

THE
BRITISH ENCYCLOPAEDIA
OF
MEDICAL PRACTICE

MEDICAL PROGRESS

1964

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FOREWORD

One great use of a Review, indeed, is to make men wise in ten pages, who have no appetite for a hundred pages; to condense nourishment, to work with pulp and essence, and to guard the stomach from idle burden and unmeaning bulk.

REV. SIDNEY SMITH, 1824

New and startling discoveries which change fundamental concepts in medicine or provide us with wholly novel weapons against disease are rare and none has been reported during the past year. Yet *Medical Progress 1964* records valuable advances in all fields and helpful reassessments of earlier experience.

Professor Ellis sums up the steady progress in both palliative and curative operative procedures and chemotherapy in peptic ulcer, diverticulosis, fulminating ulcerative colitis, and carcinoma of the breast, oesophagus, liver and prostate.

The thalidomide tragedy leaves its trace in the search for other teratogenic drugs. Many have been indicted, for example, tetracycline, cyclizine and phenmetrazine, but firm proof is lacking. There is good evidence that influenza early in pregnancy might cause foetal deformities. Indeed, many and varied are the suggested stresses (including smoking) in early pregnancy which, it is thought, can affect foetal development. These are discussed in some detail by Professor Illingworth in his section on Paediatrics. In this he deals also with recent advances in many of the commoner diseases of childhood—prematurity, retarded growth, urinary tract infection, anaemia, epilepsy, accidents including burns—and the problem of emotional deprivation in the first years of life in relation to subsequent psychological damage.

Old controversies in the immunization field still rage. Will routine smallpox vaccination be replaced by the use of antiviral drugs in contacts? Should anti-toxin be given as a routine in the prophylaxis of tetanus despite its attendant hazards, or has the time come to replace this by antibiotics and wound toilet? Do the reactions to attenuated live measles vaccine prohibit its use in general prophylaxis, and if so, how best may its risks be minimized? These and kindred problems are objectively ventilated by Dr. Christie and Professor van Rooyen. Dr. Christie's experience with ampicillin in the treatment of typhoid carriers recorded before the Aberdeen typhoid outbreak receives strong confirmation from its use in that epidemic; there is also good evidence that ampicillin can be used as an alternative to chloramphenicol in typhoid and paratyphoid fevers, and that it is probably safer, especially if repeated courses are required.

The mechanisms underlying allergic responses are still ill-understood, but Dr. Macaulay reviews what is at present known of these in several clinical states.

During the past year the alleged production of massive hepatic necrosis by halothane has been vigorously debated. Dr. Geddes, reviewing reported papers, feels that at this stage a causative relationship has not been conclusively demonstrated. This view is upheld by Professor Mushin and his colleagues who have recently reported (*British Medical Journal*, 8 August, 1964) that 'out of 15,747 halothane and 6,123 non-halothane anaesthetics there does not appear to be any important differences in the effect on the liver between halothane and non-halothane'. Newer volatile anaesthetics are under trial, and the genetically

determined clinical responses to suxamethonium are being more widely recognized. The mechanisms of such anaesthetic complications as alkalosis and vomiting are being investigated in a manner which reflects the firm scientific basis of modern anaesthesia.

One of the fascinating themes in fundamental human biochemistry is the occurrence and role of isoenzymes. Professor Latner's contribution mirrors his own important work in this field. He has shown that analysis of isoenzymes has significant diagnostic value, and may indeed throw light on the neoplastic changes which may be induced in normal cells by viral infection. The enzymatic changes in muscular dystrophies are also reported, and the possibility of detecting female carriers of the Duchenne type of muscular dystrophy by increase in serum creatine kinase values is discussed. Many newly discovered inborn errors of metabolism are described, and the striking potentialities of newer biochemical techniques are discussed.

The mortality and incidence of all forms of tuberculosis continue to fall. Early detection, BCG vaccination and chemotherapy have all played their part. Dr. Hartston's section sums up recent views on the aetiology of farmer's lung (as does Dr. Macaulay's). In other chest diseases there have been no strikingly fruitful advances.

Dr. Lodge describes the more significant conditions in which radiology is an indispensable diagnostic aid, but he discusses also the steps which have been taken to reduce the radiation hazards of diagnostic radiology to a minimum, and the untoward effects which may follow the use of contrast media, especially of the tannic-acid-containing Clysodrast and thorium dioxide (Thorotrast).

The rare condition of pyridoxin-responsive anaemia introduces Dr. Wilkinson's informative review of haematological advances. The iron-chelating action of desferrioxamine and the use of fibrinolytic agents in intravascular thrombosis are regarded as significant therapeutic advances; but the results of new agents in the treatment of the leukaemias, especially acute, are disappointing.

Professor Polson gives a comprehensive survey and appends an extensive bibliography of important developments in forensic medicine. He draws attention to recent legislation concerning the plea of 'guilty but insane', flammable clothing, and the illicit traffic in 'purple hearts' (Drinamyl). Since his contribution went to press, the manufacturers of Drinamyl have announced that the shape of the tablet will henceforth be circular.

The claim that the healing of gastric ulcers is accelerated by a liquorice preparation (Biogastrone) is supported by firm statistical evidence. Dr. Avery Jones and Professor Alstead and his colleagues discuss this medication but stress the risks of oedema, especially in the elderly. The natural history and management of achalasia of the cardia are referred to by Professor Ellis and Dr. Avery Jones, and the latter's contribution mentions also that not only iron and vitamin B₁₂ deficiency may follow partial gastrectomy but calcium metabolism may also be affected and bone disease ensue. Diverticulosis of jejunum and colon, and ulcerative colitis are among the topics of current interest examined by Dr. Avery Jones.

The increasing social and medical problems presented by the elderly, many of which are preventable ('Then why not prevented?') are clearly presented with candour and authority by Dr. Kemp. His comments on 'psychogeriatrics' and the organization of geriatric care, including the benefits from providing day hospitals, are based on a wide experience and intimate concern for improved and more generous recognition of the needs of the ageing population.

Chromosome abnormalities continue to throw light on the inheritance of disease, and of these Dr. Clarke discusses in helpful detail recent work on the

Lyon hypothesis and on mosaicism. Discussions on genetically determined responses to drugs (*pharmacogenetics*) must now refer to the anticoagulant dicumarol, corticosteroids on intra-ocular pressure and dextran in rats. Many of the recent additions to our knowledge of blood groups, of natural selection in man, and of genetically influenced diseases are noted, and a most helpful glossary is appended for novitiates in this field.

Cancer research continues to excite public as well as medical interest, yet it is a tragic reflection on the efficacy of our present methods of health education that although the evidence for the causative association of cigarette smoking and cancer of the bronchus is overwhelming, cigarette smoking continues unabated. Chemotherapy in cancer meets with occasional successes but is, on the whole, disappointing. Cytological screening in cancer of the cervix uteri, stomach and lung increases the prospect of earlier recognition, and hence eradication, and there has been much discussion on radiological examination as an adjunct to clinical examination in the diagnosis of breast cancer. Mr. Raven summarizes also in his article recent advances in fundamental cancer research.

Cerebrovascular 'accidents' are among the neurologist's commonest diagnostic problems. Dr. Michael Jefferson's review throws light on many hitherto obscure corners. He describes also the rare Whipple's disease and its occasionally dominant neurological signs, and notes the renewed interest in uraemic polyneuropathy.

The posterior subcapsular cataract following steroids in rheumatoid conditions, the role of these drugs in the genesis of glaucoma (possibly, as earlier observed, genetically determined) and the retinopathies of chloroquine therapy present, observes Professor Perkins, examples of iatrogenic disease. He discusses also trachoma and other virus diseases of the eye, and their relation to genito-urinary infections; infestation of the eye with *Toxocara canis*; and the value of electro-oculography in detecting retinal dysfunction before fundal changes or visual symptoms occur.

Professor Roaf stresses that orthopaedic surgery has much to offer to improve the lot of those victims of ankylosing spondylitis with fixed, flexed, kyphotic deformities and fixed hips, and he has useful suggestions to make on improving the function of the rheumatoid arthritic hand by surgery. He supports the recommendations of the report of Sir Harry Platt's Committee on Accident and Emergency Services and has much of interest to relate on spinal injuries, fractures (especially bone grafting and non-union) and congenital deformities (especially von Rosen and Barlow's approach to congenital dislocation of the hip).

It is most helpful to have so comprehensive and yet so concise a description and evaluation of current progress in therapeutics by Professor Alstead and his staff. Some of the drugs they mention are discussed by other contributors in their specialized sections, but there is striking agreement on where significant advances have been made.

The present-day trend in social medicine is to replace institutional by community care. This means that health and welfare authorities must shoulder a heavier burden and the Ministry of Health publication on *Health and Welfare. The Development of Community Care* summarizes the 10-year plans made by 146 local health and welfare authorities. Dr. Millar reviews this report and also others published during the year, including the Gillie Report on *The Field of Work of the Family Doctor*; the Cohen Report on *Health Education*, and the B.M.A. Report on *Deaths in the Community*. He draws attention also to recent legislation in the field of preventive medicine, and the review in 1963 of arrangements for establishing smoke-control areas under the Clean Air Act, 1955,

necessitated by the diminishing future supply of gas coke. Other matters which come under review include noise, perinatal mortality, handicapped children and food safeguards.

The frank and objective review by Professors Roth and Kiloh of drugs used in mental disorders (psychopharmacology) is most timely. It is interesting to note also the deeper clinical analysis of depressive illness. The psychological risks of the housebound housewife, depersonalization and impairment of memory following E.C.T. are among other topics discussed.

Malaria remains a world problem, and Professor Maegraith summarizes hopefully the present position—'significant overall advancement has been made towards the ultimate objective of eradication'. He discusses drug resistance in both anopheline vector and parasite. Intramuscular CI501 appears to have an important place in malarial therapy, and there is good promise of drug control of schistosomiasis, filariasis and onchocerciasis. Changing views on the use of antivenin in snake bite, and the protection afforded by deficiency in erythrocytes of glucose-6-phosphate dehydrogenase against malaria, similar to but less powerful than that conferred by the sickle-cell trait, are also reported.

The venereal disease problem continues to be dominated by its social aspects, although there has been little change in incidence in the past year in England and Wales. Non-gonococcal genital tract infections and trichomoniasis have been the subject of much study, especially their therapy.

Professor van Rooyen discusses vaccination in measles and the control of poliomyelitis by live oral vaccine on a massive scale. He is hopeful about recent advances in the chemotherapy of viral diseases, and sees in the aetiology of the Burkitt African lymphoma the possible clue of the role of viruses in neoplasia. He reviews comprehensively the present status of our knowledge of respiratory viruses, the role of the thymus in immunity, some newer antibiotics, and the use of hyperimmune human *gamma*-globulin in viral and bacterial infections.

Mr. Dempster brings up to date the review on kidney transplantation which he contributed to last year's *Medical Progress*. During the year there have been reported successful transplantations of lung in man and heart in dog, and the mechanics of rejection of transplants has in some respects been clarified. Conflicting reports continue to be published on the various methods used to suppress rejection, and the 'normal lymphocyte transfer test' described by Brent and Medawar which was discussed in last year's Foreword has, disappointingly, been shown to have no value for humans. That only 3 per cent of human kidney transplants have survived for 1 year may seem a disappointing result, but in terms of future potentialities it must be assessed as a resounding achievement.

No special section on Medicine has this year been included since all topics that might usefully have been included in such a section are covered in other sections.

We are grateful, as always, to our contributors. No Editor in Chief could have been better served by his colleagues.

Cohen of Birkenhead.

CONTENTS

	PAGE
GENERAL SURGERY	1
HAROLD ELLIS, D.M., M.Ch., F.R.C.S. Professor of Surgery, Westminster Hospital, London	
PAEDIATRICS	18
R. S. ILLINGWORTH, M.D.(Leeds), F.R.C.P., D.P.H., D.C.H. Professor of Child Health, The University of Sheffield	
ACUTE INFECTIOUS DISEASES	27
A. B. CHRISTIE, M.A., M.D., D.P.H., D.C.H. Physician Superintendent, Fazakerley Hospital, Liverpool	
ALLERGIC DISEASES	36
D. BLAIR MACAULAY, M.B., Ch.B., M.R.C.P. Consultant Allergist, Royal Liverpool United Hospitals and Liverpool Chest Hospital; Consultant Physician, Bootle Hospital, Liverpool	
ANAESTHESIA	40
I. C. GEDDES, M.D.(St. And.), F.F.A.R.C.S., D.A. Senior Lecturer in Anaesthesia, University of Liverpool; Honorary Consultant Anaesthetist to the United Liverpool Hospitals; Honorary Consultant Anaesthetist to the Liverpool Regional Hospital Board	
CHEMICAL PATHOLOGY	56
A. L. LATNER, D.Sc., M.D., F.C.Path., F.R.I.C., F.R.C.P. Professor of Clinical Chemistry, University of Newcastle upon Tyne, and Consultant in Clinical Chemistry, Royal Victoria Infirmary, Newcastle upon Tyne	
CHEST DISEASE	67
W. HARTSTON, M.D., M.R.C.P., D.T.M., D.P.H. Chest Clinic, St. Thomas' Hospital; Tuberculosis Service, London County Council; Tuberculosis Research Fellow, Medical Research Council	
CLINICAL PHARMACOLOGY AND THERAPEUTICS	72
S. ALSTEAD, D. H. A. BOYD, JANET P. BROWNING, I. W. DYMCK, C. D. FORBES, G. PARKER LEWIS, J. G. MACARTHUR, N. MACKAY, T. J. THOMSON and A. G. G. TURPIE. Staff of the Department of Materia Medica and Therapeutics, University of Glasgow	
DIAGNOSTIC RADIOLOGY	102
THOMAS LODGE, M.B., F.F.R., F.C.R.A.(Hon.) Consultant Radiologist, The United Sheffield Hospitals; Lecturer in Radiodiagnosis, University of Sheffield	
DISEASES OF THE BLOOD	111
JOHN F. WILKINSON, M.D., M.Sc., Ph.D., F.R.C.P., F.R.I.C. Consulting Physician, United Manchester Hospitals	
FORENSIC MEDICINE	123
C. J. POLSON, M.D.(Birm.), F.R.C.P., F.C.Path., M.R.C.S. Barrister-at-Law. Professor of Forensic Medicine, University of Leeds; President of the British Association in Forensic Medicine	
GASTRO-ENTEROLOGY	152
F. AVERY JONES, M.D., F.R.C.P.	
AND	
J. HOWEL JONES, M.B., M.R.C.P., Department of Gastroenterology, Central Middlesex Hospital, London	
GERIATRIC MEDICINE	157
ROBERT KEMP, T.D., M.D., M.R.C.P. Visiting Physician, Walton Hospital and Newsham General Hospital, Liverpool	
HUMAN GENETICS	166
C. A. CLARKE, M.A., M.D., Sc.D.(Camb.), F.R.C.P.(Lond.). Reader in Medicine, University of Liverpool; Consultant Physician, Liverpool Royal Infirmary and Broadgreen Hospital, Liverpool	
MALIGNANT DISEASE	178
RONALD W. RAVEN, O.B.E. (Mil.), T.D., F.R.C.S. Senior Surgeon, Royal Marsden Hospital and Institute of Cancer Research, Royal Cancer Hospital; Surgeon, Westminster Hospital; Joint Lecturer in Surgery, Westminster Medical School, University of London; Late Hunterian Professor, Royal College of Surgeons of England	

	PAGE
NEUROLOGY	191
MICHAEL JEFFERSON, D.M., F.R.C.P. Consultant Neurologist, Queen Elizabeth Hospital, Birmingham	
OPHTHALMOLOGY	203
E. S. PERKINS, M.D., Ph.D., F.R.C.S. Professor of Experimental Ophthalmology, Institute of Ophthalmology, London	
ORTHOPAEDIC SURGERY	210
ROBERT ROAF, M.A., M.Ch., F.R.C.S. Professor of Orthopaedic Surgery, University of Liverpool	
PRESENT STATE OF KIDNEY TRANSPLANTATION	220
W. J. DEMPSTER, F.R.C.S. Reader in Experimental Surgery, and Consultant in Organ Transplantation, Postgraduate Medical School of London, Hammersmith Hospital	
PREVENTIVE AND SOCIAL MEDICINE	227
E. L. M. MILLAR, M.D., M.Sc., D.P.H. Medical Officer of Health, Birmingham	
PSYCHIATRY	239
MARTIN ROTH, M.D., F.R.C.P., D.P.M. Professor of Psychological Medicine, Department of Psychological Medicine, Royal Victoria Infirmary and University of Newcastle upon Tyne	
AND	
L. G. KILOH, M.D., M.R.C.P., D.P.M. Professor of Psychiatry, University of New South Wales, Australia	
TROPICAL MEDICINE	254
B. G. MAEGRAITH, M.A., M.B., D.Phil., F.R.C.P.(Lond.), F.R.C.P.(Edin.). Professor of Tropical Medicine, Liverpool School of Tropical Medicine, University of Liverpool; Physician in Tropical Diseases, Tropical Diseases Centre, Sefton General Hospital, Liverpool	
VENEREAL DISEASES	260
C. S. NICOL, M.D., F.R.C.P. Physician in Charge of the Venereal Diseases Department, St. Thomas' and St. Bartholomew's Hospitals, London	
VIROLOGY, BACTERIOLOGY, IMMUNOLOGY AND SEROLOGY	269
C. E. VAN ROOYEN, D.Sc.(Edin.), M.D.(Edin.), F.R.C.P.(C.), M.R.C.P.(Lond.), M.C.Path. Professor of Bacteriology, Dalhousie University, Halifax, Nova Scotia	

INDEX

GENERAL SURGERY

BY HAROLD ELLIS, D.M., M.Ch., F.R.C.S.
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1963 was not a year of astonishing advances in general surgery, yet the publications which we review in these pages show well the modern trends of progress. The attempts to base surgical procedures on sound physiological as well as anatomical principles is illustrated by studies in selective vagotomy and in more conservative surgery of high gastric ulcers. The careful investigation of the patient in the post-operative period is shown by the work on bowel motility after surgery. The constant steady progress in dealing with malignant disease both by palliative and curative techniques can be seen in publications on the management of mammary, oesophageal, hepatic and prostatic cancers.

Even if these advances are only small, at least the scientific spirit in which they are made is commendable.

GASTRO-INTESTINAL SYSTEM

Carcinoma of the oesophagus

Carcinomas of the oesophagus and of the cardiac end of the stomach are often so far advanced at the time of presentation that surgery cannot cure because of local or distant spread. Thus, Miller (1962), reviewing 405 cases of carcinoma of the oesophagus treated in the Liverpool Thoracic Surgical Unit, recorded that 272 patients were considered fit for thoracotomy (67 per cent), of which only 144 were then found to be suitable for radical resection. In the majority of cases then, death is inevitable either following the prolonged miseries of dysphagia or by more acute catastrophes including haemorrhage and tracheal, bronchial or aortic fistulae. Even in the technically operable group of patients, many are, in fact, beyond radical surgical help because of extreme debility and the operation itself is formidable with a high initial mortality.

The problem remains of how to manage the dysphagia which is the presenting symptom in the majority of patients. Although short-circuit procedures have been devised in which mobilized loops of jejunum or colon are anastomosed between stomach below and oesophagus above the obstruction, these have the disadvantage of being extensive and often staged procedures in already seriously ill and doomed patients. Moreover, the operative mortality is in the region of 50 per cent and the palliative results produced are often unsatisfactory (Miller, 1962).

In 1927, Sir Henry Souttar introduced his coiled silver wire tube which could be passed on an introducer through a carcinomatous stricture of the oesophagus after preliminary dilatation. He reported an average survival of 5 months with 1 patient living for nearly 2 years. Useful though this tube is, it has the disadvantages that it is difficult to pass through an extensive growth, it cannot be used for bulky tumours or those involving extensively the upper end of the stomach, it has a narrow lumen and tends to work its way free and pass downwards into the stomach, and then per rectum.

In recent years improved tubes of plastic have been introduced (Mousseau and colleagues, 1956; Celestin, 1959). The technique of their use is fairly simple. Under a general anaesthetic oesophagoscopy is performed; a pilot bougie is negotiated through the malignant stricture. An upper abdominal incision is then made and a small gastrotomy opening fashioned. The bougie is grasped and drawn downwards, pulling with it the plastic tube which has been attached to its upper end. The tube is pulled through the stricture until its upper flange sits on the proximal end of the growth. The redundant portion of the tube is cut off and the gastrotomy closed. Fluids can be started at once and semi-solids commenced in a few days; coarse foodstuffs are, however, forbidden. Meals should be followed by a draught of soda water to clear the tube.

Individual surgeons have now performed sufficient numbers of these intubation procedures for us to assess its value. Waddington and Bickford (1962) reported their experience with 44 cases, which included not only oesophageal and cardiac tumours but also bronchial carcinomas invading the oesophagus. There were 12 early deaths, mostly in patients who were already in extremely poor general condition. Two of these deaths were due to rupture of the oesophagus. The average length of survival of the remainder was 4 months, but 1 patient lived for nearly a year. Carter and Hinshaw (1963) had 4 post-operative deaths in 20 patients, 1 being due to perforation. Good palliation was achieved in all their cases apart from 1 patient with a carcinoma of the cervical oesophagus; here severe discomfort and haemorrhage necessitated removal of the tube. It is now a general experience that the method is unsuitable for growths in this high situation.

In effect, these procedures enable the patients' last few weeks or months of incurable disease to be spent in comparative physical comfort.

Radiation treatment

Most authorities agree that tumours of the lower oesophagus, if resectable and if the patient's general condition is satisfactory, should be treated surgically; indeed, it is in this region that the majority of successes have been reported. Moreover, accurate radiation treatment of tumours at this site is difficult.

Surgery of the upper two-thirds of the oesophagus carries with it a very high mortality, and a low survival rate even after successful resection. Tanner and Smithers (1961) found reports of 246 patients with carcinoma of the oesophagus who had survived 5 years after resection; the site of the tumour was specified in 165, of which only 46 occurred in the upper two-thirds of the oesophagus. Because of these poor results and because of improved radiotherapeutic techniques, more consideration is now being given to radiation therapy. Tanner and Smithers found that 89 patients treated with radiotherapy with 5-year survival have been reported. The site was noted in 74 cases and 46 of these occurred in the upper two-thirds.

Watson (1963) presents 21 cases of carcinoma of the middle and upper thirds of the oesophagus treated by the cobalt-60 beam: 14 patients were able to complete the course of irradiation; their average survival was 29 months; 4 survived 5 years, of which 1 died at $7\frac{1}{2}$ years, the others being alive 5, 8 and 9 years after treatment. Meticulous attention to technique will reduce the hazards of irradiation necrosis or stricture of the oesophagus. This report lends strong support to the contention that radiation therapy is superior to surgical excision in the treatment of cancer of the upper two-thirds of the oesophagus, although surgery is still the treatment of choice for lesions of the lower one-third.

Selective vagotomy in duodenal ulcer

It is surprising that very little is known of the function of the vagus nerve beyond its gastric distribution. Upon passing through the oesophageal hiatus, or occasionally a short distance above it, the anterior (or left) vagus gives off a hepatic branch which passes to the right in the lesser omentum, crosses the caudate lobe of the liver, where it has a constant and easily noted position, to the porta hepatis where it joins the hepatic autonomic plexus. It supplies the liver and gall bladder, and in addition a twig descends in the lesser omentum to the pylorus and to the first part of the duodenum. Frequently, there is more than one anterior vagal trunk, each of which gives off a hepatic branch (Burge, 1961). The posterior (or right) vagus passes through the oesophageal hiatus in one or more main trunks and gives off a coeliac trunk which runs to the coeliac plexus along the left gastric artery; this branch supplies the intestine from the duodenum to the ascending colon in addition to supplying the pancreas.

It is estimated that the abdominal distribution of the vagus comprises 65 per cent of fibres to the stomach, 25 per cent to the coeliac branch, and 10 per cent to the hepatic branch. About 80 per cent of all the fibres are afferent. Electrical stimulation of the hepatic branch produces a contraction of the gall bladder, and a brisk motility response in the duodenum brought about via the fibres which pass from the hepatic

branch to the pylorus. Stimulation of the coeliac trunk produces contractions in the intestine from the duodenum to the ascending colon.

Although vagotomy combined with some form of drainage procedure has now been used widely in the treatment of duodenal ulceration for more than a decade, little attention has been paid to the possibility that widespread denervation of other intra-abdominal viscera, apart from the stomach, may be deleterious.

A number of surgeons are now reporting their preliminary investigations of the results of selectively dividing those fibres of the vagus passing to the stomach (selective gastric vagotomy) with preservation of the coeliac or hepatic trunks, or both.

In departing from the generally accepted view that success with vagotomy depends upon division of all the vagal fibres of the hiatus, selective gastric vagotomy immediately raises the question of its effectiveness in producing complete vagal denervation of the stomach.

Griffith and colleagues (1963) have shown after selective gastric vagotomy in dogs that subsequent gastric analyses with insulin stimulation show no free acid. Barium meal radiographs show the stomach to be atonic and dilated, and subsequent trans-thoracic total abdominal vagotomy does not accentuate these changes. Studies were also carried out using an open-tipped catheter in the antrum and in the small intestine of these animals. If the main vagal trunks above the diaphragm were stimulated with the vagi intact, pressure elevation occurred at all the levels tested. Selective gastric vagotomy eliminated only the gastric contractions, but if the hepatic and coeliac branches alone were divided with preservation of the gastric branches, there was complete cessation of response to electrical stimulation throughout the alimentary tract, except for the stomach and the most proximal portion of the duodenum.

Although we have a precise diagnostic method to assess the full effect of vagotomy upon the stomach by means of the secretory response of free hydrochloric acid to insulin hypoglycaemia, unfortunately we have no similar precise diagnostic methods to assess the effects of vagotomy upon the bowel, biliary tract and the pancreas. One could postulate that stasis in the biliary tract and decreased volume and enzyme content of the pancreatic juice might result in steatorrhoea and that intestinal atony might produce abdominal discomfort and distension. It is interesting, however, that the great majority of patients after total abdominal vagotomy are free of symptoms. Indeed, diarrhoea is the only undesirable feature of total vagotomy that has received attention and it must be stated that, at present, its cause remains unknown. It has been postulated that stasis in the achlorhydric stomach allows unrestricted growth of bacteria in the stomach and small intestine but there is no clear evidence of this. There is no convincing evidence that the vagus plays a part in hepatic or pancreatic function in man.

Kraft, Fry and Ransom (1962) studied 12 patients before and after vagotomy; there was no difference in the small bowel transit time of a barium meal from the pylorus to the caecum. Any discussion of post-vagotomy diarrhoea is bedevilled by the widely differing reports of its incidence. This has been placed as high as 30 per cent but most surgeons of experience will agree with Kay (1962) that some 4 per cent of patients following vagotomy will report diarrhoea sufficient to detract from the success of the operation. Rarely is this a serious complaint on the part of the patient.

Against this background it is obviously difficult to assess the value of selective gastric vagotomy. Burge and colleagues (1961) stated that in 100 patients after total vagotomy there was a 26 per cent incidence of diarrhoea. In 73 patients where the coeliac branch was preserved the incidence was 23 per cent, yet in 100 patients where both the coeliac and hepatic trunks were preserved the incidence fell to 12 per cent. On this basis they strongly advise preservation of the hepatic trunk.

Smith and Farris (1963) reported a 28 per cent incidence of diarrhoea in 100 total vagotomies; one of these was severe. They carried out various combinations of selective vagotomy in 40 patients and claimed that the incidence of diarrhoea was halved, although they found no difference between preserving both the coeliac and hepatic branches and the hepatic branch alone.

Kraft, Fry and Ransom (1962) compared 47 total and 40 selective vagotomies and claimed that the incidence of diarrhoea fell from 38 to 19 per cent in the selective cases. Most surgeons are amazed at these very high incidences of post-vagotomy

diarrhoea; one wonders how much of this is due to the return of the usually constipated patient with duodenal ulceration living on a restricted diet, to the normal bowel habits of a healthy individual on a normal full diet. It is a very common experience for a patient after a vagotomy or gastrectomy to say with delight that his bowels have now returned to one or two normal actions a day. Could this be interpreted by the enthusiast as diarrhoea?

One cannot deny that the occasional patient after a gastric operation, whether this be vagotomy or partial gastrectomy, does experience severe diarrhoea and steatorrhoea. At present this remains an unsolved mystery; a mystery which is deepened when one notes in any carefully conducted follow-up study that these diarrhoeas include transient affairs, which clear some months after operation, and even more peculiar episodic attacks in which a short burst of diarrhoea, lasting hours or days, may occur at infrequent intervals.

Obviously, the more that is known of the physiology of the vagus in man the greater the possibility of throwing some light on to this obscure subject, but further research must include accurate analysis of the number of daily stools before and after surgery and eschew subjective evidence.

Gastric hypothermia in duodenal ulcer

In 1962 enthusiastic reports appeared from Wangenstein and his colleagues in Minneapolis on the value of gastric hypothermia in the management of haemorrhage from duodenal ulceration, and also in non-complicated peptic ulcers (Wangensteen, 1962). At this stage follow-up results were short, in fact, less than 1 year.

A symposium on gastric freezing was held at the meeting of the American Gastroenterological Association in 1963 at which a number of investigators reported their experimental and clinical findings. A fall in gastric secretion certainly occurred after hypothermia but this returned to normal over a period of 6 weeks to 6 months. The procedure is not free from risk; cases were recorded in which gastro-intestinal haemorrhage followed 7 or 10 days later and there were reports of gastric ulceration occurring and occasionally of severe shock associated with this procedure. Inadvertent palpation of the frozen stomach may fracture it from the cardia to the pylorus, and there has certainly been one recorded fatality; a patient who had a severe haemorrhage 5 days after freezing, was submitted to emergency operation. Death followed because of dehiscence of the anastomosis, the stomach being so necrotic that it would not support sutures (Welch, 1963).

McIlrath and colleagues (1963), at the Mayo Clinic, reported an extensive experimental investigation using the Wangenstein hypothermia machine as supplied for clinical use; this was tested on a series of dogs and pigs. They found that the temperature of the alcohol passing through the gastric balloon does not reflect that of the gastric mucosa; this depends on the thickness of the wall of the balloon, the speed of flow of the cold perfusing fluid, the tightness of the fit of the balloon within the stomach, the rate of flow of blood in the stomach wall and the presence of general hypothermia. In small dogs, where the balloon was a tight fit against the stomach wall, extensive necrosis of the mucosa was found, or even full-thickness sloughing took place with perforation. In the larger animals patchy areas of superficial necrosis occurred whenever portions of the stomach were presumably pressed close against the gastric balloon.

These disturbing findings underline the fact that the procedure of gastric hypothermia is not free from risk; it obviously requires further careful laboratory and clinic investigation before its exact role in the management of peptic ulceration can be determined.

Surgical treatment of gastric ulcer

Dragstedt (1956) has for long maintained that duodenal ulceration is usually due to an excessive nervous phase of gastric secretion and, in contrast, gastric ulceration results from the hypersecretion of gastric juice of hormonal origin. He postulated that in the latter group there is prolonged or excessive liberation of the hormone gastrin which is produced by the gastric antrum. A hypersecretion of hormone-invoked gastric juice can be induced in dogs by transplanting the denervated antrum

of the stomach to the colon wall; this hypersecretion may be sufficient to produce ulceration of the normal gastric mucosa. Moreover, both in man and in animals, gastric stasis or obstruction can similarly produce an excessive production of gastric juice of hormonal origin with the formation of a gastric ulcer; indeed, an association between gastric ulcer and preceding pyloric stenosis due to duodenal ulceration is far from uncommon.

Dragstedt's nervous hypersecretion theory of duodenal ulceration is now well accepted and has revolutionized the surgical attitude to this lesion. Many surgeons are now in favour of the simple procedure of vagotomy combined with drainage of the stomach rather than the more mutilating high partial gastrectomy with gastro-jejunal anastomosis, which carries with it a higher risk of early and late complications (Stammers and Williams, 1963). Although Dragstedt's ideas on the aetiology of gastric ulcers are in less universal favour it is of great interest that resection of the antrum with its gastrin-producing mucosa or even simple drainage of this region is followed by healing of the gastric ulcer.

Over 40 years ago, Kelling (1918) reported the healing of a stomach ulcer after resection of the pylorus. Since then, other surgeons have recorded similar experiences. Gammie (1963) reviewed 25 patients treated at the London Hospital with very high gastric ulcers in which the antrum was resected leaving the ulcer itself *in situ*. The cases were reviewed 2-10 years later; all had remained free from symptoms and fresh barium studies of 20 of the cases showed no evidence of the original lesion. One patient developed a carcinoma in the gastric stump 3 years after the operation, a phenomenon which is not unusual even after more conventional gastrectomies.

If doubt exists at the time of the laparotomy, a frozen section can, of course, be performed to confirm or refute the benignity of the ulcer.

Farris and Smith (1963) described 18 patients with gastric ulceration treated by biopsy of the ulcer, pyloroplasty to drain the antrum and, in 15 of the cases, vagotomy. The last named was used because of evidence in no less than 10 of the cases of co-existing duodenal ulcer. One patient died of aspiration of vomit; the remaining 17 all showed radiological evidence of complete healing of the ulcer.

The results of conventional partial gastrectomy for gastric ulcer, removing the ulcer itself and the antrum and restoring continuity by gastro-duodenal anastomosis, is a highly satisfactory operation. However, in some 10 per cent of cases the gastric ulcer is situated high on the lesser curve and in some, at least, removal of the ulcer can only be performed with considerable hazard to the patient and by a very radical resection of stomach. There seems little doubt that these reports of the efficacy either of removal of the antrum with preservation of the bulk of the stomach and its contained ulcer, or simpler still, of antral drainage combined with a protective vagotomy, provide the surgeon with a useful technique in the management of this problem.

Diverticulosis of the colon

Very little has been added to the natural history of diverticulosis of the colon since the brilliant account of Telling and Gruner of Leeds was published in 1917, yet surprisingly little attention has been paid to the aetiology of this common and increasingly important condition.

Diverticulosis occurs in patients over middle age; it is almost unknown under the age of 40 years and then the percentage increases in each decade. Thus, Dearlove (1954), in an extensive post-mortem study of nearly 7,000 subjects at the Royal Adelaide Hospital, found an incidence of approximately 1 per cent in the forties, 1.7 per cent in the fifties, 3.5 per cent in the sixties and 7 per cent in subjects over the age of 70 years.

The diverticula arrange themselves in two columns alongside the lateral taeniae coli, and are often overlapped by appendices epiploicae; they never open primarily into the mesocolon as do small-bowel diverticula into the mesentery. This distribution of colonic diverticula corresponds exactly to the points of penetration of the blood vessels into the bowel wall, which no doubt produces points of weakness in the colonic muscle (Drummond, 1917). However, although these facts are well established, the reason for the formation of diverticula has remained obscure, perhaps because

too much attention has been paid to the saccules themselves and not enough to the surrounding colon.

Morson (1963a and b) carefully studied a large series of specimens removed for 'diverticulitis' at St. Mark's Hospital, London. Of 173 specimens, 112 (64.7 per cent) showed evidence of diverticulitis which was extensive in 67 and focal in 45 cases. In 61 specimens there was no inflammation at all, and 5 of these, indeed, showed not even diverticula; yet all these resections had been performed on patients diagnosed as having 'diverticulitis' on clinical and radiological grounds. However, all the specimens examined showed a striking abnormality of the smooth muscle. The taeniae coli were thickened and almost cartilaginous in consistency; the circular muscle was also much thickened and thrown into concertina-like folds with the mouths of the diverticula opening between their corrugations. The thickening seems to be due to a shortening rather than a true hypertrophy of the plain muscle cells and this shortening accounts for the characteristic redundancy of the mucosa which is itself thrown into folds and appears to be a contributory factor in the obstructive symptoms which are so frequently found in diverticular disease.

The excessive quantities of fat which are found in the sigmoid mesocolon in diverticulitis can also be explained by the bunching of the pericolic tissues as a result of this shortening of the bowel by muscular contraction.

There is good evidence to support the hypothesis that it is this thickening and contracting down of the sigmoid muscle which is the basic pathology of diverticulosis, the saccules then appearing at the points of weakness where blood vessels penetrate the muscle wall.

Confirming experiments are those of Wilson (1950) who found that he could produce diverticula of the normal appendix freshly removed at operation by cutting a defect through the muscle wall and then stimulating the appendix to contract by squeezing it; as the appendix shortened, so a 'diverticulum' appeared.

In this context, an observation made at operation by Barling (1926) is of interest. At laparotomy on a man aged 43 years he found the sigmoid colon to be thickened but free from diverticula. He then noticed that the colon contracted down over a short segment to the thickness of the index finger, and then many saccules appeared between the taeniae coli which were up to $\frac{1}{3}$ inch in diameter; this phenomenon repeated itself on several occasions.

Although Morson has done much to explain the basic pathology of diverticular disease of the colon the cause of this muscle abnormality remains unknown and stresses our present ignorance of the normal physiology of the colonic muscle.

Morphine in diverticulosis

Painter and Truelove (1963) reported their interesting studies of pressures within the human sigmoid colon, both in normal subjects and in patients with diverticulosis. Simultaneous ciné-radiography was also employed. Under resting conditions the pressure pattern in the normal sigmoid colon was very similar to that obtained from the colon affected by diverticulosis. After morphine had been given the normal bowel produced waves of higher pressure which seldom exceeded 30 mm Hg. In the colon with diverticula, non-affected portions of the sigmoid behaved once again like normal colon, but areas which were the sites of diverticula responded to morphine by producing a greatly increased number of contraction waves of high pressure. In these instances ciné-radiography demonstrated that the colon was divided by contraction rings into a series of segments whose outflow was obstructed, thus allowing high localized pressures to develop; these were seen on occasions to distend the diverticula very considerably. It is probably of practical importance that pethidine was found not to increase either the number or the force of the intracolonic pressure waves and would appear to be the drug of choice in the treatment of diverticulitis.

Fulminating ulcerative colitis

There is a close relationship between the clinical severity of an attack of ulcerative colitis at the time a patient reaches hospital and his risk of dying in that attack. This is borne out by a very careful study of the course and prognosis of ulcerative colitis in a group of 624 patients studied by Edwards and Truelove (1963) in Oxford from

1938 to 1962. The clinical severity of the attack in this study was divided into three groups. Severe attacks, characterized by severe diarrhoea with six or more motions a day with macroscopic blood in the stools, fever, tachycardia, anaemia and a greatly raised erythrocyte sedimentation rate. Mild attacks comprised mild diarrhoea of four or less motions a day accompanied by only small amounts of blood in the stools, no fever, a normal pulse, anaemia not severe and an erythrocyte sedimentation rate below 30 mm in 1 hour. Moderately severe attacks were defined as those intermediate between these two groups.

In the period 1938–1952, before the use of corticosteroids, the mortality of patients dying in the first referred attack was approximately 30 per cent in the severe group, 20 per cent in the moderate group, and 1 per cent in the mild group. In the period 1953–1963 there was little change in the mortality in the severe group, but that in the moderate group had fallen to 2.4 per cent and in the mild group to under 1 per cent.

Obviously, then, it is in this group with severe colitis that the high initial mortality lies. Within this group are those fulminating cases of ulcerative colitis characterized by dilatation of the large bowel, necrosis of the colonic wall and often perforation.

In these cases the patient is extremely ill, febrile, and dehydrated, with a rapid and sometimes uncountable pulse. The abdomen is distended, tender and there may be rebound pain. This clinical picture is often accompanied paradoxically by constipation rather than diarrhoea and by relative absence of bowel sounds. This is because of the atonicity of the severely diseased colon. In some instances the dilatation of the bowel is associated with potassium depletion but this is by no means always so, and a causal relationship rests between the colonic dilatation seen clinically and the histological appearance of smooth muscle cellular damage seen in the resected or post-mortem specimens.

The microscopic appearance is of a massive inflammatory process of all the coats of the colonic wall accompanied by infiltration of collections of acute and chronic inflammatory cells. In some cases this already dangerous situation is complicated by drenching haemorrhages from the ulcerated bowel.

Unless frank perforation has already occurred into the peritoneal cavity the treatment of these fulminating cases is first, at least, medical. Dehydration and electrolyte imbalance are corrected and the blood loss replaced. The toxæmia is treated by systemic antibiotics as well as salicylazosulphapyridine (Salazopyrin). Although some clinicians are opposed to the use of corticosteroids in the fulminating attack, most are in favour of vigorous therapy, the patient being kept in the meantime under hawk-like observation. Truelove recommended prednisolone, 10 mg four times a day together with a rectal drip of hydrocortisone hemisuccinate, 100 mg twice daily. If the patient is nauseated and vomiting, prednisolone 21-phosphate 20 mg twice daily by intravenous injection is given.

Failure to rapidly control a fulminating attack is an urgent indication for operative treatment. The standard procedure is a total colectomy, bringing up the terminal ileum and the rectal stump respectively as an ileostomy and a proctostomy. Subsequently, either an ileo-rectal anastomosis can be performed or the rectal stump excised.

Even in the hands of the most expert surgeons the mortality is inevitably high. Aylett (1963) recorded 40 fulminating cases treated over the period 1952–1961 by total colectomy with 5 deaths (12.5 per cent). Of the 35 survivors, 1 has since died from an unrelated cause, and of the remainder all but 2 now enjoy normal health. One of these exceptions has a small abdominal fistula and the other has periodic effusions into the knee joints. Aylett is in favour of urgent surgery in such cases without steroid therapy unless the patient has already received it in previous episodes of the disease.

For the less experienced surgeon who deals only occasionally with these desperate emergencies the mortality is much higher. For this reason a paper by Hickey, Tidrick and Layton (1963) is of considerable interest. They reviewed 13 patients with fulminating ulcerative colitis occurring in a 10-year period, during which time 266 patients with ulcerative colitis were admitted to the surgical department at the College of Medicine of the State University of Iowa; this fortunate rarity of the fulminating cases is common experience of all published series. In 3 of these fulminating cases

they performed a double-barrelled ileostomy, the proximal barrel diverting the faecal stream and the distal stoma being used to decompress the colon via a soft rubber tube passed into the caecum. All 3 patients recovered and, subsequently, staged total proctocolectomy was performed.

The present author has carried out a double-barrelled ileostomy in 3 patients with severe attacks of colitis using the distal stoma to irrigate the colon locally with hydrocortisone. In each case there was a gratifying remission of the severe local and general features. This method, if proved effective in a larger number of cases, would obviously be of great value to surgeons who are without extensive experience of emergency total colectomy, and are called upon to deal with these fulminating cases. The operation itself is extremely simple and may tide the patient over into a satisfactory condition for more radical surgery.

Abdominal colic

It is refreshing among the welter of modern technological and experimental work to find that there is still a place for the careful clinical study of patients.

French and Robb (1963) carried out an analysis of the time and intensity pattern of the pain experienced by 50 patients with biliary and 50 with renal colic. It is a common misconception that these pains are paroxysmal; perhaps because the word 'colic' has mistakenly come to be associated with the idea of intermittency.

In this study it was found that in biliary colic the pain usually rises to a crescendo, although the pain may be at maximum intensity from the time of onset. Occasionally, this severe pain fluctuates in intensity, but only 1 patient found it to be truly intermittent. The pain of renal origin often has a similar pattern but the fluctuating pain occurred in nearly half the cases; none had intermittent pain. In both conditions the pain is severe, the patient tends to be restless and sweating and there may be associated nausea or vomiting.

The radiation of the pain is helpful in the differential diagnosis; that of biliary disease radiates to the right scapula, the right hypochondrium or to the dorso-lumbar region. Occasionally, the pain is experienced in the left scapula or the right shoulder tip. The pain produced by a stone in the renal tract, however, is frequently associated with radiation into the hypochondrium, the iliac fossa or the groin on the affected side. Sometimes there is almost diagnostic pain radiating into the tip of the penis or into the vulva.

The accompaniments of the pain are of the greatest diagnostic value. A tinge of jaundice was noted in half the patients with biliary colic in this study. The presence of bile in the urine or clay-coloured stools is also of great importance. The passing of calculus in the urine, of course, clinches the diagnosis of renal colic, but haematuria, either macroscopic or detected by examination under the microscope, is of considerable importance. Much remains to be learned by careful clinical investigations of abdominal pain. As the late John Ryle (1926) said: 'There is no study more likely to furnish interests and rewards in practice than a concerted study of visceral or other pains. Results will come very slowly, but these need not deter. No apparatus is required, no laboratory experience is necessary and yet a valuable piece of clinical research can be pursued'.

Gastro-intestinal post-operative motility

It has generally been accepted that abdominal surgery has a definite, if transient, inhibitory effect on the movements of the whole of the gastro-intestinal tract. Certainly following any intra-abdominal procedure there is a period which lasts for some 48 hours during which the abdomen is silent on routine auscultation and during which time there is absolute constipation. As intestinal activity returns to normal there is often some colicky abdominal pain followed by the passage of flatus.

The concept of generalized atony of the whole gastro-abdominal tract following laparotomy has now been challenged by a number of workers. These investigations indicate that, following laparotomy, the ileus affects the stomach and colon but the small intestine retains its activity, although at a somewhat diminished level.

In the forefront of these investigations are those of Professor Charles Wells and his colleagues in Liverpool (Wells and colleagues, 1964). Investigations included aus-