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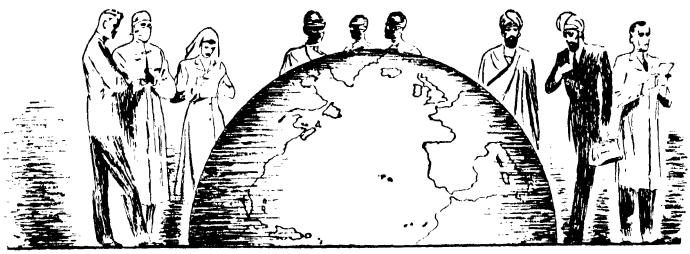
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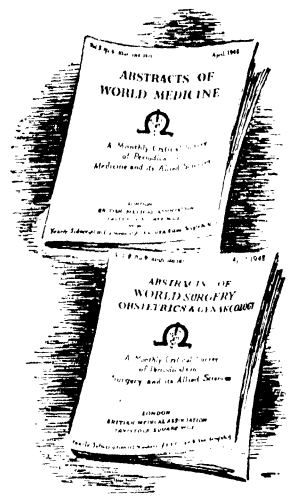
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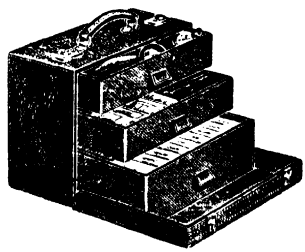
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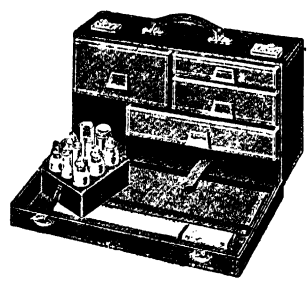


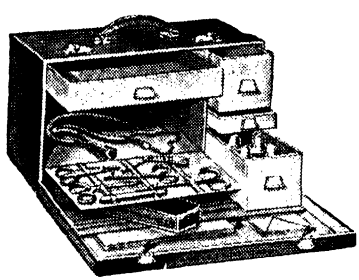
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'Iodex' presents resublimed iodine (1%) in a petrolatum base.

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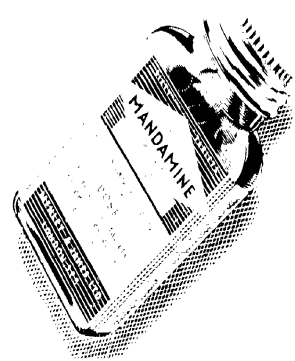
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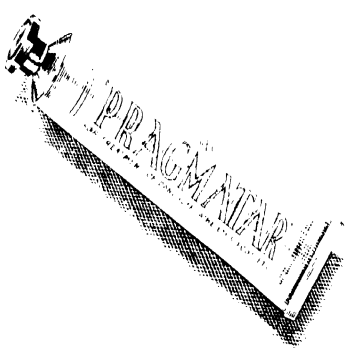
'*Ovendosyn*' *tablets :*
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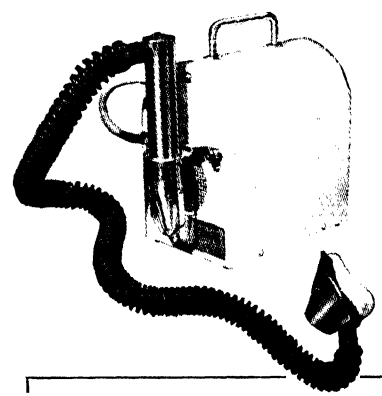
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* J. Pharm. & Pharmacol., January 1949, p. 60

† Science, 16th April, 1948, p. 397

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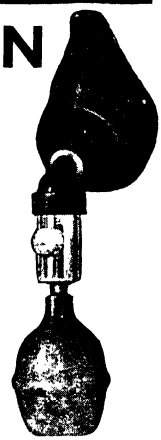
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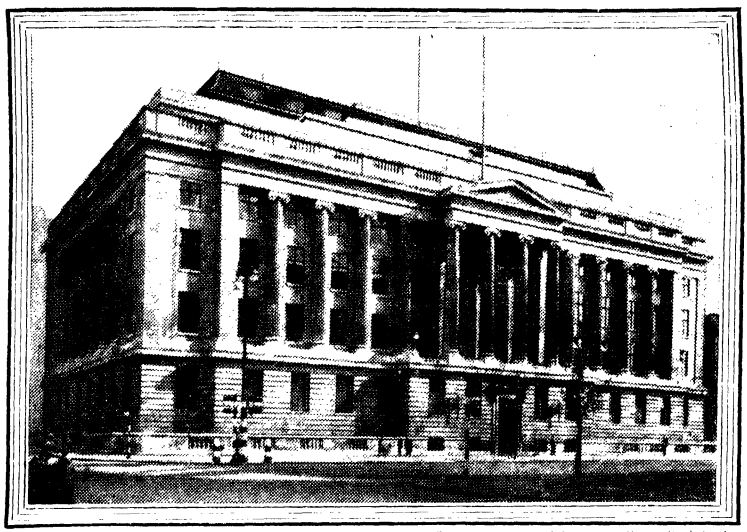
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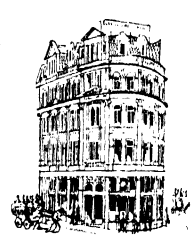
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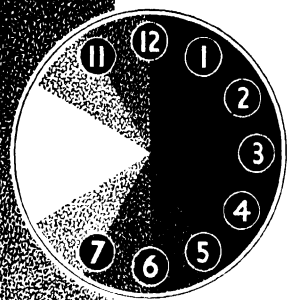
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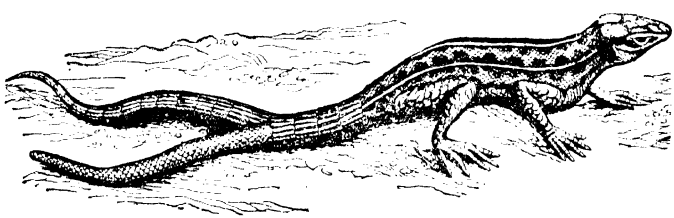
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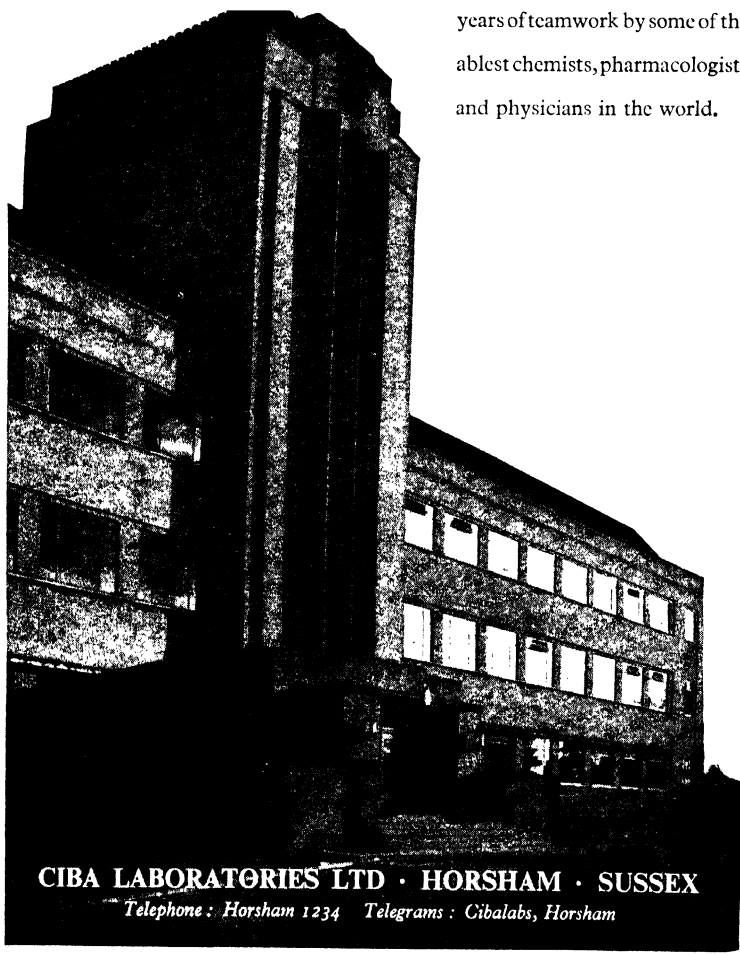
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Contents

PAGE

CONTRIBUTORS AND THEIR CONTRIBUTIONS - - - - li–lv

LIST OF PLATES - - - - - - - - lvii

PUBLISHERS' NOTE - - - - - - - - lix

REVIEW OF THE YEAR'S WORK

INTRODUCTION BY THE EDITORS - - - - - 1–8

REVIEW - - - - - - - - - - 9–406

MISCELLANEOUS

NEW PREPARATIONS AND APPLIANCES - - - - 408–419

BOOKS OF THE YEAR - - - - - - - 420–430

GENERAL INDEX - - - - - - - - 431



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(*Mental Diseases and Psychological Medicine.*)

Alcoholism and Drug Addiction—17. Leucotomy—188. Mental Diseases: General Treatment—215. Mental Diseases: Physical Treatment—216. Psychiatry: Clinical—271.

T. ANWYL-DAVIES, M.D., F.R.C.P., Physician in Charge, Department of Venereal Diseases, St. Thomas's Hospital, and Lecturer in Venereal Diseases at St. Thomas's Hospital Medical School; late Consultant and Venereologist to L.C.C.; Director of the Whitechapel Clinic; Lecturer in Venereal Diseases at the London Hospital Medical College. (*Venereal Diseases.*)

Chancroid—70. Gonorrhœa—136. Lymphogranuloma Venereum—196. Syphilis—345. Trichomonas Vaginalis—362.

HAMILTON BAILEY, F.R.C.S.Eng., F.A.C.S., F.I.C.S., F.R.S.E., Surgeon, and in Charge of the Genito-urinary Department, Royal Northern Hospital, London; Surgeon, Consolation Hospital, Lambeth; Senior Surgeon, St. Vincent's Clinic. (*Genito-urinary Surgery.*)

Adrenal Glands—14. Aneurysm of the Abdominal Aorta: Urological Manifestations—32. Bladder, Surgery of—51. Kidney, Surgery of—168. Penis, Surgery of—252. Prostate, Surgery of—266. Testis, Surgery of—349. Uræmia: The Artificial Kidney—378. Ureter, Surgery of—379. Urethra, Surgery of—382. Urinary Calculi—384. Urinary Infections, Streptomycin in—384. Vas and Seminal Vesicles, Surgery of—395.

H. STANLEY BANKS, M.A., M.D., F.R.C.P., D.P.H., Physician-Superintendent, Park Hospital, Hither Green, London, S.E.13; Lecturer in Infectious Diseases to the Medical College, St. Bartholomew's Hospital.

(*Acute Infectious Diseases.*)

Anthrax—33. Diphtheria—92. Influenza—155. Measles—209. Meningitis—210. Pneumonia, Primary Atypical—258. Rat-bite Fever—288. Rubella—315. Scarlet Fever and Hæmolytic Streptococcal Sore Throat—317. Small-pox and Vaccination—323. Typhoid and Paratyphoid Fevers—376. Typhus Fever—378. Weil's Disease—403. Whooping-cough—404.

N. R. BARRETT, M.A., M.Chir., F.R.C.S., Surgeon to St. Thomas's Hospital; Assistant Surgeon to the Brompton Hospital; Consulting Thoracic Surgeon to King Edward VII Sanatorium at Midhurst and to the Welsh National Memorial at Sully; Thoracic Surgeon to L.C.C., S.C.C., C.C.C., and the Royal Navy. (*Thoracic Surgery.*)

Bronchus, Carcinoma of—63. Cardiospasm—69. Coarctation of the Aorta—76. Heart and Great Vessels, Surgery of—143. Lung, Intralobar Sequestration of, Associated with an Abnormal Pulmonary Artery—195. Lung, Solitary Metastatic Sarcomas and Carcinomas of, Pulmonary Resection for—196. Œsophagus, Carcinoma of—238. Œsophagus, Congenital Atresia of—240. Pneumothorax, Recurrent and Chronic Spontaneous—259. Tuberculosis, Pulmonary, Surgery of—365.

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Breast Feeding—57. Burns in Children—67. Gastro-enteritis in Infants—135. Idiopathic Pulmonary Hæmosiderosis—153. Intussusception, Acute, in Childhood—164. Jaundice, Physiological, of the Newborn—165. Oral Penicillin in Infants—242. Pink Disease—256. Wilms' Embryoma—405.

W. H. BRADLEY, D.M.Oxon, M.R.C.P., Senior Medical Officer, Ministry of Health. (*Public Health, Epidemiology, and Preventive Medicine.*)

Air-borne Infection—15. Enteric Fever Spread by Pasteurized Milk—107. Immunization Procedures—153. Infectious Diseases : Certain Public Health Aspects—154. Nephritis in Textile Workers—225. Poliomyelitis Epidemic, 1947—261. Swimming-baths : Relation to Illness—339. Tuberculosis : Spread—373. World Health Organization—406.

F. A. E. CREW, M.D., D.Sc., Ph.D., F.R.C.P.Edin., F.R.S., Professor of Public Health and Social Medicine, University of Edinburgh. (*Social Medicine.*)

Social Medicine—324.

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Aphasia—34. Intracranial Hypotension—161. Louping-ill in Man—193. Meningococcosis—211. Parkinsonism—250. Toxoplasmosis—360.

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Anæmia Associated with Trauma and Sepsis—18. Anæmia, Experimental Macrocytic—18. Anæmia, Hæmolytic—19. Anæmia, Pernicious—20. Anæmia, Splenic—21. Anæmia of the Sprue Syndrome—21. Bone-marrow Aspiration—57. Iron Therapy—165. Leukæmia, Acute—192. Myelomatosis, Multiple—222. Purpura, Idiopathic Thrombocytopenic—273. Purpura, Thrombotic Thrombocytopenic—273.

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Varicose Veins, Varicose Ulcers, and Venous Thrombosis—388.

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Eye Affections : Chemotherapy—109. Eye Defects, Congenital—112. Tissue Therapy by Filatov's Technique in Ophthalmology—358.

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Bronchus, Carcinoma of—65. Intrapulmonary Calcification and Histoplasmin Sensitivity—164. Lung, Arteriovenous Aneurysm of—194. Lung, Giant Bullous Cysts of—195. Pneumo-pericardium Complicating Pneumothorax Therapy—258. Pneumothorax, Spontaneous—260. Tuberculosis, Pulmonary : Treatment—368.

MAHMOUD ERFAN, F.R.C.P.Lond., D.T.M. & H.Camb., Physician, Kasr-el-Aini Hospital, Cairo; Professor of Tropical Medicine, Fouad University, Cairo. (*Pulmonary Bilharziasis.*)

Bilharziasis, Pulmonary—48.

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Aortic Stenosis—34. Arrhythmia—39. Cardiac Infarction—68. Electrocardiography—106. Endocarditis, Bacterial—106. Heart Disease, Pulmonary—142. Heart Failure—142. Heart Murmurs—146. Heart in Scleroderma—147. Hypertension—151.

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Malaria : Modern Treatment—201.

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Anæsthesia and Analgesia—21.

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Colitis, Ulcerative : Medical Aspect—82. Gastric and Duodenal Ulcer : Medical Aspect—122. Stomach, Diverticula of—333.

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Legal Decisions and Legislation—176.

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Atom Bomb Injuries—40. Capillary Fragility—67. Coccidioidomycosis—80. Dental Caries and Fluorine—91. Erythema Nodosum—108. Leptospirosis Canicolaris—187. Nutrition and Vitamins—226. Old Age—241. Osteogenesis Imperfecta—242. Reiter's Disease—299. Reticulosis—302. Rheumatic Fever—307. Sarcoidosis—316. Tularæmia—375.

R. M. B. MACKENNA, M.A., M.D., F.R.C.P., Physician (in Charge), Dermatological Department, St. Bartholomew's Hospital; Physician to St. John's Hospital for Diseases of the Skin; Hon. Colonel, R.A.M.C., Consulting Dermatologist to the British Army. (*Skin Diseases.*)

Arsenical Dermatitis : Treatment with Dimercaptopropanol (BAL)—39. Hair : Permanent Waving—139. Kaposi's Varicelliform Eruption—166. Nitrogen Mustard Therapy in Dermatology—226. Ringworm of the Scalp : Treatment—313. Vitamin E in the Collagenoses—402.

J. W. McLAREN, M.A., M.R.C.S., L.R.C.P., D.M.R.E., Radiologist (Diagnostic) Department, St. Thomas's Hospital; late Radiologist, Royal Eye Hospital; Demonstrator of Radiological Anatomy, St. Thomas's Hospital Medical School; Examiner in Radiology, University of London. (*Radio-diagnosis.*)

Radio-diagnosis—274.

T. P. McMURRAY, C.B.E., M.Ch., F.R.C.S., Emeritus Professor of Orthopædic Surgery, University of Liverpool. (*Orthopædic Surgery.*)

Bone Tumours : Conservative Surgery in—55. Dislocation, Recurrent, of the Elbow-joint 93. Fractures, Double, and Double Non-unions, of the Shaft of the Tibia—116. Paraplegia in Cervical Spine Injuries—247. Shoulder, Painful—319. Tuberculosis of Bones and Joints : Streptomycin in 363.

SIR PHILIP H. MANSON-BAHR, C.M.G., D.S.O., M.D., F.R.C.P., D.T.M. & H., Consulting Physician to the Hospital for Tropical Diseases, London; Late Director, Clinical Division, London School of Hygiene and Tropical Medicine; formerly Consulting Physician to the Colonial Office and Crown Agents for the Colonies. (*Tropical Diseases.*)

Filariasis : Treatment with Hetrazan—114. Malaria, Aetiology of : Recent Advances—196. Malignant Malnutrition—208. Schistosomiasis (Bilharziasis)—318.

NORMAN M. MATHESON, F.R.C.S., F.A.C.S., Surgeon, Ashford Hospital, Middlesex. (*Genito-urinary Surgery.*)

Adrenal Glands 14. Aneurysm of the Abdominal Aorta : Urological Manifestations 32. Bladder, Surgery of 51. Kidney, Surgery of—168. Penis, Surgery of—252. Prostate, Surgery of 266. Testis, Surgery of—349. Uræmia : the Artificial Kidney 378. Ureter, Surgery of—379. Urethra, Surgery of—382. Urinary Calculi 384. Urinary Infections, Streptomycin in 384. Vas and Seminal Vesicles, Surgery of 395.

J. CHASSAR MOIR, M.A., D.M.Oxon., M.D.Edin., F.R.C.S.E., F.R.C.O.G., Nuffield Professor of Obstetrics and Gynæcology, University of Oxford; Director of Nuffield Department of Obstetrics and Gynæcology, Radcliffe Infirmary, Oxford; Examiner in Obstetrics and Gynæcology, Universities of Oxford and Wales. (*Obstetrics.*)

Congenital Abnormality of the Fœtus : Maternal Measles, Mumps, and Chicken-pox as a Cause 90. Labour and its Complications 171. Pregnancy Diagnosis Tests 265.

P. L. MOLLISON, M.D., M.R.C.P., Director, Blood Transfusion Research Unit, Medical Research Council. (*Rhesus Factor: Clinical Applications.*)

Rhesus Factor : Clinical Applications 303.

RALSTON PATERSON, *M.C.*, M.D., F.R.C.S., F.F.R., Director, Holt Radium Institute, Manchester. (*Radiotherapy.*)

Radiotherapy—279.

J. B. PENNYBACKER, M.D., F.R.C.S., Neurological Surgeon, Radcliffe Infirmary, Oxford. (*Surgery of the Nervous System.*)

Intracranial Infections—162. Parkinsonism : Surgical Treatment 251.

ROBERT PLATT, M.D., M.Sc., F.R.C.P., Professor of Medicine, University of Manchester; Physician, Manchester Royal Infirmary. (*Renal Diseases.*)

Renal Diseases—300.

LAMBERT C. ROGERS, V.R.D., M.Sc., F.R.C.S., F.R.C.S.E., F.A.C.S., F.R.A.C.S., Professor of Surgery, University of Wales; Director of Surgical Unit, Cardiff Royal Infirmary; Surgeon, United Cardiff Hospitals; External Examiner in Surgery, Universities of Cambridge and Belfast; Member of Court of Examiners, Royal College of Surgeons of England. (*General Surgery.*)

Aneurysm 31. Blood-vessels, Surgery of—58. Breast, Surgery of—58. Dupuytren's Contracture—96. Facial Nævi—113. Hand and Fingers, Surgery of 142. Thyroid Surgery 352. Tuberculous Cervical Adenitis—374. Varicose Ulcers—386. Varicose Veins—388. Vertebræ, Tumours of 396.

A. RENDLE SHORT, M.D., B.S., B.Sc., F.R.C.S., Emeritus Professor of Surgery, University of Bristol. (*Abdominal Surgery.*)

Abdominal Injuries 9. Abdominal Surgery, Miscellaneous 9. Appendicitis—37. Arterial Therapy 40. Colon, Surgical Diseases of—88. Diverticulitis—96. Gall-bladder and Bile-ducts, Surgical Diseases of—117. Gumma of Frontal Bone—137. Hernia 147. Hirschsprung's Disease 150. Intestinal Obstruction—156. Intestines, Surgery of 160. Liver, Surgery of—193. Mesentery, Affections of—222. Pancreas, Diseases of—243. Peritoneum, Diseases of—254. Portal Hypertension 262. Spleen, Surgery of—329.

S. LEONARD SIMPSON, M.A., M.D., F.R.C.P., Physician, Willesden General Hospital, with Charge of Endocrine and Diabetic Clinics; Endocrinologist, Princess Louise Children's Unit, St. Mary's Hospital; Consulting Physician and Endocrinologist, Soho and Samaritan Hospitals for Women; formerly Research Worker in Experimental Endocrinology, Lister Institute; Travelling Fellow, Mayo Clinic, U.S.A. (*Endocrinology.*)

Adiposity—11. Adrenal Glands—11. Diabetes Insipidus—91. Pancreas: Hyperinsulinism—247. Parathyroid Glands 249. Pituitary Gland—256. Sex Glands—319. Thyroid Gland—350.

DONALD STEWART, M.D., F.R.C.P., Medical Adviser, Austin Motor Company, James Booth & Company, and other firms; Member, Industrial Health Research Board; Member, National Advisory Council on the Employment of the Disabled. (*Occupational Health.*)

Occupational Health—229.

PERCY STOCKS, C.M.G., M.D., F.R.C.P., D.P.H., Chief Medical Statistician, General Register Office, Somerset House, London. (*Vital Statistics.*)

Vital Statistics—397.

NORMAN C. TANNER, M.B., F.R.C.S., Senior Surgeon, St. James' Hospital, London; Director, St. James' Hospital Gastro-enterological Clinic. (*Surgery of the Stomach and Œsophagus.*)

Gastric and Duodenal Ulcer: Surgical Aspect—125. Stomach, Surgical Diseases of—334.

E. D. TELFORD, M.A., M.Sc., B.Ch.Cantab., F.R.C.S., Emeritus Professor of Surgery, University of Manchester; Hon. Consulting Surgeon, Manchester Royal Infirmary. (*Surgery of the Sympathetic Nervous System.*)

Sympathetic Nervous System, Surgery of—339.

MARGARET C. TOD, M.B., Ch.B., F.R.C.S.E., F.F.R., Deputy Director, Holt Radium Institute, Manchester. (*Radiotherapy.*)

Radiotherapy—279.

MARJORY W. WARREN, M.R.C.S., L.R.C.P., Physician in Charge of Geriatric Unit and Deputy Medical Director, West Middlesex Hospital, Isleworth, Middlesex. (*Chronic Aged Sick.*)

Chronic Aged Sick—70.

F. W. WATKYN-THOMAS, B.Ch.Cantab., F.R.C.S., Surgeon, Royal National Throat, Nose, and Ear Hospital; Surgeon to University College Hospital in the Throat and Ear Department. (*Ear, Nose, and Throat Diseases.*)

Aural and Nasal Suppuration—41. Ear, Affections of—100. Nasopharynx, Tumours of: Diagnosis and Treatment—223. Œsophageal Varices—237. Postcricoid Pharyngo-œsophageal Perforation due to Endoscopy—264.

CLIFFORD WHITE, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., Consulting Obstetric Surgeon, University College Hospital; Consulting Surgeon, Samaritan Hospital for Women; Ex-President, Obstetrical and Gynæcological Section, Royal Society of Medicine; sometime Examiner of the Universities of Cambridge, Durham, London, Liverpool, Cairo, and Alexandria, and to the Royal College of Physicians and the Royal College of Surgeons of England. (*Gynæcology.*)

Dysmenorrhœa—97. Menstrual Toxin—214. Sterility and Infertility—330.

ANDREW WILSON, M.D., Ph.D., Ph.C., F.R.F.P.S.Glas., Reader in Applied Pharmacology in University College, London, and University College Hospital Medical School; Examiner in Materia Medica and Therapeutics to the University of Glasgow. (*Pharmacology and Therapeutics.*)

Analgesic Drugs—28. Aureomycin—45. British Pharmacopœia, 1948—60. Travel Sickness: Drug Treatment—361.

W. YEOMAN, M.D., Senior Physician, Royal Bath Hospital, Harrogate. (*Chronic Rheumatic Diseases.*)

Reiter's Disease—299. Rheumatoid Arthritis—308.

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List of Plates

PAGE

PLATE I.—Aneurysm of abdominal aorta - - - - 32

PLATES II, III.—Pulmonary bilharziasis - - - - - 48

PLATE IV.—Exstrophy of the bladder - - - - - 48

PLATE V.—Bladder insufflation - - - - - - 48

PLATE VI.—Resection of aortic bifurcation - - - - 54

PLATE VII.—Aortic embolectomy - - - - - 54

PLATE VIII.—Carcinoma of the breast - - - - - 58

PLATES IX–XIV.—Coarctation of aorta - - - - - 76–80

PLATES XV–XVII.—Transmeatal attico-antrotomy - - - 104

PLATE XVIII.—Gumma of frontal bone - - - - - 136

PLATE XIX.—Cartilaginous tumours of the hand - - - 142

PLATE XX.—Arm support for kidney operations - - - 168

PLATE XXI.—Aortography - - - - - - 168

PLATE XXII.—Renal papillomata (*coloured*) - - - - 168

PLATE XXIII.—Secondary carcinomata in ureter (*coloured*) - - 168

PLATE XXIV.—Sequestration of lung associated with abnormal artery 196

PLATE XXV.—Beryllium disease of the lungs - - - - 230

PLATE XXVI.—Paraplegia in cervical spine injuries - - - 246

PLATE XXVII.—Persistent priapism (*coloured*) - - - - 252

PLATES XXVIII, XXIX.—Pneumopericardium complicating pneumothorax therapy - - - - - - - - 258

PLATES XXX–XXXIII.—Recurrent and chronic spontaneous pneumothorax - - - - - - - - - 258

PLATE XXXIV.—Pregnancy diagnosis by infra-red photography - 266

PLATE XXXV.—Cancer secondary to œstrogen therapy - - 266

PLATES XXXVI–XXXIX.—Micro-radiography - - - - 274

PLATE XL.—Repair of anal sphincter - - - - - 294

PLATE XLI.—Œsophago-gastric anastomosis - - - - 336

PLATES XLII, XLIII.—Lingual goitre - - - - - 352

PLATES XLIV–XLVII.—Pneumonolysis with lucite plombage - - 368

PLATES XLVIII, XLIX.—Bilharziasis of ureter (XLIX *coloured*) - 380

PLATE L.—Varicose veins - - - - - - - 390



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Once again the publishers would like to express on behalf of their readers all over the world their very sincere sense of obligation to the Editors and contributors whose valued co-operation made this volume possible.

THE MEDICAL ANNUAL OFFICES,

BRISTOL, ENGLAND.

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THE CLASSIFICATION OF RADIOGRAPHIC APPEARANCES IN COAL-MINERS' PNEUMOCONIOSIS - *C. M. Fletcher and others*

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THE MEDICAL ANNUAL 1949

INTRODUCTION

BY THE EDITORS

MEDICINE

Several changes have taken place in our list of contributors since last year. Dr. Una Ledingham is undertaking the section of General Medicine, Dr. A. E. Barnes having retired from practice. We are indebted to him for the great care which he has devoted to this section for many years. Dr. E. W. Anderson is taking over the section on Mental Diseases and Psychological Medicine, Professor Aubrey Lewis finding his time fully occupied as Professor of Psychiatry. Dr. W. Yeoman undertakes the section on Chronic Rheumatic Disorders. Our thanks are due to Professor Aubrey Lewis and Dr. A. H. Douthwaite who have previously been responsible for these sections.

MALARIA.—Malaria still has the highest incidence of any disease. Fifty years ago the researches and discoveries of Manson, Ross, and others were thought to have solved the aetiology and that there was nothing to add. Gradually it became clear that there were phenomena yet unexplained. Thus, the erythrocytic cycle in man as then known did not account for the occurrence of relapses. It was later discovered that the fever produced by direct blood inoculation differed from mosquito-conveyed malaria and was always easily controlled by small doses of quinine. For many years advance was slow in explaining these difficulties, but the recent war afforded the necessary opportunities for research. The now famous "Malaria Research Unit" was established in 1945 at Cairns in Queensland, and large numbers of human volunteers were available. Here N. Hamilton Fairley and his associates made their fundamental researches on the "exo-erythrocytic" cycle in man. Further advances in knowledge are now recorded.

Treatment.—When quinine was the sole known drug effective in malaria treatment was simple. Quinine, however, fails to prevent blackwater fever, which indeed it definitely incites, and also to prevent relapses in *P. vivax* infections. Atebrin and pamaquin came into use after the first war. More recently a number of new drugs of varying constitution have been introduced, of which proguanil and chloroquine may be regarded as the successful survivors. Advances in the knowledge of the life-cycle of malarial parasites has made it possible to refer certain drugs to certain stages of the cycle, and for every stage there is now an efficient drug although not a complete control. Even the relapses of *P. vivax*, which are troublesome though not highly dangerous to life, are reduced to a

low incidence by the combined use of quinine and pamaquin. The treatment has thus become more complicated though more effective.

In view of its outstanding importance, Dr. G. W. M. Findlay has contributed a special article on the modern treatment of malaria.

BILHARZIASIS.—Bilharziasis is probably the most extensive disease in the world next to malaria. It has not received a fraction of the study devoted to malaria and much knowledge is lacking both as to its geographical distribution and as to its diverse manifestations.

A side-line which has been neglected until comparatively recent years is the changes in the pulmonary vessels which are produced by emboli of the ova which have escaped from their normal habitat. Attention was first called to these by F. Mainzer of Alexandria and M. F. Sorour of Cairo. Some careful studies of the pathology, radiology, and clinical features have been made by members of the Cairo Faculty of Medicine. The gross morbid anatomy of the pulmonary arteries and arterioles resembles that which is considered to be characteristic of Ayerza's disease, and the lesion was consequently called "Egyptian Ayerza's Disease" by Shaw and Ghareeb. The histology, however, is specific, and there are other differences from the accepted descriptions of Ayerza's disease.

Professor M. Erfan, of the Faculty of Medicine of Cairo University, has written a summary of the present knowledge.

The established treatment of bilharziasis is by injection of antimony compounds. Reactions, which may be severe, are common. Search is being made for a satisfactory substitute which can be administered by the mouth. Miracil D (Nilodin) is being given an extensive trial. The results in infected mice were promising, but have not been fully reproduced in man.

VITAL STATISTICS. Considerable advance has been made during the past year in completing the classifications which it is hoped will establish the statistics of various countries on a basis permitting accurate comparison. The first volume in English of the "International Statistical Classification of Diseases, Injuries, and Causes of Death" has been published, and the College of Physicians has produced a new edition of the "Nomenclature of Disease" with the object of obtaining uniformity in the naming of diseases.

The whole medical world has been yearning for "morbidity statistics" that is, for a reliable measure of the incidence of a disease in the entire population at risk, as apart from statistics of deaths and of hospital admissions. It is anticipated that the new National Health Service will render this possible in the United Kingdom, and the system of record-keeping which will be in force within the Service will have this object in view. It is to be hoped that doctors who are responsible for the treatment of patients and consequently for clinical records will not be overburdened by demands for masses of data required for some statistical study.

LEGAL DECISIONS AND LEGISLATION.—Several important decisions have been given during the last year.

Loss of Expectation of Life.—In 1934 the law was altered to give the next of kin of a person killed by negligence a claim in respect of the person's loss of expectation of life. There was wide divergence at first in the amounts awarded by different courts, but in 1940 the House of Lords held that the correct measure of damage is the loss of prospects of a happy life. Since then the amounts awarded have been smaller. For the death of a girl of four, the parents recently were awarded £200.

Control over Nurses' Agency.—Under the Nurses Act, 1948, a person who carries on an agency must obtain a licence from the local authority, which may impose certain conditions. The Middlesex County Council in issuing a licence to an agency purposed to limit the fees which a nurse might charge to a patient to a scale fixed by themselves. The agency appealed, and the King's Bench Divisional Court held that this condition was outside the powers given to the Council by the Act. According to the *British Medical Journal* this case affected about 20,000 nurses.

Legislation.—On July 5, 1948, the appointed day, the National Health Service became operative. The Criminal Justice Act, 1948, abolished penal servitude, hard labour, prison divisions and sentences of shipping, and introduced many improvements in the treatment of young offenders. The Children Act, 1948, throws on local authorities the duty of providing for children in need of care and protection. Although the number of such children is not large, the country had been shocked by some recent criminal proceedings and the subsequent report of the Curtis Committee.

Chronic and Aged Sick. The nation has suddenly realized that it is becoming burdened with increasing numbers of aged persons that is to say, individuals over the age of sixty years. Some of these aged persons are old but still active, others are old and senile, and for both these groups some State provision will be necessary owing to present difficulties of housing shortage and lack of domestic help. A third group is the "chronic aged sick", for the treatment of whom the medical profession must accept responsibility. The study of geriatrics and gerontology, unlike its subject, is in its infancy, but it is already clear that much can be done to increase the comfort of many of these old people and, fortunately, at the same time reduce the amount of personal attention which is necessary. A special article is contributed by Dr. Marjory Warren, a pioneer in the study of this important development.

The British Pharmacopœia.—The sixth edition of the *British Pharmacopœia* was issued in 1932 and followed by a series of addenda. The seventh edition, delayed by the war, was issued in September, 1948, and is a revision both of the sixth edition and of the addenda. The pruning of the drugs of the Victorian era is continued. Many friends of the nineteenth century practitioner and parent disappear, including confection of sulphur, confection of senna, and blistering fluid, the last-named possessing distinct psychological properties. It is doubtful if Easton's syrup will cease to be prescribed, although it is omitted from the *Pharmacopœia*. Sulphapyridine (M & B 693) is deleted, not for ineffectiveness but because it has finished its work as a pioneer. Blaud's

pill survives, with the proviso that it should be freshly prepared for administration. Tons of Blaud's pills must have passed unabsorbed through countless intestinal tracts, but the value of the fresh pill is undoubted. It may not always be easy to conform with the proviso. Some of the preparations now retained will be victims in the next revision. It is difficult to understand the retention of the dangerous drug amidopyrine; it should never be prescribed.

The official titles are given in Latin, e.g., paraldehydum, a system which may be thought to have outlived its generation. But it will require a firm hand to make the change.

Occupational Health and Industrial Medicine.—It is satisfactory to note the rapid increase in the influence of medical expert advice not only in mines and factories but in other occupations. With the constant introduction of new chemical methods, fresh problems arise. Beryllium is almost a newcomer in industry, but its use has increased enormously in the last three years for the coating of the tubes used in fluorescent lighting. Handling of beryllium compounds involves the risk of serious lung disease of a type distinct from pneumoconiosis. The changes were at first confused with miliary tuberculosis and sarcoidosis.

Megaloblastic Anæmia.—The most interesting recent advance has been the isolation from the liver of a crystalline compound which appears to be nearer than any known substance to the hypothetical anti-pernicious anæmia factor of Castle. It contains cobalt, but its chemical constitution is at present unknown, and it is referred to as 'Vitamin B_{12}'. Investigations are at present hampered by its scarcity and expense. It appears to have little effect on megaloblastic anæmias other than pernicious anæmia. Its relation to folic acid is uncertain but is being studied.

Hypertension.—The study of hypertension is spurred on by the great interest which the intelligentsia always exhibit in their blood-pressure, and the recent proof of influence of ascending lesions of the kidneys. There is now suggestive evidence that malignant hypertension is a secondary hypertension often due to a chronic pyelonephritis which may be unilateral. Essential hypertension on the other hand may persist for many years without interfering with ordinary activities. A number of cases of nephrectomy for hypertension is now on record. It appears impossible at present to predict the outcome of the operation. Further knowledge is necessary before a reliable prognosis can be given, but when one kidney is diseased and the other is normal, operation is generally justified.

Rheumatic Fever.—In spite of the world-wide distribution of rheumatic fever and its high incidence, it is still uncertain if sodium salicylate is curative and if it reduces the frequency of cardiac disease. No practitioner feels justified in withholding the drug and no control statistics are in existence. It is even uncertain what is the optimum method of dosage and what is the value of the addition of alkalis. Attempts are in progress to decide the dosage on the basis of the alkali reserve, but there

is no proof that this is a measure of its effective action. In view of the present high incidence of cardiac lesions, the position cannot be considered satisfactory.

THE RHESUS FACTOR.—The complexities of the Rhesus factor can only be fully grasped and certainly only remembered by specialists involved in its research. But the clinical applications are becoming clearer though not simpler. The general principles must be understood and carefully followed before any transfusion of blood or serum is given to a woman or girl at any age.

Dr. Mollison states the modern position as simply as possible.

INFECTIOUS DISEASES.—

Diphtheria.—The number of deaths in the United Kingdom is now about one-tenth of the number ten years ago. This is the direct result of active immunization, and all credit is due to the medical advisers of the Ministry of Health for the propaganda which has saved the lives of so many thousands of young children.

Rubella.—The records which are accumulating confirm the frequency of congenital abnormalities in babies whose mothers were known to have had rubella in the first two months of pregnancy. They also confirm that there is no increased incidence following measles, mumps, chicken-pox, and other infectious diseases. While the records may be accepted as proving these points, they are unsatisfactory for any definite statistical conclusions as to the exact proportion of babies in which these abnormalities occur.

SURGERY

GENERAL SURGERY.—A report from China maintains that the pain of thoracic aneurysm may be relieved by anastomosing the carotid artery to the jugular vein, to reduce the pressure. In good hands, the results of radical mastectomy for cancer may be at least as good without as with radiotherapy, before or after operation. Vitamin E is said to help resolve Dupuytren's contracture. For unsightly birth-marks on the face, removal followed by skin-grafting and tattooing with metallic oxides gives the best cosmetic results. A warning is given that patients with lingual goitre usually have no thyroid tissue in the neck, so complete removal is wrong.

ABDOMINAL SURGERY.—Modern methods have made a one-stage resection of the colon for cancer, if not obstructed, as safe as a two-stage procedure. Surgeons relate their experiences with buried skin-grafts, tantalum gauze, and other materials for the repair of difficult hernias. The correct treatment for Hirschsprung's disease is still in doubt; various medical and surgical measures are discussed. Relapsing cases of subacute pancreatitis also present a surgical problem: biliary drainage, excision of the pancreas, sphincterotomy, and resection of the splanchnic nerves are all under trial. Yet another problem, how to relieve portal hypertension causing recurrent hæmatemesis or ascites, is also discussed; injection of œsophageal varices, splenectomy, and venous anastomosis

of one kind or another are considered, but these methods all have their failures. Variations in the tone of the sphincter of Oddi account for cases in which symptoms like those of gall-stones occur without any abnormal findings at operation. For hypertension, division of the sphincter is advised, and for hypotension, resection of the splanchnic nerves. Encouraging results are reported for congenital duodenal obstruction in infants, and also in cases of irreducible intussusception. Volvulus of the sigmoid can often be relieved without operation, by passing a tube, through a proctoscope, into the twisted loop.

Gastric Surgery.—Readers will be interested in the discussion of the merits and demerits of vagotomy for certain cases of duodenal ulcer and gastrojejunal ulcer; good results are obtained in a majority of the patients, and the improvement may be maintained for four years. Gastrojejunostomy for pyloric stenosis still has its champions. Carcinoma of the proximal part of the stomach can often be treated by transthoracic resection followed by anastomosis of the œsophagus to the distal stomach.

Varicose Veins.—A special article on this subject is included. A method is described for locating a communicating vessel joining the deep and superficial veins in the leg, which must be tied if recurrence is to be avoided. Several cases of gangrene following retrograde injection of coagulants after tying the saphena vein are reported. It is no longer considered necessary to keep patients with thrombosed varicose veins in bed, as embolism comes not from the superficial but from the deep veins.

Chest Surgery.—A plea is entered for early radiography to enable a diagnosis of bronchial carcinoma to be made in time to allow of successful removal; even metastatic growths in the lung can sometimes be resected with lasting good results. Great interest is still being taken in operations on the aorta and other great vessels for coarctation, pulmonary stenosis, and similar congenital conditions, and a number of good results are reported. Relief may however be obtained sometimes by the simpler procedure of inducing pleural adhesions. Treatment of recurrent pneumothorax varies with the cause; pleurodesis is usually satisfactory. Cavities in pulmonary tuberculosis are most commonly treated by thoracoplasty, but reversed postural drainage, or surgical obliteration of the cavity, have to be considered. For cardiospasm, the mercury bougie has been supplanted by the Negus hydrostatic dilator, or in obstinate cases by Heller's operation.

Brain Surgery.—Nowhere in the body is the value of penicillin more evident than in cases of subdural abscess. Attempts are being made to abolish the tremor in Parkinson's disease by extirpation of areas of cerebral cortex, or section of the fibres in the internal capsule.

Surgery of the Sympathetic Nervous System.—A special article is included to offer guidance as to which conditions are really profited by surgical treatment, and such debatable subjects as hypertension, causalgia, and angina pectoris are reviewed.

BONE AND JOINT SURGERY.—Double fractures of the tibia unite badly, because the central portion is likely to be cut off from its blood-supply; complete and prolonged immobilization in plaster is indicated; if it fails, a bone-graft from the fibula is advised. Pressure on the spinal cord after an injury to the neck may be due to retropulsion of an intervertebral disk without fracture or dislocation; skull traction may relieve the pressure, or laminectomy may become necessary. An important cause of pain in the shoulder is damage of the long biceps tendon, which may have to be removed. Some improvement in cases of bone tuberculosis has been brought about by streptomycin.

RECTAL SURGERY.—Attention has been drawn to the frequency of fibrosis of the anus with spasm, in older women, as a cause of troublesome abdominal symptoms such as distension. Anal incontinence may be treated by surrounding the sphincter with a buried silver ring. Tattooing for pruritus ani continues to receive favourable mention. Attention is again called to the regrettable frequency with which carcinoma of the rectum has been treated on a mistaken diagnosis of piles, or colitis.

GENITO-URINARY SURGERY.—For persistent priapism, if aspiration with a large needle fails, it is best to make an incision and leave it open, using penicillin and sulphonamides to guard against sepsis. When circumcising an adult, the common mistake is to remove the prepuce too thoroughly. For hypospadias, an inlying tubular graft of skin is the best means of restoring the penile urethra. The prognosis of malignant growths of the testis is not nearly so serious as it used to be, now that surgeons explore scrotal swellings so much earlier. A technique is illustrated for the relief of stress incontinence in women. Streptomycin may be extremely effective for *B. coli* infections, but the germs soon acquire resistance to it.

OBSTETRICS.—The risk of some congenital fœtal abnormality is said to be nearly twenty times the normal if the mother contracts rubella during the early months of pregnancy, and nearly ten times the normal if she contracts poliomyelitis. If a patient with a breech presentation is seen late in pregnancy, version under deep anæsthesia, even if the legs are extended, is usually successful, and much safer for the infant than a breech delivery. The main causes of obstetric shock are prolonged labour, and retention of the placenta beyond an hour after delivery; some cases called obstetric shock are said to be due to pulmonary embolism by amniotic fluid. The question is discussed which type of Cæsarean section is safest in frankly infected cases. A new early test for pregnancy is described, namely, engorgement of the veins of the breast made visible by infra-red rays.

GYNÆCOLOGY.—In a long review of the causes and treatment of dysmenorrhœa, various remedies are considered, amongst them stilbœstrol, which is usually successful; it would appear that irregular contractions are not the correct explanation of the pain; presacral sympathectomy is

more successful for primary than for acquired dysmenorrhœa. Sterility is also discussed; it is possible to ascertain when ovulation is occurring by a biphasic variation of temperature; dienœstrol may help to embed the fertilized ovum in the uterine mucosa.

OPHTHALMOLOGY.—Penicillin is replacing the silver preparations to protect newborn infants' eyes from infections. Streptomycin is useful for some superficial infections which are unaffected by penicillin. Some chronic degenerative eye diseases are said to be benefited by "tissue therapy": the tissues injected may be placenta, or liver, or cod-liver oil.

EAR, NOSE, AND THROAT SURGERY.—Cavernous sinus thrombosis can frequently be cured by means of sulphonamides and penicillin. Gastro-enteritis in infants may be caused by a mastoid suppuration which gives almost no physical signs, and operation is called for. The remarkable fact has come to light that men who go in extensively for swimming are liable to develop exostoses of the auditory canals. Tumours of the naso-pharynx could sometimes be diagnosed before they block the nose if such signs as a blood-stained discharge, headache or neuralgia, or enlarged cervical glands, were taken seriously and followed up. The treatment of hæmatemesis by injecting œsophageal varices is discussed.

VENEREAL DISEASES.—Abdominal pain or menstrual irregularities are commoner signs of gonorrhœa than vaginal discharges or urinary symptoms. A new remedy, aureomycin, is effective in cases of lympho-granuloma. The only reliable way for a syphilitic male to avoid passing on his spirochætes is to wait for five years before marrying. Penicillin is superior to malaria in the treatment of neurosyphilis.

ANÆSTHETICS.—A warning is given against the risk of injecting thiopentone into an artery in mistake for a vein; if this occurs, heparin should be given. Some patients have an idiosyncrasy to curare, and it is suggested that a small trial dose may be a wise precaution. It is thought that the permanent paralysis which sometimes follows spinal anæsthesia is due to a "chemotaxic effect" on the spinal cord.

RADIO-DIAGNOSIS.—Considerable advance has been made in cardio-graphy. There is reason to believe that what is called short œsophagus is the result of a peptic ulcer of the lower end. Radiography is more reliable than biopsy in the diagnosis of bone tumours.

RADIOTHERAPY.—The most important new work in 1948 has been the development of supervoltage therapy, which has the advantage of attacking the deeper tissues rather than the superficial. Much work remains to be done before electron therapy can be used to treat cancer. Therapeutic use of radio-active phosphorus is mainly for leukæmia and polycythæmia, where good results are claimed; radio-active iodine helps cases of hyperthyroidism, but relapse occurs when the drug is withdrawn; there are problems with regard to storing and handling these radio-active substances.

REVIEW OF THE YEAR'S WORK

ABDOMINAL INJURIES. *A. Rendle Short, M.D., F.R.C.S.*

War Wounds.—The spate of publications on war wounds has now sunk to a trickle. C. G. Rob[1] writes on the *diagnosis of injury to the viscera*. Unnecessary exploration, with a negative finding, is no light matter; during the Italian campaign, of 66 such cases 19 died. Frequently it is easy to decide that some viscus must have been damaged. In cases of doubt, there are two signs of outstanding value: an estimate of the probable track of the missile, and repeated and prolonged auscultation of the abdomen. Persistent silence is evidence of perforated bowel; audible sounds suggest, but do not prove, that there is no visceral injury. Rigidity is a less valuable sign in military than in civil surgery. Excision of the wound in the abdominal wall often shows the necessity for laparotomy.

Historical.—D. M. Poer,[2] of Atalanta, contributes an interesting historical review of *gunshot wounds of the abdomen*. In the American Civil War, at least 90 per cent died. Some field hospitals in the First World War had a mortality of only 50 per cent, but many patients had died on the battlefield. Between the two wars, the death-rate in American civil hospitals was about 50 per cent. During the Second World War, with the aid of better transport, resuscitation methods, and chemotherapy, surgical treatment brought the percentage of deaths down to 25 in some hospitals. In American civil practice recently a mortality as low as 14 or 17 per cent has been reported.

Wounds of the Liver.—Both penetrating and non-penetrating injuries of the liver may give rise to shock with anæmia, hæmoperitoneum, biliary peritonitis, diminution in blood proteins, reduction of fibrinogen and prothrombin giving rise to increased bleeding-time, and the "hepato-renal syndrome" (J. D. Martin,[3] of Atalanta). This is commoner with extensive crushing injuries. The symptoms are hyperpyrexia, quick weak pulse, restlessness, delirium, and oliguria. There may be blood, casts, and albumin in the urine. The picture is reminiscent of 'crush syndrome' following limb injuries. Treatment is by packing the wound in the liver; oxidized cellulose, which is soluble, may be used, or a pedicled muscle graft may be turned in. Fibrin foam, or gel foam, may help to stop bleeding.

REFERENCES.—[1]*Surg. Gynec. Obstet.* 1947, **85**, 147; [2]*Ann. Surg.* 1948, **127**, 1092; [3]*Ibid.* 1947, **125**, 756.

ABDOMINAL SURGERY, MISCELLANEOUS. *A. Rendle Short, M.D., F.R.C.S.*

Abdominal Auscultation.—C. G. Rob,[1] of St. Thomas's Hospital, who became interested in the diagnosis of visceral injuries due to gunshot wounds in the war by listening to the abdomen, writes in praise of the stethoscope also in recognizing acute abdominal conditions in peace time. No doubt most surgeons have proved this for themselves. One must listen patiently for a long time, or repeatedly, before concluding that there is complete silence, but when no sounds can be heard, it is good evidence of peritonitis, with presence of intestinal

contents, pus, bile, or exudate from strangulated bowel or pancreatitis. Urine, or clean blood, will not abolish peristalsis.

Intercostal Nerve Block.—In the experience of S. Belinkoff,[2] New Bedford, Mass., intercostal nerve block prevents post-operative pain and greatly reduces the number of chest complications. Analgesia was successfully produced in 84 cases out of 100. If the incision is midline, the intercostal block should be bilateral; if it is more than one inch from the midline, a unilateral block is used. The injections are given after the patient is anæsthetized; 1 to 1½ c.c. of Novestoil (monocaine base 0·02 g., benzyl alcohol 0·05 g., benzocaine 0·03 g., sweet almond oil to 1 c.c.) is injected just under each rib from 6th to 11th, in the mid-axillary line. If the pleural cavity is entered, an effusion may follow, but it clears up. It is important to obtain good ventilation by frequently changing the patient's position, and persuading him to cough or breathe deeply. R. S. McCleery[3] and colleagues, of Columbus, Ohio, write to the same purpose. They inject further back, using 3 c.c. of 1–1000 nupercaine in peanut oil. The anæsthetic effect lasts for 48 hours or longer. Pulmonary complications fell from 13 to 6 per cent.

Early Post-operative Ambulation and Wound Disruption.—More and more surgeons are getting their patients out of bed and letting them walk to a chair and sit up for a few minutes on the day after operation, unless of course the abdominal wall is septic, or the patient shocked, debilitated, or distended. The advantages claimed are a shorter convalescence, fewer complications, and improved psychological outlook. E. A. Balcer,[4] of Chicago, reports 144 cases, including 33 partial gastrectomies, with no disruptions following. J. C. Burch and C. F. Bradley,[5] of Nashville, have had similar success; but they had 2 disruptions amongst 2046 ambulant patients. They contrast this with 9 disruptions in a series of 856 patients treated by long rest in bed. [For some reason unknown, this disaster has for a long time been commoner in the United States than in Britain.—A. R. S.] French experience, voiced by M. Luzuy,[6] of Blois, is also favourable, but he emphasizes the value of early rising as a means of avoiding phlebitis and embolism. His patients do not get up till the third or fifth day after operation. As he lost two cases from pulmonary embolism his argument is not very convincing, and other surgeons have found that early ambulation is of little value in preventing either thrombosis or embolism.

K. R. Trueman,[7] of Winnipeg, points out that wound disruption is a serious matter, and of 18 cases at his hospital 6 died. Poor suture material, and indifferent surgical technique, play a part in permitting disruption, especially in the upper abdomen, but the most important factor is protein deficiency. The third and fourth days are the most dangerous, but the accident may occur as late as the thirty-ninth day. It is sometimes safer to let things alone rather than perform a secondary suture operation. Observations by S. A. Localio[8] and others (New York) show that the protein depletion is not so much in the blood as in the tissue-proteins of fascia, where it may be as low as 18·7 per cent instead of the normal 29 per cent. Pre-operative protein therapy is advised for debilitated patients.

Abdominal Emergencies in Paraplegics.—T. I. Hoen and I. S. Cooper,[9] of New York, find that though paraplegics have often lost sensation in the lower parts of the body, they usually complain of pain as well as nausea and vomiting if an abdominal emergency develops. The pain is vague, often referred to the upper abdomen. Renal calculus, or pyelitis, may occur, and a radiograph may give help.

REFERENCES.—[1]*Lancet*, 1947, **2**, 720; [2]*Ann. Surg.* 1948, **127**, 136; [3]*Surg. Gynec. Obstet.* 1948, **86**, 680; [4]*Amer. J. Surg.* 1947, **74**, 472; [5]*Ann. Surg.* 1947, **125**, 768; [6]*Pr. méd.* 1947, **58**, 662. [7]*Canad. med. Ass. J.* 1947, **57**, 550; [8]*Surg. Gynec. Obstet.* 1948, **86**, 107; [9]*Amer. J. Surg.* 1948, **75**, 19.

ADDISON'S DISEASE. (*See* ADRENAL GLANDS.)

ADIPOSITY. *S. L. Simpson, M.A., M.D., F.R.C.P.*

Apart from indicating the association of adiposity with hypertension, pulmonary emphysema, diabetes, cardiovascular disease, nephritis, rheumatism, and cholecystitis, C. F. Gastineau and E. H. Rynearson[1] found no evidence of an endocrine cause of adiposity and no use for hormone therapy or diuretics. They look to pathological appetite, determined psychogenically or by a hypothalamic lesion, as the main cause, and restricted diet as the main treatment. Their own review appears to modify their aetiological conclusions in so far as they acknowledge adrenal cortex, castration, and hyperinsulinism types of adiposity, and refer to the Laurence-Moon-Biedl and Morgagni-Stewart-Morel syndromes. They reject the water-retention factor or the usefulness of diuretics. As a primary factor, most would agree, but there is good evidence that low-caloric diets lead to water retention and a plateau of weight stability, successfully interrupted by diuretics and a reversal of water retention as measured by total fluid intake and output.

M. M. Kunde[2] arrives at similar conclusions to Gastineau and Rynearson. He adds, however, that "the fundamental cause of obesity seems to be due to some unknown constitutional discrepancy in the metabolism. This makes it necessary for patients to exist on a dietary containing a greater proportion of protein and less carbohydrate and fat than is required for the individual who does not become excessively obese on the average American dietary".

REFERENCES.—[1]*Ann. intern. Med.* 1947, **27**, 883; [2]*Ibid.* 1948, **28**, 971.

ADRENAL GLANDS. *S. L. Simpson, M.A., M.D., F.R.C.P.*

Addison's Disease.

A Test for Adrenal Cortical Insufficiency.—To the well-known Cutler-Wilder and Kepler tests based on the concentration and excretion of salt and water and of urea, there has been added a diagnostic test based on the effects of adrenocorticotrophic hormone on eosinophil cells and on uric acid excretion (G. W. Thorn, P. H. Forsham, F. T. G. Prunty, and A. G. Hills[1]). Thus, in normal controls, an injection of pituitary adrenocorticotrophic hormone results in a fall of circulating eosinophil cells and an increase in urinary uric acid. This also happens in adrenal hypofunction secondary to pituitary hypofunction, but it does not occur when the adrenals are diseased or destroyed, as in Addison's disease, and are therefore incapable of responding.

The test is carried out fasting: 200 c.c. of water is given at 6 a.m., 8 a.m., and 10 a.m. Urine is collected from 6 a.m. to 8 a.m. and an eosinophil count is made at 8 a.m., after which 25 mg. of adrenocorticotrophic hormone is injected intramuscularly. Urine is collected from 9 a.m. to 12 noon, and another eosinophil count is carried out. The absolute decrease of circulating eosinophils is expressed as the percentage of the initial count. The two specimens of urine are analysed for uric acid and creatinine, and expressed as a uric-acid-creatinine ratio. A fall in eosinophils of 50 per cent and an increase of the uric-acid–creatinine ratio of 50 per cent excludes Addison's disease. The test really measures the capacity of the adrenal cortex to secrete the 11-oxysteroids, and not desoxycorticosterone, as only the former influences eosinophils and uric acid. The test is not reliable during severe infections or in the presence of renal disease.

Long-term Results of Treatment.—L. G. Rowntree[2] has reviewed his last 8 consecutive cases treated with adrenal cortical extract and found that 5 are still living after some ten years, and the remaining 3 lived on an average of nearly ten years. He refers to an earlier publication of records with a survival

of 18, 17, and 15 years. The writer recently saw a patient in Professor Elliott's University Clinic in South Africa who had survived some 18 years on little or no treatment, taking salt paroxysmally and being brought to hospital at long intervals in acute adrenal insufficiency, responding to cortical extract. Rowntree states that he has been able to minimize the incidence of crises by adequate treatment and supervision.

Danger of Overdosage with Desoxycortone Therapy.—This danger is becoming well recognized, and the usual form is with œdema, fluid retention, and hypertension. Some French writers (L. de Gennes, H. Bricaire, Gerbaux, Mathieu de Fossey[3]) have drawn attention, however, to the development of a form of essential hypertension, perhaps with cardiac failure, but with absence of water retention and œdema. The hypertension may be progressive even in the presence of clinical and biochemical features of intermittent adrenal insufficiency. They refer to it as a dry hypertension. Some of the doses of implanted desoxycortone that they used were exceptionally large, more than 10 times the average, e.g., 30 × 100 mg.

Effect of 11-Dehydrocorticosterone Acetate in Normal Patients and in Addison's Disease.—The isolation and synthesis of 11-dehydrocorticosterone (Kendall's Compound A—referred to as D.H.C.A.) and its action in adrenalectomized rats (glycogenesis, increasing work capacity, sodium retention, and prolonged survival) led to the hope that it might be of use in Addison's disease; especially as desoxycorticosterone, which is generally used clinically, is known to have no action on carbohydrate metabolism. Unfortunately the preliminary results reported are disappointing. F. Homburger and others[4] injected 200 to 400 mg. daily of D.H.C.A. into a normal woman of 30 and failed to alter the immediate metabolic response to repeated 48-hour fasts, or to affect carbohydrate metabolism. There was a mild retention of salt and water.

R. C. Sprague and colleagues[5] injected a woman of 37, with Addison's disease, with 200 mg. daily of D.H.C.A., and noted that "the effects on carbohydrate metabolism, studied by means of determinations of the fasting blood sugar, glucose and insulin tolerance tests, changes in the blood sugar during prolonged fasting, and estimations of urinary nitrogen were slight and in most instances of questionable significance"; nor were there any changes in blood lipoids, serum proteins, albumin-globulin ratio, or urinary phosphorus. They record similar negative results by other investigators, but refer to a paper by P. H. Forsham and colleagues[6] in which D.H.C.A. in Addison's disease produced a higher glucose tolerance curve in one patient out of three, a greater fall in serum inorganic phosphorus in two patients out of three, during glucose tolerance tests, and a consistent effect in preventing symptoms of hypoglycæmia during fasting or on low carbohydrate diets, and an increased excretion of nitrogen. Sprague and colleagues carried out a subsidiary experiment on the effects of 17-hydroxy-11-dehydrocorticosterone (Kendall's Compound E) in 20-mg. daily doses in this Addison patient, and found "a transient increase in the urinary excretion of sodium chloride; a slight carbohydrate effect, as indicated by a diminished hypoglycæmic response to insulin, and better maintenance of the blood sugar level during fasting".

Cortical Tumours.—

Diagnosis.—J. Patterson[7] says that the problem is to differentiate adrenal tumours from adrenal hyperplasia in women. Quantitatively the 17-ketosteroids tend to be above 50 mg. per 24 hours in the case of tumour and between 20 mg. and 30 mg. in the case of hyperplasia, but values as high as 80 mg. may be found in the case of hyperplasia. The detection of dehydro-iso-androsterone in tumour cases by Callow and the fact that it was largely responsible for the high-androgen content in neoplasm cases was a considerable step forward. In

another approach, Talbot divided the ketosteroids into α and β fractions, and showed that in tumours the β fraction was in great excess. Patterson's contribution is to devise a chromogenic test for dehydro-iso-androsterone which is sensitive down to less than 0·1 mg. It is easily and rapidly carried out, and depends upon the development of an intensely violet-blue colour with some green fluorescence when the urine is treated with concentrated sulphuric acid after a series of extractions and separations, details of which are given. The colour in the case of urine from adrenal hyperplasia patients is by contrast a brown one. Further, in tumour cases the final extract could be diluted until the amount of total 17-ketosteroids was no more than 0·2 mg. in the sample under test, and still a characteristic colour, which was never obtained from hyperplasia urines at concentrations of 1·0 mg. content of 17-ketosteroids. Patterson indicates that the colour may also be generated by two other substances, found with tumours and not with hyperplasia, namely, iso-androsterone and (probably) $\Delta^{3:5}$-androstadiene-17-one; but this does not depreciate its clinical value. Full references are given to previous work.

Medullary Tumours: Phæochromocytomata.—C. W. Holland and S. C. Strickland[8] record the case of a woman of 28 who complained of daily attacks of headache, palpitations, flushing of face, blanching of hands and feet, nausea and vomiting, and scanty menstruation. The symptoms were of long duration, eight years, and followed pregnancy. Attacks might be produced by lying on her left side. A flushed face was associated with circumoral pallor. One year ago sugar was found in the urine, and 12 units of insulin given daily before breakfast. Blood-pressure was 164/124, rising to 280/160 in attacks. A smooth mass was felt in the left subcostal region; 1 c.c. of 1–1000 adrenaline subcutaneously produced an attack. A phæochromocytoma was successfully removed, and almost complete freedom from symptoms resulted. The adrenaline content of the tumour was 1579 mg., compared with 5 mg. normally. The author refers to a series of 35 operated cases from the literature in which the mortality-rate was 14 per cent.

J. W. S. Blacklock, J. W. Ferguson, W. S. Mack, J. Shafar, and T. Symington,[9] although they found records of only 2 adrenal medulla tumours among 2994 autopsies in the Glasgow Royal Infirmary, are nevertheless able to present in their paper no less than 6 patients with phæochromocytoma, 5 of whom came under their observation in a very short time.

1. A soldier, aged 21, with attacks of headache, palpitations, and breathlessness, at first at intervals of six weeks and then several times a day, and of only two minutes' duration, attacks associated with facial pallor and hypertension. Death after operation.

2. A woman, aged 37, with attacks similar to the first case, but lasting five to sixty minutes and associated with nausea and anginal pains. Operation; recovered.

3. A male, aged 39, with attacks of giddiness, acute occipital pain, and black-outs; also insomnia and polyuria. The blood-pressure was 240/130, and he died before operation in a phase of mental confusion. A small phæochromocytoma, 1 cm. in diameter, was found in the upper pole of the left suprarenal.

4. A woman, aged 37, who died nine days after admission to hospital, with cough, nausea, vomiting, and diarrhœa, and no indication of a phæochromocytoma, which was found at autopsy, together with a chronic liver abscess.

5. A male, aged 37, admitted with mental confusion and hypertension, 220/110. Autopsy revealed phæochromocytoma.

6. A woman of 34, admitted with weakness and breathlessness, and a palpable tumour in the left hypochondrium. She died after removal of a malignant phæochromocytoma and left kidney.

In summary, *Cases* 1 and 2 belonged to the paroxysmal adrenal-sympathetic syndrome; *Case* 3 to the persistent hypertension group which can be confused with malignant hypertension; and *Cases* 4, 5, and 6 to the asymptomatic group. In only one patient (*Case* 6) was the tumour malignant.

In addition to features described above, attention is drawn to the widespread vasoconstriction, the thin and sometimes impalpable pulse, the pallor and coldness of the face and extremities, the prostration after an attack, the rise of serum potassium in an attack, the initiation of an attack by pain, exercise, emotion, a large intake of fluid, or by histamine injections, and hyperplasia of the islets of Langerhans in one case. Intravenous pyelography was an aid to diagnosis in two cases, and the subcutaneous injection of 0·5 c.c. 1–1000 adrenaline every half hour helped to counteract a post-operative fall of blood-pressure.

A Test for Phæochromocytoma.—M. Goldenburg, C. H. Snyder, and H. Aranow[10] point out the need for such a test in so far as a large proportion (perhaps 60 per cent) of patients with phæochromocytoma may present the picture of chronic rather than intermittent hypertension. Reference is also made to the fact that in Smithwick's series of 1000 patients undergoing sympathectomy for hypertension, an unsuspected phæochromocytoma was found in 5. Attention is also drawn to the fact that 20 per cent of phæochromocytomas are found in extra-adrenal sites.

The test is based on the fact that benzodioxanes, prepared by the introduction of an oxygen atom into the molecule of a simple aromatic sympathomimetic amine, injected intravenously in moderate doses, has a purely adrenolytic action, causing a lowering of blood-pressure when hypertension is due to an excessive amount of adrenaline in the blood. Piperidyl benzodioxane, designated 933F., was used for later studies, and the dose was 0·25 mg. per kilo body-weight, injected intravenously during the course of a slow intravenous saline drip, the actual drug being injected over a period of two minutes. There resulted an immediate fall in systolic and diastolic pressure of some 60 mm. if a phæochromocytoma was present, and this fall lasted some fifteen minutes. In essential hypertension there were only transient minor falls in blood-pressure followed by similar rises. Minor side reactions from the injection were rarely spontaneously complained of, but are enumerated as flushings, palpitations, nervousness, cold and clammy extremities, dizziness, etc. Eight cases are described, and of these two were girls, aged 11 and 13; and one in a boy aged 12. The first girl had paroxysmal hypertension giving place to chronic hypertension; the second girl had attacks of tachycardia, loss of weight, sweating, and heat intolerance, followed by hypertensive retinopathy; while the boy had outbursts of temper and irritability, later followed by attacks of headache, nausea, vomiting, abdominal pain, failing vision, and papillœdema.

The basal metabolic rate in this series, as in others, was raised in some 50 per cent, and a diagnosis of hyperthyroidism was sometimes made.

Another test not referred to in this paper is the intravenous injection of 0·05 mg. of histamine in 0·5 c.c. of normal saline solution, which produces a considerable rise of blood-pressure and induces a characteristic paroxysmal attack (G. M. Roth and W. F. Kvale[11]) (*see following article*).

REFERENCES. [1]*J. Amer. med. Ass.* 1948, **137**, 1005; [2]*Acta med. scand.* 1947, **128**, suppl. 196, 92; [3]*Pr. méd.* 1947, **48**, 541; [4]*Amer. J. Med.* 1948, Feb. 163; [5]*Ibid.* 175; [6]*Ibid.* 1946, **1**, 105; [7]*Lancet*, 1947, **2**, 580; [8]*Canad. med. Ass. J.* 1948, **58**, 330; [9]*Brit. J. Surg.* 1947, **35**, 179; [10]*J. Amer. med. Ass.* 1947, **135**, 971; [11]*Amer. J. med. Sci.* 1945, **210**, 653.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

Phæochromocytomata.—The association of *hypertension* with such tumours is well known. However, there are cases in the literature, as well as in the report

of S. D. Spatt and D. M. Grayzell,[1] in which hypertension is not present. The absence of this symptom in such phæochromocytomata makes it difficult for the authors to accept that the elaboration of pressor substances by the tumour is the only mechanism involved.

Particularly noteworthy is the fact that in the case reported by N. Alwall and H. B. Wulff[2] the paroxysmal attacks, lasting from 2 to 10 minutes, occurred as frequently as five times a day.

J. A. C. Colston[3] reports 2 cases of *bilateral phæochromocytoma in blood relations*; one was a woman of 22 years and the second her 36-year-old maternal aunt.

He draws attention to the *histamine test* of G. M. Roth and W. F. Kvale,[4] who found that by intravenous injection of 0·05 mg. histamine base in 3 patients with phæochromocytoma the rising blood-pressure was accompanied by symptoms of the typical spontaneous attack. According to E. Calkins and J. E. Howard[5] the test appears to be of value as a method of producing attacks at will and as an indication of the presence of phæochromocytoma. As far as is known, no such tumours have been found when the test was negative. In J. A. C. Colston's[3] phæochromocytomata severe attacks of paroxysmal hypertension were induced by histamine; in his opinion the great value of the test as a diagnostic procedure would seem to outweigh any possible dangers.

REFERENCES.—[1]*Amer. J. med. Sci.* 1948, **216**, 39; [2]*Acta chir. scand.* 1948, **96**, 337; [3]*J. Urol.* 1948, **59**, 1036; [4]*Amer. J. med. Sci.* 1945, **210**, 653; [5]*J. clin. Endocrin.* 1947, **7**, 475.

AIR-BORNE INFECTION.

W. H. Bradley, D.M., M.R.C.P.

In the MEDICAL ANNUAL of recent years scientific work on aerial contamination and disinfection has been reviewed. Now, in a paper delivered at the Royal College of Surgeons of England, Professor R. J. V. Pulvertaft[1] has summarized the position and pinned his flag to the mast. He writes: "Respiratory disorders, from tuberculosis and pneumonia, through sinusitis to the common cold, are far the most frequent of the diseases of mankind, and they are spread mainly through the air. The common infectious and virus diseases of childhood cause a high mortality and lifelong respiratory tract disease, and the air is again the commonest vehicle. Air-borne sepsis and cross infection are common particularly in wartime. There is still a tendency to laugh away the protagonists of the control of air-borne infection as faddists. I feel quite sure that the time will come when the methods of controlling air-borne sepsis discovered in Europe and developed in America will return fully fledged to roost in their parent country."

In general terms there are two practicable methods of air sterilization: (*a*) aerosols or mists and smokes; (*b*) ultra-violet light.

Of the first very fascinating method, it can be said that the mechanism is still largely unexplained. A limited number of antiseptics of low vapour pressure, when dissolved in low vapour pressure solvents and sprayed in the form of fine mists, can kill all droplet bacteria in five minutes or less, although the amounts used are homœopathic in their values. For example 5 ml. of 1 per cent sodium hypochlorite will sterilize 1000 cubic feet of air in less than five minutes, and less than 0·00025 g. of hexylresorcinol in propylene glycol will sterilize 1 cubic metre in a similar time. Pulvertaft likens this to a balloon-barrage effect, through collision of particles, but mathematicians suggest that the rate of kill found is more rapid than collision could explain. It is possible that there may be attraction by an electric charge on the particles. From a bacteriological standpoint the results of this method are of great interest, whatever its value in practice. Bacteria suspended in air can be as readily killed by ultra-violet light as by bactericidal mists. Indeed, from the point of view of speed and efficiency of kill there is little difference between the

methods. Ultra-violet light with a wave-length of approximately 2537A.U. is used. It is produced by quartz low-pressure mercury discharge tubes. There are no moving parts, upkeep is minimal, and the amount of electricity used insignificant.

Attractive as these methods may sound, there is need for a word of warning. Aerial contamination and the necessity for its sterilization by methods other than ventilation may be largely a bacteriologist's conception. We are still very much in the dark concerning the exact mechanism of the transmission of the upper respiratory and so-called droplet infections. While undoubtedly methods of aerial disinfection can bring about surprisingly dramatic reductions in the amount of aerial contamination, we have still to prove that aerial contamination plays a major part in the transmission of disease. There is in fact a little uneasiness on the part of the most experienced observers in this field. For example, M. Hamburger et al.[2] find droplet spread to be of much less importance in the transmission of hæmolytic streptococci than we previously thought, and as the result of long-continued experiments conclude that :—

1. Although sneezing probably accounts for a certain number of sporadic cases of hæmolytic streptococcal infection, it is not important in epidemics because it is not a common symptom, and, even if it were, very few sneezes discharge significant numbers of beta-hæmolytic streptococci into the air as droplet nuclei. Nevertheless the rare carriers whose sneezes heavily contaminate the air may be very dangerous if they do not baffle the sneezes efficiently.

2. Coughing, likewise, is important only in sporadic infections for similar reasons. This symptom is more common than sneezing.

3. Talking expels negligible numbers of hæmolytic streptococci.

4. Since the concentration of alpha (salivary) streptococci per c.c. of saliva is remarkably constant from one individual to another, the number of these micro-organisms recovered from the air in large droplets or droplet nuclei during sneezing provides a good index of the quality of sneezes.

5. A more precise understanding of the role of sneezing in the transmission of different respiratory diseases may result from a study of the concentration of the infective agent in the saliva and of the frequency of sneezing among carriers of the agent.

Others who have doubts are J. E. Lovelock and his colleagues K. R. Dumbell and E. J. Lowbury,[3] who report that the dry weight of material dispelled by handkerchief waving is about the same as that emitted by a sneeze, and since it is a matter of everyday observation that sneezing is much rarer than the using of the handkerchief, it may be that the handkerchief is a more potent source of infection than sneezing. There are good reasons for believing that talking and nose-blowing contribute fewer air-borne particles and therefore the use of the handkerchief is probably the most important single action except bed-making in the contamination of the air with micro-organisms from the respiratory tract. In their series of observations, the average number of bacteria carrying particles which can be shaken from normally used handkerchiefs was 136,000 over a series of 211 handkerchiefs shaken gently. The astounding thing is that these particles are resistant to the action of aerial disinfectants and ultra-violet rays at normal relative humidities.

When we consider that the soiled handkerchief implies a soiled hand and that the hand can travel easily as far as a sneeze and get into even less accessible places, we are indeed constrained to consider again whether contact may not play a very much greater part than droplets in the spread of upper respiratory infections.

REFERENCES.—[1]*Brit. med. J.* 1947, **2**, 517 ; [2]*Amer. J. Med.* 1948, **4**, 690 ; [3]*Lancet*, 1948, **2**, 183.

ALCOHOLISM AND DRUG ADDICTION.

E. W. Anderson, M.D., F.R.C.P., D.P.M.

Alcoholism.—H. G. Wolff,[1] opening a conference on the treatment of alcoholism, states that it has been conservatively estimated that in the United States perhaps two and a half million people are addicted to alcohol to an extent which interferes with their effectiveness; further, that of this number about 200,000 are seriously sick and that no solution of the therapeutic problem has been found.

T. A. C. Rennie,[2] whose contribution followed, stated that 10 to 25 per cent of admissions to State hospitals were for conditions associated with alcoholism. He described two main types of alcoholics: (1) The "spree" drinker; (2) The steady drinker, whom he classified into 4 groups: the man with an intolerable life problem, the psychoneurotic, the "psychotic", including manic-depressives, schizophrenics, and mental defectives, and those without any obvious personality deviation who drink because they like the taste and the effect of alcohol. Hospital facilities for the treatment of alcoholism are inadequate, but some hospitals have recently laid aside more beds for the treatment of alcoholics. The author believes that cure of the chronic alcoholic requires the integration of the psychological, medical, and social aspects of the patient's problem. He stresses the value of psychotherapy. Treatment is best carried out in hospital, and for the chronic alcoholic a stay of not less than six months is desirable. In New York State, for instance, it is not possible to convict alcoholics and a revision of the law is strongly recommended. In the treatment of acute cases he advocates insulin (25 units) and glucose (1000-2000 c.c. of a 5–10 per cent solution) in addition to vitamin B fraction to further the oxidation of alcohol in the liver, together with high caloric diet with much protein and carbohydrate.

In chronic alcoholism the author recommends abrupt withdrawal, and believes that with psychotherapy, sedation, and good nursing this has no untoward effects. He mentions also the so-called "conditioned reflex" treatment used in some hospitals in which an emetic is given along with alcohol (an injection of 0·25–1 c.c. of a mixture containing in each c.c. 0·75 mg. emetine and half as much pilocarpine and ephedrine); 70–80 per cent of cures, as measured by abstinence for periods of 2–3 years, have been claimed. In the subsequent discussion some doubts as to the value of vitamin B in acute states were expressed, and uncertainty as to the exact role played by insulin and glucose. The main stress in therapy is laid on psychotherapy and the rehabilitation of the whole individual, in which the author acknowledges the assistance of the Society known as "Alcoholics Anonymous". Unless the fundamental causes of alcoholism in the individual can be removed all symptomatic treatment is of temporary value only.

H. Revilliod[3] (1948) discusses the effect of new legislation in Switzerland, which came into force in 1943, in the treatment of alcoholism. Of 22 cantons, 16 have laws which permit compulsory internment of inebriates notified to the authorities by relatives, relieving officers, or police. Such commitment is a curative measure, not a penalty. Alcoholic out-patient clinics were established by private initiative in 1912. There are now 73 such clinics in the country as well as 9 institutions for the rehabilitation of chronic drunkards which although private enjoy support from cantonal and federal authorities. The director has, however, no power to detain or remove patients, but those interned by State authority remain under official supervision. Statistics showed that 40 per cent remained total abstainers for many years.

Morphinism.—A. Z. Pfeffer[4] discusses the occurrence of *psychosis during the withdrawal of morphine.* Such psychoses are generally considered to be toxic

in character and due to the concurrent use of other toxic agents such as alcohol, barbiturates, and other drugs. It has, however, been generally accepted that withdrawal of morphine alone can produce a psychosis. The author classifies psychoses due to morphine into: (1) Chronic psychosis due to habitual use; (2) Psychosis due to withdrawal; and (3) Psychosis due to idiosyncrasy.

In a study of 500 addicts from whom morphine was withdrawn, 12, or 2·4 per cent became psychotic during the withdrawal period. The author uses the method of gradual withdrawal giving 3 mg. phenobarbitone twice daily: 6 of the 12 patients had a chronic psychosis long before withdrawal, 4 were schizophrenic, and 2 had a "chronic alcoholic psychosis". During withdrawal 3 of the 4 schizophrenic addicts showed increased anxiety and their delusions and hallucinations became more vivid. One of the 3 became disorientated; in this last case the picture of a toxic psychosis resulted. The author concludes that withdrawal of morphine is not enough in itself to cause a psychosis, but that withdrawal may intensify the symptoms of a psychosis already existing. In other cases he found it difficult to know how much withdrawal contributed to the picture of a toxic psychosis, and how much other drugs, including alcohol, played a part; there was, however, little doubt but that anxiety was increased.

REFERENCES. [1]*N.Y. St. J. Med.* 1947, **47**, 1697; [2]*Ibid.*; [3]*Brit. J. Addiction*, 1948, **45**, 68; [4]*Arch. Neurol. Psychiat., Chicago*, 1947, **58**, 221.

AMŒBIC ABSCESS. (*See* LIVER, SURGERY OF.)

ANÆMIA. (*See also* IRON THERAPY.)

ANÆMIA ASSOCIATED WITH TRAUMA AND SEPSIS.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Under this title, Janet Vaughan[1] gives a valuable review of the attempts which have been made to elucidate the pathogenesis of this common type of anæmia.

She points out that both in infections and after injury, there frequently develops an anæmia which is either normocytic and normochromic or slightly microcytic and hypochromic. Neither iron nor liver is effective in treatment. In both conditions there is a negative balance of nitrogen, and in infections erythrocyte coproporphyrin and serum copper are high while serum iron is low. She considers that there is a defect in the synthesis of the globin part of the hæmoglobin molecule which is "part of a wider disturbance of protein metabolism dependent upon the action of breakdown products liberated from the injured tissues or by the need of injured tissues for special amino-acids". The low serum-iron is probably due to a diversion of iron from the plasma to the storage depots and does not indicate a deficiency of this element. Preliminary experimental work indicates that lack of cobalt may play an important part in the failure of hæmoglobin synthesis, but its effect in man has not yet been evaluated.

The author states that at present treatment of the anæmia should consist of a high-protein diet and the use of blood transfusions in severe or prolonged cases.

REFERENCE. [1]*Brit. med. J.* 1948, **1**, 35.

ANÆMIA, EXPERIMENTAL MACROCYTIC.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

G. M. Watson, D. G. Cameron, and L. J. Witts[1] have described the experimental production of macrocytic anæmia in rats by the formation of a blind loop of small intestine. The pathogenesis of this anæmia is not understood,

but it depends on the dilatation of the blind loop with accumulation within it of intestinal contents. The rats developed the anæmia on an average of 8 weeks following the operation and showed an increase in large and early erythrocyte precursors in the bone-marrow. The blood and marrow changes were found to respond to treatment with liver extract. In America, A. D. Welch[2] and G. E. Cartwright[3] and their co-workers have produced a macrocytic anæmia in swine by adding a folic acid antagonist to a purified diet.

The importance of this work lies in the possible development of a test in animals for the therapeutic potency of liver extracts other than their clinical trial in cases of pernicious anæmia. The latter disease has never been reproduced in animals, and although it is difficult to say what relation the experimental anæmia now reported bears to the natural disease, further developments of this work will be followed with great interest as throwing possible light on the mechanism of macrocytic anæmia.

REFERENCES.—[1]*Lancet*, 1948, **2**, 404; [2]*Proc. Soc. exp. Biol., N.Y.* 1947, **65**, 364; [3]*J. Lab. clin. Med.* 1946, **31**, 423.

ANÆMIA, HÆMOLYTIC.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

The mechanism of the hæmolytic crisis has been studied in 6 cases of congenital hæmolytic jaundice by P. A. Owren.[1] He states that during crisis there is no evidence for increased hæmolysis but that a sudden hypoplastic disturbance develops in the marrow, which is responsible for the fall in red cells, granulocytes, and platelets in the peripheral blood. Reticulocytes disappear from the blood and the onset of anæmia is associated with a lessening in the degree of jaundice. The spontaneous recovery from crisis is caused by a return of marrow activity accompanied by reticulocytosis, leucocytosis, and an increase in platelets. The author suggests that as the red cells in congenital hæmolytic jaundice have been shown by transfusion experiments to have a life span of approximately 15 days, the development of an acute aplasia in the marrow would precipitate the rapid onset of anæmia seen in the crisis period. Owren's claim that the severe exacerbations of anæmia in the hæmolytic anæmias are due to episodes of bone-marrow aplasia and not to crises of hæmolysis, is of great interest but is contrary to the views of many leading hæmatologists.

J. A. Fisher[2] of Oxford has reported on 18 cases of acquired hæmolytic anæmia and has reviewed some of the factors which may precede or precipitate the hæmolytic process. He describes the very variable effects of splenectomy in the series of cases studied and concludes that as the results of this operation cannot be predicted, it appears reasonable to maintain the patient with blood transfusions for a period of weeks or months during which time a remission may occur. If, however, the condition remains unremitting and severe, this period with transfusions will serve as a preparation for splenectomy. There was no evidence that liver therapy was of value or that iron was indicated except when hæmoglobinuria threatened to deplete the iron store of the body.

J. M. Stickney and F. J. Heck[3] have followed the results of splenectomy in 22 cases of primary non-familial hæmolytic anæmia treated at the Mayo Clinic. Half of these cases had shown microspherocytosis and increased fragility of the erythrocytes and the results of splenectomy in these cases were better than in those in which microspherocytosis was absent. The authors found no evidence that agglutinins and hæmolysins played any significant role in the production of the hæmolytic syndrome. [The reviewers are in agreement with these findings.]

REFERENCES.—[1]*Blood*, 1948, **3**, 231; [2]*Quart. J. Med.* 1947, **16**, 245; [3]*Blood*, 1948, **4**, 431.

ANÆMIA, PERNICIOUS.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Vitamin B_{12}.—Great interest has arisen within the last year from the isolation from liver of a crystalline compound which would appear to be very closely related to the long-sought anti-pernicious anæmia factor of Castle. In 1947, M. S. Shorb[1] reported finding in refined liver extracts a factor necessary for the growth of an organism, *Lactobacillus lactis* Dorner. This L.L.D. factor was present in an almost direct proportion to the potency of the liver extracts used in the treatment of pernicious anæmia. E. L. Rickes, N. G. Brink, F. R. Koniuszy, T. R. Wood, and K. Folkers[2] isolated from liver a crystalline compound which Shorb,[3] who assayed its potency value for L.L.D. factor, believed to be either wholly or partly responsible for the L.L.D. growth activity observed for liver extracts. Pending the discovery of its chemical constitution, the name vitamin B_{12} was proposed for the compound, which is known to contain the element cobalt. In clinical tests, R. West[4] obtained a positive hæmatological response in 3 patients with pernicious anæmia following the intramuscular administration of B_{12} in single doses of 3, 6, and 15 micrograms respectively. Subsequent clinical trials with vitamin B_{12} have been reported by Tom D. Spies and his co-workers,[5, 6, 7] who have used the compound in 2 cases of pernicious anæmia, 2 cases of nutritional macrocytic anæmia, 1 case of non-tropical sprue, and 7 cases of tropical sprue. In some of the cases of sprue the hæmopoietic result was very definitely suboptimal.

In Britain, Lester Smith[8] has described the preparation from 4 tons of proteolysed liver of a gramme of two red pigments, one of which has been obtained in crystalline form and is probably identical with vitamin B_{12}. C. C. Ungley[9] has reported on the hæmatinic effects of these pigments, which are active in pernicious anæmia in doses of 20 micrograms and also appear effective in subacute combined degeneration. In cases of megaloblastic anæmia other than Addisonian pernicious anæmia the material is not necessarily effective. Thus, Ungley[10] quotes a case with megaloblastic anæmia of pregnancy which showed no response to 65 micrograms, but responded subsequently to a daily dosage of 2·5 mg. folic acid. F. H. Bethell[11] and his co-workers have also reported a similar finding in a case of puerperal megaloblastic anæmia which responded to treatment with folic acid after vitamin B_{12} had failed to produce hæmopoietic or clinical improvement.

Vitamin B_{12} and the compound isolated by Lester Smith are of great academic interest but of little clinical importance at the present time because of their scarcity and great expense. [The reviewers have been informed that 1 c.c. of a highly purified liver extract such as that made by the Lederle Co. which contains 15 U.S.P. units of the anti-pernicious anæmia factor has been shown to have the activity equivalent to 15 micrograms of vitamin B_{12}.] If, however, vitamin B_{12} is synthesized, or produced cheaply from sources other than liver by new methods, a great clinical advance in therapeutics would be achieved.

The exact relationship of vitamin B_{12} to folic acid in the mechanism of normal and abnormal hæmopoiesis is at present a matter of great interest to investigators, and many important findings in this field of work may be expected in the near future.

Folic Acid.—Full reviews of this compound dealing with its chemical and clinical aspects and with a large bibliography have been written by J. F. Wilkinson[12] and L. S. P. Davidson[13] and the reader is referred to these papers for full and up-to-date information on this subject.

REFERENCES.—[1]*J. biol. Chem.* 1947, **169**, 455; [2]*Science*, 1948, **107**, 396; [3]*Ibid.* 397; [4]*Ibid.* 398; [5]*Sth. med. J.* 1948, **41**, 522; [6]*Ibid.* 523; [7]*Blood*, 1948, **11**, 1213; [8]*Nature, Lond.* 1948, **161**, 638; [9]*Lancet*, 1948, **1**, 771; [10]*Brit. med. J.* 1948, **2**, 154; [11]*Proc. cent. Soc. clin. Res.* 1948, **27**; [12]*Brit. med. J.* 1948, **1**, 771, 822; [13]*Edinb. med. J.* 1948, **55**, 400.

ANÆMIA, SPLENIC.

(*See also* ŒSOPHAGEAL VARICES; PORTAL HYPERTENSION.)

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

In last year's ANNUAL mention was made of new surgical procedures which have been developed in the treatment of the syndrome of portal hypertension. Obstruction to the flow of blood in the portal venous system may be due to fibrotic changes in the liver or to a more localized block occurring in the main portal or splenic veins. J. R. Learmonth[1] and Learmonth and A. I. S. Macpherson[2] have reported on the surgical aspects of portal hypertension and have given the results of treatment in 16 cases. In 6 of 8 patients who survived lienorenal anastomosis there was no further hæmatemesis after intervals up to 23 months and their general condition was much improved. In 3 patients in whom hæmatemesis was shown to result from thrombosis of the splenic vein, splenectomy alone has so far proved a safe and satisfactory immediate method of treatment and should result in permanent cure. The surgical assessment and operative technique in cases of portal hypertension is a highly specialized procedure and should at present be carried out only in centres where special knowledge and facilities are available. It will be several years before the value of surgical measures in this syndrome can be finally assessed, but the results so far reported are very promising.

REFERENCES.—[1]*Ann. R. Coll. Surg. Eng.* 1947, 299; [2]*Lancet*, 1948, **2**, 882.

ANÆMIA OF THE SPRUE SYNDROME.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

The blood and bone-marrow findings in the sprue syndrome have been studied in 63 cases by E. M. Innes[1] and in 45 cases by W. T. Cooke, A. C. Frazer, A. L. P. Penney, H. G. Sammons, and M. D. Thompson.[2]

The characteristic blood-picture in adult cases was macrocytosis of the erythrocytes with or without anæmia, both macrocytosis and anæmia being more marked in the non-tropical than in the tropical group. It was noted that the macrocytosis tended to persist in spite of liver therapy and in some cases after folic acid treatment as well. The bone-marrow findings varied from a megaloblastic change indistinguishable from pernicious anæmia to true normoblastic erythropoiesis, with many cases showing an intermediate picture comparable to that seen in a case of pernicious anæmia in relapse following the injection of a suboptimal dose of liver extract. The varied response to liver extracts and to folic acid is difficult to explain. The best results are obtained with folic acid when a megaloblastic anæmia is present. In some of these cases however, neither liver extract nor folic acid will restore the blood-picture to normal. The therapeutic effects are poorest in cœliac disease (where only the exceptional case responds) and best in tropical sprue. In idiopathic steatorrhœa some cases respond well, some moderately, and some not at all. While folic acid can be stated to be a more valuable therapeutic agent in the sprue syndrome than liver extract in most cases, the hope that the discovery of folic acid had yielded a specific remedy for this syndrome can unfortunately no longer be sustained.

REFERENCES.—[1]*Edinb. med. J.* 1948, **55**, 282; [2]*Quart. J. Med.* 1948, **17**, 9.

ANÆSTHESIA AND ANALGESIA.

C. Langton Hewer, M.B., M.R.C.P., F.F.A.R.C.S.

INHALATION ANÆSTHESIA

Trichlorethylene.—It is now recognized that trichlorethylene should not be given in a closed circuit owing to the possibility of chemical reaction with unsuitable soda-lime and the formation of toxic products. Various mechanical

devices have now been contrived to prevent this happening; for example, A. H. Galley[1] describes a by-pass for attachment to existing apparatus, while H. R. Marrett[2] has incorporated this safety factor in an entirely new gas-oxygen apparatus which is of very light but sturdy construction.

Respiratory Disturbances.—M. D. Nosworthy[3] has contributed a very important paper entitled "Some Respiratory Disturbances during General Anæsthesia", which is a sequel to his classical contribution on controlled respiration to the Royal Society of Medicine in 1941. An adequate summary is impossible to give here, and the reader is strongly recommended to read the original article. The author's summary is as follows: (1) Keeping the airway clear is very largely dependent on the avoidance of reflex response; (2) The various factors which influence the bronchial lumen are considered; (3) The depressant qualities of modern anæsthetic methods make the different levels of anæsthesia less easily distinguishable; (4) Marked central depression may be injurious and is not necessarily accompanied by adequate reflex suppression; (5) Examples of the results of reflex respiratory activity during anæsthesia are given.

Anæsthesia for Cardiac Surgery.—B. Raft-Smith and G. Ostlere[4] give a useful account of the anæsthetic technique evolved at St. Bartholomew's Hospital for dealing with cardiac surgery, particularly the closure of patent ductus arteriosus and pericardiectomy for constrictive pericarditis. Induction is by intravenous thiopentone (or nitrous oxide in children), followed by a few breaths of nitrous-oxide–oxygen–trilene and then ether–oxygen. A tracheal tube is then passed and narcosis is maintained by means of ether and oxygen with a semi-closed circuit. This is preferred to a completely closed system, as the dosage of ether is more delicately controllable and there is less resistance to breathing, particularly in children. Cyclopropane was tried and abandoned owing to the prevalence of tachycardia and arrhythmia. It can, however, be used in combination with curare if a co-existent condition such as pulmonary inflammation renders it desirable. Under these circumstances, cardiac irregularities are not so pronounced. If necessary, re-expansion of the lung is carried out before pleural closure by screwing down the expiratory valve, occluding the mouth and nostrils with the hand, and gently compressing the re-breathing bag.

Intravenous Anæsthesia

Accidental Arterial Injections. S. Cohen[5] has contributed an exhaustive and important paper on the results of the inadvertent arterial injection of drugs. Eight hitherto unrecorded cases of intra-arterial thiopentone are included and some idea of the serious nature of the accident is afforded by the fact that five of these patients subsequently underwent arm or forearm amputations. The incidence in Great Britain has been estimated as 1 in 55,000 injections of thiopentone. None has been reported with hexobarbitone. Pain is the first immediate effect and the pulse in the affected limb may become poor or absent. Even if it remains full, this does not preclude disaster, as it has been known to fail as late as the tenth day after the injection. The commonest abnormality predisposing to the accident is a superficial ulnar artery (*Fig.* 1). The pathology is discussed, and seems to consist usually of a combination of arterial spasm and thrombosis.

As regards treatment, the previously suggested intra-arterial procaine is probably useless, but immediate brachial plexus block with a long-acting analgesic such as amethocaine would seem to be indicated. If arterial injection is certain, the projected operation should be abandoned, if possible, as heparinization ought to be carried out at once, an initial dose of 15,000 units being

suggested in the adult. The affected artery can be exposed and the drug injected directly into it. The heparin should be followed up by dicoumarin. If it is imperative to proceed with the operation, cyclopropane is the anæsthetic of choice as it relaxes peripheral blood-vessels. The limb must be carefully watched and a decision as to exploration made within six hours. If this is judged necessary, the artery should be opened proximal to the site of injection



Fig. 1.—Veins distended with rubber band. Arrow indicates superficial ulnar artery. Gliding of needle to enter median basilic vein may lead to puncture of the artery. (*By kind permission of 'The Lancet'.*)

and the clot removed. An intra-arterial injection of heparin should be given before closure of the wound. Arterectomy is judged to be useless and is contra-indicated. The limb should then be wrapped in a sterile towel and covered with wool but *not* heated.

Muscle Relaxants

Curare.—Extended experience has shown curare to be the safest and most reliable relaxant in common use. T. C. Gray[6] points out that some patients appear to have a true idiosyncrasy for the drug, apart from myasthenia gravis, and suggests that a trial dose of 5 mg. (tubarine) should first be given to the conscious patient. If there is no effect beyond slight ptosis, a further 10 mg. can be given, followed immediately by 0·5 g. thiopentone. An airway or tracheal tube can then be inserted and unconsciousness maintained by any desired method provided that assisted or controlled respiration is carried out as indicated. It must, however, be admitted that some anæsthetists do not regard the technique as entirely safe, and prefer to add curare as required to a patient already anæsthetized. A trial dose can, of course, be equally well given to the unconscious patient. An unpleasant possibility with the technique described is that if the needle comes out of the vein before the thiopentone has been given and there is difficulty in re-insertion, the patient is subjected to the experience of being curarized but not unconscious. If the stomach is known to contain fluid, a cuffed tracheal tube should be inserted before curare is given or regurgitation may ensue.

Myanesin.—This drug was originally thought to act on the spinal cord, but A. R. Hunter and J. M. Waterfall[7] point out that it is more probable that its effect is on the basal ganglia. Myanesin will check epileptic fits in thirty seconds, which is little in excess of the arm-brain circulation time and much less than the ninety seconds which curare requires for its peripheral effect.

Extended use of myanesin has not tended to confirm its earlier promise. While it does undoubtedly cause less respiratory depression than curare for a given degree of relaxation, it is much less certain in its effect, and very large doses are sometimes necessary. Furthermore, myanesin frequently causes

venous thrombosis, and H. B. Wilson and H. E. Gordon[8] confirm that definite hæmolysis and increased red-cell fragility can be demonstrated after its administration. H. R. Griffith and W. C. Cullen,[9] in reporting 4 cases of thrombophlebitis in 120 administrations of myanesin, suggest that the solvent may be responsible. This is believed to contain propylene-glycol, ethyl alcohol, and water, and the usual 10 per cent solution is strongly hypertonic. It is possible that dilution to 2 per cent with normal saline might minimize complications.

If myanesin is inadvertently injected into an artery, gangrene of the fingers and hand can ensue, T. A. Ogilvie et al.[10] recording one such case which resulted in amputation above the elbow. There is some evidence to show that the cause of the gangrene is not intense vasospasm, as with thiopentone (q.v. in this article), but " curdling " of the myanesin which results in a shower of emboli blocking the arterioles.

Other Relaxant Drugs.—A great deal of research has been proceeding with a view to finding other muscle relaxants, and from experimental work on animals it seems likely that two may be of value. The first is the dimethyl ether iodide of *d*-tubocurarine usually known as " DME ", and the second bistrimethylammonium decane di-iodide known as " C.10 ". At the time of writing, however, observations on the effects of these compounds in man have not been completed.

Spinal Analgesia

Total Spinal Block.—Analgesia of the whole body has been produced by intrathecal injections in the past, notably by Jonnesco and Le Filliâtre, and these workers recognized that the method was a dangerous one owing to extreme falls in blood-pressure and to respiratory paralysis.

H. W. G. Griffiths and J. Gillies[11] have revived the technique for thoracolumbar splanchnicectomy and sympathectomy for essential hypertension. After premedication with omnopon and scopolamine, intravenous thiopentone up to 1 g. is given. A lumbar puncture is performed in the second lumbar space and 150 to 250 mg. procaine is dissolved in 3 to 4 c.c. cerebrospinal fluid. The patient is then turned on to his back in the steep Trendelenburg position until an appreciable fall in blood-pressure occurs. An airway is then inserted and 100 per cent oxygen is given. He is then turned into the lateral " jack-knife " position (*Fig.* 2), the pelvis being the highest point. Unconsciousness is maintained either with thiopentone or cyclopropane. Controlled respiration may be necessary, especially if the pleura is opened, but phrenic paralysis does not usually occur. The most probable explanation of this is that dilute analgesic solutions affect vasomotor fibres more than sensory, and sensory more than motor ones. After operation a 20° head-down tilt is maintained for at least eight hours.

The great advantage of this technique is that the low blood-pressure ensures an almost ischæmic operative field. The pressure is often unrecordable but the optimum is regarded as 70 mm. Hg.

In 84 operations there was one death on the table. The reader is strongly advised to read the original article very carefully before attempting this technique.

Spinal Block for Congenital Megacolon.—Most workers who have tried high spinal analgesia for the treatment of congenital megacolon have had disappointing results. E. D. Telford and H. A. Haxton,[12] however, report 12 cases in which the results were " good " in 8, " fair " in 2, and " failed " in 2. They consider that the drug and method are immaterial provided that the effect reaches the anterior roots of T.5. It is suggested that some earlier " failures "

were due to insufficient waiting, as a delay of several weeks may elapse before much improvement is seen.

Permanent Paralysis following Spinal Analgesia.—The opinion is gaining ground that permanent palsies are commoner than was formerly supposed, and a recent large-scale investigation has been made in Sweden (E. Schildt).[13] This revealed that, out of approximately 23,000 spinal blocks, 6 were followed by permanent paralysis leading to invalidism. There was no evidence of infection, and it is concluded that these disasters were due to a "chemotoxic effect" of the local analgesic on the spinal cord and its membranes. If this conclusion is generally accepted it is obviously of great medico-legal

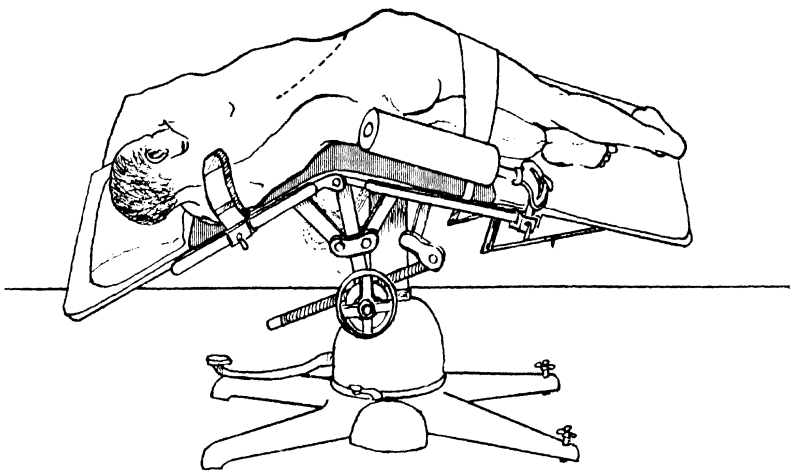


Fig. 2. Lateral 'jack-knife' position. (*By kind permission of* '*Anæsthesia*'.)

importance, as the skill and aseptic technique of the anæsthetist could hardly be called into question.

Meningitis following Spinal Analgesia. Once more we have to record cases of meningitis following spinal block. I. A. Davidson[14] describes 2 consecutive cases of hernia operated upon under 3 c.c. 5 per cent intrathecal planocaine which developed meningitis from *Ps. pyocyanea*. One patient eventually recovered after treatment with sulphamerazine, but the other died. An exhaustive attempt to trace the source of infection failed.

The increasingly large number of post-spinal meningitis cases has prompted the Public Health Laboratory Service and the London Sector Pathologists Committee to issue a memorandum pointing out some of the more obvious pitfalls in an aseptic technique.[15]

Ephedrine in Spinal Analgesia.—Ephedrine (1-phenyl-2-methylamino propanol) has been used for many years as a vasopressor drug during spinal analgesia. In 1940, F. H. Shultz[16] showed that, when injected subcutaneously, ephedrine produced local analgesia. This year J. E. Ruben and others[17] have proved that 50 mg. ephedrine injected intrathecally in man produced sufficient spinal analgesia for operating purposes, and this is probably the explanation for for the fact, long known, that ephedrine added to spinal analgesic solutions potentiates their effects. This was previously thought to be due to the vasoconstrictive action. Incidentally no rise in blood-pressure could be detected

after the intrathecal injection of ephedrine, so that the drug probably does not enter the general circulation in appreciable quantity when given by this route.

General Analgesia

Obstetric Analgesia. It has become almost impossible to keep track of all the published methods which have been tried to produce an efficient and safe analgesia for childbirth, but H. Roberts[18] has had encouraging results from a combination of pethidine and scopolamine. The initial dose consisted of 100 mg. pethidine and $\frac{1}{150}$ gr. scopolamine. This was repeated after an hour unless the os was more than three-quarters dilated, in which case the scopolamine was omitted. Further doses were sometimes necessary. The intramuscular route was used unless labour was so advanced that the pethidine had to be given in diluted form into a vein. In 500 cases the degree of relief was described as "good" in 82·2 per cent.

References.—[1]*Brit. med. J.* 1948, **1**, 996; [2]*Ibid.* 403; [3]*Anæsthesia*, 1948, July, 86; [4]*Lancet*, 1948, **1**, 647; [5]*Ibid.* **2**, 361; [6]*Proc. R. Soc. Med.* (Anæsth. Sec.), 1948, April, 2; [7]*Lancet*, 1948, **1**, 366; [8]*Ibid.* 367; [9]*Anesth. & Analges.* 1948, July–Aug., 232; [10]*Lancet*, 1948, **1**, 947; [11]*Anæsthesia*, 1948, Oct., 134; [12]*Brit. med. J.* 1948, **1**, 827; [13]*Acta chir. scand.* 1947, Jan., 101; [14]*Lancet*, 1947, **2**, 653; [15]*Ibid.* 883; [16]*Anesthesiology*, 1940, **1**, 69; [17]*Science*, 1948, **107**, 233; [18]*Brit. med. J.* 1948, **2**, 590.

ANAL FISSURE (AND ALLIED CONDITIONS).

W. B. Gabriel, M.S., F.R.C.S.

R. Turrell[1] describes the *surgical treatment of chronic anal fissure or ulcer*—these terms he regards as synonymous. Pre-operative sedation with barbiturates such as nembutal or seconal is given 1 to 2 hours before operation, followed by morphine and scopolamine. The anæsthetic preferred is a low spinal with 25–50 mg. of procaine hydrochloride. The treatment of spinal headaches is described. The use of long-acting anæsthetic solutions locally is not recommended, because they may produce an aseptic inflammatory reaction in the tissues, which may finally result in tissue necrosis and suppuration. The operation consists in the usual wide excision of the fissure together with any related crypt or polyp and the sentinel pile. The subcutaneous external sphincter is now divided in the floor of the wound, and if much fibrosis is present a small part of the muscle is excised in order to prevent early re-apposition of the muscle and to ensure ample drainage. The author prefers not to remove associated hæmorrhoids, except those close to the wound, since they frequently recede after the fissure operation. Any of the new hæmostatic agents such as gelatin sponge or oxycel may be applied locally if desired. A finger is passed on the 5th post-operative day, and the wound is completely healed within 3 or 4 weeks. It is stated that the patient is discharged from hospital after the first bowel movement, which usually occurs between the second and fourth post-operative day. The importance of post-operative management is mentioned, and the author states that in his series of 270 cases there occurred two examples of a low-grade infection in the base of the wound with a resulting sinus or fistulous tract.

E. T. Whitney[2] describes in considerable detail some important points in the *anatomy of the anal canal and its musculature*; he makes a distinction between "sphincterotomy" (division of the subcutaneous external sphincter) and "pectenotomy" (division of the pecten band). He believes that the pecten band develops beneath the transitional epithelium at the level of the anal intermuscular septum and is due to chronic infection in anal crypts and ducts as the result of which the fibromuscular insertion of the longitudinal muscle is gradually converted into a band of pearly white connective tissue. Contraction of this fibrous tissue may lead in process of time to abscesses and fistulæ from

constriction of the necks of the anal ducts, also to a *general fibrosis of the anus with a contracture of the sphincter muscles as well as of the epithelial lining of the anal canal.* Whenever this condition is met with the best treatment is division of the subcutaneous external sphincter in the posterior midline, together with a pectenotomy. The operation and its management is described in detail; the procedure is contra-indicated in the rare cases of ataxic sphincter and also when the puborectalis sling is weak and there is in consequence a deficient recto-anal angle and a tendency to prolapse.

F. C. Newton and C. A. Macgregor[3] describe 21 cases of *spasm and fibrosis of the anal sphincter* associated with a long history of severe constipation and chronic abuse of catharties, together with vague abdominal symptoms such as discomfort, anorexia, tenesmus, and excessive gas formation. Out of their 21 patients 19 were women, the average age being 55 years; the average duration of symptoms was 10 to 15 years. Examination revealed spasm and hypertrophy of both internal and external sphincters; associated anorectal lesions were of a minor character and could not have been the chief cause of the conditions described. The treatment recommended is a digital dilatation of the anus under general anæsthesia; this should be carried out slowly over a period of 10 minutes until finally four or five fingers can be inserted with ease. Frequently the subcutaneous external sphincter must be incised in the midline posteriorly in order to correct a shelf-like fibrosis. At this stage a proctoscopy and sigmoidoscopy should be done. Subsequently a high-residue diet without catharsis is resumed either immediately or after the first few days, and digital or instrumental dilatation should be begun on the 4th post-operative day. The author illustrates Young's dilators; these consist of a set of 4 graduated dilators which the patient is instructed to pass daily until normal bowel habits are restored. Periodical rectal examination should be made. Good results were obtained in all the cases reviewed and only one needed a second dilatation.

REFERENCES.—[1]*Surg. Gynec. Obstet.* 1948, **86**, 434; [2]*Amer. J. Surg.* 1948, **75**, 761; [3]*New Engl. J. Med.* 1948, **239**, 113.

ANAL FISTULA. *W. B. Gabriel, M.S., F.R.C.S.*

H. M. Young[1] discusses the *embryology of the anal canal, the anal crypts, and intramuscular glands.* He refers particularly to the work of F. P. Johnson[2] on this subject and reproduces a number of his illustrations. He describes the approved method of laying open a direct low-level fistula and emphasizes the importance of paring back the anal epithelium on either side of the severed sphincter fibres. If there is any redundance of the anal epithelium *opposite* the fistula wound a sector should be excised in order to prevent it from falling into the fistula wound. Packing the wounds with gauze subsequently is to be avoided. The author recommends sulphasuxidine or sulphathalidine both pre- and post-operatively.

J. M. Kenney[3] says that the commonly accepted methods of treating fistula-in-ano appear to be archaic and that healing by granulation involves a long convalescent period with discomfort, temporary anal incontinence, frequent dressings, and the need for careful and prolonged wound care to ensure proper healing. He describes a method of *excision of the fistulous tract*, with primary closure of the wound in layers by the use of fine, interrupted cotton sutures. The tissues round the wound are infiltrated with a penicillin solution, 2000 units per c.c., 20–100 c.c. being used. The mucosal edges are approximated with the finest catgut on atraumatic needles, and the skin with vertical mattress sutures of No. 60 cotton. No drains are inserted and the technique aims at complete hæmostasis and avoiding any dead spaces in the wound. Out of 12 patients treated by this method (all young adults between the ages of 18 and 31), primary

healing took place in 11 and no recurrence was noted over a period of 2–6 months. One case which was not infiltrated with penicillin failed to heal *per primam* and discharged some pus and cotton stitches. The author states that the successful cases were noteworthy for the short convalescent period, and absence of complications and excessive scarring. [The fistulæ treated by this method appear to have been of the direct subcutaneous or low-level anal varieties.—W. B. G.]

H. Aronsson[4] has written a voluminous and well-documented monograph on *ano-rectal infections and their sequelæ*, particularly fistulæ and incontinence. The study is based on 1052 cases of ano-rectal infections and fistulæ; 8 cases of incontinence are also described, and the available methods of treatment are examined. The author emphasizes the importance of distinguishing between the deep ano-rectal portion of the sphincter muscle and the superficial anal portion; at operation the level of the internal opening of a fistula must be accurately determined. In order to avoid recurrence the entire fistulous tract should be excised and this proved possible in all the 53 cases personally operated upon by the author. The incidence of a tuberculous infection in the fistula series proved to be between 2·5 and 5·1 per cent.

REFERENCES.—*Ann. West. Med. Surg.* 1948, **2**, 206; [2]*Amer. J. Anat.* 1914, **16**, 1; [3]*Ann. Surg.* 1947, **126**, 320; [4]*Acta chir. scand.* 1948, **96**, suppl. 135.

ANAL INCONTINENCE.

W. B. Gabriel, M.S., F.R.C.S.

The *operation* described by Thiersch more than 50 years ago has been revived by W. B. Gabriel,[1] and details are given of 11 cases treated by this method. The operation consists in placing a silver wire ring in the perianal space so as to narrow and support the anus. The chief indication has been the cases of relaxed sphincters with mucosal prolapse. The operation may also prove useful as a subsidiary procedure following operation for complete prolapse, when a patulous sphincter fails to show sufficient capacity for recovering its tone. The operation is performed under continuous pentothal anæsthesia, and the silver wire (No. 19 or 20 S.W.G.) is passed round by means of a Doyen's needle through a puncture about one inch posterior to the anus. Before the wire is twisted care is taken to ensure that the calibre of the anus will allow a forefinger to be passed. A temporary fæcal impaction in the rectum is liable to develop at first and glycerin suppositories may be required daily for a week or two after operation.

REFERENCE.—[1]*Proc. R. Soc. Med.* 1948, **41**, 467.

ANAL PRURITUS.

(*See* PRURITUS ANI.)

ANALGESIC DRUGS

Andrew Wilson, M.D., Ph.D., Ph.C.

The synthesis of analgesic drugs has been the subject of considerable pharmacological research and numerous methods have been devised for measuring the analgesic activity of drugs in animals and in man. These methods have recently be reviewed in publications by Thorp,[1] and Hewer and Keele.[2]

Methadon (Physeptone).—The disadvantages of morphine as a pain-relieving drug have been recognized for many years and attempts have been made, from time to time, to provide derivatives of this drug without its undesirable properties. A new aspect of the subject was opened up when a number of new compounds, prepared by German chemists, was made available at the close of the recent World War.[3] One of these substances *dl*-2-dimethylamine-4: 4 diphenyl-heptan-5- one hydrochloride, known in Germany as Hœchst 10820, has been studied in this country and in America. This compound has also been called amidone, miadone, dolophine, and has recently been given the

proprietary name of methadon by the Council on Pharmacy and Chemistry of the American Medical Association. In Great Britain it is marketed as Physeptone. It is a white crystalline substance, soluble in water and in alcohol, and is available for oral or parenteral administration. The compound contains an asymmetric carbon atom and is supplied as the racemic mixture. It possesses many of the characteristic actions of morphine, and it has been shown that the analgesic activity of the *l*-isomer is much greater than that of the *d*-isomer.[4, 5, 6]

The analgesic effects of methadon have been compared with those of morphine and of pethidine. Thorp, Walton, and Ofner[6] have shown that when tested on the rat, methadon is about as potent as morphine and 10 times more potent than pethidine. These results are in close agreement with those obtained by Kirchhof and David,[7] and by Robbins,[8] and are of the same order of activity as Hewer and Keele[2, 9] found when the drugs were given to human volunteers by intravenous injection. Using a different method, Christensen and Gross[10] have shown that when the drugs are administered to human subjects by subcutaneous injection, the maximum analgesic effect is produced in about 90 minutes and that methadon is three times more active than morphine and about thirty times more active than pethidine; this was also the experience of Hand[10] and Isbell and his colleagues.[11] Christensen and Gross[10] found considerable variation in response when the drugs were given by intravenous injection, a fact which was also noted by Hewer and Keele.[2] There is also considerable variation in the intensity and duration of effect when the drug is administered by mouth,[10] though Troxil[12] considered that an elixir of methadon given orally produces effects comparable with a similar dose by hypodermic injection.

The analgesic effects of methadon and of morphine are reduced in intensity and in duration when these drugs are administered subcutaneously with therapeutic doses (0·3 mg.) of atropine sulphate or hyoscine hydrobromide (Christensen and Gross[10]). These authors subsequently found that as a drug for pre-medication methadon is unsatisfactory; this was also the experience of Scott and his colleagues,[13] who considered that methadon is inferior to morphine for this purpose on account of its lack of sedative properties.

The enhancement of the analgesic action of opium derivatives by neostigmine, reported by Slaughter and Munsell[14] and by Floodmark and Wrammer,[15] holds true for methadon and for pethidine. It has been shown[10] that when neostigmine in a dose of 0·5 mg. is injected subcutaneously with methadon or pethidine, it markedly increases both the intensity and duration of analgesic action of these drugs. The mechanism of this action is not clear, though it is interesting to speculate whether the anti-cholinesterase activity of neostigmine is concerned in this effect since Eadie, Bernheim, and FitzGerald[16] have recently shown that methadon inhibits the cholinesterase activity of rat brain.

Clinical Effects.—Several reports have been published concerning the analgesic effects of methadon in a variety of clinical conditions.[7, 8, 12, 13, 17, 18] The most satisfactory relief of pain is evident in the treatment of post-operative pain, dysmenorrhœa, renal colic, and cough; the drug is of little value in controlling labour pains or the joint pains of arthritis and primary and secondary carcinoma. Troxil[12] considered that methadon given intramuscularly in doses of 7·5 to 10 mg. is more effective than morphine in doses of 10 to 15 mg., and more effective than pethidine in doses of 75 to 150 mg. This is also the conclusion of Kohlstaedt.[12] The analgesic effect lasts from three to four hours, though in some cases the action continued for about eight hours.

The incidence of side-effects is lower than with morphine, and such toxic effects are more evident in ambulant than in non-ambulant patients. The

chief side-effects are nausea, vomiting, headache, miosis, drowsiness or euphoria, and dryness of the mouth. When patients were treated with 5 mg. methadon 13 per cent complained of these, while in those given 7·5 mg. 12 per cent had side-effects, whereas in doses of 10 mg. the incidence rose sharply to 22 per cent. Troxil[12] concluded that the most effective dose of methadon which would cause the minimum of side-effects is 7·5 mg.

Although Woods, Wingarden, and Seevers[19] could find no evidence of tolerance to the drug in the Rhesus monkey, Isbell and his co-workers,[20] in an extensive series of observations on dogs and on man, have concluded that marked tolerance develops not only in respect to the analgesic action of methadon but also to its sedative and respiratory depressant actions.

Earlier and optimistic reports had suggested that methadon did not cause addiction, but there is no doubt from the work of Isbell,[20] that habituation is a marked feature of its use. This is abundantly clear from the fact that methadon when given to 12 morphine addicts completely alleviated the symptoms of morphine withdrawal. Furthermore when morphine was replaced by methadon, the latter prevented the appearance of morphine withdrawal syndrome. When the drug has been given for periods of up to six months and then stopped, the withdrawal symptoms were mild compared with those of morphine, and subsided in about ten days. In consequence, the use in Great Britain of methadon, in common with that of morphine and pethidine, is governed by the Regulations of the Dangerous Drugs Acts.

Analgesic Activity of Acetanilide. The therapeutic activity and toxic actions of acetanilide are generally ascribed to the conversion of this drug in the body to *p*-aminophenol and analine.[21, 22] Recent studies on the metabolism and fate of acetanilide (Lester and Greenberg),[23, 24] have drawn attention to the presence in the blood and plasma of substantial amounts of *N*-acetyl *p*-aminophenol. When acetanilide is given by mouth in doses of 1 g. to human subjects, the major portion of the drug is oxidized in the liver to *N*-acetyl *p*-aminophenol, which is excreted in a conjugated form in the urine, thus :—



Acetanilide	*N*-acetyl *p*-aminophenol	Conjugated *N*-acetyl *p*-aminophenol

According to Brodie and Axelrod,[25] only a small portion of acetanilide is de-acetylated to form aniline, which is the precursor of a substance, probably phenolhydroxylamine, which is responsible for the formation of methæmoglobin. It is suggested that the toxicity of acetanilide is mainly due to the formation and ultimate fate of aniline produced in this way.

There is evidence that phenacetin (acetophenetidine) is likewise transformed to *N*-acetyl *p*-aminophenol.[26]

Flinn and Brodie[27] have investigated the analgesic activity of *N*-acetyl *p*-aminophenol in man. Using the Hardy, Wolff, and Goodell method,[28] they have shown that when given by mouth in doses of 0·325 g., this substance raises the threshold for pain by about 25 per cent in two and a half hours. According to the authors, this indicates that dose for dose the analgesic effect is comparable with that found for acetanilide by Wolff, Hardy, and Goodell.[29]

Even when given in higher doses, there was no evidence of methæmoglobin formation.

This work offers a new approach to the study of these analgesic substances, not only from the point of view of toxicity, but also in regard to the relationship between analgesic and antipyretic activity.

REFERENCES.– [1]*Brit. J. Pharmacol.* 1946, **1**, 113 ; [2]*Lancet*, 1948, **2**, 683 ; [3]*U.S. Department of Commerce, Office of the Publication Board, Washington, Report No.* 981 ; [4]*J. Pharmacol.* 1946, **87**, 63 ; [5]*Anesth. & Analges.* 1947, **26**, 12 ; [6]*Nature, Lond.* 1947, **159**, 679 ; [7]*West J. Surg.* 1947, **55**, 183 ; [8]*J. Amer. med. Ass.* 1948, **137**, 594 ; [9]*Lancet*, 1947, **2**, 281 ; [10]*J. Amer. med. Ass.* 1948, **137**, 594 ; [11]*Federation Proc.* 1947, **6**, 341 ; [12]*J. Amer. med. Ass.* 1948, **136**, 520 ; [13]*Anesth. & Analges.* 1947, **26**, 18 ; [14]*J. Pharmacol.* 1940, **68**, 104 ; [15]*Acta. physiol. scand.* 1945, **9**, 88 ; [16]*J. Pharmacol.* 1948, **94**, 19 ; [17]*Federation Proc.* 1947, **6**, 345 ; [18]*Proc. Mayo Clin.* 1947, **22**, 249 ; [19]*Federation Proc.* 1947, **6**, 387 ; [20]*J. Amer. med. Ass.* 1947, **135**, 888 ; [21]*Acetanilide* Hill House Press New Haven, 1946 ; [22]*J. Pharmacol.* 1946, **88**, 87 ; [23]*Ibid.* 1947, **90**, 68 ; [24]*Ibid.* 150 ; [25]*Ibid* 1948, **94**, 29 ; [26]*Federation Proc.* 1948, **7**, 207 ; [27]*J. Pharmacol.* 1948, **94**, 76 ; [28]*J. clin. Invest.* 1940, **19**, 649 ; [29]*Ibid.* 1941, **20**, 63.

ANEURYSM.

Lambert Rogers, M.Sc., F.R.C.S.

Abdominal Aortic Aneurysm.– Of 32 cases of aneurysm of the abdominal aorta admitted to the Presbyterian Hospital, New York, in recent years, 26 were regarded as due to arteriosclerosis, the remaining 6 to syphilis. Thirty of the 32 patients were men. The arteriosclerotic aneurysms were fusiform in type, the syphilitic saccular. Vertebral erosion was not caused by the aorta in the arteriosclerotic cases but occurred in the syphilitic ones ; the explanation being that the great vessel is elongated by arteriosclerosis and so lifted away from the vertebra. Pain due to erosion, therefore, was characteristic of the syphilitic saccular aneurysms, and not present in the arteriosclerotic cases. For this reason patients with arteriosclerotic aneurysms frequently did not seek relief until on the brink of disaster. Loss of weight and a pulsating mass in the abdomen were the chief clinical features of the arteriosclerotic cases. These points are well brought out in a recent paper by A. H. Blakemore[1] of New York.

Blakemore reports encouraging results from the wiring operation of Moore and Corradi (1864 79) which he has modified and modernized. The object of his procedure is to bring about clot formation in relation to the sac walls by passing a heating current through the wire, which, where it is near the walls of the aneurysm, is not exposed to the fast-moving blood in the axial current and so becomes heated and induces clot formation. (*Plate I.*)

Thoracic Aortic Aneurysm. F. T. Ranson,[2] of Shanghai, has reported the results of 8 operations which he has performed on male Chinese patients with aneurysms eroding the anterior wall of the chest. All complained of severe pain and had positive Wassermann reactions. Under local analgesia the right common carotid and internal jugular veins were divided, their central ends anastomosed, and the distal ligated. This operation, known as Babcock's (W. W. Babcock, 1926,[3] 1932[4]) has as its object the lowering of the pressure in the aneurysm. Ranson writes of this : "Whatever happens inside the aneurysm, there is one striking immediate result of the operation, and that is relief of pain." It took place in 7 of the patients immediately the tapes controlling the anastomosed vessel were released. Seven patients left hospital improved and relieved of pain ; the eighth, whose pain was not alleviated, had a swelling "as big as a fist" on the chest wall and died of its rupture five days after the operation. The author of this paper considers the operation justified because of the relief of pain which it produces, though, as he points out, it cannot be expected to cure the patient. In the only other operation of which he has had experience for thoracic aneurysm, namely, wiring, he has not observed any relief of pain.

REFERENCES. [1]*Ann. Surg.* 1947, **126**, 195 ; [2]*Brit. med. J.* 1947, **2**, 692 ; [3]*Ann. clin. Med.* 1926, **4**, 933 ; [4]*Amer. J. Surg.* 1932, **16**, 401.

ANEURYSM OF THE ABDOMINAL AORTA: UROLOGICAL MANIFESTATIONS.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

From its very situation, an aneurysm of the abdominal aorta is prone to involve the renal arteries. It is surprising that more attention has not been given to the urological manifestations of this dire disease. The orifices of one or both renal vessels may be implicated in the dilatation, or secondarily occluded by laminated clot. B. S. Abeshouse et al.[1] describe a case ending in anuria. The surgical significance of aortic dissecting aneurysms is also discussed by D. P. van Meurs,[2] while R. Green and O. Saphir[3] describe ecchymosis of the abdominal wall as a diagnostic sign.

A. S. Warren and A. L. McQuown[4] find that no definite single aetiological factor is responsible for all cases, the most common pathological change being atherosclerosis. A study of pathological specimens permits of division into anatomical groups, one of which is of particular interest to the urologist. The renal arteries are frequently compressed by the dissection process and the resulting infarction of the kidney may produce symptoms compatible with renal colic or nephrolithiasis. The clinical criteria are sudden onset of lumbar pain, with or without radiation to the groin, associated with the laboratory findings of albumin, casts, and blood in the urine.

The experiments of J. S. Robertson and K. V. Smith[5] demonstrate that the pressure required to produce medial dissection is almost invariably far in excess of the aortic blood-pressure, even in severe hypertension.

REFERENCES.—[1]*Urol. cutan. Rev.* 1948, **52**, 196; [2]*Brit. med. J.* 1948, **2**, 599; [3]*Amer. J. med. Sci.* 1948, **216**, 24; [4]*Ibid.* **215**, 209; [5]*Quart. J. Med.* 1948, **60**, 43.

ANORECTAL GONORRHŒA.

W. B. Gabriel, M.S., F.R.C.S.

A. H. Harkness[1] states that anorectal gonorrhœa occurs more frequently than is generally supposed and is often overlooked owing to the mildness of its signs and symptoms. The condition may be secondary, chiefly in women, or in little girls with vulvovaginitis; also from the bursting into the rectum of gonococcal abscesses in the prostate, Cowper's glands, or Fallopian tubes. Primary disease occurs more frequently in men than women, and follows sodomy as a rule, but accidental infection has been known to occur from contaminated thermometers and enema nozzles, also after prostatic massage. The author then proceeds to describe the symptoms and proctoscopic findings based on an experience gained from 168 cases of primary disease in the male. Suppuration in the subepithelial connective tissues may result in abscesses and fistulæ, but this did not occur in his series once treatment had been instituted. The only blood-borne complication was arthritis, which occurred in 2 cases. The portal of entry of infection in anorectal infections is the columnar epithelium of the rectum, and it is considered unlikely that the infection travels up the bowel wall higher than the rectum. Diagnosis is usually made by smears stained by Gram's method but pure cultures can be readily obtained in some cases. Treatment is by *sulphonamide* therapy in the first instance and penicillin is given in the sulphonamide-resistant forms, but the danger of masking a concomitantly acquired syphilis has to be kept in mind, since the rectum or anal canal is frequently the site of primary syphilis; in the author's series of 168 cases the Wassermann and Kahn reactions were positive in 60 (35 per cent).

REFERENCE.—[1]*Proc. R. Soc. Med.* 1948, **41**, 476.

ANORECTAL MALIGNANT MELANOMA.

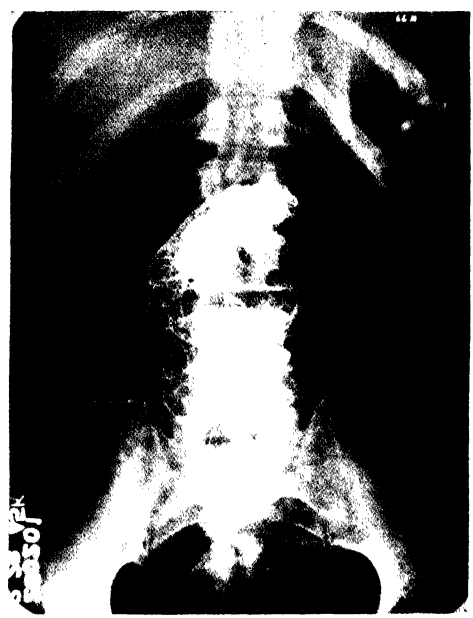
W. B. Gabriel, M.S., F.R.C.S.

R. W. Raven[1] describes the histological characteristics of malignant melanoma. The type cell is the melanoblast; this is an active cell which moves among the fibroblasts by amœboid movement and is an autonomous unit with capacity

PLATE I

ANEURYSM OF ABDOMINAL AORTA

(A. H. BLAKEMORE)



Roentgenogram of arteriosclerotic aneurysm of the abdominal aorta in a man aged 55. The fusiform aneurysm with the aorta has been occluded with wire, using the method of electrothermic coagulation and endo-arterial occlusion.

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for survival and reproduction. Melanoblasts tend to become detached and carried away to commence a new colony elsewhere in the body. A single cell can pass through the larger lymphatic channels and may become arrested in the liver, lung, or bone-marrow. In the anorectal region a melanoma may be sessile or pedunculated: lobulation and superficial ulceration usually occur and the black colour is characteristic although an amelanotic type has been described. Spread of the tumour takes place by direct extension upwards in the submucous space, by lymphatic and by venous spread. The symptomatology and treatment are described. Radical excision by the abdominoperineal route is advised when conditions are favourable. Cytological and clinical studies have shown that malignant melanoma is not radio-sensitive. Case records are described of three patients admitted to the Royal Cancer Hospital during the past 15 years. The author states that in the anorectal region over 100 cases have been reported and a bibliography is given.

REFERENCE.—[1] *Proc. R. Soc. Med.* 1948, **41**, 469.

ANTHRAX. *H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.*

Penicillin Treatment.— Successful treatment of 36 cutaneous cases of one to fifteen days' duration is described by A. C. La Boccetta.[1] Penicillin was given in three-hourly doses of 100,000 to 200,000 units for three or more days. Smears and cultures from the lesions were usually found to be negative within three days of commencing this treatment, and by that time also the lesions were regressing. There were no untoward reactions. No other specific treatment was given. Local treatment was simply a plain sterile non-adhesive dressing. It was found rarely necessary to administer narcotics or analgesics. A remarkable feature of the cases was the absence of severe pain—there was discomfort only. There were no failures in the series and it is concluded that penicillin is a safe, rapid, and effective treatment of cutaneous anthrax.

REFERENCE.—[1] *Amer. J. med. Sci.* 1948, **216**, 407.

ANUS, IMPERFORATE. *W. B. Gabriel, M.S., F.R.C.S.*

J. E. Rhoads, R. L. Pipes, and J. P. Randall[1] describe the management of certain cases of imperforate anus by a *combined simultaneous abdomino-perineal procedure*. Cases selected for this are those which correspond to Type III of the Ladd and Gross[2] classification, that is, the cases in which the rectum ends blindly at the pelvic floor so that it cannot be reached from the perineum. Details of the operation as carried out in two infants, both aged 24 hours, are described. In both cases the rectum was successfully mobilized and brought down outside the perineum. One case has done well and at 8 months the child weighed 18 lb. and he appeared quite healthy: in the other case the intestinal tract functioned satisfactorily, but the child died at 3 months, apparently from uræmia, and autopsy revealed bilateral hydronephrosis and hydro-ureter. The authors believe that the procedure they describe is preferable to an abdominal colostomy, and in the event of the bowel being accidentally opened the meconium would probably still be sterile.

In a discussion on *congenital abnormalities of the ano-rectal region* Professor John Kirk[3] gave a résumé of the developmental anatomy of the rectum and anal canal, and then proceeded to discuss various practical considerations which are of interest to all surgeons who have to deal with this region. The upper two-thirds of the anal canal are lined by entoderm and gripped by the internal sphincter; its nerve-supply belongs to the autonomic nervous system and its lymphatic drainage is intrapelvic. The lower third (not more than ½ in. (1·3 cm.) long in the adult) is formed from the proctodæum and is therefore ectodermal in origin; at the junction of these two zones is the 'pecten' or

'pectinate line' because its upper limit is the line of the anal valves. The columns of Morgagni should be known as the 'anal' columns since they are truly anal in position and were described as such by Morgagni in 1741. The lower area distal to the pecten is supplied by somatic nerves: its muscle ring, the external sphincter, is striped muscle under voluntary control; the lymphatic drainage is to the superficial inguinal glands. The instruction to be gained from a study of the comparative anatomy of this region is set forth, and the help this gives in understanding congenital malformations of the rectum and anus in man is explained.

REFERENCES. [1]*Ann. Surg.* 1948, **127**, 552; [2]*Amer. J. Surg.* 1934, **23**, 167; [3]*Proc. R. Soc. Med.* 1947, **40**, 876.

AORTA, COARCTATION OF. (*See* COARCTATION OF THE AORTA.)

AORTIC STENOSIS. *William Evans, M.D., D.Sc., F.R.C.P.*

Incidence of Coronary Artery Disease. M. J. Horan and A. R. Barnes[1] have tried to determine the degree of coronary sclerosis that occurs in patients suffering from calcareous aortic stenosis: they examined 100 patients. Some degree of coronary sclerosis was present in every case, and this degree was found to be, in a measure, inversely proportional to the degree of aortic stenosis. The most common clinical symptom was found to be dyspnœa, which occurred in 69 per cent of the cases. Of the patients, 29 per cent exhibited hypertension and 28 per cent complained of an anginal type of pain. Infarction of the myocardium was exhibited in 20 per cent of the cases. Sudden death occurred in 18 per cent.

Simulating Hyperthyroidism.—One of the most gratifying experiences in the case of patients suffering from cardiovascular disease is the treatment of patients with thyrocardiac disease. This is true whether the cardiac disability is entirely due to thyrotoxicosis or whether there is an additional independent cardiac lesion. Such patients respond so well to proper management and often have so few of the customary signs of thyrotoxicosis that physicians have been impelled to search carefully for these cases of masked thyrotoxicosis. The result is that on minor suspicion determinations of basal metabolism are frequently performed in order not to overlook thyrotoxicosis as a remediable burden in patients suffering from various types of cardiac disability. At times the decision is difficult, because there are numerous other causes of an elevated basal metabolism.

Four cases of aortic stenosis without significant pulmonary congestion or dyspnœa are reported by J. A. Smith and S. A. Levine[2] in which the patients showed definite and persistently elevated basal metabolic rates and had normal thyroid glands grossly and microscopically. They also manifested some of the other features suggestive of thyrotoxicosis. This adds another group of conditions that needs to be considered in the differential diagnosis of masked thyrocardiac disease.

REFERENCES. [1]*Amer. J. med. Sci.* 1948, **215**, 451; [2]*Arch. intern. med.* 1947, **80**, 265.

APHASIA. *Macdonald Critchley, M.D., F.R.C.P.*

Aphasia and Artistic Realization.—Th. Alajouanine[1] in his Harveian Lecture gave a fascinating account of 3 cases of aphasia occurring in a writer, a musician, and a painter respectively.

The writer was afflicted with a right hemiplegia and an aphasia of expressive type. The speech affection gradually improved, after passing through a stage of recurrent utterance the phrase reiterated being "Bonsoir, les choses d'ici bas". At the present day this manifestation has been overcome, and the chief speech

defect is to be found in a disorder of synthetic construction. *Writing, still* executed with the left hand, shows a similar type of agrammatism. *Reading*, though slow, is possible, and in several languages. Literary production is, of course, out of the question. This does not appear to arise because of any deficiency of memory, reasoning, judgement, or affectivity. He was able to criticize the æsthetic qualities of one of his own unpublished manuscripts, and he could unhesitatingly identify paragraphs which did not attain the necessary standards of efficiency.

The second case was that of a musician, Maurice Ravel. At the height of his powers he was afflicted with a complex type of aphasia of the Wernicke type. There was no hemiplegia, but some apraxia existed. Oral and written languages were diffusely impaired to a moderate degree; understanding of language was much better retained. Memory, judgement, affectivity, and æsthetic taste were not obviously altered. Writing was very faulty, largely because of the apraxia. The patient's musical faculties were impaired in an interesting fashion; musical thinking was comparatively well preserved, while there was a marked loss in musical expression, both written and instrumental. In greater detail it can be said the patient was able promptly to recognize tunes played before him, including of course his own works. He would recognize immediately any mistake in the playing, including errors of rhythm. He also noticed that the piano used for these tests was out of tune. Note reading was extremely difficult and usually impossible, though the patient was able to recognize at a glance whatever piece of music he wanted to find. Piano-playing proved very difficult, though he could manage scales, and also—with the right hand only—the beginning of "Ma Mère l'Oye". He did better when he attempted to play from memory pieces of his own composition. Musical writing was also very difficult, though easier than plain writing. Apraxic defects probably also entered here. He could sing correctly some of his melodies, but only if the first note or notes were given him. He can still attend concerts with enjoyment and pass shrewd judgement upon what he hears.

Alajouanine's third patient was a painter, a high-ranking representative of the contemporary French school. At the age of 52 he developed a Wernicke aphasia, without hemiplegia, but with some visual field defect. Understanding was fairly good, largely because of an intuitive grasp of the general meaning of a conversation. Spoken language was much impaired and marred by a considerable amount of paraphasia. Reading is a matter of difficulty and writing is executed very slowly. It is evident that his memory, judgement, and taste are not at all affected; indeed, his keen affectivity is even more acute than before his stroke. Artistic realization remains as perfect as ever. According to some critics, in fact, his painting has even perhaps gained a more intense and acute expression since his aphasia. His activity and productivity have not slowed down, and he works as rapidly as before. As the artist himself put it: "There are two men, the one who is grasped by reality to paint; the other one, the fool, who cannot manage words any more."

Alajouanine discusses the psychological and philological problems thrown up by these three cases of aphasia, and by the fact that while the musician and writer can no longer practise their art, the painter, though aphasic, can continue to paint with his old skill. The reason lies in the fact that the techniques of the musician and the writer are based upon language, while language plays but little part in plastic realization. Literary art is obviously entirely dependent upon language. For the composer the same is true, for musical language is made up of signs, where sounds represent a mere symbolism. In the case of the painter, there is no language made up of symbols. Aphasia, therefore, does not alter plastic expressive power, since it takes place outside of language.

Speech Iterations.—M. Critchley[8] has described the phenomena of speech iterations whereby certain words, phrases, or sentences are repeated incongruously and often to the exclusion of other utterances. Among this general category (sometimes spoken of as 'barrel-organisms' or as the 'ting-a-ling phenomenon') may be enumerated: stammering, palilalia, palilogia, verbal mannerisms, verbal tics (including Gilles de la Tourette's disease), echolalia, verbigeration, recurring utterance, occasional utterance, and reduplications.

Palilalia is essentially an organic affection, associated with diffuse pallido-striatal disease. It may accompany a postencephalitic Parkinsonism, or a pseudobulbar syndrome. Palilalia entails the involuntary repetition two or more times of a word, phrase, or sentence first uttered, in a clipped, hushed, and rapid fashion. It does not appear if the patient is reciting by heart any well-remembered verse or prayer, or if he reads aloud, or recites the alphabet, or counts. Palilalia is to be regarded as a disorder of speaking rather than of speech. Though it may be associated with palipraxia, it does not betray itself in anything which one might term a paligraphia.

Palilogia is merely a peculiarity of certain orators who deliberately repeat a phrase merely for the sake of emphasis.

Verbal mannerisms form an irritating trait of many careless speakers, who sprinkle their talk with a wealth of silly, trite, and almost meaningless expressions.

Verbal tics are but an extension of these, and comprise the compulsive enunciation of words devoid of congruity. Gilles de la Tourette's disease is the 'manie blasphematoire' of other authors, and also always consists in interjections of a scabrous or bawdy character.

In *echolalia* the patient repeats statements or questions put to him with or without a change in pronoun: it is a phenomenon met with in psychiatric practice, particularly among dements and schizophrenics. Another example of verbal stereotypy in psychotics is spoken of as *verbigeration*.

Recurrent utterance is a rare but essentially aphasic phenomenon. According to Hughlings Jackson, these recurring utterances may be relegated into one of four types: (1) a fragment of meaningless jargon; (2) a single word; (3) a phrase; and (4) 'Yes' or 'No'—or both of these words. Jackson thought that an 'utterance' consists in words which the patient was about to utter before losing consciousness at the time of the stroke; that is to say, a sort of 'stillborn proposition'. Gowers, however, believed that the words of a recurrent utterance were actually the last ones spoken by the patient before losing consciousness.

Occasional utterances were also originally described by Hughlings Jackson. A speechless patient—or one who is almost so—may in certain circumstances be heard to enunciate a cry, an interjection, a word, or even a sensible phrase. This occasional utterance may be quite unexpected and completely incongruous. Sometimes it becomes 'fixed' as it were, and therefore obtrudes itself as a recurrent utterance.

Reduplications are linguistic phenomena which bear a superficial resemblance to speech iterations but actually they bear no relationship to speech disorders. They are met with in the speech of primitive peoples, or of young children, as well as in such artificial languages as Bêche-de-Mer, patois creole, Chinook, or pidgin-English.

In his paper, Critchley also discussed iterations of written speech. Examples of echographia were taken from the letters written by aphasic patients, by schizophrenics, and by certain modern writers.

Speechlessness, Literacy, and Verbosity.—The various factors which determine the severity of a speech loss in a particular case were discussed by M. Critchley[8] with special reference to the literacy of the victim prior to his illness. It is

commonly believed, though it cannot yet be established, that poor education, especially as regards reading and writing, usually ensures that cerebral disease, left-sided or right-sided, is unlikely to be followed by severe aphasia. Crippling speech-loss is said to be rare in aboriginal peoples of the tropics and in those who cannot read or write. But exceptions must surely occur and further data on this score are sorely needed. Conversely it may well be inquired whether an aphasia is likely to be more severe in the case of a person who had been highly proficient in the use of language, whether written or spoken. In other words, would a relatively small cerebral softening in the left cerebral hemisphere produce much speech loss or little in the case of an orator, a poet, or an essayist? The author believed the question was much more complex than one might imagine. Possibly speech loss might prove to be severe in those who had laboriously achieved a literary technique, through much practice; while the verbose volatile mercurial individual, as much addicted to talk as to *gesture*, *might require* a comparatively large and crippling cerebral lesion to silence him. The same question is raised when one asks whether an aphasia is likely to be greater in a man than in a woman. There is, of course, a well-known sex difference as regards the faculty of speech. Girls learn to talk earlier than boys, and their speech becomes more rapid, more fluent, and more copious. But males eventually achieve a larger vocabulary, being more interested in words themselves. As Jesperson said: "A man is slower, he hesitates, he chews the cud to make sure of the taste of words." One might expect therefore that aphasia is likely to be more severe in a man than in a woman.

REFERENCES.—[1]*Brain*, 1948, **71**, 229; [2]*Post-Grad. med. J.* 1948, **24**, 19; [3]*Brit. Enc. med. Pract. interim Suppl. No.* 52, 1947, 3.

APPENDICITIS.

A. Rendle Short, M.D., F.R.C.S.

Appendicitis in Retreat.—An article by two New Zealand surgeons (W. M. Cotter and I. Gebbie[1]) bears this title. They have reviewed the mortality of three groups of cases of appendicitis-peritonitis in the years 1925–30, 1933–7, and 1944–7. The death-rate has fallen from 17 to 5 per cent. They attribute the improvement to intravenous fluids, conservative treatment of localized peritonitis including appendicitis abscess, the McBurney incision, and sulphonamides. S. O. Hoerr,[2] of Boston, U.S.A., draws similar conclusions. Only one patient died out of 382 operated on at his hospital between 1941 and 1945, though there were as many perforated cases as in previous years. He thinks the administration of sulphonamides has been the most decisive factor. The intraperitoneal use of sulphonamides has been given up. In Scotland, where appendicitis mortality is higher than in England, there were 156 deaths in 1901 and 257 in 1945, but the figure is falling. Between 1911 and 1938 over 400 died annually (J. B. de W. Molony[3]). In New York, R. N. Shallinger[4] reports a steady fall in the mortality from acute appendicitis, from 6 to 7 per cent in the 1920's to 1 or 2 per cent since 1940. The fall is just as marked in patients with diffuse peritonitis—from 20 to 4 per cent—but is less marked when abscess or local peritonitis is present. Deaths nowadays are less often the result of peritonitis and more often caused by cardiovascular complications and other non-surgical conditions. The important advice is given that if drainage is used it should never be *across* a viscus. Quite often it is good policy to drain the abdominal wall down to the peritoneum. E. L. Strohl and F. E. Sarver,[5] of Chicago, also show improving figures; their overall mortality for acute appendicitis has been reduced from 1·92 per cent to 1·48 per cent in 878 cases. After perforation, 8·25 per cent died. They use sulphonamides, but think the fall in fatalities set in before these drugs were used.

Spasm in Appendicitis.—W. H. Bowen[6] considers that there is a spasm factor in the determination of an acute attack. The appendix, already the seat of chronic inflammation, contracts down on a fæcolith, and this causes colic and obstruction distal to the blocked lumen. A purgative makes matters worse.

Appendicitis in Childhood.—H. Williams,[7] of Melbourne, writing of appendicitis in children under three, stresses the *importance of repeated examination*. It is useless to try to feel the abdomen while the child is crying. Only in 6 of his 42 patients was a diagnosis made before perforation. In 21 there was as inflammatory mass, and in 15 diffuse peritonitis. Abdominal pain with vomiting, of recent origin, should always arouse suspicion of appendicitis. In all his cases the appendix was removed; 8 died, including 7 out of the 15 with peritonitis. In this last group of cases, operation was deferred for six to twelve hours, or even longer, to allow time for treatment by warmth, intravenous fluids, and gastric suction.

I. Schulz,[8] of Milwaukee, advances evidence to show that the *dangers of the perforated appendix in children are less than they were*. Over 25 years, the mortality in 226 cases was 11·5 per cent, but during the last ten years only one child with perforated appendix died. The average age in his series was four years. He attributes the improvement to non-operative treatment for the perforated appendix. Gastric suction, intravenous fluids, small repeated blood transfusions, sulphonamides, and, lately, penicillin, have constituted the treatment. If the appendix has not perforated, of course it is removed at once. [Conservative treatment of appendicitis-peritonitis in children is not widely followed in this country, but in my own limited experience it is the better way.—A. R. S.]

Causes of Death in Acute Appendicitis.—An interesting study of 124 fatalities, spread over 20 years, is contributed by Salvador C. Menez, of Manila.[9] Of these, 8 were due to errors of technique, and 18 to mistaken diagnosis, such as removing the appendix when the stomach or bowel was perforated, or tuberculous disease present. Vascular complications such as pulmonary embolism or cardiac failure accounted for 6 deaths, and intra-abdominal hæmorrhage for 2 more.

Diagnosis of Chronic Appendicitis. A. Trojaniello,[10] of Naples, describes a "new sign". The surgeon makes firm pressure with his hand over the right iliac fossa of the patient lying flat, and asks him to cough. If he feels sharp pain in the area, the appendix is at fault. He says this sign is positive in 47 per cent of cases, the "psoas sign" in 68 per cent, and Rovsing's sign in 37 per cent.

Psychological Handling of Appendix Cases.—Two psychiatrists, S. Blenton and V. Kirk,[11] of Nashville, stress the importance of so talking to each patient as to allay his fears before operation, and afterwards to return him to normal life as smoothly as possible. [When a surgeon is too busy to give personal attention to his patients, this help from a psychiatrist team may be valuable, but it is a pity if he cannot spare time to say a few words of encouragement himself.—A. R. S.]

Mucocele of the Appendix.—M. Roux and L. M. Rognon,[12] of Paris, describe a case in which a mucocele of the appendix was large enough to form a palpable swelling. [I have operated on a mucocele as large as a coco-nut, lying behind the ascending colon. Removal was most difficult.—A. R. S.]

REFERENCES.—[1]*N. Z. med. J.* 1948, **47**, 225; [2]*Surgery*, 1947, **22**, 402; [3]*Edinb. med. J.* 1948, **55**, 153; [4]*Ann. Surg.* 1947, **126**, 448; [5]*Arch. Surg., Chicago*, 1947, **55**, 530; [6]*Brit. J. Surg.* 1947, **35**, 89; [7]*Brit. med. J.* 1947, **2**, 730; [8]*Arch. Surg., Chicago*, 1948, **56**, 117; [9]*Philipp. J. Surg.* 1947, **2**, 87; [10]*Policlinico*, 1948, **55**, 721; [11]*Ann. Surg.* 1947, **126**, 305; *J. Chir., Paris*, 1948, **64**, 5.

ARRHYTHMIA.

William Evans, M.D., D.Sc., F.R.C.P.

Repetitive Paroxysmal Tachycardia.—J. Parkinson and C. Papp,[1] reporting 40 cases showing an atypical kind of paroxysmal tachycardia, had this to say about the condition, "Paroxysmal tachycardia might be defined as sudden attacks of extreme acceleration of the heart that last from a few seconds to a few days and end abruptly as they begin. In the average patient with paroxysmal tachycardia the paroxysm is the exception: normal rhythm is the rule: the difficulty is to obtain an electrocardiogram showing the attack. We have become interested in a special variety where *recurrent paroxysms are* the rule and normal rhythm is the exception; *the difficulty now is to obtain* the normal electrocardiogram. This variety is here described as *repetitive*. It is characterized by recurring short runs of auricular, nodal, or ventricular extrasystoles, runs or paroxysms of tachycardia in fact, almost constantly present for months or for years and only occasionally interrupted by the normal sinus rhythm. We do not include under this term the recurrent brief paroxysms of tachycardia which may happen to be portrayed on an isolated electrocardiogram. It is true that in a sense they are repetitive, but this is an incident, not a clinical state like that of repetitive paroxysmal tachycardia where the play of paroxysms almost displaces normal rhythm. Its separate consideration is justified on clinical grounds for it more often affects children and young people, in whom it presents a novel problem in prognosis. There are few conditions in children of which it can be said that they are likely to 'grow out of it', but this appears to be one".

REFERENCE.—[1] *Brit. Heart J.* 1947, **9**, 241.

ARSENICAL DERMATITIS: TREATMENT WITH DIMERCAPTOPROPANOL (BAL).

R. M. B. MacKenna, M.A., M.D., F.R.C.P.

In the MEDICAL ANNUAL[1] of 1948 reference was made to British Anti-Lewisite or BAL, and it is not intended to enter here on a prolonged discussion of the use of this compound, although the introduction of this drug is a milestone in therapeutics. Suffice it to say that A. B. Carleton, R. A. Peters, and R. H. S. Thompson[2] have published a paper recording the results of a clinical trial of the use of BAL in the treatment of arsenical dermatitis. Forty-four cases are described: these were collected through the co-operation of the Ministry of Health, the Medical Departments of the Services, and the clinicians concerned. With but 4 exceptions, the dermatitis was in all cases severe and widespread, showing in addition to erythema one or more of the following features—desquamation, exfoliation, oozing, or fissuring. The drug was given by deep intramuscular injection into the buttocks. The dosage in the majority of cases was as follows: First day: one ampoule four times during the first twenty-four hours, at four-hourly intervals. Second, third, and fourth days: one ampoule morning and evening. Fifth and sixth days: one ampoule daily. The ampoules each contained 2 c.c. of 5 per cent 2:3-dimercaptopropanol dissolved in arachis oil containing 10 per cent benzyl benzoate. The injections were well tolerated, but in 14 cases boils or abscesses developed either in the buttocks or elsewhere. In 8 of these cases the abscesses developed at or near the sites of injection. Three cases ended fatally, and in 4 more it was impossible to assess the progress numerically. In the remaining 37, the mean number of days between the first injection of BAL and healing or practically complete healing was 21·5 days, a rate of cure which has never previously been reached.

Brian Russell, B. Green, and L. G. R. Wand[3] have brought forward evidence to suggest that injections of BAL can produce tetany; this may be of the low-magnesium and possibly also of the low-calcium type. They consider that

symptoms of toxicity which may follow injections of the drug may be explained as latent tetany, and suggest that the patients should be given a high-calcium diet, magnesium sulphate, and vitamin D.

REFERENCES.—[1]*Med. Annu.* 1948, 244; [2]*Quart. J. Med.* 1948, **17**, 49; [3]*Lancet*, 1948, **2**, 169.

ARTERIAL THERAPY. *A. Rendle Short, M.D., F.R.C.S.*

Arteriography as a means of diagnosis is of course well known, but Portuguese and French surgeons, notably Dos Santos of Lisbon, have recently revived arterial injection as a means of local therapy. By this route drugs can be brought to bear on a particular part of the body without spreading the effect over all the organs, especially if pressure is made by means of a rubber band to block the venous return. Arteries which lend themselves to the method are the carotid, the abdominal aorta, and the arteries of the limbs, such as the axillary, the brachial at the bend of the elbow, or the femoral at the base of Scarpa's triangle. The treatment may be given to relieve local pain, to reduce inflammation, or to promote local vasodilatation. For the relief of pain, novocain may be injected. To deal with inflammation, either penicillin, 80,000 or 100,000 units, or 10 to 15 c.c. of mercurochrome in 2 per cent solution, is given. As a vasodilator, acetylcholine may have a remarkable effect—for instance, in cases of phlebitis with œdema, or incipient gangrene. It will, however, not avert gangrene in the presence of arterial thrombosis. Antitetanic serum may be injected into the carotid artery. Relief of pain and a rapid clearing up of inflammation with lowering of temperature may be obtained by aortic injection in cases of acute appendicitis, salpingitis, pancreatitis, or renal infections. Conditions like cellulitis or acute arthritis will respond well to injection of the peripheral arteries, and so, too, will open fractures and suppurating wounds. The solution used should be nearly isotonic with the blood, or slightly hypotonic; a hypertonic injection is dangerous. Another danger is that of inducing arterial spasm; if this occurs the stellate or lumbar ganglia should be injected with novocain to relax it. To make an injection, the artery is located by its pulsation and held steady by the two fingers of the left hand; a slender needle is then inserted through the skin. When it enters the artery, the piston of the syringe will be pushed out and red blood will enter the barrel and show pulsations. After completing the injection, the proximal ligature is tightened to locate its effect, and a finger is pressed over the needle puncture. The aorta is injected at the level of the twelfth rib with the patient lying prone. The needle is made to enter four finger-breadths from the midline, and slides forwards around the side and front of the centrum of the vertebra. A. Enjalbert[1] has experience of about 50 cases of arteriotherapy, without mishap.

REFERENCE.—[1]*Toulouse méd.* 1948, **49**, 302.

ASCITES. (*See* PORTAL HYPERTENSION.)

ATOM BOMB INJURIES. *Una Ledingham, M.D., F.R.C.P.*

Most of us have a healthy fear of the potentialities of this bomb, and should know what these potentialities are and what conduct, if any, would reduce the mortality and relieve the suffering of bombed populations. The effects in man in Japan and afterwards in animals in the Bikini experiments were studied in considerable detail. The results are depressing but not unexpected.

LeRoy[1] presents a clear summary. The special and deadly property of the atom bomb being the emission of large quantities of ionizing radiation, principally gamma rays, the injuries resulting from exposure are the chief interest. While some escape was found in heavy concrete buildings or underground shelters,

the suffering was generally in proportion to the distance of the victim from the exploding bomb. Many exposed persons appeared well at first but in a few days a clear-cut syndrome appeared, initiated by severe diarrhœa and vomiting. Purpura, bleeding, fever, leucopenia, and anæmia followed, with consequent severe secondary infections. Widespread surface ulceration of the mucous membrane, of any or all parts of the gut, but chiefly of the colon, accounted for the intractable diarrhœa with dehydration and acidosis. Falling white cells to below 1500 allowed for the incidence and rapid spread of severe secondary infection. Falling platelets accounted for the purpura and hæmorrhages which complicated the already severe anæmia. Death occurred from toxæmia or infection and came about as early as four days or as late as three months after the incident. Mortality figures varying from 33 per cent to 100 per cent are quoted. Recovery was rare when the white-cell count fell to below 600, and added injury, wounds, or burns, further reduced chances of survival.

More encouraging is the advice regarding treatment, which if instituted early could reduce the death-rate. The needs are: suitable fluids to replace those lost through diarrhœa and to restore acid-base balance; control of infection by penicillin and other chemotherapy; correction of hæmorrhagic tendency and anæmia by blood transfusion.

Animals, including guinea-pigs and rats, were exposed to both under-water and air explosions at Bikini and received the degree and type of protection most commonly given to ship's crews.[2] Here, too, though the cover saved a large number of burns and injuries, it was ineffective against radiation. The symptom-complex was strikingly similar to human experience. The under-water explosion was the more lethal by reason of widespread deposition of radio-active spray. Rats showed surprising resistance towards this type of injury.

REFERENCES.—[1] *J. Amer. med. Ass.* 1947, **134**, 1143; [2] *Ibid.* 1155.

AURAL AND NASAL SUPPURATION. *F. W. Watkyn-Thomas, F.R.C.S.*

Treatment by Sulphonamides and Abiotics. It is recognized that *tyrothricin* is too toxic to be used for anything except surface application to infected areas. F. J. Otenasek and D. Fairman[1] report 2 *cases of chemical meningitis following use of tyrothricin*. In the first case, after a radical frontal sinus operation for a *Staph. aureus* infection, the cavity was frequently irrigated with 1–10,000 tyrothricin. Two days after his discharge from hospital the cavity was irrigated again. He fainted, and on recovery complained of severe headache, and vomited. In a few hours he had a temperature of 103°, neck rigidity, and a cloudy C.S.F. with 15,000 polymorphs. He was semi-comatose for a week, but recovered and left hospital a month later. The C.S.F. was sterile throughout. In three weeks time he was readmitted with headache, vomiting, and drowsiness. Ventriculograms showed dilatation of all ventricles; C.S.F. was acellular, with a pressure of 340 mm. water. Exploration showed extensive adhesive arachnoiditis. After fourth-ventricle-choroid plexectomy the patient recovered, with loss of sight in one eye, and some loss of acuity in the other. In the second case, after a frontal sinus operation, the cavity was irrigated with 1–10,000 tyrothricin; during irrigation he complained of headache, followed by pyrexia and delirium, with 2000 cells in the C.S.F. After 11 days he was discharged as convalescent. All cultures of the fluid were sterile. A fortnight later he was readmitted with headache and vomiting. The ventricles were dilated, and he died after ventriculostomy. At autopsy a breach of the dura was found behind the frontal plate; this was probably the result of a motor accident ten years previously.

A series of animal experiments showed that tyrothricin in the C.S.F. in minute quantities (1 c.c. of a 1–1000 suspension) killed 18 out of 35 animals, either immediately or in a few hours.

E. J. Pulaski and C. S. Matthews[3] report on 41 patients treated with *streptomycin* for otitis externa, otitis media, mastoiditis, brain abscess, and meningitis. In all, 41 patients were treated. Five cases of *otitis externa*, all with streptomycin-sensitive organisms, who had been under treatment for from 3½ to 36 months, were treated with streptomycin-soaked wicks or with a solution of 5000 u.c.c.: all ears were dry in 3–8 days; no relapses, no local or general toxic signs. Thirteen cases of *chronic suppurative otitis media* were treated, including 4 old mastoid cavities: 11 were improved; 5 of these were "clinically arrested"; treatment was by local instillation. Two cases of *mastoiditis*, one with *B. proteus* infection and meningeal irritation, one with lateral sinus thrombosis and a mixed infection of penicillin-insensitive streptococci and staphylococci, were treated by operation and intramuscular streptomycin; both recovered. Of 8 cases of *brain abscess* treated with intramuscular streptomycin and, in 3, instillation into the abscess, 7 recovered. There were 12 cases of *meningitis*, with 9 recoveries. In 1 fatal case the organism was *Cryptococcus hominis*, which is known to be insensitive to streptomycin *in vitro*. In all cases administration was intramuscular, in 8 intrathecal as well, and in 1 also intravenously.

A. Glorig and E. P. Fowler[3] carried out *tests for labyrinth function following streptomycin therapy* on 23 patients, all but one of whom had a normal audiogram after more than two months of streptomycin treatment. But nearly all had vestibular symptoms and signs. The first sign noted was usually a fine nystagmus on lateral gaze in either direction; this usually preceded the vertigo. The vertigo was peculiar in that, on turning in bed, the patients felt that they were continuing to turn. The same sensation was produced in turning the head; often the head was turned more than was intended. On the whole vertigo was avoided if the head was not turned. Only 6 patients did not complain of vertigo at any time. The vertigo lasted for from 5 to 50 days. Nausea and vomiting were not common. As most of the patients were confined to bed, Romberg's test was only done on 6; all showed a positive reaction after 25–30 days. All but 3 patients had loss of caloric and rotatory responses.

E. P. Fowler[4] has applied these results to the *treatment of vertigo*. If a patient has 2 g. of streptomycin daily for 3–4 weeks, no labyrinth reaction is obtained by rotation or by ice-cold douching. In only 3 cases out of 130 where vestibular disturbance was caused by the drug, did Fowler find any deafness. The patient feels weak, has mild vertigo and occasional nausea, his eyes do not focus well, and he cannot walk in the dark; in young patients these symptoms pass, but if he is over fifty they may never clear up. He has treated 4 cases of Ménière's disease with streptomycin with considerable improvement in all. The method should only be used in patients under fifty, with violent vertigo, uncontrolled by medical treatment, where the condition is bilateral, and the only possibility of relief is section of both vestibular nerves. If one side is normal and there is severe deafness on the other he believes that destruction of the labyrinth by Day's diathermy method or Cawthorne's operation is the method of choice.

Intracranial Complications.—F. Altmann and S. Karaty[5] describe 3 cases in which fatal brain abscess was secondary to *extradural abscess caused by suppuration in the perilabyrinthine cells*. In one case the patient had an acute otitis media which was said to have cleared up in a week. Seventeen years later, although the membranes were healed and the hearing normal, he died of a right-sided temporal lobe abscess, secondary to an abscess in the petrous which had eroded the petrous ridge and formed an extradural abscess. In the second case there had been recurrent discharge for twenty-four years, with a dead labyrinth. The labyrinth was surrounded by an abscess cavity, although the labyrinth itself is described as uninfected. This cavity communicated, by

blood-vessels in the wall, with an extradural abscess which, in its turn, had caused two cerebellar abscesses. In the third case there was complete loss of the membrana tensa with no evidence of cholesteatoma or of bone destruction a condition which is usually regarded as a mucosal infection and harmless to life. Here there was an abscess in the perilabyrinthine cells, with an extradural abscess and an acute cerebellar abscess. The writers remark: "Otogenic deep epidural abscess should always be suspected when signs and symptoms of a purulent endocranial complication are noticed, and there is evidence of past or present disease of the middle ear, no matter how harmless the clinical or otoscopic appearance may be."

F. L. Weille[6] describes a case of *superior petrosal and cavernous sinus thrombosis with petrositis, destructive labyrinthitis, and facial paralysis.* A twelve-year-old boy, who had had two years' discharge, got headache, vomiting, and complete facial palsy. The affected ear was totally deaf, and at operation the horizontal canal and facial aqueduct were found to be destroyed. He cleared up, and three weeks later had a slight exophthalmos. Further operation showed destruction of the whole labyrinth, and deeper destruction in the petrous. This was followed by cavernous sinus thrombosis and meningitis. Free resection of the petrous, with penicillin and sulphadiazine, and a course of heparin and dicoumarol, eventually cured him. The end-result was return of facial nerve function and of all eye movements, with a normal optic disk. [The course of the case and the operation findings suggest that this was a labyrinth destruction secondary to petrous invasion. An interesting point is that *B. proteus* was found in an orbital abscess, which formed and discharged spontaneously in the course of the cavernous sinusitis, but the organism found during the meningitis in the cerebrospinal fluid was a *Str. haemolyticus.* F. W. W.-T.]

Sir H. Cairns and F. Schiller,[7] speaking of *purulent pachymeningitis*, report the results of penicillin in the treatment of this condition. In the last twenty years they have seen 33 cases. There were 18 cases before penicillin was used; all the patients died. Of 15 treated with penicillin, 7 recovered.

Purulent pachymeningitis is an infection of the subdural space, the space that lies between the dura and the piarachnoid. This space is continuous over the whole of the brain and cord, save where it is crossed by nerves, vessels, and prolongations of the arachnoid to the dura; it does not communicate anywhere with the piarachnoid space. Infection in the space quickly passes over both cerebral hemispheres, and gives signs of a spreading paralysis, sometimes with fits. Unless and until the arachnoid barrier is passed by the organisms and leptomeningitis starts, there is little change in the cerebrospinal fluid, and little or no neck rigidity. If the patient survives the first attack the pus will be loculated by adhesions and subdural abscesses will form. These are not the same as the occasional, rare, subdural abscess secondary to an inflamed patch of dura and localized from the start.

As a rule (in at least 26 of these 33 cases) the condition follows a spreading osteomyelitis of the skull, which is usually secondary to sinusitis, not to mastoiditis. In 8 of the 33 cases there was thrombosis of dural sinuses or of cerebral veins. Since the introduction of penicillin more patients have survived, and for that reason localized subdural abscess and brain abscess have become more common in this condition; in some cases there has been cerebral infarction, and various lung complications. Leptomeningitis and ventriculitis are now less common than formerly. The only condition which is likely to cause confusion in diagnosis is cerebral thrombophlebitis. In case of doubt the dura should be opened and the subdural space inspected. In this series of cases the most common organisms were streptococci of the anaerobic, *viridans*, or non-haemolytic forms.

For treatment systemic penicillin, 100,000 units three-hourly, is given until the sensitivity of the organism has been tested; if this is normal the dose is halved. Systemic penicillin should be continued for at least eight weeks to control the bone infection. Locally, one or more catheters are passed into the subdural space through burr-holes, and 6 c.c. of penicillin 500 u./c.c. instilled at frequent intervals. The writers believe that the more the space is irrigated the less is the danger of loculation; it is a question whether a catheter should not be passed along the medial surface of the hemisphere as a routine (it is on the medial surface that loculation is most likely, and most difficult to detect) and whether the healthy hemisphere should not always be irrigated as well. If leptomeningitis is considerable, subarachnoid and ventricular penicillin is given. When the primary focus persists after treatment it should be dealt with radically, but if possible this should be deferred for some months, and penicillin given before and after operation. It is a question whether penicillin should be given as a prophylactic before operations on the sinuses and petrous bones.

In the discussion which followed,[7] F. C. W. Capps said that prophylactic penicillin had the disadvantage that, if a second course was needed, there might be an allergic reaction. Several speakers (H. V. Forster, R. L. Flett, and Norman Patterson) mentioned osteomyelitis following operations on the antrum. Donald Watson and E. D. D. Davis supported prophylactic penicillin.

F. M. Anderson[8] describes 3 cases of *subdural empyema secondary to frontal sinusitis*. From his description of these cases it seems that they were of the group described by Cairns and Schiller as "purulent pachymeningitis", with rapid advance, hemiparesis, and Jacksonian fits. He treated them by irrigation through burr-holes, penicillin, and sulphadiazine. One case of the 3 recovered.

J. L. Reid and F. McGuckin[9] report 6 cases of *cavernous sinus thrombophlebitis* seen between 1943 and 1945, with 6 consecutive recoveries. They regard Eagleton's criteria for diagnosis as too rigid. The case should be judged on the severity of the condition; the increasing orbital œdema, with proptosis and, especially, chemosis; and the increasing fixation of the eye. Diagnosis is confirmed by palpable thrombosed veins, local cyanosis, meningitis, septicæmia, etc. In the first two cases sulphonamides only were used; in the other four sulphonamides and penicillin. Unless meningeal signs are present, when sulphadiazine is indicated, they prefer sulphamethazine as less toxic and less likely to cause renal trouble. A blood-level of 8–10 mg. per 100 c.c. is maintained. The usual penicillin dose is 15,000 u. three-hourly, increased to 25,000 in some cases. In one case meningitis developed during treatment; it was checked by three injections of 50,000 u. in 2 c.c. pyrogen-free solution intrathecally. If there is much facial swelling and discoloration gas-gangrene infection should be suspected, and the serum given. This was done in two cases of the six; in one of them the infection was proved.

S. L. Fox and G. Brooks West[10] describe 3 *unusual cases of cavernous sinus thrombosis*. In one, a girl of eight, with bilateral chronic otitis media had tonsillectomy done, and a fortnight later was readmitted to hospital with a temperature of 104°, obvious toxæmia, and unequal pupils. Apart from the discharge there was no evidence against the mastoids. Radiographs showed poor pneumatization, but no bone destruction. Two hours later she had exophthalmos on the right with sixth-nerve palsy. She became unconscious and died two days later, in spite of heavy sulphonamide and penicillin treatment. The exophthalmos was unilateral throughout; unfortunately post-mortem examination was refused. In the second case there had been pyrexia and headache, for which six teeth were removed. There was a previous history of "sinusitis". He was admitted with pyrexia and slight right exophthalmos. A retrobulbar exploration did not reveal anything. With penicillin and

sulphapyridine the condition gradually improved, the exophthalmos receded, and after several months vision was normal. In this case, as in the first, there was never any bilateral exophthalmos. The third case was remarkable for the associated complications—a woman with diabetes (blood-sugar 225 mg. per 100 c.c. and acetonuria 4 +) and syphilis (Kahn 4 + and a septal perforation). Radiographs showed antral and left ethmoidal clouding. There was right exophthalmos, later spreading to the left. In this case dicoumarol was given in doses to keep the prothrombin time at 30 seconds (undiluted). The patient recovered, but bilateral optic atrophy left her totally blind.

W. A. Fairclough[11] writes of *drainage in infected cavernous sinus thrombosis*, and reports a case in which this was done. Fairclough notes that in this case, and in three earlier fatal cases, there was œdema over the mastoid, although in every case the infecting lesion was on the lip or nasal ala. He believes that this sign is due to spread of thrombosis along the superior petrosal sinus to the lateral sinus and so to the mastoid emissary vein. In the case reported, the patient, a boy of 9, had a furuncle under the nose. The left eye was closed; there was œdema and moderate chemosis and proptosis. Retinal veins were swollen, and eye movements much restricted. In 36 hours there was left mastoid œdema and early œdema and chemosis of the right upper lid and conjunctiva, in spite of sulphonamide and penicillin treatment. As the patient's condition was degenerating it was decided to drain the cavernous sinus. Under pentothal anæsthesia the upper lid was retracted, the chemotic conjunctiva incised, and a pair of closed artery forceps pushed in to the apex of the orbit, the superior orbital fissure. Here resistance increased, but the forceps were pushed in another half-inch, until the wings of the sphenoid were felt to fracture. The forceps were then partially opened "with moderate force". When the forceps were withdrawn there was escape of a little faintly pus-streaked blood. A tube was put into the depths of the wound, and irrigated hourly with penicillin. Bacteriological examination showed *Staph. aureus*. The patient recovered completely, except for severe loss of vision in the affected eye (perception of light only) and slight ptosis and divergent strabismus.

To prove that the forceps had really entered the sinus the same procedure was done on the cadaver. After the brain was removed the blades of the forceps were exactly in the sinus.

REFERENCES.—[1]*Arch. Otolaryng.* 1948, **47**, 21; [2]*Ibid.* 1947, **45**, 503; [3]*Year-book of Eye, Ear, etc.*, 1948, 283; [4]*Ibid.* 461; [5]*Arch. Otolaryng.* 1946, **44**, 525; [6]*Ibid.* 1947, **45**, 90; [7]*Proc. R. Soc. Med.* 1948, **41**, 805; [8]*Year-book of Eye, Ear, etc.* 1947, 399; [9]*J. Laryng.* 1946, **61**, 273; [10]*J. Amer. med. Ass.* 1947, **134**, 1452; [11]*Aust. N.Z. J. Surg.* 1947, **16**, 193.

AUREOMYCIN.

Andrew Wilson, M.D., Ph.D., Ph.C.

The remarkable advances which have been made in the search for antibiotic substances is reflected in the fact that to date almost 100 antibiotics or substances listed as such have been described. Some of these have resulted from the study of the fleshy fungi of the Basidiomycetes, others from bacteria, and still others from the Actinomycetes. The rather remarkable fact emerges, however, that of all the antibiotics which have been described, the chief therapeutic agents which have been developed on an industrial scale have been confined to a half-a-dozen. Thus, of the mould products, penicillin, streptomycin, fumigacin, and streptothricin have been studied in more detail, while the bacterial products, gramicidin, tyrothricin, and bacitracin, have only a limited place as chemotherapeutic agents.

Some account has recently been published of the work on a group of fungi, the Actinomycetes, in particular the genus *Streptomyces*. Several species of *Streptomyces* are characterized by the production of a yellow pigment in the mycelium or in the culture medium. *S. aureofaciens* is so named on account

of the production of a golden-yellow pigment at a certain stage in the growth of a colony of this fungus. The antibiotic obtained from *S. aureofaciens* is also faintly golden-yellow and has been named aureomycin.

In exploring the properties of this new antibiotic Duggar[1] has described how colonies of several strains of *S. aureofaciens* were grown on agar plates appropriately flooded with different assay organisms whereby the organisms were exposed to the antibiotic directly secreted by the growing colonies of *S. aureofaciens*. The organisms used for assay purposes included Gram-positive and Gram-negative bacteria and certain non-pathogenic bacteria, as well as plant pathogens and certain filamentous fungi and yeast. Antibiotic activity was particularly conspicuous against both the Gram-positive and Gram-negative bacteria *Shigella gallinarum* and *Brucella abortus*.

Aureomycin (trade name Duomycin) is a yellow crystalline substance which is soluble in acid and in alkaline solution. A 2 per cent solution of aureomycin hydrochloride in water has a *p*H of 4·5. In the dry state the drug is stable; in solution, however, the antibiotic rapidly loses its activity, particularly in the presence of broth, serum, or whole blood.

Pharmacology. When tested on a variety of animals aureomycin produces no systemic effects and does not interfere with the normal response of animals when injected with drugs such as adrenaline, acetylcholine, and histamine (Harned et al.).[2] Relatively large doses of the antibiotic can be given intravenously, the LD_{50} for mice being about 134 mg. per kilo and for rats about 118 mg. per kilo. There is no evidence of toxicity after the oral administration to mice or rats of 3 g. per kilo. The antibiotic appears to have a mild diuretic effect, which is about one-third of that given by caffeine.

Aureomycin appears in the urine about one hour after oral administration, and when given in daily doses of 1 to 2 g. to normal human subjects there is a maximum concentration in the urine within four to eight hours. The excretion is prolonged, for antibiotic activity has been demonstrated in the urine three to four days after the last dose is given by mouth. Aureomycin passes the blood-brain barrier and is present in therapeutically effective concentration in the cerebrospinal fluid of the dog about six hours after intravenous administration of the drug. Solutions of aureomycin hydrochloride when injected intramuscularly or subcutaneously are irritant, and this method of administration is not usually recommended. On the other hand, instillation of a 1 per cent solution of aureomycin borate into the eye of the rabbit produces no evidence of irritation, and Braley and Sanders[3] have used $\frac{1}{2}$ per cent solution of this drug in the control of human ocular infections without evident damage to the conjunctiva or cornea, though some patients complained of irritation of the conjunctiva after using it for forty-eight hours. Dowling and his colleagues[9] consider that effective concentrations of the antibiotic can be maintained by oral administration of the drug at intervals of six hours, and have suggested that the drug may even be effective if given every eight to twelve hours. The daily dose used in most instances was of the order of 15 to 30 mg. per kilo, and the only evidence of side effects was the occurrence of nausea, vomiting, or diarrhœa in a few cases.

Antibiotic Activity. *In vitro* studies indicate that as an inhibitor of Gram-positive cocci and Gram-negative bacilli, aureomycin is less potent than streptomycin, and, in the treatment of mice experimentally infected with these organisms, aureomycin is not as effective as either penicillin or streptomycin (Price et al.;[4] Chandler and Bliss[5]). The most interesting and promising field of investigation concerns the activity of aureomycin against the viruses of the psittacosis-lymphogranuloma group and the rickettsiæ of spotted fever, typhus fever, scrub typhus fever, and Q fever. This has been

shown in experimental infections of mice, guinea-pigs, and preparations of embryonated hen's eggs (Wong and Cox[6]).

When guinea-pigs infected with epidemic typhus, Q fever, or Rocky Mountain spotted fever were allowed to develop symptoms, subsequent daily subcutaneous injections of 5 to 6 mg. per kilo of aureomycin for three to five days rendered most of the animals afebrile within forty-eight to seventy-two hours. There appears to be a quantitative relationship between the dose of the infecting agent and the dose and time of administration of the antibiotic, since the initial phase of chemotherapy has a decisive influence not only on the prolongation of the incubation period but also on the ultimate complete or partial suppression of clinical symptoms (Anigstein et al.)[7]

The complete clearance of the infecting agent from the tissues of the host after treatment with aureomycin is not yet certain, though preliminary observations indicate that this is probably so. When mice were heavily infected with psittacosis or with lymphogranuloma venereum virus and were then treated with aureomycin, the viruses were found in the brain and liver of the animals at the seventeenth day but not at the forty-second day, whereas control animals similarly infected with small non-fatal doses and given no treatment were found to harbour the viruses after the forty-second day.

Clinical Reports. The most promising results of clinical trials concern the anti-rickettsial properties of the drug. Dowling and his colleagues[9] reported that 2 patients with Rocky Mountain spotted fever recovered dramatically during administration of 300 and 700 mg. aureomycin every six hours for five days. The rash disappeared and the temperature fell within twenty-four hours and became normal in sixty hours. In a more extended study of this disease, oral treatment with 30 mg. per kilo daily was started on the second to fifth day of the disease, and a normal temperature and clinical cure was apparent within thirty-six to seventy-two hours of the start of the treatment, and all the patients recovered fully without complications (Schoenbach et al.).[8]

The evidence on the therapeutic efficiency of the drug in epidemic typhus fever is scanty; 1 case of Brill's disease treated on the sixth day became afebrile and symptomless within forty-eight hours.

Patients with typhoid fever have varied in their response to the drug and the initial trials on a few patients have not given much convincing evidence of therapeutic value.

Three patients with brucellosis were more successfully treated, and became symptomless within seventy-two hours of treatment.

Wright and his colleagues[10] are convinced from a study of 35 cases of lymphogranuloma venereum that aureomycin is the treatment of choice. Not only is the antibiotic effective against the virus but also against the secondary bacterial invaders.

Preliminary trial of the drug in patients with ulcerated lesions due to granuloma inguinale has also been reported.

Lennette and his co-workers[11] have described promising results of treating patients with Q fever with aureomycin, and have concluded that the drug merits further study in the treatment of this disease.

Urinary tract infections due to organisms such as *B. coli aerogenes*, *B. paracolon*, *Str. faecalis*, some of which were resistant to penicillin, streptomycin, or sulphonamide therapy, have been successfully treated with aureomycin, though infections due to *B. proteus* were not controlled by this drug.

Aureomycin borate, where applied locally as ½ per cent solution, shows a wide range of therapeutic usefulness in ocular infections due to Gram-positive cocci and Gram-negative bacilli, as well as in inclusion conjunctivitis and

herpes simplex of the cornea. In some instances local therapy was supplemented by intramuscular injections of aureomycin hydrochloride.

Aureomycin represents another stage in the development of antibiotic substances, and while it has been shown to be an effective agent in tackling some problems of virus infection, there are still many opportunities for further exploration in this field.

REFERENCES.—[1]*Ann. N.Y. Acad. Sci.* 1948, **51** (2), 177; [2]*Ibid.* 182; [3]*Ibid.* 280; [4]*Ibid.* 211; [5]*Ibid.* 221; [6]*Ibid.* 290; [7]*Ibid.* 306; [8]*Ibid.* 267; [9]*Ibid.* 241; [10]*Ibid.* 318; [11]*Ibid.* 331.

BACTERIAL ENDOCARDITIS.

(*See* ENDOCARDITIS, BACTERIAL.)

BILHARZIASIS.

(*See also* SCHISTOSOMIASIS.)

BILHARZIASIS, PULMONARY.

M. Erfan, F.R.C.P. (Lond.), D.T.M. & H. (Camb.)

Pulmonary bilharziasis occurs in the early stage of bilharzial infection during the migration of the larvæ through the lungs, and at a later stage from the deposition of *Schistosoma* ova or worms.

The symptoms of the early stage have been described in *S. japonicum* under Katayama disease, in *S. mansoni* by Lawton (1917), and in *S. hæmatobium* by Fairley (1919–20). They appear within 2 to 8 weeks of the infection, last a few days to several weeks, and consist of fever, rigors, headache, anorexia, urticaria, abdominal pain, diarrhœa, cough, bronchitis, enlarged tender liver and spleen, and a very high eosinophil leucocytosis.

The following description applies to the form of the disease due to the deposition of *Schistosoma* ova or worms in the lungs.

History. Pathologically V. Belleli[1] (1885) was the first to record the presence of *Schistosoma* ova in the lungs. W. St. C. Symmers[2] (1905) reported the presence of the worms in the blood-vessels of the lungs. G. A. Turner[3] (1909) found *S. hæmatobium* ova in the lungs in 70·9 per cent of cases in South Africa. M. F. Sorour[4] (1928) described the pathological changes in pulmonary bilharziasis, and Bernard Shaw and Abou Ghareeb,[5] in 1938, published a full account of the pathology of the disease.

Clinically, R. M. Suarez[6] (1930) described cases of bronchial asthma which he attributed to pulmonary bilharziasis. S. Azmy and S. Effat[7] (1932) reported the first case of pulmonary arteriosclerosis due to bilharziasis confirmed by autopsy. After the report of this case interest in pulmonary bilharziasis grew rapidly. Several papers appeared on the subject, notably by E. Clark and I. Graef[8] (1935), H. B. Day[9] (1937), F. Mainzer[10] (1938), E. Koppisch[11] (1942), J. Silveira[12] (1944), and M. Erfan[13] (1948).

Incidence. In Egypt, where 60 per cent of the inhabitants are infected with bilharziasis, Bernard Shaw and Abou Ghareeb[5] found *Schistosoma* ova in the lungs in 33 per cent of cases of *S. hæmatobium* and *S. mansoni* infections. In South Africa Turner found ova in the lungs in 70·9 per cent of cases of *S. hæmatobium* infections. In Argentina Koppisch found ova in the lungs in 10·8 per cent of cases of *S. mansoni* infections. Silveira explains this comparatively low figure by the easier access of *S. hæmatobium* ova to the lungs by way of the vesical veins, while *S. mansoni* ova have more difficulty in reaching the lungs by way of the porto-caval anastomoses. No record of the percentage incidence of ova in the lungs in *S. japonicum* infections has been published, though few cases have recently been reported (E. C. Faust et al.,[14] 1946, H. B. Weinberg et al.,[15] 1946).

Pathology. Pulmonary bilharziasis is the result of the deposition of *Schistosoma* ova and worms in the lungs. These reach the lungs as emboli from the veins of the urinary and intestinal tracts. From the veins of the

PLATE II

PULMONARY BILHARZIASIS



A B

Fig. A. Lung, early stage, showing bilharzial miliary nodules. B. Lung, late stage, showing thickened arteries.

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PLATE III

PULMONARY BILHARZIASIS

(M. Ebeyan)

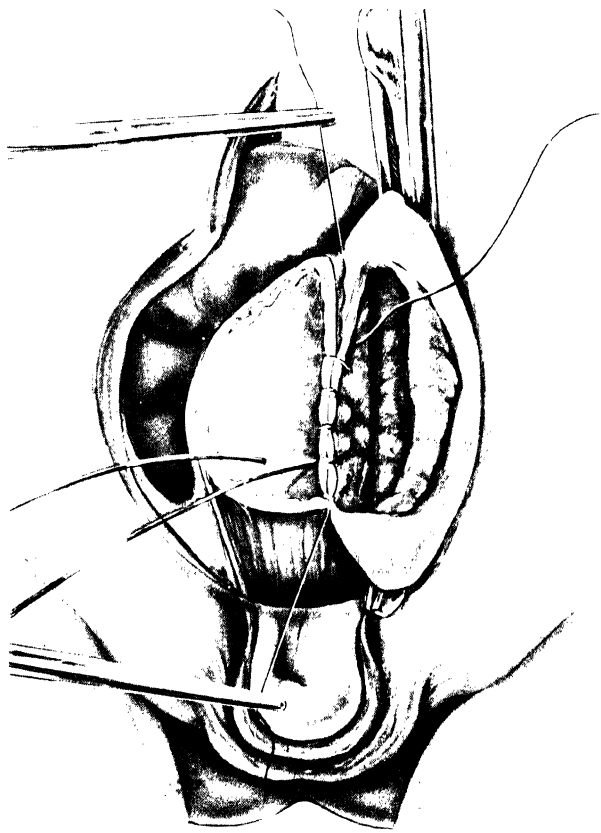


Radiograph showing mottlings in the lungs due to bilharzial nodules, increase of the hilar shadows, and marked prominence of the pulmonary conus.

PLATE IV

EXSTROPHY OF THE BLADDER

(R. Rizzi)

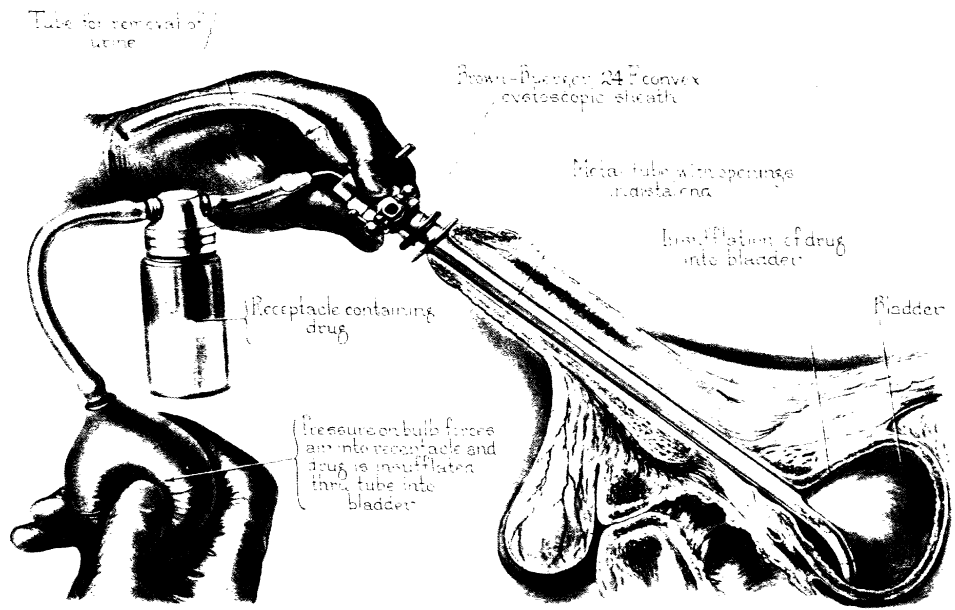


Cysto-sigmoidostomy for vesical exstrophy.

PLATE I

BLADDER INSUFFLATOR

(S. L. Wasp)



Bladder insufflator in use.

urinary tract they reach the lungs by way of the internal iliac veins and from the veins of the intestinal tract by means of the porto-caval anastomoses.

S. hæmatobium ova are more often found in the lungs than *S. mansoni* ova, but the latter produce vascular lesions more frequently than the former.

The ova, reaching the lungs as emboli, obstruct the small arterioles, pass through their walls, and lie immediately outside them. The tissue reaction round the ovum results in the formation of the bilharzial tubercle. This consists at first of the ovum surrounded by histiocytes and eosinopnil leucocytes. Later lymphocytes and one or more giant cells appear. Fibroblasts invade the tubercle and a nodular scar is formed.

The ova produce two types of lesions, parenchymatous and arterial. Parenchymatous lesions lie in relation to the bronchioles and alveoli. They are scanty in number and produce little alteration in the finer structure of the lungs. Arterial lesions, though less frequent, are more serious. They are the result of the necrosis of the walls of the arterioles produced by the passage of the ova through them. Necrosis is followed by healing with thickening and narrowing or occlusion of the lumina of the vessels. Canalization of the obstructed vessels may occur with the formation of angiomatoids. The arterial lesions may be confined to few vessels or be widespread. In the latter case dilatation and thickening of the arteries in the lungs and of the pulmonary artery and its primary branches result (*Plate II, Fig. B*). The right ventricle hypertrophies and dilates and finally fails.

To the naked eye, at a comparatively early stage, the bilharzial tubercles appear as miliary nodules on the cut surface of the lungs (*Plate II, Fig. A*). These are about ½–1 mm. in diameter, greyish in colour, firm in consistency, and are arranged in clusters or lines round the thickened arteries. At a later stage these nodules disappear and only thickened dilated vessels are seen.

The pulmonary artery and its primary branches are dilated and may reach aneurysmal size. Their walls may show atheromatous changes and their lumina may contain ante-mortem thrombi. The right ventricle is dilated and hypertrophied and its wall may be 1 cm. or more in diameter. The right auricle may also be dilated.

The worms may be present in the blood-vessels of the lungs. While living they are harmless, but when dead they produce a necrotic and focal pneumonia which appears as opaque white areas of consolidation 0·1–0·5 cm. in diameter.

For a full account of the pathology of the disease the reader is referred to the article by Bernard Shaw and Abou Ghareeb,[5] "The Pathogenesis of Pulmonary Schistosomiasis in Egypt with Special Reference to Ayerza's Disease", published in the *Journal of Pathology and Bacteriology*, 1938.

Clinical Picture.—Clinically two forms of pulmonary bilharziasis have been described: bronchopulmonary and cardiovascular.

In the *bronchopulmonary* form the pathological lesions are in the bronchioles and alveoli. Clinically bronchial asthma, chronic bronchitis, bronchiectasis have been attributed to this form, mainly on the ground of improvement on specific antimony treatment. Pulmonary fibrosis, pulmonary emphysema, pleural thickening, and even pneumothorax (Silveira,[12] 1944) have also been considered to be due to this form.

In the *cardiovascular* form the pathological lesions are primarily in the pulmonary arterioles and secondarily in the pulmonary artery and its branches, and in the right ventricle.

The clinical picture of this form is similar to that of primary pulmonary endarteritis or Ayerza's disease. However, cyanosis, which is the most striking feature of Ayerza's disease, is absent in pulmonary bilharziasis and appears only when the right ventricle has failed.

The cause of the cyanosis in Ayerza's disease is not clear. A. H. Fishberg[16] (1940) states that marked cyanosis in Ayerza's disease, without failure of the right ventricle, "indicates the presence of changes in either the capillaries or the pulmonary parenchyma interfering with gas exchange". D. E. Bedford[17] (1946) is of opinion that "the classical clinical picture of so-called Ayerza's diseases is really one of chronic lung disease and heart failure combined".

The electrocardiogram shows right heart strain (right ventricular preponderance). Arrhythmias other than extrasystoles have not been observed.

Radiologically, at an early stage some of the small branches of the pulmonary artery in the lungs, usually the basal, show nodules about 1 mm. in diameter along their course. At a more advanced stage the nodular arteries are more numerous, the arterial shadows in the lungs become intensified and the hilar shadows are increased in size and the subaortic notch is obliterated. At a still more advanced stage the hilar shadows are very much increased in size and the pulmonary artery and conus are very much enlarged, may reach aneurysmal size, and mask the shadows of the aorta and its knob. The heart has the configuration of cor pulmonale.

Diagnosis.—The only certain means of diagnosing pulmonary bilharziasis is the presence of *Schistosoma* ova in the sputum. However, the ova are very rarely found in the sputum.

Establishment of the presence of bilharziasis is essential. This consists in the demonstration of the ova in urine or fæces, sigmoidoscopic evidence of bilharziasis, rectal and liver biopsy for ova and the specific tests of bilharziasis. Eosinophilia is more marked in pulmonary than in other forms of chronic bilharziasis.

Examination of the lungs clinically is of little help, as there are usually no signs or only few crepitations and rhonchi over their bases. Radiological examination is helpful. Peri-arterial nodules, intensification of the arterial shadows in the lungs and increase of the hilar shadows may be observed (*Plate III*).

Examination of the heart, clinically and radiologically, for signs of cor pulmonale is important. Other causes of pulmonary dilatation have to be excluded, especially mitral stenosis and atrial septal defect. Mitral stenosis can be excluded by its characteristic cardiac signs, and dilatation of the left auricle observed radiologically. Atrial septal defect is differentiated by early dilatation of the right auricle, hilar pulsations, and absence of nodules in the lungs. At a late stage differentiation may be possible only by auricular catheterization.

Radiologically, miliary tuberculosis and silicosis have to be differentiated from pulmonary bilharziasis.

In miliary tuberculosis the lesions in the lungs are more widespread, and there is no dilatation of the pulmonary artery and conus. In silicosis the radiological picture is similar. Peri-arterial nodules, however, are not seen in silicosis, while extensive fibrosis is not observed in pulmonary bilharziasis.

Prognosis.—It has been mentioned previously that 60 per cent of the inhabitants of Egypt are infected with bilharziasis and that one-third of these have pulmonary bilharziasis. Post-mortem records show that 2 per cent of cases of bilharziasis die from right ventricular failure as the result of bilharzial pulmonary arterial disease.

Clinically, bilharzial pulmonary arterial disease is a much less common cause of right ventricular failure than rheumatic heart disease, hypertension, and other chronic pulmonary diseases. Right ventricular failure is late in appearance as its cause is mechanical rather than myocardial.

As a cause of chronic pulmonary disease, such as chronic bronchitis and bronchiectasis, it is difficult to give an accurate idea of its importance as it is often difficult to establish the bilharzial origin of these diseases.

Treatment.—Early treatment with antimony compounds is important. In advanced cases with enlargement of the right ventricle they must be used with caution as they are toxic to the myocardium. They are definitely contra-indicated when the right ventricle has failed.

Heart failure is treated on ordinary lines by digitalis, venesection, and mercurials. Recently J. McMichael[18] (1948) has expressed the opinion that digitalis and venesection, in heart failure of pulmonary origin, are unlikely to help and may even be dangerous. This view, however, is not shared by other authorities.

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BLADDER, SURGERY OF.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

Cystoscopy.—Last year marked the fiftieth anniversary of Joaquin Albarran's epoch-making contribution to urology in the form of a lever device for directing the course of urethral catheters into the ureters by means of the cystoscope. Albarran's contribution to cystoscopy opened up new horizons, and after fifty years remains as useful and sound in principle as the day it was conceived. (A. Puigvert.[1])

Cysto-sigmoidostomy for Vesical Exstrophy.—Implantation of the ureters into the bowel has long been an accepted treatment for vesical exstrophy. A more direct form of urinary deviation is advocated by R. Rizzi.[2] The bladder, after dissection from the abdominal wall is directly united to the sigmoid colon (*Plate IV*). Such good results have been obtained in 4 cases that Rizzi believes that cysto-sigmoidostomy should be as seriously considered as are Coffey's procedures.

Intractable Cystitis : Treatment. Since powdered sulphanilamide has proved useful in relieving pain and cleansing the ulcerations of tuberculous laryngitis, it occurred to S. L. Wang[3] that such treatment might be tried for bladder tuberculosis. A special insufflator was devised (*Plate V*) consisting of a metal tube (adapted to a 24 F Brown-Buerger cystoscope sheath) and an atomizer. Wang reports some relief in a number of patients, and believes that topical application of other drugs by this method should be considered. The other sulphonamides such as sulphadiazine and sulphathiazole are unsuitable, as they cake in the instrument. In addition to tuberculous cystitis, Hunner's ulcer, chronic interstitial cystitis, and other chronic bladder inflammations suggest a field for further study.

Inveterate Cystitis.—Apart from ureteric transplantation into skin or bowel, R. Darget[4] describes, and speaks well of, two additional procedures : (1) Denervation of the bladder by section of the nervi erigentes, followed by division of the hypogastric nerves ; (2) Local infiltration of the nervi erigentes.

Diphtheritic Cystitis.—G. Wolfsohn[5] describes a case occurring after prostatectomy in a faucial carrier. The suprapubic wound, the bladder, and anterior urethra were involved.

Thrush.—Monilial infections of the bladder must be rare. In describing such a case in a woman, O. C. Snyder[6] points out that only when the urine became strongly acid (mandelic acid) have the mycelial threads been found.

Cystitis Glandularis.—This year several surgeons have commented upon those confusing local manifestations of cystitis glandularis which may suggest a malignant bladder. The deceiving cystoscopic appearances are well shown in the study of H. R. Sauer and M. S. Blick.[7] Equally striking in its similarity to cancer is one of the histological preparations which these authors reproduce.

Vesical Ulceration following Radiation of the Cervix.—T. J. D. Lane[8] finds that the incidence of radiation effects on the bladder following treatment of cervical carcinoma is markedly falling. The appearances of the bladder after radiation injury are frequently indistinguishable from carcinoma. When ulceration occurs, the ulcer, unlike the cancer, is located low down on the posterior wall in the midline, and just above the trigone. An ulcer in this situation in a patient with a history of radiation and a bladder base, as felt per vaginam, not indurated, is much more likely to be a radiation ulcer than a malignant one.

Tumours in Vesical Diverticula.—In Paris J. Michon[9] has made a special study of such tumours; they have always been found in men, as might be expected when one recalls that vesical diverticula predominate in the male and that bladder cancer is three times more frequent in men than in women. The tumour arises at different parts of the pouch and is seven times more often malignant than innocent. It seems as if chronic infection and leucoplakia predispose to cancer. Hæmaturia is the suggestive symptom and induration on rectal examination is an important sign. At cystoscopy the orifice of a diverticulum may be concealed by clot; it can even appear so normal that the presence of a growth is unsuspected. Direct observation of the tumour is rare. Cystography should always be performed, for by this means irregularity of outline and filling defects are often detected. Special emphasis is paid to diverticulography by injecting the opaque medium directly into the sac through a ureteral catheter. Extravesical diverticulectomy after division of the neck appears indicated for fundal growths. The prognosis is very similar to that of bladder cancer. Michon is unable to share the view that extirpation gives better results than are obtained in the removal of primary neoplasms of the bladder.

Vesical Abnormalities and Diabetes Mellitus.—The diabetic atonic bladder has received too little attention. In the opinion of R. Lich and O. Grant[10] the neurological lesion is apparently one of demyelination of the posterior root fibres. Transurethral resection of the vesical neck was of value in 3 cases.

Vesical Dysfunction in Tabes Dorsalis.—J. L. Emmett and J. Beare[11] report consistently good results by means of transurethral resection of the vesical neck. The patients should be re-examined at yearly intervals, as small degrees of post-operative contracture may conceivably cause a recurrence of the obstruction.

Endometriosis of the Bladder.—A plea for routine cystoscopy in all cases of pelvic endometriosis is made by H. E. Schmitz and G. R. Baba.[12] A pathognomonic feature of bladder involvement is the cyclic vesical distress associated with the menstrual cycle. As with endometriosis lesions elsewhere, the bladder lesions regress in pregnancy so that vesical symptoms may subside completely. The lesions, however, will recur after delivery. Treatment varies according to local conditions, but H. L. Tolson and B. Skitarelic[13] report a case in which the McCarthy resectoscope served well in removing the neoplasm.

Papilloma of the Bladder treated with Podophyllin.—The success which followed the application of podophyllin to genital warts prompted its use in the treatment of vesical papillomata. J. E. Semple's[14] preliminary report suggests that results warrant further trial. With the window of the cystoscope immediately over the growth, the bladder is emptied and 3 ml. of 0·5 to 1 per cent podophyllin in liquid paraffin is introduced direct on to the papilloma. After withdrawal of the cystoscope the patient lies for half an hour on the side of the

growth and then on the opposite side for as long as possible; he micturates as the urge arises. The initial dose tests the susceptibility of the patient and the potency of the drug. If no reaction occurs, an effective dose of 5 ml. of 4 per cent podophyllin in liquid paraffin is inserted in 4 to 7 days, the patient lying on alternate sides as before. A week later a third application is carried out, using 5 ml. of 8 per cent podophyllin. The need for further applications depends on the size of the growth. Fulguration completes the destruction of the tumour.

Cancer of the Bladder.—In at least one-half of 100 cystectomies the true condition was of a greater degree of malignancy than cystoscopy biopsy had indicated (A. L. Dean[15]).

C. C. Higgins[16] rightly objects to cystectomy being utilized as a court of last resort in the treatment; with his present experience a mortality of 5 per cent or less may be anticipated. The technique varies. If the lesion involves the bladder neck a perineo-abdominal procedure is preferable. When the lesion is relatively far from the bladder neck the abdominal excision suffices.

C. C. Higgins and K. F. Hausfeld[17] write that when cutaneous metastases make their appearance, death ensues within 6 months.

Bilharzial Cancer.—H. Ibrahim[18] recounts his extensive Egyptian experience. *Bilharzia* is a very potent cause of vesical cancer, the cause being tissue imbalance from the toxin secreted by the miracidium. Bilharzial cancer is rare where bilharzial calcification is rare. These cancers differ in no way from non-bilharzial ones except in their greater malignancy and younger age-incidence. The operability rate is exceedingly low. The report ends with the dismal acknowledgement that in more than 1000 cases the cures could be counted on the fingers of a single hand; for the remainder there was no really effective palliative measure.

Treatment with Inositol.—Inositol, an important factor in animal nutrition, is a compound regarded as a member of the vitamin B group. It has been found to inhibit tumour growth in mice. W. P. Herbst and C. E. Bagley,[19] after using it in advanced malignancy in man with doses of 2–4 g. daily, believe that it reduced the size of the tumour in primary carcinoma of the bladder.

Œstrogen Treatment.—Since the bladder and prostate are of similar embryological origin, it occurred to O. Grant[20] that the œstrogenic response seen in prostatic neoplasm might well be experienced in vesical malignancy. With R. Lich, Grant reports 11 instances of vesical neoplasm along with their response to stilbœstrol. The amount used as a routine was 5 mg. daily and exceptions are recorded. They find that the most consistent effect was in the symptomatic reduction of vesical irritability. Stilbœstrol afforded subjective relief in 9 of the patients. Tumours of Grades 3 and 4, though showing histological changes due to stilbœstrol, were practically unaltered clinically. Papillomata consistently disappeared.

Carcinoma of the Bladder with Bone Metastases.—To the increasing list of tumours which involve the skeleton must be added vesical cancer. H. L. Kretschmer and J. H. McDonald[21] add 8 cases, five males and three females, with an average age of just under 60. The primary neoplasm may be an innocent-looking papilloma or a large fungating cancer. Although hæmaturia is frequent, it may be the pain of a skeletal deposit which brings the patient for investigation. Such metastases, which can occur reasonably early, are essentially osteolytic, the bones of the pelvis being most frequently invaded.

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BLOOD-VESSELS, SURGERY OF.

(*See also* ANEURYSM, VARICOSE VEINS, VARICOSE ULCERS, AND VENOUS THROMBOSIS.)

Lambert Rogers, M.Sc., F.R.C.S.

Thrombosis of the Abdominal Aorta.—A rare cause of thrombosis of the abdominal aorta is pressure from without. E. Hesse,[1] who in 1921 reviewed 73 cases of aortic thrombosis, regarded only 3 as due to external pressure, the causes of these being a uterine fibroid, carcinoma of the uterus, and a tumour of the 2nd and 3rd lumbar vertebræ respectively. G. E. Pinkerton[2] has reported a case in a man of 81, apparently due to pressure of a large osteophyte which projected from the bodies of the 2nd and 3rd lumbar vertebræ (*Fig.* 3).

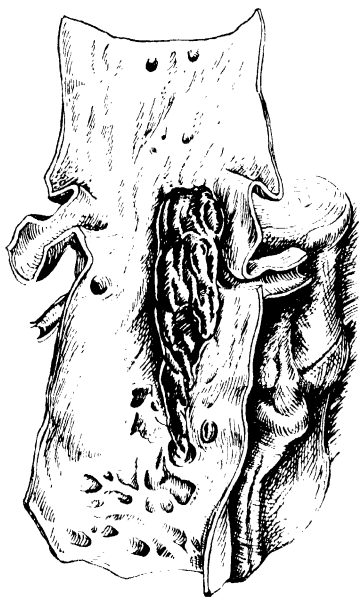


Fig. 3.—Abdominal aorta opened to show clot in portion distorted by vertebral osteophyte. (*By kind permission of* '*The Lancet*'.)

Resection of the Aortic Bifurcation.—F. W. Cooper, M. H. Harris, and J. W. Kahn,[3] of White Sulphur Springs, have recorded a remarkable case in which a ·45 calibre revolver bullet passed through the left arm and penetrated the chest of a soldier aged 22, entered the heart, and became an embolus which traversed the aorta and lodged at its bifurcation (*Plate VI, Fig. A.*) At operation the aorta was found to be about one-half of its normal diameter and tightly constricted about the foreign body. The common iliac arteries were obstructed by partially organized clot. The bifurcation was resected successfully, the aorta being ligated just below the origin of the inferior mesenteric arteries with double-zero braided silk ligatures (*Plate VI, Fig. B*). There was no untoward effect on the circulation in the legs and feet, but instead there was some improvement which was thought to be due to peripheral vasoconstriction being suppressed by division of the main vessels.

Thirty-six cases of partial or complete ligation of the abdominal aorta have now been reported in the literature, and 12 of these cases have been successful.

Aortic Embolectomy.—An additional successful embolectomy performed at the bifurcation of the aorta for saddle embolus has been reported by J. L. Keeley,[4] of Chicago. The patient, a housewife aged 52, suffered from auricular fibrillation and had been confined to bed for several weeks. Vague pains in the left leg and some weakness of muscles leading to a mild foot-drop were followed suddenly ten days later by numbness of both legs and pain in the lower abdomen. The legs soon became paralysed. Six hours after the onset of these symptoms of a saddle embolus, transperitoneal exposure of the aortic bifurcation was made under general anæsthesia, tapes were placed around the aorta and common iliac arteries and an incision 2 cm. long was made into the anterolateral aspect of the aorta at its junction with the right common iliac artery (*Plate VII*). The embolus was removed (*Fig.* 4). Free bleeding now occurred. The opening in the aorta was closed by a running mattress suture

PLATE VI

RESECTION OF AORTIC BIFURCATION

(F. W. Cooper, M. H. Harris, and J. W. Kahn)



Fig. A. Roentgenograms of abdomen with foreign body at bifurcation of aorta.



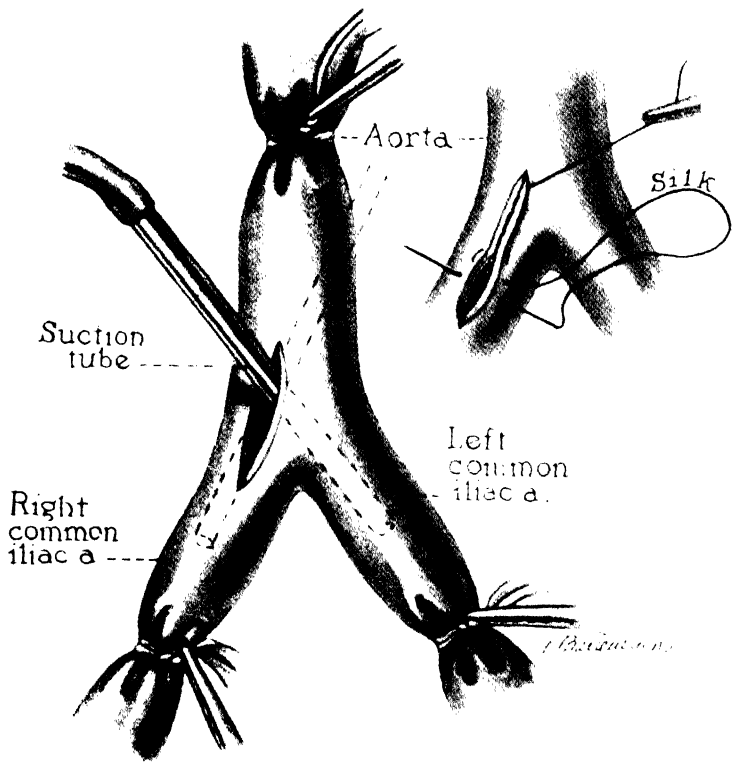
Fig. B. Operative procedure. The foreign body has been removed and a portion of the injured aorta excised. An additional segment of the damaged aorta is being excised.

Reproduced from the "Annals of Surgery"

PLATE VII

AORTIC EMBOLECTOMY

(J. L. KEELEY)



The incision in the vessel wall at the junction of the aorta and the right iliac art

of fine silk, and heparin was administered. The patient made a good recovery. This operation was performed in 1946, and at the time of the report, twenty-three months later, she was alive and well. The authors of this paper believe this to be the twenty-second reported case.

[There are two ways of dealing with embolic obstruction at the aortic bifurcation, either a direct attack as in this case, or indirectly by opening the femoral

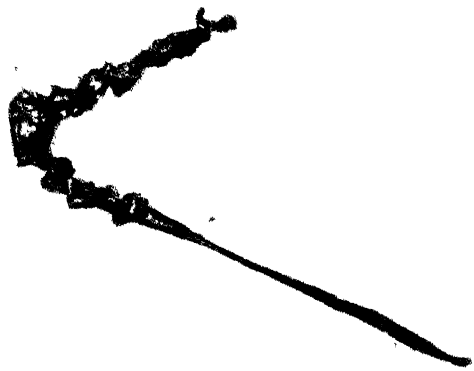


Fig. 4.—The clot as assembled after removal. The tail thrombus is from the right iliac artery and was approximately 15 cm. long. The clot from the left iliac artery was removed in several pieces. (*Reproduced from the "Annals of Surgery".*)

or external iliac artery and dislodging the clot by milking or intravascular probing as advocated by G. Nystrom[5] and others. L. C. R.]

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BONE AND JOINT, TUBERCULOSIS: STREPTOMYCIN IN. (*See* TUBERCULOSIS OF BONES AND JOINTS.)

BONE TUMOURS: CONSERVATIVE SURGERY IN.

T. P. McMurray, F.R.C.S.

Coley and Higginbottom[1] make an appeal for the use of more restricted operative procedures in the removal of bone tumours, in contrast with the present methods which invariably include high and mutilating amputation when removal of the tumour is surgically possible.

In recent years there has been a gradual tendency to rely with much greater confidence upon surgical measures rather than on roentgen therapy in the treatment of all types of benign and malignant neoplasms of bone.

In the treatment of those tumours which are known to be radio-resistant, roentgen therapy is employed only when the tumour is obviously inoperable, although occasionally it may be used to assist those few patients who will not consent to surgical procedures. The use of radiation under these circumstances is obviously palliative rather than curative, although in many instances freedom from pain and restraint of tumour growth follow on the intelligent use of this type of treatment.

The authors claim that whilst it would be highly regrettable if conservative measures were used in those instances in which complete removal of the tumour was possible only by amputation of the affected limb, yet, in their opinion, great benefit to the patient may follow on the use of more conservative procedures when the conditions are suitable. They claim: (1) That there is a definite place for selecting a conservative rather than a more radical operation; (2) That there are criteria which enable the surgeon to make a correct decision in the majority of instances; (3) That there is a measure by which the surgeon can subsequently determine whether his initial decision was justified; (4) That if judgement is exercised the patient stands to benefit rather than to suffer from the more conservative procedure.

In their definition of conservative surgery, the authors describe it as an elective procedure which either avoids amputation or, if this is impossible or inadvisable, which places the site of amputation at a level ensuring useful function in the stump of the limb.

In general it may be stated and agreed that in dealing with benign tumours of bone, conservative measures are usually adequate except in those instances where the tumour mass has destroyed the bone so extensively as to render the limb useless. Tumours which are doubtful in character and those in which malignancy is of 'low grade' must be carefully considered and a decision arrived at as to the possibility of their removal by some procedure less mutilating than amputation. In making this decision, the surgeon must be influenced by the site and extent of the growth. Thus, those tumours which are of medullary origin and which have not, at the time of examination, penetrated the cortex of the bone may be safely dealt with by local excision. On the other hand, the typical osteogenic or chondrosarcomata, which are usually of considerable size and have probably extended beyond the confines of the bony structure, are definitely unsuited to treatment by local removal.

When considering the inadvisability of the use of a more conservative procedure, the authors are influenced solely by the possibility of removing the tumour with an adequate amount of the neighbouring tissue sufficient to prevent a local recurrence and, at the same time, leaving a stump which will be useful to the patient.

It is suggested also by the authors that the wisdom or tragedy of using the conservative procedure can only be decided by subsequent events. It is claimed that if, following the operation, there is no local or regional recurrence of the tumour, conservative removal may be considered to have been the correct procedure even though distant metastasis may be discovered at a later date, because in this latter event, even high amputation would have afforded no additional protection. If unfortunately the limited removal of the affected tissue is followed by local recurrence of the disease, then the employment of this method may be classed as a grave error of surgical judgement.

The conservative methods of removal which are described are the following well-tried procedures: -

1. *Curettage.*—By this means giant-cell tumours, bone cysts, enchondromata, and fibrous dysplasia may be adequately treated. The authors in their series have one five-year survival of a chondromyxosarcoma of the upper portion of the tibia treated by this method.

2. *Partial Resection.*—This is particularly suitable in dealing with tumours of the tibia, fibula, and clavicle, which are largely subcutaneous in position.

3. *Segmental Resection and Bone-graft to repair Defect.* This well-tried procedure has been employed for many years, and it is interesting to note the figures reported by Phemister from the records of the Bone Sarcoma Registry of the American College of Surgeons, in which only 3 of the 93 patients who

have survived for the five years following operation were treated by resection.

4. *Excision.*—Chiefly applicable when bones in the distal portions of the limbs, such as the metacarpals, metatarsals, and phalanges, are involved.

5. *Amputation.*—It is rather strange to read of amputation being described as a conservative procedure, but the authors make the point that every effort should be made to save as much as possible of the limb in order that the amputation stump may be of functional value.

The authors bring forward their views on the value to patients of these more limited procedures. There can be no doubt that when dealing with simple tumours, conservative methods are always advisable so long as the limb is not irretrievably destroyed by the growth.

The problem is very different when the bone tumour is malignant in character. Risk of life is the important criterion, and if this risk is increased by the use of a local procedure, then the decision of most surgeons will be in favour of the more radical procedure of amputation well away from the area of disease.

REFERENCE.—[1]*Ann. Surg.* 1948, **127**, 231.

BONE-MARROW ASPIRATION.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

M. A. Rubenstein[1] has reported on a study of biopsy specimens of bone-marrow obtained simultaneously from the iliac crest and sternum in 216 cases showing normal and pathological findings. The diagnostic advantages of iliac-crest marrow were seen in cases of infiltrative diseases involving the bone-marrow such as metastatic lesions of various neoplastic conditions and in some instances of multiple myeloma. The technique of obtaining marrow from the iliac crest is easy and safe and aspiration may be carried out repeatedly. It would appear to be a valuable diagnostic procedure in cases where sternal puncture fails to give satisfactory information owing to difficulty of aspiration or in cases where patchy changes in the general marrow are likely to occur.

REFERENCE.—[1]*J. Amer. med. Ass.* 1948, **137**, 1281.

BREAST FEEDING.

R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.

Self-selective Breast Feeding.—C. Anderson Aldrich and Edith S. Hewitt[1] report a study upon 688 babies on a self-regulating regimen designed to allow the baby free choice of intervals between feeds and amounts of food. The babies were supervised in a well-baby clinic after their discharge from the maternity hospital.

The feeding intervals during the first month of life were irregular, being sometimes 2-, 3-, or 4-hourly or 3 or 4 meals daily. Upon the whole, the babies chose to lengthen their feeding intervals gradually so that the average in later months agreed closely with the intervals usually prescribed.

Many babies, however, had to be fed at less than 4-hourly intervals in the first two months of life. At the age of a year 91 per cent of babies had automatically placed themselves on a diet of three meals a day. At this age, 92 per cent of the babies' appetites were classed as excellent, 2 per cent as borderline, and only 1 per cent as poor. The heights and weights attained compared favourably with the accepted standards, 29·4 in. and 21·8 lb. The authors conclude that a rigid routine, even if regulated to fit the average baby at each age, will have a large group of infants poorly adjusted as far as the interval between meals is concerned.

Breast Milk Bank.—Joyce Wright and Elsie M. C. Edwards[2] describe the establishment of a frozen-breast-milk bank. They obtained this milk from a twenty-bed maternity ward, by a clean ward technique of expression. The milk was pooled, boiled, and stored in an ice-cream freezing cabinet at −12° C.

This bank yielded 894 oz. of milk in twelve months which was used for premature infants in the obstetric hospital, and for sick infants in the children's ward. The sterility of the milk and its flavour were tested after boiling, and at the fourth, eighth, and twelfth weeks of storage. The milk remains sterile, but there was a slight deterioration of flavour between the eighth and twelfth weeks.

The excellence of this bank, both in its ease of operation and the simplicity of its apparatus, should commend it to any who have the care of sick or premature infants. This same bank has, in the current year, produced over 4000 oz. of breast milk, and has supplied other hospitals.

REFERENCES.—[1]*J. Amer. med. Ass.* 1947, **135**, 340; [2]*Lancet*, 1947, **2**, 233.

BREAST, SURGERY OF.

Lambert Rogers, M.Sc., F.R.C.S.

Carcinoma. During the past year an important discussion on the treatment of carcinoma mammæ was held at the Royal Society of Medicine. Sir Gordon Gordon-Taylor,[1] after outlining the age-long history of cancer of the breast, presented the case for the radical amputation without accompanying radiotherapy, and pointed out that few of the advocates of irradiation make any reference to the morbidity from radiation therapy. Apart from unhappy local effects, the sickness, misery, and other untoward sequelæ may lower the patient's resistance to any malignant cells that may remain after surgical operation. The natural duration of untreated cancer of the breast is from 2 to 5½ years, with an average of 3½ years, so that the frequently-discussed 5-year results of treatment are hardly worthy of consideration. Sir Gordon had performed 645 radical amputations for primary cancer of the breast, and percentage survivals of Stages I, II, and III cases for 10 years respectively had been 84, 29, and 6·5. [It is doubtful whether radiation alone or any of the present combinations of surgery and irradiation can produce comparable results.—L. C. R.]

R. S. Handley[2] investigated the state of the internal mammary glands and in 20 cases removed the lymphatic gland from the second intercostal space. In 6 this gland was not involved. Both intercostal and axillary glands were invaded in 9; in 3 the axilla only was involved and in 2 only the intercostal gland.

Stanford Cade[3] has investigated the mortality of radical amputation by writing to London and provincial teaching hospital surgeons and found that in a group of 11,014 radical mastectomies the mortality was 1·65. It is emphasized that the risk to life from radical mastectomy is low.

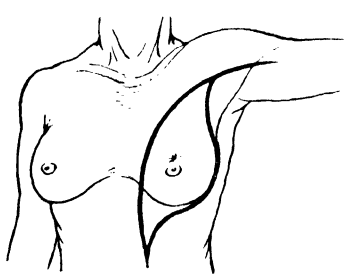


Fig. 5. Type of incision used in 11 cases of radical amputation. (*Fig.* 5 *and Plate VIII reproduced from the "Annals of Surgery".*)

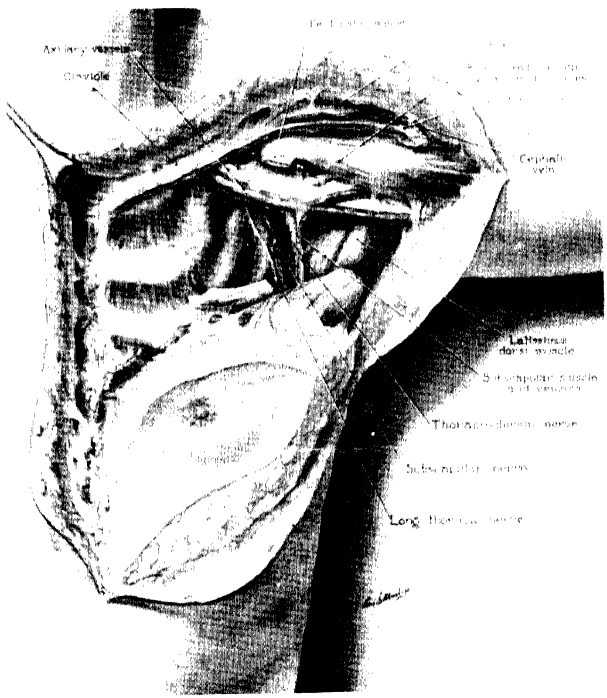
G. W. Taylor and R. H. Wallace,[4] of Boston, discussing end-results at the Massachusetts General Hospital, 1933–5, conclude that the occasional employment of prophylactic irradiation would not appear to improve prognosis.

G. G. Finney, W. C. Merkel, and D. B. Miller,[5] of Baltimore, report a consecutive series of 298 cases of cancer of the breast operated upon during the 15-year period 1930–45 of which they were able to trace 280 of the patients. Operative mortality was 1 per cent. Only 19 patients had received any radiation. Of 150 who did not die of metastases, 70 per cent showed no metastatic lesions in the axillary glands at the time of operation. The survival rates were 77 per cent after three years, 49 after five, 19 after ten, and 4 after fifteen. The type of operation performed is shown in *Fig.* 5 and *Plate VIII*.

PLATE VIII

CARCINOMA OF THE BREAST

(G. G. Finney, W. C. Merkel, and D. B. Miller)



Artist's composite drawing of radical amputation, showing extent of dissection.

[Opinion seems to have veered again to the radical amputation performed adequately and early as the most satisfactory treatment. The radiotherapeutists have not established a case for the replacement of the Halsted operation. —L. C. R.]

Dressing after Radical Amputation of the Breast (*Figs.* 6, 7).—L. N. Pollock[6] suggests the use of a vertically-placed piece of strapping. A strip of adhesive placed over a thin piece of gauze is carried from an area of skin over the lower aspect of the scapula, across the lower part of the axilla, while one hand of the surgeon is used to press the posterior axillary fold forwards and upwards. The upper and inner skin-flap is gently pushed towards the incision as the strapping is carried upwards in the infraclavicular depression which results from removal of the pectoral muscles. The strapping is now brought over the shoulder and ends where it began over the scapula. The tension is taken off the skin-flaps

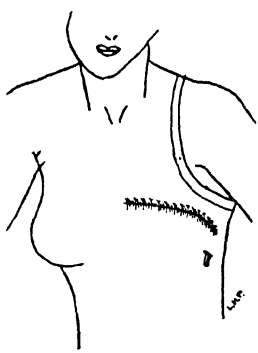


Fig. 6.—Adhesive strap approximating the upper skin-flap to the chest wall when a transverse incision is used. This minimizes the use of voluminous dressings. (*Figs.* 6, 7 *reproduced from the 'New England Journal of Medicine'.*)

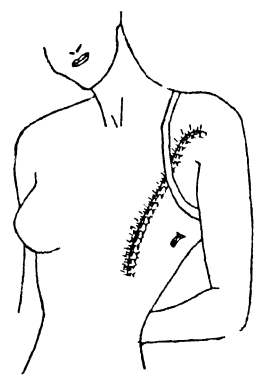


Fig. 7.—Curved adhesive strap, moulding the skin to the chest wall in a longitudinal incision. This supports the posterior axillary fold to lessen the tension on the suture line. It greatly decreases the padding needed to obliterate the dead space.

by the application of this piece of strapping, and the flaps themselves are moulded and kept applied to the concavity over which they lie after amputation of the breast. There is no need for tightly-applied constricting bandages across the chest if this method is used.

Chronic Cystic Mastitis.—H. L. Reid,[7] of Brooklyn, has raised again the question of whether chronic cystitis mastitis is a pre-cancerous lesion. Opinions as he points out, are conflicting; on the one hand, Ewing, Crile, Cheatle, and others, believe that those with the condition are no more liable to the development of cancer of the breast than those who do not have the condition. Reid has followed 26 patients from 10 to 17 years after operation for chronic cystic mastitis. Two had died from causes other than the breast condition, a third had had two local recurrences which were excised. The histological appearances were simply those of chronic cystic mastitis, and the last operation 12 years ago has not been followed by recurrence; the remaining 23 patients have remained free from recurrence or carcinoma of the breast. Not one of the 26 developed carcinoma of the breast.

Reid divides cases of chronic cystic mastitis into three groups: (1) simple chronic mastitis for which local excision of the involved area is advised; (2) chronic cystic mastitis with papillary proliferation treated similarly but watched

closely subsequently; and (3) atypical forms for which simple mastectomy is advised.

[The consensus of opinion to-day would appear to be against chronic cystic mastitis being a pre-cancerous condition.—L. C. R.]

REFERENCES.—[1]*Proc. R. Soc. Med.* 1948, **41**, 118; [2]*Ibid.* 131; [3]*Ibid.* 129; [4]*New Engl. J. Med.* 1947, **237**, 475; [5]*Ann. Surg.* 1947, **125**, 673; [6]*New Engl. J. Med.* 1948, **239**, 366; [7]*Arch. Surg.* 1948, **56**, 338.

BRITISH PHARMACOPŒIA, 1948. *Andrew Wilson, M.D., Ph.D., Ph.C.*

When the sixth *British Pharmacopœia* was published in 1932 it was intended to revise and reissue the *British Pharmacopœia* every ten years. On account of the war, however, the seventh *British Pharmacopœia* was not issued until September 1, 1948. This does not mean that revision of the *Pharmacopœia* had been suspended, for the British Pharmacopœia Commission has been actively engaged in collecting information, and in issuing *Addenda* at appropriate intervals during the sixteen years which have elapsed since the last *British Pharmacopœia* was published. It is perhaps not sufficiently appreciated that in compiling the list of drugs which are to be included in the *British Pharmacopœia*, medical and pharmaceutical authorities throughout the Commonwealth are consulted and there is considerable liaison with committees of revision of the *United States Pharmacopœia* and of the Health Organization of the League of Nations. Indeed the standardization of certain drugs is governed by international agreement, and there is some prospect that an *International Pharmacopœia* may eventually be published.

The task of the British Pharmacopœia Commission is to select drugs and to set for each a complete group of standards and assays for its control. Now the selection of drugs might reasonably be expected to be based on the pharmacological activity and clinical usefulness of a drug, but recognition must also be made of drugs which, though in frequent use, have not necessarily well-defined pharmacological activity. It is therefore not surprising to find some of the older drugs, such as Gentian, Oil of Rosemary, Castor Oil, and Catechu, in company with new and very potent drugs like Pethidine, Mepacrine, Thiouracil, Heparin, and Dicoumarol. In the case of certain new drugs for which not enough information is available for their inclusion in the *British Pharmacopœia*, approved names have been given; by this means it is hoped to restrict the use of numerous proprietary names for these drugs.

In common with previous editions, the official Latin title is given at the beginning of the description of each drug, and the drugs and their preparations are arranged in alphabetical order. There are, no doubt, well substantiated reasons for continuing this practice in contrast to that of the *United States Pharmacopœia* where drugs are given an English name. A new and interesting departure is the historical review of the *British Pharmacopœia*, which affords an opportunity for reflecting upon the extensive expert committees which are now called upon to consider the changes to be made before a new *Pharmacopœia* is issued.

The *British Pharmacopœia* holds in its 900 odd pages a wealth of information which is of interest in a particular way to three groups of the medical and pharmaceutical professions. To the manufacturing chemist it provides a detailed description of standards for purity and activity of drugs; for the practising pharmacist it affords a comprehensive list of preparations of drugs and of methods for preparing these in a manner suitable for administration. This is evident in the new descriptions for preparing tablets, ointments, and solutions for parenteral administration. The medical practitioner has learned to leave this pharmaceutical knowledge to the pharmacist and to accept from him with unquestionable reliance the preparation and dispensing of medicines

for his patients. The interest of the medical practitioner in the *British Pharmacopœia* is largely one of acquainting himself with the preparations and doses of drugs which are officially recognized.

In reviewing the changes that have occurred in the new *Pharmacopœia,* it must be remembered that the contrast is not with what was published in 1932, for it should be appreciated that by publication in the seven *Addenda* which have been issued from 1936 to 1945, a large number of new drugs and preparations have already been made official. This review, therefore, is concerned mainly with the changes that have occurred since the last *Addendum* to the 1932 *British Pharmacopœia* was issued.

Of the antibiotic substances, Penicillin and its preparations have already been made official for purposes of standardization. The standard preparation used is the Sodium Salt of Penicillin II or G. For parenteral administration there is an aqueous and an oily solution the former containing 50,000 units and the latter 125,000 units per ml., while for local administration there are two Creams and an Ointment each containing 500 units per gramme. Penicillin Eye Ointment contains 1000 units per gramme, and Lozenges for penicillin each contain 500 units. Sulphapyridine (M & B 693) and its sodium derivative have been deleted. Soluble preparations of other Sulphonamides, such as Sulphacetamide, Sulphadiazine, and Sulphathiazole, which are available for the preparation of injections, are now described as sodium derivatives, e.g., Injection of Sulphathiazole Sodium. The relatively non-absorbable compounds, Succinylsulphathiazole and Sulphaguanidine, are retained, as is Sulphanilamide. Three acridine antiseptics are described, the new Aminacrine Hydrochloride, Proflavine Hemisulphate which replaces Proflavine Sulphate, while Acriflavine is retained. The casting out of Hexamine, Buchu, and Copaiba represents a newer phase in the treatment of urinary tract infections; Calcium Mandelate is now officially recognized in common with Mandelic Acid. Preparations of organic Arsenical compounds for the treatment of syphilis now include Injections of Neo-arsphenamine, Sulpharsphenamine, and Tryparsamide.

Among the drugs available for the treatment of tropical diseases, Carbarsone, Injection of Suramin (Germanin), Injections of Potassium Antimonyltartrate. Sodium Antimonyltartrate (also of Sodium Bismuthyltartrate) and of Stibophen (Fouadin) are described; there are, in addition, an Injection of Emetine Hydrochloride and Injections of Hydnocarpus Oil and of its ethyl esters. Of the antimalarial drugs, several Quinine salts are described, the preparations of which are intended to be used only for the prevention and treatment of malaria; consequently Cinchona Bark and preparations of it, as well as the historical Ammoniated Tincture of Quinine and Easton's Syrup are deleted. Pamaquin and Mepacrine have already been described in Addenda to the *British Parmacopœia* 1932, but a new Injection of Mepacrine Methanesulphonate (Atebrin Musonate) is now included. Although Paludrine is not yet fully recognized, it has been given the approved name Proguanil.

The remarkable advance in hormone replacement therapy is reflected by the number of preparations of hormones, some synthetic and others of natural origin. Two Gonadotrophins are described, Chorionic and Serum, with corresponding preparations for parenteral administration. For the parenteral administration of œstrogenic compounds, Injections of Œstradiol Dipropionate and Œstradiol Monobenzoate are described, and there are also Tablets of Œstrone, Dienœstrol, and Hexœstrol for oral administration. Progesterone therapy may be given by Injection of Progesterone or by mouth with Tablets of Ethisterone. There are two preparations of male sex hormone: Injection of Testosterone Propionate and Tablets of Methyltestosterone. Unfortunately the difficulties of setting appropriate standards for an official extract of adrenal

cortex have not yet been overcome, but Injection of Deoxycortone Acetate (D.O.C.A.) is available for the treatment of Addison's disease. Thyroxin-sodium has been deleted and the antithyroid substances Thiouracil and Methyl Thiouracil are included.

The list of oxytocic drugs has been revised, Injection of Ergometrine Maleate has replaced the alkaloid, and Tablets of prepared Ergot are described; Ergotoxine Ethanesulphonate has been deleted. Posterior Pituitary Extract is now known as Injection of Pituitary (Posterior Lobe), and separate Injections of Oxytocin and Vasopressin are available.

Some changes in the vitamin preparations are indicated by the exclusion of powdered Vitamin B_1, Vitaminized Oil, and Solution of Irradiated Ergosterol. Vitamin K is represented by Injection of Menaphthone (Kapilon) and Tablets of Acetomenophthone (Kapilon-oral), while an Injection and Tablets of Aneurine Hydrochloride are added to the list of Vitamin B preparations.

There is considerable revision of the drugs acting on the cardiovascular system. Tablets of Prepared Digitalis and of Digoxin and Injections of Digoxin, of Theophylline with Ethylenediamine (Aminophylline), and of Ouabain (Strophanthin G) are notable additions. A place is given to two new substances, Papaverine Hydrochloride and Carbachol, and three vasodilator preparations, Erythrityl Tetranitrate, Solution of Glycerol Trinitrate, and Concentrated Solution of Nitrous Ether, have been abandoned. Many preparations of iron have rightly shared a similar fate. Iron and Ammonium Citrate, Ferrous Sulphate, and Saccharated Iron Carbonate are all that remain to support the classical preparations Parrish's Syrup and Blaud's Pill. A remarkable condition affecting the latter is that these pills should be freshly prepared for administration. It is possible that this may give rise to considerable alarm and despondency in the pharmaceutical profession. No concentrated preparation of Liver is described, though Dry Extract of Liver has been rejected. The anticoagulant substances Heparin and Dicoumarol have now been officially recognized.

There are some additions to the group of drugs acting on the central nervous system—thus Injection of Pethidine Hydrochloride (Dolantin), and Injections of Morphine Hydrochloride and of Morphine and Atropine. Preparations of the short-acting Barbiturates are now provided by Injection of Hexobarbitone Sodium (Evipan Sodium), and of Thiopentone Sodium (Pentothal Sodium), in addition to the longer acting Injection of Phenobarbitone Sodium. To some it may be a matter of regret that Carbromal has been deleted, but probably none share this for Methylsulphonal; the inclusion of Phenytoin Sodium (Epanutin) is a welcome addition, and it is noteworthy that Phemitone has changed its name to Methyl-phenobarbitone.

Picrotoxin now enjoys full official recognition as a respiratory stimulant, and Vinyl Ether and Trichloroethylene undoubtedly merit inclusion as general anæsthetics.

Amethocaine Hydrochloride (Decicain), Cinchocaine Hydrochloride (Nupercaine), Butacaine Sulphate (Butyn), and Butyl Aminobenzoate (Butesin) have joined the ranks as local anæsthetics, while Amylocaine Hydrochloride has retired from active service. Injection of Ethanolamine has replaced Injection of Sodium Morrhuate as a sclerosing agent. Although the pharmacological action of gold salts remains obscure, there is little doubt that Injection of Sodium Aurothiomalate (Myocrisin) is a much used therapeutic agent.

Injection of Neostigmine Methylsulphate (Prostigmin) and Tablets of Neostigmine Bromide are essential preparations for the treatment of myasthenia gravis, though their use in the treatment of numerous other conditions is open to question.

Many die-hard purgative preparations have at last succumbed, and we pay tribute to the passing of the Effervescent Saline Preparations of Sodium Phosphate and Sodium Sulphate, Confection of Sulphur and of Senna, Pill of Aloes and Asafetida, Tamarinds, and the Preparations of Jalap. The retention of Scammony in the name of Ipomœa makes one suspect that the reasons for deleting Jalap were not entirely pharmacological. There is a new Emulsion containing 50 per cent Liquid Paraffin and two new anthelmintics, Diphenan and Tetrachlorethylene, are described.

The list of preparations for local application has undergone many changes. The blistering agents Cantharidin and Blistering Liquid (Liq. Epispasticus) and all the plasters in company with the linseed poultice have now passed beyond the ken of the *Pharmacopœia*. New ointment bases have been described, suitable for surface action and for absorption of drugs; the emulsifying ointments prepared from the higher fatty alcohols will be a welcome change from the greasy preparations which caused such unnecessary soiling of clothes and bed linen.

There are ten official vaccines including Yellow Fever Vaccine and Typhus Vaccine; Mixed Gas-gangrene Antitoxin has been added to the list of antitoxin preparations. Antipneumococcal Serum I and II and Anti-dysentery Serum have been deleted.

Three additional diagnostic agents, Injection of Histamine Acid Phosphate, Diodone (Perabrodil), and Iodoxyl (Urosclectan-B), are now recognized.

In the therapeutic flood-tide, few will miss the substances which have been swept aside, but some will be perplexed by the presence in the *British Pharmacopœia* of certain drugs. It would be interesting to learn the reasons for preserving Krameria and Catechu, whose astringent properties are of little value except to the therapeutically destitute. Some may question the retention of Valerian, but conclude that, unlike the rose, there is something in a name. It may be justifiably concluded that the prevalence of clinical usage has alone dictated the preservation of Diamorphine Hydrochloride, Amidopyrine, and Cinchophen; for these drugs are not indispensable and can readily be replaced by substances of comparable activity and of greater safety. Unfortunately, this official recognition condones the continued use of preparations which have outlived their usefulness. It may well be, however, that in its wisdom, the British Pharmacopœia Commission has decided that if a drug is used in considerable amounts, it is better to ensure its purity and consistency by including it in the *Pharmacopœia*.

BRONCHUS, CARCINOMA OF. *N. R. Barrett, M.A., M.Chir., F.R.C.S.*

Since Graham's first successful pneumonectomy for carcinoma of the bronchus in 1933 many similar successes have been reported, and at least a few of the patients afflicted with this disease can be cured by surgical removal of the tumour. In recent years large groups of cases have been reported from various hospitals and some long-term follow-ups are now available. From these it is obvious that any patient known to have a carcinoma of the bronchus, and in whom there is no contra-indication to operation, should be treated surgically without delay.

Adrian Lambert[1] has reviewed the cases treated at the Bellevue Hospital, New York, between 1939 and 1946. There were 349 patients; 20 per cent of cases of carcinoma of the bronchus admitted were considered suitable for thoracotomy; 70 patients were explored, and of these only 25 had tumours which could be removed (7·2 per cent); 17 of these 70 patients died in hospital; and of the resectable cases 7 died in hospital; 1 patient survived 5 years. The chief cause of these gloomy figures is that the cases were not diagnosed

early enough, and the most important step in early diagnosis is radiological examination of the chest.

William F. Rienhoff[2] describes his experiences in a consecutive series of 327 patients who were referred for surgical treatment at Johns Hopkins Hospital and who were treated by operation. In 215 cases the lesion was found to be inoperable at thoracotomy, and in this group the average length of life after leaving hospital was 5 months; 112 cases were operable and the tumour was removed. Of the patients living at the present time 39 per cent have survived from 1 month to 13 years.

PNEUMONECTOMY FOR CARCINOMA OF THE LUNG (*W. F. Rienhoff*)

	No. of Cases	Total	Per-centage
Patients dying after various periods of time :—			
Less than 1 month ..	25	25	22
1 month to 6 years :			
1 month to 6 months	20		
6 months to 1 year ..	10		
1 year or more ..	6		
2 years or more ..	2		
3 years or more ..	3		
4 years or more ..	1		
5 years or more ..	1		
6 years or more ..	1		
		44	39
Patients living :—			
1 month to 6 months	12		
6 months to 1 year ..	2		
1 year or more ..	8		
2 years or more ..	5		
3 years or more ..	4		
5 years or more ..	4		
6 years or more ..	2		
9 years or more ..	2		
10 years or more ..	2		
11 years or more ..	1		
13 years or more ..	1		
		43	39
		112	100

Rienhoff stresses that the prognosis of carcinoma of the bronchus in those cases in which surgical removal is impossible, or is not attempted, is a mortality of 100 per cent, and that the figures quoted above compare favourably with the expectation of survival after surgical removal for malignant disease of the thyroid, stomach, kidney, etc.

Alton Ochsner and M. E. DeBakey[3, 4] report upon 360 patients suffering from carcinoma of the bronchus seen at the Charity Hospital of Louisiana between 1935 and 1946; 129 patients were submitted to pulmonary resection, i.e., one-third. The immediate surgical mortality in this group was caused by a certain proportion of preventable errors, but the incidence of cardiovascular complications is high and the risk must be assumed. An analysis of all patients who had been operated upon 6 months or more earlier indicated that any who survive 3 years have a very good chance of surviving 5 years. The survival rate is importantly greater when the growth is localized, and no patient who was found to have metastases at operation survived more than 3 years. Whatever analysis is made of the statistics the vital factor is early diagnosis, and the way to achieve this is routine radiography.

Frank P. Coleman[5] describes his results in 7 patients in whom the tumour had invaded the chest wall; 5 were subjected to block excision of the chest

wall and pulmonary resection; a total pneumonectomy was done in 4 and a palliative lobectomy in 1. There was 1 operative death; the patient who had a palliative lobectomy died 11 months after operation; and the remaining 3 are alive and well—6 years, 2 years, and 5 months post-operatively.

V. O. Björk[6, 7] reports upon 345 cases diagnosed and treated at the Brompton Hospital, London. Of all the patients operated upon and followed up (79), 5 per cent are alive longer than 5 years; 16 per cent longer than 3 years; 23 per cent longer than 2 years; 39 per cent longer than 1 year.

E. D. Gagnon[8] describes 508 cases admitted to the Toronto General Hospital between 1934 and 1945. Thoracotomy was performed on 86 occasions and in these resection was successfully accomplished in 49; on 5 occasions a lobectomy was done, and in this group the longest survival was 9 months. The operative mortality for the whole series was 36 per cent, but in recent times this has been reduced to 6·6 per cent (1946 figures). A quarter of all the pneumonectomies are alive to-day and apparently free from disease, their survivals ranging from 7 months to 8½ years.

REFERENCES.—[1]*Amer. J. med. Sci.* 1948, **215**, 1; [2]*Ann. Surg.* 1947, **125**, 541; [3]*J. Amer. med. Ass.* 1947, **135**, 321; [4]*Ann. Surg.* 1947, **125**, 522; [5]*Ibid.* **126**, 156; [6]*Int. Abstr. Surg.* 1948, **86**, 243; [7]*Acta chir. scand.* 1947, **95**, suppl. 123; [8]*Cancd. med. Ass. J.* 1948, **58**, 25.

Philip Ellman, M.D., F.R.C.P.

R. C. Brock,[1] E. D. Churchill,[2] and W. A. Henkin[3] stress the urgency of early diagnosis for the following reasons: (1) It is the second commonest form of malignant disease in the male; (2) The expectation of life from the time cases are first diagnosed and treated is estimated by Henkin at 8 months and by Brock at 6 months; (3) The results of pneumonectomy for localized disease in the early stage are proving increasingly favourable.

The importance of bearing in mind the possibility of bronchial carcinoma is illustrated by R. H. Jaffé's[4] series of 100 autopsy cases in which 47·5 per cent of cases were wrongly diagnosed over a period of three years, but only 30 per cent in a second three-year period, after misdiagnosed cases were presented repeatedly at clinical conferences.

Symptomatology.—Brock, Churchill, and Henkin are all agreed that *persistent cough with or without blood-streaked sputum* is a presenting symptom in at least half the cases. In fact, Brock suggests that persistent staining is almost diagnostic in a male of the 40–60 age-period.

The next most important group of symptoms are those due to respiratory infections consequent upon bronchial obstruction. In this connexion Brock and Henkin warn against the ominous character of "*slowly-resolving and recurrent pneumonias*", and in all such cases Churchill insists upon the importance of serial radiographs until the lung fields are completely clear.

Henkin lays great stress on the neglected triad of "*fever, leucocytosis, and anæmia*". Thus, out of 36 autopsied cases in his series, fever (above 99° F.) was persistently present at some time during the day in no less than 28, and of these 8 had a typical swinging 'septic' curve. In 16 cases in which multiple white-cell counts were performed, 8 had counts persistently above 10,000 per c.mm. and only one had cell-counts persistently below 10,000. In this connexion he draws attention to the fact that leukæmoid counts (above 30,000 per c.mm.) are frequently associated with bony metastases. A red-cell count of less than 4,000,000 was present in 24 of 33 cases who had repeated estimations.

Pain in the chest is present at some time in 50–60 per cent of cases, but when it occurs as a presenting symptom it suggests a grave prognosis, since it is usually due either to pleural involvement or to involvement of nerves by mediastinal deposits, either of which occurrence contra-indicates surgical intervention.

Wheezing is a common presenting symptom, Churchill estimating that it occurs in 10–15 per cent of cases. He shows how, although often transient, it differs from the wheeze of asthma by its unilateral character, of which even the patient is sometimes aware. The adage that " all is not asthma that wheezes " is indeed appropriate here.

Joint Changes.—Pulmonary osteo-arthropathy with clubbing is usually a late manifestation, but it is not usually realized that a ' rheumatoid ' type of arthritis with joint pain, swelling, and even effusions may be the presenting symptom of an otherwise ' silent ' intrathoracic neoplasm. P. Ellman[5] has briefly recorded 3 such cases, and it is a matter of great interest that in some of these cases surgical resection results in a dramatic subsidence of the joint condition.

Diagnosis.—

Radiological Diagnosis.—X-ray examination in various planes may be an indispensable preliminary to diagnosis—fluoroscopy to reveal abnormalities in respiratory dynamics, films to supply a permanent record for comparison. Nevertheless, radiological diagnosis alone is a highly fallible procedure. J. W. Olds and B. R. Kirklin,[6] who reviewed 206 microscopically verified cases, found that the definite diagnosis of bronchial carcinoma had only been suggested by the radiologist in 60 per cent of these cases.

Churchill points out that whereas the majority of cases originate centrally in a main bronchus, it is of great importance not to dismiss spherical peripheral opacities as metastases, especially where careful examination fails to reveal a primary source. He suggests that this examination should include pyelography to exclude a silent hypernephroma.

Brock advises *barium examination of the œsophagus* for every case in order to exclude distortion or narrowing which provide an important indication of mediastinal metastases.

Both Brock and Churchill are agreed that *bronchography* is often inconclusive and merely complicates further radiological study, and this is in keeping with the reviewer's experience, but *tomography* may be helpful and may show bronchial *distortion* and *obstruction*.

Differentiation from Tuberculosis.—Churchill warns that some cases of adult tuberculosis characterized by dense fibrosis may be confused with neoplasm, especially where the bacteriological findings are negative. On the other hand it is worth noting that Jaffé's series included among those wrongly diagnosed 5 cases with tubercle bacilli in the sputum. In cases where doubt persists, diagnostic lobectomy may be advisable, for " such a biopsy oftentimes proves to have been a remarkably effective method of treating the tuberculosis before cavitation is established ", says Churchill.

Bronchoscopy.—This is an invaluable early diagnostic procedure and essential as a method of obtaining a biopsy and assessing operability; 30–40 per cent of neoplasms are so situated that they cannot be reached by the biopsy forceps, and indeed when some segments of the upper lobe are involved, the surgeon may suspect inaccessibility. Nevertheless, even in these cases the bronchoscope is invaluable as a means of obtaining *bronchial secretion* from the affected area. P. A. Herbut and L. H. Clerf[7] made cytological examinations of bronchial secretion from 30 consecutive cases of bronchial carcinoma: 22 of these showed cancer cells, yet biopsy specimens showed cancer in only 11 cases. More noteworthy still is the fact that 7 cases with ' positive ' bronchial secretion had negative bronchoscopy.

Treatment.—Improving results from *lung resection* have not been paralleled by palliative measures. Henkin estimates the average survival of cases treated by *irradiation* to be only six months more than the untreated, but stresses that great (if temporary) symptomatic improvement follows.

C. P. Rhoads[8] states that *nitrogen mustards* may be expected to produce transient regression and symptomatic improvement in some 50 per cent of cases.

REFERENCES.—[1]*Brit. med. J.* 1948, **2**, 737; [2]*J. Amer. med. Ass.* 1948, **137**, 455; [3]*Ann. intern. Med.* 1947, **27**, 243; [4]*J. Lab. clin. Med.* 1935, **20**, 1227; [5]*Lancet*, 1947, **1**, 464; [6]*Amer. J. Roentgenol.* 1940, **44**, 357; [7]*J. Amer. med. Ass.* 1946, **130**, 1006; [8]*Ibid.* 1948, **136**, 305.

BURNS IN CHILDREN. *R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.*

Brenda Morrison, in an exhaustive study of 31 badly burnt and scalded children, correlates the symptomatology with the hæmatological data. She concludes that the main cause of illness and death in the early stages is the reduction of blood-volume by plasma loss, and that early and adequate replacement by transfusion is essential for recovery. The physical signs of reduced plasma-volume are thirst, peripheral vaso-constriction, drowsiness, restlessness of a spasmodic type, and eventually mental confusion and loss of consciousness. These signs are specific indications for intravenous therapy and cannot be disregarded. Hypotension is a late sign and treatment must not be delayed pending its appearance.

She finds the hæmatocrit value is more sensitive than the physical signs, as an index of fluid loss. She shows that up to 30 per cent of plasma-volume may be lost before clinical deterioration is obvious, and death probably occurs when 60 to 70 per cent of plasma has been lost. She considers that the margin of safety is greatly increased if hæmatocrit data are used in assessing plasma loss.

During the second 24-hour period "toxæmic" signs develop. These are sustained temperature, with hyperventilation, moderate but sustained hypertension, and nervous signs suggesting raised intracranial pressure. While the cause of these "toxæmic" signs is obscure, she finds clinical and post-mortem evidence of cerebral œdema in the most severe cases, which could not be attributed to the over-administration of intravenous fluids, because it may be found in inadequately resuscitated and unresuscitated cases. Hypotension occurs both during and after the administration of plasma and may persist for weeks.

During the recovery period, secondary infection and wasting are the trouble and are interrelated. She stresses the maintenance of good morale and advises the avoidance of painful dressings and treatment in this connexion.

The blood-urea did not rise very high and was normally associated with poor fluid intake when elevated.

Care must be taken in the use of sulphonamides on burnt areas because of the rapidity of their absorption in the first two days.

A leucocytosis of 30,000 to 40,000 occurs within the first few hours, subsiding gradually, to rise again with secondary infection.

Convulsions occurred from three causes—circulatory inefficiency from untreated plasma loss, hypertension during plasma and serum reactions, and a central disturbance of unknown actiology during the "toxæmic" phase.

She finds saline solutions of little use in replacing fluid, but must be given in addition to plasma when the urine output is low and the child cannot drink.

This paper is important in that it is a careful study of a common cause of death by accident in childhood. It points the way to adequate therapy by fluid replacement in burnt children.

REFERENCE.—[1]*Arch. Dis. Childh.* 1947, **22**, 129.

CAPILLARY FRAGILITY. *Una Ledingham, M.D., F.R.C.P.*

Increased fragility is common in diseases such as hypertension and diabetes, the cause being uncertain but not connected with deficiency of vitamin K, P, or C, or with reduction of platelets. *Rutin* is offered as a cure for such fragility

states, but its value is in doubt. Levitt et al.[1] discuss the problem as a whole. Capillary fragility manifests chiefly as retinopathy, especially where hypertension co-exists. Joslin's experience is quoted, where the incidence of retinopathy was 4 per cent of all diabetics, over half of whom showed skin capillary fragility. In 12 well-stabilized diabetics with marked retinal changes administration of rutin resulted in small improvement, no greater than is seen in controlled diabetics without the drug. Therefore no directly curative virtue can be attributed to rutin, though experiments should continue.

REFERENCE.—[1]*Amer. J. med. Sci.* 1948, **215**, 130.

CARDIAC. (*See also* HEART.)

CARDIAC INFARCTION.

William Evans, M.D., D.Sc., F.R.C.P.

Pain.—Since the interpretation of pain in the chest is often difficult, great advance would be achieved if a means were available for separating by objective criteria those instances which are of cardiac origin. Physical examination, radiology of the heart, and electrocardiograms cannot be interpreted in terms of functional capacity, and the therapeutic test with nitroglycerin is not always specific. H. J. Stewart, E. L. Horger, and C. W. Sorenson[1] have given their experience with the anoxæmia test as an implement of diagnosis. They preface their observations by saying that in one series of cases with a history of angina the electrocardiogram was normal in 25 per cent, and in another series of 150 patients it was normal in one-sixth or them. The authors emphasized that the presence of a normal electrocardiogram did not rule out angina pectoris. The following statements were included in their deductions of the results obtained. In none of the 26 normal subjects was a positive electrocardiographic response recorded. The anoxæmia test gave electrocardiographic evidence of coronary insufficiency in 45 per cent of the group with typical angina, compared with 13 per cent of the group with atypical pain. When pain was included, the test gave evidence of coronary insufficiency in 73 per cent of the group with angina, and in only 40 per cent of the group with atypical pain. Although only 13 per cent of the atypical cases had positive electrocardiographic changes with anoxæmia, 27 per cent experienced pain, which was approximately the same as the pain in those with typical angina; this suggests the possibility that pain of an origin other than coronary disease may be aggravated by anoxæmia. In 32 per cent of the patients with symptomatically and therapeutically typical angina pectoris this test failed to elicit changes, and in 71 per cent of the group with atypical pain the results were equivocal. If a patient has typical angina pectoris clinically, their experience led them to accept the clinical impression, although the anoxæmia test was negative.

Diagnosis.—W. Dressler and H. Roesler[2] have examined the significance of high T waves in the electrocardiogram in the early diagnosis of cardiac infarction. Twenty-seven instances of cardiac infarction were studied, in which the first electrocardiogram was taken as early as one and one-quarter hours, and not later than twelve hours, after the onset of symptoms. Follow-up tracings were obtained in all but two of these cases. In 25 cases the earliest electrocardiographic signs of infarction were high T waves, the majority of which became inverted in the healing stage of infarction. In most of the cases the high T waves were no longer present twenty-four hours after the attack. In 5 instances where the T waves persisted for several days, early mortality was as high as 60 per cent, as compared with 14 per cent in the cases where the high T waves underwent regression within twenty-four hours.

Treatment.—A report by I. S. Wright, C. D. Marple, and D. F. Back[3] summarizes the results obtained by a preliminary statistical analysis of the first 800 cases studied by the Committee for the evaluation of anticoagulants in the treatment of coronary thrombosis with cardiac infarction. In the analysis the incidence of death and of both thrombo-embolic and hæmorrhagic complications has been compared in a control series of patients who received anticoagulants (dicoumarol, heparin, or both) in addition to conventional therapy. The composition of the two groups was judged to be essentially the same. The death-rate was 24 per cent in the control group and 15 per cent in the anticoagulant group. The proportion of patients developing one or more thrombo-embolic complications was 25 per cent in the control group and 11 per cent in the anticoagulant group. The incidence of hæmorrhagic manifestations was 7 per cent higher in the specially treated group.

REFERENCES.—[1]*Amer. Heart J.* 1948, **36**, 161; [2]*Ibid.* 1947, **34**, 627; [3]*Ibid.* 1948, **36**, 801.

CARDIOSPASM.

N. R. Barrett, M.A., M.Chir., F.R.C.S.

In an important paper Wooler[1] describes the present knowledge in relation to cardiospasm. The disease may start at any age, and in his series the patients ranged from nine months to seventy-three years. At first cardiospasm affects the whole lower segment of the œsophagus between the aortic arch and the cardia and is associated with greatly increased peristaltic activity in the region; this activity may continue for half an hour or more until the contents have been pressed onwards into the stomach. This first stage may last for months until the œsophagus appears to tire of its increased efforts and to become dilated, tortuous, and paralysed. In any treatment which remedies this lesion, or in the cure which occasionally occurs spontaneously, the sequence of events is reversed and the œsophagus regains normal mobility and shape in the reverse order to which they were lost. Wooler summarizes the effects of treatment as follows:—

Total number of cases	
Treated with a Negus hydrostatic dilator	
Good result ..	
Bad result ..	
Under observation	
Treated by Heller's operation	
Good result ..	
Under observation	
Treated by Mikulicz's operation	
Good result	
Symptoms returned	
Refused treatment ..	

Great differences of opinion still exist as to the proper method of treatment. A. Ochsner and M. E. DeBakey[2] advised œsophago-gastrostomy, but although this relieves the obstruction many patients are left with distressing regurgitation of gastric contents, particularly when they are lying down (Maingot[3]). Barrett, who has performed a considerable number of œsophago-gastrostomies, has given up the operation because most of the patients developed peptic ulceration of the œsophagus within a year of the operation, and although in some the condition was relatively symptomless, in the majority there was a serious degree of secondary anæmia due to persistent bleeding.

Kay[4] describes his experiences in 17 patients treated by transpleural cardioplasties; 3 were of the Finney type and the others were performed in a manner similar to a Heineke-Mikulicz pyloroplasty. These patients were all stated to be benefited by the operation, but the author makes no statement as to the *late results* which, as Barrett has shown, are the crux of the whole matter. Similarly Gill and Child[5] report favourably upon 8 œsophago-gastrostomies,

but these authors admit that although the act of swallowing as shown by fluoroscopy was remedied, "some untoward symptoms referable either to swallowing or to the upper gastro-intestinal tract continued"; they also state: "We are at a loss to explain the persistence of symptoms . . ."

It appears that the position as regards treatment to-day is that in the early cases a few dilatations, performed with a Negus hydrostatic dilator, will generally cure the disease. It follows that there is no place for mercury bougies, barbarous instruments which long since should have been relegated to the museum, and no necessity for laparotomy with dilatation of the cardia after opening the stomach. Advanced cases respond best to Heller's operation.

REFERENCES.—[1]*Thorax*, 1948, **3**, 53; [2]*Arch. Surg.* 1940, **41**, 1146; [3]*Post Grad. med. J.* 1944, **20**, 278; [4]*Ann. Surg.* 1948, **127**, 34; [5]*Surgery*, 1948, **23**, 571.

CEREBROSPINAL FEVER.

(*See* MENINGOCOCCOSIS.)

CHANCROID.

T. Anwyl-Davies, M.D., F.R.C.P.

Treatment with Streptomycin.—Chancroids are susceptible to the action of sulphonamides, penicillin, and streptomycin. The last had proved successful in the treatment of experimentally produced chancroidal lesions, and H. C. Hirsch and S. R. Taggart[1] have now reported for the first time the clinical effect of streptomycin. They treated 15 patients: 14 received 1 g. intramuscularly of streptomycin per day in divided doses every four hours (one received 2 g. daily) until the lesions healed, which they did in from 5 to 25 days. Eleven patients healed in less than 2 weeks, and no toxic effects occurred. The authors consider the sulphonamides to be the drugs of choice on account of lower cost and simplicity of administration, but that penicillin or streptomycin may be used when the patient is sensitive, or when the infection is resistant, to the sulphonamides.

REFERENCE.—[1]*J. ven. Dis. Inform.* 1948, **29**, 47.

CHRONIC AGED SICK.

(*See also* OLD AGE.)

Marjory W. Warren, M.R.C.S., L.R.C.P.

Introduction.—During the present century there has been a steady increase in the number of persons living over 60 years of age and this number is still increasing—*see* table below.

YEAR	MEN	WOMEN	TOTAL
1901	1,071,519	1,336,907	2,408,426
1939	2,511,200	3,197,400	5,708,600
1944	2,737,000	3,590,000	6,327,000
1947	3,189,000	4,243,000	7,432,000

The increase in three years is therefore 1·1 millions.

This age shift in the population is likely to be permanent or even to increase. At the beginning of the century the ratio of persons over 60 years of age to the total population was 1 to 18, in 1947 it was 1 to 5·5.

This increase in the numbers of elderly people has been brought about by the advance of medical science, including the discovery of insulin, chemotherapy, and antibiotics, and by the progress of preventive medicine and industrial welfare during the past fifty years.

Morbidity increases with advancing years, and as the elderly are more liable to suffer from diseases of a degenerative nature or from multiple pathology, and as they are more accident prone than the young, so the numbers of sick amongst the elderly must increase. As repair of injuries in the old is slow,

and recovery from degenerative lesions only partial, the majority of such persons, when ill, fall into the groups of chronic or long-term sick.

Changes in the pattern of the social life of this country brought about during this century have materially added to the needs of the elderly. Smaller families and the greater migration of members of the family unit from the home, difficulties in housing conditions, a general shortage of nursing and domestic help, and a lessening of filial responsibilities have all played their part in increasing the isolation and loneliness of ageing people.

Of recent years, therefore, many more elderly persons have come to need and to demand care and treatment either in hospital or other suitable accommodation.

It is well known to medical and to social workers who are interested in the subject of gerontology that there are a great many patients in their own homes who need and would benefit from the medical treatment and social care which should, in the first instance, be undertaken in hospital. Such patients are known to be living, or existing, in conditions which are totally inadequate for their comfort or happiness and in circumstances where a remediable condition is rapidly deteriorating into one which is irremediable. Such conditions ultimately call for admission to hospital for a much longer period of time than would have been needed if treatment had been implemented earlier: indeed, such delay in treatment may result in need for permanent care.

The needs of the long-term sick fall under two headings: (1) medical, and (2) social, and these are often intimately related one with the other.

In the past there has been too little interest in, or treatment of, these patients. Lack of essential needs has been and still is responsible for much suffering, misery, frustration, and hardship for the afflicted and for their relatives and friends, and a great waste of hospital bed accommodation, nursing and other personnel, and home facilities, creating serious economic loss to the country as a whole. To-day the medical care and welfare of the long-term aged sick, in their increasing numbers, is a major problem and calls for a critical survey of present conditions. It is a challenge to medicine which can only be met by considerable reform and immediate action.

Definitions. As the whole subject of geriatrics is comparatively new, and as there exists still in the minds of many medical as well as lay persons a good deal of confusion as to the difference between geriatric and chronic sick, the definitions given below should help to clarify these terms.

Geriatrics.—This word was first used by Nascher in America in 1909. Derived from the Greek words "geros" and "iatrikos" it signifies the medical treatment of conditions associated with old age and ageing. It is therefore not confined to the care of long-term illness, although admittedly a considerable number of such patients will be included in the group.

Gerontology.—A less familiar term with a wider connotation, includes the study of *all* aspects of ageing—medical, psychological, social, economic, and others.

Chronic Sick.—A term which should be abandoned in favour of the phrase long-term sick—and refers to long-term sick found in all groups of patients and in all age groups from infants to the very old.

By these definitions it is clear that the geriatric service will accept appropriate new patients from outside the hospital (either from their own homes or from Homes) and may also accept some transfers from other departments *after consultation*. These transfers will probably be mainly by request from the surgical units, as after the geriatric service has been established it is to be presumed that generally those patients eligible for, but not admitted into,

the geriatric department in the first instance will have been admitted elsewhere by request of another unit, who will wish to see the patient through his illness.

Present Conditions: Disadvantages.—At the present time the long-term elderly sick, apart from those who can be cared for at home, are being treated mainly in: (1) Hospitals or Institutions for the chronic sick; (2) Blocks for chronic sick in non-teaching hospitals; (3) Nursing Homes. Such accommodation frequently offers no opportunity for classification of patients—and is often required to take more patients than should be accepted, with all the attendant evils of overcrowding. In such accommodation it is not uncommon to find, with the elderly, younger long-term sick, mental defectives, and in some cases even children. In such places there is little scope for active treatment, and no opportunity to undertake full investigation. Wards are often old-fashioned and lacking in all the modern amenities for easy nursing and congenial medical work. Resultant upon these conditions such patients seldom attract the best medical or nursing personnel and patients come to regard their conditions as hopeless from the onset.

At present there is no real co-ordination between the various authorities and no integrated service for the elderly sick. This results not only in delays in admission but also in admission to wrong accommodation, e.g., hospital beds are blocked by patients who on medical and/or social grounds need vacancies in homes for the elderly and as a direct result the hospital cannot admit patients from their own homes who urgently need medical care—and so it is not uncommon to find that emergencies occur and elderly persons with treatable medical conditions are admitted into homes without investigation and where no facilities for treatment exist.

Suggestions for Reform.

1. Large institutions or hospitals for chronic sick should be replaced as soon as possible by more modern arrangements. The disadvantages of this former type of accommodation have already been referred to.

2. A service of gerontology should be developed which will include the overall medical treatment and social care of the elderly in their own homes, in hospital, and in other suitable accommodation.

3. The principles should be accepted that the responsibility for the care of all long-term sick should be shared, but that in the interests of patients there should be medical continuity.

4. The service of gerontology should therefore be responsible for the elderly long-term sick as well as the acute or short-term elderly sick, but should *not* accept the long-term sick of the younger age-groups, of children, or psychiatric patients (that is those who are legally certified under the lunacy acts, including mental defectives).

Service of Gerontology.—The B.M.A. has set up a special committee on the "Care and Treatment of the Elderly and Infirm" and has endorsed the suggestion of a co-ordinated medical service for the elderly (*see* report published by the B.M.A., Section IV).

The service, as outlined in the B.M.A. report, for the medical care and social needs requires three types of accommodation: (1) The geriatric unit—part of the general hospital; (2) Long-stay annexes associated with the general hospital; (3) Residential homes.

The Geriatric Unit.—Comprises wards in a General Hospital, reserved exclusively for elderly patients, all of whom are undergoing investigation or active treatment and rehabilitation, so that in due course they may be discharged from such wards, either to their own homes, or, after classification, to other appropriate accommodation.

Long-stay Annexes.—Provide, under the medical supervision of the geriatric department, accommodation and nursing care for really irremediable elderly patients, who after full investigation and treatment in the geriatric department, show no promise of further improvement. These annexes may be either within the curtilage of the hospital or outside it, but, wherever situated, should remain directly under the medical supervision of the geriatric department.

Resident Homes.—Provide accommodation for elderly persons in need of reception, but not of nursing care. The residents in these Homes should advisedly be supervised as to their medical needs, when necessary, by the staff of the geriatric department.

Geriatrics. The subject of geriatrics has come to the fore recently and there is much in favour of creating within a large general hospital a geriatric unit for the investigation and treatment of elderly patients. As the success of such a unit must depend upon the interest and experience of the physician-in-charge, and as at present there are comparatively few who have had such experience, it would seem a wise measure to create experimental units in certain areas where suitable staff is available.

In these centres study of the subject can be made, different methods can be compared and those who are interested in geriatrics can be trained. Such units should get to work as quickly as possible, and in order to improve the service, should be given every possible help and assistance in development.

Such a geriatric unit, being an integral part of a general hospital, can call upon the services of all specialists when necessary and share, with other departments, the amenities of all ancillary services, should be of equal standing with other departments, and should plan a definite service and a precise role in the hospital practice.

The advantages of treating the elderly sick in such a unit are:—

1. That the patients more often make congenial contacts with each other, and definitely stimulate each other in a healthy spirit of rivalry, helpful to their rehabilitation, and in a way which they do not do when scattered in other wards.
2. That staff can be trained in the best methods of caring for and treating elderly patients.
3. That the wards can be equipped for their special needs.
4. That study of reactions and comparison of methods can be undertaken for the mutual benefit of patients and staff.
5. That such a field offers the best opportunities for research.

The Geriatric Unit.—In order to keep the geriatric unit working as efficiently as possible, it is obvious that there must be adequate opportunity for discharge either to the patient's home or elsewhere.

Regular consultations with the almoner are essential in fostering home conditions and helping in cases where social aid is needed. Such help may be a building up of the patient's home conditions—by the addition of domestic and/or district nursing service and by sundry help from the voluntary services and/or statutory bodies—or it may be in finding or choosing a Home when the social conditions demand this. Thus adequate Home vacancies are needed.

Likewise there must be a sufficiency of beds in the long-stay annexe, but a careful watch must be kept on this type of accommodation to ensure that only those who are really suitable for such long-stay annexe are transferred there. It is obvious that abuse of such accommodation, which might at times be a temptation, would lead to a repetition of to-day's unsatisfactory conditions.

Into the geriatric unit will be admitted, not only new patients, but all transfers to the geriatric service, as all must be fully screened, medically and socially, before treatment (medical and/or social) can be correctly worked out.

Within the service there must be classification and continuity of treatment.

Classification can be brought about by wards set aside for different purposes :—

1. Cot-bed wards—for those who need or will benefit by such beds.

2. Open-bed wards—with a section for incontinent patients.

3. Wards with low beds and a day room, for ambulant patients, awaiting discharge or transfer to a Resident Home. Such a ward offers educational facilities to an elderly person who is about to enter a Home permanently.

Continuity is essential for good treatment. In the past, much of the failure to treat these long-term sick patients has been due to lack of continuity and therefore to lessening of responsibility for their care.

The medical treatment and social care of the elderly sick should be undertaken by a team of workers if the best results are to be obtained. Such a team should consist of: (1) Medical staff; (2) Nursing staff of various grades and nursing orderlies; (3) The almoner, a fully trained medico-social worker, using all agencies, voluntary and statutory, as occasion demands; (4) Physiotherapists; (5) Occupational and diversional therapists, together with the services of a dietitian and chiropodist.

Functions of a Geriatric Unit.

1. To accept new geriatric patients whether short-term or long-term, and selected patients transferred from other wards.

2. Investigation and medical treatment of geriatric patients admitted as in-patients and seen as out-patients.

3. Responsibility for the medical supervision and nursing care of patients in the long-stay annexes.

4. When invited, the medical supervision and advice in residential homes concerning the care and welfare of the aged.

5. Education in the principles of treatment and care of the elderly sick and infirm.

6. Research into the conditions, medical and social, which affect elderly persons.

This concept does not of course postulate the pre-emption of all patients to the geriatric wards, but does presuppose the setting aside of certain wards where such patients may enjoy continuity of treatment and be able to be grouped for rehabilitation. Special emphasis is laid on the role of physiotherapy, both in preventing chronicity, and as the outstanding factor in the rehabilitation of elderly patients.

Co-ordinated Service.—There is experience to show that in addition to being the most economic method (with the minimum waste of staff and accommodation) such a service gives the best results to patients. It also provides the most interesting and satisfying conditions to members of the therapeutic team and at the same time offers the widest experience, both educational and clinical, and the best opportunities for research into the disease, habits, behaviour, and medical and social care of the elderly.

In order to create and maintain such a well-integrated service it is necessary to have very close liaison between the two statutory bodies concerned, i.e., the Regional Hospital Board and the Local Authorities. Such a liaison should take the form of a committee with executive powers comprising personnel who are interested and knowledgeable in the needs of the elderly sick and infirm.

At the present time it is advisable to utilize all the service and resources of both voluntary and statutory bodies. Both should set up experimental homes and units so that all methods can be given a full trial before there is any attempt to standardize.

Principles of Treatment.—It would be impossible and unprofitable to attempt, even briefly, to outline the various forms of treatment required for the different

conditions found amongst geriatric patients, but the best results can only be obtained if the following principles of treatment are implemented :—

1. Appreciation of the necessity for *complete investigation*, medical and social.
2. Appreciation of the necessity for *full treatment*, medical and social.
3. Appreciation of the need for the patient's confidence and co-operation, which must be won and jealously guarded. Without these no treatment can fully succeed.
4. Understanding of the therapeutic value of happiness and hopefulness in treatment.
5. Knowledge of the part which occupation and activity play in maintaining mental alertness and interest in improvement.
6. Restoration of as full function as possible with maintenance of the maximum independence of the patient for his personal needs.
7. Recognition of the need for active treatment for the prevention of secondary conditions. Such conditions, if they are allowed to develop, will cause not only additional pain and discomfort to the patient and much extra work for the staff, but will also hinder progress and may prevent the degree of recovery which would otherwise have been possible and probable e.g., pressure sores, stiff joints, contractures, obesity, loss of morale, apathy and disinterest, with incontinence, etc.
8. Need of care in the use of drugs which will ensure adequate rest and/or relief of pain, and yet avoid over-sedation, which in the elderly is one of the commonest single factors preventing progress in rehabilitation.
9. The importance of developing a follow-up and out-patient department. Such a department is invaluable in maintaining a patient in his own home when discharged, and in treating patients who would otherwise undoubtedly deteriorate and need treatment as in-patients.
10. Creation of an atmosphere of encouragement of all members of the therapeutic team to work harmoniously together towards the recovery of the patient and his discharge home.

Conditions for Treatment.—Although conditions for treatment of geriatric patients will in many instances be far from ideal for some years to come, the following conditions should be aimed at :—

1. Adequate staff, including all essential members of the therapeutic team already referred to.
2. Sufficient attendant help to give a ' valet service ' to patients who require help in dressing, going to toilet, etc.
3. Standard bed space with no overcrowding.
4. Easy-nursing high beds, except for patients who get up and who need low beds of a similar modern design.
5. Sufficient over-head pulleys and end-of-bed pulleys for the use of patients confined to bed. A supply of springs and slings, for the use of patients, to aid in physiotherapy.
6. Ward equipment equal to that of general medical wards, as the needs will be much the same.
7. Good lighting, bearing in mind the fact that physiologically visual acuity diminishes with advancing years.
8. Avoidance of all unnecessary steps, corners, or awkward passages.
9. Day-room accommodation for patients getting up for long periods of time.
10. Sufficient arm-chairs of suitable *and varied* types for the use of patients allowed up.
11. Rails for the support and help of patients in corridors, toilet, etc.
12. An ample supply of walking-sticks with rubber ferrules.

Summary.—

1. The problem of adequate care and treatment of elderly sick presents a major problem to health administrators and a challenge to medicine.

2. The conception of a fully co-ordinated medical and social service including a geriatric unit based on a general hospital offers a solution.

3. Such a service should be tried in special areas where staff trained in gerontology is available.

4. Such a service is based on : (*a*) Co-ordination of needs ; (*b*) Classification of patients ; (*c*) Continuity of medical care.

5. Such a service can undertake in addition to medical treatment : (*a*) Rehabilitation and resettlement of the patient ; (*b*) Research into medical and social conditions of old age.

6. Such a service working as a team with appropriate ancillary staffs can build up : (*a*) Efficiency of service for patients ; (*b*) Education of medical and nursing personnel ; (*c*) Experience of the subject as a whole.

7. It is claimed that such an integrated service must offer to patients a better service than that which can be given in a hospital for chronic diseases. In the hospital for the chronic sick both staff and patients are isolated from the more academic atmosphere of the general hospital. Under such conditions indolence is liable to develop from lack of facilities which exist in the general hospital, but which are too costly to justify duplication.

8. Finally, it is obvious that interest in and development of the long-stay annexe is essential to the well-being of the geriatric unit. It is equally true that as the geriatric unit will inevitably need vacancies in the Residential Homes it is important that the unit seeks a very close liaison with such Homes.

PLATE IX

Fig. A.—a, Aorta, ligamentum arteriosum, and part of left pulmonary artery. The upper surface of the aorta at the level of the insertion of the ligament shows the external concavity characteristic of the appearance in coarctation of the aorta. The patient was a man 51 years of age with coarctation of the aorta, who had died of bacterial endocarditis of a bicuspid aortic valve. b, The interior of the aorta in the vicinity of coarctation in a man 29 years of age. A probe runs through the narrow opening in the diaphragm-like structure which creates the aortic narrowing. The arrow of the probe lies in the aorta below the level of the coarctation. It is in contact with a corrugated intimal patch. The latter evidently results from a reaction to a jet of blood striking the wall after passing through the narrowed zone. The intimal patch is named a "jet lesion". c, Photomicrograph of a section through the jet lesion shown in b and the adjacent normal aortic wall. The normal aortic tissue lies in the left xtremity of the photomicrograph. The rest of the field shows intimal fibrosis and at phy and loss of elastic tissue in the underlying media. (Verhoeff's elastic tissue stai counter-stained with van Gieson's connective-tissue stain. × 8.)

COARCTATION OF THE AORTA. *N. R. Barrett, M.A., M.Chir., F.R.C.S.*

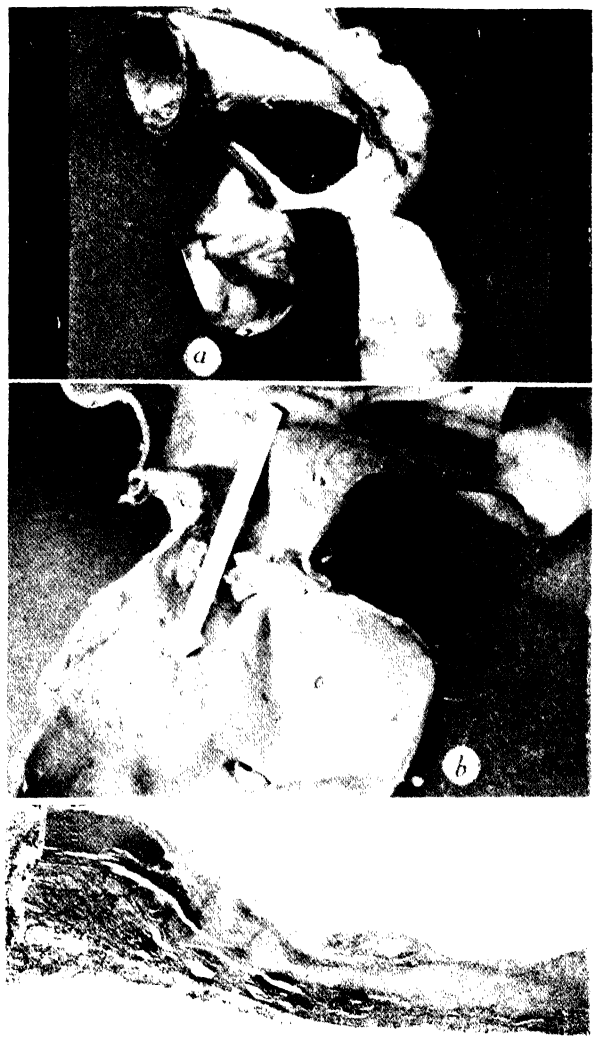
The *Proceedings of the Staff Meetings of the Mayo Clinic* dated July 21, 1948, consisted of a symposium of 9 short papers upon the subject of coarctation of the aorta. These stress new information and contain a very full list of references.

Edgar A. Hines states : "It was 100 years ago, in 1848, that the first clinical diagnosis of coarctation of the aorta was made. It has been considered as a rare anomaly of the aorta about which little could be done. Consequently, coarctation of the aorta has received only casual interest and attention from the medical profession until recently . . . This change has resulted . . . from the development of surgical methods of treatment which offer some, if not all, patients who have this often-times dangerous and life-shortening disease, a reasonable prospect of cure and a better chance to live a normal life."

History.—Norman A. Christensen gives a brief historical review of the subject in which the following are the chief points. Morgagni was the first

PLATE IX

COARCTATION OF AORTA



Plates IX XIV and Fig. 8 reproduced from the "Proceedin of the Staff Meetings of the Mayo Clin

PLATE X

COARCTATION OF AORTA—*continued*

(J. E. Edwards, N. A. Christensen, O. T. Clagett, and J. R. McDonald)



man, in 1770, to describe the condition, and Paris (Evans[1] and Abbott[2]) in 1789 and 1791 gave an account of the pathology. In 1827 Meckel (quoted by Flexner[3]) reported a case in which rupture of the right auricle had occurred; he also showed the collateral circulation and mentioned notching of the ribs for the first time. Legrand (quoted by Flexner) diagnosed obstruction of the aorta in 1835; but Maud Abbott's classical papers upon the clinico-pathological aspects were not written until nearly 100 years later. Scheele (quoted by Flexner), in 1870, demonstrated the delay of the femoral arterial pulsations, and in 1892 Potain (quoted by Flexner) described hypertension as occurring in the upper part of the body. The first successful resection of the coarctation with reconstitution of the aorta by direct anastomosis was performed by Crafoord[4] on Oct. 19, 1944 (Dcterling,[5] Blalock and Park,[6] Gross and Hufnagel,[7] Owings and Hewitt[8]).

Pathology (*Plates IX–XI*).—The pathological considerations are described in the symposium by Jesse E. Edwards and others, who make these observations: The classification of types of coarctation which is in common usage is that of Bonnet,[9] who distinguished between infantile and adult varieties. In the former the coarctation lies between the ductus arteriosus and the left

PLATE X

Fig. B.—Photomicrographs stained with Verhoeff's elastic tissue stain and counter-stained with van Gieson's connective-tissue stain. a, Longitudinal section (× 3½) through a segment of aorta removed surgically during the operation for coarctation of the aorta. The proximal portion of the segment lies to the left. The ligamentum arteriosum inserts into the proximal portion of the lower wall. An intimal aortic atheroma lies just proximal to its insertion. Distally, the superior wall of the aorta shows a curtain-like protrusion of the media into the lumen, which is materially narrowed by this phenomenon. The intima overlying the distal surface of the medial curtain is thickened, appearing as a triangular mass of tissue. b, Higher magnification (× 12) of the medial curtain and the overlying intimal tissue. The intimal overgrowth is composed largely of collagen laid down in concentric layers. At the base of the tissue, near the media, the intimal tissue contains fibres of elastic tissue, in addition. c, The anterosuperior portion of the aortic wall (× 8½) at the zone of coarctation in a female infant 5 months of age. The specimen is viewed from behind forward, so that the segment of the aorta distal to the curtain lies to the left; that proximal, to the right. There is a curtain-like protrusion of the media into the lumen of the vessel. The medial curtain is composed almost exclusively of smooth muscle. There is little, if any, elastic tissue in it. The intimal reactive fibrous tissue seen almost consistently in older patients (a and b) is absent in this infant.

The specimens illustrated in *Fig. B* support the concept that the primary alteration in coarctation is a curtain-like protrusion of the media into the lumen. The overlying intimal tissue seen in adolescence and adult life is acquired as a secondary lesion.

subclavian artery. The adult type includes cases in which the stenosis lies either at the level of the aortic insertion of the ductus or immediately beyond. In the infantile type the ductus is usually patent, in the other it is usually closed. This classification omits a number of other varieties of coarctation which have since been described. Edwards stresses the point that patency or otherwise of the ductus is chiefly important because if the ductus is closed the pulmonary arteries are normal, but if it is open there are morphological changes in the intrapulmonary arteries as well as in the aorta.

In coarctation the aorta shows a concavity of the *outer* contour of the vessel which involves the superior, anterior, and posterior aspects. This concavity involves all sides of the aorta except the lower into which the ductus is inserted. The stenosis consists of a diaphragm which lies across the lumen and which protrudes into the lumen from the outer wall. The tiny orifice in this diaphragm is eccentric and situated towards the side of the ductus. Immediately distal to the diaphragm there is often a 'jet lesion' which consists of a localized fibrous thickening of the intima: this might be a potential weak spot if an anastomosis were to be made using the area, or it might give rise to a saccular aneurysm. In the pathological museum at St. Thomas's Hospital, London,

there is a specimen showing coarctation of the aorta with a "jet lesion" which has ruptured and caused a dissecting aneurysm of the descending aorta.

The author dismisses the "skodaic hypothesis" of the origin of coarctation which holds that the lesion is caused by an overgrowth into the aorta of the tissue which proliferates to close the ductus soon after birth. In fact the basis for the narrowing is a peculiar deformity of the aortic media. "In sections through the zone of coarctation, the media of the superior, anterior, and posterior portions of the aortic wall shows a characteristic thickening

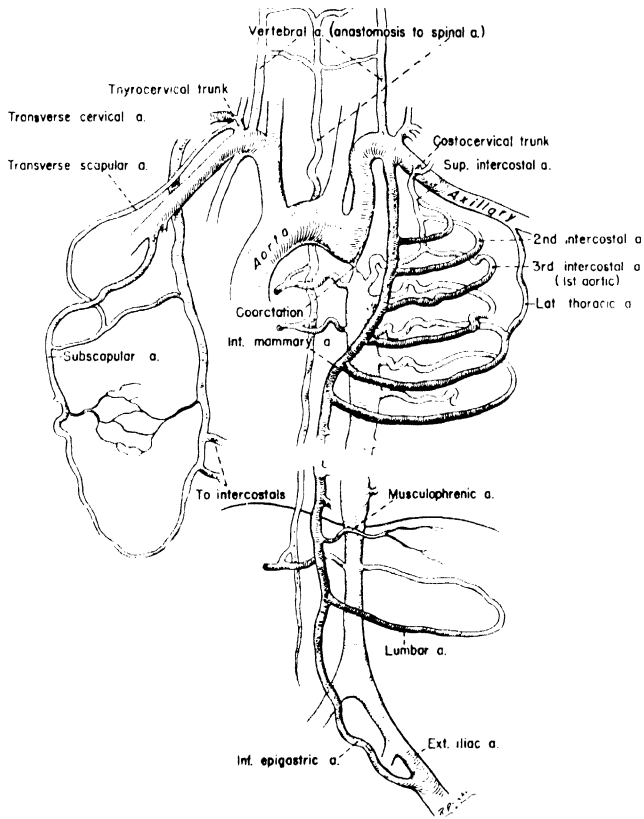


Fig. 8.—The major collateral channels in coarctation of the aorta.

which projects into the lumen, making it narrow and eccentric." In longitudinal section the localized thickening appears as a curtain, in cross-section as a sphincter.

Prognosis.—The prognosis of coarctation varies. Some patients can live a full life and attain old age, but in a group of 104, reviewed by Reifenstein, Levine, and Gross,[10] 61 per cent died before the 40th year of life. The chief causes of death were congestive heart failure, rupture of the aorta, intravascular bacterial infections, and intracranial lesions.

COARCTATION OF AORTA—*continued*

(J. E. Edwards, N. A. Christensen, O. T. Clagett, and J. R. McDonald)

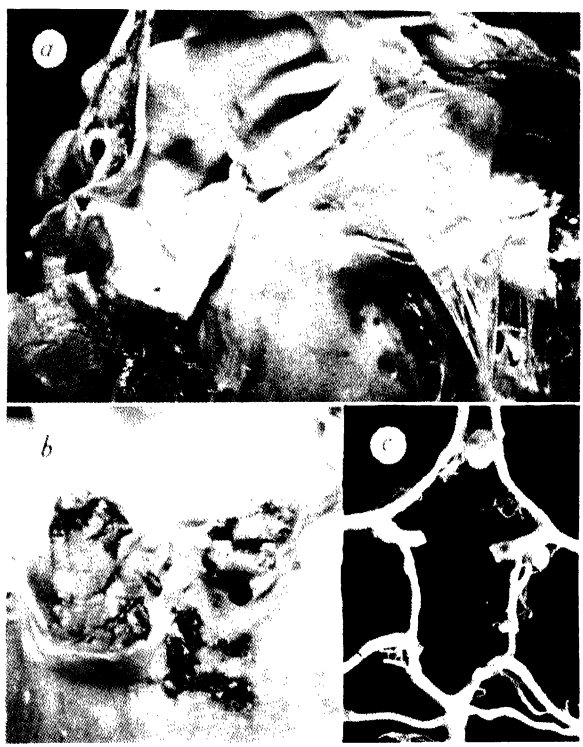
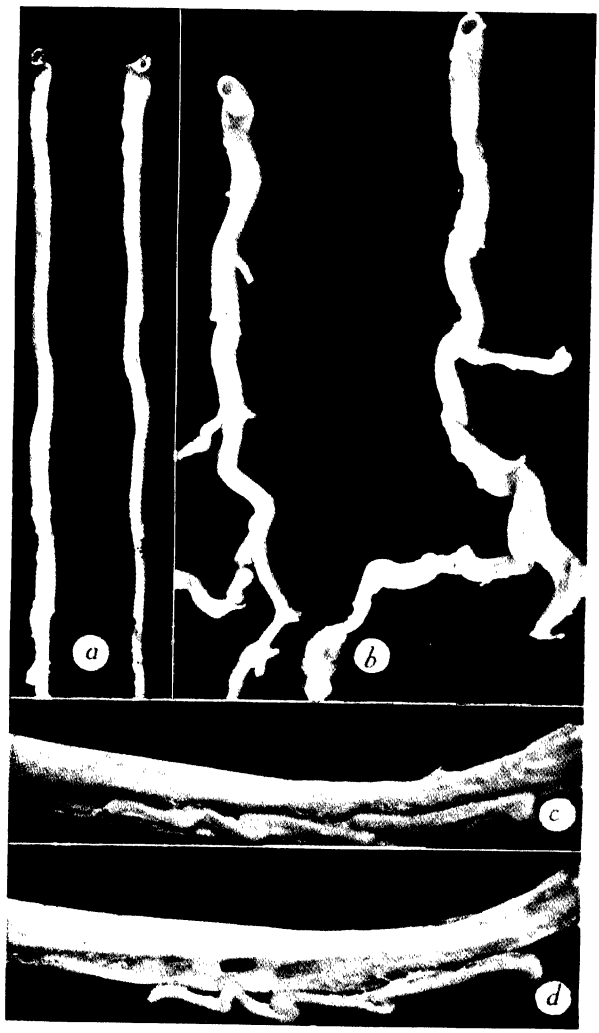


Fig. C. a. The aortic orifice and the anterior leaflet of the mitral valve in a case of aortic coarctation. The patient was a 28-year-old man. The aortic valve is bicuspid. The ventricular surface of the anterior leaflet of the mitral valve, beneath the aortic valve, shows a patch of raised tissue. This is considered as representing a reaction to trauma caused by blood regurgitating through the aortic valve. b. Bicuspid aortic valve from a case of coarctation of the aorta. The patient was a man of 25 years of age. The leaflets and the subvalvular endocardium of the left ventricle show large vegetations characteristic of bacterial endocarditis. c. The circle of Willis, viewed from below, from the patient having aortic coarctation whose heart is illustrated in a. There are two so-called congenital aneurysms of the circle, one involving the anterior communicating cerebral artery, the other the left internal carotid artery.

COARCTATION OF AORTA—*continued*

(J. E. Edwards, O. T. Clagett, R. L. Drake, and N. A. Christensen)



Myocardial hypertrophy occurring as a result of the hypertension is common, but it may also be due to bicuspid aortic valves, which are stated to be present in 23·5 per cent of cases according to Maud Abbott and 42·7 per cent according to Reifenstein. Recent papers indicate that this percentage is still rising. The bicuspid valves represent a cause of regurgitation and are a potential site for bacterial endocarditis.

Rupture of the aorta is generally due to a dissecting aneurysm of the ascending aorta and accounts for 17 per cent of the natural mortality; intracranial aneurysms involving the circle of Willis are a frequent cause of cerebral complications.

Collateral Circulation (*Fig. 8, Plates XII, XIII*).—The collateral circulation from the upper to the lower part of the body is chiefly carried by the intercostal vessels and by the arteries which anastomose around the scapula. Notching of the ribs occurs as a result of the intercostal arteries being bulbous and tortuous; it does not affect the lower border of the rib, as is commonly stated, but occurs on the inferior and anterior aspects of the main body of the rib at the point at which it joins that part of the rib which forms the wall of the costal groove.

Clinical Features.—The clinical features are described by Christensen and Hines, who review 119 cases diagnosed at the Mayo Clinic between 1925 and

PLATE XII

Fig. D.—a, A pair of normal internal mammary arteries for comparison with those in b. b, Internal mammary arteries from a case of coarctation of the aorta in a male 18 years of age. The vessels are dilated and tortuous. c, A rib and intercostal artery from a case of aortic coarctation; the internal mammary arteries in this case are illustrated in b. The intercostal artery is dilated and tortuous. At the points of greatest tortuosity of the artery there is notching of the rib. d, The same specimen as illustrated in c. The intercostal artery has been retracted, exposing the notches in the rib. The notches do not lie at the lower margin of the rib. Rather, they lie at the junction of the main body of the rib and that portion of the bone forming the posterior wall of the costal groove.

1947. The basic features are: (1) Characteristic differences in the arterial pulsations and in the indirect blood-pressure in the upper and the lower extremities; (2) The presence of one or more cardiac or cardiovascular murmurs; (3) The presence of a collateral circulation which by-passes the coarctation; (4) Notching of the ribs as seen on radiographs (*Plate XIV*) (Crafoord, Ejrup, and Gladnikoff[11] point out that notching is not always present and in an admirable paper they describe the clinical and radiological features as well as the treatment); (5) Characteristic direct intra-arterial radial and femoral arterial pulsations and blood-pressure differences (Brown, Clagett, Burchell, and Wood[12]). The sex ratio was 3·8 males to 1 female, and the ages, at the time of diagnosis, ranged from 4 to 56 years. Hypertension was the usual presenting abnormality and symptoms were generally widely varied, not characteristic; they were mild, unless there were complicating factors.

End-results of Operation.—George E. Brown and others record that, after resection of the coarctation, there is a demonstrable and measurable improvement in the circulation in the lower part of the body; and Clagett reports his surgical experiences in the management of 21 patients: "As nearly as we can determine at present, the results seem satisfactory in 12 of the 16 patients who have survived operation."

REFERENCES.—[1]*Quart. J. Med.* 1933, **2**, 1; [2]*Amer. Heart J.* 1928, **3**, 392; [3]*Ibid.* 1936, **11**, 572; [4]*J. thorac. Surg.* 1945, **14**, 347; [5]*Proc. Mayo Clin.* 1947, **22**, 124; [6]*Trans. Sth. surg. Ass.* 1944, **55**, 157; [7]*New Engl. J. Med.* 1945, **233**, 287; [8]*Ann. Surg.* 1942, **115**, 596; [9]*Rev. Médecine*, 1903, **23**, 108, 335, 418, 481; [10]*Amer. Heart J.* 1947, **33**, 146; [11]*Thorax*, 1947, **2**, **121**; [12]*Proc. Mayo Clin.* 1948, **23**, 352.

COCCIDIOIDOMYCOSIS.

Una Ledingham, M.D., F.R.C.P.

The problem of contagion in this disease is tackled by Rosenthal and Routien.[1] The point is especially important in view of the heavy incidence following troop-training in infected areas during the recent war. The causative fungus (*Coccidioides immitis*) has two developmental phases. In the human host it exists as a thick-walled spherule filled with spores, ultimately liberated by rupture of the cyst walls. The released spores develop into new spherules and so the cycle proceeds and the disease spreads. In culture, however, the fungus produces mycelial threads and cylindrical spores. These latter have been isolated from soil and were held to be the only variety infective to man. Up to now spherules were thought to be incapable of initiating the disease and man-to-man transmission impossible. Isolation was therefore unnecessary. The present experiment tends to disprove this ruling. The authors, using spherule-containing pus or sputum from human sources, produced the disease in 100 per cent of guinea-pigs inoculated. Intratracheal inoculation resulted in bilateral lung lesions, especially of the apex and associated lymph-glands. They were very similar to the human type of infection. Intraperitoneal injection resulted in a miliary spread of the disease. Spherules were seen or recovered from the tissues in both types of infection, and the disease could be transmitted from one animal to another. As well, spherules were kept viable for four months, and the experiments are still in progress. The wise conclusion is that this disease in humans must be regarded as contagious until proved otherwise. In fairness it must be said that the big majority of infections are contracted from other sources.

Reference.—[1]*Arch. intern. Med.* 1947, **80**, 343.

COLITIS, ULCERATIVE, CHRONIC: SURGICAL ASPECT.

W. B. Gabriel, M.S., F.R.C.S.

The treatment of certain cases of ulcerative colitis by surgical measures is in the ascendant, and several papers now to be reviewed place the position fairly and clearly. R. B. Cattell and E. Sacks[1] review the results at the Lahey Clinic over a 20-year period, 1927 to 1946 inclusive. During the first half of this period there was a high operative mortality and unsatisfactory results owing to lack of knowledge and experience in the management of ileostomy. They now discuss the indications for surgery under the following headings: Failure of medical management; Subacute perforation, abscess and fistula; Obstruction; Hæmorrhage; Infectious arthritis; Polyposis; Carcinoma; Segmental colitis.

They have had 12 patients in whom carcinoma has developed from chronic ulcerative colitis; the average duration of the disease in these cases was 9 years. This complication may be suspected in any patient who begins to pass blood after being quiescent for a time. Only 3 of the 12 patients operated upon are alive two or more years after operation.

Three types of surgical operations are being employed at the Lahey Clinic for ulcerative colitis, namely, ileostomy, partial or subtotal colectomy, and total colectomy. Ileostomy is usually the first procedure, and if the case is followed up for six months, it is found that as a rule one of the following three alternatives have to be adopted: (*a*) the ileostomy may be closed in a few cases—this only rarely proves to be satisfactory, and improvement can only take place if ileostomy is performed before structural changes take place in the colon; (*b*) the ileostomy is permanent while the disease remains quiescent; (*c*) the ileostomy is permanent but symptoms persist and a colectomy is subsequently required.

These three phases are carefully considered and an analysis is given of 166 patients, among whom 46 were treated by partial colectomy, and 75 had a

COARCTATION OF AORTA—*continued*

G. E. EDWARDS, O. T. CLAGETT, R. L. DRAKE, AND N. A. CHRISTY

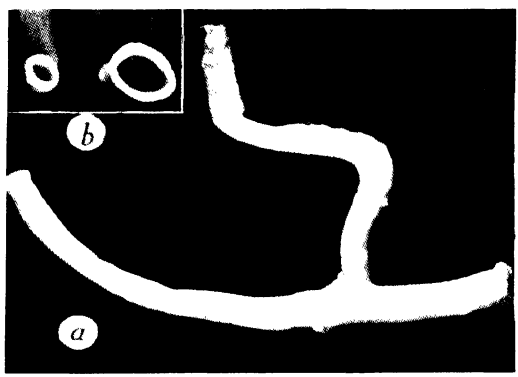


Fig. E. a. Ex

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COARCTATION OF AORTA—*continued*

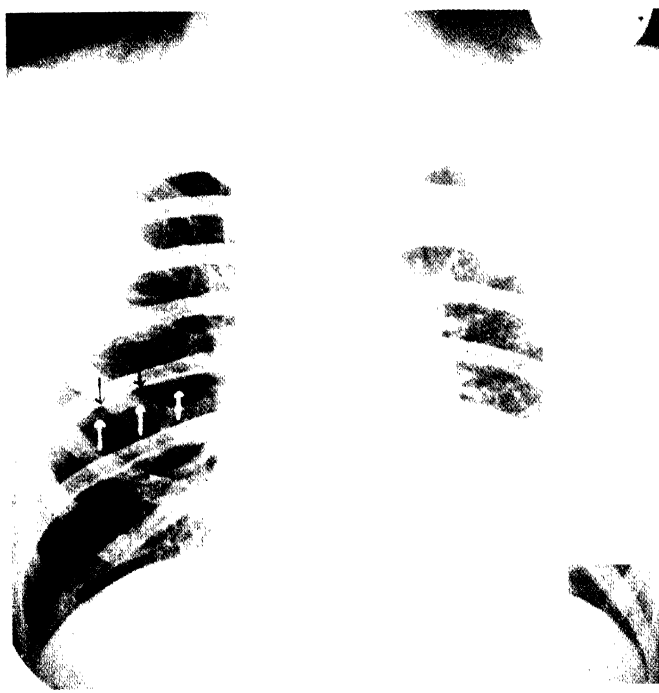


Fig. F. Coarctation of II point to the inferior margin of costal grooves.

complete colectomy performed – this term implying removal of the rectum as well as the entire colon in three stages– ileostomy, colectomy, and abdomino-perineal excision. The mortality for the whole series was 22 per cent, but in a recent series of 75 patients treated during 1945 and 1946 there were 3 deaths, or 4 per cent. The conclusion is given that this low mortality, combined with the modern management of ileostomy, justifies the surgical treatment of all patients with ulcerative colitis who do not respond satisfactorily to medical treatment.

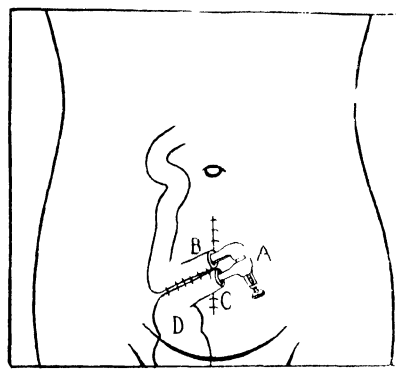


Fig. 9.— A, Clamp, made of hard aluminium alloy, in position to crush the spur; B, Ileum; C, Sigmoid; D, Rectum. (*Figs.* 9, 10 *by kind permission of the 'British Medical Journal'.*)

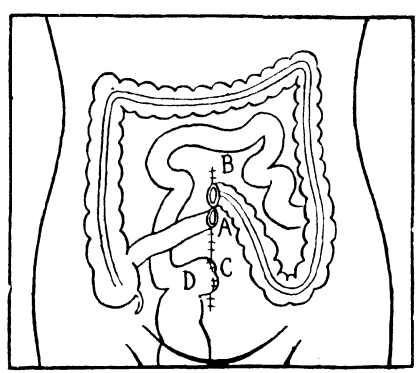


Fig. 10. A, Openings of excluded bowel; B, Ileum; C, Closed end of ileum; D, Lower segment of sigmoid

Garnet W. Ault[2] writes that after reviewing the end-results of 110 patients with chronic ulcerative colitis, he finds that 15 to 20 per cent reach an advanced stage in spite of medical treatment, and the indications for surgical treatment may be considered under two heads: (1) Specific, such as ulcerative colitis with severe constitutional and visceral degenerative changes, anorectal complications such as stricture, abscesses, fistulæ, etc., polypoid degeneration and carcinoma, obstruction and tumour mass, subacute perforation, and abscess or fistula in connexion with the colon; (2) Elective, such as focal infection, especially polyarthritis, and hæmorrhage. Surgical treatment is to be avoided in acute fulminating ulcerative colitis and in acute perforation, which is almost invariably fatal.

Sir Hugh Devine and J. Devine,[3] of Melbourne, describe in great detail the management of 11 advanced and desperate cases of ulcerative colitis; they advise a method of staged colectomy in which after an ileostomy has been established the ileum is anastomosed to the lower pelvic colon by the crush method (*Figs.* 9, 10). After a suitable interval the ileorectal anastomosis is closed by suture, and then at some future time, depending on the patient's general condition, a subtotal colectomy is carried out. As a rule the patient's general condition has dramatically improved after removal of the diseased colon and the number of motions passed per rectum gradually diminishes to about two per day. The authors stress the importance of general treatment, particularly in regard to tissue resistance and repair; essential pre-operative preparation is to correct anæmia and hypoproteinæmia.

E. C. B. Butler[4] describes *spreading ulceration of the skin as a rare but important complication of ulcerative colitis.* Reference is given to previously reported

cases, their causation being ascribed to vitamin deficiency or impaired resistance to infection. Two cases of severe ulceration involving the arms and legs are described; the condition appears to develop coincidently with an exacerbation of the colitis as shown by pyrexia, diarrhœa, and rectal bleeding. Similarly healing of the ulcers seemed to depend on cessation of the active phase, in one case after medical treatment and in the other after colectomy. Bacteriology showed no specific organism and in one case cultures were sterile for some days. The actiology is discussed, and several possible factors are mentioned such as vitamin deficiency, allergy, and lowered resistance in conjunction with secondary anæmia. As to treatment, this should be vigorous, either on medical lines with sulphonamides, penicillin, and repeated blood transfusions, or ileostomy followed by colectomy may be necessary. The best local treatment for the ulceration appeared to be excision of the entire edge of the ulcer with a diathermy knife and subsequently penicillin-sulphonamide powder was applied locally. Early skin grafting should be carried out if necessary.

REFERENCES.—[1]*J. Amer. med. Ass.* 1948, **137**, 929; [2]*Amer. J. Surg.* 1948, **75**, 325; [3]*Brit med. J.* 1948, **2**, 127; [4]*Proc. R. Soc. Med.* 1948, **41**, 474.

COLITIS, ULCERATIVE: MEDICAL ASPECT.

F. Avery Jones, M.D., F.R.C.P.

J. Groen[1] (Amsterdam) has made a particular study of the *personality and emotional difficulties* of 6 patients with ulcerative colitis. Murray and other psychiatrists have previously drawn attention to the peculiarity of character and the occurrence of psychological conflict situations in the history of these cases. Groen, as a general physician without special psychiatric experience, has taken very detailed biographical histories, having established good contact with the patients, who were made to feel that a special effort was being made to understand, and not to judge or condemn. He noted the following personality characteristics:—

1. A well-developed intellect.

2. Carefulness and neatness, often exaggerated, are striking features. There is a morbid tendency towards extreme 'decency' in words and manner. They dislike vulgar or obscene expressions and hate coarse jokes. They are particularly neat in their dress. Female patients may have a flair for fashion in dress. They are meticulous in their housework and tend to continue to keep their home in perfect order long after the disease has undermined their strength.

3. They are extremely sensitive and will brood about rudeness for days on end.

4. Although at first appearing to be very modest, they really have a very high opinion of themselves and are inwardly full of criticism of others.

5. They are extraordinarily egocentric. They may talk about helping other people, but they really do nothing for anybody outside their immediate circle.

6. Their attitude towards life is passive and they do not strive towards bettering their position.

7. They are fearful and in a difficult situation will choose the path of least resistance.

8. They are very unaggressive.

9. They have a great need for love, sympathy, and affection. If they do not receive love from others, they become utterly unhappy and helpless.

10. They have an exaggerated idealistic, sometimes a positively naïve, infantile conception of love. They think of love as a sublime adoration, attachment, and harmony between husband and wife, but consider the bodily sexual contact as something inferior. Many of them never marry or marry after long hesitation and are seldom capable of normal sexual relations.

11. In male cases, there is an abnormally strong attachment to the mother, combined with fear of the father. This marked mother fixation is probably the underlying cause of the difficulty of realizing a harmonious sexual life when adult. Many have an instinctive liking for elderly ladies, which they cannot explain. Their attitude towards other men is often reminiscent of the fear or hate they felt for their father. Some female patients may exhibit a strong fixation for their father and an aversion, usually well inhibited, for their mother.

12. The patients are reticent and in the introductory conversation the existence of mental conflict is usually denied. Later on it was always found that they had repressed and worried a great deal more than had appeared at first. They tend to be ashamed of not being able to manage their conflicts.

Individuals with this type of character structure may live in good health so long as their special wishes and desires are satisfied and as long as they live a sheltered life. Such a sheltered life may easily be upset. The mother may die or somehow may be withdrawn from the patient's orb, so that he is left behind alone. The patient may become engaged or married to a partner who is unable and unwilling to play the part of a mother substitute and this will cause acute disappointment. In the case of some female patients, the fear of what would happen was too much for them and some days before the marriage the disease broke out. In all his patients, shortly before the outbreak of their colitis, a difficult situation, requiring an active solution, had taken the place of their former sheltered life. A new situation arose, with which the patient could not cope and from which he could not escape. Such situations were particularly associated with emotional trauma, which involved the combination of acute love loss and painful humiliation. It persisted in the unconscious because there was no one to whom the patient dared to confess his difficult situation. This state of bereavement and humiliation which the patient could not solve by words or actions would precede the outbreak of ulcerative colitis by barely a few days.

The treatment consisted of giving them the opportunity to unburden their emotions and giving simple encouragement. They were told not to be ashamed of their great need for love and attachment. Their self love was gratified by telling them that they had a refined inner life and therefore a valuable personality. Their lack of outward success was consoled by pointing out that this type of personality is appreciated only by a limited category of people.

By recognizing the root cause of a conflict situation, steps could be taken to avoid a recurrence. With this simple type of psychotherapy his patients rapidly improved. Groen considers that ulcerative colitis is precipitated by a specific internal conflict, which is formulated as an acute love loss, combined with humiliation, which made the patients feel their inferiority as men or as women. Without sympathetic independent help, they could not solve their conflict and had continued to grieve.

M. Block and H. M. Pollard[2] (Michigan) review the *use of chemotherapy and antibiotics in colitis* and conclude that sulphonamides are a valuable adjunct therapy in the treatment of chronic ulcerative colitis. The sulphonamides which are sparingly absorbed and act locally in the bowel are more satisfactory than the more soluble forms. Sulphaphthalidine appears to be the drug of choice; no toxic reactions have been reported and it appears to be of value in inducing remission in about two-thirds of non-toxic cases of ulcerative colitis; 3 g. daily may be given over long periods. Penicillin is generally ineffective when given parenterally for inducing remissions, but may be valuable as additional treatment for the acute febrile phase.

J. Felsen and W. Walarsky[3] (New York) have analysed the progress of 34 patients with chronic ulcerative colitis through 50 *pregnancies*. These patients

were from a group of 421 female patients under their care. Seven pregnancies in 5 patients did not proceed to term, but 3 were induced abortions. In the remaining 43 pregnancies, all produced full-term live babies. In 30 per cent of the cases there was a temporary aggravation of the colitis, but insufficient to justify the interruption of pregnancy. In 12 per cent the condition remained unchanged, but in 58 per cent the colitis was substantially improved. Termination of pregnancy is therefore not indicated in the patient with ulcerative colitis.

REFERENCES.—[1]*Psychosomatic Med.* 1947, **9**, 151; [2]*Gastroenterology*, 1948, **10**, 46; [3]*Amer. J. Obstet. Gynec.* 1948, **56**, 751.

COLLAGENOSES, VITAMIN E IN. (*See* VITAMIN E IN THE COLLAGENOSES.)

COLON, CARCINOMA OF. *W. B. Gabriel, M.S., F.R.C.S.*

Diagnosis.—In a paper on diagnostic errors in relation to carcinoma of the large intestine, R. L. Jackman, H. A. Neibling, and J. M. Waugh[1] find that out of 232 patients with carcinoma of the colon beyond reach of a finger and sigmoidoscope, 23 patients, or 9·9 per cent, had received other treatment previously for symptoms which were in fact due to the carcinoma. For instance, 6 had been operated on for hæmorrhoids, 5 had been treated for alleged pernicious anæmia, 5 had been treated for colitis, 2 for amœbiasis, and 2 had undergone appendectomy. In 3 cases rectal polyps had been diagnosed and treated, but carcinomas at a higher level in the colon had been missed. The correct diagnosis in this group was established by roentgenograms, and in 9 further cases the diagnosis was made by laparotomy performed for relief of acute obstruction; no significant treatment had been given to this group during the immediate pre-operative period.

A paper read before the Philippine College of Surgeons by J. Estrada[2] refers to some causes of delays and errors in diagnosis and the problems presented by actual or suspected amœbiasis are indicated.

Chemotherapy and Other Adjuvants.—Some of the intricate problems connected with anæmia and hypoproteinæmia are discussed in a paper by I. S. Ravdin, H. A. Zintel, and D. H. Bender.[3] The importance of correcting these conditions before operating on the colon is evident, seeing that the under-nourished patient is more susceptible to shock, wound infection, and œdema at the site of anastomosis. Some important points concerning vitamin therapy are mentioned, and after preparation for some days with sulphasuxidine it is shown that there is an increased need for the thiamine intake in the diet and for vitamin K. The passage of a Miller-Abbott tube pre-operatively is now recommended before all operations on the colon. Chemotherapy with sulphasuxidine and sulphathalidine is useful but may be highly selective, and occasionally the usual or larger doses are without any marked effect. The latest antibiotic streptomycin, when given by mouth in the dosage of 0·25 g. every 6 hours, has rendered the fæces free of *Streptococcus fæcalis* in 8 days, with a marked reduction in the coliform group and anærobic organisms of the *Welchii* group. The effect of these drugs on the stools is shown graphically. The mean operative mortality for all operations on the colon from 1923 to 1938 was 18·4 per cent, but since 1938 the mean mortality has been 3·6 per cent. Now resection with end-to-end anastomosis is supplanting Mikulicz procedures, and one-stage operations have entirely superseded multistage operations except in the presence of perforation or obstruction. Nothing, however, replaces the gentle handling of the bowel, care in preservation of blood-supply, prevention of major soiling, and careful approximation of the bowel edges.

Another paper on similar lines with details of pre- and post-operative biochemical studies and their practical application is that by H. E. Bacon and

R. J. Rowe.[4] They consider that the very significant reduction in mortality which has taken place in recent years after operations on the colon and rectum has been due largely to the advances that have been made in preparation and after-care. The problems connected with fluid balance, protein nutrition, and the use of antibiotics are discussed, and a suitable régime is mapped out. As regards thrombo-embolism, the prophylactic measures and indications for anticoagulant therapy are described. Femoral vein ligation has apparently only been done in one case.

Surgical Management.—L. S. McKittrick[5] of Boston reviews many important historical and pathological aspects, and refers in particular to the teaching of Jamieson and Dobson (1909); their work on the lymphatic drainage of the several portions of the colon still stands and should form the basis of adequate operations for cancer of the colon. The progress of surgical technique for resection of the colon is considered, and the present trend towards one-stage primary section and anastomosis is defined. For lesions at or beyond the middle of the transverse colon the author prefers a closed type of anastomosis with a basting stitch. The following essential basic principles are stated: (1) Proper preparation of the patient for operation; (2) Optimum exposure of the segment of colon to be excised; (3) Adequate mobilization of bowel; (4) Adequate cancer operation; (5) Free blood-supply to both segments; (6) Avoidance of tension on suture line; (7) Proximal complete colostomy, if adequacy of suture line or blood-supply is in doubt. A mortality-rate of 3·6 per cent is recorded for 110 operations in which a primary anastomosis was done.

P. I. Hoxworth and J. Mithoefer[6] from Cincinnati describe in detail and with very clear illustrations their technique and management, both pre- and post-operatively, of carcinoma of the colon. For a lesion of the right half of the colon they perform a right hemicolectomy with either a side-to-side or end-to-side open anastomosis between the ileum and transverse colon: a large number of interrupted Halsted mattress sutures of No. 000 silk are used. For lesions distal to the hepatic flexure an aseptic end-to-end anastomosis is done and the technique is clearly described. Intraperitoneal implantation of sulphonamides has not been done for the past four years. The results in 144 patients with cancer of the colon are reported; of these a resection was done in 87 cases (60·4 per cent). In 16 cases the operations were classed as palliative, and in 4 cases, resection of other organs was required. The mortality for the 87 resections was 6, or 6·9 per cent. The average period in hospital for the 79 operation survivors was 26 days from time of operation. In patients who required a preliminary cæcostomy the average waiting time between cæcostomy and resection was 15 days.

A. W. Allen, C. E. Welch, and G. A. Donaldson[7] of Boston also describe the recent advances in colonic surgery. Since the introduction of the Miller-Abbott tube and the use of sulphasuxidine and sulphathalidine pre-operatively, fewer patients need preliminary cæcostomy. With a resectability rate of 95 per cent they have had a mortality-rate of only 2 per cent in 100 cases resected at the Massachusetts General Hospital between the years of 1943 and 1946; this compares very strikingly with the previous mortality of 17·5 per cent in the period 1925 to 1942. The preliminary procedures carried out in these cases are described in detail and the necessity for 5 to 7 days' preparation is stressed. A tube cæcostomy as a preliminary is only done in the presence of complete obstruction and a new method for cleansing the colon through a cæcostomy by use of a Miller-Abbott tube is described. As to technique the authors, although formerly champions of aseptic anastomosis, now favour open anastomosis in all operations of election; the inner row of sutures is of fine chromic catgut on an atraumatic needle and the outer row of non-absorbable interrupted

sutures of No. 30 cotton, preferably of the Halsted mattress type. Local sulphonamides into the peritoneal cavity or into the wound are not now used. Blood transfusions are given routinely. In suitable cases dicoumarol has been given to prevent venous thrombosis, but when anticoagulant drugs are contra-indicated, for instance, in arteriosclerosis, prophylactic superficial femoral vein interruption has been practised; it is mentioned that in their hospital this procedure has been done in 458 elderly patients without harm and it is considered to be a reasonable safeguard against thrombophlebitis and pulmonary embolism.

W. F. MacFee[8] discusses the management of lesions in the different parts of the colon and favours the aseptic type of anastomosis as a one-stage operation, but there should be no hesitation in performing proximal drainage as a preliminary, either by cæcostomy or transverse colostomy, especially in dealing with carcinoma of the splenic flexure, which is often recognized late, and in cases of obstruction, fixation, or gross infection.

Curtice Rosser[9] describes the management of surgical lesions of the left side of the colon and mentions the difficulty in diagnosis between carcinoma and peridiverticulitis with tumour formation. Endometriosis of the pelvic colon also closely simulates a constricting carcinoma. The author reports 23 resections of the colon without any operative mortality, 7 were done in stages and the remainder in one stage with immediate anastomosis; only one aseptic anastomosis was done, the remainder being by open suture anastomosis. One other matter dealt with in this paper is colostomy stenosis, and the method of correcting this by excision of a circle of skin is described; inversion of the skin margin by what is known as the Sturmdorf stitch is described and illustrated.

E. G. Muir[10] describes a method of right hemicolectomy in one stage with an antiperistaltic lateral anastomosis between the ileum and the transverse colon. The cut end of the transverse colon is not completely closed by suture and a small gap of about ½ cm. is left at the corner farthest from the anastomosis; through this a soft rubber tube about the size of a No. 12 or 13 catheter, with several lateral holes cut in the distal 10 in., is passed through the anastomosis up the lumen of the ileum; the last hole in the tube should lie in the colon. A firm closure of the colon round the tube is effected with several purse-string sutures and omentum is wrapped round. A stab incision is then made about 2 in. below the costal margin outside the rectus sheath and the ileostomy tube is brought out; the colon is sutured to the parietal peritoneum with a few stitches and the abdomen is closed. Post-operatively the patient has an intravenous drip to supply fluid for the first 48 hours and constant suction is applied to the ileostomy tube and also to an indwelling gastric tube, which is passed either before or soon after the operation. The ileostomy tube is removed after about a week; slight fæcal leakage may take place for a few days but no secondary operation for closure of the fistula has been necessary. The operation described has been performed on 20 cases without mortality.

J. E. Dunphy[11] considers that recurrent cancer of the colon and rectum should not in all cases be considered to be hopeless and beyond all possibility of eradication by further surgery provided that there is no positive evidence of distant metastases or generalized peritoneal dissemination. He relates the details of 4 remarkable cases in which extensive operations were done for recurrent cancer, with survival for 6¾ and 5½ years in two cases, and arrest for several years in the others. The fact of the primary tumour being of a relatively high grade of malignancy does not rule out the possibility of a local recurrence without distant metastases and it is suggested as a speculation that in some cases an inflammatory reaction might perhaps seal off the lymphatics at the periphery of the field. In any case the point to be stressed is that one must not give up in dealing with cancer.

REFERENCES.—[1]*J. Amer. med. Ass.* 1947, **134**, 1287 ; [2]*Philipp. J. Surg.* 1947, **2**, 101 ; [3]*Ann. Surg.* 1947, **126**, 439 ; [4]*J. Amer. med. Ass.* 1948, **136**, 975 ; [5]*Surg. Gynec. Obstet.* 1948, **87**, 15 ; [6]*Surgery*, 1947, **22**, 271 ; [7]*Ann. Surg.* 1947, **126**, 19 ; [8]*Ibid.* 125 ; [9]*J. internat. Coll. Surg.* 1948, **11**, 17 ; [10]*Proc. R. Soc. Med.* 1947, **40**, 831 ; [11]*New Engl. J. Med.* 1947, **237**, 111.

COLON, POLYPOSIS OF.

W. B. Gabriel, M.S., F.R.C.S.

In considering this condition, C. McG. Gardner[1] refers to the work of Harrison Cripps, Lockhart-Mummery, and Dukes, and states that hereditary polyposis of the colon is not a congenital disease but a Mendelian dominant transmitted by the father or mother ; the genetic defect results in excessively rapid growth of the intestinal epithelium ; areas of hyperplasia and adenomas develop, and the condition finally progresses in a large proportion of cases to carcinoma. The questions involved in conservative treatment and radical operation are discussed ; instead of doing an abdomino-perineal excision of the rectum and pelvic colon, which leaves the patient with a permanent colostomy, the author recommends a one-stage colectomy with a side-to-side ileorectal anastomosis ; this is done after the rectum has been cleared of polypi through a sigmoidoscope, and the anastomosis is done above the peritoneal reflection but well within the reach of a sigmoidoscope. The details of two cases (males aged 44 and 47 respectively) successfully treated by this method are given ; in one case over 800 polypi were counted in the specimen removed and one polyp in the cæcal region showed malignant change. Post-operatively an extra supply of protein is essential, and if this is given it appears to control a tendency to diarrhœa.

W. L. Estes, jun.,[2] relates the family history of a newly-discovered polyposis family : A woman at the age of 37 had polyposis with a carcinoma of the sigmoid, and of her 6 children all have either died of carcinoma or are known to have polyposis of the colon and rectum, either with or without carcinoma. The author makes the practical point that although 3 members of this family were symptom-free examination revealed well-marked polyposis, which shows that reliance on the history or symptoms alone may be completely fallacious. Members of polyposis families should have a regular 6-monthly survey if they are to be protected against the insidious onset of polyposis or cancer of the colon or rectum. Diagnosis is made by three procedures—digital examination of the rectum, sigmoidoscopy, and barium enema by the double contrast method with air inflation. The available methods for the surgical treatment of polyposis are reviewed, and preference is expressed for a low ileorectal anastomosis followed by colectomy, except in those cases in which there is a suspicion of a rectal carcinoma developing, when radical excision of the rectum and the entire colon should be carried out. In connexion with low ileorectal anastomosis the papers are mentioned by P. Guptill[3] and D. B. Pfeiffer and F. M. S. Patterson.[4] Treatment of polyposis by radiation is not recommended. After colectomy with ileorectal anastomosis, re-examination should be done every 6 months, with prompt fulguration of all new polyps. If cancer develops in the remaining rectal segment, abdomino-perineal excision with permanent ileostomy will be required.

In this connexion a paper by H. E. Bacon and C. H. Smith[5] might be mentioned ; they describe a method of left hemicolectomy and proctosigmoidectomy, with transplantation of the transverse colon to the anus. The indications for this procedure have varied, but among the 8 cases described we note that there were 2 cases of polyposis with malignant change. The technical details are briefly described and consist essentially in careful mobilization of the splenic flexure with preservation of the anastomosing arterial arcades between the middle colic and the left colic arteries ; in doing this transillumination is of great value. The inferior mesenteric artery is ligated close to its origin, and after the usual thorough mobilization of the pelvic colon and rectum the bowel

is brought down through the anal canal by the ' pull-through ' method so that finally the transverse colon is transplanted to the anus.

REFERENCES.—[1]*Arch. Surg., Chicago*, 1948, **56**, 75; [2]*Ann. Surg.* 1948, **127**, 1035; [3]*Surgery*, 1947, **22**, 286; [4]*Ann. Surg.* 1945, **122**, 606; [5]*J. int. Coll. Surg.* 1947, **10**, 661.

COLON, SURGICAL DISEASES OF. (*See also* COLITIS; DIVERTICULITIS; HIRSCHSPRUNG'S DISEASE.) *A. Rendle Short, M.D., F.R.C.S.*

Albert S. Lyons,[1] of New York, refers to instances in which diseases of the sigmoid, such as diverticulitis or carcinoma, may give rise to symptoms in the right iliac fossa and mislead the surgeon into removing the appendix. The error may be due to a long loose pelvic colon that falls across the lower abdomen, or it may be adherent, or bowel contents from a sigmoid perforation may invade the right iliac fossa. The deduction is that when an appendix has been removed and does not seem grossly pathological, the pelvic colon should be examined.

A. Brunschwig and P. W. Schafer,[2] of Chicago, quote 9 cases of *multiple visceral neoplasms*. For instance, there were two growths of the stomach in

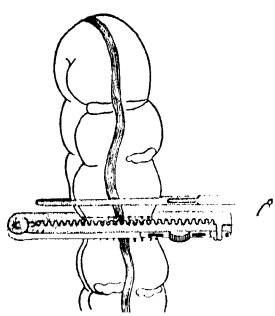


Fig. 11. Furniss clamp applied. Specimen ready for excision. (*Figs.* 11–14 *reproduced from the* ' *Annals of Surgery* '.)

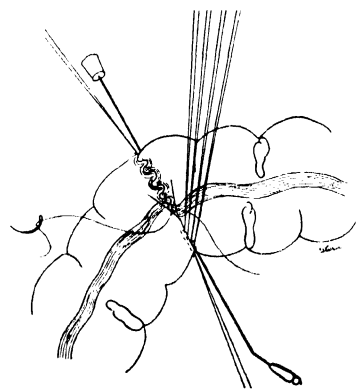


Fig. 12.—Stay sutures placed before removal of clamp. Limbs to be anastomosed held by pin. First anterior row of interrupted Lembert sutures placed.

2 cases, and two of the colon in 3 patients. The lesson, once again, is to make a thorough examination at every laparotomy and not to assume that one finding is necessarily all that is to be found.

Surgical Technique. There is a decided swing-over of opinion in favour of *one-stage resections of growths of the colon*, unless of course obstruction is present. A few surgeons still advise a proximal vent; the majority do not. The mortality, in six American clinics, has varied from 2 to 11 per cent. J. W. Hinton and S. A. Localio,[3] of New York, report 26 cases with only one death, from pulmonary embolism. There were 12 carcinomas of the right colon and 7 of the sigmoid. Preparation takes about a week and includes blood transfusion if there is anæmia, a high-protein low-residue diet, and amigen, ascorbic acid, and vitamin B daily. Succinyl-sulphathiazole is given in doses of 12 g. every day. During the first two days the bowels are emptied with the aid of magnesium sulphate. The authors use a method of aseptic anastomosis with the aid of the Furniss clamp. If a right hemi-colectomy is performed the ileotransversostomy is made end-to-side. The lumen is opened after suturing is completed, with thumb and finger (*Figs.* 11–14). At the end of the

operation a Levine tube is left in the stomach, but not used for suction unless needed. Patients are got up on the first day, and go to the toilet instead of using a bedpan.

A method of performing an *aseptic ileocolostomy without any special clamps* is described by a Dutch surgeon, J. Ten Kate.[4] The loops of bowel are brought

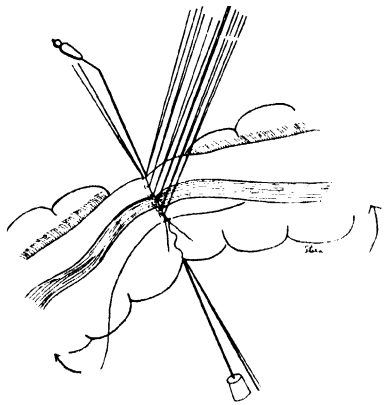


Fig. 13.—First anterior row complete. Colon rotated by turning pin clockwise or counter-clockwise. First posterior row of Lembert sutures placed.

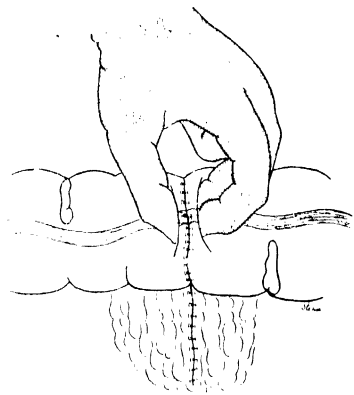


Fig. 14.—Diaphragm opened by manipulation and patency of anastomosis tested. Defect of mesentery repaired by interrupted sutures.

together side by side, and a posterior sero-serous suture inserted. An incision is then made down to but not through the mucosa of both ileum and colon, and a series of interrupted long seromuscular sutures put in, which are then hooked up out of the way. The mucosa is divided with diathermy knife, and the stitches are pulled taut and tied (*Fig.* 15). The author allows that the



Fig. 15. Left: Incision of the intestinal wall down to the mucosa. Right: Suture of the posterior seromuscular flaps. (*Reproduced from 'Surgery, Gynecology and Obstetrics'.*)

mucosa may bleed sharply from the cut edge, but no notice is taken of this, as to ligate bleeding points would abandon the aseptic principle. He says the loss of blood is never serious. [We certainly agree that bleeding from mucosa divided with the cautery can be considerable, and a wide experience would be necessary to convince us that it is innocuous.—A. R. S.]

Colostomy.—H. G. Holder and E. F. Lewison[5] relate experience with 67 colostomies following war injuries, treated by them in an American hospital in England. They found that closure by end-to-end anastomosis suffered less morbidity than those in which the spur-crushing technique was used; they had a shorter convalescence, and there were no cases of peritonitis. The anastomosis must not be made under tension, and a good blood-supply must be secured. They apply these lessons, with which we cordially agree, to the closure of peace-time colostomies. G. B. Sanders, H. Haffner, and R. B. Lynn,[6] of Louisville, come to a similar conclusion. They use the Pauchet method of closure. The peritoneum is opened and the two ends are pulled well outside. Œdematous ends are cut away. A vertical incision is made in the long axis of each loop, and a side-to-side anastomosis performed. In only one of their 72 cases did the colostomy fail to close.

REFERENCES.—[1]*Ann. Surg.* 1948, **127**, 398; [2]*Ibid.* 1947, **126**, 780; [3]*Ibid.* 1948, **127**, 12; [4]*Surg. Gynec. Obstet.* 1947, **85**, 217; [5]*Ann. Surg.* 1947, **126**, 253; [6]*Ibid.* 1948, **127**, 243.

CONGENITAL ABNORMALITY OF THE FŒTUS: MATERNAL MEASLES, MUMPS, AND CHICKEN-POX AS A CAUSE.

J. Chassar Moir, M.A., M.D., F.R.C.S. Ed., F.R.C.O.G.

It is now well known that the contraction of rubella by the mother early in her pregnancy is related to the development of congenital abnormalities in her offspring. So real is this risk that it may be regarded as a virtuous act to allow girls to contract this disease—usually mild—while they are yet young, and so avoid a possible grave danger to future offspring should an epidemic of rubella occur when that girl later marries and becomes pregnant.

Naturally one wonders whether other virus diseases—morbilli, mumps, or chicken-pox—can also derange embryonic development. Regarding chicken-pox and small-pox, evidence is already to hand that the disease can be transmitted to the fœtus in utero: Mauriceau himself the famous French obstetrician of the seventeenth century—was said to have been born pock-marked. That, however, is a rather different story, for the present question is whether the virus can interfere with normal development during the *early* weeks of embryonic life.

M. J. Fox, E. R. Krumbiegel, and J. L. Terise, of Milwaukee, give a partial answer to the question. Among 297 mothers, 589 children were born before, and 76 were conceived after, the mothers had had measles, mumps, or chicken-pox. The incidence of anomalies of development in this group of 665 children was 0·9 per cent. Of 33 live children born to the same number of married women who contracted one or other of these diseases while pregnant, 1 had a congenital anomaly, and 1 pregnancy ended in abortion at the second month.

These figures, so small in number, are quite inconclusive, and in many of the cases listed the disease was contracted *after* the first three or four months of pregnancy, when the fœtal structures are already well formed. However, they do give some indication that the diseases mentioned are unlikely to have any pronounced influence on the developing fœtus.

According to the authors of this paper, the available published information indicates that in maternal rubella the incidence of fœtal anomalies is fifteen times the expected rate of 0·9 per cent, and if the figures are restricted to mothers who develop the disease in the first four months of pregnancy, it is more than eighteen times the expected rate; similar figures for poliomyelitis are twice, and nine times, the expected rate.

[This is an important subject on which reliable information is still scanty. It is a matter in which practitioners throughout this country, acting through the Medical Officers of Health, could give great help.—J. C. M.]

REFERENCE.—[1]*Lancet*, 1948, **I**, 746.

DENTAL CARIES AND FLUORINE.

Una Ledingham, M.D., F.R.C.P.

Weaver[1] traces the advances in knowledge of the relationship between fluorine and dental caries on the one hand and mottled teeth on the other. The unsightly teeth result from faulty enamel formation in the pre-eruptive phase, providing a defective mottled surface which pigments readily. A direct association with high fluoride content of drinking water is agreed, though only a proportion of the population supplied by such water is affected. The more fortunate result of high fluoride intake is an inhibition of dental caries, though this influence may tend to be delaying rather than preventive. Arguments are advanced for and against adding fluoride to water or dispensing it in tablet form, and results from New Jersey favour its addition. Klein,[2] after an experiment lasting twenty years, reports definite and long-lasting protection in children of all ages supplied with 'high fluoride' water.

Murray and Wilson[3] in Morocco, where fluorosis is endemic, found that well-nourished European children escaped, while the local Arab population showed a high proportion of mottled teeth. This suggests that the nutritional state exerts some influence.

Local application of fluoride solution to erupted teeth is now on trial, and results so far are quite inconclusive.

REFERENCES.—[1]*Proc. R. Soc. Med.* 1948, **41**, 284; [2]*Publ. Hlth. Rep., Wash.* 1948, **63**, 443; [3]*Brit. dent. J.* 1948, **84**, 97.

DERMATITIS, ARSENICAL.

(*See* ARSENICAL DERMATITIS.)

DERMATOLOGY, NITROGEN MUSTARD THERAPY IN.

(*See* NITROGEN MUSTARD THERAPY IN DERMATOLOGY.)

DIABETES INSIPIDUS.

S. L. Simpson, M.A., M.D., F.R.C.P.

Agents Determining and Influencing the Functions of the Pars Nervosa of the Pituitary.—Professor E. B. Verney[1] continues his demonstrations that the secretion of posterior pituitary hormone—particularly the anti-diuretic hormone—is a variable physiological one determined by emotional stimuli and osmotic pressure of fluids reaching the gland. Both emotion and exercise decrease the volume of fluid excreted in the urine, and exercise probably acts through the associated emotional stimuli. This inhibition of water diuresis, like the direct effect of an injection of pitressin, is independent of the nerve-supply to the kidneys and is not caused by endogenous release of adrenaline. The nerve connexion between the posterior pituitary and the hypothalamus make this emotion effect one that might be expected, and its importance in clinical medicine will be increasingly recognized.

Origin of Thirst in Diabetes Insipidus.—J. H. Holmes and M. I. Gregersen[2] produce evidence that the thirst of diabetes insipidus results from the same mechanism as the thirst of dehydration, and that it may be abolished by pitressin or by forced fluids. In untreated diabetes insipidus there is found, as in dehydration, a decrease in plasma volume, a decrease in extra-cellular fluid volume, and in salivary flow, and increase of serum protein and serum sodium, all corrected by pitressin or successful forcing of fluid intake beyond renal excretion.

The Role of Pinealomas in the Causation of Diabetes Insipidus.—G. Horrax[3] points out that pineal tumours are one of the causes of diabetes insipidus, either by direct penetration into the hypothalamus or by the production of internal hydrocephalus, or by solitary implants or metastases of a pinealoma invading the hypothalamus (or the tuber cinereum portion of it), or by an 'ectopic' pinealoma. In all these cases, there is interruption of the supra-optico-hypophyseal tract.

Horrax describes 5 cases showing diabetes insipidus from a total of 17 cases of pineal tumour in a department of neurosurgery.

Case 1.—Child of 12. Polyuria 1 year. Penetrating pineal tumour. Ventriculogram—dilated ventricles, large pineal calcification, and tumour projecting into third ventricle. Death after operation.

Case 2.—Child of 12. Two months polyuria, etc. X-ray showed enlarged sella turcica. Cranio-pharyngioma diagnosed. Solid tumour found between optic nerves and removed. Pincaloma. Radiotherapy. Recovery.

Case 3.—Man of 20. Polyuria, headaches, and fainting spells, eight months. Ventriculogram showed dilated *lateral* ventricles and rounded mass in posterior third ventricle. Radiotherapy. Improved.

Case 4.—Male of 24. Polyuria, headaches, blurred vision, 8 weeks. Ventriculogram gave result as in *Case* 3. Radiotherapy. Improved.

Case 5.—Male of 31. In 1932, headaches, blurred vision, papillœdema. Ventriculogram gave result as in *Case* 3. Decompression and radiotherapy. Well for nine years, when he developed diabetes insipidus. Further radiotherapy. Improved.

REFERENCES.—[1]*Brit. med. J.* 1948, **2**, 119; [2]*Amer. J. Med.* 1948, April, 503; [3]*Ann. Surg.* 1947, **126**, 725.

DIPHTHERIA.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Epidemiology.—In 1946, the corrected number of notified cases of diphtheria was 11,986 and of deaths 472. Comparable figures for the two immediately preceding years were 23,199 and 934 in 1944, and 18,596 and 732 in 1945.

Active Immunization.—Under the immunization scheme 3,035,154 children have been immunized in England and Wales while still under 5 years, and 3,596,029 when they were in the age period 5 to 15 years. This gives a total of 6,631,183 protected in the period 1940–6. It is roughly estimated that, at the end of the year 1946, not less than 60 per cent of the children under 15 years had received at least one course of immunization. A beginning was made to provide *a boosting dose to those protected in infancy* before they start school life. It is most desirable that this principle should become generally established.[1]

J. A. Bell[2] has produced a report on combined immunization by alum-precipitated toxoid (A.P.T.) and pertussis vaccine, based on well-controlled field work in which A.P.T. alone was used as the control. Results, as measured by Schick tests one year after immunization, showed: (1) That two doses of the combined reagent at a four-week interval gave better protection than A.P.T. alone; (2) That the combined reagent was more effective at the age of 2 to 5 months than ordinary A.P.T. at 2 to 23 months; (3) That while immunization at 2 to 5 months was fairly effective, there were twice as many failures to immunize with each product at that age as at the age 6 to 23 months. It was concluded that combined immunization was superior to A.P.T. alone, but that if immunization were done at age 2 to 5 months, a booster dose should be given after one year.

Bacteriology.—Differentiation of *C. diphtheriæ* by serological typing of 500 strains has been carried out by L. F. Hewitt.[3] He found the serological reactions of the *gravis* group clear cut and 13 specific types were distinguished. In the *intermedius* group there were only 4 serological types and in the *mitis* group, which was less easily differentiated, there were no less than 40. No correlation of clinical severity with serological type has yet been attempted. The virulence of *gravis* strains was investigated by J. W. McLeod and D. T. Robinson.[4] More than 200 starch-fermenting strains were collected from Western and Central Europe, widely scattered cities and areas in England and Wales, two cities in Norway, Glasgow, and the Eastern Mediterranean area.

Some 5 to 6 per cent were found to be non-virulent, and if atypical *gravis* strains were excluded, this figure was reduced below 4 per cent. It is concluded that, in general, virulence tests of *gravis* strains do not justify the time and expense involved, but that they are desirable: (1) in carriers of long standing, (2) in diphtheritic lesions in unusual situations, e.g., wounds, and (3) in certain areas where non-virulent *gravis* strains are found with some frequency.

Complications.—R. M. Maher[5] shows that there are two chief types of *palatal paresis*—defective elevation of the palate due to levator paresis, and deviation of the uvula due to tensor paresis. He noted reversal of uvular deflection in 5 cases during the course of palatal paresis, and explains this on the basis of fatigue of the active muscle involved. He considers that the pattern of paresis generally in diphtheria—that is, accommodation, palate, pharynx, and predominance in the legs and right arm—all point to usage producing a fatigue effect on the end-plates as the probable precipitating factor. *Polyneuritis* in 85 soldiers in the Far East is examined by A. D. Leigh.[6] Among 150 with a history of jungle sores, he noted sensory changes around the sore two to three weeks before onset or concurrently with the polyneuritis in 25 per cent. Palatal paresis occurred in 15 cases with no history of sore throat. The symptoms and signs were remarkably uniform and *symmetrical*. There was no evidence of local paresis in the cutaneous cases. The first symptoms were tingling and numbness of fingers and toes. Postural and vibration sense were lost in severe cases. The spinal fluid in the more severe cases showed an increase in protein and, in 4 cases, a mild pleocytosis.

Penicillin Treatment.—A report of a sub-committee of the public health laboratory service (R. Cruickshank and others[7]) makes an authoritative statement, from the bacteriological standpoint, of the place of penicillin in diphtheria. Penicillin sensitivity tests were carried out on 284 strains of *C. diphtheriæ* isolated in different parts of the country. Most of the strains tested were two or three times as resistant to penicillin as the Oxford staphylococcus. *Gravis* strains were more resistant than *intermedius* and *intermedius* more resistant than *mitis* types. In the treatment of acute faucial cases, adults received 240,000 units daily, divided into four-hourly doses, and children proportionately less. With a six-day course, 23 out of 28 gave consistently negative swabs within four days of the end of treatment. This rate of disappearance of *C. diphtheriæ* is much more rapid than in the series of acute cases investigated by Wright,[8] which is taken as an adequate basis for comparison. It is therefore considered that penicillin treatment shortens the duration of carriage of *C. diphtheriæ* in acute cases. No comment is made on the question of clinical improvement. Penicillin treatment of persistent *carriers* did not give very encouraging results. In 31 carriers, rapid disappearance of the organism followed in only 13.

REFERENCES.—[1]*Ann. Rep. Min. Hlth.* 1947, 22, H.M.S.O. Lond.; [2]*J. Amer. med. Ass.* 1948, **137**, 1009; [3]*Brit. J. exp. Path.* 1947, **28**, 338; [4]*Lancet*, 1948, **1**, 97; [5]*Ibid.* 57; [6]*Ibid.* 277; [7]*Ibid.* **2**, 517; [8]*J. Path. Bact.* 1941, **52**, 129.

DISLOCATION, RECURRENT, OF THE ELBOW-JOINT.

T. P. McMurray, F.R.C.S.

The problem of recurrent dislocation of the shoulder-joint has been discussed very fully in surgical literature. The causes of redisplacement have been fully investigated, especially by Bankhart, and the principles of treatment have been generally accepted.

Although occurring as a rule in the shoulder, this complication of repeated dislocation is not unknown in other joints. This is especially so in the temporomandibular articulation, while Wainwright[1] discusses the occurrence of a similar type of disability in the elbow-joint.

The author states that he has been able to discover only 3 instances of this condition previously reported in the surgical literature; the first by Sorrel in 1935, then in 1936 Milch reported its occurrence as a bilateral disability in one patient, while in 1943 Gosman described another similar case.

The patient described in this article was a boy of twelve years who, at the age of ten, had sustained a simple dislocation of the elbow-joint as a result of a fall. After the reduction of the dislocation, the injury was treated by rest with the elbow at right angles for a period of two weeks. Following an apparent cure of the condition, redislocation had occurred on five occasions as a result of some trivial injury, usually when the elbow-joint was in a position of full extension. On each occasion the dislocation was reduced under gas anæsthesia, and on the fifth occasion the arm was immobilized in a plaster cast for a period of eight weeks. On clinical examination of the elbow, the only discoverable abnormality was a slight degree of active and passive hyperextension of the joint when compared with the normal side, and by radiographic examination it appeared that the olecranon fossa was shallow with a not very obvious deficiency in the depth of the coronoid process.

Under anæsthesia it was possible to reproduce the dislocation by a combination of downward pull and backward thrust of the forearm, this manœuvre being carried out while the patient was anæsthetized for operation.

As conservative measures of immobilization had failed it was decided that recurrence of the dislocation could only be prevented by increasing the height of the coronoid process of the ulna, which would thereby act as an effective block to the sliding forward of the lower articular surface of the humerus.

The joint was approached from the anterior aspect, the route employed being in the sulcus between the biceps tendon and the brachioradialis. On the floor of this space lay the brachialis anticus muscle, which was split vertically, giving an adequate view of the anterior portion of the joint capsule. This was found to be abnormally lax and on making a cut through its substance, the coronoid process was easily defined and prepared for the reception of a bone-graft.

Both Milch and Gosman, who had previously employed this method, had used a graft taken from the tibia, but in this instance, a flat cortical graft about three-quarters to half an inch was removed from the subcutaneous portion of the upper end of the ulna and inserted into the groove which had been previously prepared in the coronoid process. After closing the capsule, the joint was immobilized at right angles for two months. A series of radiographs taken at intervals demonstrated the subsequent partial absorption of the graft. Later the substitution of new bone became evident, and this new bone, although at first irregular in outline, was gradually moulded to conform with the contour of the lower articular surface of the humerus. This remodelling process occurred much more rapidly than would be expected. In the case of this patient it was evident that the cause of the dislocation was to be found in the abnormally shallow coronoid process and the laxity of the anterior border of the capsule of the joint, but the pathological changes in the other reported instances differed in many respects. Thus, Sorrel reported that in the patient described by him the ulnar collateral ligament was definitely deficient to such a degree that the dislocation always occurred through a lateral displacement of the humerus in the coronoid fossa.

Milch, on the other hand, was able to demonstrate in his case, which was bilateral, a true congenital abnormality of the sigmoid cavity. This was normally wide and shallow, permitting an excessive range of gliding movement of the bones of the joint.

No bony abnormality was demonstrated in the elbow-joint of the patient described by Gosman. All the ligaments were elongated and the joint could

be moved through an abnormal range in every direction, permitting the dislocation to occur in several directions.

The operation of placing a bone-graft in the coronoid process resulted in the provision of a sound joint in those instances in which it was employed. It would appear that the operation of capsulorraphy alone would be as unsuccessful as it has been in dealing with recurrent dislocation of the shoulder.

REFERENCE.—[1]*Proc. R. Soc. Med.* 1947, **40**, 885.

DIVERTICULITIS.

W. B. Gabriel, M.S., F.R.C.S.

A paper from the Mayo Clinic by J. de J. Pemberton, R. M. Black, and C. R. Maino[1] sets out in great detail *the progress which has taken place in the surgical management of diverticulitis of the pelvic colon*; in order to assess this, 389 cases of diverticulitis of the pelvic colon were divided into two groups: series A comprised 245 patients treated surgically in the years 1908 to 1940 inclusive, and series B comprised 144 patients operated upon in the years 1941 to 1945 inclusive. The chief point brought out by the authors is that *modern chemotherapy* has brought the surgical mortality-rate down from 14·7 per cent to 4·2 per cent; the drug used since 1942 has been sulphasuxidine in the dosage of 12 to 15 g. daily for 3 to 5 days before operation. It is shown that a colostomy proximal to the area involved by diverticulitis will be followed by resolution of the inflammatory reaction, and the mortality in series B proved to be 1·1 per cent compared with 5·1 per cent in series A. The patients with colostomy remained well so long as the colostomy remained effective, but of those whose colostomy was subsequently closed without a resection being done, only about one-third remained well, and in the light of this experience the authors recommend an exteriorization type of resection after an interval of 6 to 12 months after establishment of the colostomy; in the era after chemotherapy became available there were no deaths and approximately 80 per cent of patients were cured by resection, whether done as a primary operation or after colostomy. The following table summarizes the mortality-rate of the different surgical procedures in the two series of cases.

DIVERTICULITIS OF THE PELVIC COLON: SURGICAL PROCEDURES AND MORTALITY-RATE

SURGICAL PROCEDURES	SERIES A: 1908-40			SERIES B: 1941-5		
	Patients	Deaths	Per cent	Patients	Deaths	Per cent
Colostomy only	38	6	15·8	12	1	8·3
Colostomy, subsequent closure	31	1	3·2	7	1	14·3
Colostomy, subsequent exteriorization	22	3	13·6	41	0	0
Primary exteriorization	76	13	17·1	38	1	2·6
Colostomy, subsequent resection and end-to-end union	24	4	16·7	20	1	5·0
Primary resection, end-to-end anastomosis and colostomy	0	0	0	6	0	0
Primary resection, end-to-end anastomosis. No colostomy	16	2	12·5	4	1	25·0
Miscellaneous	38	7	18·4	16	1	6·2
	245*	36	14·7	144	6	4·2

* There were actually 5 patients less than 245.

The results were less satisfactory after primary resection with end-to-end anastomosis than after colostomy followed by resection. Examination of the total mortality for each series shows that it has been reduced from 14·7 to 4·2 per cent, and this they consider is due to chemotherapy, which has largely eliminated serious infections. In view of the obvious advantage of resections and of the reduced operative risk, the indications for surgical treatment are likely to be broadened.

REFERENCE.—[1]*Surg. Gynec. Obstet.* 1947, **85**, 523.

A. Rendle Short, M.D., F.R.C.S.

L. Anderson,[1] of the Mayo Clinic, writes on *acute diverticulitis of the cæcum*. He reports 8 cases, and gives a summary of about a hundred others from the literature. The patients are younger than is usual with diverticulitis of the sigmoid, and men and women are equally affected. The pre-operative diagnosis may be appendicitis, or carcinoma of the cæcum. An abscess or fæcal fistula is quite likely to form. Many varieties of surgical treatment have been used, ranging from local excision of the diverticulum to right hemi-colectomy.

R. Russell Best,[2] of Nebraska, discusses another unusual condition, *diverticulitis complicated by ileosigmoidal fistula*. This follows an attack of acute diverticulitis. The clinical picture is confusing. There may be abdominal cramps, active peristalsis, and distended loops of bowel. The patient may alternate between semi-obstruction and diarrhœa. It is not always safe to give a barium enema, but if the venture is made, it may show the fistulous connexion. Sigmoidoscopy will exclude carcinoma of the rectum or lower sigmoid colon. At operation, a large inflammatory mass is discovered. The best treatment is a lateral anastomosis of the ileal coils to by-pass the fistula, along with colostomy of the transverse colon. Best's four patients all did well. In two of them the colostomy was closed after a year.

REFERENCES.—[1]*Surgery*, 1947, **22**, 479; [2]*Ibid.* 1948, **24**, 30.

DRUG ADDICTION. (*See* ALCOHOL AND DRUG ADDICTION.)

DUPUYTREN'S CONTRACTURE. *Lambert Rogers, M.Sc., F.R.C.S.*

Dupuytren's contracture was last referred to in the MEDICAL ANNUAL for 1945 (p. 99), evidence being presented for its being an hereditary condition and not, as previously thought, traumatic in origin. Cases have been recorded of its appearance at identical ages in identical twins, further evidence in favour of its being a familial condition. Others do not accept this explanation. It is regarded by some as an inflammatory lesion, and by still others, notably R. C. Clay,[1] as neoplastic, the lesion being regarded as a fibroma. It is frequently seen in those who have never done any manual labour. Tord Skooz,[2] in a compilation of 2200 cases, found that it was six to eight times more common in men than in women, and that there were more instances in the right hand. He favoured a traumatic origin, suggesting that it is brought about by partial ruptures of the fascia. He also found that "knuckle pads", which are subcutaneous nodules found on the dorsal aspects of the fingers, are relatively common in patients with Dupuytren's contracture, and he confirmed M. Land's[3] observation made in 1941 of an abnormally high frequency of Dupuytren's contracture among epileptics, as it was present in 42 per cent of over 200 male epileptics.

C. L. Steinberg,[4] of New York, has recently drawn attention to the value of vitamin E in large doses (300 mg. daily, given in divided doses of 100 mg. three times daily) for early and moderately advanced cases. In these he claims that resolution may be complete after some months of treatment.

During the past year there have been two Canadian papers on Dupuytren's contracture, one by Stuart Gordon,[5] of Toronto, the other by R. G. Langston and E. J. Badre[6] of Vancouver. Gordon recognizes acute and chronic forms; he has seen 2 instances of the acute type in which the hand becomes swollen, stiff, and painful, and inflamed areas appear on the palm which are later sites of thickening. Pain, soreness, and interference with function are indications for treatment, which Gordon thinks should be excision of the fascia. Operation should not be done during the acute phase or during an exacerbation, but he points out that A. A. Campbell has observed that a hand from which the palmar fascia has been removed has lost 25 per cent of its gripping power. Langston and Badre, reporting their experiences of 88 cases, also advocate excision of the palmar fascia and at the same time amputation of the affected finger.

[Opinion on the treatment of this condition varies between the extremes of conservatism and of radical excision of fascia, parts of the skin, and amputation of fingers. The use of large doses of vitamin E is an innovation which would appear to be worthy of trial, and radical treatment should be reserved for only the most intractable cases in which prolonged conservative treatment—i.e., continued stretching—has failed. It is interesting to recall that the late Sir Robert Jones, who like some other surgeons had the condition himself, refused to have any operation performed and constantly stretched the contracting fingers. It may be that why the condition does not develop to any extent in the plantar fascia is because this is constantly stretched by the body-weight. —L. C. R.]

REFERENCES. [1]*Ann. Surg.* 1944, **120**, 224; [2]*Acta chir. scand.* 1946, **96** (supp. 139), 190; [3]*Acta psychiat. neurol.* 1941, **16**, 465; [4]*Med. Clin. N. Amer.* 1946, **30**, 230; [5]*Canad. med. Ass. J.* 1948, **58**, 543; [6]*Ibid.* 57

DYSMENORRHŒA. *Clifford White, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G.*

This extremely common disability is still in the very unsatisfactory state that its pathology remains almost unknown in spite of extensive research. Probably for this reason its nomenclature and classification into varieties differ in different text-books. It is almost unnecessary to state that its treatment is in a chaotic state and ranges from a psycho-analyst trying to find a father-complex to presacral sympathectomies. J. O. Haman[1] estimates that in U.S.A. 140 million hours of work are lost annually from dysmenorrhœa. Patients with acquired dysmenorrhœa starting when about 30 years of age often have physical signs of an acquired retroversion, fibroids, salpingo-oöphoritis, or endometriosis, and, since there is a definite pathology in such patients, the treatment should be simple and successful. These patients, however, constitute only a small proportion of the total, and the difficult cases are those often called primary and occurring in girls of about 17 years of age. Although commonly termed primary it is quite exceptional for the pain to come on with the first period and to recur with each subsequent period. One explanation of the 2 or 3 years' interval between the onset of the periods and the occurrence of pain is that during the first few years the bleeding is anovular. This is probably correct for a large proportion of these patients but certainly not for all, as is proved by the occurrence of pregnancy in young girls.

Taking the so-called primary cases as a whole, the pain usually starts on the first day of the bleeding and is relieved to a greater or lesser extent at the end of 24 hours. The amount of blood lost varies, but is often small. It is generally agreed that it most commonly afflicts those who pursue a sedentary occupation and are in poor general health. But many patients with primary dysmenorrhœa have pain during the whole of the period and also may complain of pain for 24 hours before the onset of the bleeding. The pain is usually colicky and cramping but radiates; there is often also a dull ache which is

felt in the back as well as in the lower abdomen. There is a tendency to sterility and the dysmenorrhœa is usually increased by sterile marriage, although the occurrence of pregnancy followed by vaginal delivery at term commonly cures the pain. Since the pain is colicky with intermissions, the idea that it is due to irregular uterine contractions trying to expel the blood has been widespread, and hence the attempt to treat the pain by atropine, which is still sometimes advised in spite of its failure to produce any improvement at all in the great majority of patients. The fact that cervical dilatation relieves some patients for a longer or shorter time has been held to support the uterine colic theory, and so does the recent work of R. Torpin, R. A. Woodbury, and G. E. Child[2] with intra-uterine bags.

It is of interest to consider what is happening in the pelvic organs shortly before and during menstruation. The endometrium has reached the full secretory or progestational phase and then degenerates; vasoconstriction of the coiled uterine arteries begins 4 to 24 hours before the onset of bleeding and then hæmorrhages occur into the deeper layers of the endometrium, forming a sub-endometrial hæmatoma. The blood forces its way to the surface of the endometrium and clots in the uterine cavity. Whitehouse postulated the presence of a fibrolysin to dissolve the clot and O. W. Smith[3] has demonstrated its existence. Hence the presence of clots in the vagina may be due to too much blood reaching the uterine cavity at one time so that a normal amount of fibrolysin cannot dissolve it or to a deficiency of fibrolysin so that a normal amount of blood cannot be dealt with. The association of vaginal clots with nulliparous dysmenorrhœa is well known. The surface layers of the endometrium are shed in every case either in small pieces or very rarely as a large membrane (membranous dysmenorrhœa). The passage of a large piece of membrane through a nulliparous cervix can cause pain just as the passage of a blood-clot, but V. S. Counseller[4] found dysmenorrhœa in only 47 per cent of patients who passed membranes. If the membrane is unusually difficult to cast off, the tension in the sub-endometrial hæmatoma will presumably be greater than usual and may be a cause of pain of a constant type which would be relieved when the blood comes away. In the ovary the corpus luteum is degenerating and blood is present in its centre; normally this blood is small in amount, but sometimes a large corpus luteum hæmatoma forms which is a definite cause of severe pain. Such a hæmatoma may explain the occurrence of severe unilateral dysmenorrhœa at long intervals in a patient who usually menstruates without pain.

The well-established fact that anovular bleeding is painless should be a strong criticism of the uterine colic theory, and tends to support the suggestion that the sub-endometrial hæmatoma may cause pain, as the hæmatoma is not present with anovular bleeding. L. W. Haus, J. W. Goldzieher, and E. C. Hamblin[5] stress that dysmenorrhœa is always associated with ovulatory menstruation - ovulation being shown either by the temperature chart or by the presence of progestational endometrium on biopsy. They therefore treated cases of severe functional dysmenorrhœa by trying to suppress ovulation by administering œstrogens. Stilbœstrol and ethinyl-œstradiol were used. Administration is started 20 days before the expected date of ovulation and is continued for 20 days. Treatment should be omitted every third cycle to ensure endometrial regression. Most investigators agree that such treatment can only cure the pain while the treatment is in progress, i.e., while a condition resembling metropathia is induced. They report on 54 patients who were given diethylstilbœstrol. With a total dosage of under 20 mg. of stilbœstrol, 36 per cent of their patients were freed from pain, and, with a total dosage of 60 mg. of stilbœstrol, 78 per cent. When treatment failed to cure

the pain there were indications that ovulation had not been suppressed. The risk of inducing floodings does not seem to be as great as might be expected and they state that no gross menstrual disturbance followed the treatment in spite of the large doses given to some patients. The grave disadvantages of deliberately producing anovular bleeding in place of true menstruation are obvious and such treatment is definitely contra-indicated if pregnancy is desired. It can only be said to be less objectionable than suppressing ovulation by testosterone. W. Blair Bell[6] suggested that uterine hypoplasia was frequently present in cases of nulliparous dysmenorrhœa. A girl of 17 would not be expected to have a large uterus, but the uterine sound usually passes nearly the full distance if a dilatation is being performed. As a result of the hypoplastic uterus theory many patients with dysmenorrhœa have been given small doses of œstrogens to make the uterus grow and not to try to suppress ovulation, but the results are disappointing. There is not any proof that those who suffer from dysmenorrhœa are producing an excess or a deficient amount of œstrogen or progesterone. Attempts to treat nulliparous dysmenorrhœa by progesterone have not been successful, although progesterone is in very low concentration in the system at the phase of the cycle when dysmenorrhœa comes on (E. C. Hamblin, C. Ashley, and M. Baptist[7]). Even if a heroic dose did cause an improvement in the pain the treatment would have to be continued every month indefinitely. In many patients progesterone increases the pain. The theory has been advanced that dysmenorrhœa is associated with vasoconstriction, but nitrites and nicotinic acid neither prevent nor relieve the pain.

Torpin and his associates[2] have used very delicate methods when repeating experiments with intra-uterine balloons. They obtained uterine contractions of high amplitude in some patients with colicky, doubling-up pains, but only very small amplitude in patients with the dull continuous ache. Unfortunately control patients who do not have dysmenorrhœa often show uterine contractions of high amplitude. In every one of 25 patients the injection of pitressin produced the characteristic dysmenorrhœa symptoms of that particular patient, including such a remote effect as headache. Pitocin, histamine, and acetylcholine caused less increase of uterine activity than pitressin. Acetylcholine and histamine injected intravenously never elicited the patients' complete menstrual pain, hence treatment of dysmenorrhœa by anti-histamine and anti-acetylcholine drugs does not appear to be a hopeful method. Some of the work on uterine contractions during pregnancy, labour, and the puerperium was reviewed in the MEDICAL ANNUAL for 1943 and 1944. Referring to the experiment of stimulating the pituitary stalk in cats it was noted that injection of epinephrine, acetylcholine, and histamine produced little expulsive effect on the uterus.

W. K. Diehl and J. M. Hundley[8] also carried out a most careful investigation of uterine motility during menstruation by means of intra-uterine bags. Their technique was extremely elaborate, the bags being retained for up to five and a half hours, so that any irritability of the uterus caused by the introduction of the bag had time to pass off before the tracings were made. They state: "A most careful comparison of the tracings revealed no significant difference in any component of contraction between those patients suffering from dysmenorrhœa and those in whom menstruation was painless. It suggests, at least, that the causative factor in dysmenorrhœa is possibly not muscular in character." As part of their research they found that viburnum prunifolium is not a panacea for menstrual pain.

There is also the question of a menstrual toxin as a cause of dysmenorrhœa. D. I. Macht and D. S. Lubin[9] described a menotoxin 25 years ago, and Macht[10] made further reports in 1943. Recently O. W. Smith[3] published elaborate

researches on this subject, which is reviewed elsewhere in this volume (*see* MENSTRUAL TOXIN).

Presacral Sympathectomy for Dysmenorrhœa.—This subject is discussed by F. M. Ingersoll and J. V. Meigs.[11] Of 111 operations performed between 1930 and 1946, 89 were for essential and 19 for acquired dysmenorrhœa. Of the 19 women with acquired pain, 52 per cent obtained complete relief, 21 per cent partial relief, and the operation failed in 26 per cent; of the primary cases, 81 per cent reported complete relief, 4 per cent partial cure, and 14 per cent were failures. In the acquired cases neurectomy was combined with any further surgery that the local condition demanded. There was no mortality among the 111 cases. Since many operators report 10 to 15 per cent failures, the authors tried to find the cause of the failure in the 12 patients with essential dysmenorrhœa. They conclude that failure was due to incomplete sympathectomy in 7, regeneration of the nerves in 2, and psychoneurosis in 3. In the hope of saving a neurotic patient from being subjected to a major operation that will not cure her, Ingersoll and Meigs tried giving 1 mg. of stilbœstrol daily, starting on the first day of the loss and continuing for 20 days, in order to prevent ovulation occurring. Any bleeding from the uterus if ovulation does not take place is an œstrogen-withdrawal bleeding and so should be painless. If the patient complains of pain with an œstrogen-withdrawal bleeding she is not regarded as suitable for neurectomy and it suggests that she should consult a psychiatrist rather than a surgeon. This is probably going too far, as œstrogens did not always stop ovulation in Haus's patients quoted above, and S. Sevett and others[12] have proved that ovulation may take place within a few days of the end of the period.

Regeneration of the sympathetic nerves has been proved to occur in cases of Raynaud's disease where a second operation demonstrated the regenerated nerves.

Of the 111 patients 24 have had children subsequent to the operation. In 8 the discomfort of labour was slight, pain being limited to the passage of the child through the vulva.

Gynæcologists know that occasionally an interval appendectomy is followed by dysmenorrhœa. Ingersoll and Meigs quote 2 interesting cases. One had painless periods from the age of 12 till 19, appendectomy was then done and dysmenorrhœa ensued, and increased till neurectomy at 23 years. No cause for her pain was found at the laparotomy but sympathectomy gave complete relief. The second case was almost identical, and 2 other similar cases are mentioned. J. P. Greenhill[13] states that he has not had failures in sympathectomies performed for dysmenorrhœa.

REFERENCES.—[1]*Amer. J. Obstet. Gynec.* 1945, 755; [2]*Ibid.* 1947, 766; *J. Amer. med. Ass.* 1947, **134**, 1081; [3]*Amer. J. Obstet. Gynec.* 1947, 201; [4]*Ibid.* 1938, 877; [5]*Ibid.* 1947, 820; [6]*J. Obstet. Gynaec.* 1923, **30**, 119; [7]*Endocrinology*, 1939, **24**, 1; [8]*Amer. J. Obstet. Gynec.* 1948, 281; [9]*J. Pharmacol.* 1923, **22**, 413; [10]*Amer. J. med. Sci.* 1943, 281; [11]*New Engl. J. Med.* 1948, **238**, 357; [12]*Lancet*, 1946, **2**, 448; [13]*Brit. med. J.* 1947, **2**, 859.

EAR, AFFECTIONS OF. (*See also* AURAL AND NASAL SUPPURATION.)

F. W. Watkyn-Thomas, F.R.C.S.

Otitis Media with Gastro-enteritis in Infancy.—This subject has been frequently discussed in the past (*see* MEDICAL ANNUAL, 1933, p. 151, and 1938, p. 154). The association between the two conditions was recognized, but there was considerable doubt as to whether it was causal or casual, and whether the otitis was the cause or the effect of the enteritis. D. W. Hall and J. E. G. McGibbon, in papers at a discussion before the Royal Society of Medicine,[1] review the present position. D. W. Hall regards the acute non-specific gastro-enteritis of infants as a special condition limited to the first year of life. The incidence

and the mortality vary considerably from year to year, as do the number of cases in which there is associated otitis media. She found that the belief that gastro-enteritis was secondary to a primary mastoid infection was untenable; many of these children had no otitis, but where there was mastoiditis, especially if 'frank pus' was found, operation gave immediate improvement. Text-book signs of mastoiditis are not found in these children; the only reliable evidence is provided by the drumhead, and here there are peculiarities in the infant which confuse the diagnosis. These differences from the older drumhead are fully and carefully described in the paper. Any child showing an abnormal drumhead was treated by immediate myringotomy, repeated if need be. If, associated with positive myringotomy, there was persistent pyrexia, persistent or increasing diarrhœa (which she finds a much more reliable indication than vomiting), sudden or recurrent dehydration, persistent failure to improve, or persistent otorrhœa associated with any of these signs, the mastoid should be opened. In such a case, both mastoids should be opened, even if one drumhead shows no signs. In some refractory cases, now seldom seen, where no cause for the symptoms can be found, the mastoid should be opened to exclude a 'silent' mastoiditis.

General anæsthesia is inadvisable, as chest complications may follow, or the child may be unduly collapsed; also, the resumption of normal feeding is delayed. Morphine, $\frac{1}{10}$ gr. to 14 lb. of body-weight, is given long enough before operation to allow it to act, and operation is done under procaine with 2 min. of adrenaline to 1 c.c. A single straight incision is adequate. Opening the antrum is not enough; all cells must be opened, and it was found that pneumatization is much more advanced than the text-books teach; in one case the zygomatic area was pneumatized at 4 weeks old. The bacteriology is confusing; in one case a child with *Str. viridans* in the throat and a *viridans* septicæmia had pneumococcus in one mastoid and *Str. hæmolyticus* in the other. Coliform organisms play a variable part, but their presence may account for the poor results of penicillin; on the whole penicillin and sulpha drugs together act better than either of them separately. One view of the diarrhœa and vomiting is that it is a 'trigger response' to some stimulus, possibly a virus, and the response, once started, can be elicited by any subsequent stimulus, of which otitis media is one. J. E. G. McGibbon reported on a series of 104 infants suffering from diarrhœa and vomiting, who were operated on for latent mastoiditis between September, 1945, and December, 1946. During this period of those who died of diarrhœa and vomiting without showing any signs of ear infection 32 were found *post mortem* to have infection of the middle ear and mastoid. In fatal cases pathological changes in the bowel were found only in about 25 per cent; rectal swabs were negative in 66 per cent, which is in favour of a virus infection, and in some brain lesions characteristic of virus infection were found. The otitis is usually secondary to nasopharyngitis by infection directly ascending the Eustachian tube or by lymphatic spread. Further, vomiting may infect the nasopharynx, or even directly the ear, by regurgitation into the tube. None of these lesions can be regarded as a separate entity; they form part of "the syndrome of acute otitis media, latent mastoiditis, and diarrhœa and vomiting which constitutes a vicious circle". McGibbon agrees with Hall on the indications, and on the lack of classical symptoms. Whether the enteritis be bacterial or virus-caused, the mastoiditis is undoubtedly bacterial. The bacteriology is uncertain; in McGibbon's series the commonest organism found was *B. coli*, usually in mixed infection, the commonest found in pure culture was *Staph. aureus*; *Str. hæmolyticus* was surprisingly rare. Mastoid drainage was done under local anæsthesia, with chloral and bromide premedication. The majority of McGibbon's patients came for operation only as a last resort, and he holds

that the mastoid should be opened if myringotomy fails to improve the condition in 24 hours. Penicillin and sulpha drugs were disappointing. Treatment of dehydration by intravenous infusion is most important; in some cases whole-blood transfusion has been a life-saving measure. In the discussion that followed there was general agreement with the opening papers.

H. S. Sharp emphasized the difficulties of diagnosis. J. Crooks remarked on the curious point that sometimes when a mastoid was opened and nothing was found, the child immediately improved. No explanation was found for this. He did not think the mastoid should be explored if there were no signs of inflammation in the ear. G. A. Fraser said that in 27 bilateral mastoid operations performed in a year on babies with gastro-enteritis, in half there were no signs of middle-ear disease, but at operation, of the 27 cases, in 2 only was a perfectly healthy mastoid found.

Aetiology of Swimmers' Exostoses of the External Auditory Canals and of Associated Changes in Hearing.– W. Stirk Adams[2] discusses the connexion between exostoses of the external auditory meatus and swimming. Many suggestions have been made as to the cause of this condition—syphilis (now discredited), gout, fractures of the meatus (which must be very rare indeed), " high alcoholic intake ", heredity, especially in association with otosclerosis. Stirk Adams traces the idea that the condition is secondary, in many cases, to swimming, back to Field in 1893. Field remarked that most of his patients who had double ivory exostoses were confirmed sea-bathers, that the condition is very uncommon in women, and of extreme rarity in hospital practice. Van Gilse, in 1938, confirmed the figures of sex ratio, and produced valuable evidence from the examination of skulls in the institute of anatomy at Leyden of the high incidence of aural exostoses among peoples who indulged much in swimming. He examined 92 students – 19 women included—of whom 55 had exostoses. Of these only 3 had no " water-history " ; 23 had no water-history and no exostoses ; 14 had a water-history without exostoses. Of 10 professors of swimming the only one who had no exostoses did not allow water to enter the ears. He believes that the exciting factor may be the intense hyperæmia deep in the meatus found after swimming. On these lines Stirk Adams reports a carefully worked-out series of cases of meatal exostoses, and a most valuable ' control '. In 22 men and 6 women with exostoses he found a history of long swimming. Whether the water was salt or fresh seemed to make no difference, nor did the swimming stroke most used. He described 2 cases in which, for a long lifetime, the patients had rolled their heads in daily baths—one hot and one cold. As a control he examined the ears of 18 boys in a school swimming team ; of these only 4 showed no alteration of the external auditory canals from the normal symmetry, and of 11 non-swimmers from the same school only 2 showed any deviation, and one of these immersed the head in hot baths.

Stirk Adams concludes that, in certain predisposed subjects, contact of water in the external meatus for long periods causes exostosis production. In a few cases only is this associated with " social deafness ". His diagrams show that the exostoses are usually of the sessile type, often a hyperostosis of the canal. None of his cases seem to have had the pedunculated, cancellous exostosis.

[It must be admitted that this paper adduces strong evidence in support of the view that the most common cause of meatal exostosis is the periosteal irritation produced by the hyperæmia described by van Gilse. The question whether such irritation can also induce changes in the mastoid or in the middle ear must be most carefully considered. It may well be that the hereditary tendency often noticed in these cases may be explained by some factor which predisposes the patient to the condition ; at the same time we should remember a familial or local tradition of swimming as a factor.—F. W. W.-T.]

Escape of Cerebrospinal Fluid into Wounds of Operations on the Temporal Bone.—H. I. Lillie and A. A. Spar[3] analyse 22 cases already recorded in the literature where fluid escaped spontaneously at, or after, operation, and report 4 more. Seven of the cases had had some form of labyrinth operation, usually the Neumann. In one case an auditory-nerve tumour had been removed. In one there had been operation on the Gasserian ganglion. In the others there was nearly always a history of one or more mastoid operations. Where the escape is through a fistula of the bony labyrinth "almost without exception" the discharge stops of itself, without any special treatment. The normal dura is strong and tough, but it may be softened by inflammation or by cholesteotomatous erosion. In operations on the petrous pyramid, especially when the dura is bound down by adhesion to the bone, it is easy to injure it. The first recorded repair of a post-operative fistula was a case of Canfield's in 1913. In this case the dura of the cerebellum was injured in the course of a labyrinthectomy, and Canfield closed the gap with a piece of dura from a dog. If the dura is normal and healthy Lillie and Spar advise suturing with silk. If this cannot be done bone should be removed until healthy dura is exposed all around the perforation; soluble 'cellucotton' is packed over the gap, and is cured by a piece of animal membrane or a flap of fascia. All splinters of bone should be removed, and bone edges smoothed down. In secondary mastoid operations there is always the danger that dura, exposed at a previous operation, may be bound to the scar.

[The cessation of flow of cerebrospinal fluid through an injured labyrinth is common experience, but it is difficult to say exactly how the arrest takes place. Even in cases of the translabyrinthine operation for meningitis, where the internal meatus was deliberately opened, in surviving patients the discharge always ceased in a week or two. In cases where one or more mastoid operations have been done, with exposure of the dura, the danger of injuring it at any further operation is minimized if a large flap is made, with the incision well behind the earlier operation area.—F. W. W.-T.]

Modifications of Operative Methods.—Mention has been made of the *endaural mastoid approach* in previous editions of the MEDICAL ANNUAL (1941, p. 101). With some years' experience it is possible to evaluate the method. For *labyrinth fenestration for otosclerosis* this is now the most usual approach, as has been taught by Lempert, Shambaugh, and others. Some surgeons (Simson Hall, 1946, p. 240) still adhere to the ordinary postauricular route. The great advantage of the Lempert endaural method in this operation is that it is easier to make the flap by it, and most surgeons find the actual labyrinth exposure is better. For this last reason the endaural method is convenient for all labyrinth surgery, especially when, as is often the case, some form of radical operation has already been done. The endaural route is a simple and convenient approach for conversion of an old simple mastoidectomy to a radical operation, or for revising an old radical operation. For the ordinary radical and modified radical operations, the majority of surgeons still prefer the postauricular approach. For acute suppurations and mastoid complications the endaural method is not much favoured in this country.

A. Tumarkin[4] has evolved a *transmeatal attico-antrotomy for chronic tympano-mastoid suppuration*. In the past this method has been generally condemned on account of its inadequacy, the difficulty of operation, and the dangers to the deep structures. Tumarkin's method avoids many of these disadvantages. It differs entirely from the orthodox endaural method—which essentially consists in displacing the auricle and soft structures backwards instead of forwards—in that there is no displacement of auricle or meatus. The operation is genuinely *intrameatal*. A flap is cut, through a wide, slotted speculum, and bone is removed with fine labyrinth gouges. There is no attempt to remove

bone by punches, and no blind struggling with the ossicles. The flap covers the greater part of the cut bony surface. (*Plates XV–XVII* and *Figs.* 16–19.)

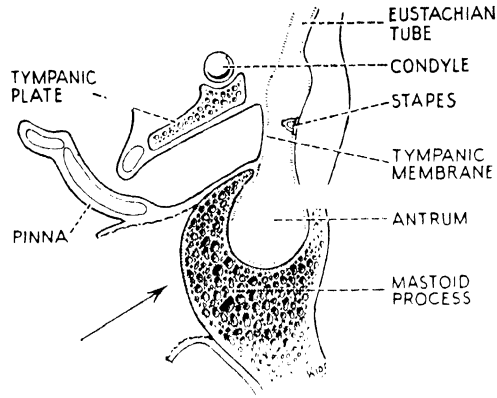


Fig. 16.—Classical radical mastoidectomy. Showing post-auricular incision and radical excision of mastoid proce (shown by shaded area).

[This is a delicate and highly skilled technique, which should give good results in suitable cases, e.g., a small attic cholesteatoma. The difficulty is to decide beforehand on the conditions within the mastoid. In most cases of chronic suppuration the bone is dense and the pneumatization poor. The most skilled radiologist may not be able to tell us what actually is the lesion hidden in dense bone; a large cholesteatoma may only be partly revealed by radiographs, and an empyema, a cavity formed by the breakdown of a chain of cells in a largely sclerotic mastoid, may escape detection entirely. For such cases the operation would be inadequate. F. W. W.-T.]

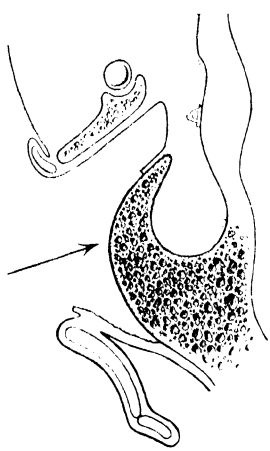


Fig. 17. Lempert's endaural anti-auricular mastoidectomy. Showing endaural excision of skin, mobilization of concha and radical excision of bone as in *Fig.* 16.

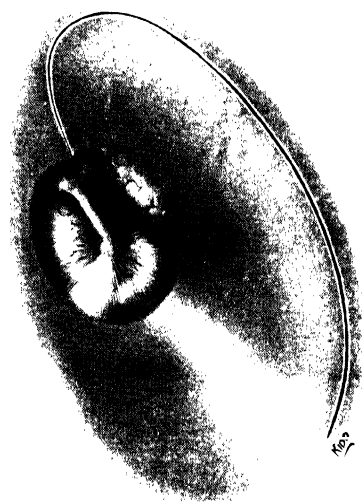
O. Popper[5] describes a *transtympanic route for labyrinth fenestration*. His incision is placed anteriorly to the tragus, and the meatal cartilage is freed from the tympanic plate and pushed back. The tympanic plate is cut away, and the membrane fully exposed. A flap, including the membrane, is turned down, and the contents of the middle ear are exposed. Popper states that he has done "almost one hundred" of these operations—not all for fenestration—and that "most of my cases have had no discharge whatever within three weeks after the packing was removed", his point being that, by avoiding any exenteration of the mastoid he avoids the moist cavity and discharge which often complicate a fenestration operation.

Effects of Multiple Sclerosis on the Auditory Nerve.—These have been studied by H. von Leden and B. T. Horton[6] in 92 patients, of whom 78 were under forty years of age: 57 per cent of the patients had normal hearing; 43 per cent

PLATE XV

TRANSMEATAL ATTICO-ANTROTOMY

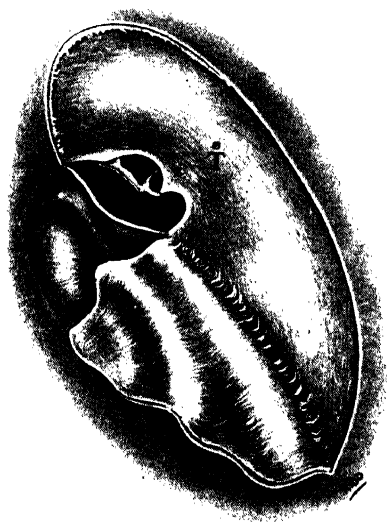
(A. Tumarkin)



XV–XVII and Figs. 16–19 by kind permiss of the edings of the Royal Society'.

TRANSMEATAL ATTICO-ANTROTOMY—continued

(A. TUMARKIN)



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TRANSMEATAL ATTICO-ANTROTOMY—continued

(A. Tumarkin)

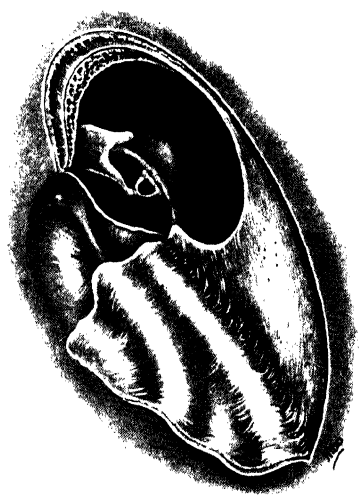


Fig. C. The bone excision completed. Showing incus, semicircular canal, facial nerve, and stapes. This shows a comparatively limited excision of bone. The exposure can easily be extended forwards, upwards or backwards. The strip of bone overlying the head of the malleus would normally be removed so as to gain access to Prussak's pouch.

had a measurable degree of deafness—a loss of over 25 decibels in one or both ears, as measured by a specially calibrated pure tone audiometer. In some cases there were defects up to 70 decibels loss for some tones. Of these patients only 12 had noticed any hearing defect, and of these 12 only 5 had defective hearing. The writers comment on this disparity between subjective and objective disturbance of function as characteristic of the condition. It was regarded as typical of the condition that there seemed to be no correlation between the degree of deafness and the severity of the disease. The tests were repeated at regular intervals to determine whether any change took place as the disease progressed. Differences up to 25 decibels were noted, but the period of observation has been too short to form any legitimate conclusion as to how this variation

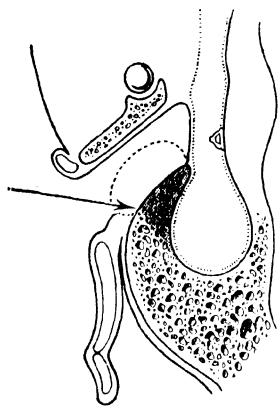


Fig. 18.—Transmeatal attico-antrotomy (author's technique). Dotted line shows skin flap turned downwards. Note limited excision of bone (shown by shaded area).

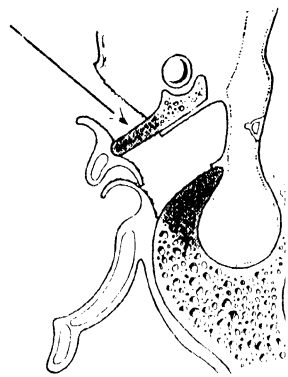


Fig. 19.—Transmeatal attico-antrotomy (Popper's route). A pre-auricular incision is made so as to expose the tympanic plate. This is excised and the external auditory canal is entered through its anterior wall. Bone excision as in *Fig.* 18.

is affected by changes in the basal condition. On the other hand, it was found that changes in vestibular activity did offer a fair indication of the general changes. As a control a similar number of normal persons were tested under the same conditions. Slight hearing changes were present in 18 per cent as against varied changes in the 43 per cent.

Neurinoma of the Facial Nerve. This is a rare condition. Only 16 cases have been reported. Of these, 13 were diagnosed clinically, 2 were discovered incidentally after death. Karsten Kettel[7] reports another case. A woman of 32 had complete right-sided facial paralysis. Seven years before she had had severe pain around, not in, the ear followed by complete paralysis of the right side of the face, with reduction of taste along that side of the tongue. Paralysis improved but never entirely cleared up; the pain remained all the time. Two months before admission paralysis again became complete. The facial nerve was decompressed, and a tumour "the size of a hazel nut" was found on the pars descendens. This case is peculiar, as the paralysis diminished and then returned, the pain was constant, and there was no sign of the swelling in the external meatus. The neurinoma usually arises from sensory nerves or sensory roots of mixed nerves. This seems to show that there are sensory fibres in the descending part of the facial nerve.

Another case is reported by Nils Lundgren.[8] A man of 41 had left-sided tinnitus and deafness for a month. The whole auditory canal was filled by a rounded polypoid tumour which arose from the postero-inferior wall. When it was snared off, a normal drum was seen, and hearing returned. There was no facial palsy except a very doubtful weakness of the left eyelid. The growth was exposed by a radical mastoid operation, and was found to arise by a broad base from the descending part of the facial nerve. It was removed, leaving only enough not to risk injury to the nerve. The cavity healed quickly, and the function of the nerve was unimpaired. Probably the early break-through into the external meatus, which made early diagnosis possible, is responsible for the absence of paralysis.

[At the postero-inferior quadrant of the meatus the nerve sometimes lies very close to the surface, a point to remember when exposing the round window in labyrinth operations.—F. W. W.-T.]

REFERENCES.—[1]*J. Laryng.* 1948, **62**, 396; [2]*Proc. R. Soc. Med.* 1949; [3]*Arch. Otolaryng.* 1947, **46**, 779; [4]*Proc. R. Soc. Med.* 1947, **40**, 761; [5]*J. Laryng.* 1946, **61**, 24, and *S. Afr. med J.* 1948, **22**, 42; [6]*Proc. Mayo Clin.* 1947, **22**, 279; [7]*Year-book of Eye, Ear, etc.* 1947, **314**; [8]*Ibid.* 1948, 246.

ELBOW-JOINT, RECURRENT DISLOCATION OF. (*See* DISLOCATION, RECURRENT, OF THE ELBOW-JOINT.)

ELECTROCARDIOGRAPHY.

William Evans, M.D., D.Sc., F.R.C.P.

Right Ventricular Hypertrophy.—G. B. Myers and H. A. Klein[1] have given an account of the electrocardiogram in 40 cases which were examined at necropsy. The following are some of the deductions they made. There was a reversal in the ratio of the amplitudes of the R and S waves in V_1 and V_6, characterized by an abnormally large R in proportion to S in V_1, a diminution in ratio in leads further to the left, and a prominent S in V_6. There was a tendency to inversion of the T wave in V_1, and absence of notching of the R wave in the same lead. Additional leads higher than and to the right of V_1 will sometimes show the presence of right ventricular hypertrophy when the S is also deep in V_6. When right bundle branch block was present the R wave in leads from the right side was prominent and notched. The presence of right axis deviation in the standard leads accompanied by inversion of the T wave in Leads II and III was not diagnostic of right heart hypertrophy, for such changes may be found in left ventricular hypertrophy and even in health.

REFERENCE.—[1]*Amer. Heart J.* 1948, **35**, 1.

ENDOCARDITIS, BACTERIAL.

William Evans, M.D., D.Sc., F.R.C.P.

Treatment.—Experience with *penicillin* in the treatment of 44 patients with bacterial endocarditis has been reported by O. Paul, E. F. Bland, and P. D. White.[1] Twenty-nine were living and considered cured. One patient died from a second attack of bacterial endocarditis, and 8 others succumbed to cardiovascular complications of the disease, although the infection itself appeared to have been overcome. Six patients died without evidence of control of the bacteræmia. Rheumatic heart disease was present in 82 per cent of cases in the series; 14 per cent were diagnosed as having congenital heart disease; 1 case was classified as having calcareous aortic stenosis. Upper respiratory infections preceded the endocarditis in 30 per cent of cases, and extraction of teeth in 11 per cent. Alpha-hæmolytic streptococcus was responsible for the infection in 82 per cent of cases. There were 5 cases of marked bacterial resistance to penicillin *in vitro*; 2 of these patients were cured.

R. J. Glaser and others[2] observed the effect of penicillin on the bacteræmia following dental extraction, and found that the administration of large doses of penicillin for twenty-four hours prior to dental extraction caused a significant decrease in incidence of bacteræmia following extraction, but failed to

prevent it in a large number of cases. The agent was particularly effective in decreasing bacteræmia after extraction of teeth from infected gums. The recommendation was made that this agent be given to all patients with rheumatic and congenital heart disease before and after dental extraction.

From the treatment of 9 cases, 8 of which recovered, W. H. Clark, S. Bryner, and L. A. Rantz[3] considered that the following facts should be known regarding penicillin treatment. The *in vitro* penicillin sensitivity of the causative organism should, if possible, be determined before therapy is instituted. The initial daily dosage of penicillin should be based on these studies. Cases with sensitive organisms should receive at least 500,000 units per day. When the causative organism is moderately or markedly resistant, 1, 5, 10, or even 20 million units should constitute the daily dosage. The duration of therapy should be approximately four weeks. More prolonged therapy is usually unnecessary if adequate amounts of penicillin are used, and increased resistance of the organism to penicillin may develop under prolonged subcurative dosage. The daily penicillin dosage should be drastically increased five- to ten-fold if the circulating blood is not promptly sterilized after treatment has been started or if relapse occurs subsequent to its completion. There will be instances of unnecessarily intensive therapy, but arrest of the infection should more nearly approach 100 per cent. The drug may be effectively administered by continuous drip or intermittent intramuscular injections. The latter method is more simple and very large individual doses of crystalline penicillin can be given with minimal local discomfort. The use of anticoagulants is not indicated. Streptomycin may advantageously be used alone or simultaneously with penicillin in some very resistant cases.

B. M. Wagner[4] has analysed the reports in the literature of 521 cases of bacterial endocarditis treated with penicillin. Clinical arrest was effected in 371 patients who have continued to remain well. Improvement took place in another 95, but the infection returned later and they died. The remaining 55 failed to respond to penicillin. His study of these cases made him emphasize the following principles of treatment. The sensitivity of the infecting organism to penicillin should be determined *in vitro* within a range of 0·1 to 1 unit per c.c. If the organism is sensitive, the dosage of penicillin should be 500,000 units daily by continuous intravenous drip. All cases should be treated as early as possible. Therapy should be continued for at least 28 days. If the patient's condition does not improve, 1,000,000 units should be given daily for 28 days. The plasma level of penicillin and the sensitivity of the organism to penicillin *in vitro* should be determined twice a week.

REFERENCES.—[1]*New Engl. J. Med.* 1947, **237**, 349; [2]*Amer. J. Med.* 1948, **4**, 55; [3]*Ibid.* 671; [4]*Amer. J. med. Sci.* 1948, **215**, 84.

ENTERIC FEVER SPREAD BY PASTEURIZED MILK. (*See also* TYPHOID AND PARATYPHOID FEVERS.) *W. H. Bradley, D.M., M.R.C.P.*

As the result of a sustained attempt to apply typing with Vi bacteriophages to a field study of endemic typhoid fever, W. H. Bradley[1] in 1943 showed that contaminated milk might do no more than give a string of single cases of typhoid spread over a long period of time. In this experience the milk, which came from a distributor who professed to pasteurize, had on certain occasions escaped adequate pasteurization. Now, as the result of experience in Wales during 1946, Dr. Thomas, the M.O.H. for Glamorgan, and his colleagues on the public Health Laboratory Staff at Cardiff have reported[2] that milk which had passed through the pasteurizing chambers into bottles contaminated by water from the jets of the washing machine caused 55 cases of paratyphoid B occurring in six months in connexion with a creamery distributing 15,000 gallons

a day to 200,000 people. The cases were spread over 12 local authority areas. The lessons are these: (*a*) Water used to rinse bottles before they are filled with milk should be potable water. (*b*) A review from time to time of all cases of enteric fever which have occurred in a district over a long period may lead to an explanation which gratifies the epidemiologist and, incidentally, prevents further disease.

Looking back over the past history of the districts in which this milk was consumed, it was found that available data fitted into the conclusion that an unexplained outbreak of 76 cases in 1941 had almost certainly been due to the same source. The writers also observed that 3 patients who did not consume the milk were boys who had bathed in the river which flowed by the creamery which was the main source of water used in the creamery. The creamery consumed 3000 gallons hourly. Chlorine, to produce a concentration of 2·5 parts per million, was injected by an automatic pulsator into the crude water, which was then passed through a Candy pressure filter to an elevated storage tank of 5000 gallon capacity. From the tank this water passed to the bottle-washing machines, where, after the initial cleansing with hot detergents, it was used for the final rinsing immediately before the bottles were filled with pasteurized milk. The bottles were rinsed both inside and outside as they passed inverted on a conveyor system. Samples of this water had often been taken from the jets of the bottle-washing machines for examination in the creamery's laboratory, and readings of 0·3–1 parts of residual chloride per million were usual, but occasionally much lower readings were obtained. Bacteriological examinations had been made periodically, and presumptive coliform bacilli often found. The river water was heavily contaminated.

REFERENCES.—[1]*Brit. med. J.* 1943, **1**, 438; [2]*Lancet*, 1948, **2**, 270.

ERYTHEMA NODOSUM. *Una Ledingham, M.D., F.R.C.P.*

The relationship of this syndrome to tuberculosis and to rheumatic fever requires clarification, especially in regard to the handling and after-care of the patient. Needless anxiety may be caused and restrictions applied on the supposition of a specific relationship. Favour and Sosman[1] do much to clear the air in a comprehensive study of 155 cases seen in Boston over the past twenty years. Their conclusions and observations agree with the experience of clinicians in this country. The disease is regarded as a hypersensitivity state contributed to by individual predisposition on the one hand and a variety of infective and chemical agencies on the other. In other words there are both constitutional and acquired factors. They remark on the wide variety of such infective agents apart from tuberculous and streptococcal infection. Coccidioidomycosis, meningococcal infections, ulcerative colitis are among those mentioned. Thus erythema nodosum is an unusual manifestation of many common diseases. The cases conformed to the average clinical type, four-fifths occurring in women, mostly between 20 and 40 years of age. There was a remarkable lack of rheumatic fever and tuberculosis in the family and personal histories. Most striking was the association with respiratory infections, over 80 per cent of these patients so suffering in the few weeks preceding the onset of their erythema. Two further points emerge. A majority of patients complained of migratory joint pains, often with swelling and sometimes with redness and hydrarthrosis. This arthritis appeared as often before as after the erythema attack. Secondly, nearly half the patients examined by X rays (67) had enlarged hilar or peri-bronchial glands with frequently associated palpable superficial glands. These findings tend to explain away the previous assumption of a rheumatic or a tuberculous basis for the syndrome.

REFERENCE.—[1]*Arch. intern. Med.* 1947, **80**, 435.

EYE AFFECTIONS. (*See also* TISSUE THERAPY BY FILATOV'S TECHNIQUE IN OPHTHALMOLOGY.)

EYE AFFECTIONS : CHEMOTHERAPY.

Sir Stewart Duke-Elder, K.C.V.O., D.Sc., M.D., F.R.C.S.

The further use of the sulphonamides and penicillin has consolidated their value in treatment of ocular infections, but during the year under review no fundamentally new observations have been made which have not already been noted in previous editions of this ANNUAL.

Penicillin.—In view of the fact that it is now becoming easy to obtain, penicillin is being used as a prophylactic for ophthalmoblennorrhœa in the newborn in place of the classical method with silver nitrate or one of its organic substitutes. Thus, a report from Italy by A. Fadda and E. Zambetti[1] deals with 689 newborn infants in whom penicillin ointment (containing 500 O.U. per g.) was applied to the conjunctival sac immediately after birth and afterwards twice daily for 5 days. Ophthalmoblennorrhœa appeared in 2 cases only (0·29 per cent). The figures of the previous years when prophylaxis was conducted according to Credé's method were 2·10 and 2·05 per cent.

Again, in America H. C. Franklin[2, 3, 4] has made a study of the bacterial content of the conjunctiva after a single instillation of penicillin ; and a comparison of the results with those obtained with silver nitrate. The infants were treated in the delivery room within an hour of birth. The eyes were either flushed with normal saline and treated with one drop of penicillin (2500 units per ml. of normal saline) or flushed with sterile distilled water and treated with one drop of 1 per cent solution of silver nitrate.

In each group the eye swabs from 10 infants were cultured during the interval up to four hours after treatment, eye swabs from another 10 were cultured four hours later, and so on through the first forty hours after treatment, making a total of 100 infants studied. No infant whose eyes contained pus was included. A swab was taken from each eye, plunged into sterile broth, and streaked across plates of McLeod's medium, blood-agar, and eosin and methylene-blue agar. The broth was then added to two tubes of blood-tryptose broth. Some cultures were incubated at 37·5° C., after sealing by the Varney method for detecting anaerobic organisms. The two plates of McLeod's medium were sealed under carbon dioxide tension, and incubated at 37·5° C. ; all the others were examined after 24 hours and, if negative, again after 48 hours, when plates of McLeod medium were also examined for *Neisseriæ*. All plates negative after 48 hours were discarded, but any negative specimens of broth were re-examined five days after inoculation ; after this period negative broths were discarded and positive ones were plated and the organisms identified.

Positive cultures were obtained in 41 per cent of penicillin-treated cases and in 45 per cent of the others. In the former, 46 organisms were isolated in the 41 positive cultures and the type and incidence of these organisms in relation to time of appearance were tabulated ; in the latter, 47 organisms were isolated in the 45 positive cultures. In the penicillin-treated cases, 30 per cent of the cultures were positive in the first 20 hours of life and 52 per cent in the following 20 hours ; in the other group, the number of positive cultures also increased with time, 36 being positive in the first 20 hours and 54 in the second. Seven anaerobic organisms were found in 93 positive cultures, 4 in group 1 and 3 in group 2. There were no gonococci.

This study indicates that penicillin compares favourably with silver nitrate as a prophylactic agent. Further study is required for interpretation of the observed increase of the bacterial flora with time in the conjunctiva of newborn infants.

The American Academy of Ophthalmology appointed a committee to investigate this matter and their report has recently been issued. The following points are emphasized : The Credé method with 1 per cent silver nitrate produces a variable degree of conjunctival irritation but has never caused ultimate visual loss ; penicillin is said to be equally ineffective against virus infections and is also relatively ineffective against coliforms, some staphylococcal, and a few gonococcal strains ; the suggested dosage of penicillin necessitates intramuscular injections which have theoretical objections, or instillation of drops on each of the first four days which requires more nursing time than with the single Credé instillation ; a single instillation of penicillin is considered inadequate

although the recently available high concentrations (100,000 units per gramme of penicillin-G ointment) may be found satisfactory. The time is thus not considered ripe to advocate replacement of silver nitrate by antibiotic drops in prophylaxis.

Streptomycin.—Most interest during the past year has been concentrated on the value of streptomycin in ophthalmology. Like penicillin, streptomycin is not absorbed into the cavity of the eye in any quantity when administered systemically, so that its value is essentially confined to external infections of the cornea and conjunctiva unless intra-ocular injections of the drug are given. Instilled into the conjunctival sac little of the drug enters the eye. Thus J. G. Bellows and C. J. Farmer[5] found that when streptomycin hydrochloride in concentration of 5000, 10,000 and 50,000 μg. per ml. of physiological salt solution was applied as a corneal bath for periods of 15 minutes to 4 hours, no penetration through the normal cornea resulted. Further experiments showed that penetration of streptomycin through the cornea can only be achieved by three methods —by iontophresis (to an aqueous concentration of 70 μg. per ml.), by use of aerosol as a wetting agent (to a concentration of 100 μg. per ml.), and by abrasion or ulceration of the corneal surface (to a concentration of 200 μg. per ml.). An alternative route is by subconjunctival injections, but experiment has shown that the administration of the drug in this way even in large doses (up to 10,000 μg.), and even combined with adrenaline to delay the rate of absorption, produces a chemotherapeutic concentration for only a short period. Injections into the anterior chamber can be used, 0·05 c.c. of 1000 μg. per c.c. solutions, introducing 50 μg. streptomycin at each injection (A. Grignolo[6]). On the other hand, P. G. Gardner and his co-workers[7] found that after an intravitreous injection of 2000 μg. of streptomycin, chemotherapeutic concentrations were maintained in the ocular fluids for over three days, the intravitreous injection acting as a depot. Streptomycin was found to have a deleterious effect on the retina when introduced into the vitreous in doses of 1·2 or 3 mg. No toxic effect on the fundus was found when given subconjunctivally.

Some experimental work has been carried out on the effect of streptomycin on ocular infections mainly superficial ones. J. G. Bellows and C. J. Farmer[8] found that three instillations of streptomycin drops (10,000 μg. per c.c.) at 2-hourly intervals prevented the progress of a *B. pyocyaneus* corneal ulcer in experimental animals. Prophylactic or therapeutic systemic streptomycin either as a continuous intravenous drip of 100,000 μg. per kilo of body-weight over 6 hours, or a similar dose in cholesterol derivatives in peanut oil with 2 per cent beeswax, limited the external inflammatory manifestations but not the progress of the vitreous abscess induced experimentally with hæmolytic streptococci. A vitreous abscess was prevented by the intravitreous injection of 100–200 μg. of less purified streptomycin or 25 μg. of streptomycin calcium given within 6–8 hours of a similar infective inoculation. A. Grignolo[9] has also studied the action of streptomycin on selected varieties of bacteria in experimental lesions of the cornea and of the anterior segment of the eye. The experimental animals were rabbits, and the organisms used included *E. coli*, *P. vulgaris*, *K. pneumonia* (Friedländer), *P. aeruginosa*, *B. subtilis*, and *Staph. aureus*. He concluded that experimental corneal infections in rabbits caused by stock inoculations of the organisms mentioned were dominated by streptomycin cream (100,000 μg. per gramme excipient administered 3-hourly) provided the treatment was started within 12 hours from inoculation; no action was present if the treatment was started later. In infection by *P. aeruginosa*, however, treatment by streptomycin cream started 8–12 hours after inoculation was not effective, as a temporary arrest only was produced in the progress of the infection. Corneal baths (100,000 μg. per c.c. for 45–60 minutes four times

daily) with streptomycin showed less action than the cream on corneal infection. Injections into the anterior chamber (50 μg. streptomycin once a day) arrested infection by *E. coli* provided they were started within 2 hours of inoculation, but if started 12 hours after inoculation there was no improvement. Six hours after inoculation by *B. pyocyaneus* intrachamber injections of streptomycin had no action. Subconjunctival injections started 2 to 12 hours after inoculation with *E. coli* and *B. pyocyaneus* did not control the infection. Direct chamber injections of streptomycin in the case of *E. coli* and *B. pyocyaneus* showed more effect than did subconjunctival injections.

In the treatment of experimental corneal infections by *S. aureus*, penicillin was more effective than streptomycin. It was shown at the same time that there was no interference between each other in the action of these two antibiotics. Confirmation of this fact was shown by experiments *in vitro* with *S. aureus*, which is sensitive both to penicillin and streptomycin, and also with *E. coli* which is sensitive only to streptomycin.

From the ophthalmological point of view the great value of streptomycin is to control superficial infections caused by the Gram-negative bacilli which are insensitive to penicillin. That the drug is effective in controlling the growth of such organisms if they are included in the conjunctival flora by simple instillation of drops at 6-hourly periods has been shown by D. Panzardi and G. Pasca[10]; it is, however, still more efficient if administered in some form of ointment, in which form it seems to be more rapid, long-lasting, and, above all, more consistent in action against the different types of saprophytic and pathogenic bacteria of the conjunctival flora.

Among conjunctival infections Grignolo treated 72 patients. He obtained good results in ulcerative blepharitis, and in acute catarrhal conjunctivitis from the staphylococcus and from Koch-Weeks's bacillus, but these results are not superior to those obtained with penicillin. In one patient suffering from gonococcic conjunctivitis streptomycin brought about a marked improvement without, however, leading to complete recovery; in 4 other cases of the same type, treatment had a poor result. One case of conjunctivitis with inclusion bodies showed a rapid disappearance of the epithelial inclusions, but only modest clinical results. In 12 cases of florid and scarred relapsing trachoma streptomycin led to a rapid sterilization of the conjunctival sac, but had no influence on the follicles or the pannus. High doses of the drug led to disappearance of Halberstaedter-Prowaczek's bodies, in a period, however, definitely longer than with penicillin. No results were seen in pneumococcic, staphylococcal, or streptococcal corneal ulcers, in superficial and deep herpetic keratitis, in epidemic keratoconjunctivitis, in pseudo-membranous conjunctivitis, and in dacryocystitis. Panzardi and Pasca treated 15 patients suffering from acute catarrhal conjunctivitis caused by a Koch-Weeks bacillus, 4 cases of gonococcal conjunctivitis, 29 cases of conjunctivitis caused by the diplobacillus of Morax-Axenfeld, and 3 cases of epidemic keratoconjunctivitis, by instilling a solution of 10,000 U.S. of streptomycin chlorhydrate per c.c., 4–6 times a day for 1–5 days running. In the first three groups of patients streptomycin therapy led to complete and definite recovery of all patients within 1–3 days. The authors did not, however, observe any effect of the antibiotic in the cases of epidemic keratoconjunctivitis.

U. Azzolini and F. Pascucci[11] reported 3 cases of Reiter's disease (hitherto very resistant to treatment) in which the conjunctival symptoms are said to have responded well although the urethral and articular symptoms showed no improvement. E. Epstein[12] reported good results in indolent corneal ulcers. A. Estrada[13] used streptomycin in a typical epidemic of keratoconjunctivitis with acute conjunctivitis, punctate keratitis, and swelling of the pre-auricular

glands, with very satisfactory results. The initial dose given was 0·80 g. per day, and in spite of the smallness of the dosage, the disease was reported cured. The largest dose given fluctuated between 2 and 6 g. a day. Altogether 35 patients were treated. The patients with advanced disease showed control of the acute inflammatory symptoms in 8 or 10 days, and in those in whom the disease had not yet fully developed, the symptoms were arrested and cure was effected in 3 to 4 days.

The response of ocular tuberculosis has not yet been well annotated. Some experimental work was done on this subject by Grignolo, who inoculated the anterior chamber of guinea-pigs with virulent tubercle bacilli and administered massive doses of streptomycin. If the streptomycin was given before the onset of symptoms, tuberculous manifestations were delayed until the cessation of treatment; if the drug was given after the tuberculous lesion was clinically apparent there was no difference from controls in the course of the infection. Clinically the same author reported 3 cases of improvement with tuberculous choroiditis out of 7 treated. On the other hand, Gracia Miranda[14] reported a case of conjunctival tuberculosis in which this method of treatment was exclusively employed. Complete recovery resulted and subjective and objective symptoms disappeared. Subconjunctival injections were made into the new-formed tissue with an isotonic solution of 10,000 units of streptomycin per c.c. every other day up to 120,000 units, together with instillations of the same solution. With the solution of streptomycin he injected 0·25 c.c. of novocain-adrenaline solution.

On the whole it would seem that streptomycin is a drug of considerable value in treating external infections of the lids, conjunctiva, and cornea when dealing with Gram-negative bacilli which are resistant to penicillin; but its value in intra-ocular infections is problematical. As in the case of penicillin, in such infections it may save the eye, but rarely as a useful seeing organ.

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EYE DEFECTS, CONGENITAL.

Sir Stewart Duke-Elder, K.C.V.O., D.Sc., M.D., F.R.C.S.

Retrolental fibroplasia - a condition wherein there appeared a mass of "fibrous tissue" behind the lens—was first classified as a clinical entity occurring in premature infants by Terry[1] in 1914. The condition was later associated with multiple cutaneous angiomata by Reese and Payne,[2] and with hydrocephalus and other cerebral anomalies by Krause,[3] who suggested the term "congenital encephalo-ophthalmic dysplasia". It is now known that the condition is not necessarily associated with prematurity; that the opacities behind the lens are visible at birth in full-term babies and may be seen to develop in premature infants. A. B. Reese[4] made the significant observation that the mothers of such children gave a high incidence of hæmorrhage during pregnancy. T. H. Ingalls[5] has made a study of this condition and collected 77 cases from the literature; 51 of the total number were in premature infants. In 12 of the 77 cases there were single or multiple hæmangiomata in the skin, and in one of Ingalls' cases gelatinous masses of hæmatomatous tissue were found post mortem at the base of the brain. Seven of 27 patients for whom there were post-natal records had evidence of cerebral 'dysplasia' in the form of hydrocephalus, intracranial hæmorrhage, or spasticity; and in the author's fatal case there was diffuse 'cortical deficiency', the basal gelatinous masses already described, hydrocephalus, and a reticular thickening of the meninges.

A significant correlation was found between the ocular and other lesions and maternal toxæmia and placental hæmorrhages. These 'maternal disturbances' occurred during the second trimester of pregnancy or a little later. At this period in normal conditions the differentiation of the primary vitreous is completed and its sheath disappears. It is suggested that this normal process of involution is arrested by fœtal anoxia resulting from maternal toxæmia or placental hæmorrhage at this time. If this hypothesis is correct it might also explain the occurrence of ordinary cutaneous hæmangiomata, and also of the rare Lindau's disease (retinal and cerebellar angiomatosis). The same theory of arrested development of particular tissues leading to aberrant growth is applied in explanation of the multiple deformities in the ocular lens, brain, and heart that occur in the developing fœtus after maternal rubella; the different distribution and character of the defects are due to the operation of the noxious agent at an earlier period of development (the first trimester of pregnancy). The multiple defects of mongolism, occurring also at an early period of fœtal life, are also explained by the same theory of arrested development of tissues by vascular faults and consequent failure of oxygen supplies. In all three syndromes there is postulated a common basic defect, which may be caused by different agents (bleeding, toxæmia, infections, and multiple or premature births), and may produce different patterns of defect according to the stage of development, the severity and site of the lesions, and the secondary changes. There is no evidence of a genetic factor.

Local treatment of retrolental fibroplasia is difficult, for any attempt to remove the fibrous tissue tends to result in failure or in a detachment of the retina.

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FACIAL NÆVI.

Lambert Rogers, M.Sc., F.R.C.S.

Eradication of the 'Port Wine' Birthmark (*Navus flammeus*).—Many forms of treatment have been used in attempting to divest the unfortunate possessor of a capillary hæmangioma of the birthmark, but few of these treatments have achieved any degree of success. Excision and skin grafting would appear to be the most appropriate procedure, but the facial blemish presented by a large area of pale grafted skin may be as noticeable as the port wine stain which it has replaced. The treatment of these lesions by tattooing permanent insoluble pigments, a method which had been suggested over 100 years ago, has had renewed interest in the last few years. In 1946, J. B. Brown, B. Cannon and A. McDowell,[1] and in 1947, J. P. Docktor and H. Conway,[2] reported successful cases in which the colour of the blemish had been effectively disguised. H. Conway,[3] of New York, now reports 28 cases so treated. Capillary hæmangiomas have been classified by G. C. Andrews[4] as (*a*) subepidermal, in which the abnormal capillaries lie under the epidermis, (*b*) dermal, in which the abnormal capillaries are in the mid-cutis and (*c*) subdermal in which they are in the subcutaneous tissue. It is only in the dermal and subdermal types that tattooing can be effective, since the inert pigments used to hide the nævus must be deposited in the derma. Tattooing may also be used to make grafted skin more closely resemble its new surroundings. The results of tattooing alone and of various combinations of grafting, undercutting, suturing and tattooing are described and illustrated. The tattooing is carried out with an electro-magnetic 'gun' fitted with six needles which enter the skin at an angle of 60° so that the pigment is injected obliquely. The pigments are mostly metallic oxides such as ochre, the yellow oxide of iron, and cinnabar. Anæsthesia is not usually necessary, and a series of treatments is required.

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FATTY LIVER DISEASE IN INFANTS. (*See* MALIGNANT MALNUTRITION.)

FILARIASIS : TREATMENT WITH HETRAZAN.

Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.

Up to 1948 it is fair to state that the medicinal treatment of filariasis has been most unsatisfactory. Therefore the announcement in 1947 by A. D. Welch et al.[1] that *hetrazan* (1-diethylcarbamyl-4-methylpiperazine hydrochloride), when injected into cotton-rats, kills the filaria parasites, *Litomosoides carinii*, which inhabit the peritoneal cavity of these animals, was received with astonishment not unmingled with incredulity. Their habitat in the peritoneum renders it comparatively easy to make accurate observations upon these filariæ. It is, at any rate, a source of considerable satisfaction to have a laboratory animal at hand in order to be available for therapeutic experiments. The great advantage of hetrazan, especially as regards its suitability for the tropics, lies in its administration by the mouth. Confirmation of its curative properties in man is now available and may be regarded as fairly satisfactory. R. L. Hewitt and his colleagues[2] have given detailed data showing the effects of hetrazan (84-L) on microfilariæ in naturally-acquired infections with filarioid worms in cotton-rats (*L. carinii*) and dogs infected with *Dirofilaria immitis*. Some 212 cotton-rats and 25 dogs were used. After oral or intraperitoneal treatment of infected cotton-rats, in doses ranging from 3 to 100 mg. per kilo, the microfilariæ count dropped suddenly within twenty-four hours, became negative, or remained very low, as long as treatment continued. In dogs, although the optimum treatment schedule has not yet been determined, it would appear that frequent administration of the drug for several weeks has to be aimed at. The field trials of hetrazan in man have been conducted by D. Santiago-Stevenson and associates[3] on 26 Porto Ricans infected with *Wuchereria bancrofti* and with microfilariæ of the nocturnal variety in their blood. The drug was given by the mouth, thrice daily, in doses ranging from 0·5 to 2 mg. per kilo of body-weight over periods of 3–21 days. In half the cases treatment was continued for 6 days or less and in the rest for 11 days or longer. At the end of forty-eight hours it was ascertained that there were no microfilariæ in the night blood of 9 and that they were markedly reduced in numbers in the remaining 17.

A more recent report by the same observers[4] describes a larger series of 74 patients, including 54 males and 20 females, studied in Porto Rico, British Guiana, and in the Virgin Islands. Of these only some 4 exhibited clinical signs of filariasis; the remainder were asymptomatic. In the majority, *regardless of dosage*, a marked reduction of microfilariæ resulted, within the space of 2–4 days after the first dose. These reductions were sustained throughout the period of treatment, but a few recurrences have been observed. Approximately one-third had negative counts from 3 to 12 months after the cessation of treatment. This is probably due to the peculiar mechanism, as F. Hawking et al.[7] have shown that the microfilariæ in the blood-stream are reinforced from reservoirs in the pleural spaces where they are not affected by hetrazan and are there removed from contact with phagocytes.

Side reactions were not serious, but included headache, nausea, vomiting, and sometimes skin rashes. None of them constituted a signal for discontinuation of treatment.

In St. Croix, Virgin Islands, hetrazan has been made available, free of charge, to every inhabitant and a great measure of co-operation has been thereby obtained. The true incidence of *W. bancrofti* incidence is somewhere about 18 to 20 per cent of the population.

The dosages used for treatment of 98 test cases were as follows :—

11 cases once daily for 5 days : 90·6 per cent reduction of microfilariæ.
39 cases thrice daily for 3 days : 92·4 per cent reduction of microfilariæ.
19 cases thrice daily for 5 days : 90·8 per cent reduction of microfilariæ.
29 cases thrice daily for 7 days : 96·9 per cent reduction of microfilariæ.

These results clearly demonstrate that substantial reductions in the counts of microfilariæ (*bancrofti*) after hetrazan by the mouth can be relied upon and would indicate increasing reduction with increasing dosage and that this reduction in the count persists in large measure for at least four weeks.

The main purpose of the St. Croix mass field experiments was directed to the prevention of infection of mosquito transmission and thereby breaking the chain.

In onchocerciasis (*Onchocerca volvulus*) the drug has been tested out in Mexico and in Guatemala. In this serious filariasis N. R. Stoll[5] has indicated that it has a really specific and rapid action. Here side reactions are frequent, sometimes serious, but of short duration. Nausea, vomiting, and extensive skin rashes are probably allergic and are due to massive destruction of the microfilariæ.

L. Mazzotti and R. Hewitt[6] (1948) state that the most convenient dose is 2 mg. per kilo body-weight, three times daily for 21 days. Where the infestation is a heavy one they commence with one third of the daily dose for the first day, two-thirds for the second day, and with the full dose for the third day, preferably administered after meals. Should allergic reactions prove severe, it may be necessary without detriment to suspend treatment for four days.

The results of treatment were checked and controlled by cutaneous biopsies. In nodules which were excised it was found that the adult worms were unaffected and were indeed normal in appearance, but the microfilariæ present in large numbers were all destroyed. This is probably due to the fact that, as Hawking and his colleagues[7] have recently demonstrated, hetrazan and its metabolic products do not have any direct action on the microfilariæ, but seem to modify them in some way (opsonize them) so that they are devoured by the phagocytes of the endothelial system and removed from the circulation.

Hetrazan has only a moderate effect on the adult worms, so that prolonged intensive treatment is necessary to destroy *Litomosoides carinii*. When 6 mg. per 100 gr. is injected intravenously into cotton-rats, 80 per cent of microfilariæ disappear in one minute and over 90 per cent in two.

Loa loa Filariasis (*Loaiasis*).—Up to date nothing has appeared in print on this West African filaria, but such information as is available has been derived from personal communications. F. Hawking[8] (1948) has treated two with severe and distressing Calabar swellings ; and in neither were microfilariæ demonstrated in the peripheral blood. In the first, two dead *L. loa* became visible under the skin, though the patient continued to exhibit symptoms. The total course of hetrazan was 17·525 g. The second case was much more severe, but the total dosage was less than half the first ; in spite of this the Calabar swellings were greatly relieved in intensity and their frequency greatly diminished.

G. J. Stefanopoulo and J. Schneider[9] in Paris have so far treated some 20 adults from W. Africa infected with *L. loa*. Seven had microfilariæ in their blood, but the majority were diagnosed by positive intradermal reactions. Forty-eight hours after the commencement of treatment the œdematous swellings decreased and then disappeared, whilst the associated pruritus was strikingly relieved. The microfilariæ disappeared very rapidly and in one only were to be found 7 days after treatment. Symptoms of loaiasis, especially

pruritus, may reappear after three weeks, but so far no return of microfilariæ has been recorded.

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FINGERS AND HAND, SURGERY OF. (*See* HAND AND FINGERS, SURGERY OF.)

FLUORINE AND DENTAL CARIES. (*See* DENTAL CARIES AND FLUORINE.)

FOLIC ACID. (*See* ANÆMIA, PERNICIOUS.)

FRACTURES, DOUBLE, AND DOUBLE NON-UNIONS, OF THE SHAFT OF THE TIBIA.

T. P. McMurray, F.R.C.S.

Hans May[1] discusses this problem, which is so frequently encountered in any busy fracture clinic. The difficulty lies in the fact that these double fractures of the tibia, although reduced with comparative ease, are particularly slow in healing and show a high incidence of non-union at one or both fracture levels.

Anatomically there are two vascular systems in the long medullated bones, the periosteal and the intermedullary. The periosteal system consists of a network of smaller and middle-sized vessels derived from the blood-vessels of the surrounding soft tissues with which they are in intimate contact. The intraosseous system is formed by three separate but intercommunicating sets of vessels, the first, that of the diaphysis, containing the nutrient artery, which enters the bone as a single trunk except in the case of the femur, where it usually divides into two branches before entering the bone ; the second that of the metaphyseal vessels, which are branches from the system of the joint capsule ; while the third group consists of the vessels directly supplying the epiphysis, extending into its substance from the vessels of the joint ligaments.

In the child these three groups of vessels are more or less distinct and separate, being connected simply by a few small delicate anastomoses ; whilst in the adult these communicating vessels become larger and more numerous and the three separate groups of the intraosseous system gradually merge to form one pattern. The vascular supply of the bone itself is virtually confined to the vessels of the intraosseous system, which receives only a few minute anastomosing vessels from the periosteal supply.

In a single fracture of the tibia both fragments of the bone remain well vascularized even if the fracture should occur through the point of entrance of the nutrient artery. Even though this main trunk has been injured the collateral circulation from the metaphyseal vessels is sufficient to secure an adequate blood-supply to both fragments.

The conditions are somewhat different when two fractures are present in the shaft. Because of its vascular arrangement the central portion of the bone in a double fracture receives no intra-osseous circulation unless by chance this middle fragment includes the uninjured nutrient artery. In the tibia the nutrient artery normally enters the bone within the proximal third on the posterior surface of the bone near the linea poplitea. Hence in a double fracture of the tibia, in which the proximal line of fracture runs through or distal to this point of entry, the middle fragment is apt to be deprived of its blood-supply and may readily become necrotic. Under these circumstances the incidence of non-union is naturally very high. The detached middle fragment can be regenerated only by the growing in of new vessels from the proximal and distal fragments, a process so slow that during its occurrence non-union may easily develop.

It may be impossible to prevent the appearance of non-union, but the chances of union occurring are greatly increased if adequate immobilization of the broken bone is employed and the developing vessels protected from the earliest possible moment.

In the author's opinion, this immobilization can be provided most satisfactorily by the application of a skin-tight plaster cast enclosing the whole limb and retained until there is radiographic evidence of consolidation.

From radiographic studies alone it is difficult or impossible to judge whether the proximal fracture line runs above or below the point of entrance of the nutrient artery, since only on rare occasions would it be possible to distinguish the small opening of the foramen nutricium. Because of this inability to determine the exact site of entry of the nutrient artery, it is preferable to treat all double fractures of the tibia by immobilization rather than by traction, as in this latter method developing vessels might be injured by movement.

Radiographic examination of the bone at a later date gives much more valuable information. Thus, if the middle separated portion of the bone does not atrophy to the same degree as the proximal and distal fragments, remaining dense and clear cut, it may be assumed that this portion of the bone has been deprived of its normal circulation. The occurrence of this complication is a clear demonstration of the overriding importance of the medullary blood-supply. Obviously each of the three fragments retains its periosteal blood-supply, but this alone is not sufficient to promote the normal changes of decalcification which precede repair of the fractured surfaces.

Unfortunately in this article no figures are given as to the probability of the occurrence of non-union following on this cutting of the blood-supply to the central fragment. Reliable figures on this point would help the surgeon to determine the correct line of treatment. They would enable him to decide whether all these fractures should be treated by prolonged immobilization or by early operation.

It is generally recognized that these double fractures of the tibia are peculiarly slow in healing, but it is also the experience of most surgeons that most of them will eventually become solid if adequately controlled.

When non-union does occur at either or both fractures, the author states that only by bone-grafting is it possible to restore bony continuity. The method suggested in the article is the transference of a portion of the fibula of the same leg, sufficient in length to bridge the gap in the tibia, and to be incorporated with the proximal and distal fragments.

The author also suggests that if the patient's general condition is such as to negative the performance of a major bone-grafting operation, an excellent result can be obtained by the transference of the fibula to the tibia in two stages as recommended by Meyerding[2] and Wilson,[3] although it is difficult to understand how the performance of the operation in two stages with two anæsthetics would be preferable to one slightly longer procedure.

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GALL-BLADDER AND BILE-DUCTS, SURGICAL DISEASES OF.

A. Rendle Short, M.D., F.R.C.S.

Anatomy. Deviations from the normal anatomy are not uncommon, and may lead to a surgical disaster. Bruce Lockwood,[1] of Detroit, was able to demonstrate a deformity by cholecystography in 41 out of 1464 cases. The commonest variation was the so-called Phrygian cap deformity, in which the fundus is folded over. E. O. Latimer[2] and two others report 3 cases of congenital absence of the gall-bladder. Milroy Paul[3] found the abnormalities

shown in *Figs.* 20, 21 in two Sinhalese women. He was able to amputate most of the gall-bladder in each case. Various abnormalities of the hepatic and cystic arteries supplying the bile-ducts are described and figured by A. L. Shapiro and G. L. Robillard.[4]

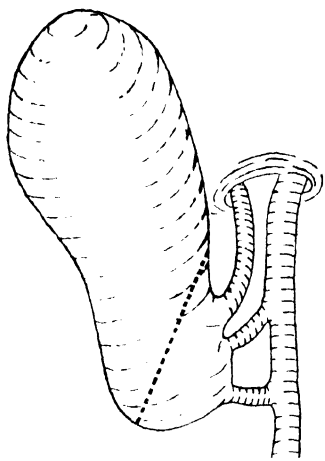


Fig. 20.—Abnormal arrangement of bile-ducts demonstrated at operation. The site of excision of the gall-bladder is indicated by the dotted line. (*Figs.* 20 *and* 21 *by kind permission of the* '*British Journal of Surgery*'.)

Acute Cholecystitis.—F. Glenn,[5] of New York, advocates early operation for acute cholecystitis, after careful preparation of the patient. At this hospital, the death-rate was 2·8 per cent in 586 cases, after operation. Those under 50 years of age nearly all did well. In ordinary, the gall-bladder was removed, but in 13 per cent of the patients drainage was thought to be safer, on account of old age, toxicity, the presence of jaundice or peritonitis, or extensive recent adhesions. In another paper,[6] he discusses acute cholecystitis coming on as a complication after some other operation such as hernia. The gall-bladder should be either drained or removed. Occasionally gas may be found in the gall-bladder during an attack of acute inflammation. C. J. Heifetz and H. R. Senturia,[7] of St. Louis, have seen 2 cases, and find 8 others in the literature. The gall-bladder may be necrotic, but only in one case was *Clostridium perfringens* found.

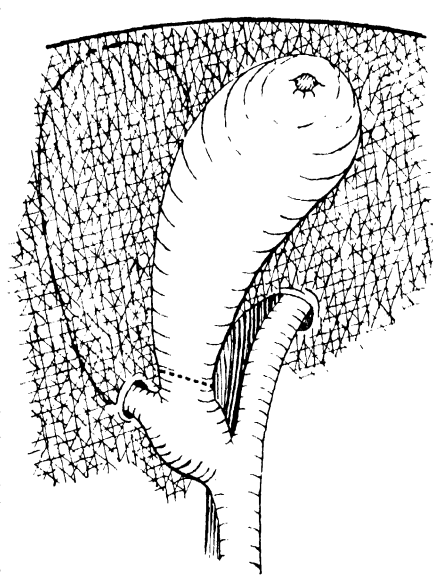


Fig. 21.—Another abnormal arrangement of bile-ducts demonstrated at operation. Hartmann's pouch was thick and scarred. The site of division of the gall-bladder is indicated by the dotted line.

J. W. Barksdale and J. H. Johnstone[8] advocate early surgery for acute cholecystitis, but interpret this to mean operation after spending 4 to 8 hours in preparatory treatment to restore the fluid and electrolyte balance. The safest time for surgery is during a quiescent interval, or within 48 hours of the onset of an acute febrile attack. The period from the third to the tenth day is well recognized as the most dangerous, and should be avoided if possible, but if the disease fails to subside, surgery is indicated, and

"it is infinitely better to do a safe drainage procedure than a heroic extirpation". With the opinions expressed in this paper there will be wide agreement.

Calcification of the Gall-bladder. P. Biocca,[9] of Florence, describes 2 cases and discusses the pathology. It is considered to be the result of chronic irritation, often from gall-stones.

Gall-stones.—As R. Adams and A. Stranahan,[10] of Boston, point out, it is important to remember that only a minority of patients with gall-stones have jaundice, 18 per cent in their experience, and only half their patients with stones in the common duct ever developed jaundice. Again, in only half the patients with jaundice was a stone found in the common duct. X-ray studies were misleading in 2·4 per cent of their cases. They always operate if stones are thought to be present, as they do not believe in the silent gall-stone theory. In nearly half their patients at operation they explored the common duct, but a stone was found only in 186 out of 504 such cases. Their over-all mortality was 0·9 per cent in 1104 cases operated on.

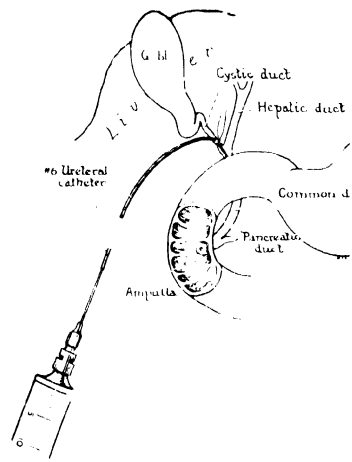


Fig. 22.—Ureteral catheter passed through small incision in cystic duct for injection of opaque medium. (*Figs.* 22, 23 *reproduced from the 'Annals of Surgery'.*)

Cholangiography (*Figs.* 22, 23).—Year by year, a number of communications appear on this subject. We may notice two papers by P. Mirizzi,[11] the father of the method, one in Spanish, and the other almost identical in French.[12]

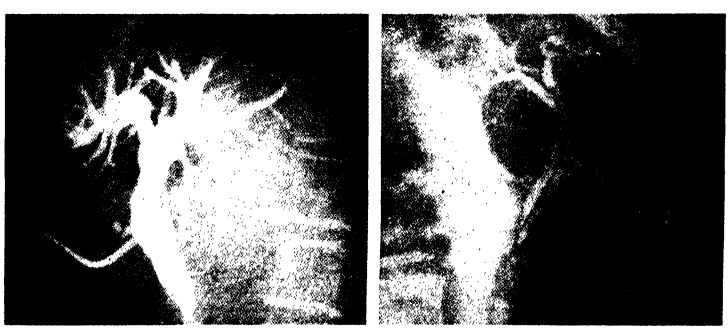


Fig. 23.—A, Common duct drainage following cholecystectomy and removal of large stone from common duct. Delayed cholangiogram reveals stone in distal end of common duct. B, After secondary operation: stone removed and patent duct demonstrated.

We also mention papers by C. E. Hughes[13] and others, of Cleveland, and by H. Hagan and H. L. Townsend,[14] of Louisville. The injection and examination may be made at the time of the primary operation, which is Mirrizzi's practice, or subsequently, introducing the dye through the T tube used for

draining the common duct. Hughes uses a 35 per cent solution of iodopyracet, and all the authors claim that ill effects are very uncommon. A small quantity of the dye, a few c.c. at a time, should be introduced, under direct X-ray visualization. The method will detect stones, strictures, atony or spasm of the sphincter of Oddi, or what Mirizzi calls 'stenosing odditis'. P. Mallet-Guy and R. Jean-jean,[15] of Lyons, add manometry of the common duct to cholangiography, during the primary operation, as the only way to detect variations in the tone of the sphincter. Sometimes hypotony, sometimes hypertony, will be found.

Surgical Technique.—R. J. McNeill Love[16] praises *diathermy dissection* in removing the gall-bladder. The needle is used to divide the peritoneal covering, the knife to dissect the gall-bladder from its bed, and the button to check bleeding from the raw area. Occasionally, in difficult cases, the button is used to destroy the mucosa. The advantage of diathermy is that the abdomen can be closed without drainage, and, as diaphragmatic breathing is thus made easier, there are fewer chest complications. His mortality in 233 cases was under 1 per cent.

F. R. Ruiz-Conde,[17] of Mendoza, has a *bayonet-shaped clamp with a long blade*, for grasping, pulling, and rotating the gall-bladder; it is removed from fundus to neck, sewing the peritoneum over the liver-bed bit by bit as the gall-bladder is dissected off.

P. Mallet-Guy and R. Koppes[18] feel that *closure without drainage* is safe in their patients, the patency of whose bile-passages has been demonstrated by cholangiography and manometry. They quote 116 cases without mishap, except that one patient died of pneumonia. Of 49 followed up, 44 had a perfect result.

Indications for Exploring the Common Duct.—R. W. Buxton and L. B. Burk,[19] of Ann Arbor, give the following criteria: palpable stone in the duct, recent jaundice, dilated or thickened duct, cholangitis, numerous small stones in the gall-bladder, induration of head of pancreas, biliary colic without stones in the gall-bladder. Other communications referred to above give a very similar list of indications.

Failed Cholecystectomy. In a paper already quoted, R. Adams and A. Stranahan[10] allow that some patients are not cured by removing the gall-bladder. The commonest cause of this misfortune was "irritable bowel or functional indigestion", 132 cases. Much less common were pancreatitis, stones left in the ducts, gall-bladder or cystic duct remnants (12 cases), biliary dyskinesia and spasm of sphincter of Oddi (7 cases), adhesions (8 cases), stricture of the common duct, or duodenal diverticulum. Their over-all mortality was 0·9 per cent in 1104 cases operated on.

N. A. Womack and R. L. Crider,[20] of St. Louis, write on the same subject. From 5 to 20 per cent of patients with symptoms of cholecystitis and with characteristic findings at operation continue to complain after cholecystectomy, and especially in cases where no stones were found. Leaving out those in whom a stone has been left behind, or the common duct has been injured and not repaired, the cause of the continued symptoms may be difficult to determine. If in the further attacks the amylase content of the blood is raised, the trouble is probably due to pancreatitis. Cholangitis, and distortion from adhesions, are improbable causes. Biliary dyskinesia, due to spasm of the sphincter of Oddi, may be important or, perhaps, atony of the common duct. It has recently been suggested that when a length of cystic duct has been left behind it may become distended and give trouble. Womack and Crider find that amputation-neuromata can be found in the stump of the cystic duct after removal of the gall-bladder, and they think stretching of these is a common

cause of recurring symptoms. They removed these by a second operation in 6 patients, most of whom were benefited.

Post-operative Stricture of the Bile-ducts.—H. F. Graham,[21] of Brooklyn, mentions a case in which obliteration of the common duct after cholecystectomy was due to cellulitis and not to injury. Damage to the duct will be followed by biliary fistula, or by jaundice coming on within 72 hours. W. H. Cole,[22] of Chicago, has operated 53 times on 39 patients for this distressing condition, which seems to be a good deal commoner across the Atlantic than in Britain. He has used a variety of methods, but is persuaded that the best results follow anastomosis of the proximal portion of the duct to a Roux Y loop of jejunum, usually with the aid of a vitallium tube. The end-to-side, or side-to-side jejuno-jejunostomy is made about 18 in. from the ligament of Treitz. This gave a good result in 82 per cent out of his cases, with no deaths. M. M. Zinninger[23] believes end-to-end repair of the injured duct is best, but it is often impossible. In 10 cases the duct was anastomosed to the duodenum without a tube; 7 of these did well. It is important to sew mucosa to mucosa.

Biliary Dyskinesia.—By this is meant abnormalities in the sphincter of Oddi, or in the common bile-duct. French and Italian surgeons continue to devote much attention to it. F. Poilleux and R. Guillet[24] agree with the conclusions of the Lyons school that symptoms of biliary colic may be due either to increased or diminished tone, and the only way to distinguish them is by manometry and cholangiography. Treatment for increased tone is partial division of the sphincter through the duodenum under manometer control. Treatment for diminished tone is by drainage of the gall-bladder or bile-duct if there is infection, or by splanchnicectomy. It is too soon to judge how permanent the benefits of these comparatively new methods of treatment will be.

P. Mallet-Guy and J. de Beaujeu[25] believe that hypotonia of the bile-ducts is often associated with chronic pancreatitis. They have practised unilateral splanchnicectomy for hypotonia over six years now and obtained good or perfect results in 90 per cent of 92 cases. The operation is not indicated if there are gross changes in the gall-bladder or bile-ducts.

The MEDICAL ANNUAL does not normally undertake to record in detail animal experimentation bearing on surgical problems, but those who are interested, and are able to read Italian, may usefully consult two papers[26, 27] dealing with the results of cholecystectomy, and also of the abolition of the sphincter of Oddi.

Biliary Infections and Emetine.—E. Melchior,[28] of Ankara, writing in German in a Swiss periodical, maintains that emetine is very valuable in the treatment of biliary infections, apart from any surgical interference. He relates 20 cases, most of them due to *B. coli*. It is given in small doses, 0·03 to 0·05 g., twice daily, either subcutaneously or intramuscularly.

Carcinoma of the Gall-bladder.—Only one patient out of 65 treated by removal of the gall-bladder at Mount Sinai Hospital, New York, lived longer than three years. F. B. Sainbury and J. H. Garlock[29] consider that the risk of malignant disease in patients with gall-stones is greater than the risk of cholecystectomy.

Carcinoma of the Bile-ducts.—Four cases in which a growth of the common duct was removed at the Mount Sinai Hospital are reported by H. E. Leiter.[30] In two of these the gall-bladder was also removed and the hepatic duct sewn to the duodenum. In the others the duodenum was resected as well. None of the patients survived long.

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Gynec. Obstet. 1947, **85**, 776 ; [11]*Prensa méd. argent.* 1948, **35**, 269 ; [12]*Lyon chir.* 1948, **43**, 385 ; [13]*J. Amer. med. Ass.* 1948, **137**, 687 ; [14]*Ann. Surg.* 1948, **127**, 810 ; [15]*Pr. méd. argent.* 1947, **45**, 509 ; [16]*Brit. med. J.* 1947, **2**, 11 ; [17]*Prensa méd. argent.* 1948, **35**, 837 ; [18]*Lyon chir.* 1947, **42**, 543 ; [19]*Surgery*, 1948, **23**, 760 ; [20]*Ann. Surg.* 1947, **126**, 31 ; [21]*Ibid.* 811 ; [22]*Canad. med. Ass. J.* 1948, **58**, 582 ; [23]*Surgery*, 1948, **23**, 337 ; [24]*J. Chir.* 1947, **63**, 550 ; [25]*Lyon chir.* 1948, **43**, 157 ; [26]*Arch. ital. Chir.* 1947, **69**, 385 ; [27]*Policlinico*, 1947, **55**, 125 ; [28]*Helv. chir. Acta*, 1948, **15**, 75 ; [29]*Surgery*, 1948, **23**, 201 ; [30]*Ibid.* 1947, **22**, 1627.

GASTRIC AND DUODENAL ULCER : MEDICAL ASPECT.

F. Avery Jones, M.D., F.R.C.P.

There is little reliable information on the *absolute incidence of peptic ulcer in the general population*, and Knutsen and Selvaag[1] provide information of great interest from Drammen in Norway. The information was derived from an analysis of medical certificates needed for extra rations for sufferers from peptic ulcer. The widespread resistance to an occupying force led to considerable misuse of medical certification, but by admirable foresight all certificates from this town of 25,830 persons for 1942 were put aside and analysed after the war. By reference to the physicians and radiologist, all cases without radiological diagnoses have been eliminated and the X-ray diagnosis confirmed in the remaining cases.

INCIDENCE OF GASTRIC AND DUODENAL ULCER PER 100 IN DIFFERENT AGE-GROUPS

Age :	20–29	30–39	40–49	50–59	*Over* 60	*Over* 20
	Men					
Gastric ulcer	0·47	1·18	2·09	1·76	1·48	1·34
Duodenal and pyloric ulcer	1·86	3·76	4·03	2·00	2·61	2·98
Total	2·33	4·94	6·12	3·76	4·09	4·32
	Women					
Gastric ulcer	0·24	0·32	0·77	0·97	1·22	0·66
Duodenal and pyloric ulcer	0·16	0·68	1·09	1·29	0·99	0·79
Total	0·40	1·00	1·86	2·26	2·21	1·45

It will be seen that the highest frequency of ulcer in men is found in age-group 40–49 with 6 per cent of male population, two-thirds being due to duodenal ulcer. The real ratio of gastric to duodenal ulcer in the population over twenty years of age is 1 : 1·85. This ratio is considerably higher in the earlier age-groups in men and falling in later decades. The lower incidence of the ulcer in the elderly and also the fall in the G.U. : D.U. ratio is apparently due to a deficiency of duodenal ulcer in the older male age-groups.

K. Schanke[2] (Norway) has studied the problem of *peptic ulcer among the fisher folk* in Vesteraalen, a Norwegian group of islands north of the Polar Circle. From 1941 to 1944 there were 232 cases treated at the Stoknarkness Hospital, probably practically all the cases of gastroduodenal ulcer occurring from a population of 43,000, 80 per cent of them living in rural areas. The disease was diagnosed for the first time in the period under review in 172 patients.

DISTRIBUTION OF PEPTIC ULCER IN 172 FISHER FOLK

Sex	*Gastric Ulcer*	*Duodenal Ulcer*	*Pyloric Ulcer*	*Hæmatemesis and Melæna*	*Total*
Men	91	31	5	4	131
Women	28	8	1	4	41
Total	119	39	6	8	172

The occupational incidence was 15·2 per 1000 among fishermen, compared with 9·3 per 1000 for all other occupational groups. Fishermen accounted for 51 per cent of all admissions to hospitals. Gastric ulcer was twice as common amongst the fishermen as among all other occupations, but the incidence of duodenal ulcer was the same in both groups. There was no evidence of a hereditary predisposition and nutritional factors could not explain the differences. The high ulcer-rate among fishermen may depend on the most irregular

mode of living entailed by their occupation, with more irregular meals and times of rest than other occupations. The proportion of duodenal ulcers was higher in the urban dwellers in this area; for men, the D.U. : G.U. ratio was 1 : 1 compared with 1 : 3 in the rural areas. These figures are compared with the high ratios reported in the literature in America (e.g., 13·6 : 1 by Jennison).

[The ratio is about 3 : 1 in London. The wide geographical variations are interesting and possibly important clues in the actiology of peptic ulcer. Schanke has made a valuable contribution in producing these figures in relation to the population at risk. The difficulty in interpreting variations in ratio is in knowing whether there is a deficiency in gastric ulcer or an excess of duodenal ulcer. All the evidence in this study points towards a true excess of gastric ulcer among the fishermen.—F. A. J.]

C. A. Flood[3] (Columbia) has *followed up a selected group of duodenal ulcer subjects* who had been treated as in-patients at the Presbyterian Hospital. The duration of the follow-up was between one and fifteen years and the entire group of 231 patients had been supervised for a total of 1603 years. Sixty-three per cent of the years had been free from symptoms of ulcer, but the remaining years were marked by one or more recurrences, of which 24 per cent were of moderate severity and 12·7 per cent were incapacitating. For the entire group there were 756 recurrences during 1603 follow-up years, a ratio of one recurrence every 2·1 years.

Most of the patients became symptom-free during the first week in hospital. In those who took longer to become pain-free the prognosis was considerably worse, and supported the view that a slow response under conditions of ideal medical treatment is an indication for consideration of surgery. Studies to determine the fundamental differences underlying the more refractory symptoms yielded no definite clues. In those patients who had had one or more gross hæmorrhages the subsequent prognosis was essentially the same as in the group as a whole except for a slightly higher percentage of incapacitating recurrences. Among 44 patients who had had two or more gross hæmorrhage 19 had further hæmorrhages during the period of observation, which averaged 7·4 years.

GROSS HÆMORRHAGE

	No. of Cases	*Average Follow-up*	*Satisfactory Years*	*Recurrences*	
				Moderate	*Severe*
All patients	109	6·8	449 (60%)	186 (25·1%)	111 (14·9%)
Multiple hæmorrhages	44	7·4	188 (58%)	77 (24%)	59 (18%)

Patients with Multiple Hæmorrhage

No further bleeding	25
1 subsequent hæmorrhage	12
2 subsequent hæmorrhages	3
3 subsequent hæmorrhages	3
4 subsequent hæmorrhages	1
Total	44 cases

Transitory obstruction of up to 50 per cent of the barium meal at six hours was observed in 36 patients, disappearing during the treatment. Their follow-up showed them to compare very satisfactorily with the group as a whole. When the obstruction persisted after the period of medical treatment, the prognosis of medical treatment was poor, but, even so, only half came to surgery. Analysis of the diet régimes during the first year of the follow-up failed to reveal evidence of a protective effect of a rigid régime. A history of unusual anxiety or fatigue was found in approximately 40 per cent of cases preceding the onset of a relapse, but similar periods of stress also occurred in many of those who remained free from symptoms.

Of the whole group, 13 per cent were subjected to surgery during the period of the study because of persistent or recurrent pain, multiple hæmorrhages,

or persistent pyloric obstruction. Five patients died from causes relating to ulcer, giving a mortality of 2 per cent.

D. T. Davies[4] (London) discusses the *medical management of peptic ulcer*, and stresses the particular importance of taking a deep personal interest in the patient, probing into his life and his environment. This must be done sympathetically and with an obvious sincerity in the desire to help, and must be done in strict privacy. The patient must be given an understanding of the anatomy and physiology of the stomach and the ease with which nervous stimuli are reflected on gastric function. The laity often think that troubles have not come singly and do not recognize the connexion between the anxiety and the dyspepsia. To do so is to become forewarned and forearmed. Diet sheets, although serving a useful function, must be modified to suit the patient and his work. The diet should have a two-hourly basis. If there is tension, and usually there is tension, in the ulcer patient, a sedative taken regularly will help to allay the bombardment of the stomach. A convenient sedative, and possibly superior to phenobarbitone, is amytal, either ¾ gr. (50 mg.) twice a day or ½ gr. (32 mg.) four times a day, and this should be continued for a year or more.

C. M. Fletcher[5] advocates the better *instruction of patients with chronic or recurrent conditions* such as peptic ulcer. The initial diagnosis and prescription of the appropriate régime must be in the hands of an experienced physician. From the onset, however, the patient should be given an insight into the rationale of his treatment and should from then on feel himself to be a pupil and ultimately a collaborator with his doctor in intelligent and careful management and follow-up of his case. Such instruction is a very time-consuming undertaking for busy practitioners, and Fletcher has written a simple explanatory pamphlet for the patient on the nature and treatment of indigestion.

[These pamphlets can be obtained from the *Practitioner* and should be of real value to doctors and patients.—F. A. J.]

H. Rafsky, M. Weingarten, and C. Kriefer[6] discuss the *onset of peptic ulcer in the aged*. Among 1800 successive admissions for peptic ulcer, there were 378 (22·2 per cent) over 60 years of age, and in 81 (4·5 per cent) the clinical history of ulcer began after the fifth decade. The short history of dyspepsia in an elderly patient particularly suggested the possibility of neoplasm, which needed full investigation and careful observation to exclude. The differentiation from an acute coronary thrombosis may be difficult, and indeed the two may co-exist. The medical treatment of uncomplicated ulcer in the aged does not present any special therapeutic problem, but it must be remembered that atropine or belladonna may precipitate acute glaucoma in older patients and that soluble alkalis should never be employed in patients with impaired renal function, the magnesium trisilicate, together with aluminium hydroxide, being recommended. Perforation occurred in 14 per cent of the elderly patients, some occurring without any previous gastric complaints. Pyloric stenosis with a short history was not infrequently seen, and responded well to medical treatment. With long-standing dyspepsia and cicatricial changes, the elderly are particularly susceptible to alkalosis, hypochloræmia, and azotæmia, and surgical treatment is imperative after correction of the fluid and electrolyte balance.

[The onset of peptic ulcer in the elderly must be kept well in mind to-day. The prognosis of the uncomplicated case is reasonably satisfactory.—F. A. J.]

C. Baker[7] (London) reports 576 admissions for *bleeding peptic ulcer* to a Birmingham municipal hospital from 1940 to 1945. There were 77 deaths (13·4 per cent). Twenty-nine per cent of the admissions were over sixty. Patients who had had a previous episode of bleeding in their past history had the same prognosis as those with no previous hæmorrhage. Patients with associated pyloric stenosis or hour-glass stomach fared badly and there were

11 deaths out of 17 patients. Among 540 patients, there was radiological or other evidence of a peptic ulcer in 329 (65·4 per cent). The majority of the remaining cases had negative radiological findings and were probably due to acute, rapidly healing ulcers. Surgical treatment is recommended when there is reasonable clinical evidence of chronic ulcer and no intercurrent disease, (*a*) with the presence of an obstructive factory, (*b*) with recurrent brisk hæmorrhage, (*c*) with persistent bleeding as indicated by the general condition of the patient, even if unassociated with further hæmatemesis or melæna. An experienced gastric surgeon is essential.

Meulengracht[8] (Denmark) provides a further report on his experiences of *early liberal feeding of cases of bleeding peptic ulcer.* There were 26 deaths among 1031 admissions. All the fatal cases, except one, were over forty years old, and many had large ulcers penetrating to the pancreas or liver, or had associated complicating diseases. Although previously he had withheld surgical treatment, as a result of this review he will in future consider surgery for patients over forty with persistent or repeated hæmatemesis and threatening to die in spite of repeated blood transfusions.

[Meulengracht popularized the feeding of bleeding peptic ulcers, and modifications of his diet have been in use over the past twelve years. It is significant that, with his extensive experience, he now agrees with many in this country that surgery has a scope in the management of severe bleeding. It must be remembered that differences in the mortality between series reflects the ease of admission as well as the efficiency of treatment. In Scandinavia, the majority of bleeding ulcers are admitted to hospital, whereas in this country many are treated at home and chiefly the more severe cases sent to hospital. F. A. J.]

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GASTRIC AND DUODENAL ULCER : SURGICAL ASPECT.

Norman C. Tanner, F.R.C.S.

Vagal Resection for Peptic Ulcer.—Many interim reports on series of vagal resections performed between one and four years ago are now available to help in judging the operation. It is much too soon to consider final judgements, though it can be said that there is thus far no evidence of large scale ulcer relapse, and most of the undesirable 'side effects' diminish with time, though a small proportion of them persist.

Technique of Vagal Resection.—The general trend is to favour the abdominal route for the operation,[1, 2, 3] except in certain cases of anastomotic ulceration where there is reason to believe that dense peritoneal adhesions may make the operation difficult or hazardous. (*See* MEDICAL ANNUAL, 1947, *Plate XVI.*) Division of the left triangular ligament and reflection of the left lobe of the liver to the right improves the exposure,[2] and further improvement may result if the xiphoid process is removed, as recommended by H. Lefevre for total gastrectomy.[3] A tube in the œsophagus helps to identify it. The nerve-trunks are felt as firm unyielding cords against the soft œsophagus when the stomach is drawn downwards. Any doubtful strands of tissue should be excised, and it must be remembered that nerve-fibres may pass down in the œsophageal musculature, or even as deep as the submucosa.

Post-operative Treatment.—Many surgeons are reporting post-operative difficulties far in excess of those which may follow gastrectomy,[4,5] and of these gastric ileus and abdominal distension are the most troublesome in the early stage. L. R. Dragstedt[6] and I. Orr[7] maintain that a strict post-operative régime will minimize these troubles. The suggested routine is to institute continuous gastric suction for four to five days after operation, the fluid and

salt balance being maintained by intravenous infusion. At the end of this time hourly feeds of one ounce are given, and if, after twelve hours, gastric aspiration shows that there is no retention, the amount of fluid is doubled, but if there is retention then a further 24–48 hours' aspiration is considered advisable. A full diet is given in 3–5 weeks after operation.

Post-vagal Resection Effects and their Management.—The occurrence of unpleasant 'side effects' after vagal resection was mentioned in the MEDICAL ANNUAL, 1948, p. 127.

One of the commonest complaints is of *a "bloated" feeling in the abdomen and foul eructations.* The foul or 'rotten egg' smell no doubt results from the altered bacterial flora due to the lowered gastric acidity in association with gastric stasis. Similar foul belching is sometimes observed in patients with obstructive gastric carcinoma.

At times not only gastric atony but *severe abdominal distension* gives rise to great anxiety in the early days after operation. Its treatment demands very careful nursing and prolonged gastric aspiration and maintenance of the fluid balance. The simultaneous performance of gastrojejunostomy and vagotomy does not prevent post-operative gastric retention;[4] indeed some observers,[5] including the reviewer, believe it may make it worse in the early days, though it minimizes the risk of persisting or later obstruction.

Urecholine (carbaminoyl -beta-methyl-choline chloride) has been used in doses of 5 mg. by injection or 10 mg. orally three times daily about half an hour before feeds for a week post-operatively. K. S. Grimson and his associates[8] thought the drug diminished gastric retention. It appears to have little clinical effect when symptoms of gastric atony are severe, although increased gastric motility may be demonstrated radiologically after its use.[9]

In cases where abdominal distension is persistent despite prolonged gastric aspiration the reviewer has had dramatic improvement from the very slow intravenous injection of pituitrin (0·1 c.c. every 15–20 seconds with a maximum dose of 1 c.c., though less is required if defæcation commences before 1 c.c. has been given). Aspiration may have to be continued, but this rather drastic method, which should not be used too freely, may just turn the scale in the patient's favour.

Diarrhœa: Mild diarrhœa, characteristically an early morning looseness, is very common, but severe or persistent diarrhœa may occur and has contributed to late fatalities.

Author	*No. of Vagal Resections*	*Mild or Temporary Diarrhœa*	*Persistent Diarrhœa*
K. S. Grimson[8]	57	20	4
L. H. Appleby[4]	66	23	1
F. D. Moore[10]	74	'over 50'	6
I. Orr[7]	115	56	1

The diarrhœa bears no clear relationship to the gastric emptying rate[11] and is possibly associated with the hypochlorhydria. Large doses of hydrochloric acid by mouth effect little improvement. Sulphasuxidine diminishes the diarrhœa in a high percentage of cases, though it may relapse when the drug is withdrawn. K. S. Grimson[8] found that some cases were relieved by gastric lavage or by urecholine. There is disagreement as to whether gastrojejunostomy has a good or bad effect on the diarrhœa.[6, 10]

Dysphagia: A. C. Ivy[12] suggested that vagectomy in man would predispose to cardiospasm, an effect noted after the operation in animals. Earlier reports did not describe this complication, but now considerable numbers of cases of dysphagia, some having the radiological features of cardiospasm, are being reported.

Author	*No. of Cases of Vagectomy*	*Dysphagia or Cardiospasm*
P. H. T. Thorlakson[13]	63	5
I. F. Stein et al.[14]	35	3
L. R. Dragstedt[6]	212	0
K. S. Grimson et al.[8]	57	20
R. Maingot[5]	46	4
I. Orr[7]	115	8

Apart from cardiospasm, which is presumably a direct result of the nerve section, dysphagia may result from trauma to the lower œsophagus, or from gastric stasis and dilatation.[8] The majority of cases recover within a few weeks without treatment. In more resistant cases octyl nitrite inhalations[5] or œsophageal bouginage may give relief. W. R. Moses[15] found some benefit from repeated posterior splanchnic nerve block.

? *Hypoglycæmic attacks*: H. D. Johnson[11] reported that about a third of his cases suffer from attacks of weakness, sweating, and faintness which often pass off in a few weeks. Two patients investigated had hypoglycæmia during an attack.

The Mortality of Vagal Resection.—Low mortalities are reported by most writers.

Author	*No. of Cases*	*Mortality*
L. H. Appleby[4]	66	
P. Thorek[16]	50	
W. Walters et al.[9]		
I. F. Stein et al.[14]		
L. R. Dragstedt[6]		
R. Colp[6]	77	1 ,,
R. Maingot[5]	46	1 ,,

In the majority of cases the fatality is not a direct consequence of the vagal section, though death from gastric and intestinal ileus may occur.[16]

Clinical Results of Vagotomy.—Follow-up reports between eighteen months and four years after vagal resection for duodenal ulcer show a 75 per cent or higher rate of satisfactory results.[10, 14, 7] Some of the unsatisfactory results are due to relapse or failure of the ulcer to heal. Others are due to gastric retention and other 'side effects', though there is no doubt that many of those with persistent gastric retention may eventually be made comfortable by the performance of gastrojejunostomy or gastrectomy.

The clinical results of the operation when performed for duodenal ulcer may vary according to whether it is performed alone or combined with pyloroplasty,[17] gastrojejunostomy, antral resection,[7] or partial gastrectomy, and the statistical and other evidence thus far produced is not sufficient to judge between them.

There is a wide measure of agreement that the operation is amply justified for anastomotic ulceration following gastrectomy[18] or gastrojejunostomy, so long as mechanical faults of the previous operation are excluded.

The weight of opinion is against the performance of vagectomy for gastric ulcer. There is the risk that the ulcer may be or may become malignant. In addition there are results of gastric ulcer appearing for the first time or increasing in size after the operation.[5, 19, 20] In contrast to these disadvantages is the very large measure of satisfaction given by gastrectomy for gastric ulcer, anastomotic ulcer being almost unknown after it.[21] A minority of surgeons support vagal resection for gastric ulcer,[4, 6] particularly if the ulcer is so high that resection would be difficult or hazardous.

Effect of Vagotomy on Gastric Function. There is evidence that vagal section reduces the night and the basal day secretions[14, 11] as well as abolishing the cephalic phase of digestion (*Fig.* 24). The accepted method of estimating the total gastric secretions in man, by continuous gastric aspiration, is not completely reliable because of losses of gastric juice, entry of duodenal juices and

bile through the pylorus, and entry of saliva through the cardiac orifice. A. M. Schoen and R. A. Griswold[22] have described a new method of estimating the rate of gastric secretion. It consists of injecting into the empty stomach an isotonic solution containing a known amount and concentration of an indicator (phenol red), and after a 15-minute period aspirating the entire gastric residue. From the values of quantity and concentration of indicator injected and aspirated, the average rates of gastric secretion can be estimated. By this method the authors found an average reduction of the basal gastric secretory rate of 36 per cent after vagotomy, estimated in 6 patients. In one person the basal secretory rate fell from 3 c.c. per minute during a period of exacerbation of duodenal ulcer to 1·2 c.c. per minute during a remission. The rate was reduced to 0·45 c.c. per minute after vagotomy.

Radiological studies shortly after vagotomy show gastric atony and dilatation in most cases. Gastric peristalsis is sluggish, ineffective, and arrhythmic or absent, and the gastric emptying time is greatly increased. Examination six

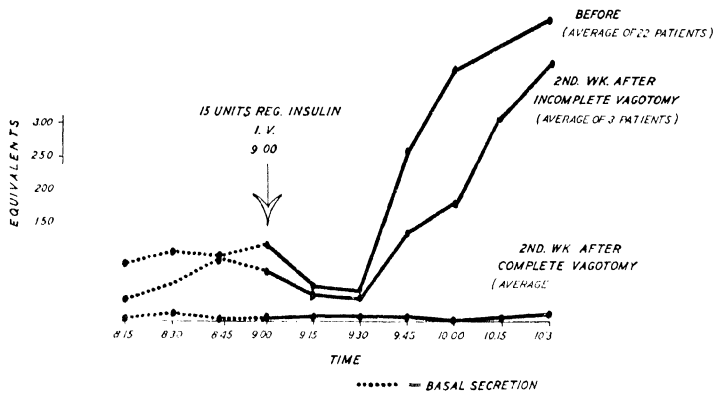


Fig. 24.—The effect of insulin on gastric acidity before and after vagotomy. (*Reproduced from 'Surgery, Gynecology and Obstetrics'.*)

to twelve months later reveals a tendency to return to normal, though in a series of cases examined by M. Ritvo and I. A. Shauffer[23] up to fourteen months after operation, none returned completely to normal.

The size of the small intestine is unaltered by vagotomy, though its motility is slow, possibly as a result of the slow discharge from the stomach.

Test for Complete Vagal Section.—The two classical tests for vagal activity are the tests for increased gastric secretion either after sham feeding or during an insulin-produced hypoglycæmia (MEDICAL ANNUAL, 1948, p. 128). The former test is difficult to carry out clinically, the latter is not entirely free from risk,[5] nor always reliable.[11] A new test has been described by F. Mandl and H. Männchen.[24] This is based on the finding of von Hess and Faltitschek in 1924 that injection of local anæsthetic into the right 7th and 8th sympathetic ganglia causes a rise in gastric acidity. Mandl and Männchen suggest that the rise may be due to vagal overaction consequent on the sympathetic block. They found that after vagal section the sympathetic block causes no rise in acidity, and the writers claim that this is a useful test for complete vagal section.

Cause of Pain Relief after Vagotomy.—There is much conjecture as to why relief of pain after vagotomy is usually immediate, and there have been

suspicions that it may be due to severances of sensory nerve-fibres from the stomach. Therefore it is interesting to learn that L. R. Dragstedt[6] and I. F. Stein and K. A. Meyer[14] reproduced ulcer pain in patients shortly after vagotomy by introducing 200 c.c. of 0·5 per cent hydrochloric acid into the stomach.

Gastrojejunostomy for Peptic Ulcer.—The entry of vagotomy into the field has stimulated the protagonists of gastrojejunostomy and gastrectomy to point out the achievements of the latter operations, so that there will be no hasty discarding of the older though imperfect operations for the doubtful advantages of the new one. In addition many surgeons are performing a combination of vagotomy with gastrojejunostomy, and there are now a number of young surgeons who are unaware of what may be expected of gastrojejunostomy alone. W. A. Cooper[25] followed up 279 posterior gastrojejunostomies performed between 1932 and 1948. Nine patients died from the operation (mortality 3·2 per cent—it would probably be less nowadays), and 257 were available for follow-up. The author points out the difficulties of grouping the cases accurately. He labels a case a failure which at any time suffers from bleeding from the upper alimentary tract, has treatment for ulcer, or clinical or X-ray evidence of recurrent ulcer, though he does not include in the failures those patients who have transient attacks of mild discomfort, belching, etc. At the time of the follow-up, in 13 cases ulcer symptoms had recurred and disappeared again without further surgical treatment. Although they were now satisfied they were classed as failures.

Following this method of classification there were 49 'failures', 75 per cent of whom had pain and 32·6 per cent haemorrhage—the rest were satisfactory. Of the 49 failures, 47 relapsed in the first five years after operation, so that if a patient with a gastro-enterostomy remain well for 5 years he will probably remain well; 37 of the 49 failures had definite recurrent gastrojejunal ulcers and there was suspicion of recurrence in the other 12.

The author found that the radiologists were accurate in showing gastrojejunal ulcer in cases where it was subsequently shown at operation where they failed to demonstrate it, it was because the ulcer was healed. Not infrequently radiologists showed duodenal craters in patients with gastrojejunostomies, but in all but one of such cases the duodenal ulcer was found to be soundly healed. [The reviewer agrees that active duodenal ulcer in the presence of a gastrojejunostomy is extremely rare.—N. C. T.]

In addition W. A. Cooper carefully reviewed the cases in an attempt to see if any particular factors influenced the end-results towards success or failure. Age appeared to have no effect, the older group being as prone to recurrence as the young. There were more failures (25 per cent) in the group where bleeding was the main symptom than in those (15 per cent) where obstruction or pain was the prominent feature.

Of the 49 failures 26 were operated on again, and 20 of them then became symptom-free. Gastrectomy was the only effective secondary operation.

The author summed up by saying that the patient with a gastro-enterostomy had an 89 per cent chance of survival with eventual cure and satisfaction. There was a 25·2 per cent chance of some recurrent symptoms, usually within five years of operation.

Gastrojejunostomy for Organic Pyloric Stenosis.—Several observers[25, 26, 28, 29] have remarked again on the better results obtained from gastrojejunostomy if it is performed for obstruction, an observation previously made by Wilkie, who claimed 90 per cent good results in such cases.[27] H. Reid and R. Marcus[28] studied the fate of 80 cases of long-standing pyloric stenosis treated between 1928 and 1938, with a minimum of 10 years follow-up. There were 2 operative deaths and 9 died before the date of the study, but none from recurrent

ulceration. Fifty-four cases were available for examination: 50 of these cases were quite symptom-free, 3 had occasional mild abdominal discomfort, and 1 had ulcer-like symptoms (and had a hæmatemesis). There were no dumping symptoms and only 1 case of anæmia. The average age of this series was 50, and as they were all resistant to medical treatment they were presumably cases of scar stenosis rather than obstruction from œdema round an ulcer. In this type of case the actual ulcerative tendency may be on the wane, but the patient is crippled by the healing process of fibrosis rather than the disease process of ulceration, and should theoretically and in fact does give the best results from gastrojejunostomy.

Treatment by Gastrectomy.

Measured Radical Gastrectomy.—A. H. Visick,[30] in a Hunterian lecture, compared his results in periods when a "moderate" gastrectomy was done for duodenal ulcer with those obtained after a very high gastrectomy in which all but the highest vas breve were divided and the remaining stomach measured 1½ in. on the lesser curve and 3 in. along the greater curve. He found that whereas a 2/3 to 3/4 gastrectomy had a recurrent rate of 3·7 per cent, the very high gastrectomy gave rise to no recurrent ulcers (*Fig.* 25). In fact the resection

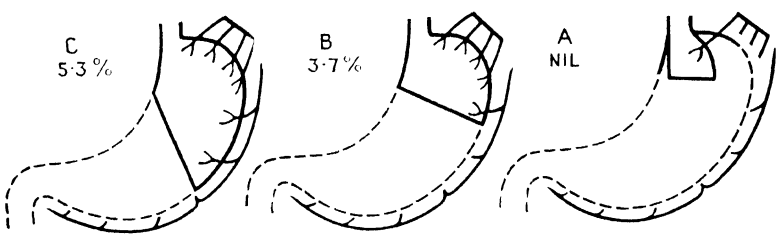


Fig. 25.—Incidence of recurrent ulcer in relation to extent of gastrectomy and blood-supply of gastric remnant: A Measured radical gastrectomy; B "Two-thirds to three-quarters" gastrectomy; C "Half to two-thirds" gastrectomy. Recurrence-rate for C is based on the report of Heuer et al. on three-month to ten-year results; it would be considerably higher if the later cases were excluded and the recurrence-rate calculated only on the two-year results as in B (present series).

(*By kind permission of* '*The Lancet*'.)

was so extensive that in 12 cases where the pyloric antrum was left unresected (a variation very prone to cause anastomotic ulceration) there was no recurrent ulceration. [The reviewer dislikes the word "radical" in Visick's description, for it is a useful word to describe the operation for carcinoma, which is not necessarily a high one, but involves resection of the glands, omenta, etc. High, or subtotal, is a satisfactory term.—N. C. T.]

Gastrectomy as a Precaution in view of the Possibility of Carcinoma.—S. F. Marshall and M. L. Welch[31] found evidence of carcinoma in 26 out of 131 resections for gastric ulcer, all believed to be innocent before and at operation, a diagnostic error of 19·82 per cent. Therefore they have adopted a more aggressive attitude to gastric ulcer, both on account of the diagnostic errors, and also because of the possibility of subsequent malignant degeneration. They recommend in particular that all prepyloric, greater-curve, and cardiac-end ulcers be treated surgically, and also gastric ulcer in any part of the stomach which does not heal rapidly with complete relief of symptoms. F. H. Lahey[32] is in favour of gastrectomy for all gastric ulcers, because the mortality of the operation is low, the results are excellent, and because many medically-treated ulcers return with carcinoma at a later date. [A diagnostic error of 19·82 per cent is higher than most surgeons would admit; no doubt the ulcers treated

surgically were the ones clinically most suspicious of carcinoma. Lahey's attitude is defensible if restricted to chronic gastric ulcers, but a gastroscopist would see many acute ulcers which heal in a few days and for which resection would not be justifiable.—N. C. T.]

Aftermath of Gastrectomy.—N. C. Lake[33] performs a valvular form of gastrectomy as described by him in 1926. Part of the divided end of the stomach is closed and the afferent loop is stitched over it (*Fig.* 26). This modification—similar to the one independently described by Finsterer—makes reflux into the afferent loop improbable. He followed up 615 cases for between two and twenty-three years. The late results were excellent in the vast majority of cases. There were no macrocytic anæmias, though a few patients had a microcytic anæmia which responded well to iron. There was a general tendency to gain weight. The appetite was improved in cases where the operation had been performed for gastric ulcer, but unchanged when it had been for duodenal ulcer. There were 6 proven and 2 suspected anastomotic ulcers, and 20 cases of persisting 'dumping' syndrome. Some of the cases had morning nausea, which disappeared when the patient got up or took food or drink. I may be relieved by sleeping on the right side, and Lake believes it to be due to the free entrance of bile into the stomach.

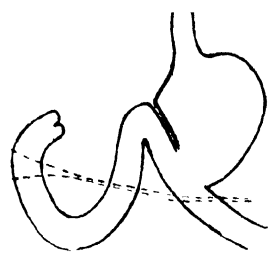


Fig. 26.—End-to-side anastomosis with restricted valvular orifice. The anastomosis is retrocolic and about two-thirds of the stomach is usually removed. The broken line indicates the level of the transverse mesocolon. (*By kind permission of the 'British Medical Journal'.*)

The *incidence of anastomotic ulceration after gastrectomy* depends primarily on the condition for which it is performed. It is a curiosity after gastrectomy for gastric ulcer unassociated with duodenal ulcer. W. Waters[34] has never seen such a case. N. C. Tanner[21] had no recurrent ulceration in 390 gastrectomies for gastric ulcer (though he found at least 2 per cent recurrent ulceration after gastrectomy for duodenal ulcer and even more after gastrectomy for gastrojejunal ulcer). Marshall and Welch (*see above*) found no anastomotic ulcers in their series. H. K. Ransom's[35] experience appears at first sight to be to the contrary, for 4 out of 127 gastrectomies for gastric ulcer developed anastomotic ulcer. He explains, however, that in all the four there was suspicion that part or all of the pyloric antral mucosa was left in situ, a variation of the normal gastrectomy which encourages the development of anastomotic ulcer.[36]

Effect of War on Peptic Ulcer Convalescents.—D. M. Douglas[26] at the end of World War II studied the conditions of three series of peptic ulcer patients, one series treated medically, another by gastrojejunostomy, and a third by gastrectomy, between 1935 and 1941. In gastric ulcer cases gastrectomy gave only 10 per cent unsatisfactory results, compared with 44·4 per cent for gastrojejunostomy and 42 per cent for medical treatment. In duodenal ulcer cases without stenosis, gastrectomy gave 9 per cent, gastrojejunostomy 29 per cent, and medical treatment 68·2 per cent unsatisfactory results. All the cases of duodenal stenosis had been treated by gastrojejunostomy, and of 15 traced 13 were symptom-free. Against these figures one must balance the greater primary mortality of gastrectomy over gastrojejunostomy. Douglas found that the war conditions appeared to have had no great effect in the progress of the cases, compared with similar series which had remained under peace-time conditions.

Gall-bladder Complications following Resection of Stomach for Peptic Ulcer.—There is no doubt that gall-bladder diseases may be encountered in patients

after they have had a gastrectomy. N. C. Lake performed 4 operations for gall-stones on his 615 gastrectomy cases, not a significantly high proportion. H. K. Ransom[35] found 3 cases of cholelithiasis in 127 patients who had had a gastrectomy. C. L. H. Majoor and T. J. T. Suren[37] found gall-stones in 7 out of 174 Billroth II type gastrectomy cases at operation. Subsequent to the operation 6 other cases suffered from gall-stone colic, the diagnoses being confirmed at a second laparotomy. These latter stones were young, and were not evident at the original operation. The authors believe that the gastrectomy predisposed to their formation; possibly the altered duodenal flow and pressure were reflected in the biliary system. Confirmation of this must await further reports in cases where the gall-bladder is routinely and minutely examined at gastrectomy operations.

Post-prandial Symptoms following Gastrectomy.—There is still a great deal of conjecture about and investigation into the cause and means of relief of the symptoms experienced after gastrectomy by a minority of patients (*see* MEDICAL ANNUAL, 1948, p. 131). It is not unlikely that more than one cause of the symptoms may be found; possibly some are of mechanical origin and some due to blood-sugar fluctuations. W. T. Irvine[38] considers that the fact that symptoms may start during or very shortly after a meal suggests a mechanical cause. In further support of this he states that symptoms are more likely to occur after a bulky meal even it is of low carbohydrate value. Studying 24 cases, he found that symptoms might appear before the blood-sugar had reached its peak, and disappear before the blood-sugar value began to fall. Irvine suggested that the mechanical distension of the bowel produces sympathetic stimulation, for the pulse is raised 10-20 beats per second during the attack, the symptoms resemble adrenaline effects, and they are unaffected by vagotomy.

Technique of Partial Gastrectomy.—T. W. Mimpriss and St. J. M. C. Birt[39] investigated their partial gastrectomy cases to see whether the anastomosis technique had influenced the end-results. They used four different techniques. The best results were obtained from the Billroth I anastomosis, though only in gastric ulcer cases. Next best was a retrocolic end-to-side gastrojejunal anastomosis using a small valve, and with the efferent loop at the greater curve. Not quite so satisfactory because of occasional trouble with the long loop was an antecolic position of the same form of anastomosis. More trouble appeared after antecolic end-to-side gastrojejunal anastomosis, with the efferent loop at the lesser curve. It produced a high percentage of complaints of symptoms of distension, lassitude, vomiting, sweating, and "bile in the throat" shortly after meals, which the authors believe to be due to the filling and distension of the proximal loop which occurs after this operation.

Gastrojejunocolic Fistula.—In the MEDICAL ANNUAL, 1944, p. 129, the occasional value of a preliminary colostomy in the treatment of gastrocolic fistula was mentioned. There has been a certain amount of enthusiasm for preliminary ileocolic anastomosis followed by gastrectomy combined with colectomy, as practised by F. H. Lahey[40] and S. F. Marshall.[41] These operations involve a colonic anastomosis, however, a grave risk in such ill patients. The performance of a proximal colostomy in the ascending colon or near the hepatic flexure is a minor and safe procedure which can be done if necessary under local anæsthesia. Its advantages are emphasized by R. F. Barber and J. L. Madden,[42] who comment on the fact that it produces marked clinical improvement, gain in weight, and terminates fæcal vomiting. Strangely enough it usually terminates the diarrhœa as well, though 2 out of 5 of their cases persisted with diarrhœa. They speculate as to why the diarrhœa should improve, and suggest that in some cases the diarrhœa may be an irritant effect due to the entry of fæces into the stomach and jejunum. Undoubtedly the diarrhœa is

at times due to the passage of food and gastric juices directly into the colon, for it may be recognized as such after voiding.

At a suitable time after the colostomy the upper abdomen is reopened, the fistula disconnected, and the colon repaired. The stomach and jejunum may also be repaired, or better still a partial gastrectomy performed. The colostomy does not add to the operative difficulties, and repair of the clean defunctioned colon is easier and practically free from the risk of producing peritonitis. Closure of the colostomy is a comparatively minor procedure once the fistula has been dealt with.

Perforation of Peptic Ulcer.—The mortality associated with perforation of peptic ulcer is showing a definite fall in recent years[43, 44, 45] (*Fig.* 27). This mortality decline must be taken into consideration when the methods of immediate gastrectomy or conservative treatment are compared with simple closure of the perforation. The main reasons for the mortality decline are the introduction of chemotherapy with the sulpha drugs and penicillin, freer use of the indwelling stomach tube, and perhaps improved methods of anæsthesia. W. T. McElhinney and C. E. Holzer[45] found their mortality reduced from 21 per cent to 10·7 per cent in the twelve-year period 1935–46, and in particular found the incidence of wound infection, peritonitis, and subphrenic abscess greatly reduced.

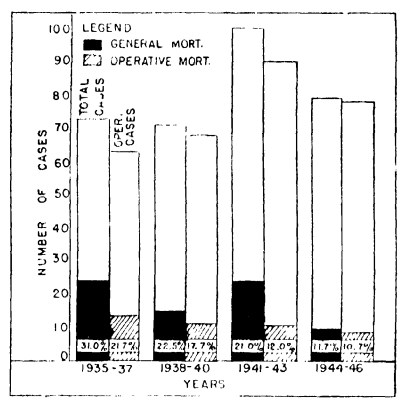


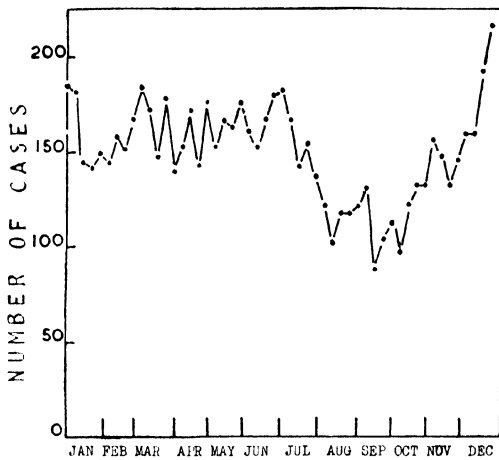
Fig. 27.—Comparison of general and operative mortality-rates by three-year periods, 336 cases seen at Cincinnati General Hospital from 1935 to 1946. (*Reproduced from 'Surgery, Gynecology and Obstetrics'.*)

Conservative Treatment of Perforated Peptic Ulcer.—No large series have been published since Hermon Taylor's series (MEDICAL ANNUAL, 1948, p. 131), and the merits of non-operative treatment remain *sub judice*. D. C. L. Bingham[46] reported 5 cases treated conservatively without mortality, and considers that the case for this type of treatment must be most carefully chosen. He suggests that: (1) The perforation should be under 8 hours' duration; (2) It should have occurred more than one hour after a meal (a full stomach presumably leads to greater soiling); (3) There should have been no large amount of fluid drunk; and (4) As far as is ascertainable the ulcer should be duodenal rather than gastric, and small in size. Suspicion of pyloric stenosis or carcinoma makes surgical treatment advisable.

Late Results following Perforation of Peptic Ulcer.—Many 'follow-ups' of cases of perforation have been made with varying results, usually between 25 per cent and 60 per cent of satisfactory late results being recorded. S. W. Moore and R. Hendricks[47] found rather unsatisfactory end-results in a following-up period varying between 6 months and 11 years. Only about a third of the duodenal ulcer cases and a quarter of the gastric ulcer cases were quite symptom-free, and 6 per cent of the survivors of perforation suffered a second perforation.

Variations in the Frequency of Ulcer Perforation with Seasons and the Time of Day.—R. A. Jamieson[48] investigated a very large number of ulcer perforations occurring in the three main Glasgow hospitals between 1924 and 1945, with

particular reference to the exact time of perforation. He found that perforations are least common in the months of August, September, and October, and then they rise to a high peak in December, from which month the rate remains fairly high until a fall in the following August (*Fig.* 28). Closer examination showed the perforation rate was fairly high in the first two weeks in July and there was a sudden fall in the latter part of July. It is probably significant that July in that part of Scotland is a holiday month and the majority of the labouring and artisan class have ten days' holiday in mid-July. This holiday is probably



Week Commencing	No of Cases	Week Commencing	No of Cases
Jan 1	185	July 2	182
.. 8	181	.. 9	166
.. 15	144	.. 16	142
.. 22	141	.. 23	155
.. 29	150	.. 30	138
Feb. 5	145	Aug. 6	121
.. 12	159	.. 13	103
.. 19	151	.. 20	118
.. 26	168	.. 27	118
Mar 5	184	Sept. 3	121
.. 12	162	.. 10	132
.. 19	146	.. 17	89
.. 26	177	.. 24	105
April 2	140	Oct 1	114
.. 9	154	.. 8	97
.. 16	172	.. 15	123
.. 23	144	.. 22	131
.. 30	176	.. 29	131
May 7	154	Nov 5	156
.. 14	166	.. 12	149
.. 21	164	.. 19	131
.. 28	176	.. 26	146
June 4	162	Dec 3	160
.. 11	153	.. 10	160
.. 18	168	.. 17	191
.. 25	180	.. 24	216
		Dec 31 (alone)	30

Fig. 28.—Perforated peptic ulcer; incidence by calendar weeks (1924-45). (*By kind permission of the 'British Medical Journal'.*)

effective in diminishing the frequency of perforation for the following 3 to 4 months.

Perforation becomes more common as the week goes on, but is relatively uncommon on Sundays and Mondays—which Jamieson suggests may be an effect of the week-end rest.

It is uncommon for perforation to occur at night. The hourly incidences of perforation rise as the day goes on, to a peak about mid-afternoon, and there is a diminution at night. Again, the lowest incidence appears in and just after the rest periods.

Jamieson could find no evidence that ulcer perforation tended to occur at any particular phase of gastric digestion, nor that severe exertion was a common precursor of perforation.

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GASTRO-ENTERITIS IN INFANTS.

R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.

Aetiology.—Professor G. Payling Wright,[1] presenting the result of a statistical study in Willesden, classified this disease complex according to J. M. Smellie[2] into "Infective", "Infectious", "Parenteral", and "Dietetic", and added "Neonatal Diarrhœa". As the result of his study, he concludes that in spite of the rise in the incidence of deaths from this condition in the late winter months, there is little evidence that parenteral infection plays an important part in its aetiology, but on the other hand there seems to be evidence that neonatal diarrhœa was increasing with the increase of the use of maternity hospitals and was likely to go on increasing. The main component of gastro-enteritis in urban communities, however, seems to be Smellie's "Infectious" form. In the past, infecting agents were spread by flies and man, the former seasonal, the latter perennial. The former has disappeared and with it the drastic hot weather epidemics. The latter continues and maintains the endemic form where mildly pathogenic organisms cause enteritis in susceptible infants.

E. Harden[3] in another study covered the district of North Kensington, London, and compared it with the Registrar General's rates for the years 1937, 1938, 1939, and 1940. In the clinical material presented, there were 148 cases with 65 deaths, a case mortality of 44 per cent. This mortality-rate he compares with other published series. In the second half of this paper, he discusses the route of invasion, the bacteriology with the possibility of a virus aetiology, the role of parenteral infection, the value of chemotherapy and of blood and blood products in treatment, and lastly epidemic diarrhœa of the newborn.

He concludes that diarrhœa and enteritis under the age of two is a heterogeneous group. He believes that most of the cases of the severe type belong to an acute infectious disorder, probably specific, which gives a mortality-rate of 33 to 50 per cent. This disease occurs in small epidemics at different times and in different places, but mainly in early months. Congregation of susceptible infants favours the development of an epidemic. Hence it is found in cities, children's wards, and nurseries of maternity hospitals. Harden does not believe the pathogen to be bacterial, but thinks it may be viral. The brunt of the infection is borne by the intestine, regional glands, and liver, but the portal of entry is not oral but may be respiratory. He finds chemotherapy of doubtful value, but says that blood transfusion exerts a specific effect. It is difficult to understand why, when he said that the portal of entry is not oral, he should go on to say that there is good evidence that the disease is caused by parenteral infection. He finds no good reason for considering epidemic diarrhœa of the newborn to be a separate entity. This interesting study reviews the work on this present problem, and although many will not agree with the author's conclusions, yet, when it is taken with Professor Wright's paper,[1] there is much common ground between them.

G. J. Budding[4] and K. Dodd[5] have presented evidence for some outbreaks of gastro-enteritis occurring with stomatitis being of viral origin. S. H. Clifford[6] goes into the question of epidemic diarrhœa of the newborn. He gives evidence to show that this syndrome is not a pathological entity, though its viral aetiology has been postulated in five epidemics. He concludes that its prominence to-day coincides with the transfer of childbirth from the home to hospital. Overcrowding of hospital nurseries being the cause, he plans for more small nurseries of eight to twelve cots, with isolation facilities. Although many outbreaks have been traced to a specific organism, yet in the majority a gross breakdown in nursing technique has also been found.

He suggests that to combat this all techniques should be tightened up and stricter supervision of these be instituted.

In this country, too, there is a general trend towards hospital childbirth, and with this has come epidemic diarrhœa in the nurseries. Those in charge of neonates in nurseries must realize the necessity for strict supervision and for the maintenance of strict barrier technique if these disasters are to be averted.

REFERENCES.—[1]*Proc. R. Soc. Med.* 1948, **41**, 182 ; [2]*Lancet*, 1939, **1**, 969, 1026 ; [3]*Arch. Dis. Childh.* 1948, **23**, 27 ; [4]*Sth. med. J.* 1946, **39**, 382 ; [5]*J. Pediat.* 1944, **25**, 105 ; [6]*New Engl. J. Med.* 1947, **237**, 969.

GONORRHŒA. (*See also* ANORECTAL GONORRHŒA.)

T. Anwyl-Davies, M.D., F.R.C.P.

Prophylaxis.—To improve the prophylactics used by the United States Forces C. P. Miller[1] produced experimental gonococcal infection of the rabbit's eye by inoculation of the anterior chamber to test the effectiveness of various prophylactic agents. The tests showed that penicillin, or 15 per cent sulphathiazole and/or 30 per cent calomel, were highly effective in an aqueous or vanishing cream base, but not in oily or greasy ointments.

Gonorrhœa in Gynæcology.—The chief symptoms of 317 women with gonorrhœa were analysed by H. Peters.[2] Urinary frequency, dysuria, and vaginal discharge were less common than abdominal pain (36 per cent) and menstrual irregularities (23 per cent). Only 13 per cent complained of a vaginal discharge, and only 7 per cent had urinary symptoms.

TREATMENT

Procaine Penicillin.—The most recent preparation to prolong the action of penicillin is crystalline procaine penicillin G. This is not, as its name suggests, a mixture of penicillin with the local anæsthetizing agent, procaine, but a true salt formed by procaine with sodium or potassium penicillin G. Suspended in oil and aluminium stearate, it is ready for use in a mobile stable form, and its sparing solubility prolongs absorption. The laboratory experiment of G. L. Hobby et all.[3] showed it to be equal to sodium penicillin G, and to persist in the blood of animals after a single injection. Herrell et al.[4] found detectable amounts of penicillin in the blood in 9 out of 10 patients twenty-four hours after a single injection of 300,000 units. This was confirmed by W. L. Hewitt et al.[5] who showed that after the same dose given to 63 patients, 58 had detectable amounts of penicillin in the blood at twenty-four hours and 21 at forty-eight hours. Similarly, P. F. Jones and R. A. Shooter[6] detected penicillin in the blood of 37 out of 45 patients between eighteen and twenty-six hours after daily injections of 300,000 units. They found that the high-peak levels usually obtained with penicillin in oil and beeswax did not occur, but that on the whole the amount of penicillin in the blood remained fairly constant throughout the twenty-four hours. Hence they conclude that a low but constant penicillin blood-level can be maintained in ambulant patients with more certainty by procaine penicillin than by penicillin in oil and beeswax, and with an absence of local reactions. H. A. Tucker and his associates[7] at Johns Hopkins Hospital treated 50 patients who had uncomplicated acute gonorrhœa. Each patient was given a single intramuscular injection of procaine penicillin G in sesame oil containing 100 to 500 units per kilo body-weight. There were no failures with doses of 250 units per kilo body-weight or higher, and the persistence of bactericidal activity was noteworthy, for nearly 50 per cent of the 24-hour specimens contained traces of penicillin. As a routine dosage in uncomplicated acute gonorrhœa, the authors recommend 0·5 mg. per kilo body-weight. For the average adult this is equivalent to 0·12 c.c. of the 300,000 units per c.c. concentration.

PLATE XVIII

GUMMA OF FRONTAL BONE

(L. J. Horst)



Front and side views of the gumma

Penicillin in Oil.—A large series of 14,756 patients with gonorrhœa was treated in the public clinics in New York with ten different schedules of penicillin. A Jacoby et al.[8] analysed their effect on the 10,156 cases who were followed long enough for assessment. A cure rate of 78 to 88 per cent was effected. The highest failure rate, 29 per cent males and 25 per cent females, occurred in those who were given only a single dose of 150,000 units of aqueous penicillin. But with a single dose of 300,000 units of penicillin in oil the failure rate was reduced to 7 per cent males and 3 per cent females.

The authors were unable to determine any relationship between the blood-levels of penicillin and its therapeutic action, and no example of penicillin resistance occurred in the series.

R. P. Hughes and C. M. Carpenter[9] studied 216 soldiers with alleged penicillin-resistant gonorrhœa, who had been hospitalized for from two to six months for treatment with intramuscular injections of several million units of aqueous penicillin without cure. Bacteriological examination revealed only 19 patients (9 per cent) to be infected with the gonococcus: These were cured with 300,000 units of calcium penicillin in oil and beeswax. The alleged penicillin-resistance was due to the erroneous diagnosis of non-gonococcal urethritis as chronic gonococcal urethritis, to faulty Gram staining, or to reinfection.

Penicillin in Ophthalmia Neonatorum.—H. C. Franklin[10] used a single instillation of penicillin for prophylaxis against ophthalmia neonatorum on 1177 infants. Crystalline sodium salt of penicillin containing 2500 units per c.c. was used, four drops being instilled into the conjunctival sac of each eye. Thirteen (1·1 per cent) infants exhibited pus in one or both eyes after penicillin prophylaxis while in the nursery, but there was no known instance of gonococcal conjunctivitis, either in the nursery or at home.

Aureomycin.—The new antibiotic, aureomycin, was found by M. Finland, H. S. Collins, and T. F. Paine[11] to inhibit completely strains of gonococci when used in concentrations of 1 microgram per c.c. or less. On a weight basis it was less effective than penicillin: but much more effective in an acid than in an alkaline medium, the reverse of streptomycin. Administered orally, it appears rapidly in the urine and is excreted continuously for two or three days after a single dose of 0·5 or 0·75 g. The overall results in 66 males with gonorrhœal urethritis were satisfactory, but they were inferior to those obtained with adequate doses of penicillin: there were 49 good results, 11 doubtful, and 6 failures. Most of the failures received a total of 1·5 g. in two or three doses during a single day, but larger doses given for two days gave results more closely resembling those obtained with penicillin. It may prove useful in cases resistant to penicillin.

REFERENCES.—[1]*Amer. J. Syph.* 1948, **32**, 437; [2]*Amer. J. Obstet. Gynec.* 1947, **54**, 517; [3]*Proc. Soc. exp. Biol.* 1948, **67**, 6; [4]*Proc. Mayo Clin.* 1947, **22**, 567; [5]*New Engl. J. Med.* 1948, **239**, 286; [6]*Brit. med. J.* 1948, **2**, 933; [7]*Amer. J. Syph.* 1948, **32**, 445; [8]*N.Y. St. J. Med.* 1948, **48**, 517; [9]*Amer. J. Syph.* 1948, **32**, 265; [10]*Sth. med. J.* 1948, **41**, 320; [11]*J. Amer. med. Ass.* 1948, **138**, 946.

GUMMA OF FRONTAL BONE. *A. Rendle Short, M.D., F.R.C.S.*

The swelling shown in *Plate XVIII* had softened and approached the skin when first seen, and arsenical injections were only just in time to avert breaking through, secondary infections, and probably bony necrosis. W.R. positive. (Case of Mr. L. J. Horn, Ebbw Vale.)

HÆMOLYTIC ANÆMIA. (*See* ANÆMIA, HÆMOLYTIC.)

HÆMOLYTIC STREPTOCOCCAL SORE THROAT. (*See* SCARLET FEVER AND HÆMOLYTIC STREPTOCOCCAL SORE THROAT.)

HÆMORRHOIDS.

W. B. Gabriel, M.S., F.R.C.S.

It is now generally held in this country that the operation of hæmorrhoidectomy is a standardized procedure soundly based on anatomical grounds by the ligature and excision operation described in *The Lancet* by E. T. C. Milligan et al.[1] It is therefore interesting to observe recent papers from other countries advocating other methods. For instance, from Switzerland there is a paper by Von J. Loessl[2] describing a modified Whitehead's operation, which he says is particularly suitable for advanced hæmorrhoids complicated by a mucosal prolapse. The operation is carried out under local anæsthesia, and after a division of the sphincter muscle in one place [? only the subcutaneous portion], the mucosal cuff is pulled down and split into three portions—left anterior, right anterior, and posterior. A flat-bladed clamp, as previously used in the clamp and cautery operation, is applied to each flap in turn and the excess of mucosa is removed with a thermocautery. The mucosal edges are further secured by placing a few catgut sutures in each segment. After completion of the operation

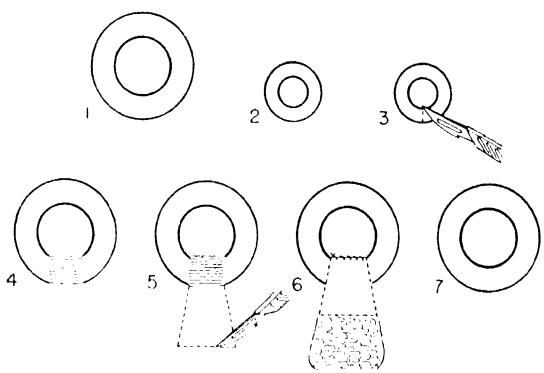


Fig. 29. Diagram illustrating preparation of sliding graft and anusotomy in plastic repair of anal stenosis, and also employed to prevent contractures following radical hæmorrhoidectomies. 1, Represents normal anal lumen; 2, A stenosed canal; 3, Indicates the anusotomy; 4, Shows the separation of the wound edges and consequent widening of the anal tube; 5, Represents the incisions for preparing the sliding skin-graft; 6, The graft has been drawn up to cover the entire surface of the anal wound except for two narrow radiating slits—a large open wound remains on the outside far from the margin; 7, Indicates the end-result. (*Reproduced from the "American Journal of Surgery".*)

the anal opening at first appears triangular, but as the mucosa retracts the anus soon assumes its original shape. A tube is inserted for 12 to 24 hours. The author states that by this method the passage of the first motion is painless, and in the course of seven years he has seen no recurrences or complications.

Carruth J. Wagner[3] advocates an excision and suture operation under low spinal anæsthesia with 10 per cent procaine (dose 0·3 to 0·4 c.c.). Details of technique and post-operative management are given. Under service conditions an average stay in hospital of 6 to 8 days was needed, but the author states that in private practice patients would be discharged on the first post-operative day.

A. Gerson Carmel[4] describes a somewhat complicated method in which a sliding graft from the perianal region is drawn up by sutures into the anal canal, and is used to cover in the raw surface left after "circumferential hæmorrhoidectomy" as he terms it. This is therefore another modification of Whitehead's operation. He describes also a further use for this method, namely, a method of rectoplasty,

in those cases in which an anal stenosis has to be relieved by a dorsal incision (*Fig.* 29). Pre-operative preparation with sulphathalidine (1 g. four or five times daily) is begun 4 days prior to operation and is continued for 7 to 10 days after operation. Spinal anæsthesia with a smaller dose than is customarily used is advocated—1 c.c. of 2 per cent procaine solution containing adrenaline 1–20,000, the dose of procaine being 20 mg.

In the subsequent discussion, Hugh Beaton recommended the use of mercurochrome as a local application at the close of a hæmorrhoid operation, followed by the application of a wick of oxycel. This is the subject of a formal paper by Marion C. Pruitt,[5] who finds oxycel a useful primary dressing after any operation in the anal region, such as hæmorrhoidectomy or operations for fistula, etc. The addition of a firm overlying dressing is considered to be important.

G. Angelo[6] reports a series of 481 patients who had some form of anorectal operation with a routine course of sulphathalidine. The great majority of the operations were for cure of hæmorrhoids, fissures, and fistulæ. The usual dosage of sulphathalidine has been 3 g. during the 24 hours before operation, and post-operatively 1 g. three times daily for 4 to 14 days depending on the operation performed. It is stated that 394 patients (82 per cent) had a normal bowel movement on the 2nd–3rd day after operation with a minimum of effort or discomfort and without the aid of laxatives, mineral oil, or enemas; by this time the stools had become soft and gelatinous and had lost most of their bulk. Owing to the elimination of most of the pathogenic organisms post-operative complications such as abscess, stricture, and hæmorrhage were not encountered. With this routine a normal bowel habit was re-established in patients who had previously been chronically constipated for many years.

REFERENCES.—[1]*Lancet*, 1937, **2**, 1119; [2]*Helv. chir. Acta*, 1948, **15**, 60; [3]*Amer. J. Surg.* 1947, **74**, 455; [4]*Ibid.* 1948, **75**, 320; [5]*Ibid.* 292; [6]*Rev. Gastroenterology*, 1948, **15**, 145.

HAIR : PERMANENT WAVING. *R. M. B. MacKenna, M.A., M.D., F.R.C.P.*

W. T. Astbury and F. O. Bell[1] have shown that keratin, the protein of mammalian hairs, is a very complex chemical compound, and is one of a great group of fibrous proteins which have a common molecular configuration and elastic properties. The structural unit of the group is a 'grid' consisting of long polypeptide chains cross-linked by means of their side-chains; the main chains of this grid are not normally extended but are drawn into a sequence of folds; when the fibres are stretched the grid is pulled out flat, only to return to its folded configuration when the tension is released. These workers have called the normal folded configuration "alpha-keratin" and the extended configuration "beta-keratin", and believe that the reversible transformation within the molecule from alpha-keratin to beta-keratin is the basis of the remarkable elastic properties of hair. Beta-keratin is just about twice as long as alpha-keratin and is about the same density.

R. G. Harry[2] has stated that, in its natural form, hair is built up of "polypeptides" which form a chain along the hair shaft. In normal hair these chains are buckled, but on stretching they are transformed into the straight form. On releasing the tension they return like coiled stretched springs to their original folded form. Without moisture the hair cannot be stretched or contracted; under tension it just breaks. If, however, the hair is wetted, stretched, and then dried in a stretched condition, little or no contraction occurs and what the hairdressers term a "water-wave" is achieved. If the temperature of the wetting agent is increased and/or is made sufficiently alkaline a chemical reaction occurs, the elasticity of the hair is relaxed, and new and somewhat unstable links between the various polypeptide chains are formed and tend to hold the hair in its new position. A stage may be reached

when the alteration becomes 'permanent' and can no longer be completely reversed. This is the 'permanent wave' and the hair now always attempts to return to its new configuration after stretching.

In the usual form of permanent waving grease is removed from the hair by the use of a shampoo. Carefully chosen hanks of hair are then wound round suitable rollers, slight tension being used. A strip of absorbent material dipped in a suitable solution is wound over the hair, which is encased in an electric heater and the hair "steamed" for the required period. Harry (from whose book these details have been obtained) states that the most satisfactory permanent waving solution contains 0·88 ammonium hydroxide in combination with a proportion of borax or sodium or potassium carbonate. He recommends the following as giving good results on average hair in about ten minutes' steaming time, this time being adjusted to suit the type of hair :—

	Per cent
Ammonium hydroxide (s.p. 0·88)	20
Sodium carbonate	4
Potassium sulphite	2
Water	74

Usually heat is applied by means of an electric current, although in one system the heaters are previously heated, applied, and then allowed to cool for the desired period. Chemical heating methods have been introduced, these usually depending on the formation of heat by a chemical process of oxidation and reduction. After the permanent waving is accomplished the curled hair is wetted, re-arranged, and dried, a water-wave being formed on top of the permanent wave.

Many of us have seen burns of varying severity occurring on the scalp as a result of the escape of steam from the wetting pads during the heating process.

In recent years a cold method of permanent waving has been introduced. In this the hair is wrapped round a roller of suitable diameter either before or after treatment with an alkaline reducing agent—usually a thioglycolate. Heat is not applied. After the hair has been satisfactorily waved, the wave is fixed by application of an oxidizing agent. This matter has been discussed at some length by R. E. Reed, F. L. Humoller, and M. DenBeste[3] in a contribution read before a meeting of the American Association for the Advancement of Science in 1946. L. Goldman, L. Mason, and W. McDaniel[4] have considered the matter from the medical standpoint, and have emphasized that the potentialities for harm possessed by commercial products should be fully investigated before they are distributed and used. R. G. Harry[5] has stated that one type of solution employed for cold waving contains approximately 6 per cent ammonium thioglycolate in water adjusted to a *p*H of 9·6 or thereabouts. He states that the hazard of using the thioglycolates in hair-waving solutions is controversial, but emphasizes that as some thirty million cold waves have been given in the U.S.A. in the last three years, and as but few complaints of dermatitis or damage have been proved to be due to the normal use of cold waving materials, such materials are reasonably safe under proper conditions of use. He emphasizes, however, that as the solutions can and do alter the chemical structure of the hair in the cold, and as the skin and hair are closely allied in composition, it is evident that given the requisite time thioglycolate must effect some change in the chemical structure of the skin. He states that it is the time factor and the purity and concentration of the solution which are the matters of importance. Goldman and his colleagues[4] quote C. P. McCord[6] as stating that primary irritation of the skin does not occur from contact with thioglycolic acid or its alkaline derivatives in concentrations below 8 per cent by volume in water—moreover, McCord[7] found

no evidence of sensitivity or allergic responses of the skin to carefully prepared ammonium thioglycolate. H. Goodman,[8] however, in a paper entitled "Dermatitis from Cold Wave Permanent Chemicals" emphasizes that the factor responsible for any skin irritation which may occur in these cases is usually a combination of thioglycolic acid, the softener, the fixative, or the keratin rather than the acid itself. He considered, therefore, that patch tests with the material alone are not satisfactory. In a case investigated by J. B. Howell[9] in which eczematous contact dermatitis developed after a cold wave, the patient did not react to the waving solution, neutralizing liquid, or shampoo, but did react to a lotion which was a detergent of unknown composition used to clean the hair before the wave.

Goldman and his colleagues[4] appear to believe that cutaneous irritation and sensitization can occur from thioglycolate, whilst the hair may become more fragile after treatment and may darken slightly, particularly if it is white. They also appear to regard systemic toxicity from cold waving as a possibility but not a matter which is of practical importance. They state that if dermatitis does develop after a cold wave the following chemicals must be considered: (1) The preliminary shampoo material; (2) The preliminary cleansing lotion; (3) The cold wave material; (4) The oxidizing agent; (5) The post-treatment shampoo; (6) The wave-setting material (usually a vegetable mucilage mixed with a little alcohol, a little alkali, and a suitable preservative), perfumes, etc.

In a preliminary group of observations on 149 women, they found that undiluted ammonium thioglycolate was a mild irritant to the skin. Twelve beauty parlour operators with contact dermatitis of the hands were examined. In no case was a positive reaction obtained to patch tests with cold wave material which the beauty parlour operators provided. Tests with shampoos give positive reactions with much greater frequency. Goldman and his colleagues recommend that beauty parlour operators should be instructed to remove all cold-waving solutions carefully from their clients' skins and to be particularly careful that these solutions do not reach skin which has been scratched or abraded. During the operation of cold waving, every attempt should be made to limit the use of materials to the least quantities consistent with obtaining a satisfactory result. They note that reactions on the hands of the beauty parlour operators are likely to be more numerous and more severe than those which occur among the patrons, and do not offer any hope for the protection of the hands of these operators under the conditions associated with present procedures, unless the operators consent to wear some sort of protective gloves.

In the *Recorder* (a London weekly newspaper) of Oct. 9, 1948, it is stated that cold-permanent-wave kits which can be used by women in the home are going to be the centre of a competitive business struggle in Britain, where the prize to the manufacturers will be in the neighbourhood of four million pounds a year profit. Lever Bros. and Unilever are early in the field in Britain with a British kit called "Pin-up". The Gillette Safety Razor Co. will put "Toni"—the best selling American kit—on the British market. Each kit is said to contain waving lotion, finishing lotion, end tissues, and curlers. The writer has no information as to whether or not these kits depend for their effect on the use of thioglycolate, but it will be interesting to see whether or not, in the near future, cases of dermatitis are attributed to the use of the lotions contained in these kits.

REFERENCES.—[1]*Nature, Lond.* 1941, **147**, 696; [2]*Modern Cosmeticology*, 2nd ed. 1944, Leonard Hill Ltd., London; [3]Quoted in *J. Amer. med. Ass.* 1948, **137**, 355; [4]*Ibid.*; [5]*Cosmetic Materials*, 1948, Leonard Hill Ltd., London; [6]*J. Amer. med. Ass.* 1946, **131**, 776; [7]*Indust. Med.* 1946, **15**, 669; [8]*Urol. cutan. Rev.* 1945, **49**, 117; [9]*Arch. Derm. Syph.* 1944, **49**, 432.

HAND AND FINGERS, SURGERY OF. *Lambert Rogers, M.Sc., F.R.C.S.*

Cartilaginous Tumours (*Plate XIX*).—Cartilaginous tumours of the fingers and hand are unsightly, interfere with function, and occasionally become malignant. J. G. Shellito and M. B. Dockerty,[1] of the Mayo Clinic, emphasize that these tumours are either enchondromas (chondromas) or ecchondromas (exostoses), a distinction made in Virchow's time and still true. The enchondromas are believed to arise from cartilage rests, the ecchondromas (or perichondromas of Virchow) from pre-cartilage at the tendinous attachments. Between 1908 and 1945 there were 42 cases of cartilaginous tumours of the hand in the Mayo Clinic; 30 were examples of enchondroma, 12 of ecchondroma. One instance of an enchondroma proving to be a chondrosarcoma occurred. When pain occurred in the enchondromas, there was a spontaneous fracture. The enchondromas occurred most frequently between 20 and 30 years of age, the ecchondromas between 10 and 25 years. The latter are bony outgrowths surrounded by a cartilaginous cap. Their X-ray appearances are characteristic, while those of the enchondromas may resemble bone cysts. Malignant change is rare, but more often affects the enchondromas than the ecchondromas.

Nearly a third of the Mayo Clinic patients with these tumours had spontaneous fractures. In one of the Clinic cases there were multiple enchondromas in a tendon-sheath. It is interesting to notice the way in which these cartilaginous tumours have a predilection for the metacarpals or phalanges, and M. L. Mason[2] has reported that enchondromas have never been found in a carpal bone.

Treatment of both types of tumour should be conservative, the tumour tissue being curetted away, leaving as much of the bone shell as possible and using bone-grafts where needed.

[This is an enlightening paper which does much to clear up the rather nebulous views which are sometimes expressed in regard to these tumours.—L. C. R.]

REFERENCES.—[1]*Surg. Gynec. Obstet.* 1948, **86**, 465; [2]*Ibid.* 1937, **64**, 129.

HEART. (*See also* AORTIC STENOSIS; ARRHYTHMIA; CARDIAC INFARCTION; ELECTROCARDIOGRAPHY; ENDOCARDITIS, BACTERIAL.)

HEART DISEASE, PULMONARY. *William Evans, M.D., D.Sc., F.R.C.P.*

Pulmonary Arteriovenous Fistula.—When a young person presents himself for medical examination with cyanosis, clubbing of the fingers and toes, and polycythæmia, the most common actiological condition is congenital heart disease. That such a picture may be associated with an arteriovenous shunt in the lesser circulation has become of increased diagnostic importance, for, with the recent advances in the field of thoracic surgery, complete cure of the condition may be effected with minimal operative risk. H. B. Burchell and O. T. Clagett,[1] reporting such a case, believe that it is the ninth case to be recognized clinically and the fifth patient to be cured by surgical treatment. They discuss the clinical syndrome consisting of cyanosis, clubbing of fingers, polycythæmia, and the characteristic murmur of an arteriovenous fistula. Cardiac enlargement, presumably depending on the size of the fistula, has only been reported twice. Radiological examination of the pulmonary field is important, for it will show a nodular lesion, often well demonstrated by tomography, which pulsates in association with increased hilar pulsation on the side of the lesion.

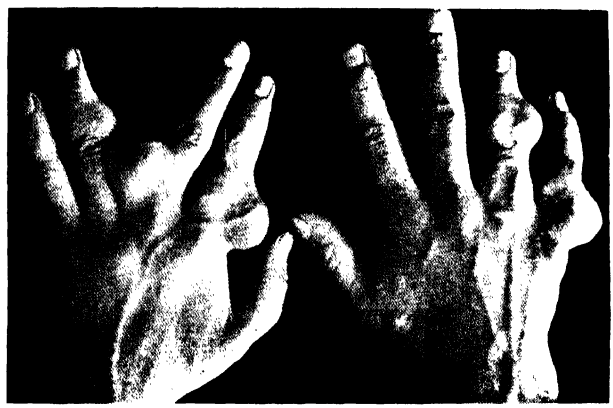
REFERENCE. [1]*Amer. Heart J.* 1948, **34**, 151.

HEART FAILURE. *William Evans, M.D., D.Sc., F.R.C.P.*

Digitalin Preparations.—P. Dick[1] tried the effect of six different commercial preparations of digitalin in 17 patients with heart failure and auricular

PLATE XIX

CARTILAGINOUS TUMOURS OF THE HAND



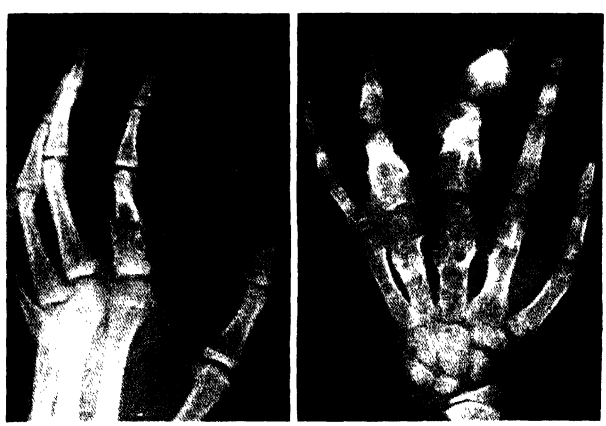


Fig. B. Left: Pathologic fracture. *Right*: Enchondromas of the hand.

fibrillation. One preparation was much less effective than the other five in two trials. He suggested that a standardized procedure for the manufacture of digitalin should be introduced, and that biological assay should be made compulsory. The variability in the potency of digitalin preparations confirmed the advisability of using digitalis leaf for continuous digitalization at the present time.

Rapid Digitalization.—Strophanthin and a number of digitalis preparations were submitted to a clinical trial by W. Evans, P. Dick, and B. Evans[2] in 20 patients with auricular fibrillation and heart failure with the object of discovering the best means of bringing about a digitalis effect quickly (rapid digitalization).

Digoxin and lanatoside C proved to be the best and digitaline (Nativelle) was scarcely less efficient. Should it be necessary to induce digitalization within two hours, digoxin as 1·5 mg. intravenously or as 2·0 to 3·0 mg. orally, and lanatoside C as 1·5 mg intravenously only, can best accomplish it. To establish adequate digitalization within four hours digoxin as 2·0 mg. by mouth is an effective method. As it is seldom necessary to obtain a digitalis effect in less than two to three hours, and as intravenous medication may be less convenient, digoxin as 2·0 to 3·0 mg. by mouth is generally the best way to induce rapid digitalization.

REFERENCES. [1]*Brit. Heart J.* 1948, **10**, 122; [2]*Ibid* 105.

HEART AND GREAT VESSELS, SURGERY OF.

(*See also* COARCTATION OF THE AORTA.)

N. R. Barrett, M.A., M.Chir., F.R.C.S.

The surgery of the heart and of the great vessels continues to occupy the attention of investigators all over the world and the advances which are being achieved are numerous and gratifying. Several points already stand out as generally referable to this branch of surgery.

A great deal of valuable *experimental work* has been done upon animals and this has not only proved the feasibility of numerous theoretical possibilities but has provided surgeons with the opportunity of perfecting details of technique before operating upon man. Some of the most interesting of these experiments are as follows:—

The perfusion apparatus described by Björk,[1, 2] working with Crafoord and Anderson, is capable of performing the functions of the heart and lungs for a sufficient time to permit bloodless intracardiac operations. Dogs, in which the venæ cavæ have been clamped for more than 30 minutes, and in which the blood-flow to the brain has been maintained artificially with a machine, have survived with no sign of organic disease. This experiment opens the way to a whole new field of endeavour.

Hamlon and Blalock[3] have tackled the problem of overcoming the disabilities incurred from complete transposition of the aorta and the pulmonary artery. In this condition the aorta arises from the ventricle which has received systemic venous blood, and the pulmonary artery from the ventricle which has received oxygenated blood. Artificial production of pulmonary venous return to the right side of the heart has been achieved experimentally by anastomosing the pulmonary veins to the right auricle or to the superior vena cava.

The circulatory changes produced by clamping the thoracic aorta have been studied by Watkins.[4] The aorta was clamped in dogs for periods of between 5 and 15 minutes and the most dangerous effects were found to occur after the sudden release of the clamps, which was apt to cause a precipitous fall in the arterial blood-pressure. These observations have an important bearing upon operations in which the aorta is temporarily occluded to control

hæmorrhage or to excise a segment of coarctation. Crafoord[5] found it necessary to clamp the normal aorta just distal to the subclavian artery for 27 minutes on one occasion, and the patient suffered no ill effect.

Claude S. Beck,[6] continuing his experiments to improve the arterial circulation of the heart, which he started in 1932, has now shown that a collateral circulation can be established in animals by grafting a systemic artery into the coronary sinus. Between 1946 and the present time 700 operations have been performed on 350 dogs and only now is the principle being applied to man. The operation consists in taking a segment of the distal end of the brachial artery, excising this segment, and using it as a free graft (because none of the thoracic vessels are of suitable size or anatomy), thus creating a new branch of the aorta by anastomosing the graft to the aorta at one end and to the coronary sinus at the other.

The technique of anastomosing one blood-vessel to another has been extended by the development of special clamps which partially occlude the vessels and so allow the circulation to continue throughout the operation (Willis Potts, S. Smith, S. Gibson[7, 8]), and by the perfection of vitallium cannulæ (Blakemore and Lord[9, 10]).

The pre-operative diagnosis of congenital cardiovascular abnormalities still presents many difficulties, and the works which are most useful in this respect are the books by Helen Taussig[11] and J. Brown.[12] It is clear that in spite of all refinements of radiography, cardiac catheterization, electrocardiography, phonocardiography, and other ancillary methods a number of mistakes are still made, and these place the surgeon who operates to overcome a supposed deformity in a difficult position, for even when the heart has been exposed he may not be able to tell what should be done (Daley[13]). The pre-operative investigations may take weeks or months to complete, and although they are often a trial to the patient and sometimes not without danger they cannot be short-circuited at present: they have at least shown that many patients can be greatly assisted and encouraged by simply living for a time in a surgical ward without any operation being performed.

Operations on the Heart and Great Blood-vessels.—These operations, which are now so frequently performed, are becoming standardized, so that amazingly low mortality-rates have been achieved. Dodrill[14] reported 24 consecutive anastomoses for Fallot's tetralogy with 4 deaths. Murray[15, 16] claimed a mortality of 7·3 per cent in tetralogy cases, and Blalock a mortality of less than 15 per cent in a series of more than 500 cases. Jones[17] operated upon 61 consecutive cases of patent ductus arteriosus and 2 patients died, whilst Gross[18] treated 91 patients and only 2 died. These successes have not been achieved without corresponding advances in anæsthesia and these have been well described by Rait-Smith and Ostlere.[19]

Although at birth there are many varieties of congenital heart disease which are associated with cyanosis, about 80 per cent of the infants who survive to adolescence suffer from Fallot's tetralogy, and it is towards the correction of this and allied abnormalities—in which the principal fault is that not enough blood is passing through the lungs—that three different methods have been used to increase the pulmonary circulation; none of these completely corrects the cardiac deformities.

1. The first successful attempts were made by Blalock and Taussig, and the brilliant surgical work of the former, who has now operated 610 times upon cyanotic children, was the starting-point for this branch of surgery. Blalock's operation[20] consists in anastomosing one of the branches of the aorta to the pulmonary artery, and "most of the patients who survive the operation are improved. This improvement varies in degree from that of patients who

are considerably restricted to those who have no limitation of their activities". Willis Potts[7, 8] widened the scope of this work by anastomosing the pulmonary artery directly to the aorta, thereby fashioning a shunt exactly like a patent ductus arteriosus. It seems probable that Potts's operation—which is easier to perform and more physiological than Blalock's—will gradually become the more widely used of the two procedures. In 1948 Potts[21] reported his experiences in 45 consecutive anastomoses in which the mortality was 8·8 per cent; 39 of the patients were "tremendously improved".

2. Sellors[22] and Brock[23] have tackled one type of pulmonary stenosis differently. The former states that observations and studies on the nature and situation of the pulmonary stenosis in Fallot's tetrad show that there are considerable variations in its extent and degree. Often there is narrowing in the conus or common pulmonary trunk or a well-marked subvalvular stenosis, but if the stenosis is localized to the valve area the relieving operation may well take a different form from the anastomosis adopted in the Blalock or Potts operations. Both these surgeons have succeeded in overcoming valvular stenosis by actually dividing the stenosed pulmonary valves. Brock states that, as it stands at present, this operation is of use in only a small proportion of cases, and until a method can be found to relieve the subvalvular stenosis (Brock has now succeeded in excising the stenosing subvalvular tissue in some cases) the Blalock operation must continue to take precedence. He also points out that a firm diagnosis of valvular stenosis can be made at operation by observing the following points: in valvular stenosis the stem of the pulmonary artery immediately distal to the obstruction is often dilated and forms a thin-walled aneurysmal-like bulge: on the other hand, if the sinuses of Valsalva are present and fully formed, it is probable that the valve cusps are normal; palpation of the first part of the pulmonary artery reveals a typical thrill if the valves are stenosed, and this is due to the fine jet of blood pouring through the pin-hole orifice. Sellors divided the stenosed valve by introducing a tenotome through the infundibular region of the right ventricle; Brock did the same thing, but he used a carefully constructed cardioscope and valvulotome.

Smithy, Pratt-Thomas, and Deyerle[24] describe a series of experiments they have performed in dogs in which the aortic valves have been successfully divided by introducing a valvulotome through the left ventricle.

3. Another method of increasing the blood-supply through the lungs is to create vascular adhesions between the lungs and the parietes. Barrett has investigated this possibility in a group of cyanotic children who, for one reason or another, were not considered suitable for any of the usual 'shunt' operations or valvulotomy. The children who were submitted to these relatively simple procedures have derived considerable benefit from them.

The *final results* of all these operations are difficult to assess, but it seems probable that the most valuable criteria of benefit lie not so much in detailed chemical analyses of the oxygen-carrying capacity of the blood, but in simple exercise-tolerance tests. The most reliable of the laboratory tests is that described by Bing and others;[24] it consists in measuring the ratio of oxygen consumption to volume of ventilation before and after exercise. In normal persons this ratio increases, in contrast with those with an inadequate pulmonary blood-flow, in whom the ratio falls.

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HEART MURMURS.

William Evans, M.D., D.Sc., F.R.C.P.

Foremost amongst the findings of a clinical and cardiographic investigation of 500 healthy subjects and patients with heart disease carried out by W. Evans[1] was the clinical identification of the *innocent mitral systolic murmurs* which continue to cause widespread unwarranted cardiac invalidism because of their common appearance. The situation and distribution of these murmurs and the effects upon them of a change in posture and deep breathing make it possible to tell them from the murmurs of organic heart disease. The phonocardiograph confirmed this clinical classification and located the murmurs either in mid-systole or late systole; it also showed the absence in such cases of auricular systolic and diastolic murmurs.

In patients with *mitral stenosis* the phonocardiograph showed that the murmur which presented clinically as a systolic murmur usually started during the P-R period of the electrocardiogram, that is, during auricular systole, as did the presystolic murmur. The common incidence of a mid-diastolic murmur immediately succeeding the third heart-sound in mitral disease, for it was found in each of 74 cases, stimulates the clinical search for this murmur in patients suspected of the condition. Should future investigation show that this is an invariable graphic finding in mitral disease it will prove to be a physical sign of inestimable value.

In *aortic valvular disease* the systolic murmur, which was an unfailing sign in the mitral area, was seen phonocardiographically to start synchronously with the start or early part of ventricular systole. The test showed the common incidence in aortic stenosis of the early diastolic murmur of aortic incompetence although this sign had not yielded to clinical auscultation. The phonocardiograph has often demonstrated an early diastolic murmur when aortic incompetence is unsuspected by casual or even careful clinical examination. On this account, too, the test has proved of great value.

The mitral systolic murmur in *hypertension*, making its appearance whenever the heart is greatly enlarged, was recorded in mid-systole and a little time after the ventricle had commenced to contract; such a finding opposes the assumption that this murmur is the outcome of mitral incompetence. Doubtless it is the result of muscular contraction, and the same murmur was found when the heart was much enlarged in *complete heart-block*. In both conditions an early diastolic murmur of relative aortic incompetence, resulting from dilatation of the aortic ring, was a fairly common event, and when it was present it served to emphasize the presence of considerable left ventricular enlargement.

The phonocardiogram in *congenital heart disease* helped to tell the innocent parasternal murmur from that of ventricular septal defect, and the innocent pulmonary systolic murmur from that of pulmonary stenosis. The test demonstrated the continuity of the murmur of patent ductus arteriosus with its accentuation in early diastole. An early diastolic murmur from pulmonary incompetence, leading up to an obvious third heart-sound, was never absent in the sound tracing from cases of auricular septal defect; when mitral stenosis was added to the congenital lesion (Lutembacher's syndrome) so were auricular systolic and mid-diastolic murmurs to the phonocardiogram. The murmur of coarctation of the aorta was written in late systole. In anæmia the murmur started in mid-systole and a diastolic murmur was not once recorded.

This phonocardiographic study of heart murmurs has shown that the quality and intensity of murmurs matter far less than their place in the cardiac cycle and in relation to the heart-sounds. Such a finding emphasizes the need for self-catechism during clinical auscultation when precise answers should be sought to 6 set questions. The questions concern the character of the first

heart-sound and similarly of the second heart-sound, the presence of more than two sounds, and the presence of murmurs connected with the first heart-sound (presystolic and systolic), with the second heart-sound (late systolic and early diastolic), and with the third heart-sound (mid-diastolic). When such simple auscultatory procedure has become custom, cardiological diagnosis will have gained immeasurably in accuracy.

REFERENCE.—[1]*Brit. Heart J.* 1947, **9**, 1, 125.

HEART IN SCLERODERMA. *William Evans, M.D., D.Sc., F.R.C.P.*

Scleroderma, if sufficiently generalized, may on rare occasions be associated with changes in the heart in some degree, and it is exceptional for such changes to be so great as to cause heart failure and death. T. East and S. Oram[1] found 9 such examples in the literature and described another which they had observed. Their case with generalized scleroderma showed scattered areas of fibrosis of the heart at necropsy and this change had given rise to complete heart-block during life and heart failure from which the patient died.

REFERENCE.—[1]*Brit. Heart J.* 1947, **9**, 167.

HERNIA. *A. Rendle Short, M.D., F.R.C.S.*

For some reason or other, there is a marked revival of interest in the treatment of hernia, and many papers describing old and new methods of operating have been published in a number of countries. Treatment by injection seems to have been dropped.

Inguinal Hernia : The Older Methods. Amongst the modifications of the classical Bassini operation may be mentioned the McArthur and the McVay methods. McArthur used a strip of fascia cut from the external oblique aponeurosis, left attached at the pubic tubercle but set free at the lateral end, as darning material. McVay ignored the inguinal ligament and sutured the inferior margin of the transversus abdominis aponeurosis with its attached transversalis fascia down to Astley Cooper's ligament on the pubic ramus. C. O. Rice and J. H. Strickler,[1] of Minneapolis, repair hernias by combining the Bassini, McArthur, and McVay methods. Their experience is small (40 cases), but satisfactory. H. H. Harkins and R. H. Schug[2] have performed the McVay operation in 367 cases with less than 1 per cent of recurrences. They point out that it is in effect the Lotheissen operation used for inguinal hernia as well as for femoral. D. Weiss[3] also sews the conjoint tendon to Cooper's ligament; he cuts across muscle-fibres of the internal oblique and transplants the spermatic cord into the incision, which is then sewn up lateral to the cord; the mesial leaf of the slit external oblique aponeurosis is then sewn to Poupart's ligament and the lateral leaf imbricated over the mesial. E. S. R. Hughes and J. T. Fathi[4] believe that it is necessary to divide and ligature the cremasteric vessels to obtain satisfactory repair, as they form a band holding the internal ring open. F. Alieri,[5] of Rome, contributes a well-illustrated article describing his modification of the Bassini operation. He uses a complicated stitch to constitute a new floor for the canal, and brings the cord through the slit in the external oblique aponeurosis, far out.

There has been an impression that the *floss silk method*, popular early in the war, led to too many suppurations calling for a second operation to remove the silk, but R. Maingot[6] says no technique is so satisfactory for large or recurrent hernias in enfeebled patients. There were 2 cases out of his last 100 in which the silk had to be removed for sepsis, but this soon cleared up with penicillin. In spite of obesity, old age, and recurrent cases, the hernia was cured in all but 3 per cent. The beginning of his floss-silk darn is shown in *Fig.* 30.

Sliding hernia, according to Carrington Williams,[7] of Richmond, Virginia, *is best dealt with through an abdominal incision. A muscle-splitting approach is made in the iliac fossa*, the herniated bowel brought up into the abdomen, and the excess of peritoneum cut away. A Bassini repair of the inguinal canal, *using a fascial strip, is carried out. A better view of the blood-vessels of the* colon is obtained than when it is approached from below, and the removal of the sac is more thorough.

C. Craig,[8] of Launceston, Tasmania, has considerable experience of the *Hamilton Russell operation*, that is, simple ligature of the sac, which is twisted and removed. There were 3 per cent recurrences in 154 operations, but as 31 large hernias were excluded from the series, this is not very satisfactory. He says that after plastic operations recurrences are often direct hernias. He advises inversion of the sac without any repair, because after this simple operation the recurrences are nearly all indirect.

G. E. Moloney, W. G. Gill, and R. C. Barclay,[9] of Banbury, darn with *nylon*, and G. H. Pratt,[10] of New York, with *steel wire*. The nylon is inserted as a

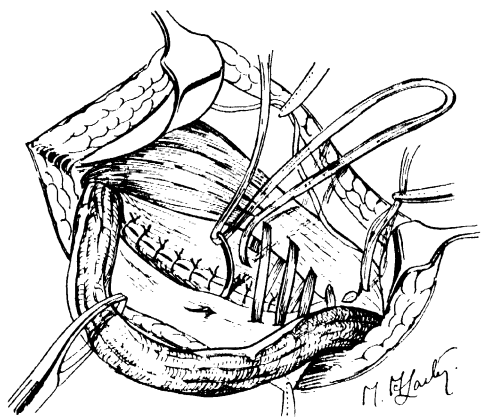


Fig. 30. Maingot's lattice repair for inguinal hernia. Start of the floss-silk darn. (*By kind permission of* '*The Lancet*'.)

loose continuous stitch uniting the internal oblique and the inguinal ligament behind the cord. It withstands sepsis better than floss silk; infection took place in 5 out of 239 patients, but all healed without extraction of the suture, and there have been no recurrences. Pratt advocates steel wire, local anæsthesia, and immediate ambulation. Interrupted stitches of No. 36 wire are used. He claims that recurrences are very few, but there were 26 cases of infection after 376 operations.

Buried Grafts.—Despairing of finding an absolutely reliable method of repair by suture, many surgeons are turning to some kind of inlay to prevent return of the hernia. *Whole-skin grafts* have been used by some, following Mair's advice. Brigadier C. M. Marsden,[11] of Milbank, W. T. West and E. S. Hicks,[12] of Brantford, Ontario, and V. Pataro and D. E. Zavalcta,[13] two Argentine surgeons, write on this subject. Marsden says that in older patients of poor physique the conjoint tendon may be too flimsy to hold Gallie strips of fascia lata, and the incision in the thigh may give trouble. This is true. At his hospital 163 cases of inguinal hernia were operated on and a whole-skin graft inserted. The patients were kept in bed three weeks. In 75 per cent of these

there was some fever two or three days after operation, but only 10 were due to infection and these were trivial, affecting the suture-holes in the skin. No grafts sloughed. The fever, whatever the cause, often lasted a week. Penicillin was not necessary. Of 136 followed up, 16 recurred; of these 12 had had operations for recurrent hernia. The recurrences were as follows: simple direct hernia, 8·3 per cent; recurrent direct hernia, 23·7; simple oblique hernia, 4; recurrent indirect hernia, 8·6 per cent. West and Hicks have had one recurrence in 25 cases. If the patient is obese, they excise a good deal of skin and fat. The Argentine surgeons report 23 cases. [These results are little if any better than those obtained by good plastic methods.—A. R. S.]

Four papers may be noticed, describing methods of repair with the aid of *tantalum gauze*. The authors are D. M. Douglas,[14] of Edinburgh, T. D. Throckmorton,[15] of Des Moines, A. R. Koontz,[16] of Baltimore, and N. C. Jefferson and U. C. Dailey,[17] of Chicago. Douglas and Koontz tried out the process on animals. Douglas has used the gauze for repairing 32 large hernias—para-umbilical, incisional, and inguinal. In the first two types the gauze was inserted between the anterior rectus sheath and the muscle. For inguinal hernia, the testis was dissected out from the scrotum and passed through a hole made in the internal oblique, and the inguinal canal obliterated by sewing the gauze beneath the external oblique aponeurosis. In 3 cases infection took place, but they healed well. There have been no recurrences. Throckmorton reports 6 successful cases, without transplantation of the testis. Tantalum is strong, pliable, and biologically inert. Koontz has used it on 5 occasions, all very obese patients with poor tissues. Jefferson and Dailey report one successful case, that of a man with a large incisional hernia.

W. Thompson,[18] of Manchester, has imbedded, beneath the cord and in front of the peritoneum and the old internal inguinal ring, a *plastic inlay* which can be cut with scissors. A notch is cut to take the cord, which is displaced outwards. He reports 20 successful cases.

Femoral Hernia.—D. F. Ellison Nash[19] describes a method of repair by using as suture material a strip of fascia, half an inch wide, cut from the external oblique aponeurosis as for the McArthur repair of inguinal hernia. It is left attached to the pubes, and is inserted to unite the inguinal ligament to the pectineal ligament.

Strangulated Hernia

J. P. Jarboe and J. H. Pratt[20] present a study of 104 cases of strangulated femoral hernia treated at the Mayo Clinic. They point out how easy it is to miss the diagnosis. A painful swelling in the groin should arouse suspicion, but sometimes it is difficult to feel, and the patient may complain of obstruction symptoms only. The approach through an inguinal incision is recommended; the incision over the femoral canal does not afford sufficient room. When the bowel was gangrenous, resection with end-to-end anastomosis was performed in 7 cases, with 3 deaths, by the inguinal route; by the femoral route in 2 cases, both fatal; and through a paramedian abdominal incision in 7 cases, with 5 deaths. On a few occasions, the gangrenous loop was reduced and exteriorized, but with poor success. Sometimes the intestine was freed by dividing Poupart's ligament, and in others Gimbernat's was incised. [Probably the use of the Miller-Abbott tube might have given better results. The method of treatment by leaving the gangrenous bowel in situ, with a free incision into it through the femoral canal, and with a side-to-side anastomosis carried out within the abdomen to short-circuit the strangulated area, is not mentioned.—A. R. S.]

C. Dennis and R. C. Varco,[21] of Minneapolis, treat strangulated hernia in the femoral canal by resection not only of the bowel but also of the ring and the sac, so that a clean end-to-end anastomosis may be carried out. They divide the inguinal ligament to give better access. It is often possible to recognize gangrene without opening the sac, which of course makes for cleaner surgery. They saved 8 out of 10 cases.

(*See also* INTESTINAL OBSTRUCTION.)

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HERPES SIMPLEX. (*See* KAPOSI'S VARICELLIFORM ERUPTION.)

HIRSCHSPRUNG'S DISEASE. *A. Rendle Short, M.D., F.R.C.S.*

According to current teaching, the sympathetic nervous system has the function of contracting the anal sphincter and relaxing the circular muscle of the colon, and the parasympathetic, derived from the second, third, and fourth sacral roots, has the opposite effects. Megacolon in infants and children would then be due to sympathetic overaction, and various operations have been recommended to break the course of the nerve-fibres to the bowel, such as presacral neurectomy, left lumbar ganglionectomy up to the second lumbar ganglion, a similar operation on both sides, or ramisectomy with removal of nerve-fibres on the inferior mesenteric artery. All these operations have given good results in a few patients followed for a short time only. Late follow-ups are badly needed. But there have been successes that were partial, and failures. Both J. A. Jenkins,[1] of Dunedin, New Zealand, and J. Lannon with Elizabeth Weller,[2] of Johannesburg, give reasons for believing that our treatment is unsatisfactory because our anatomy is wrong. That the sympathetic does not contract the anal sphincter is shown by the following observations (Jenkins): Under low spinal anæsthesia, too low to involve the lumbar sympathetic, the anal sphincter is relaxed. A presacral neurectomy does not lead to rectal incontinence nor does the patient need to rely on voluntary contraction of the sphincter to obtain control. After resection of the rectum, preserving the sphincter, it shows itself to be independent of sympathetic control. Injuries of the sacral cord and cauda equina do lead to sphincter paralysis. It is true that some degree of contraction of the anal canal may be felt when the distal end of the cut hypogastric nerve is stimulated electrically, but this may be due to spread of current to the pelvic visceral nerves. Cases are recorded in which Auerbach's plexus in the wall of the colon has been defective, but this may be the result, not the cause, of the bowel distension. Denny Brown and Robertson[3] have shown that the mechanism which controls defæcation is mediated entirely by the parasympathetic, not by the sympathetic. Lannon and Weller consider that megacolon is due to under-functioning of the parasympathetic. They quote the analogy of vagotomy, now so popular, causing atony of the stomach with gastric distension and delayed emptying. Various preparations of *acetylcholine* (urethane B. methyl choline; acetyl beta-methyl choline), which act like the parasympathetic, sometimes give good results in restoring gastric tone, and in relieving megacolon. *Prostigmin*, also, may do good. It is necessary to empty the bowel first with enemata and liquid paraffin, to give these drugs a chance.

It is difficult to see why any lasting benefit can result from *repeated spinal anæsthesia*, but E. D. Telford and H. A. Haxton[4] have followed up 12 cases

treated thus from two to twelve years previously. The average age at first treatment was seven. The anæsthesia must reach the level of the fourth thoracic vertebra, and liquid paraffin and enemata will be needed for the first week. In 8 patients, the eventual result was good, fair in 2, and there were 2 failures. In 3 of the unsatisfactory cases a sympathectomy was performed, but only in one of these did improvement follow. Spinal anæsthesia is useless in megacolon of adults.

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HODGKIN'S DISEASE. (*See* RETICULOSIS.)

HYPERTENSION.

William Evans, M.D., D.Sc., F.R.C.P.

Hypertension in Young Subjects. R. Platt[1] found that of 191 cases of severe hypertension (excluding chronic patients), there were 45 under the age of 40 years. Of these, only 13 appeared to be cases of essential hypertension. No case of malignant hypertension under the age of 34 years was seen. Young persons with the malignant type of hypertension are nearly always suffering from secondary hypertension, the underlying cause of which is often pyelonephritis, which may be on the background of a congenital abnormality. In such cases the disease may be unilateral. When cases of secondary hypertension are carefully excluded the average ages for malignant and benign hypertension in the present series were 45 and 53 years respectively. Taking into account the likelihood that patients with benign hypertension do not complain of symptoms for many years after the commencement of their disease, it seems probable that benign and malignant hypertension have a similar age of onset.

Prognosis.—An analysis was made by D. W. Blood and G. A. Perara[2] of 50 patients, who when first observed, exhibited asymptomatic and uncomplicated hypertensive vascular disease and were subsequently followed for at least ten years. The average length of observation in this selected group was seventeen years, the longest period exceeding twenty-seven years. It was found in the group studied that the initial height of blood-pressure, symptoms such as headache and palpitation, the presence of cardiac enlargement, minimal albuminuria, minor electrocardiographic changes, and retinal arteriovenous compression, bore no relationship to prognosis. Essential hypertension may be compatible with many years of survival and well-being. The favourable outlook for some patients with hypertension should be considered in evaluating the indications for and the results of such therapeutic procedures as sympathectomy.

Aetiology.—G. J. Langley and R. Platt[3] have written about the indications of nephrectomy in hypertension. They found that in nearly one-third of the cases of unilateral renal disease there were surgical indications for nephrectomy such as a large hydronephrosis, when the decision in favour of operation will be relatively easy. In the remainder a non-functioning kidney on one side with good function on the other is the most promising indication for success. Atrophic pyelonephritis, if unilateral, is more likely to meet with success than calculus or hydronephrosis. Papilloedema is not a contra-indication to nephrectomy. The operation of thoraco-lumbar sympathectomy for hypertension affords the opportunity of inspecting the kidneys, and in cases where unilateral renal disease is a possibility it should be performed first on the side of the suspected kidney. A nephrectomy can then be carried out if the indications appear to be favourable, for instance if atrophic changes, renal deformity, perirenal fibrosis, or abnormal renal arteries are found. In most failures the evidence that the renal disease was unilateral has been unconvincing.

Treatment.—R. H. Smithwick,[4] speaking on the surgical treatment of hypertension, said there were three measures which might help. Unilateral nephrectomy appears to have modified the course of the disorder in some patients. It appears to be difficult or impossible to predict the outcome. It seems permissible to remove a seriously damaged or non-functioning kidney when the other is little if at all affected. It seems unwise to remove the poorer of two involved kidneys. In general, the indications for nephrectomy should be the same in hypertensive as in non-hypertensive patients. The removal of adrenal tumours which are physiologically active is helpful. In those patients having paroxysmal hypertension the diagnosis can often be made with considerable certainty. On the other hand, paroxysmal forms of hypertension may not be due to tumours but appear to be the result of an intermittent increase in diencephalic activity. In these patients denervation of the splanchnic bed has been effective. Continued non-paroxysmal hypertension may be caused by an adrenal tumour. The diagnosis may be difficult to make, and most of these tumours have been found unexpectedly during the course of operations upon the sympathetic nervous system. In general, active adrenal tumours are rare causes of hypertension. They almost always prove to be pheochromocytomas.

Surgical intervention upon the sympathetic nervous system appears to offer many patients a reasonable chance of improvement at a minimal risk. It appears to slow the progress of the disorder. It probably is rarely if ever curative. A lessening of the severity of cardiovascular damage, as judged by favourable changes in the retinal, cardiac, or renal areas, was noted in about 60 per cent of unselected patients followed from one to five or more years. Blood-pressure levels were also modified slightly to markedly in about 60 per cent of these subjects. It is believed that at least part of the effect of the operation is due to a modification of reflex vasomotor fluctuations in blood-pressure. This effect is independent of changes in blood-pressure levels and occurs in virtually all thoroughly denervated patients. It is possible that elimination of reflex secretion of adrenaline and a stabilization of blood-flow through the denervated area may be of some importance. Extensive sympathectomy has been utilized largely in patients who have reached the stage of continued hypertension with evidence of cardiovascular damage varying from slight to marked. Experience to date indicates that at least 30 per cent of these patients are clearly unsuited for this form of treatment, and rules have been formulated in an attempt to exclude them as far as possible. If such patients are excluded, the early results in the remaining subjects are considerably better. A follow-up period of five years or more is needed to establish the circumstances under which splanchnicectomy is most likely to be worth while. It is gradually becoming apparent that patients with the best chance for good results are those in the younger age-groups with narrower pulse-pressures, with variable blood-pressures, the cardiovascular systems not too extensively damaged, and with satisfactory responses to sedation. Occasional patients develop evidence of cardiovascular damage in the stage of intermittent hypertension. In these it seems proper to consider surgical intervention. Thorough denervation of the splanchnic bed by a technique which permits exposure of the kidneys and adrenal glands appears to be the most desirable procedure for most patients. In some, total or subtotal thoracic sympathectomy may prove to be preferable.

Indications for sympathectomy in the treatment of hypertension have been arranged in the following terms by T. Findley :[5] That less reliance be placed upon prediction tests which measure the response of blood-pressure to sedation or to anæsthetization of the nervous system ; That the operation be reserved for those with severe symptoms but no gross impairment of cerebral, cardiac,

or renal function; That the operation should not be done in young individuals with mild asymptomatic hypertension because of the possibility of nerve regeneration; That sympathectomy may profitably be done on patients over 50 years of age, provided other requirements are met; That patients be told that sympathectomy offers palliation and not a cure.

REFERENCES.—[1]*Quart. J. Med.* 1948, **17**, 83; [2]*Amer. J. Med.* 1948, **4**, 83; [3]*Quart. J. Med.* 1947, **16**, 143; [4]*Amer. J. Med.* 1948, **4**, 744; [5]*Surgery*, 1948, **23**, 639.

HYPOSPADIAS. (*See* PENIS, SURGERY OF.)

HYPOTENSION, INTRACRANIAL. (*See* INTRACRANIAL HYPOTENSION.)

IDIOPATHIC PULMONARY HÆMOSIDEROSIS.

R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.

In adding 7 new cases to the literature which only has a total of 17 published cases, W. G. Wyllie, W. Sheldon, M. Bodion, and A. Barlow,[1] have classified the symptoms and signs of this rare disease so that a clinical diagnosis becomes a possibility. The symptoms are recurrent attacks, often sudden in onset, of fatigue, cyanosis, pallor, cough, often followed by vomiting, with traces or quantities of blood in sputum or vomit. The temperature may go up and abdominal pain may occur. Severe attacks can be very alarming; the patient appears to be dying. Each attack lasts from two to several days, and the patient, besides showing increasing pallor, may become jaundiced. The liver increases in size, the spleen becomes palpable, and the test for occult blood in the fæces becomes positive. Signs of right-sided cardiac failure with engorged neck veins and dilatation of the right heart may ensue. During the attacks there are scattered signs over the lung fields. Radiographs of the chest show small clear circular spaces surrounded by thickened opaque walls, giving a pumice-stone appearance, and may be confused with miliary tuberculosis, sarcoidosis, or lipoidosis. The heart shadow is enlarged and the pulmonary arc may be prominent. The blood shows a severe type of secondary anæmia. The morbid anatomical studies show an increase of reticulin, collagen, and muscle, and a decrease of elastic fibres in the pulmonary interstitial tissue. This seems to result in hæmorrhage by diapedesis and is followed by the deposition of hæmosiderin. It is not a part of generalized systemic hæmosiderosis.

It seems that this picture in children of attacks of anæmia, with hæmoptysis or hæmatemesis, acute respiratory disturbance, and cardiac failure, forms an entity which can now be suspected clinically and diagnosed by radiography, examination of the sputum, and lung puncture, for in the last two procedures the demonstration of hæmosiderin in the sputum or lung tissue clinches the diagnosis.

REFERENCE.—[1]*Quart. J. Med.* 1948, **17**, 25.

IMMUNIZATION PROCEDURES.

W. H. Bradley, D.M., M.R.C.P.

Section 26 of the National Health Service Act, 1946, has had the effect of associating general practitioners more closely with the job of raising the levels of immunity in the population as a whole, particularly against diphtheria and small-pox. Nevertheless, some practitioners have not been slow to voice criticism of local health authorities' schemes. Many feel that more should be done, particularly with regard to whooping-cough inoculation.

On reflection it will be realized that there are fundamental differences between the points of view of the administrator and the private practitioner in regard to this problem. These are related to the difference between what is desirable for the group or community in general, and what will best serve an individual

under particular conditions. The difference in point of view is, however, reconcilable, because the ultimate goal in both instances is satisfactory protection against disease, whether the unit is an individual or a community. The important thing is that each should see the other's point of view and that each should fulfil his own task without being critical of the other's attitude. In the *Medical Journal of Australia*, 1948, **2**, 158, there is a leading article which quotes, amongst others, the interesting example of the mass vaccination of over 6,000,000 people in New York State during April, 1947, upon the appearance of not more than a dozen cases of small-pox in two generations, all in the direct line of contact with an imported case. This mass vaccination is discussed by R. S. Muckenfuss, whose verdict is that the 36 cases of generalized vaccinia with 2 deaths, and 42 cases of encephalitis suspected of being post-vaccinal, constituted a negligible danger in comparison with the danger of a major small-pox epidemic.

A completely different situation is seen in relation to pertussis, because the reliability of immunization measures is still uncertain, and public health officers are still reluctant to recommend its use on a community-wide basis. Fortunately in this country, if the individual practitioner thinks whooping-cough inoculation is good for his patient, he can use it. These and other interesting topics concerning immunization procedures are discussed in the *American Journal of Public Health and the Nation's Health* of April, 1948.

INFANTS, FATTY LIVER DISEASE IN. (*See* MALIGNANT MALNUTRITION.)

INFECTIOUS DISEASES: CERTAIN PUBLIC HEALTH ASPECTS. (*See also* AIR-BORNE INFECTIONS.) *W. H. Bradley, D.M. M.R.C.P.*

Dr. Thomas Rivers[1] is the Director of the Hospital of the Rockefeller Institute of Medical Research, and a microbiologist of repute, well equipped to discuss infectious diseases from the point of view of bacterial ecology. In a paper in the *New England Journal of Medicine*, he "seriously doubts whether a decrease in incidence of certain infectious diseases and the marked decrease in the death-rate from tuberculosis in particular are largely due to the activities of health officers instead of resulting from multiple events in the population about which too little is known and over which no one has a great deal of control. Undoubtedly many of these happenings are in some way related to or controlled by ecologic laws".

More epidemiologists would be prepared to admit that the major fluctuations in the incidence of specific infections do not result from measures applied by man deliberately, and Rivers quotes as an interesting example the historic fact that malaria was once rampant in the Mohawk Valley. As the land became more densely populated and passed under cultivation, mosquito breeding places were removed, and with the advance of civilization malaria-bearing mosquitoes found ecologic conditions unfavourable and malaria disappeared without any conscious effort on the part of man. Whatever man's intention in the matter, he and the pathogenic micro-organisms each strive to keep for themselves a place in the world and therefore appear to war against each other. "The various forms of life and the different species have each a separate ecology. The epidemiologist is at all times concerned on the one hand with human ecology and on the other with bacterial ecology" (W. H. Bradley[2]).

We must attempt to keep these two aspects apart, neither should we allow ourselves to be led to the conclusion that there is room in the world for both pathogenic organism and man, and that immunity in the serological sense is the only way in which man can protect himself. One sometimes fears that nowadays it is fashionable to become nihilistic and to lose enthusiasm for the

general principles in the control of communicable disease which served our forefathers. It is indeed difficult to retain one's faith in these old principles in the face of enigmas like poliomyelitis or neonatal diarrhœa. It is all too easy to become over enthusiastic about immunological methods of control and then to lose heart when we discern their limitations.

Rivers, while attempting to establish that the trends in the incidence of disease are more natural than made by man, admits "the best way for a country to prevent the entrance and spread of (certain) diseases is to have a civilization and a standard of living that provides poor ecologic conditions for the infectious agents, their vectors, and reservoirs"; but we must admit that these are not necessarily what we would call good conditions for man, and that we are rarely able to go into action with exact information concerning the optimum conditions for the elimination of infection beyond a few rough ideas about heat and chemical disinfection, ventilation, daylight, and nutrition of the host. Perhaps we should be able to do better if instead of guessing at the optimum conditions for man, who is a difficult beast to study, we concentrated more on bacterial ecology in the hope of being able to introduce more deliberate and more specific treatments against the relatively few pathogens which bother us.

REFERENCES.—[1]*New Engl. J. Med.* 1948, **238**, 37; [2]*J.R. sanit. Inst.* 1948, **68**, 477.

INFERTILITY AND STERILITY. (*See* STERILITY AND INFERTILITY.)

INFLUENZA. *H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.*

Active Immunization. H. Mellanby, C. H. Andrewes, J. A. Dudgeon, and D. G. Mackay[1] report an investigation of influenza A inoculation in some 20,000 persons with controls during the winter of 1946–7. The study was made in Army recruiting centres, mental hospitals, and boarding-schools. In some cases, the alternate-case method of inoculation was followed, but in others whole groups were inoculated and similar groups left uninoculated, in order to study the herd immunity as well as the individual immunity in the population concerned. The results were disappointing. One reason for this was the mild clinical character and the low incidence of the disease during this particular season. In the only two Army training centres in which clear-cut results were obtained, the incidence of influenza was 7·1 per cent among the inoculated and 8·3 per cent among the uninoculated—not a significant difference. It was concluded: (1) That in the absence of a widespread epidemic the value of inoculation could not be determined; (2) That even in communities apparently favourable for inoculation, present-day vaccines had not produced any striking reduction in incidence; (3) That no conclusions can be drawn from this study about the merits of attempting to immunize whole communities; (4) That the results were much less encouraging than those reported in 1944 and 1946 from the United States. It is pointed out that recent reports from the United States indicate that in 1947 inoculation had little if any effect on the incidence of influenza. Apparently the strains of influenza A causing the 1947 epidemics were antigenically rather remote from those contained in the vaccine.

Mode of Cellular Infection. F. M. Burnet[2] reports research of a fundamental nature to study the mode of cellular infection by influenza and related viruses. It was shown that the hæmagglutinating action of these viruses was due to the presence of an enzyme which was an integral part of the virus particle surface. The substrate of this enzyme is a mucin present in the surface layer both of erythrocytes and of the respiratory and other cells which are susceptible to infection by influenza viruses. If this mucin is not present in the exposed cell surface, infection cannot take place but it does not always follow that the presence of this mucin makes the cell susceptible to infection. After some search,

another enzyme, one derived from *V. cholerœ*, was found which was active against same the substrate, and, by its use, cells were rendered insusceptible to infection by viruses of the influenza and mumps groups. The potential importance of this work is the fact that it opens up a possible approach to the chemotherapy of virus disease.

(*See also* MENINGITIS—INFLUENZAL.)

REFERENCES.—[1]*Lancet*, 1948, 1, 978; [2]*Ibid.* 7.

INTESTINAL OBSTRUCTION. *A. Rendle Short, M.D., F.R.C.S.*

Results of a composite research on intestinal strangulation by surgeons working for the London County Council[1] have been published. Most of the cases, 336 in all, were strangulated hernias, but some were examples of strangulation by a band. When gangrene was present the mortality was 48 per cent; the mortality of resected cases was 52 per cent. Points of interest that emerge were that when long lengths of intestine were involved, 50 cm. or more, the gut may fail to recover although at operation muscular contractions were seen in the affected loop and pulsation was present in the mesenteric arteries. On the other hand bowel that is black, grey, green, or yellow may be reduced, and resume its functions (14 out of 20 cases). When pulsation in the mesenteric vessels is absent, recovery is improbable. Animal experimentation convinces H. Laufman and H. Method[2] that papaverine HCl, given by injection, releases arterial spasm and enables some borderline cases to recover.

It is interesting to hear after these years of separation what Austrian surgery is doing for intestinal obstruction. P. Fuchsig and W. Maresch,[3] of Vienna, present a study of 196 cases, the general mortality being 33·7 per cent. An ileostomy in addition to release of the obstruction is of no particular value, but gastric or duodenal suction improves the outlook. For young patients in good condition ether is the best anæsthetic, but for older patients already seriously ill spinal anæsthesia is better.

K. H. Sartorius[4] puts on record the results of operation on 359 natives on the Witwatersrand, suffering from various forms of intestinal obstruction. The general mortality was 20·1 per cent, but this low rate is due to the fact that 200 of the patients were suffering from strangulated hernia, with a case-mortality of 4·5 per cent. Much the commonest cause of internal obstruction was volvulus, 98 cases, of whom 42 died. He lays stress on the value of penicillin in the after-treatment, as well as of intestinal suction and continuous intravenous fluids.

Diagnosis of Obstruction, Ileus, and Strangulation.—Without saying anything not generally known, W. H. Cole,[5] of Chicago, gives a useful account of the differential diagnosis of these conditions. When obstructive symptoms come on within a few days of an operation, and no peristaltic waves can be seen or heard, it is probably a case of ileus and can be relieved by intestinal suction. Obstruction by recent adhesions, also, will nearly always clear up with such treatment, but if there is evidence of strangulation, operation is urgently called for. Cole's list of signs of strangulation is as follows: increase of abdominal pain, or of pulse-rate, or of abdominal tenderness; appearance of muscular rigidity; development of a palpable mass; fever or leucocytosis; sudden fall of blood-pressure; or failure of suction treatment to reduce distension. [One might add localized abdominal distension, with dilated coils, as evidence of obstruction needing operation.—A. R. S.]

Non-operative Treatment.—F. I. Harris and M. Gordon,[6] of San Francisco, have a single-lumen mercury tube six feet long, which they consider superior to the Miller-Abbott double-lumen balloon tube. It is of course easy to see

with the aid of radiography how far it has passed. With a longer tube they had trouble in that the end passed sometimes through the ileocæcal valve and was difficult to withdraw, and had to be cut off and let pass per anum. Their tube made operation unnecessary in 41 out of 100 patients, as the intestine recovered function after decompression. L. Berger and S. Achs,[7] of New York, though ardent advocates of the Miller-Abbott tube, report a case in which it caused perforation of the small intestine. J. P. and T. A. Quilliam,[8] of King's College, London, find that intramuscular injection of two doses of 1·5 ml. of 0·1 per cent of di-isopropyl fluorophosphonate (D.F.P.) is more effective than pituitrin or prostigmine in stirring up peristalsis, and less toxic.

Intestinal Obstruction in Children.— Obstruction in the newborn is probably due to defects of the duodenum. Isabella Forshall,[9] of Liverpool, relates 4 cases in which the obstruction lay in this region. The dominant symptom is vomiting, beginning within 36 hours of birth, the vomit containing bile. Meconium is passed at first, then absolute constipation follows. There may be fullness in the epigastrium and emptiness of the lower abdomen. Operation should be within four days, before dehydration ruins the child's chances. Open ether is the best anæsthetic. The obstruction may be extrinsic, such as volvulus due to faulty rotation, or intrinsic. Volvulus can be untwisted. Atresia may be dealt with from within, by opening the duodenum, or a gastrojejunostomy may be performed. A tube is passed through the nose into the stomach or duodenum for after-treatment, and the child is given fluids parenterally for 48 hours, after which teaspoonfuls of water are allowed every two hours. Miss Forshall relates 4 cases, 2 being successful.



Fig. 31.—Uniting intussusceptum to intussuscipiens with parallel mattress sutures. (*Figs.* 31–34 *reproduced from 'Surgery, Gynecology and Obstetrics'.*)

Methods of operating for irreducible intussusception in infants are described by J. Peyton Barnes,[10] of Houston, and by C. Dennis,[11] of Minnesota. Barnes begins by sewing the intussusceptum to the intussuscipiens proximal to the obstruction with mattress sutures. He then brings the mass outside the abdomen and closes the parietal peritoneum around it. The intussuscipiens is then incised and the dusky or gangrenous intussusceptum pulled out and cut away (*Figs.* 31–34). A rubber tube is loosely inserted through the stoma for about 6 in. into the ileum, and suction applied for a day or two. The tube is anchored with a silk stitch to the abdominal wall. The colostomy will close spontaneously. Dennis reports 8 cases treated by ordinary resection and primary end-to-end anastomosis, with no deaths. He uses a one-layer silk suture method, with interrupted mattress stitches. The after-treatment includes oxygen, gastric suction, and sulphonamides.

(*See also* INTUSSUSCEPTION, ACUTE, IN CHILDHOOD.)

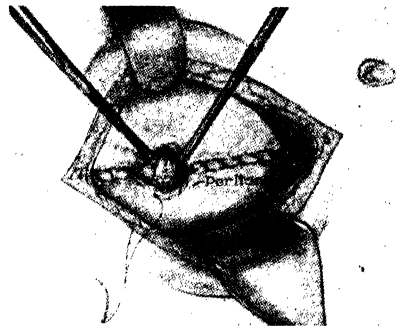


Fig. 32.—The peritoneum has been closed with the exception of a small opening. The peritoneal edges are being sutured to wall of intussuscipiens. Dotted line marks site of incision into intussuscipiens.

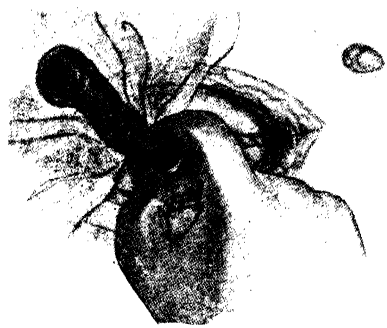


Fig. 33.—The intussusception is pulled out until the mattress suture line is felt between thumb and index finger. The intussusceptum will be sectioned a half-inch distal to this point.

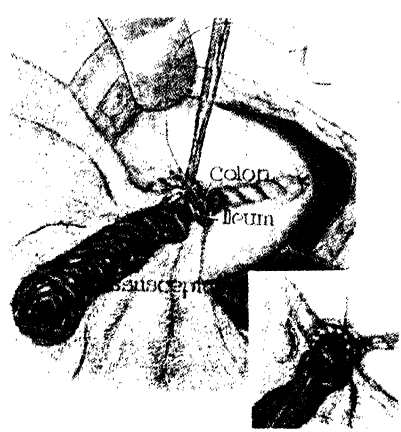


Fig. 34.—First guy suture placed through walls of intussuscipiens and intussusceptum. Inset: Intussusceptum cut half-way through, running suture being placed.

Volvulus.—Volvulus of the cæcum can be diagnosed with the help of a plain radiograph which shows the greatly distended cæcum lying in the upper left abdomen. A barium enema may visualize the beginnings of the twist in the right colon. E. L. Young[12] and two others, of Boston, advise simple reduction if the condition of the bowel is good, or Mikulicz resection and ileotransversostomy if its nutrition is impaired. There is a marked tendency to recurrence. They give details of 7 cases, one being fatal. C. Bruusgaard,[13] of Oslo, discusses volvulus of the sigmoid as seen in Norway. He mentions 91 patients admitted to hospital 168 times. In most of these cases there was torsion, but no vascular impairment. Case-histories often suggest that previous attacks righted themselves at home. The usual treatment at the Ulevaal Hospital has been to pass a proctoscope as far as the site of torsion, and then a lubricated rubber tube, 60 cm. long and as thick as a finger, is guided up past the obstruction to enter the twisted loop. A great gush of flatus and liquid faeces, with reduction of the distension, shows that the tube has been correctly passed. This method of treatment has been used with success in 123 cases over ten years. The tube is left in place for three days to prevent relapse. On one occasion it perforated the bowel. In 9 patients it failed to enter the twisted loop. It is admitted that the volvulus may return later. Operation was performed on 18 cases. In 6 of these the loop was resected in one stage, with 5 deaths. In 7 other cases a multiple-stage resection was carried out during a quiet period and all did well. The all-over mortality for the 91 patients was 14·2 per cent, which is well below that usual in series treated by surgery.

Obstruction by Growths.—In a series of acute obstructions due to carcinoma of the colon, M. L. Michel[14] records a fatality-rate of 30 per cent. It is humiliating to notice that 12 out of the 55 patients had consulted a doctor weeks or months previously, and had been put off with soft words. Four had been explored surgically and the growth missed. All of which is a salutary reminder of the necessity for a barium enema, or meal, to be repeated if there is any doubt, whenever abdominal pains or other departures from the normal arise and persist in patients past 40.

Another cause of obstruction is *endometriosis*. P. McGuff[15] and three others, in a long paper, discuss the Mayo Clinic experience of this disorder. Sixteen patients were seen. Their ages lay between 30 and 50. The diagnosis is probable in the presence of acquired dysmenorrhœa, menstrual periodicity of symptoms, sterility, pelvic pain, perhaps an ovarian cyst or uterine fibroid, and a long history of recurrent intestinal obstruction without loss of weight. A firm swelling can usually be felt in the pelvis, often in the rectovaginal septum. A barium enema shows a filling defect but with intact mucosa. The treatment is by operation, consisting of double oöphorectomy or hysterectomy, with perhaps a colostomy also. An immediate biopsy is often necessary to distinguish from carcinoma. If the endometrioma is confined to the ileum, resection is better. In a young woman, the ovaries may be left and the endometrioma removed. The end-results are good.

Foreign Bodies in the Intestine.—T. J. Snodgrass[16] has unearthed 21 cases in which a toothpick, or similar piece of wood, has been found in the intestine. On 10 occasions it had perforated the cæcum. During eight years, in a Vienna hospital, there were only two cases of perforation of the bowel by a foreign body, amongst 13,500 operated on. In one of these the abdomen had been opened three times for a swelling in the left hypochondrium before the cause was found in the shape of a piece of bone 2½ cm. long. In the other case, there was a splinter of iron lodged in an abscess in the appendix region. Both patients were unaware that they had swallowed anything unusual (O. Beutl[17]). Bezoars are concretions formed in the stomach or intestines. They are far

commoner in animals than in man. Three examples are described by C. H. Watt and J. W. Hurner,[18] two being composed of vegetable fibres and the other of hair. They all caused acute obstruction, and were relieved by surgery. All lay in the small intestine. The vegetable bezoars are usually in elderly men, the hair-balls in young women. [Hairy bezoars generally form a palpable mass in the stomach. One such seen by the editor was about five inches across.—A. R. S.]

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INTESTINES, SURGERY OF.

A. Rendle Short, M.D., F.R.C.S.

Diverticula. Two papers, by C. H. Maguire,[1] of Louisville, and by A. V. Migliaccio and C. Begg,[2] of Rhode Island, deal with illnesses arising from a *Meckel's diverticulum*. They both point out that the diverticulum often contains heterotopic tissue, such as gastric mucosa, or pancreas. In two cases in which it led off an intussusception, pancreatic tissue was found in its wall. The gastric mucosa may ulcerate, and this is one of the causes of severe melæna in children. This may be distinguished from intussusception because pure blood without mucus is passed, and there is no colic or vomiting. The ulcer may perforate. In adults, as is well known, acute intestinal obstruction may be caused. A pre-operation diagnosis is rarely possible. The treatment is resection with a wide base, to get rid of any heterotopic mucosa. In the Rhode Island series of 50 cases, only 21 had any symptoms due to the diverticulum. Amongst these there were 11 obstructions, 2 of which were produced by intussusception; 5 cases of inflammation; 4 with perforating ulcer; and 1 with melæna.

Diverticula of the duodenum and jejunum are the subject of a paper by H. Mahorner and W. Kisner,[3] of New Orleans. Duodenal diverticula are quite common, and may be seen in perhaps 1 per cent of all barium meals. The authors do not subscribe to the general opinion that they are harmless and not worth operating on. They consider that they often produce quite troublesome symptoms, especially in the second half of life. There is pain, which varies from slight discomfort to real agony, lower in the abdomen than gall-bladder pain. The relation to a meal is variable. Nausea is common, vomiting rare. There is sometimes a tendency to diarrhœa. Acute inflammatory attacks, and perforation, are rare. The diagnosis, of course, depends on the barium meal. Jejunal diverticula are uncommon, often multiple, and not far from the duodeno-jejunal junction. As a rule they are symptomless. The authors advise surgical removal for both forms of diverticula if they are giving rise to serious trouble, as little or nothing can be expected from medical treatment. If there is difficulty in finding the pouch, the intestine should be distended with air by means of a needle and syringe. The 6 patients they operated on all did well, except that one given a spinal anæsthetic was left with permanent partial paralysis of the bladder and rectum. [This terrible disaster after spinal anæsthesia receives too little notice in the literature. In one case of duodenal diverticulum under my care the sac was as large as a grapefruit and removal was quite a formidable undertaking, though the result was good. In another case there were three or four pouches and it was thought better not to operate in spite of persistent complaints.—A. R. S.]

Hypertrophic Tuberculosis of Ileum.—MM. Froehlich, Frühling, and L. Kissel-Nikès,[4] of Strasbourg, report 2 cases in which tuberculosis of the ileum produced a tumour-like mass causing chronic obstruction. One was discovered

at autopsy. In the other, a woman of 47, the mass was resected, with a good result.

Ulcers of the Small Intestine.—Tuberculous, typhoid, and malignant ulcers of the small intestine have been well known for many years, but occasionally one meets with a simple non-specific ulcer for which no definite pathological or clinical cause can be found. These also were described long ago, but no one has any extensive experience of them. J. A. Evert[5] and two others describe the 14 cases that have been seen at the Mayo Clinic. They may be recognized by bleeding, perforation, or stricturing. Four of the patients died. The authors give particulars of a further 31 cases from the literature. The general mortality is 47 per cent. The treatment is surgical. Perforations should be closed; it appears that it is not necessary to excise the ulcer, as those closed had no further trouble. For non-perforated ulcer resection was carried out 14 times, with 5 deaths.

Tumours of the Small Intestine.—Every year there are two or three papers in the journals on this subject which do not as a rule add much to our knowledge. Reference may be made on this occasion to communications from J. H. Eckel,[6] H. A. Weinberger and R. Paltauf,[7] and J. Rabinovitch[8] with three others, all of New York. Patients give a history of intermittent intestinal obstruction and of melæna. The barium meal will usually show the filling defect. Eckel relates 19 cases, 12 of them malignant; in 8 of these resection was performed, without a death. Three are alive over five years. Weinberger writes of 20 cases; most of them died soon, or later after removal, but one was well for three years, and 5 others for shorter periods. Rabinovitch discusses 15 cases of sarcoma of the small intestine; he says that in half of these a lump could be felt.

REFERENCES.—[1]*Arch. Surg., Chicago*, 1948, **56**, 65; [2]*Amer. J. Surg.* 1948, **76**, 188; [3]*Surg. Gynec. Obstet.* 1948, **85**, 607; [4]*J. Chir.* 1948, **64**, 88; [5]*Surgery*, 1948, **23**, 185; [6]*Ibid.* 467; [7]*Ibid.* **24**, 35; [8]*Surg. Gynec. Obstet.* 1947, **85**, 333.

INTRACRANIAL HYPOTENSION.

Macdonald Critchley, M.D., F.R.C.P.

The problem of low intracranial pressure—a relatively unfamiliar subject in British medicine—formed one of the topics for discussion at a combined meeting between the Neurological Section of The Royal Society of Medicine and the Société de Neurologie de Paris.

R. Leriche[1] stated that the existence of hypotension was established during the first World War as the result of the experience of head injuries. In some of these post-traumatic cases a low intracranial pressure was recorded manometrically at lumbar puncture. After subcutaneous or intravenous injection of artificial serum a series of results could be demonstrated, namely: (*a*) a rise in C.S.F. pressure; (*b*) disappearance of headache; and (*c*) bulging of the scar at the site of a cranial defect.

In 1920 it was noted that after closed head injuries the C.S.F. pressure might prove to be either high or low, and yet the clinical manifestations were identical. In the cases with low C.S.F. pressure the headache would be relieved by an intravenous injection of 40 c.c. of distilled water. The conception of a persistent hypotension seemed to explain some of the clinical correlates of a spinal-fluid fistula (coma, hyperthermia, bradycardia), all of which improved after injections of distilled water. Later it was remarked that after removal of splinters from the brain, fistulization of the ventricle might lead to symptoms referable to disordered vegetative centres—curable by water injections.

By 1922 hypotension seemed to be associable with three conditions: (1) Loss of cerebrospinal fluid into the soft tissues (as after lumbar puncture) or to the outside (as after fracture); (2) Inadequate dialysis in the choroid plexus from vasomotor disturbances (due to injury), inflammation, or sclerosis; and (3)

Enlargement of the subarachnoid spaces in patients previously trephined. Symptoms were very like those of hypertension. In chronic and otherwise intractable cases P. Puech had previously advocated ligation of the inferior internal jugular vein, and peri-carotid sympathectomy.

According to P. Puech, P. Guilly, J. Morice, and M. Brun[2] intracranial hypotension represents 7·2 per cent of all neurological cases. Trephine puncture, and direct exploration of the brain, are the only precise methods of diagnosing hypertension, because lumbar or suboccipital punctures give inadequate or even misleading information. Of their series of 238 cases, 68 per cent were 'secondary' (post-traumatic, post-operative, associated with other diseases), and 32 per cent were apparently 'primary'. Clinical manifestations comprise headache, vomiting, and occasionally papilloedema. In more severe cases consciousness may be lost and there may be paralyses or convulsions. The picture may recall that of cerebral softening or hæmorrhage. Hypothalamic symptoms are the rule. Psychiatric features may be prominent and may include depression, confusion, and episodes of mania or narcolepsy. The condition of cerebral hypotension may be acute or chronic, but in either case the pattern is similar. A prodromal period lasts a few days to several months, comprises headache, loss of weight, emotional changes, and often diabetes insipidus. These features appear especially in the morning, or when fasting, and are relieved by eating, drinking, or lying with the head low. Sudden severe manifestations may then develop, and, unless treated, may lead to coma and death. At operation the neurosurgeon observes that the dura does not pulsate; the brain appears shrunken, collapsed, and pulseless. No fluid escapes on ventricular puncture, and one hears the sound of air being sucked into it. The authors also refer to 5 cases of what they termed 'therapeutic hypotension' when radiotherapy or drug therapy was responsible.

D. Petit-Dutaillis and G. Giout[3] pointed out the possibility that hypotension and hypertension may alternate or succeed each other in the same patient.

Treatment, as outlined by these last-named authors, comprises intravenous injections of distilled water or of serum; drugs which act upon the arterial blood-pressure, capillary permeability, or the secretion of the plexuses (perfusion of adrenaline or ephedrine in serum, syncortil, pitressin). Vitamin P has been recommended. Air may be injected into the ventricles, with caution. In severe cases one may inject physiological serum, or, better, Ringer's solution, directly into the ventricles.

Prevention of hypotension is an important point in neurosurgery. At the end of an operation for removal of a hæmatoma or tumour, and also after operations upon the posterior fossa, reflection of the ventricles is a wise practice.

A recent study by G. W. Pickering[4] upon *lumbar puncture headache* is of importance in this connexion. A low cerebrospinal fluid pressure was discovered, and this feature and the accompanying headache were both returned to normal after an injection of 30 to 50 c.c. of saline. Pickering ascribes post-puncture headache to a caudad displacement of the base and posterior parts of the brain with tension on the anchoring structures, particularly the tissues around the large arteries at the base.

REFERENCES.—[1]*Proc. R. Soc. Med.* 1948, **41**, 771; [2]*Ibid.* 772; [3]*Ibid.* 775; [4]*Brain*, 1948, 71, 274.

INTRACRANIAL INFECTIONS (Subdural Abscess : Purulent Pachymeningitis.) *J. B. Pennybacker, M.D., F.R.C.S.*

There is perhaps no condition which more clearly demonstrates the life-saving value of *penicillin* than subdural abscess. F. Schiller, H. Cairns, and D. S. Russell,[1] in a study of 33 cases treated in the last twenty years, found that even

after the introduction of sulphonamides, the condition was almost invariably fatal. Of 15 cases treated with penicillin 7 recovered, and these authors consider that their results should be improved with increasing knowledge of the most effective ways of using penicillin.

Subdural abscess (or purulent pachymeningitis as the authors prefer to call it, on analogy with purulent peritonitis) is usually a sequel of *spreading osteomyelitis of the skull*, and in 29 of their 33 cases the infection began in the accessory air sinuses (23) or mastoid (6). Thus this is a complication with which ear, nose, and throat surgeons should be thoroughly familiar. The infection may penetrate to the level of the subdural space and remain largely confined to this plane with little or no leptomeningeal infection, although in some cases leptomeningitis and brain abscess may occur. Pus spreads freely throughout the subdural space as there are no obstructing septa as in the subarachnoid space. Thus the medial and inferior surfaces of the cerebral hemispheres may be as much bathed in pus as the more accessible supero-lateral surface. In some cases the pus becomes loculated to form discrete and localized abscesses in the subdural space. These are commonly on the inferior or medial surfaces of the hemisphere, are often relatively small, and are thus difficult to treat by the methods commonly employed for cerebral abscesses, i.e., aspiration or extirpation.

The effect of subdural suppuration is ultimately to paralyse that part of the cortex which lies under the pus. Where the effects are localized, e.g., paralysis of one limb, this may be due largely to pressure and local toxic effects, but often there is complete hemiplegia, hemianæsthesia, and hemianopia coming on within a few hours' time. In such cases this complete "hemisphere knock-out" is due to an infective thrombosis of cerebral veins which may extend to involve the large venous sinuses. There may or may not be epileptic attacks during the genesis of the lesion. There are general signs of illness, and if there is infected bone in an accessible part of the skull this will manifest its own signs. The spinal fluid may be little abnormal, but in some cases there is an increase in the protein and cell content of the fluid—much less than one would expect in considering that only a thin translucent membrane separates the pus in the subdural space from the cerebrospinal fluid in the subarachnoid space.

The diagnosis of subdural suppuration may be easy when a case of known osteomyelitis of the skull is 'going wrong', with evidence of gross cerebral disturbance and too little leptomeningitis to account for it. But there are cases in which a much more benign explanation has to be considered, i.e., when the neurological disorder is due solely to cerebral thrombophlebitis with, as yet, no subdural suppuration. The diagnosis, indeed, cannot be established without making burr-holes and finding the pus. It is convenient that the means necessary to make the diagnosis may also be used in treatment, because through these burr-holes penicillin may be instilled directly into the subdural space. It has been found that penicillin will pass freely from the circulating blood into the subdural space, but if there is much pus it is essential to let it out and instil penicillin directly through small catheters suitably placed. The mechanical effect of the instillations is also of some value in diffusing the penicillin and preventing loculations of pus.

In addition to the local and systemic use of penicillin, it may be necessary to administer it intrathecally if there is a sharp leptomeningeal reaction with organisms in the fluid, and in some cases intraventricular injections may also be required. These authors have found that big operations for removal of infected bone are rarely called for: it is preferable to rely on systemic penicillin administered over a long period, and to limit operations to removal of small sequestra and the draining of small abscesses. It so happens that these infections are usually due to penicillin-sensitive organisms (various types of streptococci

in 25 of their 33 cases), and the authors stress the importance of maintaining an adequate concentration of penicillin in the blood before, during, and after operations on infected sinuses.

REFERENCE.—[1]*J. Neurol. Neurosurg. Psychiat.* 1948, **11**, 143.

INTRAPULMONARY CALCIFICATION AND HISTOPLASMIN SENSITIVITY.

Philip Ellman, M.D., F.R.C.P.

Following the original observations of J. D. Aronson[1] that coccidiomycosis was probably responsible for lung calcification among Indians in certain areas in South-Western U.S.A., C. E. Palmer and others[2] subsequently adduced evidence in favour of Histoplasma capsulatum infection as a common cause of calcification in certain areas of the South-Eastern United States.

In both cases the geographical distribution of pulmonary calcifications corresponded closely to the areas of endemic infection with the respective fungi, and also showed a parallel relationship to the territorial distribution of positive reactors to the respective fungal extracts.

Although it is now known that the skin reactions to these fungal extracts are not entirely specific, as there is considerable overlap between the reactions to extracts of various fungi, it is, however, clear that in certain areas of America there are causes other than tuberculosis for a large proportion of cases of pulmonary calcification.

In order to determine whether or not a significant proportion of pulmonary calcifications in this country were associated with sensitivity to histoplasmin rather than to tuberculin, a survey of Cardiff University students was carried out, and reported on by B. H. McCracken.[3] Of 1188 students, all between 17 and 28 years old, there was X-ray evidence of calcification in 87 (7·3 per cent); 82 of these were subjected to skin tests. Of these, 67 (82 per cent) were found to be tuberculin-positive, and 15 (18 per cent) were found to be tuberculin-negative. Out of the total number of cases showing calcification, 33 were tested with 3 fungal extracts including histoplasmin, and 20 with histoplasmin only; 7 of each of these two groups were retested with higher concentrations of the same extract. Not one of these tests with fungal allergens was positive.

McCracken noted that all cases with peripheral calcifications were positive to tuberculin, a fact of possible significance, since hilar shadows were more likely to be interpreted erroneously than shadows peripherally situated.

He concluded, therefore, that in South Wales fungus infections such as histoplasmosis are not a significant factor in producing intrathoracic calcification, and it is fair to assume that this experience is generally applicable to this country.

REFERENCES.—[1]*Arch. Path.* 1947, **3**, 41; [2]*Pub. Hlth Rep., Wash.* 1945, **60**, 513, and 1946, **61**, 475; [3]*Thorax*, 1948, **3**, 45.

INTUSSUSCEPTION, ACUTE, IN CHILDHOOD. (*See also* INTESTINAL OBSTRUCTION.)

R. E. Bonham-Carter, M.D., B.Chir., M.R.C.P.

Reporting a detailed study of 100 cases from the Department of Child Health, Royal Victoria Infirmary, Newcastle-upon-Tyne, Brenda Morrison and Donald Court[1] reveal facts which they believe will help family doctors in diagnosis, as well as those responsible for treatment. The overall mortality has fallen from nearly 40 per cent to less than 10 per cent in the last thirty years, but though the mortality is below 5 per cent when treatment is started within the first twenty-four hours, it rises steeply to 20 per cent if the condition remains untreated for two days. They stress the importance of the history in diagnosis and the fact that physical signs may not be sufficient to warrant admission to hospital when the child is first seen.

As a result of close clinical study of these cases, they conclude that the text-book description of acute intussusception in childhood may have to be revised, for many of the statements appear inaccurate, and many of the physical signs stressed are late in appearance, and if treatment is delayed pending their appearance, the mortality will be high. In this connexion they point to the fact that a number of cases occur between three and six months of age, that the male predominance is not marked, and that the spontaneous passage of blood per rectum is often a late sign. They affirm that acute sudden illness between the ages of three and ten months, characterized by abdominal pain and vomiting, especially when associated with pallor and collapse, should be regarded as intussusception and sent to hospital immediately. They place more emphasis on history than on physical signs in the diagnosis, though a tumour was felt in their series in a high proportion of cases, yet they feel that the family doctor should not wait to detect this, but should send the infant to hospital upon suspicion. Rectal examination should not be omitted, for blood may be found this way. Fever was found commonly. The outlook is directly determined by the duration of the disease before treatment.

This important paper, laying, as it does, great stress upon a sense of urgency in cases of suspected intussusception should, if its precepts are followed, affect the overall mortality-rate.

REFERENCE.—[1]*Brit. med. J.* 1948, 1, 776.

IRON THERAPY.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

In the MEDICAL ANNUAL last year attention was drawn to the work of J. A. Nissim[1] who found that solutions of saccharated iron oxide could be given intravenously in doses sufficient to promote satisfactory hæmoglobin regeneration without producing undesirable reactions. A proprietary preparation of this form of iron is now available ("Ferivenin", Benger's Limited) as 5-c.c. ampoules each containing 100 mg. of elemental iron in the form of a 2 per cent solution of saccharated oxide of iron. Intravenous injection of one ampoule provides enough iron for an increase in the hæmoglobin level of approximately 4 per cent. It is usual to give 2 c.c. as the first injection and thereafter 5 c.c. every second day or twice weekly until the hæmoglobin is restored to normal. The reviewers have had considerable experience of the use of this preparation and can testify to its efficacy in promoting rapid hæmoglobin regeneration in case of iron-deficiency anæmia, and to the almost complete freedom from untoward reactions following the injections. There is no doubt, therefore, that an efficacious and non-toxic form of iron for intravenous injection is now available. At the same time the reviewers would reiterate a previously expressed opinion, that in the great majority of cases of iron-deficiency anæmia, iron by mouth produces very satisfactory results and that it is only in the following circumstances that the need to give iron by injection arises :—

1. When there is true intolerance to orally administered iron, i.e., persistence of gastro-intestinal upset even when the initial doses of iron are small.
2. When the anæmia has proved to be refractory to large doses of iron by mouth (in these cases there may be defective absorption from the intestine).

REFERENCE.—[1]*Lancet*, 1947, 2, 49.

JAUNDICE, PHYSIOLOGICAL, OF THE NEWBORN.

R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.

Following the suggestion of A. Yllp and A. Hirsch,[1] P. L. Morrison[2] has shown that the high concentration of bilirubin in the blood of the newborn infant, a concentration which increases rapidly during the first week of life,

is due chiefly to the excreting capacity of the liver of the newborn. He shows that the rate of removal of bromsulphthalein from the neonatal plasma is strikingly lower than the rate observed in healthy adults, and deduces a poor excretion capacity of the liver in the newborn from this finding also.

Upon the survival time of erythrocytes in neonatal blood, he shows that the bulk of the newborn's erythrocytes have a survival time not very much shorter than that obtained in adults, but that there is a smaller proportion of newborn red cells where disappearance from the blood is distinctly more rapid.

This is yet another proof of the differing physiology of the newborn baby.

REFERENCES.—[1]*Kinderheil*, 1913, **9**, 208; [2]*Lancet*, 1948, **1**, 513.

KAPOSI'S VARICELLIFORM ERUPTION (with a Note on other Infections with the Virus of Herpes Simplex). *R. M. B. MacKenna, M.A., M.D., F.R.C.P.*

Severe infantile eczema always presents a difficult problem. If the child is left to the care of its mother, the eczema often 'does badly' and from time to time secondary infection with pyogenic organisms may occur and may make the patient gravely ill. If the infant is admitted to hospital, the eczema may improve, but these patients readily contract diarrhœas or catarrhal chest complaints in institutions; and as their resistance to these maladies is low, they may die.

M. Kaposi[1] in 1887 was the first to draw attention to a severe generalized pock-like eruption occurring as a complication of infantile eczema. In his book he stated that the eruption consisted of flat or indented small bullæ the size of lentils or slightly larger; recent bullæ were numerous, transparent, filled with clear serum, and disseminated but with a tendency to be arranged in groups. They appear like chicken-pox eruptions, but Kaposi believed that they were not a form of chicken-pox. He described how the skin of the face, previously affected by eczema, appeared to be more intensively raised and œdematous when the bullæ formed. He noted that the patients developed a high fever of 40° C. or more and were restless.

Kaposi's varicelliform eruption develops very acutely, and in most cases it efflloresces for three to four days or a week; fresh bullæ may appear while the earlier lesions fade. Most of the bullæ burst and then heal slowly under a crust. Kaposi stated that the largest number of lesions were found on the skin previously affected by eczema. In his experience small groups of lesions might appear on the previously unaffected skin in the neighbourhood of the head, neck, shoulders, and perhaps the arms, but he had not noted any lesions occurring below that level.

Surprisingly, in view of modern experience, Kaposi thought that the malady had a good prognosis, the lesions healing within two or three weeks and the fever abating as the lesions healed. He noted that when healing does occur the area may be scarred and pigmented whilst the pre-existing eczema continues. Kaposi did not know what caused the eruption; he suggested that it might be due to a fungus!

E. B. Sims and Eric L. French[2] have recently quoted Kaposi's views at some length and have reviewed some of the literature concerning the subject. They point out that F. Juliusberg[3] in 1898 commented on the similarity of the lesions to vaccination pustules, and state that since his day it has become increasingly recognized that generalized vaccinia as a complication of vaccination is a hazard to which the eczematous patient is more prone than the healthy person; they imply that whilst he confused the issue he was probably the first to associate Kaposi's eruption with a virus malady.

In 1935 an epidemic of Kaposi's varicelliform eruption occurred in the Stobhill Hospital in Glasgow; A. D. McLachlan and M. Gillespie[4] in reporting

this epidemic admitted that the lesions suggested a virus infection, but unfortunately the material they obtained for virus studies proved to be unsuitable. H. A. Wenner[5] in April, 1944, reported a series of 3 cases from which he succeeded in obtaining a virus closely resembling, if not identical with, that of herpes simplex. Sims and French[2] quote the work of several workers who have obtained the virus of herpes simplex from the lesions of Kaposi's eruption. They note that a number of workers have shown that an attack of the eruption not only can occur in vaccinated people but also does not protect against successful vaccination subsequently in a previously unvaccinated person. They state that L. P. Barker and E. S. Hallinger[6] have described 2 cases in adults, one occurring as a complication of dermatitis, the other on a previously healthy skin after an attack of herpes on the lips. Barker and Hallinger have suggested that the name "systemic herpes simplex" should be used in preference to "Kaposi's varicelliform eruption" and suggest that the administration of moccasin venom is possibly of value in these cases. This suggestion is based on a report made by R. J. Kelley[7] on the treatment of herpes simplex with the venom.

Sims and French[2] report 9 cases of Kaposi's eruption occurring in three separate epidemics. Six of the patients died: classical herpes simplex virus was isolated from 4 of them. They note that some recent writers have stated that the prognosis of the malady is good, but consider that whilst this may be so in adults, there is a high mortality among children. This is rather to be expected, for a child is born free from herpes infection and the Kaposi's eruption probably represents the first contact the child has ever had with the virus. Such a first infection with the virus can cause a sharp fever with a variety of symptoms, and when an extensive involvement of the body surface occurs the toxæmia can be extreme. The outstanding clinical features of Kaposi's eruption, as shown in the cases described by Sims and French, are the abrupt onset, in an eczematous child, of a high remittent temperature (apparently described by some writers as "picket-fence fever") and an intense toxæmia.

As the temperature rises small vesicles up to 4 mm. in diameter appear; occasionally these are slightly umbilicated. They ulcerate, with pock formation and crusting. As the process continues, vesicles begin to appear on previously healthy skin. There is but slight enlargement of the proximal lymphatic glands. The eruption is not limited to the areas described by Kaposi. The disease may run its course and subside by lysis in from one to two weeks, or death may occur at the height of the attack; in some cases the patient dies after a lingering illness from some complication such as bronchopneumonia or mastoiditis. Sims and French found that the diagnosis can be confirmed by inoculating some of the fluid from a pustule on to the chorioallantoic membrane of a chick; after incubation for two days the infected membrane is removed, ground with sand and saline, and the resultant suspension used in a hæmagglutination test. They emphasize that it is important to prevent the malady by rigidly excluding from contact with susceptible children all persons who suffer from herpes simplex. The second important step is the immediate isolation of any suspected case at a considerable distance from any dermatological ward in a hospital. In regard to treatment Sims and French recommend the use of penicillin or sulphadiazine, the former probably being the most efficacious. Also they recommend that treatment by means of a small blood transfusion from a donor who has suffered from herpes simplex should be considered, whilst the suggestion concerning administration of moccasin venom should be remembered.

As a postscript to this essay on Kaposi's varicelliform eruption, attention may be directed to a paper by R. H. Kipping and A. W. Downie.[8] These

authors quote briefly recent work that has proved that stomatitis in children during the first six years of life is often a primary infection with the virus of herpes simplex. After the primary infection in childhood, persons carry the virus for years and may suffer from recurrent attacks of mild labial herpes. Primary herpes simplex infection in adults seems to be uncommon. Occasionally primary infection with this virus can be severe. Fatal encephalitis due to this virus has been recorded. Kipping and Downie describe a case of a motor engineer, aged 37, who developed signs and symptoms which led to a somewhat disputed diagnosis of variola, but which eventually proved to be a case of generalized infection with herpes simplex virus. It seems, therefore, that the clinical signs and symptoms which can be caused by infection with this virus are more numerous than is generally recognized.

REFERENCES.—[1]*Pathologie und Therapie der Hautkrankheiten*, 1887, Urban & Schwarzenberg; [2]*Clin. Rep. Adelaide Child. Hosp.* 1948, **1**, 99; [3]*Arch. f. Derm. u. Syph.* 1898, **46**, 21; [4]*Brit. J. Derm.* 1936, **48**, 337; [5]*Amer. J. Dis. Child.* 1944, **67**, 247; [6]*J. Amer. med. Ass.* 1947, **135**, 149; [7]*Arch. Derm. Syph.* 1938, **38**, 599; [8]*Brit. med. J.* 1948, **1**, 247.

KIDNEY, SURGERY OF.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

The Maintenance of Position in Kidney Surgery.—H. E. Carlson[1] makes a practical suggestion. The position of the patient in kidney surgery, always difficult to maintain, can be made easier by the use of side strips of adhesive tape supplemented by a *double* arm support (*Plate XX*).

Congenital Cystic Kidneys.—P. P. Lambert[2] made graphic reconstructions of polycystic kidneys of the newborn, and demonstrates that the cysts are closed cavities consisting of distended nephrons having no connexion with the renal pelvis. The same method of examination applied to the adult type of polycystic disease shows the cysts to be glomerulous dilatations developed in the course of the nephron. These graphic reconstructions offer explanations as to why the infant dies at, or before, birth while the adult survives at any rate to middle age.

Lambert stresses that between the typical polycystic form of congenital cystic kidneys and the so-called solitary cyst of the kidney many intermediate stages may be observed. In a number of instances patients with kidneys riddled with cysts remain free from serious trouble—complaining only of mild lumbar pain aggravated by hard work. On the other hand, as T. P. Grauer[3] says, infection, attacks of hæmaturia, and constant pain are frequent accompaniments; eventually uræmia sets in. Grauer agrees with most authors that surgery is indicated only for certain complications, but the reviewers sympathize with I. Dodson[4] who asks—what has medical treatment to offer these patients?

Dodson reports 2 cases of congenital cystic kidneys treated by Rovsing's operation (exposure of the kidneys and emptying the cysts). Both patients were benefited remarkably.

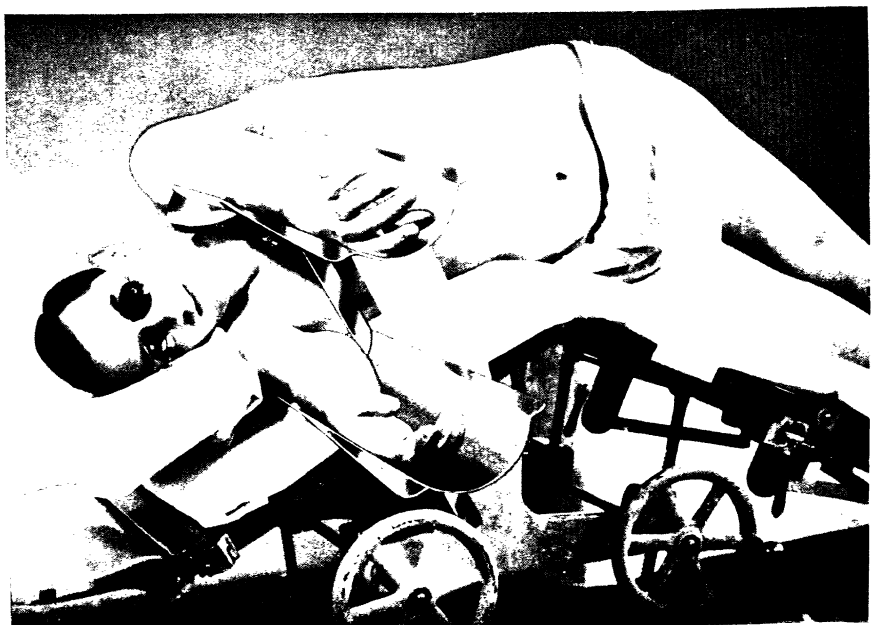
M. M. Mayers[5] has employed, apparently with excellent results, a combined procedure. So that cysts can be aspirated post-operatively, Goldstein's marsupialization of the kidney is performed, together with Young's technique for sclerosing the cysts. Quinine hydrochloride or dihydrochloride is preferred to sodium morrhuate.

Renal Manifestations of Periarteritis Nodosa.—In recent years periarteritis nodosa has been receiving increasing attention in the surgical literature. R. K. Womack and W. R. Mathews[6] regard it as a necrotizing vascular disease affecting medium-sized and small arteries and arterioles. Its clinical manifestations are varied and quite often of a bizarre nature. The disease usually involves the arteries of several organs. The urologist should be aware of the fact that the kidneys are most frequently affected, in 80 per cent of cases according to several

PLATE XX

ARM SUPPORT FOR KIDNEY OPERATIONS

(H. E. CARLSON)



Carlson's double-arm support for maintaining position in renal surgery.

PLATE XXI

AORTOGRAPHY

(W. F. Mellick and A. E. Vitt)



Combined retrograde pyelography and aortogram showing kinking of the ureter by an aberrant renal artery. Artery supplies lower half of the kidney and cannot be sacrificed without destroying much renal tissue.

PLATE XXII

RENAL PAPILLOMATA

(J. B. MACALPINE)



Bilateral renal papilloma in dye workers. The whole of the right pelvis is filled with growth; a single papilloma occupies the junction of the upper left major calyx with the pelvis.

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PLATE XXIII

SECONDARY CARCINOMATA IN URETER

(J. B. MACALPINE)



Ureterectomy following removal of kidney for hypernephroma: specimen showing the two carcinomatous lesions. (*Macalpine.*)

By kind permission of the 'British Journal of Surgery'

authorities. The aetiology is as yet unproven. First occurs necrosis of the vessel wall; this may be followed by rupture and hæmorrhage, thrombosis with infarction, or aneurysmal dilatation. The end stage is fibrosis and nodular thickening of the arterial wall and surrounding tissue.

The relative frequency of urinary symptoms has been noted by many observers. In one series hæmaturia was a symptom in 48 per cent. It may be unilateral, suggesting renal tumour. Several instances of hæmorrhage into the perirenal space, causing severe pain suggestive of renal colic, have been reported. Massive bilateral perirenal hæmorrhage has been recorded. Renal infarcts due to thrombosis are not uncommon, and periarteritis nodosa has been advanced as a cause of essential hæmaturia. Three patients exhibiting symptoms of urinary tract disease form the basis of the report by Womack and Mathews.[6] One case of suspected nephrolithiasis, another of suspected renal tumour, and one of profuse hæmaturia are reviewed. (*See also* SPONTANEOUS PERIRENAL HÆMATOMA, *below*.)

Medial Ptosis of the Kidney : a New Renal Syndrome. Little or no attention has been given to medial or lateral mobility of the kidney. G. C. Prather[7] points out that medial ptosis, which may cause symptoms, cannot be demonstrated by the usual pyelographic technique. The diagnosis can be made, however, by X-ray films using anteroposterior projection with the patient in a lateral position. Nephropexy is a simple method of correction.

Renal Complications of Hyperparathyroidism. Some years ago F. Albright and co-workers[8] described three ways in which the kidneys may be involved: Type I: pyelonephritis secondary to formation of calcium phosphate stones in the renal pelvis. Type III: acute parathyroid poisoning with anuria and death with calcium deposits in kidney parenchyma as well as in other organs, but with no chronic renal changes. Type II: a condition midway between Types I and III which simulates both chronic glomerular and vascular nephritis. In describing 4 cases, E. Burns and C. M. Whitehead[9] assent that primary hyperparathyroidism produces no specific symptoms, the majority of cases being unrecognized until complications have developed. It should be considered a possibility in every case with renal calculi. Removal of the parathyroid adenoma is the only effective treatment. Except in acute conditions of the urinary tract, such as ureteral block, the parathyroid tumour should be removed first. Urinary tract complications are dealt with according to standard urological procedures.

Renal Tuberculosis.—J. W. S. Blacklock[10] found *bovine* strains in 28·3 per cent. The bacilli were all isolated from catheter specimens taken during the day and not first thing in the morning. This proved preferable to, and more convenient than, examination of a 24 hours' specimen and the results are as reliable.

Hypertension.—To the variety of unilateral renal lesions associated with hypertension, J. D. Shea et al.[11] add a case of *thrombosis of the left renal artery*, apparently cured by nephrectomy.

Hydronephrosis : Aortography.—The present status of aortography is discussed by W. F. Melick and A. E. Vitt,[12] who find that aortograms afford yet another test of renal function in addition to demonstrating aberrant vessels as a cause of hydronephrosis. (*Plate XXI.*)

Ureteropelvic Obstructions.—As emphasized by R. B. Henline and C. J. Hawes,[13] often the sole manifestation of an obstructive renal syndrome may be a digestive upset with no urinary symptoms. The common nerve-supply of kidneys and intestinal tract is well understood and any renal irritation frequently results in indigestion. With Henline and Hawes the Foley Y plastic operation has been more successful than any other procedure, but only when combined with nephrostomy and the use of a splinting ureteral catheter for 6 weeks.

Perirenal Tumours.—In reporting a case of *fibrosarcoma*, H. G. Hanley[14] discusses the subject of perirenal tumours; by far the commonest is the *lipoma*. A characteristic feature of the perirenal tumours is their insidious onset. Symptoms may be absent until there is a large mass. Pyrexia has been noted in several fibrosarcomata. Hanley's patient, who never complained of pain, showed a dramatic return of the temperature to normal after removal of the tumour. In general, urinary symptoms are seldom reported. Renal ischæmia from pressure may occur, and marked improvement in hypertension has been observed after removal of a perirenal lipoma, together with the kidney. The ideal treatment of perirenal tumours is probably early surgical enucleation, a transperitoneal approach being the easiest. The prognosis is bad; recurrences are frequent and tend to undergo malignant change.

L. F. Greene[15] reminds us that extreme renal displacement due to malignant retroperitoneal tumours is very unlikely. In his 3 cases of really marked displacement of the kidney, the retroperitoneal tumour was benign.

Spontaneous Perirenal Hæmatoma.—In a patient with hypertension, periarteritis nodosa should be considered in the differential diagnosis (C. A. Fort[16]).

A rare cause, mentioned by J. Cibert,[17] is renal tuberculosis due to a cortical focus.

Papilloma of Renal Pelvis. K. Tzchirntsch[18] seems convinced that patients with papillomata of the urinary tract often suffer from cutaneous papillomata as well. That papillomatous disease of the bladder is more prevalent amongst dye workers than amongst members of the general population has long been known. Less well recognized is the presence of papilloma of the renal pelvis in such workers. J. B. Macalpine[19] reports 2 cases, one of which showed bilateral growths (*Plate XXII*).

Carcinoma of the Kidney.—In 10·5 per cent of 126 patients the primary growth was 'silent', and the first symptoms noticed were those due to metastases (M. Donaldson et al.[20]).

In 1932 J. B. Macalpine[21] performed nephrectomy for an adherent left *hypernephroma*. The patient was well until January, 1937, when she noticed clots in the urine; a blood-stained efflux was detected on the left, and ureterectomy carried out. The specimen (*Plate XXIII*) showed: (*a*) an elongated polypoid mass springing from just below the upper end of the ureter; (*b*) A second lesion about the size of a match-head at the junction of the middle and lower thirds of the specimen. Sections of (*a*) and (*b*) revealed tissue typical of renal cancer. This is the sole example in J. B. Macalpine's practice where a hypernephroma has produced a secondary implant on the ureteric wall. Of course, a similar phenomenon is well known in papillomatous disease. A painstaking search in the literature for authentic examples of grafting down-stream from renal carcinomata has only emphasized their extreme rarity.

Three cases of pulmonary resection for metastatic hypernephromata form the basis of a communication from D. Robb.[22] In one remarkable instance the patient has remained well 2½ years after lobectomy, 14½ years after nephrectomy, and 18½ years since the first probable clinical evidence of the hypernephroma. Pneumonectomy or lobectomy is worth doing for solitary metastases, and would seem to be the more promising the later it is called for. Robb believes that when the growth is limited to one lobe, is peripherally placed, and well encapsulated, lobectomy appears to give excellent results.

It is of interest to note that R. Cacchi[23] had a patient in whom malignant multiple tumours of the bladder bore a striking resemblance to hypernephromata.

The unusual feature of the four-year follow-up of L. T. Mann's[24] patient was the spontaneous disappearance of multiple pulmonary metastases, which were present at the time of the original nephrectomy.

Adenocarcinoma and Tuberculosis of the same Kidney.—H. A. Neibling and W. Walters[25] present a summary of 7 cases. The diagnosis is directly related to that portion of the combined disease which predominates. In no recorded instance has the complete diagnosis been made pre-operatively.

Cancer and Tuberculosis in the same Kidney.—A. Puigvert and A. O. Anguera[26] find that in 19 known cases the diagnosis of tuberculosis and tumour was established clinically in none.

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KWASHIORKOR. (*See* MALIGNANT MALNUTRITION.)

LABOUR AND ITS COMPLICATIONS.

J. Chassar Moir, M.A., M.D., F.R.C.S. Ed., F.R.C.O.G.

External Version under Anæsthesia.—One of the objects of antenatal supervision is to detect and, when possible, correct any fœtal malpresentation. This applies particularly to breech presentations, in which it has long been customary to perform external cephalic version.

The procedure is usually simple if performed soon after the thirty-fourth week, and before the fœtus has become large in proportion to the amount of amniotic fluid present in the uterus. If the operation is left until nearer term it becomes increasingly difficult, especially if the fœtal legs are extended. Added to this, there may be difficulty from unusually tense abdominal walls, especially if the patient is apprehensive and unable to relax during the necessary manipulations. In these cases anæsthesia greatly facilitates the operation. But now fresh dangers arise. First, there is the danger of the anæsthetic itself, —and for this purpose nitrous oxide, or pentothal, is useless, and a deep ether anæsthesia essential. Secondly, the operator may be tempted to use undue force, with the result that the placenta may be separated, hæmorrhage may suddenly occur, or the fœtus may die in utero. Rupture of the uterus has even been recorded. Short of these disasters, premature labour is sometimes precipitated. Because of these various dangers there has been a difference of opinion regarding version under anæsthesia, and some obstetricians have declared that the dangers of this procedure are worse than the dangers of the breech delivery which it is designed to avoid.

J. H. Peel and S. G. Clayton[1] have done a good service by collecting careful records of 236 cases of version under anæsthesia after previous failures to correct the fœtal position without anæsthesia.

Version was successfully accomplished in 87 per cent of the primigravidæ, and in 89 per cent of the multiparæ. Among cases in which the fœtus was known to have extended legs (proved by X-rays, or by the position at subsequent delivery), version was successful in 79 per cent of the primigravidæ, and in 71 per cent of the multiparæ. Regarding this matter of extended legs, during part of the investigation every patient requiring version under anæsthesia was X-rayed: this revealed that in 82 per cent of the cases in which version without anæsthesia failed, the fœtus had extended legs.

There were 14 fœtal deaths in the series, but only 4 could be related to the version, and only 2 definitely attributed to the version (cases of prolapsed cord and compound presentation). The fœtal death-rate attributable to version was therefore 1·7 per cent.

Onset of labour was precipitated in 7 cases, but without stillbirth or neonatal death. Vaginal bleeding was recorded in only 5 cases, "but slight bleeding certainly occurred in a larger number of cases". There were no stillbirths among the cases of vaginal bleeding.

Against these figures must be balanced the fœtal death-rate to be expected from breech delivery. This varies greatly in different published statistics; and in this connexion it must be remembered that workers who have good figures to present are more likely to publish their results than those who have not. Nine different reports on breech delivery are quoted in this article; the average fœtal mortality among primigravidæ was 11·3 per cent, and amongst multiparæ 9·8 per cent. These figures are certainly high, but they probably represent a fair average of the results obtained in present-day obstetric practice.

Peel and Clayton conclude: "We consider that our results are fairly representative and could easily be equalled or bettered by others. If the fœtal risk from version is 1·7 per cent, and the probability of success under anæsthesia over 85 per cent, even in cases in which version has previously failed without an anæsthetic, the operation is clearly justified. We can perhaps illustrate our opinion thus: if 1000 cases are treated by version there will be about 17 fœtal deaths due to the operation, and about 15 fœtal deaths in cases in which version fails and breech delivery occurs. On the other hand, if all the cases were delivered as breech presentations, there would be about 100 fœtal deaths due to breech delivery alone. We therefore urge the more general adoption of external version under deep anæsthesia in the cases in which version has otherwise failed, and maintain that the operation is not unduly dangerous, and that it is possible even in cases in which the fœtal legs are extended."

Obstetric Shock.—W. A. Scott[2] and H. L. Sheehan[3] have presented two full and interesting papers on shock as it is seen in obstetric practice.

Scott emphasizes the importance of trauma and blood-loss. Of 82 fatal cases in which there had been evidence of shock, in only 11 was no lesion found to account for the shock, and, of these 11, 5 were cases of internal version after 'failed forceps', and 5 were difficult forceps deliveries. Rupture of the uterus is probably commoner than is recognized clinically. Inversion of the uterus may occur spontaneously and accounts for rapid onset of shock.

In treatment, the prime requisite is to treat the shock and not to add to it by operative treatment—that should be reserved until remedial measures have been instituted and the shock shows signs of abating. Morphine should be given to allay pain and apprehension, body heat should be maintained, and the volume of the circulating blood restored by intravenous therapy. The only exception to this rule is the case in which it is necessary to stop active hæmorrhage.

Sheehan's work is based on a clinical and post-mortem study of 147 fatal cases of shock in obstetric cases. The following table indicates the cause of "shock death" in 451 obstetric necropsies at the Glasgow Royal Maternity Hospital:—

Dystocia:	
Prolonged labour	46
Rupture of uterus	20
Third Stage:	
Retained placenta	30
Placenta accreta	5
Inversion of uterus	2
"*Toxæmia*":	
Concealed and mixed accidental hæmorrhage	25
Hypertension	6
Other Conditions:	
Cæsarean section	8
Complicating diseases	5

Sheehan makes many interesting observations, some of which are at variance with current teaching. He states that hospital records show that blood transfusion has been eminently successful in reducing the death-rate from collapse consequent on blood-loss (placenta prævia, accidental hæmorrhage, post-partum hæmorrhage); they show that it has also been successful, although to a lesser extent, in reducing the death-rate from shock combined with blood-loss; but no evidence is forthcoming in hospital records to show that blood transfusion has done anything to reduce the death-rate from shock unassociated with blood-loss.

As a predisposing cause of shock Sheehan specially singles out two conditions —prolonged labour and retained placenta. He states that although it is reasonable to expect that extremely forcible delivery during the first day or two of labour would lead to severe shock, the available figures do not support this view. "In contrast, there were 46 deaths from shock in patients left for three, four, or more days in labour and then delivered with usually relatively little further trauma . . . the importance of length of labour does not appear to be sufficiently recognized." (Sheehan also points out that this type of case is also that in which chloroform, even in small doses, is likely to produce severe liver damage.)

Similarly, with regard to the removal of the placenta, he states: "No matter what the method of the removal of the placenta (spontaneous delivery, Credé, expression by pure physical force, or manual removal) there was not a single shock death in the present series when the placenta was removed in the first hour. But 35 women died of shock when the placenta was left in utero two hours or more. Some of these patients had previously undergone unsuccessful attempts to express the placenta, and it is now impossible to assess how vigorous these attempts were . . . it seems that more emphasis should be placed on the duration of the long third stage of labour than on the precise technique of the removal of the placenta."

Other conclusions are these: —

"Most of the manifestations of shock are due to a vasoconstrictor mechanism which reduces the blood-flow to skin, muscles, and abdominal viscera, though not interfering with the blood-flow through the brain. The slowing of the blood-flow through most of the body leads to a reduction of the return of blood to the right heart. This interferes seriously with cardiac function, leading to a low pulse-pressure and later to a low arterial blood-pressure. Characteristic subendocardial hæmorrhages occur in the heart, and the patients die finally from what appears to be a failure to maintain even sufficient cardiac output to supply the brain.

"In shock there occur other changes indicating an over-activity of the sympathetic relative to the parasympathetic. These include in many cases dilatation of the stomach and proximal colon. There is no evidence that any primary endocrine disturbance is involved in the production of shock.

"The vasoconstrictor changes in shock are similar to the defence mechanism which occurs in response to hæmorrhage. In shock, however, the mechanism appears to come into action without purpose, and its results are harmful. It is probably evoked by nervous or biochemical factors and not by any significant reduction of blood-volume."

[This paper contains a wealth of information on the clinical features of shock, and on the post-mortem findings in fatal cases: it well repays study in its entirety.—J. C. M.]

Pulmonary Embolism by Amniotic Fluid.—Is obstetric shock the same as surgical shock? Obviously, an obstetric patient may become shocked after a traumatizing delivery—that needs no comment. But every obstetrician of experience has encountered the much rarer condition in which, for no obvious reason, a woman suddenly collapses and may die within a few minutes or a few hours of an apparently normal, easy delivery. The term "obstetric shock" should be restricted to this particular condition. Post-mortem examination does not always reveal a cause of death. Unsuspected rupture of the uterus, inversion of the uterus, or a major vascular lesion may sometimes be found, but there remain many 'difficult' cases which defy all explanation.

In 1941 P. E. Steiner and C. C. Lushbaugh[4] threw new light on this subject. They brought forward evidence that many cases of obstetric shock, or of sudden death during or after labour, are associated with, and presumably caused by, the sudden passage of amniotic fluid and its contaminants into the maternal circulation via the uterine sinuses. Ten fatal cases of obstetric shock were recorded in which special post-mortem investigations showed the presence of multiple small emboli in the lungs, consisting of epithelial squames and other fœtal products.

P. Gross and E. J. Benz[5] now report 3 further similar cases. They were "characterized by the sudden, unexpected development of irreversible shock during labour or the immediate puerperium, and were followed very quickly by death . . . microscopically the diagnosis was established by the demonstration of extensive vascular occlusion by leucocytes and contaminants of amniotic fluid in the smaller branches of the pulmonary arteries".

They make special mention of the appearance of the blood aspirated from the pulmonary artery or the inferior vena cava. (The necessary sample of blood, they say, can also be obtained from the right side of the heart without need for post-mortem removal of the organs.) After centrifuging the blood, three strata are seen instead of the usual two. This, they state, "should be considered pathognomonic of this condition. The particulate constituents of the amniotic fluid, including mucus, being of low specific gravity, settle out as a flocculent layer above the leucocytic cream . . . both smears and sections should be made of this layer. The sections should be cut from alcohol as well as Zenker or formalin-fixed blocks of this sediment".

Pelvic Delivery after Cæsarean Section.- The old advice, "Once a Cæsarean, always a Cæsarean", is nowadays largely disregarded, provided that the patient can be observed in hospital during a subsequent pelvic delivery, and provided that the previous Cæsarean section was done for some non-recurring condition. Nevertheless, there is always some anxiety whether the uterus will, in fact, stand up to the strain of pregnancy and labour. In this connexion it should be borne in mind that a rupture of the Cæsarean section scar, because it occurs in almost bloodless tissue, does not always produce urgent or easily recognized symptoms. Further, the rupture, if it is to occur, not infrequently takes place during the later weeks of pregnancy, and before the expected onset of labour.

D. H. Hindman,[6] of Boston, records 177 deliveries in 118 patients who have had a previous Cæsarean section. There were 8 cases of ruptured uterus. Of these, 6 followed a previous classical Cæsarean section. The remaining 2 patients had previously had both classical and lower-segment operations; one ruptured the classical incision with a small extension into the lower-segment scar; the other ruptured the lower-segment scar with some extension into the bladder.

It is interesting to note that in some cases of uterine rupture there has been a normal delivery between the pregnancy that terminated in Cæsarean section and the pregnancy that has resulted in the rupture. One explanation of this is the position of the placenta; and it is well known that a placenta lying over the old Cæsarean section scar weakens that scar. It is therefore a matter of chance whether or not the scar is weakened in a subsequent pregnancy. Hindman quoted reports by previous investigators to show that in 3600 lower-segment Cæsarean sections only 0·28 per cent of ruptures occurred—one-sixteenth of the number estimated to follow classical Cæsarean section. Among other reasons for this may be the fact that the placenta is unlikely to encroach on the lower segment in any subsequent pregnancy.

Among other interesting points in this paper is the fact that Hindman routinely makes an intra-uterine examination after a normal delivery subsequent

to a Cæsarean section, in order to explore for any small rupture or weak area in the uterine scar. Not only may an unrecognized rupture be thus discovered, but information is gained which may prove valuable in the conduct of future deliveries. Of 112 cases in which this exploration was made, only 4 patients showed any febrile disturbance in convalescence, and in all of them the pyrexia was mild in character.

Which Type of Cæsarean Section ? For many years a swing from the classical Cæsarean section to the lower-segment Cæsarean operation has been apparent; and although the older operation is not entirely discredited, it is certainly outmoded. True, it can give good results but are they good enough ? What of the post-operative disturbances ? the risk of peritonitis ? the frequent adhesion of the uterus to the abdominal wall ? the chance of intestinal obstruction from adhesion of the ileum to the uterus ? and, above all, the risk of uterine rupture with subsequent pregnancies ? Are not all these complications decidedly more frequent after the uterus has been opened through its upper segment ? As for mortality-rates, a recent compilation by R. J. Heffernan and C. L. Sullivan,[7] covering no less than 14,776 lower-segment operations and 15,030 classical operations (the same operators in both cases), shows that the percentage mortality-rate in the first group was 1·52, while in the second it was 3·87. Even so, it is probable that the lower-segment group was unfairly 'weighted' with serious cases (for example, the patient having been long in labour at the time of operation); but despite this bias mortality-rate was less than half that of the other operation.

But while the lower-segment operation now holds pride of place, much discussion is taking place—especially in the U.S.A.—on the best form of that operation in frankly infected cases. Is the *extraperitoneal* approach preferable to the *transperitoneal* approach ? And, in the presence of sepsis, is either of these operations preferably to craniotomy (if necessary, on a living child) or Cæsarean hysterectomy ?

Heffernan and Sullivan discuss the first two options in these words :

"Craniotomy on the living child is mentioned only to be vehemently condemned. It has no place in modern obstetrics, and the claim that sacrifice of the baby saves the mother is disproved by the experience of Baird,[8] who reports a maternal mortality of 7 per cent in 147 cases of craniotomy. Cæsarean hysterectomy for infection adds operative shock and additional blood-loss to that of Cæsarean section, and if the patient is a young primipara the loss of the uterus may indeed be tragic. We have collected from the literature a series of 119 Cæsarean hysterectomies done for infection, with a mortality of 14·2 per cent. We believe that Cæsarean hysterectomy has no place in the treatment of infected patients but should be reserved for parturient patients with fibroids, atonic uteri, or other pathological conditions of the uterus."

The authors then present the case for the modern extraperitoneal Cæsarean operation, which they have performed on 72 occasions without a maternal death. The claim is made that this operation should be used when there is the slightest suspicion of infection, when membranes have been ruptured for a period of eight hours, when the patient has been in labour for six hours or more, or when there has been previous vaginal examination. Some excellent illustrations of the steps of the operation are included in the article; these should be studied against the background provided by the earlier publications of Waters,[9] Ricci and Marr,[10] and Norton.[11]

[Possibly Heffernan's and Sullivan's enthusiasm has led them to over-stress the importance of the extraperitoneal approach. There is no doubt that it presents considerably more technical difficulty than does the usual transperitoneal method and that the danger to the bladder, or even the ureters, is considerable. In fairness to the transperitoneal lower-segment operation it should be stated that it also gives excellent results, even in the presence of infection, provided that the peritoneal pouch at either side of the lower part of the uterus is adequately packed to prevent infected fluid from gaining access to the paracolic gutter,

and that penicillin and sulphanilamide drugs are administered both before and after the operation. Nevertheless, it is reasonable to suppose that the extraperitoneal technique further lessens the risk of peritonitis, and that, in the presence of virulent sepsis, this merit outweighs the disadvantages of that operation. It is also clear that it should be favourably considered as an alternative to Cæsarean hysterectomy.—J. C. M.]

W. J. D. Dieckmann, F. J. Bjork, and G. T. Aragon,[12] of the Chicago Lying-in Hospital, hold other views. They maintain that *hysterectomy* after Cæsarean section in infected or potentially infected patients ensures the lowest mortality, provided that the entire corpus and most of the cervix is removed. Speaking of the extraperitoneal Cæsarean operation they state:—

"Two years ago they (Cosgrave and Waters) reported 483 extraperitoneal sections with 6 maternal deaths (5 due to infection), a mortality-rate of 1·24 per cent. Since most of the operations were performed in infected or potentially infected patients (whom we would have delivered vaginally, if necessary by craniotomy, or by Cæsarean hysterectomy), this low mortality convinced us that this type of operation in the potentially infected patient is far superior to laparotrachelotomy (i.e., transperitoneal lower-segment Cæsarean section) and to difficult vaginal deliveries with their high fœtal mortality and maternal injuries, but has not convinced us that it is safer than Cæsarean hysterectomy in infected patients."

They then present statistics relating to 153 Cæsarean hysterectomies (only 19 of which were, however, performed because of infection). There was one death from peritonitis. Several cases of major complications are also recorded, including damage to bladder and ureters.

[It is clear that the operative procedure best suited to infected cases is not yet settled. Dieckmann and his colleagues are to be congratulated on frankly reporting the major complications as well as the mortality-rate—a procedure far too seldom followed. How helpful it would be if we knew the number of "near deaths", and the frequency of damage to vital structures, encountered by the advocates of the extraperitoneal method of Cæsarean section. My own practice is to use the transperitoneal lower-segment operation almost exclusively both for patients in labour and patients not in labour—and to use it, too, when Cæsarean section is needed late in labour in potentially infected cases (it would then be combined with careful packing, and pre- and post-operative chemotherapy). I should, however, make a possible exception of the patient already obviously septic; for her, provided the fœtus is not of great size, the extraperitoneal operation is probably the safer procedure. Despite the evidence put forward by Dieckmann and his colleagues I doubt whether Cæsarean hysterectomy can give superior results, although there may be special reasons for performing that operation the presence of myomata, for example. Hysterectomy at term, it should be noted, carries a special risk of damage to the bladder and ureters. The uterine supports are then softened and relaxed, and when the uterus is pulled on, the ureters may be drawn up to an unexpectedly high and therefore dangerous position.—J. C. M.]

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LEGAL DECISIONS AND LEGISLATION.

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Legal Decisions

Artificial Insemination and an Annulled Marriage.—Learned counsel have stated their opinion that a child born of an artificial insemination by donor (i.e., a man other than the husband) is illegitimate, and that such an act of

insemination is adultery.[1] It did not, apparently, occur to any of the members of the Archbishop's Committee to consider the status of a child born from artificial insemination with the husband's semen if the marriage is later dissolved. At the end of November last Mr. Justice Pearce tried[2] a petition for nullity on the ground of the husband's incapacity, which was admitted, to consummate the marriage. The husband alleged that the wife had approbated the marriage by accepting artificial insemination. The judge did not agree, and found her perfectly sincere. The evidence was that she had done her best to save the relationship by conceiving a child artificially, but had found herself unable to go on with the marriage. He granted a decree of nullity, but in doing so assumed that its effect would be to make the child illegitimate. With great respect, this surely cannot be right. As the child's status was not one of the issues before him, his remark was not a ruling and so cannot have any legal authority. The child was lawfully registered at birth as the child of the husband, because the parties were married. There is no process by which such an entry, if correct, can be altered, and so the child's registration will continue to show him as legitimate. It would be interesting to see what the court would make of an application on his behalf for a declaration of legitimacy. Herbert's Act, reforming divorce law in 1937, bears on this question. It made wilful refusal to consummate a marriage a ground for nullity proceedings, and laid down that where a child had been conceived before the marriage and legitimized by it, the child should not be rendered illegitimate by the annulment of the marriage, although the effect of a nullity decree is to state that no marriage has ever taken place. The same reasoning should surely apply to the present case. If the child had been conceived, not by artificial insemination, but by fecundation *ab extra*, how could it possibly be called illegitimate? It is not without interest that in a case before a New York court last year Mr. Justice Greenberg ruled[3] that a child was legitimate even though it had been conceived by donor semen, because the father had consented to the insemination.

Nullity after Coitus Interruptus.—Another problem raised by the provision making wilful refusal to consummate a marriage a ground for annulling it is whether coitus interruptus amounts to consummation or not. The House of Lords deliberately left this point undecided when it heard *Baxter* v. *Baxter*,[4] the case in which it refused a decree of nullity asked on the ground that the wife had refused to permit intercourse unless the husband wore a sheath. Two cases came before the Divorce Division within two days in both of which the wife prayed for a decree of nullity on the ground that the husband had always persisted in coitus interruptus. One judge granted the decree, the other refused it. In the first case[5] Mr. Justice Finnemore said, in granting the decree, that many authorities had held that there must be emission into the body of the woman to constitute consummation of marriage. Chitty on Medical Jurisprudence says that without penetration and emission there is incapacity and therefore ground for alleging non-consummation. Dr. Lushington held in a very famous judgement[6] that if intercourse is so imperfect as to be scarcely natural, it is legally speaking no intercourse at all and will not satisfy the second important end of marriage—that of providing a lawful indulgence of the passions to prevent licentiousness. The principle, said the judge, is the same whether the husband is unable to perform the act or whether he refuses to perform it: there is no proper intercourse and therefore no consummation. He distinguished *Baxter's* case,[4] for even with a sheath there may still be a form of intercourse which in these days ordinary people would accept as natural and complete and which therefore amounts to consummation. A coitus which is 'interruptus', however, cannot very well be said to be complete; it is by its nature a partial and incomplete intercourse.

Mr. Justice Wilmer, trying the other case two days later,[7] said that although he naturally had the highest regard for the view expressed by his brother judge Mr. Justice Finnemore, he could not in the circumstances regard his decision as binding on him. On the other hand, he concluded that the reasoning of the House of Lords impelled him to a different conclusion. In the present case full entry and penetration had been achieved. What followed merely affected the probability of conception, which the House of Lords has declared irrelevant. He therefore could not say that this marriage had not been consummated. Nevertheless, he was able to find that the husband's persistence in coitus interruptus although the wife's doctor, after she had seen a mental specialist, had warned him that his attitude was seriously injuring her health, amounted to cruelty. Clearly these two contrary interpretations of what the House of Lords meant in Baxter's case call for a ruling by a higher court. It is a pity that in England the decision of points of law has always to wait for a litigant. In France, where there is a mechanism for referring such questions to the Cour de Cassation for an opinion, they do these things better.

The Longest Gestation Period.—Last year this section noted a record judicially-accepted pregnancy of 346 days.[8] That record was soon broken.[9] A serving soldier, after cohabiting with his wife on August 24, 1944, went overseas and did not return until July, 1945. The wife gave birth to a child on August 12, 1945. The husband petitioned for divorce on the ground of adultery, with this gestation period of 349 days as his only evidence, for the court rejected suggestions that there was other evidence. Medical witnesses said that it was not impossible for the husband to be the father of the child, and the Court of Appeal would not infer that the wife had committed adultery. Its reasoning was that adultery has to be positively proved to a reasonable degree of probability; that there must be a point at which no court could believe that the child was conceived at the last intercourse between the parties to the marriage, but that in this particular case the court could not declare that the line had been overstepped. Sydney Smith, referring to the earlier case of *Gaskill* v. *Gaskill*,[10] mentioned the evidence of Dr. Watts Eden that children had been born after pregnancies of 323, 324, and 336 days, weighing 12·5, 14, and 16·5 lb. respectively. Such pregnancies may, it seems, persist in spite of two or even three menstruations. Dr. S. M. Wells, of Valparaiso, Chile, reported a case in the *British Medical Journal* (Jan. 15, 1949, p. 116) of a woman whose last period was on May 5 and who was delivered on April 3 of a child which hardly weighed 9 lb — 334 days maximum and about 320 probable.

It will be very interesting to see where the limits of the court's patience in this matter are reached; but that can hardly come about until the medical witnesses are prepared to assert that a given pregnancy was too long to have conceivably resulted from the last legitimate intercourse. The scientific grounds for such evidence will only be available when the mechanism of delayed birth—and even that of the onset of normal birth—have been conclusively demonstrated.

An Invalid Partnership Agreement.—Cases involving medical business relations are so rare that solicitors have had very little guidance in avoiding the pitfalls of drafting agreements between partners, between principal and assistant or locum tenens, and the like. Now and again a sensational case occurs to show that many such agreements forming the legal foundation of a practice in which more than one medical man takes part would not hold water if contested in court. The case of *Jenkins* v. *Reid*[12] is the latest of these. Dr. Jenkins, a general practitioner of Gloucestershire, took Dr. Alexander Reid into partnership on July 1, 1939. Mrs. Jenkins was also medically qualified, but took no regular active part in the practice, having work of her own, a part-time appointment at one of the antenatal clinics of the Bristol Corporation. The partnership

agreement provided that a partner who withdrew or was expelled should not at any time thereafter practise as a physician or surgeon or apothecary within a radius of ten miles of the post offices of two named towns where the partnership had surgeries. It also bound Mrs. Jenkins, during the continuance of the partnership or after Dr. Jenkins ceased in any way to be a partner, not to practise without the consent of a partner at any time thereafter as a physician or surgeon or apothecary within a radius of five miles of the two post offices, or professionally visit or consult with any of the patients of the practice, except that she could continue her own work. In August, 1939, Dr. Jenkins joined the Navy, and Mrs. Jenkins worked for the partnership during the war and even after his return. Her formal contract as an assistant was terminated in May, 1947. Wishing to continue in practice, she applied to the Chancery Division to determine whether the deed was void as contrary to public policy, too vague, and in unreasonable restraint of trade.

The courts apply a different standard to these covenants according to whether the parties are purchaser and vendor or master and servant. In the former case the restriction can reasonably be wider, because value is being paid for it; the vendor is selling goodwill and should be strictly bound against derogating from it. These considerations do not apply when the covenant restrains a servant on quitting employment. Public policy requires that every man shall be at liberty to work for himself, and shall not be at liberty to deprive himself or the State of his labour, skill, or talent by any contract that he enters into. The court held that, having regard to the wide scope of the covenant, which extended to prohibit Mrs. Jenkins from acting as a consultant or a specialist, the first part was bad as not reasonably necessary for the protection of the practice. He did not need to decide whether the first part could be severed from the second, because this was bad also. It prohibited Mrs. Jenkins from doing something which was remote or foreign to the nature of the general medical practice carried on by the partners—viz., consulting with any of the patients. This would presumably include acting as a consultant; but apart from that the whole wording was so hopelessly vague that it would be almost impossible for her or anybody else to know whether or not she was breaking her covenant. She could not even know whether a given person was a patient of the partnership. Moreover, there was no limitation of the area. He therefore declared that the restrictive clause was void, and the effect is to leave Mrs. Jenkins completely unfettered by the agreement.

Loss of Expectation of Life. When the law was altered in 1934 to give the next-of-kin of a person killed by negligence a claim in respect of the person's loss of expectation of life, the courts soon had some knotty problems to solve, which this ANNUAL chronicled from time to time. The position was eventually stabilized by the House of Lords, which held[13] that the correct measure of damages is the loss of prospects of a happy life. Mr. Justice Streatfield, therefore, had something to guide him in trying[14] a recent claim in respect of the death in a motor accident of a girl of four. The child would have lived in a slum area and would have been deserted by her mother, who had left her father, so the prospect was not happy, though it might have improved as time went on. The loss of expectation of the child in the House of Lords case had been valued at £200. The judge said that although he would have awarded less than that had he been considering like values, the depreciation of the pound sterling justified him in awarding the same amount in this case. Further, though he allowed the expense of embalming the body, thinking that this was not unreasonable, he was clear that a claim for £225 for a monument to be erected over the grave must fail. Funeral expenses within the meaning of the Assurance Companies Act, 1909, include the cost of an ordinary stone or tablet, but to

make a negligent motorist pay for a monument is beyond reasonable and proper limits.

Cruelty of an Invalid.—In this section last year, under the sub-heading " An Exacting Invalid ", a case was mentioned in which a husband sued for divorce on the ground of a rather unusual form of cruelty. He proved that his wife had for a long time been an invalid, and that she had systematically for nights on end prevented him from sleeping, demanding that he read to or talk with her ; if he showed signs of going to sleep, she unreasonably demanded that he should perform various menial services for her and stripped the clothes from his bed, moved the furniture, and switched the lights on, whereby he was deprived of sleep and suffered in health. The trial judge found that she had never deliberately set out from spite to hurt him or to prevent him from sleeping because she could not sleep ; there had been no such deliberation, malignance, or intention as to amount to legal cruelty. The Court of Appeal, however, has since reversed this decision and allowed the husband his divorce,[15] holding that malignant intention is not an essential element of cruelty. Mr. Justice Hodson dissented, not from this statement of the law, but from the finding that the cruelty was proved in fact. Both courts emphasized that the state of affairs when a cruel spouse is insane is quite different, since in that case he or she is not responsible for his acts in law.

Medical Examination of a Motorist.—The conduct of doctors when called to examine motorists charged with drunkenness in charge of a car was dealt with in an interesting case in the King's Bench Division.[16] Some police officers saw a motorist drive on the wrong side of the road without lights at night. They decided that he was drunk and took him to the station. A general order was made many years ago that whenever a man is charged with being drunk and seriously denies it, a doctor must be sent for if possible. The police surgeon accordingly came and explained that it might be in the motorist's own interest that a doctor should be allowed to examine him. The motorist did not wish to be examined, but the police surgeon was a little persistent, and ultimately the man agreed to be examined but, to use his own expression, which the Divisional Court found significant, was 'very awkward' about it. The police surgeon then certified that owing to his consumption of alcohol he was in an unfit state to drive a car. At quarter sessions he was fined £50 and had his licence suspended for a year. He appealed to the High Court on the ground that the evidence of the police surgeon was inadmissible because he had improperly examined a man who was refusing to be examined, though it was not suggested that he had used any force. The court found that the doctor had from beginning to end behaved perfectly reasonably in the interests of the motorist, and the mere fact that at one time he said : " It may be better for you " or " It may be to your advantage " that he should examine him, could not be regarded as an inducement to do something so as to come under the law which excludes confessions made as a result of persuasion, promises, or threats.

Mr. Justice Humphreys, in his judgement, made some interesting observations on a Scottish case in which the Lord Advocate had conceded that the police surgeon or other doctor summoned by the police to conduct an examination was acting as the hand of the police and not as an independent medical referee. The English court, he said, did not agree that that state of things existed in this country. The court's view was that the evidence of a doctor, whether he was a police surgeon or anyone else, should be accepted, unless the doctor himself showed that it ought not to be, as the evidence of a professional man giving independent expert evidence with no other desire than to assist the court.

Signature of a Will. The Wills Act, 1937, is very strict on the attestation of a will but lenient in the matter of its signature by the testator. He must have

a sound disposing mind and intend to sign the will, and he must do so in the presence of two witnesses, who must also sign the will, all three being present together. The testator's signature need not be in any particular form, and need not even be legible. A simple cross will do, if it is the best signature of which he is capable, if he knows what he is doing, and if he acknowledges it as his signature in some way. The signature by the witnesses in the physical and mental presence of the testator is, however, unconditionally vital. An elderly woman suffering from cancer was on the point of death and was given a strong dose of morphine.[17] Her daughter, in the presence of other members of the family and of two attesting witnesses, prepared a short codicil to her will. This was shown to the testatrix, and she was asked whether it gave effect to her wishes; she nodded assent. The daughter then put the paper before her and, supporting her on the bed, said: "If you can't sign your name, put a cross". The dying woman took the pen and began to sign her name, but when she had got as far as her initial and half her surname she stopped, and never completed the signature. The witnesses immediately signed the document, and from then onwards the testatrix was never really conscious. The case turned on whether the uncompleted signature, which she had undoubtedly acknowledged, was sufficient. The opponents contended that a testator may execute a will by putting initials or a mark provided that he forms the intention of doing so; but that if he starts out with the intention of doing any one of these things, and never departs from that intention yet never completes what he set out to do, he has not executed the will. The judge, Mr. Justice Wilmer, thought there must be some question of degree. If he could draw the inference that what she wrote was intended by her to be the best that she could do by way of writing her name, he ought to accept this incomplete signature as her signature. Bearing in mind all the circumstances, including her weakness and her difficulty in which while lying very nearly on her back, he came to the conclusion that this mark amounted to all the circumstances to a signature by her.

He had still to decide whether the witnesses had attested the document in her presence, for if she had relapsed into unconsciousness before they signed it, she would not have been mentally present. His decision, he said, depended on all the evidence. If when she broke off the signature she was overtaken by a mental blackout, she would not have been present because she would have been completely incapable of understanding what was going on. On the evidence of the doctor, however, the operation of the drug, though swift, would be gradual, inducing drowsiness and relief from pain, which would in turn induce sleep for the closing stages of her life. This seemed to the judge inconsistent with a sudden departure of her mental faculties. He thought the proper inference to draw was that throughout all these critical moments she was losing her faculties gradually. Considering that the codicil was attested immediately after she had written what she wrote, the true inference was, he thought, that she was still mentally present to a sufficient degree to make the attestation valid. Although the case was difficult and often very near the borderline, he decided that this was a validly-executed and attested codicil.

Control over Nurses' Agency.—Under the Nurses Act, 1943, a person who carries on an agency for the supply of nurses must obtain a licence from the local authority. These may impose certain conditions, including conditions as to the fees to be charged by the person, whether to the nurses or the patients. The Middlesex County Council, in issuing a licence to an agency, purported to limit its charges to a scale fixed by themselves. An appreciable proportion of the nursing staff of their hospitals is supplied by agencies, and the higher rate these nurses charge is a source of discontent to the permanent staff and an incentive to them to leave before completing training. A possible motive for

the Council's action may therefore (though it did not appear in the report of this case) have been to reduce the gap between the remuneration of agency and of permanent nurses. The Hendon justices, who allowed the agency's appeal, held that this condition was outside the powers given to the Council by the Act. The Council appealed, and the King's Bench Divisional Court upheld the justices.[18] Lord Goddard, Lord Chief Justice, said that the agency did not actually employ nurses itself but found employment for nurses on its books at the salaries which the nurses required, rendering accounts to the client, collecting the amounts, and paying it to the nurse after deducting a commission of 10 per cent. The Council had inserted a condition that the agency should not collect from a patient more than a maximum sum which the Council had taken upon itself to prescribe, quite independently of whether or not the nurse was willing to work for that amount of money. If the nurse would not work for that sum, one would arrive at the rather curious position that the agency could collect on her behalf, say, five guineas a week, and she could then say to the client that she wanted to be paid direct another two guineas a week. This was not a condition as to the proper conduct of the agency. The relevant section of the Act was aimed at undue fee-snatching by persons carrying on employment agencies; the court saw nothing in the present case to suggest that if a nurse was willing to work for the patients whom the agency found for her but required seven guineas a week, and the agency told the patient that that was the charge, that was not proper conduct by the agency. The condition attempting to control nurses' fees was therefore declared invalid. This case, according to the *British Medical Journal*, affected about 20,000 nurses, mostly in the London area.

Accident or Medical Inefficiency? A coal miner had a rare deformity of his thumb: a rudimentary second thumb which grew from the top joint. A stone flew off the shovel he was using and fractured the bone of this excrescence. He was splinted and rested, and then put to light jobs about the colliery. The thumb, however, remained painful and interfered with his work, and so he consulted his own doctor, who sent him to the emergency hospital. The surgeon advised that the superfluous bone and also the normal top joint should be removed. This was done, but the stump remained sore and disabling. The workman claimed compensation from the company, but the county court judge refused it, holding that the soreness resulted from the amputation and not the injury. The Court of Appeal, with regret, agreed.[19] A line of decisions has resulted in the principle that negligent or inefficient treatment by a doctor or other person may amount to a new cause and the circumstances may justify a finding of fact that the existing incapacity results from the new cause and not the original injury. Though submitting to this principle, Lord Greene, Master of the Rolls, did not hesitate to criticize it. He recalled that it had been first laid down in a case where the negligence was very serious, but in course of time it had reached the point where mere inefficiency is enough to exonerate the employer. The unfortunate workman is now in the position that he may call his doctor who says, "I gave this man the treatment I considered right"; and the other side may call more eminent or persuasive doctors who say that the treatment was wrong, and the judge can then find on the facts that the treatment was the cause of the disability. Such anomalies, and others which favour the workman, prove the irrelevance of the judicial method in workmen's compensation.

Silicosis not an Accident. The meaning of "accident" in workmen's compensation has been extended during the years by the beneficial interpretation of the courts, especially the House of Lords, to include the invasion of the body by an anthrax bacillus, blood-poisoning due to a long series of scratches,

and recently Raynaud's disease due to the constant vibration of a rotary instrument,[20] and hernia due to that of a pneumatic drill.[21] An attempt was made last year to induce the courts to add silicosis. This disease is not a scheduled industrial disease but is covered by a special scheme. This benefits, however, only persons who have been employed in cutting silica rock, and so a workman who became totally disabled by silicosis in a slate quarry could illogically not benefit by it.[22] He therefore attempted to bring his case within the line of "cumulative" accidents by arguing that the injury done by each particle of silica to the lungs was a separate accident in a long series. Lord Porter, giving judgement in the House of Lords, said that in silicosis it is, of course, possible to divide up the cause of the final collapse and say that each particle of silica striking upon and adhering to the lung is a separate accident; but, however analytically maintainable, the attribution of the resultant silicosis to an accidental cause is unreal. The distinction between accident and disease has been insisted upon throughout the authorities and is well founded. There must come a time when the indefinite number of so-called accidents and the length of time over which they occur take away the element of accident and substitute that of process. In his opinion disability from silicosis is one of such instances. The appeal was therefore dismissed.

Suicide and Pension.—A Scottish case[23] showed the bias in favour of the applicant that exists in the modern law of Service pensions. A Glasgow tram driver suffered from nervous disturbance after a fatal accident and gave up his job. He was called up to the Army next month, but deferred for six months. When after that interval he was taken into the Army, he drowned himself in the sea after a fortnight. His widow's application for a pension was refused by both the Minister and the tribunal, but allowed by the Court of Session. The Lord Justice-Clerk, Lord Thomson, thought that the tribunal had not properly asked itself what effect Service conditions had had on this particular man. It had concluded that the deceased had committed suicide because he was depressed when he enlisted, that the depression was a continuation of a pre-Service condition from which he had never recovered, and that his brief Army life had been "happy". The judges could not help feeling that that cryptic finding involved the idea that there was need only to establish that the deceased's Army life had been such as would not upset a normal man. This was not the proper test, and there was no evidence to enable the court to affirm that Service conditions had not played a part in aggravating the man's depression and so precipitating the tragedy. The court therefore awarded the widow a pension.

Disablement for Pension.—A soldier during his service twice strained his right ankle, which left him with a post-traumatic arthritis. It was treated, and he suffered very little ill effect for the last two years of his service. On discharge he claimed a pension on the ground of arthritis, but was refused by the Minister on the ground that there was no disability. He appealed to the High Court,[24] saying that, even so, he was still entitled to an award of entitlement, which would enable him to claim a pension should he become worse in the future. Mr. (now Lord) Justice Denning was satisfied that, under the Royal Warrant which governs pensions, there must be a 'disablement' before there can be an award of entitlement. Disablement for this purpose, however, does not mean incapacity, but "physical or mental injury or damage, or loss of physical or mental capacity". Therefore, if there is a physical injury or damage, even though it does not cause any loss of capacity at the moment, it comes within the meaning of the Warrant, and an award of entitlement may be granted which will not give rise to the actual grant of a pension unless and until incapacity appears. The claimant's post-traumatic arthritis was a "physical injury or

damage " and was therefore a disablement, but for the time being he was not entitled to any money. The judge therefore allowed the appeal and made an award of entitlement with a *nil* assessment.

Legislation

National Health Service.—On July 5, the appointed day, the National Health Service became operative. In the words of Mr. H. L. Linstead in the debate in the House of Commons on January 21, 1949, the service was on the rails and moving, but it was creaking and groaning.[25] According to the Government, 95 to 98 per cent of the population joined the scheme. Millions of persons, especially housewives, who had never before been able to afford treatment and appliances such as spectacles and dentures now flocked to take advantage of their new rights. Dentists were overrun, and their earnings had to be curtailed by special order of the Minister. By the beginning of the New Year the rush was showing signs of subsiding. The effect of the scheme on the medical profession in the first six months was catastrophic. Doctors in large industrial areas found themselves slightly better off, but elsewhere incomes fell off so seriously that thousands of practitioners were thrown into severe financial distress and anxiety. Work everywhere became much heavier. The Government promised that if by the end of March the remuneration of general practitioners was not shown to accord with the recommendations of the Spens Committee, the arrangements would be reviewed. All sides were agreed that the position would have to be remedied swiftly, but the general opinion was that so vast and novel a scheme could not be judged on its initial working. There is obviously room for great change before the next issue of this ANNUAL appears.

From the point of view of the profession, against the obvious disadvantages, Mr. R. W. Cockshut listed[26] a number of what he regarded as substantial gains. The first of these by far he thought to be the preservation of the principle of free choice. The others included the exclusion of the local authorities from the control of hospitals and general practice; the retention of private practice and competition between general practitioners, and of practice at doctors' own premises and not at health centres; no universal basic salary and consequent control of certification; the prospect of settlement of the question of compensation for loss of partnership rights (*see below*); freedom to choose a partner or assistant; freedom to set up in practice in areas not closed by the Medical Practices Committee; legal representation before the appeal tribunal; freedom of speech and criticism; consultation on the drafting of all regulations; and freedom of any practitioner to attend any woman in confinement if both desire it. He claimed that clinical freedom had thus been secured.

Medical Partnerships.—A practitioner who belongs to the National Health Service may not sell his share of a partnership practice. The Act provides for compensation for loss of goodwill, but the Medical Practice Compensation Regulations, 1948,[27] do not provide for the determination of loss and the distribution of compensation. With a view to legislation, the Minister appointed in April, 1948, the Slade Committee to consider whether the sections of the 1946 Act dealing with partnerships should be amended. The Committee, reporting in November,[28] recommended that nothing in those sections should be deemed to render unlawful the due fulfilment of obligations or due exercise of options in existing partnership agreements. It recommended certain modifications of existing obligations and options where agreements do not expressly provide for the manner in which compensation for loss of goodwill is to be divided among the partners. Where all partners have joined the service and one is obliged to sell a share of his goodwill to another, the transfer of that share should be free and the transferring partner should be entitled to compensation in lieu of

payment of the purchase price. Where a partner not participating in the scheme is under an obligation to purchase a share from a partner within the scheme, the committee think the obligation should be converted into an option; and if this option is exercised the partner who is in the scheme should take the purchase price and forgo his share of the compensation. Where a partner who has joined the service is entitled to purchase a share from a partner outside the scheme, he should on paying the contract price be entitled to compensation out of a supplementary compensation fund which should be set up. To deal with individual cases of hardship the committee recommend that every existing partnership shall be considered to contain an arbitration clause whereby questions of hardship may be determined by a single arbitrator to be nominated by the partners, or, failing agreement, by a committee of arbitration. The hardship should not, they consider, be a ground for dissolution by the court unless the arbitrator or the committee of arbitration so recommend.

Criminal Justice.—The Criminal Justice Act, 1948, abolished penal servitude, hard labour, prison divisions, and sentences of whipping. Probation orders may now contain a condition requiring the offender to submit to medical treatment with a view to the improvement of his mental condition, if the court is satisfied on the evidence of a psychiatrist that treatment is necessary and may succeed but he is not certifiable as a person of unsound mind. The order may specify treatment as a voluntary patient, or as resident patient in a specified institution, or as a non-resident patient, or by or under the direction of a specified practitioner, but the court has no further power to specify the treatment, and may only make such an order if it is satisfied that arrangements can be made for the treatment and reception of the offender. The practitioner may for good therapeutic reason, and with the consent of the probationer, move the place of treatment, but must notify the probation officer. The order lasts for a year. The court may not treat as a breach of a condition of the probation order a refusal, reasonable having regard to all the circumstances, to undergo any surgical, electrical, or other treatment.

Persons under twenty-one may now as an alternative to imprisonment be ordered to be detained in a detention centre or to attend an attendance centre (out of working or school hours), if there is accommodation at one of these institutions. Persistent offenders may be sent to a prison for corrective training for a period of two to four years, or for preventive detention for five to fourteen years. Before making the order the court must consider any report of the Prison Commissioners on the offender's physical and mental condition and his suitability for such a sentence. A court of summary jurisdiction trying a person for any act punishable with imprisonment may, if it is satisfied that the accused did the act, and—on the evidence of at least two doctors—that he is of unsound mind and a proper person to be detained, make an order with the force of a summary reception order for his reception and detention in a named institution, and must then send to the institution any information it possesses that it considers likely to help in dealing with the accused. The court may also remand an accused person in custody or on bail for not more than three weeks for medical examination and report, and the person may be received for that purpose into an institution under the Mental Treatment and Mental Deficiency Acts; but by the Mental Deficiency (Amendment) Regulations, if the institution is already full the person cannot be received into it without the consent of the Minister. The term "Broadmoor institution" has been substituted for "criminal lunatic asylum", and "Broadmoor patient" for "criminal lunatic", as an expression of a more rational and curative attitude towards persons who have committed crimes for which mental disease has rendered them irresponsible. The Act will, when implemented, restore this country's previous supremacy in the treatment of young offenders.

Children.—The defects of the country's provision for children in need of care and protection were dramatically brought to light by recent criminal proceedings and the report of the Curtis Committee. With commendable promptness the Government and Parliament have passed the Children Act, 1948, which goes a considerable distance in the required direction. It throws on local authorities the duty to receive into their care (i.e., by boarding-out or in homes) orphans, deserted children, and children who otherwise cannot be properly accommodated, maintained, or brought up, and of furthering their best interests and giving them opportunity for the proper development of their character and abilities. The authority must keep the child as long as his welfare appears to require it until he is 18. They must, whenever to do so seems consistent with the welfare of the child, try to secure that he is taken over by a parent or guardian, or by a relative or friend of the same religious persuasion. In proper cases the authority may resolve to adopt all the rights and powers of a parent or guardian. Unless a probation or supervision order is made, an authority cannot refuse to have a child committed to their care as a 'fit person' by order of a court. The Home Secretary will make regulations for boarding-out and the conduct of homes, and may close a home, or order an authority to remove a child from a voluntary home. The provisions for visiting and inspection are improved. An authority may arrange for the emigration of children, and provide hostels for persons over school age but under 21, and contribute towards the cost of maintaining, educating, or training persons over 18 but under 21. Voluntary homes are to be registered and their conduct is subject to regulation. Local authorities must advise and befriend up to the age of 18 all children over school age who have ceased to be in the care of a local authority or of a voluntary organization, unless they are satisfied that the interests of the child do not require it. The provisions of various Acts for the protection of child life are extended from children under 9 to all children of school age, and in certain cases to children up to 18. Local authorities must establish a children's committee and appoint, subject to the approval of the Home Secretary, a children's officer (who will usually be a woman), and the Home Secretary is to appoint an advisory council on child care for England and Wales and another for Scotland.

Radio-active Substances. In view of the imminent great expansion of the use of radio-activity, the Government introduced and Parliament passed the Radio-active Substances Act to secure protection for the health of workpeople and of the public against the harmful effects of exposure to dangerous radiation. The Minister has wide powers to make regulations, after consulting with a powerful advisory committee appointed after consultation with the Royal Colleges, the medical corporations, the Medical Research Council, the Faculty of Radiologists, the Physical Society, the Department of Scientific and Industrial Research, and the British X-ray and Radium Protection Committee. The Act prohibits the sale or supply to the public of medicines or toilet preparations containing more than a prescribed quantity of radio-active material, except by a doctor or dentist holding a licence for the purpose from one of the Health Ministers or by a chemist under the authority of a prescription from a licensed doctor or dentist. The administration of radio-active substances even by licensed doctors and dentists is limited. The use of irradiating apparatus emitting rays above a certain strength to be laid down is subject to licence, but specified classes of persons may be exempted. Regulations may lay down codes of safety precautions for protection in premises where radio-active substances and irradiating apparatus are used, and in hospitals and laboratories. The Minister may also ensure by regulation that waste products from factories and the like are safely disposed of. The Minister of Supply may manufacture, process, and distribute radio-active substances, and the Government hopes to

improve the supply of radio-active substances of all kinds for medicine, research, and industry. Import and export control is to continue. The restriction on the doctor's freedom of treatment which the Act implies is bound to be distasteful, but the case for it is good, and the strong representation of the profession on the advisory body should prevent the restriction from becoming vexatious.

Factories.—The Factories Act, 1948, amends the principal Act of 1937 in some important respects.[29] The examining surgeons are now to be called "appointed factory doctors". Where there is no appointed factory doctor, the medical officer of health for the administrative county or county borough will act instead. Young persons under 16 entering factory employment and work on ships and building for the first time have to be certified fit, and re-examination will be required at least once a year. This provision partly implements an international labour convention of 1946. The powers of the Minister to require medical supervision are widened to cover changes in the conditions of work and the arrival of a consignment of suspected material. Courts of summary jurisdiction may prevent and stop the use of industrial premises regarded as unsuitable from the point of view of the safety, health, or welfare of the employees.

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LEPTOSPIROSIS. (*See also* WEIL'S DISEASE.)

LEPTOSPIROSIS CANICOLARIS. (*See also* WEIL'S DISEASE.)

Una Ledingham, M.D., F.R.C.P.

Infection with *L. canicola* is a common infection of dogs in most parts of the world. The animals remain potentially infectious for months after recovery, the organisms being excreted in the urine. Leptospirosis in man was thought until now to be almost always due to *L. icterohæmorrhagiæ*, as under 100 cases of the *canicola* infection were reported from all over the world, only one case coming from England. Two recent reports, however, suggest that the disease is commoner than this, 17 cases in Amsterdam[1] and 4 cases in England[2] being diagnosed within sixteen months. Infection was contracted through known association with dogs in five-sixths of the two series and the organism was recovered from the offending dog on several occasions. Happily, other human contacts with these dogs neither developed the illness nor showed any serological evidence of it. The almost uniform onset was acute, with high fever, intense headache, dizziness, vomiting, or muscle pains. Conjunctivitis, rashes, and epistaxis sometimes followed. Most striking was the meningeal aspect. Not only was Kernig's sign positive together with other signs of meningeal irritation, but protein and cells in the C.S.F. were consistently raised. There is thus a striking resemblance to Weil's disease. The cells were either lymphocytes or mononuclears. In contrast to Weil's disease, gross leucocytosis was not seen and normal blood-counts were the rule. Precise diagnosis is only made by specific agglutination tests, the titre rising after the second week to 1–3000 up to 1–10,000. The authors make a strong plea for consideration of this disease in cases of lymphocytic meningitis and think that less severe types of infection will be diagnosed more frequently if the possibility is borne in mind.

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LEUCOTOMY.

E. W. Anderson, M.D., F.R.C.P., D.P.M.

There is much activity in this field of study from many angles. This procedure, introduced as a form of therapy is shedding *inter alia*, an increasing light on the functions of the frontal lobe, studies which constitute a considerable and important sector of the growing edge of psychiatry to-day. It would be impossible in this space to review the substantial literature of the past year in all aspects of the subject; only one or two points are selected for comment and one or two illustrative articles, mostly of clinical bearing, reviewed. In general, the published reports vary between individual cases such as that of W. Sargant and C. M. Stewart,[1] who report dramatic recovery with restitution of working capacity in a war hysteric, and the case of gross organic psychosis reported by J. W. Friedlander and R. S. Banay[2] and reviewed in detail below. Other recorded results lie between these extremes. It is widely recognized that this diversity of experience rests on a number of variables, one of which is certainly the lack of scientific selection and study of the individual cases, not merely before, but also after operation. Thus L. Frankl and W. Mayer-Gross[3] stress the necessity for study of the patient's pre-psychotic personality, the changes referable to the illness up to the time of operation, and comparison of these with the post-operative effects. Since it is well known that improvement can follow leucotomy up to a period of two years or even more after operation, an adequate follow-up must extend over this time, and in the event of death an autopsy should be performed. Meyer and McLardy found themselves hampered in their study mentioned below through lack of adequate data before and after operation. As A. Meyer[4, 5] remarks elsewhere, "prefrontal leucotomy furnishes us on an unprecedented scale with an experiment on human frontal lobe structure and function". The situation has been summed up forcefully by W. C. Halstead, H. T. Carmichael, and P. C. Bucy[6] as follows: "Unfortunately, aside from their value as vital statistics, it is impossible to assess the validity of these findings [results of leucotomy]. At no point have there been other than superficial attempts made to standardize the criteria for the pre-operative and post-operative clinical status of a patient: not a single patient has been adequately studied. For a moral and social responsibility to do this, there has been substituted a phenomenal array of case statistics. Unfortunately the pyramiding of unknowns is scarcely a pathway to knowledge." [There would seem much to be said for the limitation of leucotomy to a few centres staffed by personnel with the necessary training in clinical, psychological, pathological, and social investigation.—E. W. A.]

Another factor is the site of the cut. A. Meyer, whose work on this problem is widely known, has, with T. McLardy, in a clinico-anatomical investigation of 40 cases, shown that unfavourable sequelæ followed a posterior cut much more often than with an anterior, 42 clinical items as against 8 in a series of 40 cases. (The authors define posterior cut as one involving the posterior half of the orbital region, the striatum, the pre-motor region (Brodmann's areas 6 and 44), the region of the external capsule, or any combination of these). Further, the survival period of cases with posterior cuts is on the average much less, 6½ months as against 1½ years with more prefrontal cuts. Also, whereas only 1 case with a posterior cut out of 17 with bilateral involvement of the striatum or the posterior orbital region or both died from an intercurrent disease, 10 out of 18 cases with an anterior cut did so, and posterior cuts, especially if they involve the striatum or posterior orbital region, tend to determine "delayed post-operative death". The personality change tended to be most severe when the posterior lesion was most widespread. Some degree of change occurred in 8 of the cases with lesion limited to the prefrontal region. The authors conclude, therefore, that personality change does not depend upon, but is amplified by, damage to

the posterior region of the frontal lobes. The authors stress this, since it is at variance with D. O. Hebb's[7] contention that personality is not affected by almost complete removal of both prefrontal regions. Again, such symptoms as general restlessness, vasomotor, and trophic changes, nutritional deficiency (2 cases), hyperpyrexia (3), and respiratory disturbance (1) were all associated with posterior cuts. One case of uræmia occurred, but its relationship to the brain damage was considered doubtful. Since 4 cases with posterior cut confined to the external capsule showed no sequelæ it is clear that the anatomical substrate involved does not include the external capsule, insular cortex, or uncinate fasciculus, which was involved bilaterally in at least 3 out of 4 cases. Eight cases showing persistent incontinence had had a posterior cut, and only 1 anterior. Epilepsy was associated in 2 cases with an anterior cut. In the third case with posterior cuts the relationship to the operation was doubtful, since this symptom did not appear till 2 years after the operation and 2 courses of E.C.T. had been given in the interval.

That the site of operation is related to many of the undesirable sequelæ of leucotomy, notably personality deterioration and incontinence, has stimulated investigation into improved or modified surgical techniques. Thus R. G. Heath and J. L. Pool[8] have resected bilaterally the rostral part of Brodmann's area 9. The more caudal portion was left on account of its proximity to the motor and speech areas. Anæsthesia is induced with intravenous pentothal and maintained by nitrous oxide and oxygen. Details of the operation are given, but limitations of space bar detailed description.

The desired segment of cortex is removed by cutting at right angles to the brain to the fullest extent of the grey matter and no further. All segments included the rostral, one-third of the superior frontal gyrus, and an adjacent portion of the middle frontal gyrus. The medial portion of the superior frontal gyrus was always included. The average duration of the operation was 5½ hours. There were no post-operative surgical complications. All patients were ambulatory within days of the operation. No case of post-operative epilepsy was reported.

The authors state that they have carried out the procedure on a large number of cases, but only the 4 followed up for longer than 8 months are reported. One of these was a woman of 58 with a manic-depressive illness of 28 years' duration who was referred for surgical treatment on account of destructiveness, abnormal eroticism, and dirty habits; 12 months after the operation it was stated that she was very well. No details are given. The second, a woman of 42, had a schizophrenic illness of 4 years' duration, with delusions, auditory hallucinations, "confusion", and periods of over-activity and destructiveness. The hallucinations disappeared after the operation. During the 3rd week after operation her garrulity and distractibility began to subside and she was eventually discharged home and later resumed work satisfactorily outside. In this patient some defect in abstraction, and of foresight, was reported. The latter improved somewhat. Her behaviour was never embarrassing. Her blood-pressure, initially 186/114, slowly dropped to 160/90 after the operation. Of the 2 other cases, 1, a catatonic schizophrenic of 32, showed no essential improvement, though again the hallucinations seemed to have disappeared and the thought disturbance was less prominent; the other patient, a hebephrenic of 22 whose hallucinations also disappeared after the operation, did not improve much, but his family were able to manage him at home.

No incontinence, trophic changes or œdema, or convulsions occurred after operation in any case. Social behaviour did not deteriorate and no post-operative apathy or retardation [*sic*] was observed.

The authors attribute the absence of complications with this procedure to the fact that a large proportion of the radiation between the cortex and lower centres remains intact. Their results thus support those of Hebb.

W. Freeman[9, 10] has proposed leucotomy by the transorbital route. This is a development of a suggestion made by A. M. Fiamberti[11, 12] before the war and later carried out by him, in which briefly the frontal lobe is penetrated through the orbital plate by a sharp instrument which is moved laterally and medially through 15–20° thus destroying a triangular area in the anterior part of the frontal lobe. Electro-shock is the anæsthetic of choice. Complications occurred in 3 out of more than 100 operations. In all of these cases there was bleeding, with severe inertia and paralysis in one and "mild hemiparesis" in another. The advantages claimed are similar to those of topectomy as already described by Heath and Poole (loc. cit.), and are said to consist in the absence of undesirable personality changes, although tactlessness and indolence are occasionally noticed. Some patients are stated to have returned to their household duties within a week of operation. The operation is thought, in accordance with the views of this school, to have a more beneficial effect on some symptoms than on others. Thus, anxiety and emotional tension are said to be reduced or eliminated, and depressive ideas, phobias, and obsessional thoughts usually to improve, whilst fixed delusions, hallucinations, and motor compulsions or ties remain essentially unchanged. In consequence patients with involutional depression and anxiety states are said to do well, as also schizophrenics, who improve but relapse. Patients with long-standing and intractable pain have not responded as well as to leucotomy. In chronic schizophrenia the operation is usually contra-indicated. One 'advantage' cited is that the psychiatrist can easily learn to carry out the operation by himself. [It is unlikely that this will be universally acclaimed as such. E. W. A.]

On the assumption of Freeman and Watts that the affective changes following leucotomy are due to atrophy of areas in the thalamus following severance of connexion between thalamus and cortex, attempts have also been made, as mentioned by Freeman, to destroy a few minute areas in the thalamus by electro-coagulation.

F. Reitman,[13] in a follow-up study of 60 out of 250 patients discharged who had remained well after leucotomy, found that discharge was significantly more frequent when a low vertical incision was used, and that personality modification could be obtained better by the orbital than by other incisions. He attributed these changes to structural damage to the lower quadrants of the frontal lobe, i.e., to destruction of a particular site, which is not in accordance with Meyer's results to date, which afford no grounds for belief in narrow localization of specific mental functions. Reitman found that patients showing introversion, lack of initiative, and shallow affect tended to respond more favourably to the low vertical cut. He shows the influence of a fairly well preserved pre-operative personality in ultimate adjustment. None of the patients with this cut showed post-operative convulsions.

Amongst recent results of leucotomy may be mentioned those by M. Greenblatt, R. E. Arnot, J. L. Poppen, and W. P. Chapman[14] from the Boston Psychopathic Hospital. An open operation is used (Poppen). The plane of section passes just in front of, sometimes through, the anterior horn of the lateral ventricle, ending below at the sphenoid ridge. From October, 1943, to April, 1946, 247 patients had the operation. One essential condition of operation is that patients should have had an adequate trial of other modes of therapy beforehand, but disturbed behaviour was sometimes an indication.

Of 154 cases operated on before October, 1946, a group of 147 has been followed up to April 1, 1947, periods from 6 months to 3½ years after operation.

There were 2 operative deaths from convulsive seizures, giving a mortality of 1·4 per cent. Results were classified into "good", i.e., free from psychotic symptoms and able to work; "poor", i.e., still suffering from gross psychotic symptoms and a burden to family or community; and "fair", i.e., showing variable alleviation of symptoms. The authors report that the operation was worth doing in 88 cases (65 per cent), that 36 (26 per cent) gave gratifying results, and "stellar" results were achieved in 12 (9 per cent). Of 98 schizophrenics the results in 20 per cent were "good", in 37 per cent "fair", and in 40 per cent "poor". Paranoid cases did best and hebephrenics worst. Of 14 cases of involutional psychosis (unspecified), 13 improved and 8 out of 14 were in good condition. Out of 4 obsessionals, 2 did well and 2 fairly well.

Schizophrenics with good pre-psychotic adjustment, abrupt onset, and good residual integration of personality did best in accord with universal experience. Age had no noteworthy effect on the results, in contrast to Reitman's experience, who found that patients under 45 were more likely to do better. Symptoms most frequently relieved by lobotomy were tension, fear, anxiety, overconscientiousness, and the like. These diminished remarkably in a high percentage of cases. Depression, aggressiveness, solitariness, hallucinations, and delusions were less frequently improved. The familiar sequelæ of laziness, irritability, untidiness, tactlessness, gain in weight, and seizures after operation are reported, but no figures given. Laziness, i.e., aspontaneity and inertia, was the most consistent post-operative complaint. Epileptiform seizures occurred in 10 per cent of the cases; 20–25 per cent continued to wet for longer than 1 week after operation. The Rorschach after operation showed more perseveration and stereotypy and less phantasy, but fewer restrictions on the patients' emotional expression. Abstraction tests revealed more concrete performance, indecision, and a difficulty in shifting attitudes. The authors stress that the personality changes are complicated and varied and should be interpreted with great caution. Physiological tests suggested a greater sensitiveness to stimuli of both divisions of the autonomic system after operation.

In the subsequent discussion W. Freeman[15] suggested that better results could be obtained by better selection of cases. The cardinal indication was emotional tension, but the choice of patients from a family able to give him the necessary after-care and careful choice of operation were also most important. L. C. Kalinowsky[16] obtained his best results in psychoneurotics.

W. Mayer-Gross and L. Frankl[3] report a follow-up of the first 170 patients operated on in the Crichton Royal Hospital between February, 1943, and June, 1946: 77 of these were discharged from hospital, 9 had to be readmitted, leaving 68, 28 men and 40 women. More than half of the 68 patients (one-fifth of the total) were earning their living, and more than three-quarters were usefully employed. The authors, pointing out that the symptoms following leucotomy are those of the frontal lobe syndrome, suggest as a theory of the treatment that the operation if successful provides the patient with a new framework of personality within which he must reconstruct his life, and that as experience of the re-education of patients with head injury has shown, this may well take years. Accordingly the original premorbid personality should not have a decisive effect on the final result, but the data available did not permit of definite conclusions on this.

J. W. Friedlander and R. S. Banay,[2] commencing their article with the remarks of Halstead, Carmichael, and Bucy already quoted, report in detail a gross organic psychosis following leucotomy. This case had been reported by one of the authors (R. S. B.[17]) in 1942: A sexual psychopath, who had apparently benefited by leucotomy in 1941, had stabilized for a year and had then progressively deteriorated until in 1945 he was first recognized as psychotic

and in 1947 was childish, incontinent, and showed trophic changes in his foot. The abnormal sexuality had persisted after operation. The E.E.G. showed changes suggestive of an epileptic record. Despite deterioration by clinical standards, there was a remarkable dearth of positive findings by psychological tests. The results of 6 of the tests were probably significant, although in the absence of pre-operative data it was impossible to be certain. There was evidence of defective abstraction as measured by the Vigotsky blocks and Koh's Block Design; disturbances of immediate memory (Knox Cube), of sustained attention (Robinson Deliberation Test), of ability to learn from experience (Porteous maze), and intellectual deterioration (Babcock-Levy), and since these results conformed to the clinical picture, they were regarded as significant. A Rorschach test done a few months after operation showed no evidence of cerebral damage, and after 5 years the abnormalities found were slight as compared with the clinical picture. The authors remark that lack of significant test results may well be due to a lack of significant tests, and that since, in a large series of cases it is found that pre-operative impairment equals post-operative defect, the inevitable conclusion must be that there is no appreciable change in general mental ability so long as no tests exist which differentiate clearly between functional and organic impairment. The authors attribute the result in this case not to the site of the operation, which was done in accordance with Freeman and Watts's technique, but to the operation itself. The differential diagnosis between this patient's psychosis and other organic conditions is discussed and the other possible conditions on the whole satisfactorily eliminated.

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LEUKÆMIA, ACUTE.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Treatment by Aminopterin.—Hitherto no form of treatment has been available which can favourably influence the course of *acute* leukæmia. X-ray treatment produces no improvement and may indeed increase the rapidity of the downhill course. In recent years various drugs have been shown to produce beneficial effects in *chronic* leukæmia—viz., urethane (*see* MEDICAL ANNUAL, 1947, p. 167), the nitrogen mustards (MEDICAL ANNUAL, 1948, p. 220), and radio-active phosphorus (MEDICAL ANNUAL, 1946, p. 196), but none of them has helped the acute type.

This consideration enhances the importance of the recent observations of S. Farber and his colleagues at Harvard Medical School.[1] Farber had found that folic acid and folic acid conjugates (teropterin and diopterin) seemed to produce an acceleration of the leukæmic process in children with acute leukæmia. Accordingly it was decided to determine the effect of folic acid antagonists (pteroylaspartic acid, methylpteroic acid, and 4-amino-pteroyl-glutamic acid). Farber and his colleagues describe the results obtained by the use of 4-amino-pteroyl-glutamic acid (aminopterin), which is the most powerful of these antagonists, in 16 children with acute leukæmia during a period of five and a half months (November, 1947, to April 15, 1948). The anti-vitamin was given by intramuscular injection. Many of the children were moribund at the beginning of treatment. Of the 16 cases, 10 showed "clinical, hæmatological, and pathological evidences of improvement of important nature of three months' duration" at the time of the report. Six did not respond well;

4 of these are now dead and 2 showed no improvement. Full details are given of 5 of the cases, and the remarkable changes which were observed are worthy of close study by all who are interested in this subject.

The report is a preliminary one and the authors make no extravagant claims. They point out that the remissions are temporary in character and that aminopterin is a toxic and dangerous substance (stomatitis seems to be the first manifestation of toxicity, but continuation of the drug can produce complete aplasia of the bone-marrow). More important than the actual results are the implications of this work. So far as the reviewers are aware this is the only form of treatment which may affect the course of acute leukæmia beneficially in certain cases. As the authors say, their studies "justify a search for other antagonists to folic acid that are less toxic than aminopterin and may be even more powerful". Future results will be awaited with great interest.

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LIVER, SURGERY OF. *A. Rendle Short, M.D., F.R.C.S.*

Laparoscopy and Biopsy.—Three Argentine surgeons, M. R. Castax, A. L. Maggi, and H. E. F. Stocker,[1] describe a method of obtaining fragments of the liver for biopsy by means of "laparoscopy" (called in this country cœlioscopy or peritoneoscopy) by nipping out a fragment of the liver with forceps, and electrocoagulation to check hæmorrhage. They give a report of 5 cases, with histological pictures, showing cirrhosis and other changes.

Amœbic Abscess.—E. H. Drake and T. A. Warthin,[2] working at an American Veterans' Hospital, discuss the treatment of amœbic abscess of the liver. Open operation and drainage has a high mortality, involves a prolonged period of convalescence, and is only advised in the presence of secondary infection. In ordinary, the best treatment is needle aspiration combined with chemotherapy, by which they mean courses of emetine with penicillin alternating with vioform, 1 g. t.d.s. If the abscess has opened into the lung, chemotherapy alone may be sufficient to cure. They relate 6 cases.

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LOUPING-ILL IN MAN. *Macdonald Critchley, M.D., F.R.C.P.*

Louping-ill is a disease of sheep in the Scottish border district, known to farmers for over a century. W. A. Pool et al.[1] proved that it is due to a filter-passing virus. J. MacLeod and W. S. Gordon[2] demonstrated the vector to be the sheep tick (*Ixodes ricinus*). The illness, as it occurs in sheep, consists in fever lasting three or four days. Then, after a short afebrile period, the temperature rises again. Dullness, inco-ordination, tremors of the head, salivation, and champing of the jaws develop. The sheep may make leaping movements (hence the term "louping-ill"), and after a stage of cerebellar ataxia, the sheep is no longer able to stand. Paralysis supervenes and is followed by coma and death.

Although "tick-borne fever" is a distinct disorder of sheep, it is believed that louping-ill does not develop until the animal has already developed tick-borne fever.

The morbid anatomy of louping-ill in sheep consists in a meningo-encephalomyelitis with a particular involvement of the Purkinje cells of the cerebellum.

In 1934 T. M. Rivers and F. F. Schwenkler[3] described 4 laboratory workers who had been taken ill; they had previously worked with the virus of louping-ill. The sera of all 4 patients neutralized this virus. Other similar cases were recorded by H. Wiebel[4] and by K. Wesemeier.[5] Of these 6 cases, 5 resembled a meningo-encephalitis, and the other one an influenza. The C.S.F. was examined in 4 of these cases: in 1 it was normal; in 3 there was a high lymphocyte count and a raised protein level.

G. Davison, C. Neubauer, and E. Weston Hurst[6] have recently reported 2 more cases of meningo-encephalitis due to the virus of louping-ill. One patient was a laboratory worker in contact with the virus and the other was a farmer in the Border area. The authors have many interesting observations to make. They believe that the clinical picture in man is as variable as that of poliomyelitis. Cases may perhaps occur with only a mild non-specific illness, with rapid recovery. A few days after laboratory exposure to the virus, in a typical meningo-encephalitic case, there develop malaise, headache, and fever, which continue for about a week. Then comes an afebrile period of a fortnight or so. Once again symptoms appear, this time with greater intensity. Headache is now severe, and is accompanied by fever, vomiting, drowsiness (may be associated with nocturnal sleeplessness), confusion, tremor. The pulse is slow. There may be stiffness of the neck, cranial-nerve palsies, and papilloedema. A blood-count shows a leucocytosis of 10,000 to 20,000 per c.mm. with 70 to 80 per cent neutrophils. The C.S.F. may show an increased cell-count (50 to 500 cells per c.mm., predominately lymphocytes) and a slightly raised protein level. The temperature drops in a few days, and the symptoms clear up in a week or so.

Clinical variations may occur in the foregoing picture, and the cell-count in the C.S.F. may contain an excess of polymorphs.

Diagnosis is confirmed by virus-neutralization tests.

There may well be a close relationship between louping-ill and Russian spring-summer encephalitis of man and animals.

REFERENCES.—[1]*J. comp. Path.* 1930, **43**, 253; [2]*Ibid.* 1932, **45**, 240; [3]*J. exp. Med.* 1934, **59**, 669; [4]*Klin. Wschr.* 1937, **16**, 632; [5]*Deut. Arch. klin. Med.* 1938, **182**, 451; [6]*Lancet*, 1948, **1**, 453.

LUNG. (*See also* BRONCHUS, CARCINOMA OF; INTRAPULMONARY CALCIFICATION AND HISTOPLASMIN SENSITIVITY; PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY; PNEUMOTHORAX, SPONTANEOUS; TUBERCULOSIS, PULMONARY.)

LUNG, ARTERIOVENOUS ANEURYSM OF. *Philip Ellman, M.D., F.R.C.P.*

C. G. Barnes, L. Fatti, and C. M. Pryce[1] believe that the rare lesion hitherto described as a cavernous hæmangioma of the lung, whose clinical syndrome was recorded as such in the MEDICAL ANNUAL, 1948, is not a true vascular tumour and that it is, in fact, an arteriovenous aneurysm. The syndrome should be carefully differentiated from cyanotic congenital heart disease and polycythæmia rubra vera, and in a few cases it has been regarded as bronchiectasis and pulmonary tuberculosis. The number of cases apparently recorded to date is 25, including 2 further cases recorded by the authors. Intense cyanosis and clubbing in varying degree, increasing dyspnœa, transient attacks of faintness, giddiness or convulsions due to cerebral anoxæmia, hæmorrhage in the form of hæmoptysis or epistaxis, and capillary hæmangiomata of the skin and mucous membranes are the major symptoms and signs. Examination reveals no abnormality of the heart either clinically, radiologically, or electrocardiographically; the blood-pressure is normal.

The lungs are normal unless the aneurysm is large and situated near the costal surface of the lung, when a systolic murmur sometimes continuing into diastole may be heard, and this important physical sign was heard in 12 of the 25 reported cases. Splenic enlargement is unusual. The arteriovenous shunt leads to remarkable circulatory adjustments with a great increase in blood volume, due to the polycythæmia.

Radiographically the aneurysm is seen as a circumscribed opacity with no surrounding inflammatory reaction, and on screening it may pulsate, varying in size with forced inspiration and expiration. Surgery in the form of local

excision, lobectomy, or pneumonectomy is indicated, depending on the extent of the lesions.

In addition to a full review of the literature, the pathology of the 2 cases recorded is fully described and the genesis of the lesion is discussed.

REFERENCE.—[1] *Thorax*, 1948, **3**, 148.

LUNG, GIANT BULLOUS CYSTS OF. *Philip Ellman, M.D., F.R.C.P.*

In a comprehensive review of this subject P. R. Allison[1] points out that these cysts are an expression of underlying bronchial disease, either in the form of inflammation or scarring. Air passes into the area of lung supplied by the diseased bronchus more easily than it can escape during expiration, so that local over-inflation occurs with formation of a cyst. This may arise either by stenosis of a small bronchus or a bronchiole, or (in the case of bronchiectatic subjects) by ulceration of the wall of a bronchus with escape of air into the interstitial tissue of the lungs. Allison shows that whereas they have usually been regarded as of pathological rather than clinical interest, they can produce symptoms apart from those of their underlying cause.

In his series of 6 such cases the principal symptoms were attacks of acute chest pain in 3, and right shoulder pain in a fourth, which was probably referred from pressure on the phrenic nerve, as it disappeared after a therapeutic phrenic crush. Multiple cysts were present in 3 cases. The presenting symptoms were as follows: Attacks of dyspnœa, 3; attacks of acute chest pain, 3; localized 'tightness' or fullness in the chest, 3; belching, 1; paroxysmal tachycardia, 1. In the case with attacks of tachycardia, Allison noted at post-mortem examination that a bullous cyst lay over the pericardium.

The frequency with which the cysts produced dyspnœa out of proportion to any bronchitis and emphysema present is noteworthy. This may be due either to simple compression of lung tissue or, as Allison suggests, by the increased tension acting as a governor to the Hering-Breuer reflex.

In the radiograph these cysts may easily be mistaken for a localized pneumothorax—a differential diagnosis which may be impossible clinically. Allison warns against attempting differential diagnosis with a pneumothorax needle, for if the cyst wall is pierced, a tension pneumothorax is almost inevitable, and often does not manifest itself in acute form for a few days.

Treatment.—The ideal treatment is excision, but many of the subjects are unsuitable for operation by reason of bronchitis and emphysema, or multiplicity of cysts. In these cases Allison gets good results from phrenic paralysis—especially in cases where the lower lobe is involved. He suggests this is probably because the piston-like action of the diaphragm—possibly in conjunction with pleural adhesion over the cyst—plays a big part in inflating this section of the lung.

REFERENCE.—[1] *Thorax*, 1947, **2**, 169.

LUNG, INTRALOBAR SEQUESTRATION OF, ASSOCIATED WITH AN ABNORMAL PULMONARY ARTERY.

N. R. Barrett, M.A., M.Chir., F.R.C.S.

This condition has recently been reviewed by a number of authorities (Pryce;[1] and Pryce, Holmes Sellors, and Blair[2]), and is of importance not only because of the baffling clinical lesions which may develop in the chest but because of the pitfalls which await the surgeon who endeavours to remove the abnormal tissues. The abnormality referred to is of two parts—namely, first, an ectopic, or sequestered, segment of lung which may be contained within the normal lung or separated from it, and, secondly, one or more large systemic arteries, arising most commonly from the aorta either above or below

the diaphragm, and supplying the ectopic segment with its blood-supply. The arterial abnormality without the bronchopulmonary deformity has been recorded quite frequently, and a striking example is the case described by Maugars,[3] a French medical student of the revolutionary period (*Plate XXIV*). Such segments of lung are liable to become infected and are generally diagnosed as pneumonia; if suppuration occurs the lesion then resembles bronchiectasis, cystic disease, or empyema, and operation has usually been undertaken for one of these conditions. Even at operation the true nature of the abnormality may not be suspected, and in one case the patient died of hæmorrhage in consequence (Harris and Lewis[4]). The artery concerned is elastic, and, although it arises from the aorta, it is a pulmonary structure; in size it may often be as large as the radial artery. The dislocated segment of lung may be cut off from the bronchial tree, and probably any communication which does exist has been acquired as a result of secondary ulceration.

The treatment is surgical removal of the abnormal parts.

REFERENCES.—[1]*J. Path. Bact.* 1946, **58**, 457; [2]*Brit. J. Surg.* 1947, **35**, 18; [3]*J. Med.* 1802, **3**, 453; [4]*J. thorac. Surg.* 1939, **9**, 666.

LUNG, SOLITARY METASTATIC SARCOMAS AND CARCINOMAS OF, PULMONARY RESECTION FOR. *N. R. Barrett, M.A., M.Chir., F.R.C.S.*

John Alexander and Cameron Haight[1] have recently reviewed this important subject and added a number of new cases to the literature. They point out that the appearance of a presumed solitary metastatic lesion in the lung is not rare, and that, unless treated surgically, these patients almost invariably die. The first patient in whom both the primary and the lung metastasis were removed was reported by Barney and Churchill[2] and the patient is alive and well 12 years later. The present report includes 19 new cases, in addition to the 5 already in the literature. There was one death as a direct result of the lobectomy or pneumonectomy operations, and out of the whole 24 patients the tumour has recurred elsewhere so far in 11, leaving 12 who appear to be cured. These 12 were operated upon 12, 7, 6, 5, 4, 3, 1¼, and 1 year ago respectively, and the 4 other patients have been done within the last few months.

Six of the 8 sarcoma patients and 6 of the 15 carcinomata are well, which suggests that the outlook may be better in the former than the latter.

REFERENCES.—[1]*Surg. Gynec. Obstet.* 1947, **85**, 129; [2]*J. Urol.* 1939, **42**, 269, 1944, **52**, 406.

LYMPHADENOPATHY. (*See* RETICULOSIS.)

LYMPHOGRANULOMA VENEREUM. *T. Anwyl-Davies, M.D., F.R.C.P.*

A new antibiotic, *aureomycin*, seems to be highly effective in the treatment of the viruses of the psittacosis and lymphogranuloma venereum group. L. W. Wright et al.[1] have treated 25 patients suffering from lymphogranuloma venereum. The buboes in 8 patients, proctitis in 3, and a rectal stricture in 14 cases, were all considerably improved. At last a specific remedy may have been found, and further experiences with it are awaited with interest.

REFERENCE.—[1]*J. Amer. med. Ass.* 1948, **138**, 408.

MALARIA, AETIOLOGY OF: RECENT ADVANCES. *Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.*

Recent discoveries have fundamentally altered our knowledge of malaria to such an extent that accounts of the life-history of the malaria parasites in text-books will have to be revised and all the illustrations will have to be redrawn (*Fig.* 35). For some time past it had become obvious that there were

PLATE XXIV

SEQUESTRATION OF LUNG ASSOCIATED WITH ABNORMAL ARTERY

(D. M. Pryce, T. M. Sellors, and L. G. Beattie)

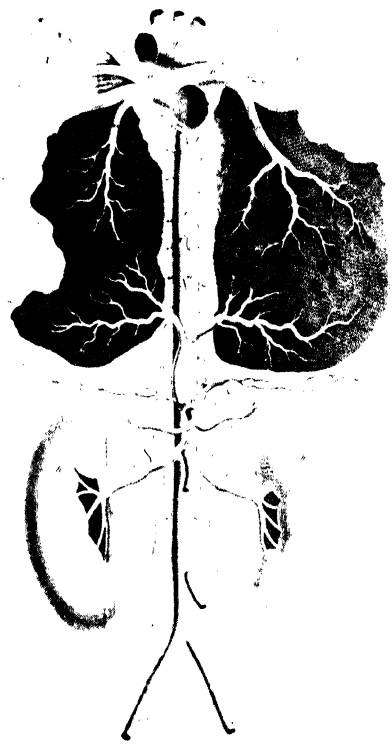


Illustration by Maugars of the abdominal artery in his case

By kind permission of the 'British Journal of Surgery'

certain gaps in our knowledge in order to explain the latency of the infection and the mechanism of relapses which constitute such a feature of malaria. At the time of Ross's discovery of the complete life-cycle of the plasmodium in the mosquito it was assumed that there was little more to be learned. However,

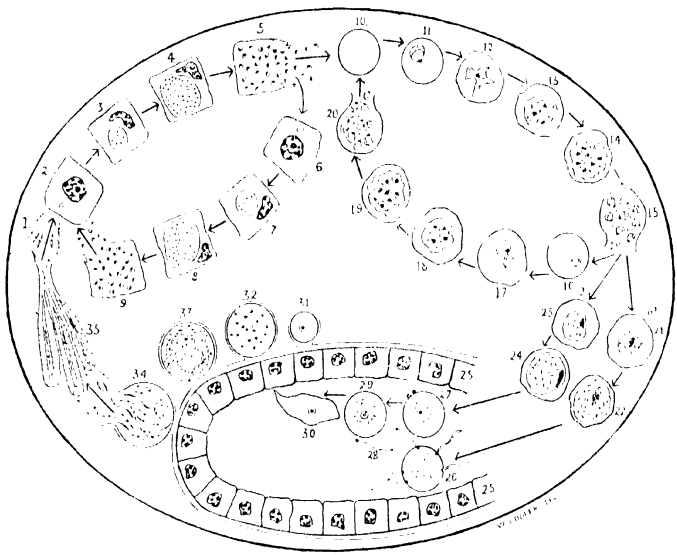


Fig. 35. Life cycle of *Plasmodium cynomolgi*, a type of mammalian malaria parasite.

1, Sporozoites from salivary glands of mosquito enter liver cells.

2, Liver cell containing early stage of pre-erythrocytic parasite.

3, 4, Stages in development of the pre-erythrocytic schizont in liver cells.

5, Fully developed pre-erythrocytic schizont rupturing and releasing pre-erythrocytic merozoites.

6, Liver cell containing merozoite of an exo-erythrocytic cycle of schizogony.

7–9, Remaining stages in exo-erythrocytic schizogony ending in second generation of merozoites.

(Exo-erythrocytic cycle)

10, Red cell of circulating blood.

11–14, Stages in erythrocytic schizogony in circulating blood.

15, Fully developed erythrocytic schizont rupturing and releasing erythrocytic merozoites and gametocytes.

16–20, Repetition of erythrocytic schizogony.

21, 22, Development of male gametocyte or microgametocyte in circulating blood.

23, 24, Development of female gametocyte or macrogametocyte in circulating blood.

25, Wall of stomach of mosquito.

26, Exflagellating microgametocyte producing microgametes in stomach of mosquito.

27, Macrogametocyte extruding polar bodies and so becoming macrogamete.

28, Microgamete free in stomach of mosquito and seeking macrogamete.

29, Zygote, formed by fertilization of macrogamete by a single microgamete.

30, Oökinete or travelling vermicule formed by elongation of zygote. It is about to penetrate epithelial lining of stomach.

31, Oöcyst, formed by oökinete after penetration of stomach wall of mosquito. It lies under elastic membrane on outer surface of stomach.

32, 33, Stages in development of oöcyst with production of sporozoites.

34, Rupture of mature oöcyst with dispersion of sporozoites, most of which enter salivary glands of mosquito.

35, Salivary gland of mosquito containing mature sporozoites.

(After H. E. Shortt and P. C. C. Garnham, by kind permission of the authors, the editor of the 'Transactions of the Royal Society of Tropical Medicine and Hygiene', and the Secretary of the Society.)

in 1902 F. Schaudinn[1] claimed to have observed the penetration of the sporozoites, derived from the salivary glands of the infected anopheles, into the red blood-corpuscles, in which he thought that they developed to complete the asexual and sexual cycles in the peripheral blood, a process now known as the "erythrocytic cycle". For the next thirty years this observation was assumed to be correct and was figured as such in every diagram of the text-books of the world, in spite of the fact that repeated attempts by other workers had failed to confirm the work of this great authority.

Gradually it began to dawn that some other explanation must be necessary. The introduction of malaria therapy by Wagner-Jauregg in the decade following the end of the First World War afforded splendid opportunities for detailed clinical studies of malaria under controlled conditions unobtainable in the tropics. Soon it became apparent that the fever produced by direct blood inoculation differed in several important aspects from naturally-acquired, mosquito-conveyed malaria, especially in the benign tertian form (*Plasmodium vivax*) most commonly employed in this type of therapy. It was pointed out, especially by W. Yorke and J. W. S. Macfie[2] in 1924, that the blood-induced disease was easily controlled by small doses of quinine which are quite inadequate for the suppression of clinical malaria in the tropics or for the prevention of relapses. In the blood-produced disease the incubation period was sometimes a very short one, whilst with sporozoite-produced infection it was much longer, being never less than 5–8 days. To explain this discrepancy S. P. James[3] in 1931 made the original suggestion that the sporozoites, on entry into the human body, instead of penetrating blood-corpuscles, as had been generally accepted, passed directly into the tissues, where they underwent a peculiar development in the cells before entering the blood-stream. This suggestion received considerable support when in 1936–7 it was proved by G. Raffaele,[4] W. Kikuth and L. Mudrow,[5] that such a cycle did take place normally in the malaria-like parasites of canaries—*Plasmodium cathemerium* and *P. relictum*. They demonstrated that the sporozoites entered the endothelial cells of blood-vessels in the internal organs. Non-pigmented merozoites were produced within the cells and persisted for several generations. These stages were later termed cryptomerozoites, or cryptozoic merozoites, by C. Huff and F. Coulston,[8] and the whole tissue-stage the exo-erythrocytic cycle. In 1937 a similar cycle was described by S. P. James and P. Tate[6] in *P. gallinaceum*, the malaria parasite of fowls, which is more closely related to the human plasmodia than are the other avian parasites. In 1943 E. Reichenow and L. Mudrow,[7] in Germany, and in 1944 C. Huff and F. Coulston,[8] in America, showed conclusively in chickens that sporozoites when injected into the skin were taken up by macrophage cells and transported to the spleen and other internal organs where they underwent the exo-erythrocytic (or E.E.) cycle for 3–4 generations before the cryptomerozoites were able to penetrate the red blood-cells and initiate the *erythrocytic* cycle and thus produce symptoms in these birds.* This stimulated malariologists to experiment further with the malaria parasites of monkeys, several of which, especially *P. knowlesi* and *P. cynomolgi*, closely resemble those of man. But in this direction protozoologists were foiled from proving the E.E. cycle in mammalian malaria by the application of Huff and Coulston's technique. The next step forward was the demonstration of E.E. forms of the plasmodium of the bat in the endothelial cells in 1946 by R. D. Manwell,[9] in *Pteropus gouldi*, and in 1947 by G. C. Mer and N. Goldblum.[10] Shortly afterwards, in Kenya, P. C. C. Garnham[11]

* In *P. gallinaceum* two forms of cryptomerozoites are produced, macro- and micro-merozoites, of which the latter enter erythrocytes, whilst the former serve to continue the tissue-cycle.

(1947) found cysts in the liver of monkeys (*Cercopithecus*) with a blood infection of *Plasmodium kochi*. In these cysts pigmentless protozoal masses were demonstrated which obviously represented the E.E. cycle in these animals. There were, however, some objections, as this parasite is more nearly related to the *Haemoproteus* or *Halteridium* of birds, and belongs to a different genus now renamed *Hepatocystes*. Any doubts that remained were dispersed in 1948 by H. E. Shortt, P. C. C. Garnham, and B. Malamos[12] in their work upon *P. cynomolgi* of monkeys, a species almost identical with *P. vivax* of man. By employing a new technique, consisting of the injection of large numbers of ground-up infected anopheles mosquitoes, they found in the liver of the monkey which was sacrificed numerous large plasmodial masses, 25–30μ in diameter, which in their morphology and staining reactions closely resembled the tissue forms of bird malaria already referred to. Although this possibility had been in the minds of protozoologists for several critical years it may seem surprising that this discovery was not made before. Probably this was due to the technique employed of using large numbers of infective sporozoites, and to some extent it may be ascribed to the comparatively large size of the plasmodial masses when research workers were looking in the tissues for some comparatively small body. Moreover, the bird experiments had led their thoughts astray from the liver as the cradle of the parasite when those of chicken malaria develop primarily in the macrophage cells of the skin.

It was now realized that it was only a matter of opportunity before a similar E.E. cycle could be demonstrated for the benign tertian parasite (*P. vivax*) in man. In this direction it must now be stated that a very distinct pointer had been given by the original and fundamental researches of N. H. Fairley and his associates[13] of the Malaria Research Unit at Cairns, Queensland, in 1945. There for the first time it had been possible to employ human volunteers for the production of malaria and to use them as experimental material. Amongst many other important observations the most pregnant was the demonstration that sporozoites inoculated by infected mosquitoes could be recovered from the blood for 7 30 minutes only after the infecting mosquito bite, but that after this time a non-infective period ensued of eight days in the case of *P. vivax*, or five to six days—a shorter period– in *P. falciparum*, before it was again possible to reproduce malaria in another individual by blood inoculation. This appeared to indicate clearly that the parasites had been locked up in some solid organ during this silent period which prevented them from being transferred to another individual.

Very shortly after their work on *P. cynomolgi* (1948),[14] H. E. Shortt and P. C. C. Garnham, together with G. Covell and P. G. Shute[15] (1948), were able to prove the E.E. cycle in *P. vivax* in man in a human volunteer who consented to have a biopsy of his liver performed seven days after a massive infection with sporozoites. The general procedure was the same. Some 3600 anopheles mosquitoes (*A. atroparvus*) were infected with *P. vivax* on two successive feeds. Fourteen days after the last infecting feed the survivors were set to feed on the volunteer on two successive days. It is recorded that 2010 fed and it was shown by sample dissections that 86 per cent were infected. Further, to make doubly certain, the salivary glands of 200 others were dissected in Locke's fluid and injected intravenously. A piece of the patient's liver was removed seven days later. It must be explained that the subject had undergone malaria therapy with the homologous strain of *P. vivax* some 22½ months previously and had developed, so it seems, a certain amount of immunity to this strain of the parasite. As infection had been effected on two successive days it was expected that forms of the sixth and seventh day might be present. The sections were stained with a special modification of Giemsa stain (H. E. Shortt and W. Cooper,[16] 1948). Ovoid

plasmodial masses were found in the hepatic cells which closely resembled those of *P. cynomolgi*. The earliest forms were larger, being about 42 μ in longest diameter, containing as many as 800 chromatin masses. The fully developed stage (*cryptoschizont*) ruptured and permitted the segmented forms, or *cryptomerozoites*, to escape into the blood and thus to enter the red blood-corpuscles. This would suggest that an attack of malarial fever was imminent, but no fever took place. The patient's general condition was normal and he continued to show no ill-effects of the operation. No malaria parasites have been found in his blood and he appears to be completely immune to *P. vivax*. It therefore appears probable that highly potent immune bodies are produced in the serum so that the invading cryptomerozoites are killed and phagocytosed. A further study of this liver has demonstrated a round-cell infiltration at the site of the ruptured liver cells. These cell-accumulations consist of lymphocytes, endothelial and plasma cells which lie in relation to branches of the portal vein. This seems to fall into line with the observations of pathologists, especially F. W. Vint[17] (1931), who has shown that periportal round-cell infiltration is a common feature of Africans who have been much exposed to malaria. Possibly it is one of the factors which might go to explain the frequency of hepatic cirrhosis in malarious countries. These remarkable discoveries do not explain the whole story, because it is clear that not all the human malaria parasites have identically the same E.E. cycle. Probably that of the subtertian (*P. falciparum*) differs in form as well as in time.

What then constitutes a relapse? Does the establishment of blood infection terminate the exo-erythrocytic cycle or does it persist as a low-grade infection of the liver for prolonged periods? In a recent paper H. E. Shortt and P. C. C. Garnham[18] (1948) have described the persisting E.E. cycle in *P. cynomolgi*, and there are good reasons for believing, as already stated, that this holds good also for *P. vivax*. In a second monkey which was killed at a time that a relapse of malaria was expected cryptoschizonts were demonstrated in the liver cells some three and a half months after a sporozoite-induced infection, and by these means it was shown that the E.E. cycle persists long after the establishment of the blood infection.

It is now possible to summarize this new knowledge as follows: The inoculation of sporozoites by the infected mosquito is followed by development of the pre-erythrocytic cycle (E.E. cycle) in the parenchyma cells of the liver with ultimate production of *cryptomerozoites*. Some of those which escape phagocytosis enter red blood-corpuscles in the hepatic capillaries to produce in due time a clinical attack of malaria, but, on the other hand, other cryptomerozoites enter normal liver cells and repeat the process, which continues indefinitely, irrespective of whether the erythrocytic or blood cycle is present, or held in check by antimalarial drugs, or even as the result of naturally-acquired immunity. This immunity, however, operates solely against the blood forms and destroys those merozoites which are destined to enter red blood-corpuscles. Probably those which enter liver cells to maintain the E.E. cycle are protected from the destructive effects of immunity by their intracellular habitat; but when the active immunity of the human host is impaired, it is no longer active against those merozoites which are destined to recommence the *erythrocytic* cycle, and these enter the red blood-corpuscles in order to initiate a clinical relapse.

REFERENCES.—[1]*Arb. Kais. Gesundhamt. Berl.* 1902, **19**, 169; [2]*Trans. R. Soc. trop. Med. Hyg.* 1924, **18**, 1; [3]*Ibid.* 1931, **24**, 477; [4]*Riv. Malariol.* 1936, **15**, 318; [5]*Klin. Wschr.* 1937, **16**, 1690; [6]*Nature, Lond.* 1937, **139**, 545; [7]*Dtsch. Tropenmed. Z.* 1943, **47**, 289; [8]*J. infect. Dis.* 1944, **75**, 231; [9]*Amer. J. Hyg.* 1946, **43**, 1; [10]*Nature, Lond.* 1947, **159**, 444; [11]*Trans. R. Soc. trop. Med. Hyg.* 1947, **40**, 719; [12]*Brit. med. J.* 1948, **1**, 192; [13]*Trans. R. Soc. trop. Med. Hyg.* 1945, **38**, 311; [14]*Ibid.* 1948, **41**, 785; [15]*Brit. med. J.* 1948, **1**, 547; [16]*Trans. R. Soc. trop. Med. Hyg.* 1948, **41**, 427; [17]*Konga and E. A. med. J.* 1931, **7**, 349; [18]*Brit. med. J.* 1948, **1** 1225.

MALARIA : MODERN TREATMENT.

G. M. Findlay, C.B.E., M.D., Sc.D., F.R.C.P.

Chemotherapeutic Drugs

During the last ten years there have been notable advances in the chemotherapy of malaria.

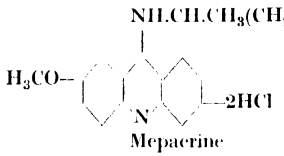
Until after the First World War the only drugs available for the treatment of malarial infections were quinine and the other cinchona alkaloids, cinchonine, quinidine, and cinchonidine. The relative ineffectiveness of these compounds was shown by the high death-rate from malaria of troops in East Africa and in the Jordan Valley, and by the complete immobilization of allied armies in the Balkans. The Germans, cut off from the main supplies of cinchona bark in the Dutch East Indies, were in even more desperate straits : they were, however, stimulated to investigate the possibility of obtaining synthetic drugs which could replace the naturally occurring cinchona alkaloids. The first of these compounds was pamaquin, originally known as beprochin, plasmoquin, plasmochin, and, in French-speaking countries, as præquine. In human malaria this compound, 6-methoxy-8-diethylamino-*iso*pentylamino-quinoline, was found to be unsuitable for general use as the dose necessary to destroy the asexual forms in the blood-stream is only slightly less than the toxic dose. Pamaquin, however, has a powerful action on the gametocytes. Further investigations in Germany dispensed with the 6-methoxy-quinoline nucleus, which was replaced by a 2-chloro-7-methoxyacridine ring, although the same dialkylaminoalkylamino side chain was retained. This compound, now known as mepacrine, is 2-chloro-5-diethylamino-*iso*pentylamino-7-methoxy-acridine dihydrochloride : it has also been called atebrin, atabrine, quinacrine, and erion.

At the beginning of the Second World War there were thus two other compounds available, in addition to the naturally occurring alkaloids of cinchona. In France, rhodoquine or Fourneau 710, 6-methoxy-8-diethylamino-*n*-propylaminoquinoline, a homologue of pamaquin with a similar action, was also used to some extent. Very little was known of the action of mepacrine either in the treatment or prevention of malaria.

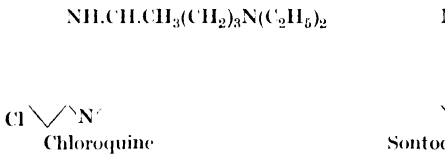
With the loss of Java to the Japanese the supply of cinchona bark became limited, and though quinine was synthesized in 1944 by R. B. Woodward and W. E. Doering[1] the process is too complicated for use on a manufacturing scale. Attention was therefore directed to a thorough investigation of the antimalarial potentialities of mepacrine and to the antimalarial activity of a host of new compounds. In America more than 14,000 compounds were examined, tests being carried out largely on malaria in birds and monkeys (F. Y. Wiselogle[2]). In Great Britain by a logical series of steps the acridine nucleus of mepacrine was replaced first by a pyrimidine and later by a biguanide ring, leading finally to the formation of N_1-*p*-chlorophenyl-N_5-*iso*propyl-biguanidine, formerly known as paludrine and more recently as proguanil (F. H. S. Curd et al.,[3] 1945). In Germany prior to 1939 another 8-amino-quinoline, " certuna ", differing from pamaquin only by one less methyl group in the side chain, was found by W. Kikuth[4] to have a more powerful gameto-cytocidal action than pamaquin but to be useless in *vivax* malaria. In America, pentaquine, 6-methoxy-8, 5′-*iso*propylaminoamylaminoquinoline, was similarly developed.

Another device which was exploited in Germany before the war was the breaking down of the mepacrine molecule into its constituent parts. In this way 7-chloro-4-(4-diethylamino-1-methyl-butylamino)-3-methylquinoline was obtained. This compound, originally termed sontochin and now known as

sontoquin, santoquine, and nivaquine (SN 6911), was given a limited clinical trial by the Germans in North Africa (Kikuth[5]), where some of it was captured by the Americans. Sontochin was not easy to prepare in large amounts, but a compound differing only by the presence of a methyl group was found to be highly active by American observers. This compound is chloroquine (aralen, resochin, SN 7618), 7-chloro-4-(4-diethylamino-1-methylbutylamino)-quinoline, which differs from nivaquine only in the absence of a methyl group.



Mepacrine



Chloroquine Sontochin (Nivaquine)

One other 4-aminoquinoline is of interest, Cam-Aqi or camaquine, 7-chloro-4-(3′-diethyl-amino-4′-hydroxyanilino)-methylquinoline (A. Halawani et al.,[6] 1947).

A compound of a different type, metachloridine (SN 11,437), has also been used in the chemotherapy of human malaria: 2-sulphanilamido-5-chloropyridine was first shown to have a chemotherapeutic action in avian malaria: later investigations resulted in the production of N′-(5-chloro-2-pyrimidyl metanilamide, or 2-metanilamido-5-chloropyrimidine).

Chemotherapeutic Action of Antimalarial Drugs

The antimalarial action of drugs is closely associated with the biology of malarial plasmodia, for :—

1. The four species of plasmodia which parasitize man, *Plasmodium falciparum*, the causal agent of malignant tertian malaria; *P. vivax*, the causal agent of benign tertian malaria; *P. malariæ*, the causal agent of quartan malaria; and *P. ovale* do not all react uniformly to antimalarial drugs.

2. Within each species of plasmodium there are certain strains which show quantitative differences in their reactions to chemotherapeutic drugs.

3. The different stages in the life cycle of malarial parasites show qualitative differences in their reaction to drugs.

These various qualitative and quantitative differences are brought out by a consideration of the effects of drugs on the various stages in the life cycle of plasmodia.

Sporozoites.—When the anopheline mosquito infected with malaria takes a blood meal it injects sporozoites from its salivary glands into the blood-stream. These sporozoites continue in the blood-stream probably for not more than 30 minutes before entering reticulo-endothelial cells. Possibly because they represent a resting stage and their metabolism is low, no drugs are known which attack the sporozoites of human malarial parasites, but the sporozoites of *P. gallinaceum* in the chicken are apparently destroyed by 2-hydroxy-3-β-decalyl-propyl-1, 4-naphthoquinone (D. H. Clarke and M. Theiler,[7] 1948).

Primary Exo-erythrocytic Forms.—On entering reticulo-endothelial cells the sporozoites have been termed cryptozoites, which in turn give rise to meta-cryptozoites (C. G. Huff and F. Coulston[8]). These metacryptozoites at the end of 10 to 14 days rupture the reticulo-endothelial cell and enter red cells as schizonts, where they form rings which grow and finally segment into a number of merozoites. The primary exo-erythrocytic forms are destroyed by a number of drugs which are termed true causal prophylactics. Pamaquin in large doses acts as a true causal prophylactic both against *P. vivax* and *P. falciparum* but owing to its toxicity cannot be generally used for daily doses of 80 mg. of the base are required on the day before infection with sporozoites, on the actual day of infection, and on the six succeeding days (S. P. James[9]). Proguanil (paludrine) was shown by N. H. Fairley and his colleagues[10] to act as a true causal prophylactic against New Guinea strains of *P. falciparum*. These results have now been confirmed with one African strain of *P. falciparum*. Against New Guinea strains of *P. vivax* proguanil appears to act as a partial causal prophylactic, being sometimes successful and sometimes unsuccessful. The cinchona alkaloids, mepacrine, chloroquine, metachloridine, and the sulphonamides do not act as true causal prophylactics against any human malarial parasites. Against *P. gallinaceum* in birds sulphadiazine and certain other sulphonamides (G. R. Coatney and W. C. Cooper[11]), as well as metachloridine (S. Brackett and E. Waletzky[12]), do act as true causal prophylactics.

Asexual Blood Cycle.—When once the red cells have become infected the parasites become vulnerable to a large number of drugs differing widely in chemical constitution. The asexual blood parasites can be removed from the blood-stream temporarily by cinchona alkaloids, mepacrine, chloroquine, proguanil (paludrine), sulphonamides, and metachloridine. In the case of infections due to *P. falciparum* there is evidence to show that in a considerable proportion of cases infected with strains of differing origin mepacrine and chloroquine if administered over a considerable period will entirely eliminate the infection. In the case of *P. vivax* relapses will inevitably occur after a shorter or longer interval. This difference between the two species of parasite is due to the fact that in the case of *P. vivax* the exo-erythrocytic forms persist in the tissues, with some strains almost indefinitely ; the asexual blood cycle can thus be re-initiated after long intervals ; in the case of *P. falciparum* the exo-erythrocytic forms die off rapidly, so that if the asexual blood forms are all destroyed there is no reservoir from which this cycle can be restarted. A. J. Sinton and W. Bird,[13] however, showed that by the combined use of pamaquin and quinine the exo-erythrocytic forms of *P. vivax* could be eradicated from the tissues. These observations have been amply confirmed : similar good results may be obtained with a combination of pentaquine and quinine.

Sexual Cycle. From the asexual stage of the parasites there arise male and female gametocytes. If the patient with gametocytes in his blood is not bitten by an anopheline mosquito the gametocytes die out, but if the infected blood is taken up into the stomach of the mosquito the male gametocyte fertilizes the female gametocyte, which then penetrates the stomach wall of the mosquito giving rise to an oöcyst in which sporozoites are formed, thus[3] completing the cycle. The gametocytes of *P. falciparum* and to a less extent of other malarial parasites are rapidly destroyed by pamaquin and other 8-aminoquinolines. Drugs such as mepacrine which rapidly eliminate asexual forms from the blood-stream will naturally prevent the formation of gametocytes, although they will not destroy them once they are formed. Proguanil does not destroy the gametocytes while they are in the blood-stream of the

vertebrate host, but does interfere with fertilization and with the formation of the oöcyst in the anopheline mosquito (M. J. MacKerras and Q. N. Ercole,[14] P. G. Shute and M. Maryon[15]). L. Whitman[16] has shown that in *Aëdes aegypti* the sexual cycle of *P. gallinaceum* may be similarly inhibited by feeding with 2-hydroxy-3-β-decalyl-propyl-1, 4-naphthoquinone.

It is thus possible to control in some degree every stage in the life history of the malarial parasite.

Chemotherapeutic Treatment of Malaria in Man

The treatment of malarial infections of man is not a simple problem, for the populations which suffer from malaria are almost always divisible into two unequal groups : (1) Indigenous inhabitants who are exposed repeatedly to the same strain or strains of parasite and constitute the overwhelming majority of those infected ; (2) Immigrants who arrive in a malarial zone without previous exposure to the local strains, are only temporarily exposed to infection, and have but slight chance of reinfection. The first group is not, however, homogeneous : it consists of adults who have acquired both tolerance and a specific immunity to a particular strain, of very young children without either tolerance or specific immunity, and of people with intermediate degrees of tolerance and immunity. In " tolerance ", the host limits the degree of reaction, as shown by signs and symptoms, to a given infecting dose : in " specific immunity ", the host specifically inhibits the multiplication of the parasite (C. R. B. Blackburn[17]). Each generation of the indigenous inhabitants acquires specific immunity at the cost of a high death-rate in infancy. In Group I the object must be to allow the development of immunity without permitting acute attacks to endanger the life of the individual or to interfere with his normal enjoyment of life. If the development of immunity is prevented in childhood, the non-immune or partially immune adult becomes liable to severe attacks and if he lives in an area where *P. falciparum* is present he may suffer from blackwater fever. In the case of Group II the object is (1) to prevent the development of acute attacks by the use, if possible, of a true causal prophylactic ; (2) to control acute attacks as rapidly as possible ; and (3) to eradicate persisting exo-erythrocytic forms, thereby, in *vivax* malaria, preventing relapses : in other words there should be radical cure of infection and true causal or at least clinical prophylaxis.

In assessing the value of antimalarial drugs it is thus important to keep in mind the object for which the drug is administered, the type of person to whom the drug is being given, and the reactions which may be caused by the drug.

Infections due to *P. falciparum*.—Although the parasites of malignant tertian malaria may give rise to severe symptoms they are comparatively readily controlled by antimalarial drugs.

Quinine and other cinchona alkaloids should be avoided in the treatment of *falciparum* infections. By eliminating quinine both in the treatment and prevention of malaria in West Africa it was possible to prevent the onset of blackwater fever in European troops (G. M. Findlay and A. C. Stevenson[18]). The advantage of quinine lies in its low toxicity and in the rapidity of its action in removing parasites from the blood and lowering the temperature.

Mepacrine, 0·3 g. daily, is slightly slower than quinine, 30 gr. daily. J. Bryant[19] was the first to show that with a larger dose of mepacrine during the first 24 hours of treatment the results were as good as those with quinine. In West Africa in a controlled series of cases it was found that 0·8 g. during the first 24 hours of treatment, followed by 0·4 g. on the second and third days, and 0·3 g. for a further 3 days, a total of 2·5 g. in 6 days, was superior to the usual 0·3 g. daily, and no more toxic : it was also more rapid in its action than

quinine (G. M. Findlay et al.[20]). Mepacrine has now been found to act rapidly on strains of *P. falciparum* from all parts of the world. Though some doubt has, however, been thrown on the correlation of plasma concentration and therapeutic response (E. K. Marshall, jun., and E. H. Dearborn[21]), carefully controlled experiments by J. A. Shannon et al.[22] and J. A. Shannon and D. P. Earle, jun.[23] suggest that the minimum concentration of mepacrine in the plasma necessary for the alleviation of symptoms is 30 μg. per litre. Other observers have found that therapeutic response is more closely correlated with oral dosage than with plasma concentration. If daily administration of mepacrine is continued for 6 or 7 weeks after an acute attack the infection will be entirely eradicated (S. F. Kitchen and P. Putnam,[24] N. H. Fairley et al.[25]). Mepacrine is readily absorbed from the intestinal tract and there are few reports of non-absorption, whereas quinine may not be absorbed in a certain percentage of people.

Chloroquine will also rapidly control acute infection due to *P. falciparum*, though further investigation on a larger number of strains is still necessary. An initial dose of 0·6 g. of the base, followed 6 to 8 hours later by 0·3 g. and then by a single dose of 0·3 g. on each of two consecutive days, will remove symptoms in from 24 to 48 hours, while parasites disappear from the bloodstream in from 48 to 72 hours. This régime will also eliminate infections due to *P. falciparum* (R. F. Loeb et al.[26]).

Proguanil (paludrine) will also rapidly control *falciparum* infections. B. G. Maegraith et al.[27] found that what were probably radical cures followed doses of 200 to 400 mg. daily for 14 days, while clinical cures resulted from 20 mg. daily for 14 days or 500 mg. daily for 4 days. Clinical cures of New Guinea strains were obtained by N. H. Fairley et al.[28] with a single dose of 100 mg. These results have generally been confirmed with Asiatic strains of *P. falciparum*, but with strains from tropical Africa doses of 300 mg. daily are necessary for at least 7 days, the response is slower than with mepacrine, and radical cure does not result. A more rapid action is gained by combining mepacrine and proguanil.

Suppression and Causal Prophylaxis.—Quinine and mepacrine are not true causal prophylactics, since they do not prevent the development of exo-erythrocytic forms. They do, however, suppress the asexual blood forms. Mepacrine 100 mg. daily was shown by N. A. Fairley et al.[25] to be superior to quinine with New Guinea strains and the same was true in field experiments in West Africa. N. H. Fairley et al.[29] (1946), however, found that one strain of *falciparum* malaria existed in the Aitaipe-Wewak area for which 0·2 g. daily was not always sufficient to prevent infection. The majority of failures with mepacrine suppression are due to failure to take the drug daily.

Proguanil will act as a true causal prophylactic with New Guinea strains if taken in a dose of 100 mg. once weekly (N. H. Fairley et al.[28]). There is, however, increasing evidence that with some strains from tropical Africa daily doses of 100 mg. cannot always be guaranteed to act as a suppressive.

Chloroquine has been used as a suppressive against strains of *P. falciparum* in India and Africa (K. Goldsmith,[30] G. Doucet[31]): weekly doses of either 0·25 or 0·3 g. of the base give excellent results. Chloroquine, like mepacrine, is not a true causal prophylactic, but unlike mepacrine it need be taken only once a week and it does not stain the tissues.

Gametocytocidal Action.—The gametocytes of *P. falciparum* are attacked by pamaquin and other 8-aminoquinolines in doses of 0·03 g. daily for 5 days. These compounds, however, have very little action on the asexual forms.

Infections due to *P. vivax.*—Acute infections due to *P. vivax* are readily controlled by chemotherapeutic drugs, and owing to the fact that there is not

the same tendency to develop blackwater fever there is no objection to the administration of quinine. Some strains of *P. vivax*, particularly those of Italian origin, are more resistant to quinine than those of Indian origin (P. G. Shute[32]) : concentrations of quinine in the plasma of 6 mg. per litre produce a complete interruption of the asexual cycle. Mepacrine, chloroquine, and proguanil also bring the asexual cycle to an end. In the case of chloroquine, H. Most et al.[33] used three treatment schedules : (1) 1·0 g. of the diphosphate in 24 hours, (2) 1·5 g. in 4 days, (3) 2·0 g. in 7 days. H. H. Gordon et al.[34] found chloroquine equal to mepacrine in controlling acute attacks when the following doses of the base were given : 2·0 g. in 6 days, 1·2 g. in 3 days, or 0·8 g. in 3 days. The initial dose is 600 mg., followed by 300 mg. after 6 to 8 hours and a single dose of 300 mg. on each of the next two days. Concentrations of 10 μg. per litre of blood are essential to bring about cessation of the asexual cycle. Proguanil is also an active schizonticide in *vivax* malaria. Comparatively small doses are effective, and according to R. D. C. Johnstone[35] there is little difference in the rapidity of response to 50 mg. daily for 10 days and 500 mg. daily for 10 days. In India a single dose of 100 mg. ends the acute attack in 74 per cent of cases (M. K. Afridi[36]) : doses of 300 mg. give slightly better responses.

None of these drugs alone brings about radical cure, because they do not destroy the exo-erythrocytic forms.

Various forms of treatment have been tested with a view to the total eradication of infection. The results may be summarized briefly as follows :—

Drug	No. of Cases Treated	No. of Cases Relapsed	Percentage of Relapses
Quinine	182	158	86·8
Mepacrine	1136	509	44·8
Proguanil	315	138	40·6
Chloroquine diphosphate	126	81	64·2
Nivaquine	183	72	39·3
Pentaquine (base)	40	13	22·5
Pamaquin	7	7	100·0
Quinine and pamaquin	1325	178	13·4
Quinine and pentaquine	187	28	15·9
Proguanil and pamaquin	411	68	16·5
Proguanil and pentaquine	5	4	80·0
Proguanil and quinine	10	9	90·0
Quinine and metachloridine	5	4	80·0
Chloroquine and metachloridine	5	4	80·0
Pamaquin and metachloridine	5	5	100·0
Quinine, pamaquin, and mepacrine	29	5	17·2
Pamaquin and mepacrine	98	59	61·0
Mepacrine and sulphamerazine	112	77	69·0
Intermittent quinine and pamaquin	45	0	0·0
Intermittent mepacrine	42	12	28·6

It will be seen that the best results are obtained with a combination of quinine and either pamaquin or pentaquine. The usual dosage of quinine is 2·0 g. daily accompanied by 30 mg. of pamaquin continued for 10 to 16 days. R. W. Berliner et al.,[37] however, have given 90 mg. of pamaquin daily. J. F. Monk et al.[38] have obtained the best results with three courses of quinine, 2 g. and pamaquin 30 mg. daily continued for 7, 5, and 5 days so that the whole course lasts for 31 days. Of 45 patients given this course none relapsed during an observation period of 180 days. There is thus a possibility that a high percentage of *vivax* infections can be eradicated.

Suppression of vivax Infections.—No drug has yet been found which acts as a true causal prophylactic of infections due to *P. vivax*. N. H. Fairley et al.[28] found that proguanil inhibited the appearance of asexual forms in the

red cells while the drug is actually being taken. Occasional instances of an acute attack have been noted with daily doses of 100 mg. If proguanil is used as a suppressive this dosage must be taken daily in hyperendemic areas throughout the year, in areas where the disease is seasonal only during the period of prevalence. Chloroquine has the advantage that it needs to be taken only once a week in doses similar to those used against *P. falciparum* ; in addition chloroquine does not stain the skin as does mepacrine.

Toxic Reactions

The reactions due to antimalarial drugs are as a rule infrequent. This is specially true of quinine and other cinchona alkaloids.

Quinine, however, is a general cytoplasmic poison and occasionally reactions are seen. These are : (1) Hypersensitivity : the patient displays buzzing in the ears and deafness after therapeutic doses which do not affect the normal person. (2) Idiosyncrasy : signs and symptoms such as skin rashes which do not occur in normal persons. (3) Acute poisoning has occurred after 240 gr. (4) Wrong administration : death occurred after 1 g. given intravenously. (5) Acute hæmolytic anæmia : 12 cases have been recorded, not necessarily after large doses. (6) Amblyopia may also occur after moderate doses : just under 250 cases have been recorded. (7) Agranulocytosis and purpura are very rare.

Mepacrine also gives rise to certain toxic symptoms : it stains the skin yellow but this is of no consequence. It may cause slight symptoms of nausea and abdominal discomfort, but these usually pass off rapidly. The main toxic reactions are : (1) Skin eruptions : (*a*) Dermatitis with, rarely, exfoliative dermatitis ; (*b*) A lichen-planus-like eruption ; (*c*) Blue pigmentations on nails, and hard palate. (2) Psychoses : Among 90,221 persons recorded there were 149 cases, an incidence of 1·65 per 1000 (G. M. Findlay[39]). (3) Aplastic anæmia, agranulocytosis, and acute hepatitis are very rare. (4) In those engaged in manufacturing mepacrine there may be a yellow discoloration of the conjunctiva in the interpalpebral space and a slight dulling and yellowing of the cornea (I. Mann[40]) ; œdema of the corneal cells may very rarely occur in those taking large doses (F. M. Reese,[41] 1946).

Chloroquine.—Reactions are rather more frequent than with mepacrine. Nausea, vomiting, anorexia, abdominal cramps, diarrhœa, dizziness, pruritus, urticaria, and skin rashes have been noted. The suggested suppressive dose of 300 mg. once a week, if persisted in, may, as suggested by O. G. FitzHugh et al.,[42] be near the toxic level.

Nivaquine has produced a very low rate of toxic reactions : a few instances have been noted of nausea and vomiting, diarrhœa, and tinnitus (H. H. Gordon et al.[34]).

Pamaquin may give rise to asthenia, cyanosis, vomiting, and gastralgia. The cyanosis is most noticeable in the lips, tongue, and finger-nails, and occasionally in the lobules of the ears. It is due to the formation of methæm-albumin. In addition to this change in the blood pigments, acute anæmia, sometimes associated with hæmoglobinuria, and neutrophilic granulocytopenia may be seen.

Pentaquine has a very similar reaction.

Proguanil occasionally causes mild gastro-intestinal upsets if taken on an empty stomach, probably due to inhibition of gastric secretion (J. H. Burn and J. R. Vane[43]). Itching, puffiness, and erythema of the face, palms of the hands, and soles of the feet are uncommon. Desquamation may occur in these erythematous areas.

Drug Resistance

It is not easy to produce any degree of drug resistance in plasmodia against quinine or mepacrine. *P. gallinaceum* has been rendered resistant to minimal effective doses of pamaquin after 8 months' exposure (A. Bishop and B. Birkett[44]). Proguanil, however, gives rise to resistant strains comparatively readily; *P. gallinaceum* in chickens, and *P. cynomolgi* in monkeys have been made resistant, and there is evidence that *P. falciparum* and *P. vivax* in man may also become drug-fast (A. Bishop and E. W. McConnachie,[45] J. Williams et al.,[46] F. Hawking and W. L. M. Perry,[47] A. R. D. Adams and D. R. Seaton,[48] E. M. Lourie and D. R. Seaton[49]). These facts must be taken into account in adopting any suppressive régime.

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MALIGNANT MALNUTRITION (Kwashiorkor, Fatty Liver Disease in Infants).

Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.

The syndrome which has been observed in the West Indies by J. C. Waterlow[1] clearly belongs to a group of related conditions. An important member of this group is the disease known in Africa as *kwashiorkor* ("red boy") of which the first account was given by C. D. Williams[2] (1933) on the Gold Coast. H. C. Trowell[3] (1937) has given a detailed description of it in Uganda, S. L. Kark[4] (1943) in Basutuland, T. Gillman and J. Gillman[5] (1945) in Johannesburg, W. Hughes[6] in Nigeria (1946), B. A. S. Russell[7] (1946) in Ashanti, and M. Gelfand[8] (1946) in S. Rhodesia. Apparently the same syndrome has been reported in Mexico (1934), San Salvador, Cuba, Costa Rica, and Guatemala.

Trowell in tropical Africa describes it as an acute and fatal disease attacking infants in the first few years of life. It is characterized by œdema, "crazy-pavement" skin, diarrhœa, cheilosis, stomatitis, generalized skin pallor, straight and scanty hair. Neurological changes may occur but are slight and terminal. Microcytic or macrocytic anæmia are variable features.

In the disease as observed in the West Indies the main features were œdema, muscular wasting, and fatty infiltration of the liver. It differed in some respects from the disease of Africa known as kwashiorkor in that a number of lesions characteristic of it are often absent. These are depigmentation of the skin and hair, "crazy-pavement" dermatosis, ulceration of the buccal mucosa, and fissuring of mucocutaneous junctions, some of which are probably caused by a vitamin B_2 complex deficiency; but both the West Indian and the African diseases differ from the commoner deficiency states in three directions—fatty infiltration of the liver, high mortality, and resistance to dietetic treatment. Probably the fatty liver must be regarded as the fundamental lesion, and it is this feature which renders it resistant to treatment and

responsible for deaths. It is suggested that the West Indian fatty disease is seen in a relatively pure form, whereas kwashiorkor is a multiple deficiency state. In the West Indies fatty liver disease begins soon after weaning and is due probably to inadequate feeding after breast feeding has been stopped. Inadequacy of feeding at this stage is reflected in the weight curve of West Indian babies, which shows a marked falling-off during the six months after weaning.

The main complaints were œdema and vomiting. There was gross muscular wasting, but subcutaneous fat was not completely lost. The liver was enlarged and in some there was mild glossitis and angular stomatitis. Anæmia was of moderate severity. The serum protein concentration was reduced; the total protein in 8 out of 14 cases was less than 4·5 g. per 100 ml., the reduction being mainly in the albumin fraction.

In the 4 fatal cases there was gross fatty infiltration of the liver, and the same lesion was demonstrated by means of liver biopsy. There was no evidence of liver necrosis, but a moderate amount of iron pigmentation was present. In treatment there was no evidence that methionine, choline, or inositol had any beneficial effect, but improvement occurred on a high intake of milk.

It is suggested that cirrhosis of the liver in Africans develops as a result of preceding fatty infiltration and therefore represents the final stage of the disease. The question is raised of the part played by hepatic, pancreatic, and intestinal insufficiency in the production of steatorrhœa, but no definite conclusion is possible.

Œdema is considered to be the result of hypoprotinæmia, and this, in turn, is attributed to low protein intake. Fatty liver infiltration is considered to be the result of malnutrition. The source of the liver fat is thought to be *exogenous*, whereas in wasting diseases it is *endogenous*. This exogenous fat, in animal experiments, only occurs when there is a relatively high caloric intake and this harmonizes with observations in the West Indies. In babies dying of undernutrition the findings were very different. In contrast with African fatty liver disease in infants the West Indian type is seen in relatively pure form, uncomplicated by evidence of avitaminosis. This together with failure of vitamins in treatment suggests that the fatty change is not the result of any known vitamin deficiency.

The similarity of the descriptions of this fatty liver disease of the tropics with that described in Germany and Central Europe in children fed on excessive carbohydrate dietaries and generally known as *Mehlnahrschadung* of Czerny and Keller[9] (1906) is apparent. This European disease is produced also by overfeeding with carbohydrates and improves on a milk dietary.

REFERENCES.—[1]"Fatty Liver Disease in Infants in the British West Indies", *Spec. Rep. Ser. med. Res. Coun.* No. 263, 1948; [2]*Arch. Dis. Childh.* 1933, **8**, 423; [3]*Ibid.* 1937, **12**, 193, *Trans. R. Soc. trop. Med. Hyg.* 1940, **33**, 389; [4]*S. Afr. J. Med. S.* 1943, **8**, 106; [5]*Arch. Path.* 1945, **40**, 239; [6]*Trans. R. Soc. trop. Med. Hyg.* 1946, **39**, 437; [7]*Arch. Dis. Childh.* 1946, **21**, 110; [8]*Clin. Proc.*, Capetown, 1946, **5**, 135; [9]*Des Kindes Ernährung, Ernährung-Störrungen, u. Ernährungs Therapie*, 1906 (2nd ed. Leipzig, 1928).

MEASLES.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Epidemiology.—Notifications of measles in 1946 numbered 160,402, and there were 204 deaths. The low fatality-rate of 0·13 is remarkable. Its causes are complex and not fully understood.[1]

Prevention and Attenuation.—Gamma globulin, prepared in U.S.A. from human serum, was tested in Great Britain by a sub-committee which reports to the Medical Research Council.[2] Tests were carried out on contacts of measles of various ages in hospital, schools, nurseries, and at home, mainly in Glasgow and London. It was shown that gamma globulin prepared by Cohn's method

contains measles antibodies in high concentration, and that the volume of this gamma globulin required for the prevention and attenuation of measles is about half the volume of convalescent measles serum required for the same purpose. Although gamma globulin is thus superior to convalescent measles serum, it did not give full protection in the doses used, but in all cases either protection or attenuation was obtained. A batch of out-dated gamma globulin (used some two years after its preparation) showed but little diminution in potency from that of the fresh batches. No local or general reactions followed the injection of gamma globulin. [Preparation of this gamma globulin required an elaborate low-temperature plant and a large amount of alcohol. It does not follow that the gamma globulin so far manufactured in Britain has the same potency as the American product. H. S. B.]

J. Stokes, jun., et al.[3] could not find any evidence of serum hepatitis in 3000 measles contacts injected with gamma globulin. They consider either that the virus of serum hepatitis may be destroyed in the processing or that the gamma globulin may contain antibodies to this virus as well as to that of measles. M. C. Blanchard et al.[4] felt that reliance could not be placed on either of these possibilities, and recommended that the filtered serum before processing should be sterilized by exposure to ultra-violet light in a rotating tube.

REFERENCES. [1]*Ann. Rep. Min. Hlth*, 1947, 26, H.M.S.O. Lond.; [2]*Lancet*, 1948, **2**, 41; [3]*J. Amer. med. Ass.* 1948, **138**, 336; [4]*Ibid.* 341.

MECKEL'S DIVERTICULUM. (*See* INTESTINES, SURGERY OF—DIVERTICULA.)

MEGACOLON. (*See* HIRSCHSPRUNG'S DISEASE.)

MENINGITIS. *H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.*

Penicillin-resistant Bacterial Meningitis.—C. Wilson[1] reports 14 cases treated with *streptomycin*. The causal organisms included *B. coli*, *Ps. pyocyanea*, *Staph. pyogenes*, *Proteus*, and *Str. faecalis*. The infection was controlled in 11 of the 14 cases. Streptomycin is therefore a valuable new therapeutic agent in pyogenic meningitis due to penicillin-resistant organisms. W. Lewin and R. L. Vollum[2] treated 6 such cases, with 4 recoveries (one relapse), 1 death, and 1 unchanged.

Actinomycosis Meningitis. J. R. Jacobson and R. B. Cloward[3] report what is claimed to be the first recorded cure of this condition. It was effected by combined *penicillin*, *sulphadiazine*, and *streptomycin*.

Influenzal Meningitis.

Streptomycin Treatment.—C. Wilson[4] reports to the Medical Research Council on 34 cases. An organism of Pittman type b was grown from the spinal fluid in all of them before the treatment was begun. The infection was controlled by streptomycin in 25 and treatment failed in 9. There was no significant difference in age, duration, or C.S.F. changes between the two groups, but, clinically, the unsuccessful cases appeared to be more severe. When treatment was successful the C.S.F. usually became sterile within twenty-four hours of the first intrathecal injection. Streptomycin was effective in 13 cases which had relapsed on other treatment. A relapse with streptomycin treatment occurred in 4 cases, but further treatment of these with streptomycin alone was successful. The principal cause of failure was development of resistance by the organism; this occurred in 7 of the 9 failures, sensitivity changing from 0·5 to as high as 5000 units in one to four days. Since development of resistance is thus a serious drawback, it was decided to use in future trials a combination of streptomycin, penicillin, and sulphonamides from the start. [It will be recalled that H. Alexander and G. Leidy[5] recommended treatment of severe cases with combined streptomycin, *antiserum*, and sulphonamides.—H. S. B.]

P. M. Smythe[6] treated 11 of the above cases with the dosage recommended, usually 20 mg. of streptomycin per lb. of body-weight daily, divided into six intramuscular injections, together with a daily intrathecal injection of 25 to 100 mg. in 5 ml. of saline, the dose varying with the age of the patient and the severity of the disease. Treatment by both routes was continued until the C.S.F. had been sterile for a week. Of the 11 cases, 3 died.

REFERENCES.– [1]*Lancet*, 1948, **2**, 446; [2]*Ibid.*; [3]*J. Amer. med. Ass.* 1948, **137**, 769; [4]*Lancet*, 1948, **2**, 445; [5]*Med. Annu.* 1948, 165; [6]*Lancet*, 1948, **2**, 485.

MENINGOCOCCOSIS. *Macdonald Critchley, M.D., F.R.C.P.*

In his Milroy Lectures (1945) H. Stanley Banks[1] utilized his exceptional experience of cerebrospinal fever. His observations are based upon 706 cases admitted to the Park Hospital between January 1, 1939, and June 30, 1947. The lectures are of extreme value as well as interest and they form an important landmark in the literature of this subject. Banks first of all deals with the question of terminology. Believing that 'cerebrospinal fever' is no longer an adequate term to embrace all the protean features of the disease, Banks suggests the generic expression 'meningococcosis' on the analogy of tuberculosis and trichinosis.

This wartime period was interesting in that it witnessed a decline in favour of serotherapy (which the author had already rejected as unnecessary); the stabilization of chemotherapy with the various sulpha drugs; and the introduction of penicillin. These years also include an epidemic period, namely, during the triennium 1940, 1941, and 1942. Of these years 1940 easily held the greatest number of cases, and in each year March was the peak month.

The death-rate over the whole period 1939–47 proved to be 7·36 per cent, and as there was no selection of cases, the mortality included patients admitted to hospital in a moribund state.

When Banks's cases were tabulated with respect to age-incidence and mortality, it was found: (1) There were far more cases in infants under one year than in any other single year of life; (2) The incidence declines with age, except for the period 15 to 25 years; (3) After the age of 35 there is a sharp drop, and after the age of 55 another and still sharper drop, in incidence; and (4) Case-fatality rates are high only at the extremes of life, the lowest level being between 15 and 25 years.

As regards the manner of invasion of the nervous system, Banks holds the stages to be, ordinarily: (1) A phase of nasopharyngeal infection, usually subclinical; (2) Bacteræmia; and (3) Meningitis. Banks is dubious about R. W. Fairbrother's[2] contention that the meninges are involved from the nasopharynx via perineural pathways. The intermediate stage of bacteræmia seems to have been clearly proved, although it may be quite short, i.e., a matter of minutes or hours in ordinary types, and two or three days in exceptional cases. A rash is to be observed at this stage in 25 to 50 per cent of cases.

Varieties. – The 'ordinary' types are encountered in at least 90 per cent of all clinical cases, but Banks pays particular attention in his lectures to the rarer forms. Their atypical characters often lead to errors or delays in diagnosis, and for such reason they deserve especial notice.

Chronic meningococcal septicæmia was an important manifestation of meningococcosis in the army during the period 1940–42. The clinical picture, according to Banks, is characteristic: (1) Bouts of pyrexia every two or three days, with or without rigors and sweating; (2) Recurring crops of papules—often petechial—over the trunk or limbs; (3) Raised circular erythematous areas resembling erythema nodosum; and (4) Pains in bones, joints, muscles, tendons, and fasciæ. Such cases should be investigated by means of a blood-culture, though

a negative result is frequent. Unless treated with sulphonamides, such cases may linger on for months or even years, either subsiding eventually or culminating in meningitis.

Acute diffuse encephalitis is the name applied to a type where the patients show the ordinary symptoms of meningitis for 24 hours or so, and then lapse into deep coma. Stertor, paralysis, and papillœdema are characteristic signs. The condition responds little, if at all, to sulphonamides, and death is common within a period of 3 to 7 days. Banks's series of 706 patients contained 13 such cases (with 7 deaths and 6 recoveries). Histological studies of the brain were made in 4 instances. The lesions to be expected in this acute diffuse encephalitic form of meningococcosis comprise congestion and œdema of the brain, perivascular lymphocytic infiltration, and widespread thromboses. Purulent meningitis was also present, though considerably modified if sulphonamides had been administered during life. Degenerative changes within the neurones may be demonstrable in a diffuse manner in the cerebrum, cerebellum, brain-stem, and cord. In 2 of the cases there were clusters of polymorphs suggesting incipient abscess formations (L. S. Banks and J. E. McCartney[3]). Absence of primary demyelination distinguishes these cases from the so-called acute hæmorrhagic leuco-encephalitis (W. B. Wartmann and I. C. Hanger[4]).

Fulminating meningococcal septicæmia may prove fatal in from 4 to 48 hours. Banks found no clear-cut distinction between cases with mainly neurological and those with circulatory involvement—as has been taught in the past. Banks prefers to divide this fulminating septicæmic group into three sub-groups: (1) encephalitic; (2) adrenal; and (3) mixed encephalitic-adrenal. The author deprecates the term 'Waterhouse-Friderichsen syndrome', believing this syndrome to be of composite pathology, in the clinical manifestations of which the important question of the degree of consciousness is not considered.

Of the *encephalitic* sub-group there were 6 examples, all fatal within 48 hours. A sudden onset of fever, vomiting, and anorexia leads rapidly to lethargy, stupor, and then coma. Convulsions occurred in the younger subjects. A petechial rash—not massively purpuric—appeared within 12 to 18 hours of the onset. Meningococci could be found within the blood. The morbid anatomy comprised hæmorrhagic brain changes with a commencing purulent meningitis. There were no adrenal lesions.

The *adrenal* sub-type was encountered in 13 cases, with 8 deaths. Main symptoms comprise sudden fever, malaise, and a generalized petechial rash which rapidly became purpuric—often massively so. Meningeal symptoms developed later. The mental state remained clear almost to the end. The blood-pressure was low. Meningococci could be demonstrated within the blood. Pathological studies revealed congestion of the brain and meninges, together with bilateral hæmorrhages within the adrenals.

In the *mixed encephalitic-adrenal* type, early deep coma is associated with a purpuric rash and low blood-pressure. In the author's series there were 5 such cases, all fatal. The post-mortem changes comprised a combination of the foregoing two sub-types. Occasionally the pituitary gland was also involved.

The classification here depicted still does not adequately account for all the observed clinical varieties. *Focal encephalitic lesions*, for example, may occur and cause sudden and unexpected collapse and death at a stage when the meningitis seems to be subsiding satisfactorily. Banks also mentions, briefly, *mild* and *abortive forms* especially occurring during an epidemic. The *chronic form* of the disease has become much rarer since the use of the sulphonamides. Other uncommon types of meningococcosis include *primary meningococcal ophthalmia*; *meningococcal hepatitis*; and *meningococcal pneumonia*.

Complications and Sequelæ.—Some of the older complications and sequelæ are nowadays rarely seen (e.g., pericarditis, neuro-radiculitis, hydrocephalus, and the chronic forms of the disease). To-day the three commonest after-results seem to be labyrinthitis, arthritis, and cranial-nerve palsies. Of these the first is the most important as it is associated with permanent deafness.

Labyrinthitis is due to direct infection of the perilymph from the subarachnoid space. Both vestibule and cochlea are usually affected. The defect of balance is usually relieved after a few months, but a permanent high-tone deafness in one or both ears is a common sequel (5 to 7 per cent of the author's series, the incidence being lower in the 15 to 30 year age-group).

Joint complications occurred in 4·7 per cent of Banks's cases, and consisted in arthritis, bursitis, and tenosynovitis.

Of *cranial-nerve palsies* the commonest were the 6th, 7th, 3rd, and 4th nerves (in that order). The paralysis is not permanent but may last up to four months, the average being 2 to 3 weeks.

Rare sequelæ—some of which found no place in Banks's series—include neuritis or radiculitis; hemiplegia; spastic paraplegia; focal epilepsy; thrombosis of the superior longitudinal sinus; iridochoroiditis; glycosuria; bronchopneumonia. The author refers to hydrocephalus arising from subarachnoidal adhesions as a much more frequent residium in the pre-sulphonamide days. Moreover, exudate may collect in the dorsal part of the cord and lead to adhesions, pressure on nerve-roots, or on the spinal cord itself.

Psychiatric sequelæ are also discussed. They consist in persistent headache, and are often associated with an hysterical overlay or prolongation, especially in military personnel. Accompanying symptoms include impaired powers of concentration, backache, insomnia, depression, postural dizziness, poor appetite, irritability, and other symptoms (which are almost identical with the post-concussional syndrome occurring after head injuries). In Banks's experience such symptoms are not permanent but tend to disappear within a year or two. The role of suggestion on the part of medical attendants is emphasized, and admission to hospital should as far as possible be avoided. Banks quoted the opinion expressed earlier by S. L. Ballard and H. G. Miller:[5] "Many of these symptoms are frankly hysterical in nature, and they are strikingly correlated with predisposition to psychoneurosis, as determined by psychiatric study of the personality. They are only partly correlated with the severity of the acute illness."

Treatment.—Ordinarily, the disease is best treated by chemotherapy alone, penicillin not being necessary. Sulphathiazole and sulphadiazine are the best drug in Banks's experience. Sulphanilamide should be given when renal blockage is feared, and either it or sulphamezathine in congestive heart failure. The scale of dosage used is that advocated by the Medical Research Council. The best drug for intravenous use is soluthiazole (M & B).

Spinal drainage is rarely necessary. Morphine should be avoided as it increases a tendency towards retention of urine. Sodium Amytal gr. 3 combined with paraldehyde min. 120 is useful, or else Somnifaine (Roche) 2 ml. intramuscularly or by mouth, repeated if necessary.

The management advocated by Banks for special syndromes may well be quoted in detail:—

Fulminating Septicæmia of Adrenal and Mixed Types.—

a. Combat the infection with sulphathiazole or sulphadiazine combined with systemic penicillin in high dosage.

b. Combat shock by adrenal replacement therapy, especially adrenal cortical extract—e.g., Eucortone 5 ml. or more intramuscularly every four hours; plasma intravenously seems also to be indicated in the present state of our knowledge.

c. Combat anoxæmia with oxygen, especially the oxygen tent for a child.

d. Combat any special complications—e.g., hyperglycæmia with insulin; dehydration with salines, etc.

Fulminating Septicæmia of Encephalitic Type.

a. Combat the infection with intravenous and intramuscular soluthiazole and penicillin.

b. Feed the patient by nasal tube.

c. Combat dehydration with parenteral or rectal saline.

d. Combat the œdema of the brain with intravenous hypertonic glucose.

Acute Diffuse Encephalitic Syndrome.

a. Combat the infection with intravenous and intramuscular soluthiazole and penicillin until consciousness is restored, and thereafter with sulphonamides by mouth.

b. Feed the patient by nasal tube.

c. Correct dehydration.

d. Give 20 ml. of 50 per cent glucose intravenously to reduce œdema of the brain, and repeat as necessary.

Prophylaxis.—Banks asserts that it is vain to attempt to isolate carriers. Mass prophylaxis by administration of sulphonamide is not without success. Quarantine of contacts is useless. Prophylactic sprays may even be harmful. Fomites, unless very recently contaminated, do not convey the infection. The routine use of masks by attendants or patients in the acute stage is impracticable and unnecessary.

REFERENCES. [1]*Lancet*, 1948, **2**, 635, 677; [2]*J. clin. Path.* 1947, **1**, 10; [3]*Lancet*, 1942, **1**, 219; [4]*Amer. J. med. Sci.* 1944, **208**, 234; [5]*Lancet*, 1945, **2**, 273.

MENINGO-ENCEPHALITIS (Louping-ill). (*See* LOUPING-ILL IN MAN.)

MENSTRUAL TOXIN. *Clifford White, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G.*

The existence of a menstrual toxin was demonstrated by D. I. Macht and D. S. Lubin[1] 25 years ago. O. Watkins Smith[2] has recently published the results of her 8 years' work on the subject. The method of obtaining the toxin is briefly as follows: After being centrifuged, the menstrual discharge separates into 3 layers, a supernatant serum, a bottom layer of red blood-cells, and a middle layer containing endometrial debris. The washed cells are not toxic, the serum is slightly toxic, and the washed endometrial debris contains most toxin. To estimate toxicity an immature male rat is injected subcutaneously and the dose that causes death in 8 hours is considered the minimum lethal dose (M.L.D.). After elaborate purification an atypical large-moleculed euglobulin is obtained which is thought to contain the toxin. It is extremely labile, being destroyed by a temperature of 45° C.; in aqueous suspension toxicity disappears fairly rapidly even if it is kept at a temperature below freezing. The only means of preserving the toxicity of the euglobulin is by rapid freeze-drying. Further experiments showed that the toxicity is not due to hæmolysis or to bacterial action. That bacterial action had nothing to do with the formation of the toxin is proved by noting that the toxicity gets less instead of more when the specimen is allowed to stand at room temperature, by finding toxin in endometrial scrapings obtained aseptically, and by passing it through a Seitz filter. It was found that endometrium obtained directly from the uterus just before and during menstruation was 3 or 4 times as toxic as endometrium taken at other times. This suggests that the premenstrual withdrawal of hormonal support permits catabolic changes in the endometrium which result in the formation of a highly toxic material. Further, it was found that post-ovulatory material contained more

toxin than material obtained from patients with anovular menstruation, and it is of interest to note that anovular menstruation is painless.

The rat killed by the injection of the euglobulin toxin shows constant post-mortem changes which are the result of vasoconstriction and local stasis. The injection is given subcutaneously in the nape of the neck. Within 12 hours the animal shows a bloody discharge from the eyes and nose, and it is usually dead after 24 hours. Autopsy shows a mottled liver, swollen pale kidneys, and enlarged purple adrenals.

V. Menkin[3] caused a pleural exudate in dogs by injecting turpentine, and from the exudate obtained a toxin which is called 'necrosin'. This necrosin is also a euglobulin, and the pathological effects of necrosin are found to be similar to those of the menstrual toxin. Since Menkin's necrosin results from tissue damage, their similar actions suggest that the menstrual toxin also results from tissue damage. Immunity to the menstrual toxin can be produced by repeated injections of sublethal amounts, and the serum of an immunized rabbit prevents death in a rat given a M.L.D. of toxin. The same serum affords equally good protection against a lethal dose of canine necrosin.

The euglobulin is fibrinolytic as well as toxic, which may have a bearing on the causation of dysmenorrhœa. The circulating blood of normal women at the time of menstruation differs from that obtained between catameniæ, and contains, in the euglobulin fraction, fibrinolytic and pyrogenic bodies.

Further work to connect the toxin with pregnancy toxæmia is proceeding. G. van S. Smith[4] suggests that all the symptoms connected with menstruation, except mammary engorgement, are due to the menstrual toxin. He thinks that premenstrual tension may be attributed to prolonged absorption of the toxin from a secretory endometrium before it degenerates. Diuresis occurs immediately menstruation starts, and is probably to get rid of the toxin and hence of the premenstrual molimina. He suggests that primary dysmenorrhœa is due to an exaggerated effect of the euglobulin toxin. During menstruation there is evidence of a protective pseudoglobulin in the circulating blood; its protective quality only becomes evident after removal of the toxic euglobulin fraction. Why the two bodies do not neutralize each other in the blood is unexplained. To test the dysmenorrhœa theory, 4 patients with primary dysmenorrhœa were given injections of the protective pseudoglobulin intramuscularly, and relief or prevention of the cramps seemed to result provided the material was injected within 2 hours of the onset of the pain. The series is much too small on which to form conclusions.

REFERENCES.—[1]*J. Pharmacol.* 1923, **22**, 413; [2]*Amer. J. Obstet. Gynec.* 1947, **2**, 201; [3]*Science*, 1943, **97**, 165; [4]*Amer. J. Obstet. Gynec.* 1947, **2**, 212.

MENTAL DISEASES. (*See also* LEUCOTOMY; PSYCHIATRY, CLINICAL.)

MENTAL DISEASES: GENERAL TREATMENT

E. W. Anderson, M.D., F.R.C.P., D.P.M.

Penicillin has shown promising results in *neurosyphilis*. Whether it can by itself influence the pathological process is less certain. The findings, therefore, of R. H. F. Smith and V. R. de Morais,[1] who examined histologically the brains of 4 paretics who had been treated by penicillin are of great interest; especially since no similar previous reports have appeared. Two of these patients had shown clinical as well as serological improvement; the 2 which did not were juvenile forms and 1 of them was a Lissauer type. Examination of the brains of the 2 improved cases showed less intense inflammation than in untreated cases, resembling that found after malarial therapy. The iron-reaction was positive in all 4, but least in the improved. No spirochætes were found in any

of the 4 brains. The authors are naturally guarded in drawing conclusions from such a very small number of cases, but they consider that penicillin alone may be capable of directly influencing the disease process.

REFERENCE.—[1]*J. ment. Sci.* 1948, **94**, 70.

MENTAL DISEASES: PHYSICAL TREATMENT.

E. W. Anderson, M.D., F.R.C.P., D.P.M.

1. Electronarcosis.—A number of papers have appeared on this subject, but relatively few considering its comparative novelty. A. S. Paterson and W. L. Milligan[1] (1947) have described their technique of electronarcosis using the Shotter-Rich apparatus. They reported results on 20 schizophrenics who had been ill for varying durations. In most cases 12 treatments a month had been given. They claimed encouraging results but gave no figures. This they followed up by separate communications to the Royal Society of Medicine (1948). Paterson[2] (1948) gave the following results in 35 schizophrenics:—

	Total	*Recovered and Working*	*Improved and Working*	*No, or Slight, Improvement*
Group I. Previous attack with recovery	9	7 at work	1 at work	1
Group II.—Ill less than 1 year	10	7 at work	2 at work	1
Group III.—Ill more than 1 year (av. 3·2 yr.)	16	4 at work	3 at work	9

He confirmed the observations of E. B. Tietz[3] (1947), R. W. Medlicott[4, 5] (1947, 1948), and W. L. Milligan[6] (1948). Medlicott's figures for all types of schizophrenia, apart from "acute schizophrenic reaction states" and "undetermined" cases, show that paranoids alone (37·5 per cent) returned to the premorbid level, whilst the others only achieved at best recovery at a reduced level, and that older paranoid types do better than younger hebephrenics. Paterson believes that these older patients do better with electronarcosis than with insulin. He compared the results of E.C.T. with electronarcosis in schizophrenics: 6 patients out of 14 who failed to respond to E.C.T. are said to have recovered with electronarcosis, 3 improved, and 5 were no better. The possibility of synergic action between the two forms of treatment is suggested.

Sixteen cases of severe depression were also treated with electronarcosis, 13 of whom had shown no response to E.C.T. A good recovery was claimed for 12 of these patients; the other 4 showed no lasting improvement. Nine cases of psychoneurosis were treated with electronarcosis and all but 1 improved.

W. L. Milligan (1948), who followed, reported results in 70 cases of schizophrenia, 10 of whom were children. He claims complete remission in 44 per cent, social recoveries in 17 per cent, and "social defects" in 8 per cent; 16 per cent improved in hospital, and in 14 per cent no improvement took place. None of the 10 children improved. Excluding the children his results were as follows:—

	Total	*Per cent*				
		A	B	C	D	E
Adults alone	60	52	20	10	10	8

(A = Complete remission; B = Social recovery; C = "Social defect"; D = Improved in hospital; E = No improvement.)

He gives the following results for adults according to duration of illness:—

	Total	*Per cent*				
		A	B	C	D	E
Less than 1 year	7	100	—	—	—	—
,, ,, 2 years	17	88	12	—	—	—
,, ,, 5 ,,	40	60	20	7	10	2
More ,, 5 ,,	20	34	20	15	10	20

In many cases of schizophrenia, especially hebephrenic and paranoid forms, the treatment had the effect of activating the psychosis, producing excited and

violent behaviour; 10 paraphrenics responded quite well to treatment. W. Grey Walter[7] (1948), in the subsequent discussion, professed scepticism as to the nature of the effects described. He suggested that following experiments he had conducted some years previously to discover the margin between the maximum therapeutic and minimum lethal dose of current in E.C.T. he had obtained a loss of consciousness similar to that described in electronarcosis which he interpreted as due to gross over-stimulation of a large part of the central nervous system. He considered that the technique of electronarcosis produced just this over-stimulation and the use of the term "electronarcosis" was therefore misleading. It seemed to him possible that the therapeutic effect depended primarily upon over-stimulation, exhaustion, and reconditioning rather than upon the induced repose akin to natural rest claimed by the writers.

Although nearly all the authors hold that the procedure is essentially safe with due precautions, G. Garmany and D. F. Early[8] (1948) reported 3 types of complication in some patients of a series of 28 to whom they had given electronarcosis. In 1 case hæmoptysis occurred, in 2 severe clouding of consciousness, which in 2 patients lasted many days; in neither of these 2 patients was there evidence of cerebral vascular disease, and although psychometric tests showed no deterioration, the possibility of such permanent change caused them concern. The third and most important complication was collapse, which occurred in 7 patients, with only 2 of whom the authors were prepared to continue treatment. The symptoms were greyish pallor, imperceptible pulse, tachycardia, and sighing infrequent respiration. They obtained no lasting improvement in any of the 21 cases of schizophrenia they treated, although not all of this number finished treatment.

A. S. Paterson and Glyn Davies[9] (1948), replying to these criticisms at length, stated that they had only seen hæmoptysis occur in E.C.T. but never in electronarcosis, that confusion was an unimportant complication, and that with care and appropriate measures (curare) the risk of circulatory collapse could be minimized.

W. L. Milligan[10] (1948), who also replied, stated that in over 1100 treatments only 2 cases of cardiac collapse occurred, and only one hæmoptysis for which no chest pathology could be found. He believed that a confusional state had therapeutic value rather than otherwise.

Of the complications of the treatment, *memory defects*, usually transient, are reported by all the writers (Paterson (1948), Milligan (1948), Medlicott (1947), Tietz (1947)). These are said to be nearly always transitory. Milligan (1948) reports one case of a sudden short circumscribed amnesia after a social function, but the possibility of alcohol, as one factor at any rate, could not, it would seem, be completely eliminated in this case. Medlicott (1947) reports the rapid appearance of memory defects following daily treatment in the first few cases, but in many intelligent patients no failure was found on testing. The most striking defects, however, were not for immediately recent events, but for more remote, in some cases extending up to the previous two years. In one case this amnesia was persistent, but the patient appeared to have made a satisfactory recovery. Medlicott (1948) also reports transient confusional episodes following electronarcosis. He found no permanent adverse change in the mental condition of any patient. In two of his cases epileptic fits seemed to have been released by the treatment [as in one patient later under the reviewer's care].

The *blood-pressure* may rise alarmingly to as high as 260/160 (Paterson) after completion of treatment, in 15 cases of Medlicott's, where the increase reached hypertensive levels. In two cases this caused some anxiety. The estimation of resting blood-pressure during a course of treatment is recommended, and if a steady rise occurs treatment should be discontinued.

Three cases of *vertebral compression fractures* were recorded by Tietz (1947), but no more after curare was administered as a routine. Medlicott (1947) reported no fractures in his series. No other report of fractures with electro-narcosis has been found.

[It is, of course, too early to assess the value of this therapy; the published figures are small and discrepant, and results like those of Paterson and Milligan (1948) and Tietz (1947), particularly for old schizophrenics, must excite surprise. One cannot dismiss lightly the complications reported, and until more is known about this procedure the proper attitude is one of reserve. E. W. A.]

2. Electro-convulsive Therapy. A large number of papers continue to appear, but interest has been shifting from the statistical results of treatment to the *modus operandi*, to modifications of technique, to the use of the treatment in other forms of mental illness than depressive states, and to complications. Among the more important recent publications not so far reviewed in the MEDICAL ANNUAL is that of H. H. Dedichen[11] (1946), who made a follow-up investigation of shock-treated cases (1459 cases, 803 women, 656 men). Of these, 1087 (565 women, 522 men) received convulsion therapy, mostly with pentrosol; 159 females and 84 males were treated by insulin; and the rest had combined treatment. The incidence of relapse in 495 patients of this group was studied over a 4-year period. The whole material was controlled by 969 non-shock-treated cases from 3 mental hospitals. The results were statistically evaluated. The author divided his cases into 3 groups: (1) Uncomplicated schizophrenia; (2) Hebephrenic-paranoid and katatonic syndromes with manic-depressive or confusional features; (3) Pure manic-depressive illnesses. In Group 1 (schizophrenic illnesses) the percentage of remissions was 63·3 for the treated and 14·7 for the controls in cases with a duration of 0–6 months. Group 2 cases of similar duration showed 77·4 per cent remissions in shock-treated and 46·9 per cent of controls. Group 3 showed 81·7 per cent for shock-treated and 82·0 per cent for the controls. In those cases with duration of illness 6 months–1 year the figures in percentages were: Group 1, shock-treated 12·3, controls 7·9; Group 2, shock-treated 62·8, controls 33·3; Group 3, shock-treated 75·8, controls only 16 in this group. Of cases of duration 1–2 years: Group 1, shock-treated 12·3, controls 7·9; Group 2, shock-treated 29·5, controls 32·0; Group 3, 33·3 among convulsion-treated. Of cases of duration 2–5 years only Group 1 had a large enough number of cases for comparison: shock-treated 10·7, controls 8·7.

The author found significant differences between the treated and the non-treated in Group 1 for cases of duration 0–6 months (6·3 times standard error) and a probable significance (2·5 times standard error) for cases with duration 6 months to 1 year, but no significant differences for cases of longer duration. In Group 2, 0–6 months (4·7 times standard error) 6–12 months (3·3 times standard error); but for Group 3 no differences were found between the two groups. These results of shock treatment of manic-depressive illness are at variance with the majority of published reports, and suggest a more critical attitude to the long-term benefits at least of shock therapy in affective disorders. On the other hand Dedichen's figures for shock-treated schizophrenics are equally noteworthy, and at variance with general experience.

H. S. Rubinstein[12] (1948), pointing out that a number of patients show emotional reactions to E.C.T., modifies the orthodox technique by giving pentothal sodium (4–8 c.c. of a 5 per cent solution, through one minute beforehand). The author believes that although the convulsion is avoided this method is as effective as the ordinary procedure. He finds it useful in aged subjects and in giving treatment to those who have already sustained a vertebral fracture. No complications were observed in over 500 treatments.

H. C. Solomon, A. S. Rose, and R. E. Arnot[13] (1948) report on the use of E.C.T. in general paralysis. Thirteen patients during the previous year were given E.C.T. in addition to malaria and penicillin. They describe 3 patients who, after the antisyphilitic treatment had been given, were yet so disturbed that their continued detention in hospital was necessary and whose residual symptoms were removed by E.C.T. In one case where extreme restlessness was endangering the life of the patient, E.C.T. by removing this symptom probably saved life. The patients with affective features responded, but E.C.T. was of little value in cases presenting schizophrenic syndromes. No serious complications arose.

It is well known that the E.E.G. after E.C.T. shows a convulsive pattern. Prima facie there would seem to be considerable risk of inducing or unmasking a latent clinical epilepsy by this treatment in the presence of an abnormal E.E.G. which is generally considered a contra-indication. There seems no risk with patients with normal records. In over 1000 cases with normal pre-treatment E.E.G.'s, no patient developed spontaneous seizures, as reported by R. M. Taylor and B. L. Pacella[14] working at the New York Psychiatric Clinic. These authors investigated a series of 56 patients all of whom had abnormal E.E.G.'s. The records were compared before and after treatment. The abnormal records fell into 4 groups: (1) Convulsive; (2) A slow-wave group; (3) A fast-activity group; and (4) A focal-abnormality group. They observed that the E.E.G.'s did not attain the marked slow-wave activity characteristically following E.C.T. for periods significantly longer than patients with normal pre-treatment records. There were, however, 6 exceptions to this. Two patients developed spontaneous convulsions, beginning about 6 to 8 weeks respectively after an otherwise normal course of therapy. One of these had only one convulsion, the other, despite anti-convulsant medication, had regular convulsions over a period of 3 years.

Of the whole group only about 4 per cent developed seizures, and of those showing 'convulsive' tracings 8 per cent. The question is raised whether E.C.T. should be given to known epileptics. Although one of the authors, Pacella, with Barrera,[15] had shown an increased risk of shock treatment to epileptics, the present authors state that if the patient is kept on anti-convulsant drugs there are no appreciable untoward effects. Four of the patients of this series with a history of epileptiform seizures maintained on anti-convulsants showed no tendency to increased seizures. Patients with evidence of arteriosclerosis showed more marked and more prolonged amnesia and confusion than did the remainder of the group, regardless of the character of their E.E.G.'s. They conclude that E.E.G. abnormalities of whatever degree do not by themselves constitute a contra-indication to E.C.T. except where a focal and expanding lesion is suspected.

[These conclusions, whilst reassuring, cannot be accepted as final, and in the meantime, pending further investigation in a much larger number, it would seem well to continue to exercise care in practice in administering E.C.T. to patients with abnormal E.E.G.'s.—E. W. A.]

The risk of fractures following E.C.T. has been investigated from the radiological angle by J. R. Lingley and L. L. Robbins[16] (1947), who studied 230 patients who had received E.C.T. at the McLean Hospital, Waverly, Mass., from September, 1940, to February, 1946. These patients received anything from one treatment to several series. The current was calculated to produce a convulsion of 45 seconds' duration. Great care was taken during the treatment to prevent sudden hyperflexion. Routine X rays of the thoracic and lumbar spines were taken before treatment and afterwards if there was any evidence suggesting fracture. Of the 230 patients, 53, or 23 per cent, sustained

fracture of one or more bones, including 110 vertebræ, a percentage far in excess of that given so far as following E.C.T. The incidence was greater in males than in females, and in the young and the old rather than the middle-aged. In Dedichen's series fracture of the vertebral column occurred in 88 cases and fracture of the neck of the femur in 9, which gives a percentage of roughly 7 to 8 for his total number of shock-treated cases.

P. E. Huston and C. R. Strother[17] investigated the effect of shock therapy on mental functions.

It is well known that electric shock produces as an immediate effect an 'organic' syndrome characterized by so-called confusion, disorientation, and memory disturbance, and that in general the greater the number of shocks, the shorter the interval between them, and the older the patient the greater the impairment. Such effects are usually transitory, but not infrequently leave an amnesia for most or all of the period of shock treatment. The authors point out that absence of clinical evidence of residual intellectual impairment after some 6 to 8 weeks is not conclusive proof that some degree of impairment does not persist, as suggested by the complaints of memory disturbances, for several months afterwards in some cases.

Seventy-five patients, 26 men and 49 women, of whom 51 were diagnosed manic-depressive, 22 involutional melancholics, and 2 psychoneurotics, were investigated with the Babcock and Shipley Hertford tests of deterioration. Only co-operative patients were included. No patient was suffering from a formal disorder in thinking, other than retardation or occasional distractibility. Administering the Babcock test on an average 11 days after shock there was a slight but not statistically significant improvement. On the Shipley test the improvement was probably significant. When the same tests were used after a follow-up interval averaging 189 days, there was relatively great and significant improvement on both tests. Using a control group of 17 normals of the same age and vocabulary level as the patients, the results obtained from the latter were not significantly lower. The authors concluded that for the population studied and under the conditions of the experiment E.C.T. did not produce any significant impairment of mental efficiency after an interval of 6 months. No correlations were found between age and improvement from test period to test period. There was some evidence that patients receiving a greater number of shocks were affected more in mental efficiency than those receiving a lesser number of shocks.

The neurological signs and complications of E.C.T. have been reviewed by W. Korliner,[18] who concludes that there is not sufficient evidence at hand indicating that in human beings structural brain changes are referable to electric shock treatments. It is more likely that physiological and possibly chemical rather than structural changes occur. But that in general, where brain pathology exists before the treatment, such as tumour and advanced cerebral arteriosclerosis, electric shock treatments may complicate structural brain changes causing neurological complications and even death.

He concludes that electric shock treatment is safe and in most instances without untoward effects. With correct evaluation of indications and contra-indications, no permanent damage is produced in persons who undergo these treatments.

There is nevertheless perceptible in the recent literature an increased awareness of the risks of E.C.T. and other physical methods of treatment, and of a more critical attitude to results so often enthusiastically claimed. R. Kaldeck[19] (1948) stresses our inadequate knowledge of the changes caused by E.C.T. and states—what is too often forgotten—that "the simple question of what current does to brain structure has not been answered satisfactorily".

He reports the case of a woman of 31 suffering from a "schizoaffective" psychosis who developed a complete hemiplegia after E.C.T. which lasted several days and disappeared gradually, leaving no residual signs. There was no evidence of cerebral vascular disease. He reviews the previous literature, refers to C. W. Olsen's[20] case of unilateral convulsions and transient hemiplegia in a senile psychotic treated with E.C.T., and mentions the studies of E. C. Milch,[21] who observed spasm of the retinal arteries usually before the generalized convulsions in patients receiving E.C.T., and of L. Alexander and H. Loewenbach,[22] who found arteriolar constriction within the path of the current, but with doses much higher than those used clinically. Kalieck suggests that similarly in his case vascular spasm might have led to reversible damage in the brain.

O. A. Will and M. A. Neumann[23] also stress that a number of questions have not been completely answered; first, what the relapse rate is of patients treated with E.C.T. as against the untreated, and secondly what possibility exists of producing irreversible, incapacitating, organic changes in the cerebrum by the electric current and the vascular alterations associated with the convulsion. There is a divergence of opinion over the incidence of these changes, but there must be few psychiatrists who have not seen a handful of such at least. The authors point out that at the moment, owing to the lack of follow-up studies of the adjustment of the patient after treatment, and because of the comparatively few careful psychological investigations which have been made up to date, it is impossible to say that no significant damage to the brain can be done by any number of electroconvulsive treatments. They believe that organic cerebral cortical changes may be produced by E.C.T. and that the reversibility of such changes has not been fully established. They go on to report a fatality following E.C.T. in a man of 46 treated for depression. The patient had been curarized. Death resulted apparently from respiratory failure. The authors do not discuss the possibly complicating role of curare, but appeared satisfied that this did not contribute to the issue. A post-mortem examination was performed. No focal lesion was found in the brain, but microscopically widespread neuronal damage was present, the most prominent change being central chromatolysis. The authors review the literature of deaths from E.C.T., and, including their own case, find 33. The number of treated cases is, however, unknown, and a number of fatalities are probably not reported. The majority of the patients were over 40. Sixteen of the patients had received less than 9 shocks before death. Of the total number, 26 were apparently related to the therapy. The use of curare was reported in only 4 cases. Twelve of the patients died of cardiac failure, 2 of respiratory failure, and 2 of either respiratory or cardiac failure; 8 patients died of complications initiated by the therapy; in 7 cases details were not available. The autopsy findings were incomplete, but no lesion could be identified as a characteristic result of the passage of an electric current or due to the muscular or vascular changes associated with the convulsion. The authors stress the need for careful physical overhaul before initiating this form of treatment. They add that despite the low mortality-rate of E.C.T. this treatment cannot be given lightly and without a careful evaluation of the details of each patient's physical and psychiatric condition. They regard E.C.T. as a traumatic therapy which causes at least transient alteration in the brain. Before convulsive therapy can be accepted as the most desirable and effective means of treatment, as perhaps the majority do regard it, careful investigation and follow-up studies must be made, which is not to deny its effectiveness or value in modifying or eliminating depression, especially perhaps in involutional illnesses. The authors deplore the substitution of shock therapy for detailed psychiatric study [in which the reviewer concurs]

since this may lead to erroneous conclusions and might hinder progress in the study of social and psychogenic factors in the causation of emotional disturbances.

In Dedichen's series of patients treated by convulsive therapy alone (1147) and those treated by combined insulin-pentrosol (129), 5 deaths (0·4 per cent) occurred which could be traced to the treatment.

REFERENCES.—[1]*Lancet*, 1947, **2**, 198; [2]*Proc. R. Soc. Med.* 1948, **41**, 575; [3]*J. nerv. ment. Dis.* 1947, **106**, 150; [4]*N.Z. med. J.* 1947, **46**, 280; [5]*J. ment. Sci.* 1948, **94**, 793; [6]*Proc. R. Soc. Med.* 1948, **41**, 581; [7]*Ibid.* 585; [8]*Lancet*, 1948, **1**, 444; [9]*Ibid.* 536; [10]*Ibid.* 537; [11]*Acta psychiat. Kbh.* 1946, suppl. 37 (also abst. *Exc. med.* 1948, **1**, 494); [12]*Arch. Neurol. Psychiat., Chicago*, 1948, **59**, 517; [13]*J. nerv. ment. Dis.* 1948, **107**, 377; [14]*Ibid.* 220; [15]*Amer. J. Psychiat.* 1945, **101**, 783; [16]*Radiology*, 1947, **48**, 124 (abst. *Int. Abs. Surg.* 1947, **85**, 394); [17]*Amer. J. Psychiat.* 1948, **104**, 707; [18]*Ibid.* **107**, 1; [19]*Arch. Neurol. Psychiat., Chicago*, 1948, **59**, 229; [20]*Bull. Los. Angeles Neur. Soc.* 1944, **9**, 171 (quoted Kaldeck); [21]*Arch. Neurol. Psychiat., Chicago*, 1941, **45**, 848; [22]*J. Neuropath. exp. Neurol.* 1944, **3**, 139; [24]*J. nerv. ment. Dis.* 1948, **107**, 105.

MESENTERY, AFFECTIONS OF.

A. Rendle Short, M.D., F.R.C.S.

Mesenteric Vascular Occlusion. J. D. Rives and two colleagues,[1] of New Orleans, have seen 11 cases. They say arterial occlusion, due usually to emboli from the heart, is commoner than venous thrombosis, of which portal hypertension is the commonest cause. More clinically useful is the classification into immediate occlusion, and more gradual, the latter being rather more frequent. In the immediate cases, gross cardiac disease is usually present. Pain, tenderness, shock, distension, and leucocytosis are nearly always present. In the more gradual cases, mild colic, with or without diarrhœa, progresses to partial intestinal obstruction, with early disappearance of peristalsis. There may be blood in the stools. X rays may show distension of the small intestine, and perhaps colon also. There was 1 recovery amongst 8 operated on.

Mesenteric Cysts.—Probably these may have a variety of origins. Some contain chylous fluid, some are lined with intestinal mucosa, and a few are dermoids with stratified epithelium. A very probable suggestion to account for the majority of the recorded examples is that of Dowd, who considers that they may be relics of pronephros, or mesonephros, giving rise to retroperitoneal cystic collections. Milroy Paul,[2] of Ceylon, relates a case of successful removal. The cyst blocked the pelvis and caused attacks of intestinal obstruction. In some recorded cases, marsupialization has been carried out instead of incision, and the cyst has not refilled. Simple aspiration may be sufficient.

REFERENCES.—[1]*Ann. Surg.* 1948, **127**, 887; [2]*Brit. J. Surg.* 1948, **35**, 308.

MYELOMATOSIS, MULTIPLE.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Diagnosis.—There is little doubt that multiple myelomatosis is a more common disease than is generally believed. Cases which show the usual features of pain in the back, the characteristic X-ray appearances in the bones (especially the skull), a marked increase in the serum globulin, and Bence-Jones proteosuria, are easy to diagnose. But it is important to remember that frequently the picture is not so clear, and, in particular, the possibility of myelomatosis should be kept in mind in any adult who complains of back pain and in whom X-ray examination reveals only osteoporosis. In such cases examination of sternal marrow should be regarded as an essential part of the investigation, since in practically all cases the typical myeloma cells are present in this situation. E. D. Bayrd and F. J. Heck[1] have recently published a useful account of the various manifestations based on analysis of 83 cases.

Treatment.—It is now a matter of importance that the diagnosis of myelomatosis should not be missed. Until recently the only form of treatment in general use was X-irradiation, which did little to alleviate the symptoms. As

a result of Snapper's work we can now relieve pain for a considerable time in some cases.

The hyperglobulinæmia which is a feature of most cases of myelomatosis is found also in kala-azar. The remarkable therapeutic effects of stilbamidine in the latter disease led I. Snapper[2, 3] to use this drug in myelomatosis. From the outset it became apparent that dramatic relief of the bone pain, which is so often the main symptom, occurred in almost all the patients treated. It is not claimed that the disease is cured or indeed that the clinical course, apart from the pain, is significantly altered; several years will be necessary to allow accurate assessment of the full effects. But there can be no doubt that we now have available a method of treatment which should not be denied to any patient with myelomatosis in whom pain is severe.

Unfortunately, stilbamidine is troublesome to use. It is given intravenously (initial dose, 50 mg., second dose after two days, 100 mg., and thereafter 150 mg. either daily or every second day until a total of 4-5 g. has been given). Venous thrombosis at the site of injection often follows. Intramuscular injection usually gives severe pain. Snapper has recommended a low-protein diet during treatment. The pain is relieved or greatly reduced after the fourth or fifth injection, as a rule.

Observations in patients suffering from generalized bone metastases, from mammary carcinoma, and from other diseases, have shown that stilbaminide does not act as a general analgesic for bone pain. Snapper[4, 5] believes that the drug dissociates the protamine-ribonucleic acid compound in the cytoplasm of the myeloma cells and forms an insoluble stilbaminide-ribonucleic-acid complex which forms granules in the cytoplasm which are basophilic with the common hæmatological stains.

More recently pentamidine, another aromatic diamidine, has been used. Apparently it is sometimes effective when stilbamidine has failed to relieve the pain, but sometimes the reverse is true. Pentamidine is easier to administer, since it may be given intramuscularly with little or no discomfort.

[One of the reviewers (H. W. F.) has had experience of both these compounds in myelomatosis and has found a remarkable improvement in the bone pain. In one patient treated with stilbamidine this has already lasted nearly a year; in another given pentamidine the effect was equally striking but of much shorter duration.]

In some cases of myelomatosis there is little or no pain, the presenting feature being a severe anæmia refractory to all the usual forms of treatment. There is insufficient evidence at present to justify the use of stilbaminide in this group.

REFERENCES. [1]*J. Amer. med. Ass.* 1947, **133**, 147; [2]*Ibid.* 157; [3]*Ibid.* 1948, **137**, 513; [4]*Blood*, 1946, **1**, 534; [5]*Ann. intern. Med.* 1947, **27**, 541.

NASAL SUPPURATION.

(*See* AURAL AND NASAL SUPPURATION.)

NASOPHARYNX, TUMOURS OF: DIAGNOSIS AND TREATMENT.

F. W. Watkyn-Thomas, F.R.C.S.

E. D. D. Davis[1] has seen 34 cases in the past twenty-five years. There were 19 cases of carcinoma, 4 of lymphosarcoma or lymphoma, 10 of angiofibromata, and 1 of myxosarcoma of doubtful origin. Two of the angiofibromata were really sarcomatous, and recurred some time after removal.

Early diagnosis is delayed, because the growth lies in a cavity which is difficult to inspect, and because the patient does not notice anything until the growth is large enough to produce mechanical signs, by which time—if malignant—it is too advanced for successful treatment.

Of the carcinomata the first sign in 3 cases was Eustachian obstruction with fluid in the middle ear—the 'auricular type'. In 6 cases the first sign was enlargement of cervical glands; this is the first sign in lympho-epithelioma or lymphosarcoma. In another 6 cases the first signs were neurological—headache, bitemporal or vertical; fifth-nerve neuralgia, especially in the region of supply of the auriculotemporal nerve; occasionally upper cervical neuralgia, and paralysis of the sixth and later of the third cranial nerves. When a cranial-nerve palsy is the first sign it is probably due to a growth starting in the body or great wing of the sphenoid. Proptosis is a late sign. Nasal symptoms, a blood-stained nasal or nasopharyngeal discharge with headache and epistaxis, in a patient of the cancer age are always suspicious. Treatment of malignant growths in this region is limited to deep X-ray therapy, as they are inoperable when first seen. This is the only treatment which offers any hope of success. The author found radium most unsatisfactory, as it caused severe reaction with pain and irritation, and was frequently followed by metastases.

The bleeding fibroma is benign, and occurs in boys between the age of 10 and 20. Davis has never seen a case in a girl, or a true angiofibroma appearing after the age of 25, nor has he ever seen or found any record of a case in which the growth disappeared spontaneously. Biopsy is unsatisfactory and misleading, as it is difficult to remove a really large enough piece without copious bleeding. The tumour can be dealt with by enucleation or by diathermy. If enucleation through the nose or nasopharynx is impossible the best attack is by Nélaton's operation, making a window through the hard palate. This damages the nose less than does a lateral rhinotomy. Davis has not found ligation of the external carotid much use, and has found radium implantation unsatisfactory.

A. J. Gardham, speaking of malignant tumours, said that sixth-nerve palsy was the commonest ocular sign, and was followed in about one-third of the cases by a third-nerve palsy. These were late signs, and often indicated intracranial extension. Displacement of the globe was a very late sign. Fifth-nerve neuralgia was the most common cause for the patient consulting a neurologist; palsies of the nerves of the jugular foramen were also sometimes seen. Patients usually came to the general surgeon for enlarged cervical glands of unknown cause; these glands were easy to mistake for tuberculous glands, as they were soft and often bilateral. Sometimes the first sign was swelling in the temporal fossa. Pathologically the picture was an infiltrating tumour of the cranial base which spread submucously and subperiosteally without much ulceration. There were two curious points about these growths—the geographical distribution (in Hong Kong they accounted for some 25 per cent of malignant surgical lesions), and the close relation to septic conditions. Treatment was entirely by deep X rays or teleradium. Immediate results were good, but recurrence was the rule. Cases with evidence of intracranial spread were best left alone. He had tried to relieve the fifth-nerve neuralgia in these cases by injection of the Gasserian ganglion, but had never succeeded.

H. Martin, H. E. Ehrlich, and J. C. Abels[2] analyse 29 cases of *juvenile nasopharyngeal angiofibroma* seen between 1927 and 1946. The condition is not common; at the Memorial Hospital, where about 2000 cases of head and neck neoplasms are admitted each year, there are among these usually 1 or 2 cases of this kind; the condition is found only in pubescent males. In this series the average age of onset was 14; the youngest patient was 9 years old. One patient of 36 was admitted, but he had had symptoms since 16. The writers suggest that this sex-age predilection is due to some endocrine disturbance. They noted that most of their patients were physically and emotionally underdeveloped sexually. The error might be either deficiency of androgen, or

overproduction of œstrogen. There is some evidence that hyperæmia of mucous membranes is a function of œstrogen, and that the mechanism is probably due to production of acetylcholine. Thus œstrogen treatment is helpful in atrophic rhinitis, and the gangrene of ergotism can be prevented by œstrogen dosage. On this view the growth starts as by abnormal stimulation of the local vascular system; the fibrous tissue, at first only a supporting stroma, becomes predominant as the œstrogen effect diminishes; when the patient reaches sexual maturity the growth becomes less vascular and more fibrous, and eventually regresses. His explanation is the only one which satisfactorily explains the history and distribution of the growth. [Although the writers frequently mention the regression of the growth when sexual maturity is reached, and, in fact, largely base their method of treatment on this belief, they do not produce much definite evidence on the point. E. D. D. Davis (*see above*) has never seen this happen.—F. W. W-T.] They agree with Davis as to the difficulties of histological diagnosis by biopsy. The picture is usually clear enough—nasal obstruction with recurrent epistaxis in a boy of the sensitive age. They have found no satisfactory evidence that a true juvenile angiofibroma ever undergoes malignant change.

Taking the position that the growth will eventually recede without damage if the dangerous period of hæmorrhages can be tided over, they avoid surgery as much as possible, limiting it to those cases where the growth is already bulky and difficult to treat by irradiation. If surgery is needed they agree with Davis that the soft palate should not be split, and that the Langenbeck and Ollier operations are to be avoided. For severe hæmorrhage, not only as a preliminary to surgical removal, one or both external carotids should be ligated; packing for severe hæmorrhage is dangerous, as it encourages spreading sepsis, with further hæmorrhage, and infection of middle ear or sinuses. Irradiation, like surgery, should not be 'too aggressive'. They report several cases of radionecrosis of the palate, and other complications. The best line of treatment they believe is carefully controlled irradiation, either by deep therapy or by interstitial radium, with administration of testosterone—either testosterone propionate or methyl testosterone or both, in doses adequate to encourage the secondary sex characteristics without disturbance of emotional balance. The excretion of urinary ketosteroids and X-ray examination of the ossification centres should be made at regular intervals.

[As 'constructive evidence' in favour of spontaneous regression it is fair to quote the rarity with which these tumours are found in adult life. One case in this series was a man of 36, who had had symptoms for 20 years, but such cases are exceedingly rare.—F. W. W-T.]

REFERENCES.—[1]*Proc. R. Soc. Med.* 1947, **40**, 707; [2]*Ann. Surg.* 1948, **127**, 513.

NEPHRITIS IN TEXTILE WORKERS. *W. H. Bradley, D.M., M.R.C.P.*

Professor Robert Platt[1] reviewed the data presented in the Registrar General's Decennial Supplement of 1931 against the background of the records of 161 cases carefully investigated in his own department in Manchester. The result is a salutary one, for he concludes that the deaths from so-called nephritis in textile workers are in all probability due to hypertension, and can be as easily explained by natural variations in the genetic constitution of an inbred population as they can by environmental influences. This should be borne in mind before making the assumption that such deaths are due to "the inhalation of textile dusts".

In certain textile trades there may be influences at work whose effect is to hasten or even to initiate cardiovascular and renal disease. Professor Platt's investigations do not disprove such a possibility, but suggest that before setting

out on a laborious, time-consuming, and expensive investigation into the cause and prevention of nephritis in textile workers we should need more evidence that it exists. In particular we should require evidence that there is a renal syndrome amongst textile workers which is in some way different in its incidence, symptomatology, or course from hypertensive disease in the general population.

At the moment investigations into the diseases apparently associated with several industries are fashionable. It might be more profitable to obtain overall morbidity statistics for the whole population and establish a firm base line before we embark on many of these studies.

REFERENCE. [1]*Brit. med. J.* 1947, **2**, 771.

NITROGEN MUSTARD THERAPY IN DERMATOLOGY.

R. M. B. MacKenna, M.A., M.D., F.R.C.P.

The use of mustard gas in the treatment of various disorders was discussed in the MEDICAL ANNUAL of 1948.[1]

E. D. Osborne, J. W. Jordan, F. C. Hoak, and F. J. Pschierer[2] have discussed this method of treatment in reticuloses with cutaneous manifestations. They note that from the clinical standpoint only two compounds have been discussed, viz.: tris (beta-chloro-ethyl) amine hydrochloride and methyl-bis (beta-chloro-ethyl) amine hydrochloride. The usual doses employed have been 0·1 mg. per kilo of body-weight given in one injection intravenously on four successive days, making a total dose of 0·4 mg. per kilo. Symptoms such as nausea, vomiting, and diarrhœa, as well as effects on the blood-forming organs, may follow the injections, and the total leucocyte count declines progressively for 15–25 days but returns to normal usually within 2 weeks after the maximum reduction. Osborne and his colleagues describe the treatment of 5 cases treated with nitrogen mustard. Of these, 2 patients with advanced mycosis fungoides responded dramatically, but they noted that the improvement was likely to be only temporary. In one of these cases, which presented a confluent erythemato-squamous eruption, the rash completely disappeared after the injections. One immediate and dramatic effect of this form of treatment in mycosis fungoides has been the early relief of severe itching. The third case in their series was an example of lymphosarcoma; he was moribund when treatment was given, but there was some improvement in the condition of his skin before his death. The fourth case was one of Hodgkin's disease associated with multiple hæmorrhagic sarcoma of Kaposi. Treatment with nitrogen mustard did not produce any change in the skin lesions. The fifth case was a woman suffering from chronic disseminated lupus erythematosus. Four weeks after her fourth injection the eruption, which had been severe and had resisted very many other forms of treatment, had almost completely disappeared. Nevertheless the authors are careful to note that they are not advocating the use of nitrogen mustard therapy for a disease of a chronic inflammatory nature.

The present trend of opinion in Britain in regard to this matter appears to be that the use of nitrogen mustard can greatly relieve the intolerable itching which sometimes occurs in Hodgkin's disease and may relieve the cutaneous manifestations of other reticuloses, but the therapy is more palliative than curative, and can only be administered safely and satisfactorily under carefully controlled conditions.

REFERENCES.—[1]*Med. Annu.* 1948, 220; [2]*J. Amer. med. Ass.* 1947, **135**, 1123.

NUTRITION AND VITAMINS.

Una Ledingham, M.D., F.R.C.P.

Starvation.—World War II provided conditions in which starvation was all too common in large sections of populations throughout the world. *Nutritional*

œdema is one of the better known consequences of insufficient food and was closely studied in Germany and following German occupation of other countries. Sinclair[1] summarizes some of the known facts and adds some new ones. It is of note that 11·3 per cent of the Dutch population suffered famine œdema, while 4·1 per cent only of Germans were affected. Three causes are recognized: thiamine deficiency; hypoproteinæmia with low plasma-albumin levels; and the last type, possibly an early form of the second, which is specially considered. Œdema arose on diets as variable as 600 to 1800 calories daily with protein up to 50 g. to which animal protein contributed one-third. It came on rapidly following cold or exertion and varied considerably with varied salt intake. Most persons had lost weight and complained of associated nycturia. Of other evidences of under-nourishment, acrocyanosis of the hands is particularly noted. Surprisingly the plasma protein, albumin fraction, and cystine values were within normal range both in Dutch and German subjects, and the slight fall in colloidal pressure was insufficient to account for the œdema. However, evidence was clear of diminished nitrogen content of plasma protein in œdematous subjects, suggesting strongly that the quality rather than the quantity of albumin is at fault. There was no apparent thiamine deficiency, and treatment with B_1 was useless. *Nycturia* is assumed to result from an exaggeration of the normal effect of posture on renal tubule function, whereby increased resorption occurs in the upright position. Either greater secretion by the posterior pituitary or alternatively a shunt through the renal juxtamedullary capillaries (as suggested by Trueta), may be responsible. Enlargement of the suprarenals is observed in both famine œdema and in wet beri-beri, and because of the variation of such œdema with altered salt intake, further investigation is indicated.

It might be expected that starvation conditions would decrease resistance to infection, but Gell[2] found otherwise amongst a large German population existing on 1000-calorie diet. Antibody formation in these almost famished subjects was found to be little lower than amongst healthy army controls. That no widespread epidemic has swept Germany since the end of the war supports these findings.

One strange result of recovery from starvation is displayed as *gynæcomastia*.[3] American soldiers in Japanese prison camps developed this when their diet improved. After liberation, with the provision of a generous diet, it appeared in 50 per cent of ex-prisoners, but regressed completely in six months. Seemingly androgen and œstrogen production recover before liver function, and œstrogen blood-levels are temporarily uncontrolled.

There are more details of the heartbreaking experience of allied prisoners in Japanese hands. Multiple vitamin-deficiency states developed, contributed to by the prevalence of tropical disease and the physical effort literally forced out of them in a shocking climate. Whitfield[4] confirms that the clinical picture was seldom a clear-cut and specific vitamin-deficiency disease. Rather was there an unfamiliar and ill-defined syndrome with some recognizable features and unexplained additional features. The distressing 'painful feet' state developed in nearly 10 per cent of men in one camp. The diet was deficient in all essentials, especially in riboflavin and other components of the vitamin B_2 complex. White rice bulked large with small amounts of green leaves and a little fat. After a warning tiredness in the feet a persistent deep ache in the ball of the foot was followed by intolerable burning and tingling in the soles. Finally, after about four months the syndrome was complete with excruciating pain in the feet and calves, much worse at night. Cold, often brought about by immersion of the legs in iced water, gave slight relief only. Evidence of severe peripheral nerve injury such as gross ataxia, loss of power, wasting, or foot-drop was not apparent. Pantothenic acid deficiency is suggested, together

with thiamine and riboflavin lack. The latter was widely evident as scrotal dermatitis, angular stomatitis, glossitis, and conjunctivitis. Atypical cardiac beri-beri appeared when barley and beans were substituted for rice. Thirty cases fell victims rapidly and within ten days to a state characterized by sudden weakness and exhaustion with palpitation, breathlessness, irregular pulse, and attacks of cardiac asthma. Recovery was slow with no immediate response to thiamine. Gross vitamin B_2 defects were not apparent.

Reid and Wilson[5] paint an even more horrifying picture in their story of difficulty and disease in Thailand. In spite of appalling diet, lack of sanitation, and incredible hardship, evidences of vitamin B_2 deficiency were rare. Most of the states accorded with lack of thiamine, and at one time 80 per cent of this force suffered some degree of beri-beri.

Food. *Bread* is still in the limelight, and in the United States agene processing of flour is to be prohibited. In Britain, however, the findings of Sir Edward Mellanby's committee indicate that the process is harmless to man. This distinguished worker[6] goes further into canine hysteria precipitated by agene-treated flour. Using the commercial proportion of NCl_3 to flour he found: that the toxic agent was not in the fat fraction but was confined to the gluten fraction; that it existed in greater degree in the gliadine than in the glutelin fraction; and that it survived chemical processes involved in the experiment.

Vitamins. Interdependence between the various members of the vitamin B complex is now acknowledged. It is common experience that large doses of one component may precipitate a relative deficiency of another. Davidson and Girdwood[7] follow up their experience with folic acid. Five cases developed clear signs of deficiency states during treatment with this vitamin. In 4 this appeared as acute and rapidly progressive peripheral neuritis. As well, one had burning pain in the soles, and one other angular stomatitis. The fifth case escaped neuritis but showed widespread signs of B_2 deficiency. These complications were resistant until liver treatment was started, when all made steady improvement. This danger must be recognized, and when folic acid is used it should be supplemented always by liver in some form.

Vitamin C requirements are finally fixed at 30 mg. daily by the M.R.C.[8] Actually, 10 mg. daily protected against clinical scurvy including poor wound repair. The same small dose cured moderate degrees of induced scurvy. Total deprivation caused no ill health for over four months, when hyperkeratosis of hair follicles was the only abnormal feature. Skin hæmorrhages followed after six months' depletion and gum changes not for nine months. Exacerbation of acne, consistently observed, is previously not reported. While 10 mg., therefore, is a minimal protective dose, the safer figure of 30 mg. daily allows for a margin of protection. Early deficiency states are discussed by Leitner.[9] Numerous factors are involved as well as insufficient ingestion. Absorption and utilization may be interfered with or there may be increased requirements for particular vitamins during disease processes. Either excretion or destruction may be facilitated. Deficiencies are more often multiple than single, and symptoms and signs are not specific. Little help can be obtained from laboratory findings in these early cases and a presumptive diagnosis may depend on the dietary history.

In the midst of confused thinking and multiple prescribing a welcome paper from the pen of Leslie Harris[10] tells us which vitamins matter and which can safely be ignored. Those definitely essential to man include only A and B_1, three components of the B_2 complex (nicotinic acid, riboflavin, and folic acid) and C, D, and K. In a second group, believed but not proved clinically significant are E, F, and P, together with the B_2 components biotin and choline. The third group, demonstrated only by animal experiment, consists of the remaining

B_2 elements—pyridoxin, pantothenic acid, inositol, and para-amino benzoic acid (paba). Their clinical importance is even more uncertain. Classical descriptions of manifest deficiency states relating to the first group are included, with a useful estimate of daily requirements and a list of suitable foods. Indications for legitimate clinical use are also given. Contrary to early hopes, biotin neither protects against nor cures grey hair, seborrhœa, or other skin complaints (Oppel[11]). Vitamin E is valueless in muscular dystrophies and in habitual abortion. There is no proof that vitamin K influence capillary fragility. Inositol and paba assist by stimulating intestinal flora to synthesize nutrients. The latter in addition inhibits the bacteriostatic action of sulpha drugs, and is on trial as an anti-infective agent.

REFERENCES.—[1]*Proc. R. Soc. Med.* 1948, **41**, 541; [2]*Ibid.* 323; [3]*Ann. intern. Med.* 1948, **28**, 792; [4]*Brit. med. J.* 1947, **2**, 164; [5]*J.R. Army med. Cps*, 1948, **89**, 149; [6]*Brit. med. J.* 1947, **2**, 288; [7]*Lancet*, 1948, **1**, 360; [8]*Ibid.* 853; [9]*Brit. med. J.* 1948, **1**, 917; [10]*Ibid.* 1947, **2**, 681; [11]*Amer. J. med. Sci.* 1948, **215**, 76.

OCCUPATIONAL HEALTH.

Donald Stewart, M.D., F.R.C.P.

Health of the Agricultural Worker.—The number of agricultural workers in this country at the present time is approximately 1,100,000,[1] but the Economic Survey of 1948[2] showed that another 60,000 workers are required by 1951 if national recovery is to be maintained. The potential contribution that industrial medicine can make to assist this occupational group has been outlined by G. F. Keatinge and R. Littlewood.[3] Drift of workers away from the land has been a feature common to all developing countries. There has been disparity between agricultural and industrial wages, a marked difference in hours of work, rural housing conditions were less satisfactory, and up-to-date health services were frequently denied to the country-dweller. The labour force now on the land is ageing, for the children of farm workers often choose other occupations. To prevent withdrawals from the industry the Government have cancelled the call-up of farm workers, and the duration of the Essential Work Order has been extended. With the application of modern and scientific methods of farm work certain occupational hazards occur– for example, poisoning by tolyl mercuric acetate used in treating seeds, by methyl bromide in insecticides used on fruit, by fluorine compounds found in artificial fertilizers, by arsenical compounds in sheep dip, and by tar derivatives used in the preservation of timber. Diseases such as abortus fever, glanders, and anthrax are communicable from animals to man. Specialized medical supervision of the agricultural worker at his place of work has not been practicable in the past due to the small size of British farms. But if larger units can be organized, and this is the plea of Keatinge and Littlewood on economic grounds, then an occupational health service for this group can readily be organized: new entrants can be properly placed in work; the health and welfare of young persons and women on the land can be adequately supervised; an adequate first-aid service can be instituted; and expert advice on toxic hazards can be readily available.

Health of Workers in Atomic Energy Establishments.—Much of the work of the Ministry of Supply's Atomic Energy Establishment at Harwell has recently been revealed.[4] This establishment was founded in November, 1945. Harwell is a former R.A.F. station, and all the hangars and most of the buildings have been adapted for the purpose of carrying out fundamental research and development in atomic energy. Protection of the health of the workers at the establishment is a specific responsibility of the Ministry. This, briefly, ensures that no members of the staff are exposed to excessive radiation. There has been instituted a combination of individual monitoring, permanent local monitoring in active areas, and further surveys as required, including the taking of air samples. The Medical Research Council's standard is that the total

integrated dosage of the individual should in no case exceed 0·5 r per week, but the present average for the establishment is less than one-fifth of this figure. Individual monitoring is based on the use of three different types of recorder: a radiation-sensitive pocket film, collected weekly and developed at the National Physical Laboratory under controlled conditions (films showing more than the usual darkening are reported by telephone); a pocket condenser, of the size of a nasal inhaler (charged to a prescribed voltage and gradually discharged by exposure to radiation); and an instrument resembling an overgrown fountain-pen by which the individual can make his own observation of dosage received at any time. Fixed radiation meters are also provided throughout the plant; a glance at the 'clock' is thus sufficient to inform the individual worker whether he is above or below the accepted dosage rates. All workers are given a full medical examination on joining, including blood-count, and this is repeated periodically.

Beryllium Disease. A recent report by J. N. Agate[5] of a case of delayed pneumonitis in a beryllium worker emphasizes the need for close and prolonged observation of persons in this country coming into contact with beryllium. Beryllium occurs naturally as a double silicate of beryllium and aluminium. In compound form it has an ever-widening use in industry in the manufacture of radio and cathode-ray tubes, neon-sign lighting, incandescent lamps, X-ray windows, electric heating elements, refractory bodies, gas mantles, vitreous enamels, and textile fibres, while alloys containing beryllium are also growing in popularity. Recent reports from the United States of America show that the handling of beryllium compounds is attended by a risk (*a*) of serious acute or chronic lung disease, and (*b*) of skin disease. Harriet Hardy and I. R. Tabershaw[6] found 17 cases in one factory where fluorescent lamps were manufactured. Here exposures to a phosphorescent powder, zinc beryllium manganese silicate, varied from five months to five years. Clinically these patients showed cough, dyspnœa, undue fatigue, and often remarkable loss of weight. In 2 cases the liver was enlarged, in 2 the spleen, in 2 there was adenopathy, and in 2 skin granulomata. The lung X-ray showed three stages - 'granularity', reticulation, and nodulation (*Plate XXV*). The disease described in this series was chronic, but there was serious interference with working capacity.

Agate's case showed similar clinical features and residual disability. It occurred in a physicist, aged 36, engaged from 1936 in research and development of filament and mercury-vapour lamps and tubular fluorescent lamps. His contact with the powders containing beryllium was confined to one year, 1941-2. After that his contact was negligible. Symptoms were noted first in 1945, three years after his last significant exposure, and he died in 1948.[7] First diagnosis on radiological grounds was acute miliary tuberculosis, later it was called Boeck's sarcoidosis. But the lung condition was only part of a more generalized pathology, liver biopsy showing focal granulomatous lesions. The report of the coroner's inquest on this man was given publicity in the public press. It was probably the first case of its kind in Great Britain. Death was due to granulomatous fibrosis of the lungs and failure of a hypertrophied right heart. The microscopic appearances in the lungs somewhat resembled silicosis and sarcoidosis, but were not typical of either.[7] These microscopical appearances were later confirmed by F. R. Dutra,[8] even in cases where the exposure had been solely to beryllium oxide.

R. S. Grier, P. Nash, and D. G. Frieman[9] have described 3 cases of subcutaneous granulomata in persons who had cut themselves on fluorescent lamps, and 2 cases of skin granulomata accompanied by pulmonary granulomatosis. (Skin lesions previously found in the handling of beryllium compounds were contact dermatitis and indolent skin ulceration, but these were due only to

PLATE XXV

BERYLLIUM DISEASE OF THE LUNGS

(HARRIET HARDY)

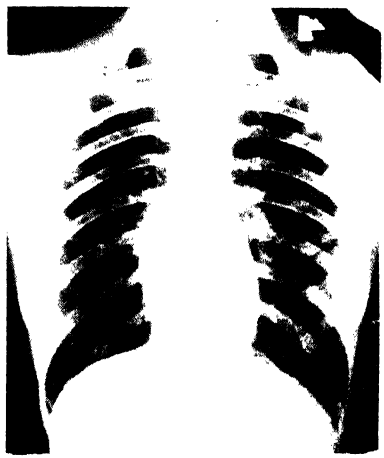


Fig. A. S. P. S. Aug. 27, 1944. Lungs before onset of symptoms.



Fig. B. S. P. S. June 7, 1943. Typical example of the 'nodular' stage of the disease.

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contact with the soluble salts.) The first of these cases resulting from contamination of a cut was that of a boy of 12 who, while playing on a dump where old fluorescent lamps lay, cut himself with some of the glass on the right side of the neck. Three months later a number of small painless swellings were found at the site of injury. Spectroscopic examination of biopsy material from the nodules showed 27 micrograms of beryllium per 100 g. tissue. (This is about the same concentration of beryllium as that found in lung lesions of patients, described by Hardy and Tabershaw,[6] who had died of pulmonary granulomatosis.)

Environmental studies in a number of American factories producing beryllium compounds from the ore and in laboratories using beryllium for research purposes were carried out by M. Eisenbud, C. F. Berghout, and L. T. Steadman.[10] At these places employees had been discovered to be suffering from beryllium pneumonitis by H. S. Van Ordstrand,[11] H. S. Martland and others,[12] and J. C. Aub and R. S. Grier.[13] Compounds studied were atmospheric contaminants in the work area; these included dust and mist of beryllium sulphate, dust and mist of beryllium fluoride, dust and fumes of beryllium oxide, and metallic beryllium. In machine shops and metallurgy laboratories exposure was due to metallic beryllium dust and, if the metal was cast or welded, to the oxide fumes. Acute pneumonitis was shown to be caused by beryllium sulphate, fluoride, oxide, and metallic dust. A number of acute cases resulted from a single excessive exposure. An exposure to the fluoride for 20 minutes is known to have produced 3 cases of acute pneumonitis.

Agate points out that the commercial use of beryllium in Great Britain has developed considerably during the past 3 years, so more cases of beryllium disease, manifesting itself as acute or delayed pneumonitis or as a skin disease, may well be expected. Substitution of other compounds in place of beryllium is obviously the best preventive measure, but where it must still be used close attention will have to be paid to suppression of dust and fumes at the place of work and adequate schemes of regular health supervision instituted.

In February, 1949, the Ministry of National Insurance added beryllium poisoning to the list of industrial diseases prescribed under the National Insurance (Industrial Injuries) Act, 1946. In future any employed person who contracts beryllium disease may therefore claim industrial injury or disablement benefit. In a fatal case death benefit may be paid.

Pneumokoniosis of Coal Miners. An account of the work of the Medical Research Council's Unit investigating pneumokoniosis among coal miners in South Wales was given by C. M. Fletcher.[14] By the end of 1945 approximately 10,000 men from that area alone had been certified as suffering from the disease. This figure underlines the size and seriousness of the problem. A leading article in the *British Medical Journal*[15] pointed out that "the survival of the nation depends on coal, and if the nation is to attract men to this industry and then keep them in it, the dust problem must be solved". Fletcher showed that there has been much complacency in the past among those medical men held to have special knowledge in this field. The incidence of the disease is related to quantitative rather than qualitative differences in the dust. There is no great difference in incidence between steam-coal areas and anthracite areas. The incidence of the disease is higher in South Wales than the rest of the country, as is the dust concentration. High concentration is found in anthracite pits with poor ventilation, and in steam-coal pits where mechanical methods have been introduced without corresponding dust suppression. The post-mining employment of certified cases of pneumokoniosis requires special provisions other than those already planned. Progression of the disease, demonstrated by X-ray findings, takes the form of localized shadows which develop into large massive shadows to which the name "progressive massive fibrosis" is applied.

Development appears to be independent of continued exposure to dust. Evidence suggests that infection, perhaps tuberculosis, superimposed on a lung already occupied by dust is responsible for the development of progressive massive fibrosis. Prevention may in the future be achieved by dust suppression. At present it can be assured only by periodic medical and X-ray examination of all underground coal miners. Treatment is only symptomatic, but much can be done by reassurance and exercise in early cases.

A detailed study of the progression of pneumokoniosis after exposure to dust has ceased was carried out by Alice Stewart and others.[16] Some 3500 miners who contracted the disease in the anthracite and steam-coal pits of South Wales were followed up after they had been away from the mines for two to fifteen years. The subsequent mortality-rates of men who left the mines during the 'early' stage of pneumokoniosis were higher than normal. Those who did not leave underground work until the disease had reached an 'advanced' stage had often higher mortality-rates after leaving the pit. Descriptions of 654 cases showed that the disease frequently continues to progress after removal from the dust hazard, and suggests that the late results are due to infection superimposed on generalized pulmonary fibrosis. This progression after leaving the mine was more frequent among the younger men and less frequent among men who worked entirely out of doors during this period. In its early stages the disease is often symptomless and even in later stages dyspnœa on exertion may be the sole manifestation. In men with advanced disease a particular type of black spit may occur which is associated with breakdown of large areas of diseased lung tissue. The overall incidence of open tuberculosis was less than 3 per cent, the specific criterion of diagnosis being sputum examination. In the absence of tuberculosis the disease frequently progresses slowly, and apart from dyspnœa produces little disturbance in general health despite gross X-ray changes. Progression is often accompanied by a raised erythrocyte sedimentation-rate, and periods of arrest by a normal sedimentation-rate. Early stages of the disease are not associated with any conspicuous manifestation in corpuscular volume, but in more advanced stages anæmia is common.

Pneumokoniosis of Welders (Welders' Siderosis).—Siderosis found among welders is a benign form of pneumokoniosis. The iron-oxide dust apparently does not set up fibrosis of the lungs and the welders show little or no disability. A. T. Doig and A. I. G. McLaughlin[17] now hold that the iron-oxide dust can be slowly eliminated from the lung, and that the abnormal X-ray shadows can disappear when the worker gives up welding and has no further contact with fumes. (*The Lancet* points out[18] that this is in striking contrast with the prognosis in silicosis, which may progress even if no more silica dust is inhaled.) In a re-examination of 15 welders examined nine years or more previously they found that of 7 men with normal X-rays at the first examination 5 were still normal, 1 showed suspicious changes, and 1 definite reticular changes; of 6 men who had originally shown well-marked changes 4 still had the same condition; and 2 men with previous suspicious changes now had definite reticulation. All these men had continued at work and were in good health. In 2 cases with previous lung changes, 1 now not at risk and the other only occasionally on welding, subsequent X-rays were normal or less intense, thus suggesting that the iron-oxide dust can be eliminated from the lung parenchyma after some years.

Insurance against Industrial Disease. During the year 1948 the report was issued of a committee set up by the Minister of National Insurance to advise on the principles which should govern the selection of diseases for insurance under the National Insurance (Industrial Injuries) Act, 1946.[19] The committee holds that the Workmen's Compensation tests as recommended by the Samuel

Committee in 1906, and applied before a disease was scheduled, are no longer appropriate. Now particular cases must normally be attributable with reasonable certainty to the nature of employment. Subject to this overriding principle the primary consideration should be whether the disease is specific to an occupation, or, if not specific, whether the occupation causes special exposure to risk of the disease. Incidence alone is not a conclusive test of risk.

Industrial Injuries Act, 1946.—Under the National Insurance (Industrial Injuries) Act, 1946, new regulations concerned with prescribed diseases (previously scheduled diseases under the Workmen's Compensation Acts) have been issued.[20] These important regulations include rules for deciding the date of onset of a prescribed disease, certain modifications of the Act relating to benefits, procedure for determining claims, special provisions for pneumokoniosis and byssinosis, and the constitution and duties of pneumokoniosis medical panels, and pneumokoniosis medical boards. The First Schedule to these regulations sets out, by name, each disease now (at 1948) on the list of prescribed diseases, together with the occupations in which persons have to be employed to qualify for benefits under the Act. These diseases include practically all the conditions scheduled under the old legislation; there has been some re-grouping and a widening of definitions—for example the separate 'diseases' of dermatitis, ulceration of the skin, and ulceration of the mucous membrane of the nose or mouth, all provoked by dust or liquids, are now grouped into one category. The Schedule also gives the various occupations in which a man suffering from pneumokoniosis may claim benefits under the Act. These include a wide variety of jobs other than coal-mining or pottery manufacture such as fettling or blasting of metal castings with adherent siliceous substance and jobs requiring the use of a grindstone.

Notifiable Industrial Diseases under the Factories Act, 1937.—Under the Factories Act, 1937, fourteen occupational diseases have still to be notified to the Factory Department of the Ministry of Labour. The incidence of these diseases for 1944–8 is shown in the accompanying table.

INCIDENCE OF NOTIFIABLE DISEASES, 1944–8
(Abstracted from The Ministry of Labour Gazette)

POISONING BY					
Lead	41 (5)	45 (2)	47 (8)	58 (3)	49 (2)
Phosphorus	1	—	—	—	—
Mercury	7	5 (1)	1	—	2
Arsenic	3	—	1	—	3 (1)
Manganese	1	—	—	—	—
Carbon bisulphide	1	—	—	—	3
Aniline	55	31	19 (1)	17	12
Benzene (chronic)	1 (1)	1	1 (1)	—	1 (1)
Toxic jaundice	12 (1)	6 (2)	1	—	4 (1)
Toxic anæmia	12 (6)	7 (2)	1 (1)	3 (3)	—
Compressed air	1 (1)	1	—	—	28
Anthrax	8 (3)	7	14 (1)	21 (2)	32
Epitheliomatous ulceration	205 (20)	215 (9)	245 (32)	210 (19)	233 (18)
Chrome ulceration	121	94	98	300	147

Figures in brackets indicate deaths, and include all fatal cases reported, whether or not they have been included in these or previous returns.

Factories Act, 1948.—The Factories Act, 1948, which amends the Factories Act, 1937, received the Royal assent on July 30, 1948. The provisions of the new Act relating to the medical supervision of young workers, suitability of factory premises, and miscellaneous amendments of the Factories Act, 1937, came into force on October 1, 1948. The decision to extend the system of medical examination of young persons employed in factories is important. Previously

when a young person under 16 years of age was taken into employment in a factory he or she could not remain in that employment for more than fourteen days unless certified as fit for it by a doctor appointed by the Factory Department of the Ministry of Labour. (This doctor now, under the new Act, will be known as the Appointed Factory Doctor. Previously he was known as the Certifying Factory Surgeon and, later, the Factory Examining Surgeon.) Young persons aged 15, 16, and 17 years will now be medically examined, also within fourteen days of first employment; previously only those of 15 years of age were required to be examined. Another new provision is that, until the juveniles reach the age of 18, re-examination is required at least once a year. The scheme is also extended to include young persons working in building operations and works of engineering construction, and employed in repairing, refitting, painting, loading, unloading, and coaling ships in harbour or wet dock as well as in shipbuilding yards. The Act also stipulates that facilities for sitting are to be provided and maintained "where any employed persons have, in the course of their work, reasonable opportunities for sitting without detriment to their work"; and also "where a substantial proportion of any work can properly be done sitting" then seats have to be provided. These seats will have to be of suitable design, construction, and size, with foot-rests if necessary. These provisions do not come into legal force until October, 1950.

Health of Iron-founders. On July 19, 1948, the Minister of Labour and National Service made The Factories (Cleanliness of Walls and Ceilings) (Amendment) Order, 1948, under the Factories Act, 1937. This affects the health of iron-founders. Under the provisions of Section 1 (c) of the Act, inside walls and partitions of rooms, and ceilings in factories, are required in the interests of health to be washed, painted, white-washed, or colour-washed at least once in every fourteen months. Hitherto, under the Factories (Cleanliness of Walls and Ceilings) Order, 1938, some iron-foundries or parts of them were exempt from this requirement. In their Report published last year[21] the Joint Advisory Committee, set up by the Chief Inspector of Factories to advise on methods by which general working conditions in iron-foundries could be improved, recommended that the exemption should be removed. The amending Order gives effect to the Committee's recommendation and as from August 1, 1948, all iron-foundries are subject to the general requirement of Section 1 (c) of the Act, except as regards those parts of the walls and ceilings which are above 20 ft. from the floor and which remain exempt under provisions of the Order of 1938.

Human Factors in Industry.—In December, 1947, the Lord President of the Council set up a Panel on Human Factors in Industry as a permanent part of the Government's Committee on Industrial Productivity. An account[22] of the initial work of the Panel included a programme of research into the design and measurement of human performance, the effects of ageing on industrial productivity, methods of joint consultation, intra-management relations, the status, selection and training of foremen, and the effect on production of the size of the work unit. Sir George Schuster is chairman of this Panel, and at the annual meeting of the British Medical Association in 1948 he opened a discussion on human relations in industry.[23] In his view industrial medical officers, through the intimate and individual nature of their vocation, have an important effect for good in this field. They can assist industrial productivity in three ways: by attempting to fit the man to the job and the job to the man; by using their opportunities for sympathetic contacts with individuals; and by planning and directing a positive health policy among groups of workers. In a leading article[24] the *British Medical Journal* discussed Sir George Schuster's proposals. To fit the man to the job or the job to the man it was necessary for the profession to

know more about work and working conditions. One immediate opportunity to do this was during the study of disabled workers and the problems of their resettlement. Success in placing disabled men and women in suitable jobs through mutual co-operation meant that relationships of the right sort were established. There was urgent need for training of industrial medical officers in how to link human understanding with the day-to-day realities of occupation.

At the 1948 International Congress on Mental Hygiene *mental health in industry* was defined by W. Line[25] as another name for the human factor. He insisted that doctors must take the leadership in research in this field. Investigations into the health of the juvenile at his place of work was an important basic research leading to potentially great improvements in mental health among future industrial generations. At the same conference G. R. Hargreaves[26] pointed out that, while the doctor might be leader in research teams in certain fields, in other places and in different situations the chemist or engineer might be the pivot, or the sociologist. Research in human relations is governed by the tempers and emotions of individual human beings and depends on the participation both of managers and employees. The human factor in industry cannot be considered in isolation, nor can it be investigated in the laboratory. There is need, therefore, for all those taking part in future investigations to appreciate these fundamental issues.

In discussing the *relationship of modern psychiatry to occupational health*, D. Stewart[27] pointed out that matters such as the interpretation of collective attitudes or worker discontent had hitherto come mainly within the sphere of the industrial psychologist. Now, with the recent expansion of occupational health services, a greater opportunity to resolve some of these problems is offered through the less remote medical approach. Understanding of causes of disharmony among worker groups has to be supplemented by practical recommendations. The intimacy and warmth of the clinical approach, based on an accurate knowledge of man's normal physical and mental make-up, thus plays an important part in maintaining health and morale and the productivity of industrial workers. Industry requires doctors versed in both industrial and psychological matters rather than the academic psychiatrist who is often remote from industrial reality. Selection for occupation can be assisted by knowledge of psychological method, as can rehabilitation and resettlement; the young worker needs special supervision; and training in industry goes beyond instruction in accident prevention and personal hygiene. Training for management, the need for which is shown in a recent report by a committee set up by the Minister of Education,[28] needs the closest collaboration of doctors.

A recent broadsheet by P. E. P.[29] maintains that good working conditions alone do not make for good fellowship in industry, nor do batteries of personnel record cards without close human contacts. Output and labour turnover offer a rough measure of relations, as does absenteeism. Morale suffers less when the conveyor belts are kept going; it is therefore related to factors such as the flow of raw materials and the overall efficiency of managers who are the responsible planners of production. Systems of joint consultation and information, which allow a two-way contact between managers and workers with outlets for grievances, are complementary to good management and are essential for harmony at the place of work.

Stress diseases, so termed by Lord Horder, were described by Sir Stafford Cripps[30] as arising " not from what in the past we regarded as illness or disease but from those once vague and rather despised causes which passed under such names as neurasthenia ". There is a close relation between stress disease and industrial morale. In organizations where absenteeism due to this cause is at a minimum there is proper and sound selection of employees, adequate chances

for promotion, full knowledge on the part of the employees of the purpose and objects of the work, and stability in the organization itself. In the view of Sir Stafford Cripps the medical schools have a serious responsibility to see that social and industrial problems are given their rightful place in the educational syllabus. At the same time, he maintained, departments of commerce and other similar university faculties must devote some of their curriculum to the questions of human relations in industry. In this way the problem can be tackled simultaneously from both sides, and this is necessary for success.

Industrial Rehabilitation.—The Ministry of Labour and National Service continues to maintain responsibility, under the Disabled Persons (Employment) Act, 1944, for industrial rehabilitation, resettlement, and employment of disabled persons. (*See* MEDICAL ANNUAL, 1948, p. 231.) At the end of 1948 the Disabled Persons Register contained the names of some 908,000 individuals, of whom 70,300 were unemployed. Analysis of the register showed that 42 per cent of cases were surgical, 35 per cent medical, and 6 per cent psychiatric cases. Industrial Rehabilitation Units were opened, during 1948, in Birmingham, Coventry, Felling, Leicester, Denton, Cardiff, Leeds, Hull, and Edinburgh, and are planned for 1949 at Liverpool, Swansea, Sheffield, and Glasgow. Part-time medical officers have been appointed to each unit on a sessional basis. About thirty Medical Interviewing Committees have been established in different parts of the country. The purpose of these committees is to advise the Disablement Rehabilitation Officer (the D.R.O.) on the physical and mental capacities of disabled persons as required, in relation to their employability; resettlement of difficult cases can thus be more readily assured. The Ministry has appointed a number of part-time regional medical advisers to supervise Industrial Rehabilitation Units and Government Training Centres and give general advice to those regional officials of the Ministry more closely concerned with disablement problems. The Minister's National Advisory Council on the Employment of the Disabled, a statutory body under the Disabled Persons (Employment) Act, continues to hold a watching brief, on behalf of the Minister, in all matters coming within the purview of the Act. Among problems to which attention has been given are the scope, functions, and training of the D.R.O., the link between hospitals and the medical profession as a whole with these new national schemes, employment of the tuberculous, and the need for research into re-settlement. In this last connexion the Ministry of Labour, on the advice of the National Advisory Council, has approached the Medical Research Council, which has agreed to carry out investigations in this field.

The Disabled Persons Employment Corporation Limited continues to expand its activities. The current programme of the Corporation has been extended to provide for 118 factories capable of employing approximately 10,000 severely disabled persons. Of these factories thirty-eight were open at November, 1948.[31] Special attention is being paid to the need for permanent sheltered work for cases of tuberculosis, and over twenty Remploy factories will be specially set aside for these cases.

Occupational Morbidity.—An investigation into occupational morbidity, based on absenteeism due to sickness and accidents in two factories with a combined population of 4341 men and 743 women, was carried out by I. Sutherland and G. P. B. Whitwell.[32] Men engaged on manufacturing processes had a lower incidence of certified sickness measured by the system recommended by the Industrial Health Research Board,[33] and a lower lost-time rate, than those employed in non-production departments. This might have been due to less fit men taking the lighter jobs. Male clerical workers paid weekly had a greater incidence of certified sickness, and a higher lost-time rate, than those who were paid monthly. 'Colds' and 'influenza' were the commonest specified causes

of absence, although the average duration of absence from these causes was less than for other diseases. A ' long ' absence was defined as one where thirty working days or more were lost. The percentage of occurrences involving long absences varied from 2·1 per cent for colds and influenza to 32·8 per cent for accidents at work.

Studies on age and wastage in industrial populations, published by R. Padley,[34] dealt with the relation of age to the risk of incurring specific diseases and to morbidity in an employed population. The data concerned large groups of insured persons and was collected by the Department of Health for Scotland. The relative age-incidence of a number of diagnoses was given and possible implications discussed. There is constancy of relative age-incidence both for total morbidity and for individual diagnoses. Women tend to incur accidents relatively more often as they grow older. The incidence among men, on the other hand, tends to decline with age. The great part of this differential is accounted for by accidents resulting in fracture.

The value of *vaccination in industry as a preventive of respiratory disease* is a continually recurring question. Results of vaccination in industry with influenza A and B vaccine during the 1947 epidemic in the United States have been recounted by Anna Baetjer[35] from information supplied by thirteen firms. Some 37,000 individuals were vaccinated, and over 39,000 workers acted as controls. Data from six companies showed a lower rate of respiratory disease or influenza in the vaccinated group, but the rates from seven companies were higher or not significantly different in the two groups. Although the lower rates of respiratory illness among the vaccinated groups in the six companies suggested a beneficial effect of the vaccine, analysis of the records indicated that other factors were probably responsible for these differences. This view is supported by the other seven companies, by consideration of these data in relation to the general characteristics of the epidemic, and by the negative results of other studies made during this period. The data presented in this paper did not show a consistent reduction in sickness during the 1947 epidemic as a result of vaccination, but this does not necessarily imply that influenza vaccination will be of no value to industry in future epidemics.

REFERENCES.—[1]*Min. Labour Gaz.* 1948, **12**, 419 ; [2]*Economic Survey*, 1948, Cmd. 7344, H.M.S.O. ; [3]*Lancet*, 1948, **2**, 281 ; [4]*Brit. med. J.* 1948, **2**, 263 ; [5]*Lancet*, 1948, **2**, 530 ; [6]*J. industr. Hyg.* 1946, **28**, 197 ; [7]*Lancet*, 1948, **2**, 937 ; [8]*Amer. J. Path.* 1948, **24**, 1137 ; [9]*J. industr. Hyg.* 1948, **30**, 228 ; [10]*Ibid.* 281 ; [11]*J. Amer. med. Ass.* 1945, **129**, 1084 ; [12]*J. med. Soc. N. Jersey*, 1948, **45**, 1 ; [13]*Proc. Ann. Meeting Amer. Industr. Phys.*, Boston, 1948 ; [14]*Brit. med. J.* 1948, **1**, 1015, 1065 ; [15]*Ibid.* 1088 ; [16]*Brit. J. industr. Med.* 1948, **5**, 120 ; [17]*Lancet*, 1948, **1**, 789 ; [18]*Ibid.* 800 ; [19]*Report of Committee on Industrial Diseases*, 1948, Cmd. 7557, H.M.S.O. ; [20]*National Insurance (Industrial Injuries) (Prescribed Diseases) Regulations*, 1948, No. 1371, H.M.S.O. ; [21]*Report of the Joint Advisory Committee on Conditions in Iron-foundries*, 1947, H.M.S.O. ; [22]*The Times*, Aug. 10, 1948 ; [23]*Brit. med. J.* 1948, **2**, 505 ; [24]*Ibid.* 521 ; [25]*Proc. internat. Congress on Mental Hlth*, 1948, London ; [26]*Ibid.* ; [27]*Lancet*, 1948, **1**, 737 ; [28]*Education for Management*, 1947, H.M.S.O. ; [29]*Planning*, 1948, **14**, No. 279 ; [30]*Lancet*, 1948, **2**, 30 ; [31]*Min. Labour Gaz.* 1948, **12**, 412 ; [32]*Brit. J. industr. Med.* 1948, **5**, 77 ; [34]*Industr. Hlth Research Bd. Rept.* 1944, No. 85, H.M.S.O. ; [34]*Brit. J. soc. Med.* 1947, **1**, 218 ; [35]*Industr. Med.* 1948, **17**, 171.

ŒSOPHAGEAL VARICES.

(*See also* ANÆMIA, SPLENIC ; PORTAL HYPERTENSION.)

F. W. Watkyn-Thomas, F.R.C.S.

Treatment by Injection of a Sclerosing Solution.—H. J. Moersch[1] reviews a series of cases in which he has tried this method. These cases are due either to Banti's syndrome of portal hypertension or to earlier hepatitis. Massive gastro-intestinal bleeding is the characteristic symptom, and patients with untreated varices usually die from repeated hæmorrhages. In 1939 Crafoord and Frenckner suggested treatment of these cases by injection of the œsophageal varices with a sclerosing solution under endoscopy, and in 1941 Moersch made a preliminary report on 11 cases treated by this method. In the present paper he reviews the results in 10 of the original cases (one case omitted from lack of

follow-up) and on 12 additional cases. All 22 cases have been followed up for three years or more.

The cases were classified as follows: (*a*) Patients with Banti's syndrome who had undergone splenectomy before treatment of the œsophageal varices by injection; (*b*) Patients in whom the varices were secondary to hepatitis and had had no surgical treatment; (*c*) Patients with Banti's syndrome who had splenectomy performed during the course of treatment of the œsophageal varices by injection. In group (*a*) there were 16 patients, 11 men and 5 women, aged from 11 to 61; 13 had had gastro-intestinal bleeding before splenectomy, and all had had copious hæmorrhages since. Of these patients 8 have had no more bleeding; 5 have died, and 3 have had further hæmorrhages. In group (*b*) were 3 cases. Two seem to have recovered completely; one died of hæmorrhage after three years of freedom from bleeding. In group (*c*) there were 3 cases. Two have recovered; one still has hæmorrhages.

From the available figures, age, sex, duration of the condition, and frequency of hæmorrhages have no relation to the result that is to be expected from œsophageal injection. Moersch believes that failure is due to varices in the stomach. Of 10 unsuccessfully treated patients 6 were found to have gastric varices when examined by the gastroscope. Radiographs, although of great value, cannot be relied on to show this condition, so gastroscopy should be done in every case before trying sclerosing injections of the œsophagus; if gastric varices are present there is not much hope of success by œsophageal treatment.

In the discussion on this paper, C. O. Patterson said that he had been using the method since 1943, and his results were similar to those of Moersch. His youngest patient was 3 years old, his oldest 66. In some of the cirrhosis group ascites had disappeared. There is some risk of damage to the aorta, pericardium, or pleura. Some patients had substernal distress, pain in the back, or pyrexia for a few days, and anaphylactic reaction to the injecting agent had been reported.

Moersch reports that one of his patients had a normal confinement without any return of bleeding, but advises against severe exertion, and warns us that patients are in some danger during any acute respiratory infection, as the accompanying œsophagitis predisposes to bleeding. There are eight references and four illustrations of specimens.

REFERENCE.—[1]*J. Amer. med. Ass.* 1947, **135**, 754.

ŒSOPHAGUS. (*See also* CARDIOSPASM.)

ŒSOPHAGUS, CARCINOMA OF. *N. R. Barrett, M.A., M.Chir., F.R.C.S.*

Santy and Mouchet[1] have reviewed the subject of carcinoma of the œsophagus and state that surgical treatment is justifiable because of the great frequency of the disease, its serious consequences, its failure to respond to any other method of treatment, and its relatively long period of operability after the first symptoms have been experienced. In 1939 Ballivet was only able to collect 24 cases which he believed had been cured, whilst to-day the number in the literature exceeds 400. The operative mortality has dropped from 70 per cent in 1940 to less than 15 per cent in some clinics to-day.

Raven[2] has investigated the clinical and the pathological features in a series of 277 patients admitted to the Cancer Hospital, London. His analysis shows that many delayed as much as 4–5 months between the time they first had symptoms and the time when medical aid was sought, and only 40 per cent of patients came up within 3 months. The killing nature of the disease is shown by the fact that 67·1 per cent of the patients *untreated by surgery* had died within 6 months of diagnosis being made. Of the patients treated by

high-voltage irradiation 30·6 per cent died within 3 months and 55 per cent within 6 months; the figures for *radium therapy* are equally bad, for 37·2 per cent died within 3 months and 76·7 per cent within 6 months. A study of 108 patients who died of the disease revealed that 57·4 per cent had metastases but 42·5 per cent had not, and thus it is reasonable to assume that, even diagnosed as late as these cases are to-day, about 4 out of 10 are still operable.

Holmes and Schulz[3] have shown that in their hands no patients treated by super-voltage radiation survived more than 2 years.

Sweet[4] reported the results of surgical operations in 213 patients treated at the Massachusetts General Hospital between 1939 and 1947. The growth was resectable in 66 per cent of cases, and there was no important difference in operability between the low and the high lesions. Of the 141 patients suffering from carcinoma of the cardia and of the lower œsophagus who were treated by radical resection and primary anastomosis 93 made an uncomplicated recovery, and 25 others recovered ultimately, whilst 23 (16·3 per cent) died as a result of the operation. The operation for removal of growths situated in the middle and upper thirds of the gullet is more dangerous, and of the 50 patients in this group the operative mortality was 22 per cent. These operations have not as yet been practised long enough to assess their late results, but all the patients (except 2) who survived the operations referred to above have been traced, and it is known that, to date, the *survival-rate* is as follows: 77 per cent six months or longer; 50 per cent twelve months or longer; 31 per cent eighteen months or longer; and 37·5 per cent for two years. Sweet also stresses that in carcinoma of the œsophagus the most distressing symptom is dysphagia, and, like many other surgeons, he is an advocate of palliative resections or short-circuit operations even in the case of inoperable or irremovable tumours.

John H. Garlock,[5] working at the Mount Sinai Hospital, New York, has again advanced our knowledge of how to resect growths and perform primary reconstitution of the alimentary canal in the mediastinum in one procedure, by describing a new operation for growths in the upper third of the œsophagus. He has demonstrated that in a patient of average height the stomach could be mobilized sufficiently to permit its transplantation *above the apex of the chest* without impairment of its vitality, and that it could then be anastomosed to the cervical œsophagus in the neck. Harold Wookey,[6] of Toronto, has also contributed to this aspect of the subject by describing his operation for lesions of the hypopharynx and the upper œsophagus. The procedures he describes should be compared with those of Watson and Pool.[7]

In June, 1948, *Surgery* devoted a whole number to the subject of carcinoma of the œsophagus and of the cardiac end of the stomach; 10 important papers are included and should be consulted by all who have to treat these cases. It seems fair to summarize these papers by observing that all authors agree that surgical excision is the only possible curative measure at present; that the patients do not come up and are not diagnosed soon enough to give surgical excision a really good chance of success; that despite this defect an increasing number of patients are being cured every year; that the details of operative technique are well established; that the operative mortality is not excessive; that the principle of primary resection with direct anastomosis in the mediastinum is accepted; that palliative operations to overcome dysphagia are justifiable; and that even better results may soon be expected.

Garlock[8] has given details of the points which he considers specifically important as follows:—

1. There seems to be fairly general agreement now that the question of anæsthesia is of paramount importance. I am convinced that, unless the anæsthetist is thoroughly competent, the surgeon should not undertake this operation. In talking to many surgeons who have

attempted œsophageal resections in appreciable numbers, I have been impressed with the fact that many of them have been severely handicapped by serious problems of anæsthesia. This has been particularly noticeable with the foreign surgeons, who are now visiting America in increasing numbers. The anæsthesia of choice to-day, on the basis of an extensive experience with various modalities, is intratracheal gas-oxygen-ether.

2. For cancers of the middle third of the œsophagus it is no longer necessary to utilize the Torek operation. It is now possible to restore normal gastro-intestinal continuity by the operation of supra-aortic œsophago-gastrostomy, originally described in January, 1944. By an accurate ligation of the blood-supply of the stomach, one can mobilize the organ to such an extent that it can be brought to the apex of the chest without jeopardizing its vitality, and anastomosed to the stump of the œsophagus. Recently, in a patient with a carcinoma just above the arch of the aorta, I was able to bring the stomach through the apical aperture of the chest and anastomose its cardiac end to the œsophagus in the lower part of the neck without impairment of its blood-supply. The utilization of the stomach in effecting these high anastomoses has made unnecessary the various complicated plastic procedures which employed tubes of stomach wall and loops of jejunum in an attempt to restore œsophago-gastric continuity. The operation of supra-aortic œsophago-gastrostomy is a recent development in œsophageal surgery.

3. Since Phemister's first successful œsophago-gastric anastomosis in 1938 for cancer of the distal part of the œsophagus, most surgeons have adopted this procedure as a routine measure for tumours of the lower œsophagus and upper stomach. Until recently, this was accomplished by a transthoracic transdiaphragmatic route. Frequently, after the patient had been subjected to a formidable transthoracic exploration, an inoperable tumour was disclosed by reason of extensive metastases below the diaphragm. It is for this reason that I suggested some years ago the great desirability of demonstrating a resectable tumour by the simple expedient of an abdominal exploration alone. If the growth was found operable the abdominal wound was closed and a transthoracic resection was then done. A recent development of this thought has been the perfection of a combined abdomino-thoracic incision with simultaneous exposure of both the upper abdomen and the left thoracic cavity. This incision has simplified in no small measure the whole problem of the surgical treatment of cancer of the lower œsophagus and upper stomach. Because the incision is a large one, the approach is more direct and all operative manœuvres can be carried out under direct vision with minimal trauma. This has been clearly discernible in the much smoother post-operative course, the lower mortality, and decreased incidence of post-operative complications. The combined abdomino-thoracic approach has a wide field of applicability and should be the exposure of choice for total gastrectomy.

4. Increasing experience during the past five years has effected some changes in the technical details of these operations. The important ones may be mentioned briefly.

a. The left leaf of the diaphragm should be put at rest by pinching the phrenic nerve above the diaphragm.

b. It is not necessary to apply clamps to either the œsophagus or stomach in order to minimize contamination. The œsophagus may be kept empty by an indwelling Levine tube during the operation. The stomach can be emptied by suction.

c. In the performance of the anastomosis, it has been clearly demonstrated that interrupted silk sutures should be used if one is to avoid a stricture. I am inclined to agree with Sweet that the excision of a button of gastric wall the approximate size of the œsophageal lumen also aids in the prevention of stricture.

d. Slight telescoping of the suture line by drawing the stomach over it and anchoring of the stomach to both edges of the mediastinal pleura will prevent drag on the suture line.

e. It is important to anchor the diaphragm around the transplanted stomach in such a way as to prevent herniation of abdominal contents into the chest.

f. We have never found it necessary to use an indwelling Levine tube during the post-operative period. In fact, there may be some danger from pressure necrosis on the suture line.

g. There seems to be general agreement that underwater drainage of the chest for at least a few days post-operatively is desirable.

h. Before closure of the operative wound, 50,000 to 100,000 units of penicillin should be injected into the pleural and abdominal cavities. It probably has some local beneficial effect.

REFERENCES.—[1]*J. Chir., Paris*, 1947, **63**, 505; [2]*Brit. J. Surg.* 1948, **36**, 70; [3]*Amer. J. Roentgenol.* 1946, **55**, 533; [4]*J. Amer. med. Ass.* 1947, **135**, 485; [5]*Surgery*, 1948, **24**, 1; [6]*Brit. J. Surg.* 1948, **35**, 249; [7]*Surgery*, 1948, **23**, 893; [8]*Ibid.* 906.

ŒSOPHAGUS, CONGENITAL ATRESIA OF.

N. R. Barrett, M.A., M.Chir., F.R.C.S.

The commonest (80 per cent) congenital abnormality of the œsophagus is complete atresia: the upper segment ends blindly in a pouch and the lower segment communicates with the trachea near to the bifurcation. This deformity is incompatible with life, but can now be corrected by operation in many cases. One of the first to recommend surgical treatment in these cases was Cameron Haight,[1, 2] and the reader will find ample descriptions of the methods of diagnosis and treatment in articles by Haight, Humphreys,[3] Daniel,[4] Ladd,[5] Lam,[6] Longmore,[7] Franklin,[8] and Sweet.[9]

Early diagnosis is essential if the patient is to have a chance of successful operation, and Franklin states that all babies with attacks of cyanosis and choking, made worse by feeding, must, until the contrary is proved, be

assumed to have a congenital atresia. The most important method of diagnosis is to pass a soft rubber catheter through the mouth until it is arrested and to inject 1 c.ml. of lipiodol. The child should then be screened, and if atresia is found the oil must be sucked out. A radiograph of the chest and the upper abdomen affords valuable evidence by showing the presence or absence of an air-bubble in the stomach and the normality or otherwise of the lungs. If air is present in the stomach complete atresia cannot be present.

Pre-operative management consists in correcting dehydration, and in keeping the upper pouch as dry as possible by frequent aspirations. Penicillin can be instilled. Most authorities, including Franklin, who has now operated successfully many times, advocate a general anæsthetic; they set up a blood transfusion and are prepared to do an operation which may take anything up to four hours. It is surprising but true that these apparently ill and delicate infants will tolerate such an operation. The œsophageal obstruction is approached through a right intercostal incision with division of one or two adjacent ribs posteriorly. Every effort should be made to do the job extrapleurally. After the ends of the œsophagus have been isolated and mobilized the anastomosis between the upper and the lower segments is done with interrupted stitches of silk or thread and this is facilitated by passing the catheter, which is already in the upper pouch, onwards into the lower segment. The fistulous communication with the air-passages is closed off with sutures. After operation the mediastinum is drained. A fistula, which fortunately does not often persist, may develop. The mediastinal drainage-tube is connected to a water-seal bottle; oxygen and penicillin are exhibited and nasopharyngeal aspirations are continued. The exact details of the post-operative management, and especially the feeding of the infants with breast milk, are as important as the operation itself, and must be studied by any who would attempt to cure atresia. Full details and advice will be found in the recent papers quoted above.

Sweet[9] has recently described a technique for dealing with that small group of cases in which for one reason or another direct continuity of the œsophagus cannot be re-established after the ends have been mobilized and the tracheal fistula closed. The method, which has been successfully applied in 2 infants, consists in performing an intercervical œsophago-gastric anastomosis after bringing the stomach up through the chest. This must be an even more formidable procedure than direct anastomosis, but the fact that immediate success can be achieved is already established, although the late results will be interesting to observe, for any operation in a child or adult in which the stomach is either anastomosed to the œsophagus, or mobilized so that it is transposed into the mediastinum, carries the risk of serious late possible complications.

REFERENCES.—[1]*Surg. Gynec. Obstet.* 1943, **76**, 672; [2]*Ann. Surg.* 1944, **120**, 623; [3]*Surgery*, 1944, **15**, 801; [4]*Ann. Surg.* 1944, **120**, 764; [5]*New Engl. J. Med.* 1944, **230**, 625; [6]*Surgery*, 1946, **20**, 174; [7]*Arch. Surg., Chicago*, 1947, **55**, 330; [8]*Lancet*, 1947, **2**, 243; [9]*Ann. Surg.* 1948, **127**, 757.

OLD AGE. (*See also* CHRONIC AGED SICK.) *Una Ledingham, M.D., F.R.C.P.*

There is increasing compassionate recognition of the medical and social problems of old age. They merit at least as much interest as those of lower age-groups and must loom larger as the years go by and as advances in prophylaxis and therapeutics allow for more of us to acquire the doubtful privilege of surviving the biblical span. Sheldon[1] studied the health and living conditions in an unselected group of 477 old people. Women on the whole had increasingly poor health with advancing age, few being exceptionally well at 85. Their hold on life, however, is greater and they tend to live longer than old men.

The latter succumb rapidly after 80, only those in exceptional health surviving. Apart from defined disease the elderly suffer greatly from declining function of the cochlea and labyrinth. Deafness and vertigo are common problems, and these, together with deterioration of postural sense and co-ordination explain the frequent accidents to which they are liable. Old people dislike the dark and are much handicapped by the loss of their visual aid. The position socially is more cheerful than appears at sight. Many live alone but are near to children, friends, and relations on whom they depend for companionship and help. These relations come forward in illness and the old people are kindly nursed in their homes. Many make up for their inevitable weaknesses by taking on such tasks as the care of grandchildren or nursing the sick. These burdens are often too heavy for their health and strength. Sadly enough beyond this age old people themselves become the burden. Assistance for younger people with such relations should be arranged for. More institutions of the right type are needed, while the help of kindly sympathetic persons could be recruited to the 'home help' ranks.

REFERENCES. [1]*Lancet*, 1948, **1**, 621; [2]*Ibid.* 517.

ORAL PENICILLIN IN INFANTS.

R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.

J. H. Moseley[1] reviews the previous work on the administration of penicillin by mouth, and points out that most of this work had been done on infants under a month of age. In a careful study, he has shown that adequate serum levels of penicillin can be obtained by administering penicillin by mouth before feeds. He concludes that penicillin may be successfully given to infants under six months by mouth, as reliably as sulphonamides, provided massive doses are used and given when the stomach is empty. He thinks this the route of choice in severely ill babies, but it is contra-indicated when vomiting or persistent diarrhœa is present; the relaxed and frequent stools seen so often in infantile infections are, however, not a contra-indication. The size of dose must be based upon the age rather than the weight of the infant. He recommends: 0–6 weeks, 20,000 units 3-hourly, or 30,000 units 4-hourly; 6–12 weeks, 40,000 units 3-hourly, or 60,000 units 4-hourly; 12–26 weeks, 50,000 units 3-hourly, or 70,000 units 4-hourly. In older children, he finds the use of oral penicillin a matter of trial and error, because of the variability of absorption.

REFERENCE. [1]*Arch. Dis. Childh.* 1948, **23**, 93.

OSTEOGENESIS IMPERFECTA.

Una Ledingham, M.D., F.R.C.P.

Disturbance of genes determining mesenchymal development is postulated, and this view has some support, as no confirmatory evidence of metabolic, endocrine, or other dysfunction has appeared. Kellogg[1] reports a family where 17 affected members are included in 5 generations. As well as the characteristic multiple fractures, blue sclerotics, blue tympanic membranes, and deafness, exophthalmos was noted in two-thirds of the cases. This association is not previously recorded, and no mention is made of the degree of cranial deformity or to the relationship of the exophthalmos to the size and shape of the orbit. The author reminds us that the disease is transmitted by affected females, that half the children of such women will develop the disease, that unaffected persons do not transmit the disease, and that therefore a generation is not skipped. He recommends properly that even minimally affected persons should be made familiar with these facts.

REFERENCE.—[1]*Arch. intern. Med.* 1947, **80**, 358.

OSTEOPOROSIS.

(*See* PARATHYROID GLANDS.)

PANCREAS, DISEASES OF.

A. Rendle Short, M.D., F.R.C.S.

A 500-page report has been issued of an International Congress held at the University of Louvain[1] in July, 1948, to discuss modern work on the pathology of diseases of the pancreas. It is difficult to summarize, because so many topics are briefly dealt with, but some of the observations are noted in the following paragraphs.

Acute Pancreatitis.—J. Howard and R. Jones[2] find that in 50 per cent of human cases there is a communication between the biliary and pancreatic ducts when the ampulla of Vater is blocked. H. Wapshaw,[3] of Glasgow, investigated the amount of blood diastase and lipase in 10 cases of acute pancreatitis; in the early stages there was a very marked increase of both ferments, but within a few days they had returned to normal. C. G. MacGuire and A. J. Conte,[4] of New York, find that if there is no increase of blood diastase within the first 24 hours of symptoms, acute pancreatitis can be excluded; later, the test is of little value. They think a history of a recent heavy meal is of some significance. Some 60 per cent of the patients had had previous milder attacks. They report 30 cases. Their policy is to operate in the necrotic cases as soon as shock passes, but not when œdema only is present. They allow that the distinction is difficult. The operation is described as "supportive", but sometimes they drained or removed the gall-bladder. Six out of their 23 operated cases died.

J. R. Paxton and J. H. Payne,[5] of Los Angeles, relating 307 cases, saw a mortality of 44·7 per cent in those treated by surgery and 21·3 when conservative measures were used. Usually nothing useful could be done even at operation. They call attention to variations in the clinical picture; a diagnosis of acute cholecystitis was often made, or of acute intestinal obstruction. Some began with what was thought to be acute gastritis after a bout of alcoholism. In late cases, there was often a palpable swelling in the epigastric region. Vomiting of blood, or bloody diarrhœa, was present in a few patients. Shock was absent in 80 per cent of their cases. A plain X-ray often showed segments of ileus in the upper abdomen. The conservative treatment recommended is gastro-intestinal suction, intravenous fluids, morphine, and atropine. They think X-ray therapy helps in the acute phase. H. Paschoud,[1] of Lausanne, and F. Tondeur,[1] of Brussels, also advise against operation, but if the abdomen is opened to clear up the diagnosis it may be helpful to remove any stones in the gall-bladder or to drain it. [We agree that conservative treatment is usually safest when the diagnosis is rendered virtually certain by the diastase test. Late collections of fluid in the lesser sac may need to be evacuated.—A. R. S.]

R. Horton[6] does useful service by calling attention to the chronic relapsing course taken by some cases of subacute pancreatitis. This is by no means uncommon. The diagnosis is suggested when the cholecystogram is normal in patients who appear to be suffering from acute cholecystitis. If the pain is severe and the attacks are frequent, surgery may have to be considered. Pancreatectomy has been proposed, but seems too severe. Thoracolumbar sympathectomy cured one case. Internal or external biliary drainage is usually the best treatment; it cured 7 patients and relieved 4 others, but failed in 6. To these may be added 4 cases operated on at Guy's Hospital: 2 were cured and 1 relieved by cholecystenterostomy. H. Doubilet and J. H. Mulholland[7] of New York recommend sphincterotomy of the sphincter of Oddi to relieve such cases. The common duct is opened and a curved forceps armed with a knife-blade is passed down through the ampulla of Vater, and the sphincter is slit from within the duct (*Figs.* 36–38). L. A. Hulst,[1] of Utrecht, remarks that in these patients there may be palpitations, tachycardia, and pain under

the heart going through to the back. P. Mallet-Guy and J. de Beaulieu,[1] of Lyons, report 7 cases in which a large part of the pancreas was removed to stop the pain of recurrent attacks: 1 died, 4 were cured, and in 2 the pain

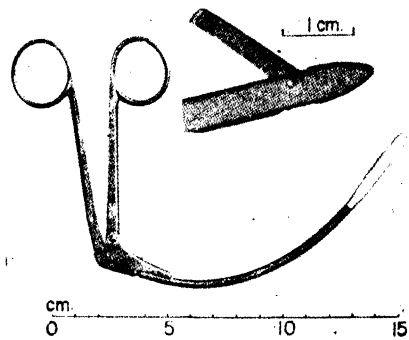


Fig. 36. Endocholedochal sphincterotome. The length and curvature of the instrument are adapted to insertion into the duodenum through the common duct. Since the handle and knife are in the same side and plane only the anterior free lip of the papilla of Vater can be cut. The length of the effective section is 1 cm.

returned, no doubt from involvement of the head of the pancreas left behind. Of 44 cases treated by splanchnicectomy, results were classified thus: 61 per cent perfect, 9 per cent very good, 16 per cent good, and 14 per cent poor.

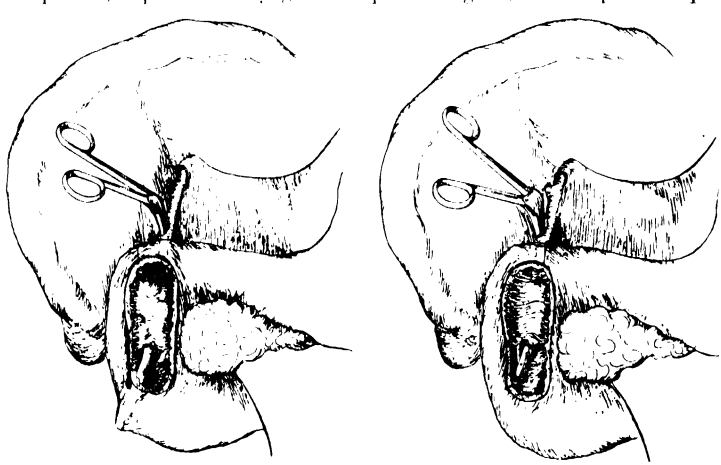


Fig. 37 *Fig.* 38

Figs. 37, 38.—Endocholedochal sphincterotomy. The instrument is inserted through the common duct into the duodenum until it elevates the anterior duodenal wall (*Fig.* 37). The blade is then opened to convert the instrument into a hook and the instrument withdrawn until it catches the papilla. On closure, the sphincter of Oddi is sectioned in one plane.

A. Gasbarrini[1] calls attention to the relative amounts of fats and fatty acids in the fæces (index of Zoja) for accurate diagnosis of pancreatic lesions.

Hyperinsulinism. E. Delannoy and J. Paris,[1] of Lille, and D. Cock and M. Hendrickx, of Alost, describe cases cured of attacks of hypoglycæmia, in

which no islet tumours were found, by hemipancreatectomy, but Rene Leriche mentions two failures, with one success.

Pancreatic Calculi.—A number of papers have appeared on this subject of late years. It would seem that cases are more often overlooked than diagnosed, in spite of the fact that the stones show in a good radiograph. E. L. Eliason and R. F. Welty,[8] of Philadelphia, report 9 patients operated on, with 1 death. The best approach is by a transverse incision, exposing the pancreas through the gap between the stomach and the transverse colon. The stones can usually be felt, and the duct can be cut down upon to extract them. L. Martin and J. D. Canseco,[9] of Baltimore, describe 21 cases of generalized calculosis of the pancreas, causing serious pain. Treatment is difficult. They have tried removal of as many stones as possible, ligation of the duct, splanchnicectomy, partial and total removal of the pancreas, each in a few patients. They are inclined to prefer ligation of the duct.

Pancreatic Cyst.—An Indian surgeon, R. Mahadevan,[10] of Madura, has treated 5 cases of pseudocyst by primary anastomosis to the jejunum (4 cases) or to the stomach (1 case). One died; the others all did well over several years. He made a stoma of 1½ in.

Cancer of the Pancreas. This condition, and its treatment, continue to arouse much interest. G. F. Dashiell and W. L. Palmer,[11] of Chicago, and G. B. Silver and R. K. Lubliner,[12] of New York, discuss the diagnosis. Pain is nearly always present, usually dull and persistent. It often radiates to the back. Jaundice is seen in two-thirds of the cases. The gall-bladder was palpated in 58 per cent. Loss of weight was rapid and very significant; so was steatorrhœa. In about a quarter of the patients there was glycosuria (Dashiell and Palmer). Silver and Lubliner give the appended table for distinguishing growths of the head and of the body of the pancreas.

CLINICAL DIFFERENCES IN INVOLVEMENT OF THE HEAD AND BODY OF THE PANCREAS

SIGNS AND SYMPTOMS	HEAD	
..	Epigastric and right sided. Less severe and less frequent	Epigastric, left sided and back pain. Severe and almost universally present
..	Infrequent. Sugar tolerance disturbances also infrequent	Diabetes and sugar tolerance disturbances frequent
Ascites	Infrequent	Common
Metastases	Few clinically	Diffuse and widespread
Thrombosis and œdema ..	Not frequent	More common; frequently disseminated thrombosis
Splenomegaly	Rare	More common
Steatorrhœa and creatorrhœa	Occasionally present (10 per cent)	Less frequent
ndings		s likely to ha
X-ray defects ..	Reflected in pyloric area and first, second, and third parts of duodenum	Reflected in stomach and first portion of duodenum

Most surgeons find tumours of the head much the commoner, but in their series the proportion was 57 per cent of the head to 43 per cent of the body. V. E. Siler and M. Zinniger,[13] of Cincinnati, add to this list of significant symptoms the value of persistent presence of occult blood in the stools as suggestive. They carried out a removal of the bile-duct, duodenum, and head of pancreas in 5 cases, some by a one-stage and some by a two-stage operation. They advise implantation of the pancreatic duct into the jejunum. One patient was still alive after 2½ years, another died after 7 years.

A. Brunschwig,[14] of Chicago, and C. G. Child,[15] of New York, present their experience of one-stage pancreatico-duodenectomy for growths of the head of the pancreas or ampulla of Vater (*Fig.* 39). Brunschwig has 7 cases without a death, and Child collects records of 22, treated by various surgeons, with

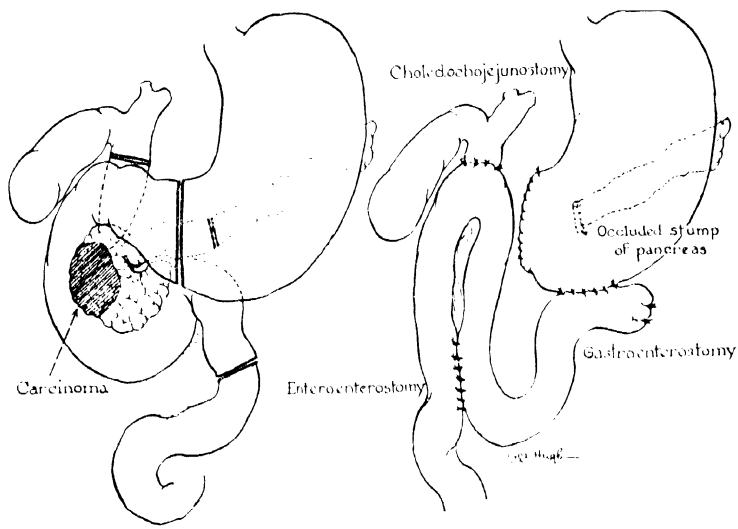


Fig. 39.—Diagram of one-stage pancreatico-duodenectomy without implantation of the transected pancreas into the jejunum. (*Figs.* 36–39 *reproduced from* '*Surgery, Gynecology and Obstetrics*'.)

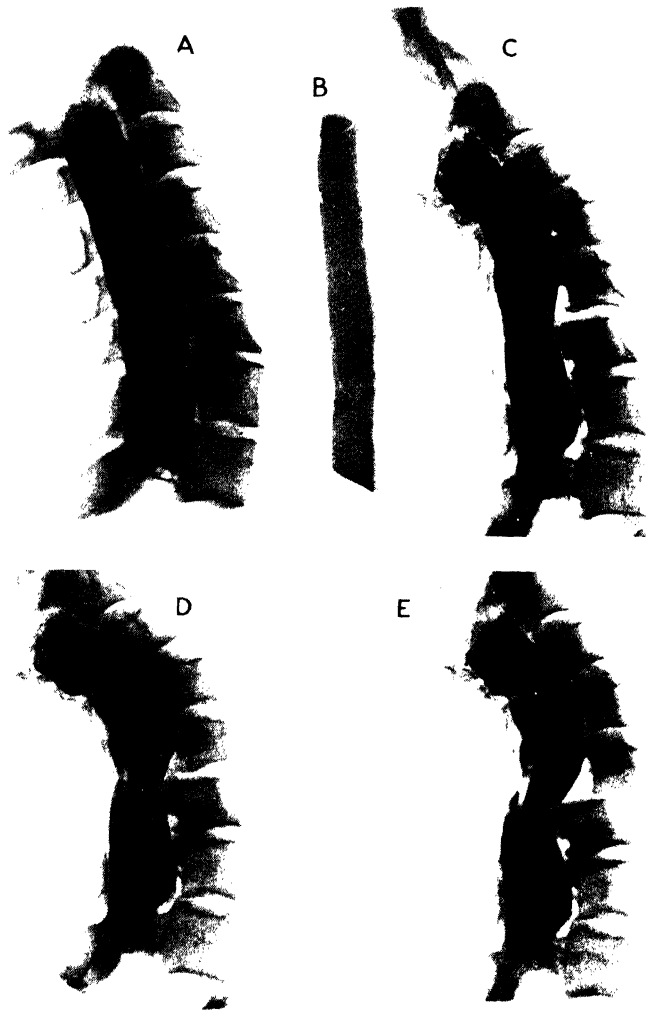
6 post-operative deaths, 4 from recurrence, and 9 apparent successes, 2 of them over three years. Four of Brunschwig's patients suffered recurrence; 3 kept well. At the Mayo Clinic, resection has been carried out 11 times for benign disease and 38 times for carcinoma, with a death-rate of 21 per cent. Eight patients were alive and well over two years (J. M. Waugh[16]).

J. Morley[17] advises a two-stage operation if the patient is seriously ill, as his cases were. The first stage is cholecystgastrostomy, and the second the resection, with a gastrojejunostomy, and ligature of the pancreatic duct. Of 6 patients dealt with, 1 died soon and 3 later, 1 has cholangitis, and 1 is well at eleven months. Many years ago he had a carcinoma of the ampulla, verified by section, but not removed, which underwent spontaneous cure. The patient died of coronary thrombosis in 1944.

PLATE XXVI

PARAPLEGIA IN CERVICAL SPINE INJURIES

(ROLAND BARNES)



Experimental displacements of cal spine in which the dural sac has be filled with lipiodol. A shows the sp dural position and C, D, E show degr of flexion dislocation. B is a soft ti size. In C there is subluxation of t artic ar processes. In D one articular proc locked. In E both articular proces are ocked. The spinal cord is not compr by the displaced neural arches until t lea one articular process is locked.

PANCREAS : HYPERINSULINISM. *S. L. Simpson, M.A., M.D., F.R.C.P.*

Tumours of the Islets of Langerhans. A paper by R. Lopez-Kruger and M. B. Dockerty[1] is based on the records of 38 patients presenting themselves with the syndrome of spontaneous hypoglycæmia during the past twenty years, and on a review of 10,314 consecutive general necropsies. Routine examination of the latter revealed 44 asymptomatic islet cell adenomas of the pancreas. The lesions found responsible for clinical hypoglycæmia were : (1) Benign adenomas, 70 per cent ; (2) Islet cell adenomatosis, 2 per cent ; (3) Histologically malignant but non-metastasizing islet cell tumours, 20 per cent ; and (4) Metastasizing islet cell carcinomas, 8 per cent.

One case of islet cell adenomatosis is described and is worth recording here. A 34-year-old white woman had experienced for 11 years transitory episodes of diplopia, faintness, weakness, and perspiration. Recently there were attacks of unconsciousness, with incontinence and convulsive twitches : blood sugar 36 mg. per 100 c.c. On September 24, 1943, a pancreatic adenoma was removed but symptoms soon recurred. On April 4, 1944, the entire tail of the pancreas was removed for multiple small adenomas which had not been palpable at the time of the first operation. At least 8 of these nodules measured 1 cm. in diameter. The case was complicated by a functioning parathyroid adenoma, which was successfully removed.

From a surgical angle, it is stated that blind resection of the tail of the pancreas will remove 50 per cent of tumours ; resection of the body as well as the tail will account for about 20 per cent more. Total pancreatectomy will occasionally be necessary for some of the small buried tumours located in the head of the gland, which is the site of about 20 to 30 per cent of the neoplasms. Very rarely (2 per cent) the tumour will have an extrapancreatic location.

REFERENCE. —[1]*Surg. Gynec. Obstet.* 1947, **85**, 495.

PARAPLEGIA IN CERVICAL SPINE INJURIES. *T. P. McMurray, F.R.C.S.*

R. Barnes[1] discusses the incidence of paraplegia in various types of injury of the cervical spine. In the opening paragraph it is stated that more than half the patients suffering in this way die as a result of complications of spinal cord injury, while many of the survivors are left with varying degrees of paralysis.

One of the most puzzling features of injuries of the cervical spine is the lack of correlation between the degree of vertebral displacement and the severity of the spinal cord lesion. Thus, with the cord irretrievably damaged there may be no radiographic evidence of bone injury, while in other patients gross dislocation and distortion of the cervical vertebræ may be accompanied by no sign of nerve injury. It is commonly believed that in these injuries of the cervical spine the cord is damaged by direct pressure of the dislocated neural arches, and in the absence of radiographic changes it is assumed that following considerable displacement spontaneous reduction of the dislocation has taken place. This view, although generally held, is not in the author's opinion supported by experimental or post-mortem observations.

Radiographic study of specimens in which the dural sac has been filled with lipiodol shows quite clearly that the dislocated neural arches do not produce a narrowing of the spinal canal sufficient to compress the cord until there is locking of at least one articular process (*Plate XXVI*). Once the articular processes are locked the dislocation is, as a rule, stable, and reduction cannot be obtained without manipulation. The author is of the opinion, as a result of post-mortem specimens and from direct observations at operation, that spinal cord injury can occur in the absence of any vertebral dislocation, and unless there is clear radiographic evidence of fracture of articular processes, which would permit spontaneous reduction, some other cause must be responsible.

Types of Cervical Injury. The cervical spine may be injured by excessive movement, either in flexion or extension, and in this paper, which is based on 22 patients suffering from paraplegia, there were 15 instances in which the injury was caused by excessive flexion, while the remaining 7 were due to hyperextension.

Three types of flexion injury may be recognized—(1) anterior dislocation, (2) crush fracture of a vertebral body, (3) acute retropulsion of an intervertebral disk—while the lesions produced by hyperextension may be classified under two headings—(1) posterior dislocation, and (2) injury to an arthritic spine.

Flexion Injuries of the Cervical Spine.

Cervical Dislocations. In dislocation of the cervical spine, cord injury may be caused by a combination of two factors—(*a*) pressure on the dorsal surface of the cord by the dislocated neural arches, and (*b*) a coincident compression of the ventral surface of the cord by the pressure of retropulsed disk material. As a result of a lengthy experience the author is of the opinion that in the treatment of this type of injury extension by means of the skull calliper is the treatment of choice, as its effective use results in a reduction of the dislocation without the risk of further injury to the already suspect cord.

Acute Retropulsion of an Intervertebral Disk. In this series there were 3 instances of this type of injury, each resulting from a forcible flexion of the head on the trunk. In none was there any evidence of bony injury in the cervical spine, but in every instance there appeared to be a distinct narrowing of one intervertebral space. In the treatment of this type of injury traction by the cranial calliper will restore the normal depth of the interval between the approximated vertebræ, and it is probable that with this opening out of the intervertebral space some portion of the protruded disk will return to its normal situation between the vertebræ, and so relieve pressure on the cord. If, however, there is no recovery of paraplegia within a few days following application of the skull traction laminectomy should be considered, even when the Queckenstedt test is negative.

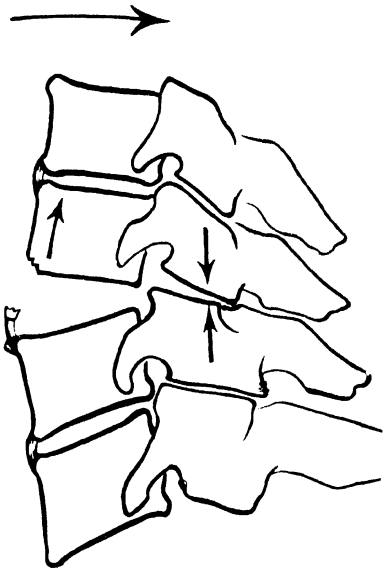


Fig. 40. Mechanism of hyperextension injury of cervical spine. The anterior common ligament is torn or avulsed with a bone fragment. There is no dislocation of articular processes. (*Plate XXVI and Fig.* 40 *by kind permission of the "Journal of Bone and Joint Surgery".*)

Crush Fracture of the Cervical Spine. Four of the patients in the series had sustained crush fracture of cervical vertebræ without evidence of dislocation. Post-mortem examination of two fatal cases indicated that the cord was severely crushed, although there was no sign of dislocation of the articular processes. The two patients who recovered had incomplete paraplegia from the first, and yet there was poor recovery of function during a period of two years following the injury. In the author's opinion the treatment of compression fracture of the cervical spine complicated by paraplegia should be on similar lines with skull traction.

Hyperextension Injuries in Arthritic Spines.—Six of the patients under review sustained this type of injury, and it is interesting to note that all six were over fifty years of age. Although there was strikingly little radiographic evidence of recent bony injury, only one patient recovered, even though there was complete paraplegia in only one instance. The occurrence of this type of injury has been previously noted by Crooks and Birkett (1944).

Mechanism of Injury.—The injury probably occurs because of a certain loss of mobility of the spinal column. At the age at which this type of injury usually occurs the normal kyphosis of the dorsal area is increased, with a corresponding increase in the cervical lordosis. Because of an accompanying loss of mobility the spine cannot be protected by the usual instinctive flexion of the cervical spine, the head is forced backwards, and the anterior common ligament is torn, or a small flake of bone is detached from the vertebral margin (*Fig.* 40). Continuation of the force causes a gross separation of the bones on the anterior surface of the spine, but as there is no bony locking the gap disappears as soon as the force ceases to act.

It is not clear how this hyperextension produces the severe injury to the cord, but two possible explanations are advanced—(1) spinal concussion, or (2) traction injury at the moment of extreme hyperextension.

Treatment.—In the opinion of the author there is no justification for the use of calliper traction in these hyperextension injuries of a spine in which arthritic changes are present. The intervertebral disk is not displaced backwards into the spinal canal, and cannot, therefore, be the cause of the spinal cord injury. In addition, any slight alteration of the vertebral bodies is easily corrected by moderate flexion of the neck. It is in fact not advisable under these circumstances to use any external splintage or plaster, of which these elderly patients are so intolerant. The treatment advised is the use of a small pillow, by which the patient is made more comfortable, and which cannot cause any further injury to the cervical spine.

REFERENCE.—[1] *J. Bone Jt Surg.* 1948, **30**, 234.

PARATHYROID GLANDS.

S. L. Simpson, M.A., M.D., F.R.C.P.

Hyperparathyroidism.—H. U. Stephenson and W. L. McNamara[1] give an excellent review of the physiology and pathology of hyperparathyroidism. The average weight of a normal parathyroid gland is 35 mg. and its size 6 × 4 × 2 mm. Each has a thin capsule and the colour is putty tan, pink or greyish-yellow. The blood-supply is the inferior thyroid artery. Adenomas consist of chief or principal cells, which usually make up the bulk of a normal gland. Polyhedral and poorly outlined, the cytoplasm is scant and faintly acidophilic, and the nucleus is round, sharply demarcated, and large. Hyperplasia of the chief cells occurs secondary to renal disease, rickets, osteomalacia, multiple myeloma, and carcinomatous bony metastases.

Idiopathic hyperplasia, with hyperparathyroidism, usually involves the 'water clear' or 'wasserhelle' cells, which are modifications of chief cells, sharply outlined and larger, with extensive vacuolation of cytoplasm and a hyperchromatic and eccentric nucleus. Normally these cells may occur singly and/or in groups. The oxyphil cells are large, polyhedral, well defined, with a reddish-pink cytoplasm and a nucleus, not so hyperchromatic as most of the chief cells. The oxyphil cells occur after puberty, forming large islands, and have no known function.

Adenomas of chief cells are very rarely malignant. Collip thinks that the primary action of parathormone is to stimulate osteoclasts which lead to resorption of bone and liberation of calcium, whereas Albright postulates a primary lowering of the renal threshold for phosphorus and increased phosphorus excretion.

Clinically, hyperparathyroidism is not necessarily manifested by osteoporosis or raised alkaline phosphatase, and a parathyroid adenoma has been found to be the cause of multiple renal calculi.

The case here presented is a man of 70 admitted with symptoms of two years' duration; two fractures, loss of weight, polyuria, pruritus, and anorexia. X rays showed general osteoporosis with cystic areas. Several serum calcium determinations ranged between 14 and 19·5, and phosphorus between 3·4 and 4·4 mg. per 100 c.c. The non-protein nitrogen varied between 49 and 200 mg. Alkaline phosphatase was only slightly elevated (6·8 Bodansky units). Laparotomy revealed a parathyroid adenoma $3\frac{1}{2} \times 3\frac{1}{2} \times 2$ cm. weighing 10 g. Unfortunately he died, and autopsy revealed calcium deposited in considerable amounts in the parenchyma of the kidneys.

Osteoporosis.—F. Albright[2] defines osteoporosis as "that category of decreased bone mass where the disturbance is a failure of the osteoblasts to lay down bone matrix"; and thus differentiates it from osteomalacia, where there is a disturbance of the calcification of the osteoid, and osteitis fibrosa generalisata, where there is increased bone destruction. He postulates three steroidal imbalances as a cause of osteoporosis:—

1. Old age, with atrophy of bone as one of multiple tissues and responding to œstrogens and androgens, the latter stimulating protoplasmic anabolism by the retention of nitrogen, phosphorus, potassium, and sulphur.

2. Post-menopausal, relieved by œstrogens, which diminish calcium excretion and stimulate osteoblasts.

3. Cushing's syndrome, where there is an excess of adrenal cortical 'S' hormone (11-oxysteroids) which produces a striking increase in urinary calcium excretion, as does adrenotrophic hormone, and which inhibits osteoblastic activity. Testosterone reduces the steroid content of the adrenals and the secretion and excretion of 11-oxysteroids. The adrenal 'N' hormone, androgenic, acts like testosterone.

Disuse and starvation are other factors producing osteoporosis.

REFERENCES.—[1]*Amer. J. med. Sci.* 1948, **215**, 381; [2]*Ann. intern. med.* 1947, **27**, 861.

PARATYPHOID FEVER. (*See* TYPHOID AND PARATYPHOID FEVERS.)

PARKINSONISM.

Macdonald Critchley, M.D., F.R.C.P.

Treatment with Parpanit. Parpanit (or G.2747) is a synthetic product prepared by Messrs. Geigy of Basle. It is chemically related to Trasentin and Dolantin. E. Grünthal[1] thought because of its pharmacological properties that it might prove of service in the treatment of Parkinsonism. His therapeutic tests proved encouraging and benefit was also reported by K. Hartmann,[2, 3] by R. Domenjoz,[4] and by G. Bickel and J. P. Dubois.[5] V. Davini and A. Borellini[6] used this drug in 10 cases and they, too, believed that Parpanit can relieve Parkinsonism spasm. Most benefit came on after 15 to 30 days. Two patients noted an interesting change in their body scheme: they asserted that their limbs "felt strangely light, as if made of rubber or immersed in water" and that they "were unable to tell exactly where the end of a limb was".

In Great Britain, a report on the use of Parpanit has recently been made by W. F. Dunham and C. H. Edwards[7] on a series of 25 patients. Their work confirmed the usefulness of Parpanit in Parkinsonism, though patients varied as to whether they fared better on this drug or on the more usual solanaceous drugs. The optimum individual doses varied from 0·025 g. to 0·1 g. The side effects of Parpanit include giddiness, weakness, dry mouth, and blurred vision.

REFERENCES.—[1]*Schweiz. med. Wschr.* 1946, **76**, 1286; [2]*Ibid.* 1289; [3]*Therap. Umschau* 1947, **3**, pt. 2; [4]*Schweiz. med. Wschr.* 1946, **76**, 1282; [5]*Rev. méd. Suisse Rom.* 1947, **67**, 708; [6]*Minerva Med.* 1948, **39**, 432; [7]*Lancet*, 1948, **2**, 724.

PARKINSONISM : SURGICAL TREATMENT.

J. B. Pennybacker, M.D., F.R.C.S.

There has recently been a good deal of unfortunate publicity in the lay press about the surgical treatment of Parkinsonism, unfortunate because sufferers from this affliction have been led to believe that it can be cured. It cannot, nor do any of the surgeons working on this problem claim that it can. There may be some cases in which the disability can be lessened by suitable surgical procedures, and with growing knowledge and experience selection of such cases and appropriate procedures should be within the competence of most neurologists and neurological surgeons.

The study of involuntary movements has always fascinated neurologists, and much useful clinical and pathological information has been gathered through the years. But, apart from diagnosis and classification, there have been few contributions to therapy, either by medicine, orthopædic, or physical methods. It was natural that with increasing knowledge of the anatomy and physiology of the motor pathways surgical efforts would be made, and Horsley was experimenting as long ago as 1909. But for the next twenty years or so the young specialty of neurological surgery was developing its technique on the commoner and more urgent problem of intracranial tumours, and it is only within the last twenty years that there has been time and opportunity to devote to the more subtle problems of neurophysiology presented by involuntary movements. Most of the work has been done on human material as it is difficult to produce involuntary movements in animals, and most of it has been done in America where neurosurgical services are more freely available than in this country.

In a brief critical review of the subject Paul C. Bucy[1] describes the effects of *extirpation of certain areas of the cerebral cortex* on abnormal involuntary movements such as in choreo-athetosis. By electrical stimulation he identifies the cortical representation of the upper and lower limb, and then excises the precentral gyrus and part of the adjacent frontal gyri by a subpial dissection. This of course causes a considerable paralysis, but if the involuntary movements have been so disabling as to lead the patient and his medical advisers to feel that a hemiplegia without involuntary movement is preferable, the operation is justifiable. The most suitable cases are those in young subjects in whom the movements are wholly or largely confined to one side of the body, and in whom the affection does not seem to be progressive, as obviously an operation will not affect the course of a progressive disease. Such cases are few, and this means that each one should be made the subject of intensive study and critical appraisal of results.

Regarding tremor, as opposed to the involuntary movements of choreo-athetosis, Bucy considers that it is impossible to abolish tremor by any procedure which does not interrupt the pyramidal tract, and this means inducing a certain amount of paralysis. As the exchange of tremor for weakness is of doubtful advantage, as Parkinsonism is usually a progressive affection, and as the other symptoms of Parkinsonism are not affected by operation, he feels that cortical extirpations are of very limited usefulness, and that probably not more than 1 in 500 cases is suitable for operation.

Another type of operation which has been devised for Parkinsonism is *section of the fibres in the anterior limb of the internal capsule*. In describing this procedure Jefferson Browder[2] stresses the fact that it too is in the experimental stage, but he is on the whole more optimistic about the possibilities of this operation than Bucy is about cortical extirpation. He has found that it is possible to abolish tremor without inducing paralysis, or more than minimal weakness. In selecting suitable cases, he states that they should be under 50 years of age, tremor should be the chief cause of disability, and this should be largely confined

to the limbs of one side. In 9 such cases, tremor was abolished in 6, largely abolished in 1, and abolished for six or eight weeks in 2. Of 6 patients with bilateral involvement, 3 died after operation, and although tremor was abolished on one side in the other 3, he did not feel that the general situation had been improved in any of them. As this operation entails a considerable incision in the brain it is not surprising that 1 of the 12 survivors subsequently developed epilepsy. Browder makes no extravagant claims for the operation and rightly concludes that it is worthy of further trial in suitable cases. One great difficulty is that by present standards suitable cases are few and far between, and unless a surgeon is doing this operation often enough to become thoroughly familiar with the anatomy in the depths of the brain, it may be difficult or impossible for him to know just what he has done.

There is no doubt that interest in this problem will continue, and more results will be available for study as time goes on. At present, however, the surgical treatment of Parkinsonism must be considered in the experimental stage.

REFERENCES. [1]*Amer. J. Surg.* 1948, **75**, 257 ; [2]*Ibid.* 264.

PENICILLIN, ORAL, IN INFANTS. (*See* ORAL PENICILLIN IN INFANTS.)

PENIS, SURGERY OF. *Hamilton Bailey, F.R.C.S., F.A.C.S.*
Norman M. Matheson, F.R.C.S., F.A.C.S.

Persistent Priapism. H. Bailey[1] classifies the causes as: (1) *Nervous* (traumatic, organic, poisoning by aphrodisiacs). (2) *Vascular* (primary thrombophlebitis of prostatic plexus, secondary thrombophlebitis due to leukæmia or sickle-celled anæmia ; B. Levant and R. Stept[2] are under the impression that the relationship of sickle-celled anæmia to priapism is probably not so rare as it appears ; priapism may be actually the first clinical manifestation of the disease). (3) *Secondary carcinoma* (in the corpora or pelvic venous plexus).

Priapism due to vascular causes is the largest and most important group : there is every reason to believe that the clotting commences behind the erector muscles in the formed veins that connect the venous honeycomb of the phallus with the pelvic plexus. That thrombosis of the deep dorsal veins is the most usual case of vascular priapism is substantiated by the observation that in 5 out of 6 cases the corpora cavernosa alone are involved. Trauma plays an extremely small part in the production of pelvic thrombosis. No justification is found for the statement that hyperpiesis is a frequent cause.

Division of nerves and muscles is a theoretical concept of treatment ; ligation of the dorsal arteries is fundamentally unsound (*Plate XXVII*). It is probable that the non-success of *aspiration* is in part due to the employment of an unsuitable needle. French's blood transfusion needle should be the standard instrument. More success has attended *incision* than aspiration, but it is no panacea, for 2 cases so treated developed gangrene. Asepsis should be perfect and it is a mistake to sew up the wound. Incision with drainage under the protection of sulphanilamide and penicillin is recommended (*a*) when aspiration has failed, (*b*) when the priapism has been present for a week or more.

Peyronie's Disease. R. E. Fricke and J. H. Varney[3] inform us that Hugh Cabot has called Peyronie's disease one of the more common rare diseases of the penis. The tunics of the corpora cavernosa or the intercavernous septum or both are involved in induration which may result in formation of a plaque, nodule, cord, or band, readily palpable and superficial, although not attached to the overlying skin. The corpus spongiosum and urethra are not involved. On erection the presence of this plaque or band causes an abnormal bending of the penis, usually without pain, although pain may be present. The plaques exhibit bundles of collagen fibres with fibroblasts between them and resemble

PLATE XXVII

PERSISTENT PRIAPISM

(HAMILTON BAILEY)



Commencing gangrene following incision of a corpus cavernosum with suture combined with ligation of the dorsal arteries.

By kind permission of the "British Journal of Surgery"

keloids. In long-standing untreated plaques, calcium and bone may be formed. The aetiology of the fibrous plaques is unknown. The disease usually occurs in middle-aged patients and many more cases have been reported in recent years. Although present methods of treatment are unsatisfactory, Fricke and Varney believe that more than half the patients should receive definite benefit from *radium therapy* by the technique employed for keloids.

Circumcision of the Adult.—J. R. Elder[4] makes some observations on this subject. This is an operation which frequently gives disappointing results, the patient exchanging one disability for another. Its object is not the ablation of the foreskin but its reduction in such a fashion as to preserve its important function of clothing the shaft of the penis in the erect state. A bloodless technique, which obviates the common fault of removing too much skin, is described.

Hypospadias with Enlargement of the Prostatic Utricle.—F. S. Howard[5] discusses this interesting subject. It has been suggested that hypospadias in the male is an intersexual manifestation rather than an isolated fusion defect. If this theory is correct, congenital enlargement of the utricle might be expected to occur frequently in hypospadiac individuals and the degree of differentiation of the Müllerian ducts in the female direction should vary in proportion to the severity of the penile deformity. F. Howard studied 14 unselected males undergoing treatment for hypospadias. In 10 of these an abnormal degree of development of the utero-vaginal tract was found upon endoscopic and radiographic investigation. There is a close correlation between the degree of differentiation of the structures of Müllerian derivation and the severity of penile and other genital anomalies. The cases are described in three groups (*Figs.* 41, 42, 43). In penile hypospadias, the utricle is normal. In penoscrotal and perineal hypospadias, the utricle is markedly enlarged and may communicate with a well-developed uterus.



Fig. 41.—Hypospadias, Group I. Penile hypospadias is the only abnormality present. The testicle, prostate, seminal vesicle, and utricle are normal. This constitutes a minimal degree of feminization. (*Figs.* 41–43 *reproduced from "Surgery, Gynecology and Obstetrics".*)

As F. Z. Havens[6] rightly states, treatment is particularly difficult. Many methods have been described, and it is amazing that no writer gives an analysis to show the percentage of good results. Attention is drawn to an as yet unpublished report on the use of the inlying tubular graft in 29 cases of major hypospadias. Good results were obtained in 27 cases, a fair result in 1, and there was one failure. Worthy of note is the fact that the greatest success is secured if the graft is not inserted until about 16 years.

Penile Cancer.—Reviewing 43 cases treated at Bellevue Hospital, J. Zausner[7] comes to the conclusion that early circumcision seems to offer protection, and that the disease is frequent among syphilitics. Early lesions may be treated with X rays and/or radium; a combination of surgery and radiation is preferred for advanced cases.

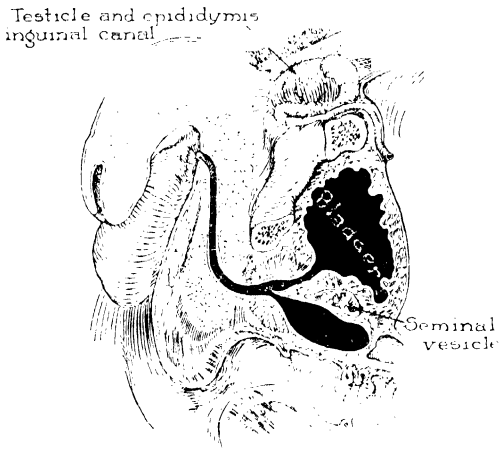


Fig. 12. Hypospadias, Group II. There is a penoscrotal hypospadias. The testicle is incompletely descended. The penis, prostate, and seminal vesicle are smaller than normal. The utricle is enlarged. Here, feminization is more marked.

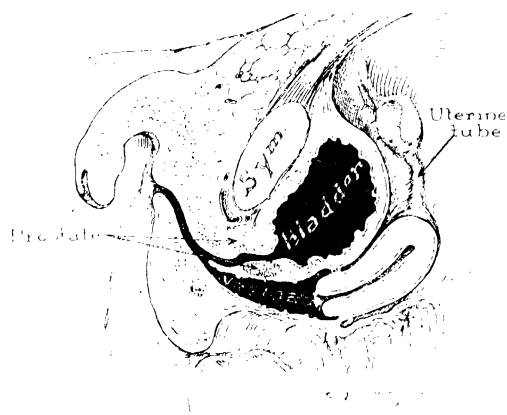


Fig. 13. Hypospadias, Group III. The penis resembles a large clitoris. The urethral meatus is perineal. An atrophic testis with a rudimentary epididymis lies in contact with the uterine tube in the pelvis. A well-developed uterus and vagina are present. The prostate is under-developed and seminal vesicles and vasa are absent. Feminization is extreme.

REFERENCES. [1]*Brit. J. Surg.* 1948, **35**, 298; [2]*J. Urol.* 1948, **59**, 328; [3]*Ibid.* 627; [4]*Brit. J. Urol.* 1948, **20**, 17; [5]*Surg. Gynec. Obstet.* 1948, **86**, 307; [6]*Ibid.* **87**, 239; [7]*Radiology*, 1948, **50**, 786.

PERITONEUM, DISEASES OF. *A. Rendle Short, M.D., F.R.C.S.*

Talc Powder in Peritoneal Cavity. Warnings that talc powder shed from gloves can do harm in the peritoneal cavity have received expression in former numbers of the MEDICAL ANNUAL. A Swiss surgeon, C. Klemm,[1] repeats these warnings and describes 3 cases in which at a second laparotomy granulations were found containing magnesium silicate. They simulated tuberculous

peritonitis in one case, regional ileitis in another. The second operations were for obstruction symptoms. Klemm suggests that potassium bitartrate might well be used instead of talc, as it does not injure the peritoneum in animal experimentation.

Chemotherapy.—V. M. Coppelson,[2] of Sydney, gives his patients a covering dose of 60,000 units of penicillin before abdominal operations, and leaves 200,000 units in the peritoneal cavity, distributed with a spoon. In cases of intestinal obstruction or peritonitis, 100,000 units are given intramuscularly every one or two hours and 200,000 units left inside. For the delayed (Ochsner Sherren) treatment of appendicitis, or acute cholecystitis, 50,000 to 100,000 units are given every few hours. For bowel resections he prescribes sulphonamides by mouth for several days pre-operatively, and penicillin at the time. He gives no figures, but has a strong general impression that patients do better when treated on these lines. E. J. Pulaski,[3] with two other U.S. Army surgeons, report on the use of streptomycin in 63 cases of peritonitis of various types. They think it is beneficial in the presence of spreading peritonitis, but it is not a cure-all, and is of little value for localized peritoneal suppuration. Five of their patients died. It may well be used with penicillin. They give 2–4 g. daily, intramuscularly, in divided doses. H. J. Silvani[4] and four others, working at San Francisco, were less satisfied with the streptomycin therapy; in 9 of 13 cases it did little or no good. Given by mouth in animals, it failed to control intestinal organisms sufficiently to make operations on the bowel safer (E. J. Poth[5] and four others).

Ascites (*see also* PORTAL HYPERTENSION).—Various surgeons (Crosby, Tannahill) have advised the insertion of a glass flange forming a "peritoneal button" for the cure of chronic ascites. K. J. Welch,[6] of Boston, relates 2 cases, both of which failed to improve. A kind of cyst formed in the abdominal wall.

Chronic Encapsulating Peritonitis.—A very good description of this rare condition, with 2 personal cases and a consideration of the literature, is given by an Italian surgeon, B. Sciacca.[7] He thinks most of the cases are of congenital origin. The symptoms and X-ray signs are not definite enough to point to a diagnosis. The palpable swelling may be thought to be a uterine fibroid, or a mesenteric cyst.

Pneumococcic Peritonitis.—A very full description of this condition is given by Gino Tartarini,[8] of Pisa. He classifies the evolution of the disease into four stages or groups (*after* Fèvre): pneumococcic septicæmia; diffuse purulent peritonitis; multiple abscesses in the abdomen; localized pneumococcic peritonitis. Apparently, on the Continent the circumscribed form is commoner than the diffuse; the mortality as given by various authors quoted is about 10 per cent in the form with localized abscess, and 80 per cent with diffuse peritonitis. Surgeons differ as to whether early operation is called for. Tartarini gives particulars of 7 cases, all in girls under ten. All were operated upon, and all recovered. Antipneumococcic serum, sulphonamides, and penicillin are also helpful. [The main argument in favour of laparotomy is the risk of missing an appendicitis-peritonitis. Early diarrhœa, herpes labialis, or signs of pneumonia in the chest, may clarify the diagnosis. But there are reasons for believing that even in cases of appendicitis with diffuse peritonitis and toxæmia, conservative treatment is better than immediate operation. Of course, pus in a localized abscess must be let out. The cases with multiple abscess are a therapeutic problem.—A. R. S.]

REFERENCES.—[1]*Helv. chir. Acta*, 1947, **14**, 141; [2]*Med. J. Aust.* 1947, **2**, 292; [3]*Surgery*, 1947, **22**, 889; [4]*Surg. Gynec. Obstet.* 1947, **85**, 721; [5]*Ibid.* 1948, **86**, 641; [6]*New Engl. J. Med.* 1947, **237**, 735; [7]*Arch. ital. Chir.* 1947, **69**, 3; [8]*Ibid.* 311.

PERNICIOUS ANÆMIA. (*See* ANÆMIA, PERNICIOUS.)

PEYRONIE'S DISEASE. (*See* PENIS, SURGERY OF.)

PHÆOCHROMOCYTOMATA. (*See* ADRENAL GLANDS.)

PINK DISEASE. *R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.*

J. Warkany and D. M. Hubbard[1] found mercury in appreciable amounts in the urine of 18 out of 20 cases with pink disease, and in some of these the excretion of mercury continued for several weeks. The 2 patients in whom no mercury was found were not typical, being eight and fourteen years old respectively. In a control series, no mercury was found in 80 per cent of cases, and in the few who showed mercury it appears that they were excreting less than the cases of pink disease. It is suggested that parents have administered mercury medicinally to these children before the onset of the disease, by giving 'teething' powders or calomel, or by the application of ammoniated mercury to the skin.

Following this work, Lee Burings and George Lewis[2] treated a case of pink disease with British Anti-Lewisite (B.A.L.), having demonstrated mercury in the urine and obtained a history of the ingestion of calomel. The dosage of B.A.L. was 3 mg. per kilo of body-weight in a 10 per cent oily solution, preceded by ½ c.c. of 2 per cent novocaine, given deep in the buttocks every four hours. A reduction in the urinary mercury occurred after nine days, and the symptoms, except photophobia, subsided after nineteen days' treatment.

Confirming this work, G. Fanconi and A. Bozteyn[3] found mercury in the urine of no less than 19 out of 20 patients with pink disease, who had been treated with mercury shortly before the onset of the disease. These authors are of the opinion that pink disease is a neuro-allergic reaction to toxic substances, one of which is mercury. They also found a rapid disappearance of symptoms following the elimination of mercury from the body after treatment with B.A.L.

REFERENCES. [1]*Lancet*, 1948, **22**, 289; [2]*Pediat.* 1948, **32**, 63; [3]*Helv. paed. Acta*, 1948, **3**, 264.

PITUITARY GLAND. (*See also* DIABETES INSIPIDUS.)

S. L. Simpson, M.A., M.D., F.R.C.P.

Simmonds's Disease.—There have been two recent symposia on the Simmonds's-Sheehan syndrome, one at the Royal Society of Medicine, London, in November, 1947,[1] and another at the Royal Academy of Medicine, Ireland, in April, 1948.[2] H. L. Sheehan spoke at both. He defined Simmonds's disease as the "clinical syndrome which results from a long-standing and very severe destructive lesion of the anterior pituitary". He emphasized that the continued conception of emaciation as part of the syndrome prevented recognition of the same, and was contrary to fact, and that some patients even gained weight. A. W. Spence postulated that the adiposity might be due to simultaneous injury of the tuber cinereum. He felt that the term Simmonds's disease should be "applied only to those cases exhibiting panhypopituitarism brought about by an organic lesion". Simmonds's disease responded to thyrotrophic hormone, whereas myxœdema did not. Differentiation from advanced anorexia nervosa rested mainly on the discovery of an initial psychological factor in the latter. Russell Fraser described the intravenous insulin hypersensitivity and hypoglycæmic unresponsiveness, the low 17-ketosteroids, and the low basal metabolism in Simmonds's disease. The reviewer (S. L. S.) dealt mainly with treatment. Thyroid was moderately useful but must be given gradually, or acute reactions, possibly acute adrenal insufficiency, might be induced. The scalp hair was

improved, but there was no effect on the absent pubic and axillary hair. Thyrotropic hormone was dangerous. Desoxycortone was of some use in increasing strength and appetite but it was easy to induce dangerous overdosage with water retention even on moderate dosage. Pituitary adrenocorticotrophic hormone was of moderate temporary use, increasing strength and giving some increase in pubic hair. Testosterone by injection, or methyl testosterone by mouth, was the most valuable therapeutic approach, resulting in increased weight, strength, and libido, a return of pubic, axillary, and eyebrow hair, and a darkening of the hair of the head. Simpson recorded a new observation that progesterone acted similarly to testosterone, although with less power relatively, and in particular produced growth of pubic, axillary, and eyebrow hair. Œstrogens failed to affect the absence of pubic and axillary hair, but the scalp hair increased in abundance, lustre, and colour. Gonadotrophins were of little or no use. Spontaneous hypoglycæmia must be guarded against and looked for. Armstrong reported the successful use of pituitary corticotrophin.

T. N. A. Jeffcoate, at the Irish symposium, brought forward therapeutic evidence much in line with that of Simpson. He found gonadotrophins of little or no value. Pituitary corticotrophin was generally of no value, but one patient reported increased strength, some pigmentation of the skin, and ability to tan in sunlight, and slight axillary sweating. Pituitary thyrotropin was of no value and thyroid might be dangerous. Desoxycorticosterone was of no value. Œstrogens restored a senile type of vulva, vagina, and uterus to normal and improved facial colour (capillary change); they failed to pigment skin or nipples or produce growth of pubic or other hair, or to affect dryness of skin and axillæ.

Androgens, a total of 100 mg. injected each week, were beneficial and well tolerated without virilism resulting. They produced increased strength, growth of pubic and axillary hair, eyebrows, and eyelashes, some darkening and improved texture of facial hair and axillary sweating. Jeffcoate recognized that where œstrogens affect pubic and axillary hair, as in ovarian agenesis, the pituitary and adrenal glands are functioning.

Jeffcoate reported an interesting example of Simmonds's disease in a woman of 41, treated by the implantation of a portion of an adrenal cortex adenoma removed from a girl of 4 with sexual precocity. The effects lasted for 6 months, and were increased strength, return of body and breast pigment, slight increase in pubic hair, growth of scalp hair with thickening and improvement of texture and darkening, and growth and darkening of the eyebrows.

In his further review (Royal Academy of Medicine, Ireland), H. L. Sheehan added to his original 19 cases, 22 further cases coming to autopsy since 1940. The lesion was an ischæmic infarction, always associated with thrombosis of parts of the vascular supply of the gland. The necrosis began about the time of parturition. Within 6 hours there was a peculiar œdematous appearance of the pituitary tissue, with some hyperchromasia of nuclei, and actual necrosis was not detectable until 12 hours post-partum. The severity of the lesion depended upon the degree and duration of the circulatory collapse, and the commonest obstetrical factors were post-partum hæmorrhage and retained placenta. Occasionally necrosis of the posterior pituitary gland also occurred and diabetes insipidus resulted; but the symptoms were minimized because the anterior lobe was also necrosed. Sheehan also referred to a total of 81 clinical cases of severe hypopituitarism living for many years after a presumed anterior pituitary necrosis, and estimates that the probable incidence of the lesion is 1–2500 as judged clinically, and 1–800 coming to autopsy.

D. K. O'Donovan dealt with diagnosis, and J. F. Cunningham with obstetrical shock.

Transplantation of the Hypophysis of a Cadaver in Simmonds's Disease.—This paper (E. Kubanyi[3]) is extracted only to show fallacious diagnosis and reasoning. Following some rat experiments, the hypophysis was removed from autopsy cases within two hours and immediately transplanted in the cervical region to be in touch with a good carotid blood-supply and 'penetrating' sympathetic nerves. However, the 4 cases are obviously cases of anorexia nervosa, and where the photograph is clear, abundant pubic hair is seen before treatment. The first patient, a woman of 41, first started symptoms at the age of 15. She 'recovered' after the implantation. The second was a girl of 17, who recovered at first but later relapsed and died with pulmonary tuberculosis as a complication. The third, an adolescent of 19, died with tuberculosis. The fourth, an adolescent, also 19 years old, 'recovered'. It is, of course, well recognized in this country that apart from neoplasms in the pituitary region, Simmonds's disease occurs mostly in married women after parturition, whereas anorexia nervosa is nearly always a disease of adolescence with an obvious psychological background.

REFERENCES. [1]*Proc. R. Soc. Med.* 1948, **41**, 187; [2]*Irish J. med. Sci.* 1948, **270**, 241; [3]*Lyon. chir.* 1947, **42**, 265.

PNEUMONIA, PRIMARY ATYPICAL.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

G. E. O. Williams[1] studied 51 cases admitted to a R.A.F. hospital and suggested that patchy consolidation, migration of the pneumonic process from one lobe to another, and the presence of cold agglutinins in a titre of 1 in 64 or more, seem to form a triad distinguishing one group of this disease from the remainder.

[It would be interesting to know in further studies whether such a group is or is not associated with Eaton's virus. H. S. B.]

H. G. Alton and M. D. Hickey[2] describe a small highly infective outbreak in all 5 members of a secluded family in an Irish country district. All these cases showed a rise in cold agglutinin titre, mostly well over 1 in 64. The authors point out that cases arising from a single source tend to give similar findings in this respect.

REFERENCES. [1]*Lancet*, 1947, **1**, 865; [2]*Ibid.* 1948, **1**, 559.

PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY.

Philip Ellman, M.D., F.R.C.P.

Whilst congenital defects of the pericardium are not so uncommon, the literature reveals that only 3 reported cases have been detected during life. Two of these were discovered at operation, and only Dahl (1937) has reported a case detected after pneumothorax induction.

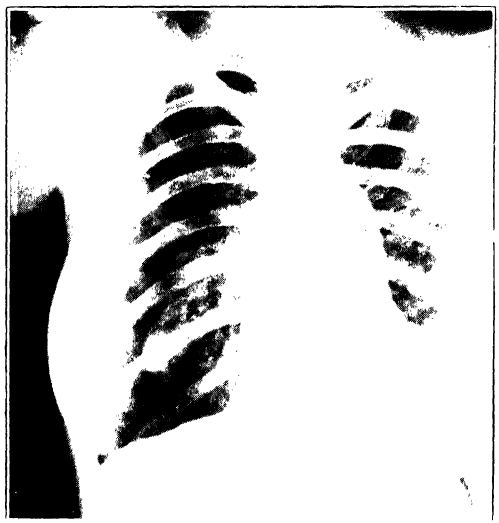
P. Ellman and K. Hussain[1] report 2 cases of pulmonary tuberculosis in which a pneumopericardium was found at routine X-ray examination, one of whom was receiving a right-sided artificial pneumothorax, and one a left-sided pneumothorax. They discuss the anatomical and embryological factors concerned in the production of a congenital pleuropericardial defect, and point out that it is sometimes extremely difficult to appreciate the significance of certain linear shadows seen at the left border of the heart on radiological examination, and recommend that where the appearances are suggestive of pneumopericardium thoracoscopy should be performed, and if possible iodized oil injected into the opening to see whether it really communicates with the pericardium.

As an illustration of this, they describe a case of pulmonary tuberculosis with similar radiological appearances due to a mediastinal hernia with an acquired interpleural communication. Ellman and Hussain suggest that partial defects of pericardium causing congenital pleuro-pericardial fistula may be less

PLATE XXVIII

PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY

(P. Elman and K. Hussain)



Pneumopericardium (left) after induction of a right pneumothorax

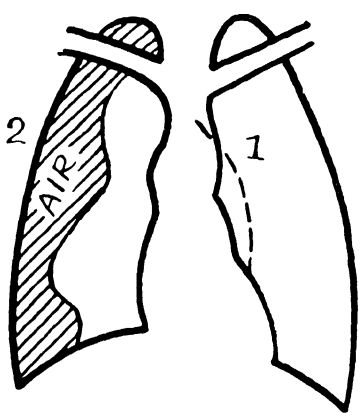


Fig. B. Line diagram of *Fig. A*, showing 1, V left pneumopericardium 2, V right artificial pneumothorax.

PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY—*continued*



Fig. C.—Film showing an acquired interpleural communication (? mediastinal hernia ?) simulating a pneumopericardium. The linear shadow at the left border of the heart here arises from a level beyond the upper limit of the pericardium and not at the aortic knuckle.

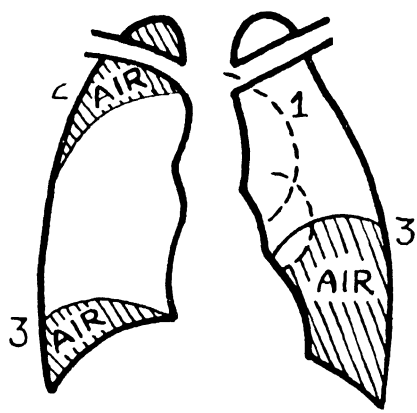


Fig. D.—Line diagram of *Fig. C*. 1. Acquired interpleural c
2. Pneumothorax. 3. Pneumoperitoneum.

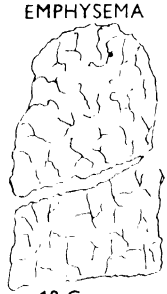
Plates XXVIII, XXIX, by kind

PLATE XXX

RECURRENT AND CHRONIC SPONTANEOUS PNEUMOTHORAX

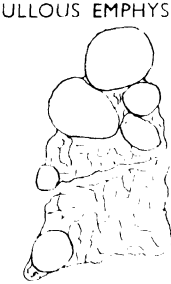
(R. C. Brock)

EMPHYSEMA



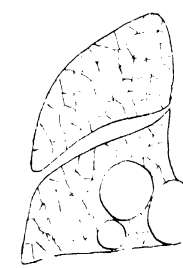
12 Cases

BULLOUS EMPHYSEMA



13 Cases

CYSTIC LUNG



10 Cases

POLYCYSTIC LUNG



1 Case

APICAL BULLA



15 Cases

NORMAL



6 Cases

TORN LUNG



2 Cases

APICAL SCAR



6 Cases

'CUCKOO-SPIT'



4 Cases

RECURRENT AND CHRONIC SPONTANEOUS PNEUMOTHORAX—*continued*

(R. C. Brock)

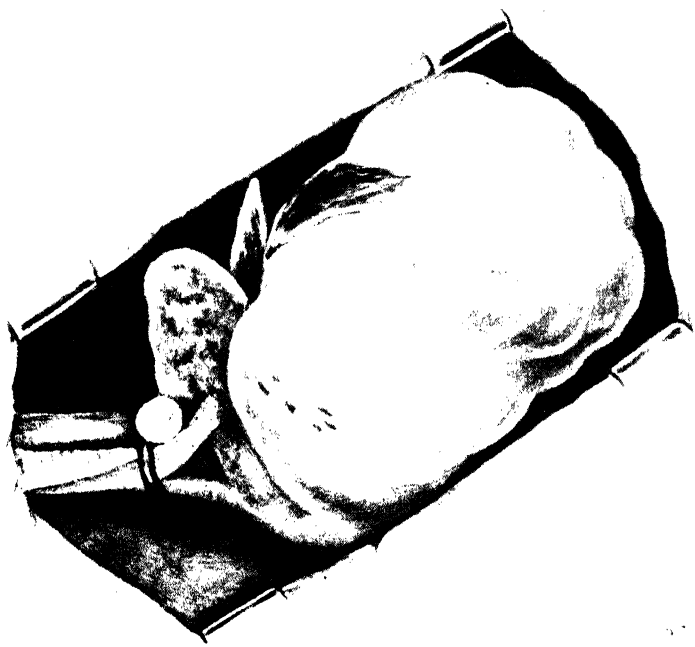


Fig. 1.—Woman, aged 30, with chronic spontaneous pneumothorax, showing the appearances seen at thoracotomy.

PLATE XXXII

RECURRENT AND CHRONIC SPONTANEOUS PNEUMOTHORAX—*continued*

(R. C. Brock)



Fig. B. Same patient, showing a cystic lower lobe.

RECURRENT AND CHRONIC SPONTANEOUS PNEUMOTHORAX—*continued*

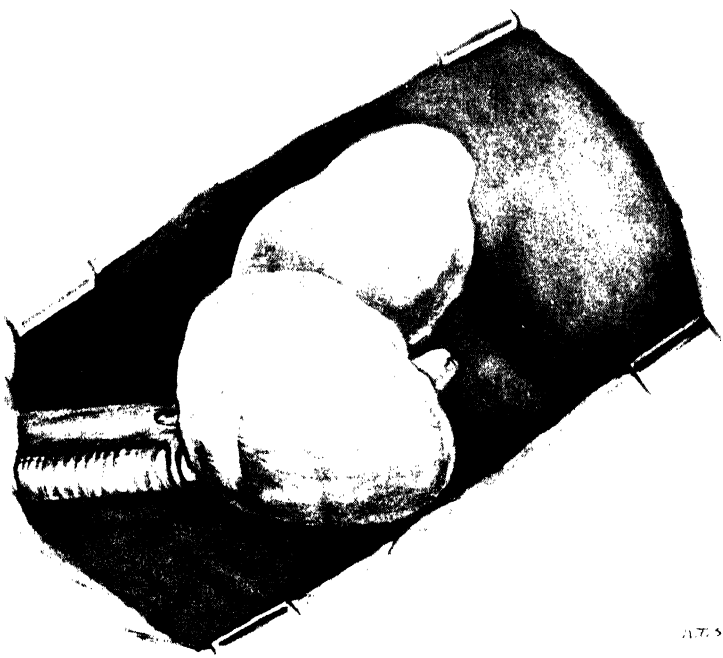


Fig. C. Same case, showing the expansion of the upper and middle lobes that began as soon as the cystic lower lobe had been removed and the partial volvulus corrected.

uncommon than has been hitherto thought. If so, this could have considerable significance in view, first, of the possibility of tuberculous effusions, thereby entering the pericardium and setting up a tuberculous pericarditis, and secondly, of possible symptoms arising with pericardial distension in pneumothorax treatment. (*Plates XXVIII, XXIX.*)

REFERENCE.—[1]*Thorax*, 1948, **3**, 129.

PNEUMOTHORAX, RECURRENT AND CHRONIC SPONTANEOUS.

N. R. Barrett, M.A., M.Chir., F.R.C.S.

An important paper by R. C. Brock[1] describes the manifestations of recurrent and of chronic spontaneous pneumothorax: it is based upon a careful personal study of 71 cases.

In 'pneumothorax simplex' the lung generally re-expands in two or three weeks, but in the cases under consideration it was still collapsed after several months (in 46 cases the average length of collapse was fifteen months); 25 of the cases presented as recurrent spontaneous pneumothoraces. *Tuberculosis was not the causal factor* and the author emphasizes the point that once tuberculosis has been excluded there is a tendency to regard these conditions as occurring in the presence of a normal lung and to adopt a *laissez-faire* policy in treatment: in fact chronic and recurrent pneumothoraces are manifestations of many types of lung abnormalities.

About nine groups or types can be identified (*Plate XXX*):

Generalized emphysema	12
Bullous emphysema	13
Asthma and bronchitis with emphysema	
Large solitary bullæ or cystic disease	
Diffuse polycystic disease	
Small bullæ (mostly apical)	
Apical scar	
Leak or tear seen	
Areas of "cuckoo-spit"	
Various (Tooth extraction, 1; Staphylococcal abscess, 1; Drainage of empyema, 1; Tuberculous pleurisy, 1)	
No cause	

It will be apparent from this table that the principal aetiological factor may lie in the pleura, as when adhesions cause the lung to tear and hold open the rent, or when the elastic tissue is defective in quality or quantity. It may be subpleural, as when there is rupture associated with bullæ arising either in connexion with an old scar or with destructive emphysema; subpleural leakage may also occur from defective alveoli. The chief causal disease may be emphysema or congenital cystic disease, or it may lie in the major bronchi as in giant valvular bullæ; it may be chronic bronchitis, asthma, or bronchiectasis. In any event it produces chronic and often crippling ill health which generally completely defies medical remedies.

The pathology, the symptomatology, and the diagnosis are described in detail, and illustrations of cases given (*Plates XXXI–XXXIII*).

The treatment advocated is as follows. Conservative expectant management of the first attack of 'pneumothorax simplex' is sound; the lung generally re-expands and the patient is cured. If the condition recurs or if the lung fails to re-expand early the case must be fully investigated to find the cause, and thoracoscopy is an essential part of the investigation. If the lesion is due to a large bullous cyst then the cyst must be excised or a lobectomy performed (8 cases); if, however, cystic disease has been excluded the author

states that the logical treatment is pleurodesis produced by instilling a small amount of strong silver nitrate into the pleural cavity (5 to 10 minims of 10 per cent solution).

SPONTANEOUS PNEUMOTHORAX: TREATMENT

Lobectomy	8
Pleurodesis	53 patients
11 bilateral	64 sides
Silver nitrate	52 patients
9 bilateral	61 sides
Poudrage	3 sides
Cauterization of adhesion ..	2 patients
No treatment	12 patients

Brock states that pleurodesis is a most satisfactory form of treatment once cystic disease has been excluded: it is free from risk. This paper is followed by a valuable list of relevant and original articles.

Allison[2] discusses *giant bullous cysts* and states that they are caused by inflammation with a valve-like stenosis of the bronchus, or by ulceration and perforation of the lateral wall of the bronchus. They probably grow slowly and produce dyspnœa by lung replacement and compression, or by rupture causing a tension pneumothorax. The surgical treatment of the intact cyst is described as follows: phrenic nerve crush in small basal lesions and, if successful, phrenic avulsion later; excision of the cyst and suture of the bronchial opening where the cyst is large and causing compression collapse of neighbouring lung; excision and lobectomy when the cyst occurs either in or adjacent to a bronchiectatic lobe.

REFERENCES. [1]*Thorax*, 1948, **3**, 88; [2]*Ibid.* 1947, **2**, 169.

PNEUMOTHORAX, SPONTANEOUS. *Philip Ellman, M.D., F.R.C.P.*

R. M. Myerson[1] has published a valuable series of 100 consecutive cases of spontaneous pneumothorax, of which 64 per cent were known or found to have an underlying lung lesion and 36 per cent were apparently healthy persons. Some fundamental differences in the two groups are well demonstrated. Similarly B. Hyde and L. Hyde[2] surveyed 63 cases of benign idiopathic pneumothorax and compared certain features with 25 cases of spontaneous pneumothorax in known tuberculous subjects.

Age Incidence. In Myerson's series the average age of 36 healthy cases was 27 years, while Hyde found that 75 per cent of cases were under 40 years of age. On the other hand, Myerson's 64 cases with underlying disease averaged 46 years, and he points out that the occurrence of the condition in people over 45 strongly suggests underlying pulmonary disease.

Symptomatology.—In Myerson's group 20 per cent of cases gave a history of unusual exertion prior to the episode. Only 2 (3 per cent) of Hyde's cases gave such a history. Every single patient gave a history of chest pain. Dyspnœa was very common (83 per cent of Hyde's cases), but nowhere was there a direct relationship to the degree of atelectasis.

Fever was present in only 11 per cent of Hyde's cases and never persisted beyond a few days. Myerson's healthy cases had an 8·5 per cent incidence of short fever.

Cough was present in 14 per cent of Myerson's healthy cases. He noted, however, that cough and fever were common in the diseased group, and Hyde suggested that if no other cause for persistent fever (over one week) is found, a pneumothorax should not be regarded as benign.

Clinical Findings. One of the prominent features of the benign group is the rapidity of re-expansion: 70 per cent of Hyde's cases re-expanded within 7 weeks, and Myerson's healthy cases had an average hospitalization of 11 days.

Both papers showed a striking predominance of males in the benign group (i.e., 80 per cent in each case).

None of Hyde's 63 healthy cases showed pleural adhesions, whereas he mentions that all of 25 consecutive cases complicated by tuberculosis admitted to the same hospital showed adhesions.

Pleural fluid was completely absent in 65 per cent of Hyde's cases. Of 23 cases where fluid was present, only two had fluid above the level of the diaphragm. In both these, pure blood, presumably from a pleural tear, was aspirated but 13 of Hyde's 25 tuberculous cases had fluid above the level of the diaphragm.

Sedimentation-rate was normal in 22 of 30 patients estimated in Hyde's series, and only slightly elevated in the remaining 8.

Causes.—Even in cases with underlying lung disease there are many causes other than tuberculosis, which accounted for 59 per cent of Myerson's 64 cases with underlying disease. The causes were: tuberculosis, 38; emphysema, 5; bronchiectasis, 5; post-pneumonic empyema, 4; carcinoma, 3; asthma, 3; lung abscess, 3; pneumonia, 2; infarct, 1. It is noteworthy that only 38 of 100 consecutive pneumothoraces in this series were due to tuberculosis.

Follow-up.—In Hyde's series 18 patients were followed up with serial films for periods up to 8 years. None showed evidence of disease.

Of 21 cases in Myerson's series followed up for periods up to 12 years, only 1 developed tuberculosis (after four recurrences).

Recurrences. The incidence of recurrence in healthy cases appears to vary from 10 to 30 per cent in different series. In Hyde's series there were 19 per cent recurrences, and only 14 per cent in Myerson's series. Only 2 of Hyde's cases had over three recurrences.

REFERENCES. [1]*New Engl. J. Med.* 1948, **238**, 461; [2]*Amer. J. med. Sci.* 1948, **215**, 427.

PNEUMOTHORAX THERAPY, PNEUMOPERICARDIUM COMPLICATING.

(*See* PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY.)

POLIOMYELITIS EPIDEMIC, 1947.

W. H. Bradley, D.M., M.R.C.P.

The Medical Officer of Health who has to deal with a high prevalence of poliomyelitis is faced with a number of almost insoluble problems. The intense public interest and alarm must be satisfied at a time when he is fully occupied with the day-to-day administration associated with the outbreak. Nevertheless, several Medical Officers of Health have contrived to record their experience during the 1947 epidemic. One of the most helpful descriptions comes from Dr. W. P. Sweetnam,[1] of Eccles, the borough which suffered the highest attack-rate of any local authority district. There were 1·09 notifications per 1000, with a case fatality-rate of 6·5 per cent.

The epidemic was confined for nearly six weeks to the western half of the borough by a canal which restricted communications between the two halves. Dr. Sweetnam concludes that the chief factor in the spread of infection was human contact, in which abortive cases and healthy carriers played a major part, and asserts that the presence of the virus in the nasopharynx of patients and carriers was of much more importance for the spread of infection than was its presence in fæces. Viewing in retrospect the wide distribution of cases, and the high attack-rate in this borough, one cannot help having some doubt about the efficacy of the accepted preventive measures; however, Dr. Sweetnam feels that although these measures are not likely to stop an epidemic, they will certainly slow down its spread. Since epidemics nearly always abate with the onset of cold weather, this 'slowing down' may be expected to result in a large number of susceptible persons remaining untouched who might otherwise have become permanent cripples.

The widely held view that cases of overt poliomyelitis are to be regarded as the severer examples of a carrier epidemic makes the recognition of early non-paralytic cases of special importance. Colonel G. J. Dixon[2] (1948) made an assay into clinical epidemiology, to see if the abortive cases and those "below the clinical horizon" could be identified early amongst the population of Catterick Camp, numbering some 18,000 persons. This procedure resulted in the admission of 8 paralytic cases, including a fatal one, 10 probably abortive cases, and 8 suspects. Colonel Dixon had every opportunity of observing this material from the very beginning of the disease, and his clinical descriptions are therefore of special interest. They are as follows :—

"*Symptomatology of Paralytic Cases.*—An acute onset, with headache, stiffness and pain in the back, occasional vomiting, and twitching of the muscle groups which later became paralysed, was the rule. However, five of the eight paralytic cases had been slightly indisposed for about a week; only one had sought advice, and he had felt well enough to go on leave hitch-hiking the day before he was finally taken ill.

"Objectively the early cases presented with pyrexia ranging from 101° to 102° F. (38·3° to 38·9° C.), slight drowsiness, and furred tongue. The most characteristic sign was stiffness of the back, especially pronounced in the lumbar and dorsal spine, where the immobility was almost complete, making the body rigid like a plaster cast. Limitation of neck flexion prevented the chin being flexed more than half-way to the chest wall; Kernig's sign was present after flexion of 45°. The combination of these factors made it impossible for the patients to sit up in bed. Elicitation of these signs usually produced pain in the back in either the mid-dorsal or the lumbar region. The skeletal muscles were often tender on palpation, and localized pains occurred in the regions later paralysed. The pyrexia became remittent, with maximal temperatures varying between 100·8° and 102° F. and lasting three to six days. Only one case developed anything resembling 'dromedary' pyrexia observed in certain other epidemics (A. M. McFarlan, G. W. A. Dick, and H. J. Seddon,[3] 1946). This child had fever of 102° F. for three days and meningism, then after two symptom-free days developed a minor palsy of one leg with recrudescence of pyrexia to 99° F.

"*Presumed Abortive Cases.*—Ten of the suspected cases never developed sufficient signs or symptoms to warrant an unequivocal diagnosis. Their main interest lies in the fact that six of them occurred in Catterick Camp between July 23 and Aug. 28 and so coincided with the paralytic cases. Their illnesses were characterized by backache, headache, stiffness in the neck, and fever. In two meningism occurred; three vomited, and another two developed doubtful paresis of short duration. In six of these patients subjected to lumbar puncture the cerebrospinal fluid was found to be abnormal.

"The clinical findings in these 10 patients are similar to those labelled non-paralytic poliomyelitis by A. E. Casey, W. I. Fishbein, I. Abrams, and H. N. Bundesen[4] (1946) among 14 children who became ill five to twenty-five days after being in contact with the same febrile case of poliomyelitis. M. B. Andelman, W. I. Fishbein, A. E. Casey, and H. N. Bundesen[5] (1946) at the same time examined the cerebrospinal fluid of 19 contacts suspected of suffering from subclinical poliomyelitis, and found the protein content to be above 45 mg. per 100 ml. in 79 per cent, as against a similar finding in only 10 per cent of 10 non-contact control children who had suffered a febrile illness not thought to be due to the virus of poliomyelitis."

It must be admitted that the confident diagnosis of poliomyelitis before the development of palsy is almost impossible. In 16 patients suspected, it was possible, later, to diagnose other diseases in 8, and in 2 only was there abnormal cerebrospinal fluid.

With regard to the epidemiology of this outbreak, the cases were spaced in time in much the same way as occurred in outbreaks described by Casey and other American writers. There was a suggestion of a higher incidence of vague undifferentiated indisposition in the camp occurring as a background to the outbreak of paralysed cases. It is of some interest that during the period of the outbreak there were extremely few flies or other insects in the camp, sanitation was good, and intestinal diseases, apart from a small epidemic of mild gastro-enteritis in September and October, were absent.

REFERENCES.—[1]*Brit. med. J.* 1948, **1**, 1172; [2]*Ibid.* 1175; [3]*Quart. J. Med.* 1946, **15**, 183; [4]*Amer. J. Dis. Child.* 1946, **72**, 661; [5] *Sth. med. J.* 1946, **39**, 706.

PORTAL HYPERTENSION. (*See also* ANÆMIA, SPLENIC; ŒSOPHAGUS, VARICES OF.) *A. Rendle Short, M.D., F.R.C.S.*

It has been known for many years that severe or fatal hæmatemesis may be associated with enlargement of the spleen, and in most cases the blood seems to come from œsophageal varices the result of portal hypertension.

Splenectomy has proved itself a very uncertain remedy. Amongst the suggestions which have been made to prevent recurrent bleeding are injection of the varices, through an œsophagoscope, with a coagulant; injection of the gastric vein along the lesser curvature of the stomach; lienorenal venous anastomosis; formation of an Eck fistula; ligature of the splenic artery; and gastrectomy. Another consequence of portal hypertension is of course ascites.

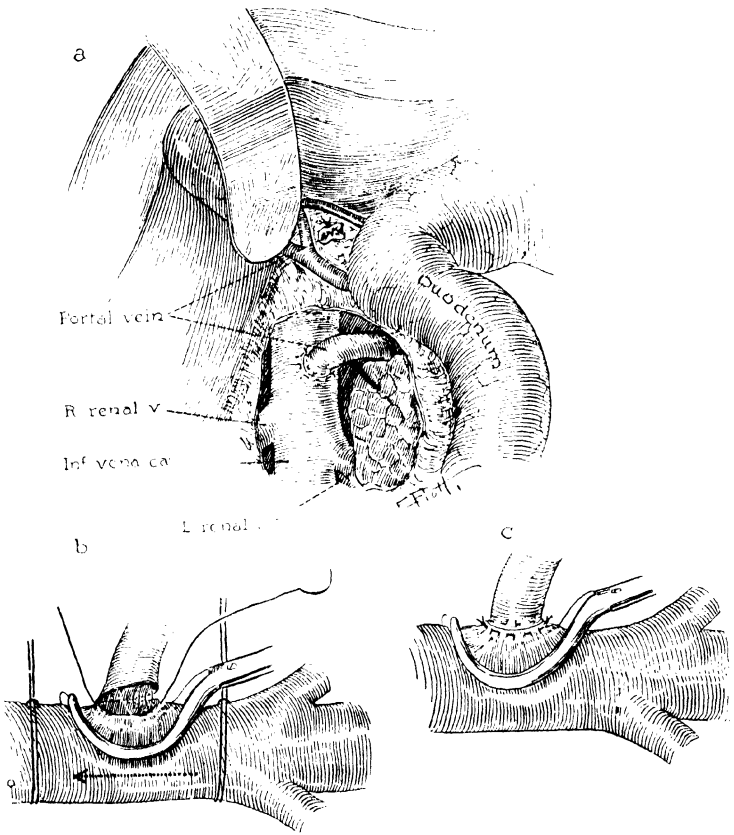


Fig. 44.—a, Completed suture portacaval anastomosis. b, Anastomosis of the end of the portal vein to the side of the vena cava above the renal vein entrances with the Thomas Smith clamp in place. Note free caval flow beneath the clamp. c, Anastomosis completed. Note everting type of suture. (*Reproduced from 'Surgery, Gynecology and Obstetrics'.*)

D. B. Phemister and E. M. Humphreys,[1] of Chicago, consider that splenectomy, portacaval shunts, and injection of œsophageal varices are the only methods that have given success so far. Splenectomy usually fails. At the Mayo Clinic, injection of varices was successful in 12 out of 22 cases, but in 7 it failed. The portacaval shunt may be impossible because the spleen has been removed, or because of cavernomatous or fibrous changes in the portal vein. They have treated 2 cases, after splenectomy and injection of varices had failed, by total gastrectomy in the one, and resection of 3½ in. of œsophagus

and 2½ in. of stomach, by the thoracic route, in the other. There was some return of the bleeding in the first, but not severe. The second case is recent.

R. Linton,[2] of Boston, maintains that if a surgeon removes the spleen in these cases he should perform a lienorenal venous anastomosis at the same time, as it will be impossible later. In one of his cases, after several other operations, and repeated injection of varices, had failed, splenectomy with lienorenal anastomosis stopped the bleeding. In another, a boy of 12, splenectomy and injection of varices with sodium morrhuate were tried without success, but anastomosis of the superior mesenteric vein to the inferior vena cava gave a good result, with no further bleeding so far, over two years. In another patient, after failed splenectomy, the inferior mesenteric vein was used for the shunt, successfully. In a fourth case, splenectomy, and anastomosis of inferior mesenteric vein to the vena cava, both failed, and Eck's fistula proved to be impossible on account of changes in the portal vein.

C. S. Welch,[3] of Boston, describes a method of making an Eck fistula. He uses a curved clamp (*Fig.* 44) so as to avoid even temporary blocking of the vena cava, because if the flow is obstructed for ten minutes anuria due to kidney damage may follow. A three-zero Deknatel suture, everting the vein wall, is inserted. His patient, a man of 24, had had several big haemorrhages not controlled by splenectomy. The œsophageal varices were well shown in a barium swallow. The operation was too recent for a final result to be known.

J. Devine[4] relates a case of lienorenal anastomosis for ascites in a woman of 34 who had been tapped many times at intervals of five weeks. The barium swallow demonstrated no varices. At operation, a fine cirrhosis of the liver was found. The pressure in the splenic vein, measured by a needle manometer, was over 400 mm. of water. The spleen was removed and the splenic vein joined to the renal vein end-to-side over a vitallium tube. The abdomen continued to fill up with fluid but did not need tapping for 24 weeks. T. C. Everson and W. H. Cole,[5] of Chicago, have tied the splenic artery in three cases of ascites in men, performing an omentopexy at the same time. One did well, another died, and in the third ascites returned. One of the patients was an alcoholic.

REFERENCES.—[1]*Ann. Surg.* 1947, **126**, 397; [2]*New Engl. J. Med.* 1948, **238**, 723; [3]*Surg. Gynec. Obstet.* 1947, **85**, 492; [4]*Med. J. Aust.* 1947, **2**, 14; [5]*Arch. Surg., Chicago*, 1948, **56**, 153.

POSTCRICOID PHARYNGO-ŒSOPHAGEAL PERFORATION DUE TO ENDOSCOPY.

F. W. Watkyn-Thomas, F.R.C.S.

J. C. Goligher[1] points out that gastroscopy is not entirely riskless. Œsophageal or pharyngeal perforation is a recognized danger in endoscopy. Mosher in 1935 reported 19 perforations in 938 œsophagoscopies, mostly at the site of the lesion, but some, independent of the lesion, at the pharyngo-œsophageal junction. In 1944 Hoover reported 2 such cases in his group of 8 œsophageal perforations.

Goligher reports 2 cases. In both a tube was passed under local anæsthesia without any difficulty. In the first case the patient complained of pain in the neck on the following morning, but could swallow fluids. In the evening there was swelling in the neck and spreading emphysema. On the sixth day the neck was explored, but only a little frothy fluid was found. She died on the eighth day, and at autopsy an abscess was found behind the pharynx, spreading from the base of the skull to the tracheal bifurcation. There was a longitudinal perforation in the posterior pharyngeal wall just below the lower edge of the cricoid.

In the second case swelling and emphysema were noticed three hours after passage of the tube. Under general anæsthesia a tube was passed as far as the

cricoid, but no perforation was seen. The neck was explored by incision along the anterior border of the left sternomastoid, the lobe of the thyroid was freed to allow rotation of the larynx, and a circular perforation, half-an-inch across, was found just above the pharyngo-œsophageal junction. This was sutured over a rubber tube in two layers, a drain was left in the wound, and a Ryle's tube passed and left for 36 hours for feeding. The patient recovered without any wound infection, and ate normally on the tenth day. Afterwards he was readmitted to hospital for gastrectomy for carcinoma of the stomach—the condition for which he was being examined at the time of the accident—and made a satisfactory recovery.

Goligher does not believe that cricopharyngeal spasm played any part in the causation of these 2 cases; the well-known weakness of the posterior wall in this position may be a contributing factor, but the most important factor, in his opinion, is the prominent forward convexity of the bodies of the 5th, 6th, and 7th cervical vertebræ, which is accentuated if the head is fully extended for the introduction of the endoscope. Further, these bodies are seldom perfectly smooth, and may be grossly deformed by spondylitis, etc. On these grounds he avoids excessive extension of the neck, and advises trying to lift the back of the tongue and the larynx forward with the left hand while passing the tube. Routine radiography of the cervical spine is a small addition to the radiographs always considered necessary in these cases, and might reveal dangerous bony deformations.

Goligher strongly advises operation at the earliest moment if there is indication of a perforation in the region of the pharyngo-œsophageal junction. If endoscopy has been done for stricture or neoplasm lower down, particularly if a biopsy or a dilatation has been done, the perforation is most likely to be at the site of the lesion; in other cases the most likely spot is at the junction. If this is so, immediate suture is the proper course. Probably with modern advances in intrathoracic surgery it would be possible to deal with a perforation of the thoracic portion in the same manner.

REFERENCE. [1] *Lancet*, 1948, I, 485.

POSTERIOR LEVATOR SPACE, ABSCESS OF.

W. B. Gabriel, M.S., F.R.C.S.

H. Courtney[1, 2] describes a space which he believes exists behind and lateral to the rectum, and situated between the superior and inferior layers of the levator muscle. Infection of this space begins in one of the posterior anal crypts. Symptoms are those of a deep perirectal abscess, and on clinical examination tenderness is elicited by external pressure between the tip of the coccyx and the anus. With a finger in the anal canal a bulging of the posterior wall is evident and may simulate a submucous abscess. These abscesses, however, should not be drained into the anal canal; they should be opened by a posterior midline incision which separates the fibres of the coccygeal portion of the external sphincter; a counter-opening may be needed on one side by a slightly curved incision which spares the external sphincter. Operation in stages is usually necessary and if at the primary operation the involved crypt and the main tract can be located it should be marked with a seton.

REFERENCES.—[1] *N.Y. St. J. Med.* 1947, **47**, 2552; [2] *Amer. J. Surg.* 1948, **75**, 405.

PREGNANCY DIAGNOSIS TESTS.

J. Chassar Moir, M.A., M.D., F.R.C.S. Ed., F.R.C.O.G.

Twenty years have elapsed since the specific changes in the mouse's ovaries, consequent on the injection of urine from a pregnant woman, were observed by Aschheim and Zondek and made by them the basis of a pregnancy diagnosis

test. Innumerable modifications have since been suggested, some of which—such as the Friedman test in the rabbit—have proved of considerable value. In recent years much use has been made of the South African claw-toed toad (*Xenopus laevis*), the female of which lays eggs within twelve hours of the injection of an extract of pregnancy urine (Hogben test).

In 1947, Galli Mainini[1] found that the male frog of the species *Bufo arenarum* promptly responds to gonadotrophic hormone and that active sperms appear in the cloaca after an injection of pregnancy urine. The test has the advantages that the result is obtained in the remarkably short time of three hours, that the frog can be used repeatedly, and that special preparation of a urine-extract is not required.

This test has been reported on by Haines[2] in this country. To date, the results appear to be comparable to those of the original Aschheim-Zondek test; and if this is confirmed by an extended trial a valuable new test has become available. Workers in this country will naturally ask whether our own common frog or toad will also obligingly act as an indicator of pregnancy. Investigations are now being made and an answer should be forthcoming in the near future.

An entirely different approach to the pregnancy diagnosis problem is made by K. Bowes, S. H. Riterband, and J. E. Andrews.[3] These workers have found that engorgement of the breast-veins occurs at a surprisingly early stage in pregnancy (8 to 10 weeks). The changes can be readily displayed by infra-red photography, and may supply, it is suggested, a simple means of diagnosing pregnancy (*Plate XXXIV*).

REFERENCES. [1]*Sem. méd., B. Aires*, 1947, **54**, 337; [2]*Lancet*, 1948, **2**, 923; [3]*J. Obstet. Gynaec.* 1948, **55**, 285.

PRIAPISM. (*See* PENIS, SURGERY OF.)

PROCTITIS. *W. B. Gabriel, M.S., F.R.C.S.*

The clinical findings and sigmoidoscopic picture of granular proctitis are described by E. H. Cluer.[1] Case reports are given of 3 patients who were treated by *succinyl-sulphathiazole suppositories*; these were inserted into the rectum every night while the patients were in hospital and then on alternate nights after discharge. All 3 patients showed remarkable improvement both as regards symptoms and also proctoscopic findings, but were admittedly all fairly recent, the first case treated having been followed up for a period of 5 months only. The author considers that this method of applying sulphonamides to the rectal mucosa may prove to be the best and most economical method, superior to retention enemas, and not requiring in-patient treatment. Instructions for preparing the suppositories are given; each one contains 3 g. of the succinyl-sulphathiazole and 7 g. of cocoa butter.

REFERENCE.—[1]*Lancet*, 1947, **2**, 168.

PROSTATE, SURGERY OF. *Hamilton Bailey, F.R.C.S., F.A.C.S.*
Norman M. Matheson, F.R.C.S., F.A.C.S.

Modern Trends in Prostatic Surgery.—For a clear understanding of this subject, Walter Galbraith's[1] Presidential Address to the Urological Section of the Royal Society of Medicine should be consulted. Galbraith makes it clear that no single operative procedure is suitable for all types of prostatic obstruction—an opinion shared by R. Ogier Ward[2] and A. Jacobs,[3] as well as D. Antonio[4] when he writes that the merits or demerits of an operation should not be weighed by the difficulty or ease with which it can be performed. Galbraith, who finds the Freyer operation to be the most commonly practised prostatectomy amongst general surgeons, has ceased to use the Thomson-Walker operation. He has performed perurethral resection on 26 per cent of patients, including a period

PLATE XXXII

PREGNANCY DIAGNOSIS BY INFRA-RED PHOTOGRAPHY OF BREAST VEINS

(K. Bowes, S. H. Rutherland, and J. E. Andrews)

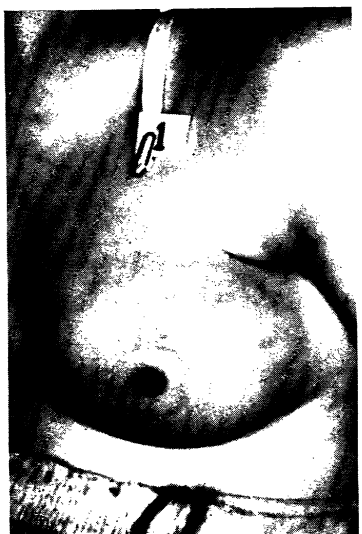


Fig. A. Primigravida. Diagnosed "negative", correctly.

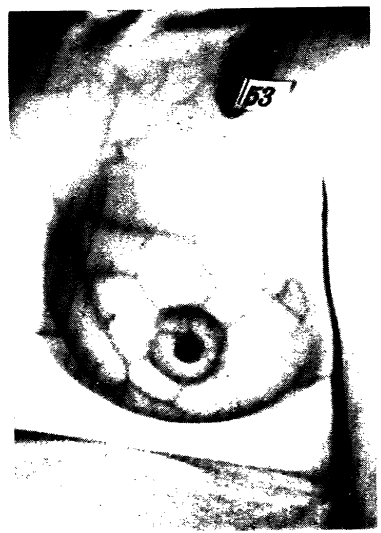


Fig. B. Primigravida. Diagnosed "positive", correctly.



Fig. C. Multigravida. Diagnosed "positive", correctly.

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PLATE XXXV

CANCER SECONDARY TO ŒSTROGEN THERAPY

(G. REIMANN-HUNZIKER)



Bilateral carcinoma of the male breast following œstrogen therapy for cancer of the prostate.

in which it was used almost exclusively. Galbraith dislikes the large size of the cold punch and believes that with a large adenomatous gland perurethral prostatectomy is a much more serious procedure than radical suprapubic operation. On the modified Harris technique Galbraith reports most favourably. If 2 cases, which are not strictly operation deaths, be excluded, his hospital mortality is 1·5 per cent and the total 3·1 per cent. Galbraith is careful to state that his results with the Harris operation detract in no way from his admiration for T. Millin's excellent method, which, through later experience, he might use more frequently. Wilson Hey's teachings are discussed. The two-stage prostatectomy is undoubtedly a safer procedure for the inexpert, but for the specialist the one-stage operation is much to be preferred from all points of view. Galbraith performed the two-stage operation in approximately 6 per cent of all cases. For early cancer the perineal route is good, but the retropubic approach of Millin seems preferable.

Prostatic Obstruction.—As A. Jacobs[5] points out, it is the degree of obstruction and not the size of the prostate that constitutes the chief indication for operation. Permanent suprapubic drainage is highly undesirable, and must be regarded as a confession of failure. Out of 310 operations for prostatic obstruction carried out in the past 2 years, Jacobs employed cystostomy as the sole procedure in only 11.

Post-prostatectomy Obstruction.—That various degrees of obstruction are extremely frequent after suprapubic prostatectomy is the finding of A. E. Goldstein[6] and S. W. Rubin. The post-operative passage of sounds should be a routine. Their thorough perusal of the literature confirms the belief that complete occlusion of the vesical orifice is very rare after the suprapubic operation. In reporting 3 such cases, they come to the conclusion that complete obstruction occurs almost exclusively at the junction of the bladder and prostatic cavity; it was so placed in all recorded cases. Theoretically, a total obliteration of the urinary channels can occur when the prostatic bed is involved. An impacted calculus might prevent micturition. As late causes, recurrence of benign prostatic hypertrophy or carcinoma are to be considered. When complete occlusion develops, a very persistent and profusely draining suprapubic fistula is diagnostic; through this the cystoscope can be inserted and the occluding diaphragm visualized. It may also be seen in the cystogram. Prevention of complete occlusion following operation is possible by the utilization of an indwelling urethral catheter. In the established case treatment consists in suprapubic cystostomy and incising the diaphragmatic obstruction over a urethral sound.

Heterotopic Bone Formation after Suprapubic Prostatectomy.—B. S. Abeshouse[6] finds that the new bone may be in the scar, rectus sheath, or surrounding a fistula. It varies from spicules to plates extending along the incision. Maximum growth occurs within one to two months after operation. There is no symptom complex, the diagnosis being made by palpation and X rays. The most likely explanation is metaplasia of connective tissue. Treatment is surgical removal.

Modification of Resectoscope.—The improved instrument described by J. Iglesias de la Torre[7] can be used by one hand so that at the same time the surgeon can reach the rectum with the other. The disposition of rings for handling the sheath and moving the loops are shown in *Fig.* 45.

Hæmolysis after Transurethral Resection.—Sterile water used for irrigating during resection may enter the periprostatic venous plexus. If forced into veins it can produce hæmolysis, thus damaging the kidney as does transfusion with incompatible blood. A fatal case is reported by C. D. Creevy,[8] who recommends 4 per cent glucose for irrigation. R. M. Nesbit and S. I. Glickman[9] favour 1·1 per cent solution of glycine.

Tuberculous Prostatic Urethritis : a Suggestive Diagnostic Sign.—When the prostatic urethra is seen to be slightly dilated, with a trabeculated floor and 'golf-hole' prostatic ducts, tuberculosis of the prostate gland should be suspected (J. K. Lattimer[10]).

Cancer. Benign enlargement and carcinoma are distinct and separate lesions of the prostate, even though they commonly occur together. The literature is full of reports of malignant degeneration and of tumours arising in areas of benign prostatic enlargement. There is reason to believe that neither occurs, or at least very rarely. These pronouncements, coming from such an authority as F. Hinman,[11] greatly help in the clarification of our conceptions of prostatic pathology.

In an analysis of 399 cases of prostatic cancer, M. Donaldson et al.[12] find that in as many as 21 per cent the first symptom pointed to the possible presence

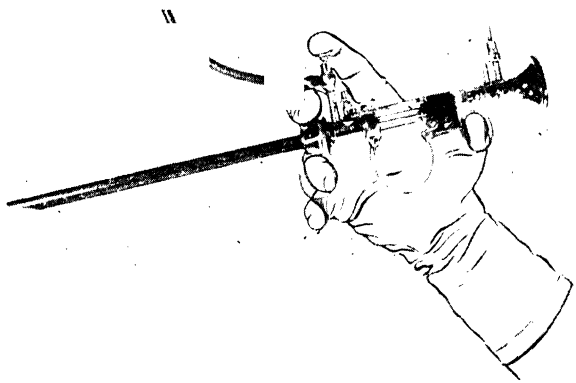


Fig. 45. Iglesias de la Torre's modified resectoscope fo

of a metastasis ; this is in striking contrast to carcinoma of the bladder, where metastases caused initial symptoms in 1 to 2 per cent.

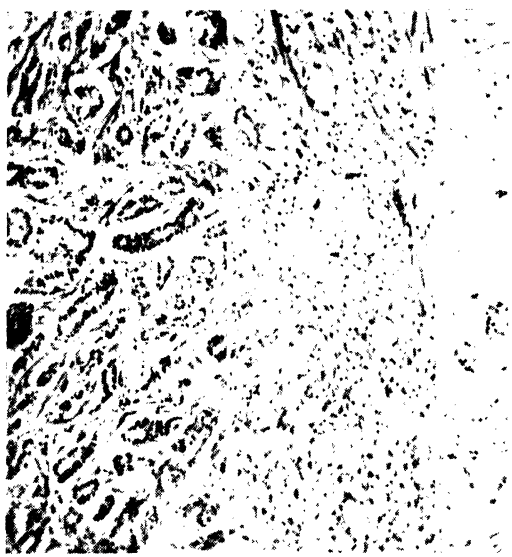
M. S. Hovenanian and C. L. Deming[13] report for the first time the successful heterologous transplantations of prostatic cancer in guinea-pigs. When so transplanted, cancer of the human prostate lost a fundamental activity, the production of acid phosphatase. In male castrated guinea-pigs, human cancer of the prostate did not grow.

Separate Estimation of Enzymes in the Acid Phosphatase Group. E. J. King and G. E. Delory[14] remind us that there are at least two acid phosphatases in the blood other than that coming from the prostate. One is found in red cells and another occurs normally in the serum. F. K. Herbert[15] employs incubation with alcohol to inactivate the prostatic component and thus to determine it indirectly. More recently M. A. M. Abul-Fadl and E. J. King[16] observed that 0·5 per cent formaldehyde completely inactivates red-cell acid phosphatase and destroys most of the normal serum enzyme, but has no effect on the prostatic enzyme. For clinical purposes the following limits for formaldehyde-stable serum acid phosphatase are suggested :

Normal values :	0·3 units per 100 ml. serum
"Suspicious" :	3·1–5 units per 100 ml. serum
Prostatic :	5·2 units per 100 ml. serum

Diagnosis of Metastases.—The value of *combined* blood examinations is emphasized by R. N. Boylan and J. H. Tillisch.[17] With skeletal metastases, the acid phosphatase was normal in 34 per cent, the sedimentation rate in 23 per cent, and the alkaline phosphatase in 14 per cent. It is to be noted that the combined acid and alkaline phosphatase values and the sedimentation rate were normal in 2 per cent of cases.

Treatment. F. R. Kilpatrick[18] reminds us that even before orchiectomy or hormone treatment was carried out some of the patients survived 3 to 5 years. The best results are obtained in adenocarcinoma. The more undifferentiated



a *b*

Fig. 46.—Serial biopsy specimens of prostatic carcinoma during œstrogen treatment, showing regression of the tumour: *a*, Initial; *b*, After 10 days; *c*, 17 months later. (*J. D. Fergusson.*)

cancers do not respond to œstrogenic therapy or orchiectomy (R. T. McCabbery and E. Hess[19]).

J. D. Fergusson[20] considers that the greatest danger in connexion with œstrogen therapy lies in it being regarded as a panacea for all urinary disturbances arising from prostatic cancer. The evil consequences of urinary obstruction and sepsis demand that ample measures be taken for their prevention and relief, and for this reason the use of œstrogens must often be regarded as supplementary to perurethral resection and chemotherapy.

A prostatic cancer may lose many of its malignant characteristics during œstrogen therapy. In some cases seen for the first time after receiving treatment, the local condition may prove unrecognizable. *Fig.* 46 shows the histological changes in prostatic cancer during œstrogen treatment.

It is pointed out by C. L. Deming et al.[21] that prostatic cancer treated with small doses of œstrogen becomes tolerant to the hormone, which explains the refractory phase so often seen clinically.

After an experience with 3 cases in which adrenalectomy was done as a last resort, H. T. Cox[22] concludes that it seems as if this operation, on present evidence, may be dismissed as a practical measure.

Cancer of Breast in Male secondary to Œstrogenic Administration.—As W. Abramson and H. Warshawsky[23] recall, in 1932 A. Lacassagne made the first report on the development of breast cancer following injections of œstrogens in male mice of a strain in which the incidence was high in the female. These experiments were confirmed, and W. U. Gardner[24] showed that hereditary factors were of great importance in determining the influence of œstrogens on mammary cancer. In presenting their case of cancer of the breast in a male who was undergoing œstrogenic treatment for prostatic carcinoma, Abramson and Warshawsky[24] are of the opinion that there is strong evidence that there is a causal relationship between the hormonal therapy and the development of the cancer. The total amount of diethylstilbœstrol used was 1097 mg. The treatment extended over a period of 489 days.

From Switzerland G. Reimann-Hunziker[25] discusses the effect of œstrogenic hormones upon the male, especially in relation to the mammary glands. He gives a description of a 68-year-old patient suffering from carcinoma of the prostate which was treated by implantation of ovocycline. This treatment led to the development of gynæcomastia; following a second implantation bilateral mammary cancer occurred (*Plate XXXV*). While this complication is clearly exceptional, the author advises that the greatest caution should be exercised in the administration of œstrogenic hormones. The breasts should be subjected to regular examination and due attention should be paid to any familial history of cancer. Similar instructions are given by U. Musiani.[26]

F. H. Entz[27] regards his case of cancer of the male breast following stilbœstrol therapy as being probably metastatic in origin. The literature on the relation of sex hormones to cancer is steadily increasing. A case of cancer of the male breast with metastases is reported by R. Karpat and C. A. Kuehn.[28] Following castration there was a spectacular improvement in the pulmonary secondary deposits.

REFERENCES. [1]*Proc. R. Soc. Med.* 1948, **41**, 73; [2]*Lancet*, 1948, **1**, 472; [3]*Brit. med. J.* 1948, **1**, 1231; [4]*Philipp. J. Surg.* 1947, **11**, 145; [5]*J. Urol.* 1948, **60**, 499; [6]*Ibid.* **59**, 50; [7]*Ibid.* 890; [8]*Ibid.* 1217; [9]*Ibid.* 1212; [10]*Ibid.* 326; [11]*J. Amer. med. Ass.* 1947, **135**, 136; [12]*Brit. Emp. Cancer Campaign Ann. Rep.* 1947; [13]*Surg. Gynec. Obstet.* 1948, **86**, 29; [14]*Post-Grad. med. J.* 1948, **24**, 299; [15]*Quart. J. Med.* 1946, **59**, 221; [16]*J. Path. Bact.* 1948, **50**, 149; [17]*J. Urol.* 1948, **59**, 391; [18]*Clin. J.* 1948, **77**, 11; [19]*J. internat. Coll. Surg.* 1948, **11**, 68; [20]*Post-Grad. med. J.* 1948, **24**, 312; [21]*J. Urol.* 1948, **59**, 215; [22]*Lancet*, 1947, **2**, 425; [23]*J. Urol.* 1948, **59**, 76; [24]*Arch. Path.* 1939, **27**, 138; [25]*Helv. chir. Acta*, 1948, **15**, 242; [26]*J. d'Urol.* 1948, **54**, 215; [27]*J. Urol.* 1948, **59**, 1203; [28]*Urol. cutan. Rev.* 1948, **52**, 521.

PRURITUS ANI.

W. B. Gabriel, M.S., F.R.C.S.

H. E. Bacon and C. E. Hardwick[1] discuss the actiology of pruritus ani, particularly from the biochemical aspect. They refer to the work of L. H. Slocumb (*see* MEDICAL ANNUAL, 1945, p. 258), who advised correction of a high alkaline *p*H in the rectum by dietetic management. The authors conclude that pruritus ani is a form of chemical dermatitis with variable skin changes. *Treatment* recommended is partly dietetic and partly local: lactose suppositories inserted at bedtime tend to prevent leakage of rectal discharge containing a high *p*H. The local care is outlined and consists in cleansing with saturated boric lotion, application of mercurochrome solution, and keeping the area dry with boracic powder. Treatment for fungus infection is to be borne in mind, also anti-allergic treatment. The findings in 125 cases of anal pruritus are tabulated and it is noted that in 107 cases some form of surgical treatment to correct 'anorectal pathology' was required.

A paper on the treatment of intractable pruritus ani by *tattooing with mercury sulphide* by R. Turell and A. W. M. Marino was reviewed in the MEDICAL

ANNUAL for 1943, p. 273. Now a further paper by R. Turell[2] is noted, based on an analysis of 93 patients treated between October, 1938, and November, 1942, and followed up for varying times from 6 months to 4 years. The author concludes that tattooing with mercury sulphide is an effective form of treatment for intractable anal pruritus when characteristic cutaneous changes have taken place : it is contra-indicated in patients with any inflammatory condition of the colon and rectum ; local lesions such as haemorrhoids or anal stenosis should be corrected surgically before tattooing is undertaken. As a general rule patients without cutaneous changes are not likely to benefit from tattooing. The article is illustrated by some interesting photomicrographs of specimens of tattooed skin, and the instruments used are illustrated.

REFERENCES.—[1]*J. med. Soc. New Jersey*, 1947, **44**, 446 ; [2]*Surgery*, 1948, **23**, 63.

PSYCHIATRY : CLINICAL. *E. W. Anderson, M.D., F.R.C.P., D.P.H.*

Despite an enormous amount of patient research in all relevant fields, clinical, psychological, pathological, biochemical, and others, the *aetiology of schizophrenia* remains essentially obscure. As M. Bleuler[1] in an admirable review remarks, schizophrenia, which accounts in the whole world for one-half of the admissions to mental hospitals and three-quarters of their total inmates, remains aetiologically much the same mystery as all mental disorders were some 100 years or so ago. Refuting the suggestion that clinical research in schizophrenia has come to a standstill, the author gives some of the results of his own investigations. Although the clinical features of schizophrenia have been carefully studied, the course of the illness has not received the same attention. Since the new methods of treatment were introduced the deficiencies of our knowledge were such that the basis was lacking for an appraisal of the merits of these. Whilst what happened to the patient at certain crises of his life was known, knowledge of the patient's whole life was not. Over the last 15 years the author, in an investigation of over 500 cases, found that 95 per cent fell into the following categories :—

1.	Acute course proceeding to deterioration	(5–15 per cent)
2.	Chronic ,, ,, ,, ,,	(10–20 per cent)
3.	Acute ,, ,, ,, defect	(not over 5 per cent)
4.	Chronic ,, ,, ,, ,,	(5–10 per cent)
5.	Circular ,, ,, ,, deterioration	(hardly over 5 per cent)
6.	,, ,, ,, ,, defect	(30–40 per cent)
7.	Recovery after a circular course	(25–35 per cent)

(The figures given are derived from studies made at different places and represent upper and lower limits).

He summarizes his results as follows :—

a. The ultimate outcome of the disease for a quarter each of the cases is severe deterioration, severe defect, slight defect, and recovery.

b. Schizophrenia tends to a circular (remittent) more frequently than to a simple progressive course.

c. Of the remittent forms only an insignificant fraction go on to complete deterioration. After several previous remissions deterioration hardly ever occurs.

d. The insidiously beginning forms proceed in the majority of cases to deterioration, in a minority to defect, and only exceptionally to recovery.

e. Of the cases beginning acutely barely a quarter deteriorate, barely a half recover with defect, and a good quarter make social or complete recovery.

The author investigated the incidence of schizophrenia in remote Swiss villages and found it broadly equivalent to that of New York. The author believes it premature to postulate the biological unity of schizophrenia, and thinks research more likely to be fruitful if based on small subgroups for each of which a unitary aetiology might exist. In the absence of a definite pathology,

genetic and personality researches form the only data for the delimitation of such groups. His investigations have suggested that different familial, characterological, and bodily dispositions correspond to the 7 groups mentioned, but no figures are given. He draws attention to the fact that a schizophrenia may develop out of an hysterical or anankastic constitution, which is certainly in accord with the clinical experience of others, and not only from a 'schizoid' background. In consequence the aetiological importance to be attached to environmental factors varies from one form to another, the significance of a particular noxa being determined by the particular constitution. He expresses scepticism as to the value of the newer methods of treatment. Follow-up studies showed that 6 months after termination of shock treatment approximately one-third of the social and fully recovered cases had relapsed, and 3 to 5 years after treatment only about one-quarter had remained well; that despite such treatment the 'rhythm' of the episodes remained the same before and after treatment, and that the personality of those who recovered with treatment was sounder on an average than that of those who did not. Shock treatment has not diminished the total number of chronic schizophrenics in the hospital, although by now nearly all these patients had had such treatment in the past. The author asks whether it would not be paradoxical if a specific treatment were discovered for a disease whose origin is so obscure and doubtful?

The existence of a so-called 'schizophrenia simplex' is doubted by some, who refer such cases to the hebephrenic group. O. Kant[2] found that out of 741 schizophrenics at the Worcester State Hospital, Mass., 49 (6·6 per cent) were diagnosed as schizophrenia simplex; 64 cases, 46 men and 18 women were investigated. In only 2 cases was there no definite evidence of psychotic experiences such as hallucinations or delusions. Where it was possible to be certain, the age of onset ranged from 12 to 29. In all but 2 onset was gradual; 26 (61·9 per cent) had hereditary tainting with various functional psychoses, mostly schizophrenia. Lack of sexual adjustment, aggressiveness, and introversion were the commonest pre-psychotic personality features. Leptosomes predominated, and a majority (60 per cent) had been shiftless workers. Loss of contact was not prominent in the early stages. The majority showed at the time of onset aggressiveness, sexual or alcoholic indulgence, or vagrancy, or combinations of these. In every case he found a history of lack of aggressiveness or a disorganized home environment. He suggests that the personality of these patients is such that the elaboration of a defensive psychotic symptomatology is not possible. He believes surprisingly, that the simple schizophrenic is in better contact with reality than other schizophrenics. He explains some of the other symptomatology on similar psychodynamic lines.

The problem of the *relationship of psychosis to organic cerebral disease* is discussed by J. W. Friedlander and B. J. Kesert[3] in a report of a case of amyotrophic lateral sclerosis. The patient was a man of 50 who had complained since August, 1943, of pain, paræsthesia, and weakness of his right leg. Irrational behaviour was first noticed in September, 1945, and examination revealed a profound dementia. Air studies showed general cerebral atrophy. He died in December, 1946. The problem of whether the psychosis occasionally associated with amyotrophic lateral sclerosis is causally related or merely coincidental is reviewed. From the 34 cases reported in the European and American literature it is evident that both relationships occur. Unfortunately no autopsy was possible in this case, but the authors argue that apart from the possibility of a coincidental Alzheimer, the psychosis in this case was directly related to cerebral involvement due to the disease.

REFERENCES. —[1]*Wien. Z. f. Nervenheilk.* 1948, **1**, 129; [2]*Psychiat. Quart.* 1948, **22**, 141; [3]*J. nerv. ment. Dis.* 1948, **107**, 243.

PULMONARY BILHARZIASIS. (*See* BILHARZIASIS, PULMONARY.)

PULMONARY HEART DISEASE.—(*See* HEART DISEASE, PULMONARY.)

PULMONARY TUBERCULOSIS, SURGERY OF. (*See* TUBERCULOSIS, PULMONARY, SURGERY OF.)

PURPURA, IDIOPATHIC THROMBOCYTOPENIC.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Pathogenesis.—Although the beneficial effect of splenectomy in idiopathic thrombocytopenic purpura has been realized for many years (*see* MEDICAL ANNUAL, 1945, p. 261), the role of the spleen in the pathogenesis of this disorder has for long been the subject of argument. One theory has been that the spleen in this disorder removes platelets from the circulation and destroys them (thrombocytolysis); the other has postulated that the spleen gives rise either to an abnormal substance which prevents the normal formation of platelets by megakaryocytes in the marrow or to an excessive amount of a normal inhibitor of platelet production. Careful studies of the sternal marrow in recent years leave little room for doubt that the second theory is the correct one. W. Dameshek and E. B. Miller[1] have found in idiopathic thrombocytopenic purpura a relative increase in megakaryocytes with greater percentage of immature forms and a marked decrease of mature forms showing platelet formation. Rapid and complete reversal of those changes followed splenectomy. L. R. Limarzi and E. M. Schleicher[2] described similar findings and noted that before splenectomy many of the megakaryocytes showed a hyaline cytoplasm with absence of azurophilic granules. More recently E. H. Valentine[3] has reported studies of 3 cases of idiopathic thrombocytopenic purpura and 11 control cases. In the controls 56 to 80 per cent of the megakaryocytes in the sternal marrow showed evidence of platelet production. In the cases of purpura there was a marked depression of platelet-forming activity by the megakaryocytes, but forty-eight hours after splenectomy, platelet production had returned to normal levels.

These studies are important not only from the theoretical standpoint. They indicate that the characteristic megakaryocytic changes should be sought for and found before the diagnosis of idiopathic thrombocytopenic purpura can be regarded as firmly established and before the operation of splenectomy is recommended.

REFERENCES.—[1]*Blood*, 1946, **1**, 27; [2]*J. Amer. med. Ass.* 1940, **114**, 12; [3]*Amer. J. med. Sci.* 1947, **214**, 260.

PURPURA: THROMBOTIC THROMBOCYTOPENIC.

Stanley Davidson, M.D., F.R.C.P.
H. W. Fullerton, M.D., M.R.C.P.

Physicians in general, and hæmatologists in particular, realize that the diagnosis in cases of purpura may be a matter of considerable difficulty. One of the most useful investigations is the platelet count. This serves to divide cases of purpura into two groups: (*a*) non-thrombocytopenic; and (*b*) thrombocytopenic. In (*a*), the non-thrombocytopenic group, it is believed that the essential defect lies in the capillaries, which are damaged in a generalized or a patchy manner, and we find purpura due to this defect in a wide variety of conditions such as severe infections (especially septicæmic), drug intoxications (e.g., with sulphonamides), chronic diseases of kidney and liver, C-avitaminosis (scurvy), the anaphylactoid purpuras of Schönlein and Henoch, and as an

inherited abnormality (hereditary familial purpura). In (*b*), the thrombocytopenic group, the platelet count is usually below 75,000 per c.mm., and the main conditions to be considered are idiopathic thrombocytopenic purpura (*see previous article*), and the diseases which result in a marked reduction of megakaryocytes in the bone-marrow, viz., aplastic anæmia, the leukæmias, pernicious anæmia, severe hæmolytic anæmias, diffuse malignant disease of bones, myelosclerosis, and osteosclerosis.

Occasionally cases may be encountered in which both platelet deficiency and capillary damage appear to be present, but, in general, the separation of cases of purpura according to the platelet count serves a useful purpose and greatly facilitates diagnosis. However, recent reports indicate that some cases of thrombocytopenic purpura cannot be accounted for by an inhibition of platelet formation (idiopathic thrombocytopenic purpura) or by reduction of megakaryocytes in the bone marrow (aplastic anæmia, the leukæmias, etc.). P. J. Fitzgerald, O. Auerbach, and E. Frame,[1] in an article entitled "Thrombocytic Acro-angiothrombosis (Platelet Thrombosis of the Capillaries, Arterioles, and Venules)", and K. Singer, F. P. Barnstein, and S. A. Wile,[2] under the heading "Thrombotic Thrombocytopenic Purpura; Hæmorrhagic Diathesis with Generalized Platelet Thrombosis", draw attention to a rare condition which has not yet been diagnosed in life. Approximately 12 cases have now been reported of a disease which is characterized by acute purpura hæmorrhagica, fever, thrombocytopenia, anæmia, and a rapidly progressive fatal course. The essential findings at autposy, as described by Fitzgerald, Auerbach, and Frame, are numerous thrombi, composed of platelets, in capillaries, arterioles, and venules, and a variable degree of endothelial proliferation. They were unable to decide which of these lesions was the primary one, but the thrombocytopenia is considered to be due to a sweeping-up of platelets from the circulation in the formation of the platelet thrombi. W. Dameshek[3] considers that the disorder may well be more common than was previously thought. Probably it should be considered as a possibility in any case of apparent idiopathic thrombocytopenic purpura which runs a rapid downhill course. It may be possible to diagnose "thrombotic thrombocytopenic purpura" in life by careful examination of sections of the sternal marrow which would show (1) the characteristic endothelial changes and platelet thrombi, (2) a normal number of megakaryocytes which, in contrast to idiopathic thrombocytopenic purpura, show no inhibition of platelet formation.

References.—[1]*Blood*, 1947, **2**, 519; [2]*Ibid.* 542; [3]*Ibid.* 597.

RADIO-DIAGNOSIS. *J. W. McLaren, M.A., M.R.C.S., L.R.C.P., D.M.R.E.*

Micro-arteriography.—A. E. Barclay[1] has developed a new technique for close study of the renal vascular system in great detail, managing to get enlargement up to × 250 of sections of the human kidney showing glomeruli and surrounding capillary network in the kidney. The finding of an arteriovenous shunt in the renal substance in cases of shock is of obvious value, and the technique opens up a new field of research.

Sections of the organ to be studied (from 120 μ to 450 μ) are washed and placed in a 50 per cent mixture of glycerin and water and transferred to a thin waxed paper. This is placed in a special holder with the film, which is mounted directly on the X-ray tube (to prevent vibration) and the X-ray film made. The X-ray tube is a special tube used for crystallography with a molybdenum target and beryllium window, and the film, which has to be of a fast but not granular type, is a maximum resolution film. The kilovoltage used was of a very low order of 20 kv. or under. It was found that thorotrast was a very suitable medium for contrast injection *in vivo* in the experimental animals

PLATE XXXVI

MICRO-RADIOGRAPHY

(A. E. Barclay)

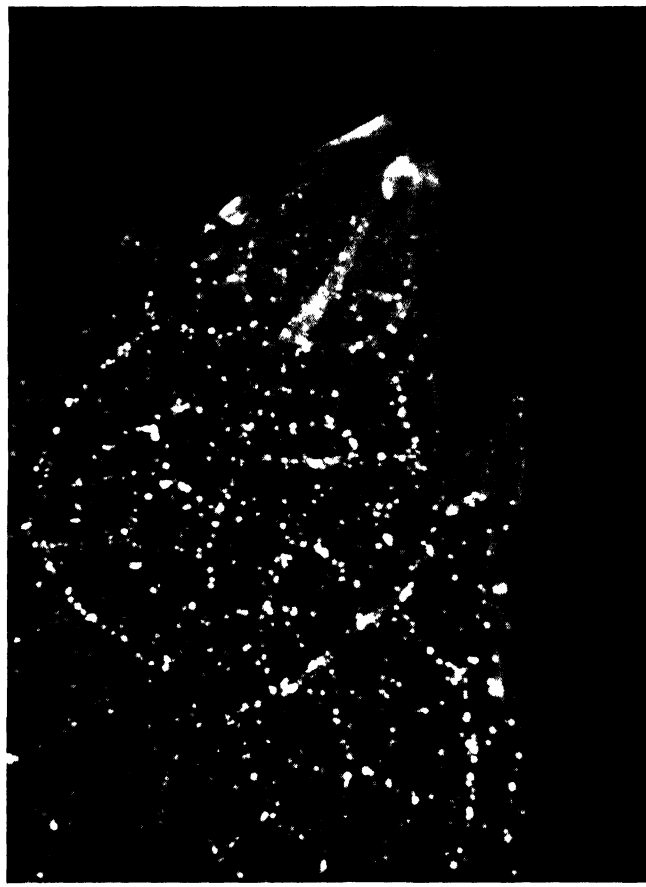


Fig. 1. Rose leaf, showing spots of minerals that have travelled from the ground up to the leaf through the sap channels. (× 50.)

PLATE XXXIX

MICRO-RADIOGRAPHY—*continued*

(A. E. Barclay)

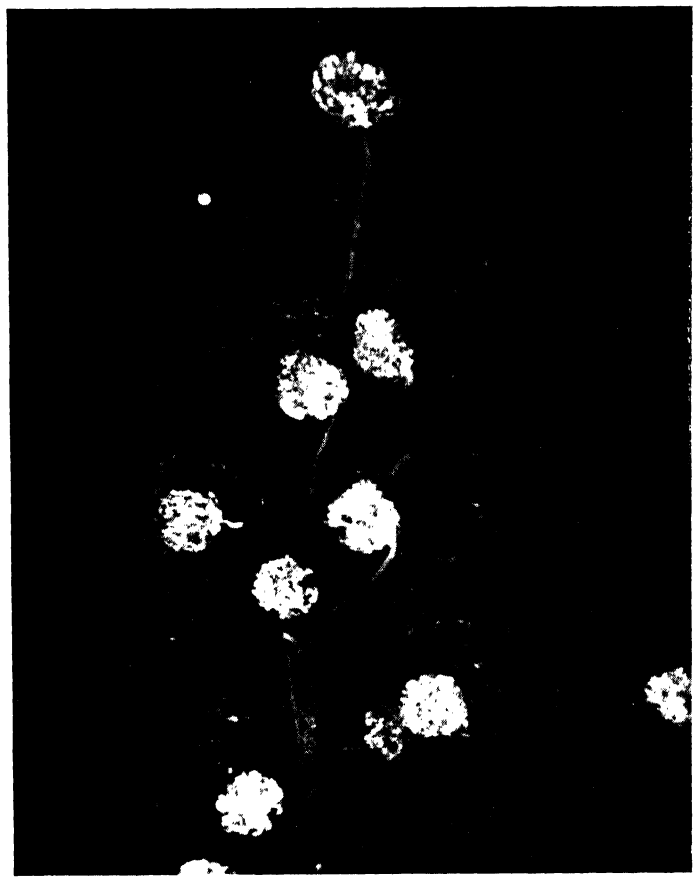


Fig. D. Micro-arteriography. Glomeruli in human kidney, from a case of traumatic uræmia. The capillary bed is very imperfectly filled, and no efferent vessels are seen leaving the glomeruli. (× 50.)

used, and this could also be combined with indian ink to stain the sections at the same time.

The method is one which can be used by research workers in many studies of the vascular system in selected organs of the body and may greatly increase our knowledge of the capillary patterns. (*Plates XXXVI–XXXIX.*)

Pulmonary Hæmosiderosis (Scott Park[2]).—In cases of *mitral stenosis* pulmonary hæmosiderosis may be shown to be present in rare instances. In such cases, in addition to the congestive changes, there will be seen in both lung fields multiple, small, radio-opaque foci measuring from 1 mm. to 5 mm. in diameter, but usually of the order of 2 mm. These foci are fairly dense rounded opacities closely packed in the mid-regions of the lung fields, also extending to the periphery and bases, but not to the apices. The appearance is compact not varying with the congenital changes. Post-mortem examination shows that these foci are groups of adjacent alveoli containing phagocytes with hæmosiderosic material. This is probably due to the late results of hæmorrhage into terminal air-passages, possibly from varicose bronchiolar veins.

Angiocardiography.—The last year has seen considerable advances in this field, but there is still a considerable amount of work to be done on the technical side of the examination. The radiological part of the technique is quite a complicated one, and for full examination it is essential to take a fairly long series of X-ray films at short intervals from the time of the completion of the injection of the contrast medium. Of the main methods at present employed none completely fulfils all requirements. Full-size films can be used in mechanically controlled cassette stands or tunnels but it is difficult to ensure rapid enough change to cover all the stages of the examination. The use of 5-in. strip film for indirect radiography has been shown to be of value, but leaves much to be desired in detail (Hills). It is essential that if angiocardiography is to be of real diagnostic value there should be maximum detail on the film. The use of 5-in. film, however, has advantages in that it can be viewed directly without projection.

It is probable that the solution to the problem will lie in the use of indirect radiography with a film of 70 mm. size. This will ensure speed for the maximum number of exposures—up to 4 exposures a second can be taken, and though projection of the resultant film is often advisable it can be looked at directly. The advent of brighter fluorescent screens will no doubt in the near future materially help in the method of indirect radiography.

Peptic Ulcer of the Œsophagus.—Allison[3] maintains that short œsophagus is usually an acquired condition due to defects in the diaphragm which allow a sliding hernia of the stomach. In early stages the œsophagus may remain elastic so that the hernia can be reduced, but after peptic ulceration and fibrosis have developed permanent shortening occurs. Seventy-four cases of peptic ulceration have been studied by Allison, and in the adult group of cases (63) the following radiological points are made. Adequate screening and full examination is required. The length of a stricture as seen by the narrowed stream of barium may be misleading unless the lower margin is ascertained by forcing barium back to the lower end of the stricture. A short œsophagus will nearly always be found, and part of the stomach adjoining the cardia will be demonstrated in the mediastinum, and the change in the mucosal folds will mark the position of the cardia. This can also be ascertained by applying a Cushing clip at the mucosal junction through an œsophagoscope.

The following are given as the main types found in cases under review :—

1. Short œsophagus with gastric hernia but without obvious deformity of the œsophagus, the condition being leucoplakia and acute superficial erosions.

2. Stenosis of the œsophagus without short œsophagus and gastric pouch. The explanation is to be found in the presence of heterotopic gastric mucosa.

3. Complete œsophageal obstruction.

4. Smooth short stenosis of the œsophagus with gastric pouch (1·5 cm. or less).

5. Smooth long stenosis (over 1·5 cm.).

6. Distorted channel without stenosis but with shortening and gastric pouch. Produced by irregular scarring or inflammatory infiltration of the œsophageal wall.

7. Irregular stenosis resembling a carcinoma. The presence in these cases of a gastric hernia suggests benign rather than malignant change.

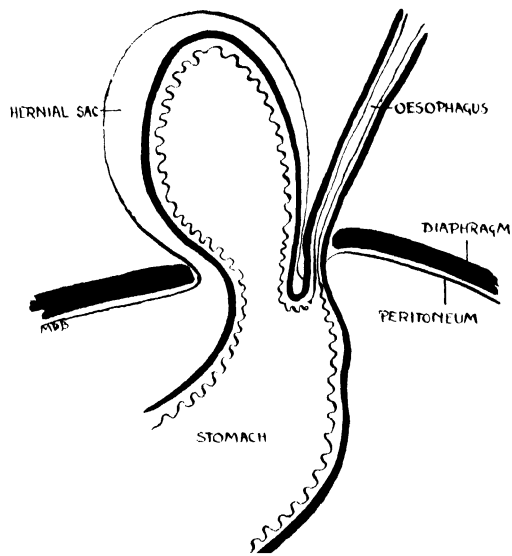


Fig. 47.—Para-œsophageal hiatal hernia. (*Figs.* 47–51 *by kind permission of* '*Thorax*'.)

8. Crater. This is a rare radiological finding.

9. Patulous cardia. With a free flow back of barium from stomach to œsophagus in the prone position.

10. Associated para-œsophageal gastric hernia. In these cases the cardia may be well above the diagram.

11. Indefinite. Only a few cases fall into this category with satisfactory radiological examination.

Where there is any defect in the diaphragm peptic ulceration may occur in the œsophagus if the defect is such as allows the constant presence of acid in the œsophagus.

Allison shows the varying types of herniation diagrammatically (*Figs.* 47–51). In type 1 para-œsophageal hiatal hernia (*Fig.* 47) acid does not invade the œsophagus and ulceration occurs, but in types 2 to 5, in a sliding hiatal hernia with a short œsophagus (*Fig.* 48) or complicated by a para-œsophageal pouch (*Fig.* 49)—and in the condition of 'bulging hernia' (*Fig.* 50) and heterotopic gastric mucous membrane without hernia (*Fig.* 51), ulceration may occur.

Achalasia of the Cardia with Œsophageal Carcinoma.—Achalasia produces a condition favourable for the subsequent development of carcinoma in the

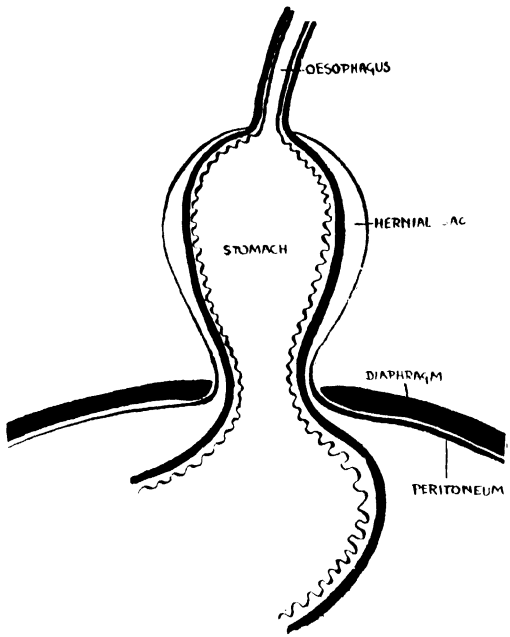


Fig. 48. - Sliding hiatal hernia with œsophageal shortening.

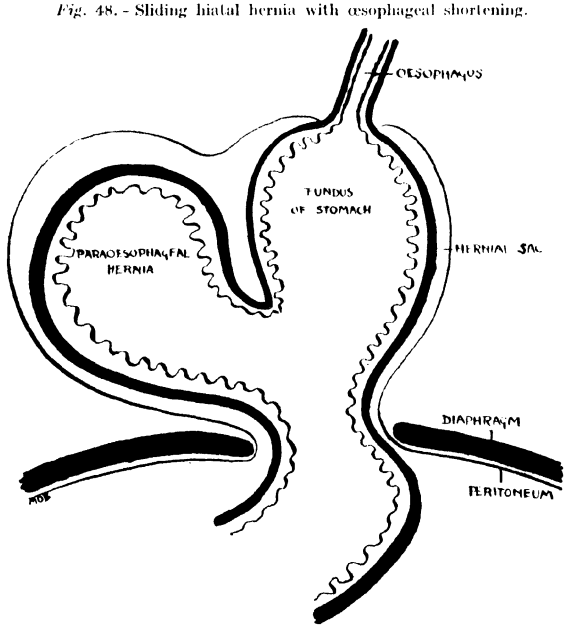


Fig. 49.—Sliding hiatal hernia complicated by para-œsophageal pouch.

œsophagus, and this condition may be very difficult to demonstrate radiologically. Carcinoma should be suspected in a case of achalasia when, after

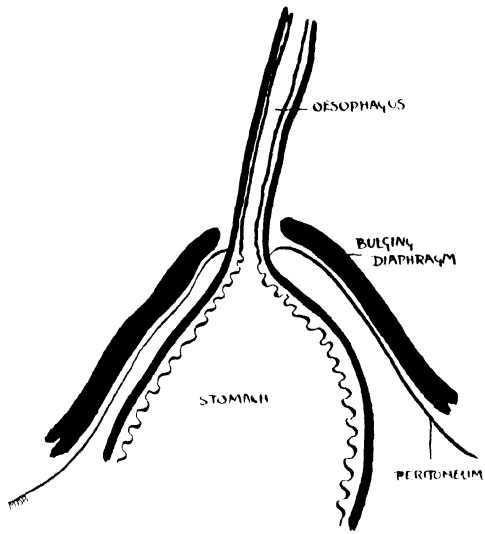


Fig. 50. 'Bulging hernia'.

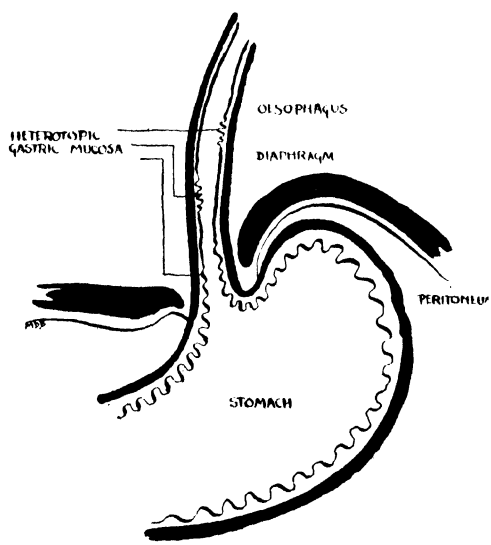


Fig. 51.—Heterotopic gastric mucous membrane without hernia.

a symptom-free interval, a recurrence of dysphagia with a marked weight loss, blood-stained vomit, and retrosternal pain occurs.

Achalasia produces an œsophagitis, and frequently ulceration and malignancy may supervene on the repair process. Baer and Sicher[4] give details of a series of cases of carcinoma of the œsophagus occurring in such conditions. It is of great importance that carcinoma should be recognized in these cases, as the possibility of surgical treatment at the present time can afford relief to the patient.

Polyostotic Fibrous Dysplasia.—This disease, originally called 'osteitis fibrosa disseminata' by Albright, is one which occurs in childhood and ceases after puberty. The main features are bony deformity with spontaneous fractures. Usually the disease is unilateral, but cases involving both sides of the skeleton have been described. The actiology of the disease is unknown, but as congenital stigmata may occur it has been thought to be due to developmental errors. The essential abnormality is a fibrosis of the marrow changing the compact bone into spongiosa, bending and expanding the long bones. The epiphyses are not affected. Accompanying endocrine and pigmentary changes may occur, and while the parathyroids are normal the serum-phosphatase is sometimes raised. The radiological changes in this condition are diagnostic. The affected bones show: (1) Broadening or expansion; (2) Thinning of cortex; (3) Rarefied and trabeculated and cystic appearance; (4) Secondary deformities. The long bones are most often affected especially the femur, but the base of the skull frequently shows sclerosis. Differential diagnosis is mainly from Paget's disease, Ollier's disease, and hyperparathyroidism. A. C. Bingold[5] reviews in detail a case report of the condition.

Diagnosis of Tumours of Bone.—Brailsford[6] points out that the essential evidence respecting a tumour of bone is whether it is simple or malignant. He stresses that while the clinical history of the patient may help in diagnosis, it often does not, and that too much reliance is placed on the pathologist for fully proving the nature of the tumour, with the result that biopsy is too frequently resorted to. Ewing's warning, that "few surgeons realize the limitations in the histological diagnosis of bone tumours and the conditions which simulate or accompany them", is too frequently disregarded. The histological reports on bone tumours produce a very wide variety of indecision in the findings, with the use of terms which allow of too much latitude for positive diagnosis. Simple and malignant tumours can simulate one another in both early and late stages.

The risks of biopsy are not inconsiderable, not only in the risks of anæsthesia and surgical exploration, but also in the risk of dispersal of the tumour cells. Consideration of all the facts concerning biopsy, as to whether the results can be relied on, the method, and the interpretation for surgical treatment, has caused Brailsford to consider biopsy as usually not a justifiable procedure. He considers it to be too dangerous, not reliable enough for accurate diagnosis in early cases, and often resorted to too early in the general clinical investigation.

Radiology can allow the continued investigation of the tumour without harm to the patient, and should be part of the general investigation of the patient. This of course places a considerable responsibility on the radiologist, whose report should be more often conclusive. It is because of the tendency for vague reporting on bone tumours that so much reliance has been put on biopsy.

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RADIOTHERAPY.

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Supervoltage Therapy.—The most important new work in 1948 has been the development of supervoltage therapy. A point has now been reached when voltages of from one to three million volts have passed the purely experimental

stage and are being used for treatment in a number of hospitals, while extremely high voltages, up to 100 million volts, are the subject of physical studies. These supervoltages are being obtained from the betatrons now working in several centres. From the Department of Physics of the University of Illinois, G. D. Adams and his collaborators[1] discuss the application of the betatron to medical therapy. Their important paper explains the difficulties of measuring dosage from high-energy roentgen radiation produced in a narrow beam from the 22-M.e.v. betatron. Details are given of the method of collimating the beam and of shielding from stray radiations both of electrons and of strong roentgen rays. Compensating filters improve the characteristics of the beam by selective absorption to reduce the low-energy content and, by proper shaping, to make the intensity distribution across the beam fit a predetermined scheme. Finally a method of monitoring the dose during treatment is suggested.

An equally careful study by E. E. Charlton and H. E. Breed[2] discusses the depth doses obtained with roentgen rays for energy levels from 20 to 100 million electron-volts. They worked with roentgen radiation generated by the 100-M.e.v. electron accelerator in the Research Laboratories of the General Electric Company. The film density method of measuring in a pressboard phantom was used with densitometer measurement of the films exposed. Relative ionization was measured with the standard victoreen and thimble meter. The use of this method requires elaborate precautions but it has produced a series of most interesting isodose curves for radiations at 20 to 100 M.e.v. A paper of this type cannot be summarized, but its importance is indicated when it can be said that it brings appreciably nearer the possibility of selecting the depth in the tissue at which the maximum ionization will be produced by choosing the correct voltage. This would provide over a wide range a favourable ratio of energy absorbed in the desired region to that absorbed in the rest of the volume through which the radiation must pass.

L. S. Skaggs and collaborators[3] also report experimental work with the 22-M.e.v. betatron, about which E. M. Uhlmann says in an introduction that concentration of energy is at the end of the beam so that the overlying tissue will receive less intensive radiation than the actual tumour, a reversal of the conditions under which radiotherapy is at present administered. To achieve this the electron beam itself, and not the X ray produced by allowing it to strike a target, is necessary, and the energies at which the betatron releases electron beams must be such that the required penetration is obtained. To produce a free beam of electrons it is necessary to have an unobstructed path. The technical difficulties of obtaining the electron beams are very great, and the authors describe the ingenious arrangements they have used to overcome their difficulties and to bring out through a window a well-collimated beam of electrons which produces at a distance of one metre from the window ionization equivalent to that produced by 100 r per minute of X rays. This beam can be visualized by a fluorescent screen placed at a slight angle, and penetration was measured by the use of films in a pressed wood phantom. Its extreme penetration was 6 cm. for a 13-M.e.v. beam of electrons, which is in agreement with theoretical predictions.

Much work remains to be done before electron therapy can be used in the treatment of cancer. E. H. Quimby,[4] speaking in the discussion which followed this paper, said: "It would seem that we have an instrument for putting our energy right where we want it. That means of course that the radiologist has to find out, much more definitely than ever he did before, right where it is that he does want it." R. R. Newell[5] agreed that this would be "an extraordinarily difficult and delicate clinical operation", an opinion with which all experienced radiotherapists must agree.

The clinical *use of supervoltage X-ray therapy in the one to three million volt ranges* is now providing material for analysis. R. Dresser[6] reports the use of 3 million volts in the treatment of a number of cases. The distance is 100 cm. with filtration equivalent to 20 mm. of lead, the intensity is from 80 to 100 r per minute, and the depth dose for small portals is approximately double that for 200 kv. This high depth dose makes it possible to treat many deep-seated lesions from a single field, and the absence of severe skin reactions is a great advantage. J. G. Trump[7] discusses the physical basis for the high skin tolerance of supervoltage roentgen rays and shows that the ionization produced in the surface region is both less than that available some distance below and is composed of electrons of relatively high average energy. This high average energy disappears when the radiation beam has traversed a distance below the surface equal to the range of the highest energy electrons which the beam can produce. After this it acquires the full complement of low-energy secondaries, so that its effect is little different from that of low-voltage roentgen rays.

The *skin reaction of human skin to radiation of different qualities* is described, and it is found that the threshold erythema dose for 20-M.e.v. radiation is very high. This is a quality effect explained by the absorption of high-energy radiations by the Compton process, resulting in forward directed electrons of high energy. It is only after these electrons have passed through the first few millimetres of tissue and the electromagnetic radiation is accompanied by the full complement of low-energy secondaries that maximum biological effect is obtained.

The use of new types of radiation must be tested by animal experiments, and T. C. Evans[8] describes the *effect of small daily doses of fast neutrons on mice*. It was found that the effects were in general similar to those of roentgen rays, but that the r/'N' ratio varies from one effect to another and is greater for small daily doses than for acute exposures. The lens was particularly susceptible to neutron irradiation, cataract being produced very easily, but in general the ratio was in the region of 12 r equals 1 'N'.

A practical study of the *use of one million-volt X-ray plant* was presented by G. S. Innes.[9] He described its development and application from the point of view of the physicist, and discussed the advantages of radiation at a million volts and the ionization produced at different levels in the tissues. He showed isodose curves for a number of different set-ups to illustrate the ease with which a desired tumour dose can be obtained. I. G. Williams,[10] speaking in the same symposium as a radiotherapist, described the use of the plant for the treatment of patients: 726 cases were treated, nearly all advanced cases of malignant disease. The conditions treated were cancer of the breast, tongue, antrum, larynx, œsophagus, bronchus, bladder, rectum, and anal canal, and a few odd cases in other sites. The results are on the whole similar to those obtained with the more usual voltages, but the material was probably more advanced than the average of cases treated, and there were some long survivals of such conditions as cancer of the rectum, where the advantages of a higher voltage probably explains a favourable response not often obtained.

Another method of treatment which seeks to improve the depth dose is *rotation therapy*, the theory and clinical application of which are described by S. J. Hawley.[11] It allows a proportionately high dosage to be delivered to a cylindrical volume of tissue about the axis of rotation and can therefore be used to eradicate any centrally placed tumour in the trunk. The isodose curves for a narrow portal are circular, and the dose falls off rapidly from centre to periphery. Seventy-one patients were treated, at first with very low doses because of the volume of tissue involved. Cases treated later received doses of 4000 r in 4 weeks from a skin dose of 2700 r, and good palliation with minimal reactions is claimed.

Study of the *changes produced in tumours by ordinary high-voltage irradiation* continues, and J. W. Hall and M. Friedman[12] examined by serial biopsy 28 lesions of the mouth, including the tonsil, treated by fractionated external irradiation at 200 kv. The average daily tumour dose was 275, and total tumour dose averaged 6000 r to 6500 r in 23 to 28 days ; 24 patients were treated. The biopsy material showed three main histological changes : acute cell death, progressive enlargement to giant-sized tumour cells, and radiation keratogenesis. The authors conclude that a single biopsy taken between the seventh and eleventh days during a course of fractionated irradiation will yield considerable information concerning the sensitivity of the tumour and the effectiveness of the irradiation technique.

Radio-active Isotopes.—Work on the use of radio-active isotopes continues, and the British pile at Harwell is now in production, although it can only supply relatively small quantities of the isotopes needed for therapy. The help received from the United States has included visits by a number of scientists specially qualified to advise on the use of isotopes, and one of them, J. H. Lawrence, delivered the Sir James Mackenzie Davidson Lecture on the subject " Some Tracer and Therapeutic Studies with Artificial Radio-activity ".[13] He began with a summary of the method of producing radio-active isotopes, then discussed some tracer investigations of rheumatoid arthritis. These have shown that there is a decreased circulation in the extremities of arthritics. It has also been possible, using labelled gold, to investigate the mechanism and site of action of gold in animals suffering from chemically induced arthritis. It was found that gold is taken up in relatively large quantities in the liver and kidneys, where it produces its toxic action, but that the uptake is also greater in the involved synovia, the ratio being about ten to one between involved synovia and surrounding normal tissue. Therapeutic use of radio-active phosphorus is still mainly for the treatment of leukæmia and polycythæmia, and the best results have been obtained in polycythæmia, where they can be excellent even when leukæmia and gross enlargement of the spleen are present. Chronic myeloid and lymphatic leukæmia give results which although not entirely satisfactory are probably better than those of the methods which have hitherto been used. A special example of selective uptake is that of iodine in the thyroid and of radio-active colloid chromophosphate in the liver. Radioyttrium and zirconium colloids are taken up selectively by bone-marrow and are now being used in the treatment of leukæmia and of certain diseases of the liver and spleen. The carcinogenic hydrocarbon dibenzanthracene has been labelled with radio-carbon, and it has also been shown that labelled tyrosine is taken up by melanotic tumours, by the thyroid, and by the adrenals, but the concentration is too small to suggest a therapeutic use for radio-carbon in tyrosine. The possibility of producing fission in uranium 235 in the tissue has also been investigated. A mouse previously injected with uranium containing U 234 was irradiated with neutrons and an auto-radiograph of a section showed the localization of the uranium atoms and thus where fission was produced. This appeared to be mainly in the phagocytic cells of liver and spleen. A point has been reached when an animal can be injected with uranium which is relatively harmless in itself, then irradiated by slow neutrons. The U 235 atoms will capture these neutrons and local fission will liberate amounts of energy enough to damage or even destroy the organ in which the atoms have been selectively absorbed.

A paper which cannot be summarized, but which is essential to those who are using radio-isotopes for therapy, is by L. P. Marinelli, E. H. Quimby, and G. J. Hines.[14] It provides the *tables necessary for dosage determination* for the many different types and qualities of radiation produced by the disintegration of the radio-isotopes likely to be used for tracer studies or for therapy.

A preliminary report on the clinical *use of radio-active iodine in the treatment of Graves' disease* is now available. E. R. Miller, M. H. Soley, and M. E. Dailey[15] point out that the possibility of using I 131 depends on the ability of the gland to take up iodine so that it can only be used in Graves' disease when the gland is not saturated with iodine and in certain types of cancer. The authors describe their method of obtaining accurate measurements which has allowed them to study the effects of small doses of radio-iodine on patients with the characteristic symptoms of hyperthyroidism. Striking improvement has been obtained but has not been permanent because the quantities available for administration were too small, but better results from larger doses are confidently predicted. The method of studying the uptake of radio-active isotopes by auto-radiography has also been further developed. The uncertainty as to exposure time can be reduced by a formula which determines the quantity of radiation from the data available regarding the rate of decay, the initial activity per unit surface of the tissue section which makes the auto-radiograph, and from various other factors. Auto-radiographs give a clear picture of the distribution of the radio-isotope, and may for instance outline an inactive tumour in the thyroid or show the patches where normal activity continues. This technique using radio-iodine has been successful in demonstrating thyroid function, but auto-radiography with P 32 would need doses which would be dangerous because of the wider distribution of this element in the body. The conclusion is reached that this method should only be used for patients who are receiving treatment with radio-active elements. Auto-radiography has also been used by D. Findlay and C. P. Leblond[16] to study the partial destruction of the thyroid of rats by large doses of radio-iodine. Damage is increased by the retention of the radio-iodine within the thyroid follicles.

The question of the *administration and operation of a radio-chemical laboratory* needs special attention. F. C. Henriques and A. P. Schrieber[17] describe the contamination and health hazards which are problems in laboratories handling beta and gamma activities at millicurie levels. They discuss the practical design of a 'hot' laboratory for safe and efficient operation. Contamination is considered in relation to the half life of the product; health hazards depend on the amount and energy of the activity present. The employer is responsible for the health of the employee, and must therefore make one person responsible for all activity stored or in use, who must keep a record of all persons receiving activity and of its ultimate disposal. One careless person may endanger all, but a check can be kept by the use of film badges. If one wearer consistently shows higher exposure than others it indicates a careless worker. How easy it is to be careless is shown by the elaborate rules drawn up for 'hot' laboratories using beta and gamma emitters and by the ingenious methods which have been devised to allow processing by remote control of radio-active isotopes. A paper such as this shows that no 'hot' laboratory should be installed without the most careful consideration of the dangers of storing and handling high-energy products. Radio-active elements are given as drugs and can be used in any hospital, but need the co-operation of physician, radiotherapist, and physicist if they are to be used for administration to patients.

Dosage problems in isotopes are the subject of continuous study from the point of view of general effect on the tissues. An interesting paper is that on the *effects of radiation on hæmopoiesis* by J. S. Lawrence, A. H. Dowdy, and W. N. Valentine.[18] Certain facts are recognized :—

1. The cells in the circulating blood are to all intents and purposes relatively resistant to radiation.

2. The peripheral blood-picture produced by radiation is affected markedly at any one period following irradiation by the length of life of the different

morphological elements in the peripheral blood. The life span of all of these has not been completely established, but roughly there is complete replacement of all white cells in 10 to 12 hours, of blood-platelets in 4 to 5 days, and of red cells in about 120 days. Changes in the white cells therefore appear very soon, changes in the platelets after those in the white cells, and changes in the erythrocytes only after a long interval, often masked by the regeneration which occurs well within the life span of this element.

3. The effect of radiation on the peripheral blood-picture is influenced by the radio-sensitivity of the various parent cells.

4. The ability of the tissue to regenerate is of great importance. It is suggested that all the tissues are capable of active regeneration. Radiation effects have been studied in the blood of rats treated in various ways with single and divided whole-body irradiation and doses to one area. A graph shows the changes

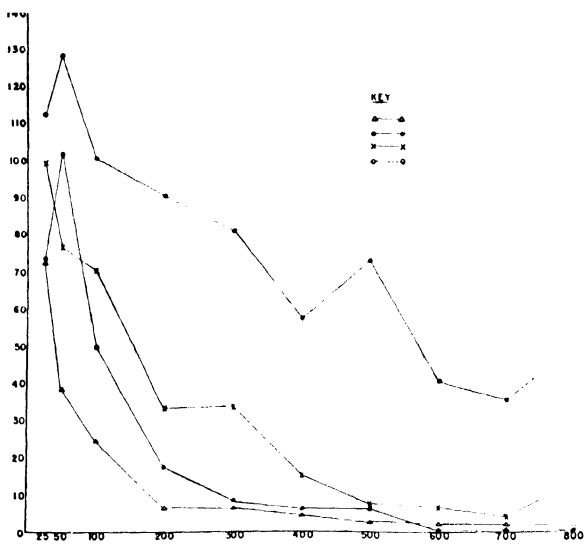


Fig. 52.—Changes in the various cellular elements of the blood with increasing doses of radiation. The time chosen for each element was that interval after radiation exposure when definite diminution of that element was first noted. (*Data of Suter and associates.*)

in the various cellular elements in the blood with increasing doses of radiation (*Fig.* 52).

C. H. G. Price has also made observations upon the lymphopenia of X-ray irradiation.[19] He studied 16 cases treated by means of three large fields 30 × 30 cm. for cancer of the ovary. The tumour dose was 2800 to 3500 r, treatment was given each day, and was equally fractionated over about 4 weeks. Curves were plotted against the integral dose. The reaction of the lymphocytes follows a characteristic path under standardized conditions of exposure, and the author believes that the rapid fall which takes place immediately may be the result of direct effect on the cells, while the slower fall later is due to indirect effect.

The platelet-count may also be an indication of the effect of irradiation, and W. M. Court Brown[20] believes that it is more accurate than the white count.

It may be used both for estimating irradiation effect and for observing the response of leukæmia. Accurate counting of platelets needs practice and a good microscope—the technique is similar to that used for the red cells.

An effect due to high dosage is *myelitis of the cervical spinal cord*, which has been recorded by G. Boden.[21] This is a form of late radiation necrosis which had not previously been recognized because the result simulated metastases. It followed two types of treatment both of which included the cervical spine: large-field treatment with moderate doses and small-field treatment with tolerance doses. Ten cases are described, 5 of whom died. Now that the danger is known it can be avoided by keeping doses which are delivered to long sections of the cord at levels below 3000 r in 3 weeks, and, where small fields with beam direction are used, by placing the field so that high doses on the cord will be avoided. The dose to the cord should be routinely investigated in the same way that the dose in the tumour is determined.

Malignant Disease

Cancer of the Breast.—G. E. Richards[22] discusses some of the factors which determine success or failure in treatment. The material consisted of 1189

Table I.—Survival Table—3, 5, and 10 Years in Relation to Stage of Disease

Stage	Survival			
	No. of Cases	3 years	5 years	10 years
		per cent	per cent	per cent
I	166	89	81	59
II	240	73	54	28
III	503	58	38	21
IV	198	34	16	8
V	45	13	3	0
Unclassified ..	37	—	—	—
Total	1189	59	43	26

cases, and the survivals are shown in *Table I.* He takes up the question of the effect of the size of the tumour, of its rate of growth, and lymph-node involvement. He also analyses the relation of cancer of the breast to the menopause. From all the facts considered he gives a clinical index of malignancy and relates it to survival. He prefers pre-operative treatment by X-ray therapy, and discusses its influence on the results of treatment, comparing the methods of treatment in *Table II.*

Table II.—General Summary. 5-year Survival

Stage	'Conventional' Surgery plus Post-operative Radiation	Pre-operative Radio-therapy	Gain
	per cent	per cent	per cent
I	81	—	—
II and III	43	50	7
IV and V	13	45	32
Clinical Index			
10–30	82	100	18
31–40	41	66·6	25·6
41–60	4	39	35

Method	5-year Survival	Selection of Cases to Date
	per cent	
Untreated	22	All stages
Surgery alone	30	All stages
Surgery, plus post-operative radiotherapy	43	All stages, borderline cases predominating
Pre-operative radiotherapy plus surgery	47	Late stages only, early stages excluded
Pre-operative radiotherapy, plus radical mastectomy	51	Mostly advanced cases

treatment in *Table II*. Finally he presents a series of interesting isodose curves taken from different planes in the breast.

Another contribution to the X-ray therapy of the breast is by F. M. Allchin and C. W. Wilson.[23] They describe the use of jigs made of perspex to allow the breast to be irradiated as a body of a known geometrical shape. Bridges and triangles are used and the space between the jig and the skin surface is filled in with scattering material.

J. Maisin[24] has collected statistics from a large number of sources for surgery alone to compare with the results obtained with pre- and post-operative radiation. He divides the cases by stage and concludes that a Stage I Steinthal surgery alone gives a 65 per cent five-year survival, and, in Stage 2, 26·8 per cent. If radiotherapy is added it makes little difference in Stage 1, but if Stages 1 and 2 are taken together about 50 per cent survive five years. He also analyses the effect of adding X-ray sterilization and the results of treatment by radiotherapy alone. There is a very extensive bibliography.

The technique of treatment for cancer of the breast remains a controversial problem. R. McWhirter[25] describes the technique of local mastectomy followed by a full course of X-ray therapy, using tangential fields to deliver a dose of 3750 r in three weeks to chest wall and axilla. The results of this method of treatment are shown in *Table III*, which should be compared with his other table (*Table IV*) which gives the results of treatment by *radical* mastectomy and post-operative irradiation of a similar type.

Table III.—Survival Rate of all 'Operable' Cases in the Period 1941–5. Main Method of Treatment—Simple Mastectomy and Post-operative Radiotherapy. Total Cases, 941

Years after Treatment	Number of Cancer Deaths	Number Exposed to Risk	Chance of Dying in any one Year	Survival Rate
				per cent
1	75	941	0·080	92·0
2	76	668·5	0·114	81·6
3	57	440	0·130	71·0
4	31	230·5	0·135	61·5
5	8	88	0·091	55·9

A possible way to improve the treatment of bone metastases from cancer of the breast is suggested by L. Reynolds, T. Leucutia, J. C. Cook, and K. E. Corrigan.[26] They use colloidal lead orthophosphate to enhance the effect of X-ray therapy. This compound has a certain toxic action in itself, and in addition the heavy lead atoms deposited within the tumour emit under the influence of the roentgen irradiation secondary electrons which also act on cancer cells. This method has been used for 20 years in a series of 355 cases of bone

metastases. The palliative effect was excellent, and the average survival was three years. It is now hoped that the method may be improved by the introduction of tagged phosphorus and it is also suggested that tagged lead may be used.

Table IV.—Survival Rate of all 'Operable' Cases in the Period 1935–40. Main Method of Treatment—Radical Surgery and Post-operative Radiotherpay. Total Cases, 56[illegible].

Years after Treatment	Number of Cancer Deaths	Number Exposed to Risk	Chance of Dying in any one Year	Survival Rate
				per cent
1	94	568·5	0·165	83·5
2	102	472·5	0·216	65·5
3	52	366	0·142	56·2
4	42	307·5	0·137	48·5
5	24	261	0·092	44·0

Malignant Disease in Gynæcology.—This is the subject of a number of good papers in the James Heyman Anniversary Number of *Acta radiologica*.[27] L. Adler[28] reviews the history of treatment of *cancer of the cervix* by surgery and radiotherapy and describes the methods by which he obtained 39·4 per cent survival in the patients treated. P. Jacoby from Odense,[29] V. Kahanpää and J. O. Kankkunen from Helsinki,[30] L. Martindale from London,[31] and H. Swanberg from Illinois[32] using the 1933 Report edited by Professor Heyman all report results of treatment. D. Den Hoed, Rotterdam,[33] E. Peterson, Denmark,[34] and G. I. Strachan, Cardiff,[35] all describe complications which may arise during treatment by radiation of cancer of the uterine cervix. M. C. Tod,[36] Manchester, discusses optimum dosage in the treatment of cancer of the cervix by radiation. Doses are calculated at a designated point A, and the conclusion is reached that with the techniques used which are described the optimum dose level for radium only is between 7500 r and 8500 r in 7 to 10 days. With a combination of radium and X-rays it is between 9500 r and 10,500 r in 4 to 6 weeks. Doses in excess of these suggested are liable to produce a high percentage of high-dose effects.

An excellent informative paper by H. L. Kottmeier[37] records his clinical and experimental observations on radiotherapy in *functional uterine hæmorrhage*. He believes that attempts to produce a temporary amenorrhœa in young patients are seldom satisfactory, and believes that if young patients are sterilized of necessity during the treatment of cancer of the cervix they may have menopausal symptoms several years later. The literature is reviewed and evidence is given that as little as 280 r to the ovary will result in complete sterilization in patients over 40 years and that 650 r given to anterior and posterior fields over the pelvis, the treatment suggested by Forssell, has obtained satisfactory results over many years. Heyman prefers to use intra-uterine radium conveniently introduced at the time when the necessary dilatation and curettage is carried out. A careful study has been made of the dose distribution from intra-uterine radium, and measurements made at laparotomy show that with 650 mg.-hours, the dose now preferred by Heyman, the ovaries receive from 350 to 400 r although this dose is not evenly distributed. Finally there is a very full discussion of the effects of sterilization by the different methods available on the secretion of the gonadotropic hormone as measured in the urine, and the degree of ovarian activity is found to be higher in patients treated by radium than in those treated by X rays. It is also concluded that the effect

of radium application upon uterine bleeding is partly produced by its effect on the endometrium.

Benign Conditions

There is little that is new in the *treatment of benign conditions* by radiotherapy. M. Riebeling[38] writes from Mexico, where the disease is very prevalent, on the treatment of *external infections due to B. anthracis*: 36 cases with local lesions were treated, 20 of them complicated by systemic manifestations. Treatment was by means of small doses of radiation given as often as every 12 hours if the patient was very ill. In less acute cases doses of 85 r were given every 2 or 3 days. An immediate response was always obtained and all the cases treated recovered.

J. F. Kelly, D. A. Dowell, and J. E. Dowling[39] discuss the *evolution of rational dosage in the prevention and cure of infections*. They conclude that if the best results are to be obtained radiotherapy must be begun at an early stage, and that no patient should be allowed to die of a bacterial toxæmia without receiving the benefit of X-ray therapy.

The treatment of *angioma* is the subject of a comprehensive paper by Simone Laborde.[40] She points out the need for care because of the effects on the underlying tissues, particularly in the neighbourhood of the epiphyses. A large number of photographs show the great success she has achieved in the treatment of these lesions, and she proposes a minimum dose obtained by radium application which can be counted on to give the best cosmetic result.

Folke Jacobson[41] describes the treatment of *keloids* at the Radiumhemmet, 1921–41. The material comprises 625 cases, many caused by vaccination for small-pox. The main treatment has been the application of radium in flat containers, and the dose has been counted as an average dose at 1 cm. tissue layer and has varied between 600 r and 1200 r. Very large lesions should be treated with X rays because the dose will then be more uniform. A satisfactory result is obtained in about 74 per cent of the smaller lesions which have not been present for a very long period.

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RAT-BITE FEVER.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Rat-bite fever may arise from two distinct infecting agents. Not all cases are due to rat-bites, and in the absence of a clear history, bacteriological evidence is alone conclusive. Infection with *Spirillum minus* (originally called *Spirocharta morsus muris* by its Japanese discoverers in 1916–17) is the commoner variety and many cases are on record. Diagnosis is made by observing the spirillum in thick blood-films. The incubation period is seven days or more. The rarer variety is due to *Streptobacillus moniliformis* (Levaditi), first described by Schottmüller in 1914 and classified by him as a streptothrix. Diagnosis is made by blood-culture. The incubation period is short (three days or more). Penicillin treatment is rapidly effective in both varieties. A case of the streptobacillary type in a laboratory worker is described by L. R. W. Lominski, A. S. Henderson and J. W. McNee.[1] Severe febrile illness with a rash on trunk and limbs developed forty-eight hours after the bite of a hooded rat. Treatment with penicillin was completely successful, the disease being cured at once.

Reference.—[1]*Brit. med. J.* 1948, **2**, 510.

RECTUM, CARCINOMA OF.

W. B. Gabriel, M.S., F.R.C.S.

Many new papers are available for study this year, and almost every aspect is well covered by new and interesting papers containing a wealth of detailed information, with statistics on operability rates, operative mortality, and end-results.

Diagnosis.—R. J. Jackman, H. A. Neibling, and J. M. Waugh[1] are impressed with the large number of patients who continue to be seen with carcinoma of the large intestine and yet have been receiving treatment for some other supposed condition, with delay in establishing a correct diagnosis. Out of 817 patients studied, 634 (or 77·6 per cent) had carcinomas situated in the rectosigmoid, rectum, or anal canal, and in 444 of these the growth was palpable with a finger, either directly or as an extra-rectal mass. Yet of these 444 cases no less than 102 (or 23 per cent) had received treatment for some other alleged condition; for instance 42 patients had undergone surgical treatment for hæmorrhoids and 4 of these had been operated upon twice, 35 patients had been injected for piles, 4 had been operated upon for fissure, 4 for fistula, and 4 others for some other form of anorectal operation. Three patients were wrongly treated for colitis, 3 for amœbiasis, and 7 others had received electrical or palliative treatment for hæmorrhoids. A further group of 132 patients had rectosigmoid lesions which were visualized on sigmoidoscopy, and of these 34, or 25·8 per cent, had received some other treatment previously, either surgical or medical, while the carcinoma was missed. It appears, therefore, from this important analysis, that 1 in every 4 of these cases of carcinoma of the rectum and rectosigmoid had received unnecessary previous treatment when the growth was all the time within easy reach by ordinary clinical methods.

In a Chairman's address to the Section of Gastro-Enterology and Proctology of the American Medical Association, Martin S. Kleckner[2] spoke of the importance of a thorough training in general surgery, particularly in the surgery of the colon, for those who intended to specialize in proctology. He referred to the need for taking a proper history and for thorough physical examination, not only of the rectal lesion itself, but of the area above it by sigmoidoscopy, and in addition a barium enema examination was frequently required. He then proceeds to analyse 441 cases of cancer of the large bowel. Change of bowel habit was the earliest symptom (64 per cent), next came bleeding (22 per cent), and tenesmus (7 per cent). The time interval between the first symptom and medical consultation was appalling, seeing that out of 304 cases investigated 259 delayed for over six months and 142 for over one year. A considerable lag of time also took place before the patient was referred by the general practitioner to a specialist, and out of 189 investigated there was a delay of over one year in 70. Diagnostic and therapeutic errors took place in 100 out of 441 cases, or 22·7 per cent: 25 cases were given medical treatment for colitis, constipation, etc.; 75 cases received unnecessary surgical treatment, and among this group more than half (42) were wrongly treated for hæmorrhoids.

T. Hendelberg[3] states that although in older patients, in what is known as the cancer age, the possibility of acute peritonitis being due to perforation of a cancer is usually kept in mind, in young people little attention is paid to this possibility. He then proceeds to relate the details of 5 patients between the ages of 22 and 34 with cancer of the rectum or descending colon, who were admitted to hospital with acute inflammatory complications such as peritonitis or periproctitis. These cases were seen in the course of five years, and the author concludes that in cases of perforative peritonitis in young people special attention should be paid to the large intestine, and that, in cases of fistula, proctoscopy and biopsy should be done, with X-ray investigation also if necessary. The bibliography of carcinoma of the colon and rectum in young subjects is reviewed.

Pathological Factors.—R. K. Gilchrist and Vernon C. David[4] consider that owing to the difficulty of identifying the rectosigmoid junction on a surgical specimen it is preferable to divide cancer of the rectum into two groups: (1) Those which are partially or completely below the peritoneal reflection; these they classify as extraperitoneal carcinoma of the rectum (112 cases). (2) Those which are entirely covered by peritoneum anteriorly and are below the promontory of the sacrum; these they designate as "intraperitoneal carcinoma of the rectum" (55 cases). Concerning the first group the following two tables are given; it will be noted particularly that in the group of 69 cases with lymphatic metastases 43·5 per cent developed recurrences in less than 5 years, the incidence of local and liver recurrences being striking.

Table I. 112 Extraperitoneal Rectal Carcinomas

	Number	Per cent
Alive 5 to 10 years	58	51·8
Post-operative deaths	12	10·7
Lymph-node metastases present	69	61·9
Of 69 with node metastases alive 5 years ..	26	37·5
Of 43 without node metastases alive 5 years	32	74·4

Table II.— 112 Extraperitoneal Rectal Carcinomas

Recurrence	69 with Node Metastases		43 without Node Metastases	
	Number	Per cent	Number	Per cent
Local	16	23·2	2	4·6
Liver	11	15·9	2	4·6
Lung, bone, general	3	4·3	2	2·3
Total	30	43·5	5	11·6

The favourable prognosis in this group, especially in those without lymph-node metastases, is evident. Retrograde metastases to nodes 1 to 5 cm. below the tumour occurred in 7 out of 153 tumours below the sacral promontory. Post-mortem examinations have shown that the ordinary methods usually fail to show outlying metastases and the authors consider that the widest possible resection is indicated particularly in carcinomas below the peritoneal reflection; here the Miles operation gives the best chance of cure. Further, in lesions above the peritoneal reflection, where the tumours are large or have palpably enlarged lymph-nodes, abdomino-perineal excision will give a greater chance of cure as compared with resection and end-to-end anastomosis.

Relationship to Fistula-in-ano.—In a perusal of the literature I. Skir[5] has found records of at least 50 cases in which cancer has developed in fistulæ, or in scars following operations for fistulæ or abscesses. He finds it difficult in some cases to be certain whether the fistula antedated the cancer, and considers that if a fistula has been present for 10 years or more before malignancy supervened, this arbitrary limit should suffice to eliminate doubtful cases. On this basis he finds that 14 out of the 50 cases collected qualify, and in addition he describes 3 fresh cases, 2 of them in negroes, in which fistulæ of 10, 30, and 55 years' duration respectively developed carcinomatous changes. The growths

were all of the mucinous or colloid type, and the origin of this variety of growth in the perianal tissues is discussed: origin in glandular epithelium in relation to the anal crypts is thought to be the most likely explanation.

Group Statistics.—A very detailed paper with much statistical information is published by E. J. Ottenheimer.[6] His study has been made possible by a remarkable effort by the Division of Cancer Research in Connecticut, whereby duplicate hospital records of all patients suffering from cancer have been made available since 1935. During the 11-year period studied, 1610 patients with cancer of the rectum were admitted into 27 general hospitals; of these only 6 hospitals had more than 100 cases of rectal cancer in the period. Complete follow-up data were obtained in over 97 per cent of cases. Microscopical proof of malignancy was obtained in 1188 cases, while in 422 there was only a clinical diagnosis, and these two groups are separated in many of the subsequent tables. Grading into three grades has been practised. The resectability-rate rose from 46 per cent in the early years studied to 62·4 per cent in 1944, with an average of 52·3 per cent for the entire period. Of the 621 resections performed, 74·6 per cent were one-stage abdomino-perineal operations and 25·4 per cent were done in two stages either by the Lahey method or by colostomy and perineal excision; there has, however, been a striking increase in the one-stage operations during the last three years.

The rising operability-rate has been accompanied by a lowering of operative mortality; for instance, between 1935 and 1940 the operative mortality after one-stage resection was 25·2 per cent, whereas in the last five years in 332 cases it had dropped to 16·5 per cent. The mortality-rate for two-stage operations has tended to rise slightly, being 26·6 per cent for the entire period, and this indicates that this type of operation is now reserved for poor-risk patients. The causes of death are tabulated, peritonitis and shock being the most frequent, and next came cardiovascular failure. Pulmonary embolism accounted for 8·4 per cent of deaths. The 5-year survival- and cure-rates are set out according to different methods of calculation; in the microscopically proved cases 11·5 per cent were cured at the end of 5 years. The suggestion is made that further improvement in results might be possible if the care of these cases could be concentrated in a few centres.

[A very similar figure for the 5-year survival-rate, namely, 11·1 per cent, was recorded in the *British Empire Cancer Campaign Annual Report* for 1946, p. 162, on the basis of 1422 primary cases studied.—W. B. G.]

Surgical Management.—H. E. Bacon and Caleb H. Smith[7] describe the arterial supply of the distal colon, with a coloured chart showing the approved points of arterial ligation in 8 patients in whom the colon was to be mobilized with a view to transplantation to the anus. Familiar names such as Sudeck and Hamilton Drummond occur in this paper, and it is agreed with Drummond that the best place for the ligation of the inferior mesenteric artery is immediately below the first sigmoid artery; in some cases the entire left side of the colon has been excised and the stump of the transverse colon has been brought down to the perineum with its viability maintained by the middle colic artery (*see* p. 87).

R. Russell Best[8] reviews the history of the subject from the time of Littré (1710), and illustrates in particular the method of anterior resection and anastomosis (8 cases); conservative sacral resection and anastomosis after abdominal mobilization and cæcostomy has been performed in two instances, and conservative sacral resection alone in one case. No end-results are given because the cases reported were recent, and so far as sphincter function is concerned it is reported to be adequate and in most cases remarkably satisfactory. The author remarks, however, that the conservative operation is more difficult,

more time-consuming, and with a higher incidence of infection when an awkward anastomosis is attempted; in obese and poor-risk patients abdomino-perineal excision or posterior excision without anastomosis would seem to carry less risk, but even so the author appears to advocate sphincter-preserving operations if the end-results do not vary more than 5 to 10 per cent from the results for abdomino-perineal excision with permanent colostomy.

A. S. Graham[9] gives a carefully considered report on current trends in surgery of the distal colon and rectum, and concludes that the recent transient trend towards sphincter-preserving operations is likely to be short-lived, but that one noticeable trend which will probably be universally accepted is towards the performance of single-stage operations rather than multiple-stage operations for lesions in any segment of the large intestine, i.e., in the colon by immediate anastomosis after resection, and in the rectosigmoid and rectum by a one-stage combined abdomino-perineal excision.

T. E. Jones, J. R. Robinson, and G. B. Meads[10] have reported a series of 137 conservative abdomino-perineal excisions without operative mortality. A statistical analysis is given; 87 per cent had a palpable lesion on digital examination of the rectum and only 13 per cent required a sigmoidoscopy to establish the diagnosis. Routine biopsy is not considered to be necessary. The average stay in hospital after operation was 18·3 days. The one factor which is considered to be chiefly responsible for so few post-operative complications is the use of alloy steel wire through all layers in closing the abdominal wound. The most common and troublesome complications were urinary infection and retention of urine.

F. W. Rankin and C. C. Johnston[11] advocate abdomino-perineal excision as the operation of choice for cancer of the rectum and rectosigmoid and analyse 336 cases of cancer of this region seen during the seven years 1934–41. Abdomino-perineal excision was done in 167 cases, with a mortality of 5·3 per cent. Colostomy and posterior resection was done in 56 cases, with a mortality of 9 (or 16 per cent): this operation is now being done very occasionally and its use is steadily decreasing, whereas the abdomino-perineal excision has been done in 71·7 per cent of the group submitted to some sort of resection.

R. A. Thomas, Philip S. Kline, and L. Seed[12] present an analysis of 844 cases of carcinoma of the rectum and rectosigmoid admitted to the Veterans Administration Hospital, Hines, from 1931 to 1946. In the list of symptoms, bleeding from the rectum occurred in 76·5 per cent of the patients, and in 36 per cent it was the first symptom noted. In the cases dealt with since 1940 the abdomino-perineal excision has been the most frequently performed operation —175 cases, with a mortality of 10·6 per cent. The survival-rate after various types of treatment is described, and it is considered that for inoperable cases adequate radiation does prolong life and that its use as a palliative is justified. After abdomino-perineal excision the 5-year survival-rate (22 cases) was 45·5 per cent, while in a group of 58 cases treated by perineal excision it was 32·1 per cent. A comparison with cases which had no treatment or colostomy only, gave one inescapable conclusion, namely, that a carcinoma of the rectum or rectosigmoid should be resected even in the most adverse circumstances.

Turning now to conservative methods of rectal resection, various new papers are available for study. C. W. Mayo and R. S. Smith[13] have published a critical analysis of 200 cases of low anterior resection for growths situated between 5 and 15 cm. above the anus. An effort was always made to divide the bowel at least 2 cm. below the growth, and the two most important factors in regard to the anastomosis are accurate union of the rectum and pelvic colon and avoidance of tension on the suture line. The operative mortality in the series of 200 cases was 9, or 4·5 per cent, and in 100 cases in which

a colostomy was performed at the time of the resection, the mortality was 3 per cent, and in 100 cases done without colostomy the mortality was 6 per cent. A striking difference between the two series was apparent when hospital morbidity was considered: thus, in the cases without colostomy 82 per cent were out of hospital within one month, and all but one of the 94 were dismissed in less than two months after operation; whereas in cases with colostomy only 4 per cent were discharged from hospital within a month, and only 7 out of 97 patients were dismissed within two months from operation. Owing to the recent completion of these cases survival-rates cannot be given.

H. E. Bacon and R. J. Rowe[14] discuss the management of 560 cases of malignant disease of the sigmoid, rectosigmoid, rectum, and anus; of this number 467 were resected, or 80·1 per cent, with a mortality of 26 (5·5 per cent). Conservative procto-sigmoidectomy by the pull-through technique has been done in 317 patients, with 15 deaths (4·7 per cent). They state that the 5-year cure-rate is 52·6 per cent, which figure includes those done for palliation. That the cases have not been specially selected is shown by a table which includes 47 cases in which resection of other organs was required, such as small intestine, bladder, uterus, vagina, etc. The same authors, in an additional paper,[15] report 4 cases in which carcinoma of the rectum was complicated by pregnancy (one patient being 3 months pregnant at the time of operation and in the other three the pregnancy had terminated a few months earlier). Abdomino-perineal procto-sigmoidectomy was done in all 4 cases, with recovery. The authors have made an exhaustive search of the literature and have collected 35 cases in which a rectal growth complicated by pregnancy was considered to be operable and 24 in which it was inoperable. The types of operation performed are detailed, and the authors give their opinion as to the most suitable procedure according to the stage of the pregnancy: if seen in the last 3 months of pregnancy they recommend Cæsarian section and hysterectomy followed by excision or resection of the growth 2–4 weeks later.

Much statistical material is presented for study in a paper by O. H. Wangensteen and R. W. Toon.[16] During the years 1945 and 1946, 78 per cent of patients with cancer of the rectum and rectosigmoid had some type of radical operation performed: an abdomino-perineal excision was done in 44 cases (56·4 per cent) and a conservative anastomotic operation in 34 cases (43·6 per cent). The rectal function after anterior resection is considered to be much better than it is after the pull-through operation. Conservative procedures are contra-indicated for lesions at 8 cm. or less from the anus, as well as for advanced growths of borderline operability in the rectal ampulla, when abdomino-perineal excision is the procedure of choice. Local recurrence took place in 7 out of 63 conservative resections (14 per cent), but there was no example of local recurrence after resection of lesions between 14 and 20 cm. above the anus, and at this level a conservative operation gives as good a prospect of cure as does abdomino-perineal excision.

The subsequent discussion is illuminating and important. On the one hand we see the remarks of Dr. T. E. Jones, who is a firm advocate of abdomino-perineal excision and in this paper reported a series of 535 operations done between 1942 and 1946 with a mortality of 20 (3·7 per cent); then on the other hand J. M. Waugh of Rochester recorded the opinion that for lesions of which the lower edge is 5 cm. or more above the pectinate line conservative operations are just as curative as the Miles procedure, with a mortality approximately the same. He mentioned a series of approximately 100 pull-through operations with one hospital death, and gave the following Table of 5-year survival-rates after anterior resection:—

Table III.—Anterior Resection (Non-palliative Operation): Five-year Survival-rates for Different Levels (Dr. Dixon's Data)

Distance from Dentate Line	All Cases		No Nodal Involvement		Nodal Involvement	
	Number	5 Yr. Survival-rate	Cases	5 Yr. Survival-rate	Cases	5 Yr. Survival-rate
cm.		per cent		per cent		per cent
6–10	74	63·7	32	72·4	42	57·1
11–15	97	70·2	58	78·8	39	57·7
16–20	101	66·9	60	71·5	41	60·4
All levels	272	67·7	150	74·0	122	58·5

W. F. Nickel and A. I. Chenoweth[17] review the recent literature dealing with conservative resection of the rectum and record their experiences with the Babcock-Bacon 'pull-through' operation in a series of 68 patients operated upon in New York Hospital between 1932 and 1946. Their paper is well illustrated, and the details of the perineal stage are clearly described. The operation mortality was 13·2 per cent. The 9 deaths, however, took place in the years preceding 1941, since when they have had a series of 23 cases without a death; this improvement is due, they consider, to improved anæsthesia and better pre- and post-operative care, particularly increased attention to nutritional requirements and especially proteins and vitamins. The advent of sulphonamide drugs and penicillin has, of course, played a part. The survival-rate in this series is 62 per cent for a 3-year period (61 patients being considered), and 40 per cent for a 5-year period (with 55 patients under consideration). The functional results in 34 patients has been assessed as perfect in 3, good in 7, fair in 10, and poor in 14.

E. G. Muir[18] gives a general review of the present position of excision of the rectum, and describes the essential pathological requirements, particularly in regard to anterior resection and also the 'pull-through' method. In a series of 86 consecutive cases of cancer of the rectum and rectosigmoid he has done a radical combined excision in 49 cases and a conservative resection in 21 (out of 72 cases submitted to some form of resection). There were only 2 deaths in this series. For the conservative resections he believes that a preliminary transverse colostomy lessens the risk of infection and should always be employed. The use of penicillin and sulphonamides has reduced the mortality of all methods of rectal resection to a low figure.

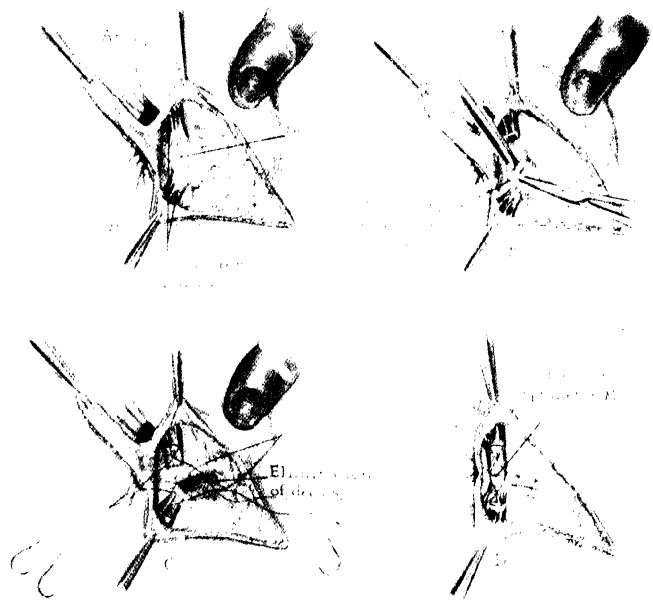
A paper from India on cancer of the rectum is of interest and some striking points are brought out by E. J. Borges[19] of Bombay. First the incidence in the various communities is considered, and it is concluded that cancer of the rectum is fairly evenly distributed among the different communities in India. The sex incidence was in the proportion of 3 males to 1 female. Biopsy is considered to be of great importance in diagnosis and it is mentioned that 19 patients referred with a diagnosis of cancer were proved by biopsy to have inflammatory lesions. Out of 87 cases biopsied, no less than 33 (nearly 40 per cent) proved to be squamous carcinomas, and the author speculates as to the explanation of this very high incidence. The various types of surgical treatment are discussed, and preference is stated for the one-stage abdomino-perineal excision of Miles; out of 113 cases, however, 51 were too far advanced for any sort of treatment, and radical operation could only be carried out in 30, thus giving as the author admits, a distressingly low operability-rate.

References.—[1]*J. Amer. med. Ass.* 1947, **134**, 1287; [2]*Ibid.* **135**, 545; [4]*Acta chir. scand.* 1945, **92**, 339; [4]*Ann. Surg.* 1947, **126**, 421; *Surg. Gynec. Obstet.* 1948, **86**, 359; [4]*Amer. J. Surg.* 1948, **75**, 285; [6]*New Engl. J. Med.* 1947, **237**, 1; [7]*Ann. Surg.* 1948, **127**, 28; [8]*Surg. Gynec. Obstet.*

PLATE XL

REPAIR OF ANAL SPHINCTER

(R. Turell, J. B. Gordon, and Kemp Davis)



A. Appearance of lesion at operation; B. Muscle ends freed, scar excised; C. One needle with suture is passed transversely through belly of muscle about 0·75 cm. from severed end and then each needle is traversed obliquely within the muscle substance so as to emerge on the side at the edge of each severed end, the suture strands at each muscle end are then tied; D. Muscle ends approximated cleanly by tying the suture strands.

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1948, **86**, 98 ; [9]*Ann. Surg.* 1948, **127**, 1022 ; [10]*Arch. Surg., Chicago*, 1948, **56**, 109 ; [11]*J. Amer. med. Ass.* 1948, **136**, 371 ; [12]*Arch. Surg., Chicago*, 1948, **56**, 92 ; [13]*Ann. Surg.* 1948, **127**, 1046 ; [14]*N.Y. St. J. Med.* 1948, **48**, 607 ; [15]*Sth. med. J.* 1947, **40**, 471 ; [16]*Amer. J. Surg.* 1948, **75**, 384 ; [17]*Surgery*, 1948, **23**, 480 ; [18]*Brit. med. J.* 1948, **2**, 286 ; [19]*Indian J. Surg.* 1947, **9**, 121.

RECTUM, INJURIES OF.

W. B. Gabriel, M.S., F.R.C.S.

W. S. McCune[1] gives a detailed description of 41 patients with *wounds of the rectum and anal sphincter*, who were admitted into a special hospital under the direction of Dr. Harry B. Stone. The patients were between the ages of 20 and 36 years, and in all but one case the wounds were due to shell fragments or machine-gun fire. Most of the patients had had débridement of the wounds and a temporary colostomy before admission. After a régime of sphincter and gluteal exercises 11 patients regained adequate sphincter control and the colostomies were closed with satisfactory results. The treatment given to the remaining 30 patients is described : patients with high rectal fistulæ had the tracts excised and a plastic repair carried out ; those with scar involvement of the anal sphincter had a local plastic operation ; and those with complete sphincter loss had a fascial plastic operation as described by Stone, sterile ox fascia being used. Patients with complete sphincter loss and extensive scarring with loss of gluteal function, constituted the most serious group in whom no sphincter repair could be devised. Four out of the seven cases had an abdomino-perineal excision done with conversion of their loop colostomies to terminal colostomies ; this operation got rid of the mucous discharge on to the perineum. Two patients were left with an uncontrolled perineal colostomy, and both were, on the whole, disappointed and might need abdomino-perineal resections later.

R. Turell, J. B. Gordon, and K. Davis[2] record a method of *repairing the external sphincter ani* by excising intervening scar tissue and then suturing the muscle ends together with No. 0 catgut on atraumatic needles by the Bunnell method. A few interrupted sutures are put into the tissues deep to the muscle in order to obliterate any dead space and take tension off the sphincter muscle. The subcutaneous tissues are approximated with interrupted sutures and the skin is left unsutured. Sulphonamide and antibiotic therapy is employed before and after operation. They consider that the advantage of this method is that it avoids strangulation of muscle-fibres by the sutures. (*Plate XL.*)

Closure of Colostomies.—Somewhat related to the question of injuries to the rectum is the subject of closure of colostomies. A paper on this subject by Roettig, Glasser, and Barney, was reviewed in the MEDICAL ANNUAL for 1948, p. 292. The present paper, by C. S. Hertz and D. H. Poer[3] deals with 32 patients who were admitted to hospital for closure of colostomies or large bowel fistulæ following gunshot wounds. Many useful details of management are described, and the authors stress the importance of pre-operative care, particularly in regard to diet, mechanical cleansing of the bowel to get rid of inspissated mucus in the distal loop, and chemotherapy with sulphathalidine. The method of closing a colostomy by suture is described ; after closure of the opening into the colon by two rows of sutures, the authors advise opening the peritoneum and replacing the bowel into its normal position within the peritoneal cavity ; they believe that this is an important step in preventing a post-operative incisional hernia. In some cases where it was not considered safe to use an enterotome, an open intraperitoneal suture was done, either by simple transverse suture or by a standard anastomosis either end-to-end or side-to-side. In all the cases the abdominal wall was closed without drainage and all healed without infection developing.

REFERENCES.—[1]*Surgery*, 1948, **23**, 653 ; [2]*Amer. J. Surg.* 1948, **76**, 89 ; [3]*Ibid.* 1947, **74**, 163.

RECTUM, MUCOSAL POLYPS OF.

W. B. Gabriel, M.S., F.R.C.S.

G. E. Binkley and D. A. Sunderland[1] describe the clinical and histological characteristics of three types of benign adenomatous tumours: (1) areas of hyperplasia, (2) adenomas, and (3) papillary adenomas.

Papillary adenomas are soft and spongy, usually single, sessile, and varying in the thickness of the villous processes; they can be divided into four groups: (*a*) tumours that are clinically and microscopically benign; (*b*) those which show atypical changes microscopically; (*c*) those in which there are islands of adenocarcinoma; (*d*) fully developed infiltrating carcinoma with areas of benign tumour still remaining. The treatment according to the stage of the lesions is described. Radiation therapy is reserved for cases of incomplete removal. Radical excision of the rectum is needed when the disease is not controlled by local treatment or when induration is noted at the base of the tumour and also when adenocarcinoma has clearly developed. All patients treated conservatively need very careful observation subsequently, since there is a marked tendency for those tumours to recur; malignant change is frequent in recurrent tumours.

[In this paper the term "papillary adenoma", from the description and illustrations, appears to be identical with what is usually known in this country as a villous tumour or villous papilloma.—W. B. G.]

Further points in the diagnosis and treatment of mucosal polyps of the rectum are made by N. W. Swinton.[2] He considers that the majority of polypi in this region are adenomatous and must be considered to be pre-malignant lesions. The incidence of mucosal polyps in the adult population is much greater than has been previously suspected; for instance, N. W. Swinton and A. D. Haug[3] in a series of 1843 autopsies found benign mucosal polyps in 311 cases, or 7 per cent, and L. C. Helwig[4] in a large autopsy series reported an incidence of 9·5 per cent. For the detection of mucosal polyps in the rectum and colon it has been shown that over 50 per cent are within the reach of a 10-inch sigmoidoscope; the mere detection of a polyp is easy, but it requires much skill and experience to determine the presence and extent of malignant change and the type of treatment indicated. A series of 22 cases is reviewed in which the diagnosis of malignancy was made sufficiently early to enable local excision or destruction of the polyp to control the disease. The histological criteria of malignancy are discussed, together with the important points in the clinical estimate of malignant change such as induration, ulceration, and fixity of the tumour. The subsequent recorded discussion is of interest, particularly in regard to the essential service of a pathologist skilled in this branch of work, and also the importance of a careful 3-monthly follow-up of patients who have had a polyp removed.

J. R. Colvert and C. H. Brown[5] give a statistical study of 235 cases of rectal polyps; a follow-up for 5 or more years was done in 174 cases. The incidence of polypi in routine proctoscopic examinations was only 2·3 per cent. Patients with rectal polyps rarely have symptoms referable to the polyps, hence a routine rectal examination should be considered an essential part of a gastro-intestinal examination. Barium enemas, particularly by the double contrast method, are considered to be of great importance in the diagnosis of colonic polypi. Ulceration recurred 7 times as frequently in malignant polypi as in a similar number of benign polypi. Of the 16 malignant polyps that were found, none had a malignancy higher than Grade II. The conclusion is reached that malignancy either starts very early in rectal polyps or is present from the start, and the prompt removal of rectal polyps in this group of cases resulted, without major surgery, in a 5-year cure in 13 out of 14 patients with malignant change.

H. E. Bacon and G. G. Broad[6] have published a paper which deals with many important points in the incidence and pathogenesis of adenomatous polyps and their relation to malignancy of the large bowel. A carcinoma which develops from an adenoma is usually of a low grade. The literature is reviewed, and the findings of many independent investigators indicate the following five factors which point to a close relationship between intestinal adenomas and malignancy :—

1. Intestinal adenomas develop into the malignant state in a significant proportion of cases.
2. The similarity in respect to the age incidence between adenomas and carcinomas.
3. The similarity in respect to their location in the sigmoid colon and rectum in the majority of cases.
4. The frequent co-existence of both benign and malignant processes in the same individual.
5. The feature of multiplicity of adenomas and carcinomas.

The irresistible conclusion is that intestinal adenomas should be considered as pre-malignant lesions and should be treated by destruction or removal in all instances.

REFERENCES.—[1]*Amer. J. Surg.* 1948, **75**, 365 ; [2]*Ibid.* 369 ; [3]*Lahey Clin. Bull.* 1947, **5**, 84–8 ; [4]*Surg. Gynec. Obstet.* 1947, **84**, 36–50 ; [5]*Amer. J. med. Sci.* 1948, **215**, 24 ; [6]*Rev. Gastroenterology*, 1948, **15**, 284.

RECTUM, PROLAPSE OF.

W. B. Gabriel, M.S., F.R.C.S.

T. G. Orr[1] discusses the aetiology of complete rectal prolapse and considers that it is primarily a developmental defect, namely, an abnormally loosely attached rectum with a deep peritoneal cul-de-sac, which predisposes to a hernia. He describes an abdominal operation in which two strips of autogenous fascia lata are sutured to each side of the rectum ; the strip on the left side is passed through a puncture made through the base of the pelvic mesocolon, and with the rectum held suspended both fascial strips are firmly sutured to the dense fascia above the promontory of the sacrum. Finally the peritoneal cul-de-sac is obliterated by two or more rows of interrupted silk sutures and a fold of peritoneum is sutured to the front of the rectum on each side in order to cover the fascial strips. Case reports of 4 patients treated by this method are given.

H. T. Hayes and H. B. Burr[2] in discussing the treatment of complete prolapse of the rectum, mention 2 cases in which an abdominal operation was carried out, and Roscoe Graham's method was attempted but proved to be technically impossible ; therefore instead of suturing the levatores ani together in front of the rectum as recommended by Graham, they brought the lateral ligaments across and sutured them together in front of the rectum with one or two linen sutures. This prevented the anterior rectal wall from prolapsing through the defect between the levatores, and the operation was concluded by obliterating the peritoneal pouch and also by carrying out a sigmoidopexy in the left iliac fossa in the standard fashion after raising a peritoneal leaf. Finally a rectal tube was passed up from below into the rectum and sigmoid and left in situ for three days. A complete cure resulted in both of these cases and no plastic operation was required on the sphincter muscles.

J. E. Dunphy[3] describes a combined perineal and abdominal operation, for which, he states, he claims no originality. First a rectosigmoidectomy is carried out and the levatores ani are sutured together in front of the rectum ; the bowel suture is done with the aid of four stay sutures and then each quarter segment is approximated by a continuous blanket stitch of fine catgut. The abdominal operation is done as a separate procedure some days later, and

consists essentially of a Moschcowitz procedure to obliterate the pouch of Douglas plus a colopexy to the left lateral wall of the pelvis. The results in 4 cases have been gratifying, the period of observation varying from 4 months to 1 year 8 months.

REFERENCES.—[1]*Ann. Surg.* 1947, **126**, 833; [2]*Amer. J. Surg.* 1948, **75**, 358; [3]*Surg. Gynec. Obstet.* 1948, **86**, 493.

RECTUM, STRICTURE OF.

W. B. Gabriel, M.S., F.R.C.S.

M. Popesco-Urlueni and C. Axente,[1] of Bucharest, discuss in great detail the pathology and clinical aspects of lymphogranulomatous strictures of the rectum. The virus of Nicolas and Favre's disease has a great predilection for the lymphatic system, and in the production of rectal strictures the primary inoculation may be either intrarectal or intravaginal, the latter being much more frequent. The problem, however, is very complex, and it is suggested that there is a close connexion between the virus of lymphogranuloma and Ducrey's bacillus, possibly with another microbe. Whichever the point of inoculation, rectal or vaginal, the lesion always begins at the level of the rectal mucosa and from there extends outwards.

Treatment is discussed, and the authors refer to the well-known paper of Gatellier and Weiss (1934), who condemned surgical treatment on the grounds that it led only to recurrence or incontinence. The usual lines of medical treatment are described: a left iliac colostomy has previously been considered to be indispensable for overcoming increasing rectal stenosis, for putting the rectum at rest, and for giving perineal abscesses and fistulæ a chance to heal. Considering surgical treatment, the authors believe that the bad results of surgery, as propounded by Gatellier and Weiss, who had 90 per cent failures, were due to the fact that the operations as then performed were all of the low perineal type. Unless the upper part of the excision reaches healthy tissues recurrence is certain. Neither rectoscopy nor X rays can be relied upon to define the upper limit of the intestinal infiltration, and therefore abdominal exploration is essential to decide upon operability and the type of resection required. The authors quote Dimitriu, who in 110 cases explored found that only 3 were suitable for a perineal operation. In doing a rectocolic resection the authors made the following test: they marked the upper limit of the infection as tested macroscopically and then subsequently by means of serial sections the microscopical limit was determined; they showed that the macroscopical test was wrong by 3 to 4 cm.

The principles of surgical treatment are next set out, and the necessity for a wide, complete excision of the diseased part is emphasized. In 31 cases the methods employed were as follows: 5 perineal resections, 22 abdomino-anal resections, and 4 colostomies. Various technical details of abdomino-anal resection are discussed, one point being that no attempt is made to excise elephantiasis of the anus or vulva, nor to open up fistulous tracts; all these will get well spontaneously. A Whitehead approach is made, and finally the rectum, which may be very thick from the accompanying periproctitis, is mobilized and brought down. The colon is sectioned approximately 10 cm. beyond the anus, and the perirectal space is drained by two rubber tubes placed one on each side between the new rectum and the sphincter. Post-operative care is described, and complications listed are prolapse, cicatricial stenosis, and incontinence. Recurrence does not actually take place and what is called recurrence is actually continuation of the disease due to an inadequate surgical intervention. As to results, out of 5 intrasphincteric perineal resections there was 1 operation death, 2 resulting cures, and 2 recurrences. Out of 22 abdomino-anal pull-through operations there were 2 deaths, and 18 perfect results, 13

being between 5 and 8 years after operation. Two patients developed cicatricial strictures at the level of the anus following sloughing of the exteriorized colon: this accident happened in two cases in which the colon had been sectioned too close to the anus and this decided the authors to leave a longer amount outside in future. The patients with stricture are in good health and attend for dilatation. The writers conclude that surgical treatment correctly applied cures the condition, with anatomical and functional restoration.

REFERENCE.—[1]*J. Chir.* 1947, **63**, 363.

REITER'S DISEASE. *Una Ledingham, M.D., F.R.C.P.*

This syndrome continues to excite interest, and though the aetiology remains uncertain, the clinical pattern becomes increasingly plain. Pinck[1] describes fully 12 cases seen personally in two years. All were young males suffering the classical triad of urethritis, conjunctivitis, and arthritis. Diarrhœa, often described as a preliminary finding, had preceded the onset in 1 case only. Superficial lesions of the penis occurred in 3 cases. No case showed spread to the upper urinary tract, but in 3 the prostate was involved. Urethritis appeared first in three-quarters of the cases, followed by conjunctivitis and arthritis. The infection was moderate, but of frankly purulent type, and though the acute stage was short there was a tendency to relapse. Arthritis proved the most serious aspect of the illness. The onset was with sudden fever, leucocytosis, raised E.S.R., and migratory polyarthritis. Affected joints were hot, red, tender, and swollen, and knees and ankles were commonly involved. Aspiration (5 cases) gave serous fluid containing little protein but many cells. Cultures were always sterile. Improvement was slow and no case recovered under three months, some persisting longer. As usual no causative organism was recovered. This author's experience suggests that the disease is more common than usually thought. He emphasizes that the aetiology remains obscure, the course long, relapse frequent, and that no definite treatment is yet available.

Young and McEwen,[2] on the other hand, regard the disease as a complication, possibly allergic in nature, of bacillary dysentery. They describe 14 cases of arthritis following dysentery, half of which had also conjunctivitis and urethritis, thus qualifying for Reiter's diagnosis.

Baines[3] holds still different views, and draws comparison with abacterial pyuria. While agreeing that treatment is generally unsatisfactory, he maintains that the local urethral condition responds to N.A.B. An attempt to determine aetiology was made by Dunham et al.[4] They prepared a filtrate of allantoic fluid previously contaminated with material from the urethral and conjunctival discharges of a classical case of Reiter's disease. This filtrate was injected intraperitoneally into 40 mice, 60 per cent of which developed conjunctivitis, all the 20 controls escaping.

REFERENCES.—[1]*Amer. J. med. Sci.* 1947, **214**, 76; [2]*J. Amer. med. Ass.* 1947, **134**, 1456; [3]*Brit. med. J.* 1947, **2**, 605; [4]*J. Urol.* 1947, **58**, 212.

W. Yeoman, M.D.

The syndrome arthritis, conjunctivitis, and urethritis, commonly known by the name of one of the observers who published a series of cases, has come into prominence in recent years and cases have been reported from all over the world. Paronen[1] has now collected all the references on the subject and reports on 344 cases, the majority of which followed an outbreak of Flexner's dysentery on the Karelian Isthmus in 1944; 70 per cent of the cases showed the complete triad of the syndrome, and 97·3 per cent had articular manifestations. Earlier reports suggested that the disease was confined to men, but in this series 34 women and 4 children were affected. Complete investigations confirmed previous reports that venereal disease is not a causative agent in

the urethritis ; 74 cases of pleurisy and 23 cases of carditis were other complications noted, but there was no reason to suppose that either the heart or lungs suffered permanent damage.

Isolated cases appear in this country, and the condition should be borne in mind when dealing with a case of polyarthritis of sudden onset. It is necessary to differentiate between Reiter's syndrome, where the polyarthritis is the prominent feature, rheumatic fever, and rheumatoid arthritis.

Prognosis is good as regards immediate recovery and no permanent impairment of function in the organs affected need be anticipated. Treatment is symptomatic and none of the treatments had any effect on the natural course of the disease, which appears to be self-limiting.

REFERENCE.—[1]*Acta med. scand.* 1948, **130** (suppl.).

RENAL DISEASES. (*See also* NEPHRITIS IN TEXTILE WORKERS.)

Robert Platt, M.D., F.R.C.P.

To the serious student of renal physiology and pathology, undoubtedly the most important work in recent years is Gamble's book on the *chemical anatomy of extracellular fluid.*[1] Much of the material which the author uses is based on the work of others such as Peters, Darrow, and Newburgh, but nowhere else is this information so attractively, fully, and clearly presented. Many points of practical importance in renal disease emerge from studies of this kind. For instance the osmotic work done by the kidney in excreting urea is greatly lessened by increasing urinary volume and by increasing the blood-urea, both of which changes occur naturally in chronic renal disease. Restriction of protein intake will lessen the load still further, but salt restriction will act adversely since salt will then be conserved by maximum reabsorption from the glomerular filtrate, a process requiring energy on the part of the tubule cells. Another important lesson is that there are two causes of the acidosis so common in advanced renal disease ; the retention of anions such as HPO_4 and SO_4, and the loss of sodium and other bases in an attempt to excrete acids by a kidney which has lost much of its power to produce a highly acid urine or to synthesize ammonia.

Another book which requires mention is Addis on *glomerular nephritis,*[2] an interesting work largely devoted to three subjects : experimental work on removal of portions of the kidney in rats, in which Addis and his co-workers showed that the rats on a low-protein diet lived and maintained health for a longer period than others given diets rich in meat ; a description of the author's rapid methods of assessing the pathological and chemical state of renal patients by tests which can be used in an out-patient department ; and a plea for low-protein diets in all cases of renal insufficiency. *Diet in renal disease* has been subject to a good deal of pendulum action during the last few decades. The old protein restriction was shown to be harmful in many cases of renal œdema with massive albuminuria and low plasma protein, and many authors started to treat all renal cases on high-protein diets. Quite recently Vagn Mortensen[3] has claimed that cases of acute (scarlatinal) nephritis recover at least as quickly on a high-protein as on a low-protein diet, but not all observers would agree with such a conclusion. In œdematous (Type II) nephritis, high-protein low-salt diets are still mostly in use, but in chronic renal failure most authors now advocate a low-protein intake with adequate salt. Borst[4] treats uræmic cases on a high-calorie salt-free diet of butter and sugar followed by a more permanent low-protein diet consisting largely of rice, flour, butter, cream, sugar, vegetables, and fruit. He claims that many such patients can maintain an active life on only 25 g. of protein per day provided that total calories are adequate. Lippmann and Persike[5] have treated 21

uræmic cases on a diet containing 0·5 g. of protein per kilo of body-weight per day to which was added an amount of protein equal to that lost in the urine. They also stress the desirability of providing an adequate calorie intake and about 3 litres of fluid daily. According to these authors when such a diet was given the clinical condition of most of the patients improved remarkably within a few days, the serum urea was reduced, and to a less extent the serum creatinin. As far as possible the patients were treated as out-patients and many of them were able to lead relatively normal lives despite azotæmia and anæmia. The anæmia was treated when necessary by transfusion of concentrated red cells. Before leaving the subject of diet it is interesting to note that Nielsen and Bang[6] confirm an observation which has been made by others that on a diet poor in protein the urea clearance falls. They show that although this is the case, the inulin clearance, and therefore the glomerular filtration rate, falls to a much less extent. The fall in urea clearance is therefore probably not a factor which need be taken into account in considering the effect of low-protein diets.

Davson, Ball, and Platt[7] describe two types of *renal lesions in periarteritis nodosa*. The first type is a widespread necrotizing glomerulitis, and these cases are liable clinically to terminate in uræmia without hypertension. In the second type there is evidence of either active or healed periarteritis nodosa involving larger branches of the renal artery. Many of these cases have had severe hypertension during life. The authors consider that the characteristic glomerular necrosis which they describe in the first group can be distinguished from other types of renal lesion such as focal embolic nephritis, Type I nephritis, or malignant nephrosclerosis, and in most of their cases the clinical course was quite unlike that of any known form of nephritis.

The treatment of certain urinary infections by streptomycin has received further attention. Carroll, Allen, and Doubly[8] have particularly studied infections by *Pseudomonas æruginosa* (commonly called *Bacillus pyocyaneus*), as these are usually resistant to treatment by mandelic acid, sulphonamides, and penicillin. *Pseudomonas* infection of the urinary tract can be a serious condition and may arise as a complication of other disorders of the urinary tract or as a result of catheterization and surgical treatment. The infection is often accompanied by severe symptoms such as fever with rigors and dysuria. Ulceration of the mucous membrane of the bladder may occur. *In vitro* studies showed that the effectiveness of streptomycin varied with the reaction of the medium and was greatest at *p*H 7·6. This is a practical advantage, as the organism tends to produce a highly alkaline urine, which is the reason why mandelic acid is rarely effective; 39 patients were treated, and it was found that if the organism were sufficiently sensitive to streptomycin *in vitro* clinical response was satisfactory, but highly resistant strains occur and may readily be induced by insufficient dosage of streptomycin. It is therefore important to treat patients adequately from the commencement; 3 g. of streptomycin daily for seven days was used by these authors. In cases where the organism was resistant to streptomycin, mandelic acid treatment was successful if a urinary acidity of *p*H 5·5 could be obtained.

A number of further attempts have been made to *dialyse the blood in uræmia* by peritoneal irrigation and by the artificial kidney. These methods were referred to in this article last year. It must be confessed that the reviewer is not impressed by the result of these methods, but this is partly because they cannot be expected to produce permanent benefit in chronic and advanced renal failure, and because the few cases in which recovery from acute anuria has occurred might well have recovered spontaneously. Using Kolff's artificial kidney, Bywaters and Joekes,[9] and McLean, Ripstein, de Leeuw, and Miller[10]

record their experiences. The former authors have had some trouble with pneumonia, œdema, sepsis, and one subdural hæmorrhage, presumably due to the heparin which has to be used in this method. Their cases included two of acute glomerulonephritis with uræmia, neither of which was successful. Two out of 12 cases recovered, one suffering from post-traumatic and the other from post-operative anuria. Alwall,[11] and Alwall and Norvitte,[12] describe a new type of artificial kidney which has considerable advantages in being able to dispense with the rotating couplings used in the Kolff apparatus. Heparin dosage can thus be reduced. Murray, Delorme, and Thomas[13] also describe a new apparatus. All of these act on the principle of dialysis through a cellophane membrane.

Accounts of attempts to dialyse the blood by peritoneal irrigation come from Reed,[14] Buckley and Scholton,[15] and Grossman, Ory, and Willoughby.[16] It is clear that dialysis of this type removes a considerable amount of urea from the blood and materially reduces the blood-urea and non-protein nitrogen. In successful cases dialysis can be continued for many days, but there are always present the dual dangers of sepsis and of producing disturbances in the composition of the extracellular fluid. Very few successful results have been recorded, but that is partly for the reasons already given, namely, that many cases are unsuitable for this kind of treatment. At present in cases of acute uræmia with anuria in which life is threatened peritoneal irrigation would seem to be the most practical method of attempting artificial purification of the blood.

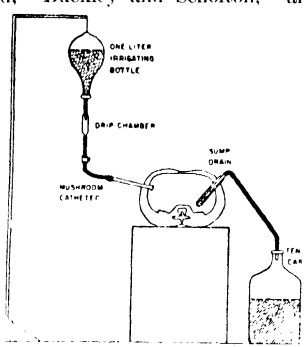


Fig. 53.—Diagram of peritoneal irrigation system. (*Reproduced from the 'Journal of the American Medical Association'.*)

The method consists essentially in inserting a tube through a small incision into the peritoneum. Another tube equipped with a sump and drain is put in on the other side of the abdomen (*Fig.* 53). The solution used for dialysis is usually a modified Tyrode's solution to which may be added glucose, sodium bicarbonate, heparin, penicillin, and streptomycin.

REFERENCES.—[1]*Chemical Anatomy of Extracellular Fluid*, Harvard University Press, Cambridge, Mass., 1947; [2]*Glomerular Nephritis*, Macmillan, New York, 1948; [3]*Acta med. scand.* 1947, **129**, 321; [4]*Lancet*, 1948, **1**, 824; [5]*Arch. intern. Med.* 1947, **80**, 579; [6]*Acta med. scand.* 1948, **130**, 382; [7]*Quart. J. Med.* 1948, **18**, 175; [8]*J. Amer. med. Ass.* 1947, **135**, 683; [9]*Proc. R. Soc. Med.* 1948, **41**, 411; [10]*Canad. med. Ass. J.* 1948 **58**, 433; [11]*Acta med. scand.* 1947, **128**, 317; [12]*Ibid.* suppl. 196, 250; [13]*Arch. Surg.* 1947, **55**, 505; [14]*Proc. R. Soc. Med.* 1948, **41**, 409; [15]*New Engl. J. Med.* 1947, **237**, 431; [16]*J. Amer. med. Ass.* 1947, **135**, 273.

RETICULOSIS.

Una Ledingham, M.D., F.R.C.P.

The war continues against the old enemy *Hodgkin's disease and allied primary lymphadenopathies*. It is waged chiefly on the therapeutic front and little has been added to our knowledge of causation or clinical findings. Relationship between these diseases and lymphatic leukæmia and lymphosarcoma is recognized, but many atypical cases are seen falling outside precise diagnosis. Bodley-Scott[1] remarks that the therapeutic aims are to destroy pathological tissue and to maintain general health. *Radiotherapy*, though only palliative, still holds first place and much symptomatic improvement is achieved thereby. However, it is doubtful if permanent benefit derives, and the discouraging fact emerges that there is little evidence that life is prolonged by such treatment.

The use of *nitrogen mustard* is steadily increasing, especially for the radio-resistant case. It is clear that in Hodgkin's disease the drug brings about effective even if temporary remission. Cure, however, is not yet in sight. In the United States there is more enthusiasm. Winthrobe et al.[2] report notable improvement in a wide range of diseases including Hodgkin's disease, lympho-sarcoma, and leukæmia. All workers agree that pain and thrombosis at the injection site are frequent and that systemic toxic reactions must be expected. In the peripheral blood an early fall of lymphocytes is followed by neutropenia, platelet reduction, and anæmia. If the drug is proceeded with, a complete aplasia follows. Details of dosage and the method of administration are given in these papers and experiments with an orally effective preparation are in train.

Giant Follicular Lymphadenopathy (Lymphoid Follicular Reticulosis) is attracting notice and its specific nature becoming more clearly defined. Relatively few cases are reported, but the erroneous diagnosis of Hodgkin's disease must account for many more. The responsibility for accurate diagnosis rests with the histologist. Rubenfeld[4] assumes the disease to be a precursor of many better known states. Either the original morphology persists, or, more usually, and sooner or later, alteration occurs and transformation into lymphatic leukæmia, lymphosarcoma, or other types of sarcoma takes place. This mutation comes about when the follicles rupture and abnormal cells escape into the gland substance. The power of mutation is considered as inherent property of the disease. Nineteen cases are reported, half of which were in the early stage, the others exhibiting sarcomatous progression. The dominating clinical feature was localized enlargement of superficial lymph-glands, indistinguishable from those of other reticuloses. Skin lesions were seen in 5 patients, and loss of weight, weakness, and a variety of symptoms in others, though general health was remarkably good. Leucopenia persisted in 4 cases. The results of radio-therapy accorded with the histological grouping. The glands in giant follicular lymphadenopathy regressed rapidly with relatively small doses, but where sarcomatous alteration had occurred the masses were much more resistant. Trebled doses were needed and a slower and smaller regression achieved, sometimes only after a latent period. Results were encouraging, with 60 to 66 per cent of patients remaining well for five or more years. Variability in radio-sensitivity previously reported may be explained by this conception of the disease. *Radio-isotopes* are already in use, and it will be interesting to know what improvements can be accomplished.

REFERENCES.—[1]*Proc. R. Soc. Med.* 1947, **40**, 617 ; [2]*Ann. intern. Med.* 1947, **27**, 529 ; [3]*J. Amer. med. Ass.* 1948, **137**, 849.

RHESUS FACTOR : CLINICAL APPLICATIONS.

P. L. Mollison, M.D., M.R.C.P.

Rh Antigens. Although our knowledge of the Rh system of antigens is still growing rapidly, there is fortunately only one antigen, D, which need be taken into account by the clinician.[1] This is the antigen which is concerned in almost all cases of Rh incompatibility. People can be satisfactorily classified as Rh-positive or Rh-negative by simply testing their erythrocytes against an anti-D serum : the majority (83 per cent) give positive reactions and are called Rh-positive ; the remainder (17 per cent) are Rh-negative. In passing, it may be noted that Rh antigens are inherited from each parent, and everyone inherits either D or its allele d from his father and D or d from his mother. Thus Rh-positive people may have a single or double dose of D, i.e., they may have the antigenic constitution DD or Dd ; Rh-negative people have the antigenic constitution dd, and these are the only people who can get immunized to the Rh factor (D) and produce anti-Rh (anti-D).

It may be very important to know whether a man is DD or Dd, because in the former case he is bound to hand on D to all his children, whereas if he is Dd he will sometimes hand on d and thus, although Rh-positive himself, may father a Rh-negative child.

Rh and Pregnancy.—A Rh-negative woman, if pregnant with a Rh-positive fœtus, may become immunized to Rh, presumably by the passage of minute amounts of blood from the fœtus across the placenta; anti-Rh can then be detected in her serum. This antibody in turn passes across the placenta and causes damage to the fœtal erythrocytes, setting up a hæmolytic anæmia; the clinical manifestations of this are described below.

A Rh-negative woman carrying a Rh-positive fœtus for the first time only rarely forms anti-Rh, perhaps only once in 200 or 300 times. (This rule does not apply if the woman has previously been transfused with Rh-positive blood – *see below.*) The second Rh-positive fœtus, however, immunizes about 1 in 12 of Rh-negative women. This does not mean that 1 in 12 of all Rh-negative women become immunized in their second pregnancy, because, of course, some will be married to Rh-negative husbands and others will be married to heterozygous (Dd) husbands and thus have some Rh-negative children. Some women may only become immunized after having 3 Rh-positive infants, or may even has as many as 5 or more Rh-positive infants without forming antibody. Since families of two or three children are commonest nowadays, it is clear that the majority of Rh-negative women will never have enough pregnancies to get immunized against Rh.

Rh and Transfusion. A single transfusion of Rh-positive blood, given to a Rh-negative person, causes the formation of anti-Rh in almost 50 per cent of cases (L. K. Diamond[2]). Thus it is clear that blood transfusion is a far more effective stimulus to the formation of anti-Rh than is pregnancy. Repeated transfusions of Rh-positive blood given to a Rh-negative person almost always cause the formation of anti-Rh. In such cases successive transfusions have a progressively less valuable effect; at first the transfusion may simply be followed by fever and slight jaundice, but if these signs are ignored and further transfusions of Rh-positive blood are given, hæmoglobinuria and renal failure may be produced.

Since anti-Rh does not occur spontaneously in the serum of Rh-negative people, a first transfusion can only be immediately dangerous if the patient is a woman who has been sensitized by pregnancy. Before the Rh factor was discovered, there were many catastrophies following transfusions given to women in the puerperal period. In these cases we now know that the patient was Rh-negative and had anti-Rh agglutinin in her serum as the result of two or more pregnancies with Rh-positive fœtuses, and that the donor was Rh-positive.

Although a single transfusion of Rh-positive blood is thus only likely to be immediately fatal if the patient is a Rh-negative woman who has been sensitized by pregnancy, there is one common insidious danger which is even now not sufficiently widely realized. It has been mentioned above that a single transfusion of Rh-positive blood given to a Rh-negative person causes the formation of anti-Rh in some 50 per cent of cases. This means that if a Rh-negative girl or young woman is given a transfusion of Rh-positive blood and later becomes pregnant with a Rh-positive fœtus, her very first infant is likely to be affected with hæmolytic disease, and, what is worse, with a severe form of the disease. The mortality of such infants is about 50 per cent, despite treatment. It is all too common for a Rh-negative woman to be unable to bear any healthy children because in the past she has been transfused with a single bottle of Rh-positive blood.

Forms of Rh Antibody.—Rh antibodies occur in two forms which unfortunately have been given many different names. The kind of antibody first discovered was a 'saline agglutinin'; that is to say, it was found to agglutinate saline suspensions of Rh-positive cells just as do the naturally occurring anti-A and anti-B agglutinins. For some time after this discovery there was much confusion because some women who were obviously sensitized to Rh could not be shown to have any anti-Rh of this kind in their serum. It was then found that their serum contained a form of anti-Rh which would 'coat' Rh-positive cells and actually prevent them from being agglutinated by the saline agglutinating form of anti-Rh. The second form of Rh antibody is sometimes called 'blocking' or 'incomplete', or, since it will agglutinate Rh-positive cells if they are suspended in albumin, 'albumin' antibody.

Albumin antibodies occur more commonly than saline agglutinins and have a more serious significance from a prognostic point of view. Furthermore, high titres of albumin antibody, say 1 in 128 or more, have on the average a slightly more serious significance than low titres (I. Davidsohn and K. Stern[3]). Nevertheless exceptions to this rule are so common that in an individual case measurements of titre are of little value.

The fact that antibodies are part of the globulin fraction of human serum is the basis of the valuable antiglobulin or 'Coombs' test. This test can be used to detect the presence of Rh antibodies in the following way: A serum suspected of containing the albumin form of anti-Rh is incubated with known normal Rh-positive cells. If anti-Rh is present, it coats the Rh-positive cells. The presence of this 'coat' can then be demonstrated by testing the washed cells against an anti-globulin serum: strong, rapid agglutination occurs if the cells are coated.

Infants with hæmolytic disease of the newborn have their red cells coated with Rh antibody at birth and for some weeks afterwards. Therefore if their washed erythrocytes are tested directly against an anti-globulin serum, they will agglutinate. This test, the direct Coombs test, is always positive in hæmolytic disease of the newborn and is of very great value in diagnosis.

Compatibility Tests before Transfusion.—From what has been said in the previous section, it will be understood that many sera which contain anti-Rh will not agglutinate Rh-positive cells suspended in saline, but will agglutinate them if they are suspended in albumin or plasma. Unfortunately, because of the occurrence of rouleaux formation, tests made in protein media are harder to interpret than tests made in saline, and it is very difficult to devise a single, simple compatibility test. The most satisfactory procedure is to do two tests, a test in saline and an indirect Coombs test.

If a single test is used, the donor's cells can be suspended in plasma or 20 per cent bovine albumin and mixed with an equal volume of the recipient's plasma. After 30 minutes the tube is centrifuged and the sediment is then examined under the microscope for agglutination. In cases of great urgency, Diamond's rapid slide test can be used. Three drops of the donor's whole blood (oxalated) are mixed with one drop of the recipient's serum and rocked gently over a lighted surface. If no agglutination occurs within five minutes, the bloods can be considered compatible. Unfortunately this test is not very satisfactory for the detection of weak Rh antibody of the albumin agglutinin type.

Hæmolytic Disease

Hæmolytic disease may be so severe as to cause death in utero at about the twenty-fourth week of pregnancy, or may be so mild that only the most careful blood examinations after birth will reveal its presence. Infants who die in utero probably die from severe anæmia; such infants often have widespread œdema—

hydrops fœtalis. If these infants are born alive, they seldom survive for more than 24 hours. Examination of their cord blood shows severe anæmia, erythroblastæmia, and hyperbilirubinæmia. Less severe cases show mild anæmia at birth; this may be masked after birth by the physiological transfer of blood from the placenta, which occurs immediately after the child has been born. After birth jaundice rapidly develops—*icterus gravis neonatorum*—and plasma bilirubin values of 20–30 mg. per cent are frequently reached between the second and fifth days of life. During this period a proportion of the infants become lethargic and die with or without signs of damage to the central nervous system. These infants usually die from medullary failure and at autopsy are found to have damage to the basal ganglia and medullary nuclei—*kernicterus*. A few infants who develop abnormal signs during this phase but survive, later show signs of permanent damage to the central nervous system, such as spasticity, mental defect, or athetosis. Fortunately, these cases make up only about 10 per cent of all the sufferers from hæmolytic disease. Less severe cases of hæmolytic disease show no anæmia at all in the cord blood and develop only mild jaundice subsequently. Nevertheless they may become anæmic during the second week of life or later.

Treatment of Hæmolytic Disease.

a. Antenatal.—If Rh antibody is first found by routine antenatal testing in the serum of a woman who has never been transfused and has never given birth to an affected infant, this antibody is not usually detectable before about the fifth month of pregnancy. The fœtus is thus only exposed to the action of anti-Rh for 4 or 5 months or less, and the mortality in such infants is low (only about 10 per cent). Many are so mildly affected that they can only be diagnosed by the direct Coombs test. However, in subsequent pregnancies the fœtus is exposed to the action of anti-Rh throughout the greater part of intrauterine life, and the mortality rises to 50 per cent or more; stillbirths are common.

It is clearly tempting to try to remove the infant from the bad effects of the antibody as soon as possible, and for this reason premature induction of labour is widely practised. Nevertheless, it is very difficult to say just how valuable a measure it is. When the mother has previously had an affected infant or a transfusion of Rh-positive blood, and has anti-Rh in her serum from the beginning of pregnancy, it seems reasonable to advise induction of labour even as early as the thirty-fifth week, in view of the fact that death of the fœtus during the last few weeks of pregnancy is not uncommon. However, if anti-Rh is simply found on routine examination in the serum of a woman with no previous history of sensitization, it is probably unwise to induce labour before the thirty-seventh week, since, in view of the good prognosis, one does not want to run the undue risk of prematurity.

b. Treatment of the Infant after Birth.—Until recently the standard treatment has been the transfusion of Rh-negative blood to combat anæmia. Recently various techniques have been introduced for carrying out exchange transfusion. By this procedure approximately 450 c.c. of the infant's blood is withdrawn and, simultaneously, 500 c.c. of Rh-negative blood is injected. This operation produces a 90 per cent exchange of red cells. The most widely favoured technique is that of carrying out both withdrawal and injection of blood through a fine plastic catheter passed up the umbilical vein within a few hours of birth (L. K. Diamond[4]). It is too early to say whether this treatment can produce a significant fall in the mortality and morbidity of hæmolytic disease, but it seems probable that it will do so. In any case, the treatment is likely to replace simple transfusion because it is easier to carry out than the series of transfusions which otherwise have to be given to the infant. In most cases

after the initial exchange transfusion, the infant requires no further treatment (P. L. Mollison and Marie Cutbush[5]).

REFERENCES.—[1]*Med. Res. Coun.* Memo. No. 19, "The Rh Blood Groups and their Clinical Effects", 1948, H.M. Stationery Office, London; [2]Personal communication, 1947; [3]*Amer. J. clin. Path.* 1948, **18** 690; [4]*Proc. R. Soc. Med.* 1947, **40**, 546; [5]*Lancet*, 1948, **2**, 522.

RHEUMATIC FEVER.

Una Ledingham, M.D., F.R.C.P.

Frank *rheumatic fever connected with hæmolytic streptococcal epidemics* proved a major source of disability in the U.S. Navy in the recent war, the rate per 1000 increasing from 0·73 in 1940 to 2·29 in 1944. Quin[1] presents a careful study of the problem based on findings in 7575 patients admitted to a naval hospital during the year beginning March, 1945. The incidence was very much greater in training centres than at sea or in foreign stations. These centres were placed in areas where rheumatic fever is common amongst the population, and the conditions allowed for crowding and insufficient ventilation. The average age of onset was notably high (between 17 and 19 years), and most attacks occurred in the first six to twelve months of Navy life. Respiratory infection preceded the attack in three-quarters of the cases. The new recruit must be regarded as susceptible, and the crowding of infected with susceptible people favours the continuance of streptococcal epidemics, with consequent increase in rheumatic fever cases.

That *rheumatic pneumonitis* is a clinical entity has been long agreed, though the exact nature of the disease process is not agreed. All emphasize the primary nature of the lesion as distinct from secondary congestive lung complications of rheumatic heart disease. These congestive changes may mask the presence of the primary pneumonitis, rendering diagnosis difficult and assessment of incidence impossible. Muirhead and Haley[2] review the position, emphasize the true rheumatic basis of the lesion, and present a case in support. A young woman with mitral stenosis suffered repeated attacks of congestive cardiac failure associated with unaccountable intermittently raised temperature. Blood-cultures were negative in spite of the raised white-cell count. Before death consolidation of the right lung developed with characteristic X-ray and clinical findings. Post mortem revealed evidence of old and active rheumatic heart disease and extensive lung changes consistent with both active and chronic pneumonitis.

Treatment.—The curative properties of sodium salicylate are still in doubt. Reid[3] maintains that it can cure, and takes a normal E.S.R. as the best criterion of cure, though admitting a poor best. These interesting and helpful facts emerge from his report. There was wide variation in the plasma salicylate levels of patients taking equal doses of the drug. The fall of E.S.R. depended on the plasma level attained; it was most rapid at a concentration of 30 to 40 mg. per 100 c.c., and not affected at levels below 20 mg. per 100 c.c. Relapses and remissions coincided with fall and rise of the plasma level. When sodium bicarbonate was given in addition, the plasma concentration was less and the urinary concentration proportionately more. This suggests that the alkali facilitated excretion of salicylate and hindered achievement of effective plasma levels. Initial maximum concentration in the blood was followed consistently by a fall, in spite of maintenance of drug intake. This fall is accompanied by a rise in the alkali reserve and urinary *p*H, and conversely a rising salicylate concentration coincides with a falling alkali reserve and urinary *p*H. The inference is that alteration of acid-base balance determines the fall in plasma salicylate level. A possible explanation is that the drug causes acidosis which may be over-corrected by physiological reaction. For cure the dose of salicylate must be dictated by blood and urine estimations; alkali should be withheld, and effective dosage continued until the E.S.R. has fallen. The frequent practice of reducing the drug on symptomatic relief is strongly condemned.

As this advice entails the intake of large doses of sodium salicylate for long periods it is useful to know when to expect toxic symptoms and what such symptoms will be. Graham and Parker[4] found that four-fifths of 70 patients developed toxic symptoms. These appeared in definite order and related directly to the initial plasma concentration of salicylate. Tolerance was acquired later. Tinnitus, deafness, nausea with mild vomiting occurred in nearly half the patients and indicated an approach to the optimum plasma salicylate concentration of 35 mg. per 100 c.c. These mild symptoms can be ignored, but toxic effects were more serious when concentration rose above the therapeutic level. Persistent vomiting and hyperventilation are especially serious, and hæmorrhage, though rare in this series, accounted for the only fatality. Sodium bicarbonate is the proper antidote for salicylate overdosage.

Parker et al.[5] add to the known factors influencing concentration. Salicylate was as effective when given rectally as orally and intravenous therapy has no place in straightforward cases. Conversely to the action of bicarbonate, ammonium chloride or para-amino benzoic acid causes a rise in plasma levels. Fluid intake should exceed 3 pints daily, plasma concentration being virtually unaffected by higher intakes, while lower intakes cause a sudden increase in the concentration which may reach danger level. A therapeutic dose of 0·8 g. daily per stone of body-weight is suggested.

REFERENCES.—[1]*Arch. intern. Med.* 1947, **80**, 709; [2]*Ibid.* 328; [3]*Quart. J. Med.* 1948, **17**, 139; [4]*Ibid.* 153; [5]*Ibid.* 229.

RHEUMATISM, INFECTIVE. (*See* REITER'S DISEASE; RHEUMATOID ARTHRITIS.)

RHEUMATOID ARTHRITIS. *W. Yeoman, M.D.*

Anæmia in Rheumatoid Arthritis.—Though it has been recognized for a long time that hypochromic anæmia is almost always present in a case of rheumatoid arthritis at some stage of the disease, no satisfactory explanation has ever been given for the cause, and the response to treatment has been discouraging. Nilsson[1] has now collected and fully reviewed the literature on the subject and used this as a background for his investigation of 436 patients.

He compares the serum iron content in cases of rheumatoid arthritis with normals and notes that it is lower in women than in men in both normal and pathological material. He investigates the response to iron therapy by the oral and intravenous routes and notes that serum iron does not rise so high in the rheumatoids as in the normals.

In the case of the intravenous injections the serum iron is estimated before the injection and at intervals of 5 minutes, 1 hour, and 2 hours after. A series of normal and polyarthritis cases are compared which shows that the iron disappears more rapidly from the circulation in the polyarthritis cases by a statistically significant amount. This cannot be due to faulty absorption so it must be due to absorption into the iron stores, or more rapid excretion. More probably the former, for Greenberg et al.[2] have shown that the liver and spleen absorb larger quantities of iron during infections than in normal states. In the severer cases the iron disappeared more rapidly from the serum than in the milder ones. The conclusion is drawn that it is not the iron therapy which regulates the hæmoglobin percentage but the course of the basic disease. In addition to the above the behaviour of serum copper was investigated, both in normals and patients suffering from various forms of infection. These examinations showed that whereas serum iron has a diurnal variation this is not the case with copper, and in the abnormal series the serum copper was considerably raised above the normal figure except in a case of nephrosis—

probably amyloid – and one of arteriosclerosis. This decrease in serum copper in cases of amyloid disease is worth further investigation, and the increase in infectious states is significant in view of the recently introduced therapy in rheumatoid arthritis.

Treatment

Treatment with Heavy Metals. – A new development is the introduction of preparations of copper salts. An organic copper compound was first used by German workers, but Forestier and Certonciny[3] were the first to publish a critical account of the results in 44 cases. The compound used was cupro-allyl-thiourea-sodium-benzoate, which is water-soluble and contains 19 per cent copper. It is excreted chiefly by the intestine but the excretion is slow and continues after the cessation of injections. It accumulates in the liver and to a less extent in spleen and kidneys, and though it is more toxic to animals than the gold salts, in man tolerance is considerably greater. The solution is given intravenously and the authors generally employed 10 c.c. of doubly distilled water for 0·25 g. of copper. It is important that none of the solution should escape into the perivascular tissues, for a very painful reaction will thus be caused lasting six to eight hours. The initial dose suggested is 0·10 g. which is quickly increased to 0·25 g. Injections are given twice a week and the total dose varies from 2·5 to 5 g. per course. The interval between the first two courses is a month and between the later courses two to three months.

The results in cases of long standing were not so good as with gold but in cases showing resistance to gold the copper caused improvement which was frequently rapid. In the early cases of polyarthritis of less than a year's duration the result was remarkable. Of 13 cases treated, 12 showed rapid improvement both clinically and by the fall in the sedimentation-rate of the erythrocytes. No toxic effects were noted.

[The only objection the reviewer has so far discovered in this method is the difficulty of giving the injection. The solution is almost of the colour of venous blood, and in many of the subjects the veins are of small calibre. – W. Y.]

Pursuing this line of treatment, Forestier, Jacqueline, and Lenoir[4] report a series of 55 cases treated with an aqueous solution of cupro-oxyquinoline sulphonate of methylamine by the intramuscular route. The injections are almost painless, but in some cases 2 c.c. of 2 per cent novocain or scurocain were added in the syringe. The dose used was 0·50 g. per injection twice or sometimes three times weekly till 6 or 9 g. were given in the course, i.e., twelve or eighteen injections. Four weeks elapsed between the first and second courses and six to eight weeks between subsequent courses. The results are tabulated in the table below.

No toxic reactions were noted, but 2 cases had a focal reaction and 3 a skin eruption of short duration. It will be noted that out of 19 cases which had become either intolerant or resistant to gold therapy 12 were notably improved by the copper salt. Intolerance to gold does not appear to be a contra-indication to giving copper. One of the reported cases had developed severe albuminuria during a course of gold injections, but this decreased during the course of copper and the arthritis improved. One case of psoriasis associated with the arthritis improved during the course, and this fact has also been noted by Christin. [So far the intramuscular preparation is not available in this country, but when it is this line of treatment will be worth investigating in a large controlled series. The improvement in the skin in the case of psoriasis is interesting, because, in the author's experience, this condition is invariably made worse by a course of chrysotherapy. – W. Y.]

	No. of Cases	Results			
		Excellent	Good	Mediocre	Nil
Chronic polyarthritis of less than one year's duration :—					
Copper only	4	—	4	—	—
Copper following chrysotherapy	1	—	1	—	—
Chronic polyarthritis of more than one year's duration :—					
Copper only	13	3	7	2	1
Copper following chrysotherapy	18	2	9	2	5
Gonococcal arthritis	4	—	2	1	1
Gout, chronic polyarthritis	3	2	1	—	—
Chronic hydro-arthrosis	4	2	1	1	—
Ankylosing spondylitis	3	2	—	—	1
Mono-arthritis	2	1	1	—	—
Coxitis	2	—	—	1	1
Discogenetic disease	1	1	—	—	—
	55	13	26	7	9
Percentage	—	24	47	13	16

BAL in Gold Toxicity.—Reference was made in the MEDICAL ANNUAL, 1948, to the use of BAL (British Anti-Lewisite Solution—the approved name is *dimercaprol*) in the treatment of toxic reactions due to heavy metals. Macleod[5] reports the results of the use of BAL in 15 cases of gold toxicity which included 2 cases of acute hepatitis and one of hypoplastic anæmia; 11 patients had dermatitis and 2 had stomatitis in addition. One of the hepatitis cases on the fifth day of the treatment after a dose of 1300 mg. BAL complained of nausea, epigastric discomfort, and diarrhœa, so the injections were stopped. The icteric index had fallen from 17 to 8 units during this time. One month later there was a relapse and 500 mg. BAL was given over a period of 2 days, but again the injections had to be stopped because of nausea, vomiting, and severe abdominal pain. However, the patient's condition rapidly deteriorated and her condition appeared to be hopeless, so a further 1000 mg. BAL was given during the period of 11 days and the patient recovered. The case of hypoplastic anæmia due to gold did not improve and there was no change in the peripheral blood or bone marrow after the administration of BAL.

Toxic Reactions to BAL.—Toxic effects usually begin 20 minutes after injection, with a return to normal in from 45 minutes to 2 hours. Among the toxic effects produced are various paræsthesiæ, lacrimation, blepharospasm, nausea, abdominal pain, vomiting, unrest, exhaustion, and a transient rise in blood-pressure. Local pain at the site of the injection is frequently encountered. Doses up to 5 mg. BAL per kilo of body-weight can be given with safety, and even up to 8 mg. per kilo the effects are transitory. These doses can be safely given in the presence of severe kidney damage, but a daily dose of 3 mg. of BAL per kilo of body-weight or even less is advisable in cases of gold hepatitis.

Russell, Green, and Ward[6] considered that the toxic symptoms produced by BAL are due to latent tetany: "The symptoms and signs in both conditions may be summarized as manifestations of increased excitability of motor, sensory, and secretory nerves, the vegetative nervous system, and the higher centres. The maintenance in the pericellular fluid of equilibrium between calcium, magnesium, and hydrogen ions on the one hand, and sodium, potassium, and hydroxyl ions on the other, is vital for the health of the cells controlling the heart-beat, the contractility of plain and striped muscle, and the transference of impulses at the neuromuscular junction and through synapses." They therefore concluded that the tetany is of the low-calcium, low-magnesium

type and can be obviated by providing a high calcium diet, magnesium sulphate, and vitamin D. With these precautions they considered a daily dose of 3·14 mg. per kilo of body-weight should not produce a toxic reaction.

Dosage of BAL.—Macleod does not advocate a stereotyped dosage, and advises each case to be treated individually, and suggests that if it is desired to give energetic treatment the doses may be administered 4-hourly or even 3-hourly. He states: "Though relapse in the symptoms of rheumatoid arthritis following treatment with BAL has not been a feature of the present cases, it is probably undesirable for several reasons to use BAL in quantities larger than necessary to control the toxic symptoms. In the first place, though BAL has not resulted in an increase in the symptoms of rheumatoid arthritis in the present series, the experience of others has led to a different conclusion, and a larger series of cases may prove relapse in the rheumatoid arthritis to be a frequent undesirable sequel to BAL therapy. On theoretical grounds relapse would be expected if BAL caused an increase in urinary excretion of gold. Secondly, it is well known that cases of rheumatoid arthritis developing toxicity often show a very good improvement in the joint symptoms. Over-treatment of the toxic reactions may therefore be undesirable. Lastly, gold toxicity is usually insidious in its onset, the risk is that it may progress to a dangerous degree—for example, from mild dermatitis to severe exfoliation, or from mild hepatitis to acute yellow atrophy. If the toxic reactions can be averted at an early stage such danger may be averted and the beneficial effect of gold on the joints be allowed to continue."

Spinal Pumping.—In previous editions of the MEDICAL ANNUAL reference has been made to the technique of spinal pumping introduced by Speransky. Savage[7] reports on 4 cases so treated but cannot claim the good results of the Gillmans.[8] Speransky devised the technique because he considered rheumatoid arthritis to be a nervous dystrophy. As one of the effects of the treatment all observers have reported severe sweating, rise in skin temperature, and dilatation of the peripheral vessels, and it was this effect on the peripheral circulation which led Boueck and Lowman[9] to use this treatment in a novel combination. After the spinal pumping a course of typhoid-vaccine–autohæmotherapy was commenced. This course consisted of 6 fever sessions covering a period of 3 to 4 weeks. At the same time as the T.A.B. vaccine was given intravenously 10 c.c. of the patient's blood was withdrawn from the arm and re-injected into the gluteal muscles. In the intervals between the fever sessions nicotinic acid was given in sufficient dosage to produce a flushing effect: this was given twice a day in doses of 200 mg. (100 mg. in 2 doses at 15-minute intervals) before the midday and evening meals.

The series consisted of 27 cases having an average age of 34 years, and all could be classified as chronic, having had numerous well-recognized types of treatment during the course of their illness, the duration of which ranged from 15 to 22 years.

The authors describe 5 cases in detail, but unfortunately the results of the whole series are not tabulated clearly and no attempt is made to group the effects of this treatment or correlate them with blood and biochemical examinations. Nicotinic acid in the doses prescribed appeared to alleviate peripheral vasomotor symptoms and "in all cases the major effect from use of the Speransky pumping was in alleviating peripheral fibrositic and vasospastic symptoms".

[The scientific reasoning advanced to justify this treatment is not clear, but it would seem to rank with the 'shock therapy' class of remedies. That an advanced case of rheumatoid arthritis is able to endure a spinal pumping

followed by 6 intravenous injections of T.A.B. in the space of 4 weeks speaks well for the inherent toughness of patients suffering from this disease process. The effect of a course of intravenous T.A.B. does improve the peripheral circulation for a time, and it may have the effect of turning a case which is becoming steadily worse into one which has a remission. This, however, is only temporary and is not curative, and it remains to be seen how many cases treated by the methods described sustain their improvement. W. Y.]

Rheumatoid Arthritis an Allergic Phenomenon.—The theory that the joint lesions in rheumatoid arthritis are the result of an allergic reaction to some infective agent or metabolic process has been advanced periodically for many years. The advocates of this theory point to the continued and universal failure to discover any infective agent in the fluid withdrawn from infected joints, and the fact that it is common to obtain a history of asthma, fever, or urticaria either in the patient or a near relative. Following this line of thought Novotny[10] has devised a method of *desensitizing patients suffering from rheumatoid arthritis by transplanting a portion of the capsule of a damaged joint to the subcutaneous tissues in the lower quadrant of the abdominal wall.* The size of the transplanted tissue averages 2 by 4 cm. and is taken from the capsule of the knee-joint in the suprapatellar area. Only in one case did the transplanted tissue necrose and become discharged. Twelve cases were treated, the ages ranging from 18 to 60 years, and all except one had had several courses of gold and X-ray treatment. In 11 cases there was reduction of pain and swelling and increased mobility in the affected joints. The case in which the transplant necrosed had been bedridden for 2 years and was in poor general condition; 7 cases have remained markedly improved over a period ranging from 9 to 17 months; 2 cases had a complete relapse and 2 a partial relapse in the course of a year. In the series was a case of gout of 28 years' duration, and though the serum uric acid was 9·2 mg. per cent 6 months after the operation, there was such an improvement in his joints that he was able to resume his business 3 months after the operation and his condition remained stable 12 months later.

Intra-articular Injections.—In the MEDICAL ANNUALS of 1945 and 1946 the injection into arthritic joints of solutions of *acid potassium phosphate and lactic acid with procaine* was noted and discussed. Since then this treatment has been used by many observers with varying results, and the method has now been in use long enough for an assessment to be made as to how long the temporary benefit previously reported has been maintained. So far no such report has been published. One of the criticisms of this method has been that no reports have been published giving a series of controls, but now Baker and Chayen[11] in publishing a series of 52 cases have gone some way to meet this objection. They used 3 solutions for this purpose and the injections were given mainly into the hips and knees. The cases were observed for periods varying from 6 to 18 months, and the number of injections per patient ranged from 2 to 22 with average of 10. The solutions used were: (1) Lactic acid in 2 per cent procaine, *p*H 5·4; (2) 0·5 per cent procaine adjusted to *p*H 7·6 with sodium phosphate, i.e., about normal joint *p*H; (3) Normal saline. The results of treatment in the 52 cases irrespective of the injection fluid used were as follows:—

	No. of Cases
1. No improvement	13
2. Slight improvement (continuing injections) ..	7
3. „ „ (ceased „) ..	4
4. Moderate „ (continuing „) ..	
5. „ „ (ceased „) ..	
6. Great „ (continuing „) ..	
7. „ „ (ceased „) ..	

The results of treatment of 70 joints by intra-articular injection according to the solutions used were as follows:—

		Solution		
		I	*II*	*III*
1.	No improvement	14	6	—
2.	Slight improvement (continuing injections) ..	5	5	—
3.	,, ,, (ceased ,,) ..	3	1	—
4.	Moderate ,, (continuing ,,) ..	5	6	1
5.	,, ,, (ceased ,,) ..	4	2	—
6.	Great ,, (continuing ,,) ..	1	—	1
7.	,, ,, (ceased ,,) ..	12	4	—

The reasoning which induced Waugh to start this treatment was his estimation of the *p*H of synovial fluid in damaged joints, which he found to be alkaline. He hoped by injecting an acid solution to restore the joint fluid to a normal *p*H. Therefore any injection used in a control series should have the same *p*H value, and it is unfortunate that the observers quoted above did not use fluids of the same *p*H value for all their injections; nevertheless their conclusions are significant, for they state that "we are becoming more and more convinced that most of the benefit is the result of the lubricating action of the fluid". That the local anæsthetic effect of the injected fluid should be considered is shown by Granbard, Kovacs, et al.,[12] who injected 15 cases of destructive arthritis of the hip with procaine intravenously. A total of 137 injections were given, averaging 9 per patient. "The amount of procaine is calculated at 4 mg. per kilo body-weight, dissolved in isotonic saline solution to make a 0·1 per cent solution to be given over a 20-minute period. For example, a 60-kilo individual received 240 mg. of procaine in 240 c.c. of isotonic saline solution at the rate of 12 c.c. of solution per minute." The dosage is repeated at weekly intervals, and used in this way procaine is not an anæsthetic but an analgesic. It was found that procaine administered intravenously was 8 times more concentrated in traumatized or inflamed tissues than in normal tissues. No attempt is made to assess the amount of improvement, but all cases have been followed for 12 months. In one case of rheumatoid arthritis the improvement was only temporary, but in the remaining 14 cases relief of pain and increased mobility was reported in every case.

This preliminary investigation appears to support the view that it is the procaine content of the fluid injected into the joint which is important and not the *p*H of the solution.

REFERENCES.—[1]*Acta med. scand.* 1948, **130**, (suppl. 210); [2]*J. clin. Invest.* 1947, **26**, 121; [3]*Pr. méd.* 1946, No. 64, 884; [4]*Ibid.* 1948, No. 29, 351; [5]*Ann. rheum. Dis.* 1948, No. 3, 143; [6]*Lancet*, 1948, **2**, 169; [7]*Brit. med. J.* 1948, **1**, 496; [8]*Amer. J. med. Sci.* 1946, **211**, 448; [9]*Ibid.* 1948, **215**, 198; [10]*Acta med. scand.* 1948, **129**, 524; [11]*Lancet*, 1948, **1**, 93; [12]*Ann. intern. Med.* 1948, **28**, 1106.

RINGWORM OF THE SCALP: TREATMENT.

R. M. B. MacKenna, M.A., M.D., F.R.C.P.

R. T. Brain, K. Crow, H. Haber, C. McKenny, and J. W. Hadgraft[1] have discussed the possibility of treating ringworm of the scalp without removing the hair either by means of X rays or by the administration of thallium acetate. They state that the work of S. Rothman[2] and his colleagues indicated that a certain fraction of the free fatty acids extracted from adult human hair could inhibit the growth of *Microsporon audouini* in concentrations of 0·0002–0·0005 per cent. Pelargonic acid was the main constituent of this fraction, but success did not follow its therapeutic use, probably because of its lack of penetrating power. Attention was therefore directed to the use of penetrating vehicles which might carry an effective fungicide to the bases of the hair follicles and make possible the cure of scalp ringworm by simple inunction or even by painting the scalp without preliminary epilation.

Brain and his colleagues refer to recent American work concerning this matter, and state that G. M. MacKee, F. Herrmann, and F. L. Karp[3] found that the most promising results in the treatment of ringworm of the scalp were obtained with a preparation containing cetyltrimethylammonium pentachlorphenate 3·5 per cent in " intraderm ". The latter consists of a combination of sodium alkylbenzene sulphonate 5 per cent, phenazone 12·5 per cent, propylene glycol 10 per cent, sulphonated castor oil 10 per cent, and distilled water. The *p*H was adjusted to 4 by the addition of citric and propionic acids. An acid shampoo was used in conjunction with this application. In a series of 59 cases of infection with *Microsporon audouini* 54 per cent of the children were cured in an average period of 14 weeks. Brain and his colleagues used phenylmercuric nitrate and salicylanilide as fungicidal agents, incorporating these with suitable wetting agents. The Crill series of wetting agents (marketed by Croda Ltd., London) appeared to possess satisfactory properties and Crill No. 6 was chosen, for it produces the greatest reduction of surface tension of the series. Crill No. 6 is an ethylene oxide derivative of sorbitan monolaurate. Of various formulæ tried the following appears to have been the most satisfactory :

Phenylmercuric nitrate	5 g.
Crill No. 6	100 ml.
Solution of citric acid and sodium propionate	20 ml.
Carbowax '1500'	to 1000 g.

Melt together the carbowax '1500' and Crill No. 6 over a water-bath ; add the phenylmercuric nitrate, previously triturated with the solution of citric acid and sodium propionate, and continue heating until the phenylmercuric nitrate is completely dissolved. Allow to cool.

The method of use was as follows : -

The hair was cut short and kept short throughout the treatment ; a linen cap was worn for twenty-four hours continuously ; every morning the scalp was washed with soap and hot water and scrubbed with a nail-brush, particular attention being paid to the infected patches. The ointment was applied three times a day with a tooth-brush for five minutes. The use of the nail-brush is an interesting suggestion ; the brush, applied with gentle vigour, helps to dislodge the infected hairs which are caught up by the coarse bristles and are easily removed from the follicles.

The children's scalps reacted in various ways to the treatment, the range of reaction varying from slight redness and scaling to varying degrees of pustulation. An inflammatory reaction was welcomed, and in cases where it was absent it was intentionally provoked. Improvement could usually be seen between the first and seventh weeks of treatment, and when a case became negative to examination under Wood's ray it remained so.

Twenty-two cases were treated ; these included 8 of *M. audouini* infection, 9 of *M. felineum* infection, 1 due to *T. endothrix*, and 4 due to unidentified microspora ; 17 of these cases were cured in an average time of two and a half months. In this small series of cases, the authors found no significant differences between the response to treatment of the human and that of the animal type of ringworm.

This interesting paper taken in conjunction with recent American work seems to indicate that in time an effective and thoroughly reliable treatment of ringworm of the scalp—which does not necessitate removal of the hair by X rays—will be evolved. It is interesting to note that Brain and his colleagues are careful to emphasize that preliminary removal of the hair, even when followed by old-time remedies, still affords the quickest prospect of cure.

REFERENCES.—[1]*Brit. med. J.* 1948, **1**, 723 ; [2]*Science*, 1946, **104**, 201, *J. invest. Derm.* 1946, **7**, 43.

RUBELLA. *H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.*

C. Wesselhoeft[1] gives a much fuller account of rubella than is obtainable from most text-books. Its infectivity is high in children's institutions but low in schools, and it is more common in adults than measles. The virus can be isolated from throat washings during the first forty-eight hours of symptoms but not thereafter. Infectivity precedes the eruption by a day or two. Isolation after the appearance of the rash is often ineffective as a measure of control, and isolation beyond the period of the rash is of doubtful value. The rash resembles fairly closely that of serum-attenuated measles, scarlet fever (especially the second day of the rubella rash), glandular fever, erythema infectiosum (which is rare in Britain and U.S.A.), roseola infantum or exanthem subitum, the rash of which appears after three days' fever, rickettsial diseases, late serum rashes, drug eruptions, and erythema multiforme. Complications include a mild form of polyarthritis, thrombopenic purpura, encephalomyelitis, unilateral retrobulbar neuritis, and polyneuritis. The incidence of post-rubella encephalitis has been estimated at 1 in 6000 cases.

Congenital Malformations.—By combining various observations from Australia and U.S.A., Wesselhoeft shows that of 122 babies whose mothers were known to have had rubella in the first two months of pregnancy, 118 had congenital defects and only 4 were normal. For the last five months of pregnancy the figures in 26 instances were 6 congenital defects and 20 normal. All reports except that of M. J. Fox and H. M. Bortin[2] confirm the Australian findings. In the past five years, the combined literature of U.S.A., Australia, and Britain reports only 52 normal children [this may be a serious under-statement.—H. S. B.] and 521 children with serious congenital defects following maternal rubella. Among the latter there were 221 eye defects, 243 deafness, 221 heart lesions, 74 microcephalus, 25 mental retardation, 20 gross dental deformities, 3 pyloric stenosis, 2 obliteration of bile-ducts, 1 spina bifida. It is estimated that congenital defects associated with rubella have an incidence about ten times greater than that of other congenital deformities. Measles, mumps, chicken-pox, herpes zoster, and influenza in pregnancy have also been followed by such congenital defects as deafness, patent ductus arteriosus, microcephaly, and pyloric stenosis, but to a very small extent compared with rubella. The available evidence [which may well be incomplete—H. S. B.] points to a ten to one chance (521 to 52) that rubella in pregnancy will be followed by congenital defects. Fox and Bortin's conclusions from their data are considered to be faulty. A few cases have been reported in which congenital deformities occurred following attacks of rubella *before* conception.

Prophylaxis.—Free exposure of children to rubella in the community is not recommended since some of those contracting it might infect pregnant women; but free exposure of girls in institutions and in homes where there are no pregnant women is advised.

Treatment.—There is no satisfactory treatment at present for the pregnant woman who contracts rubella. Swan and his associates suggested that abortion would be justified, but there are no legal grounds for this, since danger to the *mother* must be proved. A liberal interpretation of the law might be obtained if it were shown that a mother, in virtue of the knowledge which she possesses, might become "a mental and physical wreck". Three therapeutic abortions have been reported. The evidence suggests grounds for amendment of the law in respect of rubella.

C. Swan[3] discusses rubella in pregnancy as an aetiological factor in *stillbirth*. A survey was made in S. Australia in the seven years 1939–45, and 764 stillbirths investigated. In 16 of these cases the mother had had rubella in pregnancy, and in 13 of the 16, rubella occurred in the first four months of pregnancy—the

'critical period'. No other infectious diseases appeared to show any predominance in the early months of pregnancy such as is manifested with rubella. It is suggested that rubella may be a factor in the causation of stillbirths by damaging the embryo early in pregnancy.

Prevention of Rubella.—F. M. Burnet and his co-workers[4] transmitted the disease from filtered throat washings to 9 out of 16 women student volunteers. It was shown that the virus was present in high concentration in throat washings taken from patients at the height of the rash. Such washings, if frozen, remain active indefinitely, and, it is suggested, might be used to reproduce the disease in young girls in closed communities, e.g., in boarding-schools or holiday camps. Gamma globulin processed from rubella convalescent serum was given to 22 presumably susceptible pregnant women all of whom had been in proved or possible contact with rubella. None developed a rash. This passive method of protection is, however, an uncertain one, since a fœtus might be damaged from rubella before a woman knew herself to be pregnant.

Congenital Malformations following Maternal Measles, Mumps, and Chicken-pox.—These have been investigated by M. J. Fox et al.[5] These diseases are notifiable in Milwaukee. A survey of notified cases in 1942–5 by public health nurses revealed the following: (1) The incidence of congenital anomalies in a group of 665 children born before, or conceived and born after, the mothers had measles, mumps, or chicken-pox was 0·9 per cent. This is regarded as the normal or expected rate of congenital defects. (2) None of the 22 children born of pregnancies complicated by mumps and none of the 4 children born of pregnancies complicated by chicken-pox showed congenital defects; only 1 of 7 children born of pregnancies complicated by measles had an anomaly—hare-lip. (3) There was no evidence that when conception took place subsequent to recovery from measles, mumps, or chicken-pox, there was any relation between these diseases and the development of anomalies in the offspring.

REFERENCES.—[1]*New Engl. J. Med.* 1947, **236**, 943, 978; [2]*J. Amer. med. Ass.* 1946, **130**, 568; [3]*Lancet*, 1948, **1**, 746; [4]*Rep. Director Walter and Eliza Hall Inst. Melbourne*, 1947–8; [5]*Lancet*, 1948, **1**, 746.

SARCOIDOSIS.

Una Ledingham, M.D., F.R.C.P.

Two special series represent the increasing frequency of this diagnosis. McCort et al.[1] saw 28 cases while working in an Army radiotherapy centre. There is thus an unusual proportion of young males, the material being drawn from army personnel. Because of the nature of the hospital, too, whereby a large number of mediastinal tumours were referred, the proportion of intrathoracic glandular involvement was unusually high. As well as the mediastinal group, superficial glands were enlarged in almost every case, and the diagnosis was made by biopsy of these glands. Often extremely small and apparently innocent, the smallest gland may show diagnostic features, and they should be searched for and examined in all suspects. As well as the well-marked glandular features, other systems were much involved and all types of the disease recognized. In over one-third the eyes were affected, with associated parotid gland swelling in a quarter of these. The uveo-parotid syndrome was therefore mostly incomplete. Only 2 patients had skin sarcoids and only 6 had bone lesions. Disease of the lung parenchyma was manifest in over a half of the cases, showing chiefly as reticular shadows spreading from the hilum. It is noteworthy that the paratracheal group of glands was involved in all cases and the peribronchial group in nearly all; larger shadows on the right depended on the anatomically greater number of glands on that side. Calcification was not seen, and the lobulated edge to the hilum shadow was consistently preserved. These points helped to distinguish sarcoidosis from tuberculous and malignant lesions respectively. As usual, plasma protein was increased and skin tuberculin tests

negative. Finally, radiotherapy, tried in 2 cases, proved of no value and is not recommended.

The second series reported by Robinson and Hahn[2] comprises 5 proved and a further 3 suspected cases occurring in siblings, distributed amongst two unrelated negro families. The apparent rarity of the family association is remarked.

REFERENCES.—[1]*Arch. intern. Med.* 1947, **80**, 293; [2]*Ibid.* 249.

SCARLET FEVER AND HÆMOLYTIC STREPTOCOCCAL SORE THROAT.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Epidemiology. The annual numbers of notified cases of scarlet fever since 1943 have been 116,034, 92,671, 73,687, and 56,730. The mildness continued: the deaths registered in the same period were 134, 107, 84, and 43.[1]

Complications.—*Purpura fulminans* is a rare and interesting complication of the convalescent stage of scarlet fever. Anderson, Ferguson, and Landsman[2] describe a case. A correspondent later pointed out that this case was indistinguishable from the Schönlein-Henoch syndrome (anaphylactoid purpura) and emphasized the relation of this disease to a preceding streptococcal infection.

The Post-streptococcic State. Rantz, Boisvert, and Spink[3] contribute important observations on the *sequelæ of hæmolytic streptococcal sore throat.* This is part of the valuable studies carried out by the Commission on Hæmolytic Streptococcal Infections, of the U.S. Army. Amongst 299 cases in soldiers, there were 72 which showed a persistent high erythrocyte sedimentation-rate or clinical manifestations of illness for three or more weeks after the acute stage. The latter included 19 cases of *arthritis* (rheumatic fever) with E.C.G. evidence of carditis in 9; 14 cases of *late fever* occurring after a clinically normal interval of five to eighteen days, with E.C.G. evidence of carditis in more than one-third; *carditis* alone in 11 cases, according to E.C.G. but not clinical evidence; *late lymphadenitis* in 8 cases, in none of which was there evidence of re-infection; *pneumonitis* of patchy distribution (rheumatic pneumonia) in 3 cases; *purpura* (non-thrombopenic) in 2 cases.

The arthritis never followed monotype infections by Type 17 or Type 1. Bacteriological or clinical evidence of re-infection was obtained in 5 of the 19 cases of arthritis; re-infection is regarded as an important factor in arthritis. Evidence of a *continuing reaction* was often present during the latent period before the arthritis, e.g., high E.S.R. and abnormal E.C.G.

All these disorders were believed to be manifestations of the same pathologic process, which might be termed the "post-streptococcic state". It is suggested that the explanation is an immunological reaction occurring in persons sensitized to some product of the hæmolytic streptococcus as a result of previous infection by this organism. Large amounts of sodium salicylate, sulphonamides, and a short course of penicillin in the acute stage did not prevent the development of these late non-suppurative complications.

Treatment.—*Penicillin therapy* of scarlet fever was investigated by Jersild[4] of Copenhagen in 1000 cases. He gave 90,000 to 150,000 units (according to the patient's age) twice daily for six days. In a series of 200 cases compared with 200 sulphanilamide-treated controls, he found that streptococci disappeared from the nasopharynx in some 93 per cent to 97 per cent and did not reappear in the next four weeks (other observers have not had such a favourable result), that the average febrile period was four to five days compared with seven days in controls, that no otitis or nephritis developed as complications, that the antistreptolysin titre was raised little above normal over a period of three weeks, and that the sedimentation-rate fell to normal in three weeks, while both of these were high in the controls. The rash was not influenced by the treatment. The average stay in hospital was only eight days. [This paper is profusely

illustrated with graphs, but the figures are too small to justify general application of the findings. The age-incidence of the patients is not given. Nearly as good results, although without the total abolition of otitis media as a complication, have been reported in this country following the use of antitoxin. But antitoxin, according to the literature, does not seem to have produced very good results in Scandinavia generally.—H. S. B.]

REFERENCES.—[1]*Ann. Rep. Min. Hlth*, 1947, 25. H.M.S.O. Lond.; [2]*Brit. med. J.* 1948, **2**, 549; [3]*Arch. intern. Med.* 1947, **79**, 401; [4]*Lancet*, 1948, **1**, 671.

SCHISTOSOMIASIS (BILHARZIASIS).

Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.

The treatment of such a widespread parasitic disease as schistosomiasis on a worldwide scale by antimony compounds, which must be injected either intramuscularly or intravenously, has many drawbacks and objections. Therefore the introduction of a drug which has a schistosomicidal action and can be administered by the mouth offers many obvious advantages.

Miracil D (*Nilodin*), a fine yellow powder (hydrochloride of 1-methyl-4-B-diethylamino-ethyl amino-thioxanthone)—a thioxanthone derivative—was first synthesized by Mauss in the I. G. Farben at Elberfeld. Subsequently satisfactory results were obtained by W. Kikuth in mice infected with both common species of schistosoma—*S. haematobium* and *S. mansoni*. F. Hawking and W. F. Ross[1] (1948) find that it has an irritant action on tissues, giving rise to inflammation and necrosis at the site of injection. It is more toxic when given intravenously and may produce venous thrombosis. By the mouth in man 0·2 g., repeated daily, was well tolerated. The method of A. L. Latner and colleagues[2] was used for estimation. This is a simple colorimetric method in which the miracil extracted from 5 ml. of blood is dissolved in 0·04 N HCl and read by a Skekker absorptiometer with ultra-violet light. About 7 per cent of an ingested dose was excreted in the urine and less in fæces, so that the drug disappeared from these excretions in 2 to 3 days after treatment.

J. M. Watson and colleagues[3] (1948) have done an extensive research in Egypt by confirming the lethal action of miracil D on mice, jerbils, and monkeys infected with *S. mansoni* and *S. haematobium*. In man, when given by the mouth, it appears to exert singularly few untoward reactions. In lower doses it is erratic, appearing to cure some, whilst failing in others, but in higher and more frequent doses the results were more favourable, and up to 300 mg. were given at 12-hour intervals for as long as 14 days. Indications for cure were based on the disappearance of viable ova from the urine and fæces, the cessation of haematuria, and obvious improvement in the physical condition of the patient.

A. Halawani, J. M. Watson, and colleagues[4] (1948) have more recently reported that of 16 patients infected with *S. haematobium*, 10 received total doses of 2 to 5 g. during 5–10 days; none of these was cured; 3 others were given 7·5 g. during 8–10 days: of these 2 were cured and 1 relapsed. Muscular twitching occurred in a few patients and excessive sweating in others. The skin was stained yellow. Three of the patients treated also suffered from *S. mansoni* dysentery. The results in these were unsatisfactory. Miracil does not have a direct action on the eggs.

It is concluded that the effective dose of miracil is not less than 18–20 mg. per kilo daily for 7–8 days and that the blood concentration must reach 0·3 mg. per 100 ml.

REFERENCES.—[1]*Brit. J. Pharmacol. Chemotherapy*, 1948, **3**, 167; *Trans. R. Soc. trop. Med. Hyg.* 1947, **41**, 133; [3]*Ibid.* 1948, **42**, 37; [4]*J. R. Egypt. med. Ass.* 1948, **31**, 272.

SCLERODERMA, THE HEART IN. (*See* HEART IN SCLERODERMA.)

SEMINAL VESICLES, SURGERY OF. (*See* VAS AND SEMINAL VESICLES.)

SEX GLANDS. *S. L. Simpson, M.A., M.D., F.R.C.P.*

Male Hypogonadism.—In 1943, Heller, Nelson, and Roth,[1] and in 1946, Heller and Nelson,[2] described "functional prepuberal castrates" with agenesis, hypoplasia or atrophy of the testis, complete azoospermia, and eunuchoid characteristics, but short or normal stature, unlike the taller eunuchoids. The urinary excretion of 17-ketosteroids was low or low normal, and the follicle-stimulating hormones high. Klinefelter, Reifenstein, and Albright,[3] in 1942, described a similar or identical syndrome with partial testicular hypoplasia or atrophy, and with gynæcomastia, and this is sometimes referred to as Klinefelter's syndrome. J. W. Goldzieher and E. C. Hamblen[4] review this work and investigate 8 further cases, indicating discrepancies or conflicts in their findings. Thus normal or increased numbers of Leydig cells might be associated with low androgens (17-ketosteroids) and high gonadotrophins (F. S. H.) and vice versa; nor was any quantitative relationship found between gonadotrophins and androgens; nor did these assays bear a quantitative relationship to the degree of incompleteness of the clinical picture.

Gynæcomastia was observed in the presence of normal or increased Leydig cells and with normal penis, and the ketosteroids or gonadotrophins were often normal. They suggest that studies of mitochondria and the Golgi apparatus of the Leydig cells might give a better indication of function.

The reviewer is of opinion that the Klinefelter-Heller syndrome has been unnecessarily complicated by excessive theorizing. It is one of partial or complete eunuchoidism, together with congenital absence of or pathological destruction of seminiferous tubules, but without the excessive height of eunuchoids, and sometimes with dwarfism. The cause of the latter is unknown but a concomitant defect of the pituitary growth factor is a reasonable supposition. It is recognized that a measurement of follicle-stimulating gonadotrophins indicates the function of the seminiferous tubules and not necessarily of interstitial cells, and that adrenal androgens contribute to the assay of 17-ketosteroids.

Hypogenitalism during the Usual Time of Puberty.—L. M. Hurxthal draws[5] attention to the value of testicular biopsy in the differential diagnosis of hypogonadism. Simple immaturity, e.g., spermatogonia without spermatozoa, is found in pituitary hypogonadism and will respond to therapy or may evolve unaided. Sclerosis of tubules and few or absent Leydig cells are found in eunuchoidism, and such testes are incapable of response. In the third type, the tubules are sclerosed but the Leydig cells are present in clumps and secondary sex characteristics are normal. The usual test for gonadotrophins only indicates follicle-stimulating hormone and therefore gives no certain indication of the state of the interstitial cells.

It is indicated that some recent experimental work is difficult of clinical correlation. Thus Simpson and Evans found that luteinizing hormone might stimulate testicular tubules in amounts that had no effect on interstitial cells, and that testosterone might stimulate tubules in hypophysectomized rats. Nelson and Merckel found that the capacity of steroids to maintain spermatogenesis was not proportional to their androgenic power.

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SHOULDER, PAINFUL. *T. P. McMurray, F.R.C.S.*

This, as yet unsolved, surgical problem is discussed by H. Hitchcock and C. O. Bechtol,[1] who describe very fully and carefully the conditions present in a series of patients who came under their observation complaining of pain and disability in the shoulder region.

The authors state that lesions of the tendon of the long head of the biceps are among the more frequent causes of pain and disability of the shoulder-joint. They believe also that there are certain anatomical factors which, when present, predispose the patient to this disability, and of these the most significant is the presence of the supratubercular ridge of bone described by A. W. Meyer.[3] The probability of pain being present in the joint is considerably increased if, in addition to the supratubercular ridge, there is at the same time an abnormally shallow bicipital groove on the humerus. When these two conditions are present, the tendon of the biceps is not firmly held in its groove and is therefore subject to the recurring trauma of complete or partial dislocation with the inevitable result of injury to its surface.

In support of this statement of the great importance of the bicipital tendon in producing a painful condition of the shoulder-joint, the authors relate the history of 4 patients, the first a man aged sixty who had fallen six months previously and struck the flexed right elbow. Three weeks after the accident he complained of pain in the right shoulder region with tenderness on pressure over the bicipital groove. Clinically there was practically no movement at the joint, and radiographic examination indicated that the head of the humerus and the bicipital groove were normal in outline.

At operation the biceps tendon was found to be grossly injected; its smooth, shiny surface was lost and the tendon was fixed by adhesions to the transverse humeral ligament, to the bicipital groove, and to the deep aspect of the pectoralis major tendon. When the shoulder was elevated it became obvious that the portion of the tendon lying in the upper part of the groove became lax, while the intra-articular portion of the tendon became buckled and nipped on full abduction of the arm.

As it was evident that the normal movement of the tendon in the groove could not possibly be restored, the tendon was sutured to the bottom of the bony groove and its upper intra-articular portion removed. The shoulder was then manipulated and the intra-articular adhesions were felt to give way. Eight weeks after operation complete and painless movement had been restored and the patient returned to work.

The authors justify their use of this operation by stating that, as a result of previous failures, they realized that simple division of the adhesions of the tendon to the bicipital groove would be followed by failure and that removal of the upper portion of the tendon was an essential part of treatment in order to prevent the inevitable intra-articular nipping which would have followed.

The second patient was a workman who, following a straight downward pull of the arm, complained of an acute burning pain in the shoulder-joint. He complained also that following this injury an uncomfortable snapping feeling could be felt in the anterior area of the joint. This snapping could be controlled by firm digital pressure over the line of the bicipital groove, and the radiographic examination indicated that whilst the contour of the head of the humerus was normal the bicipital groove in each humerus was particularly shallow, although pain was only present on the injured side.

At operation it was evident that the groove in the humerus was abnormally flat, and the biceps tendon could be easily displaced over its inner margin. In this instance there appeared to be no abnormality of the tendinous cuff, a circumstance which could be explained by the fact that operation was undertaken eight weeks after the original accident. As in the case of the first patient the operation consisted in the anchoring of the tendon into the bicipital groove and the removal of its intra-articular portion. The result was excellent, the man returning to work eight weeks following this procedure.

The third and fourth patients described suffered in a similar way with dislocation of the tendon and acute pain and tenderness in the line of the groove. In the case of patient number three, not only was the tendon dislocated on to the lesser tuberosity, but it was also impaled in this position by a bony spike which projected forward from the surface of the bone. All four patients were treated by the same technique, and the results are reported to be painless shoulders with a normal range of movements.

Anatomical Observation.—In order to determine the incidence of the supratubercular ridge and variations in the depths of the bicipital groove as possible causes of injury to the tendon, 100 humeri were examined.

The Supratubercular Ridge of Meyer.—This ridge, which, when present, projects immediately proximal to the inner wall of the bicipital groove, pushes the biceps tendon against the transverse humeral ligament, thereby producing abnormal pressure on its substance and favouring dislocation.

In the 100 humeri examined the ridge was well developed in 8, while in 59 it could be recognized as a slightly sharpened anterior margin In addition to the ridge, a spur was present on the anterior aspect of the lesser tuberosity in 50 per cent of those in which a ridge was present, but this exostosis was never present when the ridge was absent.

Variations in the Depth of the Bicipital Groove.—In the examination of these 100 humeri considerable variation was demonstrated in the depth of the bicipital groove. The simplest method of indicating the functional depth of the bicipital groove is by determining the angle at which its inner wall is placed in relation to its length. This angle varies considerably. Thus in eight instances in this series the medial wall of the groove made an angle with the floor of less than 45° as compared with the normal which is approximately 70°.

Functional Anatomy.—Contrary to the general impression, in movement round the shoulder the tendon of the biceps does not slide in its groove, but the humerus moves on the fixed tendon during all movements of the joint. From abduction to complete elevation of the arm, a given point in the bony groove moves along the tendon for a distance of one to one and a half inches. The movement is facilitated by the presence of a synovial pouch which extends from the shoulder-joint to line the bicipital groove for the greater part of its extent.

Movements of the humerus on the tendon occur in all stages of elevation of the shoulder whether this be effected through forward flexion or by simple abduction. As these movements are nearly always associated with strong flexion and supination of the elbow, the tendon of the biceps is rendered exceedingly taut, and if, while the elevation is taking place, the arm is rotated inwards, the tendon exerts strong pressure on the inner wall of the groove, working round the lesser tuberosity as a sling round a pulley. On the other hand, when the arm is in full external rotation, the tendon occupies the floor of the groove and only in this position of the arm can the long tendon of the biceps act directly on the shoulder-joint and enhance the power of abduction of the joint.

Diagnosis.—In the presence of a lesion affecting the tendon of the long head of the biceps, the most constant physical finding is tenderness on pressure over the tendon at any point in its course.

Dislocation of the tendon complete or incomplete may be differentiated from a peritendinitis by the test of L. C. Abbott and J. B. Saunders,[3] which is carried out as follows: After full abduction of the shoulder, the arm, which is held in complete external rotation, is slowly brought to the side of the body in the plane of the scapula. At some point during this movement a palpable click can be felt as the biceps tendon, forced against the lesser tuberosity, becomes dislocated from its groove.

Radiographs are of little value in arriving at the diagnosis except in so far as they exclude other conditions, although occasionally it may be possible to demonstrate an abnormally shallow bicipital groove or even the presence of a spur on the lesser tuberosity, while a supratubercular ridge, when present, may be demonstrated in anteroposterior views taken with the arm in external rotation.

The authors do not suggest that physiotherapy should never be used in the treatment of painful frozen shoulder, but they state that when painful frozen shoulder does not clear up under manipulation and the ordinary physiotherapeutic methods, especially when this failure is associated with persistent tenderness over the tendon of the long head of the biceps, it is reasonable to assume that the cause of failure is the presence of inflammation and adhesions round the tendon.

It should not be forgotten that peritendinitis of the long head may not be the only pathological condition present in the shoulder. It may be associated with other lesions of the joint such as injury to the tendon of the supraspinatus muscle, and failure to recognize the presence of the peritendinitis may lead to disappointing results of treatment of the more obvious lesion.

Operative Procedure.—In performing the operation an S-shaped incision should be employed over the deltoid-pectoral interval; the incision is used in order to prevent the development later of a hypertrophied scar, which is comparatively frequent after the use of a straight incision. When the muscles have been retracted a careful investigation of the tendinous cuff and the subacromial bursa should always be made as a preliminary step. Adhesions and peritendinitis of the biceps tendon do not usually become obvious until a clear view is obtained by incision of the capsule and of the transverse humeral ligament. When the tendon is exposed, abduction of the arm will demonstrate whether the tendon works freely in its groove or whether it is bound down by adhesions. If this latter condition be present, the proximal portion of the tendon will buckle with abduction. If adhesions are present and the tendon is bound to the humerus, the operation proceeds as follows: With an osteotome a bed is made in the groove by elevating a portion of the floor from the outside inwards. The tendon is now roughened and sutured under this bony flap while the portion of the tendon lying above the transverse ligament is resected. Manipulation of the shoulder now completes the operative procedure and restores a full range of movement to the joint.

The fixation of the tendon to the bone should always be made in the bottom of the groove. If the tendon is fixed to either tuberosity, a prominence is produced which becomes painful by pressure against the acromion on abduction of the arm, while fixation of the tendon to the pectoralis major is also inadvisable as the cross pull on the tendon causes considerable discomfort.

Post-operative Care.—The shoulder should be kept at rest until the stitches are removed, when the arm is put through a full range of passive movements at least three times a week. At the end of six weeks, when the tendon has become firmly attached to the humerus, free active and passive movements can be employed with confidence.

The authors' experience of the treatment of lesions of the long head of the biceps by this method has been most gratifying. Loss of pain and the rapid return of function have been characteristics, the only residual disability being a slight loss in the power of abduction when the arm is in external rotation—a loss which is scarcely appreciable to the patient and causes little inconvenience.

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SIMMONDS'S DISEASE. (*See* PITUITARY GLAND.)

SKIN DISEASES. (*See* ARSENICAL DERMATITIS; HAIR—PERMANENT WAVING; KAPOSI'S VARICELLIFORM ERUPTION; NITROGEN MUSTARD THERAPY IN DERMATOLOGY; RINGWORM OF THE SCALP; VITAMIN E IN THE COLLAGENOSES.)

SMALL-POX AND VACCINATION.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Epidemiology. Fifty-six cases of small-pox were reported in England and Wales in 1946, of which 14 died. Of these cases, 15 were infected abroad, 13 being by ship and 2 by air. The remaining 41 were civilians infected in this country in thirteen separate outbreaks. The clinical features indicated that in every instance the disease imported was of the major Asiatic variety, although in some vaccinated persons it assumed a clinically mild form with an extremely modified and sparse eruption.

Post-vaccinal encephalitis occurred in 3 cases with 1 death in 1946. All 3 cases were connected with a primary vaccination performed at school age or later, a practice which has repeatedly been deprecated by the Ministry except in special circumstances. The fatal case received an inoculation against yellow fever within a few days of vaccination against small-pox. It seems advisable that *primary* vaccination should, if possible, be separated from yellow fever inoculation (another attenuated virus which has on occasions shown neurotropic properties) by an interval of at least three weeks.[1]

L. H. Murray and W. H. Bradley[2] report that 79 cases of small-pox occurred in this country in 1947, the highest number recorded since 1934. They all seem to have derived their infection from one or other of two importations.

The main point of interest was the extreme modification of the rash in some instances. The primary infecting case in one of the outbreaks had only a few spots and was considered at first to be a case of chicken-pox. Two cases had only five or six spots, which were so modified as to be quite unlike the rash of small-pox. In such difficult cases laboratory assistance with the diagnosis should always be sought. There were some failures of vaccination 'takes', which were subsequently shown to be due to the use of lymph which had been badly stored after issue. *Lymph not used within seven days of issue should always be discarded.* The laboratory tests available are described, namely, unfixed smears from macules and papules for the microscopic test, scrapings from papules, vesicles, and pustules for the culture test, and the patient's serum after the first week of the disease for antibodies. Specimens should not be sent from persons who have been recently successfully vaccinated. Where a laboratory test is positive it should be regarded as overruling a hesitant clinical opinion. Mass vaccination is not now encouraged in this country. It should only be considered when an outbreak appears to be out of control.

Post-vaccinal Encephalomyelitis.—E. T. Conybeare[3] ably reviews this subject. In the twenty years 1927–46 there were 222 known cases, of which 110, or 50 per cent, were fatal. Nearly half the cases and deaths were in the school age-group five to fifteen years. Only 16 cases, of which 6 were fatal, are known to have followed a re-vaccination, and in only 10 of these 16 cases was there evidence that a primary vaccination done in infancy had been successful. In the remaining 206 cases the disease followed primary vaccination or the vaccinal state was unknown. There did not appear to be any association of groups of cases with particular batches of lymph, nor did the method of vaccination appear to influence incidence or severity. The interval between vaccination and onset of neurological symptoms ranged from two to twenty-eight days, with a mean of 10·9 days. The following four clinical groups were recognized: *myelitis without encephalitis* 10 per cent, *encephalomyelitis* 10 per cent, *encephalitis* 75 per

cent, and *meningeal reaction* 5 per cent. In 55 of the 110 fatal cases histological examination was carried out and confirmed the clinical diagnosis. It is estimated that over 4,000,000 infant vaccinations were done during this twenty-year period, with 21 infant deaths, gaving a death-rate from the complication of primary vaccination of infants of the order of 5 per million. But this estimate includes the three years 1927–9 when post-vaccinal encephalitis was uncommonly frequent. In actual fact, in ten of the twenty years no infant deaths were certified from this cause. After primary vaccination at school age, the data are insufficient to calculate the incidence, but in Holland it has been shown that encephalomyelitis has been from ten to thirty times as frequent at this age as in infancy. In young adult males after *primary vaccination* the mortality-rate has been calculated at between 4 and 5 per million, and after *re-vaccination* just under 1 per million.

The End of Compulsory Vaccination. Compulsory infant vaccination was abolished by the National Health Service Act on July 5, 1948. C. Killick Millard[4] reviews the history of compulsory vaccination.

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SOCIAL MEDICINE.

F. A. E. Crew, M.D., F.R.C.P. Ed., F.R.S.

The disputation concerning the *exact nature of social medicine, and its relationship to public health* continues. Thus B. Benjamin,[1] in the course of a paper on the *statistical assessment of public health*, remarks: "a great deal of paper and verbosity has been expended in recent years upon 'social medicine' as if distinct from the science of public health which has been in the making in this country for over a century. The sooner it is realized that a mere change of title does not contribute to the solution of nor change the nature of outstanding problems of public health the more rapidly will constructive measures be taken to raise the application of preventive medicine to the higher level which is universally demanded." There is some misunderstanding here. The title was changed not in order to distinguish between social medicine and public health but to indicate that the problems and activities of public health had become so altered as to make desirable a new name signalizing the nature and direction of these alterations. Social medicine is distinct from public health only in the same sense that public health in its time became distinct from medical police. These three are variants of one and the same general corpus of knowledge, differing one from the other in that each of them is a harmonization of one and the same mutable discipline to the circumstances prevailing at different periods in the social evolution of this country. The difference in the contents of social medicine and public health is not to be recognized by comparing that of social medicine and that of public health within the last decade, but by contrasting the content of social medicine with that of public health as defined by, for example, E. Chadwick[2] and J. Simon.[3]

Social medicine is the result of the transformation of public health into a social science. As a result of this development medicine is now claiming its right to be included among, and to assume a position of considerable importance within, the social sciences. These developments are recorded and described by J. A. Ryle[4, 5] and F. A. E. Crew.[6] A. Davidson,[7] from his position as Chief Medical Officer of the Department of Health for Scotland, describes how in recent decades the emphasis in public health has been moving away from pathogenic micro-organism to socio-economic circumstance, from disease to health, and how in health-promoting measures the State has been claiming an expanding role. The individual (the unit in clinical medicine), he states, is no longer regarded as the unit in so far as the health services are concerned, but

has become replaced by the family and the household. The 'family doctor' is no longer an individual but a team. He shows how in increasing measure medicine, sociology, economics, and psychology have become integrated so that the content of public health has changed. For an historical account of the means by which Scotland attempted in the past to control the epidemic diseases, to relieve destitution, to improve the environmental conditions of the people, and to provide for them adequate medical care, the recently published book of T. Ferguson[8] is a positive mine of information.

This continuing uncertainty concerning the nature and content of social medicine has, of course, had its repercussions upon the teaching of this subject in the medical curriculum. This topic receives the attention of J. B. Grant,[9] whose unique position enables him to consider these matters against the background of developing medicine throughout the whole of the world. He concludes that the essential requirement for the teaching of social medicine is a community in which the student can go through the routines and apply the techniques of social diagnosis and therapy. He advocates that each medical school should assume responsibility for a model health service within a given community and that a Health Centre should be assigned to the social medical department for teaching purposes. He emphasizes the importance of the social worker, presenting the view that she bears the same relationship to the effectiveness of social medicine as does the nurse to clinical medicine. It remains to be shown whether the Health Centre, as conceived by Grant, will indeed prove to be the best milieu in which social medicine can be taught at the vocational level. It seems probable that the Health Centre, as we shall know it, will be primarily a means whereby curative medicine may be exercised under circumstances more advantageous to all concerned than those which obtain in the consulting rooms of individual general practitioners. But the exponents and practitioners of social medicine are not all of a kind, are not all graduates in medicine. They are a compound team which must include representatives of a variety of disciplines, the variety being determined by the nature of the investigation to be undertaken or the work to be done. Among them will be found the social psychologist, the sociologist, the geographer, the economist. It therefore seems not improbable that the laboratory in which social medicine will be expanded will be not the health but the community centre.

In another paper, A. Strom,[10] writing as a professor of hygiene, discusses the type of curriculum he himself would choose. This would deal in the main with a consideration of those diseases in the aetiology, development, or spread of which some factor or factors within the social environment is implicated, and secondly with those diseases which because of their nature and incidence create social problems of considerable magnitude. The course would also include an introduction to demography, vital statistics, medical economics, health education, eugenics, sociology, and social economics.

It is of interest to note that the term social medicine is assuming a very different connotation in the United States of America. L. H. Bauer and W. W. Bauer,[11] for example, show that there social medicine would seem to be a term given to those projects which have for their object the provision of curative medical services to the general public other than by government action.

J. H. Sheldon's[12, 13] *survey of 477 elderly people of pensionable age* in Wolverhampton fulfils an important task since it presents the total problem of the aged with its manifold medical and social ramifications and interconnexions. The social pattern of this random sample and the functioning of their minds and bodies were scrutinized and studied with the help of a detailed questionary. After giving an account of the physical state of the subjects and of the main physical symptoms complained of by them, the author goes

on to deal in similar fashion with their mental state, the social structure of their homes, and the problems arising from illness among these old people. He explodes quite a number of popular misconceptions and applies the corrective of exact recording to many vaguely held notions on the subject of old age. The main impression which he conveys would seem to be that old people are on the whole less handicapped than our clinical experience would tend to make us think. This book, packed with facts set down by a competent observer, is of the very greatest value and constitutes an irresistible invitation to further and more detailed investigation.

Two more papers dealing with the same subject are worthy of note. In that of J. V. Walker[14] there is nothing that can claim any originality in respect of method or conclusions; yet the paper is of value in that the survey was carried out personally by a medical officer having much experience in this field. That of J. W. Affleck[15] bears upon the same general question and is a study of a group of 788 old people in Leeds. He presents the interesting observation, doubtless not new to many, that there is a distinct unwillingness to leave the hospital bed on the part of the hospitalized aged sick, since for these discharge means the return to a lonely life and a hopeless struggle against cold, hunger, and discomfort.

A publication of the greatest interest is the report of a survey carried out by a joint committee of the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee.[16] The purpose of this inquiry was to provide accurate *information concerning the availability of the maternity services to different social classes and in different parts of the country, the use made of these services, their effectiveness in educating mothers and reducing mortality and morbidity amongst mothers and infants, the need for domestic help during pregnancy and the puerperium, and the nature and extent of present expenditure on childbirth.* It shows that the municipal antenatal services are used by all members of the community and that one-third of the mothers in the most prosperous social group make use of them, and that women in full-time work during pregnancy do not receive less antenatal care than non-working mothers, many of them leaving work soon after becoming pregnant. It discusses the varying proportion of women entering hospital for their confinement in different parts of the country, attributing these variations to lack of accommodation and transport difficulties in the main. It seems to suggest that although many women would prefer a good domiciliary midwifery service, in present circumstances there is little doubt that were accommodation available the habit of hospital confinement would become as established here as it is in America. The risks of stillbirth and neonatal death in home and institutional deliveries are compared. The Committee suggests, therefore, that either the number of institutional maternity beds must be greatly increased or better housing conditions and an efficient home help service established. The main complaint of mothers in this inquiry was of lack of analgesia. At the present time relief of pain is most frequently available to those who can afford a medical practitioner to deliver them. Difficulties of transport and shortage of persons suitably trained make it less common for those delivered by a midwife to receive analgesia. The cost of childbirth is then discussed. It would appear that the average cost for the well-to-do is £57 and for the manual worker £36, a high proportion of the total expenditure in all groups being on non-medical items, and even the new benefits and allowances cover only a relatively small proportion of the actual costs. The report reveals that the establishment and maintenance of lactation depends more upon the quality of antenatal supervision than upon care given during the puerperium, and that such antenatal supervision is more important than any other biological, social, or economic factor that was

considered. It seems to establish that the risks of stillbirth and prematurity are greater for those women who remain at work during the later stages of pregnancy, even when these make the same use of antenatal services as non-working women, and that medical care is by no means all that is required by mothers during the later weeks of pregnancy and after confinement. The provision of domestic help would seem to be essential. The problem of the unmarried mother is then discussed. It would seem that economic circumstance makes it more probable that she will remain at work longer and return to work sooner (the alternative frequently being destitution), that she tends to come under antenatal supervision at a much later stage of pregnancy, that she is rarely delivered by a doctor, and is most unlikely to receive analgesia. This report reveals many defects in the existing organization of the maternity services and its recommendations are all essentially practical.

A paper by E. J. Williams[17] on the *decline in the proportion of breast-fed babies* is worthy of mention. Although the conclusions reached are of no great significance this pilot survey does throw light upon the proper design of such investigations.

The public health, the well-being of an organized society, can be measured by the use of certain demographic yardsticks. Amongst these are movements of the birth-, death-, and fertility-rates and natural increase, since these are reflections of the reactions of human beings to circumstances and conditions within their total external world. A report by P.E.P.[18] constitutes a comprehensive, fully documented and simply presented account of *population trends* together with a fair and objective consideration of what these trends imply and an outline of a *population policy* designed at least to maintain the present quantity and quality of our people. Although this report contains little that is peculiarly new, either in respect of factual information or of interpretation, there is no other book of recent appearance which presents so complete an account of this particular subject, for in it are integrated and synthesized the results of the labours and ponderings of the many who in recent years have written upon it. Emerging from the argument concerning population trends and the retreat from parenthood comes the suggestion that the objective of a population policy must be to achieve a stable fertility at a level involving an average number of about 2·5 children in each family. The methods to be adopted for the achievement of this objective are set out in detail: maternity grants, family allowances, social insurance, tax rebates, the provision of suitable houses, and other environmental health services. It is clearly recognized that the removal of the economic burdens of parentage are not in themselves sufficient to persuade people to increase the size of their families. It is suggested that to the Minister of Health should be given an additional portfolio of Minister of Population, and that within the National Health Service there should be an organized Family Welfare Service in which the medical practitioner would be the advisor of those about to marry and the guardian of the child yet to be conceived. There is no doubt that for the present the recommendations made are far in advance of public opinion or of the ability on the part of the medical profession to give effect to them; but nevertheless the argument presented and the recommendations made are fundamentally sound and well merit the consideration of all who are concerned with such projects as planned migration or the relief of man-power shortage by the importation of displaced persons.

Of great interest to students of social medicine will be the work of Stocks on the *statistics of rheumatic diseases*, an account of which is to be found in a text-book on the subject edited by W. S. C. Copeman.[19] In this it is recorded that out of 16·7 million days of incapacity for work within a year amongst insured men muscular rheumatism accounted for 220,000 days, lumbago for

194,000, rheumatoid arthritis for 131,000, osteo-arthritis for 64,000, subacute and articular rheumatism for 40,000, rheumatic fever for 11,000, chorea for 4000, together with arthritis (unspecified) 201,000, and rheumatism (unqualified) 702,000. These are figures given in the report on incapacitating sickness in the insured population issued by the Department of Health for Scotland in 1937 8. The records maintained by the Emergency Medical Services are used to display the contributions to total illness amongst men of osteo-arthritis and muscular rheumatism. They show that these increased rapidly as age advanced whilst that of rheumatic fever declined, that amongst men under 25 two-fifths of all rheumatic illness consisted of rheumatic fever and its sequelæ, one-fifth of other forms of arthritis, and two-fifths of muscular or undefined rheumatic conditions, and that at ages 33–44 rheumatic fever contributed less than one-tenth, other arthritis about a quarter, and muscular types over three-fifths.

Rheumatic fever in Denmark, where it is a notifiable disease, is then discussed, the annual notification rate during 1938–43 in this country being 74 per 100,000 persons. It is pointed out that a comparable rate for England and Wales would be 30,000 cases annually, that about 7 out of every 1000 infants born can be expected to have rheumatic fever before the age of 15, and that subsequently another 38 attacks would be expected amongst the survivors. The author, using the records of the London County Council for 1938, suggests that about 2½ per cent of London's child population were suffering from or had experienced some form of rheumatic infection. From other figures provided by medical boards of the Armed Forces, the Canadian Civil Service, various New York hospitals, a Ministry of Health social survey, and individual workers in the field of rheumatic disease, the author draws many conclusions of very great interest.

A paper dealing with *morbidity of various kinds* is that of A. Davidson,[20] who reviews pre-war analyses of sickness in insured persons which were presented in the reports of the Department of Health for Scotland. It is revealed that in the insured population of Scotland (1·8 millions, 37 per cent of the total population) in 1938 between a quarter and a third of those displaying chronic diseases were under 35 years of age; incapacitating illness lasting more than three days accounted for the loss of 25·9 million working days and only a relatively slight proportion of this loss was contributed from 30 onwards by chronic sickness lasting throughout the year. This paper then deals with the findings of a review made between 1937 and 1939 of 50,000 patients whose illnesses had lasted more than three months, which revealed that the proportions disabled by the most common conditions were: rheumatism 1 in 7, cardiovascular disease 1 in 8, peptic ulcer and other digestive disease 1 in 10, other important causes being injury and psychoneurosis; that the incidence of sickness was particularly high under 40, and that there was great need for early treatment and close co-operation between the general practitioner and the specialist services whenever recovery failed to follow quickly upon simple treatment.

Such as are interested in *social resettlement as part of medical therapy* will find much of interest in a paper by A. E. Turner et al.[21] It deals with the provision of an industrial milieu in which severely disabled and crippled men may recapture their self-esteem. It would appear that this venture is remarkable for the striking change that is displayed by the disabled, a new happiness, enthusiasm, and sense of corporate life being easily discernible in them after comparatively short periods of time.

A new line of most profitable research is suggested by the paper of M. M. Johnstone and M. E. Hosker,[22] in which the *sex differentials with respect to diseases* are discussed and the *incidence of certain diseases in married and unmarried*

women respectively contrasted. According to this preliminary investigation marriage would indeed seem to be a relatively healthy occupation, since married women suffer a higher mortality than single women and men from only two diseases—diabetes and cancer of the uterus. The paper would seem to indicate that, with the exception of appendicitis, every disease which causes a higher mortality amongst men than amongst women also causes a higher mortality amongst single than amongst married women. It would seem to follow therefore that differences in respect of occupation must play some part in determining the differential risk of these diseases to men and women.

To those medical officers of health who are re-orienting themselves to changing circumstances consequent upon the introduction of the new health services the two papers by B. Benjamin,[1, 23] to one of which reference has already been made, must prove of value. The author, having made the point that the factual information upon which policy is based must be provided by a statistical department, shows that such activity must be discriminatory, and thereafter suggests what particular statistical activities the M.O.H. should sustain.

The harvest of 1948 is greatly enriched by the publication of the Heath Clark lectures of 1948, on *British pioneers of social medicine*, delivered by Major Greenwood.[24] The author, defining social medicine as that application of medical and scientific knowledge to the prevention and relief of suffering and to the raising of a standard of living which can only be effected by social agencies and by co-operation, renders great service by resurrecting for our guidance those historical figures who in their day laid the sure foundations on which we now build. Writing with great elegance, great knowledge, and even greater sympathy, he depicts the personalities and critically assesses the work of those who during recent centuries have found great pleasure in doing sums, sums which shed light upon the public health, and also of those to whom the sums meant much and who translated their meaning into political action.

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SPINE INJURIES, CERVICAL, PARAPLEGIA IN. (*See* PARAPLEGIA IN CERVICAL SPINE INJURIES.)

SPLEEN, SURGERY OF. (*See also* PORTAL HYPERTENSION.)

A. Rendle Short, M.D., F.R.C.S.

Ruptured Malarial Spleen. Traumatic rupture of the enlarged malarial spleen is common in tropical countries; spontaneous rupture does occur, but is rare. J. M. Lubitz,[1] of New Orleans, describes a case in a war veteran, aged 37. The patient was in bed with a malarial attack, and had vomited

shortly before rupture. There was sudden severe pain, slight general rigidity, marked tenderness and spasm in the left hypochondrium, and no peristalsis was audible. The spleen could not be felt. Recovery followed splenectomy, eight hours after onset, with the aid of blood transfusion. The mortality in published cases is about 30 per cent. No doubt the failures are more likely to pass unrecorded.

REFERENCE.—[1]*Ann. Surg.* 1948, **127**, 40.

SPLENIC ANÆMIA. (*See* ANÆMIA, SPLENIC.)

SPRUE. (*See* ANÆMIA OF THE SPRUE SYNDROME.)

STERILITY AND INFERTILITY.

Clifford White, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G.

S. R. Meaker[1] states that sterility is the "inability to initiate the reproductive process on the part of a couple who have desired and who have attempted to reproduce for a reasonable length of time, ordinarily at least a year", and infertility is "the failure to produce a viable child". Thus a patient who gives birth to a macerated fœtus because of erythroblastosis is infertile but not sterile. These definitions are not accepted by everyone. Some regard sterility and infertility as meaning the same thing. The problems of sterility and infertility remain difficult: the literature is enormous, but there is a tendency to carry out more and more investigations which do not necessarily lead to any practical results as regards treatment. This is especially the case as regards infertility, so it is simpler to consider the question of sterility. Twenty-five years ago it was regarded as a great advance when it was proved that in a large proportion of sterile marriages it was the husband who was at fault. The percentage of cases in which the male is at fault has been given at 25 to 60 per cent. C. Coghlan[2] found a high proportion of male infertility among prisoners returned from Japanese prison camps and attributed it to lack of vitamin E. Gynæcologists stress that the male must be examined as well as the female, but since the number of male patients with gross anatomical abnormalities or palpable inflammatory masses is small, the examination really consists in an examination of the seminal fluid. This examination has become more thorough recently; not long ago a pathologist was content to send in a report simply stating whether spermatozoa were present or not; whereas now the amount of the ejaculation, the sperm count, the percentage and types of abnormal spermatozoa, the duration of mobility under specified conditions, and the presence of blood and pus are usually recorded. Similarly the proportion of women consulting their doctor because of sterility who have pelvic abnormalities discoverable on bimanual examination is small (especially if a congenital retroversion is no longer regarded as an abnormality), and so the investigation of the patency of the tubes by I. C. Rubin[3] was a great advance.

In a monograph issued in 1947, Rubin[4] states that he was investigating the use of collargol in Vienna and published a paper on the subject in May, 1914,[5] while in America W. H. Carey[6] published a paper on the same subject in March, 1914. Owing to the clinical disadvantages of the use of collargol Rubin[7] turned his attention to inflation and inflated his first patient with oxygen in November, 1919, in New York. She became pregnant within 2 months and was delivered of a child at term. His first series of inflation cases was published in 1920. By this time oxygen had been replaced by carbon dioxide because its more rapid rate of absorption from the subphrenic space lessened the duration of the discomfort referred to the shoulder. Rubin's valuable book contains over 400 pages, and it is impossible to abstract it

adequately but a few further points of special interest may be selected. It is stressed that insufflation (or lipiodol) should always precede a myomectomy intended to relieve sterility, because if the tubes are patent the myomectomy may be postponed as pregnancy is possible, whereas if the tubes are occluded at the uterine end myomectomy should be performed and the patency of the tubes again investigated after the operation, as, unfortunately, it frequently happens that the removal of the tumours kinks the tube or a hæmostatic ligature may occlude its lumen. Repeated insufflation should be carried out soon after the operation of salpingostomy to keep the new ostium patent. Insufflation may be carried out before advising contraceptive precautions, as they are unnecessary if the tubes are not patent. The question of tubal spasm must be excluded in all cases but is not always easy to do. If the pressure of gas or lipiodol in the uterus is raised very slowly spasm is less likely to occur than if a sudden and violent rise of pressure occurs. Atropine with or without morphine or pethidine may be administered twenty minutes before the operation with good results especially with nervous patients. The utmost gentleness is essential, as the less the patient is frightened and hurt the less the chance of spasm. The injection of a radio-opaque fluid such as lipiodol has the great advantage of showing the site of the tubal obstruction, and, in spite of theoretical objections, it does not seem to damage the tube; hence it has become increasingly popular and many gynæcologists have given up inflation in favour of lipiodol. Rubin followed up insufflation by lipiodol in 99 patients of one recorded series; in 9 patients where insufflation showed non-patency, lipiodol under high pressure showed a slight degree of patency, whereas, on the other hand, 8 patients showed some degree of patency with insufflation but tubal closure with lipiodol. In other words both procedures seem to be of exactly equal value in demonstrating patency. Insufflation when a kymograph is used enables tubal contractions to be observed, and so the vigour of the tube to be assessed.

L. Bonnet,[8] of Paris, by observations on the rate of flow of gas at a given pressure, attempts to estimate the calibre of the Fallopian tube to see if it is big enough to transmit an ovum which normally measures 200 μ.

When the question of performing a plastic operation on an occluded tube arises it is of the utmost importance to know whether the obstruction is at the fimbrial end or at the isthmus, as many surgeons think that attempts to restore the patency of the tube should be limited to cases of fimbrial obstruction, because the results of operation if the occlusion is in any other portion of the tube are so bad. A. Hamant[9] found 40 per cent of closures at the isthmus and 60 per cent fimbrial whereas comparable figures by S. A. Robins and A. A. Shapiro[10] are 18·7 and 82·3. The condition of the rest of the tube besides the site of the occlusion is of importance when considering the advisability of performing a plastic operation. After gonorrhœal salpingitis the ciliated epithelium of the tube is destroyed, the sealed end of the tube is drawn in, and extensive mucosal agglutination is present. The prognosis from plastic surgery in such a case is obviously poor. In cases of perisalpingitis the epithelium of the tube is not affected and the prognosis is better. In some cases of suppurative perisalpingitis the fimbriæ are not even closed; the writer once evacuated a pint of pus by posterior colpotomy and the patient had a living child at term within a year.

In the great majority of patients complaining of sterility, the tubes are patent to lipiodol or inflation and further information is obtained from examination of an endometrial biopsy. If it shows the secretory phase of the menstrual cycle, it indicates that ovulation has taken place and so metropathia and anovular menstruation can be excluded. Endometrial biopsy by means of

a suction curette can be done without anæsthesia, but it has certain disadvantages. To show the secretory phase the biopsy has to be done a few days before the expected onset of the period, whereas insufflation and lipiodol injections are best done a day or two after the period is ended. Thus the patient has to be subjected to manipulations twice in a month, and specimens obtained with a suction curette are not always satisfactory. For these reasons it may be easier for the patient to keep a record of her temperature; a biphasic curve is evidence that ovulation has occurred. The woman takes her temperature by the mouth every morning before rising and finds that it is mostly about 98°. If it drops to 97·5 on the 13th day and rises to 98·5 on the 14th day and remains raised for the next few days, it is strong evidence that ovulation has occurred. The temperature varies with each patient the essential thing is a rise of 0·5 to 0·9 F. If ovulation is expected to take place on the 14th day, it is usual to advise that coitus should occur, if possible, on the 13th, 14th, and 15th days so as to catch the ovum if ovulation happens a day earlier or later than usual.

The *p*H of the vaginal secretion is not now thought to be so important as it formerly was, although a very highly acid secretion immobilizes spermatozoa. The estimation of the B.M.R. in both husband and wife is popular in the U.S.A. K. M. Grant[11] lays stress on hypothyroidism as a cause of infertility, and states that a B.M.R. of −7 to −10 is an indication for treatment by thyroid extract, although many regard these figures as being within the normal range. Blood cholesterin determinations, sugar tolerance tests, pregnandiol assays between the 20th and 24th days, and a radiograph of the sella turcica are asked for by some.

Œstrogen and progesterone prepare the endometrium for the embedding of the ovum. If the fertilized ovum takes several days to traverse the length of the Fallopian tube (as many believe) there is a good chance that the endometrium will be ready for its nidation, but if the fertilized ovum reaches the uterus unduly quickly the necessary changes in the endometrium may not be complete. For this reason R. Christie Brown[12] suggests, among other things, that patients should take 0·6 mg. of dinœstrol and 10·0 mg. of ethisterone daily from the 16th day before the anticipated onset of the period until the onset of the period, when the drugs are stopped since menstruation shows that attempts to aid the nidation of the ovum shed on about the 14th day has failed. It should be noted that the administration of these hormones may delay the onset of menstruation for a few days. He also thinks this treatment is useful for patients who have repeated miscarriages and in whom no other cause for miscarriage has been found. After about the 16th week of pregnancy the placenta secretes progesterone freely as well as œstrogen, hence it is not usual to continue to administer hormones after the 16th week of gestation.

Some cervical discharges are spermatolytic and demand treatment if severe and septic. Many patients who have cervical erosion conceive easily and a congenital erosion is probably not a deterrent to pregnancy. A bad acquired erosion, as frequently seen in a patient complaining of "one-child sterility", may be cauterized with the electric cautery and the cervical canal scraped with a sharp spoon on the same occasion.

The state of the cervical plug of mucus has received more and more attention in recent years. A solid plug of tough mucus in the cervical canal, if it does not soften and become free at about the time of ovulation, is referred to as a cervical block. The mucus plug should soften to receive the sperms at about the time of ovulation. Grant states that some of the credit given to insufflation of patent tubes rightly belongs to the passage of the insufflation-cannula through

the cervical canal; but whereas it used to be thought that there was a stenosis of the cervix which required mechanical stretching, it is now thought to be an unduly tough plug of mucus which should be disturbed. The administration of œstrogens is stated to increase the receptivity of the cervical mucus to spermatozoa this has been shown by the post-coital examination of the cervical mucus. E. Viergiver and W. T. Pommerenke[13] have investigated the cervical mucus and find that it is most abundant, most translucent and acellular, and possessed of lowest viscosity at the time of ovulation. They find that cervical mucus contains a fermentable reducing substance and quote J. MacLeod's[14] statement that sperms require a utilizable carbohydrate as a substrate in order to maintain their mobility. He has shown that in a glucose-free medium at body temperature many spermatozoa lose their mobility within 2 hours, whereas if adequate glucose is present and the oxygen tension is low, maximal motility is retained for at least 12 hours *in vitro*.

It is probable that in some patients more than one factor is contributing to the sterility; thus a woman who is rapidly increasing in weight does not easily conceive, and such a patient may have to be put on a reducing diet, with thyroid medication if indicated; her cervicitis may require treatment as well as her tubes being inflated or injected, and the fact that she is ovulating established.

REFERENCES.—[1]*Human Sterility*, 1934; [2]*J. Mount Sinai Hosp.* 1947, **3**, 167; [3]*J. Amer. med. Ass.* 1920, **75**, 661; [4]*Utero-tubal Insufflation*, 1947, C. V. Mosby Co.; [5]*Zbl. Gynäk.* 1914, **38**, 658; [6]*Amer. J. Obstet. Gynec.* 1914, **69**, 462; [7]*Surg. Gynec. Obstet.* 1915, **20**, 435; *J. Mount Sinai Hosp.* 1947, **3**, 141; [8]*Rev. franç. Gynec.* 1929, **24**, 81; [10]*New Engl. J. Med.* 1931, **205**, 380; [11]*Amer. J. Obstet. Gynec.* 1948, **3**, 419; [12]*Brit. med. J.* 1948, **2**, 851; [13]*Amer. J. Obstet. Gynec.* 1947, **3**, 459; [14]*Endocrinology*, 1941, **29**, 583.

STOMACH. (*See also* GASTRIC AND DUODENAL ULCER.)

STOMACH, DIVERTICULA OF. *F. Avery Jones, M.D., F.R.C.P.*

S. P. Bradow and M. A. Spellberg[1] (Chicago) report 26 new cases. Although there are only 150 cases recorded in the literature it is less of a medical curiosity than these figures suggest, and the incidence is 0·015 per cent of the total admissions at the Veteran's Administration Hospital, Illinois. The common site is on the posterior wall of the lesser curvature just below the cardio-œsophageal opening, where it may closely simulate a large gastric ulcer radiologically. In this situation they are always congenital in origin. Elsewhere, traction diverticula may occur, particularly near the pylorus. The diagnosis is suggested by finding a mobile sac with a well-defined smooth shadow in this position. Barium is commonly retained six to twenty-four hours. The demonstration of a neck to the sac, with gastric rugæ lining it, is confirmatory evidence, and the diagnosis may be firmly established gastroscopically.

The condition may be entirely symptomless. Melæna or hæmatemesis, vomiting, belching, epigastric pain, relieved or aggravated by food, may occur. Fifteen of the 26 cases had other intra-abdominal diseases which undoubtedly contributed towards the symptoms. Because of the frequency with which they can be asymptomatic, their mere presence must not be accepted as accounting for the patient's symptoms and a careful search must be made for other causes.

If the symptoms are mild, a medical régime with bland diet and alkalis after meals will bring relief. Gastric lavage and postural drainage may be helpful when retention in the diverticulum is present. Surgical treatment is only occasionally indicated for the cardiac diverticula, but a laparotomy is advisable for patients with an apparent diverticulum in the lower two-thirds of the stomach because malignant lesions may give rise to a mistaken diagnosis of diverticula in this region.

REFERENCE. [1]*Gastroenterology*, 1948, **11**, 59.

STOMACH, SURGICAL DISEASES OF. (*See also* GASTRIC AND DUODENAL ULCER, SURGICAL ASPECTS.)

Norman C. Tanner, F.R.C.S.

Carcinoma of the Stomach.

Early Detection.—Further suggestions have been made to find a solution of the problem of the early detection of gastric cancer, which has so far defeated all efforts but on which the hopes of surgical benefit must rest. F. B. St. John, P. C. Swenson, and H. D. Harvey[1] in 1944 had subjected 2413 random patients over the age of 50 to brief fluoroscopic examination of the stomach, and found two silent carcinomas and one lymphosarcoma. O. H. Wangensteen,[2] taking into account the well-known association of hypochlorhydria or achlorhydria with gastric tumours, examined with special care, using radiology and gastroscopy, 464 patients who had a histamine-fast achlorhydria. In this group 50 were found to have simple gastric polyps and 3 had carcinoma. Only one of the carcinomas was early and this one was missed radiologically. [There is a tendency to discredit fractional and other types of gastric analysis in diagnostic clinics. They give a valuable pointer to a probably cancer-prone group. If gross blood is present in the stomach it is even more suspicious of carcinoma.—N. C. T.]

Aggressive Attitude to Carcinoma.—In view of the hopeless outlook of the patient with unresected gastric carcinoma, the chance of cure and the good chance of palliation that gastric resection can give, an aggressive attitude is more than ever justifiable. G. T. Pack[3] warns against refusing surgical help to the cancer sufferer because of an unnatural pride in low figures for operative mortality. [This pride should be reserved for operations of convenience for non-malignant conditions, e.g., duodenal ulcer.—N. C. T.] The aggressive attitude is expressed in a higher resection-rate, more extensive glandular resections, higher gastric resections, resection of the peritoneum of the lesser sac, or of neighbouring invaded organs, e.g., pancreas, liver, colon, providing there are no distant hepatic, peritoneal or other metastases. G. McNeer and A. James[4] reporting 15 cases of resection of the stomach together with an adjacent organ, found that of 6 cases who were operated on over five years ago, 4 were still alive.

The diminution in operative mortalities which has occurred in late years, and the consequent freer use of high and total gastrectomy, have increased resectability rates. D. State et al.,[5] in reporting 586 cases of gastric carcinoma treated between 1936 and 1945 inclusive, found that whereas in 1936 the operability, resectability, and mortality rates were 57, 28, and 25 per cent, in 1945 these rates were 88, 80, and 4·9 per cent. His 10-year figures were similar to those previously reported by G. T. Pack and G. McNeer. Comparison of statistical data for 10-year period:

	Dr. Wangensteen and Associates	*Drs. Pack and McNeer*
Number of gastric cancers	586	683
	per cent	per cent
Operability	76	79
Resectability	52	35
Operative mortality:		
Resection	16·6	Subtotal Total
Gastro-enterostomy	24	
Resection survivors:		
5 years	21·5	
Total gastrectomy	10	18·3 } Radical
Transthoracic cardiectomy	None listed	17·0 } procedures

Gastric resection is also valuable palliation. The average survival after resection in those who ultimately expired was 22·4 months and the majority were comfortable up to within a few weeks of death. On the other hand, C. E.

Welch and A. W. Allen[6] found that if the gastrectomy was only meant to be palliative, that is, that it was known that cancer was left in the abdomen, then the life expectancy averaged 8 months.

Prognosis of Resected Gastric Carcinoma.—In the MEDICAL ANNUAL, 1948, p. 319, the relationship between the macroscopic appearance of gastric carcinoma and its prognosis after resection was discussed. Further evidence that Borrmann's classification may be valuable in this respect is given by S. N. Maimon, W. L. Palmer, and J. B. Kirsner.[7] Out of 377 patients, 115 (30·8 per cent) survived gastric resection, 30 (7·4 per cent) survived 5 years or more. Of the growths of the 30, 26 were Borrmann *Types I* and *II*, 4 were *Type III*, and none were *Type IV* (*Fig.* 54). This agrees with Schindler's findings. Histo-

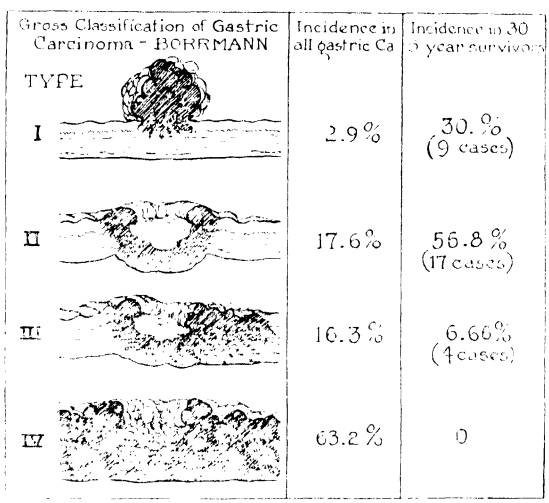


Fig. 54.—Prognosis in gastric cancer. (*Reproduced from the "American Journal of Medicine".*)

logically the tumours of the five-year survivors were of all types, though there were less infiltrative lesions than in the group who survived one year or less. The writers state that the size of the tumour bore little relationship to the degree of malignancy and life expectation, 26·6 per cent of the five-year survivors having had palpable masses.

The Incidence of Gastric Cancer.—Superficially there appear to be quite marked variations in the incidence of carcinoma of the stomach in different parts of the world. A careful analysis by G. T. Pack and G. McNeer[8] demonstrates that the reported incidence varies directly, with but few exceptions, with the economic status, educational and medical facilities, and life expectancy of the community or country. Cancer of the stomach occurs most frequently between the fiftieth and seventieth year, and the incidence is not unnaturally lower in countries such as the U.S.S.R., Bulgaria, Romania, and India, where fewer than 15 per cent of the inhabitants reach the age of fifty. Japan is an exception in that there is a high mortality-rate from the disease despite the fact that only 15·3 per cent of its inhabitants reach the age of fifty. The areas where low incidence rates are reported for gastric carcinoma are areas where life expectancy is low and the facilities for recognition and registration of the disease are poor.

The writer concludes that at a common level of longevity, economic security, and public health education and opportunity, it is probable that the incidence of gastric cancer would be approximately the same the world over.

The rare occurrence of gastric carcinoma in youth must not be forgotten. Out of 1913 cases of gastric carcinoma, M. Block, A. H. Grief, and H. M. Pollard[9] found 20 cases under the age of 31. During the same time 50 benign ulcers of the stomach occurred in patients under 31, so that there is about a 30 per cent chance that a gastric ulcerative lesion in a patient under 31 will be carcinoma.

Cytological Examination of Gastric Aspirate for Carcinoma.—With such an insidious disease as carcinoma of the stomach any simple and safe diagnostic procedure which gives a reasonable proportion of definite results is worthy of consideration. Cytological methods as an aid to diagnosis were largely fostered by Papanicolaou in 1928, who made observations on the uterus. The method depends on the observation that most malignant growths desquamate cells which can be identified after suitable fixation. In the stomach a great difficulty is the rapid digestion of such cells which occurs. The method recommended by R. M.

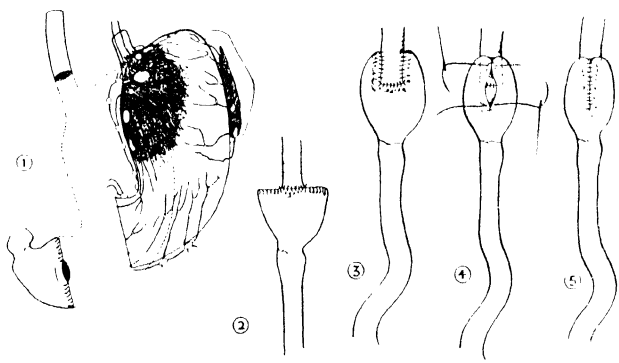


Fig. 55. Technique of œsophago-gastric anastomosis after transection through pyloric antrum.

Graham, H. Ufelder, and T. H. Green[10] is to aspirate fasting gastric contents, and send them to the laboratory at once. The secretion is centrifuged, the sediment spread on a glass slide, and placed in a fixative of ethyl ether and 95 per cent alcohol for at least 15 minutes. This secretion must be fixed within half an hour of withdrawal. It is then stained by Papanicolaou's method. The authors describe the microscopic appearances that may be found. Using this method in 50 cases, a positive result was correctly given in 15 of 24 with gastric carcinoma, and incorrectly given in 1 of 26 without carcinoma (a case of benign gastric ulcer).

Œsophago-gastric Anastomosis after Transthoracic Resection of the Upper Stomach.—It has become an accepted method of reconstruction, after resection of carcinoma of the cardia and upper stomach, to close the cut end of the residual stomach and make an anastomosis between the œsophagus and the anterior surface of the stomach. N. C. Tanner[11] (Rome Assembly, 1948, Internat. Coll. Surg.) finds that end-to-end anastomosis of the œsophagus to part of the cut end of the stomach gives excellent results. In 12 such cases there were no leakages and no stenosis followed it being possible post-operatively to pass a full-sized œsophagoscope through the stomata with ease. In addition it

PLATE XLI

ŒSOPHAGO-GASTRIC ANASTOMOSIS

(N. C. Tanner)



Radiograph after end-to-end œsophagogastric anastomosis. In this case the stomach "angles" were not stitched against the side of the œsophagus.

enables the surgeon to remove more stomach, or alternatively to make the anastomosis with less tension.

The technique of anastomosis varies, depending on the amount of gastric tissue removed. If most of the stomach is removed, a triangular part of the pyloric antrum is left (*Fig.* 55). The method of closure Tanner found secure in such a case is to close part of each end of the cut surface and anastomose the œsophagus to the middle part. The two angles left are then brought against the side of the œsophagus and sutured to it, thus greatly strengthening the anastomosis (*Fig.* 55).

If much of the stomach is conserved, as is permissible in the case of squamous-celled tumours of the lower œsophagus, or tumours very localized to the cardia (though the glands around the left gastric artery must always be removed), then an oblique cut end results (*Fig.* 56). Much of the lesser-curve side and a minimum of the greater-curve side is closed and again an end-to-end anastomosis is made. This gives added length to the stomach, enabling the anastomosis to be made with less tension. The lesser-curve side is then inverted,

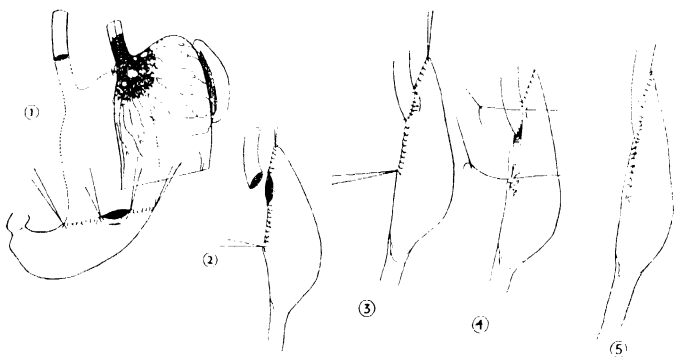


Fig. 56.—Technique of œsophago-gastric anastomosis after transection through body of stomach.

the greater-curve end is stitched against the side of the œsophagus to take off the strain (*Fig.* 56) and if possible a third row of sutures is used to give added safety (*Plate XLI*).

In the more extensive upper gastric neoplasms it is necessary to remove the whole stomach. In such cases he transects the jejunum and mobilizes it after the method of Roux, and makes an end-to-end œsophago-jejunostomy.

Total Gastrectomy for Carcinoma. With the lowering mortality after total gastrectomy it can be performed with less hesitation than in the past. G. T. Pack, G. McNeer, and R. J. Booker[12] do not agree that total gastrectomy is necessary for all gastric carcinomas (*see* MEDICAL ANNUAL, 1948, p. 319), because most deaths following subtotal gastrectomy for carcinoma are due to distant metastases and not local recurrence. On the other hand, there is a tendency to perform abdominal total gastrectomy in cases where a transthoracic approach would have given a better chance of extirpating the upper limits of the growth. It must be remembered that there is intramural extension for 3 to 4 cm. beyond the obvious limits of the disease. In 44 total gastrectomy cases H. K. Ransom[13] examined tissue at the two cut ends and found carcinoma in the cut œsophagus in 21 and in the cut end of the duodenum in 13 of the cases.

Surgical Technique of Total Gastrectomy.– Pre-operative lavage of the stomach with N/10 hydrochloric acid is said to reduce the bacterial content[12] and is desirable in those cases with a low gastric acidity.

It cannot be over-emphasized that where the œsophagus is involved, or even where the growth is within 3 to 4 cm. of the cardiac orifice of the stomach, the abdominal route is inadequate, difficult, and dangerous.

When the abdominal route is used R. de Vernejoul[14] confirms Lefevre's suggestion that the lower œsophagus should not be mobilized for fear of impairing its blood-supply. On the other hand, most American and British surgeons have made a point of œsophageal mobilization. There is a considerable following for H. Lefevre's[15] methods on the continent of Europe. He makes a point of excision of the xiphoid process to improve visualization. He has further developed the 'sandwich' method of œsophagojejunal anastomosis. A loop of jejunum is brought up, transected, and the cut ends closed. The efferent loop is fixed first to the diaphragm and then to the posterior surface of the œsophagus and an end-in-side œsophagojejunostomy is made into it. The afferent loop is stitched high over the front of the œsophagus and stitched to the efferent loop so that the œsophagus is sandwiched between them, and of course the loops are short-circuited.

Results of Total Gastrectomy. F. H. Lahey[16] points out that the mortality of total gastrectomy depends very largely on correct selection of cases for the operation. In his clinic the mortality for the last 43 cases had dropped to 16 per cent. After following up 87 operative survivors he stated that 50 per cent survived 12 months, 30 per cent 24 months, and 21 per cent 3 years or more. H. K. Ransom's results were somewhat similar. He summarized them as follows: of the operative survivors one-third live under 6 months, one-third live between 6 and 12 months, and out of 41 cases 3 survived 5 years. R. Smithwich[17] reported a patient alive and well 10½ years after total gastrectomy for carcinoma.

Neurogenic Tumours of the Stomach. There is some confusion between neurogenic and smooth-muscle neoplasms of the stomach, because of the difficulty in differentiation histologically. J. P. West and G. Knox[18] reported 8 nerve-sheath tumours. These tumours tend to ulcerate and bleed and may become malignant. Pain is not a prominent symptom, though all the 8 had vague epigastric distress. Radiologically the tumours are seen as smooth rounded filling defects: sometimes central ulceration can be recognized.

Every effort should be made to determine the nature of the tumour at operation, particularly of those near the cardia, because the benign lesions only require local excision, and not massive gastric resection. Microscopic section of the nerve-sheath tumours in most cases discloses spindle-shaped cells, with palisading nuclei and some giant nuclei. In some cases swollen hypertrophic tortuous nerve-trunks may be seen at the periphery of the tumour.

Prolapse of Gastric Mucosa through the Pylorus. There is good radiological evidence that the mucosa of the pyloric antrum may at times prolapse into the first part of the duodenum. Some writers have claimed that the prolapse produces symptoms and may require surgical treatment.[19] It is the reviewer's opinion that no good case has yet been made out for this. I. A. Ferguson[20] reported that the condition was found in 7·7 per cent of 297 radiological examinations. He reported 6 cases in which severe digestive disturbances occurred, hæmatemesis and melæna in 4 of them. Before accepting this as a symptom producing abnormality, one must exclude the possibility of other explanations of the symptoms. The series so far produced appear to have been diagnosed on incomplete evidence and gastroscopy appears to have been omitted in the majority, so that the possibility of gastritis or acute ulcer has not been disproved.

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SUBDURAL ABSCESS.

(*See* INTRACRANIAL INFECTIONS.)

SWIMMING-BATHS: RELATION TO ILLNESS.

W. H. Bradley, D.M., M.R.C.P.

The epidemic of poliomyelitis in 1947 called for considerable speculation, on the part of laymen and doctors alike, concerning the part played by the swimming-bath in the dissemination of disease.

Dr. J. Roswell Gallagher,[1] the School Physician of Phillips Academy, Andover, Massachusetts, studied the question through the seven-year period 1941 to 1947, choosing as his period of observation the first eight weeks of the year when respiratory disease is at its highest incidence. He compares the sickness rate in two groups of young men—a 'swimming' group averaging 117 each year and a 'non-swimming' group of 500. The swimming group contained only members of the Academy swimming team and those taking part in competitive swimming. No other persons in this large boys' boarding-school were allowed to use the swimming pool.

The number of days lost as the result of respiratory-tract illness and the number of admissions to the sick rooms for the same cause were both about 14 per cent greater amongst the swimmers than amongst those who did not use the pool. There was, however, considerable yearly variation in both the incidence and the number of days lost from this type of illness. It is clear that swimming pools used in the winter require careful supervision so that excessive respiratory illness may be avoided, but when careful control is exercised and when normal conditions exist, there is, on the basis of this experience, no reason to expect a higher incidence of respiratory infection amongst swimmers. In the presence of a highly communicable disease, however, these data suggest that it is desirable to take extra precautions: this applies particularly to mumps and measles, which seem to spread more rapidly amongst swimmers.

The writer concludes that in the presence of careful control and reasonable precautions the benefits of the swimming pool were not overbalanced by its effect upon either the frequency or the duration of illness. These observations cannot, of course, be applied to poliomyelitis and other summer epidemics.

REFERENCE. [1]*New Engl. J. Med.* 1948, **238**, 899.

SYMPATHECTOMY FOR DYSMENORRHŒA.

(*See* DYSMENORRHŒA.)

SYMPATHETIC NERVOUS SYSTEM, SURGERY OF.

E. D. Telford, M.A., M.Sc., F.R.C.S.

The operation of sympathectomy, by which one means cord-ganglionectomy and not the obsolete perivascular method, has been extensively practised for a quarter of a century. During these years the number of conditions for which the operation has been performed would make a list well-nigh comparable to an Index of Diseases. Many of these interventions have been entered upon with an enthusiasm quite unhampered by the facts of anatomy or physiology, and the results have inevitably been disappointing.

The results obtained by responsible workers to-day may fairly be divided into three groups.

In the first may be placed those lesions, e.g., hyperidrosis, some types of chronic vascular disease, and the chronic ulcers of anterior poliomyelitis and

of erythrocyanosis, in which the results are good. Here the operation may be advised with confidence.

The second, or intermediate group, is a large one and includes such conditions as hypertension, some forms of the Raynaud phenomenon, thrombo-angiitis obliterans, chronic 'varicose' ulcers, and the causalgias. With these the results in any considerable series of cases will be found perplexingly variable, but on the whole worth-while.

In the third group, one would put the failures. In these, e.g., the constipation of ptosis, the massive gangrenes, glaucoma, and retinitis pigmentosa, sympathectomy should not be done.

It is in the intermediate group that most of the research is needed, especially in the sorting out of types and the clarifying of indications. The bulk of the literature of the past year is naturally concerned with these objects, and here the question of the place of sympathectomy in *hypertension* takes up the chief share of the work.

Anatomy. Because accurate anatomical data are essential to a properly planned sympathectomy a paper by Mitchell[1] is welcome. This paper contains illustrations of the exquisite dissections of the sympathetic nervous system for which the author is well known. Mitchell points out how widespread in origin and distribution are the fibres which should be interrupted in an ideal operation for hypertension. Some fibres may come from the phrenic, from the coeliac plexus, and even from the first and second thoracic ganglia via the adventitia of the aorta.

Mitchell concludes, however, that the great majority of the sympathetic fibres and all those considered to be of most importance in hypertensive operations can be eliminated by bilateral removal of the splanchnic nerves and by extirpation of the thoracic sympathetic trunks as high as their fourth ganglia. This may be regarded as the optimal upper limit of the operation. The lower limit should include the second, or, perhaps better, the third, lumbar ganglia.

A further and somewhat disquieting contribution to anatomy is made by Tord Skoog,[2] who describes the finding of ganglia outside the usually accepted limits and in positions in which they must escape the ordinary sympathectomy. He states, for instance, that intermediate ganglia were present in the rami communicantes of the cervical region in all specimens which he examined. These ganglia contained sympathetic ganglion cells and may be found in close relation to the spinal nerves.

These findings may explain the early relapses after operation, in that important pathways have not been divided. As regards the later relapses, usually attributed to regeneration, Skoog points out that anatomical restoration of the severed sympathetic chain has never been demonstrated and therefore it is not unreasonable to assume that a smaller number of undamaged neurones may gradually develop function over a widened peripheral area.

Relapses, Early and Late.—The question of relapse is the subject of an important paper by Haxton,[3] who carries on the work done in 1939 by Simmons and Sheehan. As the result of much careful and detailed observation on a large range of sympathectomized patients, both recent and old, he concludes that regeneration is the most probable explanation of the later relapses. Although there are some cogent objections to this view it must be admitted that in the present state of our knowledge regeneration does supply the most likely answer.

Vascular Spasm. Kolodny[4] has a short but interesting paper in which he studies the reactions following the use of a tourniquet and of venepuncture in the limbs, using encephalographic methods. He considers that a vascular

spasm at one point sets off a reflex chain of similar spasms throughout the body. Our present-day approach to vascular problems is thought to be faulty by this author. We have, in the past, considered as independent clinical entities such conditions as angina pectoris, migraine, vascular cerebral insults, Ménière's syndrome, idiopathic epilepsy, essential hypertension, and pylorospasm. We should look at all these and other spastic conditions as manifestations of the same pathogenesis, namely, vascular spasm, rather than as unrelated and independent lesions.

Hypertension.—The greater part of the literature is, as one would expect, devoted to the various approaches of surgical methods in hypertension.

McGregor,[5] on a basis of 50 personal cases, gives a very competent review of the subject to date. This paper may be consulted with advantage by any surgeon who is taking up this branch. The history and development of the work is concisely stated and operative methods are given in great detail with most helpful illustrations. The conclusions may be summarized as follows: The results of operation are remarkable, 80 per cent of patients achieving a well-worth-while fall in the resting diastolic pressure and 90 per cent obtaining relief of symptoms. The damage done to eye-grounds, myocardium, and kidney is reversible by operation in a notable percentage of cases. These satisfactory results are, for the most part, sustained in follow-ups for periods as long as eleven years. Medical and surgical methods should be considered not as mutually antagonistic but as complementary measures of treatment. Without wishing in any way to detract from the value of this excellent paper the reviewer would, from his own experience, regard these conclusions as erring on the side of optimism.

Craig and Abbott[6] discuss the surgical considerations in the treatment of hypertension. Since this condition is due to a great variety of causes they insist on the need for a classification of types before any evaluation of treatment can be made. The common primary grouping of cases is into: (1) Essential hypertension, about the cause of which little is known; and (2) Secondary hypertension, due to many different but usually well-understood causes. The authors point out the strong familial tendency to hypertension, stating that where both parents suffered from hypertension the incidence in the children was as high as 45 per cent.

In this paper cases of essential hypertension are classified in four groups: (1) Slight to moderate increases in blood-pressure, often becoming normal after rest, with mild and usually symptomless sclerosis of retinal arteries; (2) Moderate to severe hypertension, moderate sclerosis of retinal arteries, and occasionally venous thrombosis, but clinical symptoms not necessarily present. (3) Moderately severe hypertension and angiospastic retinitis with an exudative retinopathy almost always associated with clinical symptoms; (4) Severe hypertension, angiospastic retinitis, œdema of optic disks, and always clinical manifestations of hypertension.

This grouping does not indicate the degree of hypertension, although the blood-pressure is often higher in one group than in the group which numerically precedes it. The hypertension may progress from group to group until Group 4 is reached.

The fatality rate among patients of Group 1 or Group 2 is 30–40 per cent respectively within four years. The rate in Group 3 is 78 per cent, and in Group 4 it is 98 per cent again within a period of four years.

Clearly, the operative prognosis is better in the earlier groups, and patients over 50 years with high diastolic pressure, together with those patients who have shown a high pressure over a long period of time, are not likely to do well after operation.

The need for caution and time in evaluating results is stressed, and the authors conclude by agreeing with White's apt summary of the position in which he states: "There is good reason to believe that the hands of the clock can be set back for a number of years in the majority of younger patients who have not been permitted to progress to the stage of advanced degeneration or of changes in heart, kidney, or brain."

Malignant Hypertension.—The term malignant is a loose, not to say, unfortunate one since it implies nothing more than the more acute and rapid types of the disease. In this group some authors think that sympathectomy should not be done. Peet,[7] however, reports the results in 162 cases diagnosed as malignant and treated by operation between November 1933 and December 1941. All the cases showed: (1) A rapidly progressive deteriorating clinical course of recent onset; (2) Severe neuroretinitis with definite papilloedema of one diopter or more; (3) High diastolic blood-pressure; and (4) Evidences of constitutional involvement.

The operation performed was a supradiaphragmatic resection of the greater, lesser, and least splanchnic nerves and excision of the eighth, ninth, tenth, eleventh, and twelfth thoracic ganglia. This was done on both sides in one stage. The operative mortality was 10 per cent and the five years survival rate of 143 patients was 21·6 per cent. Generally speaking there was definite improvement in retinal signs, in blood-pressure, and general condition. Peet concludes that surgical treatment offers some hope to victims of this disease, which is usually rapidly fatal under other forms of treatment.

Selection of Cases. The selection of patients for operation is always anxious and difficult. Hinton and Lord[8] discuss this problem and outline a set of definitions which serve to estimate the degree of damage in each of the four important organs, i.e., brain, eye, heart, and kidney. The progress of the disease in each of these four organs is divided into two stages for each of which certain marks are awarded. Whilst this paper contains much useful information it is clear that selection by marks, already tried out in many other diseases, can at the best give only a rough indication; it can never replace judgement and clinical experience.

Causalgia. Shumacker, Speigel, and Upjohn[9] have an important article on the treatment of causalgia by sympathectomy. The study is based upon observations on 90 patients with war injuries. In 83 of these a preliminary paravertebral block by 0·5 per cent procaine was performed. Some writers have reported instances in which this method alone has given permanent results, and on this subject the figures given in this paper are of interest. In 21 cases treated by repeated procaine block, 18 were freed from pain for prolonged periods by the first injection, but when relief from the first injection was limited to the period of sympathetic paralysis the subsequent blocks gave no more prolonged respite from pain. When each successive block resulted in a shorter period of relief no permanent alleviation was obtained by further injections. On the other hand, those patients who were eventually rendered free from pain by procaine blocks generally noted progressively longer periods of freedom following each successive injection.

Where preganglionic thoracic or lumbar sympathectomies were done the results were excellent. Over 80 per cent obtained complete and lasting relief or were left with only trivial discomfort.

Paravertebral Block.—The year has seen a notable increase in the use of this method by procaine and other agents. Its uses are many. It may be employed in diagnosis to determine to what extent the sympathetic system shares in the symptoms; it may be used before a projected operation to determine the extent and area which is likely to be affected by actual section of the ganglionic

chain, and it may be practised to give a permanent break in sympathetic conduction. Further, by combining a radio-opaque substance with the injection fluid precise and sometimes very instructive evidence can be had on the position and spread of the injected fluid.

Mandl[10] gives a lengthy and detailed account of the therapeutic value of sympathetic block in a number of diseases, such as angina pectoris, asthma, peripheral vascular disease, and the causalgias. He gives, for instance, the results in a collected series of 249 cases of angina, stating that good results were claimed in 83 per cent, whilst in a series of personal cases the good results were 68 per cent.

Mandl's[11] book on paravertebral block gives excellent details of technique, and discusses the results in a great variety of diseases with notable fairness and restraint. This is a work which must be consulted by any surgeon interested in this field.

There has been a good deal of work on paravertebral block using a 10 per cent watery solution of phenol. The results would appear to be permanent, but it is as yet too early to speak definitely on this point. It may be that the anatomical risks will prove too much for its routine employment in the upper thoracic region, save perhaps in such cases as severe angina, where considerable risk may justifiably be undertaken. But the method is easy and safe in the lumbar region and it is interesting to speculate how far paravertebral block may replace open operation.

Angina Pectoris. The possibility of the relief of severe angina by sympathectomy has interested many surgeons. White and Bland[12] have a paper based on work done at the Massachusetts General Hospital during the past 20 years. They believe that resection of the upper thoracic ganglia, or section of the corresponding spinal sensory roots, is preferable to paravertebral alcoholic block, but that in half of the worst sufferers the risk of operation would be too grave; for these the paravertebral block is the procedure of choice.

In all cases treated by upper thoracic ganglionectomy, from stellate down to and including the third thoracic ganglion, there has been complete relief from pain in precordium and arm. In patients treated by paravertebral block 84 per cent gave excellent to fair results. The drawback to be feared after block is intercostal neuralgia, which is a cause of major complaint in some 10 per cent of cases.

A somewhat different view is taken by Danielopolu.[13] He considers that whilst excision of the stellate ganglion may abolish pain, the result may be actually harmful to the disease itself by dividing fibres of dilator function. For this reason it is better to attack the sympathetic chain in the neck above the stellate ganglion, dividing not only the chain but the cardiac branches, the vertebral nerve, and those rami which run from the stellate ganglion to the lowest cervical and first dorsal nerves. By this method good results have been obtained in 70 per cent against 38 per cent for stellectomy.

Varicose Ulcer.—Most surgeons practising sympathectomy have endeavoured to estimate its results in chronic varicose ulcers. During the year scarcely any work has been published on this subject, but Borrie and Barling[14] have revived interest by giving an account of 4 cases of ulcers of long standing, with successful results in 3. It may be objected that the number is too few and the lapse of time since operation is too short. The reviewer in a much larger series observed for from 10–15 years has obtained not more than 50 per cent of successful results. The subject of the results likely to be obtained in these intractable ulcers offers a promising field, but needs much further investigation into causes and pathology before operation can be advised with any confidence of success.

Hyperidrosis.—From time to time patients are seen in whom excessive sweating is much more than a social nuisance because it prevents them from earning their living in certain types of work. Such are workers in fine textiles and paper where the dripping hands can spoil the material. Haxton[15] reports on a series of 12 such cases operated upon by Telford during the past 15 years. The results were good without exception, and the author concludes that a prolonged and probably permanent cure is effected by sympathectomy.

The same writer[16] has an interesting paper on the very difficult subject of gustatory sweating. This is a troublesome type of sweating of the face provoked at once by certain foods. The exciting food is usually of a spicy or acid nature but it is remarkable how frequently the patient will give chocolate as a cause. The subject is beset by difficulties and anomalous findings. To mention but two: whilst the ordinary cervical sympathectomy does not cure the trouble, it can be temporarily abolished by a block of the upper thoracic chain, but, strangely enough, a definite and not inconsiderable number of patients who, for various reasons have undergone the usual section of the upper thoracic chain, subsequently develop some degree of gustatory sweating. This paper gives a full account of the present views, and although necessarily inconclusive it is one which must be consulted by all workers on this very puzzling lesion.

The Raynaud Phenomenon in Workers using Vibratory Tools. It has been known for at least forty years that the continued use of tools vibrating at high speeds can cause serious and usually permanent disability. Prolonged work of this kind develops a Raynaud phenomenon in the hands. This occurs in attacks during which the worker is totally unfit for his work either fine or coarse. Seeing that these attacks may happen several times a day and may last for from a few minutes to several hours the worker's chance of regular employment is small. Unfortunately, the attacks tend to get worse after the use of these tools has been given up. The condition is known among the workers by the expressive term "dead hand", and was the subject of a discussion, opened by Telford, at the Ninth International Congress of Industrial Medicine held in London in September, 1948. Although many interesting clinical facts were brought to light, and, in particular, an ingenious way of recording and analysing the noxious vibrations was demonstrated by Agate,[17] it must be admitted that no satisfactory method of either prevention or treatment is as yet known.

Ménière's Syndrome. The cause of this rare but very disabling disease is unknown, but Passe and Seymour[18] are of opinion that vasoconstriction is the main factor. They report a series of 12 cases treated by stellectomy and division of the vertebral artery; the operations were all unilateral. They claim complete relief of the vertigo in all but one patient, but state that the effects on the tinnitus are unpredictable.

Sympathectomy in Gynæcology.—Davis[19] has an informative paper on this subject in which he discusses at length the presacral and other forms of sympathectomy. After a very clear description of presacral resection he gives the results available in an extensive search of the literature. On the basis of his own experience of 86 presacral operations for dysmenorrhœa he concludes that the only type for which the operation is unquestionably indicated is the primary spasmodic case. Here the results are excellent, but although the secondary types may show improvement the result is always problematic.

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SYPHILIS.

T. Anwyl-Davies, M.D., F.R.C.P.

Infectivity

A. O. F. Ross[1] quotes two unusual cases in which the infectivity of the semen in a treated syphilitic supports the view that the time factor is of more value than blood tests in answering the question, When is a male who has had syphilis non-infectious? In both, treatment had been given (2·4 mega units of penicillin in one case), signs of syphilis were absent, and the serology was negative (for 3 years in one patient); and yet the wives were infected. As the author states, everyday experience implies that a male whose infection is of more than 5 years' duration, whether his serological tests are negative or positive, is unlikely to infect his wife. But the advice that should be given to an adequately treated male is that he should not attempt to procreate children until 5 years after the date of his infection.

Diagnosis

Cysticercosis Cerebri mistaken for Cerebral Syphilis. A. A. Williams[2] (Middlesbrough) reports the case of a regular soldier who had served seven years in India. He had no history of venereal disease, but was discharged from the Army because of epileptic fits attributed to cerebral syphilis. On discharge, he reported to Middlesbrough General Hospital complaining of repeated attacks of epilepsy. He had slurring speech and was mentally dull. The only physical sign was early optic atrophy. He received bismuth, penicillin, and malaria therapy without benefit and was discharged, only to be re-admitted three months later with epileptiform convulsions occurring every five minutes; death took place three days later. At necropsy the surface of the brain was found to be studded with considerable numbers of small cysts of cysticercosis.

Multiple Lesions in Primary Syphilis. I. W. Kuhl and H. Boggs[3] present results of a study which contradicts the general impression that multiple lesions in primary syphilis are rare. The study covers 2023 patients with primary and secondary syphilis, 742 with early latent syphilis, and 718 in other stages. In primary syphilis, the chancres were single in 378 (58 per cent), multiple in 251 (38·5 per cent) and indeterminate in 23 (3·5 per cent). Of all persons seen, 51·8 per cent were males, and the authors conclude that there is no tendency for one sex to have multiple primary lesions more frequently than the other.

Diagnostic Value of Herxheimer Pyrexia. Herxheimer reactions are known after intramuscular, intravenous, and oral administration of aqueous solutions, peanut oil, and wax suspensions of penicillin in early syphilis. The most persistent, highly diagnostic, and easily measured manifestation is an elevation of temperature. With commercial penicillin, pyrexia occurs in 30 to 70 per cent of adults with early syphilis. T. W. Farmer[4] has collected the data from twenty co-operating clinics in the United States of 939 patients with early syphilis who were given 2,400,000 to 4,800,000 units of crystalline penicillin G. Of this group, 384 (41 per cent) had febrile reactions, which occurred with equal frequency and severity in sero-negative primary, sero-positive primary, and secondary syphilitic cases. Above 100° F. was considered a febrile reaction and the temperatures were recorded rectally every four hours. In 121 patients the temperature was recorded every two hours to determine its relation to dosage. Within a wide range (10 to 120,000 units per kilo body-weight) the incidence remained relatively constant (40 to 50 per cent) and independent of the dosage. Febrile reactions were absent with very small doses (1 to 5 units per kilo body-weight) but they occurred with single doses of penicillin (10 to 80 units per kilo body-weight), as little as one-tenth of the amount required to render syphilitic

lesions dark-field negative. The generally accepted hypothesis is that the reaction is due solely to the sudden destruction of large numbers of spirochætes with the liberation of split proteins or endotoxins, and small initial doses of 1000 units are recommended to prevent this. But this paper shows that they may occur with as little as 500 units (10 units per kilo body-weight), that even the repetition of such small doses may cause repeated Herxheimer reactions, and that the reaction is not directly related to the number of spirochætes in the body.

Syphilitic Aoi

I. O. Woodruff[9] states that syphilis of the aorta and its complications comprise 13 to 15 per cent of all cardiac diseases found at necropsy. Of 41 patients with primary aortitis dying in Bellevue Hospital, New York, between 1929 and 1946, 68 per cent died after reaching their 50th year, although 67 per cent of these did not show symptoms until that age; 45 per cent with aneurysms lived beyond the age of 60, and 70 per cent survived to their 50th birthday. Syphilitic aortic aneurysm occurred in 49 per cent of the Bellevue Hospital series. The writer advises bismuth for the commencement of treatment of patients with uncomplicated syphilitic aortitis, rather than the more active spirochæticides.

To determine the effect of antisyphilitic treatment, B. Webster and G. G. Reader[6] examined the microscopical sections of syphilitic aortitis from 45 necropsies of patients whose clinical records of treatment were available. The degree of inflammation was recorded by a rating scale of 1 to 4, according to the amount of lymphocytic infiltration, the presence of plasma cells, and the amount of perivascular infiltration and endarteritis. The patients were divided into three groups according to whether they had received 'adequate', 'inadequate', or no treatment. The minimum 'adequate' treatment was considered to be approximately 20 arsenical and 20 bismuth injections. All the 19 untreated cases (100 per cent) had an active syphilitic process as shown by an active cellular infiltration of the aorta, while only 3 of 19 adequately treated cases (16 per cent) showed an active type of syphilitic aortitis. No correlation was demonstrable between the duration of the infection and activity of the aortitis. The authors concluded that adequate specific therapy with arsenic and bismuth does profoundly modify the inflammatory process of syphilitic aortitis.

Syphilis of the Stomach

The gastroscopic appearances of late syphilitic lesions have been described by C. O. Patterson and M. O. Rouse.[7] Three types of lesion were seen: ulcers; tumours; or an infiltrative process leading to a leather-bottle stomach. The mucosal margins of the ulcers were livid, slightly brown or violaceous in colour, serpiginous and irregular in outline.

L. Kurthi[8] has described them as shallow ulcers with irregular edges and pink bases, but without the œdema which usually surrounds the simple peptic ulcer. In a series of 3066 cases of peptic ulcer observed in 16 years, 52 (1·7 per cent) were syphilitic; of these, 4·9 per cent were gastric, and 0·5 per cent duodenal. The symptoms did not differ from those in cases of non-syphilitic origin, but the ordinary treatment caused no response. Gastric hypoacidity occurred in 42 patients, and occult blood in 12.

I. R. Schwartz[9] made gastroscopic observations on 12 patients with secondary syphilis; then treated them with penicillin and noted its effect. In these cases of early syphilis the gastroscopic picture was similar to that of chronic superficial gastritis, with reddening, increased high lights, and œdema. Before treatment 9 had hypochlorhydria. Penicillin caused a rapid amelioration in 10, and normal acid values in 7, of the 12 patients.

Neurosyphilis

It has been generally accepted that neurosyphilis is rare in the negro. M. J. Cook[10] found this to be untrue and founded on the lack of adequate diagnostic facilities, particularly in examination of the cerebrospinal fluid. Using modern clinical and laboratory methods, he investigated 1028 patients in Trinidad and obtained a neurosyphilis rate of 20 per cent in unselected syphilitic cases. He found severe neurosyphilis frequent enough, but thought its severity sometimes tempered by endemic malaria, which was 20 to 80 per cent in some areas from which the patients were drawn.

Treatment with Penicillin

At St. Thomas's Hospital, a new delayed-action preparation of procaine penicillin containing 2 per cent aluminium stearate was tested by S. B. van der Merwe against the standard *Staph. aureus* strain. Adequate blood levels were maintained for at least 50 hours after a single injection of 300,000 units, and for at least 72 hours after 600,000 units. The preparation manipulated easily and caused no local pain.

A report by the Syphilis Study Section, National Institute of Health, U.S. Public Health Service,[11] summarizes the principal facts of clinical importance regarding penicillin. Since 1943, at least 500,000 patients with syphilis in various stages have been treated with this antibiotic. Intramuscular injection in oil and wax, a practical method in the treatment of syphilis which does not require hospitalization, provides effectively bactericidal blood-levels of at least three to five times the duration provided by aqueous penicillin in comparable dosage. Although possible penicillin resistance has been reported in experimental rabbit syphilis and in clinical late benign gummatous syphilis, little evidence exists at present of penicillin-resistant syphilis analogous to arsenic- and bismuth-resistant syphilis or sulphonamide-resistant gonorrhœa. The recommended schedule for ambulatory treatment with crystalline penicillin in oil and wax consists of intramuscular administration of 6,000,000 units in 10 injections over a period of 10 days. Available information indicates that penicillin should be withheld in syphilitic aortitis with aortic regurgitation, saccular aneurysm, or coronary disease, until after preparatory treatment with heavy metals; five or more million units of penicillin should then be followed by small dosages (25,000 to 40,000 units) over a period of at least 15 days. For patients with dementia paralytica, taboparesis, or primary optic atrophy, a total of 10 to 20 million units of penicillin, administered over a period of 12 to 20 days, with induced malaria, is advised.

Neurosyphilis.— W. P. Boger, R. B. Baker, and W. W. Wilson[12] have shown that penicillin does penetrate into the cerebrospinal fluid. This has been confirmed clinically by J. P. Martin[13] in 24 patients: 8 with G.P.I., 5 with tabes, 2 with optic atrophy, and 9 with meningo-vascular syphilis. Excluding the tabetics and those who defaulted, 18 cases were arrested. In most cases the Wassermann reaction of the cerebrospinal fluid became negative in one year and the cell content reached normality within two months. Except for the Lange reaction and total protein content, the cerebrospinal fluid returned to normal within twelve months in all cases in the series. The routine treatment was 5,000,000 units of aqueous penicillin intramuscularly at the rate of 60,000 units every 3 hours.

The author believes that penicillin alone is sufficient in most cases of neurosyphilis, and that, with the possible exception of acute G.P.I., malaria therapy and its risks of 8 to 10 per cent mortality will seldom be justified.

J. H. Stokes, H. P. Steiger, and G. D. Gammon[14] have issued a fourth serial report from the University of Pennsylvania on the treatment for the third year

with penicillin alone of 361 cases of neurosyphilis. In the aggregate of the cerebrospinal fluids, 52 per cent were reduced to normal and 74 per cent markedly improved. The first 39 cases did well; 64 per cent had normal or nearly normal fluids and 82 per cent were improved. The spinal fluids were improved in 61 per cent of G.P.I. cases; 61 per cent of taboparetics; 75 per cent of tabetics; 73 per cent of meningovascular syphilis; and 77 per cent of asymptomatic neurosyphilis. Only 14 of 317 spinal fluids became worse. The clinical response among 179 cases remained much the same for 1946 as for the previous year in the total improvement group; paresis, 63 per cent; taboparesis, 63 per cent; tabes, 60 per cent; and meningovascular neurosyphilis, 79 per cent. Marked symptomatic improvement occurred in paresis, 46 per cent; taboparesis, 35 per cent; tabes, 33 per cent; and meningovascular neurosyphilis, 47 per cent. The proportion of marked improvement cases increased so notably during the last year that penicillin therapy, like malaria, possibly has a long period of cumulative improvement after treatment is begun or stopped.

Penicillin seems to assert itself in most cases during the first 120 to 200 days, and is more effective in dealing with abnormalities in the spinal fluid than with symptoms. Its good effect, however, ranges through all the stages of neurosyphilis from asymptomatic neurosyphilis to paresis. In paresis, the response to penicillin alone rapidly overtakes that of malaria in the second year and equals it in the third year of observation, especially in its durability of effect. Penicillin equals malaria in symptomatic improvement and produces superior results on the cerebrospinal fluid. Similarly, in taboparesis and meningovascular neurosyphilis the fluid improvement under penicillin surpasses that obtained with malaria, and the clinical improvement is equal. In tabes, the clinical results are one-third better than those with malaria in the second and third years, and the percentage of normal spinal fluids is twice as high after penicillin as after malaria in the same period.

Failures with Penicillin.—Penicillin has distinct limitations in its therapeutic efficacy. F. W. Reynolds[15] points out that it may ultimately prove less effective in the later stages of infection than during the more acute early phase of the disease. Treatment failures observed among 550 patients at Johns Hopkins Hospital were due to: (1) *Penicillin resistance.* A patient was reported with gumma of the penis, the diagnosis being substantiated by evidence of syphilis of at least ten years' duration, destructive nature of the lesion, repeatedly negative dark-field examinations and smears for Donovan bodies, and persistently high serologic titre. Although the lesion failed to heal after 4,800,000 units of penicillin, complete response was obtained with mapharside and bismuth. (2) *Clinical progression despite penicillin therapy.* Of 82 patients with late asymptomatic neurosyphilis treated with penicillin alone and followed for a minimum of six months, 6 were re-treated with malaria, usually with additional penicillin. In one case symptoms disappeared completely, but among 24 patients with general paresis there were 6 whose psychoses became worse after penicillin alone; 1 died and the rest were committed to mental hospitals. Only 9 of 33 tabetics benefited from penicillin alone, while 18 were unchanged and 6 were worse. Ataxia, urinary symptoms, and sensory disturbances frequently became more severe following therapy. Penicillin alone was found to be of little value in primary optic atrophy and of no value in Erb's spastic paraplegia. (3) *Recurrence of late lesions following penicillin.* One case is described in which relapsing osseous lesions and a serpiginous syphilide developed following penicillin therapy; another patient twice had reactivation of a cutaneous gumma. (4) *Development of new lesions following penicillin.* A patient was treated originally for late unclassified neurosyphilis with apparently favourable results, but sixteen months after a course of 8,000,000 units of penicillin evidence

developed of cardiovascular syphilis with aortic regurgitation. Therefore the author emphasizes the necessity for caution in the use of penicillin alone for the treatment of late syphilis.

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TESTIS, SURGERY OF.

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Pathology of Mumps Orchitis. The examination of biopsy specimens by C. W. Charny and D. R. Meranze[1] has shown that œdema is not a conspicuous feature ; nor is there a large accumulation of hydrocele fluid. The germinal epithelium, including the spermatogonia, is irreparably damaged. The only cells surviving are Sertoli cells. There is no evidence of pressure atrophy. These considerations lead to the conclusion that the present-day practice of draining the hydrocele and/or incising the testis capsule on or after the third day do not prevent ultimate destruction of the acutely inflamed tubule.

Distribution of the Testicular Artery.—Micro-arteriography is a new and precise means of radiological diagnosis. The injection experiments of R. G. Harrison and A. E. Barclay[2] reveal considerable variation in the artery to the testis. The commonest arrangement is for the vessel to pass to the testis, with few or no convolutions, giving branches to cord and epididymis on the way. At the posterior testicular border it divides into two branches which ramify over the lateral and medial surfaces respectively. Fine branches passing through the mediastinum testis are of little functional significance. Terminal branches are given from the superficial testicular artery at various points over the free surface of the testis.

The Malignant Testis.—H. R. Sauer et al.[3] present a review of 202 cases. Enlargement of the testicle represented the most common complaint ; painless swelling was associated most frequently with the seminoma group, while painful enlargement occurred more often with embryonal growths or terato-carcinoma. When the diagnosis is in doubt exploration is the procedure of choice. In no case should needle puncture or biopsy be resorted to. They quote G. F. Cahill's[4] observation that excretory urography, when showing lateral displacement of the ureter, may indicate pre-aortic node involvement when palpation fails.

An important argument, advanced by Sauer against pre-operative deep X-ray therapy is that a sterilizing tumour dose will render a histological diagnosis of malignancy impossible. Orchiectomy with regional lymph-node dissection is advocated for radio-resistant tumours. Simple orchiectomy plus irradiation is preferred for the more radio-sensitive seminomas.

Accurate clinico-pathological diagnosis after simple orchiectomy will make possible the proper selection of definitive treatment. Simple orchiectomy followed by radiation therapy appears to be sufficient for seminomas. Radical resection of the retroperitoneal nodes is indicated for all other malignant tumours (L. G. Lewis).[5]

Multiplicity of primary malignant growths in general is receiving more and more prominence as attention is directed to the multifocal origin of cancer. R. A. Willis[6] has examined 5 instances in which seminoma and teratoma co-existed. E. D. Gagnon[7] reports a case of seminoma of the testis associated with carcinoma of the colon.

It is of interest to note that R. D. Gill and R. B. Howell[8] record an example of primary (simultaneous) bilateral testicular malignancy, occurring in normally placed gonads.

L. C. Lewis,[9] finding 12 of 13 tumours in cryptorchids to be seminomas, points out that this is the common tumour in the atrophic or maldescended testis.

After stating that the term prolan is a misnomer which should no longer be used, V. Vermooten and W. F. Hettler[10] comment upon the gonadotropic hormones; the one in pregnancy urine was found to be elaborated by chorionic tissue and is known as chorionic gonadotropic hormone (C. G. H.) and bears no relation to the pituitary. However, the hormone found in the urine of castrates and of women past the menopause is presumed to be associated with activity of the anterior pituitary and is known as follicle stimulating hormone (F. S. H.). In interpreting results the synergic effect on C. G. H. by F. S. H. must be borne in mind. The presence of C. G. H. in the urine of a male is an indication of chorionic tumour tissue. Its decrease means removals or regression of the tumour, its increase may mean spread of the disease or may be the result of an increase of F. S. H. and its synergic effect. On the other hand, the presence of F. S. H. in male urine is merely an indication of decreased androgen output or a 'castration effect'. While the castration effect may be due to destruction of testicular tissue by tumour it may also result from other causes such as castration or irradiation.

Exploration of doubtful cases and the careful scrutiny of all hydroceles is the sound advice of J. K. Ormond and J. W. Best.[11] Most encouraging is their statement that the prognosis of malignant tumours of the testicle has greatly improved in the past 25 years. They can even claim that it is now better than the prognosis of malignant disease of any other organ in the genito-urinary tract in the male, excepting carcinoma of the penis.

Interstitial-cell Tumours. The interstitial cells of Leydig are of connective tissue origin and spheroidal or polyhedral in shape. Tumours of these cells are common in dogs. I. I. Price[12] finds records of 15 such tumours in man, and reports one in an undescended testis. There is usually a well-marked capsule and with one exception these neoplasms have been benign. Interstitial-celled tumours have been induced by the implantation of stilboestrol-cholesterol pellets. When arising before puberty, signs of sexual and somatic precocity have occurred, features which have been seen to regress after removal of the growth.

L. C. Lewis[9] has encountered 2 such cases, occurring in well-developed men of 25 and 37 years. Fresh-tissue examination revealed reddish-brown solid tumours occupying the entire testis without gross evidence of remaining tubular elements. Both patients, after radical orchiectomy, are well over 1½ years. Lewis thinks that perhaps the radical gland dissection was not indicated. These tumours, while usually benign, may become malignant.

Genital Tuberculosis in the Male. The investigations of J. W. S. Blacklock[13] showed the *bovine* type of bacillus to be responsible for 27·3 per cent (chiefly epididymitis). The almost identical percentage in renal tuberculosis (28·3) lends support to the view that the direct pathway of infection is via the urine.

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THROMBOSIS, VENOUS. (*See also* VARICOSE VEINS, VARICOSE ULCERS, AND VENOUS THROMBOSIS.)

THYROID GLAND. *S. L. Simpson, M.A., M.D., F.R.C.P.*

Thyrotoxicosis.—

Summary.—This year's brief review will be limited to modifications of thiouracil therapy, selection of cases, and the results of long-term therapy. Methyl thiouracil has been used in this country and propyl thiouracil in America,

and they are equally effective and relatively free from toxicity. H. P. Himsworth has discarded the initial 600 mg. daily dose of methyl thiouracil for an equally effective smaller dose of 200 mg. which is monthly halved down to 50 mg. daily or less. T. S. Danowski and others found that the simultaneous administration of iodine reinforced the effect and produced a less vascular, more colloid, gland. H. R. G. Poate recorded that when methyl thiouracil had produced a normal or subnormal metabolism, the addition of thyroideum siccum favourably influenced the exophthalmos and the size of the thyroid gland.

Whereas most large centres have reverted to thyroidectomy, after preparing the patient with methyl thiouracil, Himsworth continues to advocate the latter's use over long periods, and D. M. Dunlop states that only 19 of 149 patients required thyroidectomy, particularly *middle-aged* people with nodular goitre. Eight of his patients had successful pregnancies under 'cover' of methyl thiouracil. H. Cookson and F. H. Staines found that of 15 cases of nodular goitre with auricular fibrillation, treated by methyl thiouracil, normal rhythm returned in 8 cases, in 4 of which a congestive heart failure cleared up, and they indicate that "thiouracil produced its best results in toxic goitre in elderly patients and in young subjects with smooth goitres of moderate size". All are agreed that treatment must be continued at least six months and preferably twelve months before the methyl thiouracil is omitted, and then some 50 per cent of patients do not relapse within the next two years. In Denmark, E. Meulengracht, K. K. Jensen, and K. Schmith, found that nodular goitres respond more slowly, but that for thyrotoxicosis in general "non-operative treatment for the present will be the normal routine in our department". R. C. Grauer, H. de Walt, and C. W. W. Elkin consider it dangerous to use thiouracil for nodular goitre and raise the possibility of it proving carcinogenic. E. P. McCullagh, R. E. Hibbs, and R. W. Schneider found that thyrotoxicosis complicating acromegaly did not respond to thiouracil.

Methyl Thiouracil and Thiourea. H. P. Himsworth[1] says that 200 mg. daily is sufficient (100 mg. b.d.). Intermittent auricular fibrillation usually disappears completely. Continuous fibrillation may do so, but if not, the temporary addition of quinidine will restore normal rhythm. "At present, it can be said that a patient starting thiouracil treatment has about a 3 to 1 chance of securing an apparently permanent remission after about 9 to 21 months of treatment." Treatment must be continued for months after the condition is under control. As regards the leucocytes, "so long as the total count is not below 3000 per c.mm. and the polymorphonuclear cells constitute 50 per cent of the total, this fall can be disregarded". After 6 weeks, 50 mg. daily; after 6 months, 50 mg. every other day, and after another 3 months, cease thiouracil. Blood-counts and B.M.R. are not essential. Although thiourea has produced carcinoma in rats after some years, Himsworth does not believe that any case has resulted in man.

T. S. Danowski et al.[2] found thiourea effective and its action reinforced by the simultaneous administration of a strong solution of iodine, 5 to 15 drops daily. A withdrawal of the iodine often produced an exacerbation. Iodine acts by inducing a 'resting phase' and blocking thyrotrophic hormone while not disturbing the essential inhibition of synthesis of thyroxine by the thiourea.

H. R. G. Poate[3] found that when metabolism was normal or subnormal, the addition of thyroideum siccum favourably influenced exophthalmos, or the size of the goitre, particularly if these were not of more than 6 months duration. A preliminary eosinophilia indicated the probability of toxic complications.

In D. M. Dunlop's[4] series, out of 149 patients, only 19 were subjected to thyroidectomy. He says thiouracil is the treatment of choice for (1) young people, (2) old people, (3) relapse after operation. He is doubtful about its use

in middle-aged people with nodular goitre. Eight of his patients had successful pregnancies under 'cover' of thiouracil.

H. Cookson and F. H. Staines[5] found that, of 15 cases of nodular goitre with auricular fibrillation, normal rhythm returned in 8. Four of them had congestive heart failure which cleared up rapidly. In 40 of 95 patients, remissions occurred following cessation of therapy, but 15 subsequently relapsed. Thiouracil produced its best results in toxic goitre in elderly patients, and in young subjects with smooth goitres of moderate size.

Experience with methyl thiouracil in other countries, e.g., Denmark, is of interest. Incidentally, E. Meulengracht et al.[6] mention that there was an epidemic of thyrotoxic goitre in 1941 reaching its maximum in 1944 and diminishing since. They treated 134 cases, giving 250 mg. of methyl thiouracil three times daily for 6 weeks, 250 mg. once daily for 4 weeks, and 125 mg. or less daily for 6 months. They met with no serious toxicity and of 50 cases that had left off treatment entirely for some 10 months, only 5 relapsed, and in 15 the goitre had grown much smaller or disappeared. Temporary enlargement of the goitre may be troublesome in nodular goitre, and in one case, operation was necessary. Nodular goitres also respond more slowly than diffuse primary goitres. The authors report favourably on eye signs, including exophthalmos. They believe that most women patients prefer a goitre to a scar. They conclude that "non-operative treatment is preferred by the patients and for the present will be the normal routine in our department".

Propyl Thiouracil. R. C. Grauer, H. de Walt, and C. W. W. Elkin[7] say that in follow-ups of propyl thiouracil patients, the serum cholesterol was not found to be of value. It rises within one month of treatment and the raised values persist regardless of subsequent clinical fluctuations. B.M.R. and galactose index were both more reliable. Folic acid did not prevent agranulocytosis, and folic acid, pyridoxine, and penicillin were of no use if the thiouracil were continued. Of these, penicillin only was found of use in agranulocytosis and that by combating infection rather than stimulating granulocytosis. The writers used thiouracil as preparation for operation and for cases that relapsed after operation. They consider it dangerous to use thiouracil on a nodular goitre, since thiouracil has proved to be experimentally carcinogenic for the thyroid gland in the presence of a general carcinogenic agent such as 2-acetylamino fluorene.

E. P. McCullagh, R. E. Hibbs, and R. W. Schneider[8] find that 300 mg. per day is the ideal dose. Large adenomatous goitres respond more slowly in some instances, but, taking averages, there are no great differences. In some young people there is relative resistance and progressive enlargement of the thyroid gland. Thyrotoxicosis complicating acromegaly did not respond at all. In a small group, iodine (10 to 30 mg. daily) was given concurrently with propyl thiouracil to eliminate the vascularity of the thyroid gland and the bruit. The favourable response and time relations were not essentially different from using propyl thiouracil alone.

REFERENCES.—[1]*Brit. med. J.* 1948, **2**, 61; [2]*Amer. J. med. Sci.* 1948, **215**, 123; [3]*Med. J. Aust.* 1947, **2**, 93; [4]*Edinb. med. J.* 1948, **55**, 257; [5]*Brit. med. J.* 1947, **2**, 759; [6]*Acta med. scand.* 1946, suppl. 206, 293; [7]*Amer. J. med. Sci.* 1948, 215, 63; [8]*Ibid.* 1947, **214**, 553.

THYROID SURGERY.

Lambert Rogers, M.Sc., F.R.C.S.

Thyrotoxicosis. Sir Carrick Robertson,[1] of Auckland, New Zealand, reports his experience of 350 cases of thyrotoxicosis treated between January, 1945, and September, 1947.

He regards the following as contra-indications to treatment with thiouracil: (1) Signs of pressure on the airway; (2) Toxic nodular goitre; (3) A retro-laryngeal upper pole of the thyroid (*Fig.* 57); (4) Pronounced exophthalmos

PLATE XLII

LINGUAL GOITRE

(EMIL GOETSCH)

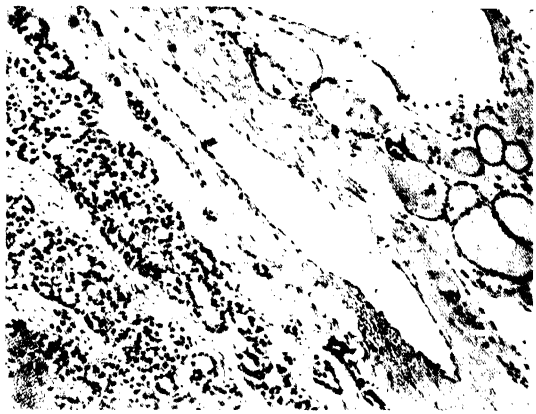


Fig. A. Photomicrograph of normal-appearing thyroid follicles in the fibrous stroma adjoining the capsule of the lingual nodule. Below the capsule one sees a sudden transition to the foetal type of thyroid often seen in adenoma of the cervical thyroid gland. (× 90.)

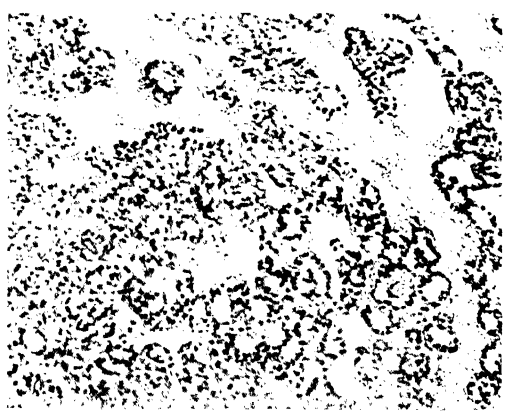


Fig. B. The parenchyma in the depth of the lingual tumour presents the appearances characteristic of the cellular foetal adenoma. The compact masses of cells, the cellular cords, and the minute follicles are lacking in definite architecture. (× 90.)

Plates XLII, XLIII reproduced from the "Annals of Surgery

PLATE XLIII

LINGUAL GOITRE—*continued*

(EMIL GOETSCH)

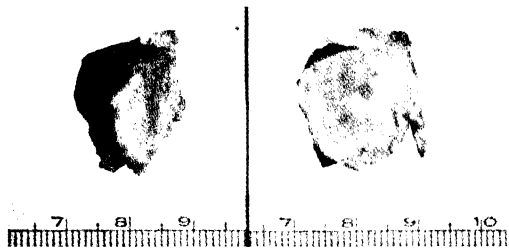


Fig. C.—Photographs of the gross specimen of tissue resected from a lingual thyroid tumour. On the right the mucosa covering the tumour shows a minute dark area, indicating the probable location of the foramen cæcum. On the left a lateral view of the specimen.



Fig. D.—Photomicrograph of lingual thyroid tumour. Note the large distended colloid acini lined by a single layer of low cuboidal cells and the thin layer of mucosa covering the tumour. (× 104.)

approaching the so-called malignant type, usually found in those over 35 years of age; (5) Predominance of heart symptoms; (6) Nervous depression; (7) Absence of facilities for blood-counts.

He regards the indications for thiouracil as: (1) Young people with Graves' disease; (2) Predominance of nervous symptoms other than depression; (3) Elderly patients who are bad surgical risks; (4) Recurrent thyrotoxicosis after operation (these patients usually respond quickly to 0·2–0·3 gr. of thiouracil daily); (5) As preparation for operation.

[This is an important review of the present position regarding the use of thiouracil. Opinion is turning back to surgery as the most effective treatment and in the long run the safest. There can be no doubt about the dangers of these thiourea drugs and only recently another potential one has come into the picture since H. D. Purvis and W. E. Griesbach[2] have produced adenocarcinoma of the thyroid of rats by the continued administration of thiourea over a period of 2 years. L. C. R.]

Thyrotoxicosis due to Struma Ovarii. A remarkable case in which thyrotoxicosis in a married woman aged 53 was due to hyperactive thyroid tissue in an ovarian dermoid has been reported by K. A. McGarrity and L. F. Dodson,[3] of Sydney, New South Wales. At operation for metrorrhagia the patient, who was thyrotoxic and exophthalmic, was found to have a left ovarian cyst with a solid area in it. The solid area consisted for the most part of thyroid tissue, some of which was of adult type; other parts resembled the fœtal gland or a fœtal adenoma (*Figs.* 58–60). After removal of the cyst her thyrotoxicosis disappeared and she gained two stones in weight. Cases of a similar type, though rare, have been recorded by S. L. Moench[4] and others. S. D. Gusberg and D. M. Danforth[5] have described cases in which thyroidectomy has not relieved the symptoms of thyrotoxicosis, but later removal of one of these ovarian dermoids containing thyroid tissue has alleviated the condition.

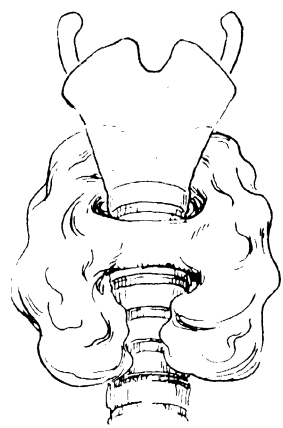


Fig. 57. Diagram of upper poles of a toxic goitre winding round the back of the larynx. The right upper pole contains a small nodule or adenoma. (*By kind permission of "The Lancet".*)

Thyroiditis. More than half a century has passed since Bernard Riedel in Jena presented his original report on the condition that has since come to be known after him. Sixteen years after this Hashimoto reported what he considered to be a distinctly separate clinical and pathological condition now known as struma lymphomatosa. To-day there is little doubt that Riedel's thyroiditis and Hashimoto's disease (struma lymphomatosa) are separate entities. The confusion regarding them which was due to Ewing's having considered them as stages in the one disease, has been clarified by a number of writers (*see* MEDICAL ANNUAL, 1939, p. 503, 1941, p. 374), among the most recent being H. M. Goldberg and J. Dawson[6] of Manchester and George Crile[7] of Cleveland, Ohio. S. F. Marshall, W. A. Meissner, and D. C. Smith,[8] of Boston, writing from the Lahey Clinic on 187 cases of chronic thyroiditis seen there over an 18-year period (1928–46) among some 25,000 operations for thyroid disease, draw attention to the difficulty of making a pre-operative diagnosis. In this series a correct pre-operative diagnosis was made in only 44 of the 187 cases; 78 of the cases were of the Hashimoto type. Operative



Fig. 58. Dissection of cyst and thickening in its wall. (*Figs. 58–60 reproduced from the "Medical Journal of Australia".*)



Fig. 59. Thyroid tissue present in tumour showing an area with large ac filled by colloid.

treatment may be necessary to ascertain the nature of the lesion and distinguish it from malignant disease or to relieve tracheal compression. Partial thyroidectomy or excision of the isthmus is all that is usually required.

In his paper Crile points out that Riedel's struma is more often unilateral, while struma lymphomatosa involves the whole gland, and while adenomas are frequent in Riedel's disease they rarely if ever occur in the lymphadenoid goitre. Although lymphadenoid goitre is rare in men, he has seen two instances. He regards lymphadenoid goitre as part of a systemic disease, and Riedel's thyroiditis as a proliferative fibrosis usually centring about a degenerating adenoma.

Lingual Goitre.—During the past year, Emil Goetsch,[9] of Brooklyn, has contributed an important paper on lingual goitre. Thyroid tissue may be present at the foramen cæcum along with a normal thyroid gland, or its presence at the foramen may be due to non-migration of the thyroid anlage and may represent therefore the whole of the thyroid apparatus. Very occasionally aberrant thyroid tissue is found in the body of the tongue. The first recorded case of lingual goitre is that of W. Hickman[10] reported to the Pathological Society of London in 1869; since then numerous cases have been reported in the literature.

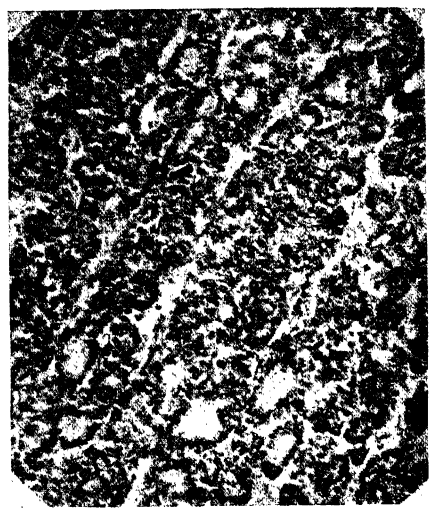


Fig. 60. An area of thyroid tissue present in tumour showing small closely packed acini resembling 'fœtal thyroid'.

Emil Goetsch records 3 cases which he has operated upon at Long Island College Hospital, namely, a woman aged 30 and girls aged 12 and 8 respectively. In the first, the lingual thyroid was the size of a golf ball; the greater part of it was removed and section showed that in part it resembled a fœtal adenoma (*Plate XLII, Figs. A, B*). The lingual thyroid was apparently the only thyroid tissue this patient possessed, as no cervical thyroid was palpable and after operation she developed hypothyroidism for which thyroid extract was required. In the child of 12, a biopsy was first performed, followed later by partial excision of the tumour, which appeared to be an atypical fœtal adenoma, though in part it resembled embryonal parathyroid. In the third case the lingual tumour was the size of a large olive (*Plate XLIII, Fig. A*) and its histological structure that of a simple colloid goitre with some small areas of hyperplasia (*Plate XLIII, Fig. B*). After operation she had hypothyroidism for which thyroid extract was administered.

Lingual goitres probably arise because of functional thyroid insufficiency in those who possess them and it is only rarely that a cervical thyroid gland is present in these patients. Goetsch's paper is a valuable addition to the analysis of lingual thyroids made by M. L. Montgomery[11] and L. T. Buckman.[12] At least 90 per cent of the patients possessing lingual goitres suffer from pressure symptoms such as dysphagia, dysphonia, and dyspnœa. These symptoms

usually arise in early life, either late childhood or adolescence. The tumours are situated at the foramen cæcum and are spherical or oval in shape. They are usually smooth in outline and darker in colour than the surrounding tongue. Occasionally carcinoma has been reported in a lingual goitre (A. F. Tyler,[13] A. P. C. Ashurst and C. Y. White,[14] and L. M. Levi and F. D. Hankins[15]), but unless metastases are present the microscopical diagnosis is notoriously difficult from fœtal adenoma, as Sir James Berry[16] pointed out some years ago in the case of some goitrous cervical glands. Lingual malignant goitre usually occurs in men over 35 years of age.

The differential diagnosis of lingual goitre must include adenoma, angioma, fibroma, lipoma and non-thyroid cysts, lymphosarcoma, and carcinoma.

Aberrant Lateral Goitre. Recent references to lateral aberrant thyroids were made in the MEDICAL ANNUAL for 1943 (p. 349) and 1947 (p. 364). The association of these aberrant masses with malignant disease of the thyroid has been recognized since 1903 when H. C. Low[17] drew attention to it. Two views are held regarding this association; one that these masses are metastases from a malignant lesion in the lateral lobe of the thyroid gland on the same side of the neck; the other that they are of congenital origin and probably arise from the ultimo-branchial bodies, a view held by F. H. Lahey and B. J. Ficarra[18] of Boston. G. Crile,[19] who also was formerly of this opinion, now regards them as metastases from a tumour of the thyroid. In 16 cases which he reports of papillary tumours of the lateral cervical region, a primary tumour was found in each case on careful examination of the thyroid. He remarks that the lateral cervical tumour may continue to form until the primary tumour in the thyroid is removed. This is often very small and may be difficult to find. Following its removal the lateral nodules cease to appear. These nodules rarely invade muscles or blood-vessels and block dissection of the neck is not necessary. X-ray therapy is not helpful.

[To sum up, recent opinion favours the view that lateral aberrant thyroids are metastatic nodules from a carcinoma, often minute, in the lateral lobe of the thyroid on the same side of the neck. This lobe should be removed along with the nodules. Block dissection is not necessary. X-ray treatment is not helpful.—L. C. R.]

Aberrant Mediastinal Goitre. J. G. Rives,[20] of New Orleans, comments on the rarity of intrathoracic aberrant thyroid masses. Among publications in English he has been able to trace only 14 unquestionable cases. Crile, Smith, Touroff, and others have, however, reported multiple papillary carcinomatous masses in the thorax which may have either arisen as aberrant thyroids or been metastases. Rives reports 3 cases of mediastinal aberrant goitre and advises removal from a cervical approach when possible, as was done in his first case; in the other two he had to open the chest. He comments on the danger of tension pneumothorax from small pleural tears which may result if a trans-sternal approach is made, and the necessity if such occurs of opening the pleura widely to prevent the valvular action of a small opening.

The reviewer has recently operated on one such case of aberrant mediastinal goitre in a women aged 54. A large adenomatous left lobe, the lower part of which was retroclavicular, was removed and the wound was about to be closed when it was noticed that there were still distended veins on the left side. On digital exploration, a nodular mass of thyroid tissue was found between the origin of the left common carotid and the aortic arch and quite unassociated with the tumour which had been removed. This mass was also removed and proved to be histologically similar to the main tumour.—[L. C. R.]

Cancer.—A number of recent papers deal with cancer of the thyroid. Marcel Dargent,[21] writing from the anti-cancer centre in Lyons, advocates thyroidectomy

with block dissection as illustrated (*Figs.* 61–64). If total thyroidectomy is to be carried out, the two internal jugular veins are dissected out and the vein draining the more affected lobe is resected. The parathyroids are dissected away from the thyroid and grafted into the stump of the sternomastoid muscle.

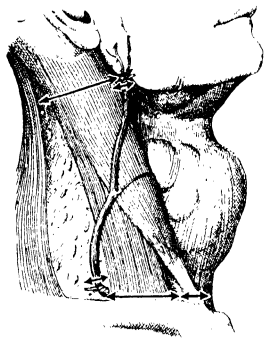


Fig. 61.—Incisions for thyroidectomy and block dissection of neck. (*Figs.* 61–64, *by kind permission of* '*The Lancet*'.)

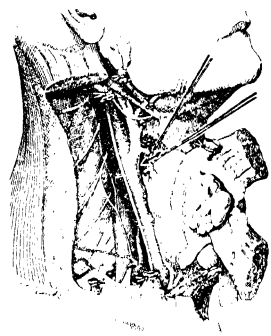


Fig. 62. Resection of sternomasto and external jugular veins.

Comparatively few cases are found to be suitable for operation and only 16 have proved so of 210 seen at the Lyons centre since 1940.

With Paul Guinet[22] the same author has written on that curious condition of so-called benign metastasizing goitre noted in 1875 by Cohnheim, who called it 'adenoma metastatique' or 'benign metastasizing goitre', and now generally recognized as carcinomatous. The condition was referred to in last year's

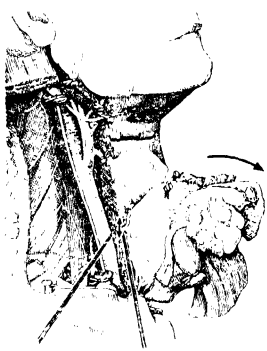


Fig. 63.—Resection of facial, lingual, and superior thyroid veins and superior thyroid artery.

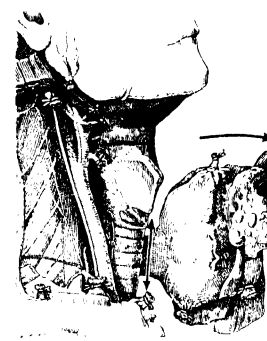


Fig. 64.—Isolation of recurrent laryngeal nerve, with dissection of its accompanying lymph-glands.

MEDICAL ANNUAL (p. 339). Dargent and Guinet have no doubt that the condition is a carcinoma.

Abraham Troell,[23] of Stockholm, found the incidence of malignancy in goitre cases to be approximately 6 per cent (42 cases of a total of 4500), and that malignant adenomatous goitre occurring in patients over 50 years of age with a *brief history, change in voice, shortness of breath, and a very high sedimentation*

rate, has a particularly bad prognosis. R. C. Horn, jun.,[24] and his associates from the University of Pennsylvania, find an incidence of 3 per cent in 2079 goitres operated upon, and in view of the small risk of operation for benign nodular goitre recommend the excision of all nodular goitres unless there are strong contra-indications. The majority of thyroid carcinomas are of the papillary or malignant adenomatous types. They find that thyroid carcinomas occurring in the younger age groups tend to be of the less malignant pathological types and less advanced in their growth when they come under observation. B. McSwain and W. Diveley,[25] of Nashville, Tennessee, found an incidence of 1·88 per cent (of 1168 specimens of thyroid glands) and also advise removal of the single thyroid nodule because it may already be malignant when it is first observed. From Massachusetts, T. J. Anglem and M. L. Bradford[26] find a high incidence of cancer in the single adenoma (9 per cent of 363 cases), and in common with those already quoted and with many others, advocate the removal of all single thyroid nodules.

[The incidence of cancer of the thyroid is thus somewhere between 1·5 and 6 per cent of all goitres. Its commonest form is the malignant adenoma. The solitary thyroid nodule should be removed, especially if it is undergoing recent increase in size, in firmness, or fixation. Cancer of the thyroid would appear to be more serious when it occurs late in life in a rapidly growing adenoma than when it appears in younger subjects.—L. C. R.]

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TISSUE THERAPY BY FILATOV'S TECHNIQUE IN OPHTHALMOLOGY.

Sir Stewart Duke-Elder, K.C.V.O., D.Sc., M.D., F.R.C.S.

Of recent years, and particularly within the last year, a great deal of interest has been excited by the 'tissue therapy' advocated by Filatov, a Russian ophthalmologist, who, more than fifteen years ago, transplanted corneæ taken from the cadaver some hours after death and preserved for some hours before use. Gradually experience showed that with prolonged refrigeration of the cadaver's cornea, up to even fifteen days, certain of its properties were enhanced, particularly the property of clearing the opaque recipient cornea. He deduced from this that such behaviour was likely to be shared by tissues other than the cornea and experimented systematically with various tissues, both animal and vegetable, on various ocular affections, some even extra-ocular. It was found that, under refrigeration, the skin and the placenta acquired to a very high degree the property of 'biological stimulation'. The workers on this subject, however, have not been narrow in their choice of tissues to employ, either by subconjunctival or subcutaneous implant, as they have used cornea, skin, cartilage, retina, choroid, placenta, brain, spleen, liver, and muscular and nervous tissue.

The tissues used are taken from the cadaver not more than six to eight hours after death. All cases in which there has been cachexia, syphilis, infective processes, or a long 'dying period' (more than six hours) are unsuitable donors. The optimum cases are those of accidental or other forms of sudden death. The action is said to depend on 'biogenic' stimulants—products of disintegration of animal tissues exposed to conditions unfavourable for their existence. These products, when used therapeutically, have a stimulating influence on

tissues and are not the result of the death of cells but are said to be produced by the cells in their fight for life. Cod-liver oil is also employed, for it contains products of the disintegration of hepatic tissue.

Preparation and mode of employment of preserved placenta: A placenta derived from a young woman is taken soon after delivery, put into a sterile jar, and kept on ice for 7 days. It is then dried for an hour at a temperature of 60° to 80°; finally it is sterilized in an autoclave. Pieces of placenta so prepared can be implanted either under the skin or subconjunctivally. For subconjunctival implantation a piece 2 × 3 × 2 mm is chosen. If the tissue is found friable, a piece taken from the periphery so as to include a little of the amniotic membrane will prove less friable. After subconjunctival injection of novocain, the conjunctiva is incised and undermined to a depth of 2 cm.; the graft is then pushed to the bottom of the pocket. No suture is used. It is inadvisable to use non-sterilized placenta; autoclaving does not destroy its properties.

Extracts of placenta are prepared by taking tissue treated as above and triturating it in a mortar. For each gramme of the triturate 100 g. of sterilized distilled water are added and well stirred; then it is left to stand for an hour at a temperature of 10°–15° C. Subsequently it is heated to boiling for 2 minutes. Next, it is filtered through several layers of gauze. It is again heated to boiling and passed through filter-paper. The filtrate is put into ampoules of 1 c.c., sealed, and autoclaved at 120° C. for an hour. The ampoules are then preserved in the cold. The extract should be bacteriologically controlled. As it should be albumin-free, ampoules showing sediment should be rejected. The extract is administered as a subdermal injection of 2 to 4 c.c., given every two days in a series of 25 to 30. The injections are painless. After an interval of a month or two, a second series may follow. It is advantageous to combine the injections with subconjunctival implantation.

Preparation and mode of employment of placental lavage: Placentas derived from clinically healthy women, serologically negative, are stored at a temperature of 2° to 4° C. for from 7 to 18 days. Then they are put through a mincer; the mince is then ground into a paste in a mortar. This paste is mixed with physiological serum and injected *per* o the rectum of the patient by means of a rubber enema syringe. Dosage: First lavage 2 g. of placenta in 30 to 40 c.c. of serum. At each subsequent lavage the dose is increased by 0·5 g. up to 6 or 8 g. The lavage should be maintained for 24 hours. The lavage is repeated every two days, 10 to 15 lavages constituting a series.

Preparation of the preserved skin of the cadaver: The skin is freed from the subcutaneous cellular tissue, preserved in the cold in the same way as the placenta, but used without sterilization. It is used either in pieces of various dimensions insinuated under the skin of the arm or on grafts placed at the temple. For grafting Filatov uses trephines of 12 to 14 mm.

Cod-liver oil as a biological stimulant: For injectable cod-liver oil, sterilized and dried ampoules of neutral glass must be used. After filling, the ampoules must be sterilized for one hour three times at 70° C. They should be kept cool in the dark. Before use the ampoules should be warmed. A series of 10 to 30 injections of 1 to 2 c.c. are given intramuscularly. After an interval of 2 to 3 months the injections may be repeated. To infants a teaspoonful of cod-liver oil is given every two days 30 or 40 times [presumably *per os*].

A large number of ophthalmological conditions have been treated by these methods, most of them of the degenerative type. The most common have been primary pigmentary degeneration of the retina ('retinitis pigmentosa'), myopic chorioretinal degeneration, old corneal opacities, interstitial keratitis, traumatous pannus, and optic atrophy. The best results have been claimed after subconjunctival implantation of placenta together with subconjunctival injections of placental serum.

The results of such treatment are difficult to assess. Filatov himself claims good results in a very high percentage of cases of retinitis pigmentosa, and an improvement of vision in all cases (71) of myopic degeneration, findings generally corroborated in the countries of Eastern Europe such as Hungary (Szanto[1]) and Jugoslavia (Matavuli[2]); but these results have by no means been substantiated elsewhere. One of the most favourable reports emanates from Switzerland (Neuenschwander[3]), which details the results of the treatment of 39 cases of retinitis pigmentosa (34 implantations, 5 conjunctival injections): in 18 cases improvement of vision, visual field, and dark-adaptation objectively could be registered. Of remarkable interest were the subjective observations of the patients, as early as ten days after the beginning of the treatment: they spontaneously said that they saw better and more clearly, were able to read better than before, and could see objects in the dark they did not see before. Sufficient experience of the results had not been gained to determine whether the results are permanent or not; but the author reported 5 cases in which the improvement lasted at least three months without new implantation. These results, however, are not by any means universally

confirmed by those from France (Dollfus, Barrois, and de Grenedau[4]; Touland[5]) or America (Gordon[6]). The last author, for example, thoroughly followed 128 cases of retinitis pigmentosa the treatment of which included cod-liver-oil injections, cod-liver-oil concentrates, shark-liver oil, placental implantations, and in one case human-liver implant. In many cases more than one line was pursued. Of the 128 cases analysed, some degree of subjective improvement was elicited in 34 (26·5 per cent). Of these, 15 improved their acuity by one line only of Snellen's type and only one by as much as three lines in one eye. In most of the cases, one eye alone was improved. Eleven cases also showed some improvement in the visual field. Some cases reported deterioration during the course of the treatment, and there were other examples where one eye improved and the other deteriorated. Many cases reported such subjective improvements as less sensitivity to glare and better night vision (though dark-adaptation tests only revealed a definite improvement in 6 out of 21 cases examined in this way).

On the whole it would seem that such conditions as recent corneal opacities may be improved: the well-known effect of Denig's operation for tracheomatous pannus probably illustrates the same action. But in the types of disease for which the treatment is most enthusiastically advocated, such as retinitis pigmentosa and myopic degeneration, objective improvement is rare (if, indeed, it exists), while the subjective tests employed are open to psychological influences. Moreover, such subjective improvement as is obtained seems to disappear in a few months, necessitating repeated injections. There is, indeed, no claim that such a condition as retinitis pigmentosa can be cured, but only that useful vision may be obtained for a longer period. If that were indeed the case, the treatment would be of great value; but the course of events seems very reminiscent of the many 'treatments' of such degenerative diseases (as the stripping of the sympathetic plexus from the carotids enthusiastically practised for some years at the beginning of this century for retinitis pigmentosa), all of which have had their advocates for a variable period of time. The basis of the treatment may, however, exemplify a biological principle of considerable interest.

REFERENCES. [1]*Szemeszeti tanulmanyok*, 1948, 26; [2]*Srpski Arkhev.* 1947, **45**, 309; [3]*Pravis*, 1947, **36**, 858; [4]*Ann. Oculist.* 1947, **180**, 681; [5]*Arch. opthal. Paris*, 1948, **8**, 33; [6]*Trans. Amer. Acad. Ophthal.* 1948, **53**, 191.

TOXOPLASMOSIS.

Macdonald Critchley, M.D., F.R.C.P.

Toxoplasma has been known to be pathogenic to animals for 40 years, and to man since 1939. These human cases are not common, and until recently none have been recorded in Great Britain.[1] Quite recently, however, a human case, in a child, was reported in Kent by N. M. Jacoby and L. Sagorin.[2]

Their patient, a male infant of four months, was admitted to hospital because of persistent crying, loss of appetite, and a large head, of a week's duration. On examination the infant was found to be hydrocephalic, the circumference of the head measuring 17½ in. and the anterior fontanelle bulging. Both eyes were rather prominent and were deviated to the left; nystagmus was observable. The pupils responded sluggishly to light. On ophthalmoscopy a very widespread choroido-retinitis was visible as well as an optic atrophy. No other neurological abnormality could be found. There were a number of small nodules (up to ¾ in. in diameter) over the dorsum of both feet. Radiographs of the skull showed, in addition to cranial thinning, small areas of calcification. Ventricular fluid contained 4 lymphocytes per c.mm.; protein 80 mg. per cent; chlorides 702 mg. per cent; and sugar 57 mg. per cent.

The diagnosis was made by demonstrating neutralizing antibodies in the mother's serum, and a weak or dubious positive reaction in the infant's serum.

This neutralization test was carried out in the State Bacteriological Laboratory of Stockholm, as there are apparently no such facilities in England.

Discussing the diagnosis of human toxoplasmosis, Jacoby and Sagorin point out that there are two clinical types—the congenital and the acquired. The latter may occur either in children or in adults. An interesting and valuable account of this disease appeared in one of the American journals in 1947.[3] The leader-writer in *The Lancet*[1] recognizes 5 forms of human toxoplasmosis: (1) A congenital necrotizing encephalitis; (2) An acquired encephalitis in older children; (3) An acute toxoplasmosis with maculo-papular rash in adults; (4) A chronic encephalitis in adults; and (5) A symptomless infection. The first of these types is the commonest. It is characterized by a hydrocephalus which may be associated clinically with twitchings or convulsions. Two important physical signs are intracerebral calcification and chorioretinitis. Jaundice is common, and may be accompanied by an enlargement of the liver and of the spleen. There may be an actual hæmorrhagic diathesis. The blood-picture is normal, while the C.S.F. may show an increase both in cells and in protein; the fluid may be yellow in colour. If the infants survive, they become blind and mentally defective.

The later cases in childhood are characterized by headache, vomiting, fever, convulsions, enlargement of the spleen and of the lymph-glands. The clinical picture may suggest the diagnosis of cerebral tumour. Adult cases may be either acute or chronic. In the former, there is a sudden development of raised temperature with a rash and respiratory symptoms. Chronic cases show low-grade encephalitic pictures. The diagnosis rests upon the demonstration of parasites either in the C.S.F. during life (rarely), or in smears and sections at autopsy. The latter should be inoculated into mice or guinea-pigs. The technique for the demonstration of antibodies has been described by A. B. Sabin and J. Ruchman.[4]

The morbid anatomy of the early and more acute cases consists in multiple macroscopic areas of necrosis within the brain-stem and cerebral cortex. There are also miliary and subependymal granulomata, and perivascular cuffing. There may be widespread areas of softening throughout the brain, and, less often, the spinal cord. Parasites are demonstrable in the nervous system, as well as at times in the viscera and muscles.

As Jacoby and Sagorin point out, toxoplasmosis may prove to be an important cause of disease in man in this country, for this infection has been found in animals within the London Zoo as well as in the dog.

No specific treatment has yet been identified, but encouraging results have been obtained from the use of the various sulpha drugs, especially sulphapyradine.

REFERENCES. [1]*Lancet*, 1948, **2**, 934; [2]*Ibid.* 926; [3]*J. Amer. med. Ass.* 1947, **133**, 852; [4]*Proc. Soc. exp. Biol., N.Y.* 1942, **51**, 1.

TRAVEL SICKNESS: DRUG TREATMENT.

Andrew Wilson, M.D., Ph.D., Ph.C.

For some, the prospect of a journey is an experience to be anticipated with much delight and interest; for others, less fortunate, it may be an ordeal both harrowing and humiliating. It is perhaps not surprising that a great variety of drugs has been used for the prevention or treatment of travel sickness. The majority of these have been chosen because of their action on the central nervous system; some, like amphetamine, ephedrine, or caffeine, because they are known to stimulate the brain; others, such as barbiturates, bromides, or chlorbutol, because they produce depression of the cerebral cortex. These drugs have all been shown to have no effect in controlling motion sickness.[1, 2]

Atropine and drugs which have actions resembling it, such as hyoscine and *l*-hyoscyamine, have also been employed. These substances have been used alone or in combination with other drugs; for example, the Royal Canadian Sea-sickness Remedy which contains hyoscine, hyoscyamine, and niacin, and the Army Motion-sickness Remedy which consists of hyoscine, atropine, and niacin.[3] There is no evidence however that aneurine, nicotinic acid (niacin), or pyroxidine contribute to the effectiveness of these remedies.[4]

During World War II, considerable attention was given to the investigation of methods of preventing sea and air sickness, and interesting accounts of this work have been published by Holling, McArdle and Trotter,[1] and by Smith,[2, 5] Hemingway,[6] and Tyler.[3] These reports unanimously agree that the most effective drug for the prevention of motion sickness is hyoscine hydrobromide.

When given by mouth in a dose of 0·6 mg. ($\frac{1}{100}$ gr.), hyoscine hydrobromide caused a greater reduction in sea-sickness rate than did any other drug. Consistently better results were obtained when twice this dose (1·2 mg.) was used; thus, Holling, McArdle, and Trotter found that 0·6 mg. hyoscine protected 57 per cent of susceptible subjects, whereas in the groups which were given twice this dose, 73 per cent were protected. Atropine sulphate 1 mg. ($\frac{1}{60}$ gr.) and *l*-hyoscyamine hydrobromide 1 mg. were each of the same order of efficacy as that of 0·6 mg. hyoscine hydrobromide. The protective action of the drug begins about an hour after administration by mouth, and a single dose is effective for between four and six hours. Repeated doses of 0·3 mg. ($\frac{1}{200}$ gr.) hyoscine hydrobromide given at six-hourly intervals have been used for periods up to forty-eight hours without any obvious side-effects.

Dryness of the mouth and slight difficulty in mastication were observed by the subjects who had taken 1·2 mg. of hyoscine, but there was no evidence of drowsiness or impairment of physical or mental ability. According to Keil[7] eye symptoms are not experienced unless the drug is given in doses greater than 1·5 mg.

The mode of action of hyoscine in controlling motion sickness is unknown.

REFERENCES. [1]*Lancet*, 1944, **1**, 128; [2]*Amer. J. Med.*, 1948, **4**, 649; [3]*C.I.M. Report*, 1944, 336; [4]*A.A.F. School of Aviation Medicine Project*, 1943, 142; [5]*A.A.F. School of Aviation Medicine Research Report*, 1945, 333; [6]*Ibid.* 1942, 31; [7]*Ibid.* 1943, 157.

TRICHOMONAS VAGINALIS. *T. Aneyl-Davies, M.D., F.R.C.P.*

E. M. Macdonald and A. L. Tatum[1] investigated the action *in vitro* of various chemical agents on 24-hour cultures of *Trichomonas hominis*, *Trichomonas vaginalis*, and *Trichomonas fœtus*. They found that detergents of both anionic and cationic types usually caused dissolution, without prior evidence of immobilization, of the organisms as soon as the agents were added.

At St. Thomas's Hospital, E. E. Philipp,[2] after testing the effects of the more common remedies, including acetarsone, silver picrate, phenyl mercuric acetate, and phenyl mercuric nitrate, investigated along similar lines. He observed a similar detergent action with Cetavlon, not on cultured organisms but on those taken directly from the vagina and watched under the dark-ground microscope. At first, slowing of the movements of the trichomonads was accompanied by a slight clouding of the field; and then the organisms seemed to 'fade away' and disappear. A pessary containing 3 per cent Cetavlon, 50 per cent glycerin, 3·5 per cent agar, and 43·5 per cent distilled water of about 130 gr. weight, was used. This is large enough for a considerable part of the vaginal mucosa to come into contact with it. The Cetavlon diffuses slowly out of the pessary which breaks up and dissolves over a period of several days, but it does cause a mild burning sensation for the first few hours. In a series of 30 cases, the discharge and irritation ceased in most cases within two or three days and the

vaginal flora recovered from Grade II or III to Grade I and its normal content of Doderlein's bacillus. No definite claim is made, but investigations along the same lines may be profitable.

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TUBERCULOSIS OF BONES AND JOINTS: STREPTOMYCIN IN.

T. P. McMurray, F.R.C.S.

Streptomycin, an antibiotic, was discovered by Schatz, Bugie, and Waksman[1] in their search for an antibacterial agent which would be effective against Gram-negative bacilli. Following its discovery it was used first in the treatment of experimentally produced tuberculosis in animals, and as a result of many trials it was found to have highly satisfactory inhibitory and healing effects on well established tuberculosis in the guinea-pig.

The drug was first used in the treatment of clinical tuberculosis in 1944, and the early observations indicated that streptomycin had also a favourable action on certain forms of pulmonary tuberculosis in the human being. As a result of continued study of its effects it became obvious that streptomycin was the treatment of choice in such forms of the disease as miliary tuberculosis, tuberculous meningitis, tuberculous enteritis, and draining sinuses connected with tuberculous infections.

W. H. Bickel, H. H. Young, K. H. Pfuetze, and T. Norley[2] discuss the use of streptomycin in the treatment of bone and joint tuberculosis. Although it has such beneficial effects its use is not entirely free from risk, and unless carefully administered may be accompanied by certain toxic manifestations. Thus, vestibular disturbance is noted fairly frequently, particularly when 2 g. or more of the drug is given each day, more especially when this dosage is continued over long periods.

Serious renal damage was rarely encountered in patients whose renal function was normal at the start of the treatment, and although deafness is occasionally encountered during the administration, this phenomenon is only seen in those patients in whom large doses are employed. So-called sensitization phenomena are seen occasionally, characterized by the appearance of chills, fever, cutaneous rash, and vomiting. If these complications should become obvious the patient can usually be desensitized with small daily doses of 50-100 mg., the amount being gradually increased until the desired daily dose is reached. In the opinion of the authors these toxic manifestations are prevented, or at least greatly diminished, if the daily dosage does not exceed 1 g.

Dosage.—Further experience and investigation with streptomycin is necessary before a decision can be reached as to the amount of the optimum daily dose. Similar observations are also necessary to determine the duration of treatment and the frequency with which the drug should be administered. At present the impression has been gained that 1 g. should be given intramuscularly each day in divided doses every 8 to 12 hours for 90 to 120 days continuously.

Streptomycin Resistance.—It may be observed that during the course of treatment streptomycin-resistant strains of the tubercle bacillus are often found to have replaced the sensitive strains during the third and fourth months of treatment, a phenomenon which is still incompletely understood. When this alteration in the character of the bacillus has occurred further treatment by streptomycin is useless. It is not always easy to recognize this change in the reactions of the bacilli, but the recovery of the tubercle bacilli from a discharging sinus usually indicates that the change has taken place.

Analysis of Clinical Records.—Sixteen patients suffering from bone and joint tuberculosis were treated during the course of this investigation. In 14 patients the infection was tuberculous, proved by histological examination or by

guinea-pig injection. In the 2 instances in which tuberculosis was not proved, a positive smear for acid-fast bacilli was obtained from chronic discharging sinuses.

In these 16 patients 19 joints were involved by the disease; the joints involved were as follows: 4 knees, 4 spinal infections, 3 ankles, 3 wrists, 2 shoulders, 1 elbow, 1 ilium, and 1 sternoclavicular joint. One patient had infection of an elbow and an ankle, another suffered from infection of an ankle and a sternoclavicular joint with draining sinuses from a tuberculous empyema, while a third patient had involvement of both shoulder-joints with multiple draining sinuses; the second and third of these patients suffered at the same time from pulmonary tuberculosis.

The duration of treatment with streptomycin varied between sixty-six and a hundred and ninety-six days, with an average duration of a hundred and twelve days. The average total dose of streptomycin was 134 g. while the daily intramuscular dose varied between 0·75 and 2 g. Mild to moderate toxic symptoms became evident in 9 of the 16 patients, but in one instance only were the symptoms sufficiently severe to warrant cessation of the administration of the drug. This patient who had received 2 g. daily for seven days developed an extensive urticarial rash with a temperature of 102° F., œdema of the face, and severe nausea and vomiting. Treatment was discontinued for six weeks, and after the administration of desensitizing doses of 0·1 g. every four hours, it was possible to return to the routine administration of 1 g. daily.

Mild toxic symptoms appeared in 8 patients, evidenced by the occurrence of slight subjective dizziness, while 6 patients developed objective staggering, and in one instance only was there a complaint of tinnitus. Dizziness and staggering disappeared in most patients on a reduction of the dosage of streptomycin, but in 3 instances these symptoms persisted for eighteen months after the complete cessation of the administration of the drug. It is interesting to note that in none of these 16 patients was there any complaint of deafness either during treatment or after its cessation. The results of laboratory studies, with the exception of the sedimentation rate, were completely uninfluenced by the streptomycin therapy.

The authors give full clinical records of each of the 16 patients treated by streptomycin. One patient suffered with chronic discharging sinuses of the thorax from tuberculous empyema and a bronchopleurocutaneous fistula. Two courses of streptomycin were given in this case; the first course was inadequate both as to the amount given and the period of treatment; the second course of the recognized strength and length led to complete healing of the sinuses which had previously resisted two operations of thoracoplasty.

One patient suffered from discharging sinuses of both shoulders associated with far advanced bilateral pulmonary tuberculosis. Both sinuses from the shoulders were healed within a month after the administration of streptomycin, and these sinuses have remained healed for a period of five months since that time. Although the patient appeared to improve rapidly, sternal and scapular abscesses developed two and four months respectively after the administration of streptomycin had ceased.

Of the 16 patients in this investigation 9 were considered to have reacted favourably to treatment by streptomycin as their sinuses were healed, their general condition was improved, and their improvement was confirmed by radiographic examination.

No benefit to the patient was observable in 4 cases, although in no instance could it be said that the drug had caused any retrogression in the patient's condition. In the case of one other patient there appeared to be a slight general improvement.

The conclusions reached by the authors were that, considering the poor response to treatment of these conditions in the past, this preliminary survey gave a very genuine encouragement for the future.

They feel that 1 g. of streptomycin daily for ninety days is a satisfactory course of treatment in the light of present knowledge.

REFERENCES.—[1]*Proc. Soc. exp. Biol., N.Y.* 1944, **55**, 66; [2]*J. Amer. med. Ass.* 1948, **137**, 682.

TUBERCULOSIS, PULMONARY, SURGERY OF.

N. R. Barrett, M.A., M.Chir., F.R.C.S.

During the last few years the surgery of pulmonary tuberculosis has been reconsidered and the relatively static point which had been reached has given origin to a number of new ideas and clinical trials. None of these have yet advanced to the stage of being placed or accepted in treatment, but all seem to hold interesting possibilities.

French surgeons have been the chief sponsors of *speliotomy* or open cavity drainage and the operation has been given a trial. It differs from the form of cavity drainage which was advocated by Monaldi in that the latter relied upon maintaining a continuous relatively negative gas pressure inside the cavity, which was achieved by introducing a fine catheter and applying continuous suction. Speliotomy consists in removing the 'roof', i.e., all the superficial tissues and that part of the wall of the cavity which abuts upon the surface of the lung and so in laying the cavity open in such a way that a pack can be introduced and that healing by granulation may occur. The operation can only be performed when pleural adhesions are present, or have been created, and is applicable to cavities of moderate size near the surface of the lung. Within these limits it has its usefulness in a small group of cases which cannot, for one reason or another, be treated by relaxation therapy or excision; but few would regard speliotomy as the first method of treatment in any given case. The chief disadvantage of the operation is the tendency of the disease to spread to other parts of the lung.

Dillwyn Thomas[1] and his associates at Sully Hospital have been concerned with the management of that group of patients whose cavities are of such a type, or so situated anatomically, as to be unsuitable for relaxation therapy; two different approaches have been tried. The first, "*reversed postural drainage*", has now been carefully assessed. It consists in nursing the patient continuously in such a position that the cavity is dependent, i.e., it is the opposite to ordinary postural drainage as applied to the lung. The position must be maintained absolutely continuously by the patient for several months on end, and brings up many difficulties in nursing as well as taxing the endurance of the patient. A plaster bed—fixed in the desired position—is one way of achieving the posture. The manner in which "reversed postural drainage" or "postural retention" works is not known, but it is most efficacious in the management of tension cavities; these either reduce in size very rapidly or slowly fill up with sputum and become 'blocked'. It has been a matter of experience that if a cavity can be kept blocked for about six weeks it will probably resolve and heal. Time has shown that although this method will greatly benefit many types of cavity there is a tendency to recurrence as soon as the patient reverts to normal posture, and for this reason Dillwyn Thomas has done thoracoplastics as a final procedure on many of the patients; but it must be stressed that the majority of these were at first quite unsuitable for thoracoplasty and that a number have been controlled by "postural retention" alone.

The second method of treatment which has been applied at Sully by D. Thomas and Cleland is *surgical obliteration of the cavity*. They were impressed

by the fact that in many cases the relatively positive intracavitary pressure, induced probably by tracheobronchitis in the small bronchi in the vicinity, seemed to be the main factor in maintaining the cavity and that in this group of patients relaxation therapy had very little effect upon the cavity. The problem was met by doing an open thoracotomy, and, after having divided local adhesions, the cavity was widely opened in such a way that by introducing through-and-through stitches into the lung it could be totally obliterated, folding one wall over the other. The success of such a procedure hinged upon whether or not it would be followed by leak of tuberculous material from the lung, with the subsequent development of a tuberculous empyema, or of a spread in the lung. Neither of these two complications has occurred in the small group of patients so far treated, and in all the cavity seems to have healed.

Another trend has been to find a way of combining the benefits of extrapleural pneumothorax with those of thoracoplasty, without the disadvantages of either. Surgeons have sought to evolve an operation which would relax as much or as little of the lung as was required (and not as much as might be dictated by considerations such as embedding the scapula); which could be performed in one stage; and which would not produce either the deformity or the risk of basal atelectasis associated with thoracoplasty. The operation must avoid the disadvantages of an extrapleural pneumothorax, namely post-operative bleeding into, or infection of, the dead space which had been created. In 1943 M. Konstam,[2] working at Milford Sanatorium, began to *fill the "Semb space" created by the usual first-stage thoracoplasty with air and subsequently with oil.* She found that some small apical lesions could be controlled in this way after only 3 ribs had been removed. The procedure was also valuable as a temporary expedient in a patient who required a more extensive thoracoplasty to cover the lesion but who had developed a complication so that the second-stage operation had to be postponed for months or weeks. At about the same time Brock began to develop his operation, which utilized the principle of *apicolysis maintained by an osteoplastic flap.* He mobilized the upper part of the lung, and then, having relaxed the lesion, fashioned a flap of bones and intercostal structures, taken from the third, fourth, and fifth ribs which he fixed by sutures to the chest wall, fore and aft, in such a way that the lung could not re-expand to its original position. This operation has now been performed upon a number of patients, and the results have been fairly good; but it is a major procedure and not one to be lightly undertaken.

More recently Wilson[3] and Grow and Dwork[4] have developed the old principle of plombage after apicolysis, but have advocated the introduction of *lucite balls.* These balls, which are used to fill the space created by an extrapleural type of operation, are made of methyl methacrylate, which is a plastic substance, and which is stated to be absolutely non-irritating to the tissues. They do away with the necessity of refilling the extrapleural space with air, and, provided that a large effusion does not occur, they seem to be efficacious (*Figs.* 65, 66, *and Plates XLIV XLVII*).

Morriston Davies[5] has used the same idea but has preferred a *polethene pack.* This substance is also a plastic but is made in sheets and is soft and resilient like fine rubber. Morriston Davies packs sheets of polethene into the extrapleural space he has created and believes that the method is preferable to lucite balls because the 'plomb' is not so rigid and therefore not so likely to be resented by the tissues.

Barrett has maintained the position of the lung after an extrapleural mobilization by holding it down with a cap of *tantalum gauze* moulded to fit the apex and sewn all round to the chest wall at about the level of the 6th or the 7th rib posteriorly and the 3rd rib anteriorly; after this operation the

extrapleural space fills with serum and blood, but this organizes and does not require any treatment.

The introduction of *streptomycin* has already made some important differences to the surgery of pulmonary tuberculosis, but the supply has been closely controlled by the Medical Research Council. For this reason no surgeon in

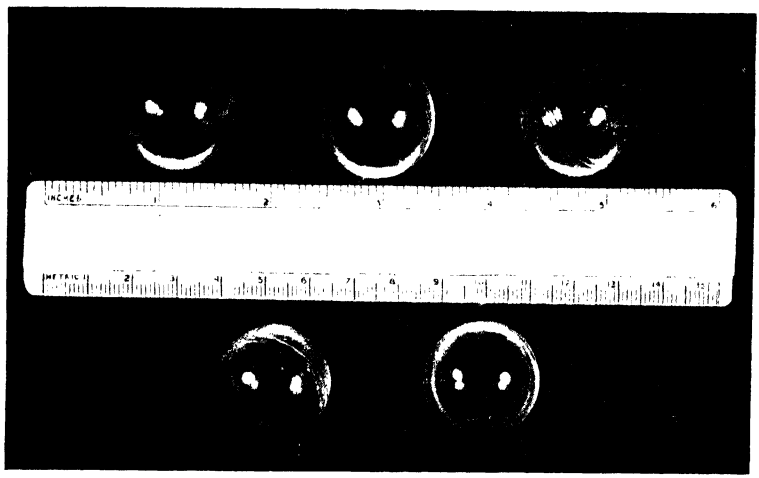


Fig. 65.—Lucite spheres (1 in.) used for plombage after extrapleural pneumonolysis. (*Figs.* 65, 66, *and Plates XLIV–XLVII by kind permission of "The British Journal of Tuberculosis and Diseases of the Chest".*)



Fig. 66.—Showing axilliary approach for apicolysis, the incision being made over the anterior axillary fold.

Great Britain has, as yet, been able to acquire a large personal experience and only general observations can be made. Tuberculous tracheobronchitis (Judd[6]) is undoubtedly benefited by the exhibition of this antibiotic, but it is manifest that if the lesion has progressed to the stage of fibrotic bronchial stenosis then the problem is one of mechanical bronchial obstruction. A second group of patients who have responded well are those who develop a spread of disease into the base of the lung, or in the opposite lung after thoracoplasty; it is difficult sometimes to be sure that the lesion is not a simple non-specific pneumonitis, but in cases known to be tuberculous a most gratifying response has often been obtained. This type of spread was, in the past, most serious for the patient, not only because the completion of the thoracoplasty had to be delayed, but because the new lesion often became established and progressive. Streptomycin has also enlarged the scope of lobectomy and pneumonectomy in the management of pulmonary tuberculosis, and so striking have some of the results been that the pendulum has probably swung too far towards radical excisions in some countries. Removal of the principal, or the most active, tuberculous focus is a general surgical maxim, which has worked well in other parts of the body, and excision of tuberculous lung has, in the past, been delayed because it was a matter of experience that without the cover afforded by streptomycin there was a prohibitive risk of tuberculous bronchial fistula in the stump remaining after lobectomy or pneumonectomy, of tuberculous empyema, or of tuberculosis in the remaining lung. It is now clear that, if the cases be chosen with discretion, there is a great future for this type of operation.

REFERENCES.—[1]Communicated to the Society of Thoracic Surgeons of Great Britain and Ireland in November, 1947; [2]*Thorax*, 1948, **3**, 247; [3]*J. thorac. Surg.* 1948, **17**, 111; [4]*Brit. J. Tubere.* 1948, **42**, 25; [5]*Thorax*, 1948, **3**, 189; [6]*J. thorac. Surg.* 1947, **16**, 512.

TUBERCULOSIS, PULMONARY: TREATMENT. (*See also* PNEUMOPERICARDIUM COMPLICATING PNEUMOTHORAX THERAPY.)

Philip Ellman, M.D., F.R.C.P.

Para-aminosalicylic Acid (P.A.S.).— The original work which laid the foundations for the discovery of P.A.S. was carried out by F. Bernheim,[1] who showed that small amounts of sodium salicylate have a profound effect on the metabolism of *M. tuberculosis*, and suggested that it was used as a metabolic substrate in the respiratory enzyme system of the organism. In 1946 J. Lehmann[2] confirmed this and showed that only pathogenic strains of tubercle bacilli were thus affected. He therefore examined a large series of compounds related to salicylic acid, in the hope that one of them might prove capable of entering into substrate competition in a manner analogous to the sulphonamides competing with para-aminobenzoic acid. Of all the compounds tested P.A.S. was by far the most active.

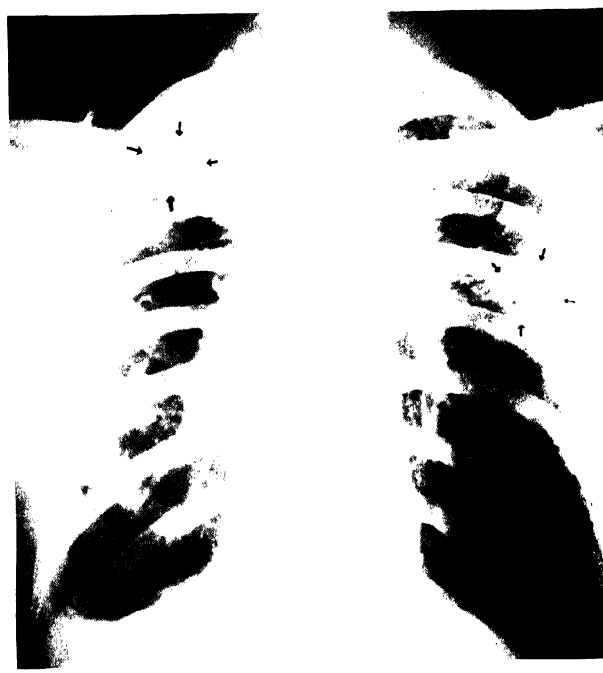
Animal experiments by various workers, notably W. H. Feldman[3] and G. P. Youmans[4] were not uniformly successful, but indicated that P.A.S. could considerably modify the course of experimental infection in guinea-pigs and mice.

Since 1946 various clinical trials have been reported, but all of them have in common that they were performed on small series of cases and without scientific controls. Thus there is no evidence (comparable to that obtained by the Medical Research Council with streptomycin) showing the effect of P.A.S. therapy in a carefully controlled series of pulmonary tuberculosis cases. This, however, has in part been due to technical production difficulties causing scarcity of supplies.

The earliest clinical trials were by Lehmann,[2] who reported good results from oral administration in daily doses of 10–15 g. given in 8-day courses at

PNEUMONOLYSIS WITH LUCITE PLOMBAGE

G. E. Grow and R. E. Dworsky



G. L. Showing cavities in both right and left lungs

PNEUMONOLYSIS WITH LUCITE PLOMBAGE—*continued*

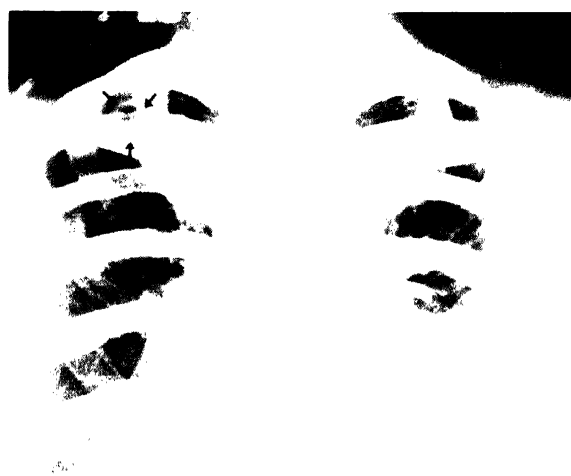
G. B. Grow and R. E. Dworkin



G. L. After extrapleural pneumonolysis. Cavities no longer visible.

PNEUMONOLYSIS WITH LUCITE PLOMBAGE—*continued*

G. B. Grow and R. E. Dworkin



G. G. K. Showing cavity in right upper lobe.

PNEUMONOLYSIS WITH LUCITE PLOMBAGE—*continued*

J. B. Grow and R. E. Dworko



G. G. K.—After extrapleural pneumonolysis. Cavity no longer visible.

8-day intervals. The fall in patients' body temperatures was prompt and marked, temporary or permanent, and coincided with periods of treatment. It was accompanied by a definite improvement in the general condition, a gain in appetite and weight, and a fall in the E.S.R. There was also improvement in red-cell count and hæmoglobin. No symptoms of salicylism were observed, and Lehmann concluded that control of fever was not a salicylate effect.

G. Vallentin[5] reported on a series of 75 cases with variable results. The greatest success was in cases of exudative pulmonary disease, where he obtained the same response as Lehmann and noted in addition sputum-conversion and improved X-ray appearances. Relapses were frequent, however, if treatment was suspended too soon. There was no effect on 6 cases of miliary and meningeal disease, and the effect on tuberculous empyemata was disappointing. Toxic symptoms reported by Vallentin were kidney irritation and albuminuria, and gastro-enteritis (especially diarrhœa).

In Britain the first clinical trials with P.A.S. were reported by T. G. Dempsey and M. H. Logg[6] who treated a total of 19 patients. Six cases of pulmonary disease received the drug orally in daily doses of 14–20 g. In these patients the drug exerted a favourable effect, but the authors did not regard their results as conclusive, since therapy had been intermittent on account of irregular supplies. They were able to report, however, that the temperature and E.S.R. fell rapidly a few days after the beginning of treatment, and that over the space of a few weeks there was a fall in pulse-rate and an increase in weight, vital capacity, and hæmoglobin. The amount of sputum decreased and the number of bacilli present were reduced, while the morphology of the organism changed, first becoming beaded and striated, then becoming replaced by acid-fast granules. The patients' general condition and radiological pictures improved, and the authors were impressed by the reduction in size of lung cavities.

A. Erdei[7] reported on 6 cases treated over a period of 60 days. All 6 were given 12 g. daily in divided doses at 3-hour intervals. The most striking effect of the drug was the very great improvement in the patient's general condition that occurred about the third day, especially in toxic, anorexic, and apathetic patients. This worker also noted a considerable fall of temperature and E.S.R., a reduction in cough, cessation of night sweats, and a gain in appetite and weight. Sputum was diminished and bacilli much sparser, becoming granular and tending to clump. Radiological changes were well marked in that considerable 'hardening' and retraction of apical lesions occurred, the size of cavities diminished, and areas of soft mottling cleared up. Prior to treatment with P.A.S. these patients had received 6·9 mega units of penicillin without benefit. Cultures of sputum after three weeks on P.A.S. were sterile after 6 weeks' incubation, and remained so even when para-aminobenzoic acid was added to the medium to antagonize any P.A.S. present. During treatment all 6 cases developed a slight leucocytosis (12,000 to 14,000 c.mm.) with monocytosis (up to 16 per cent). No toxic symptoms were observed by Erdei, who thought that higher doses could and should be used.

Thus at present it would appear that P.A.S. frequently produces marked symptomatic improvement and that it appears to have a concomitant 'hardening' effect on the dangerous type of spreading exudative lung tuberculosis. Its full place in the therapeutics of pulmonary tuberculosis will not, however, be known until the conclusion of large-scale controlled observations recently inaugurated by the Ministry of Health.

Streptomycin.—The Medical Research Council Committee's report[8] is an exemplary and rigorously controlled investigation of 107 patients with pulmonary tuberculosis. The numbers were necessarily limited since the supply of streptomycin during the investigation was restricted. The controlled investigation

and statistical analysis should serve as a model in relation to chemotherapeutic trials with this or any other substance in the future for it is as near a laboratory experiment as is practicable. The expert committee decided to confine their attention to one particular type of case, namely, acute progressive bilateral pulmonary tuberculosis of presumably recent origin, bacteriologically proved unsuitable for collapse therapy, and between the ages of 15 and 25 (later extended to 30). In fact the type of disease selected was one considered hitherto unsuitable for any other form of treatment than bed-rest. The reviewer, who provided a few cases, had occasion to appreciate the rigorous adherence of the selection committee to this type of case.

Of the 107 cases, 55 were treated by streptomycin plus bed-rest (S. cases), whilst 52 (C. cases) were treated by bed-rest alone.

The 55 streptomycin patients received 2 g. of streptomycin divided into 4 6-hourly doses daily by intramuscular injection for 4 months, though some of the earlier ones were treated for rather longer periods up to 6 months. [It is more than likely with our present knowledge of dosage that 1 g. per day would have been adequate.—P. E.] No toxic effects necessitated stopping treatment, but vestibular disturbance was common. The 52 control patients were treated in the same hospitals with the same régime apart from the streptomycin therapy. (Patients were assigned to one or other group by random selection, and only after acceptance as suitable for the trial.) At the end of six months 4 S. (7 per cent) patients and 14 C. (27 per cent) patients had died, but 27 S. (51 per cent) patients and 4 C. (8 per cent) patients had improved considerably (radiologically). These results serve to indicate the beneficial effect of streptomycin. Slight or moderate improvement was noted in 18 per cent of S. cases and 25 per cent of C. cases. Apart from those who died, deterioration was seen in 18 per cent of S. cases and 34 per cent of C. cases.

The main difference between S. and C. series is among the patients clinically acutely ill on admission: thus, among patients having on admission evening temperatures of 101° F. (38·3° C.) or over, 13 of 24 S. patients and 2 of 19 C. patients showed improvement radiologically. More S. patients than C. patients showed clinical improvement, but the difference between the two series is smaller than in respect of radiological changes.

Improvement in S. cases was greatest in the first three months. After the end of this period many S. cases began to deteriorate. At the end of six months examinations for tubercle bacilli were negative in 8 S. cases and 2 C. cases. The best result in S. cases were seen in the first months of the treatment.

Results of tests for streptomycin sensitivity of infecting strains are given for 41 cases. In 35 cases tests revealed *in vitro* resistance from 32 to over 8000 times that of the original strain or the standard H37Rv. In most cases streptomycin resistance emerged in the second month of treatment. It seems probable that streptomycin resistance is responsible for much of the deterioration seen in streptomycin cases after first improvement.

The improvement was assessed clinically, by serial radiographs, and sputum conversion. The chest X rays were viewed independently by two radiologists with specialized experience in chest radiology and a clinician, and improvement consisted in the main in resolution of the exudative lesions, which tended to occur earlier in the streptomycin cases and later in the control cases. It is significant that analysis of the results according to degree of illness of the patients on admission showed that streptomycin cases made a greater response than the control cases in the more acutely ill with higher temperatures, but in both groups there was a better response when initial gross cavitation was absent. Large cavities did not close in either group.

The well-known tendency in the course of treatment experienced by American writers for *streptomycin-resistant tubercle bacilli* to occur during treatment was equally experienced in the course of this clinical trial. This would, no doubt, account for clinical improvement in the first month and subsequent stagnation in some of the cases. This streptomycin resistance is of great clinical significance and if the organism develops resistance after a short period of treatment then, from the patient's standpoint, we must assume that a course of streptomycin may be effective possibly only once during the long illness of the individual. Hence the risk arises that if streptomycin is indiscriminately used in unsuitable cases, streptomycin-resistant organisms may be disseminated, rendering more and more cases resistant to streptomycin. The physician has therefore a great responsibility placed upon him in relation to the use and abuse of streptomycin from the wider Public Health standpoint.

The field of streptomycin therapy in pulmonary tuberculosis is therefore, in the state of our present knowledge, restricted to lesions of recent origin of a progressive nature and unlikely to respond to bed-rest or even collapse therapy alone. It may also be of use in acute contralateral spreads after artificial pneumothorax or thoracoplasty. All chronic fibroid and fibro-cavernous lesions would therefore be excluded.

Hence we may conclude that streptomycin is of value in the treatment of acute forms of pulmonary tuberculosis. Its value in the treatment of ulcerative lesions of the main bronchi, larynx, and pharynx has been confirmed. It is being used increasingly prophylactically against extension of the disease after surgery in pulmonary tuberculosis, but in this sphere further experience will be required to indicate whether in fact the patient may not, in the long run, be worse off, for were the disease to relapse late resistant organisms may have developed which would perhaps render the patient unresponsive to the drug.

The M.R.C. committee's first report[9] on tuberculous meningitis has confirmed the American experience that in most cases streptomycin would prolong life, in many it could produce considerable improvement, and in a few clinical cure was possible. This state of affairs, it must be admitted, is an advance on the previously hopeless situation in this disease.

Pneumoperitoneum. – Since A. L. Banyai[10] first recommended this procedure over a decade ago, there has been a great divergence of medical opinion concerning its value and the indications for its use, but it is becoming more widely used and there is an increasing literature on the subject. In selected cases there is good reason to believe that pneumoperitoneum can favourably influence the course of pulmonary tuberculosis, and there are certain distinct advantages of pneumoperitoneum over pneumothorax. In competent hands it is a relatively safe procedure with few possible complications. Recent studies show that it may assist in relaxing diseased tissue, which is regarded as the principle factor responsible for beneficial effects in collapse therapy.

There are conflicting reports concerning the value of procedure, used alone or in association with phrenic crush, although there is substantial evidence to show that it can alone frequently produce sufficient lung relaxation, but if the disease is unilateral its combination with phrenic crush is likely to be more beneficial. Certain observers maintain that the combination of phrenic crush and pneumoperitoneum may produce permanent diaphragmatic paralysis.

For the wise use of pneumoperitoneum it is necessary that its indications and contra-indications should be reasonably well-defined. Let us confess, in the first place, that an anatomically successful pneumothorax or a good thoracoplasty where there is no apparent risk are preferable to the relatively simpler pneumoperitoneum, but in active exudative disease, unsuitable for pneumothorax and too ill for a plasty operation, pneumoperitoneum may be

an excellent initial measure. In unsuccessful artificial pneumothorax, initial pneumoperitoneum may also prove very helpful. In old fibrocavernous disease its value is doubtful, and in tuberculous tracheobronchial disease, with or without bronchostenosis, as well as tuberculous bronchiectasis, it may even be contra-indicated. The excellent recent publications, among them those of H. C. Trimble, J. Lloyd Eaton, G. L. Crenshaw, and I. Gourley[11] in America and R. Y. Keers[12] in Britain, deal comprehensively and critically with the subject. Keers finds in his experience that, used as a simple procedure, its most notable success was found when the disease was confined to the lower zone. He also finds pneumoperitoneum of value in recent exudative disease and cavitation where pneumothorax is impracticable and may be complicated by undesirable sequelæ.

Trimble and Eaton[13] report a study of 407 consecutive cases of tuberculosis treated with pneumoperitoneum from 1934 to 1946. The literature was reviewed, the technique was discussed briefly, and several cases were presented which illustrated the type of disease most suitable for treatment and the results obtained. The complications were analysed. Significant complications were observed in 6 per cent of the series. The clinical status of the patients at the end of the study was reviewed.

Including all of the patients with cavities totalling not more than 8 cm. in diameter, there was a total of 171 such patients. Ninety-six, or 56 per cent, became arrested, and another 27, or 16 per cent, were definitely improved. On the other hand, of the 52 patients with cavities larger than 8 cm., only 10, or 19 per cent, became arrested, with an additional 13 patients definitely improved. This illustrates the fact that the best results are found with the single cavities, but the results are good in all cavities whose total diameter does not exceed 8 cm. At this point there is a sharp decline in the expectancy of arrest.

Analysis of the position of the cavity, whether apical, mid-lung, or basal, showed that the position in the lung had but little bearing on the results which may be expected from pneumoperitoneum therapy. The percentages of each group, those arrested, improved, unsatisfactory, and dead, as compared with the three separate locations of the cavity, are extremely close, but slightly more favourable results were observed in the treatment of the basal cavities.

The authors feel that building on a foundation of bed-rest plus a short period of institutional care for educational purposes, therapeutic pneumoperitoneum is an excellent procedure. They conclude that the purpose of pneumoperitoneum is to achieve an adequate mechanical rise of the diaphragm, thus reducing the motion of the diaphragm with ordinary respiration. To be maintained, large weekly refills are necessary, guided by fluoroscopy.

Manometric readings are of minimal value as a guide to the extent of the collapse. Phrenic-nerve operations are usually not necessary and are used only for specific and definite indications, which are few.

Adequate pneumoperitoneum is a valuable collapse procedure in the treatment of pulmonary tuberculosis. The authors' immediate and long-term results amply confirm this. The period of complete bed-rest is much shortened, complications are not excessive, and are rarely serious. Their indications for pneumoperitoneum therapy have been greatly widened because of: (1) the good results obtained; (2) as compared with bed-rest alone, the shortened period of complete bed-rest with the resultant economic saving to the patient, the low exacerbation and recurrence rate, the more rapid conversion of sputum, and the possibility of changing to a more radical collapse procedure should the need arise; (3) as compared with pneumothorax, the fact that pneumoperitoneum can be initiated in nearly all patients, the fact that it is a completely reversible

procedure and can be stopped at any time without danger of a non-expansile lung or pleural complications, the possibility of reinitiating it should the need occur, and the relative lack of complications.

REFERENCES.—[1]*Science*, 1946, **92**, 204, and *J. Bact.* 1941, **41**, 387 ; [2]*Lancet*,], 15 ; [3]*Proc. Mayo Clin.* 1947, **22**, 473 ; [4]*J. Bact.* 1947, **54**, 409 ; [5]*Svenska Läkartidn*, **43**, 2047 ; [6]*Lancet*, 1947, **2**, 871 ; [7]*Ibid.* 1948, **1**, 791, and **2**, 118 ; [8]*Br. med. J.* 1948, **2**, 769 ; [9]*Lancet*, 1948, **1**, 582 ; [10]*Amer. Rev. Tuberc.* 1934, **29**, 603 ; [11]*Ibid.* 1948, **58**, 251 ; [12]*Brit. J. Tuberc.* 1948, July ; [13]*Amer. Rev. Tuberc.* 1948, **58**, 251.

TUBERCULOSIS : SPREAD. *W. H. Bradley, D.M., M.R.C.P.*

The epidemiology of tuberculosis has become the subject of a wholesome, if heated, discussion in the *Journal of the Medical Association of Eire*. It all starts with an essay in clinical epidemiology by Dr. James Deeny,[1] who is Chief Medical Adviser to the Department of Health, who carried out his study in order to discover what medical-social features were common to people who died from tuberculosis, and what epidemiological relationship existed between persons dying from the disease, or what links there were which might show how the disease spreads in relation to deaths. The investigation was carried out in a manufacturing town of 15,000 population in Northern Ireland, providing a homogeneous sample both socially and from an occupational point of view, since the vast majority were employees in factories in one industry. All the deaths occurring in a twenty-five-years period from 1919 to 1944 and certified to be due to tuberculosis, were examined. These numbered 498. The people in the town were inclined to blame certain processes in their staple industry as a factor causing deaths from tuberculosis, but on examination this was not found to be the case. Certain striking observations emerged ; almost one-third of the deaths took place in houses in which there were two or more deaths : in fact, very many deaths were related in time and proximity, and could be grouped into small outbreaks affecting limited areas and extending in their effect through a number of years. Inter-familial spread appeared to be of the greatest importance. Instances were seen where, within a short time, sometimes even weeks, several deaths took place in the same family, indicating a violent and overwhelming infection of all members of a family at the same time, often caused by one person, and seemingly unrelated to any family weakness, lack of immunity or capacity to resist the disease. Apart from inter-familial spread, of all the possible associations between one death and another, the strongest link was proximity of residence. Deeny concludes that tuberculosis is a 'slow-motion' epidemic, and it is only by studying the links between one death and another that the really epidemic nature of the disease can be appreciated. The necessity to isolate infectious cases becomes more obvious and imperative. Concentration on the relatively small number of acute and very infectious cases, and the prevention of the few chronic patients from spreading the disease, is the most promising method of approach to the spread of tuberculosis in Ireland.

Other writers in the same journal, Dr. P. J. Galvin[2] and Dr. Noel Brown,[3] disagree with Dr. Deeny. The latter believes, with Professor Greenwood, that "it is not scientific or modern-minded, or anything but foolish, to try to believe that any other prophylaxis of this particular crowd disease is so important as raising the economic level . . . of the crowd". Dr. Galvin challenges Deeny's statistics, and shows how most of his findings could be readily explained as chance phenomena. But some of these arguments are rather precious. The fact remains that tuberculosis spreads in slow-motion epidemics, and that improvement in living conditions is not the only answer to an epidemic disease.

REFERENCES. [1]*J. med. Ass. Eire*, 1947, **21**, 82 ; [2]*Ibid.* 1948, **22**, 22 ; [3]*Ibid.* 26.

TUBERCULOUS CERVICAL ADENITIS. *Lambert Rogers, M.Sc., F.R.C.S.*

Hamilton Bailey[1] tells us that, of the 800 lymph-nodes in the body, 300 lie in the neck. He has traced the history of our knowledge of tuberculous invasion of these nodes. Since 1882, when Clifford Allbutt and Pridgin Teale first advocated extirpation of the involved glands, there has been a reversion to conservative measures, a rise in conservation which Bailey claims should now be followed by a decline, as he is an ardent advocate of operative treatment. He points out that the portals of entry to the invaded glands are the various parts of Waldeyer's ring, i.e., the faucial or pharyngeal tonsils respectively, or the teeth (*Fig.* 67). Whereas the anterior triangle is reached from the faucial tonsil by way of lymphatics to the chief or jugulo-digastric (Wood's) gland and so into the anterior triangle, the adenoids may drain directly into the posterior triangle and enlarged glands may first appear here. Hamilton Bailey recognizes four stages in the progress of the disease: (1) where it is confined to glands; (2) caseation within the deep fascia; (3) spread through the deep fascia (collar-stud abscess); (4) discharging sinus. He protests against aspiration even by

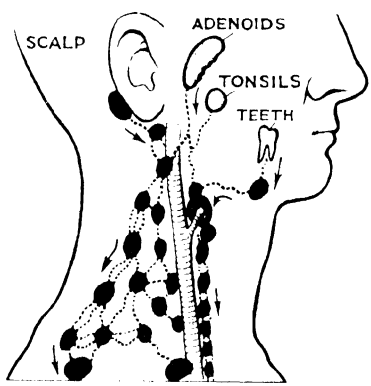


Fig. 67. Portals by which tubercle bacillus enters lymphatics of neck. (*Figs.* 67–69 *by kind permission of "The Lancet".*)

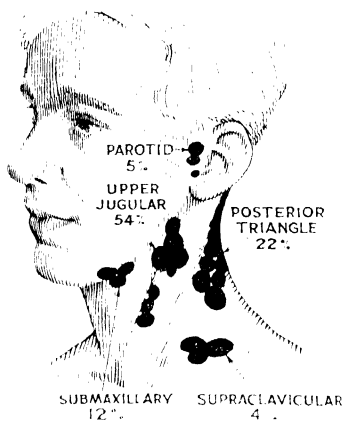


Fig. 68. Various groups of cervical lymph-nodes affected by tuberculosis, founded on 372 consecutive cases. The 3 per cent not labelled are divided between mid-jugular group shown and submental group not shown.

Calot's oblique method. He likewise condemns scraping, and points out that Volkmann designed his spoon for scraping away necrotic pieces of bone—"curettage is not divorced from the disaste of disseminating tuberculosis".

He advocates the following treatment: 1) If admission to hospital cannot be obtained within a week and there is a pointing abscess, cautery puncture and its evacuation, and the placing of a sterile pad of gauze so that it is held firmly in place over the area of the puncture by a viscopaste bandage which also splints the neck; (2) The removal of diseased tonsils and adenoids [and presumably also carious teeth (F. B. Moorhead[2] has found tubercle bacilli in decayed root pulp)]; (3) Adequate surgery; (4) Adequate convalescence—two or three months in an appropriate institution. In the surgical extirpation of involved nodes he draws attention to the importance of their regional grouping (*Fig.* 68) and the desirability of removing the particular group of glands through a transverse incision (*Fig.* 69).

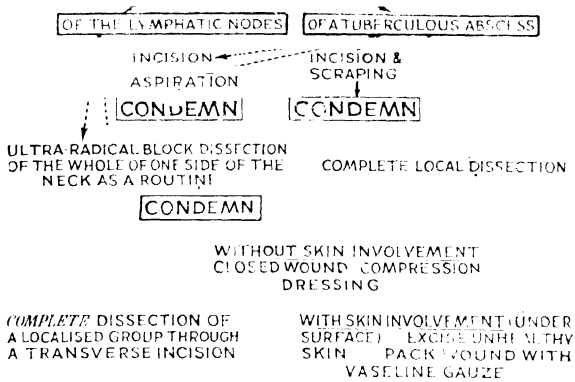


Fig. 69.—Scheme of general principles of operative treatment of tuberculous cervical adenitis.

REFERENCES.—[1]*Lancet*, 1948, **1**, 313; [2]*Dent. Summ.* 1912, **32**, 142.

TULARÆMIA.

Una Ledingham, M.D., F.R.C.P.

Reports chiefly from the United States record consistently successful results with *streptomycin*. Opinion is unanimous that this dangerous and sometimes fatal disease can now be controlled and a successful outcome anticipated. The optimum dosage remains in doubt, and some manifestations are less tractable, notably lymphatic glandular enlargement.

Johnson et al.[1] report 5 cases, some seriously ill with a hitherto bad prognosis. Both typhoidal and ulcerative types are included. In each case infection resulted from handling wild rabbits. With streptomycin fever and constitutional signs responded promptly, and the enlarged glands subsided in the one case where treatment was instigated early. If fluctuation was already obvious at the outset of treatment the mass of glands required surgical drainage and even local injections of streptomycin proved valueless.

Benson and Harwell[2] summarize their findings in 56 cases from twenty-two Veterans' Hospitals distributed in the U.S., with equally good results. Over three-quarters of these cases had the pneumonic type of disease, and they are grouped separately in view of the previously heavy mortality. All 15 cases recovered, clinical improvement being obvious in two days, fever controlled within six days, and the total duration of illness reduced to under four weeks. The larger ulcero-glandular group reacted similarly. Local lesions improved rapidly, as did fever and general toxæmia, but the enlarged glands were more resistant, some remaining unaffected and others proceeding to fluctuation and open breakdown. Foshay[3] carries the point further, and assuming streptomycin to be positively effective makes an attempt to settle the proper dosage. In view of the toxicity of this drug the smallest effective dose should be prescribed and even half a gram is suggested for as short a time as two or three days. All reports agree that immunity response is unchanged, the characteristic rising titre reaching a maximum in the second and third week as in the untreated case. In spite of the occasional large doses and known side reactions frequently seen with streptomycin only a few toxic reactions developed. They were skin reactions of varying type and of moderate degree.

REFERENCES.—[1]*Amer. J. med. Sci.* 1947, **214**, 645; [2]*Ibid.* 1948, **215**, 243; [3]*Amer. J. Med.* 1947, **2**, 467.

TYPHOID AND PARATYPHOID FEVERS.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

Epidemiology. The corrected number of notifications of typhoid fever in 1946 was 493 and of paratyphoid fever 736. Deaths from typhoid were 38, giving a case fatality-rate of 7·7 per cent, which compares favourably with the 10·6 per cent recorded in 1945. [There was a high proportion of children in 1946.—H. S. B.] Deaths from paratyphoid were 16, giving a case fatality-rate of 2·2, compared with one of 6·4 in 1945. In the summer of 1946 an outbreak of 104 cases of typhoid fever occurred in Aberystwyth. Almost all the sufferers had consumed ice-cream made and sold by a particular manufacturer. The organism recovered from the patients was of Vi-phage Type C and the manufacturer and vendor was found to be a urinary carrier of the same organism. He had suffered from enteric fever in 1938. The ice-cream consumed was made by a method which did not involve any heating of the mixed ingredients. Ice-cream has repeatedly in the past been established as the vehicle of infection in outbreaks of enteric fever. Regulations (S. R. and O, 1947, No. 612) were accordingly made on April 2, 1947, requiring that the ingredients used to make ice-cream should be subjected to pasteurization after mixing and then to rapid cooling.[1]

W. E. Thomas et al.[2] report 48 cases of paratyphoid B in one county which were traced to *pasteurized* milk. The infection was introduced in a creamery by means of the water used for washing the milk bottles. The main source of this water was a nearby river, and the water was chlorinated to an extent of 2·5 parts per million. Samples of this river water yielded *S. paratyphi B* of phage Type 1 on three out of four occasions. The same phage type of organism was found in all the cases. It is pointed out that milk-borne diseases do not always occur in explosive outbreaks, but that when contamination is intermittent, many such outbreaks produce a few cases spread over a considerable time. In this case, 55 cases were notified in twelve different local authority areas. Water used to rinse milk bottles should be potable. Investigation of the incidence of paratyphoid locally since 1939, when the creamery was opened, showed that in the summer of 1941 there was an epidemic of paratyphoid with exactly the same distribution as in 1946. (*See also* ENTERIC FEVER SPREAD BY PASTEURIZED MILK.)

Complications. F. F. Kane[3] records a case of acute *intestinal obstruction* in typhoid fever from band formation a rare and interesting surgical complication. M. Detlefsen,[4] in a monograph on the *surgical complications* of typhoid fever, does not mention intestinal obstruction.

Perforation occurs one to five times in every 100 cases, and may be not always in the lower 60 cm. of ileum, but in the appendix, cæcum, or any part of the colon, including the sigmoid flexure. There may be two perforations. Diagnosis depends on the sudden acute nature of the attack, the collapse with weak suddenly-risen pulse-rate, the fall of temperature, and the local tenderness and rigidity. Rectal examination reveals sensitiveness of the recto-vesical pouch. A middle incision makes the search more easy. In rare cases, the perforation is not of the bowel but of the gall-bladder. The symptoms may even arise from a suppurating mesenteric band, or, exceptionally, from organisms penetrating the peritoneal cavity without a perforation. After suturing a perforation it is advisable to drain the abdomen. The complication is very serious, the death-rate, even after the operation, being 92 to 93 per cent.

Other complications requiring surgical intervention include *cholecystitis*, *appendicitis*, and *abscess of the spleen*. In the *carrier* state the gall-bladder should not be removed until it is certain that it is infected, and probably not within two years of the attack. Foci in the appendix, bones, and kidney should

be carefully excluded. *Bone lesions* due to typhoid call for early recognition and treatment. Their discharges are just as infective as those from the bowel. In the surgical management of such wounds and sinuses unremitting care is necessary to prevent the spread of typhoid infection.

Two cases of *paratyphoid osteomyelitis* are reported by R. Rozansky, E. N. Ehrenfeld, and Y. Matoth.[5] It is uncommon. Only 21 cases have been reported. One case occurred in a one-year old infant, the youngest case on record. The other case was a recurrence, thirty-two years after the acute attack, of a spondylitis between the 3rd and 4th lumbar vertebræ for which the patient had been put in plaster at the time of the acute attack. The lumbar spine is involved in about 70 per cent of cases showing spine lesions. The affinity of typhoid and paratyphoid bacilli for the bone-marrow has long been recognized.

Treatment.—Clinical trials of *synergistic penicillin and sulphathiazole* in the treatment of typhoid fever as suggested by J. W. Bigger[6] and C. J. McSweeney[7] have been proceeding without apparent success. C. G. Parsons[8] summarizes the results obtained at various Army centres in the Middle East. While it is admitted that McSweeney's recommendation of two four-day courses separated by an interval of two days was not strictly followed, the conclusion drawn was that the treatment would have to produce much more dramatic results in the way of a rapid cure of the illness if the disturbance to the patient of repeated injections was to be counterbalanced. It is also admitted that the treatment was rarely instituted early in the first week, but it is pointed out that in McSweeney's cases treatment was also started late in the illness. G. Bevan et al.,[9] in a report to the Medical Research Council on the Aberystwyth cases treated at various centres, also state that the treatment was disappointing. They did not observe the speedy disappearance of toxæmia and subsidence of pyrexia described by McSweeney. A considerable proportion of patients yielded positive blood-cultures shortly after completion of the treatment. The typhoid strain responsible for the outbreak was not more resistant to the action of penicillin and sulphathiazole than were four other strains tested *in vitro*. The authors were so disappointed that they felt it necessary to warn against the indiscriminate use of this treatment.

Carriers.—R. M. Fry et al.[10] report to the Medical Research Council from the Public Health Laboratory Service that attempts were made to clear 17 chronic typhoid carriers of infection by the *penicillin-sulphathiazole method*. At first 8 cases were given a continuous course similar to that employed successfully by Comerford et al.[11] in 2 cases. All 8 cases resumed excreting typhoid bacilli soon after the end of the course of treatment. Next, much larger doses were given over a period of twenty-one days with rest intervals, and in 8 cases there was one apparent success. Then, in 2 cases the enormous amounts of 40,000,000 units of penicillin and 12 g. sulphathiazole a day were given on three occasions. Both attempts were unsuccessful. *In vitro* tests of sensitivity had shown that a concentration of 8 units penicillin per ml. inhibited growth for forty-eight hours of 11 out of 16 strains, and the remaining 5 were inhibited by 16 units per ml. The action of sulphathiazole depended on the size of the inoculum. Inhibition was obtained with a concentration of 5 mg. per 100 ml. with 100,000 organisms but not with 1,000,000. The authors concluded that although *in vitro* tests suggested that typhoid carriers might be cleared by some combination of penicillin and sulphathiazole, the result of therapeutic trials was not encouraging. There were only 3 apparent successes out of 17 cases in spite of the very large amounts of the drug that were used.

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TYPHUS FEVER.

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

A case of *murine* typhus in London is described by T. B. Dunn.[1] A Russian-born egg-tester at the London docks, who claimed that he had never suffered from typhus in Russia, had been for many years in London, and had recently been testing eggs from Poland, contracted the disease. He had no evidence of louse infestation but admitted to being frequently bitten by fleas. The acute clinical illness lasted twelve days and ended by crisis. A vivid profuse maculo-papular rash (later partly petechial) appeared on the seventh day on the arms and spread to the trunk and lower limbs, but not to the face, palms, or soles. The Weil-Felix reaction on the eleventh day was positive in a titre of 1/125 for *Proteus OX* 19 but not for *OX* 2 or *OX* K. Three days later the titre rose to 1/500. The diagnosis of murine typhus was confirmed by the use of rickettsial suspensions as antigens, the antibody titre being 1/2560 against murine rickettsiæ and 1/640 against epidemic louse-borne rickettsiæ.

Treatment.—*Chloromycetin*, an antibiotic obtained from a soil streptomyces, was found by J. E. Smadel et al.[2] to be active and non-toxic in the treatment of a few cases of louse-borne and murine typhus in Mexico. A further report by Smadel, in collaboration with Lewthwaite and Savoor of Malaya, at the International Congress of Tropical Medicine, Washington, 1948, announced highly successful results in 25 cases of scrub typhus. Among these, the duration of fever after the first dose averaged thirty-one hours. There were no deaths and no complications, whereas among 12 control cases, 2 had serious complications, 1 died, and the duration of fever was two-and-a-half times as long as in the treated cases. The appropriate dosage ultimately worked out for scrub typhus was 6 g. administered over twenty-four hours, *by mouth* in divided doses at frequent intervals. Another antibiotic of the same type, *aureomycin*, which can be given by mouth and is relatively non-toxic, is also active against rickettsiæ as well as against a variety of Gram-negative and Gram-positive bacteria.

REFERENCES.—[1]*Brit. med. J.* 1948, **1**, 979; [2]*Proc. Soc. exp. Biol., N.Y.* 1948, **68**, 12.

URÆMIA : THE ARTIFICIAL KIDNEY.

(*See also* RENAL DISEASES.)

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

"Waste products excreted by the kidneys have been removed from the body via artificial routes, such as peritoneal irrigations, with or without gastric lavage, and by *in vivo* dialysis." With these words, E. E. Muirhead and A. F. Reid[1] introduce us to the *artificial resin kidney*, the construction of which they describe. Experiments have demonstrated minimal reactions to haemolysis, and a simple method of maintaining *p*H and osmolar concentration steady.

At a discussion at the Royal Society of Medicine, E. G. L. Bywaters and A. M. Jockes[2] described the results obtained at the Post-Graduate Medical School with the Kolff artificial kidney. It consisted of a cellophane tube rotating in a Ringer bath through which blood flowed from an artery and back to a vein. The bath water (100° C.) contained glucose 1·5–2·0 g. per cent, and chloride, sodium bicarbonate, and potassium in physiological concentrations. The most suitable case was one of tubular or 'lower nephron' disease. Twelve cases had been dialysed, including 2 complete recoveries. E. M. Darmady[3] pointed out that the ultimate success of dialysis will depend on the composition of the dialysing fluid. The experience of R. W. Reid[4] confirmed that, by peritoneal dialysis, urea, and presumably other toxic products, can be removed from the blood-stream. His present belief is that intermittent injection and withdrawal is better and safer than continuous perfusion. Of various solutions used, Reid found that the most satisfactory was probably 5 per cent glucose in saline; he

believes that peritoneal dialysis has a part to play in the modern treatment of uræmia. It should only be used in cases of temporary renal suppression when there is a definite hope that the kidneys will recover sufficiently to maintain life; it must be used with the greatest care, for it is a dangerous procedure.

That the artificial kidney enables one to tide over a patient during the crucial time when the kidneys might be recovering from an acute catastrophe is indicated in the report of A. M. Jockes and G. M. Ball.[5] In their patient with accidental hæmorrhage and bilateral cortical necrosis of the kidneys, it was possible to maintain life for as long as 28 days in the absence of any significant renal function.

Much has been written on the use of peritoneal lavage in the treatment of anuria. The novel idea of inserting a Miller-Abbott tube and employing the small intestine as a dialysing membrane is reported by H. H. Marquis and F. P. Schnell.[6] They find that by massive perfusion flow the blood non-protein and urea nitrogen can be maintained at reasonably low levels in an anuric individual.

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URETER, SURGERY OF.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

Management of the Surgically Traumatized Ureter.—This important subject is dealt with at length by T. D. Moore.[1] Unilateral injury may be entirely unrecognized, particularly if simple ligation has occurred. The most common sequelæ of ureteric injury are uretero-vaginal or uretero-abdominal urinary fistulæ.

1. *Injury recognized Immediately.*—Simple ligation of one ureter is probably seldom noticed at the time of operation. If so discovered, immediate de-ligation followed by the insertion of a ureteral catheter would appear adequate. Acute angulation may be managed in the same way. Crushing by a clamp is more serious and requires essentially the same management as a severed ureter because of the probability of subsequent sloughing or cicatricial contracture. The governing principle should be conservation of the involved kidney. End-in-end anastomosis (Pozzi) has proved more satisfactory than end-to-end. If the ureter has been severed low in the pelvis probably a better procedure than anastomosis of its ends would be re-implantation into the bladder. Cutaneous ureterostomy is mentioned only for condemnation. Under certain circumstances e.g., with a patient in profound shock, ligation may be the operation of choice. Sacrifice of the involved kidney by ligation or nephrectomy is to be condemned except under most urgent circumstances.

2. *Injury recognized Late.* Unilateral ligation or ureteric occlusion from acute angulation secondary to sutures probably occurs more often than is generally believed. In many cases urinary leakage from vagina or abdominal incision is the first evidence of a ureteral injury. If both ureters have been occluded complete anuria may be erroneously diagnosed as 'suppression'. Failure to demonstrate urine in the bladder 6 to 12 hours following a difficult pelvic operation makes a cystoscopic examination mandatory. If cystoscopy confirms the suspicion of bilateral ureteral occlusion, an immediate unilateral nephrostomy may prove to be life-saving. With the patient in a desperate condition de-ligation as usually practised is undoubtedly hazardous, in that the abdomen is re-opened and the surgeon carries out an extensive search for offending ligatures, which may be extremely difficult to find. With ureteral catheters, the cystoscopist can literally prod the obstructed points, permitting the surgeon quickly to clip ligatures and also facilitating the detection of more than one ligated point if present. He should not be satisfied until both catheters have passed into the renal pelves.

From Hungary, J. Merényi[2] also makes a plea for closer co-operation between urologist and gynæcologist. As far as ureteral anastomosis is concerned he finds end-to-side union preferable to end-to-end, which is liable to be followed by marked stenosis.

Ureteral Blood-supply after Wertheim's Operation.—According to J. P. Michaels,[3] the consensus of opinion is that fistulæ following the Wertheim operation are brought about by disturbance of the blood-supply of the ureter. The ureter is chiefly supplied by arteries arising from the distal abdominal aorta and common or internal iliacs. These ureteral vessels may be single, double, or triple. On reaching the ureter they divide into ascending and descending branches which anastomose freely above and below. When dissecting the ureter from its bed every precaution should be taken to preserve the peri-ureteral arterial plexus.

Retro-caval Ureter. According to B. C. Corbus[4] the retro-caval ureter has been a relatively little discussed cause of hydronephrosis; 39 cases have been reported. It is failure of the normal vena cava to develop, with the persistent functioning of the posterior cardinal vein in its place, that creates the anomalous condition. The diagnosis of retrocaval ureter can be made only by X rays. In the retrograde pyelogram, catheterization of the ureter reveals a curve with the convexity toward the midline opposite the 3rd and 4th lumbar vertebræ. Dislocation of the ureter to or beyond the midline should call this possibility to mind. In the oblique pyelogram, the retro-caval ureter will impinge against the lower spine, whereas the normal ureter will fall away from it.

Ectopic Ureter. Two cases are described by A. M. Meads,[5] one opening into the vestibule and the other into the upper vagina. It is important to observe that intravenous urograms failed to show an ectopic ureter in either case, nor did indigocarmine appear in the ectopic ureteral fluid.

Periarteritis Nodosa. This chronic systemic disease affects the urinary tract in over 80 per cent of reported cases. In the patient described by R. S. Fisher and H. H. Howard[6] the ureters were unusually and extensively involved. The ureterograms showed changes not found in other pathological conditions.

Calcareous Abdominal Glands. Unless a definite kink or deviation of the ureter can be shown, the presence of such glands can be dismissed as of little urological significance (J. A. Ross[7]).

The Bilharzial Ureter.

Pathology.— Studies by N. Makar[8] shed light on the channels traversed by bilharzial worms from the portal system to the ureters. Apart from the mesenterico-ureteral anastomosis which he has demonstrated, the portal and systemic veins communicate in a plexus overlying the last two or three inches of the ureter; the middle rectal veins anastomose with veins from the above-mentioned ureteric segments and also with the vesico-prostatic plexus. The worms travel against the blood-stream to the ureters and thereafter mainly in the direction of the ureteric lumen.

Makar describes the lesions formed from bilharzial units as: (1) *Hyperplastic*: Nodules and papilloma-like bodies. Ureteric papillomata are smaller and not so friable as those of the bladder, but when the tube is much dilated they may attain fairly large dimension; calcification may be marked (*Plate XLVIII*). Bilharzial ureteritis cystica (*Plate XLIX*) is more frequently seen than is a similar lesion in the bladder. Epithelial hyperplasia of the ureter rarely passes on to carcinoma. (2) *Hypoplastic*: Sooner or later fibrosis kills incarcerated miracidia. With the cessation of irritation from their secretion, epithelial hyperplasia comes to a standstill; fibrosis proceeds further and calcification in ova ensues. The mucosa covering such ova, undergoing atrophy, gives a wash-leather appearance to which the term 'sandy patches' has been applied. Epithelial atrophy

PLATE XLVIII

BILHARZIASIS OF URETER

(N. Makari)



Fig. 1. Showing calcified bilharzial papilloma in the left ureter simulating ureteric calculus

Plates XLVIII, XLIX by kind permission of the "British Journal of Surge

PLATE XLIX

BILHARZIASIS OF URETER

(N. MAKARI)



Fig. B. Bilharzial ureteritis cystica

can lead to complete desquamation. It is common to find such denuded areas carpeted with granulation tissue on which encrustations can develop. While ulceration is not so common as in the bilharzial bladder, superficial small ulcers may be encountered, probably due to sloughing of papillomata. Secondary infection is a frequent complication, rarely giving rise to peri-ureteric suppuration; this has been known to cause fistulæ. However, the common result of bilharzial infiltration is a dense fibrosis leading to stenosis. The above lesions may occur in part or in the whole of the ureter. The disease is quite commonly bilateral. Hydronephrosis does not differ from the non-bilharzial condition.

Treatment. In a preliminary report, N. Makar[8] states his impressions: Specific antibilharzial treatment and that of any secondary infection should precede surgery. Strictures limited to the terminal inch of the ureter may be dilated by bougies through a cystoscope; the method has a limited scope. Dilatation of the stenosed portion above the bladder is carried out after ureterostomy proximal to the stricture. In very tough strictures a fine tenotomy knife may serve as a ureterotome. After dilatation, a fine rubber tube is passed proximally for a few inches, its other end being pushed into the bladder: at the end of about a week the catheter is removed cystoscopically. Excision of the stricture, followed by end-to-end anastomosis, is an excellent procedure, but is only applicable to more proximally situated lesions. Implantation of the ureter into the bladder after resection of its stenosed segment is indicated in some severe cases. Bilharzial papillomata lying at the ureteric orifices or peeping into the bladder can be fulgurated cystoscopically. At higher levels excision is carried out after ureterostomy. Should the papillomata be numerous or of large size the portion of the ureter harbouring them would have to be resected. Under certain circumstances nephrectomy seems justifiable. When the results of operative and non-operative methods are compared, the balance is definitely in favour of operative intervention, especially in severe lesions. Of the different surgical procedures, excision of the bilharzial affected parts followed by ureteric anastomosis has given the best results and the least post-operative trouble.

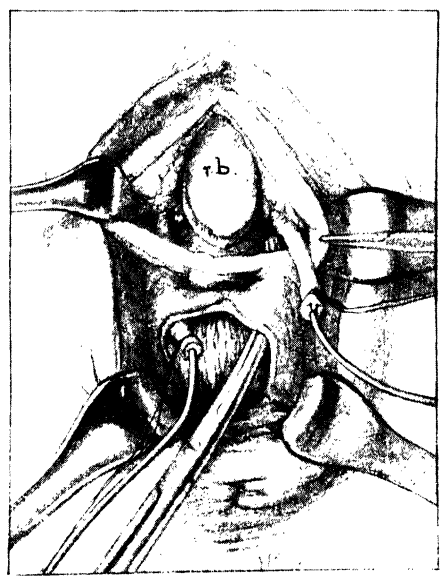


Fig. 70. Postero-lateral vaginal and ureters brought down to rectu *(Wolff, jun.)*

Transvaginal Ureterorectal Anastomosis.—As H. D. Wolff, jun.,[9] rightly asserts, infiltrating malignancy of the trigone and vesical orifice is a vexing problem. He has shown that transvaginal ureterorectal anastomosis is possible with normal vaginal structures (*Fig.* 70). The procedure seems worthy of consideration in certain cases of urinary incontinence, vesico-vaginal fistulæ, elusive ulcer,

and tumours of the bladder neck and urethra. Among the advantages of the perineal or transvaginal approach seem to be: (1) an easier single-stage procedure with minimal shock; (2) an extraperitoneal approach; and (3) the reserve possibilities for secondary anastomoses if the primary procedure is unsuccessful. It must be noted, however, that Wolff is careful to advise that the operation is not as simple as his illustrations suggest and that further experience will be necessary to establish its advantages.

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URETHRA, SURGERY OF.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

The Female Urethra.—

Urethrotrigonitis.—S. H. Bassow[1] emphasizes that urethrotrigonitis is constantly diagnosed inaccurately as cystitis. For viewing the bladder neck and female urethra, there is no instrument to compare with the McCarthy panendoscope. If this is fitted with a retrograde lens telescope, the surgeon has got the finest equipment possible. In those cases presenting granulomatous urethritis, treatment by Hegar's dilators, followed by progressive dilatation with a straight Kollmann's dilator and instillation of silver nitrate, ranging in strength from $\frac{1}{4}$ to 1 per cent, is often effective. When polypi, papillæ, and cysts are present they should be destroyed with the resectoscope, carried out under low spinal anæsthesia. Those with lesser involvement can be treated by fulguration under local anæsthesia.

E. Hock[2] also thinks the favourable effects of urethral dilatation in the condition depends on the analogy of the female urethra with the prostate gland. The female urethra contains mucus-secreting glands homologous with the male prostate, and these glands, by the dilatation, are emptied of pent-up secretion in the same way as in the case of prostatitis.

Stress Incontinence of Urine.—It is important to differentiate between extreme precipitancy of micturition, i.e., urge incontinence, and the stress variety. Precipitancy may be the result of urinary infection. Another troublesome cause is urethrotrigonitis unassociated with infection (T. Millin and C. D. Read[3]).

P. Schneider[4] considers that the basis of stress incontinence is a secondary insufficiency of the vesical sphincter *caused by the change in position of the bladder* rather than a direct injury to the sphincter itself. R. Tauber[5] maintains that the principal objective of surgical intervention is to lend fascial support to the floor and the dropped neck of the bladder. Special emphasis is laid on the formation of a *transverse supporting fascial band*, effected by the twin-stitch technique illustrated in *Fig.* 71. Excellent results followed 25 such operations.

According to P. A. Treahy and H. K. Pacey,[6] the most important finding is descent of the front wall of the vagina with the urethra and bladder base. The sphincter mechanism is not at fault and the bladder musculature adopts a purely passive roll during the stress. They describe a vaginal operation, using the pubo-coccygeal muscle for repair, which has given extremely satisfactory results.

Technique of cystography in stress incontinence: T. Millin and C. D. Read[3] advise that a No. 20 F. Malecot catheter be passed on a stylet into the bladder. The bladder is emptied, 6–10 oz. of 10 per cent sodium iodide solution is introduced, and the catheter spigotted. The patient stands against an X-ray screen with the tube centred on the upper border of the symphysis. She is requested to take a breath and to remain immobile for the first exposure. She is then asked to strain as in defæcation and a second exposure is made on the same

film, i.e., a double exposure. The second film reveals the bladder neck in its position when the intra-abdominal pressure is raised.

Urethral Stricture.—Pathologically, a urethral stricture is not formed by scar tissue in the wall of the urethra alone but by the contraction of fibrous tissue

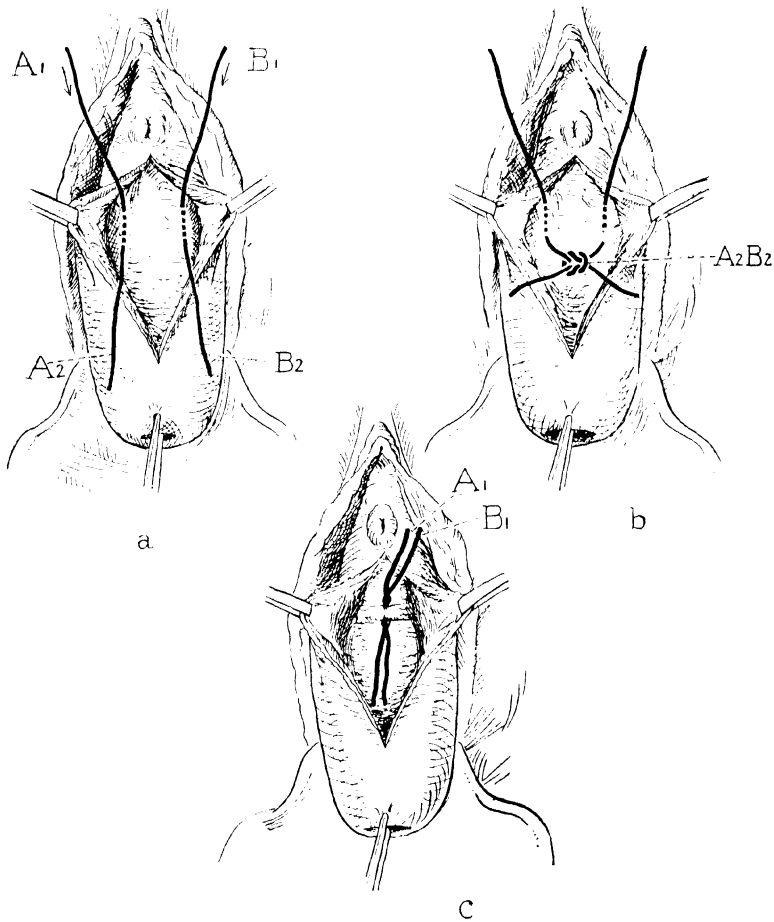


Fig. 71.—Formation of the transverse band. *a*, The twin stitches, A 1, A 2, and B 1, B 2, are applied to the right and left of the bladder neck in the sphincter region; *b*, A 2 and B 2 are tied first, and left long; *c*, A 1 and B 1 are united, resulting in the formation of the band. (*R. Tauber.*)

which replaces the corpus spongiosum for its entire thickness. The scar tissue is the result of inflammation or thrombophlebitis of the corpus spongiosum (D. E. Beard and W. E. Goodyear[7]).

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URINARY CALCULI.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

Composition.— H. W. McKay et al.[1] write on an analysis of 200 cases of urinary calculi. The chemicals observed in the stones, in order of frequency, are as follows: (1) Calcium carbonate; (2) Calcium phosphate; (3) Urates; (4) Mixtures of calcium carbonate, calcium phosphate, and urates; (5) Oxalate.

Aetiology. The experimental studies of A. Wahid[2] show that the most important aetiological factor lies in obstruction to the urinary flow.

Avitaminosis or diet played only a minor part in a series reported by H. K. Sangree.[3]

Dissolution of Urinary Calculi.— L. D. Keyser et al.[4] point out the long-overlooked fact that the organic framework of a stone is an object of attack as important as the crystalline matter. They present positive evidence that enzyme treatment (0·5 per cent urease) *in vitro* accelerates and intensifies the action of solution G on alkaline calculi.

Recurrent Postural Renal Calculi: Treatment. In a study of recurrent stones complicating recumbency after war wounds, J. C. Kimbrough and J. Furst[5] point out that removal of the calculi is only one aspect of the management: it may be misplaced effort unless there is appropriate post-operative care to prevent recurrence. Calculi in the kidney are foreign bodies, always cause damage, and should be removed. One cannot predict when infection will cause serious damage or when obstruction will convert the 'silent' stone into one of grave emergency. Time should not be lost in awaiting spontaneous passage. Dissolution with various irrigating solutions has proved unsatisfactory. Manipulation with catheters, loops, and other devices is often dangerous. Pyelotomy is the operation of choice, but is rarely possible as a secondary procedure. Nephrolithotomy may be employed in primary or secondary operations when the stone is readily accessible through the renal substance. A subcapsular approach reduces to a minimum the damage to the kidney and adjacent organs. Nephrostomy drainage and a ureteral splint are usually employed.

Ureteric Calculi: Treatment.—The size of the calculus is of considerable importance in indicating the line of treatment. As C. C. Higgins and J. G. Warden[6] point out, of equal importance is the size of the ureter below the stone. These authors find that vaginal ureterolithotomy has received but scant attention; if a calculus can be palpated on vaginal examination, it may be readily removed by that route. They have encountered no fistula formations or other complications. At the Cleveland Clinic the management of each case is individualized; there, ureteral catheter manipulations are found to be superior to mechanical stone extractors, and the trend is definitely toward conservative management by manipulation rather than by open surgery.

References.—[1]*J. Amer. med. Ass.* 1948, **137**, 225; [2]*Indian J. Surg.* 1947, **9**, 141; [3]*J. Urol.* 1948, **59**, 842; [4]*Ibid.* 826; [5]*J. Amer. med. Ass.* 1948, **137**, 219; [6]*Ann. Surg.* 1948, **127**, 257.

URINARY INFECTIONS, STREPTOMYCIN IN.

Hamilton Bailey, F.R.C.S., F.A.C.S.
Norman M. Matheson, F.R.C.S., F.A.C.S.

It would appear that streptomycin is the most valuable agent thus far developed in the treatment of certain bacillary infections of the urinary tract.

At the Medical Society of London, Sir Alexander Fleming[1] expressed the opinion that streptomycin had a powerful effect on *B. coli*. The results within 24 hours in some infections were marvellous; if the infection did not disappear within 24 to 48 hours, the chances were that the organisms had become resistant. There was either a quick result or no result at all. It was as well in *B. coli* cases to give as big a dose as practicable. E. W. Riches[2] spoke of

complicated cases in which he had concentrated on organisms which were not responsive to other drugs. Doses of 3 g. a day up to a total of 12 g. were given. *Ps. pyocyanea* had disappeared in 14 out of 20 cases; ***B. proteus*** in 4 out of 4; but *B. coli* was not always eliminated. He did not believe that results should be assessed solely on the bacteriological picture. It was not to be expected that a permanent sterilization of the urine would be obtained in the presence of gross organic disease. The great value of streptomycin urologically was in post-operative or more particularly in post-radiation infections.

A series of 61 patients with infection due to *B. coli*, *Ps. pyocyanea*, *proteus*, *Staph. pyogenes*, and *Str. faecalis* has been reported by C. Wilson.[3] In roughly half the cases the infection has been controlled by intramuscular administration of 3 g. of streptomycin daily for one to three days. Failure has almost always been due to the development of resistance. Streptomycin has a limited value where there is an underlying condition which is apt to lead to recrudescence.

The most striking finding in the bacteriological study of the patients of F. K. Garvey and T. E. Canning[4] was the development of resistance to streptomycin by organisms initially sensitive to the drug. From the results of their study, it is evident that the effectiveness of streptomycin is short-lived in the course of therapy, and once bacteria become resistant they remain so. It is also evident that therapeutic failure was due to bacterial fastness or resistance. In chronic cases with complications that necessitate surgical interference, the drug should be withheld until after such factors have been removed as far as possible. The authors recommend that 2·0 to 3·0 g. daily in divided doses every 4 hours, dissolved in sterile water, be given for 3 days and not longer than 5 days. Continued small prophylactic doses should never be used, as this tends to incomplete sterilization and the development of resistance. Alkalinization of the urine augments the therapeutic effect of the drug. Although few toxic effects were noted in this series, toxicity is a potential hazard and must receive serious consideration. Streptomycin is not innocuous and cannot be used indiscriminately as can penicillin.

C. G. Bandler and colleagues[5] report on the use of streptomycin in 15 cases of various urological conditions; their conclusions have been confirmed, with wider experience, that where ordinarily used chemotherapeutic and antibiotic agents have been inadequate, streptomycin apparently proved to be life-saving. When organisms are susceptible to streptomycin, the urine may be completely sterilized. The failure to correct underlying lesions, such as obstructive factors, is definitely responsible for the occurrence of infection following streptomycin therapy and may be a factor in the development of bacterial resistance. An important finding is that *in vitro* tests of susceptibility cannot always be relied upon to determine the effect in the patient. In some cases it has been observed that following administration there has been improvement, despite the fact that bacteria were still present in urine cultures—indicating that streptomycin has been, perhaps, effective in altering the pathogenicity of the organisms. There was an incidence of over 25 per cent of toxic reactions in the series reported. In view of the potential toxicity of the drug, its prophylactic use should not be indiscriminate.

A. D. Wright[6] operated ten times in ten years on a patient with recurrent renal calculi. Never during this time was the urine free from gross pyuria and a mixed urinary infection for which every method of treatment was employed. With streptomycin the urine became sterile for the first time. Streptomycin was used for seven days in all—1,000,000 units daily in three-hourly doses—and the diseased calices were also irrigated with streptomycin solution—1000 units per ml. for seven days after operation. Six months later the urine was clear of infection and the kidney of stone and the patient free from symptoms.

C. Mrazek[7] finds that in urinary infections there are two serious limitations to the successful use of the drug: (1) The establishment of a free-flowing urinary drainage is prerequisite if a satisfactory result is to be obtained; (2) The organisms which are sensitive to streptomycin at the beginning of treatment may rapidly become insensitive to it.

The same author says that the toxicity of streptomycin is somewhat greater than that of penicillin, but is quite low when compared with other therapeutic agents. Toxic reactions include: (1) Irritation and pain at site of injection; (2) Histamine-like responses: flushing, headache, arthralgia, urticaria, and fever. (3) Sensitization phenomena: fever and rashes. (4) Occasionally during prolonged streptomycin treatment tinnitus, vertigo, and, more rarely, deafness develop; unless the circumstances are desperate, streptomycin should be discontinued immediately. (5) Renal irritation: number of casts, albumin, and red cells are increased.

After treating 15 patients suffering from *urinary tuberculosis* with intramuscular streptomycin, E. N. Cook and L. F. Greene[8] come to the conclusion that a daily dose of 1 to 2 gr. is the most useful. While the efficacy of the drug in destroying tubercle bacilli in the urinary tract is still not established, they believe that streptomycin has a beneficial effect and that in 3 of their patients the disease has been arrested. The authors are careful to add that streptomycin is not a substitute for surgery, but may be a helpful adjunct.

E. W. Riches[9] found that in urinary tuberculosis there had been no proved cases of permanent disappearance of tubercle bacilli from the urine, but a certain amount of clinical improvement had been observed, as shown by the increased capacity of the bladder.

J. T. MacLean et al.[10] are of the opinion that tuberculous epididymitis responds very slowly, if at all, to streptomycin therapy.

REFERENCES.—[1]*Brit. med. J.* 1948, **2**, 831; [2]*Ibid.* 832; [3]*Ibid.* 552; [4]*J. Urol.* 1948, **60**, 176; [5]*Ibid.* **59**, 96; [6]*Brit. med. J.* 1948, **1**, 499; [7]*J. Urol.* 1948, **60**, 524; [8]*Ibid.* 187; [9]*Brit. med. J.* 1948, **2**, 832; [10]*Canad. med. Ass. J.* 1948, **58**, 537.

VACCINATION. (*See* SMALL-POX AND VACCINATION.)

VARICOSE ULCERS. *Lambert Rogers, M.Sc., F.R.C.S.*

These ulcers are usually found just above the internal malleolus over the lower part of the area of skin drained by the great saphenous vein. Chronic venous stasis, lymphœdema, and local phlebitis are factors in their production. Their chronicity and intractability are well known. W. M. Cooper,[1] of the New York Polyclinic, advocates their treatment

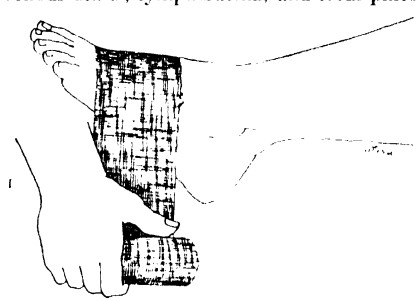


Fig. 72.—The Dome Boot (bandage) is started with one horizontal turn applied around the foot and, when completed, the bandage is directed obliquely over the heel, etc.

by high ligation and division of the great saphenous vein if varicose and incompetent, a coal-tar paste preparation to the ulcerated area, and the use of a modified Unna's-paste boot (*Figs.* 72–75). The boot is retained for one week, when a new one is applied.

[The treatment recalls that of the application of elastic adhesive bandages which has largely replaced the use of Unna's paste in this country.

Compression by the adhesive reduces œdema, and so enhances the local circulation and promotes healing.—L. C. R.]

Writing on the same question, N. Garber,[2] of Johannesburg, warns against the use of antiseptics and antibiotics in case an intractable dermatitis is pro-

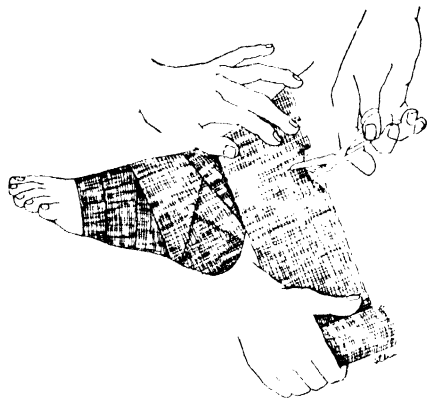


Fig. 73.—After the heel has been adequately covered, the same method of application, i.e., one horizontal turn of the bandage followed by an oblique half turn and cut, is carried out. This ensures a flat application of the bandage to the skin surface.



Fig. 74.—The bandage after it has been cut as described under *Fig.* 73.

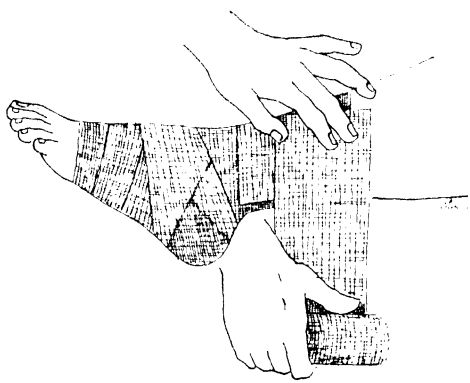


Fig. 75.—The bandage is continued as described in text with a horizontal turn encircling the limb and a one-half oblique turn, after which bandage is again cut and the same technique is carried out until the calf is covered. (*Figs.* 72–75 *reproduced from the "American Journal of Surgery".*)

duced. He points out the need to deal with the vein above and not the local lesion, and is averse to sclerosing therapy. He advocates the multiple resection operation for obliteration of the varices.

REFERENCES.—[1] *Amer. J. Surg.* 1948, **75**, 475; [2] *S. Afr. med. J.* 1948, **22**, 173.

VARICOSE VEINS.

Lambert Rogers, M.Sc., F.R.C.S.

A note of warning in a frequently practised procedure is sounded by reports from some frank writers in Australia, J. S. T. T. Hill,[1] R. P. Booth,[2] and J. H. Young,[3] who record cases of gangrene of the leg following high ligation of the great saphenous vein and injection of its distal segment. In one case 20 per cent saline was used for the injection, in two other cases 'Ethamolin'. The operation was performed under general anæsthesia in one case, under local in the other two. The first case resulted in amputation through the thigh, the other two patients retained their legs but lost the use of the musculature of the anterior compartment the muscles of which became necrosed and fibrous. The patients were a man aged 47, a woman aged 30, and a woman aged 25 respectively. The reasons suggested for the calamitous sequel are that either reflex arterial spasm was produced or that there was a pre-existing and undetected arteriovenous connexion of some magnitude, probably in the popliteal fossa. It is suggested that should the onset of such spasm be detected, treatment should be by immediate spinal anæsthesia; in one of the three patients, 2 per cent novocain solution was injected around the femoral artery and some relief of pain followed, but the leg had to be amputated later.

[We should be grateful to these Australian surgeons for publishing accounts of these cases and thereby drawing attention to the danger of high saphenous ligation and injection through a catheter of the distal part of the saphenous vein. Whatever the explanation, whether it be induced arterial spasm or a communication between vein and artery as has been suggested, the danger would appear to be in the injection. It is difficult to think that the classical Trendelenburg operation of excision of an inch of the terminal part of the vein alone could induce these disasters.—L. C. R.]

REFERENCES.—[1]*Med. J. Aust.* 1948, **2**, 238; [2]*Ibid.* 476; [3]*Ibid.* 477.

VARICOSE VEINS, VARICOSE ULCERS, AND VENOUS THROMBOSIS.

Harold Dodd, Ch.M., F.R.C.S.

DIAGNOSIS

A New Diagnostic Test.—J. G. Slevin[1] describes a multiple 4-tourniquet test which is sensitive, simple, and quick. He claims that: (1) It locates accurately incompetent communicating veins in the thigh and leg and determines simultaneously the state of the valve at the sapheno-femoral junction. (2) When the effectiveness of the Brodie-Trendelenburg and the new multiple tourniquet tests was compared on two series of veins, the older test showed that 21 per cent needed high and low ligation as against 57·5 per cent indicated by the new test. Simultaneous incompetence of the external and internal saphenous veins was present in 9 per cent. (3) The recurrence rate after the new test was 3 to 4 per cent, against 10 to 25 per cent with the older test.

Technique. The patient lies on the couch, the leg is raised, and the veins are emptied. Four tourniquets tight enough to constrict the superficial veins are applied to the upper, middle, and lower thigh, and immediately below the knee. The patient stands, and within thirty-five seconds the constrictions are removed serially, beginning with the lowest, while the veins are observed, noting first the efficiency of the external saphenous vein. A rapidly filling section before the highest band is released indicates a double-positive Brodie-Trendelenburg test—i.e., incompetence at the sapheno-femoral junction and of a communicating vein immediately below the band where the filling appeared. The site is noted, the test repeated, and the exact location is pencilled with silver nitrate; this mark remains for several weeks and even after the part is prepared for operation.

Slevin remarks that the importance of an incompetent external saphenous vein has been under-estimated; he finds it in 9 per cent of patients; also that

incompetent communicating veins are the chief cause of the recurrence of varicosities.

Injection Treatment

Injections are reserved for the lesser manifestations of the condition, and after the operation for them.

Solutions.

Phenol-Glycerin-Glucose-Gelatin Solution This consists of phenol crystals 2 per cent, glycerin 30 per cent, glucose 30 per cent, autoclaved gelatin, ¼ per cent in aqueous solution (called P.G.G.G.), and in the reviewer's experience has proved very successful. It is well tolerated constitutionally, and causes a non-painful but tender non-incapacitating thrombosis of moderate extent. When injected paravenously an immediate sharp pain occurs, but this passes off as the anæsthetizing effect of the phenol develops. No necrosis or ulcer follows. Transient giddiness may be experienced, but fainting, etc., has not occurred in over 3000 cases. Patients are injected lying down or sitting. The dose is 2 to 3 ml.; two or three injections per visit are made.

Sodium Tetradecyl Sulphate (Sotradecol).—Good reports of the sclerosing effects of sodium tetradecyl sulphate are given by Dingwall et al.[2] and E. J. Orbach.[3] It is innocuous paravenously and constitutionally. Orbach says it gives 88 per cent against 84 per cent obliterations; only 1 per cent against 9 per cent local reactions; and no sloughs, against up to 5 per cent with the usual sclerosants. L. Reiner[4] and S. R. Hirschmann[5] also report on it favourably.

A Radio-opaque Sclerosant. Boyd[6] recommends the following:

Sodium ortho-hippurate
Mono-ethanolamine oleate
Benzyl alcohol
Dose 1 to 3 ml.

Injection of Varicose Veins by Preliminary Air-bubble. E. J. Orbach[3] injects varicose veins while the patient is standing and gives a preliminary injection of 1 ml. of air. He claims that this minimizes the paravenous injection of sclerosing fluid by causing a tell-tale subcutaneous emphysema. By delaying the dilution of the scarifying medium with blood, it gives greater obliteration with less local reaction and necrosis of tissue. It results in fewer failures.

Allergy to Injections.—Allergic reactions to injections of quinine, urethane, sodium morrhuate, and sylvasol are reported by C. E. Taylor[7] and Melton et al.[8]

Operative Treatment

Boyd's[9] remark is illuminating: "I believe that varicose veins are primarily due to a congenital deficiency or weakness of the valves. The condition is progressive. No single operation is likely to cure them."

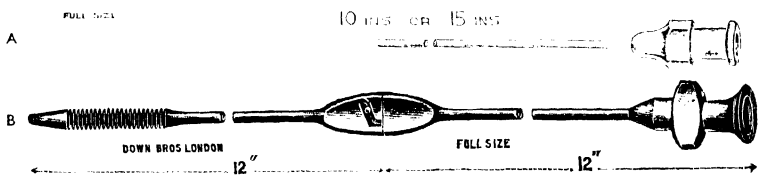


Fig. 76. Rough-headed needles for scarifying the interior of the internal or external saphenous vein. A, Small head for use from ankle; B, Extending pattern passed down from the groin.

Dodd[10, 11, 12] recommends the following procedure for the successful treatment of varicose veins: (1) Division of the internal or external saphenous varicose vein with the adjacent branches from the femoral and popliteal veins respectively.

(2) Destruction by internal abrasion and injection of the trunks of the internal or external saphenous vein from the malleolus to their terminations. This prevents their refilling by present or future incompetent intramuscular communicating veins. (3) Later the injection of the remaining subcuticular varicosities with small quantities of sclerosing fluid.

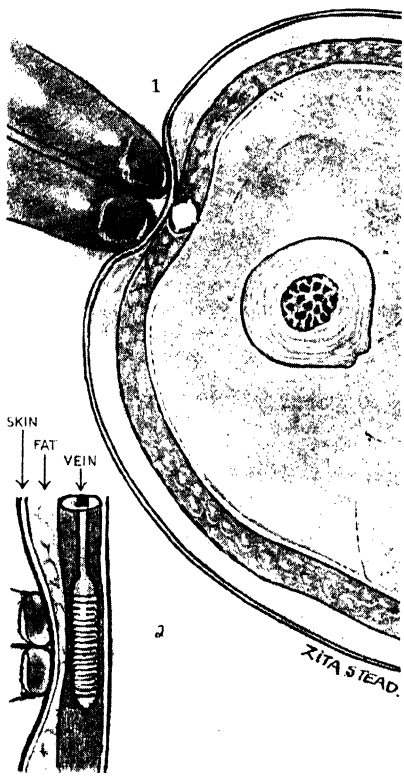


Fig. 77. Diagram illustrating the use of the rough-headed needle to scarify the interior of the internal or external saphenous vein. The surgeon's fingers externally press on the vein where the needle is and the latter is moved up and down 1 to 2 inches at a time.

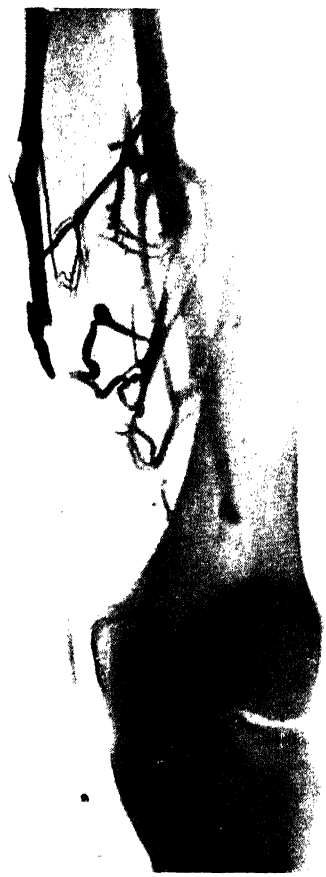
This procedure is also advised by R. R. Foote,[13] Dickson Wright,[14] and A. de Wulf.[15] The internal saphenous vein is ligated at the groin (through a large incision to give a full exposure) and the ankle. Dickson Wright introduces up to 100 ml. of 30 per cent saline, divided between these two divisions. [The reviewer has discontinued the use of 30 per cent saline because it occasionally causes sloughing; instead he employs P.G.G.G. solution *see* Injection Treatment.]

The interior of the vein is abraded by a long rough-headed needle (Dodd,[12] Foote[16]) (*Figs.* 76, 77) in lengths of 1 to 2 in., after which 1 to 2 ml. of P.G.G.G. is injected section by section, 7 to 10 ml. in all being inserted from the groin to the knee. Occasionally it is possible with an extending needle to abrade to the lower third of the leg, but generally the needle passes only to the knee. Opinions vary as to the value of these retrograde injections at the groin. Boyd and Robertson[17] contend that they are useless and dangerous because the sclerosant passes into the femoral and popliteal veins; though they are safe and effective when given downwards at the knee.

The internal saphenous vein is exposed at the ankle and a smaller long rough-tipped needle is introduced, usually to the knee. Up to 7 ml. is inserted in all, alternating with scraping for 1 to 2 in. at a time. Sometimes the needle is held up by a communicating vein in the lower third of the thigh or leg. If this occurs, the communicating vein, if appreciable clinically, is exposed, divided, and the opening in the deep fascia is closed. Its whereabouts may be disclosed by a blow-out, or the opening in the deep fascia may be felt like a buttonhole. There may be œdema surrounding. Occasionally a communicating vein goes from the internal to the external saphenous above or below the knee.

VARICOSE VEINS

(A. M. Boyd)



Venogram showing filling of femoral and upper third of popliteal vein following injection of Pyelectan into distal end of divided saphenous vein at the groin.

By courtesy of Professor A. M. Boyd and the British Medical Journal

The inefficient communicating vein at the lower third of the leg is nearly always present in varicose ulcers. It may require ligation and division before permanent healing is obtained.

These perforating vessels convey sclerosants to the deep veins, especially those in the lower third of the thigh (Boyd and Robertson,[17] and Kinmonth[18]). They may cause deep thrombophlebitis and possibly embolism, thus keeping patients in bed when activity is essential.

The External Saphenous Vein.—Slevin says that this vein is varicose and inefficient in 9 per cent of cases. When it is difficult to find in the popliteal space, Dickson Wright suggests that the vessel should be exposed in the middle of the calf and a long probe or olive-headed needle slipped up the vein until it impinges at the union with the popliteal vein. This point is exposed and the vein and its branches are ligated and divided. The portion traversed by the needle is mechanically abraded and 3 ml. of sclerosant is introduced. The injection is small because the external saphena communicates freely with varicose veins in the soleus and gastrocnemius muscles (Turner Warwick).[19] Thrombosis of these is denoted by swelling and pain in the calf muscles and partial incapacitation.

P.G.G.G. Solution.—P.G.G.G. solution[20] is effective and safe locally and constitutionally. Volumes of 20 ml. per leg have been used, injecting small quantities at a time and alternating with the internal scraping of the vein. In advanced bilateral varices, including those of the external saphenous vein, 45 ml. has been given. The procedure does not thrombose all the subcuticular varicosities; this is not the aim of the operation. Patients are seen at increasing intervals of 1, 2, 3, 4, 5, and 6 months for three years, and persistent varices are injected with 2 to 3 ml. of P.G.G.G. solution. Slevin advises supervision for one year.

Summers[21] advises excision of the internal and or the external saphenous vein from their terminations to the malleoli, with division of the communicating veins, performed through multiple incisions and using a Mayo stripper when possible. He uses no sclerosants.

Complications of Operations for Varicose Veins

Recurrence and deep thrombophlebitis may follow varicose vein operations.

Stalker[22] deals with recurrent varicose veins in the same way as with a primary affection. Of his patients 1 in 5 have previously been operated on for varicose veins. He finds that high ligation, division, and injection, including if necessary the small saphenous vein, cure a large number.

In addition, segmental ligations, or excision, or a complete or partial stripping, may be required. Inadequate exposure of the internal saphenous is a cause of recurrence, which may also arise because of the progressive nature of varicosities—i.e., further veins degenerate into varicosities. He considers that the significance of small saphenous incompetence in persistent varicose veins is not sufficiently realized.

According to Boyd and Robertson[23] recurrence may be due to inadequate operation, limited incision, branches being overlooked, and also to subsequent defects developing in the communicating veins which may refill the internal saphenous vein at the lower third of the thigh, 1 in. below the knee, or from a connexion with the short saphenous vein: these should be ligated. [It is because of these faulty vessels that the reviewer aims to destroy the trunk of the internal saphenous.—H. D.]

Deep thrombophlebitis may follow retrograde injection of the saphena magna at operation or occasional injection later. When Pyelectan was injected into the varicose great saphenous vein distally at the groin in 12 consecutive patients, it passed into the lower femoral vein (*Plate L*). When the fluid was injected downwards at the knee, it remained mainly in the superficial varices. This is

a safe insertion. The contrast medium sometimes remains in the deep veins, denoting a sluggish circulation, and often leading to endothelial damage, chemical venospasm, and perhaps to deep thrombophlebitis.

The authors conclude that retrograde injection of the internal saphenous vein at the groin is inadvisable, but that it is safe at the knee in 3-ml. doses.

Thrombophlebitis in Varicose Veins. Thrombophlebitis may follow a blow or occur spontaneously. The infection may be derived from infected nasal sinuses, tonsils, teeth, or gall-bladder. The traditional treatment of rest in bed is now being abandoned. Patients are kept up and about and given sedatives for the pain. A pad of felt is applied to the uppermost part of the thrombosed area and a firm adhesive supporting bandage (Lestreflex, Elastoplast, Dalzoband) is put on from the groin to the toes. No cases of pulmonary embolism have occurred in the reviewer's experience, nor has he seen one reported. Mayer,[24] who also advises this treatment, first seeks and removes the focus of infection. He changes the bandage every third day.

Operation for Thrombophlebitis in Varicose Veins. When the internal saphenous vein is affected, especially in cases of massive thrombosis, it is ligated and injected promptly but without the introduction of the long needle. The clot has been found to stop $\frac{1}{2}$ to $\frac{3}{4}$ in. distal to the union of the internal saphenous vein with the femoral vein. After ligation, 3 ml. of sclerosant (preferably P.G.G.G. solution) is slowly injected into the solid vessel. The fluid runs in easily between the clot and the vein wall, and causes a chemical phlebitis; it fixes the thrombus to the vein wall, and resolution follows. [Six of the reviewer's patients so treated have recovered uninterruptedly.—H. D.]

Deep Venous Thrombosis : Thrombophlebitis and Phlebothrombosis.—Venous thrombosis is receiving increasing recognition, and many articles have been written about its various aspects. Elkin,[25] Ochsner,[26] and Boyd[27] have discussed the subject of deep venous thrombosis in the legs, which is commoner than is generally realized. It may follow confinement to bed of adults after injuries (e.g., fractured femur), operations below the diaphragm, parturition, medical illness, especially where the heart and vessels are affected (Greenstein);[28] after the treatment of varicose veins, either by operation with retrograde injection, or by injection alone; lastly, it occasionally appears spontaneously in health (Boyd,[27] McCutcheon and Cantey[29]), especially in the elderly. Elkin estimates the incidence in hospital to be 0·5 per cent to 1·5 per cent; dehydration and tobacco increase the clotting tendency. Hunter et al.[30] consider that "the greatest single factor favouring thrombus formation in the lower extremity is sudden confinement to bed of a previously ambulatory older person".

Thrombophlebitis and phlebothrombosis are different entities.

Phlebothrombosis implies the formation of a non-adherent and non-inflammatory clot which can therefore become an embolus. It is due to stasis (compression of the veins), blood changes, and tissue damage; the heart and vessels are diseased in 63·6 per cent of cases (Greenstein). It develops in the posterior tibial venæ comites, never in the anterior tibial vessels. It is usually bilateral and spreads into the thigh, but may stop at the adductor magnus opening, at the groin, or where the external iliac vein is crossed by the internal iliac artery (Boyd).[27]

Phlebothrombosis is "an emergency which should take precedence over any other type of operation with the exception of massive hæmorrhage" (Ochsner and DeBakey[33]). Treatment is by bilateral ligation of the saphena magna and femoral vein below the entrance of the profunda femoris vein.

Hamilton Bailey[34] emphasizes the importance of deep femoral thrombosis. He describes the technique of femoral vein ligation and thrombectomy. Ligation of the vena cava is recommended for bilateral cases. Fontaine[35] expresses the

same opinion, and states that the distal end of the thrombus is white, like a snake's head, and after its extraction the vein bleeds.

Zilliacus[36] reports the serious after-effects of deep thrombosis of the legs in 680 patients; only 6 per cent had normal legs when followed up 6 to 14 years afterwards; œdema, heaviness, ulceration, and varying degrees of incapacitation were present in the rest.

Thrombophlebitis, according to Ochsner, begins with inflammation of the wall of the deep or the superficial veins, to which a white thrombus adheres, so that embolus from it is rare unless sepsis digests the clot attachment. Further, he has shown, both clinically and experimentally, that an inflammatory process involving a large vein produces marked spasm of the homolateral arterioles, causing a severe ischæmia and œdema of the extremity. This is present in thrombophlebitis, and when it affects the deep veins of the legs and extends to the groin or common iliac vein, phlegmasia alba dolens is declared.

Both thrombophlebitis and phlebothrombosis may be guarded against by early exercise and walking (not sitting or standing about) and breathing exercises. Compression bandages before and after operation are useful, and heparin prophylactically is effective (E. V. Allen).[31]

A. W. Allen[32] ligated the superficial femoral vein prophylactically before operation in 458 patients over 65 years of age; 5 developed thrombophlebitis and 1 a fatal embolus, against 55 and 26 respectively in a similar untreated group. [An impressive finding.—H. D.]

In such injuries and in those diseases which are so frequently followed by embolism, as amputation and hip fractures in the elderly, Elkin believes that prophylactic superficial femoral vein ligation is the method of choice. Heparin and dicoumarol are invaluable after phlebothrombosis is detected.

Thrombophlebitis and white-leg are relieved by a paravertebral lumbar sympathetic block, injecting 30 ml. of 2 per cent procaine daily until relief is obtained. Boyd says: "The treatment should be regarded as an emergency and not put off until the next day." If there is septic phlebitis with chills the inferior vena cava is ligated (Elkin).

Varicose Ulceration of the Legs

Compression Bandage Treatment of Varicose Ulceration.—This follows the lines laid down by Dickson Wright[37] in 1930, using a firm supportive bandage, with a rubber-zinc adhesive spread; Elastoplast is a well-known preparation of this kind; the writer finds that the frequent allergic reactions to the rubber-zinc adhesive can be avoided by: (1) Painting the foot and leg with tinct. benzoin. co. or 50 per cent aqueous ichthyol. (2) Applying the bandage correctly, first encasing the ankle behind, in front, and at the sides with longitudinal strips. (3) Using Lestreflex (St. Dalmas, Leicester), which is a new bandage spread with the old-fashioned emplastrum saponis. No instance of sensitiveness has been met. When eczema is present, an under-bandage of Ichthiopaste or of Dalzoband is put on loosely and support is supplied by a Lestreflex or an Elastoplast bandage over it.

Foote[38] also describes bandaging in varicose conditions.

Division of Peripheral Nerves Supplying Painful Ulcers of Leg and Ankle.—This is recommended by C. E. Corlette[39] and P. E. Roland.[40] The nerve-supply to the ulcer is cut either immediately above it by undermining the skin superficially and deeply with a tenotome under local analgesia (Corlette), or by division of the internal saphenous nerve at the knee or of the sural and cutaneous branch of the superficial peroneal nerve below and outside of the knee (Roland).

Treatment of Resistant Varicose Ulcers by Lumbar Sympathectomy.—J. Borrie and E. V. Barling[41] report 4 cases of chronic varicose ulcers, unhealed

after operation on the varicose veins and the usual remedies, which healed after lumbar sympathectomy. A preliminary paravertebral injection established that vasodilatation of the tibial arteries was feasible. They laid stress on the cold blue pulseless limb with atrophic osteo-arthritis, indicating a deficient blood-supply. After operation an elastic stocking is necessary for the leg to protect it from "trauma from without and œdema from within".

Ischæmic Ulcer of the Leg.—Some ulcers which occur after a white-leg or deep thrombophlebitis are not strictly varicose in origin. The condition is the result of a long-standing impairment of the blood-supply from arterial spasm. This produces a painful, cold, cyanosed, pulseless foot; there is trophic osteo-arthritis of the joints of the foot and leg with resultant stiffness. The muscles and tendons are weak, matted, and wasted. There may be some varicose veins, but these are secondary to the damaged valves of the deep veins and are not as a rule a prominent feature. The ulcer is an end-result in a chronically impoverished limb. Gangrene of the toes might occur later.

Treatment is primarily directed to increasing the blood-supply by interruption of the lumbar sympathetic chain, first by a paravertebral injection of procaine; if this causes the foot to become warm, a similar injection of carbolic acid 10 per cent (10 ml.) is made or lumbar sympathectomy is performed. The leg is bandaged as for a varicose ulcer. The enlarged veins, when present, are treated if necessary, but this is secondary to the fundamental factor of anæmia of the part.

Hypertensive-Ischæmic Ulcer of the Leg.—F. Martorell,[42] E. A. Hines and E. M. Farber,[43] J. W. Valls-Serra,[44] and L. Oller-Crosiet[45] describe an unusual form of ischæmic ulcer of the leg in women over 40 years with chronic hypertension. The ulcer is situated about the external malleolus and the lower third of the outer leg in a pigmented area. It is due to localized arteriolitis with thickening and occlusion of the affected vessels. The dorsalis pedis pulsation is easily palpable. Because of the impaired blood-supply, reaction and healing are extremely slow, no matter what remedy is used. Varicose veins are not present.

Paravertebral Injection

Mention of the paravertebral lumbar sympathetic injection by 2 per cent procaine is made because this is being increasingly used. It is employed for relieving the œdema caused by the spasm of the arterioles and venules of the legs after injuries to them, during and after phlegmasia alba dolens. It is of diagnostic value in cases of ischæmic ulcer of the leg and incipient gangrene. If after such an injection the limb becomes warmer, the pulse of the dorsalis pedis artery perceptible, or the range of the oscillometer reading increased, then lumbar sympathectomy is likely to be successful for these ailments.

Technique.—A No. 20 needle with a stylet 12 cm. long, two syringes, one of 2 ml. and another of 20 ml., sterilized by boiling, and a 30-ml. ampoule of procaine 1 to 2 per cent (boiling decomposes procaine) are required. The patient lies laterally on the operating table with the side to be injected uppermost. The head is flexed to the knee and a soft pillow is placed in the hollow of the waist; the transverse processes of the lumbar vertebræ are thereby separated.

The aim is to place the injection at the antero-lateral surface of the bodies of the 1st, 2nd, and 3rd lumbar vertebræ, where the lumbar sympathetic chain lies. The needle is inserted 3 finger-breadths laterally from the midline at the level of the 2nd lumbar spinous process at an angle of about 60° to 70° to the surface of the skin, inclined towards the midline (*Fig.* 78). At a depth of 4 to 5 cm. the needle will impinge on the transverse process of the 2nd lumbar vertebra; it is withdrawn slightly and deflected either above or below this in the original direction and is pressed in another 4 cm. When the needle is felt

to strike the lumbar vertebra it is withdrawn and reinserted so that it glances tangentially over the side of the vertebral body. The 2-ml. syringe is applied and suction induced to ensure that the needle is not in the superior vena cava, aorta, or other sizable vessel. If blood appears, the needle is withdrawn slowly while aspiration is continued until blood ceases to appear. A pause of 2 to 3 minutes allows the puncture to seal. The procaine is then gently injected.

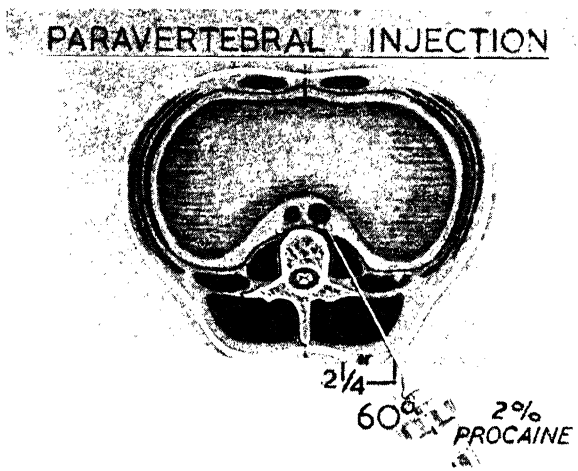


Fig. 78.—Paravertebral

The analgesic diffuses up and down the antero-lateral surface of the lumbar vertebræ, infiltrates, and paralyses the sympathetic chain. The patient is kept still with the head low for 10 to 15 minutes to avoid faintness.

If the injection is correctly placed, and the arteries to the leg can dilate, the foot will be appreciably warmer in 30 minutes, and will remain so for several hours. When given for a white-leg the instillation may be repeated daily or on alternate days on four to five occasions, when recovery is usual.

REFERENCES. [1]*Amer. J. Surg.* 1948, **75**, 469 ; [2]*Surgery*, 1948, **23**, 599 ; [3]*J. internat. Coll. Surg.* 1948, **11**, 396 ; [4]*Proc. Soc. exp. Biol., N.Y.* 1946, **62**, 49 ; [5]*N.Y. St. J. Med.* 1947, **47**, 1367 ; [6]*Proc. R. Soc. Med.* 1948, **41**, 633 ; [7]*Brit. med. J.* 1948, **2**, 573 ; [8]*New Engl. J. Med.* 1947, **25**, 940 ; [9]*Proc. R. Soc. Med.* 1948, **41**, 633 ; [10]*Brit. med. J.* 1944, **2**, 814 ; [11]*Ibid.* 1947, **2**, 708 ; [12]*Ibid.* 1948, **2**, 355 ; [13]*Practitioner*, 1948, **160**, 386 ; [14]*Proc. R. Soc. Med.* 1948, **41**, 631 ; [15]*Belg. Tijdschr. Geneesk.* 1947, **3**, 109 ; [16]*Lancet*, 1948, **1**, 579 ; [17]*Brit. med. J.* 1947, **2**, 452 ; [18]*Proc. R. Soc. Med.* 1948, **41**, 632 ; [19]*Rational Treatment of Varicose Veins and Varicocele*, 1931, 86, London ; [20]*Brit. med. J.* 1948, **2**, 838 ; [21]*Amer. J. Surg.* 1948, **76**, 72 ; [22]*Ibid.* **75**, 688 ; [23]*Brit. med. J.* 1947, **2**, 452 ; [24]*Surgery*, 1947, **21**, 843 ; [25]*Sth. Surg.* 1948, **14**, 61 ; [26]*Ibid.* **14**, 477 ; [27]*Manchr. Univ. med. Sch. Gaz.* 1947, Oct. ; [28]*S. Afr. med. J.* 1945, **19**, 350 ; [29]*J. S. C. med. Ass.* 1947, **44**, 37 ; [30]*Surgery*, 1945, **17**, 178 ; [31]*Quart. Bull. N.W. Univ. med. Sch.* 1946, **20**, 1 ; [32]*Surg. Gynec. Obstet.* 1947, **84**, 519 ; [33]*J. Amer. med. Ass.* 1940, **114**, 117 ; [34]*Brit. med. J.* 1947, **1**, 594 ; [35]*Mém. Acad. Chir. Paris*, 1948, **73**, 662 ; [36]*Nord. med. Tidskr.* 1948, **37**, 624 ; [37]*Clin. J.* 1930, **59**, 577 ; [38]*Practitioner*, 1947, **158**, 60 ; [39]*Surgeon's Guide to Local Anæsthesia*, 1948, 331, Wright, Bristol ; [40]*Brit. med. J.* 1948, **2**, 399 ; [41]*Ibid.* 202 ; [42]*Act. Cuerpo Facult. Inst. policlin.* 1945, Dec. ; [43]*Proc. Mayo Clin.* 1946, **21**, 337 ; [44]*Act. Cuerpo Facult. Inst. policlin.* 1946, **3**, Sept.-Oct. ; [45]*Med. clin. Rev. mens. Barcelona*, 1947, **3**, 175.

VAS AND SEMINAL VESICLES, SURGERY OF. *Hamilton Bailey, F.R.C.S., F.A.C.S.* *Norman M. Matheson, F.R.C.S., F.A.C.S.*

Anastomosis of Vas Deferens after Purposeful Division for Sterility.—In view of the mass sterilization for the purpose of racial discrimination in certain parts of Europe, great credit goes to V. J. O'Conor[1] for bringing his experiences to the

notice of the profession. The normal testis continues to produce spermatozoa for an indefinite period after ligation of the vas. O'Conor finds that reunion of the vas may be successfully accomplished in from 35 to 40 per cent. He advises that the pessimistic outlook for relief of the vasectomized younger men in Europe should be revised and surgical aid granted to those who request it.

Primary Carcinoma of Seminal Vesicle (*Fig.* 79).—Although this rare condition

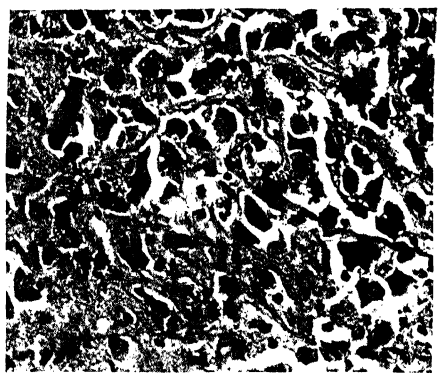


Fig. 79.—Microphotograph of section through vesicular tumour (×220). (*E. M. Gee.*) (*By kind permission of the 'Journal of Urology'.*)

has only been recorded on 21 occasions between 1883 and 1943, E. M. Gee[2] is able to add an additional 2 cases; in both a mass could be felt rectally.

A paper from Philadelphia by Lt. E. McCrea[3] also deals with primary carcinoma of the seminal vesicles. In all 3 cases personally observed three symptoms were constant, namely, frequency of urination, difficulty of urination, and hæmaturia. The hæmaturia as observed was not frank bleeding, but rather a mixture of urine, blood, and blood-clots, together with masses of cellular debris.

Treatment is unsatisfactory. It is only likely to improve by acting on the advice of E. M. Gee that where a suspicious mass is found in prostate or vesicle, consideration should be given to its exposure for biopsy with a view to radical excision.

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VERTEBRÆ, TUMOURS OF. *Lambert Rogers, M.Sc., F.R.C.S.*

The vertebral column may be the site of a wide variety of either primary or secondary neoplasms. Some idea of the different types and their relative incidence may be gathered from a recently published paper by J. P. Guri,[1] of Iowa, who has studied the records of patients with tumours of the vertebral column seen in the hospitals of the State University.

There were 2 examples of hæmangiomas; one of these which had not caused symptoms was found at autopsy in the body of the eighth thoracic vertebra, the other produced cord compression in the lower cervical region. The cervical region is less often the site of these tumours than the dorsal and lumbar parts of the column. Two cases of giant-cell tumour occurred, one in a boy of 13 in the sacrum, the other in a girl of 13 also in the sacrum. A sacral tumour in a man aged 54 proved to be a chordoma, while a woman of 45 had a chondroma at the side of the body of the sixth thoracic vertebra. This tumour recurred

after two operations and ultimately destroyed the patient, but its histological appearance at no time showed signs of malignancy. Another chondroma occurred in the sacral region of a man aged 61 who 7½ years after its removal was alive and well. There were 7 cases of fibrosarcoma, 6 of which were either lumbar or sacral in position. With the exception of one case, all of these patients were dead within 27 months; the exception, a man aged 57, had a tumour lying in the angle between the spinous and transverse processes of the lower dorsal and upper lumbar regions and was alive and well 7½ years after its removal. Microscopical studies confirmed the diagnosis of fibrosarcoma. A case of chondrosarcoma was encountered in the thoracic spine of a man aged 65. X-ray examination showed destruction of the body of the 8th thoracic vertebra. This patient died 14 months after decompressive laminectomy and radiotherapy. An osteogenic sarcoma was present in the cervical region of a man of 23 who succumbed to operation. Four patients with Hodgkin's disease had destruction of vertebræ, either in the lower cervical or the upper thoracic regions, but in one case there was generalized vertebral involvement. Complete spinal block at the level of the second lumbar vertebra was present in one of these cases. Ten cases of multiple myeloma occurred in patients between 40 and 78 years of age, eight of whom were men. In all of these death had occurred in from 4 months to 6 years.

Fifty cases of vertebral destruction by metastases were also found, and in these the site of origin of the primary tumours was as shown in the accompanying table.

	No. of Cases
Carcinoma of the breast ..	32
Carcinoma of the prostate .	7
Hypernephroma	3
Ewing's tumour	1
Chondrosarcoma	1
Bronchogenic carcinoma ..	1
Carcinoma of the skin	1
Carcinoma of the rectum ..	1
Carcinoma of the cervix ..	1
Fibrosarcoma of the cervix ..	1
Osteogenic sarcoma	1
	50

The spinal metastases in the cases of the breast tumours occurred from 4 months to 11 years after removal of the primary tumour.

[Although there is a certain amount of assumption in this paper, since autopsy or biopsy verification of the diagnosis has not been made in all the cited instances, it is, nevertheless, an interesting and valuable overall survey of the types of tumour which involve the vertebral column, either primarily or by metastasis from neoplasms elsewhere. —L. C. R.]

REFERENCE.—[1]*Surg. Gynec. Obstet.* 1948, **87**, 583.

VITAL STATISTICS. *Percy Stocks, C.M.G., M.D., F.R.C.P.*

The year 1948 was outstanding in the history of vital statistics by reason of three events of the first importance: the Sixth Decennial Conference for Revision of the International List of Causes of Death, held at Paris in April, and covering a wider field than its title suggested; the issue by the First Assembly of the World Health Organization at Geneva in July of the first International Health Regulations, dealing entirely with health statistics; and the publication at the end of the year of the first volume of the new *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death* (English edition). These events together marked the fructification of long-continued efforts to make possible a real comparability of death-rates in different countries, and also the beginning of a new era of national and international morbidity statistics. Another event having a profound influence

on the future of morbidity statistics in Britain was the inauguration of the National Health Service in July. The publication at the end of 1948 of the sixth edition of the *Nomenclature of Disease* of the Royal College of Physicians was also significant because uniformity in the naming of diseases and aetiological agents cannot but improve the quality and accuracy of sickness records.

It is most desirable that the medical profession should know something about these happenings, for, in hospital practice at least, a knowledge of the new statistical code of diseases, symptoms, and injuries will become increasingly necessary; and students can hardly be left in ignorance of it. In this year's article, therefore, precedence will be given to these matters and an attempt made to explain them in simple terms.

International Conference at Paris, April, 1948. At the conference for the fifth revision of the International List of Causes of Death in 1938 it had been resolved that the "joint committee" which had been responsible for preparing for that revision should undertake not only the next revision but also "the preparation of international lists of diseases, in conjunction with experts and representatives of the organizations specially concerned". The transfer of responsibility for such matters to the new World Health Organization necessitated some modification of procedure, and the steps actually taken to implement this resolution have been summarized in the MEDICAL ANNUAL of 1948, p. 363. In another resolution the U.S. Government had been requested, in co-operation with other countries and organizations, to continue the study of the problem of selecting the main cause of death when several causes are mentioned on a death certificate, with a view to reaching international agreement on that important question. Despite the difficulties occasioned by the war, work on each of these problems had advanced beyond all expectation by 1948, and the Conference for the Sixth Revision was presented by the Expert Committee appointed by the Interim Commission of W.H.O. with a comprehensive programme for consideration. The representatives of 29 nations during the first day of their meeting paid a compliment to the Committee by approving unanimously the new Classification designed to serve the purposes of morbidity as well as mortality statistics. The Expert Committee, of which I was chairman, was empowered to finish off the Classification; and its adoption and publication in English, French, and Spanish by the World Health Organization was recommended. An Intermediate List of 150 groups, an Abbreviated List of 50 for local tabulations of deaths, and a Special List of 50 groups for Social Security statistics were recommended for inclusion in the international manual, subject to the provision that coding must always be done first by the full list. Rules for using the lists in national statistics were also recommended, and the World Health Organization subsequently embodied them in the International Regulations.

The Conference then considered the proposals of the United States Sub-Committee on Joint Causes of Death that a standard form of death certificate be used, allowing the certifying doctor to indicate what he believed to be the underlying cause, and that the cause so indicated should be used for primary statistical tabulations unless the Classification directs otherwise. This principle, which was accepted by the Conference, has been practised by the General Register Office in England and Wales since 1940. For those countries which have used rigid rules of preference disregarding the order of statement of causes by the certifier, the change will break the continuity of statistics for many diseases and necessitate the use of "conversion ratios" (similar to those in the Registrar-General's Statistical Review for 1940, Appendix B1). The need for this reform has been well illustrated by a study of the recent trend of death-rates attributed to diabetes by the official statistics of U.S.A. (*Public Health*

Reports, 1948, **63**, No. 41, 1334). Out of a sample of 341 death certificates containing any mention of diabetes, 309 had another cause mentioned, and by operation of the coding rules at present in force in U.S.A. 294 were classified to diabetes, whereas the certifier indicated that diabetes was merely a contributory cause in 144 of them. By the system used in England and Wales since 1940 and now to be adopted internationally, only 150 would have been classified to diabetes. This shows that the diabetes death-rates in countries which have continued to use arbitrary rules preferring one disease over another have been misleading, and the same applies to a number of other diseases. The removal of this obstacle to international comparability between death-rates, which has been striven for since 1938, should now make possible real comparisons between mortality in New York, Montreal, London, and other cities, and it marks an important forward step.

The Conference also discussed the question of international definitions of live- and stillbirth, on which it was evident that agreement could not be obtained until more statistical data have been collected. In some countries registration systems still allow a live-born child who dies within a few days and before birth registration has been effected to be registered as stillborn, thus making statistics of live- and stillbirths, and of infant mortality, invalid for comparison with those of other countries. Interpretations of what constitute signs of life also differ, and the criterion of 28 weeks of gestation which forms the basis of the legal distinction between stillbirth and abortion in the United Kingdom is not accepted in some of the United States. Recognizing these difficulties and the urgent need for uniformity of definitions, the Conference requested the World Health Organization to refer the matter for study by an Expert Committee on Health Statistics, and in the meantime to ask all nations to use the British definitions for purposes of official statistics until such time as an international agreement has been reached. These recommendations were carried into effect later by the First World Health Assembly. The definition of abortion laid down in the Classification includes "premature confinement of less than approximately 7 months or 28 weeks gestation", thereby fixing the gestation limit for stillbirth.

The Conference recommended that the World Health Organization should set up a permanent Expert Committee on Health Statistics to study "problems in the field of health statistics, including recording of births, diseases, and deaths". Particular problems mentioned for study and appropriate action were (1) multiple causes, (2) vital data according to residence, (3) standardization of rates, (4) definitions and classification of fœtal and infant mortality. The importance of a competent statistical service within the World Health Organization was stressed.

Special studies to be undertaken in certain countries subject to approval of their governments were recommended, including the following in which the United Kingdom was asked to co-operate: —

Cancer registers and statistics.

Methods of presenting statistics of multiple causes of death.

Methods for obtaining reliable statistics on the frequency and causes of fœtal death, including classification by periods of gestation.

International Statistical Classification of Diseases, Injuries, and Causes of Death.—The Manual containing the new classification consists of two volumes. The first consists of an historical introduction; a list of the 3-figure categories a tabular list of principal conditions included in each category, with definitions, notes, and suggested 4th digit sub-groups where such subdivision seemed useful; condensed lists of 150 and 50 groups for the special purposes mentioned in the regulations; method of dealing with death certificates on which more

than one cause is entered; international regulations. The second volume consists of an alphabetical index of all conditions likely to occur on medical records with code numbers assigned to each, compiled by an Index Sub-Committee of the Expert Committee, most of the indexing work being done in Washington. These volumes can be obtained from H.M. Stationery Office.

The general arrangement of the Classification of Diseases follows that of the international list, which has been found more serviceable than any alternative which could be devised. A new section of Mental, Psychoneurotic, and Personality Disorders has been inserted, whilst the Chronic Poisoning section is included with acute poisoning and the section for Old Age is merged in a combined section of Symptoms, Senility, and Ill-defined Conditions. The numbering is on a decimal system, suitable for machine cards. Disease groups have numbers from 001 to 799, with suggested subdivisions in many instances, denoted by a fourth digit. Accidents, Poisoning, and Violence, with group numbers from 800 to 999, are classified in two ways, first according to external cause (the E code with numbers E800–E999), and then according to nature of injury (N code with numbers N800–N999). Every injury finds a place in both lists and each code will usually be assigned, since injuries cannot be studied satisfactorily from either aspect alone. The kind of place where an accident occurred is indicated by a 4th digit in the E code.

The structure of the classification is best illustrated by a few examples, which are given below. It must be understood that the included terms beneath a title are common descriptions likely to be found written on medical records, and are not necessarily those recommended by a modern nomenclature nor are they all sufficiently precise to enable good statistics to be obtained. In the example below it would be better if 080.3 could be omitted, but in practice it will often not be stated whether actual paralysis was present or not, and a number must be provided for the coding of such records. Words in parentheses may be present or absent without making any difference to the code number; and the same applies to words inset below a description which is not followed by a colon (e.g., "acute", "anterior", and "epidemic" in No. 080.1 below). If, however, a descriptive term is followed by a colon it signifies inclusion of that description only when modified by one or other of the words inset below it (e.g., "Hypertensive vascular" in No. 447 below). The letters NOS signify "not otherwise specified", that is, without any more precise description.

080. *Acute poliomyelitis.*

This title excludes conditions specified as late effects or sequelæ or present one year or more after onset (081).

080.0. *Specified as bulbar or polioencephalitis.*
- Polioencephalitis (acute) (bulbar)
- Polioencephalomyelitis (acute)
- Infantile paralysis (acute)
- Poliomyelitis (acute)
- Poliomyelitis (acute) anterior

} Specified as bulbar

080.1. *With other paralysis.*
- Acute atrophic spinal paralysis
- Paralytic infantile paralysis
- Poliomyelitis (acute)
  - anterior
  - epidemic

} With paralysis except bulbar

080.2. *Specified as nonparalytic.*
- Poliomyelitis (acute)
  - anterior
  - epidemic

} Specified as nonparalytic

080.3. *Unspecified.*
- Infantile paralysis
- Poliomyelitis (acute)
  - anterior
  - epidemic

} Unspecified whether paralytic or nonparalytic

081. *Late effects of acute poliomyelitis.*

Paralysis or any condition specified as a late effect or sequela of acute poliomyelitis (to synonym in 080), or present one year or more after onset of poliomyelitis.

Another example of a run of numbers, forming part of the "hypertensive diseases", is shown below together with the related category of renal sclerosis taken from the section "nephritis and nephrosis". (No. 450, also referred to, is the number for general arteriosclerosis. Nos. 440–443 resemble 444–447, but with associated heart disease.)

444. *Essential benign hypertension without mention of heart.*
Hyperpiesia
Hyperpiesis
Hypertension:
NOS
arterial
benign
essential
primary (benign)
Any condition in 447 if described as benign

445. *Essential malignant hypertension without mention of heart.*
Malignant hypertension
Any condition in 447 if described as malignant

446. *Hypertension with arteriolar nephrosclerosis without mention of heart.*
Arteriolar nephritis
Arteriosclerosis of kidney
Arteriosclerotic nephritis
Hypertension of kidney
Nephrosclerosis
Any condition in 594 with hypertension

447. *Other hypertensive disease without mention of heart.*
Arteriosclerotic hypertensive vascular disease
Hypertensive vascular:
degeneration
disease
} Not specified as benign or malignant
Any condition in 450 with mention of hypertension

594. *Other renal sclerosis.*
Atrophy
Cirrhosis
Cirrhotic
Degeneration
Gouty
Gouty nephritis
} (of) kidney
Interstitial nephritis NOS
Renal:
cirrhosis
dwarfism
infantilism
rickets
sclerosis

This title excludes hypertension with arteriolar nephrosclerosis (442, 446)

Transport accidents are classified by external cause in great detail, viz.:

Railway accidents (E800–E802)
Motor vehicle traffic accidents (E810–E825), distinguishing what the injured person was doing, whether a collision occurred and (by the 4th digit) the kinds of vehicle involved.
Motor vehicle non-traffic accidents (E830–E835)
Other road vehicle accidents (E840–E845)
Water transport accidents (E850–E858)
Aircraft accidents (E860–E866)

Non-transport accidents (E870–E936) can be coded by a 4th digit according to place of occurrence, for example, a home accident is defined as one occurring in the following places:

0. *Home.*
Apartment
Boarding-house
Farm-house (but not farm buildings and land under cultivation)
Home
Home premises
House (residential)
Private:
driveway or walk to home
garage
garden to home
Yard to home
Any other non-institutional place of residence

As an example of the complexity of a classification designed to provide statistics according to the state of knowledge at the present time, *hepatitis* may have to be coded in any one of the following categories according to the information given about it:–

092. Infectious hepatitis
580. Acute and subacute atrophy of liver

582.	Suppurative hepatitis and liver abscess
583.	Other diseases of liver
642.5.	Other toxæmias of pregnancy
652.	Abortion with toxæmia, without mention of sepsis
686.	Other forms of puerperal toxæmia
770.	Hæmolytic disease of newborn (erythroblastosis)
{ E943.	Post immunisation jaundice and hepatitis
{ N997.	Reactions and complications due to non-therapeutic medical and surgical procedures
{ E951.	Therapeutic misadventure in infusion or transfusion
{ N998.5.	Serum jaundice

Supplementary classifications are provided for: Special conditions and examinations without sickness (Y00–Y09), Admissions for convalescent care, plastic treatment, and fitting of prosthetic devices (Y10–Y18), Classification of live-births according to type of birth (Y20–Y29), Classifications of causes of stillbirth (Y30–Y39), Prophylactic inoculation and vaccination (Y40–Y49), Impairment due to birth injury, congenital malformations, and musculoskeletal diseases (Y50–Y59), Impairment due to other diseases and accidents (Y60–Y69), Absence or amputation of major or minor members due to diseases, congenital malformations, and injuries (Y70–Y79), Blindness and deafness following diseases or injuries (Y80–Y89).

VITAMIN E IN THE COLLAGENOSES.

R. M. B. MacKenna, M.A., M.D., F.R.C.P.

The work of J. F. Burgess, of Montreal, concerning this matter has attracted attention, and his recent paper[1] has caused considerable discussion.

Briefly, Burgess has suggested that cases of chronic lupus erythematosus, sclerodermia, morphœa, dermatomyositis, granuloma annulare, and lichen sclerosus et atrophicus have shown varied response to the administration of vitamin E, but in general the response has usually been favourable.

Burgess uses large doses of vitamin E (400–600 mg. daily), and apparently he uses a mixture of tocopherols. In some cases he administers 100–300 mg. intramuscularly twice a week.

Burgess's article in *The Lancet* was followed by a letter from R. D. Sweet,[2] who stated that he had treated 22 cases of chronic lupus erythematosus with vitamin E, all for at least ten weeks, and 16 of these cases were treated for more than four months. The majority were of many years' standing, 11 having been going on for more than ten years, 5 for between five and ten years, and only 2 for less than two years. All except 4 had previously been treated unsuccessfully with one or more of the common gold, bismuth, or arsenic compounds; none of the cases showed evidence of other disease. Sweet used alpha-tocopherol, administering this by the mouth, and no patient was considered to have failed to respond unless he had received no less than 200 mg. daily for two months; most cases had 250–300 mg. for a longer period. Not a single case improved dramatically under this treatment: 4 improved slightly, 11 were quite unchanged, and 7 became worse. Sweet therefore concluded that alpha-tocopherol is without value in the treatment of lupus erythematosus.

K. Hickman[3] has pointed out that the dosage ratio is probably higher for alpha-tocopherol than for any other vitamin. If the average total human content is 3500 mg. in all tissues and the daily intake is 15–20 mg. he considers that the minimum period of half adjustment to change of intake is 138 days and may be much longer if the quantity absorbed is less than that ingested. He emphasizes that Canadian workers are using alpha-tocopherol as a drug and not at nutritional levels. He makes a plea that physicians should make proper adjustment between dosage and time of treatment.

My own experience with vitamin E has been that I have yet to see a case of granuloma annulare which did not appear to respond fairly rapidly to

doses of 10–20 mg. alpha-tocopherol by the mouth thrice daily. Given in large doses either by the mouth or by injection there seems to have been some slight remission in the tightness and discomfort of various cases of sclerodermia, but no marked remission or great improvement in the disease; in but two or three cases of lichen sclerosus et atrophicus small doses of the vitamin (20 mg.) given by the mouth appear to have relieved the pruritus vulvæ which happened to be a predominant symptom in these cases, but this amelioration of symptoms has not been noted by other workers.

The use of the vitamin given either by injection or by the mouth in doses up to 300 mg. daily to cases of lupus erythematosus of the chronic type has not been encouraging, although in a few of these cases some benefit appears to have followed the administration of the vitamin.

The present position in regard to the use of vitamin E in dermatology in England varies between frank scepticism and a vague feeling that in the treatment of the collagenoses the administration of vitamin E is helpful but not by any means definitely curative; the fact that it is helpful suggests that an investigation of the biochemistry of this vitamin in these maladies might possibly help us to solve the riddles of their actiology.

REFERENCES. [1]*Lancet*, 1948, 2, 215; [2]*Ibid.* 310; [3]*Ibid.* 1, 652.

WEIL'S DISEASE (Leptospirosis Icterohæmorrhagica).

H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.

J. C. Broom and J. M. Alston[1] analyse 195 cases occurring in England in 1940–6, which were all diagnosed serologically in their laboratories. Any degree of agglutination was regarded as suspicious, but when the titre was 1 300 or less further samples were examined to test for the rise in antibody content which takes place in this disease.

Treatment. H. M. Patterson[2] describes successful *penicillin* treatment of 6 cases. As adjuvants he gave 2 mg. vitamin K daily, increased to 10 mg. if hæmorrhage or jaundice were present; ferrous sulphate and liver extract for anæmia; and hexamine and sodium diphosphate gr. 10 every eight hours right through convalescence in order to keep the urine acid and so help to destroy the large numbers of leptospiræ found in the urine for many weeks in convalescence.

Leptospirosis Canicolaris. Four cases are reported by L. J. M. Laurent et al.[3] Only 2 cases had previously been reported in England. In 3 of the 4 cases there was a history of frequent contact with a dog, 2 of which had been in bad health. All 4 cases showed the meningeal form of the disease, although this is not invariable. Onset included headache and fever in all, with vertigo or vomiting or abdominal pain. During the illness, eye signs developed in all—conjunctival or ciliary injection, photophobia, inequality of pupils, mistiness of vision, and blurring of edge of retinal disk. Stiff neck was present in all and Kernig's sign in 3. Three had a morbilliform rash in the form of small red spots or larger macules like erythema nodosum. Herpes labialis was present in 1. The spleen was palpable in 1. Diarrhœa, pulmonary congestion, epistaxis, and nephritis have been noted by others but were not present in this series. The spinal fluid showed 290–1320 cells (almost all lymphocytes), and 20 to 400 mg. protein per 100 ml. The blood-picture was little abnormal except for a relative lymphocytosis in 1. One had recurrent headaches up to ninety days, and another had a relapse with headache and fever at the twenty-first day. The disease was mild and jaundice did not occur. Most cases of this disease are anicteric and deaths are very rare. A clinical diagnosis is not readily made. *The presence of a severe conjunctivitis, rash, and signs of meningeal irritation are notable pointers.* The disease is the same as "maladie des porchers" or

"swineherd's disease" which is endemic and occupational in Savoy. (*See also article* LEPTOSPIROSIS CANICOLARIS.)

REFERENCES.—[1]*Lancet*, 1948, **2**, 96; [2]*J. Amer. med. Ass.* 1947, **134**, 1077; [3]*Lancet*, 1948, **2**, 48.

WHOOPING-COUGH. *H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H.*

Epidemiology.—Notifications of whooping-cough in 1946 numbered 92,936, and there were 808 deaths, giving an (immediate) fatality-rate of 0·87 per cent which was lower than the rate of 1·1 per cent for 1945. Whooping-cough is most fatal to infants under the age of one year, and protective measures whether by immunization or by attempts to prevent contact with the disease, should be thus directed primarily to the pre-school child.[1] S. D. Collins,[2] by analysis of the results of a series of canvasses of families living in different parts of the United States in the early 1930's, showed that of 100 infants aged six to twelve months exposed to a case of whooping-cough in a household nearly 100 will become infected.

Immunization.—Following the disappointing results reported by McFarlan, Topley, and Fisher,[3] further extensive trials using other types of vaccine are at present being carried out by the Medical Research Council. Until a prophylactic of proved reliability is forthcoming the Ministry cannot sponsor a mass immunization scheme. Whooping-cough immunization can be carried out at the same time as diphtheria immunization.[1] R. T. Mummery[4] reports on the preparation and use of whooping-cough vaccine. The best medium contains 50 per cent of *human* blood; the younger the culture the better the vaccine; in practice, however, in order to obtain sufficient growth, it is necessary to incubate the cultures for forty-eight hours, but this period should never be exceeded; there is no cogent evidence that alum-precipitated vaccine is antigenically superior to a straight heat-killed phenol-preserved vaccine; it is an advantage to combine the vaccine with diphtheria prophylactic provided that adequate doses of each antigen are combined in suitable proportions; three doses, each of 10,000 million organisms, given at monthly intervals, followed one year later by a boosting dose, and by a similar boosting dose three years later on entry to school, yield satisfactory results; immunization is worth attempting at six months of age, but better results are to be anticipated if it is postponed to nine months of age; duration of immunity with such a course is almost absolute for six months, and slowly wanes over the next six months; even if immunization fails to give complete immunity it rarely fails to mitigate the severity and duration of an attack.

J. A. Bell[5] reports on combined immunization with an alum-precipitated mixture of diphtheria toxoid and pertussis vaccine, based on well-controlled field studies involving 1238 children during the period 1941–7. Two doses were used at four-weeks interval, each dose containing 10,000 million *H. pertussis* organisms. It was shown that substantial protection was conferred against clinical pertussis when the first dose was given to children either at two to four or at five to twenty-three months af age.

Complications of Immunization.—R. K. Byers and F. C. Moll[6] submit a rather disturbing report on *encephalopathies* following prophylactic pertussis vaccine. They collected 15 cases of convulsive encephalopathy occurring some twenty minutes to seventy-two hours after inoculation with pertussis vaccine. These were all children aged five to eighteen months, 12 being male and 3 female, and were all admitted to Boston Children's Hospital during the nine years 1939–47. The previous history seemed to be negative for any known sensitivity agent. The family history was clear in at least 12 cases. There was no significant geographical grouping or concentration in the district. In 12 cases the vaccine inoculated was a straight pertussis one and in 3 cases had been

combined with diphtheria or tetanus toxoid. In 6 cases the reaction was explosive following the first dose, in 3 following the second dose, and in 6 following the third. The salient symptom was *convulsions*, varying in duration from a few minutes to several days. Consciousness was impaired in all cases. In 6 cases, symptoms included hemiplegia, exaggerated reflexes, or Babinski's sign. In most cases the spinal fluid showed a moderate increase of protein and lymphocytes. The blood-picture was a polymorph leucocytosis. The duration of the acute illness varied from thirty-six hours to ten days. In the follow-up only one child appeared normal. In 2 cases there was progressive dementia and recurrent fits ending fatally. In 9 cases there were cerebral palsies and recurrent convulsions. In 6 cases ventricular dilatation is said to have been demonstrated. In 4 of 10 cases tested, encephalograms were found abnormal. The authors point out that during the same period, 8 cases of post-vaccinal encephalitis were admitted, and that, accordingly, encephalopathy following pertussis immunization may be the more common or the more severe of these two conditions. The aetiology of this disturbing complication is quite unknown. The authors consider that some constitutional factor is probably involved and at the same time query whether a specific toxin is the cause. [Until recently British pertussis vaccines seem to have been less potent immunizing agents than the American. Will this encephalopathy be found to be a measure and a penalty of vaccines with an increased antigenic potency ?—H. S. B.]

Diagnosis.—W. C. Cockburn and H. D. Holt[2] compare the results obtained with per-nasal and post-nasal swabs in the diagnosis of pertussis. From thirty pairs of swabs taken simultaneously, all were positive by the per-nasal method and twenty-three by the post-nasal method. The plates inoculated from the per-nasal swab were much less contaminated with other organisms than those inoculated from the post-nasal swabs. Although the per-nasal swab is thus apparently more reliable for the isolation of *H. pertussis* than the post-nasal swab, it may sometimes yield a negative result even in the early stages of pertussis.

References. [1]*Ann. Rep. Min. Hlth*, 1947, 27. H.M.S.O. Lond.; [2]*Publ. Hlth Rep., Wash.* 1948, **63**, 69; [3]*Brit. med. J.* 1945, **2**, 205; [4]*Publ. Hlth*, 1948, Nov., 28; [5]*J. Amer. med. Ass.* 1948, **137**, 1276; [6]*Pediatrics*, 1948, **1**, 437; [7]*Mon. Bull. Min. Hlth*, 1948, **7**, 156.

WILMS' EMBRYOMA. *R. E. Bonham-Carter, M.B., B.Chir., M.R.C.P.*

In 1941, W. E. Ladd and R. P. White[1] summarized the literature and found 38 probable cures out of 563 cases. Their own series showed a survival rate of 23·3 per cent in 60 cases treated by operation, observed for a minimum period of two years.

Since then, W. Wersel, M. B. Dockerty, and J. T. Preistly[2] have published a series of 42 patients treated by operation, with 7 patients surviving for from two to twenty years. A. L. Dean[3] published a series of 20 patients in whom irradiation was the only form of treatment, 5 patients being alive five years later, the criticism of this paper being that it was not stated whether a histological diagnosis was made or not.

H. K. Silver[4] presents 18 cases of the neoplasm, nephrectomy being done in 13, with a survival in this nephrectomized group of 10 patients for between two and a quarter and fifteen years since operation, a survival-rate of 76·9 per cent. Only 2 patients were adults. The youngest was only three days old. Hypertension occurred in 7 out of 8 patients in whom the blood-pressure was recorded. He found no correlation between age of onset, degree of hypertension, presence of haematuria, and eventual outcome. He used no standard treatment, but points out that all 4 patients in whom both pre- and post-operative irradiation was done are alive, and that all the survivors had a nephrectomy. The following table gives the results of nephrectomy and irradiation in their series :

Treatment	Outcome		Survival Time
	Alive	*Dead*	
Nephrectomy alone	3	1	16 yrs., 10 yrs., 9 yrs.
Nephrectomy and post-operative irradiation	3	2	11 yrs., 5½ yrs., 2½ yrs.
Pre-operative irradiation, nephrectomy, post-operative irradiation	4	0	7½ yrs., 4½ yrs., 4½ yrs., 2¼ yrs.

This is the best survival-rate yet recorded, and holds out great hopes, but it should be noted the survivors who were treated with pre- and post-operative irradiation have not been observed for so long as those in the other two groups. Silver rightly stresses the importance of early diagnosis.

References. [1]*J. Amer. med. Ass.* 1941, **117**, 1858; [2]*J. Urol.* 1943, **50**, 399; [3]*N.Y. St. J. Med.* 1945, **45**, 1213; [4]*J. Pediat.* 1947, **31**, 643.

WORLD HEALTH ORGANIZATION. *W. H. Bradley, D.M., M.R.C.P.*

The First Health Assembly was held in the Palais des Nations, Geneva, in July, 1948. Fifty-two member states sent delegations and thirteen other countries were represented by observers. Dr. Brock Chisholm (Canada) was appointed Director-General of the World Health Organization.

It is of some historical interest that until this meeting the United States had not accepted the Constitution of the World Health Organization without certain reservations, particularly one permitting withdrawal from W.H.O. at twelve months' notice. In spite of this, the United States was admitted to full membership of the Organization at the July meeting.

The business of the Assembly was mainly concerned with the organization of W.H.O. Six Regional Areas covering the world were delineated. Attempts were made to obtain proper geographical representation on the Executive Board, whose statutory obligations were defined.

A programme of work to be undertaken by the Executive Board was drawn up. It was decided to concentrate on seven main fields during the first year, cholera, tuberculosis, maternity and child health, venereal disease, nutrition, environmental sanitation, and public health administration, including the welfare of seafarers. Fifteen expert committees working in these fields were authorized, some of the references being: Administration of International Sanitary Conventions, Unification of Pharmacopœial and Biological Standards, and the Classification of Disease. In relation to the last it is of historical interest to record that for the first time an international body has now formulated and adopted a nomenclature of disease and laid down a system for the compilation and publication of mortality and morbidity statistics.

Some of these expert committees will work in co-operation with other United Nations organizations, for example the Nutrition Committee with F.A.O. and the Nomenclature Committee with I.L.O.

The World Health Organization has also taken important steps towards interchange of medical information between nations. Two hundred Fellowships are to be granted, and medical literature and teaching equipment made available to backward countries. In serious epidemics the World Health Organization will provide an emergency service.

It was unanimously agreed that Geneva should be the headquarters of the Organization. There will be a small sub-office in New York, and a temporary Special Administration Office in Europe to deal with health rehabilitation of war-devastated countries in that area. A Second Health Assembly is to be held in Europe, probably in June, 1949. In the meantime, the Executive Board will continue to function under the Chairmanship of Dr. Shousha Pasha, with Dr. Evang of Norway and Dr. Yung of China as Vice-Chairmen.

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A Spencer Support for Nephroptosis is designed to support the abdomen from below, upward and backward. A Kidney pad is provided as prescribed by Doctor.

Because each Spencer is individually designed for the specific condition and made from the detailed measurements and posture description of the patient, exact fit and restful comfort are assured, and the support will not ride up or slip out of place. All Spencer Supports are designed to correct mal-posture, provide abdominal uplift and to place the pull on the pelvic girdle, not on the spine at, or above, the lumbar region. They are scientifically designed for simple and easy adjustment.

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THE PRACTITIONERS' INDEX

RECENT PHARMACEUTICAL AND DIETETIC PREPARATIONS, MEDICAL AND SURGICAL APPLIANCES, ETC.

In this Section we give short descriptions of the new Pharmaceutical Products and Medical and Surgical Appliances of the past year. It should be understood that the information is supplied by the Makers. We invite all those concerned with the Medical Manufacturing Industries to co-operate with us in making this section valuable for present and permanent reference.

A short written description of each article is required, with the advantages claimed for it, and with the Maker's name and address appended. The Editors cannot accept reference to circulars or catalogues as a compliance with these conditions, and cannot undertake to compile descriptions from such material.

In the section on Drugs, their composition, principal applications, and dosage should be stated in the fewest possible words.

PHARMACEUTICAL PREPARATIONS

Abidec Drops.—In this product the fat-soluble vitamins A and D are solubilized and are presented in combination with the water-soluble vitamins B_1, B_2, C, and nicotinamide in the form of a stable, non-oily, non-alcoholic solution. Each 10 minims contains vitamin A, 5000 I.U.; vitamin D, 1000 I.U.; vitamin B_1 (aneurine hydrochloride), 1 mg.; vitamin B_2 (riboflavin), 0·4 mg.; nicotinamide, 5 mg. and vitamin C (ascorbic acid) 25 mg. Abidec Drops permit the administration of these important vitamins to infants and children in a small dosage which is well tolerated and which may be added to the infant's feed without appreciably altering its taste or appearance. Available in 10-c.c. vials with dropper. (Parke, Davis & Co., Hounslow, Middx.)

Acorza Liquidum. A combination of codeine and papaverine in a flavoured syrup base which is claimed, on the results reported by F. Hutter (*Wein. klin. Wschr.*, 1937, **1**, 376) and Diehly (*J. Amer. med. Ass.*, 1933, **101**, 2042) to cure or improve at least 75 per cent colds within 24–48 hours. Two doses of 3i followed by one dose of 3iii (detailed instructions with vial). NOT suitable for children. Pack: 23 mls., sufficient for one treatment. (Forsters (Pharmaceuticals) Ltd., Seaham, Co. Durham.)

Adaprin Tablets. Composition: Each tablet contains acetomenaphthone (vitamin K analogue) 10 mg. and nicotinamide (the P.P. factor of the vitamin B complex) 50 mg. Indications: For the treatment and prevention of chilblains. Dosage: Treatment—one tablet four times daily; Prevention—one or two tablets daily. Packing: Containers of 25, 100, and 500 tablets. (Ward, Blenkinsop & Co. Ltd., 6 Henrietta Place, London, W.1.)

Aluminium Paste Boots. A paste containing 10 per cent finely powdered aluminium in a liquid paraffin and zinc oxide base. For the protection of the intestinal mucosa around pathological and surgical fistulæ. Supplied in jars of 4 oz. (Boots Pure Drug Company Limited, Nottingham.)

'Anthisan' Cream. Brand of mepyramine maleate cream; 2 per cent mepyramine maleate in water-miscible base. Indications: (1) In the local symptomatic treatment of skin conditions of an allergic or sensitization type, either alone or in association with oral 'Anthisan' treatment; (2) As a powerful anti-pruritic in all conditions characterized by intense itching. Method of administration: Applied directly to the affected parts. Two or three applications a day usually suffice. Supplied in containers of 1 oz. and 1 lb. The powerful anti-histaminic and analgesic properties of 'Anthisan' are probably responsible for the marked efficacy of this product. (Pharmaceutical Specialities (May & Baker) Ltd., Dagenham.)

'Auralgicin'.—

Composition:—		
	Benzocaine	1·5% w/v
	Ephedrine hydrochloride	1% w/v
	Phenazone	5% w/v
	Chlorbutol	1% w/v
	Pot. hydroxyquinoline sulphate	0·1% w/v
	Glycerin	q.s.

Indications: Ear-drops for the treatment of acute and subacute otitis media. Method of application: Apply hourly until the pain disappears, thereafter apply every three hours for one to two days. (Manufactured by Benger's Limited, Holmes Chapel, Cheshire.)

'Banocide' Brand Diethylcarbamazine. A synthetic non-metallic compound (1-diethylcarbamyl-4-methylpiperazine citrate) with specific chemotherapeutic activity *in vivo* against many types of filarial parasites, particularly *Wuchereria bancrofti* and *Onchocera volvulus*. It is well tolerated and causes rapid disappearance of microfilariæ from the blood. 'Banocide' is administered orally in the form of 50 mg. compressed products, the dosage for individual cases being based on body-weight (2 mg. per kilo three times a day for four weeks). For mass treatment, a dose of 100 mg. to adults, or 50 mg. to children, once daily for three to five days, has been recommended. 'Banocide' is issued in containers of 20, 100, 1000, and 5000 products. (Burroughs Wellcome & Co. (Th. Wellcome Foundation Ltd.), 183–193, Euston Road, London.)

'Becosym'. Previously available for oral use only, 'Becosym' is now issued for injection in twin-ampoules which preserve the B-complex factors in a stable form and provide a solution which is speedily absorbed without causing pain. One injectable dose contains 10 mg. aneurine hydrochloride, 4 mg. riboflavin, 40 mg. nicotinamide, 4 mg. pyridoxine, and 5 mg. of panthenol, a pantothenic acid preparation. Intramuscular or intravenous injection of these five important vitamin B factors is advisable in urgent cases and whenever absorption from the gastro-intestinal tract is likely to be unsatisfactory as in enteritis, colitis, steatorrhœa, sprue, etc. 'Becosym' ampoules are issued in boxes of 6 and 50 twin ampoules. (Roche Products Ltd., Welwyn Garden City, Herts.)

Befolin Tablets. Each tablet contains anecarine hydrochloride 1 mg., riboflavine 1 mg., nicotinamide 20 mg., and folic acid 1·7 mg. Indications: Sprue, pellagra, beri-beri, nutritional anæmia of pregnancy (especially in cases in which there is gastro-intestinal disturbance), polyneuritis, chronic alcoholism, and other disorders caused by deficiency of the vitamin-B complex. Dosage, three times a day, after meals: Adults, one to three tablets; Children, one tablet. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Benadryl. In addition to its issue for oral and parenteral administration, Benadryl is now supplied in the form of an Elixir in bottles of 4 and 16 fl. oz. containing 10 mg. Benadryl in each fluid drachm. For topical application Benadryl Cream is available in 1-oz. collapsible tubes containing 2 per cent Benadryl in a water-miscible base. (Parke, Davis & Co., Hounslow, Middx.)

Benylin Expectorant. A palatable raspberry-flavoured syrup containing, in each fluid ounce, Benadryl, 80 mg.; ammonium chloride, 12 gr.; sodium citrate, 5 gr.; chloroform ½ gr.; and menthol, ¼ gr. It is indicated in the treatment of coughs and other congestive symptoms associated with the "common cold". Its pleasant flavour makes it acceptable to children. Issued in bottles of 4 and 16 fl. oz. (Parke, Davis & Co., Hounslow, Middx.)

Bioglan Anti-Migraine. Indicated for all types of true migraine, also for sick headache where associated with neuritis. Supplied in capsules for oral administration. Composition: Peptone gr. 3, embryonin gr. ½, magnesium thiosulphate gr. 3, theophyllin B.P. gr. 1, phenacetin B.P. gr. 3, caffeine B.P. gr. ½, ergotamine tartrate mg. 1. Three doses daily immediately before meals. Following prolonged investigation, it is now known that migraine has to be regarded as an allergic manifestation. Many cases of sick headache are *not* migraine, but are caused by an underlying neuritis. It is necessary to bear in mind that migraine is a symptom, a consequence, but never a disease. Neuritis, on the other hand, *is* a disease and Bioglan Anti-Migraine will be found useful for the sick headache that is an accompaniment. (Bioglan Laboratories Ltd., Hertford, Herts.)

Bioglan Anti-Thyroid. Indications: All the various stages of hyperthyroidism, including Graves' disease. Many of the so-called nervous hearts, or forms of anxiety, depression, irritability, sudden spells of fatigue, are due to a thyrotoxic condition. The formula contains all those principles which are directed against the thyroid hormone and to calm the vegetative system. Supplied in capsule form for oral administration. Composition: Sodium thiosulphate gr. 7, pancreas (anti-thyroid principle) gr. 7, orchitin gr. 2, ovary gr. 2, quinine sulphate gr. ½, vitamin A 10,000 I.U. Three doses daily immediately before meals. Where, however, the B.M.R. is higher than 20 per cent, a dose should be prescribed every two hours until the improvement is striking and the B.M.R. has decreased. In all cases amelioration of nearly all the characteristic signs and symptoms can be expected within 14 days. Treatment can then be prolonged on two doses daily, later tapering off to one dose. (Bioglan Laboratories Ltd., Hertford, Herts.)

Bioglan Vitaminisers. Indicated for all cases of vitamin deficiency, tissue acidity, fatigue, lack of concentration and endurance, exhaustion, and depression. Supplied in a hard-shell capsule to be taken three times a day before meals. Composition: Potassium phosphate B.P.C. gr. 3, calcium phosphate B.P. gr. 3, magnesium phosphate B.P.C. gr. 1½, urea B.P. gr. ½, adrenal cortex gr. 1. The task of these mineral salts is to bring about a better utilization of all the various vitamins by alkalizing the tissues and strengthening the electric forces of the tissues. This action will be directed by the proper mineral balance of potassium and phosphorus within the tissues being increased while sodium (salt) will be depressed. Individuals unable to assimilate vitamins are frequently encountered in Great Britain, but in tropical and semi-tropical countries they are much more common. In hot countries perspiration involves an increased intake of salt: hence the greater need for the Bioglan Vitaminiser. To speed up recovery after infectious diseases, a double dosage (two capsules thrice daily) for the first ten days will be found to be most useful. It has recently been demonstrated that patients on sulphonamides are particularly susceptible to general vitamin deficiency, presumably due to the drying up of the body's natural sources of supply. Hence the need for the augmented vitamin dosage (especially B) where patients are undergoing sulpha drug therapy. (The Bioglan Laboratories, Ltd., Hertford, Herts.)

Calcium 'Diuretin' with Phenobarbitone (Knoll). A combination of theobromine and calcium salicylate with phenobarbitone. Intensive purine medication without excessive sedation. To relieve anxiety and nervous tension in spastic cardiovascular conditions. (Savory & Moore Ltd., Welbeck Street, London, W.1.)

'Chronalgicin'.

Composition:		
	Mild silver proteinate B.P.C.	10% w/v
	Mono phenyl ether of ethylene glycol	2% v/v
	Phenyl mercuric nitrate	0·1% w/v
	Urea	20% w/v
	Ephedrine sulphate	1% w/v
	Industrial methylated spirits	10% v/v
	Water	q.s.

Indications: Application for the treatment of chronic otitis media. Method of use: Care is taken in application to ensure entry of solution into the middle ear. It may be necessary to continue treatment for some weeks before a dry ear is obtained. (Manufactured by Benger's Limited, Holmes Chapel, Cheshire.)

Collumina Suspension. A suspension containing 5 to 6 per cent aluminium hydroxide, suitably preserved and flavoured. Indications: For the adjuvant treatment of peptic ulcers, ulcerative colitis, hyperacidity, etc. Dosage and Administration: 1 to 3 drachms (4-12 c.c.) in about four times the volume of water. (Evans Medical Supplies Ltd., Speke, Liverpool, 19.)

Collumina Tablets. Tablets containing active aluminium hydroxide. These tablets are especially convenient for travellers. Indications: Same as for the liquid preparation above. Dosage and Administration: One to three tablets chewed and washed down with a little water. (Evans Medical Supplies Ltd., Speke, Liverpool, 19.)

Crookes Stilboestrol and Lactic Acid Pessaries. Stilboestrol 1 mg., lactic acid 1 per cent. in a gelatin base. Indications: Senile atrophic vaginitis, kraurosis vulvae and pruritus vulvae, and *Trichomonas vaginalis* infection. Dosage: One or two pessaries daily or as prescribed. Packed in *boxes of 6*. (Also available, pessaries containing stilboestrol 5 mg., lactic acid, 1 per cent, in boxes of 6). (The Crookes Laboratories, Ltd., Park Royal, London, N.W.10.)

Crookes Vitamin B Complex Tablets. Aneurine hydrochloride 1 mg., riboflavine 1·25 mg., mesinamide 10 mg., yeast powder 225 mg. in sugar coated tablets. Indications: Nutritional deficiencies. Dosage: One or two tablets daily, or as prescribed. Packs: 25, 100, and 1000 tablets. (The Crookes Laboratories Ltd., Park Royal, London, N.W.10.)

Crystules. Aqueous crystalline suspensions of hormones for depot therapy lasting several weeks. Crystules are available as follows:

Perandron Crystule, 2 c.c., containing 50 mg. testosterone propionate B.P.

Luteocyclin Crystule, 2 c.c., containing 50 mg. progesterone B.P.

Oocyclin B Crystule, 2 c.c., containing 10 mg. oestradiol monobenzoate B.P.

Percorten Crystule, 2 c.c., containing 50 mg. deoxycortone acetate B.P.

Dosage: One or two Crystules by intramuscular injection 02 mg. nupercaine is included to produce local anaesthesia. (Ciba Laboratories Ltd., Horsham, Sussex.)

'Cuprelone'. Composition: Cuproallyl-thiourea-metasodium benzoate, containing approximately 19 per cent copper. Indications: As a substitute for gold in rheumatoid arthritis, certain forms of tuberculosis, and skin diseases (e.g., lupus erythematosus); also used in disseminated sclerosis and trigeminal neuralgia. Dosage: 10 to 100 mg. given intravenously in graduated doses. Packings: Ampoules of 10 mg., 25 mg., 50 mg., 75 mg., 100 mg. (Bayer Products Limited, Africa House, Kingsway, London, W.C.2.)

Deoxycortone Acetate B.D.H. An ester of the principal hormone of the suprarenal cortex, desoxycorticosterone, which is prepared synthetically and conforms with the specification for Deoxycortone Acetate B.P. It is indicated specifically in the treatment of Addison's disease. Other indications are the prevention of surgical shock, the treatment of toxaemia resulting from burns and other toxaemic states, muscular dystrophy, chronic fatigue, asthma, hypotension, and intestinal obstruction and intussusception. Deoxycortone Acetate B.D.H. is administered intramuscularly in doses of 2 to 10 mg. daily. For toxaemic states and intestinal obstruction 2 to 5 mg. every two hours may be given. Pellet implants of Deoxycortone Acetate B.D.H. in doses of 50 to 200 mg. are indicated in Addison's disease. For intramuscular injection, ampoules of 5 mg. in 1 ml. and 10 mg. in 1 ml. are available and for implantation, pellets of 50 mg., 100 mg., and 200 mg. are issued. (The British Drug Houses Ltd., Graham Street, London, N.1.)

D.F.P. Boots. Sterile 0·1 per cent solution of diisopropyl fluorophosphonate in arachis oil. For the treatment of glaucoma, post operative paralytic ileus, and myasthenia gravis. Supplied in bottles of 10 ml. and boxes of 6 2 ml. ampoules. (Boots Pure Drug Company Limited, Nottingham.)

D.F.P. (Di-Isopropyl-Fluorophosphonate). A synthetic compound whose action resembles but has been found more effective than those of physostigmine and neostigmine. Indications: glaucoma, myasthenia gravis and ileus paralyticus.

Eye drops, 0·05 or 0·1 per cent. in arachis oil. Dosage: Two or three drops daily, later reduced to one drop.

Injection solution, 0·1 per cent in ampoules of 2 c.c. Dosage: from 2 c.c. twice hourly to 0·25 c.c. daily. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Dienoestrol Ointment B.D.H. An ointment containing 2·5 per cent Dienoestrol B.D.H. in an emulsifying wax base. It is recommended especially for the treatment of meteorismal and senile dermatoses, and for such conditions as acne vulgaris, of long standing, acne rosacea, ichthyosis capitis, verrucae seniles, keratoderma, chaulmoogra and other dermatoses arising from disturbances due to hormonal imbalance. The ointment is applied lightly to the affected areas, half an inch of "ribbon" of ointment, well rubbed in, being used daily. Issued in collapsible tubes containing 1 oz. (The British Drug Houses Ltd., Graham Street, London, N.1.)

'Diparcol'.—Brand of diethazine hydrochloride; β-diethylaminoethyl-N-phenthiazine hydrochloride. Indications: When administered continuously, 'Diparcol' has been found to produce symptomatic improvement in a significant minority of cases of Parkinson's syndrome and certain other extra-pyramidal disorders. Dosage and method of administration: Parenteral use is rarely indicated. Oral administration should commence with small daily doses of 2 to 5 tablets each containing 0·05 g. The daily dose is then increased until the most effective dosage is reached. (This may vary between 0·5 and 1·5 g. per day.) Supplied as: Tablets—sugar-coated—in containers of 100 × 0·05 g., 500 × 0·05 g., 50 × 0·25 g., and 500 × 0·25 g. Solution: Ampoules of 5 c.c. (each 5 c.c. contains 0·25 g. diethazine hydrochloride). As the sudden withdrawal of this drug may give rise to serious reactions, continuity of supply is of unusual importance and may be critical. (Pharmaceutical Specialities (May & Baker) Ltd., Dagenham.)

Diphtheria Prophylactic P.T.A.P. ('Wellcome' Brand). A suspension of highly purified diphtheria toxoid adsorbed on aluminium phosphate. Its method of preparation is designed to reduce to a minimum protein and nitrogen compounds other than the specific toxoid. Each c.c. contains at least 50 Lf. doses of toxoid and 10 mg. of aluminium phosphate. It is similar to P.T.A.P. introduced by Holt (*Lancet*, 1947, I, 282, 286, and 385), but a newer method of obtaining the pure toxoid is used and the aluminium phosphate is prepared differently. The comparative effectiveness of P.T.A.P. and A.P.T. cannot be fully evaluated as yet. The elimination of foreign protein in this new preparation should make it less likely to produce untoward reactions, particularly in older children and adults. A more definite statement cannot be made, as pure toxoid is itself a protein substance and may give rise to some reaction. Antigenicity tests show that P.T.A.P. is as good as A.P.T. in exciting the production of antitoxin, but whether this effect is as lasting is not yet certain. A.P.T. contains, in addition to the specific toxoid, a considerable amount of bacillary protein the role of which in the production of 'complete' immunity is not known. It must be regarded as possible that this material, removed in the preparation of P.T.A.P., may play a valuable part in preventing diphtheria in actively immunized subjects. Two doses, each of 0·5 c.c., at intervals of four weeks to three or even six months, are recommended. P.T.A.P. is issued in rubber-capped bottles of 1 c.c. and 10 c.c. (Prepared at the Wellcome Research Laboratories. Supplied by Burroughs Wellcome & Co. (The Wellcome Foundation Ltd.), 183 193, Euston Road, London.)

'Edrisal'.—In the symptomatic treatment of pain, this preparation provides not only the traditional analgesic action of aspirin and phenacetin, but also the unique anti-depressant effect of 'Benzedrine'. This double action makes 'Edrisal' particularly useful in a wide range of conditions characterized by pain and the mental depression that almost always accompanies pain. 'Edrisal' has been found unusually successful in dysmenorrhœa, relief being obtained by 293 out of 329 patients in one series and by 283 out of 301 in another. Other indications include: simple headache, influenza, sinusitis, neuralgia, and nausea and joint discomfort. The usual dose is two tablets, repeated in three hours if necessary. 'Edrisal' is issued in bottles of 25 and 250 tablets, each containing amphetamine ('Benzedrine') sulphate ½ gr., aspirin 2½ gr., phenacetin 2½ gr. Samples and literature are available on the signed request of physicians. (Manufactured and distributed by Menley & James, Ltd., 123 Coldharbour Lane, London, S.E. 5, for Smith Kline & French International Co., owner of the trade marks 'Edrisal' and 'Benzedrine'.)

Esidrone. A potent well-tolerated mercurial diuretic. Available in ampoules of 2 c.c. each containing 0·14 g. sodium salt of pyridine-dicarboxy-β-methoxy-α-hydroxy-propylamine theophylline (equivalent to 0·045 g. mercury). Indicated in cardiac œdema, renal œdema, cardiac asthma, ascites due to any cause, and obesity. The action is enhanced by previous administration of ammonium chloride. Dosage: 2 c.c. two to three times a week intramuscularly or intravenously. (Ciba Laboratories Ltd., Horsham, Sussex.)

'Estigyn'.—Ethinyl Œstradiol B.D.H., which is one of the most potent œstrogens known and is highly effective orally, is an ethinyl derivative of the naturally occurring œstrogen, œstradiol. It is indicated in the treatment of hypo-ovarianism, in menopausal disorders, for the inhibition of lactation, and in prostatic carcinoma. The dosage is 0·01 mg. to 0·05 mg. or more, one to three times daily. 'Estigyn' is issued as tablets containing 0·01 mg. and 0·05 mg. The 0·05 mg. tablets are scored to facilitate the administration of smaller doses if required. (The British Drug Houses Ltd., Graham Street, London, N.1.)

'E.S.T.P.' Dusting Powder (Martindale). Ether-soluble tar distillate, zinc oxide, amylum, and talcum. Particularly indicated in intertrigo, moist eczemas, and peri-anal pruritus. (Savory & Moore Ltd., Welbeck Street, London, W.1.)

Ethinyl (Œstradiol 'Pabyrn'. A most potent orally active natural œstrogen of low toxicity. Indications: Menopausal disorders; hypo-ovarianism; control of lactation; amenorrhœa; prostatic carcinoma. Packings: Tablets of 0·01 and 0·05 mg. (Paines & Byrne Ltd., Greenford, Middlesex.)

Ethisterone B.D.H. Tablets each containing 25 mg. in bottles of 25 and 100 are now available in addition to those of 5 mg. and 10 mg. formerly issued. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Etiecylin Linguets. Contain 0·01 mg. and 0·05 mg. Ethinyl œstradiol, the most potent orally active œstrogen. Indicated in menopausal disturbances, amenorrhœa, and other conditions associated with an œstrogen deficiency; also for symptomatic relief in prostatic carcinoma. Dosage: 0·01 mg. to 0·1 mg. daily by sublingual absorption. (Ciba Laboratories Ltd., Horsham, Sussex.)

'Ferrivenin'. Composition: Saccharated oxide of iron. Each 5-c.c. ampoule contains the equivalent of 100 mg. of iron in the form of a 2 per cent solution for intravenous administration.

Indications: For the treatment of hypochromic microcytic anæmias, especially those which prove refractory or intolerant to oral iron, and where a quick response to treatment is required, as in pre-natal iron deficiency and prior to surgery. Dosage: The contents of one ampoule will raise the haemoglobin level by 4 per cent and dosage may be calculated accordingly. (Manufactured by Benger's Limited, Holmes Chapel, Cheshire.)

Folbyden Tablets.—Each tablet contains 1·7 mg. of folic acid and 3 gr. of molybdenized ferrous sulphate. Folic acid restores haematopoiesis in macrocytic anæmias. Fortification of iron with traces of molybdenum has been reported to increase the rate of haemoglobin-formation. Indication: Normocytic anæmias that do not respond to liver extract or folic acid alone. Dosage: One tablet three times a day, preferably after meals. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Fungicidal Ointment—Boots.—Containing 5 per cent undecylenic acid, and 20 per cent zinc undecylenate in a water-miscible base. Indicated in the treatment of tinea pedis and other dermatophytoses. Supplied in tubes of 1 oz. approx. (Boots Pure Drug Company Limited, Nottingham.)

Fungicidal Powder—Boots. A dusting powder containing 2 per cent undecylenic acid and 20 per cent zinc undecylenate in a base of talc, starch, and kaolin. For the prophylaxis and treatment of tinea pedis and other dermatophytoses. Supplied in sprinkler tins of approximately 2½ oz. (Boots Pure Drug Company Limited, Nottingham.)

Gelatin Sponge, A. & H. A sterile, dry, haemostatic sponge, made by whipping a solution of gelatin into a foam and drying and sterilizing the product. Indications: Surgery, including neurosurgical, genito-urinary, abdominal, thoracic, aural, dental, orthopædic, and cardiovascular operations. The sponge is cut into pieces of the size and shape required for the operations, and is placed in sterile normal saline solution. The air and the saline solution are squeezed out. The sponge is pressed upon the bleeding point for at least two or three minutes, until it adheres. It remains there until it is absorbed. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Gertonin Tablets and Ampoules. Powerful hydrocholoretics of low toxicity. Composition: Tablets—Each tablet contains 0·25 g. dehydrocholic acid. Ampoules—contain 20 per cent solution of sodium dehydrocholate. Indications: For diseases of the gall-bladder and bile-passages; for diuresis in œdema of cardiac origin; rheumatoid arthritis; toxic hepatitis and hepatic dysfunction; as an adjunct to surgery, cholecystography, and arsenotherapy; for determining arm-to-tongue circulation time. Contra-indications: Complete mechanical biliary obstruction: should be used with caution in the presence of severe hepatitis such as acute yellow atrophy of the liver; injections of the solution are contra-indicated in bronchial asthma. Dosage: Oral—One or two tablets two to three times daily after meals. Parenteral—5 to 10 c.c. injected slowly on the first day. 10 c.c. on the second and third days. The maximum intravenous dose is 10 c.c. Packing: Tablets—Containers of 25 and 100. Ampoules—Boxes of 5 × 5 c.c. and 5 × 10 c.c. ampoules. (Ward, Blenkinsop & Co. Ltd., 6 Henrietta Place, London, W.1.)

Gluco-Thricil.—A stable combination of ephedrine (1 per cent) and the antibiotic tyrothricin (1–5000) in an isotonic dextrose base containing solubilizing and stabilizing agent. Gluco-Thricil possesses several advantages as a nasal decongestant. It is readily miscible with nasal secretions, is non-irritating, does not adversely affect ciliary action, and possesses a high penetrating power. Tyrothricin combines high bacterial activity with low tissue toxicity. Issued in bottles of 1 fl. oz. with dropper. Each batch of Gluco-Thricil is assayed to ensure full antibiotic activity. (Parke, Davis & Co., Hounslow, Middx.)

Heparin (Evans). A pure and pyrogen-free physiological anticoagulant prepared from mammalian lung. The potency is assayed against the International Standard. (This is believed to be very nearly equal to the "Toronto" unit upon which the International Standard was based). Solutions of Heparin (Evans) are extremely stable. Indications: The two main uses for heparin are as an anticoagulant *in vitro* and as a therapeutic agent *in vivo*. In the former it has been found to have many advantages in morphological and chemical analyses of blood. Therapeutically, its value and comparative safety is being increasingly recognized in mesenteric, coronary, and cerebral thrombosis, post-operative thrombophlebitis and embolic complications, vascular surgery, and blood transfusions. Dosage and Administration: As heparin is inactive orally it is usually administered intravenously. It may be given by single injection or continuous intravenous drip. The clotting time of the patient's blood should be maintained between fifteen and twenty minutes and heparin administration should be stopped immediately if a rigor or spontaneous bleeding occurs. For the interrupted dose-method 5000 units may be administered at intervals of four hours up to a total of 25,000 units per day. In the continuous drip method 10,000 to 20,000 units are added to one litre of 5 per cent sterile dextrose or isotonic sodium chloride solution, which is injected at the rate of about twenty drops per minute. The effects of heparin are dissipated in about 3 hours following injection. If an immediate effect is desirable, 5 to 10 ml. of a sterile 1 per cent solution of protamine sulphate is given intravenously, which brings the coagulation time of the blood instantaneously to normal. (Evans Medical Supplies Ltd., Speke, Liverpool, 19.)

'Heptalgin'. 6-morpholino-4:4-diphenylheptanone-3 hydrochloride. Known during early trials as "CB 11". A potent analgesic giving relief from pain in a wide range of conditions. Little or no accompanying cortical depression and slight depressant effect on the respiratory centre. Effective in 15 to 30 minutes orally, or 2 to 3 minutes intramuscularly; duration of effect 3 to 4 hours orally or 1 to 2 hours intramuscularly. Intravenous administration is undesirable. Oral dosage 10 to 30 mg. Intramuscular dosage 10 mg. Tablet of 10 mg. in bottles of 25 and 100. 1-c.c. ampoules of 10 mg. (Glaxo Laboratories, Ltd., Greenford.)

Histostab Compound Solution.— A solution of 2-(N-phenyl-N-benzylaminomethyl)-*imin*azoline sulphate 1 2000 and 2-(naphthyl methyl)-imidazoline nitrate 1–4000. An effective preparation combining antihistamine and vasoconstrictor drugs for the relief of hay fever and allergic conditions of the eye. Supplied in bottles of ½ fl. oz. (Boots Pure Drug Company Limited, Nottingham.)

Histostab, Injection of.—A sterile solution of 2-(N-phenyl-N-benzylaminomethyl)-iminazoline methanesulphonate. For the treatment of allergic conditions. Supplied in boxes of 6 ampoules, each ampoule containing 0·1 g. Histostab in 2 ml. (Boots Pure Drug Company Limited, Nottingham.)

Histostab Oral Tablets.— Each tablet contains 0·1 g. of 2-(N-phenyl-N-benzylaminomethyl)-imnazoline hydrochloride. For the treatment of allergic conditions. Supplied in bottles of 25 tablets. (Boots Pure Drug Company Limited, Nottingham.)

Hyperduric Atropine.—Contains $\frac{1}{75}$ or $\frac{1}{100}$ gr. of atropine, as mucate, in each cubic centimetre. Combination with mucic acid prolongs the action of the atropine to three hours. Indication: Preparation of children for tonsillectomy. Dosage (subcutaneously) $\frac{1}{150}$ to $\frac{1}{75}$ gr. of atropine, according to age. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Hyperduric Hyoscine.—Contains $\frac{1}{75}$ gr. of hyoscine, as mucate, in each cubic centimetre. The action of the hyoscine is greatly prolonged by combination with mucic acid. Indications: With analgesics and hypnotics in labour, and to control the tremors and spasticity of paralysis agitans and post-encephalitic Parkinsonism. Dosage (subcutaneously): In labour, 0·25 to 1 c.c.; in paralysis agitans and Parkinsonism, 0·25 c.c. daily or every second day. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Injection of Procaine Penicillin, A. & H. Contains, in each cubic centimetre, 300,000 units of penicillin and the equivalent of 120 mg. of procaine base, the two forming a chemical compound which is suspended in sterile arachis oil containing 2 per cent of aluminium stearate. Indications: To provide prolonged effective concentrations of penicillin in the blood in infections by penicillin-sensitive micro-organisms. Dosage: intramuscularly, 1 c.c., or sometimes 2 c.c. or more, daily. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

'Kapilon'. A water-soluble analogue of vitamin K. Ammonium salt of menaphthone carboxymethoxime. For prophylaxis and treatment in all forms of hæmorrhage associated with low prothrombin such as neonatal hæmorrhage. Prothrombin deficiency in obstructive jaundice, non-tropical sprue, ulcerative colitis, hæmoptysis, and hæmorrhages from intensive quinine or salicylate therapy. Chronic urticaria is often greatly benefited by vitamin K therapy. Infant's dosage 0·5 c.c. Adults' dosage 1 c.c. Boxes of 6 × 1 c.c. ampoules containing 10 mg. water-soluble 'Kapilon'. 'Kapilon' is also issued as oral tablets and liquid, containing oil-soluble vitamin K analogue. (Glaxo Laboratories, Ltd., Greenford.)

Liver Extract (P., D. & Co.).—Liver Extract (P., D. & Co.) for parenteral use is a relatively "crude" extract containing the anti-anæmic activity of liver, together with other factors of the vitamin B complex. It is clinically assayed and contains two U.S.P. injectable units per c.c. Issued in 10-c.c. vials. (Parke, Davis & Co., Hounslow, Middx.)

Lynoral Tablets.— The most potent œstrogen known. Derived from the natural œstrogen. Composition: Ethinyl œstradiol (17-ethinyl-$\Delta^{1,3,5}$-$^{(10)}$-œstratriene-3:17-diol). Indications and Dosage: Menopause: 0·005 mg. to 0·05 mg. daily. Amenorrhœa: 0·05 mg. daily for 20-day spells with 10-day intervals. Inhibition of Lactation: 0·1 mg. b.i.d. for 2 days, then 0·05 mg. b.i.d. for 2 days, then 0·05 mg. once daily for 3 days. Induction of labour: 6 tablets of 0·05 mg. every 2 hours up to 15 doses. Menorrhagia: 0·3 mg. daily from 5th to 25th day of cycle (plus progesterone 5 mg. daily from 21st to 25th days). Essential dysmenorrhœa: 0·05 mg. daily for 24 days beginning at least 24 days prior to the next period. Acne: 0·15 mg. to 0·30 mg. daily. Carcinoma of the prostate: 1 to 3 mg. daily. Carcinoma of the senile breast: 0·15 to 0·7 mg. daily. Tablets each containing 0·01 mg. or 0·05 mg. of pure crystalline ethinyl œstradiol. The 0·05 mg. tablets are scored for halving. (Organon Laboratories Ltd., Brettenham House, Lancaster Place, W.C.2.)

Methyl-testosterone B.D.H.— Tablets containing 10 mgs., 25 mgs., and 50 mg. have now been introduced. They are indicated for the treatment of severe cases of mastitis, mastodynia, dysmenorrhœa, and metrorrhagia, for breast cancer and metastases therefrom in the female, and for severe cases of eunuchoidism and eunuchism in the male. Issued in bottles of 25 and 100. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Myanesin Brand Elixir (Elixir of Mephenesin B.D.H.). A pleasantly-flavoured palatable elixir containing 1 g. of Mephenesin (*α*: *β*-dihydroxy-*γ*-(2-methylphenoxy)-propane) in each 15 ml. Has been found to be effective in such conditions as epileptiform convulsions, spastic hemiplegia and paraplegia, cerebral diplegia, and the muscular spasm of arthritis, osteo-arthritis, and tetanus. Myanesin Brand Elixir is also of some value in paralysis agitans. The usual dosage of Myanesin Brand Elixir is one tablespoonful (1 g. of Mephenesin) from one to five times daily according to the response obtained. Myanesin Brand Elixir is issued in bottles of 8 and 40 fl. oz. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Naphthocaine Jelly.— A water-soluble jelly containing 1 per cent naphthocaine hydrochloride, useful for relief of pain in all conditions permitting surface anæsthesia. It is of particular value in hæmorrhoidectomy or in inoperable cases of hæmorrhoids, and is highly satisfactory for anæsthetizing the urethra prior to cystoscopic examination and urethral dilatation for adhesion or strictures. Issued in ½-oz. collapsible tubes with elongated nozzles. (Parke, Davis & Co., Hounslow, Middx.)

'Neodrenal' Brand Isopropyl Adrenaline. *A new 'oral' preparation of adrenaline for bronchial asthma. A potent bronchodilator: well tolerated, prompt in action, adrenaline injections unnecessary, superior to ephedrine.* Issued in the form of *sublingual tablets* and *a spray* solution. (Savory & Moore Ltd., Welbeck Street, London, W.1.)

'Neo-Epinine' Brand Isopropylnoradrenaline. *A recently developed homologue of adrenaline for the treatment of bronchial asthma.* Equal to adrenaline and superior to ephedrine in anti-asthmatic activity, it is effective when taken sublingually or by oral inhalation. Thus the necessity of giving injections is avoided. 'Neo-Epinine' is relatively free from the cardiovascular and other side-effects of adrenaline and does not give rise to the sleeplessness and excitability produced by ephedrine. Issued as 'Tablond' Brand Compressed products for *sublingual administration, each containing* 20 mg., in bottles of 25, 100, and 500; dosage varies considerably but, in general, 10 to 30 mg. (½ to 1½ products) should be given three times a day initially. For oral inhalation, a 1 per cent Spray Solution is available in bottles of 10 c.c. (Burroughs Wellcome & Co. (The Wellcome Foundation Ltd.), 183 193, Euston Road, London.)

'Neo-Octon' (Knoll). Isoamylamino-methylheptane a new synthetic antispasmodic Indicated in conditions in which it is desired to relieve smooth muscle spasm. It is well tolerated and gives prompt relief. (Savory & Moore Ltd., Welbeck Street, London, W.1.)

Oestroform. The principal use of Oestroform by implantation is for the relief of menopausal symptoms. Such symptoms can usually be controlled by an implant of 20 mg., the implant remaining effective for six months or more. Pellets containing 20 mg. of oestradiol in tubes of 1 pellet. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Paromin. Coated tablets containing organically combined iodine equivalent to 1 gr. of 0·5 per cent iodine content thyroid: high potency, well tolerated. Indications: Obesity; hypothyroidism. Packings: Bottles of 100 tablets. (Paines & Byrne Ltd., Greenford, Middlesex.)

P.A.S. (Para-aminosalicylic Acid.) *A chemotherapeutic agent which inhibits the growth of tubercle bacilli.* Composition: Supplied as the solid sodium salt dihydrate, 100 g. of which are equivalent to 72·5 g. P.A.S. Indications: For the treatment of certain forms of tuberculosis. Dosage: Oral 15 to 25 g. daily in divided doses. Intrapleural 10 c.c. of a 20 per cent solution weekly. (Ward, Blenkinsop & Co., Ltd. 6 Henrietta Place, London, W.1.)

P2G Sclerosant. A sterile solution containing 2 per cent phenol, B.P., 25 per cent dextrose, B.P., 30 per cent glycerin, B.P., in water for injection, B.P. Indicated in the injection treatment of varicose veins, and, indirectly, in the treatment of varicose ulcers and varicose eczema. Supplied in vials of 30 ml. (Boots Pure Drug Company Limited, Nottingham.)

Penicillin Chewing Gum, A. & H. Contains 5000 I.U. of penicillin in each piece. Indications: For maintaining prolonged local concentration of penicillin in infections of the mouth by penicillin-sensitive micro-organisms, e.g., tonsillitis, Vincent's angina, pyorrhœa, and streptococcal sore throat, and before and after tonsillectomy, particularly if the tonsils are infected. Dosage: Three or four pieces daily, each to be chewed for two to four hours, between meals. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Penicillin Ophthalmic Discs. Each disc contains 250 I.U. of penicillin (calcium salt), B.P. Indicated in the treatment of blepharitis, acute conjunctivitis, and superficial corneal ulcers. Supplied in tubes of 20. (Boots Pure Drug Company Limited, Nottingham.)

Penicillin Oral Tablets (Potassium Salt). Tablets containing 50,000 and 100,000 I.U. of penicillin (potassium salt), with or without 0·5 g. of sodium citrate per tablet. Indicated in gonorrhœa, childhood infections, and where parenteral penicillin therapy is impracticable. Supplied in bottles of 20, 100, and 500 tablets. (Boots Pure Drug Company Limited, Nottingham.)

Penicillin Preparations B. W. & Co.

Crystalline Penicillin G. For use where a particularly pure form of penicillin is required. Storage in a refrigerator is not required. Issued in containers of 0·1 mega unit.

Crystalline Procaine Penicillin G in Oil ('Wellcome' Brand). A suspension of the crystalline procaine salt of penicillin G, 300,000 I.U. per ml., in a vehicle consisting of arachis oil with 2 per cent of aluminium stearate. The penicillin is slowly liberated from the site of injection, so that widely spaced injections suffice to maintain a therapeutically effective concentration of penicillin in the blood. Both procaine penicillin and the vehicle are well tolerated. The preparation is given by intramuscular injection, the minimum daily dose in infections due to the more penicillin-sensitive organisms being 300,000 units (1 ml.); less susceptible infections may need a minimum dose of 600,000 units (2 ml.). Issued in rubber-capped bottles of 10 ml.

'Tablond' Brand Penicillin for Oral Administration. The issue of a 100,000 I.U. product (scored for division into two), as an addition to the 20,000 I.U. strength already available, enables doses of 20,000, 50,000, and 100,000 units, or multiples of these, to be given conveniently. The new product is issued in tubes of 10 products.

'Wellcome' Brand Penicillin Oil Wax Suspension. Now available in two strengths—300,000 and 125,000 I.U. per c.c., each in rubber-capped bottles of 10 c.c.

(Burroughs Wellcome & Co. (The Wellcome Foundation Ltd.), 183 193 Euston Road, London.)

Penicillin Snuff. A simple and efficient means of producing an even concentration of penicillin in the nose and upper pharynx. It contains 5000 I.U. of penicillin (calcium salt) B.P. per grainme in a lycopodium and lactose base. Supplied in containers of 120 gr. (Boots Pure Drug Company Limited, Nottingham.)

Penicillin Solution-Tablets B.D.H. Each solution-tablet contains 10,000 I.U. of penicillin calcium salt. These tablets are convenient and economical in dispensing small quantities of penicillin preparations for external use. Penicillin Solution-tablets B.D.H. are also suitable for oral administration. The tablet should be dissolved in water and taken with sodium citrate or milk to inhibit inactivation. Dosage is four times that which is required by injection. Penicillin Solution-tablets B.D.H. are packed in tubes of 10; tubes are packed singly or in boxes of 6. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Pernivit. A combination of Acetomenaphthone B.P. 7 mg. and Nicotinic Acid B.P. 25 mg. in tablet form for the treatment of chilblains at all stages of development. Dosage for adults, 2 to 9 tablets daily, and for children, 1 to 6 tablets daily. Pernivit is issued in bottles of 50 and 500 tablets. (The British Drug Houses Ltd., Graham Street, London, N.1.)

'Persedon'. The trade mark 'Persedon' is applied to a new sedative and hypnotic of unique composition, chemically described as 3,3 diethyl-2 4-diketotetrahydrooxazine. Belonging neither to the barbituric acid group nor to the oxides, the drug represents an entirely new type of hypnotic. The safety margin is wide. The therapeutic effect is rapid but not unduly prolonged, and 'Persedon' can therefore be taken during the night when only a few additional hours of sleep are desired. It is issued in tablets of 0·2 gm. in packages of 20, 100, and 500. (Roche Products Ltd., Welwyn Garden City, Herts.)

Pethidine-Scopolamine 'Roche'. The sedative action of pethidine hydrochloride is not pronounced, and when amnesia is desired it has been found advantageous to combine pethidine with scopolamine or hyoscine. Pethidine Scopolamine 'Roche' has an analgesic and anti-spasmodic action and also produces sedation; it is reported to be unsurpassed by any other drug or combination of drugs for the relief of pain in labour. Each 2-c.c. ampoule contains pethidine hydrochloride 100 mg., scopolamine gr. $\frac{1}{150}$ (0·43 mg.). Pethidine Scopolamine 'Roche' is issued in boxes of 12 and 100 ampoules. (Roche Products Ltd., Welwyn Garden City, Herts.)

Phenobarbitone and Hyoscine Tablets. Each tablet contains phenobarbitone sodium, B.P. gr. $1\frac{1}{2}$, hyoscine hydrobromide, B.P. $\frac{1}{200}$ gr. A powerful combination of phenobarbitone sodium and hyoscine hydrobromide for the treatment of acute anxiety states and allied conditions. Supplied in bottles of 25 tablets and 100 tablets. (Boots Pure Drug Company Ltd., Nottingham.)

Picrotoxin, Injection of, B.P. A 0·3 per cent sterile aqueous solution of picrotoxin for the treatment of severe barbiturate poisoning. Supplied in boxes of 6 ampoules, each ampoule containing 3 mg. picrotoxin per ml. Also supplied in vials of 20 ml. (Boots Pure Drug Company Limited, Nottingham.)

Priscol. A powerful vasodilator. Is 2-benzyl-1:4:5-imidazoline hydrochloride. It acts on the autonomic nervous system producing dilatation of small blood vessels. Indicated in peripheral vascular disorders, Raynaud's syndrome, thrombo-angiitis obliterans, intermittent claudication, and ophthalmic conditions in which hyperæmia is required. Dosage is initially small and gradually increased according to patient's tolerance and requirements. Tablets 25 mg., ampoules 1 c.c. 10 mg., and for local application ointment 10 per cent W/W and solution 10 per cent W/V. (Ciba Laboratories Ltd., Horsham, Sussex.)

Procaine Penicillin G Oily Injection. Each c.c. contains 300,000 units penicillin combined as procaine penicillin in a sterile suspension in arachis oil. Of the total procaine penicillin content not less than 90 per cent by weight is the procaine salt of penicillin G. Produces a prolonged penicillin concentration in the blood. 1 c.c. intramuscular injection provides a therapeutic level lasting for 24 hours in most cases. Rubber capped vials of 10 c.c. (Glaxo Laboratories, Ltd., Greenford.)

Progestin B.D.H. An additional strength of solution has now been introduced for convenience in administering the larger dose now prescribed in cases of threatened abortion and severe metrorrhagia. Issued in ampoules containing 25 mg. in 1 ml. in boxes of 1, 3, and 12 ampoules, and in rubber capped vials of 10 ml. (25 mg. per ml.). Implantation pellets are used primarily in the treatment of habitual abortion. Pellets containing 100 mg. in tubes of 1 pellet. (The British Drug Houses Ltd., Graham Street, London, N.1.)

Pyribenzamine. A potent well-tolerated antihistamine. Is N-benzyl-N(2-pyridyl)-N'-dimethyl-N-methylenediamine monohydrochloride. Indicated in all allergic conditions, including urticaria, hay fever, drug reactions, angioneurotic edema, allergic eczema, and pruritic dermatoses. Dosage: 0·05 to 0·6 g. daily (children's dosage being proportionate to age). Tablets 0·05 g., 1·0 g. (suitable for children) 0·02 g. dr. (Ciba Laboratories Ltd., Horsham, Sussex.)

Rohaden Tablets and Ampoules. Composition: Proteolytic-free gastro-intestinal tissue extracts. Indications: For the treatment of duodenal and gastric ulcer; duodenitis and gastritis. Dosage: Parenteral: Deep intramuscular injections of 1 c.c. daily or on alternate days to a total of 12 to 16 injections. Oral: One tablet three times daily before meals concurrently with the injections, and thereafter, one tablet three times daily for a further four weeks and two tablets daily for two weeks. Presentation: Boxes of 6 1 c.c. ampoules for gastric ulcer. Boxes of 6 2 c.c. ampoules for duodenal ulcer. Tubes of 50 tablets.
(Makers: Robapharm Laboratories Ltd., Basle, Switzerland. Suppliers for the U.K. and Eire: Ward, Blenkinsop & Co. Ltd., 6 Henrietta Place, London, W.1.)

Steramide Ag. Composition: A solution combining the chemotherapeutic activity of sulphacetamide sodium (30 per cent) with the antiseptic properties of silver vitellin (5 per cent). Indications: For the local treatment of ocular and nasopharyngeal infections. Dosage:

Apply by instillation at regular intervals. Packing: 15-c.c. and 25-c.c. pipette bottles. (Ward, Blenkinsop & Co. Ltd., 6 Henrietta Place, London, W.1.)

Streptomycin Glaxo. Streptomycin trihydrochloride calcium chloride complex, consisting almost entirely of the salt of streptomycin A: 1 g. streptomycin base 1,000,000 'S' units antibacterial activity. Indicated as therapeutic treatment supplementary to recognized surgical procedures and general measures, in tuberculous meningitis, miliary tuberculosis, some forms of pulmonary tuberculosis. In non-tuberculous infections such as septicæmia, meningitis, tularæmia, plague, bacterial endocarditis, pneumonia, when the infection is not amenable to penicillin. Intramuscular dosage, 1 to 3 g. daily. Intrathecal dosage 0·05 to 0·1 g. daily. Oral dosage 0·5 to 1 g. daily. Issued in rubber-capped vials each containing the equivalent of 1 g. streptomycin base. Supplies for use in U.K. and N. Ireland are allocated and distributed by Ministry of Health on a regional basis. (Glaxo Laboratories, Ltd., Greenford.)

Suspension of Sulphathiazole Boots. Contains 2 g. sulphathiazole per fluid ounce, in a flavoured vehicle. Especially useful for the administration of sulphathiazole to children. Supplied in bottles of 6 fl.oz. (Boots Pure Drug Company Limited, Nottingham.)

Tabs. Phenobarbitone and Belladonna. Containing phenobarbitone B.P. ¼ gr. with dry extract of belladonna ¼ gr. Indicated in cases where it is desired to check the action of secretory glands; to relieve gastric spasm; as a mild sedative; as an ancillary treatment to the oil-inhibitive therapy for peptic ulcer by means of 'T.O.C.' Brand Trisilicate-Oil-Vitamin C Emulsion. Also useful in the treatment of whooping-cough, migraine, and epilepsy. Dose: one, two, or three tablets as directed. Packed in bottles of 25 and 100 tablets. (C. J. Hewlett & Son, Ltd., 35 43, Charlotte Road, London, E.C.2.)

Tampovagan Pessaries with Penicillin, Sulphanilamide and Sulphathiazole. Each pessary contains penicillin 5000 I.U., sulphanilamide 0·25 g., and sulphathiazole 0·25 g. Dosage according to the physician's directions. (Camden Chemical Co. Ltd., 61, Gray's Inn Road, London W.C.1.)

T.E.P.P. (Tetra-ethyl Pyrophosphate). A synthetic compound whose action closely resembles those of physostigmine and neostigmine but differs somewhat from that of D.F.P. (di-isopropyl-fluorophosphonate). It is effective by mouth. Its action is more even than that of neostigmine. Indication: Myasthenia gravis. Tablets containing 1, 2, and 5 mg. Dosage (maintenance): 8 to 12 mg. daily. Ampoules containing 5 mg. in 1 c.c. Dosage: 0·4 to 1 c.c. (2 to 5 mg.). (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Testosterone Propionate B.D.H. A new increased strength solution has now been introduced for the treatment of breast cancer in the female, for metastases therefrom, and for the prevention of recurrences after mastectomy. It is also indicated in severe cases of metrorrhagia, mastitis, and mastodynia, and in the male, for severe cases of cunuchoidism and cunuchism. Issued in ampoules containing 50 mg. in 1 ml. and in ampoules of 100 mg. in 2 ml. in boxes of 1, 3, and 12 ampoules. In rubber-capped vials of 10 ml., each ml. containing 50 mg. The principal indications for implantation of testosterone propionate are cunuchoidism and cunuchism in the male. In the female, testosterone propionate implants have proved of value in controlling severe metrorrhagia. Dosage in cunuchoidism is 100 mgs., which is effective for three months. In advanced cases of cunuchoidism and cunuchism several 100-mg. pellets may be required. In the female, three or even more 100-mg. pellets may have to be implanted. Pellets containing 100 mg. in tubes of 1 pellet Testosterone Propionate B.D.H. Testosterone B.D.H. implantation pellets are also available and the indications and dosage are the same as for Testosterone Propionate B.D.H. implantation pellets. However, pellets of testosterone propionate are absorbed less rapidly than those of testosterone. (The British Drug Houses Ltd., Graham Street, London, N.1.)

'Tineafax' Brand Compound Undecylenate Ointment and Undecylenate Powder. For the treatment of tinea pedis ("athlete's foot"). Undecylenic acid is not only active against dermatophytic fungi but it affords the blandness essential for prolonged prophylaxis and treatment. It does not break down skin in the manner of many fungicides, because it is related to the normal constituents of sweat; it is active over alkaline as well as acid *p*H ranges, and is considerably resistant to dilution by bathing and perspiration. In addition to the zinc salt of undecylenic acid, the ointment contains bactericides and other fungicides (zinc naphthenate, terpineol, phenyl mercuric acetate); and, as aids to penetration, 'Sudermo' brand Mesulphen and methyl salicylate. The ointment, which is applied night and morning, is intended for treatment; the Powder, dusted into socks and shoes, for prophylaxis. 'Tineafax' ointment is issued in tubes of 1 oz. (approx.). 'Tineafax' Powder in tins of 2 oz. (Burroughs Wellcome & Co. (The Wellcome Foundation Ltd.), 183 193 Euston Road, London.)

'T.O.C.' Brand Trisilicate-Oil-Vitamin C Emulsion. This preparation consists of a suspension of magnesium trisilicate in an emulsion of arachis oil together with a solution of vitamin C in the continuous phase. It is suitably flavoured with lemon. The *p*H of the emulsion lies between 6·0 and 7·0, so that the loss of vitamin C by alkaline hydrolysis is eliminated. Indicated in conditions of vagal overtone, peptic ulcer, and cases of anxiety neurosis and hypersensitivity leading to excessive gastric secretion. Doses: In cases where 2-hourly feeding has been ordered, 2 teaspoonfuls half an hour after each meal; where feeds are at 4-hourly intervals, 4 teaspoonfuls half an hour afterwards. Packed in bottles of 8 fl. oz. Also in bottles of 90 fl. oz. for dispensing. (C. J. Hewlett & Son, Ltd., 35 43, Charlotte Road, London, E.C.2.)

'Travikalm'. Genatosan Travel Sickness Tablets.—Composition: B.V.U. 3 gr.; Hyoscine hydrobromide $\frac{1}{200}$ gr. Indications: For prevention and cure of travel sickness on land, sea, or in the air. Dosage: 2 tablets to be taken one hour before commencement of journey. 1 tablet may be repeated at four hourly intervals, if required, during the journey. Not more than 6 tablets to be taken in 24 hours. Children under 14 years, half the adult dose. (Manufactured by Genatosan Limited, Loughborough, Leicestershire.)

Tuberculin Diagnostic Jelly (Evans). In recent years Monrad in Copenhagen and Tytler and Paterson in this country have described tuberculin jellies for use in a manner similar to Moro's ointment. Evans Tuberculin Diagnostic Jelly contains 95 per cent old tuberculin. Application: A small portion of the jelly about the size of a match-head is applied to a cleansed area between the shoulder-blades. Full directions are enclosed in each box. (Evans Medical Supplies Ltd., Speke, Liverpool. 19.)

Vioform Cream and Ointment.—Containing 3 per cent W/W iodochlorhydroxy-quinoline, a non-irritant antibacterial and fungicidal substance. Indicated in all infections of the skin, particularly those associated with pruritus—seborrhœic and atopic dermatitis, eczema, psoriasis, athlete's foot, and sycosis barbæ. (Ciba Laboratories Ltd., Horsham, Sussex.)

Virormone-Oral Methyl Testosterone. Orally active form of testosterone. Indications: Male infertility; hypogonadism; male climacteric; metropathia haemorrhagica. Tablets 5 and 10 mg. (Paines & Byrne Ltd., Greenford, Middlesex.)

Virormone-Salve. A readily absorbed salve containing testosterone. 1½ oz. jar = 90 mg., 1½ oz. jar = 225 mg. (Paines & Byrne Ltd., Greenford, Middlesex.)

Virormone Suppositories. Each containing 15 mg. male hormone. Packings: Boxes of 6 and 12. (Paines & Byrne Ltd., Greenford, Middlesex.)

'Visco-Pyelosil'. Brand of Diodone Solution (35 per cent), rendered viscous. A contrast medium, specially suitable for use in hysterosalpingography, as the viscosity prevents flow back at introduction; Probably also useful for vesico-urethrography and visualization of sinus cavities. Technique in hysterosalpingography by is essentially as for iodized oils, but rapid dispersal due to miscibility with body fluids avoids globulation, risk of oil embolism, and later irritation from unabsorbed material. Ampoules of 10 c.c. (Glaxo Laboratories, Ltd., Greenford.)

'Viskiosol' Six.—Brand of diodone viscous solution; sterile solution containing 50 per cent of diodone together with 6 per cent of polyvinyl alcohol. Indications: A water soluble contrast medium specially prepared for use in hysterosalpingography. May also be employed for urethrography and visualization of sinuses. Method of administration: As required. Administered by the same technique as used for iodized oil. Supplied: as ampoules of 15 c.c. Being water-soluble, it does not cause embolism should extravasation occur. Peritoneal spill is demonstrated within a short time of making the injection. (Pharmaceutical Specialities (May & Baker) Ltd., Dagenham.)

s 'Pulvex'. Containing vitamin A 2050 I.U.; vitamin D 300 I.U.; nicotinamide 7.5 mg.; ascorbic acid 15 mg.; riboflavin 0.5 mg. supplement. (Paines & Byrne Ltd., Greenford, Middlesex.)

Whooping-Cough Vaccines, 'Wellcome' Brand. Prepared from recent or freeze-dried strains of *Haemophilus pertussis* isolated by the cough-plate method in the smooth virulent phase I (Leslie and Gardner). Although Whooping-cough Vaccine does not confer a degree of immunity comparable with that induced by diphtheria prophylactics, wide experience amongst clinicians indicates its value in reducing the incidence and severity of the disease. Dosage consists of a series of three injections, each of 10 000 million organisms, given intramuscularly or deeply into the subcutaneous tissues at intervals of one month. Issued as 'Wellcome' Brand Whooping-cough Vaccine, 10 000 million organisms per c.c. and as 'Wellcome' Brand Whooping-cough Vaccine (Alum Precipitated) Double strength containing 20 000 million organisms per c.c.; each in rubber-capped bottles of 1 c.c. and 10 c.c. (Prepared at the Wellcome Research Laboratories. Supplied by Burroughs Wellcome & Co. (The Wellcome Foundation Ltd.), 183 193, Euston Road, London.)

MEDICAL AND SURGICAL APPLIANCES

Arthrodesis Pin Clamp. Mr. John Charnley, F.R.C.S., of Manchester Royal Infirmary, in an article in the *Journal of Bone and Joint Surgery*, August, 1948, describes a method of positive pressure in arthrodesis of the knee-joint. He quotes Albert Key's, stating that knees treated by compression union was achieved in an unusually short space of time. With Charnley's apparatus, two Steinmann pins are driven above and below through the incised joint and these pins are connected with two clamps at each end and force is exerted by screwing down the thumb-nut. Mr. Charnley, in his article, describes a special Thomas's splint with a split ring to use with his clamp. Reference should be made to the original article. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.) (*See illustration, Advt.*, p. 43.)

Automatic Air Truss Pad and Holder. A new idea project beyond the edges of the bakelite holder so that absorption to any sudden exertion or other bodily movement control of the hernia by the elastic bands of this truss the

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Bifurcated Plates. Mr. J. S. Batchelor, F.R.C.S. of Orpington has devised some special plates to use for his operation of excision of the femoral head and neck. The illustration (*see Advt.*, p. 45) shows these plates in position. For full description of the operation reference should be made to the *Post Graduate Medical Journal*, May, 1948. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.)

Calgitex Alginate Gauze and Wool, Hæmostatic, Absorbable, and Soluble. Prepared from Alginate in the forms of Wool and Gauze. All Calgitex Alginate products are 100 per cent absorbable. For use in cases of cuts, burns, ulcers, wounds, and dental hæmorrhages; also particularly useful in arresting troublesome capillary hæmorrhage in internal operations. Supplied in Fast Absorption Rate (approx. time 72 hours) and Slow Absorption Rate (approx. time 2 to 3 weeks.)

Endaural Surgery. A special grade of Calgitex Alginate Ribbon Gauze (E.N.T.—Very Slow Absorption Rate) is available to E.N.T. Surgeons for use as a post-operative dressing; can be left in place during the whole of the post-operative period and easily withdrawn.

All Gauzes supplied in convenient sizes packed in glass vials sterilized ready for use. Wool in sterilized packets. All Calgitex Alginate products can be re-sterilized if necessary and are compatible with drugs and antiseptics, including penicillin. (Manufactured by Medical Alginates Limited, Wadsworth Road, Perivale, Middx. Sole agents to the Medical Profession: Chas. F. Thackray, Ltd., Park Street, Leeds, 1, and 38, Welbeck Street, London, W.1.)

Corneal Graft Holder. Mr. John Foster, F.R.C.S., of Leeds, has devised a holder for corneal grafts which consists of a chromium-plated strainer in a small glass receptacle. The donor graft is kept on the strainer in saline solution, and when it is required the strainer can be lifted out of its container with a pair of forceps, the graft being ready to be placed in position. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.) (*See illustration, Idxt.*, p. **45**.)

Eyeball Rotating Forceps. In the *British Journal of Ophthalmology*, March, 1949, Mr. Lindsay Rea, F.R.C.S., writes as follows: "Every ophthalmic surgeon is aware of the difficulty of rotating the eyeball downwards without obscuring his view. Whether he himself or his assistant holds the conjunctival forceps, the hand holding the instrument comes up and gets in the way. The idea occurred to me to make a forceps as illustrated (*see Idxt.*, p. **46**). Each blade terminates with a bent arm which is toothed for catching the conjunctiva. The conjunctiva is seized at 6 o'clock and the spring clip fastened. The forceps then lies on the sterile towel on the patient's cheek. By simply pulling the forceps down, the eyeball can be rotated downwards, the view being uninterrupted. Many uses will be found for this instrument. With it, muscle suture is unnecessary. It always occupies a place on my operating table." (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.)

Hip Prosthesis.—Mr. Norman S. Martin, F.R.C.S., of Belfast, being dissatisfied with the results of using Smith-Petersen's hip cups for treatment of degenerative conditions of the hip, notably chronic arthritis, has designed a hip prosthesis, as shown in illustration (*see Idxt.*, p. **47**). His operation is designed to relieve pain, as it simply entails cutting off the osteo-arthritic head and part of the neck, the normal ball-and-socket fulcrum action of the hip being lost, as there are no muscles for the hip-joint to act on; by putting in this hip prosthesis he gets quite good hip action. The instruments are made in three sizes, and can be supplied by Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.)

Instruments for Internal Fixation of the Hip by means of a Lag-screw.—This is a method devised by Mr. G. K. McKee, F.R.C.S., of Norwich, of intra- and extra-articular arthrodesis of the hip in which immobilization can be obtained by internal fixation only. The whole procedure is carried out under direct vision by using Brackett's incision and approach. The articular cartilage is removed from the exposed portion of the femoral head and acetabulum, and then the lag-screw is inserted through the femoral neck, which is drilled out so that a sliding fit is obtained. The coarse thread at the upper end is made to engage in the ilium and gives firm anchorage there. The three-hole plate is secured to the lateral aspect of the femoral shaft and the two parts are then connected by a small hexagonal nut. As the shaft of the screw is a sliding fit in the neck of the femur, any tightening of this nut causes impaction of the joint line, but before this compression effect is used, the joint cavity is packed with cancellous bone from the ilium and an extra-articular graft is applied to the superior aspect. The advantages claimed by this method are that: (1) Plaster is completely avoided; (2) X-ray control at the time of operation is of secondary importance; (3) Early ambulation is possible—three weeks; (4) Rapid bony fusion of the joint takes place as a result of the early weight-bearing, firm fixation, and the use of spongy bone from the ilium for grafting. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.) (*See illustration, Idxt.*, p. **47**.)

Intubation Cannula. Mr. Alfred Walford, F.R.C.S., of Cambridge, has evolved a modification of Asherson's antrum intubation cannula for the treatment of maxillary sinusitis by instillation of penicillin. In the *Journal of Laryngology*, January, 1949, he writes: "Instead of repeated antral puncture, a curved cannula is inserted into the antrum and left in situ for five days. Twice daily, through this, the antrum is aspirated and well washed out with normal saline. The saline is displaced by a syringe full of air and 150,000 units of penicillin in 3 c.c. glycerine of tragacanth introduced. The outer end of the cannula is then closed with a metal bung. Both antra can be treated at once, but strict aseptic technique for aspirations and instillations must be observed. By curving the cannula and having different sizes, it has been found possible to insert and leave them in situ in both children and adults, without pain, or discomfort caused by the straight type. The cannulæ, which are fixed in position by means of tapes, are strapped to the face." The instruments are supplied in three sizes, for adults, children, and infants. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.) (*See illustration, Idxt.*, p. **46**.)

Kirschner's Wire with Eye at End. For operative treatment of fractured phalanges by stainless steel wire suturing, Mr. V. C. Snell, F.R.C.S., uses a 4-in. Kirschner (1·5 mm. diameter) wire with eye at end for making a hole in the fragment of the phalanges. These Kirschner wires can be supplied by Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.)

Laryngo-Pharyngoscope.—Since their late premises in Great Portland Street were demolished by enemy action in early 1941, F. Davidson & Co., now at 24a Watford Way, Hendon, N.W.4, have, until recently, been unable to supply their direct vision instrument. They have now been able to make arrangements whereby the demand for this is gradually being satisfied. (F. Davidson & Co., 24a, Watford Way, Hendon Central, London, N.W.4.) (*See illustration, Advt.* p. **43.**)

Maw's Minimatic Automatic Electric Sterilizer.—Maw's Minimatic Sterilizer embodies all the latest improvements in miniature sterilizer design. These include the following special features: Safety cut-out fitted to prevent damage to Sterilizer in the event of it boiling dry. Visible pilot light which works in conjunction with cut-out. Seamless boiler with reinforced base to prevent leakage and warping of boiler. Removable tray fitted with special handles allowing it to rest clear of water. The working capacity of the Minimatic is 4 pints and the time taken to reach boiling point with this amount of water is approximately 25 mins. Boiling time varies according to amount of water used. Standard Model suitable for A.C. 200/110 v., 200/220 v., 200/250 v. D.C. Model to order only. Wattage 600. Boiler Dimensions, 11 in. × 5½ in. × 5½ in. (S. Maw, Son and Sons, Ltd., Aldersgate House, Barnet, Herts.)

Sterivac Cannulæ.—These are manufactured from polythene, which is a transparent plastic substance. The inert character of polythene allows Sterivac Cannulæ to be inserted into the vein for a considerable time without causing local inflammatory reaction. *Indications*: Clinical reports show that transfusion can be maintained continuously into the same vein for periods up to 7 days. Sterivac Cannulæ are also used for cardiac catheterization. *Sterilization*: This is effected by boiling or immersion in a suitable antiseptic such as 1 per cent Cetrimide. *Sizes*: Internal diameters 0·5 mm. (No. 1), 1·0 mm. (No. 2), 1·5 mm. (No. 3), and 2 mm. (No. 4), in boxes of five yards. (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

Twin Chisels. For ischiofemoral arthrodesis, Mr. H. A. Brittain, F.R.C.S., of Norwich, has devised a twin chisel. The chisels have a screw to separate them; one chisel has a slot and shoulders to receive the other. After the osteotomy has been performed by the male chisel, it is tapped gently inwards until it engages in the ischium, and the female chisel is introduced below the male chisel. The two chisels are separated by means of the screw, thus making a V-shaped slot to receive the graft. The male chisel is then withdrawn, the greater trochanter hooked upwards with a retractor, and the graft tapped in along the female chisel; as it is tapped in, the female chisel is withdrawn. For full description of the use of this instrument, reference should be made to the *Journal of Bone and Joint Surgery*, November, 1948. (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.) (*See illustration, Advt.*, p. **47.**)

Varicose Vein Needle with Torpedo End. In the *British Medical Journal*, August 14, 1948, Mr. Harold Dodd, F.R.C.S., writes as follows: "The needles illustrated (*see Advt.*, p. **46**) have been used by me continuously since October, 1946. Their purpose is to abrade the interior of the internal or external saphenous vein at the operation of ligature of varicose veins. The larger extending needle is passed down the saphena magna from the groin and will occasionally travel to its full length, i.e., to well below the knee. The skin is pressed down over the rough end of the needle with the fingers and by short up and down movements the venous endothelium is mechanically scarified, thus ensuring rapid thrombosis, which will be followed by resolution and permanent obliteration of the internal saphenous trunk where it has been so treated. The smaller needle is inserted at the internal malleolus and usually passes up to the knee. This section is similarly lacerated internally. Both sections of the extending needle are made to fit a Record syringe so that sclerosing fluids can also be introduced. The roughened ends have been arrived at by repeated experiments with Down Bros. to whom I am indebted for their courtesy and assistance. I was introduced to this endothelial destruction by Dr. Field, who had seen it used by Mr. Riddoch of Birmingham, who kindly presented me with his needle. By their use a small volume of sclerosing fluid is required and permanent destruction of the internal or external saphenous veins is certain." (Down Bros. and Mayer & Phelps, Ltd., 32–34, New Cavendish Street, London, W.1.)

BOOKS OF THE YEAR

A List of English and American Medical Works and New Editions Published During the Preceding Twelve Months

For the convenience of our readers works in this list can be ordered through John Wright & Sons Ltd., Publishers of the 'Medical Annual', 42/44, Triangle West, Bristol, 8.

ANÆSTHESIA

Aids to Anæsthesia (The Students' Aids Series). By Victor Goldman. 2nd ed. Pp. 324. 85 illus. *Baillière* - - - - - - - - - - - 7*s.* 6*d.*

Anæsthesia for the Poor Risk, and Other Essays. By William W. Mushin. Pp. 75. *Blackwell* - - - - - - - - - - - 7*s.* 6*d.*

Conduction, Infiltration and General Anæsthesia in Dentistry. By Mendel Nevin and P. G. Puterbaugh. 5th ed. Pp. 428. 288 illus. *Kimpton* - - - - 42*s.*

Elementary Anæsthesia. By W. N. Kemp. Pp. 400. 100 illus. *Baillière* - 27*s.* 6*d.*

Obstetric Analgesia and Anæsthesia. By Franklin P. Snyder. Pp. 401. Illus. *Saunders* 32*s.* 6*d.*

Pediatric Anæsthesia. By M. Digby Leigh and M. Kathleen Belton. Pp. xv + 240. Illus. with photographs and drawings. *Macmillan* - - - - - - 27*s.* 6*d.*

Recent Advances in Anæsthesia and Analgesia. By C. Langton Hewer. 6th. ed. Pp. 380. 149 illus. *Churchill* - - - - - - - - - - 21*s.*

Textbook of Anæsthetics. By R. J. Minnitt and John Gilles. 7th ed. Pp. 562. 250 illus. *Livingstone* - - - - - - - - - - - 30*s.*

ANATOMY, PHYSIOLOGY, HISTOLOGY, MICROSCOPY, BIOLOGY

Aids to Biology (The Students' Aids Series). By R. G. Neill. 2nd ed. Pp. 287. 21 illus. *Baillière* - - - - - - - - - - - 6*s.*

Aids to Embryology (The Students' Aids Series). By J. S. Baxter. 4th ed. Pp. 188. 45 illus. *Baillière* - - - - - - - - - - - 5*s.*

Anatomy and Physiology and the Cause of Disease (Baillière's Elementary Tropical Handbooks). By John P. Mitchell. 2nd ed. Pp. 240. 89 illus. *Baillière* - - 5*s.*

An Atlas of Anatomy. By J. C. Boileau Grant. 2nd ed. Pp. 521. 591 illus. *Baillière* 60*s.*

Bailey's Textbook of Histology. Ed. by Philip E. Smith and W. M. Copenhaver. 12th. ed. Pp. 850. 500 illus. *Baillière* - - - - - - - - - 38*s.* 6*d.*

Essentials of Zoology. By George E. Potter. 2nd. ed. Pp. 544. 224 illus. *Kimpton* 20*s.*

First Year Physiological Technique. By Alex Comfort. Pp. 96. Illus. *Staples* 7*s.* 6*d.*

Functional Neuro-Anatomy. By A. R. Buchanan. Pp. 242. 199 illus. *Kimpton* 32*s.* 6*d.*

Hallmarks of Mankind. By F. Wood Jones. Pp. 86. 23 illus. *Baillière* - - 10*s.* 6*d.*

A Handbook of Dissectors. By J. C. Boileau Grant and R. A. Cates. 3rd ed. Pp. 249. 19 illus. *Baillière* - - - - - - - - - - 16*s.* 6*d.*

Human Embryology and Morphology. By Sir Arthur Keith. 6th ed. Pp. xii + 690. 578 illus. *Arnold* - - - - - - - - - - - 40*s.*

Human Histology. A Guide for Medical Students. By E. R. A. Cooper. 2nd ed. Pp. 444. 257 illus. (4 coloured). *Lewis* - - - - - - - - - 27*s.* 6*d.*

Human Physiology. By F. R. Winton and L. E. Bayliss. 3rd ed. Pp. 592. 248 illus. *Churchill* - - - - - - - - - - - - 25*s.*

Introduction to Physiology. By W. H. Newton. Pp. 280. 143 illus. *Arnold* 7*s.* 6*d.*

Introductory Botany. By Alexander Nelson. Pp. 488. 121 illus. *Livingstone* - 22*s.* 6*d.*

Laboratory Technique in Biology and Medicine. By E. V. Cowdry. Pp. 269. *Baillière* 22*s.*

Living Anatomy : A photographic atlas of Muscles in Action and Surface Contours. By R. D. Lockhart. 1st ed. Pp. 71. 149 illus. *Faber* - - - - - - - 12*s.* 6*d.*

A Method of Anatomy. By J. C. Boileau Grant. 4th ed. Pp. 850. 800 illus *Baillière* 38*s.* 6*d.*

Microbiology and Pathology. By Chas. F. Carter. 4th ed. Pp. 800. 200 illus. *Kimpton* - - - - - - - - - - - - 25*s.*

Mycoses and Practical Mycology. By N. Gohar. 134 illus. Pp. 221. *Baillière* - 25*s.*

Neuroanatomy. By Fred A. Mettler. 2nd ed. Pp. 536. 357 illus., 33 in colour. *Kimpton* 50*s.*

Oral Histology and Embryology. By Frederick B. Noyes. 6th ed. Pp. 433. 284 illus., and 15 plates, 11 in colour. *Kimpton* - - - - - - - - 37*s.* 6*d.*

Physiology of Exercise. By Laurence E. Morehouse and Augustus T. Miller. Pp. 353. 51 illus. *Kimpton* - - - - - - - - - - - 25*s.*

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General Index

The more important articles are in heavy type

PAGE

ABDOMINAL aorta, thrombosis of (*Fig.* 3) 54
aortic aneurysm (*Plate I*) 31
urological manifestations .. 32
auscultation 9
distension after vagal resection 125, 126
emergencies in paraplegics 10
glands, calcareous 380
injuries 9
surgery, miscellaneous 9
Abdomino-perineal excision in rectal cancer 292, 293
operation, combined simultaneous, for imperforate anus 33
Abdomino-thoracic incision in carcinoma of œsophagus 240
Aberrant goitre 356
Abidec drops 408
Abiotics in aural and nasal suppuration 41
Abortion, definition of 309
Absenteeism, investigation of 236
Abscess, amœbic, of liver 193
extradural, caused by perilabyrinthine suppuration 42
of posterior levator space 265
subdural 162
— in purulent pachymeningitis .. 43
Accident or medical inefficiency, legal decision on 182
Accidental arterial injections (*Fig.* 1) 22, 24
Acetanilide, analgesic activity of .. 30
Acetylcholine in megacolon 150
Achalasia of cardia with œsophageal carcinoma 276
Acorza liquidum 408
Actinomycetes, antibiotics from 45
Actinomycosis meningitis 210
Adaprin tablets 408
Addison's disease 11
Adenitis, cervical, tuberculous (*Figs.* 67–69) 374
Adenocarcinoma and tuberculosis of same kidney 171
"Adenoma metastatique" 356
— papillary of rectum 296
— parathyroid 249
Adenomatosis, islet cell 247
Adiposity 11
Adrenal cortical insufficiency, test for .. 11
glands 11
hyperplasia, diagnosis of cortical tumours from 12
replacement therapy in meningococcosis 213
tumour causing hypertension .. 152
— type of fulminating meningococcal septicæmia 212, 213
Adrenaline, Neodrenal Brand Isopropyl 444
Aerosols in air sterilization 15
Age and wastage in industrial populations 237
Aged, onset of peptic ulcer in 124
sick, chronic 70
Agene processing of bread 228
Agricultural worker, health of 229
Air sterilization 15
Air-borne infection 15

PAGE

Air-bubble, preliminary, in injection of varicose veins 389
"Albumin" antibody 305
Alcoholism 17
and drug addiction 17
Allergic reaction theory of rheumatoid arthritis 312
Allergy to injections for varicose veins .. 389
Alpha-tocopherol in collagenosis 402
Aluminium paste 408
Ambulation, early post-operative, and wound disruption 10
Aminopterin, treatment of acute leukæmia by 192
Amniotic fluid, pulmonary embolism by 173
Amœbic abscess of liver 193
Amputation of bone tumours .. 56, 57
— breast (*see* Mastectomy)
Amputation-neuromata of cystic duct .. 120
Amyotrophic lateral sclerosis, psychosis associated with 272
Anæmia associated with trauma and sepsis 18
in carcinoma of bronchus 65
— colon 84
— **experimental macrocytic** 18
— **hæmolytic** 19
iron-deficiency, "Ferivenin" in .. 165
— megaloblastic, vitamin B_{12} in .. 20
— **pernicious** 20
in rheumatoid arthritis 308
splenic 21
of sprue syndrome 21
Anæsthesia and analgesia 21
for cardiac surgery 22
external version under 171
inhalation 21
— intravenous (*Fig.* 1) 22
— in operations for carcinoma of œsophagus 239
Anæsthetics in *British Pharmacopœia* .. 62
Anal canal, crypts and intramuscular glands, embryology of 27
— — and its musculature, anatomy of 26
— — **fissure and allied conditions** .. 26
— — or ulcer, chronic, surgical treatment 26
— **fistula** 27
— **incontinence** 28
— pruritus 270
sphincter, external, repair of (*Plate XL*) 295
— — spasm and fibrosis of 27
— wounds of rectum and 295
— stenosis, rectoplasty in (*Fig.* 29) .. 138
Analgesia, anæsthesia and 21
— general 26
— in labour 326
— obstetric 26
— spinal (*see* Spinal analgesia)
Analgesic drugs 28
Anastomotic ulceration after gastrectomy, incidence 131
Aneurysm (*Plate I*) 31
— **arteriovenous, of lung** 194
— complicating coarctation of aorta .. 79
Angina pectoris, anoxæmia test in .. 68

PAGE

Angina pectoris, sympathectomy for .. 343
Angiocardiography 275
Angiofibroma, juvenile nasopharyngeal 224
Angioma, radiotherapy for 288
Anorectal gonorrhœa 32
— infections and their sequelæ 28
– **malignant melanoma** 32
– region, congenital abnormalities of .. 33
Anorexia nervosa and Simmonds's disease 256, 258
Anoxæmia test *in* cardiac infarction .. 68
Antenatal services, value of 326
'Anthisan' cream 408
Anthrax 33
— radiotherapy in external infection of 288
Antibiotics 45
– in *British Pharmacopœia* 61
– chemotherapy and, in colitis 83
Anticoagulants in cardiac infarction .. 69
Antiglobulin test for Rh antibodies .. 305
Antimony compounds in pulmonary bilharziasis 51
Anus, general fibrosis of, with contracture of sphincter muscles 27
– **imperforate** 33
Aorta, abdominal, thrombosis of (*Fig.* 3) 54
– **coarctation of** (*Plates IX–XIV, Fig.* 8) 76
– thoracic, clamping of 143
Aortic aneurysm, abdominal (*Plate I*) .. 31
— **urological manifestations** .. 32
– – thoracic 31
— bifurcation, resection of (*Plate VI*) .. 54
– embolectomy (*Plate VII, Fig.* 1) .. 54
– **stenosis** 34
– valves, bicuspid 79
– valvular disease 146
Aortitis, syphilitic 346
Aortography in hydronephrosis (*Plate XXI*) 169
Aphasia 34
– and artistic realization 34
Apicolysis maintained by osteoplastic flap 366
– plombage after (*Plates XLIV–XLVII, Figs.* 65, 66) 366
Appendectomy, dysmenorrhœa following 100
Appendicitis 37
– acute, causes of death in 38
– in childhood 38
— chronic, diagnosis of 38
— complicating typhoid 376
— in retreat 37
– – simulated by disease of colon .. 88
– – spasm in 38
Appendicitis-peritonitis, conservative treatment 38, 255
Appendix cases, psychological handling 38
— mucocele of 38
Aralen (*see* Chloroquine)
Arrhythmia 39
Arsenical dermatitis : treatment with dimercaptopropanol (BAL) .. 39
Arterial injections, accidental (*Fig.* 1) 22, 24
– **therapy** 40
Arteriosclerosis, aneurysm of abdominal aorta in 31
Arteriovenous aneurysm of lung 194
– fistula, pulmonary 142
Arthritic spine, hyperextension injuries in (*Fig.* 40) 249
Arthritis following hæmolytic streptococcal sore throat 317
– migratory, associated with erythema nodosum 108
– in Reiter's disease 299
– – **rheumatoid** 308
– – in carcinoma of bronchus 66
Arthrodesis pin clamp 417
Artificial insemination and annulled marriage 176

PAGE

Artificial kidney 301, 302
— **in uræmia** 378
Ascites 255
– in portal hypertension 264
Aspiration, bone-marrow 57
– in priapism 252
Atabrine (*see* Mepacrine)
Atebrin (*see* Mepacrine)
Atom bomb injuries 40
Atomic Energy Establishments, health of workers in 229
Atresia, congenital, of Œsophagus .. 240
Atrial septal defect, diagnosis from pulmonary bilharziasis 50
Attico-antrotomy, transmeatal, for chronic tympano-mastoid suppuration (*Plates XV–XVII, Figs.* 16–19) 103
Auditory meatus, external, actiology of exostosis of 102
— nerve, effects of multiple sclerosis on 104
Aural and nasal suppuration 41
– suppuration, intracranial complications 42
'Auralgicin' 408
Aureomycin 45
– antibiotic activity 46
– clinical reports 47
— in gonorrhœa 137
– lymphogranuloma venereum .. 47, 196
– pharmacology 46
— in typhus 378
Auscultation, abdominal 9
Automatic air truss pad and holder .. 417
Auto-radiography 283
Ayerza's disease 49, 50

BABCOCK-BACON pull-through operation 294
Babcock's operation for thoracic aortic aneurysm 31
Bacillary dysentery, Reiter's disease as complication of 299
Bacteræmia following dental extraction, effect of penicillin on 106
Bacterial endocarditis 106
Bactericidal mists 15
Bacteriology of diphtheria 92
BAL in arsenical dermatitis 39
– dosage of 311
— in gold toxicity 310
— pink disease 256
— toxic reactions to 310
Bandage for varicose ulcer (*Figs.* 72–75) 386
'Banocide' Brand Diethylcarbamazine 409
Banti's syndrome, œsophageal varices in 237, 238
Barium examination of œsophagus in carcinoma of bronchus 66
'Becosym' 409
Befolin Tablets 409
Benadryl 409
Benylin Expectorant 409
Beprochin (*see* Pamaquin)
Beryllium disease (*Plate XXV*) 230
Bezoars causing obstruction 159
Biceps, tendon of, lesions of 320
Bicipital groove, variations in depth 320, 321
Bicuspid aortic valves 79
Bifurcated plates 417
Bile-duct(s), anatomy of (*Figs.* 20, 21) .. 117
– carcinoma of 121
– common, indications for exploring .. 120
– **gall-bladder and, surgical diseases** (*Figs.* 20–23) 117
– increased or diminished tone in .. 121
— post-operative stricture of 121
Bilharzial cancer 53
— ureter (*Plates XLVIII, XLIX*) .. 380
Bilharziasis 318

PAGE
Bilharziasis pulmonary (*Plates II, VI*) .. 48
— — clinical picture 49
— — diagnosis (*Plate III*) 50
— — history 48
— — incidence 48
— — pathology (*Plate II*) 48
— — prognosis 50
— — treatment 51
Biliary dyskinesia 121
— infections and emetine 121
Bioglan anti-migraine 409
— anti-thyroid 409
— vitaminisers 409
'Biological stimulation' 358
Biopsy, danger of, in bone tumours .. 279
— endometrial, in sterility 331
Biotin 229
Birthmark, port wine, eradication of .. 113
Blackwater fever, prevention of 204
Bladder (*see also* Cystitis; Vesical)
— cancer of 53
— endometriosis of 52
— papilloma of, treated with podophyllin 52
— — **surgery of** (*Plates IV, V*) 51
— thrush of 54
Blalock's operation for Fallot's tetralogy 144
Bleeding peptic ulcer 124, 125
Blood, dialysis of (*Fig.* 53) .. 301, 378
— transfusion, compatibility tests previous to .. ..
— — exchange, in hæmolytic disease ..
— — Rh and .. ..
Blood-pressure, high, complicating electromarcosis 217
Blood-vessels, great, operations on heart and 144
— — surgery of 143
— **surgery of** (*Plates VI, VII, Figs.* 3, 4) 54
Bone(s) and joints, tuberculosis of, streptomycin in 363
— lesions due to typhoid 377
— metastases from breast cancer, treatment 286
— — cancer of bladder with 53
— **tumours, conservative surgery in** .. 55
— — diagnosis of 279
Bone-graft in recurrent dislocation of elbow-joint .. ..
Bone-grafting in double fracture of tibia 117
— following segmental resection of bone tumour 56
Bone-marrow aspiration 57
Books of the Year 420
Brain abscess, streptomycin in 42
Bread, agene processing of 228
Breast, amputation of (*see* Mastectomy)
— cancer (*Plate VIII, Fig.* 5) 58
— — radiotherapy in 285
— **feeding** 57
— — decline in 327
— — self-selective 57
— male, cancer of, secondary to administration of œstrogens (*Plate XXXV*) .. ..
— milk bank .. ..
— **surgery of** (*Plate VIII, Figs.* 5–7) ..
Breech presentation, version under anæsthesia in .. ..
British Anti-Lewisite 39
— **Pharmacopœia, 1948** 60
Brock's operation in valvular stenosis .. 145
Brodie-Trendelenburg test for varicose veins .. ..
Bronchial secretion, examination of, in carcinoma of bronchus .. ..
Bronchoscopy in diagnosis of carcinoma of bronchus 66
Bronchus, carcinoma of 63

PAGE
Bronchus, carcinoma of, diagnosis 66
— — symptomatology 65
— — treatment 66
Brucellosis, aureomycin in 47
'Bulging hernia' of stomach (*Fig.* 50) .. 276
Bullous cysts, giant, and pneumothorax 259, 260
— — — **of lung**
Buried grafts in repair of hernia 148
Burns in children 67

C.10 28
Cæcostomy, preliminary, in carcinoma of colon 85, 86
Cæcum, diverticulitis of, acute 96
— volvulus of 159
Cæsarean section, choice of type 175
— — pelvic delivery after 174
Calabar swellings, hetrazan in 115
Calcareous abdominal glands 380
Calcification of gall-bladder 119
— **intrapulmonary, and hæmoplasmin sensitivity** 164
— of ureter, bilharzial (*Plate XLVIII*) 380
Calcium 'Diuretin' with Phenobarbitone (Knoll) 409
Calculi, pancreatic 245
— **urinary** 384
Calgitex Alginate Gauze and Wool Hæmostatic, Absorbable and Soluble 418
Cam-Aqui 202
Camaquine 202
Cancer (*see also* Carcinoma)
— bilharzial 53
— of bladder 53
— — with bone metastases 53
— breast (*Plate VIII, Fig.* 5) 58
— — in male secondary to administration of œstrogens (*Plate XXXV*) 270
— — radiotherapy in 285
— cervix, radiotherapy in .. .. ..
— pancreas (*Fig.* 39) 245
— penile 253
— of prostate (*Fig.* 46) 268
— thyroid (*Figs.* 61–64) 356
— — metastatic nodules from 356
— and tuberculosis in same kidney 171
— in vesical diverticula .. .. ..
Capillary fragility .. ..
— hæmangioma, eradication of .. ..
Carcinoma(s) (*see also* Cancer)
— of bile-ducts 121
— **bronchus** 63
— **colon** (*see also* Colon, Carcinoma o
— — causing intestinal obstruction 159
— complicating polyposis of colon 87
— — ulcerative colitis 80
— developing from rectal polyp .. , 297
— of gall-bladder 121
— and gastric ulcer 130
— of kidney (*Plate XXIII*) .. 170
— nasopharynx 224
— **œsophagus** 238
— — achalasia of cardia with .. 276
— primary, of seminal vesicle (*Fig.* 7 396
— **of rectum** 289
— — diagnosis 289
— — group statistics 291
— — pathological factors .. 290
— — relationship to fistula-in-ano 290
— — surgical management .. 291
— **and sarcomas, solitary metastatic, lung, pulmonary resection for** . 196
— of stomach (*Plate XLI, Figs.* 54–5) 334
— thyroid and thiourea .. 351, 52, 353

PAGE

Cardia, achalasia of, with carcinoma of œsophagus 276
Cardiac (*see also* Heart)
— **infarction** 68
— surgery, anæsthesia for 22
Cardioplasty, transpleural, in cardiospasm 69
Cardiospasm 69
— after vagal resection 126
Cardiovascular abnormalities, congenital, pre-operative diagnosis of .. 144
— system, drugs acting on, in *British Pharmacopœia* 62
Caries, dental, and fluorine 91
Carriers, diphtheria, penicillin for .. 93
— typhoid 377
Cartilaginous tumours of fingers and hand (*Plate XIX*) 142
"Castrates, functional prepuberal" .. 319
Causalgia, sympathectomy for 342
Cavernous sinus thrombophlebitis .. 44
— — thrombosis 43, 44
— — — infected, drainage in 45
Cavity, pulmonary, reversed postural drainage of 365
— surgical obliteration of 365
Cellular infection by influenza virus, mode of 155
Central nervous system, drugs acting on, in *British Pharmacopœia* 62
Cerebral disease, organic, relationship of psychosis to 272
— syphilis, cysticercosis cerebri mistaken for 345
Cerebrospinal fever (*see* Meningococcosis)
— fluid, escape of, into wounds of operations on temporal bone 103
"Certuna" 201
Cervical adenitis, tuberculous (*Figs.* 67–69) 374
— block 332
— dislocations 248
— erosion and sterility 332
— mucus 332
— spine, crush fracture of 248
— — **injuries, paraplegia in** (*Plate XXVI, Fig.* 40) 247
— injury, types of 248
Cervix, cancer of, radiotherapy in .. 287
Cetavlon in *Trichomonas* infection .. 362
Chancroid 70
Chemotherapeutic action of anti-malarial drugs 202
— drugs in malaria 201
— treatment of malaria in man 204
Chemotherapy and other adjuvants in carcinoma of colon 84
— in amœbic abscess of liver 193
— and antibiotics in colitis 83
— in diseases of peritoneum 256
— diverticulitis of pelvic colon 95
— **eye affections** 109
Chicken-pox, maternal, and congenital abnormalities of fœtus .. 90, 316
Childbirth, cost of 326
Childhood, acute intussusception in .. 164
— appendicitis in 38
Children, burns in 67
— intestinal obstruction in 157
— legislation concerning 186
Chloromycetin in typhus 378
Chloroquine in malaria therapy 202, 203, 205, 206, 207
— toxic reactions to 207
Cholangiography (*Figs.* 22, 23) 119
Cholecystectomy, failed 120
— surgical technique 120
Cholecystitis, acute 118
— complicating typhoid 376

PAGE

Chondroma of hand and fingers 142
Choreo-athetosis, involuntary movements of 251
'Chronalgicin' 410
Chronic aged sick 70
— — — conditions for treatment .. 75
— — — co-ordinated service for .. 74
— — — *present conditions* 72
— — — principles of treatment .. 74
— sick, definition 71
Circumcision of adult 253
Coal miners, pneumokoniosis of 231
Coarctation of aorta (*Plates IX–XIV, Fig.* 8) 76
Coccidioidomycosis 80
Cod-liver oil as biological stimulant .. 359
Cœlioscopy 193
Coitus interruptus, nullity after 177
Colectomy in carcinoma of colon .. 85
— polyposis of colon 87
— ulcerative colitis (*Figs.* 9, 10) .. 80
Colitis, ulcerative, chronic, surgical aspect (*Figs.* 9, 10) 80
— — **medical aspect** 82
— — personality and emotional difficulties 82
Collagenoses, vitamin E in 402
Collateral circulation in coarctation of aorta (*Plates XII, XIII, Fig.* 8) 79
Collumina Suspension 410
— Tablets 410
Colon, carcinoma of 84
— — diagnosis 289
— — surgical management 85 (*Figs.* 11–15) 88
— pelvic, diverticulitis of, surgical management 95
— **polyposis of** 87
— resection of, in diverticulitis of pelvic colon 95
— — technique .. 85, (*Figs.* 11–15) 88
— **surgical diseases of** (*Figs.* 11–15) .. 88
Colostomy 90
— closure of 295
— in diverticulitis of pelvic colon .. 95
— preliminary, in gastrojejunocolic fistula 132
— stenosis 86
Compatability tests before transfusion .. 305
Compression bandage treatment of varicose ulceration 393
'Conditioned reflex' treatment of alcoholism 17
Congenital abnormality of fœtus due to "maternal disturbances" .. 113
— — — **maternal measles, mumps, and chicken-pox as cause** .. 90
— **atresia of œsophagus** 240
— cystic kidneys 168
— **eye defects** 112
— heart disease, heart murmurs in .. 146
— — — operations for 144
— malformations due to rubella during pregnancy 315
Conjunctiva, infections of, streptomycin in 111
Conjunctivitis in Reiter's disease .. 299
Convulsions following whooping-cough immunization 405
Convulsive therapy in mental disease .. 218
'Coombs' test for Rh antibodies .. 305
Copper salts in rheumatoid arthritis .. 309
Cor pulmonale in pulmonary bilharziasis 50
Corneal Graft Holder 418
Coronary artery disease, incidence of .. 34
— thrombosis with cardiac infarction, anticoagulants in 69
Cortical extirpation in Parkinsonism .. 251

PAGE

Cortical tumours, diagnosis 12
Cough in carcinoma of bronchus 65
Cranial calliper in cervical injury .. 248
Cranial-nerve palsies following meningococcosis 213
Crill No. 6 in ringworm of scalp 314
Criminal Justice 185
Crookes Stilboestrol and lactic acid pessaries 410
— Vitamin B Complex Tablets .. 410
Cruelty of invalid, legal decision on .. 170
Crush fractures of cervical spine 248
Cryptomerozoites 200
Crystalline Penicillin G. 414
— — — in oil ('Wellcome' Brand) .. 414
Crystules 410
'Cuprelone' 410
Cupro-allyl-thiourea—sodium benzoate in rheumatoid arthritis 309
Cupro-oxyquinoline sulphonate of methylamine 309
Curare 23
Curettage of bone tumours 56
Cushing's syndrome, osteoporosis of .. 250
Cystectomy in bladder cancer 53
Cystic disease causing pneumothorax .. 259
— duct, amputation-neuromata of .. 120
— kidneys, congenital 168
— mastitis, chronic 59
Cysticercosis cerebri mistaken for cerebral syphilis 345
Cystitis, diphtheritic 51
— glandularis 52
— intractable, treatment (*Plate V*) .. 51
— inveterate 51
Cystography in stress incontinence, technique 382
Cystoscopy 51
Cysto-sigmoidostomy for vesical exstrophy (*Plate IV*) 51
Cysts, giant bullous 260
— — — **of lung** 195
— mesenteric 222
— pancreatic 245
Cystological examination of gastric aspirate for carcinoma 336

"DEAD hand" 344
Death-rates, international comparability between 398
Dehydro-iso-androsterone, test for .. 13
Dental caries and fluorine 91
— extraction, effect of penicillin on bacteræmia following 106
Deoxycortone Acetate B.D.H. 410
Dermatitis, arsenical: treatment with dimercaptopropanol (BAL) .. 39
— and permanent waving 141
Dermatology, nitrogen mustard therapy in 226
Desensitization in rheumatoid arthritis .. 312
Desoxycortone therapy, danger of overdosage 12
D.F.P. (Di-Isopropyl-Fluorophosphonate) 410
— Boots 410
D.H.C.A. (11-Dehydrocorticosterone) .. 12
Diabetes, capillary fragility in 67
— **insipidus** 91
— mellitus, vesical abnormalities and .. 52
Dialysis of blood (*Fig.* 52) .. 301, 378
Diamond's rapid slide test for compatibility 305
Diathermy dissection in removal of gall-bladder 120
Diarrhœa after vagal resection 126
— neonatal 135
Dienostrol Ointment B.D.H. 410

PAGE

Diet in renal disease 300
Dietary in adiposity 11
Digitalin preparations in heart failure .. 142
Digitalization, rapid 143
Digoxin in rapid digitalization 143
Dilatation of œsophagus in cardiospasm 70
Dilators, Young's 27
Dimercaprol (*see* BAL)
Dimercaptopropanol (BAL), treatment of arsenical dermatitis with 39
'Diparcol' 411
Diphtheria 92
— immunization combined with whooping-cough immunization 464
— Prophylactic P.T.A.P. ('Wellcome' Brand) 411
Diphtheritic cystitis 51
Disabled persons, rehabilitation and resettlement of 235, 236
Disablement for pension, legal decision on 183
Disease, statistical classification of .. 400
Dislocation(s), cervical 248
— **recurrent, of elbow-joint** 93
Diverticula 160
— **of stomach** 333
— vesical, tumours in 52
Diverticulitis 95
"DME" 24
Dome boot (bandage) for varicose ulcer (*Figs.* 72–75) 386
Dressing after radical amputation of breast (*Figs.* 6, 7) 59
Droplet infections, transmission of .. 16
Drug addiction, alcoholism and 17
— — methadon and 30
Duodenal diverticula 160
— **and gastric ulcer: medical aspect** .. 122
— — **surgical aspect** (*Figs.* 24–28) .. 125
— ulcer (*see also* Peptic Ulcer)
— — subjects, follow-up of 123
Duomycin 46
Dupuytren's contracture 96
Dyskinesia, biliary 121
Dysmenorrhœa 97
— menstrual toxin and 215
— presacral sympathectomy for 100, 344
Dysphagia in carcinoma of œsophagus, palliative measures 239
— after vagal resection 126
Dysplasia, polyostic fibrous 279

EAR and nose suppuration 41
— **affections of** (*Plates XV–XVII, Figs.* 16–19) 100
— operations on modifications of operative methods 103
— suppuration, intracranial complications 42
Ecchondromas of hand and fingers .. 142
Echolalia 36
Eck fistula in portal hypertension (*Fig.* 44) 264
Ectopic ureter 380
Eczema, infantile 167
'Edrisal' 411
Elbow-joint, recurrent dislocation of .. 93
Elderly, medical service for 72
Electrocardiography 106
— in cardiac infarction 68
Electro-convulsive therapy in mental disease 218
Electron therapy 280
Electronarcosis in mental disease .. 216
11-Dehydrocorticosterone acetate, effect of 12
Embolectomy, aortic (*Plate VII, Fig.* 4) 54

PAGE

Embolism, pulmonary, by amniotic fluid 173
Embryoma, Wilms' 405
Emetine, biliary infections and 121
Emotional and personality difficulties in ulcerative colitis 82
Empyema, subdural, secondary to frontal sinusitis 44
Encephalitic type of fulminating meningococcal septicæmia 212, 214
Encephalitic-adrenal type of fulminating meningococcal septicæmia 212, 213
Encephalitis, acute diffuse 212
— post-vaccinal 323
Encephalomyelitis, post-vaccinal .. 323
Encephalopathies following whooping-cough immunization 404
Enchondroma of hand and fingers .. 142
Endaural mastoid approach 103
Endocarditis, bacterial 106
Endocholedochal sphincterotomy (*Figs.* 36–38) 243
Endometrial biopsy in sterility 331
Endometriosis of bladder 52
— causing intestinal obstruction .. 159
Endoscopy, posterior pharyngo-œsophageal perforation due to .. 264
Enteric fever spread by pasteurized milk 107, 376
Ephedrine in spinal analgesia 25
Epidemic diarrhœa of newborn 135
Epidemiology of tuberculosis 373
Epilepsy, E.C.T. (electro-convulsive therapy) and 219
Eructation, foul, after vagal resection .. 126
Erythema nodosum 108
Erythrocytic cycle in malaria .. 198, 200
Esidrone 411
Essential hypertension, classification of 344
'Estigyn' 411
'E.S.T.P.' Dusting Powder (Martindale) 411
Ethinyl Œstradiol 'Pabryn' 411
Ethisterone B.D.H. 411
Etiocyclin Linguets 411
Eumuchoidism 319
Exchange transfusion in hæmolytic disease 306
Exo-erythrocytic cycle (E.E.) in malaria 198, 200
— — effect of drugs on 203
Exostosis of external auditory canal, swimmers' 102
— hand and fingers 142
Expectation of life, loss of, legal decision on 179
External version under anæsthesia .. 171
Extracellular fluid, chemical anatomy of 300
Extradural abscess caused by perikabyrinthine suppuration 42
Extraperitoneal carcinoma of rectum .. 290
Eye affections : chemotherapy 109
— **defects, congenital** 112
Eyeball Rotating Forceps 418

FACIAL nævi 113
— nerve, neurinoma of 105
Factories Act, 1948 .. .. 187, 233
— — 1937, industrial diseases notifiable under 233
— legislation on 187
Factory doctor, appointed .. 187, 233
Fallopian tube, occluded, operation on .. 331
— — patency of, tests for 330
Fallot's tetralogy, operations for .. 144
Fatty liver disease in infants 208
Feeding of bleeding peptic ulcer .. 125
Female urethra 382
Femoral hernia 149
Femoral hernia, strangulated 149
— thrombosis, deep 392
— vein ligation, prophylactic 393
"Ferrivenin" 165, 411
Fever in carcinoma of bronchus 65
Fibroma, bleeding, of nasopharynx .. 224
Fibroplasia, retrolental 112
Fibrosarcoma, perirenal 170
Fibrosis, progressive massive 232
— and spasm of anal sphincter 27
Filariasis : treatment with hetrazan .. 114
Filatov's technique in ophthalmology, tissue therapy by 358
Fingers, surgery of hand and (*Plate XIX*) 142
Fissure, anal 26
Fistula, anal 27
— gastrojejunocolic 132
— ileosigmoidal, diverticulitis complicated by 96
— post-operative labyrinthine, method of repair 103
— pulmonary arteriovenous 142
Fistula-in-ano, relationship of rectal carcinoma to 290
Flexion injuries of cervical spine .. 248
Flexner's dysentery, Reiter's disease as complication of 299
Floss silk method in repair of hernia (*Fig.* 30) 147
Fluorine, dental caries and 91
Fœtus, congenital abnormality of : maternal measles, mumps, and chicken-pox as cause 90
Folbyden Tablets 412
Folic acid causing deficiency states .. 228
— — in pernicious anæmia 20
— — sprue syndrome 21
Foreign bodies in intestine 159
Fourneau 710 201
Fracture(s), crush, of cervical spine .. 248
— **double, and double non-unions, of shaft of tibia** 116
— following electro-convulsive therapy 219
Frontal bone, gumma of (*Plate XVIII*) 137
— sinusitis, subdural empyema secondary to 44
Fulminating meningococcal septicæmia 212, 213
"Functional prepuberal castrates" .. 319
Fungicidal Ointment—Boots 412
— Powder—Boots 412
Furniss clamp in resection of colon (*Fig.* 11) 88

GALL-BLADDER, anatomy of (*Figs.* 20, 21) 117
— **and bile-ducts, surgical diseases** (*Figs.* 20–23) 117
— calcification of 119
— carcinoma of 121
— complications following gastrectomy for peptic ulcer 131
Gall-stones 119
Gametocytes, effects of drugs on 203, 205
Gamma globulin in measles 209
Ganglionectomy, upper thoracic, for angina pectoris 343
Gastrectomy, aftermath of 131
— measured radical 130
— partial, technique of 132
— for peptic ulcer (*Figs.* 25, 26) .. 130
— — — gall-bladder complications .. 131
— post-prandial symptoms following .. 132
— as precaution against carcinoma .. 130
— total, for carcinoma 337
— valvular form (*Fig.* 26) 131
Gastric aspirate, cytological examination of, for carcinoma 336

PAGE

Gastric carcinoma (*Plate XLI, Figs.* 54–56) 334
— **and duodenal ulcer : medical aspect** .. 122
— — — **surgical aspect** (*Figs.* 24–28) 125
— function, effect of vagotomy on .. 127
— mucosa, prolapse of, through pylorus 338
— resection in carcinoma of stomach (*Figs.* 54–56) 334, 335
— retention after vagal distension
— ulcer (*see also* Peptic Ulcer)
— — vagal resection not advised in 127
Gastro-enteritis in infants .. 135
— — otitis media in 100
Gastrojejunocolic fistula 132
Gastrojejunostomy for peptic ulcer 129
Gelatin Sponge, A. & H. .. 412
Genital tuberculosis in male .. 350
Geriatric(s) 73
— definition .. ..
— patient (*see* Aged Sick, Chronic)
— service .. ..
— unit .. ..
— — functions of .. ..
Gerontology, definition .. ..
— service of .. .. ..
Gertonin Tablets and Ampoules .. 412
Gestation period, longest 178
Giant follicular lymphadenopathy 303
Gilles de la Tourette's disease ..
Glomerular nephritis .. ..
Glomerulitis, necrotizing, in periarteritis nodosa 301
Gluco-Thricil 412
Goitre, aberrant lateral 356
— — mediastinal 356
— " benign metastasizing " .. 357
— lingual (*Plates XLII, XLIII*) 355
— lymphadenoid 353, 355
— nodular, thiouracil contra-indicated for 355
Gold toxicity 310
Gonadotropic hormones, and malignant testis 350
Gonorrhœa 136
— ***anorectal*** 32
— in gynæcology 136
— penicillin-resistant, alleged .. 137
— prophylaxis 136
Grafts, buried, in repair of hernia 148
Granuloma annulare, vitamin E in 402
Granulomata in beryllium disease 230
Granulomatosis, pulmonary, in berylli disease 230
Graves' disease, radio-active iodine in .. 283
Gumma of frontal bone (*Plate XLIII*) 137
Gunshot wounds of abdomen 9
Gustatory sweating 344
Gynæcology, gonorrhœa in 136
— malignant disease in 287
— sympathectomy in 344
Gynæcomastia following starvation .. 227

HÆMANGIOMA, capillary, eradication of 113
Hæmatoma, spontaneous perirenal .. 170
Hæmolysis after transurethral resection 267
Hæmolytic anæmia 19
— disease 305
— — test for 305
— — treatment 306
— streptococcal infection, rheumatic fever connected with 307
— — spread of 16
— — **sore throat, scarlet fever and** .. 317
— — — — sequelæ of 317
Hæmopoiesis, effect of radiation on (*Fig.* 52) 283

PAGE

Hæmorrhage, functional uterine, radiotherapy in 287
" Hæmorrhoidectomy, circumferential " 138
Hæmorrhoids (*Fig.* 29) 138
Hæmosiderosis, idiopathic pulmonary .. 153
— pulmonary, radio-diagnosis of .. 275
Hair : permanent waving 139
Hamilton Russell operation for inguinal hernia 148
Hand and fingers, surgery of (*Plate XIX*) 142
Handkerchief and disease transmission .. 16
Hashimoto's disease 353
Headache, lumbar puncture 62
Health Centres 325
— **occupational** (*Plate XXI*) 229
Hearing, changes in, associated with swimmers' exostosis of external auditory canal 102
Heart block, complete, heart murmurs in 146
— disease, congenital, heart murmurs in 146
— — — operations for 144
— — **pulmonary** 142
— **failure** 142
— — in pulmonary bilharziasis .. 51
— and great vessels, operations on .. 144
— — — **surgery of** 143
— **murmurs** 146
— in pulmonary bilharziasis .. 49, 50
scleroderma 147
Heavy metals, treatment of rheumatoid arthritis with 309
Heparin (Evans) 412
Hepatitis, œsophageal varices secondary to 237, 238
'Hepato-renal syndrome' 9
'Heptolgin' 412
Hernia (*Fig.* 30) 147
— " bulging ", of stomach (*Fig.* 50) .. 276
— femoral 149
— hiatal, through defective diaphragm (*Figs.* 47–49) 275
— inguinal 147
— sliding 148
— strangulated 149
— — causing intestinal obstruction .. 156
" Herpes simplex, systemic " 167
— — virus of, infections with 168
— — — in Kaposi's eruption 167
Herxheimer pyrexia, diagnostic value .. 345
Heterotopic bone formation after suprapubic prostatectomy 267
— gastric mucosa (*Fig.* 51) 276
Hetrazan, treatment of filariasis with .. 114
Hiatal hernia through defective diaphragm (*Figs.* 47–49) 275
Hip, Instruments for Internal Fixation of, by means of Lag-screw .. 418
— Prosthesis 418
Hirschsprung's disease 150
Histamine test of phæochromocytoma 14, 15
Histoplasmin sensitivity, intrapulmonary calcification and 164
Histostab Compound Solution 413
— injection of 413
— Oral Tablets 413
Hodgkin's disease 302
— — nitrogen mustard therapy in .. 226
Hospital, General, geriatric unit in .. 72
Hormone(s), gonadotropic, and malignant testis 350
— preparations in *British Pharmacopœia* 61
— therapy in sterility 332
Human factors in industry 254
Hydronephrosis, aortography in (*Plate XXI*) 169
Hydrops fœtalis 306
Hyoscine hydrobromide in travel sickness 362
Hyperduric Atropine 413

PAGE

Hyperduric Hyoscine 413
Hyperextension injuries in arthritic spines (*Fig.* 40) 249
Hyperidrosis, sympathectomy for .. 344
Hyperinsulinism 244, 247
Hypernephroma (*Fig. XXIII*) 170
Hyperparathyroidism 249
— renal complications of 169
Hypertension 151
— aetiology 151
— associated with phæochromocytoma 14
— essential, classification of 341
— — thoraco-lumbar splanchnicectomy and sympathectomy for .. 23
— heart murmurs in 146
— malignant 342
— **portal** (*Fig.* 44) 262
— — treatment of syndrome 21
— prognosis 151
— renal lesions associated with 169
— treatment 152
— — surgical 340, 341, 342
— in young subjects 151
Hypertensive-ischæmic ulcer of leg .. 394
Hyperthyroidism, aortic stenosis simulating 34
Hypertrophic tuberculosis of ileum .. 160
Hypertrophy, right ventricular, electrocardiogram in 106
Hypogenitalism during usual time of puberty 319
Hypoglycæmia due to various pancreatic tumours 247
Hypoglycæmic attacks after vagal resection 127
Hypogonadism, male 319
Hypophysis, transplantation of, in cadaver, in Simmonds's disease .. 258
Hypoproteinæmia, pre-operative treatment of, in carcinoma of colon .. 84
Hypospadias with enlargement of prostatic utricle (*Figs.* 41–43) 253
Hypotension, intracranial 161
Hysterectomy, Cæsarean .. 175, 176

ICE-CREAM, typhoid and 376
Icterus gravis neonatorum 306
Idiopathic pulmonary hæmosiderosis .. 153
— **thrombocytopenic purpura** 273
Ileocolostomy, aseptic, with special clamps (*Fig.* 15) 89
Ileosigmoidal fistula, diverticulitis complicated by 96
Ileostomy in ulcerative colitis 80
Ileum, hypertrophic tuberculosis of .. 160
Ileus, obstruction and strangulation, diagnosis of 156
Immobilization in plaster cast in double fracture of tibia 117
Immunization, active, against influenza 155
— — in diphtheria 92
— **procedures** 153
— in whooping-cough 404
Imperforate anus 33
Incision in priapism 252
Incontinence, anal 28
— of urine, stress (*Fig.* 71) 382
Indigestion due to renal irritation .. 169
— instruction of patients on 124
Industrial disease, insurance against .. 232
— — notifiable, under Factories Act, 1937 233
— Injuries Act, 1946 233
— rehabilitation 236
Industry, human factors in 234
Infancy, gastro-enteritis in, otitis media with 100

PAGE

Infantile eczema 167
Infants, fatty liver disease in 208
— **gastro-enteritis in** 135
— irreducible intussusception in (*Figs.* 31–34) 157
— **oral penicillin in** 242
Infectious diseases : certain public health aspects 154
Infertility, sterility and 330
Inflammation, arterial therapy in reduction of 40
Influenza 155
— vaccine, results of industrial vaccination with 237
Influenzal meningitis 210
Inguinal hernia (*Fig.* 30) 147
Inhalation anæsthesia 21
Injection of Procaine Penicillin, A. & H. 413
— treatment of thrombophlebitis in varicose veins 392
— — varicose veins 389, 390
Injuries of rectum (*Plate XL*) 295
Inositol in bladder cancer 53
— use of 229
Insemination, artificial, and annulled marriage 176
Instruments for Internal Fixation of Hip by means of Lag-screw 418
Insufflation in testing patency of Fallopian tubes 331
Insulin and glucose in alcoholism .. 17
Insurance against industrial disease .. 232
Intercostal nerve block 10
International Conference at Paris, April, 1948 398
— List of Causes of Death .. 397, 398
— Statistical Classification of Diseases, Injuries, and Causes of Death 397, 399
Interstitial-cell tumours 350
Intervertebral disk, acute retrovulsion of 248
Intestinal obstruction (*Figs.* 31–34) .. 156
— — in children 157
— — complicating typhoid 376
— — due to diverticulum 160
— — — growths 159
— — *non-operative treatment* 156
Intestine(s), foreign bodies in 159
— small, tumours of 161
— ulcers of 161
— **surgery of** 160
Intra-articular injections in rheumatoid arthritis 312
Intracranial complications of aural and nasal suppuration 42
— **hypotension** 161
— **infections (subdural abscess : purulent pachymeningitis)** 162
"Intraperitoneal carcinoma of rectum" 290
Intrapulmonary calcification and histoplasmin sensitivity 164
Intravenous anæsthesia (*Fig.* 1) .. 22
— therapy in burnt children 67
Intubation Cannula 418
Intussusception, acute, in childhood .. 164
— distinguished from diverticulum .. 160
— irreducible, in infants, methods of operating (*Figs.* 31–34) 157
Invalid, cruelty of, legal decision on .. 180
Iodine, radio-active, in Graves' disease .. 283
Iron therapy 165
— — in anæmia in rheumatoid arthritis 308
Iron-founders, health of 234
Irradiation in bronchial carcinoma .. 66
— high-voltage, in carcinoma of œsophagus 239
— — histological changes produced in tumours by 282
— in Wilms' embryoma 405

Irreducible intussusception in infants, methods of operating (*Figs.* 31–34) 157
Ischæmic ulcer of leg 394
Isotopes, radio-active 282

"JACK-KNIFE" position, lateral (*Fig.* 2) 23
Jaundice, congenital hæmolytic, crisis in 19
— **physiological, of newborn** 165
Jejunal diverticula 160
Jejuno-jejunostomy in post-operative stricture of bile-ducts 121

Joint changes in carcinoma of bronchus 66
— complications following meningococcosis 213

'KAPILON' 413
Kaposi's varicelliform eruption .. 166
Katayama disease 48
Keloids, radiotherapy for 288
Kendall's Compounds 12
Kernicterus 306
Kidney, adenocarcinoma and tuberculosis of same 171
— artificial 301, 302
— carcinoma of (*Plate XXIII*) 170
— congenital cystic 168
— medial ptosis of 169
— **surgery of** (*Plates XX–XXIII*) .. 168
— — maintenance of position in (*Plate XX*) 168
Kirschner's Wire with Eye at End .. 418
Klinefelter's syndrome 319
"Knuckle pads" in Dupuytren's contracture 96
Kolff artificial kidney 301, 378
Kwashiorkor 208

LABOUR **and its complications** ..
— induction of, in hæmolytic disease 306
— prolonged, and obstetric shock .. 173
Labyrinth fenestration for otosclerosis, approach to 103
— — transtympanic route 104
— function, tests for, following streptomycin therapy 42
— repair of post-operative fistula of .. 103
Labyrinthitis following meningococcosis 213
Lanatoside in rapid digitalization .. 143
Langerhans, tumours of islets of .. 247
Laparoscopy and biopsy 193
Laryngo-Pharyngoscope 419
Lavage, placental, preparation and mode of employment 359
Legal decisions and legislation 176
Legislation 184
Leptospirosis canicolaris 187, 403
— **icterohæmorrhagica** 403
Leucocytosis in carcinoma of bronchus .. 65
Leucotomy 188
Leukæmia, acute 192
Lingual goitre (*Plates XLII, XLIII*) .. 355
Lipiodol in testing patency of tubes .. 331
Lipoma, perirenal 170
Literacy, speechlessness and verbosity .. 36
Live- and stillbirth, international definitions of 399
Liver Extract (P., D. & Co.) 413
— fatty infiltration of, in malignant malnutrition 208
— **surgery of** 193
— wounds of 193
Loa loa filariasis, treatment with hetrazan 115
Loaiasis, treatment with hetrazan .. 115
Lobectomy for metastatic hypernephroma 170
Lobotomy 191
Long-term sick, elderly 71
Louping-ill in man 193
Lucite balls for plombage (*Fig.* 65) .. 366
Lumbar puncture headache 162
— sympathectomy for resistant varicose ulcers 393
Lung, arteriovenous aneurysm of .. 194
— **giant bullous cysts of** 195
— **intralobar sequestration of, associated with abnormal pulmonary artery** (*Plate XXIV*) 195
— resection in bronchial carcinoma .. 66
— — **cinomas of, pulmonary resection for** .. ..
Lupus erythematosis, disseminated, nitrogen mustard therapy in ..
— — vitamin E in 402, 403
Lutembacher's syndrome, heart murmurs in 146
Lutocyclin Crystule 410
Lymphadenoid goitre ..
Lymphadenopathy 302
— giant follicular 303
Lymphogranuloma venereum 196
— — aureomycin in 47
Lymphogranulomatous stricture of rectum 298
Lymphoid follicular reticulosis 303
Lymphopenia of X-ray irradiation .. 284
Lynoral Tablets 413

MCARTHUR operation for inguinal hernia 147
McCarthy panendoscope 382
Macrocytic anæmia, experimental .. 18
McVay's modification of Bassini operation for inguinal hernia 147
Maingot's repair for inguinal hernia (*Fig.* 30) 147
Malaria, aetiology of: recent advances (*Fig.* 35) 196
— in man, chemotherapeutic treatment of 204
— **modern treatment** 201
Malarial spleen, ruptured 329
Male hypogonadism 319
Malignant disease in gynæcology .. 287
— — radiotherapy in 285
— — hypertension 342
— **malnutrition (kwashiorkor, fatty liver disease in infants)** 208
— **melanoma, anorectal** 32
— testis 349
Malnutrition, malignant (kwashiorkor, fatty liver disease in infants) .. 208
Manometry of bile-ducts .. 120, 121
Marriage, annulled, artificial insemination and 176
— relation of, to incidence of disease .. 328
Mastectomy, radical operation (*Plate VIII, Fig.* 5) 58
— — — dressing after (*Figs.* 6, 7) .. 59
Mastitis, chronic cystic 59
Mastoid drainage in gastro-enteritis in infancy 101, 102
Mastoidectomy, classical radical operation (*Fig.* 16) 104
— Lempert's endaural antauricular (*Fig.* 17) 104
Mastoiditis, streptomycin in 42

PAGE

Mastoiditis with gastro-enteritis in infancy 101
Maternal toxæmia, congenital abnormalities arising from 113
Maternity services, availability of, and use made of 326
Maw's Minimatic Automatic Electric Sterilizer 419
Measles 209
— maternal, and congenital abnormality of fœtus 90, 316
Meckel's diverticulum 160
Medial ptosis of kidney 169
Mediastinal goitre, aberrant 356
Medical examination of motorist, legal decision on 180
— partnerships, legislation on 184
— and Surgical Appliances 417
Medicine, social 324
Medullary tumours 13
Megacolon 150
— congenital, spinal block for 24
Meg [illegible] B_{12}
Mehlnahrschadung .. ..
Melanoma, anorectal malignant 32
Membranous dysmenorrhœa 98
Memory defects complicating electronarcosis 217
Ménière's disease, streptomycin therapy 42
— syndrome 344
Meningitis 210
— actinomycosis 210
— chemical, due to tyrothricin 41
— following spinal analgesia 25
— influenzal 210
— penicillin-resistant bacterial 210
— streptomycin in 42
— tuberculous, streptomycin in 371
Meningococcal septicæmia, chronic .. 211
— — fulminating 212
— — — treatment 213, 214
Meningococcosis 211
— complications and sequelæ 213
— prophylaxis 214
— treatment 213
— varieties 211
Meningo-encephalitis due to louping-ill 193
Menstrual toxin 214
Mental diseases : general treatment 215
— — **physical treatment** 216
— health in industry 235
Mepacrine in malaria therapy 201, 203, 204, 205, 206
— toxic reactions to 207
Mercury sulphide, tattooing with, in pruritus ani 270
— in urine in pink disease 256
Mesenteric cysts 222
— vascular occlusion 222
Mesentery, affections of 222
Metachloridine in malaria 202, 203, 206
Metastases in cancer of prostate 268, 270
"Metastasizing goitre, benign" .. 356
Methadon 28
— clinical effects 29
Methyl thiouracil 350, 351
Methyl-testosterone B.D.H. 413
Micro-arteriography (*Plates XXXVI–XXXIX*) 274
— of testicular artery 349
Miliary tuberculosis, diagnosis from pulmonary bilharziasis 50
Milk, pasteurized, spread of enteric by 107, 376
Miller-Abbott tube in carcinoma of colon 84, 85
Miracil D in schistosomiasis 318

PAGE

Miscarriage, repeated, hormone therapy in 332
Mitral stenosis 146
— — diagnosis from pulmonary bilharziasis 50
— — pulmonary haemosiderosis in .. 275
— systolic murmurs, innocent 146
Mongolism, theory of cause 113
Morphine, methadon and .. 28, 29
Morphinism 17
Mother fixation in ulcerative colitis .. 83
Motorist, medical examination of, legal decision on 180
Mucocele of appendix 38
Mucosal polyps of rectum 296
Multiple tourniquet test for varicose veins 388
Mumps orchitis : pathology of 349
— maternal, and congenital abnormality of fœtus 90, 316
Murine typhus 378
Murmurs, heart 146
Muscle relaxants 23, 24
Myanesin 23
— Brand Elixir of Mephenesin 413
Mycosis fungoides, nitrogen mustard therapy in 226
Myelitis of cervical spinal cord due to irradiation 285
Myelomatosis, multiple 222
Myomectomy in sterility 331
Myringotomy in mastoiditis associated with gastro-enteritis 101

NÆVI, facial 113
Nævus flammeus, eradication of, by tattooing 113
Naphthocaine Jelly 413
Nasal suppuration, aural and 41
Nasopharynx, tumours of : diagnosis and treatment 223
National Health Service 184
'Necrosin' 215
Needle, rough-headed, for scarification of varicose vein (*Figs.* 76, 77) .. 389
Negus hydrostatic dilator 70
'Neodrenal' Brand Isopropyl Adrenaline 414
'Neo-Epinine' Brand Isopropylnor-adrenaline 414
Neonatal diarrhœa 135
'Neo-Octon' (Knoll) 414
Neoplasms, multiple visceral 88
Nephrectomy in hypertension .. 151, 152
— Wilms' embryoma 405
Nephritis, glomerular 300
Nerve block, intercostal 10
Neurinoma of facial nerve 105
Neurogenic tumours of stomach 338
Neurosyphilis in negroes 347
— penicillin in 347
Newborn, epidemic diarrhœa of 135
— intestinal obstruction in 157
— ophthalmoblennorrhœa in, penicil as prophylactic 109
— **physiological jaundice of** 165
Nilodin in schistosomiasis 318
Nitrogen mustards in reticulosis therapy in dermatology 303
— — treatment of bronchial carcinc 226
Nivaquine in malaria 202, 206
— toxic reactions to 207
Notifiable Industrial Diseases under Factories Act, 1937 233
Novestoil in intercostal nerve block 10
Nullity after coitus interruptus .. 177

PAGE

Nurses' agency, control over 181
Nutrition and vitamins 226
Nutritional œdema 226
Nycturia in starvation 227
Nylon in repair of hernia 148

OBSTETRIC analgesia 26
— — shock 172
Obstruction, ileus and strangulation, diagnosis of 156
— intestinal (*see* Intestinal Obstruction)
— — post-prostatectomy 267
— — prostatic 267
— — ureteropelvic 159
Occasional utterances 36
Occupational health (*Plate XXI*) .. 229
— — — relationship of psychiatry to .. 235
— — morbidity 236
Ocular (*see also* Eye)
— infections, aureomycin in 47
— tuberculosis, streptomycin in .. 112
Oddi, sphincter of, abnormalities in .. 121
Œdema, nutritional 226
Œsophageal varices 237
— — — and portal hypertension .. 262
Œsophago-gastric anastomosis after transthoracic resection of upper stomach (*Figs.* 55, 56) 336
— — — **in congenital atresia of œsophagus** 241
Œsophago-gastrostomy in cardiospasm .. 69
— supra-aortic, in carcinoma of œsophagus 240
Œsophagus, barium examination of, in carcinoma of bronchus 66
— **carcinoma of** 238
— — achalasia of cardia with 276
— **congenital atresia of** 240
— peptic ulcer of, radio-diagnosis of (*Figs.* 47–51) 275
— short, due to defective diaphragm .. 275
Œstroform 414
Œstrogen therapy in prostatic cancer (*Fig.* 46) 269
— — — — cancer of breast secondary to (*Plate XXXV*) 270
— treatment in bladder cancer 53
Old age 241
— — osteoporosis of 250
— — survey related to problems of .. 325
Onchocerciasis (*O. volvulus*), treatment with hetrazan 115
Ophthalmia neonatorum, penicillin prophylaxis in 137
Ophthalmoblennorrhœa in newborn, penicillin prophylaxis in 109
Ophthalmology, tissue therapy by Filatov's technique in 358
Oral penicillin in infants 242
Orchiectomy in cancer of prostate .. 269
— tumour of testis 349
Orchitis, mumps, pathology of 349
Osteitis fibrosa disseminata 279
Osteo-arthropathy, pulmonary, in carcinoma of bronchus 66
Osteogenesis imperfecta 242
Osteomyelitis, paratyphoid 377
— of skull, spreading, subdural abscess due to 163
Osteophyte, vertebral, causing aortic thrombosis (*Fig.* 3) 54
Osteoporosis 250
Otitis externa, streptomycin in 42
— media, chronic suppurative, streptomycin in 42
— — with gastro-enteritis in infancy .. 100
Otosclerosis, labyrinth fenestration operation for 103

PAGE

Ovarian cyst, thyrotoxicosis due to (*Figs.* 58 60) 352
Ovocyclin Crystule 410
Oxycel in anal operations 139
Oxytoxic drugs in *British Pharmacopœia* 62

PABA, uses of 229
Pachymeningitis, purulent 43, 44, 162
Pain, arterial therapy in relief of .. 40
— in cardiac infarction 68
— chest in carcinoma of bronchus .. 65
— dysmenorrhœa 97
'Painful feet' in Allied prisoners of war 227
— **shoulder** 319
Palatal paresis complicating diphtheria 93
Pallalia 36
Pallilogia 36
Paludrine (*see* Proguanil)
Pamaquin in malaria .. 201, 203, 206
— toxic reactions to 207
Pancreas, cancer of (*Fig.* 39) 245
— **diseases of** (*Figs.* 36–39) 243
— **hyperinsulinism** 247
Pancreatic calculi 245
— cyst 245
Pancreatico-duodenectomy for cancer of pancreas (*Fig.* 39) 246
Pancreatitis, acute 243
— subacute (*Figs.* 36–38) 243
Pancndoscope, McCarthy 382
Pantothenic acid deficiency 227
Papillary adenoma of rectum 296
Papilloma of bladder treated with podophyllin 52
— renal pelvis (*Plate XXII*) 170
Papillorata, bilharzial, of ureter 380, 381
Para-aminosalicylic acid (P.A.S.) in pulmonary tuberculosis 368
Paralysis, cranial nerve, following meningococcosis 213
— permanent, following operations under spinal analgesia 25
Paralytic cases of poliomyelitis, symptomatology 262
Para-œsophageal hiatal hernia (*Fig.* 47) 276
— pouch complicating hiatal hernia (*Fig.* 49) 276
Paraplegia in cervical spine injuries (*Plate XXVI, Fig.* 40) 247
Paraplegies, abdominal emergencies in .. 10
Parasympathetic nervous system, anal function of 150
Parathyroid glands 249
— tumour, renal complications of .. 169
Paratyphoid osteomyelitis 377
— **and typhoid fevers** 376
Paravertebral block 342
— injection of ischæmic ulcer 394
— — technique (*Fig.* 78) 394
Paresis, palatal, complicating diphtheria 93
Parkinsonism 250
— **surgical treatment** 251
Paromin 414
Paroxysmal hypertension 152
— tachycardia, repetitive 39
Parpanit, treatment of Parkinsonism with 250
Partnership agreement, invalid, legal decision on 178
— medical, legislation on 184
P.A.S. (Para-aminosalicylic Acid) .. 414
— therapy in pulmonary tuberculosis .. 368
Pasteurized milk, spread of enteric by 107, 3 6
"Pectenotomy" 26
Pelvic delivery after previous Cæsarean section 174
Penicillin in anorectal gonorrhœa .. 32
— cavernous sinus thrombophlebitis .. 44

PAGE

Penicillin chewing gum, A. & H. .. 414
— in diseases of peritoneum 255
— eye affections 109
— meningococcosis .. 211, 213, 214
— neurosyphilis 215
— oil in gonorrhœa 137
— in ophthalmia neonatorum 137
— Ophthalmic Discs 414
— **oral, in infants** 242
— — Tablets (Potassium Salt) 414
— Preparations B. W. & Co. 414
— procaine, in gonorrhœa 136
— in purulent pachymeningitis 43, 44
— Snuff 414
— Solution-Tablets B.D.H. 415
— standard preparation 61
— in subdural abscess 162
— syphilis, Herxheimer reactions .. 345
— therapy in anthrax 33
— — bacterial endocarditis 106
— — diphtheria 93
— — scarlet fever 317
— — syphilis 347
— — — failures 348
— — Weil's disease 403
— in rat-bite fever 288
— resistance 348
— in ulcerative colitis 83
Penicillin-resistant bacterial meningitis 210
Penicillin-sulphathiazole in typhoid .. 377
Penile cancer 253
Penis, surgery of (*Plate XXVII, Figs.* 41–43) 252
Pension, disablement for, legal decision on 183
— suicide and, legal decision on .. 183
Pentamidine in myelomatosis 223
Pentaquine 201, 203, 206
— toxic reactions to 207
Pentothal sodium in electro-convulsive therapy 218
Peptic ulcer (*see also* Duodenal Ulcer; Gastric Ulcer)
— — in aged, onset of 124
— — bleeding 124, 125
— — convalescents, effect of war conditions on 131
— — gall-bladder complications following gastrectomy for 131
— — gastrectomy for (*Figs.* 25, 26) 130
— — gastrojejunostomy for 129
— — incidence of 122
— — medical management of 124
— — of œsophagus, radio-diagnosis of (*Figs.* 47–51) 275
— — perforation of (*Figs.* 27, 28) .. 133
— — — variations in frequency (*Fig.* 28) 133
— — vagal resection for 125
Perandren Crystule 410
Precorten Crystule 410
Perforation of appendix in childhood .. 38
— complicating typhoid 376
— of peptic ulcer (*Figs.* 27, 28) 133
Periarteritis nodosa 380
— — renal lesions in 301
— — — manifestations 168
Peripheral nerves, division of, in varicose ulcer 393
Perirenal hæmatoma, spontaneous .. 170
— tumours 170
Perisalpingitis, tubes after 331
Peritoneal cavity, talc powder in .. 255
— irrigation, attempts to dialyse blood by (*Fig.* 52) 302, 379
Peritoneoscopy 193
Peritoneum, diseases of 254
Peritonitis, acute, due to perforation of cancer 289

PAGE

Peritonitis, appendicitis 37, 38
— chronic encapsulating 255
— pneumococcic 255
— streptomycin in 255
Permanent waving of hair 139
Pernicious anæmia 20
Pernivit 415
'Persedon' 415
Personality changes and leucotomy .. 188
— and emotional difficulties in ulcerative colitis 82
Pertussis (*see* Whooping-cough)
Pethidine, methadon and 29
Pethidine-Scopolamine 'Roche' .. 415
Petrosal and cavernous sinus thrombosis, superior 43
Peyronie's disease 252
P.G.G.G. solution for varicose veins 389, 391
Phæochromocytomata 13, 14
— bilateral, in blood relations .. 15
— tests for 14, 15
Pharmaceutical preparations 408
Pharmacopœia, British, 1948 60
Pharyngo-œsophageal perforation, post-cricoid, due to endoscopy 264
Phenobarbitone and Belladonna Tabs. .. 416
— Hyoscine Tablets 415
Phenol in paravertebral block 343
Phenol-glycerin-glucose-gelatin solution for varicose veins .. 389, 390, 391
Pheochromocytoma (*see* Phæochromocytoma)
Phlebothrombosis 392
Phlegmasia alba dolens 393, 394
Phonocardiographic investigation of heart murmurs 146
Phrenic paralysis in giant bullous cysts of lung 195
Physeptone 28
Physiotherapy for chronic aged sick .. 74
"Picket-fence fever" 167
Picrotoxin, Injection of, B.P. 415
Pincalomas, role of, in causation of diabetes insipidus 91
Pink disease 256
Piperidyl benzodioxana test for phæochromocytoma 14
Pituitary gland 256
— pars nervosa of, agents determining and influencing functions of .. 91
Pituitrin in abdominal distension .. 126
Placenta, extracts of 359
— preserved, preparation and mode of employment 359
— removal of, incidence of obstetric shock and 173
Placental hæmorrhages, congenital abnormalities arising from 113
— lavage, preparation and mode of employment 359
Plasma volume, reduction of, in burnt children 67
Plasmochin (*see* Pamaquin)
Plasmodia, drug-resistance of 208
— effects of drugs on stages of life-cycle of 202
— life-cycle of (*Fig.* 35) 196
Plasmodium falciparum, infections due to, control of 203,
— *vivax*, infections due to, control of 203,
Plasmoquin (*see* Pamaquin)
Plastic inlay in repair of hernia 149
Pleurodesis in pneumothorax 260
Plombage after apicolysis (*Plates XLIV–XLVII, Figs.* 65, 66) 366
Pneumococcic peritonitis 255
Pneumokoniosis of coal miners 231

PAGE
Pneumokoniosis, regulations concerning 233
— of welders 232
Pneumonectomy for carcinoma of bronchus 63
Pneumonia, primary atypical 258
— slowly-resolving and recurrent, in carcinoma of bronchus 65
Pneumonitis, beryllium 230, 231
— rheumatic 307
Pneumopericardium complicating pneumothorax therapy (*Plates XXVIII, XXIX*) 258
Pneumoperitoneum in pulmonary tuberculosis 371
Pneumothorax, acute, diagnosis from giant bullous cysts of lung .. 195
— **recurrent and chronic spontaneous** (*Plates XXX–XXXIII*) 259
— **spontaneous** 260
— **therapy, pneumopericardium complicating** (*Plates XXVIII, XXIX*) 258
Podophyllin, treatment of bladder papilloma with 52
Polethene pack in pulmonary tuberculosis 366
Poliomyelitis epidemic, 1947 261
— swimming-baths and 339
Polyneuritis complicating diphtheria .. 93
Polyostic fibrous dysplasia 279
Polyposis of colon 87
Polyps, mucosal, of rectum 296
Population trends and policy 327
'Port wine' birthmark, eradication of, by tattooing 113
Portacaval shunt in treatment of portal hypertension 263
Portal hypertension (*Fig.* 44) 262
— — treatment of syndrome 21
Postericoid pharyngo-œsophageal perforation due to endoscopy .. 264
Posterior levator space, abscess of .. 265
Post-operative ambulation, early, and wound disruption 10
— stricture of bile-ducts 121
Post-prandial symptoms following gastrectomy 132
Post-prostatectomy obstruction .. 267
Post-streptococcic sickle 317
Postural renal calculi, recurrent, treatment 384
— "retention" ("reversed postural drainage") in pulmonary tuberculosis 365
Post-vaccinal encephalomyelitis .. 323
Pott's operation for Fallot's tetralogy .. 145
Præquine (*see* Pamaquin)
Pregnancy complicating rectal cancer .. 293
— **diagnosis tests** (*Plate XXXIV*) .. 265
— rubella in, in causation of fœtal malformation 315
— Rh and 304
— ulcerative colitis complicating .. 83
Premature infants, retrolental fibroplasia in 112
"Prepuberal castrates, functional" .. 319
Presacral sympathectomy for dysmenorrhœa 100, 344
Priapism, persistent (*Plate XXVII*) .. 252
Priscol 415
Procaine block in causalgia 342
— injections in rheumatoid arthritis .. 313
— paravertebral injection of (*Fig.* 78) .. 394
— Penicillin G Oily Injection 413
— — in gonorrhœa 136
— — Injection of, A. & H. 413
Proctitis 266
Procto-sigmoidectomy, conservative, in rectal cancer 293
Progestin B.D.H. 415
PAGE
Proguanil in malaria 201, 203, 204, 206
— resistance to 208
— toxic reactions to 207
Prolapse of gastric mucosa through pylorus 338
— **rectum** 297
Propyl thiouracil 352
Prostate, cancer of (*Fig.* 46) 268
— **surgery of** (*Plate XXXV, Figs.* 45, 46) 266
Prostatectomy, suprapubic, heterotopic bone formation after 267
Prostatic obstruction 267
— urethritis, tuberculous 268
— utricle, enlargement of, hypospadias with (*Figs.* 41–43) 253
Prostigmine in megacolon 150
Protein deficiency and wound disruption 10
Pruritus ani 270
Pseudomonas infection of urinary tract, streptomycin in 301
Psittacosis, aureomycin in 46, 47
Psychiatric sequelæ of meningococcosis 213
Psychiatry: clinical 271
— present-day relationship to occupational health 235
Psychological handling by psychiatrists of appendix cases 38
Psychoses occurring during withdrawal of morphine 17
— organic, following leucotomy .. 191
— relationship of to organic cerebral disease 272
Psychotherapy in alcoholism 17
— ulcerative colitis 83
Ptosis, medial, of kidney 169
Puberty, time of, hypogenitalism occurring during 319
Public health, relationship of social medicine to 324
Pulmonary arteriovenous fistula .. 142
— **artery, abnormal, intralobar sequestration of lung associated with** (*Plate XXIV*) 195
— bilharziasis (*see* Bilharziasis, Pulmonary)
— embolism by amniotic fluid 173
— **hæmosiderosis, idiopathic** 153
— — radio-diagnosis of 275
— **heart disease** 142
— metastases in hypernephroma .. 170
— **resection for solitary metastatic sarcomas and carcinomas of lung** .. 196
— stenosis, operations for 145
— tuberculosis, streptomycin in 367, 369
— — **surgery of** (*Plates XLIV–XLVII, Figs.* 65, 66) 365
— — — streptomycin and 367
— — **treatment** 368
Purgatives in *British Pharmacopœia* .. 63
Purpura fulminans complicating scarlet fever 317
— **idiopathic thrombocytopenic** 273
— **thrombotic thrombocytopenic** .. 273
Purulent pachymeningitis 162
P_2G Sclerosant 414
Pyloric stenosis, organic, gastrojejunostomy for 129
Pylorus, prolapse of gastric mucosa through 338
Pyribenzamine 415
Pyrexia, Herxheimer, diagnostic value .. 345
Pyuria, abacterial, Reiter's disease and .. 299

Q FEVER, aureomycin in 46, 47
Quinacrine (*see* Mepacrine)
Quinine contra-indicated in tertian malaria 204

PAGE

Quinine in malaria 201, 206
— substitutes for 201
— toxic reactions to 207

RADIATION in bone tumours 55
— breast cancer 58
— of cervix, vesical ulceration following 52
— effect of, on haemopoiesis (*Fig.* 52) .. 283
Radio-active isotopes 282
— sclerosant for varicose veins 389
— substances, legislation on 186
Radio-chemical laboratory, administration and operation 283
Radio-diagnosis (*Plates XXXVI-XXXIX, Figs.* 47–51) 274
Radiography in beryllium disease .. 230
— carcinoma of bronchus 66
— idiopathic pulmonary haemosiderosis 153
— pneumokoniosis 231, 232
Radio-iodine in Graves' disease 283
Radio-isotopes in giant follicular lymphadenopathy 303
Radiotherapy (*Fig.* 52) 279
— in benign conditions 288
— malignant disease 285
— reticulosis 302
Radium, intra-uterine, in functional uterine haemorrhage 287
— therapy in carcinoma of œsophagus .. 239
— — Peyronie's disease 253
— — tumours of nasopharynx 224, 225
Rat-bite fever 288
Raynaud phenomenon in workers using vibratory tools 344
Rectoplasty in anal stenosis (*Fig.* 29) .. 138
Rectoscope, modification of (*Fig.* 45) .. 267
Rectum and anal sphincter, war wounds of 295
— **carcinoma of** 289
— **injuries of** (*Plate XL*) 295
— **mucosal polyps of** 296
— **prolapse of** 297
— resection of, conservative methods .. 292
— **stricture of** 298
Recurrent dislocation of elbow-joint .. 93
— postural renal calculi, treatment .. 384
— utterance 36
— varicose veins 391
"Red boy" disease 208
Reduplication 36
Rehabilitation, industrial 236
Reiter's disease 299
Relapse in malaria, aetiology of 200
Renal artery, thrombosis of 169
— calculi, recurrent postural, operative treatment 384
— — — streptomycin in 385
— complications of hyperparathyroidism 169
— **disease** (*Fig.* 53) 300
— — diet in 300
— — unilateral, in hypertension .. 151
— manifestations of periarteritis nodosa 168
— pelvis, papilloma of (*Plate XXII*) .. 170
— tuberculosis 169
— vascular system, micro-arteriography of 274
Respiratory disease, vaccination in industry as preventive of 237
— disturbance in anæsthesia 22
— infections, upper, transmission of .. 16
— tract illness, swimming-baths and .. 339
Resochin (*see* Chloroquine)
Reticulosis 302
Retinitis pigmentosa, tissue therapy in 359, 360
Retro-caval ureter 380
Retrolental fibroplasia 112

PAGE

"Reversed postural drainage" in pulmonary tuberculosis 365
Rh antibody, forms of 305
— antigens 303
— and pregnancy 304
— transfusion 304
Rhesus factor : clinical applications .. 303
Rheumatic diseases, statistics of .. 327
— **fever** 307
— — incidence of 328
— pneumonitis 307
Rheumatism, infective (*see* Rheumatoid Arthritis)
Rheumatoid arthritis 308
— — allergic reaction theory 312
— — treatment 309
Rhodoquine 201
Riboflavin deficiency 228
Ribs, notching of, in coarctation of aorta (*Plate XIV*) 79
Rickettsia, aureomycin in .. 46, 47
Riedel's thyroiditis 353, 355
Ringworm of scalp, treatment 313
Robaden Tablets and Ampoules .. 415
Rocky Mountain spotted fever, aureomycin in 47
Rotation therapy 281
Rubella 315
— maternal, and congenital abnormality of foetus 90, 113, 315
Ruptured malarial spleen 329
Rutin in capillary fragility 67

SALINE agglutinins 305
— Salpingitis, gonorrhœal, tubes after 331
Santoquine (*see* Nivaquine)
Saphenous ligation, high, and injection of saphenous vein, dangers of .. 388
— vein, varicose, division and scarification of (*Figs.* 76, 77) 389
Sarcoidosis 316
Sarcomas and carcinomas, solitary metastatic, of lung, pulmonary resection for 196
Scarlet fever and hæmolytic streptococcal sore throat 317
Schistosoma infection (*see* Bilharziasis)
Schistosomiasis (bilharziasis) (*see* Bilharziasis)
Schizophrenia, aetiology 271
— electronarcosis in 216
— leucotomy in 189, 190, 191
— simplex 272
Scleroderma, heart in 147
Sclerosing solution, treatment of œsophageal varices by injection of .. 237
Sclerosis, multiple, effects on auditory nerve 104
Scrub typhus, chloromycetin in 378
— — fever, aureomycin in .. 46, 47
Segmental resection of bone tumours .. 56
Seminal fluid, examination of 330
— vesicle, carcinoma of, primary (*Fig.* 78) 396
— — **surgery of vas and** (*Fig.* 78) .. 395
Sepsis, anæmia associated with trauma and 18
Septicæmia, chronic meningococcal .. 211
— fulminating meningococcal .. 212, 213
Sex differentials with respect to diseases 328
— **glands** 319
Shock, obstetric 172
— treatment in schizophrenia 272
Shoulder, functional anatomy of .. 321
— **painful** 319
— — diagnosis 321

PAGE

Shoulder, painful, operative procedure .. 322
Siderosis, welder's 232
Sigmoid, volvulus of 159
Signature of will, legal decision on .. 180
Silicosis, diagnosis from pulmonary bilharziasis 50
— not an accident, legal decision on .. 182
Simmonds's disease 256
Skin of cadaver, preserved, preparation of 359
— disease, beryllium 230, 231
— grafts, whole, in repair of hernia .. 148
— reaction to radiation of different qualities 281
— spreading ulceration of, complicating ulcerative colitis 81
"Skodiac hypothesis" in coarctation of aorta 77
Skull traction in cervical injury 248
Sliding hernia 148
Small-pox, epidemiology 323
— mass vaccination for 154
— **and vaccination** 323
Sneezing and disease transmission .. 16
SN 7618 (*see* Chloroquine)
Social medicine 324
— resettlement 328
Sodium salicylate in rheumatic fever .. 307
— — toxic symptoms 308
— tetradecyl sulphate solution for varicose veins 389
Soluthiazole in meningococcosis 213, 214
Sontochin (*see* Nivaquine)
Sontoquin (*see* Nivaquine)
Sore throat, hæmolytic streptococcal, scarlet fever and 317
Spasm in appendicitis 38
— and fibrosis of anal sphincter .. 27
— vascular 340
Speech reiteration 36
Speechlessness, literacy and verbosity .. 36
Speliotomy in pulmonary tuberculosis .. 365
"Sphincterotomy" 26
— of sphincter of Oddi in pancreatitis (*Figs.* 36–38) 243
Spinal anæsthesia, paralysis of bladder and rectum after 160
— — repeated, in treatment of Hirschsprung's disease 150
— analgesia (*Fig.* 2) 23
— — ephedrine in 25
— — meningitis following 25
— — permanent paralysis following .. 25
— block for congenital megacolon .. 24
— — total (*Fig.* 2) 23
— cord, myelitis of cervical, due to irradiation 285
— pumping in rheumatoid arthritis .. 311
Spine injuries, cervical, paraplegia in (*Plate XXVI, Fig.* 40) 247
Splanchnic bed, degeneration of, in hypertension 152
Splanchnicectomy in biliary dyskinesia .. 121
— hypertension 152
Spleen, in idiopathic thrombocytopenic purpura 273
— **surgery of** 329
Splenectomy in hæmolytic anæmia .. 19
— idiopathic thrombocytopenic purpura 273
— portal hypertension 262, 263
Splenic abscess complicating typhoid .. 376
— **anæmia** 21
Spontaneous pneumothorax 260
Sporozoites, effect of chemotherapeutic drugs on 202
Spotted fever, aureomycin in .. 46, 47
Sprue syndrome, anæmia of 21
Sputum, blood-streaked, in carcinoma of bronchus 65

PAGE

Starvation 226
Statistics, vital 397
Steel wire in repair of hernia 148
Stellectomy in angina pectoris 343
Stenosis, aortic 34
— mitral 146
Steramide-Ag 415
Sterility and infertility 330
Sterilizer, Maw's Minimatic Automatic Electric 419
Stevvac Cannulæ 419
and Lactic Acid Pessaries, Crookes' 410
Stillbirth, rubella in pregnancy and .. 315
Stomach, carcinoma of (*Plate XLI, Figs.* 54–56) 334
— **diverticula of** 333
— neurogenic tumours of 338
— sliding hernia of, and short œsophagus (*Figs.* 47–51) 275
— **surgical diseases of** (*Plate XLI, Figs.* 54–56) 334
— syphilis of 346
Strangulated hernia 149
Strangulation, ileus and obstruction, diagnosis of 156
Streptomycin in carcinoma of colon .. 84
— Glaxo 416
— in meningitis 210
— ophthalmology 110
— peritonitis 255
— pulmonary tuberculosis 369
— — — surgical treatment 367
— resistance 363, 370, 371, 385
— therapy in aural and nasal suppuration 42
— — chancroid 70
— — tests for labyrinth function following 42
— toxic reactions to 386
— treatment of urinary infections by .. 301
— **in tuberculosis of bones and joints** .. 363
— tularæmia 375
— **urinary infections** 384
Stress diseases 235
— incontinence of urine (*Fig.* 71) .. 382
Stricture of rectum 298
— ureter, bilharzial 381
— urethral 383
Struma lymphomatosa 353
— ovarii, thyrotoxicosis due to (*Figs.* 58–60) 353
Subdural abscess 162
— — in purulent pachymeningitis .. 43
— empyema secondary to frontal sinusitis 44
Succinyl sulphathiazole suppositories in proctitis 266
Suicide and pension, legal decision on .. 183
Sulphadiazine in malaria 203
— meningococcosis 213
Sulphamezathine in meningococcosis .. 213
Sulphanilamide in intractable cystitis .. 51
— meningococcosis 213
Sulphasuxidine in carcinoma of colon 84, 85
— diverticulitis of pelvic colon 95
Sulphathalidine in anorectal operations 139
— carcinoma of colon 84, 85
— ulcerative colitis 83
Sulphathiazole in meningococcosis .. 213
— penicillin and, in typhoid 377
— Suspension of—Boots 4–6
Sulphonamide(s) in appendicitis .. 37
— aural and nasal suppuration 41
— cavernous sinus thrombophlebitis .. 44
— chancroid 70
— malaria 203

PAGE

Sulphonamide(s) in meningococcosis 211, 213
— standard preparations 61
— therapy in anorectal gonorrhœa .. 32
— in ulcerative colitis 83
Supervoltage therapy 279
Supratubercular ridge of Meyer .. 320, 321
Suspension of Sulphathiazole—Boots .. 416
Swimmers' exostosis of external auditory canals, aetiology of 102
Swimming-baths : relation to illness .. 339
Sympathectomy for angina pectoris .. 343
— causalgia 342
— *in* gynæcology 344
— for hyperidrosis 344
— hypertension .. 151, 152, 340, 341, 342
— lumbar, for resistant varicose ulcers 393
— paravertebral lumbar, for thrombophlebitis 393
— presacral, for dysmenorrhœa 100, 344
— relapses after 340
— results of 339
— for varicose ulcer 343
Sympathetic nervous system, anal function of 150
— — — **surgery of** 339
Synergistic penicillin and sulphathiazole in typhoid 377
Syphilis 345
— aneurysm of abdominal aorta in .. 31
— diagnosis 345
— infectivity 345
— primary, multiple lesions in 345
— of stomach 346
— treatment with penicillin 347
— — — — failures 348
Syphilitic aortitis 346
Systolic murmurs, innocent mitral .. 146

T.A.B. vaccine in rheumatoid arthritis 146
Tabes dorsalis, vesical dysfunction in 52
'Tabloid' Brand Penicillin for Oral Administration 414
Tabs. Phenobarbitone and Belladonna .. 416
Tachycardia, repetitive paroxysmal .. 39
Talc powder in peritoneal cavity .. 254
Tampovagan Pessaries with Penicillin, Sulphanilamide and Sulphathiazole 416
Tantalum gauze pack in pulmonary tuberculosis 366
— — in repair of hernia 149
Tattooing of facial nævi 113
— with mercury sulphide in intractable pruritus ani 270
Teeth, carious, and tuberculous adenitis 374
Temperature during ovulation 332
Temporal bone, operations on, spontaneous escape of cerebrospinal fluid into wounds of 103
T.E.P.P. (Tetra-ethyl Prophosphate) .. 416
Testicular artery, distribution of .. 349
Testis, malignant 349
— **surgery of** 349
Testosterone in juvenile nasopharyngeal angiofibroma 224
— Propionate B.D.H. 416
Tetany induced by BAL 39
— latent, due to BAL 310
Textile workers, nephritis in 225
Thioglycolate in permanent waving .. 140
Thiopentone, intra-arterial 22
Thiouracil therapy in thyrotoxicosis .. 350
— — — indications and contra-indications 352
Thiourea, methyl thiouracil and .. 351
Thirst, origin of, in diabetes insipidus .. 91
Thoracic aortic aneurysm 31
Thoracoplasty, first stage, filling of "Semb space" in .. .. ..
Thoraco-lumbar splanchinectomy and sympathectomy .. ..
Thrombocytopenic purpura, idiopathic .. ..
— — **thrombotic** .. ..
Thrombophlebitis 393
— cavernous sinus 44
— deep, following injection of varicose vein (*Plate L*) .. ..
— in varicose veins .. ..
Thrombosis of abdominal aorta (*Fig.* 3)
— cavernous sinus (*see* Cavernous Sinus Thrombosis)
— deep venous .. ..
— priapism due to .. ..
— of renal artery 169
— superior petrosal and cavernous sinus 43
Thrombotic thrombocytopenic purpura .. 273
Thrush of bladder 51
Thyrocardiac disease, masked 34
Thyroid, cancer of (*see* Cancer of Thyroid)
— **gland** 350
— — retrolaryngeal upper pole of (*Fig.* 57) 352
— **surgery** (*Plates XLII, XLIII, Figs.* 57–64) 352
Thyroidectomy in cancer of thyroid (*Figs.* 61–64) .. .. ..
Thyroiditis .. ..
Thyrotoxicosis due to stroma ovarii (*Figs.* 58–60) 353
— masked 34
— treatment 350 352
Tibia, double fractures and double non-unions of shaft of 116
Tics, verbal 36
'Tincafax' Brand Compound Undecylenate Ointment and Undecylenate Powder 416
Tissue therapy by Filator's technique in ophthalmology 358
'T.O.C.' Brand Trisilicate-Oil-Vitamin C Emulsion 416
Tomography in carcinoma of bronchus .. 66
Topectomy, Heath and Poole's .. 189, 190
Toxoplasmosis 360
Tracheobronchitis, tuberculous, streptomycin in 368
Transmeatal attico-antrotomy for chronic tympano-mastoid suppuration (*Plates XV–XVII, Figs.* 16–19) ..
Transtympanic route for labyrinth fenestration (*Fig.* 19) .. .. ..
Transurethral resection, hæmoptysis after .. ..
Transvaginal ureterorectal anastomosis (*Fig.* 70) .. ..
Trauma and sepsis, anæmia associated with 18
Travel sickness drug treatment 361
'Travikalm'-Genatosan Travel Sickness Tablets 416
Tremor in Parkinsonism, abolition of .. 251
Trichlorethylene 21
Trichomonas vaginalis 362
Tropical disease, standard drugs for .. 61
Truss Pad and Holder, Automatic Air .. 417
Tuberculin Diagnostic Jelly (Evans) .. 417
Tuberculosis and adenocarcinoma of same kidney 171
— **of bones and joints : streptomycin in** 363
— differentiated from carcinoma of bronchus 66
— genital, in male 350
— of ileum, hypertrophic 160
— miliary, diagnosis from pulmonary bilharziasis .. ..

PAGE

Tuberculosis, ocular, streptomycin in .. 112
— pulmonary (*see* Pulmonary Tuberculosis) 109
— renal 260, 261
— spontaneous pneumothorax and 373
— **spread** 386
— urinary, streptomycin in 374
Tuberculous cervical adenitis (*Figs.* 67–69) 54
— cystitis, sulphanilamide in 371
— meningitis, streptomycin in 236
— patients, employment of 268
— prostatic urethritis 368
— tracheobronchitis, streptomycin in .. 375
Tularæmia 55
Tumours of bone, conservative surgery in 2
— — diagnosis 2
— changes produced in, by high-voltage irradiation 247
— of islets of Langerhans 223
— **nasopharynx : diagnosis and treatment** 170
— perirenal 161
— of small intestine 396
— **vertebræ** 52
— in vesical diverticula 109
Twin Chisels 109
Tympano-mastoid suppuration, chronic transmeatal attico-antrotomy for (*Plates XV–XVII, Figs.* 16–19) 103
Typhoid carriers 377
— **and paratyphoid fevers** ..
Typhus fever .. .. ..
— — aureomycin in .. ..
Tyrothricin, toxicity of .. ..

ULCER(S), ischæmic, of leg 394
— — of small intestine 161
— syphilitic, of stomach 346
— **varicose** (*see* Varicose Ulcers)
Ulceration, anastomotic, after gastrectomy, incidence 131
— of skin, spreading, complicating ulcerative colitis 81
— vesical, following radiation of cervix 52
Ulcerative colitis (*see* Colitis, Ulcerative)
Ultra-violet light in air sterilization .. 15
Uræmia, artificial kidney in 378
— dialysis of blood in (*Fig.* 53) 301, 378
Urecholine in gastric retention 129
Ureter, bilharzial (*Plates XLVIII, XLIX*) 380
— ectopic 380
— retro-caval 380
— **surgery of** (*Plates XLVIII, XLIX, Fig.* 70) 379
— surgically traumatized, management of 379
Ureteral blood-supply after Wertheim's operation 380
Ureteric calculi, treatment 384
Ureteritis cystica, bilharzial (*Plate XLIX*) 380
— prostatic tuberculous 268
— in Reiter's disease 299
Ureterolithotomy, vaginal 384
Ureteropelvic obstructions 169
Ureterorectal anastomosis, transvaginal (*Fig.* 70) 381
Urethra, surgery of (*Fig.* 71) 382
Urethral dilatation in urethrotrigonitis .. 382
— stricture 383
Urethrotrigonitis 382
Urinary calculi 384
— **infections, streptomycin in** 384
— tract infections, aureomycin in .. 47
— tuberculosis, streptomycin in .. 386
Urine, stress incontinence of (*Fig.* 71) .. 382
Uterine hæmorrhage, functional, radiotherapy in 287

PAGE

Uterus, rupture of, Cæsarean section scar of 174
Utricle, enlarged, with hypospadias (*Figs.* 41–43) 253

VACCINATION, compulsory, end of 237
— in industry as *preventive of respiratory disease* 237
— **small-pox and** 223
Vaccines in *British Pharmacopœia* .. 62
— whooping-cough 404
Vagal resection, cause of pain relief after 128
— — clinical results of 127
— — effect of, on gastric function (*Fig* 24) 127
— — mortality of 127
— — for peptic ulcer 125
— — — — ' side effect ' after 126
— section, test for complete 128
Vagotomy (*see* Vagal Resection)
Valvular disease, aortic 146
— stenosis, operation for 145
Varicelliform eruption, Kaposi's 166
Varicose ulceration of legs 393
— — **ulcers** (*Figs.* 72–75) 386
— — — sympathectomy for 343
— — **varicose veins and venous thrombosis** (*Plate L, Figs.* 76–78) .. 388
— **veins** 388
388
— — injection treatment 389
— — Needle with Torpedo End .. 419
— — operative treatment (*Figs.* 76, 77) 389
— — — complications 391
— — thrombophlebitis in 392
— — **varicose ulcers and venous thrombosis** (*Plate L, Figs.* 76–78) .. 388
Varices, œsophageal .. .. ..
Vas deferens, anastomosis of, after division for sterility 395
Vas and seminal vesicles, surgery of (*Fig.* 78) 395
Vascular occlusion, mesenteric 222
— spasm 340
Vasodilation, local, arterial therapy to promote 40
Venous thrombosis, deep 392
— — **varicose veins, varicose ulcers and** (*Plate L, Figs.* 76–78) 388
Ventricular hypertrophy, right, electrocardiogram in 106
Verbal mannerisms 36
— tics 36
Verbigeration 36
Verbosity, literacy and speechlessness .. 36
Version, external, under anæsthesia .. 171
Vertebræ, tumours of 396
— — cerebral apparatus for electronarcosis .. ..
— fractures following electro-convulsive therapy 219
Vertigo, streptomycin therapy in .. 42
Vesical abnormalities and diabetes mellitus
— diverticula, tumours in .. ..
— dysfunction in tabes dorsalis .. ..
— exostrophy, cysto-sigmoidoscopy for (*Plate IV*) 51
— ulceration following radiation of cervix 52
Vibratory tools, Raynaud phenomenon in workers using 344
Villous tumour of rectum 296
Vioform Cream and Ointment 417
Virormone-Oral Methyl Testosterone .. 417
Virormone-Salve 417
Virormone Suppositories 417
Viruses, cellular infection by influenza and related 155

PAGE

Viscera diagnosis of injury to 9
Visceral neoplasms, multiple 88
'Visco-Pyelosil' 417
'Viskiosol' Six 417
Vital Statistics 397
Vitamin(s) B in alcoholism 17
— — complex 228
— — — Tablets, Crookes 410
— B_{12} 20
— C, requirements of 228
— deficiency states in Allied prisoners of war 227
— **E in collagenoses** 402
— Dupuytren's contracture 96, 97
— evaluation of 228
— **nutrition and** 226
— preparations in *British Pharmacopœia* 62
— therapy in carcinoma of colon .. 84
Vitaminorum Capsules 'Pabryn' .. 417
Volvulus 159

WAR wounds 9
Water injections in intracranial hypotension 161
'Waterhouse-Friderichsen syndrome' .. 212
Weil's disease (Leptospirosis icterohæmorrhagica) 403
Welder's siderosis 232
'Wellcome' Brand Penicillin (Oil-Wax) Suspension 414
Wertheim's operation, ureteral blood-supply after 380
Wheezing in carcinoma of bronchus .. 66
Whitehead's operation, modified, for hæmorrhoids 138
White-leg 393
Whooping-cough 404
— inoculation against 153, 154
— vaccines, 'Wellcome' Brand .. 417
Will, signature of, legal decision on .. 180
Wilms' embryoma 405
Wiring operation for aortic aneurysm ..
Workmen's compensation, legal decisions concerning 398, 399, 406
World Health Organization
Wound(s) disruption, early post-operative ambulation and 10
— of liver 9
— war 9

X-RAY examination (*see* Radiography)
— plant, one million-volt .. 21
— therapy (*see also* Radiotherapy)
— deep, in tumours of nasopharynx 224, 225

YOUNG offenders, treatment of .. 185
— persons, medical examination of 233
Young's dilators 27

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Classified Index to Advertisements

(For Alphabetical Index, *see page* 3, and for Index to Books Advertised, *see page* 6.)

PAGE

ACCOUNTS, MEDICAL—
Book-keeping System (*H. K. Lewis*) . .

ALCOHOLISM AND DRUG ADDICTION
Caldecot Hall, Nuneaton . . . .
Ecclesfield, Staplehurst . . . .
Hampstead, Highfield & Elmhurst, Co. Dublin . . . . . .
Northwoods, Winterbourne, Bristol . .

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Steeper, Hugh, Ltd. . . . .

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Bryce, Wm. . . . .
Foyles . . . . . .
Lewis, H. K. & Co. Ltd.

CHEMISTS, DRUG MANUFACTURERS, Etc.
Allen & Hanburys Ltd. . . 40, 41
Anglo-French Drug Co. Ltd. . . xiii, 38
Aspro Ltd. xxviii
Bayer Products Ltd. xxvii
Boots Pure Drug Co. Ltd. . . . xlv
Brand's Essence 32
British Drug Houses Ltd. . . xxii
British Schering Ltd. . . . lviii
Burroughs Wellcome & Co. . .
Ciba Ltd. . . . . .
Collis Browne's (Dr.) Chlorodyne
Ferris & Co. Ltd. Back Endpapers 53
Glaxo Laboratories Ltd. . . . 1
Hommell's Hæmatogen & Drug Co. . . 19
Iron Jelloid Co. Ltd. xxiii
McPherson, John E. & Sons, Whisky 48
Menley & James Ltd. . . . . ix xx
Moore Medicinal Products Ltd. . . xxiii
Napp, H. R. Ltd. . . Front Endpaper
Organon Laboratories Ltd. . . Bookmark
Oxo Ltd. 27
Paines & Byrne Ltd. xxvi
Parke, Davis & Co. xxix
Pharmaceutical Specialities (Ma Baker) Ltd. . . . Front aper
Pure Products Ltd. 23
Roche Products Ltd. . . .
Savory & Moore Ltd. . . .
Smith, T. & H. Ltd. . . .
Thackray, Chas. F. Ltd. . .

CONVALESCENT, INVALID, AND MATERNITY HOMES
Duchy House Clinic . . . .
Maghull Homes for Epileptics, Liverpool . . . . . .
Ruthin Castle, North Wales, Private Hospital for Internal Diseases . . ii
Stoneycrest Nursing Home . . . xxxii

EDUCATIONAL INSTITUTIONS, SCHOOLS, Etc.
Apothecaries of London, Society of . . xliii
Institute of Psycho-Analysis 50
University Examination Postal Inst. 20

ENGRAVERS—
Sun Engraving Co. Ltd.
Swann, John & Son Ltd.

FUNCTIONAL NERVOUS DISORDERS
Archer Nerve Training Colony Langley Rise Ltd., King's Langley 34
Bowden House, Barrows-on-the-Hill . . 37
Burden Neurological Institute . . 38
Caldecote Hall, Nuneaton 30
Mount Pleasant & St. Margaret's, Walton, Cleveden xxxiii
Retreat, The, York 35

INSTRUMENTS AND APPLIANCES, BANDAGES, Etc.
Aerosols Ltd. xxi
Beatson, Clark & Co. Ltd. . . . 48
Bell (John) & Croyden vii
British Electrical Development Association 36
Brooks Appliance Co. Ltd. . . . 4
Curtis, H. E. & Son, Ltd. . . . 50
Dalmas, A. de St. 49
Davidson, F. & Co. 42, 43
Down Bros. and Mayer & Phelps Ltd. 44, 45, 46, 47
Genito-Urinary Mfg. Co. Ltd. . . 39
Gowlland Ltd. 52
Hawksley, T. Ltd. xliii
Ody, Salmon Ltd. 48
Ritchie, George B. & Co. . . . xliv
Robinson & Sons Ltd. 51
Spencer (Banbury) Ltd. . . . 107
Spirella Co. of Great Britain Ltd. . . iv
Steeper, Hugh Ltd. 50
Tampax Ltd. xxxi
Thackray, Chas. F. Ltd. . . . vi

INSURANCE OFFICES
Medical Sickness, Annuity and Life Assurance Society Ltd. . . . xxxiv
Royal Medical Benevolent Fund . . 25
Scottish Widows' Fund and Life Assurance Society xlvi

LIBRARY (MEDICAL AND SCIENTIFIC)
Lewis, H. K. & Co. Ltd. 9

MEDICAL SCHOOLS—

The Glasgow Eye Infirmary
Institute of Ophthalmology
Manchester Royal Infirmary School of Massage and Medical Gymnastics
Postgraduate Medical School
University of Bristol
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University of Sheffield

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Ashwood House 31
Bailbrook House, Bath 37
Barnwood House, Gloucester 20
Burden Neurological Institute 38
Camberwell House xxxi
Cheadle Royal Mental Hospital, Cheadle 38
Chiswick House, Pinner 34
Elmhurst, Glasnevin, Co. Dublin 31
Fenstanton, Burnham, Bucks 20
Fiddington House 23
Grove House, Church Stretton
Hampstead, Glasnevin, Co. Dublin
Haydock Lodge, Newton-le-Willows
Heigham Hall, Norwich
Highfield, Drumcondra, Co. Dublin
Laverstock House, Salisbury
Mount Pleasant, & St. Margaret's, Walton, Clevedon x
Normansfield 23
Northwoods, Winterbourne, Bristol 34
Old Manor, Salisbury
Peckham House, S.E.
St. Andrew's Hospital, Northampton

PERIODICALS—

Abstracts of World Medicine
Abstracts of World Surgery
Annals of the Rheumatic Diseases
British Heart Journal
British Journal of Industrial Medic
British Journal of Pharmacology Chemotherapy
British Journal of Social Medicine
British Journal of Surgery

PAGE

British Journal of Venereal Diseases iii
British Medical Journal iii
Disease in Childhood iii
Journal of Clinical Pathology iii
Journal of the Faculty of Radiologists lx
The Journal of Laryngology and Otology 18
Journal of Neurology, Neurosurgery and Psychiatry iii
The Lancet 14
Medicine Illustrated
The Medical Clinics of North Ame
The Medical Officer
The Medical Press 17
The Surgical Clinics of North America xxxvii
Thorax iii

PHOTOGRAPHIC SERVICES—

Fallowfield (Jonathan) Ltd. 23

PUBLISHERS—(*see also* **Index to Books**, p. 6)

Baillière, Tindall & Cox v
British Medical Association iii, v
Butterworth & Co. (Publishers) Ltd. xl, xli
Churchill, J. & A. Ltd. xxxviii, xxxix
Ferrier (Donald) xxxv
Harvey & Blythe Ltd. xxxiii
Headley Brothers 18
Heinemann, Wm. (Medical Books) Ltd. xlii
Lewis, H. K. & Co. Ltd. 9, 10, 11
Livingstone, E. & S. Ltd.
Oxford University Press
Pharmaceutical Press, The
Saunders, W. B. Co. Ltd.
Scientific Publishing Co.
Sylvio Publications
Wright, John & Sons Ltd. xliii, xliv, lx, 21, 22

SANATORIA FOR TUBERCULOSIS

Cotswold Sanatorium, Cranham, Gloucester xxxiii
Mundesley Sanatorium 27
National Children's Home and Orphanage Sanatorium, Harpenden 32
Pendyffryn Hall Sanatorium, Penmaenmawr 33

Alphabetical Index to Advertisers

Aerosols Ltd. .. .. ..
Allen & Hanburys Ltd., Chemists and Surgical Instruments ..
Anglo-French Drug Co. Ltd. .
Apothecaries of London, Society of
Ashwood House .. .. ..
Aspro Ltd., Chemists .. .. .
Archer Nerve Training Colony Langley Rise Ltd., King's Langley .. .

Baillbrook House, Bath, Mental 37
Baillière, Tindall & Cox, Publishers .. 15
Barnhouse House, Gloucester, Mental .. 20
Bayer Products Ltd., Chemists xxvii
Beatson, Clark & Co., Ltd., Medical Glass Manufacturers .. . 48
Bell (John) & Croyden vii
Boots Pure Drug Co. Ltd. xlv
Bowden House, Harrow-on-the-Hill, Functional Nervous Disorders .. 37
Brand's Essence 32
British Drug Houses Ltd. xxii
British Electrical Development Association 36
British Medical Association .. .. iii, v
British Shering Ltd. lviii
Brooks Appliance Co. Ltd. 4
Bryce, Wm., Medical Bookseller .. xxxii
Burden Neurological Institute 38
Burroughs Wellcome & Co. xxv
Butterworth & Co. (Publishers) Ltd. xl, xli

Caldecote Hall, Nuneaton
Camberwell House xxxi
Cheadle Royal Mental Hospital, Cheadle 38
Chiswick House, Pinner, Mental Hospital 34
Churchill, J. & A. Ltd., Publisher xxxvi, xxxix
Ciba Ltd., Hormone Preparation .. xlviii
Collis Browne's (Dr.) Chlorodyne .. xxiii
Cotswold Sanatorium, Cranham, Gloucester xxxiii
Curtis, H. E. & Son, Ltd., Appliances .. 50

Dalmas, A. de St. 49
Davidson, F. & Co., Darling Opticians 42, 43
Down Bros. and Mayer & Phelps Ltd., Surgical Instruments 44, 45, 46, 47
Duchy House Clinic xxxii

Eccleshield, Staplehurst, Alcoholism .. xliv
Elmhurst, Glasnevin, Co. Dublin, Mental 31

Fallowfield (Jonathan) Ltd. 23
Fenstanton, Burnham, Bucks, Mental Home 20
Ferrier (Donald) xxxv
Ferris & Co. Ltd. Back Endpapers, 53
Fiddington House 23
Foyles, Booksellers 16

PAGE
Genito-Urinary Mfg. Co. Ltd., Surgical Instruments 39
The Glasgow Eye Infirmary 38
Glaxo Laboratories Ltd. Pharmaceutical Preparations 1
Gowlland Ltd. 52
Grove House, Church Stretton, Mental Hospital xxxii
Hampstead, Glasnevin, Co. Dublin, Mental 31
Harvey & Blythe Ltd. (Publishers) .. xxxiii
Hawksley, T. Ltd., Appliances xliii
Haydock Lodge, Newton-le-Willows, Mental Hospital 31
Headley Brothers, Publishers 18
Hegham Hall, Norwich, Mental Home .. 28
Heinemann, Wm. (Medical Books) Ltd. xlii
Highfield, Drumcondra, Co. Dublin, Mental 31
Hommell's Haematogen & Drug Co. .. 19

Institute of Ophthalmology 30
Institute of Psycho-Analysis 50
Iron Jelloid Co. Ltd. ..

Lancet, The 14
Laverstock House, Salisbury, Mental Home 35
Lewis, H. K. & Co. Ltd., Publishers and Medical Library 9, 10, 11
Livingstone, E. & S. Ltd., Publishers .. 13

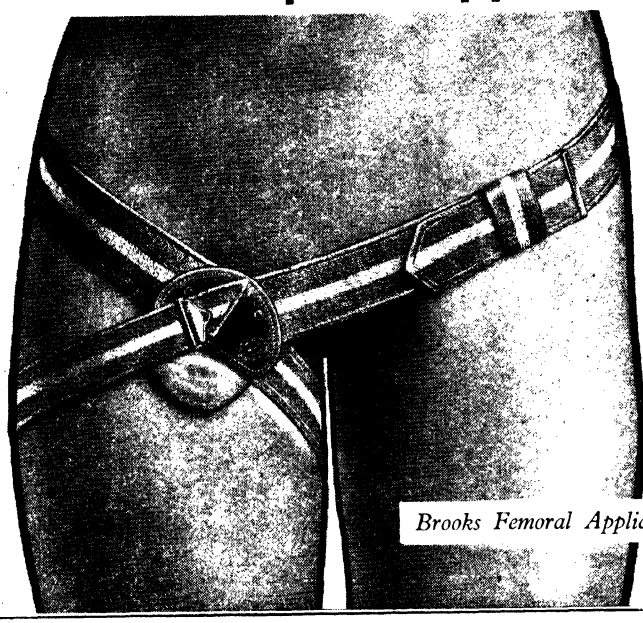
McPherson, John E. & Sons, Whisky .. 48
Maghull Homes for Epileptics, Liverpool 35
Manchester Royal Infirmary School of Massage and Medical Gymnastics .. 27
Medical Officer, The 16
Medical Press, The 17
Medical Sickness, Annuity and Life Assurance Society Ltd. xxxiv
Menley & James Ltd., Chemists .. ix–xx
Moore Medicinal Products Ltd. .. xxiii
Mount Pleasant, Walton, Clevedon, Nervous Disorders xxxiii
Mundesley Sanatorium 27

Napp, H. R. Ltd. .. Front Endpaper
National Children's Home and Orphanage Sanatorium, Harpenden 32
Normansfield 23
Northwoods, Winterbourne, Bristol, Mental Home 34

Old Manor, Salisbury, Mental Hospital .. 37
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	PAGE
Peckham House, S.E.15, Mental ..	5
Pendyffryn Hall Sanatorium, Penmaenmawr	33
Pharmaceutical Press, The	xxxvi
Pharmaceutical Specialities (May & Baker) Ltd.	Front Endpaper
Postgraduate Medical School	26
Pure Products Ltd.	23
Retreat, The, York, Mental Hospital ..	
Ritchie, George B. & Co.	
Robinson & Sons, Ltd., Surgical Dressings	
Roche Products Ltd., Chemists	
Royal Medical Benevolent Fund ..	
Ruthin Castle, North Wales, Private Hospital for Internal Diseases ..	
St. Andrew's Hospital, Northampto Mental ..	
St. Margaret's, Wall , Clevedon, Nervous Disorders	xxxiii
Salmon Ody Ltd.	48
Saunders, W. B. Co. Ltd. ..	xxxvii
Savory & Moore Ltd., Chemists ..	lvi
Scientific Publishing Co.	18
Scottish Widows' Fund and Life Assurance Society	xlvi
Smith, T. & H. Ltd.	xxx
Spencer (Banbury) Ltd.	407
Spirella Co. of Great Britain Ltd ..	iv
Steeper, Hugh, Ltd., Artificial Limbs ..	50
Stoneycrest Nursing Home	xxxii
Sun Engraving Co. Ltd.	36
Swain, John & Son Ltd., Engravers ..	18
Sylviro Publications	46
Tampax Ltd.	
Thackray, Chas.	
University of Bristol	24
University of Liverpool	28
University of Sheffield	xxxi
University Examination Post. Inst. ..	20
Wright, John & Sons Ltd., Publishers	xliii, xliv, lx, 21, 22

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Index to Books

Advertised in the Present Volume

PAGE

Abdominal Operations (MAINGOT) *Lewis* 11
Account of the Schools of Surgery, Royal College of Surgeons, Dublin, 1789–1948 (WIDDESS) .. *Livingstone* 13
Affections of the Eye in General Practice (REA) .. .. .. *Lewis* 11
Anatomy of the Eye and Orbit (WOLFF) *Lewis* 10
Atlas of Bone-Marrow Pathology (ISRAELS) .. .. *Heinemann* xlii
Aviation Medicine (BERGIN) *Wright*
Aviation Medicine in its Preventive Aspects (FULTON) *Oxf. Univ. Press*

Background of Therapeutics (BURN) *Oxf. Univ. Press* 12
Basic Facts of Health Education *Pharm. Press* xxxvi
Basic Principles of Ventilation and Heating (BEDFORD) .. *Lewis* 11
Blood Transfusion (ED. KEYNES) *Wright* 21
B.M.A. Annual Proceedings, 1948 *Butterworth* xl
Bone Marrow Biopsy: Hæmatology in the Light of Sternal Puncture (LEITNER, BRITTON, AND NEUMARK) *Churchill* xxxviii
Breast Feeding (NAISH) *Oxf. Univ. Press* 11
British Pharmaceutical Codex *Pharm. Press* xxxvi
British Surgical Practice (CARLING AND ROSS) .. .. .. *Butterworth* xl

Cardiography (EVANS) .. *Butterworth* xl
Cardiology (EVANS) .. *Butterworth* xl
Cardiovascular Disease (EAST) *Lewis* 11
Chest Disease in General Practice (ELLMAN) .. .. .. *Lewis* 11
Chest Examination: Correlation of Physician and X-ray Findings in Diseases of the Lung (TRAIL) *Churchill* xxxix
Child Health and Development (ELLIS) *Churchill* xxxviii
Clinical Endocrinology (MARTIN AND HYNES) .. .. *Churchill* xxxviii
Clinical Examination of the Nervous System (MONRAD-KROHN) .. *Lewis* 10
Common Skin Diseases (ROXBURGH) *Lewis* 11
Companion in Surgical Studies (AIRD) *Livingstone* 13
Comparative Anatomy and Physiology of the Larynx (NEGUS) *Heinemann* xlii
Complete Outline of Fractures *Heinemann* xlii
Conduct of Life Assurance Examinations (BROCKBANK) .. .. *Lewis* 11
Conquest of Malaria (JARAMILLO-ARANGO) *Heinemann* xlii
Critical Studies in Neurology (WALSHE) *Livingstone* 13
Cum Notitia (ALEXANDER) *Wright* 21
Cystoscopy and Urography (MACALPINE) *Wright* 21

Deformation and Flow (REINER) *Lewis* 10
Delayed Union in Fractures of the Long Bone (STARR) .. *Butterworth* xl
Diseases of the Ear, Throat and Nose (MCLAGGAN) .. .. .. *Lewis* 11
Diseases of the Eye (MAY AND WORTH) *Baillière* 15
Diseases of the Eye (PARSONS AND DUKE-ELDER) .. .. *Churchill* xxxix

Eden and Hollands' Manual of Obstetrics (BREWS) .. .. *Churchill* xxxix
Elementary Anatomy and Physiology (WHILLIS) .. .. *Churchill* xxxviii
Essentials of Orthopædics (WILES) *Churchill* xxxviii
Extra Pharmacopœia (MARTINDALE) *Pharm. Press* xxxvi
Forensic Medicine (SMITH AND FIDDES) *Churchill* xxxviii
Fractures and Dislocations (HOSFORD), revised by COLTART) .. *Lewis* 11

German-English Medical Dictionary (SCHOENEWALD) .. .. *Lewis* 10

Hæmolysis and Related Phenomena (PONDER) .. .. *Churchill* xxxviii
Hale-White's Materia Medica, Pharmacy, Pharmacology and Therapeutics (DOUTHWAITE) .. *Churchill* xxxviii
Handbook of Dental Surgery and Pathology (PERKINS) *Sylviro Publications* 16
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Handbook of Ophthalmology (NEAME AND WILLIAMSON-NOBLE) *Churchill* xxxix
Handbook of Surgery (MECKIE AND MACKENZIE) .. .. *Livingstone* 13
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Human Physiology (WINTON AND BAYLISS) *Churchill* xxxix

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Lawson Tait, 1845–1899 (FLACK) *Heinemann* xlii

Malignant Disease and its Treatment by Radium (CADE) .. *Wright* 21
Major Endocrine Disorders (SIMPSON) *Oxf. Univ. Press* 12
Management in Obstetrics (CLAYE) *Oxf. Univ. Press* 12
Manual of Pathology (GREEN) *Baillière* 15
Manual of Surgery (ROSE AND CARLESS) *Baillière* 15
Marriage Counselling (MACE) *Churchill* xxxviii
Massage and Remedial Exercises (TIDY) *Wright* 21
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Medical Education (ROBERTS) .. *Lewis* 11
Medicine (CLARK-KENNEDY) *Livingstone* 13
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Minor Surgery (LOVE) .. .. *Lewis* 11
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Modern Practice in Dermatology (MITCHELL-HEGGS) .. *Butterworth* xli
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Modern Practice in Ophthalmology (STALLARD) .. .. *Butterworth* xli
Modern Practice in Psychological Medicine (REES) .. .. *Butterworth* xli
Modern Psychiatry in Practice (NEUSTATTER) .. .. *Churchill* xxxix
Modern Trends in Dermatology (MACKENNA) .. .. *Butterworth* xli
Modern Trends in Diagnostic Radiology (MCLAREN) .. .. *Butterworth* xli
Modern Trends in Ophthalmology (SORSBY) .. .. *Butterworth* xli
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Pharmaceutical Pocket Book *Pharm. Press* xxxvi
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Practice of Refraction (DUKE-ELDER) *Churchill* xxxviii
Premature Baby (CROSSE) *Churchill* xxxix
Principles and Practice of Rectal Surgery (GABRIEL) .. .. *Lewis* 10
Progress in Clinical Medicine (DALEY AND MILLER) .. .. *Churchill* xxxviii
Psychological Aspects of Clinical Medicine (BARTON HALL) .. .. *Lewis* 11

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Rational Medicine (TODD) *Wright* 21

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Short Practice of Surgery (BAILEY AND LOVE) .. .. .. *Lewis* 10
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Synopsis of Medicine (TIDY) *Wright* xliii, 21
Synopsis of Neurology (TATLOW) *Wright* xliii
Synopsis of Obstetrics and Gynæcology (BOURNE) .. .. *Wright* xliii

	PAGE
Synopsis of Physiology (SHORT, PRATT, AND VASS) .. .. *Wright*	xliii
Synopsis of Regional Anatomy (JOHNSTON) *Churchill*	xxxix
Synopsis of Surgery (GROVES) *Wright*	xliii
Synopsis of Surgical Anatomy (MCGREGOR) *Wright*	xliii
Taylor's Principles and Practice of Medical Jurisprudence (SMITH) *Churchill*	xxxix
Textbook of Anæsthetics (MINNITT AND GILLIES) .. .. *Livingstone*	13
Textbook of Bacteriology (FAIRBROTHER) *Heinemann*	xlii
Textbook of Genito-Urinary Surgery (WINSBURY WHITE) *Livingstone*	13
Textbook of Gynæcology (PEEL) *Heinemann*	xlii
Textbook of Gynæcology (SHAW) *Churchill*	xxxix
Textbook of Medical Treatment (DUNLOP, DAVIDSON, AND MCNEE) *Livingstone*	13
Textbook of Medicine (CONYBEARE) *Livingstone*	13
Textbook for Midwives (SHAW) *Churchill*	xxxviii
Textbook of Midwifery (SHAW) *Churchill*	xxxviii
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Textbook of the Rheumatic Diseases (COPEMAN) .. .. *Livingstone*	13
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Varicose Veins (FOOTE) .. *Butterworth*	xl
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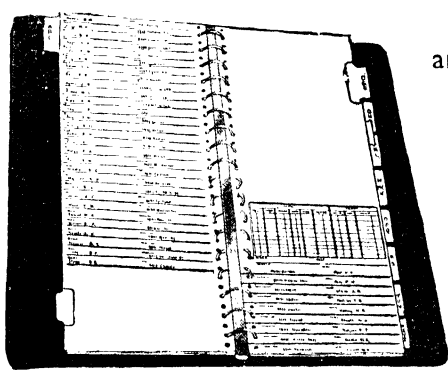
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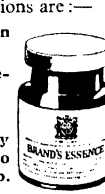
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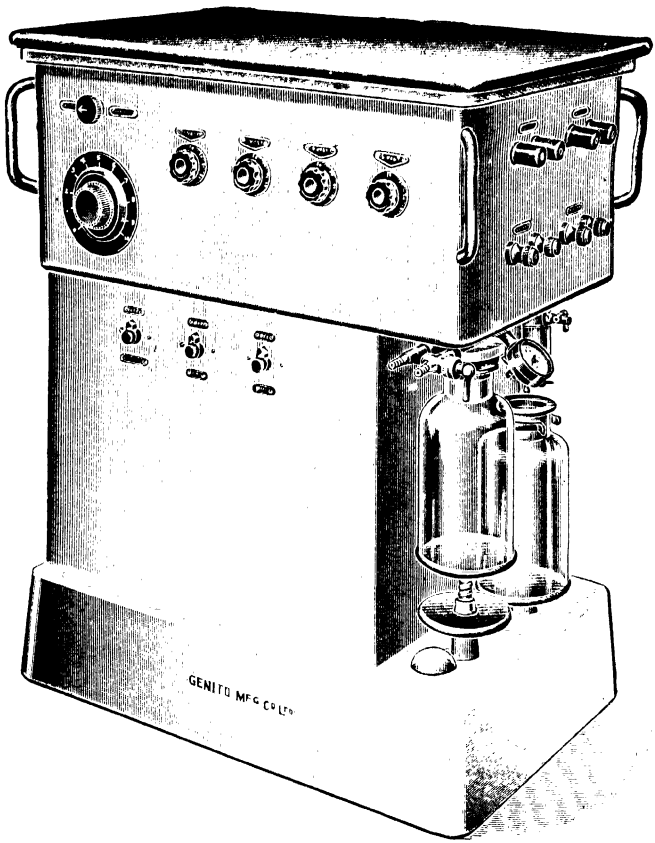
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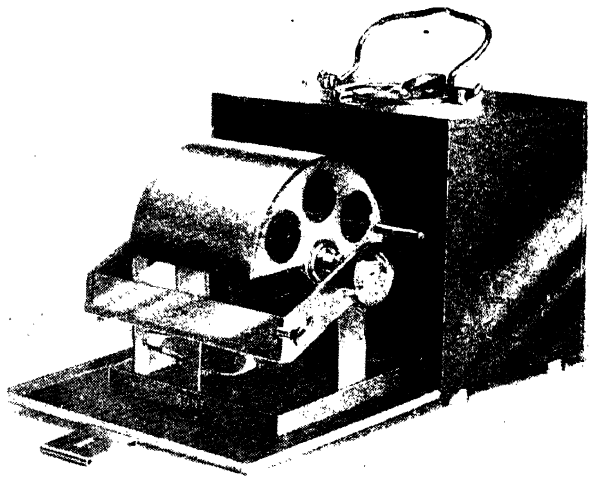
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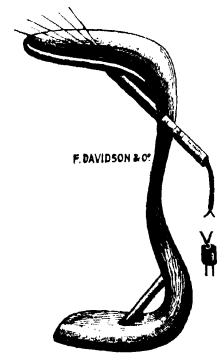
PROCAINE PENICILLIN OILY INJECTION A & H

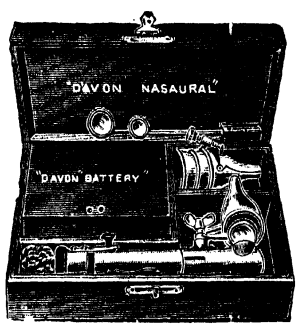
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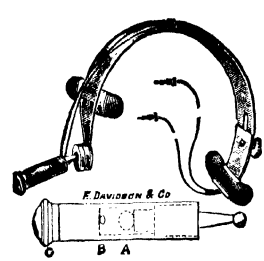


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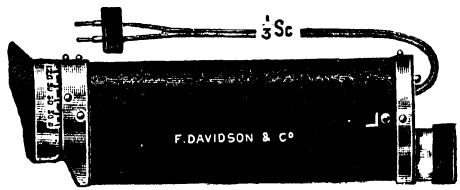
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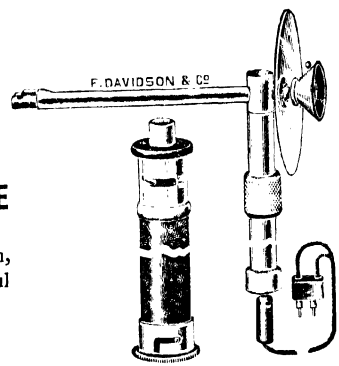
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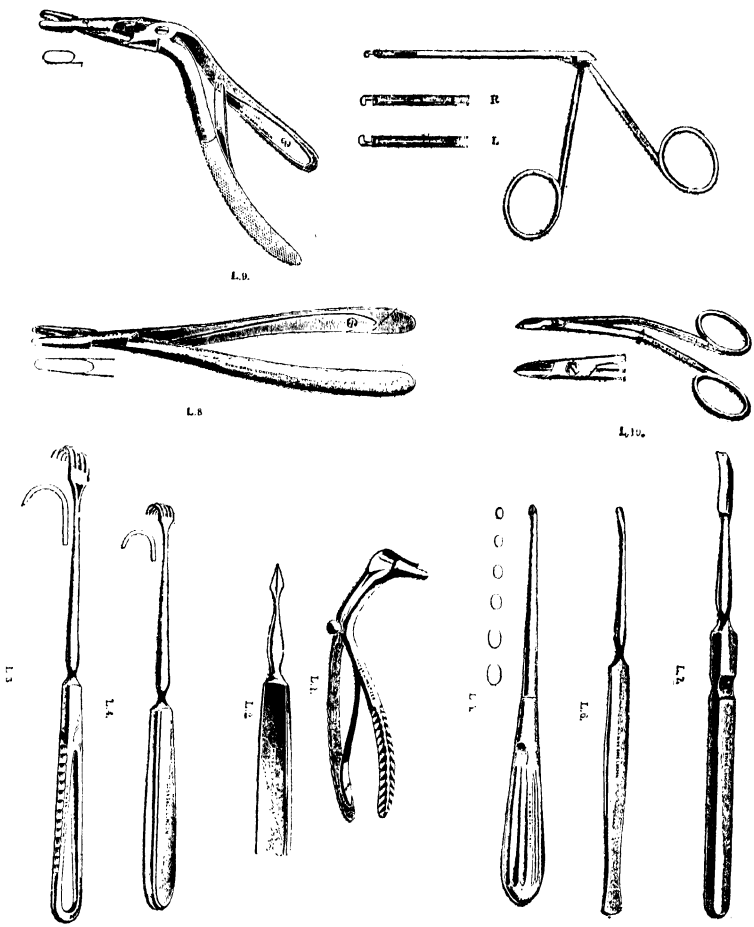
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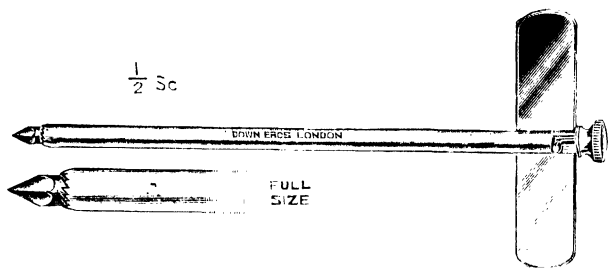
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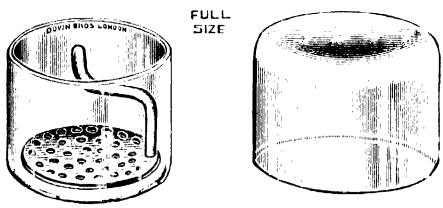
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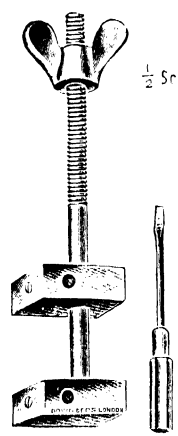
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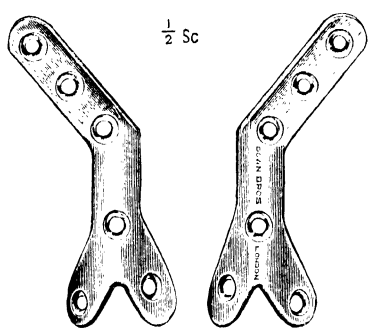
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Description, see page 418

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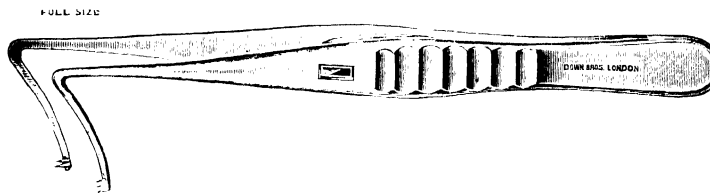
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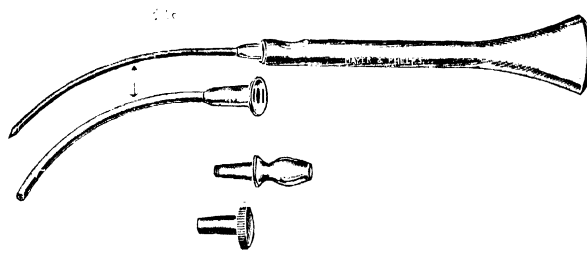
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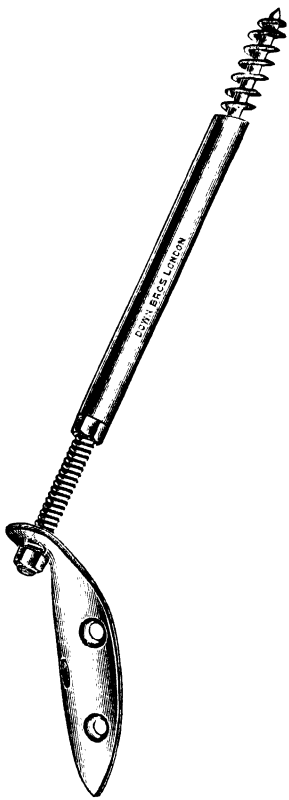
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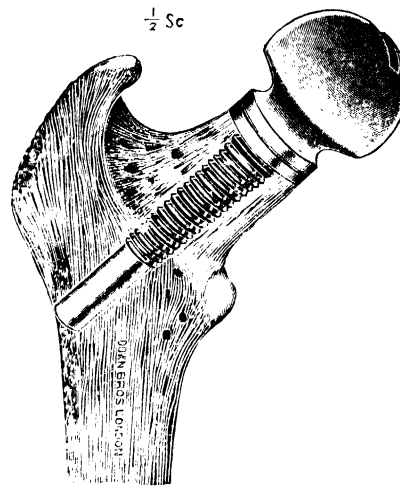
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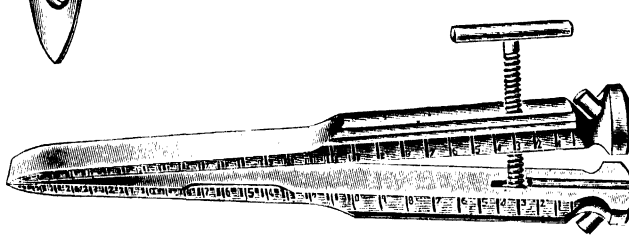
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McKEE'S LAG SCREW
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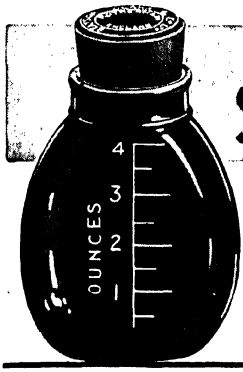


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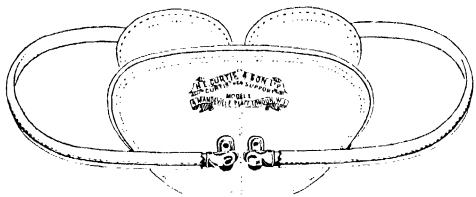


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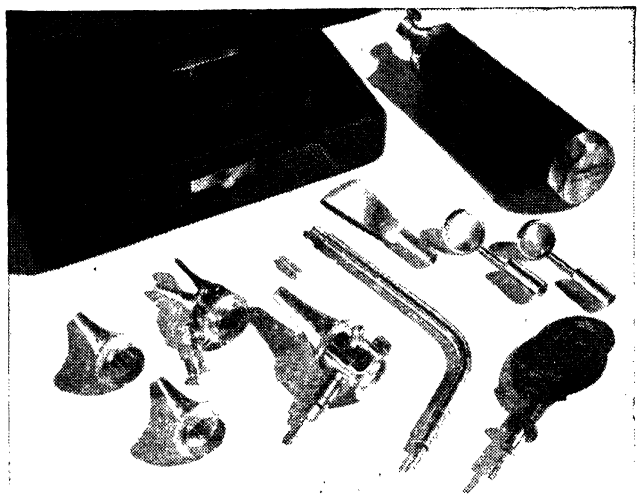
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