RES MEDICA
Journal of the Royal Medical Society

Contents

Copyright Royal Medical Society. All rights reserved. The copyright is retained by the author and the Royal Medical Society, except where explicitly otherwise stated. Scans have been produced by the Digital Imaging Unit at Edinburgh University Library. Res Medica is supported by the University of Edinburgh's Journal Hosting Service: http://journals.ed.ac.uk

ISSN: 2051-7580 (Online) ISSN: 0482-3206 (Print)
Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, May 1961, 2(4)
doi: 10.2218/resmedica.v2i4.369

26.5.61

Volume II, No. 4 May 1961

RES MEDICA

THE JOURNAL OF THE ROYAL MEDICAL SOCIETY

Contents

PRICE ONE SHILLING

See the BANK OF SCOTLAND *FIRST*...

about the EASY way to deal with regular payments . . .

Rather than depend on your calendar to remind you of the need to fulfil regular-payment commitments, why not simply ask the BANK OF SCOTLAND to be your memory?

The Banker's Order service is designed to make life SO MUCH EASIER!

BANK OF SCOTLAND

Take
a second opinion

you'll find the next

GUINNESS

just as good as the first

G.E.3454C

THE TROUBLE WITH SECURITY . . .

. . . *IS THAT ONE CAN NEVER BE SURE OF IT LASTING*

Supposing you were ill for a considerable time. Would your practice and consequently your income suffer ? This Society, run by Doctors for Doctors, specialises in Insurance for the Medical Profession.

Non Cancellable With Profit
SICKNESS AND ACCIDENT INSURANCE.
LIFE ASSURANCE.
PERSONAL PENSION POLICIES.

When you are buying a car or equipment why not ask for details of the Hire Purchase Scheme of our sudsidiary company—the Medical Sickness Finance Corporation of 7 Cavendish Square, London, W.1. Telephone Museum 9348.

Write to the General Manager and Actuary

* MEDICAL SICKNESS SOCIETY

3 CAVENDISH SQUARE, LONDON, W.1.

Telephone: MUSeum 1686 (10 lines)

*** MEDICAL SICKNESS ANNUITY AND LIFE ASSURANCE SOCIETY LIMITED**

RES MEDICA

THE JOURNAL
OF
THE ROYAL MEDICAL SOCIETY

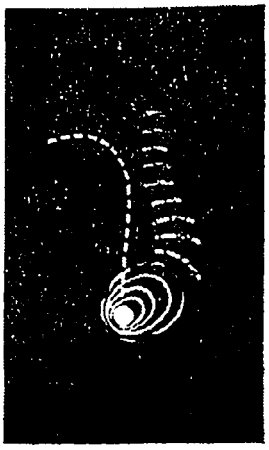
Editor
N. A. BOYLE

Editorial Committee
J. L. CHRISTIE
D. H. K. SMITH
R. L. MARSHALL
Dr. D. J. CLARK

Published by

THE ROYAL MEDICAL SOCIETY
7, MELBOURNE PLACE
EDINBURGH, 1

The management of Pain



DF 118

DIHYDROCODEINE BITARTRATE

a potent oral analgesic

In general practice DF 118 fills the gap between Tab. Codein. Co. and Morphine. It causes fewer side effects than other analgesics of equal potency and is not D.D.A.

	PACK	BASIC N.H.S. PRICE
Tablet of 30 mg.	25	5s. 0d.
do.	100	16s. 8d.

DUNCAN FLOCKHART OF EDINBURGH

The Doctors' House

Duncan, Flockhart & Co. Ltd., Edinburgh 11. adf 288

DEBILITY AND/OR LOSS OF WEIGHT
THE DIAGNOSTIC APPROACH

By CHARLES W. SEWARD, M.D., F.R.C.P.E.

Based on an address delivered to the Royal
Medical Society, on Friday, 11th November, 1960.

Nor bring to see me cease to live,
Some doctor full of phrase and fame
To nod his sapient head and give
The ill he cannot cure a name.

—MATTHEW ARNOLD

These last few decades have given us greatly increased precision of diagnosis and therapeutic power, and we, no longer merit Matthew Arnold's rebuke. These revolutionary changes have been produced as a result of a great spirit of free enquiry, a search for facts and their explanation. Such a search is dependent initially on the development of a working hypothesis, and this is just what a tentative diagnosis is. From this point our search is for facts uncoloured by accepted authority, popular opinion or personal prejudice.

In medicine Galen of Pergamum was the "Master" for many centuries, and from 200 A.D. the dead hand of Galen's authority lay upon medicine for over 1300 years. The mighty Leonardo da Vinci first questioned Galen's views and in England in 1620 Francis Bacon in his "Novum Organum" urged men to abandon their four idols—accepted authority, popular opinion, legal bias and personal prejudice. Yet, despite Leonardo da Vinci and Bacon and even the revolutionary work of Harvey in 1628, it was not until the time of Lister (1860) that medicine ceased to be a traditional empirical art bound to the words of the Master and accepted authority.

There are for us three kinds of facts, viz. symptoms, signs and the results of investigations, and upon these we base our diagnosis. It is because of the difficulty in setting down an accurate account of the first of these that medicine will be for ever an art.

THE HISTORY AND SYMPTOMS

We have to get down upon our history sheet what is in the patient's mind; the patient may be truthful or untruthful, exaggerating or minimising, garrulous, forgetful, nervous, confused or senile, not to mention deaf or stupid. He may even omit a vital piece of information not thinking it to be important as in the following two instances.

(1) "I recall seeing a pale woman with epigastric pain. Having got her story without leading questions I was compelled to seek for a cause of her probable anaemia. Had she lost any blood recently? Oh yes, she had vomited more than a pint the previous week."

(2) "Another woman was sent because of diarrhoea of 10 years duration. Did she then remember the onset? Yes, she had been troubled with constipation and had seen her doctor. What did he advise? He instructed her to take half an ounce of Epsom Salts every morning. Had she done so? Yes, she had never missed a day since!"

Another difficulty is the translation of the patient's idiom into clinical concepts which may be handled. The patient may tells us of "chills," "liver attacks," stomach trouble" or "anaemia," which terms may mean nothing or something quite different to the doctor as compared with the patient. It is sometimes taught that we should let the patient tell his own story, only guiding him where necessary. Experience seems to indicate, however, that one should restrain the patient's natural tendency to tell his tale and keep to the opening question, "Of what do you complain?"

It is my habit to select the significant symptom, which is by no means that of which the patient complains, as in the following example.

"The patient complains of breathlessness, chest pain on exertion, or epigastric pain. We note however that he is pale and that the haemoglobin estimation shows marked anaemia. Further enquiry reveals that his symptoms date from an occasion a few weeks ago when he felt faint during an evacuation of the bowel. On further enquiry it is found that he was sweating at the time and that the stools he passed were black, he presumed the latter to be due to something he had eaten."

The significant symptom here is not dyspnoea, sternal or epigastric pain or even anaemia. It is melaena, the cause of which must be investigated.

Confronted with the history and our findings on examination, there are two ways of approaching the problem of diagnosis. Firstly one may conjecture that it may be this or it may be that, or secondly a rational and systematic consideration of the significant symptom or sign and its possible causes may be undertaken.

PRELIMINARY CONSIDERATIONS

Variations in the degree of "energy" possessed by persons in normal health are very great. Some are almost indefatigable, whilst others have tired readily all their lives, yet no disease of body or mind may be found, intake of food has been adequate in quality and quantity, and the musculature is normal. This individual variation is not necessarily related to weight, height or posture and such subjects suffer illness no more frequently and no more severely and die no sooner than their more vital brethren.

Debility or readily induced fatigue sometimes amounting to exhaustion is one of the commonest symptoms. It baffles the patient to describe and the physician to analyse, but when it has an organic basis it is commonly accompanied by loss of weight.

Loss of weight, considered alone for the moment, may be physiological. It occurs in many in the summer and is often marked in new arrivals in the tropics, who may lose as much as two stones. This is presumably due to a diminished intake through a loss of appetite in the hot weather, the physiological overcoat being thus discarded. People also lose flesh after middle age as a rule, again presumably due to a diminution of appetite.

THE DIAGNOSTIC APPROACH

The first step is to find out the duration of the symptoms, and then to check for any other symptoms that have not been volunteered, such as thirst, frequence of micturition or dysuria, palpitations, etc. Positive answers to the latter particularly may lead us rapidly to a tentative diagnosis, such as diabetes, thyrotoxicosis or pyelonephritis.

Before considering the 3 main headings, there are two groups of 3 symptoms each of which should be first enquired for and excluded.

Pyrexia. A chronic fever as from brucellosis or sub-acute bacterial endocarditis may exist without the patient being aware of it. If there is such a possibility the temperature should be checked twice daily or even 4-hourly and charted. The general symptoms of pyrexia must be sought and a white cell count and determination of the blood sedimentation rate should be carried out.

Anaemia. This should be remembered for it is by no means always obvious, as in the following instances.

"I recall a sallow black-haired spinster of 60 years, she had been 'anaemic all her life'; she had never had a blood examination but had been constantly on iron therapy. I calculated that she had consumed ½ ton of iron. Half convinced I sent her for a haemoglobin estimation, it was 117%."

"Again, I saw an apple-cheeked young farmer's wife sent with dyspnoea attributed to her heart and having been warned against exertion. She had had a child two months previously, lochia had persisted due to subinsolution and the haemoglobin was 54%."

The correct medical reaction to the sight of a pale patient or any other with suspected anaemia is not to prescribe iron but to estimate the haemoglobin; a white cell count and blood sedimentation rate determination should also be carried out. The haemoglobin estimation takes only 5 minutes and no medical bag should be considered complete without a haemoglobinometer.

Chronic Pain. This and the resulting sleeplessness and fatigue may induce loss of appetite and consequent deficient intake.

Intake is strictly speaking from the mucous membrane of the small intestine. It must therefore be ascertained if the food taken in by the mouth reaches it and remains in contact for an adequate period to allow absorption to take ploce. Having regard to this there is another set of three symptoms all to do with the alimentary tract.

Dysphagia. Difficulty or pain in swallowing, or the regurgitation of food swallowed may be present, and if so it should be presumed to be the cause of the debility and loss of weight, and investigated.

Vomiting. If this is more than occasional it should be regarded as the significant symptom and followed up.

Diarrhoea. Whilst this topic will be considered under the main heading of Malabsorption, it should if present be the symptom investigated.

It may be claimed that patients will not complain of debility and loss of weight rather than these six symptoms, but this is not necessarily so. Patients complain of that symptom which concerns them most and it is not necessarily the significant one.

Having made these preliminary exclusions, the possible cause of the debility and loss of weight may be considered under the following three headings viz. deficient intake, malabsorption and deranged metabolism.

DEFICIENT INTAKE

Careful questioning of the patient or family should establish whether the food intake is reduced or unaltered from former habit. Reduction may have been produced voluntarily or involuntarily.

Intake may be reduced involuntarily when deprivation occurs in prison camps or poverty-stricken communities. Whilst the latter may apply to up to half the population of the world, deficient food intake due to poverty in Britain is very rare nowadays. Indeed malnutrition in a shabby or dirty house suggests alcoholism or mental deficiency rather than frank poverty.

Malnutrition from inadequate feeding may be seen in infants but the demands of appetite of older children and adolescents should overcome this. However, the rapid increase in weight in many youths after joining the Army in the last war showed, though not necessarily from poor homes, they had not previously received a properly balanced diet.

Intake may be restricted voluntarily e.g. there is the occasional case of the old person living alone on a diet of toast and tea.

Depression and Anxiety. Intake may be reduced because of loss of appetite from anxiety, grief or depression. This should become clear in the course of an interview with the patient or from friends and relations. Food may be reduced deliberately in the following of food fads or slimming courses, though patients who are thin due to this latter cause are unlikely to appear on this account. They may however be brought by parents or complain of debility. This cause of debility and loss of weight differs in degree rather than in kind from :

Anorexia Nervosa. This is seen characteristically in girls 15 - 25 years of age, but may occur in older women. They are moody, resentful and irritable but astonishingly energetic. Amenorrhoea is usual, the body is emaciated and often covered with downy hair. The disease may be a " killer " and, like drug addiction, requires handling by a psychiatrist.

Drug Addiction. In this country the commonest form of addiction is to alcohol. Loss of weight may not be evident until cirrhosis has begun, since beer drinkers particularly, are often fat. In later stages the loss of weight may also be masked by ascites.

MALABSORPTION

If intake has evidently been adequate and yet loss of weight has occurred, we must consider whether the food taken has been properly absorbed. Absorption of all food elements may be impaired and this is expressed by the term " malabsorption syndrome." The symptoms and signs are pleasingly explicable when each element is considered as to its deficiency, e.g. protein and nitrogen loss with wasting and oedema, iron loss with hypochromic anaemia, vitamin B_{12} or folic acid loss with macrocytic anaemia, etc. The loss of water and electrolytes, especially potassium, in such cases may well account for the muscular weakness experienced.

Impaired absorption may be endogenous, being due to actual enteritis as biopsies have shown, or exogenous. In practice it is better to consider the latter first.

EXOGENOUS CAUSES OF MALABSORPTION

Operation Sequelae. A history of abdominal operations and the presence of one or more scars raises this possibility. Operations such as gastrectomy, resection of part of the small intestine for mesenteric thrombosis, strangulated hernia, etc., may give rise to the formation of fistulae or a blind loop thus producing malabsorptive symptoms.

Chronic Pancreatitis may present as diarrhoea or as debility and loss of weight. It may arise silently or following an acute or recurring sub-acute pancreatitis. Epigastric pain, vomiting and fatty diarrhoea may occur. In distinction from the coeliac syndrome the blood picture is normal.

Hepatic Cirrhosis. Portal hypertension with congestion of the gastro-intestinal tract produces anorexia, nausea, vomiting and flatulence. The facies may be typical and the spleen is palpable ; liver function tests are called for.

ENDOGENOUS CAUSES OF MALABSORPTION

Regional Enteritis. Debility and loss of weight with diarrhoea which may resemble ulcerative colitis are the features of this fairly rare disease; in the course of treatment resection and blind loops may have left little healthy intestine. Ileo-colitis when the lower ileum is involved in ulcerative colitis can produce a similar effect.

Coeliac Syndrome. Tropical sprue is rarely seen in Britain, though several cases have occurred in former residents in the tropics. Steatorrhoea may be in the form of coeliac disease of young children or the idiopathic steatorrhoea of adults. It has been shown that in a series of 163 cases of malabsorption 66% were accounted for by coeliac syndrome.

Jejunal diverticulosis and nowadays intestinal tuberculosis provide two rare endogenous causes of malabsorption

DERANGED METABOLISM

These causes may be classified under four main headings.

(1) *Infective Causes.*

Sepsis. This has become rather unfashionable in recent decades but people still exist with silent tooth abcesses, chronic tonsillitis, diseased gallbladders and even chronic appendicitis, who benefit after their removal. The commonest form is pyelo-nephritis.

Arthritis. This will surely display itself by pain, swelling and stiffness of the joints but chronicity may draw the patients attention rather to debility.

Hepatitis

(i) Infective Hepatitis. Whilst a history of recent jaundice or transient dark urine or pale stools should be asked for, the possibility of the "sine ictero" form must be borne in mind. For example in two large epidemics in soldiers in the Middle East jaundice was absent in 10% and 33% of cases. In this country such cases may easily be overlooked. There should be history of a febrile attack usually with gastric pain, nausea, vomiting, headache, malaise and incomplete recovery. No evidence may remain save a tender, enlarged liver and abnormal liver function tests.

(ii) *Glandular Fever.* A history of recent or not so recent fever with enlarged glands, sore throat, perhaps a rash and occasionally jaundice maye be obtained in a patient with debility and occasional fever and sweats. The blood film may still show atypical lymphocytes and the Paul Bunnell test may remain positive for many weeks. Liver function tests will show parenchymatous damage.

(iii) *Chronic Hepatic Amoebiasis.* This is seldom seen in Britain, though cases may be expected as an aftermath of infection in people returning from the Middle or Far East. A frank history of diarrhoea with blood and mucous is not always obtained. The liver is enlarged and the stools may contain cysts.

Syphilis and malaria are relatively rare causes and tuberculosis is on the wain. Endocarditis in its sub-acute form may elude us by not coming into our minds, such cases are uncommon rather than rare and may present as anaemia and fever.

(2) *Toxic Causes*

Uraemia. An investigation is incomplete of course without an examination of the urine and the finding of proteinuria leads us to think of uraemia. The earliest symptoms are usually alimentary i.e. vomiting and sometimes diarrhoea.

Sarcoidosis and periarteritis nodosa are rare causes though in my personal experience cranial arteritis is less rare.

(3) *Endocrine Causes*

All the ductless glands may be responsible for debility and loss of weight when their functions are disturbed, e.g. the pituitary in Simmonds' disease, the thyroid in thyrotoxicosis and hypothyroidism, the thymus in myaesthenia gravis, the suprarenal in Addison's disease, etc.

(4) *Neoplastic Causes*

Lest they should be omitted it will perhaps be best to consider neoplasia of the leucocyte and the plasma cells of the reticulo-endothelial system first i.e. leukaemia and myelomatosis respectively. Hodgkin's disease may also be considered in this context. It may present as enlarged glands or fever or may be revealed by X-rays of the mediastinum.

Cancer. Occult cancer is the underlying anxiety of the doctor and patient alike, especially when the latter is in middle or later life. In the absence of any leading symptoms or signs each system in turn must be fully investigated. If all the main systems i.e. alimentary, respiratory, renal, cardiovascular and neurological are fully examined and these are supplemented by special investigations of the thyroid suprarenals and bones some twenty possible primary sources will have been covered.

The individual causes in this outline have necessarily received but scant attention. However, if the 6 primary exclusions and the 3 main headings and their sub-divisions are remembered the rest will readily be recalled.

"To conclude, I have tried to outline my method of approach to a pair of symptoms which must haunt every surgery and out-patient clinic daily."

YOUR MEDICAL BOOKSHOP

Progress in Clinical Surgery
Series II by various authors under the editorship of RODNEY SMITH. **£2 10s. 0d.**

Clinical Endocrinology
LAURENCE MARTIN. 3rd Edition. **£1 8s. 0d.**

The Newborn Child
DAVID G. VULLIAMY **15s. 0d.**

Progress in Clinical Medicine
DALEY & MILLER. 4th Edition. **£2 10s. 0d.**

A Pocket Gynaecology
CLAYTON. 4th Edition. **12s. 0d.**

The Essentials of Materia Medica
Pharmacology and Therapeutics by R. H. MICKS. 8th Edition. **£1 10s. 0d.**

CAIRNS BROTHERS

MEDICAL BOOKSELLERS

2 and 3 TEVIOT PLACE, EDINBURGH, 1

Telephone—CAL 6563

THE NATURE OF LEUKÆMIA

By J. A. BARROWMAN, B.Sc.

Based on a dissertation read before the Royal Medical Society on Friday, 18th November, 1960.

The classification of leukaemia as a pathological process has proved difficult, as it exhibits features of more than one of the main disease types. It is most widely recognised as a neoplastic disease, but it does not behave entirely in this way; the remitting and relapsing course of the chronic leukeamias is not at all typical of the malignant diseases. In some respects, leukaemia resembles a profound metabolic disturbance, while its presentation and course in the acute form are similar to those of a fulminating infection. This last comparison is rather difficult since severe local infection and even septicaemia are sometimes found in association with the acute types of leukaemia. Although a viral agent has been established as causative in avian leukaemias, no micro-organism has yet been shown to be associated with the human forms of the disease. The uncontrolled proliferation of primitive cells of the leucopoietic system and the capacity of these cells to infiltrate various tissues with an eventual fatal termination is in keeping with a neoplastic process and may represent an extreme form, in company with such conditions as diffuse myelomatosis. However, local deposits of leukaemic tissue such as chloroma are not as common as the local type of myeloma.

What more specific evidence exists to indicate that leukaemia is a neoplasia? Cytological study of malignant cells shows them to have certain general characteristics which include a high proportion of nuclear material in the cell, numerous mitotic figures and abnormalities of the nucleus, the presence of giant cell forms, and basophilism of the cytoplasm. In other words, these cells show rapid and disordered growth and division, and are immature. These criteria of malignancy are all fulfilled by the immature cells of the human leukaemias. Although mouse leukaemias are in some respects different from the human disease, certain basic similarities exist, and in the mouse the disease appears to be a neoplasm, responding to therapeutic measures which are effective against neoplastic tissue in general. It has been suggested that the initial disorder is not located in the leucocytes but rather in some mechanism which governs the proliferative activity of the white cell precursors. The question of the stimulus of leucocyte proliferation is a very interesting one. The leucopoietic tissues can respond to the invasion of the body by micro-organisms by a great proliferation which is promptly suppressed when the infection has been overcome. This " shutting off " of the response is critical and it has been proposed that leukaemia may result as a self-regulating growth after a period during which there is a reversible state of excessive proliferation of the cells under the stimulus of some humoral mechanism. Certainly, leukaemia in its acute form often follows a systemic infection after a variable period. On the other hand, some workers believe that the tendency to the development of the disease may remain latent for a long time and the initiation may depend on some disturbance of the normal physiological response to infection.

Leukaemia is a disease of leucopoietic tissue rather than a disorder of the peripheral blood. The peripheral blood represents a dynamic "pool" reflecting production, release from the marrow, extra-vascular migration and destruction of the leucocytes, and in health, therefore, may be a fairly good index of creation of the cells and their disposal. In leukaemia there is frequently a disturbance of this pool and consequently it may not reflect the production-destruction processes very well. This[15] is often seen in cases of acute leukaemia, where marrow aspirates show an abnormal accumulation of immature white cells which is not reflected in the peripheral blood at that time (Aleukaemic leukaemia), although eventually the abnormal process in the marrow will reveal itself in the peripheral blood. Leukaemias, which virtually always reveal themselves ultimately as a disturbance of the circulating white cells, either in numbers or in morphology, have been variously proposed as disorders of these processes of maturation, release, migration, and destruction, in addition to the obvious one of proliferation.

One of the most interesting theories is that leukaemia represents an arrest of maturation of white cells at an early stage in their development with consequent accumulation of these immature cells and with an accompanying proliferation of the precursors. This would result from a metabolic defect of the leukaemic cell either genetically determined or in response to some extrinsic factor such as a humoral agent or a virus.

In 1925, Minot and Isaacs showed that a transfusion of white cells in man resulted in a rapid disappearance of these cells from the circulation of the recipient and this led to the suggestion that leukaemia might be a disturbance of elimination rather than of production. Bierman and co-workers showed that transfused leucocyte elimination which is rapid in the healthy person is defective in leukaemias. It has been estimated that only about 1% of the body's living leucocytes are circulating and that the degree of saturation of the pool of non-circulating leucoctyes may determine clearance rates. A high degree of saturation of this pool in leukaemia could explain the defective elimination. Certainly, it is hard to see how the extensive proliferative changes seen in the marrow could be secondary to impaired clearance, whereas the reverse could well be true. A fundamental physiological mechanism which is not well understood and which is clearly disturbed in the leukaemias is the process of release of white cells from the marrow.

There are two further interesting phenomena which may be considered in connection with leukaemia. These are the leukaemoid re-actions and the relationship of aplastic disorders of the marrow.

The term leukaemoid reaction is used to describe changes in the blood and blood-forming organs bearing a close resemblance to those of leukaemia. The condition is not usually associated with the severe thrombocytopenia frequently observed in the leukaemias and this serves to distinguish the two conditions. The principal disorders associated with the leukaemoid reaction are severe infections, including tuberculosis, and widespread malignant tissue deposits. The explanation which is offered for the phenomenon when seen in infection is one of an exaggerated physiological response to the organismal invasion and in severe infections, such as septicaemia, white cell counts of as much as 100,000 per c.mm. with a proportion of immature types are found. Viral infections and whooping cough produce a high count of circulating lymphocytes, the peripheral blood resembling that found in chronic lymphatic leukaemia. All these reactions subside with the termination of the infection. Tuberculosis differs from the other infections in that it can produce an immense variety of marrow reactions ranging from aplasia to hyperplasia of

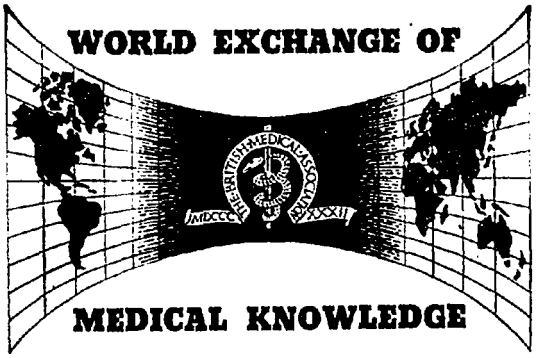
any one of the elements with such results as polycythaemia vera or thrombocytosis. Myelofibrosis may be of tuberculous origin and the disease here is essentially similar to the idiopathic type. It must be assumed here from the variety of disorders, that the mechanism is one of reaction to the bacillus, perhaps a hypersensitivity, rather than a general response to infection as described above.

When secondary malignant tumours involve the bone marrow extensively there is often found a severe anaemia and thrombocytopenia with the appearance of immature white and red cells in the peripheral blood. This condition is difficult to diagnose and it must be remembered that true leukaemia is frequently associated with malignant disease elsewhere in the body.

Preceding the development of a frankly leukaemic blood and marrow picture by a variable period, there is sometimes seen an aplastic state of the marrow involving most elements and this swings round to the opposite extreme quite quickly. Again, throughout the course of the established disease, there is a tendency to a swing to the aplastic condition for a short time. The metabolic processes going on at these times can only be imagined and it is possible that some physiological defence mechanism, perhaps an immunological response results in this aplasia with a subsequent emergence of a new line of genetically different cells. This might be part of the remarkable "side-stepping" property of the leukaemic cells evidenced by their similar response to presently available chemotherapeutic agents.

Leukaemia is at present a very challenging problem and development of successful therapy for the disease may well lead the way to treatment of all malignant conditions. Until the nature of the disease and its aetiology and pathogenesis are elucidated, therapy must be purely empirical. Big gaps still remain in our knowledge of the processes of maturation, release, and destruction of white cells. What mechanism underlies the spontaneous remissions so frequently observed in the disease and what governs the transformation of chronic leukaemia to the acute terminal form? Are the leukaemias of childhood the same disease as seen in the adult? What determines the change from a chronic lymphocytosis to chronic lymphatic leukaemia?

The chromosomal anomalies recently demonstrated in the chronic myeloid types and the absence of any consistent abnormality of this kind in the acute leukaemias are discoveries which at present pose more problems than they solve. Leukaemia is a disease of enormous complexity with difficulties on every side; much work remains for medical scientists in every field, in its investigation.



BRITISH MEDIC/
PUBLIC/

One of the main objects of the BRITISH MEDICAL ASSOCIATION is the promotion of the medical and allied sciences by collecting and disseminating the results of current research and practice. For many years, therefore, the Association has been extremely active in medical publishing, and it is today responsible for a comprehensive range of general and specialist journals.

BRITISH MEDICAL JOURNAL

Foremost among these is the BRITISH MEDICAL JOURNAL, the most authoritative and widely read medical periodical in Great Britain. For more than 100 years the B.M.J. has furnished the profession with a continuous weekly record of current developments in every field of medical science and practice.

SPECIAL JOURNALS

The growth of specialisation in modern medicine has led to the need for more and more specialist journals. Today the Association publishes no fewer than thirteen of these, each containing original articles, review articles, clinical and technical information and reports of research and experiment.

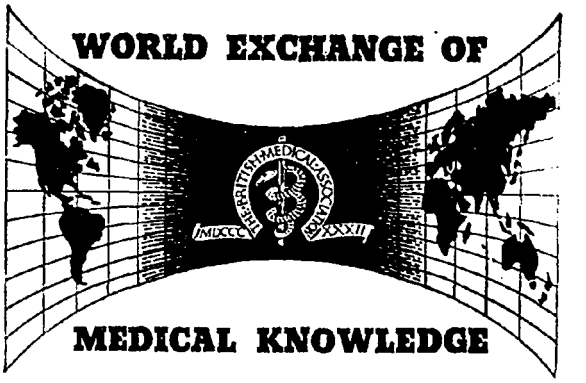
ABSTRACTING SERVICES

Another of the Association's activities consists in abstracting important articles appearing in medical periodicals throughout the world. The results are made available to the profession in two journals, ABSTRACTS OF WORLD MEDICINE and OPHTHALMIC LITERATURE. The former, a critical selection of abstracts grouped in broad classifications, is essentially a guide to work in progress in the world's medical centres; with the minimum expenditure of his time and effort it enables the specialist to keep in touch with current developments in other fields and the general practitioner to keep abreast of modern movements. OPHTHALMIC LITERATURE covers every branch of ophthalmology.

BRITISH MEDIC
B.M.A. HOUSE, TAVISTOCK

AL ASSOCIATION

ATIONS



BRITISH MEDICAL JOURNAL

A journal of international repute which serves as a continuous weekly record of current developments in every field of medical science. *Annual Subscription: British Isles £7 7s. Abroad £4 4s.*

ABSTRACTS OF WORLD MEDICINE

This journal covers the whole field of clinical medicine and allied medical sciences in each issue, and presents each month concise, informative, readable abstracts of the best of the original papers published throughout the world—selected from over 1,500 medical journals. *Monthly. Annual Subscription, £4 4s.*

SPECIALIST JOURNALS

ANNALS OF THE RHEUMATIC DISEASES.
Quarterly. Annual Subscription, £3.

ARCHIVES OF DISEASE IN CHILDHOOD.
Bi-monthly. Annual Subscription, £4 4s.

BRITISH HEART JOURNAL. *Bi-monthly. Annual Subscription, £4 4s.*

BRITISH JOURNAL OF INDUSTRIAL MEDICINE.
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF PHARMACOLOGY AND CHEMOTHERAPY.
Bi-monthly. Annual Subscription, £6 6s.

BRITISH JOURNAL OF PREVENTATIVE AND SOCIAL MEDICINE.
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF VENEREAL DISEASES.
Quarterly. Annual Subscription, £3.

GUT. *Quarterly. Annual Subscription, £3.*

JOURNAL OF CLINICAL PATHOLOGY.
Bi-monthly. Annual Subscription, £4 4s.

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY.
Quarterly. Annual Subscription, £3.

MEDICAL AND BIOLOGICAL ILLUSTRATION.
Quarterly. Annual Subscription, £3.

THORAX. *Quarterly. Annual Subscription, £3.*

BRITISH JOURNAL OF OPHTHALMOLOGY.
Monthly. Annual Subscription, £6.

OPHTHALMIC LITERATURE. A comprehensive abstracting service covering ophthalmic journals and articles of ophthalmic interest from all countries of the world. *Six issues and index yearly. Annual Subscription, £4 4s.*

Combined subscription with British Journal of Ophthalmology, £9.

AL ASSOCIATION

SQUARE, LONDON, W.C.I.

POISONING BY BRITISH PLANTS

By R. W. M. CORNER

Based on a Dissertation read before the Royal Medical Society, on Friday, 4th November, 1960.

The properties of poisonous plants have been recognised for thousands of years. To-day we see the active constituents of some such plants, accurately determined and concentrated in tablets and mixtures, used in the practice of therapeutics.

Cases of poisoning by plants though now uncommon, do still occur occasionally. Various factors are responsible for the drop in incidence over the last century. The general standard of living has been raised and people no longer require to supplement their diet with roots and fruits on pain of starvation, when mistakes are liable to occur. Better education combined with suspicions as to the wholesomeness of various fruits provides a barrier against reckless indulgence. Farming is carried out intensively and crops are cleaner than before, thus reducing possible contamination of grain. The potential murderer or suicide now has the vast range of dangerous drugs to choose from provided he can obtain them. Many of the plants themselves have now a limited distribution. The using of any available land for grazing or ploughing and the drainage of marshes, burning of scrub and felling of timber has reduced the available habitats.

Children are most frequently the victims. Babies are well-known for placing any object in their mouths and young children eat strange fruits to find out how they taste. The sweet berries may be enjoyed and are therefore the most dangerous, whereas the bitter ones will most probably be spat out. Mistaken identity has provided many tragedies. Ignorance is the cause of such accidents. When sections of the community are evacuated from the city to the country during times of strife, such accidents are liable to increase. Mental defectives may chew leaves or fruits being unaware of the dangers, and pregnant women occasionally take too much of a vegetable abortifacient.

The poisons themselves may be divided into two main groups; the ALKALOIDS and the GLYCOSIDES. A third group is that of intensely irritant volatile oils.

The ALKALOIDS are complex basic substances, being the products of plant metabolism. They are extremely potent, producing effects in minute quantities, and are therefore highly dangerous. They act predominantly on the central nervous system and post-mortem appearances are minimal.

HEMLOCK (Conium maculatum) contains the volatile alkaloid CONIINE which was the first alkaloid to be synthesised in the laboratory. The plant is an umbellifer belonging to the parsley family, and is distributed in waste places throughout the British Isles. It was used as the state poison of Athens, Socrates being a victim. Up to the year 1880, of 17 cases recorded in Britain 12 were due to the accidental eating of the plant. In one case death occurred 3½ hours after the plant was eaten in mistake for parsley. The motor nerve-endings are affected first and finally the central nervous system is paralysed, death occurring from respiratory failure.

COWBANE (Cicuta virosa) is very similar to Hemlock but is much rarer, being found only in marshes. The active principle is cicutoxin. The rootstock is especially poisonous in the Spring and is fatal to cattle. Of 31 cases of human poisoning, 14 died. In many cases violent tetanic convulsions occurred, so severe as to resemble strychnine poisoning.

WATER DROPWORT (Oenanthe crocata) is another umbellifer containing oenanthetoxin. It is much commoner than the previous plant but has a westerly distribution and is found in ditches. The large root resembles that of a parsnip and the leaves that of celery, so many mistakes have arisen. In Woolwich many years ago, 6 out of 21 convicts died after eating the root and recently in Barrow-in-Furness children died from eating the root which has a not unpleasant taste. Signs of poisoning are those of an initial stimulation and then depression of the nervous system with gastro-intestinal irritation.

TOBACCO (Nicotiana tabacum). Though not a British plant, tobacco is grown in Britain and cases of nicotine poisoning have arisen in livestock. It is mentioned here for interest because *nicotine* was the first pure alkaloid to be used criminally. This occurred in France and the poison was administered forcibly by a Count Bocarme to a M. Fougnies. Death occurred in 5 minutes and in order to hide traces of nicotine, the Count poured concentrated acetic acid into the mouth and over the body of the victim. Accidental poisoning has arisen from the application of tobacco-leaf poultices, nicotine being absorbed through the intact skin. The lethal dose is probably about 6 mg. of the purified alkaloid.

OPIUM POPPY (Papaver somniferum) is found in waste places and is recognised by its purple flowers and greenish waxy stems and foliage. The milky latex obtained from multiple incisions on the unripe capsule contains the opium alkaloids. Poisoning by the poppy itself is almost unknown in this country though in 1875 a boy of 3½ years died after drinking water in which two poppy heads had been placed. To-day, overdoseage by morphine is the cause of death. The differential diagnosis in the last stages is pontine haemorrhage but morphine poisoning can be distinguished from this encephalic lesion by the usual subnormal temperature compared with the 2-3°F. rise in the latter condition.

MONKSHOOD, WOLFSBANE (Aconitum napellus) contains the extremely toxic alkaloid aconitine. The purple hooded flower-spike is very common in gardens being related to the Delphiniums. It grows wild in woodlands, in the southern counties of England. From mammalian experiments it has been found that 1 part aconite in 1½ million parts blood is fatal within a few minutes. The heart slows then becomes quick and irregular, there is dyspnoea, progressive motor paralysis, convulsions, and death occurs from asphyxia. From 87 cases in the European literature, only 2 cases were murder and 7 were suicides, the remainder being accidental. A common mistake is to confuse the root with that of horse-radish. A wife murdered her husband in 1841 by scraping the root over some cooked vegetables and disguising the bitter taste with pepper. The unfortunate man died in 3 hours. About 4 grams of the root were used. The tingling and numbness of the tongue and mucous membranes of the mouth is characteristic. In Germany during the latter part of the nineteenth century a Dr. Meyer treated a patient with aconitine nitrate for neuralgia. The patient soon became very ill and his wife blamed the medicine. She gave her husband a cup of strong tea which almost certainly saved his life by precipitating the alkaloid. To prove to the wife that the medicine could have nothing to do with her husband's illnes, Dr. Meyer drank 4 mg aconitine nitrate in some wine. This unfortunate man died in 5 hours showing the terrible results of his aberrant thought.

Deadly Nightshade, Belladonna (Atropa belladonna) has a southerly distribution in the British Isles being rare in Scotland. It is found in woodland thickets and near old buildings, growing up to 6 feet high. It produces glossy-black berries which are sweet to taste and are therefore attractive to children. The fingers are stained purple with the juice. The plant contains the alkaloids, hyoscine, hyoscyamine and atropine in all its parts, and poisoning from the berries gives rise to the signs of atropine poisoning. There is a dry mouth, dysphagia, dilated pupils and loss of accommodation. The skin is a dry and warm and a scarlatiniform rash may be present. As the temperature is often raised, Scarlet Fever may be suspected. The central nervous system is affected and a feature of the usual delirium is the ceaseless picking at real and imaginary objects in the final stages. 5.2 g 11 oz. atropine of the root of Belladonna caused the death of a woman, and 14 berries have killed a child. Serious symptoms have occurred from the solution reaching the pharynx by the lacrimal duct and nose.

Thornapple (Datura strammonium) is found in waste places in Southern England and extends into Scotland. It is not native to Britain. The fruit is spiked and contains many seeds which were used in the East for criminal poisoning. 100 seeds will produce severe symptoms. The alkaloids are similar to the previous plant.

Henbane (Hyoscyamus niger) is another such plant containing hyoscyamine. It is native to Britain and was used by the old herbalists. It is however rather rare.

Laburnum (Cytisus laburnum) is the tree which produces the masses of yellow blossoms in the late spring and is grown in gardens and parks. The alkaloid cytisine is contained in all parts of the plant and as it has a sweet taste combined with an attractive appearance it has been the cause of many accidents with children. From 150 cases of poisoning of which 120 were accidental only 4 deaths were recorded. Features of poisoning are vomiting, abdominal pain, and convulsive movements of the limbs followed by narcosis.

Yew (Taxus baccata) is the plant characteristic of churchyards and which is very slow growing. Some yews are reported to be 2000 years old. The alkaloid taxine is responsible for the poisonous property but traces of prussic acid and ephedrine have been isolated. The scarlet berries consist of a mucilage surrounding the seeds. The mucilage is non-poisonous but the seeds are deadly. The berries therefore should be left alone. From 32 cases of accidental poisoning, 9 were from the berries and the rest from the leaves. The mortality rate was 62.5%. Death occurs rapidly after the onset of symptoms from central respiratory paralysis and cardiac arrest.

Autumn Crocus (Colchicum autumnale) is the source of colchicine used in the treatment of gout and in the study of cytology because of its inhibition of the later stages of mitosis. It has not been found to be of any real value in the treatment of cancer. The plant itself grows in grassland in the southern part of England, being absent from Scotland. Prior to 1880, 55 cases were collected from the literature. The mortality rate was 83%. The majority were mistakes in the preparation of the drug and the rest were due to eating the plant, especially the seeds. The main feature of the poisoning is the delayed lethality. In 1941 a woman of 42 years took 60 mg. She lived 8 days. Her blood-picture showed a decrease in circulating leucocytes and platelets and cells in arrested metaphase were observed in the liver, spleen and lymph glands. Charles Darwin experimented with Colchicine, applying it to the leaves of insectiverous plants (Drosera) but obtained no conclusive results.

Poisonous Fungi. The poisonous fungi have an evil reputation and rightly so but only very few are really toxic. Ergot of Rye (Claviceps purpurea) attacks all members of graminea (grasses, cereals) and is present in this country today on grasses. The seed-heads are covered by the purplish-black fruiting bodies about ⅓" - 1" long. Crops on the continent are still contaminated in some areas with this fungus. In 1770, an epidemic in France affected 600 people of which 16% died. A case occurred in this country at Wattisham in Suffolk in 1762. A labouring family with 5 children lost various parts of their lower limbs from a dry gangrene. They all survived and it was found that wheat crop from which they made bread was contaminated. There are two forms of poisoning from the Ergot alkaloids—the convulsive acute form in which the central nervous system is affected, and the gangrenous, chronic form in which the vessels of the limbs are principally affected.

Amanita Muscaria is the red-capped fungus with white warts on the surface. It contains muscarine. Atropine is the obvious antidote for cases of poisoning. The natives of the Kamchatka peninsula in N.E. Siberia eat the dried fungus to produce a feeling of intoxication. Since muscarine is excreted in the urine, they consider this liquid very precious and confirmed drunkards can keep up a week's debaucherie on a few fungi.

Amanita Phalloides (Deathcap) is the most deadly of all fungi and is commonly mistaken for the mushroom. Amanita phalloides, however, has an olive-yellow cap, white gills, and its stem fits in a socket or cup at ground-level. The mushroom has pink or brown-black gills and has no socket for the stem. In 53 cases of poisoning, 75% were fatal. Phalloedin is the active principle which causes fatty degeneration and necrosis of the kidneys and liver. Symptoms appear from 3 - 48 hours after ingestion and death follows within 12 - 18 hours.

Poisonous Glycosides. The poisonous glycosides form the other large group. They are chemical substances which break down on fermentation or by the action of dilute mineral acids to form sugar and compounds which are poisonous.

The Foxglove (Digitalis purpurea) is the well-known source of digitalis. Poisoning from the fresh plant is almost unknown because of the bitter taste of the leaves. The early clinical features of poisoning from overdoseage are those of anorexia, nausea, vomiting and undue slowing of the pulse.

The Cherry Laurel (Prunus laurocerasis) is a cyanogenetic plant, e.g. one that forms Prussic acid (HCN). It contains the glycoside amygdalin. Bitter Almonds, the kernels of plums, peaches and cherries and the pips of apples all contain HCN, and all have been fatal to children. A maid who ate 72 G (2½ ozs) of Bitter Almonds died in 1½ hours.

The Potato (Solanum tuberosum) is poisonous when green. It contains solanine which acts on the central nervous system and haemolyses red-blood cells producing urinary signs and symptoms. Storage of green potatoes in complete darkness for a fortnight makes them edible, the solanine disappearing during storage.

Woody Nightshade or Bitter-Sweet (Solanum dulcamara) also contains solanine. Its red berries have caused a number of fatalities in children. Black Nightshade (Solanum nigrum) has black berries and is abundant as a weed in gardens throughout England.

An example of a plant containing an intensely irritant oil is the Daphne (Daphne mexereon) which is a garden shrub whose pink blossoms appear before its leaves in Spring. 12 of the red berries have caused the death of a child.

There are many other poisonous wild plants which cause gastro-intestinal

symptoms when taken in moderate quantities but which must be taken in very large amounts to produce fatal results. Examples of these are the PRIVET, IVY and the BRYONIES.

Prompt treatment is necessary in all acute cases of poisoning but particularly so with the vegetable ones because of their rapid action. After general measures have been taken, the removal and inactivation of the poison is carried out by gastric lavage with dilute $KMnO_4$ until the return is colourless. Tannic acid, tincture of Iodine and activated charcoal when left in the stomach are used to inactivate alkaloidal poisons.

REFERENCES

BRITISH POISONOUS PLANTS. Forsyth, 1954.
COLCHICINE. Eigsti and Dustin, 1954.
FLORA OF THE BRITISH ISLES. Clapham, Tutin and Warburg, 1952.
FORENSIC MEDICINE. Kerr, 1957.
FORENSIC MEDICINE. Smith and Fiddes, 1955.
HANDBOOK OF TREATMENT OF ACUTE POISONING. Bensley and Joron, 1958.
PLANTS POISONOUS TO LIVESTOCK. Long, 1917.
POISONS, THEIR EFFECTS AND DETECTION. Blyth, 1906.

MEDICAL AND DENTAL DEFENCE UNION OF SCOTLAND LTD.

Benefits Offered by the Union :

Defence of claims for alleged negligence in professional work, including unlimited indemnity and costs.

Defence of claims against a principal in respect of acts by an assistant or locum.

Advice on difficulties arising out of professional practice.

All benefits available to members in Scotland, England, Wales, Northern Ireland, Isle of Man, and Channel Islands, and to Short Service and National Service Officers with H.M. Forces in any part of the world, provided the total Commissioned Service does not exceed five years.

Benefits of Membership for new graduates date from the date of application provided duly registered at that date.

Subscriptions for new graduates £1 for first three years, thereafter normal subscription of £2. No Entry Fee for new graduates. Full particulars and Forms of Application for Membership can be obtained from the Secretary.

C. C. MILLAR, T.D., C.A.

105 ST. VINCENT STREET, GLASGOW, C.2

E. & S. LIVINGSTONE, LTD.

Surgery is Destined to the Practice of Medicine

The Hunterian Oration, 1959, delivered by
SIR REGINALD WATSON-JONES

81 pages. 81 illustrations. 21s.

Textbook of Medicine

Thirteenth Edition. Edited by SIR JOHN CONYBEARE, K.B.E., M.C., D.M., F.R.C.P., and W. N. MANN, M.D., F.R.C.P.

1,008 pages. 102 illustrations. **45s.**

Cerebral Palsy in Childhood and Adolescence

A Medical, Psychological and Social Study

Edited by JOHN L. HENDERSON, M.D., F.R.C.P.(Ed.).

360 pages. 10 illustrations. **About 35s.**

Disease in Infancy and Childhood

Third Edition. By RICHARD W. B. ELLIS, O.B.E., M.A., M.D., F.R.C.P.

722 pages. 328 illustrations. **55s.**

Pathology of Infancy and Childhood

By AGNES R. MACGREGOR, M.D., F.R.C.P.E., F.R.C.O.G.

639 pages. 399 illustrations. **75s.**

The Development of the Infant and Young Child: Normal and Abnormal

By R. S. ILLINGWORTH, M.D., F.R.C.P., D.P.H., D.C.H.

324 pages. 95 illustrations. **27s. 6d.**

Scientific Aspects of Neurology

Leeds Neurological Sciences Colloquium, 1959-60

Edited by HUGH GARLAND, T.D., M.D., F.R.C.P.

276 pages. 102 illustrations. **50s.**

A Short Manual of Venereal Diseases and Treponematosis

Second Edition. By R. C. L. BATCHELOR, M.A., M.B., Ch.B., D.P.H., F.R.C.S.(Ed.), F.R.C.P.(Ed.), and MARJORIE MURRELL, M.B., B.S., F.R.C.S.(Ed.), D.P.H.

332 pages. 89 illustrations. **25s.**

Techniques of Thoracotomy

By B. T. LE ROUX, M.B., Ch.B. (Cape Town), F.R.C.S.(Ed.).

102 pages. 139 illustrations. **55s.**

The Closed Treatment of Common Fractures

Third Edition. By JOHN CHARNLEY, B.Sc., M.B., F.R.C.S.

284 pages. 434 illustrations. **50s.**

The Eye in General Practice

Second Edition. By C. R. S. JACKSON, M.A., B.M., B.Ch., D.O.M.S., F.R.C.S.

160 pages. 27 illustrations. **21s.**

The Principles and Practice of Medicine

Fifth Edition. Edited by SIR STANLEY DAVIDSON, B.A., M.D., F.R.C.P., M.D.(Oslo), F.R.S.(Edin.).

1,124 pages. 99 illustrations. **35s.**

Human Nutrition and Dietetics

By SIR STANLEY DAVIDSON, A. P. MEIKLEJOHN, M.A., B.Sc., D.M., M.R.C.P., and R. PASSMORE, M.A., D.M.

856 pages. 73 illustrations. **84s.**

Textbook of Physiology and Biochemistry

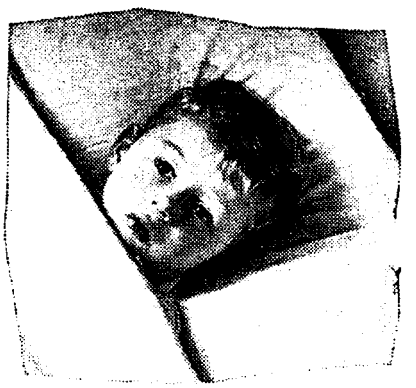
By GEORGE H. BELL, B.Sc., M.D., F.R.F.P.S.G., F.R.S.E., J. NORMAN DAVIDSON, M.D., D.Sc., F.R.I.C., F.R.S., and HAROLD SCARBOROUGH, M.B., Ph.D., F.R.C.P.

Fifth Edition. **In active preparation.**

COMPLETE CATALOGUE SENT ON REQUEST

TEVIOT PLACE, EDINBURGH

Debilitated patients



During prolonged illness

After severe illness

Post-menopausal Osteoporosis

Build up these patients with 'Anapolon' the new, effective anabolic agent

When vitality is low, the appetite poor and when the patient is temporarily unable to assimilate a fully adequate diet, then it is that 'Anapolon', the new anabolic agent, can produce remarkable results.

'Anapolon' is distinguished by its ability to promote the retention of nitrogen and other elements essential for tissue building. It restores the metabolic balance, stimulates the appetite and facilitates recovery in cases of febrile or wasting disease, impaired development in children, menopausal and senile osteoporosis, surgical procedures, burns and other injuries.

Anapolon
oxymetholone TRADE MARK

Tablets (5 mg.) in 25's, 100's and 500's. Basic N.H.S. costs 19/-, 70/- and 340/- respectively.

A PRODUCT OF THE SYNTEX CORPORATION

IMPERIAL CHEMICAL INDUSTRIES LIMITED
PHARMACEUTICALS DIVISION WILMSLOW CHESHIRE
Ph. 104

RES MEDICA

MAY, 1961

MEDICAL EDUCATION

It seems almost traditional now that medical students should be to some degree critical of the mode of conduct of their courses. In the last ten years or so it has also become fashionable for the governing bodies of medical schools to discuss and experiment with new methods of teaching and the content of courses. Practically all are agreed that the already lengthy course should not be extended, therefore the required measures will entail a judicial pruning of the present curriculum to enable the newer subjects and courses e.g. psychological medicine and general practice methods to be included.

In the United Kingdom, the General Medical Council is the all-important governing body and their Directive of 1957 has done much to stimulate thoughts and ideas along the lines of revision and re-organisation of the medical course. It is this body which lays down the minimal requirements of a medical curriculum, but in their Directive they delegated much responsibility as to the actual conduct of the course to the individual medical schools, and added their now almost famous rider that there should be "less instruction and more education."

The medical student's own opinions hold but little sway in such alterations at present. However the Association for the Study of Medical Education has recently agreed that it would be at least interesting to tap these ideas. Therefore it was under their auspices that the recent questionnaire was sent out to all medical students in the United Kingdom. The association consists of representatives from all British medical schools and various other individuals interested in medical education and meets in London, but the actual survey is being conducted from the Department of Public Health of Edinburgh University.

On the whole the questionnaire has been received favourably by the students and the response is reported to have been excellent, although the organisers are still anxious to receive the few hundred unreturned copies. A few criticisms may be made of it, for example there is a noticeable lack of questions about teaching methods and the whole thing may be construed by the sceptic to be merely a mass psycho-analysis of the medical student population. It must be realised, however, that space in the questionnaire and the time that may be spent in correlating the results, are at a premium. Also in connection with the first criticism it would be difficult to ask questions about such things without offending members of staff, an occurrence which the Association, as a relatively unofficial body, is anxious to avoid.

An interim report of the survey is expected in about nine months time, but the final fully correlated report, in book form, will not be ready for about

two years, so its effect will not be felt for at least three. The task ahead of the organisers in examining and classifying all the various ideas of 12,000 medical students is, needless to say, protean, so the long time lapse though unfortunate is unavoidable. The report once produced will be sent to all the relevant associations and interested persons and of course to all the medical schools who have taken part, to whom also will be sent private reports containing data applying to them individually. The governing bodies of these medical schools need pay absolutely no heed to this report, since in a sense it is entirely unofficial. However, it is greatly to be hoped and expected that they will do so.

Despite the discouraging prospect of this long time lapse, an interregnum of stagnation need not be anticipated, since the various medical faculties are at present undertaking considerable advances individually. In Edinburgh steps are already being taken to offer would-be students, with suitable marks in 'Advanced Level' G.C.E. examinations, exemption from the 1st Professional course. These arrangements should definitely be employed by 1962 and may be even in the coming academic year. Also in the near future the Medical Faculty will be meeting to take the initial steps in a process of large-scale revision of the rest of the medical course.

The fact that these alterations are being taken in hand before the arrival of the A.S.M.E. report and the apparent lack of authority of the latter when it does arrive, may make it appear obsolete and even impotent. However, as already implied, it is an opportunity for the medical students of this country to express their opinions in a unified and acceptable manner, which otherwise would not have been available to them. The organisers of this survey are also anxious to point out that this recent survey is only a beginning, for they have plans for several other projects e.g. longitudinal studies following students throughout their courses in order to see how their ideas and opinions are modified. This present survey and the future efforts of A.S.M.E. cannot affect the present generation of students to any great extent, but for those in the future it is to be hoped that the medical schools of this country, if not student Utopias, will at least be fitted to provide a medical education, better geared to the wishes and requirements of their students.

THE CEREBELLUM

Many experiments performed recently to investigate the functions of the central nervous system have suggested for the cerebellum a wide role in the overall physiology of movement.

Phylogenetically, the cerebellum appears as an outgrowth of the vestibular nuclei, and has developed in proportion with the cerebum. Comparative anatomy suggests that the great size of the cerebellar hemispheres is a reflection of the wide range of movement possible to the limb appendages. Ablation experiments performed upon lower animals suggest that the vermis is, by contrast, concerned with the posture and locomotion of the body as a whole. The only agreed function of the cerebellum is that of aiding the regulation of posture and the smooth and accurate execution of movements.

Although certain cerebellar lesions are known to result in the appearance of "intention tremor," its exact causation is unknown. In Rhesus macacus monkeys the most intense tremors and ataxia are produced by lesions of the

dentate and interpositus nuclei. In man, the dentate projection to the precentral cortex constitutes the bulk of the cerebellar efferent connections.

It has been shown further that the occurrence of ataxia and tremor depends largely on the presence of an intact sensorimotor cortex.

An old idea, now largely substantiated, is that the cerebellum attends to the successful completion of movements initiated by the cerebral cortex. While the apparent regulation of the g-efferent system by the anterior lobe of the cerebellum and multiple somatotopic representation of the body, fit admirably into this picture, sensory representation and visual and auditory projections were unexpected. However the eye and ear do provide important information to be co-ordinated with that from the proprioceptive system in the execution of desired movements.

It is tempting to speculate further and compare the cerebellar control of the afferent input from the muscle spindles with the observed reduction of the post-synaptic intensity of afferent impulses resulting from stimulation of central structures, including the brain stem reticular formation, the sensorimotor cortex and the anterior vermis of the cerebellum.

Whatever the role of the cerebellum, let it be emphasised that in spite of much evidence that is factual and suggestive, the complexity of the problems involved renders much evidence indecisive and precise knowledge is minimal.

MINIATURE X-RAY IN EARLY T.B.

At present two main methods are in use for the early detection of asymptomatic T.B. Firstly the use of Miniature Mass Radiography (M.M.R.) and secondly the application of Heaf and other multipuncture methods.

The X-Ray is by far the better of the two and theoretically the ideal situation would be to X-Ray all the population every year. However, in Britain at present, this is not possible due to the cost of such a scheme, the lack of machines and an insufficient number of trained staff. Even at present, the units available are unable to satisfy the demand.

The success of the X-Ray campaign depends on a good public support, but recent figures show—

(a) 90% co-operation was only achieved in one small area and then only after intensive propaganda.
(b) 70% could be expected with normal propaganda.
(c) 25% only where little propaganda was used.

When investigating why people did not attend it was found that besides the usual reasons such as lack of time, too far away, etc., a certain proportion refused to go because they felt perfectly fit, and failed to appreciate the presence of an asymptomatic phase of the condition.

This is the really important finding from the survey and indicates much must be done to ensure that no early cases escape detection.

Thus we may ask should an X-Ray be made legally compulsory as in Norway and parts of Australia, in an attempt to find these early cases? However it is doubtful if this is the ideal way. A better idea is to insist on X-Ray at regular intervals for all those engaged in employment which brings them in close contact with a large percentage of the general public. Shop assistants, transport employees, school teachers, nurses, etc., are the groups in whom such regular surveys should be attempted. Regular visits to factories, schools and other such centres is also of the utmost importance.

In many hospitals in the U.S.A. all patients admitted are automatically given a screening X-Ray, surely a scheme well worth serious consideration since this method shows a relatively high incidence of positive findings.

In general then, the efficiency of case finding could be increased by a direct instruction of the public and especially those in the danger groups, and by the most effective use of available resources.

MEDICINE AND THE LAYITY

Medicine is a subject in which a very large proportion of the general public takes a considerable interest. This is to be expected, since no-one knows when he may need the attention of a doctor. This interest is reflected in the popularity of medical articles in lay publications, and of medical broadcasts. Up to a point, this is not unwholesome; it is all to the good if the public has a general knowledge of hygiene and of the early signs of disease. The virtue of dissemination of information on these topics is obvious.

But the danger always exists that this interest may become too great. The individual who is far too introspective, who carefully studies himself for the first sign of anything abnormal and who in fact, becomes the typical hypochondriac is only too familiar. There is no doubt that one of the chief factors contributing to this sort of personality is the amount of medical information that is published quite unnecessarily in non-medical periodicals.

Recently, in addition to articles in the press, there have appeared "documentary" television programmes dealing with medicine and these seem worthy of discussion. There can be no doubt about the excellent quality of these broadcasts and of their very good intentions. Their dispassionate, matter-of-fact approach to medical matters is a welcome answer to the melodramatic atmosphere that so commonly shrouds these topics in the popular press. Moreover, by demonstrating successfully treated cases, they may reassure patients about to undergo similar treatment and increase public confidence in the medical profession generally.

Numerous pitfalls, however, await those who produce such programmes. For example, it is exceedingly difficult, in the short time available, to explain a fairly complicated disease process and demonstrate its treatment to a completely uninitiated audience; and it often seems quite likely that a broadcast intended to remove some of the mystery from the physician's or surgeon's work will in fact leave the audience more baffled than ever. It is even possible, despite the care that is taken by the speakers to explain, that a patient may be misled into thinking, for example, that surgery is the only, or at least the best remedy for his condition, when it is really undesirable in his case.

Again there is the question of broadcasting film of surgical operations. Although this shows how satisfactory surgery can be in the treatment of certain disorders, many members of the public regard it as rather repulsive. Patients about to undergo similar operations themselves may indeed be quite horrified at the spectacle, and the wisdom of showing this sort of procedure to so wide an audience is a matter for conjecture.

The nature of broadcasting is such that it reaches an exceedingly large audience, especially in this country where choice of programmes is so limited. Also it must be admitted that a serious broadcast of the type in question may have a considerable influence on the opinions of many people. Given that medical broadcasts are desirable, their content must be carefully made up; and most certainly those concerned with their production carry a substantial responsibility both to the public and to the profession.

AUSCULTATION OF THE HEART - III.

By R. W. D. TURNER
O.B.E., M.A. (Cantab.), M.D., F.R.C.P.Ed., F.R.C.P.Lond.

MURMURS

Give me a calm and thankful heart,
From every murmur free.
—from a hymn by Anne Steele, 1760.

The essential difference between a sound and a murmur is that the former is due to sudden alteration in the speed of blood flow whereas a murmur results from turbulence developing in the blood stream. A murmur is usually of longer duration and of higher frequency than a sound. The principal factors which influence turbulence are the velocity of flow, the density and viscosity of the blood and the diameter of the vessel. Another important factor is that a narrowed orifice, as from valvular stenosis, will give rise to eddies beyond the obstruction. A similar effect is produced by a relatively narrow vessel opening into a wider one as in dilatation of the first part of the aorta or pulmonary artery.

Murmurs may be heard in systole or diastole or may appear to be continuous throughout systole and diastole.

Diastolic and continuous murmurs are always due to organic disease but a systolic murmur may be present not only without any functional disability but without any clinical, radiographic or electrocardiographic evidence of organic heart disease.

In all cases in which a murmur is heard there should be noted, as described in Part I of this paper, the area over which it is audible, the position of maximal intensity, the direction of apparent radiation, the intensity (preferably graded), the quality (using simple adjectives), and, where possible, the precise timing in systole or diastole. It should also be noted whether it is associated with a palpable thrill and if there is any abnormality of the heart sounds. In cases of doubt phonocardiography, radiography, electro-cardiography and other accessory methods of examination may be required before a firm conclusion can be drawn.

SYSTOLIC MURMURS

Systolic murmurs may occur in association with various forms of acquired or congenital heart disease or as an isolated finding unassociated with any evidence for organic disease and may then be termed innocent, incidental or functional. A functional murmur is due to turbulence in the absence of significant structural abnormality.

However, it is not always possible to be certain that an apparently innocent systolic murmur is not due to mild organic heart disease nor, of course, from a single examination that such disease may not in time be progressive.

The chief danger is usually that of engendering anxiety and it is very important indeed to avoid this and also the imposition of unwarranted restrictions.

Infants and children must be kept under observation and examined at intervals because at this age it is quite impossible to be certain as to the nature of a systolic murmur.

In young adults it is best to arrange for re-examination after say 12 months at any rate but at the same time to give strong reassurance that no restrictions in activity are indicated and a normal life can be lead in every way.

In older patients an isolated systolic murmur can usually be ignored but it should be remembered that an aortic systolic murmur may signify valvular stenosis which does not become of dynamic importance until quite late in life, for example, after the age of 50.

CLASSIFICATION OF SYSTOLIC MURMURS

INNOCENT
1. Pulmonary
2. Apical
3. Parasternal

ORGANIC
- A. *Forward Flow*
  - 1. Aortic
    - Aortic stenosis or sclerosis
    - Increased flow (Aortic incompetence)
    - Coarctation of aorta
  - 2. Pulmonary
    - Pulmonary stenosis
    - Increased flow
      - Physiological
      - Left to Right shunts
- B. *Backward Flow*
  - Mitral or Tricuspid incompetence
  - Ventricular septal defect

DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS

If a systolic murmur can be heard its characteristics should be noted as described above and also if there is any associated thrill, diastolic murmur, change in heart sounds or other evidence for heart disease.

Aortic Systolic Murmur

The most usual cause for a systolic murmur that is loudest in the aortic area is aortic stenosis but a similar murmur may derive from sclerosis of the valve, dilatation of the ascending aorta or increased left ventricular stroke volume as in aortic regurgitation. Normally a systolic murmur may be heard just above the clavicle and occasionally it is also audible just below.

Pulmonary Systolic Murmur

The most usual cause for a systolic murmur that is loudest in the pulmonary area is normal blood flow in the young; or increased blood flow with exercise, emotion, pregnancy, anaemia, thyrotoxicosis or with a left to right shunt; or pulmonary stenosis.

Left Parasternal Systolic Murmur

The most usual cause for a systolic murmur that is loudest at the mid or lower left sternal border is one of the innocent varieties, tricuspid incompetence or congenital heart disease.

Mitral Area

The most usual cause for an apical systolic murmur is mitral incompetence or an apparently innocent murmur.

It must be remembered that the murmur of aortic stenosis may be loudest at the left sternal border or even at the apex and that a basal systolic murmur 'conducted into the neck' is not diagnostic of aortic stenosis but may be present in pulmonary stenosis or congenital heart disease. Other causes for a praecordial systolic murmur include coarctation of the aorta and patency of the ductus arteriosus in infancy or with pulmonary hypertension.

If one comes to think of it, it is remarkable that blood flow through the heart, past valves and protuberances and round bends should be so silent and not surprising that minor irregularities of no structural consequence should cause eddies associated with a murmur.

AORTIC SYSTOLIC MURMURS

An aortic systolic murmur may be due to aortic valvular stenosis or sclerosis, to increased blood flow across the valve or to dilatation of the ascending aorta.

Aortic Stenosis

Characteristically the murmur of aortic stenosis is loudest in mid-systole because this corresponds with the period of maximal blood flow.

Usually it can be appreciated by ear that the murmur ends before the second heart sound and often that there is a distinct gap between the first heart sound and the beginning of the murmur. Phonocardiographically it can be shown to be "diamond-shaped".

An aortic systolic murmur may be loudest in the "aortic area," over the sternum or down the left sternal border or sometimes even at the apex.

Unless faint it can also be heard over the carotid arteries in the neck.

Even when the murmur is not loudest to the right of the upper sternum signifying its probable source of origin it may be recognised as originating in the aortic valve because it is also well heard in this region and in the neck and because of associated features such as a systolic thrill maximal over the right upper chest, weakness or absence of the aortic second sound and from the fact that the murmur is loudest in mid-systole.

There may also, of course, be an early diastolic murmur from associated aortic incompetence.

It is important to emphasise that the loudness of the murmur bears no close relation to the degree of stenosis.

PULMONARY SYSTOLIC MURMURS

A pulmonary systolic murmur may be due to pulmonary stenosis, to increased blood flow across the pulmonary valve or to dilatation of the main pulmonary artery. A pulmonary systolic murmur is probably the most frequent of all innocent murmurs.

Pulmonary Stenosis

As with aortic stenosis the characteristic murmur of pulmonary stenosis is loudest in mid-systole corresponding with the period of maximal ejection and as with aortic stenosis there is no close relationship between the intensity of the murmur and the degree of stenosis.

The murmur is usually accompanied by a systolic thrill and the intensity of the thrill corresponds with the loudness of the murmur.

In pulmonary stenosis the second heart sound may be finely split, widely split, faint or absent depending on the degree of stenosis.

Increased Pulmonary Blood Flow

A systolic murmur from increased blood flow across the pulmonary valve may be associated with any hyperkinetic state such as pregnancy, anaemia or thyrotoxicosis. It is often also heard in young persons especially on exercise.

In pathological states increased pulmonary flow may be associated with a left to right shunt e.g. with patency of the ductus arteriosus, an atrial septal defect or a ventricular septal defect.

Parasternal Systolic Murmurs

A systolic murmur which is loudest at the mid or lower left sternal border is usually due to tricuspid incompetence, congenital heart disease or is one of the innocent varieties.

Tricuspid Incompetence

Tricuspid incompetence may be due to organic deformity of the cusps from rheumatic endocarditis or to dilatation of the valve ring from cardiac failure. In severe cases systolic pulsation in the jugular veins and over the liver may be present. This murmur often increases in intensity during deep inspiration.

Congenital Heart Disease

The most usual cause is a ventricular septal defect. In such cases a corresponding systolic thrill is usually palpable.

Innocent Murmurs

This subject is discussed on page —

APICAL SYSTOLIC MURMURS

A systolic murmur which is loudest at the apex always raises the possibility of mitral incompetence and is perhaps the most frequent source of uncertainty. If there is a past history of rheumatic fever, the murmur is heard out towards the left axilla, and if there is any radiographic evidence of left atrial enlargement this diagnosis must be made. Even if there is no other abnormality whatsoever it still cannot be denied that minimal rheumatic mitral disease may be developing and, if possible, the examination should be repeated a year later. However, the undesirability of making an error and diagnosing organic heart disease when none is present is far more important and of so much greater potential harm than mistaking a minor organic murmur that this slight risk may reasonably be taken. In the occasional instance even bacterial endocarditis may subsequently develop in mild rheumatic mitral disease but on balance there can be no question that this risk also should be accepted. *From the practical point of view minor mitral incompetence is of no dynamic significance and the patient should be reassured that the heart is healthy.*

ISOLATED SYSTOLIC MURMURS

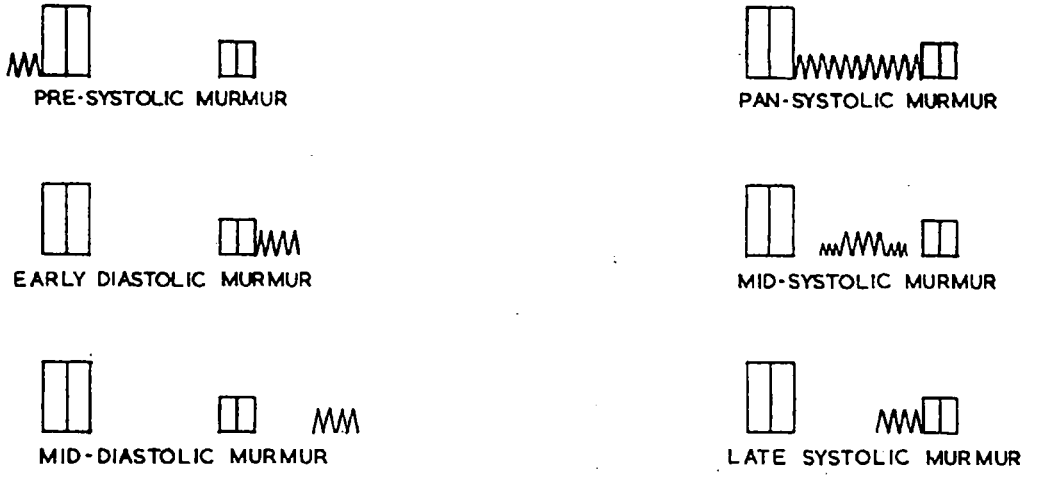
Isolated ('innocent,' 'incidental' or 'functional') systolic murmurs are of frequent occurrence in health and often pose a problem for the physician either because such a finding is made during the examination of a patient who has some condition unrelated to the heart or during the routine medical examination of school children, or of candidates for the armed forces, superannuation or life insurance.

When there is evidence of cardiac enlargement or when a diastolic murmur

is also heard, organic disease of the heart can be diagnosed with confidence but frequently no other abnormality is present. In such cases attention to detail, experience and commonsense are all important. The decision that a murmur is innocent depends not only on the absence of any evidence of organic heart disease but on the characteristics of the murmur itself.

The history is unlikely to be helpful in the type of case under consideration because symptoms related to the heart will not be present. If there is an unequivocal past history of rheumatic fever, more potential significance must be attached to a murmur but so often a history of possible rheumatic fever is inconclusive. Also a patient who has had rheumatic fever may have an innocent murmur and it is well known that some 40 per cent. of all those with unequivocal evidence of rheumatic heart disease give no history of rheumatic fever.

The characteristic features of the various organic conditions associated with a systolic murmur including valvular and congenital heart disease have already been described.



HEART MURMURS

The physician must make quite sure that there is no clinical evidence of cardiac hypertrophy or enlargement, that there is no thrill, that the heart sounds and the pulses are normal and that no diastolic murmur is present. If there is any doubt about enlargement a radiograph should be taken.

Isolated systolic murmurs unassociated with any recognisable form of heart disease may be loudest at the apex, at the base or at the left sternal border.

In general it may be said that the louder the murmur the more likely is it to be of organic origin and few murmurs louder than Grade 2-3 are innocent. Also the harsher the murmur the more likely is it to be organic.

Innocent murmurs tend to be of relatively short duration and of high frequency but inevitably the dividing line from organic murmurs is not sharp. Also they tend to vary with respiration, posture and pressure of the stethoscope on the chest wall more than do organic murmurs.

Late Systolic Murmur

A particular variety of innocent murmur is one which develops in *late* systole shortly before the second heart sound, is loudest at the apex and may amount to Grade 3 or more in intensity.

This characteristic murmur is of maximal intensity at the apex and just

before the second sound. The first part of systole is silent. The murmur may be so loud and harsh that on this account it is often mistaken for organic heart heart disease. It is therefore all the more important to recognise. Unfortunately, as so often in medicine, there is no absolute rule and it is probable that a late systolic murmur may occasionally be associated with organic mitral incompetence, possibly with shortening of the chordae tendinae.

Pulmonary area

A pulmonary systolic murmur, loudest to the left of the upper sternum, is a frequent finding especially in young people and in pregnancy. Presumably it is due to blood flowing through the pulmonary valve but there is no evidence of valvular stenosis, dilatation of the pulmonary artery or any other abnormality.

Parasternal

These murmurs are usually of maximal intensity between the apex beat and the sternal border and may be faint or loud, fine or coarse but are of short duration and end about mid-systole. There will be no thrill or change in heart sounds.

CLASSIFICATION OF DIASTOLIC MURMURS

EARLY
- Aortic incompetence or Pulmonary incompetence.

MID
1. Mitral stenosis or Tricuspid stenosis
2. Increased flow
   - Mitral
     - Patent ductus arteriosus
     - Ventricular septal defect
   - Tricuspid
     - Atrial septal defect

LATE
- Mitral or Tricuspid stenosis

PRE-SYSTOLIC MURMURS

In patients with sinus rhythm a pre-systolic murmur may be due to stenosis of the mitral or tricuspid valves.

Mitral Stenosis

The classical physical signs of mitral stenosis are a loud slapping first heart sound preceded by a pre-systolic murmur, and an opening snap followed by a rumbling mid-diastolic murmur.

This cadence gives rise to the onomatopoeic "fftou ta ta rrou" first described by Duroziez.

The first or pre-systolic element of this sequence occurs late in ventricular diastole, synchronous with the forceful rapid passage of blood into the ventricle produced by atrial systole. It is therefore only heard in patients with sinus rhythm and disappears with the onset of atrial fibrillation.

This murmur is usually loudest at the apex and may be accompanied by a thrill.

An isolated pre-systolic murmur, that is without an associated mid-diastolic murmur, is only found in the early or mild stages of mitral stenosis.

Tricuspid Stenosis

A pre-systolic murmur similar in quality to that of mitral stenosis may be

heard in patients with tricuspid stenosis. This possibility should always be considered in patients with mitral valvular disease, especially if the pre-systolic murmur is well heard in the region of the sternum and is louder in deep inspiration which increases blood flow across the valve. In such cases there is likely to be a prominent 'a' wave in the jugular venous pulse.

Occasionally a pre-systolic murmur is heard in patients with aortic incompetence but without mitral stenosis and has been called the Austin Flint murmur after the man who first described it. The importance of this murmur has been exaggerated and its mechanism of production is still disputed. It will therefore not be discussed further.

MID-DIASTOLIC MURMURS

A mid-diastolic murmur may be heard in mitral or tricuspid stenosis or in patients with increased blood flow across the valve without stenosis, i.e. with an intracardiac shunt.

The most characteristic sign of mitral stenosis is a long rumbling mid-diastolic murmur, loudest at or localised to the apex. If, as is so often the case, atrial fibrillation is present there will be no pre-systolic murmur but there may be a loud first heart sound and an opening snap as already discussed.

This murmur is best heard or may only be heard if the patient is lying down and turned towards the left side or if blood flow is increased by exercise. These manoeuvres, therefore, should be part of the routine examination of any patient suspected of having valvular heart disease.

It used to be thought that a mid-diastolic murmur at the apex was diagnostic of mitral stenosis but with the increased precision in auscultation which came with phonocardiography and in particular with the stimulus to careful auscultation brought by the advent of cardiac surgery, it has been recognised that a murmur similar in time but usually different in quality may occur in patients with congenital heart disease, associated with increased blood flow across the mitral valve.

EARLY DIASTOLIC MURMURS

An early diastolic murmur, i.e. one beginning immediately after the second heart sound is characteristic of aortic or pulmonary valvular incompetence.

These two causes are not always easy to differentiate, the distinction, when possible, being made not from the qualities of the murmurs but from consideration of associated features.

Aortic Incompetence

This is usually loudest in the 3rd and 4th intercostal space close to the left sternal border. It may also be heard in the "aortic area" and, if loud, at the apex. When the murmur is audible at the apex it can usually be appreciated that there is no gap between the second heart sound and the beginning of the murmur, in contrast to the mid-diastolic murmur of mitral stenosis when there is a distinct gap and possibly an opening snap as discussed below.

The murmur is usually best heard with a diaphragm chest piece and with the patient sitting up or standing and with the breath held in expiration. It is well to remember these points if quiet murmurs are not to be overlooked.

The murmur of aortic incompetence is usually high pitched and blowing in quality. If harsh or musical and especially if heard best to the right rather than to the left of the sternum some cause other than rheumatic fever should be considered such as syphilis, bacterial endocarditis or trauma.

Although, in general, a loud murmur will be associated with severe incompetence there is no close correlation between these two features and many striking discrepancies. The severity of valvular incompetence and consequent regurgitation cannot in fact be assessed by auscultation but only by examination of the peripheral circulation and by seeking evidence of left ventricular hypertrophy. However, the signs of aortic incompetence are often modified by associated valvular stenosis.

With free regurgitation there will be a full, bounding "water hammer" or Corrigan pulse and a low diastolic blood pressure with a high systolic pressure and therefore a high pulse pressure. Exaggerated arterial pulsations may be obvious in the carotid and other arteries and capillary pulsation in the nail beds or retinal vessels. A "pistol" shot may be heard over a medium sized vessel such as the brachial or femoral artery if the vessel is lightly compressed with the bell of the stethoscope.

Pulmonary Incompetence

As early diastolic murmur from pulmonary incompetence was first described by Graham Steele in a patient with severe pulmonary hypertension from mitral stenosis. This murmur is similar in quality to that of aortic incompetence and likewise will be audible down the left sternal border. It is impossible to distinguish the two by auscultation and the probability as to which valve is at fault must be decided by seeking signs of aortic regurgitation in the peripheral circulation on the one hand and of pulmonary hypertension on the other.

Pulmonary hypertension will be indicated by a loud second heart sound and clinical or electrocardiographic evidence for right ventricular hypertrophy. There will also be radiographic enlargement of the main pulmonary artery.

CONTINUOUS MURMURS

The most frequently heard continuous murmur is that due to patency of the ductus arteriosus, a condition with which the student should be familiar. The murmur is that of an arterio-venous fistula but the differential diagnosis will not be discussed being the province of the specialist.

* * * *

In the first part of this paper it was suggested that the recently introduced Leathan modification of the Bowles stethoscope was probably best. Further experience has shown that this model has certain defects and the student is therefore advised to use the standard bell and diaphragm chest piece manufactured by Messrs. Thackray of Leeds.

PARRY AND PARRY'S DISEASE

By R. I. LEGGE

Based on a Dissertation read before the Royal Medical Society on Friday, 18th November, 1960.

THE MAN

In 1778 the Charter of Incorporation was granted by George III to the presidents and associates of the Medical Society of Edinburgh, confirming Robert Freer, James Melliar, Andrew Wardrop and Caleb Parry in their office as Presidents. Caleb Parry, whose name appears here, became a highly esteemed practitioner at Bath and like Heberden acquired a life long habit of taking notes. He described the first recorded case of facial hemiatrophy in 1814, of congenital idiopathic dilatation of the colon in 1825, and in 1786 he left an account of *exophthalmic goitre* so complete and original that it more justly entitles him to the honour of its discovery than either Flajani in 1800, Graves in 1835, or von Basedow in 1840.

Caleb Hillier Parry was born on October 21st 1755, at Cirencester, near Gloucester, where his father Joshua was a non-conformist minister. His early education was at the grammar school in Cirencester, where he met Edward Jenner: and the latter dedicated his epochal "Inquiry in the Causes and Effects of the Variolae Vaccinae" to "C. H. Parry, M.D., at Bath, My Dear Friend." At the age of 18, Parry became a student of medicine at Edinburgh, in the days when William Cullen dominated the scene. Parry spent two of his undergraduate years in London, but when he returned in 1777, he was elected a president of the Medical Society of Edinburgh. And it was during his term of office that the Royal Charter was achieved, an honour which remains unique for an undergraduate society.

At the end of the same year in which he graduated M.D., 1778, Parry settled in Bath, which city he hardly left even for a day.

At the beginning of his career in Bath, Parry found that the practice of medicine did not demand all his time, so he devoted his leisure to the collection of fossils. Gradually, however, he acquired a very large practice and increasing occupation in more human relics prevented further progress in his work on fossils. It would appear appropriate then that Parry, the most prominent physician at that fashionable health resort, should have attended John Hunter when he stayed in Bath in 1785 and suffered some anginoid symptoms; but the great authorities have found no evidence for this.

So Parry must have been a cultivated man with wide interests; an omnivorous reader, no mean metaphysician and keenly interested in natural history and its practical applications. His portrait shows him to have been remarkably handsome; he must have been a charming personality. He died on March 9th, 1822, some five years after being inflicted with a right hemiplegia, and aphasia.

THE DISEASE

Definition: Hyperthyroidism connotes hyperactivity of the thyroid gland and hypersecretion of its hormone; thyrotoxicosis is the clinical synonym. The structural correlate of this excessive secretion is hyperplasia of the thyroid epithelium. Other more or less independent components are the ocular changes and a group of nervous manifestations; and both of these may persist virtually unchanged after the hyperthyroidism has been eradicated. In 1935, Harrington and his co-workers established the fundamental fact that the glandular secretion in hyperthyroidism, though excessive in amount, is not qualitatively different from normal.

The comparative simplicity of the thyroid gland is evidenced by its secreting but one hormone—thyroxine—which regulates the rate of metabolic activity within the cells of the body.

Etiology: Numerous factors have been put forward to explain what is still unknown. Firstly, it is possible to produce all the clinical features of thyrotoxicosis, with the notable exception of exophthalmos, by administration of thyroid extract in excessive amounts. Secondly, partial extirpation of the gland leads to improvement of some or all of the symptoms and signs. But since psychical trauma, sexual maladjustment and infection frequently precede or initiate the symptoms, it seems likely that the normal relationship of the thyroid and the pituitary is disturbed in thyrotoxicosis.

Incidence: Thyrotoxicosis may occur at any age, but is most commonly seen during the third and fourth decades. And there appears to be a general predominance of female patients in all the series.

Clinical Features: These are legion, and perhaps it is not inappropriate to set out first those factors which led Parry and many others to the idea of such a syndrome. He describes his first case of *Enlargement of the Heart in connection with Enlargement of the Thyroid Gland* in 1786, and this includes references to many interesting features: the syndrome followed an infection; it began in the fourth decade; the patient suffered violent palpitations; she had a tachycardia of 156 per minute and the pulse showed an irregularity which to-day would be termed atrial fibrillation; she suffered dyspnoea indicative of pressure symptoms; she subsequently developed increasing goitre and exophthalmos; and the author says that she appeared agitated and distressed. This is surely a remarkable collection of signs and symptoms for the year 1786. But it was some 27 years later that Parry came to a full realisation of the disease, when he stated that his attendance on three similar cases in 1813 suggested to him some connection "between the malady of the heart and the bronchocele." Robert Graves, who was Physician to the Meath Hospital in Dublin, published his findings entitled *Newly Observed Affection of the Thyroid Gland in Females* in 1835; and Carl von Basedow published his findings in what was probably the first autopsy in a case of recognised exopthalmic goitre in 1848. From Basedow's time, until the end of the nineteenth century, attention was concentrated mainly on exophthalmic goitre as such, but some of Parry's cases did not exhibit exophthalmos; so Parry must have realised that there were two types of thyrotoxicosis.

An acute onset with or without an initiating factor is rare. The patient is more likely to complain of some vague indefinite feeling of anxiety, restlessness, or irritability towards the children. It is often held however that the appearance of a vivacity and dynamic spontaneity is but an accentuation of pleasing feminine characteristics, and the slight exophthalmos gives a glint to the eye which is not unattractive. But the fully developed case will present

with thyroid enlargement, exopthalmos, tachycardia with palpitations, tremor of the hands, fatigue and loss of weight. The possibility of thryrotoxicosis without thyroid enlargement raises the question of ectopic thyroid tissue, e.g., in the retrosternal position where it may cause respiratory embarrassment from tracheal compression.

(a) Eye Signs: The numerous ocular abnormalities bring to mind more names from the past. Von Graefe is remembered by the physician for his discovery of lid lag, a separate entity from exophthalmos. The problem of exophthalmos is not fully understood but it does seem certain that the sympathetic nerve sensitivity produced by the excess of thyroxine can lead to contraction of the intraorbital smooth muscle, which will produce exophthalmos and may obstruct the venous return, so giving rise to oedema of the orbital muscles, which would accentuate the position. Jeffroy noticed the inability to contract the occipito-frontalis muscle as evidenced by the absence of wrinkling of the forehead ; whilst Stellwag thought the absence of blinking significant ; and Möbius found inability to sustain convergence a feature of the disease.

(b) Cardoivascular Signs: Parry's inclusion of the heart within the syndrome leads directly to these. The tachycardia which is almost invariably present persists during sleep and is thus differentiated from the functional variety, for in thyrotoxicosis the raised metabolic rate which is inherent in the disease demands more oxygen, and this, together with the direct stimulatory action of thyroxine on the heart, is bound to produce a marked tachycardia. The raised pulse pressure is accounted for by the decrease in the diastolic pressure with a comparatively normal systolic pressure. The young patient will compensate for this, but in the older patient it will often lead to decompensated cardiac failure, with atrial fibrillation. The ECG will show characteristic changes in 30% of cases and ECG examination must be carried out pre-operatively to assess the state of the myocardium. A systolic bruit will be heard over the gland if the latter is very vascular, and may be possible to palpate this—the feeling of a bag of worms.

(c) Locomotor Signs: The patient may notice the tremor when pouring out the tea, but the clinician may best elicit the tremor by placing a sheet of paper on the patient's outstretched hand. There may be weakness of the skeletal muscles, and a true myasthenic element responsive to neostigmine has been reported. This weakness may of course be due to the marked loss of weight which often occurs as a result of an excess of catabolism over anabolism. This accounts for the patient's voracious appetite, which is often insatiable.

(d) Endocrine Signs: Disturbances of mentstruation and pregnancy are to be expected in any endocrine upset which involves the whole of the body's metabolism. Though menstruation may be normal, it is often suppressed partially or completely. It is physiological for the thyroid to enlarge during pregnancy, and pregnanacy has been named as a precipitating factor ; but when pregnanacy supervenes in an established case of hyperthyroidism, the condition may be unaltered or even ameliorated.

(e) Other manifestations: Excessive perspiration may be troublesome, and on shaking hands with the patient, it may be possible to reach a diagnosis at the first consultation ; for in thyrotoxicosis the palms are warm, as distinct from the cold sweat of the anxiety state.

(f) Laboratory Investigations: The essential action of the thyroid gland is to increase the metabolic rate of the cells throughout the body. Thus an increase in the Basal Metabolic Rate is inherent in the diagnosis ; but efforts to achieve the basal state are so seldom fruitful that this procedure is not adopted nowadays. The degree of lowering of the serum cholesterol is significant : the normal

range of 150-220 mg% is usually lowered to 80 mg%. Signs of demineralisation may be seen on skeletal x-rays, and this negative calcium balance is confirmed by the finding of excessive calcium loss in the faeces with normal levels of serum calcium and phosphorus, but the serum phosphatase values are often raised. Since thyroidectomy alleviates this, and the reverse is found in myxoedema, it must be assumed that thyroxine exerts a direct effect upon the metabolism of calcium and phosphorus. Most cases of thyrotoxicosis can be confirmed by the finding of a raised serum protein-bound iodine, but it is not every laboratory that has the facilities for this determination. A small diagnostic dose of radio-active iodine—5 microcuries—will show whether the gland is hyperactive, and there is no real hazard in such a small dose.

Treatment: Experience has shown that the course of thyrotoxicosis, which untreated is a series of exacerbations and remissions, may be favourably modified by the use of small doses of iodine, and be interrupted temporarily or permanently by the administration or thiourea or its derivatives, or of the salts of radio-active iodine, or by subtotal thyroidectomy. In the last decade wide practical experience has been gained in the use of antithyroid drugs and radio-active iodine, and more adequate medical preparation has improved the results of surgery. Consequently each case can now be considered on its own merits, and one therapeutic route tailored to it.

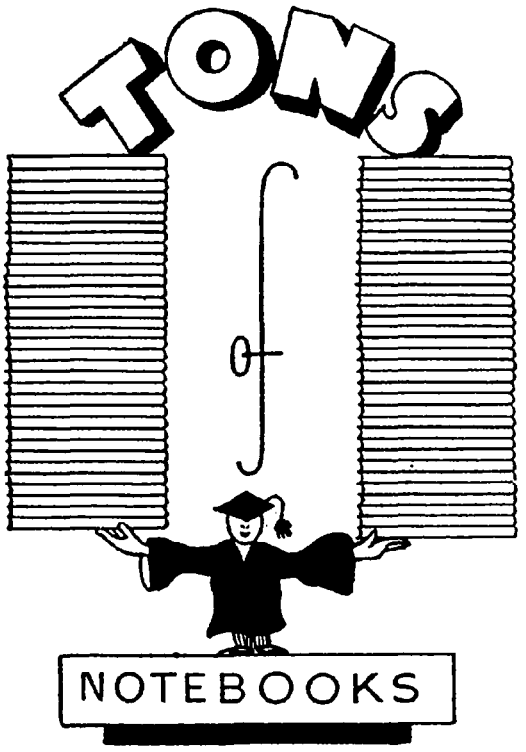
(a) *Antithyroid drugs*: It has been shown that drugs of the thiouracil series inhibit the combination of iodine with tyrosine. Carbimazole was introduced as producing fewer side-effects than methylthiouracil, particularly to combat the production of agranulocytosis by the latter. Carbimazole is, however, slower in action and is usually given in one tenth the dosage of methylthiouracil as it has been reported to be ten times as effective. Potassium perchlorate on the other hand is a rival and more recent antithyroid preparation which inhibits the iodine-trapping mechanism of the thyroid gland. It is a simple inorganic compound and is therefore unlikely to sensitise the haemopoietic system. A full investigation into these various drugs has been carried out by Crookes in Glasgow. One of his series involved the following four daily drug dosages — (1) 600 mg methylthiouracil; (2) 600 mg potassium perchlorate; (3) 1000 mg potassium perchlorate; (4) 60 mg carbimazole. The results of this showed that the higher dosage of potassium perchlorate was the most effective and was attended by the least side-effects; whilst carbimazole was not as effective in one tenth dosage as methylthiouracil. In addition, no evidence could be found that potassium chlorate increases the vascularity of the gland at surgery. It would seem then that potassium perchlorate may replace carbimazole as the antithyroid drug of choice, even in those cases which undergo a course of medical therapy prior to surgery.

(b) *Surgery*: The surgical approach is chosen on certain definite indications. The patient may choose it in preference to 12 months' drug therapy which cannot guarantee success; or she may be considered unlikely to persist with the prolonged regimen of medical treatment. Signs and symptoms of pressure are an indication for surgical intervention, and operation may be a suitable alternative when sensitivity to the drugs arises. Cases of secondary thyrotoxicosis are less likely to respond to drugs, and these together with those who do not respond to a prolonged medical regimen are candidates for surgery. Subtotal thyroidectomy, removing 7/8 of the gland, is not a hazardous procedure in experienced hands, but its few dangers should be borne in mind, particularly if a repeat operation is being considered. The possibility of interference with the recurrent laryngeal nerve necessitates direct laryngoscopy both before and after operation. A careful dissection to leave a posterior layer

of the gland covering the parathyroids will obviate any disturbance of the blood supply to the latter. Severe haemorrhage and thyroid crises are distinct rarities nowadays. The specific response of the thyrotoxic patient to iodine as a pre-operative measure is a remarkable phenomenon. For 5 - 10 minims of Lugol's iodine three times a day will produce a rapid decline in symptoms, slowing the pulse, increasing the body weight, and decreasing the metabolic rate. But its benefit is only felt for about two weeks. Thus iodine has no effect on the duration or progress of the disease, and there is now experimental evidence to show that iodine merely prevents the thyroid from giving a maximal response to the stimulus of thyrotrophin.

(c) *Radio-active Iodine:* Deep x-ray therapy is no longer recommended, but good results are now being achieved with I-131 ; for the hyperplastic gland shows such an avidity for the radio-active iodine that a therapeutic concentration is more than easily obtained without damage to the rest of the body. Gene mutation and carcinogenesis are theoretical possibilities which have not yet been seen in man, but are factors which usually preclude the use of radio-active iodine during the reproductive years of life.

Hyperthyroidism is one of the key problems of internal medicine, for in one direction it overlaps toxic nodular goitre, and the relationship of primary to secondary thyrotoxicosis is still not understood. It also merges into the anxiety states, autonomic imbalance and neurocirculatory asthenia. Exophthalmos is still an unsolved problem. And perhaps there may even be some inkling of truth in the contention that hyperthyroidism should be called *Parry's disease.*



BROWN
OF THE
MOUND

STATIONERS
and PRINTERS

NORTH BANK STREET
EDINBURGH
Telephone CAL 5960

NUTRITIONAL BLINDNESS

By DONALD S. McLAREN

M.D.(Edin.), Ph.D.(Lond.), D. T. M. & H. (Eng.)
East African Institute for Medical Research, Mwanza, Tanganyika.

Based on an address delivered to the Royal Medical Society on Friday, 2nd December, 1960.

It is a tragic fact that in large areas of the world today despite the continuing advances in medical science many thousands of people, the majority young children, are going blind every year as a result of malnutrition. As will become apparent as this subject unfolds, we know enough about the ways in which deficiency of vitamin A and vitamins of the B complex destroy vision to be in a position to prevent much of the needless suffering. It will also be shown that there are important areas in this field where we are still ignorant, especially of the long term effects of malnutrition acting very early in life on certain parts of the eye.

Due not only to lack of time but also to the dearth of reliable data and information upon which to base an appraisal I shall not deal with certain aspects of this subject. For example, we do not yet know whether or not malnutrition plays any part in the disease process of trachoma or in the development of pterygium. We are also ignorant of the importance of an underlying deficiency of nutrients in making the conjunctiva and cornea more susceptible to infectious processes.

Leaving such speculations strictly aside my purpose is to summarize present knowledge of certain nutritional eye conditions and also perhaps to enlarge the horizon of your thinking by introducing you to some fresh problems and new concepts.

1 *VITAMIN A*

Undoubtedly deficiency of Vitamin A with its outstanding spectrum of eye signs ranging from night blindness and xerosis conjunctivae to xerophthalmia and keratomalacia merits pride of place in our consideration. I have no hesitation in saying that in terms of numbers affected and damage done this is still the Number One vitamin deficiency disease in the world.

(a) *Extent.* Although occurring all over Europe and North America until about the beginning of this century, it has been in the highly populous technically underdeveloped countries of the world that it has taken its heaviest toll. The records of one eye hospital in Indonesia over the past 15 years show no less than 10,000 cases of xerophthalmia. Throughout the whole of Asia, Latin America and in certain parts of Africa Vitamin A deficiency is a continuing problem.

(b) *Effects.* Blindness, frequently total, occurs mainly in very young children and more frequently in boys than in girls. The true nature of the condition is frequently not recognised by the doctor and even if recognised sight has often already been destroyed when the patient is first seen. This is all

the more tragic because of the excellent preventive and early curative effects of good sources of Vitamin A or carotene. As the most severely affected are children those that survive constitute a problem for the community over many years.

A second important effect of Vitamin A deficiency is the threat it presents to life itself. In the laboratory many young deficient animals die before they ever develop xerophthalmia. Although, with the remedy to hand, we cannot study this point in man there seems no reason to doubt from the severity of the general condition of these children that many untreated cases do not survive. Thus Vitamin A deficiency is one of the few, and easily the most important, of the diseases that kill as well as blind. I have previously described the anterior segment changes which occur in Vitamin A deficiency.[1] Fig. 1 shows what I call "xerophthalmia" being the same as "xerosis conjunctivae et corneae." The bulbar conjunctivae of this 18 month old Gogo baby of Central Tanganyika were markedly dry and wrinkled and the corneae were hazy, the stroma infiltrated but there was no loss of integrity of the cornea. In Fig 2 we see commencing keratomalacia in a baby of the same age from the same area, where the cornea is heavily vascularized and as a whole is beginning to undergo liquefaction or colliquative necrosis characteristic of this condition. In certain parts of the world[2] keratomalacia is a frequent accompaniment of protein malnutrition or Kwashiorkor, and Fig. 3 shows this in a two year old boy in Guatemala.

Besides being a public health problem of the first magnitude Vitamin A deficiency also poses a number of problems of great interest and importance and requiring more research. These may be mentioned here without any attempt being made to elaborate on these subjects.

1. The function of Vitamin A at the cellular level, outside the retina is still not known. Recent work of Wald, who has contributed so much to our knowledge of the biochemical basis of vision, and his associates[3] may have provided the key to unlock this door. From detailed studies of the development of Vitamin A deficiency in the rat they have postulated that, as in the retina so also elsewhere, Vitamin A may be necessary to act as a stabiliser of protein.

2. Undoubtedly Vitamin A is linked with protein in many aspects of its metabolism and the part which protein deficiency may play in affecting the development and severity of xerophthalmia is still not clear, although probably a minor one.[4]

Many points about the epidemiology of Vitamin A deficiency are still far from clear. For instance it was found that there was a high incidence of keratomalacia in Orijas as compared with Khonds in a series of cases treated in India despite the fact that Khonds much more frequently attended the hospital. Dietary inquiry and other data failed to provide an explanation but differing tribal customs concerning the resumption of sexual intercourse after parturition did. A social anthropologist would find a very fruitful field here in which to work.

4. There is no reliable means of detecting Vitamin A deficiency in any but its most devastating late stages in the most susceptible age group, the young child of 6 months—3-4 years. Plasma Vitamin A levels are not of value for early detection and dark adaptation studies require co-operation. The development of such a test would be invaluable in field studies and public health work.

5. That the presence of Bitot's spots indicates Vitamin A deficiency has been copied from textbook to textbook until it has become axiomatic. However there have always been those who found no response of these lesions to even prolonged Vitamin A therapy and more recently it has been shown[5] that

they are not always accompanied by impaired dark adaptation nor are the serum Vitamin A levels lower than in controls. Vitamin A deficiency would seem to be only one, of perhaps a number, of possible causes.

6. Reversible structural changes have, from time to time, been reported in the human fundus in Vitamin A deficiency[6, 7, 8] and it has been suggested, without any real evidence that some of the choroido-retinal changes in onchocerciasis may in part be due to lack of Vitamin A.

2. *THE VITAMIN B COMPLEX*

I propose to deal briefly with three main eye conditions in this section. They are (1) the retrobubar neuritis resulting in nutritional amblyopia; (2) corneal epithelial dystrophy, and (3) corneal neovascularization.

(1) *Nutritional amblyopia*

This condition has been known and described for nearly 100 years but we are today very little nearer to an understanding of its nature. This is not surprising in view of the fact that the literature on the subject consists largely of reviews of the present literature and descriptions of clinical signs and and dietary response of a few more cases. Most Japanese authors have associated amblyopia with beriberi and there are numerous accounts of pellagra in which it is included in the symptomatology. Thousands of cases occurred in the Far East prisoner of war camps, during World War II. Certain parts of the West Indies, [9, 10] West Africa [11, 12] and part of Japan [13] are endemic foci of the condition at the present time although it is probable that it occurs in many other areas but lack of specialized facilities may prevent its recognition.

Clinical features. Young adults are usually affected although there is one report of an outbreak in children.[14] Almost invariably the amblyopia is but part of a widespread neuropathy. The ocular findings consist of impairment of central vision and the presence of roughly symmetrical central, para-central or centro-cecal scotomata larger for red than for white test objects with intact peripheral fields. Commonly there is slight pallor of the temporal portion of the discs. In the few cases examined histologically[15] the degeneration of myelinated fibers was restricted to the zone of the papillomacular bundle. Thus clinically and pathologically nutritional amblyopia appears to be identical with tobacco-alcohol amblyopia[16] and distinct from those of proven toxic origin in such as methyl alcohol and quinine. Although there is general agreement that a deficiency of Vitamin B complex is involved some favor thiamine[17] others riboflavin[18] and others more recently Vitamin B_{12}[19] in the treatment of these identical conditions. In East Africa the writer[20] has had dramatic improvement in three cases previously refractory to thiamine and riboflavin therapy in response to Vitamin B_{12}.

It may reasonably be predicted that nutritional amblyopia will become of increasing importance and show a large apparent, if not actual, increase as more and more people demand a higher degree of visual acuity for reading and for precision work in industry.

(2) *Corneal Epithelial Dystrophy*

This name was first given to a form of punctate keratitis by Metivier[9] in Trinidad frequently complicating a generalized Vitamin B complex deficiency state. Without knowledge of this report similar changes were found in many prisoners of war in the Far East and it was suggested that they were identical. Nanagos[21] in the Philippines also claimed good response with B-complex therapy. However many accounts of nutritional amblyopia made no reference

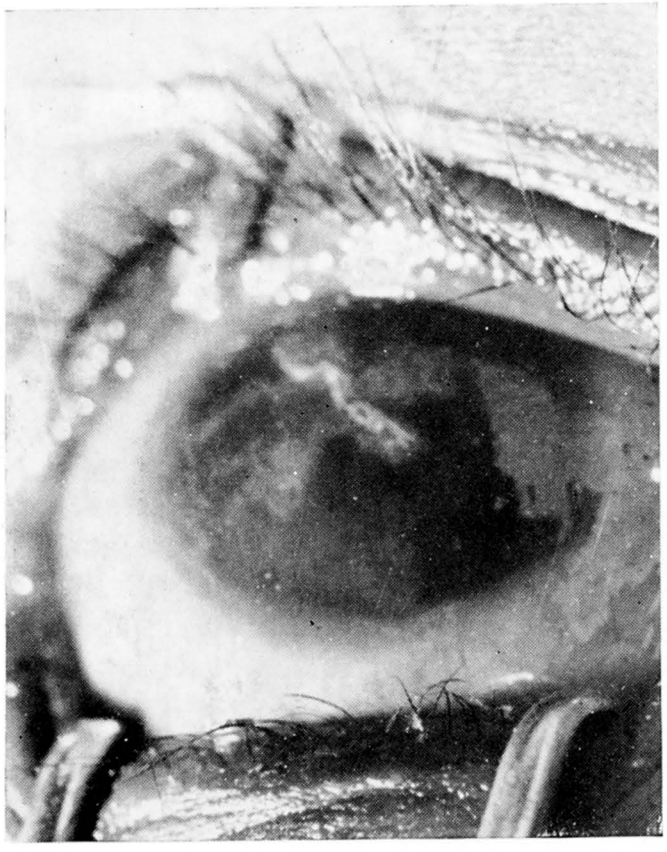


Fig. 1. "*Xerosis Cunjunctivae et Corneae.*" The eye of a young Gogo baby.

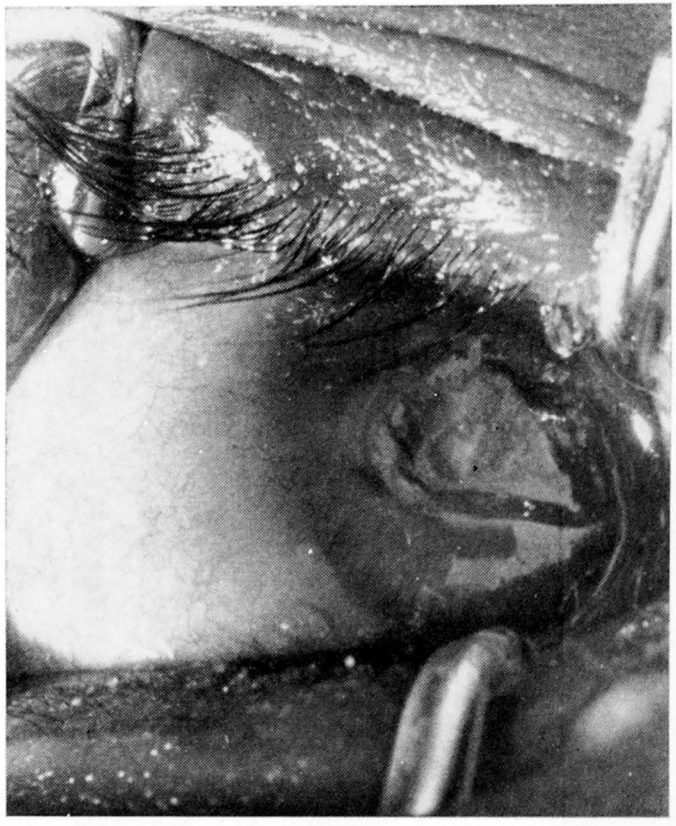


Fig. 2. "*Keratomalacia.*" The eye of a young Gogo baby showing marked corneal vascularisation and commencing colliquative necrosis of the whole cornea.

a fresh start for corticoid therapy

βetnelan

an entirely new anti-inflammatory steroid

Here is a steroid having increased anti-inflammatory activity with a decreased possibility of side effects. Betnelan, the most potent steroid available for clinical use,

is devoid of salt retention activity
has negligible effect on potassium balance
causes no mental depression

and shows promise of clinical superiority in other respects.
For short-term therapy a "**2:1:½**" dosage scheme is suggested.
For example, in acute asthma, severe eczema, urticaria, shock and other conditions for which corticoids are indicated systemically, the dosage may be
2 tablets t.i.d. for 2 days followed by **1** tablet t.i.d. for 2 days and ½ tablet t.i.d. for 2 days.
For maintenance, dosage need be no more than ¼ tablet twice daily.

BETNELAN is presented as scored tablets containing 0·5 milligrams betamethasone in bottles of 30, 100 and 500.

Dose for dose, Betnelan is the lowest priced of all corticosteroids available today.

Betnelan (betamethasone) is an entirely new parent compound developed in Britain by Glaxo Laboratories Ltd. Its merits are derived from its unique chemical structure—the beta position of 16 methyl group in the formula 16β-methyl-9∝-fluoroprednisolone (betamethasone) *representing more than 20 new stages of manufacturing complexity.*

BETNELAN Trade Mark

better—for safety: activity: economy

GLAXO LABORATORIES LIMITED

to corneal involvement. It is now known that there is a wide variety of kerato-conjunctivitides in the tropics, mostly of virus origin and in Tanganyika the writer found as many as one third of all African hospital patients admitted for other than eye diseases had active punctate keratitis or inactive scars. In the absence of better evidence for a nutritional etiology it would seem to be advisable not to regard this as a separate entity. In the writer's view the most likely explanation is that the epithelial and subepithelial changes of superficial punctate keratitis are of varied etiology and are enhanced by deficiency of B vitamins although this at present is purely speculative.

3. *Nutritional Corneal Vascularization*

Invasion of the corneal substance by capillary loops from the limbus has accompanied a variety of deficiency states in experimental animals but as far as we know is limited in man to that seen late in xerophthalmia and that attributed to ribo-flavin deficiency. The first description of ocular hyporiboflavinosis[22] occurring in pellagrous patients included inflammatory factors which suggest that there was complicating infection. There is no reason to doubt that the corneal vascularization at least responded to riboflavin. Although the muco-cutaneous lesions of riboflavin deficiency frequently accompany pellagra corneal vascularization is an unusual feature and it rarely, if ever, occurred in prisoners of war with nutritional amblyopia. Pellagra is a multiple deficiency state and the diet which caused it in the Southern United States was quite different from the pellagragenic diet in other parts of the world. In East Africa the writer has failed to find a single case of pellagra with corneal vascularization nor does it accompany angular stomatitis, perleche and magenta tongue. Several riboflavin deficiency trials in man have failed to produce corneal vascularization. In summary it would seem that, although riboflavin deficiency may in man occasionally produce corneal vascularization as in experimental animals, this is rather uncommon.

3. *Discrete Colliquative Keratopathy*

I have applied[20] this descriptive but rather cumbersome name to a fascinating condition of the cornea first described in malnourished South African Bantu children by Blumenthal.[23] As far as I know it has not been reported outside Africa. I did not see it during my 5 years in India and in other Asian and Central American countries. I have shown pictures of the disease (Fig. 6) but ophthalmologists there have not recognized it. To my mind this casts serious doubt on a purely nutritional theory of etiology and in my experience in East Africa it seems to have a distinct seasonal incidence; all my cases have occurred during the rainy season October - May. The essential process here is a quiet dissolving away of the cornea confined to a small area usually about 5 or 7 o'clock with a striking absence of accompanying symptoms or history of trauma. The rest of the cornea appears grossly normal but under the slit-lamp there is usually minimal vascularization. Iris prolapse follows corneal softening and may be asymptomatic. Some of the examples I have seen have been in children admitted to hospital for other conditions and in whom the iris prolapse has passed unnoticed by the medical staff. More than once I have heard of mothers bringing their children to the doctor and asking him to remove the " black speck " from the front of the eye i.e. the prolapsed iris, showing that frequently mothers are more observant of their children's welfare than those who attend them medically. There is no clear response to vitamin therapy or protein feeding and in this respect and by its nature discrete colliquative keratopathy is to be distinguished from keratomalacia. The

prolapse may be abscissed but is probably best left alone and healing with leucoma adherens is the inevitable end result.

4. *Cataract*

Several nutritional deficiencies, including riboflavin, certain amino acids and protein[24] are known to result in cataract in experimental animals. Other preliminary work[25] which, because of the exceedingly critical nature of the experimental condition, it has so far not been able to repeat suggest that prolonged protein deficiency in the mother rat may lead to congenital cataract and defects involving connective tissue and ground substance elsewhere in the eye. This work suggested that the cataractous process in the human lens might possibly be speeded up as a result of nutritional deficiency in early life.

In many countries where malnutrition is rife so-called "Senile" cataract is very common and appears to occur at a significantly earlier stage than elsewhere. Unfortunately these statements have as their basis only the experience and impressions of practitioners as no really objective study has been made. However the evidence is very considerable and is all consistent with these views. It has been shown[26] in Tanganyika that by the age of 7 years or so the large majority of African children already have minimal cuneiform water-cleft opacities in the extreme periphery of the lens. Children of the Indian community in East Africa also have these opacities but they were not found in a group of 100 European children of the same age many of whom had spent most of their life in Africa. These opacities appear to increase in number, intensity and size with age developing over the years into intumescent and mature cataract in many of those living until late middle age and old age. It is not known yet, of course, whether malnutrition is really playing any part in this process. If it is then it is probably acting very early in life. It has been possible to examine a few children known to have survived severe marasmus or kwashiorkor and they do not show grosser changes than most for their age. It may well be that the responsible factor is acting even earlier on probably in the first few months of intra-uterine life when the lens along with the rest of the eye and the nervous system is growing and differentiating more rapidly than other tissues and might be regarded to be especially susceptible to nutritional, as it is to other insults.

5. *Refraction*

From time to time the possible role of dietary deficiency in the aetiology of myopia and other errors of refraction has been mooted, usually wildly speculative in nature and without any real evidence. It must be admitted that the idea in itself is not in any way outlandish for it is known that the overall refraction of the eye is dependent upon the growth and development of the various parts of the eye. Nutritional deficiency occurring in the early formative months might reasonably be expected to adversely affect the growth of these tissues and also the organizing power which the retina appears to possess over this process.

In the Central Province of Tanganyika periods of severe food shortage have occurred several times during the past one hundred years and thousands of Gogo tribes people are reckoned to have died from starvation during the most recent famine in 1953-4. With the object of seeing whether the refractive state of young children who had survived this famine was adversely affected nearly one thousand children in the area were refracted and the results compared with data for African and Indian children in non-famine areas. When analysed the data for the famine area children showed very marked abnormalities in three main respects. (1) The spread of mean refraction values in the

range of the aberrations of emmetropia was much greater than normal. In the non-famine area data there were no representatives higher than +1.5 and −2.5 D whereas in the famine area data values occurred out to the limits of + and −4.0 D. (2) Beyond the limits of emmetropia and its aberrations, that is to say axial ametropia, there were 27.5 times as many representatives for the famine area data, the majority of these being high myopia. (3) When the data were analysed for the incidence of mixed astigmatism and anisometropia of a degree of 1.0 D and more it was found that these conditions were both present 5-7 times more commonly in the famine area.

Here again, in conclusion, we cannot yet say whether malnutrition really is involved or not, although it may well be. Even assuming the cause to be malnutrition there are many possibilities as to its precise nature. The importance of Vitamin A in the retina for scotopic vision is well known and it might well be important much earlier in life. Although there is a continuing xerophthalmia and keratomalacia problem in infants of that area I know of no report of such gross refractive errors from any other part of the world where this is is severe deficiency of Vitamin A. At present I would rather favour total inanition of starvation as being responsible. However, this is a good note upon which to end, calling attention to our great ignorance and the need for much more work in this important but hitherto largely neglected "no man's land."

REFERENCES

1. McLAREN, D. S. (1956) J. troj Pediat. 2, 135.
2. McLAREN, D. S. (1959) Bull. Wld. Hlth. Org. 19, 303.
3. DOWLING, J. F., WALD, G. (1958) Proc. Nat. Acad. Sci. 44, 648.
4. McLAREN, D. S. (1959) Brit. J. Ophthal. 43, 234.
5. DARBY, W. J., McGANITY, W. J., McLAREN, D. S., PATON, D., ALEUM, Z., and MEDHEN, M.G. (1960) Pub. Hlth. Rep. 75, 738.
6. MIKAMO (1915) Nippon Gank Zasshi, December cited by Elliot, R. H. Tropical Ophthalmology, Oxford Univ. Press.
7. FUCHS, A. (1959) Amer. J. Ophthal. 48, 101.
8. SIE BOEN LIAN (1960) Adr. Ophthal. 10, 49.
9. METIVIER, V. M. (1941) Amer. J. Ophthal. 24, 1265.
10. CRUICKSHANK, E. K. (1956) W. Ind. med. J. 5, 147.
11. MOORE, D. F. (1930) W. Afr. med. J. 4, 46.
12. MONEY, G. L. (1959) W. Afr. med. J. 8, 3.
13. IRINODA, K., and SATO, S. (1954) Tohoku J. exp. Med. 61, 93.
14. WHITBOURNE , D. (1947) Amer. J. Ophthal. 30, 169.
15. FISHER, C. M. (1955) Canad. Serv. med. J. 11, 157.
16. VICTOR, M., MANCALL, E. L., and DREYFUS, P. M. (1960) Arch. Ophthal., N.Y. 64, 31.
17. CARROLL, F. D. (1944) Amer. J. Ophthal. 27, 713.
18. SMITH, D. A., and WOODRUFF, M. F. A. (1951) Med. Res. Coun. Spec. Rep. Ser. No. 274 H.M.S.O. London.
19. HEATON, J. H., McCORMICK, A. J. A., and FREEMAN, A. G. (1958) Lancet, ii, 286.
20. McLAREN, D. S. (1960) Proc. Nutr. Soc. 19, 89.
21. NANAGAS, P. J. (1953) Arch. Ophthal., N.Y. 49, 536.
22. SYDENSTRICKER, V. P., SEBRELL, W. H., CLECKLEY, H. M., and KRUSE, H. D. (1940) J. Amer. med. Assoc. 114, 2437.
23. BLUMENTHAL, C. J. (1950) S. Afr. med. J. 24, 191.
24. McLAREN, D. S. (1959) Brit. J. Ophthal. 43, 78.
25. McLAREN, D. S. (1957) Proc. Nutr. Soc. 16, xxiii.
26. McLAREN, D. S. (1960) J. trop. Med. Hyg. 63, 101.

Accidental Haemorrhage

By JAMES MOWAT

Based on a dissertation read before the Royal Medical Society on Friday, 28th October, 1960.

Edward Rigby of Norwich, in a treatise on uterine haemorrhage published in 1776, first shed light on the problem of bleeding from the vagina during later pregnancy. In this essay he differentiated between an accidental haemorrhage and the haemorrhage of a placenta praevia. From his observations accidental haemorrhage was defined as "bleeding from a normally situated placenta, after the 28th week of gestation, and up to the end of the second stage of labour."

Accidental haemorrhage is divided into three varieties:

1. Revealed Accidental Haemorrhage.—where the bleeding is entirely external;
2. Concealed Accidental Haemorrhage.—where there is no sign of blood externally;
3. Mixed or Combined Accidental Haemorrhage.—which shows features of both concealed and revealed.

The most important of these is the concealed variety and there are four ways in which a haemorrhage may remain concealed:

1. A retroplacental haemorrhage occurs in the central area of the placenta, but the margins of the placenta remain adherent to the uterine wall.
2. If the placenta becomes completely separated the membranes remain attached to the uterine wall.
3. The blood may burst through the membranes into the amniotic sac mingling with the liquor, and immersing the foetus in a blood bath (Lesser 1951).
4. When the foetal head is accurately applied to the lower uterine segment so that the blood cannot make its way past it into the vagina.

In spite of these mechanisms it is much more common for blood to escape externally; a concealed accidental haemorrhage thus becomes a mixed accidental haemorrhage.

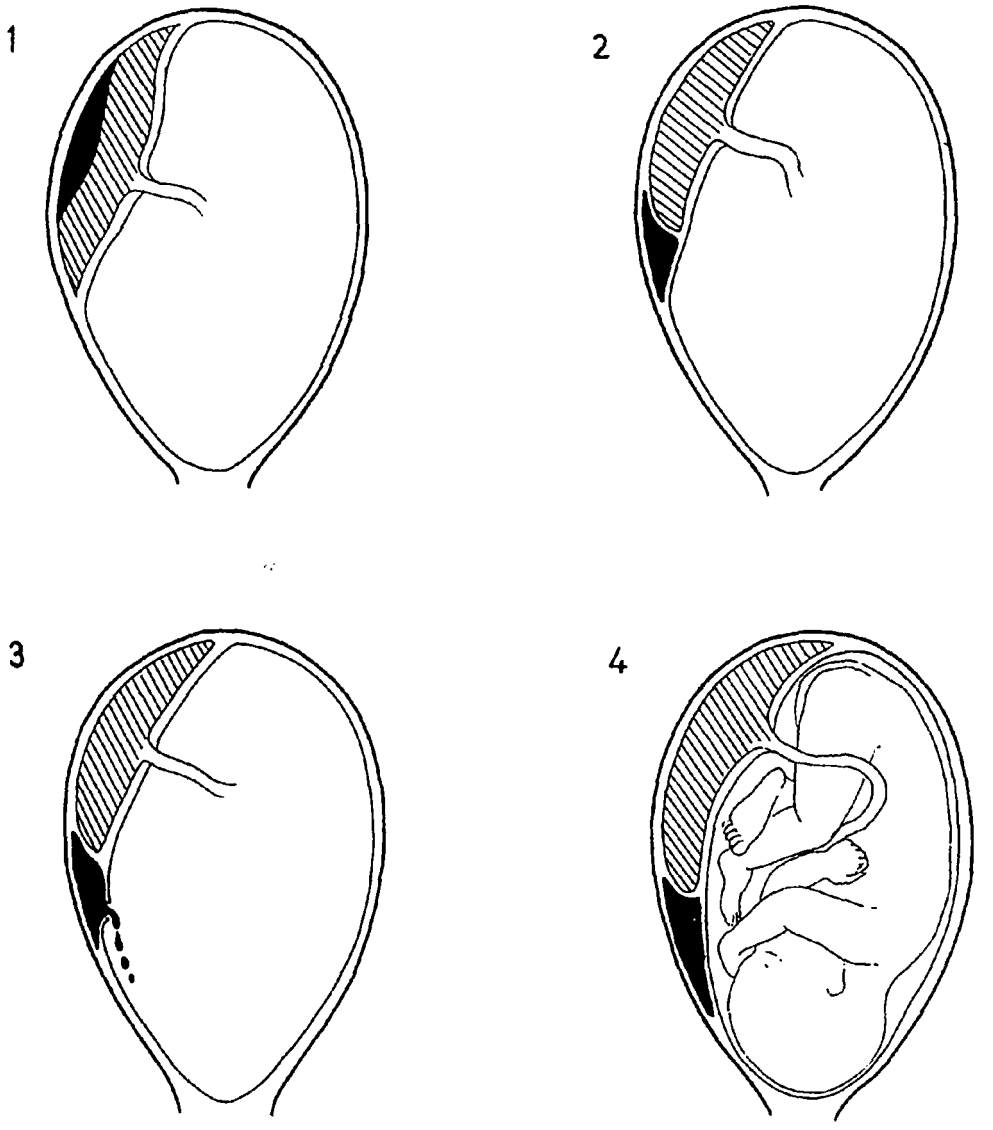
Incidence

This varies in different pubished series, but in Britain the average incidence is about 1.5% i.e. 3 in every 200 pregnancies. In America however this figure is much lower, being about 1 in every 600 pregnancies. This variation may in part be explained by differing criteria in diagnosis, and in the type of cases included under accidental haemorrhage (S.M.M.P. Annual Report 1960. p. 5). Concealed accidental haemorrhage, makes up about 12 - 16% of the total accidental haemorrhages.

Aetiology

There is no known one cause of accidental haemorrhage. It is probably for this reason that so many causes have at one time or another been evoked.

Rigby conceived of accidental haemorrhage as a feature secondary to certain external factors—"separation of the placenta must be owing to some accidental circumstance, to violence done to the uterus by blows or falls, to



The four types of concealed accidental haemorrhage (for key see text opposited).

some peculiar laxity of the uterine vessels from badness of habit or fever, or to some influence of passion of mind, suddenly excited such as fear or anger."

Trauma definitely seems to be a predisposing factor, but in a minority of cases. The trauma may be direct e.g. a severe blow on the abdomen, or indirect e.g. severe exertion, coitus, or heavy lifting. An important obstetrical factor is ante-natal versions, and this is why these should not be performed under general anaesthesia.

At the present time the most important actiological factor is thought to be pre-eclampic toxaemia. The incidence of this toxic variety varies with different authors, some with an incidence as high as 90%, while others are equally emphatic with the incidence of 5%. The criteria for the diagnosis of P.E.T. is obviously of importance in comparing the differing figures. The correct definition of P.E.T. must be used i.e. the raised B.P., with oedema (latent or obvious), and later albuminuria. In many instances P.E.T. has been diagnosed by the presence of albumin in the urine *after* the haemorrhage. This is misleading since the albuminuria may very well be due to the shock accompanying the haemorrhage. That pre-eclampsia is not the entire answer is seen by looking at the small number of accidental haemorrhages in those with P.E.T. Hypertension must also be mentioned as being an important aetiological factor (5 - 10%).

Any abnormality in the attachment of the placenta, or deficient attachment, may be a cause of premature separation.

(1) It is often noticed that women admitted with acc. haems. have had A.P.H.s. (Including abortions) in previous pregnancies. This must surely point to some inherent maternal defect, preventing good placental attachment or causing early separation, since no other pathology can be demonstrated.

(2) Interference with the normal structure of the uterine wall e.g. as a result of previous operations such as D. & C., myomectomy, or Caesarean Section, or if a tumour is present, may result in poor placental attachment.

C. S. Russell (Douglas 1955) has found that there is a fall in the level of urinary pregnanediol prior to accidental haemorrhage in those under observation because of repeated accidental haemorrhages. Whether this endocrine disturbance is primary or is a manifestation of general metabolic or pathological upset, is unknown.

It is thought that hydramnios and twin pregnancies may precipitate premature placental separation. Authors holding these views are divided into two schools of thought, one believing that the mechanism is the sudden release of an abnormally high intra-uterine pressure when the membranes rupture, and the other group considering the cause to be the pressure of a bulky uterus on the inferior vena cava, interfering with the venous return from the placenta.

Among other factors suggested are :

Chronic endometritis,
Severe torsion of the uterus,
Shortness of the umblilical cord (causing traction during labour).

Accidental haemorrhage is seen more often in the multiparous than the primigravida patient, and in a series from the records of the S.M.M.P., the unbooked multips showed a high proportion of the numbers admitted with accidental haemorrhage. Age of the patient seems to be of little significance.

Pathology

The initial lesion is thought to be a decidual haematoma which interferes with the function of the immediately overlying and now separated placental area. If the initial bleeding is from a blood vessel at or near the edge of the placenta, no further separation may occur, the blood tracking down between the chorion and the uterine wall to the cervix. In such cases the haemorrhage is limited and the foetus is not likely to be embarrassed—revealed type of haemorrhage. Fish (1951) claims that a marginal sinus rupture is of this type.

If separation occurs further in towards the centre of the placenta there may be no vaginal bleeding, and only a tender spot felt on abdominal palpation—in such a case the shed placenta shows a small depression containing fresh or

organised blood clot, depending on its age. More often the extent of the haemorrhage increases to produce further placental separation until the margin of the organ is reached and blood escapes. (Holland 1959).

There have been many suggestions as to the reason for the initial bleeding which causes the placental separation. In 1915 Williams described degenerative lesions in the intima of the small uterine arteries, and he suggested these vascular changes were due to the toxaemic process, (and thus anoxia). Bartholomew (1953) describes the placental pathology in acc. haem. as being identical with that found in pre-eclampsia and eclampsia. At any rate there are units of placental tissue which appear grossly or sharply circumscribed, round or oval, slightly firm areas. This may be a local or generalised lesion. Microscopically the villous capillaries are dilated from a diameter of 3 rbcs. to 20 rbcs., or they may be ruptured. General ischaemia of the placental bed from maternal vascular disease or athersclerosis of decidual arterioles must have nothing to do with it, Bartholomew argues, since the pathological picture is that of sharply demarkated areas. Infarction may produce haemorrhage and placental separation.

In the more severe case, either at post-mortem or operation, the uterus may be seen to be enlarged, purplish red in appearance, and with extravasated blood infiltrating its muscle fibres, and penetrating into the uterine ligaments. This classical picture, known as the Couvelaire Uterus, is associated with a decreased coagulability of the blood, a hypofibrinogenaemia, which allows the blood to penetrate the pelvic structures owing to the deficiency of the clotting mechanism. The Couvelaire uterus interferes with uterine retraction, and thus leads to further grave bleeding.

Douglas (1955) in a series quotes 75% incidence of Couvelaire uterus in patients whose delivery was beyond 3 hours of placental separation. In a series of 100 cases with 7 maternal deaths, Browne (1952) found Couvelaire lesions in 5, not in one, and unknown in one.

Marginal sinus rupture can only be diagnosed by examination of the placenta (Firth 1951). At the margin of the placenta a grossly dilated blood vessel may be noted, showing evidence of rupture, and containing blood clot continuous with blood clot outside. The placenta must be a wide membrane placenta.

Clinical Features

The signs and symptoms vary in each case from the mild barely noticeable ones, to the typical full blown picture of a severe concealed accidental haemorrhage.

In the revealed type vaginal bleeding is usually the only symptom. Although the vaginal bleeding may be a presenting feature in the mixed variety, pain is more often the first symptom. The pain may vary from backache and slight crampy abdominal pain, to the severe, sudden, and agonising pain characteristic of a severe concealed haemorrhage. After a variable period in the concealed variety there is usually some vaginal bleeding—and the haem. becomes a mixed accidental haemorrhage.

Mild cases of concealed haemorrhage may only be diagnosed after the delivery of the placenta, when retroplacental clot is noticed.

This, however, is not necessary to diagnose the severe case, where the woman presents in a shocked condition, pale, sweating, restless, and complaining of severe abdominal pain. There may be little or no vaginal bleeding, but where it has occurred, the shocked condition of the patient is out of all proportion to the revealed blood loss. The bleeding may not only come from the vagina, but from mucous membranes e.g. gums; haematemesis and haematuria may also occur.

The pulse is taken and shows a tachycardia. The B.P. is low—though a B.P.

of e.g. 140/90 is not uncommon—repeated readings however will show a downward trend. A high reading should make us think of a superimposed toxaemic state.

When the urine is tested, albumen is found, often in massive quantities. The albuminuria may be due to the shock-albuminuria syndrome, or it may have been present before the haemorrhage, because of pre-eclampsia. Oliguria may occur due to the renal embarrassment and in the most severe cases this may proceed to anuria.

On examination of the abdomen, the uterus is tense, rigid, and exhibits the typical woody hardness of concealed haemorrhage. It is extremely tender. Because of the rigidity of the uterus it is well-nigh impossible to determine whether there are any uterine contractions, and palpation of the foetal parts is impossible.

Progressive increase in the size of the uterus is an ominous sign, indicative of continuing bleeding. The blood insinuates itself into the uterine musculature and even into the uterine ligaments—producing the Couvelaire uterus as mentioned previously.

It may be impossible to hear the foetal heart beat on ausculation. Indeed in cases of this severity it is probable that the foetus has died in utero, though this must not necessarily be assumed.

Vaginal examination is required to diagnose the position of the foetus and stage of labour.

In retrospect most of the cases presenting with such severe symptoms have had warning episodes, chiefly a deep-seated backache, or a slight lower abdominal pain. Since backache is such a common accompaniment of pregnancy, it is quite to be expected that it will not arouse any suspicion on the part of the woman, or indeed of her practitioner. Lower abdominal pain may produce some anxiety, and prevention, or at least an awareness of the underlying pathology of this pain, may be important in more rapid treatment.

Complications

1. *Hypofibrinogenaemia*

The normal level of fibrinogen in the maternal blood is 400 - 700 mg.%; below 100 mg.% the blood is deprived of its coagulative activity.

DeLee in 1901 thought that accidental haemorrhage was aggravated by the blood being unable to clot, but it was not until 1936 that Dieckmann suggested that decrease in blood fibrinogen was the factor responsible.

Hypofibrinogenaemia follows the placental separation. Then the incoagulable state of the blood gives rise to

1. enlargement of the original retroplacental haematoma
2. Couvelaire uterus
2. post-partum haemorrhage

The mechanism producing hypofibrinogenaemia, is thought to be (Larkin 1957)—thromboplastin is injected into the maternal circulation from the placenta which is a rich source of thromboplastin. As a result intravascular fibrin is formed. At the same time, as a result of shock, an active fibrinolysin is released which becomes absorbed on to the intravascular fibrin as latter is in process of being formed, and destroys it. In this way large quantities of fibrin are continually being formed and destroyed in the circulating blood.

Owing to shock and generalised vascular spasm the blood supply to the liver is reduced. As long as this situation is maintained the liver does not replenish fibrinogen to the circulation, though in its normal state it is capable of doing so quite rapidly.

A viscious circle is thus set up in which the blood becomes incoagulable and will remain so, so long as the patient is shocked. As long as the blood is

incoagulable the patient will go on bleeding. The more bleeding, the deeper the shock becomes. In order to break this circle shock must be combated and the uterus emptied. The condition of shock should not be allowed to continue long enough to endanger the kidneys.

2. *Anuria*

Fortunately anuria is not a common complication of accidental haemorrhage, although some degree of oliguria is common.

Several theories have been postulated as causing anuria :

1. Shock and its accompanying low blood pressure may produce it. In this case anuria occurs early and is transitory in nature.
2. If the shock is of greater severity and causes primary vasospasm of the arterioles to the nephrons, it may lead to cortical necrosis and its irreversible anuria. [Sophian (1955) associates the utero-renal reflex with this.]
3. Some authors (Browne & Browne 1960) think that a toxin absorbed from the uterine muscle is responsible, while Johnstone & Kellar (1957) mention 5-hydroxytryptamine.
4. Schneider (1954) blames fibrin deposition in efferent and afferent arterioles and in the glomeruli as the cause of renal necrosis. Sheenan & Moore (1952) oppose this theory and claim that these thrombi are the result of vasoconstriction, and not the cause.

Management

In revealed haemorrhage, the management is more or less straightforward. Immediate bed rest in hospital is necessary. Sedation may be needed to allay anxiety. If the patient is already in hospital e.g. a haemorrhage in a pre-eclamptic confined to hospital, oxygen may be administered during the bleeding if it happens to be a bit profuse.

Although the bleeding is usually not enough to warrant blood replacement, there may be some place for blood transfusion in a woman who is slightly anaemic.

An X-ray to exclude the presence of a placenta praevia must be mentioned as essential while the patient is in hospital.

Whatever else is done, increased vigilance on the part of the obstetrician is a duty which should not be neglected.

In the more severe case of mixed or concealed haemorrhage, there is no time for delay in treatment. Usually in such cases, the safety of the mother is the primary consideration, the infant's welfare taking second place. Active treatment is required immediately ; in domiciliary practice the flying squad has its part to play in resuscitating the patient and bringing her into a well-equipped maternity hospital.

On arrival at the hospital the mother's condition must first be assessed. Shock must be combated by the use of blood transfusion and stimulants. The longer the delay in instituting treatment for shock, the greater the shock becomes, and the greater is the risk of complications such as renal cortical necrosis arising.

Morphine should be used to combat the severe abdominal pain, and to allay anxiety. Reassurance by the obstetrician is of course of great help to the patient.

Hourly clot observation tests are begun to test for the ability of the blood to clot and for its stability. If there is hypofibrinogenaemia, 2-4G of fibrinogen is given intravenously ; it may be necessary to repeat this dosage.

Catherisation will confirm the presence of albumen in the urine. Frequent samples of urine should be taken e.g. every hour, and the volume measured. Should the urinary excretion fall, some obstetricians advocate that bilateral splanchnic block should be performed. Barry (1955) and O'Sullivan and

Spitzer (1946). Recourse to such a measure is not common. Anuria will not of course gives rise to trouble until some time after delivery. Bull's regime is important in such cases, and it may be necessary to alert the artificial kidney team. A renal biopsy to differentiate between renal cortical and tubular necrosis is a possibility since renal cortical necrosis has a fatal outcome, whereas a patient with tubular necrosis may be tided over by dialysis, until recovery of kidney function.

Since prompt evacuation of the uterus best serves the interests of both mother and child, this should be the aim, as much as is compatible with safety.

Artificial rupture of the membranes should be done whether delivery is to be by the abdominal or vaginal route, and this is done at the vaginal examination. An A.R.M. is of importance for the following reasons:

(i) it relieves shock
(ii) it breaks the utero-renal reflex
(iii) it reduces thromboplastin liberation
(iv) it stimulates uterine contractions

Although almost all authorities are agreed on the necessity of doing an A.R.M., the use of pitocin is still a much debated procedure. The main objections to its use are:

(i) an aggravation of the renal vasopasm,
(ii) rupture of the uterus in grandmultips,
(iii) increased expression of noxious substances from the placental site into the maternal circulation—i.e. thromboplastin, which will eventually further decrease fibrinogen concentration. There is also the chance of causing an amniotic fluid embolism.

Only recently has it been advocated that pitocin should be used to speed up delivery, and the indications are that the objections to its use are more theoritical than real.

If there is no progression in labour, and the shock has been corrected—the mother being now in the best condition possible in the circumstances—a Caesarean section should be carried out as soon as possible.

Whether to do a Caesar or whether to wait to see if labour will progress is the most difficult decision to make.

The shorter the period of time from the acute onset of the placental separation until the ultimate delivery, the less is the likelihood of the development of some of the dreaded maternal complications, and of losing a baby whose heart is heard on admission. Little time should be wasted in waiting to see whether a birth via naturalis is going to be possible. Eastman (1956) prefers to wait 10-12 hours to see if the A.R.M. is going to bring about delivery, while Bysshe (1951) agrees to a 6 hour limit—by which time the foetus if not already dead, is in a very precarious position.

Tied up with the question of time to delivery is the question of whether the woman is in labour or not, and whether there is any cervical effacement or dilatation. The presence of labour is not a contra-indication to a Caesar. The progress in the descent of the head is the only real indication of the progress of labour.

The condition of the foetus is, of course, of great importance. Should the foetus be alive and in good condition, then there may be some justification for delaying to see whether vaginal delivery is possible, though this is probably a better reason for doing a Caesar, especially in the more severe case. If there is any slowing or irregularity of the foetal heart, a Caesar becomes imperative. Each case will be decided on its own merits.

Maternal Prognosis

This depends on a number of factors among which are:

1. Type of haemorrhage, i.e. revealed or concealed;
2. Extent of placental separation;
3. Total blood loss (including P.P.H.);
4. Degree of hypofibrinogenaemia;
5. Presence of Couvelaire uterus;
6. No. of hours between placental separation and treatment;
7. Presence or renal damage;
8. Associated maternal disease e.g. vascular disease.

In revealed and mixed types of haem. the mortality is about 1.5% whereas in concealed haem. the maternal mortality is as high as 10%. The prognosis has greatly improved recently due to such factors as the flying squad, blood transfusions, fibrinogen, and the artificial kidney.

Foetal Prognosis

Although the prognosis for the mother has shown a vast improvement in the last number of years, there has been little improvement in the foetal prognosis.

Johnstone and Kellar (1955) quote a foetal loss of 45% for mixed and revealed haemorrhages, and 90% for concealed haemorrhages. There is no further need to stress the importance of accidental haemorrhage, the above figures do all that is necessary.

One reason for the high foetal mortality is the high incidence of prematurity. Although those weighing over 2000G (4.4 lbs.) have approx. 100% chance of survival, it falls to 80-90% from 1500 to 2000G, and under 1500G (3.3 lbs.) the survival rate falls off rapidly. Major anomalies e.g. anencephaly, make up a proportion of the unavoidable foetal loss. The main case of death is, as might be expected, anoxia.

By way of prevention not much can be done; the aetiology is largely unknown, and the haemorrhage occurs with such dramatic suddenness.

At the moment the greatest benefit will be derived from the quicker and more efficient active treatment of the woman once the calamity has befallen her. The instruments for this are at hand, but a continual reappraisal of the problems involved, and a self-criticism of past failures is an absolute necessity, if a better foetal prognosis is to be anticipated.

REFERENCES INCLUDE:

BARTHOLOMEW, R. A. et al. (1953) Amer. J. Obst. Gyn. 66, 1042.
BROWNE, F. J. and BROWNE, J. C. McCLURE (1960) "Antenatal and Postnatal Care." (Churchill, London).
DeLEE, J. B. (1901) Amer. J. Obst. Dis. Wom. 44, 785.
DIECKMANN, W. J. (1936) Amer. J. Obst. Gyn. 31, 734.
DOUGLAS, R. G. (1955) J. Obst. Gyn. Brit. Emp. 62, 710.
EASTMAN, N. J. (1956) "William's Obstetrics."
FISH, J. S. et al. (1951) Amer. J. Obst. Gyn. 61, 20.
FISH, J. S. et al. (1955) "Haemorrhage of late pregnancy."
HOLLAND, Sir EARDLEY (1959) "British Obstetric Practice."
JOHNSTONE, R. W. and KELLAR, R. J. (1957) "Textbook of Midwifery" (Black, London).
LARKIN, I. M. and PHILLIP, E. E. (1957) J. Obst. Gyn. Brit. Emp. 64, 215.
RIGBY, E. (1776) "An essay on the uterine haemorrhage which precedes the delivery of the full grown foetus."
SHEEHAN, H. L. and MOORE, H. C. (1952) "Cortical Necrosis and Concealed Accidental Haemorrhage."
WILLIAMS, J. W. (1915) Sing. Obst. Gyn. 21, 541.

EYE CHANGES IN DISSEMINATED SCLEROSIS

By A. D. CHALMERS

Based on a Dissertation read before the Royal Medical Society on Friday, 18th November, 1960.

What is probably the first written account of the clinical features of disseminated sclerosis is contained in the diary of Augustus D'Esté, the illegitimate son of Prince Augustus Frederick, and grandson of George III. The first manifestations of the disease in his case, as in some 30% of all such patients, were referable to the eyes. In 1822, we read, he journeyed to visit a much-loved relative; "On my arrival I found him dead. I attended his funeral—there being many persons present I struggled violently not to weep, I was however unable to prevent myself so doing; shortly after I was obliged to have my letters read to me and their answers written for me, as my eyes were so attacked that when fixed upon minute objects, indistinctness of vision was the consequence. Until I attempted to read or cut my pen, I was not aware of my eyes being in the least attacked. Soon after I went to Ireland, and without anything having been done to my eyes they completely recovered their strength, and distinctness of vision."[3] It is interesting to note the temporal relationship of the onset of symptoms in this case, to a period of emotional stress, a relationship which has been much discussed in connection with disseminated sclerosis, but which has little statistical evidence in its support.

As indicated above, there is general agreement on the approximate incidence of eye-disease early in the course of disseminated sclerosis. On the overall incidence of eye changes there is less agreement, but it does appear that a high proportion of sufferers from disseminated sclerosis do, at some time during its course, exhibit signs or symptoms of eye-disease. For example the report of one series of investigations puts the incidence of ocular signs in disseminated sclerosis as high as 83%.

The three main mechanisms by which the disease process affects the eyes are by the production of retrobulbar neuritis, nystagmus and oculomotor disorders. Other effects on the eyes, less useful diagnostically, are alterations in pupillary characteristics, and changes in the appearance of the retinal veins.

RETROBULBAR NEURITIS

Just as the cervical spinal cord appears to be particularly vulnerable to the disease in its early stages, so the optic nerve suffers early in a significant number of cases. It is difficult, even in any one series, to establish a definite figure for the incidence of retrobulbar neuritis as an early symptom, because in many cases a number of years elapse between the first attack and the appearance of any other manifestations of the underlying disease e.g. Adams found a latent period of over 15 years in 8% of 389 cases. However, by careful and specific history-taking, several authors have estimated that an attack of

retrobulbar neuritis heralds the disease in 13-23% of cases. By similar means the overall incidence of retrobulbar neuritis in the whole course of the disease was shown to be only slightly higher (up to 30%). It also would appear that all the workers in this field are agreed that this particular manifestation always occurs early in the natural history if it appears at all.

In view of the numerous theories which have tried to connect the onset of disseminated sclerosis with local stress of various kinds, it is interesting to note that Adams et al. investigated the connection between occupation and the form of the presenting symptoms, and that the only positive correlation they were able to obtain was between the clearly defined group of brain workers and the incidence of retrobulbar neuritis as an initial symptom.

The effects of retrobulbar neuritis may be considered under the headings of (a) acute and (b) persistant.

(a) Acute. In the acute stage symptoms are more marked than signs. The commonest complaint is of mistiness or blurring of vision, in some cases progressing to complete blindness in the affected eye. This was probably the mechanism by which D'Esté's initial symptoms were produced. In most cases the affection is unilateral, but in a few instances both eyes have been reported to be involved together.[8] However it does appear that an eye is never affected twice.

If the eyes are examined during the acute attack, the common finding in the visual fields is a central scotoma of a size which depends, among other things, on the proximity of the lesion to the nerve head. The pupillary reaction to light is sluggish and ill-maintained in some cases, while the appearance of the nerve head may be surprisingly normal, being only a little paler and less well-defined than in the normal eye. In the severe case with total blindness, a mild papillitis may be seen with a few small haemorrhages. Relatively few patients complain of pain during the retro-bulbar neuritis of disseminated sclerosis, but in those who do, the pain is usually increased by eye-movement.

(b) Persistant. After the acute attack subjective recovery is usually good. On examination, however, persistant defects of vision may be found in quite a high percentage of cases. Wybar found that visual acuity and performance in Ishihara's colour discrimination test were significantly diminished in about one half of the eyes previously affected by retrobulbar neuritis, and that of 33 such eyes, 11 showed central or paracentral scotoma and 13 showed peripheral field contraction. The incidence of pallor of the optic disc varies quite widely in different series and this is hardly surprising since it is subject to individual interpretation by the observer. However it does seem that about one-third of all cases of disseminated sclerosis show pallor of one or other optic disc. Wybar has shown that there is no exact correlation of this finding with a history of retrobulbar neuritis. It is interesting to note that the stigma of temporal disc pallor, widely revered as a diagnostic sign, is not enthusiastically reported by most authorities.

NYSTAGMUS

The frequency of nystagmus was well recognised by the early writers on the subject, and this sign is included in the most famous of the many "triads" set out as aids to diagnosis i.e. Charcot's Triad of nystagmus, scanning speech and intention tremor. More modern writers are also agreed on its frequency, and it is now generally accepted as occurring in from 20 to 40% of early cases, and in from 40 to 70% of late cases. Thus far agreement is general, but on

the topic of the precise nature of the nystagmus of disseminated sclerosis less unanimity is noted. Both vertical and horizontal types are reported; the monocular variety is not uncommon; and Wybar has stressed the diagnostic importance of ataxic nystagmus, in which on lateral fixation oscillations are most prominent in the abducted eye. Subjective awareness of nystagmus (oscillopia) is also reported in a small number of cases. Because of the prolonged natural history of the disease very little work has been done on the correlation of nystagmus with anatomical location of lesions in the central nervous system. However, Savitsky and Ranzell, in a series of well-documented and autopsied cases, found plaques of demyelination in the medial longitudinal bundles of 2 patients who had showed nystagmus.

OCULOMOTOR DISORDERS

Ocular imbalance, manifest to the patient as diplopia, usually without apparent squint, is the presenting symptom of the disease in about 15% of cases, and its overall incidence in the disease course is usually about 30%. Palaysis of the sixth cranial nerve is the commonest cause of this symptom in disseminated sclerosis; third nerve palsies occur much less frequently and all are agreed that the fourth cranial nerve is spared in the great majority of cases. Because of the relative sparing of the third nerve, ptosis is not common but may occur. Physical examination may fail to reveal any demonstrable occular palsy, but in about 10% of cases some abnormality is discovered, usually in the form of simple limitation of adduction or abduction.

Apart from diplopia, supra-nuclear optic palsies may be discovered on examination in some 15% of those suffering from this disease. In these cases there is no diplopia and the clinical abnormality consists of paralysis of conjugate movement with persistence of reflex movement in the paralysed muscles. Thus, for example, a sudden loud noise may cause the patient's eyes to deviate in the direction of the paralysis, because of the persistence of connections from the auditory cortex to the optic nuclei.

PUPILLARY DISORDERS

One pupillary abnormality often described in disseminated sclerosis is the phenomenon of hippus, in which continued variations occur in the size of the pupil in sufficient amplitude to be definable by the eye of the observer. It is difficult to be definite about the usefulness of this sign as an aid to diagnosis, since no two series have produced comparable results for its incidence. For example, in one series of 264 cases collected from the literature hippus was not mentioned once, while in another series of 91 cases observed by an ophthalmic surgeon bilateral hippus was present in 37% of these patients. Here, as so often in medicine, the sign will not be detected unless it is specifically looked for. Again there is disagreement about changes in the pupillary reflexes, the incidence of which is, in any case, small. The consesus of opinion seems to be that the light reflex is absent in a small number of cases (less than 5%), and that in a very few of these cases, the fully developed Argyll-Robertson is present, in the absence of cerebro-vascular syphillis.[6] Changes in pupillary size are not now believed to be of any diagnostic importance in disseminated sclerosis, and the old view that myotic pupils were common in this disease now finds no favour.

RETINAL VEIN CHANGES

The changes which occur in the retinal veins as a result of disseminated sclerosis are described as sheathing. In this condition a thin white line is

observed on either side of the column of blood in one or more retinal veins. The affected veins are always more than two disc-diameters away from the optic disc, and the arterioles are not affected. Vitreous opacities may also be present in the region of the affected vein. Similar changes may occur in the retinal veins and arterioles as the result of chorioretinitis, diabetis mellitus or hypertension, but in all these cases other associated ophthalmoscopic changes serve to indicate the primary cause of the abnormality. A reliability of about 80% can be claimed for this sign in the diagnosis of disseminated sclerosis,[5] but unfortunately (from the diagnostic viewpoint) of all patients with disseminated sclerosis, only 10% demonstrate this sign.

These are the principal changes which occur in the eyes of a patient suffering from disseminated sclerosis. Taken as a whole, and in conjunction with an adequate history and complete physical examination, they may be of considerable help. But it is worth emphasising that, neither these eye changes nor any other isolated sign, is pathognomonic of the disease. For example, nystagmus was observed in a patient with progressive paraplegia, due, not to disseminated sclerosis, but to an operable spinal tumor. At present the diagnosis of disseminated sclerosis is important from the point of view of exclusion of any potentially tractable condition, but it is equally important to bear in mind that some advance in treatment, comparable in effectiveness to that of antobiotics in infection, or insulin therapy in diabetes may at any time be made. It is with this possibility constantly in view that the early diagnosis of disseminated sclerosis should be made.

References include:

(1) Adams D. K., Sutherland J. M., Fletcher W. B. (1950). B.M.J. 2, 431.
(2) Adie W. J., (1932) B.M.J. 2, 927.
(3) Firth D., (1948) " The Case of Augustus D'Esté." Cambridge.
(4) McAlpine D., Comptson N. D., Lumsden C. E.. (1955). " Multiple Sclerosis." Livingstone.
(5) Rucker C. W., (1948). Proc. Ass. Res. Nerv. Ment. Dis., 28, 396.
(6) Savitsky N. and Ranzell L. (1948). Proc. Ass. Res. Nerv. Ment. Dis. 28, 403.
(7) Symonds C. P. (1930) Lancet 2, 19.
(8) Wybar K. C. (1952) Proc. R. Soc. Med. 45, 315.

BOOK REVIEWS

INTRA-ABDOMINAL CRISES by K. D. Keele, M.D., F.R.C.P., and N. M. Matheson, F.R.C.S., M.R.C.P., F.A.C.S. Pp. 397. Published by Butterworths. Price 50s. plus 2s. by post.

It has become increasingly obvious that the ancient distinction between physician and barber surgeon is an unreal one; and nowhere is this more obvious than in the field of abdominal disorders. Edinburgh has recognised the need for close collaboration between physicians and surgeons in the shape of the gastro-intestinal unit at the Western General Hospital.

However, in most hospitals there remains the difficulty of deciding whether a patient with abdominal symptoms should be moved to a medical or surgical ward for further care. This decision often rests with the house physician or house surgeon, and can be a very important one. It is in these situations that the information in this book will prove most valuable, as it is written by a consultant physician and consultant surgeon at the Ashford Hospital in Middlesex.

The book does not set out to be a comprehensive textbook of gastro-enterology. It describes not only the common and uncommon gastro-intestinal emergencies, but also the gynaecological and urological disorders as well as some some of the extra - abdominal disorders which can produce abdominal symptoms. It is mainly concerned with diagnosis, although it does give some hints as to management.

It would not be very useful as a reference book in an emergency but more as a source of background knowledge. It is a very interesting book to read, and it is well produced in a lurid orange binding with a number of useful photographs, X-rays and diagrams.

Undergraduates would learn a great deal from this book which would be of value in practical medicine. It seems expensive, but it would be an excellent book to borrow.

J.A.R.F.

DILLING'S CLINICAL PHARMACOLOGY, revised by Stanley Alstead, C.B.E., M.D., F.R.F.P.S., F.R.C.P. Lond., F.R.C.P.Edin., F.R.S.Edin. and others. 20th Edition, Pp. 860. Published by Cassel & Company Ltd. Price 30s. net.

This textbook is notable for the wide limits of the topics discussed under the heading of pharmacology. The authors have succeeded in gathering together under each chapter heading the physiological principles involved in the working of each system and have attempted to relate the pharmacology of the drugs under discussion to them. They go on to carefully and logically show the rationale of the use of the drugs in medicine. At the same time, wherever possible, they demonstrate that the same pharmacological actions are also responsible for the toxic actions and side-effects. In this way it is possible to assess the benefit of a drug to the patient against a background of knowledge which also allows the risks involved to be estimated.

The topics under consideration are illustrated by reference to a limited number of representative preparations at present in common use. In each case the drug is discussed under several headings. The sources of the drug are mentioned and reference is made to chemical composition; the pharmacological actions are then considered with emphasis on those which have therapeutic applications; the side-effects and toxic actions are correlated, where possible, to the pharmacological actions and finally the therapeutic uses of the drug are considered and attention is drawn to the most appropriate preparations and methods of administration. This basic layout is followed by a brief discussion of similar drugs and their advantages.

The main advantage of this textbook is the way in which physiology, medicine and pharmacology have been interrelated. Although this may be a disadvantage to those trying to cram for an examination, it is surely the most logical presentation.

The main fault in this book is its thoroughness. The authors have been reluctant to leave anything out and at the same time have allowed themselves to prevaricate upon relatively subtle details. In other places one must read through a whole paragraph before finding that the drug is now obsolete. In some chapters, in their attempt to integrate pharmacology, the authors have failed to restrict themselves to the salient features and allowed too much space to long-winded generalisations.

The appendix runs to 187 pages, about 20% of the total material in the book, and contains a formulary, a course of practical instruction for Glasgow students and a section on pharmaceutical chemistry, all of which make the book far too large.

The production of the book can only be criticised on the use of two different sizes of type used in the text. It was difficult to decide whether the paragraphs in smaller print were considered less important or more difficult to understand. Perhaps the publishers were also unsure since only careful examination allows one to detect the difference in print size.

In conclusion, I think this book, due to the inclusion of excessive material, is of more use for selective revision than for an initial understanding, for which it was designed.

J.S.K.

MEDICAL EVIDENCE IN PERSONAL INJURY CASES, by Dorothy Knight Dix, Q.C., and Alan H. Todd, M.S., F.R.C.S. Pp. xii & 244, 17 illustrations. Published by H. K. Lewis & Co. Ltd. Price 42s. net.

This compact book is authoratively written by two authors both widely experienced in their own fields. All aspects of personal injury are covered briefly but quite adequately. Sound advice is given on legal aspects of medical examination, the presentation of medical evidence and the writing of medical reports. The nature and degree of the injuries sustained are dealt with in a systematic fashion chapter by chapter e.g. knee joint, shoulder, spine, c.n.s., etc. The book ends with possibly its most useful chapter dealing with the do's and don't's for a medical practitioner giving evidence in the witness box.

This book, although as Lord Birkett says in the forward "fills a long felt need", is not one that the medical student will probably find time to read, but it is almost definitely a must for the library of a qualified medical practitioner.

W.H.L.

TOXICITY OF INDUSTRIAL METALS, by Ethel Browning, M.D. 1st Edition 1960, 325 pages. Published by Butterworths. Price 50s., plus 1/9 postage.

This book is intended for "those concerned with the industrial use of metals" and biochemists. Fourty-four metals are dealt with in reasonable, but not excessive detail. After the text on each metal a very full reference list is added so that this book may be used as a starting point for fuller research.

Dr. Browning's aims are most modest since this book will also most certainly appeal to the interested undergraduate with time at his disposal. He will learn much about those metals in a very short space of time owing to the lucid and informative style of the book.

Unfortunately Phosphorus, because it is not defined as a metal, and calcium, sodium and potassium which despite their great physiological importance are of little consequence from the industrial point of view, are not included. There are no illustrations.

R.A.B.

CORRECTION OF SUBNORMAL VISION. Norman Bier, F.B.O.A. (Hons.), F.A.A.O., D.Orth. vi 231 pp., 133 illus. Butterworth & Co. Ltd., 1960. 50s.

It is all too easy for a practitioner or student to take the services of the ancillary professions for granted. Too often a patient is sent to the appropriate department with vague references to treatment which could cover the whole of the speciality.

The book under review affords one way of understanding the principles of the work undertaken by a vital branch of the ophthalmological profession. The author has considerable experience on both sides of the Atlantic, and intends that it should be used primarily by studendts working for Diplomas in Ophthalmic Optics and Orthoptics, and it is essentially a practical book with no more theory than is absolutely essential.

The work can be regarded as divided into three sections. The first two chapters form an introduction, dealing with visual subnormality in general, and in children in particular. After descriptive chapters on the types of aids available, almost half the book is devoted to clinical procedures of testing and fitting. Throughout the book, one is impressed by the use of lucid explanatory photographs.

A fairly extensive bibliography completes a volume which will reward anyone who wishes to read outside the standard fifth year ophthalmology course.

P.J.S.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY, by Hamilton Bailey. 13th Ed. Bristol: John Wright and Sons, Ltd., 1960. Pp. 928+xvi; 1142 illustrations. Price, 75s.

Bacon wrote that some books are to be tasted, others to be chewed, and a few to be thoroughly digested. It is a pleasure to review a book which can be briefly consulted and systematically read, with both pleasure and profit.

The latest edition of "Physical Signs" provides an even more comprehensive collection of clinical facts than its eminent predecessors. The book begins with a review of some basic clinical states and a survey of "lumps and bumps". After discussing the signs of local inflammatory lesions and giving a clear and concise account of the examination of bones and joints, the author systematically relates the clinical features of affections of the various systems and parts. The whole has been expanded in order that it may be of more use to post-graduate students and in order to keep up with recent advances.

The value of this book cannot be questioned. It is now in its 175th thousand, and German, Turkish, Spanish, Bulgarian and Jugoslav editions have been published. It provides a wealth of clinical information which should help students of medicine at all levels, both undergraduate and post-graduate. Some of the signs may have been rather outmoded by technical advances, but they serve as a reminder of the value of clinical examination. And great benefit and pleasure may be derived from eliciting a physical sign and making a diagnosis, thereby anticipating the results obtained from the ubiquitous test tube and its biochemical mentor. Perhaps some, in particular the undergraduates, may be irritated by the constant use of eponyms at a time when they are becoming less fashionable but most will be soothed by their interest in reading the many footnotes concerning the distinguished men of medicine and surgery of the past and present.

The book is beautifully and lavishly illustrated. Many of the diagrams show Mr. Bailey's unique gift of providing a simple, pictorial aid to the over-burdened undergraduate memory. There is an excellent index. It is unfortunate that the price has been increased to 75s. It is certainly well worth the money.

The recent death of Mr. Hamilton Bailey has meant the loss of one of the great teachers of surgery. This book will ensure that the influence of this great teacher will continue for a long time.

G.W.K.D.

THE CATARRHAL CHILD. By John Fry, M.D.(London), F.R.C.S.(Eng.). 1st Edition Pp. 139, 32 tables, 14 figures. Published by Butterworths, London, 1961. Price 25s.

This is a little book dealing with one of the common problems in general practice, the catarrhal child syndrome. The author, a G.P. in Beckenham, Kent, has taken the trouble, over the past ten years, to study and follow up 750 such children and he now presents his findings in the form of this book. It is refreshing to read a medical book aimed at doctors from consultant to G.P., at nurses and even at lay men and women i.e. the parents concerned, without even a mention of the student. Thus it is possible to examine the pearls without too much of a swinish glance.

The book takes the form of ten short chapters each admirably set out in sub-chapters with headings in bold type, so that even the most casual reader can remember the subject of his perusal. Each chapter also has a summary containing the main points of its theme clearly set out and enumerated. I found the most delightful aspect of the book was the use of plain and direct English. Short paragraphs state their content clearly and with exuberant rhetoric, so that the reader finds himself drawn into the argument and stimulated to think for himself.

The subject is treated from the social medicine point of view rather than as a purely clinical condition, bearing out the old maxim "Treat the patient and not the disease". The author covers the field completely, choosing one of the main features of the syndrome as the subject of each of his chapters, ranging from "The Problems" to the more prosaic "Tonsils and Adenoids". He supports his arguments well with statistics compiled from his own experience, presented in the form of the many figures and tables. He is also not afraid to include the opposing points of view, which are clearly stated, complete with references.

I can thoroughly recommend this book for its well-balanced outlook on this syndrome, especially the chapters concerned with "Antibiotics" and "Tonsils and Adenoids".

The book is well printed and strongly bound, but it comes complete with a dust jacket faced with a substance which displays a remarkable affinity for finger prints.

R.W.

Reflections

Memory, as those of us who sit examinations well know, is a lying jade at the best of times. Thus any subjective review of events occuring in the past session must be fragmentary and impressionistic. What follows is not a considered analysis of progress made and future objectives, but an armchair reverie.

Dr. David Stafford Clark opened the 224th session with a most elegant address which captured the imagination of the audience that filled the debating hall. This was a successful start and the promise of an excellent series of dissertations, talks and addresses to follow was entirely maintained. It is not however, the public face of the society which concerns me here, the articles of this journal are sufficient testimony of its workings. I shall attempt briefly to cast a lingering look behind and summon up the more personal impressions gleaned in the past session.

The vigour with which the members engage in "Private Business" is the essential measure of the success or otherwise of a session. In this respect the 224th was unusually fortunate. However there is room for improvement and all too often members look on the society as a lending library with an optional lecture course. This apathetic attitude must be dispelled. "The more a member puts into the society the more he derives from it," is admittedly an old Tory jingle but experience repeatedly proves it to be true.

It is customary to discuss medical matters at Second Private Business. This year we augmented these proceedings by a series of discussions on the society, its constituion and its laws. To aid us in these debates we had the report of the Questionnaire Committee, which had been formed to feel out the attitude of the members to their society.

Needless to say the laws of the society forbid me to write on such *in camera* sessions. It is possible to reveal that many evenings were spent in self-analysis and an endeavour was made to allow, if not a wind of change, at least a fresh breeze to clear away some of the anachronisms that burden society business.

The various committees enjoyed successful seasons. The library committee under the iron rule of Mr Legge, was conducted with exemplary efficiency. We understand that the unenvitable task of cataloguing the library continues and is nearing completition. The museum looked particularly tidy this year and the medicine demonstrations provided an ever present source of solace on wet wintry afternoons.

Of the house committee I shall say nothing save that thanks to the prompt action of Sir Derrick Dunlop the Society has a new roof and our caretakers can sleep calmly, safe in the knowledge that the eagle which surmounts our premises will not take off and dive headlong into the street below. This stone eagle, like the ravens of the Tower, is a symbol of continuity and steadfastness for the society.

This year was marked by an abundance of social occasions. The Presidents' Annual Dinner achieved its customary success. Dr. Gaddum, our guest of honour, proved decisively that it is possible for him to bestride the two cultures of art and science. (This theme was to recur in the Senior President's unique appraisal of this subject in his valedictory address.) The dinner itself

was a gastronomic triumph. The marriage of Vouvray Sec '59 to a salmon mayonnaise filled us with admiration for the matchmaker, Mr Wilson.

There was another more intimate yet no less memorable dinner for Sir David Henderson before receiving an honorary fellowship from the society. We were all most fortunate in having this opportunity of honouring such a famous product of the Edinburgh School.

The Museum Committee celebrated its centenary year, and what better excuse for yet another dinner. Those present immortalised the occasion by inscribing their names on a specially prepared bread roll, which it is hoped will be preserved in the museum to be a marvel for future generations. It is but rarely that one is given such an opportunity of carving one's name for posterity. There were many other occasions, beer and skittles, industrial visits (to Sandemans and the Scotsman), a film show; all most successful and of course the annual ball, happily restored this year to the Carlton Hotel.

What of next year? The stage seems set for Mr Friend (The Senior President Elect) to lead the society to further achievements in its 225th year.

SOCIUS

DAVID STUART MURDOCK

We regret to announce the death of David Murdock in the Edinburgh Royal Infirmary on 25th April, 1961. As a medical student in his fifth year he was an active member of our Society. He was also well known in the University Squash and Swimming Clubs and took an active interest in amateur dramatics. Among his student friends many will remember him for his friendly and generous nature.

We would like to convey our deepest sympathy to his family and friends at this time of their sudden bereavement.

THE ROYAL MEDICAL SOCIETY

OFFICE-BEARERS DURING THE 224th SESSION

Senior President:

E. A. W. SLATER

Junior Presidents:

G. W. K. DONALDSON, A. D. CHALMERS, W. S. UTTLEY

Secretaries:	*Aedilis:*	*Actorum Moderator:*
J. A. CALVERT J. A. R. FRIEND	E. B. RITSON	J. MOWAT

Librorum Custos:	*Musei Custos:*	*S.R.C. Representative:*
R. I. LEGGE	R. W. M. CORNER	P. J. SWARBRICK

COMMITTEES

House: H. J. Gold, R. A. Bailey, M. J. Grayson, J. M. S. Johnstone.

Library: J. D. Lyon, R. M. Milne, M. R. Higgins, J. G. Hope.

Museum: A. Trickett, D. C. Cameron, G. G. Thomas, T. S. Kerr.

Public Business: A. Andrew, W. H. Leach, R. Butler, D. H. Morison.

JOURNAL

of the

ROYAL COLLEGE

of

SURGEONS

of

EDINBURGH

Published Quarterly: October, January, April, July

Annual Subscription: 21s. post free

Editor: JOHN BRUCE

C.B.E., T.D., P.R.C.S. Ed., Hon. F.A.C.S., Hon. F.R.C.S. Eng.

For Your Bookshelf 1961 . . .

TEXTBOOK OF MEDICAL TREATMENT

Edited by Sir D. M. Dunlop, F.R.C.P. (Edin. and London), Sir Stanley Davidson, F.R.C.P. (Edin. and London) and S. Alstead, F.R.C.P. (Edin. and London).

New 8th Edition (May 1961). Approx. 1050 Pp. 33 Illus. **Price 60/- (post 2/-)**

"The book is thoroughly recommended. Students and practitioners should own the latest edition. This is one of the most useful, informative and interesting books in present-day medicine."

Samson Wright's APPLIED PHYSIOLOGY

Revised and edited by Prof. E. Neil and Prof. C. A. Keele.

New 10th Edition (May 1961). 632 Pp. 480 Illus. **Price 60/- (post 2/-)**

"This edition has been more extensively revised than any of its predecessors without in any way sacrificing the original style and plan of the book—so bringing it into line with modern teaching."

PROGRESS IN CLINICAL MEDICINE

Edited by R. Daley, F.R.C.P. and Henry Miller, F.R.C.P.

New 4th Edition (April 1961). 356 Pp. 25 Illus. **Price 50/- (post 1/9)**

"Important advances in medicine during the five years since the appearance of the third edition have demanded a complete rewriting of the text. An important addition to current medical literature."

Why not become a subscriber to . . .

FERRIER'S MEDICAL LENDING LIBRARY

. . . and keep up-to-date ?

We operate the ONLY "On Demand" Medical Lending Library which guarantees the supply of books, both British and American, immediately upon publication and upon request. Enquiries cordially invited. Prospectus sent post free.

Special REDUCED Terms for Undergraduates, Hospitals, Libraries and kindred Institutions.

SYMPTOMS AND SIGNS IN CLINICAL MEDICINE

By E. Noble Chamberlain

7th Edition (Ready soon). About 540 Pp. 383 Illus. **Price: About 42/- (post 1/9)**

"Describes the common symptoms and physical signs of disease, and takes the reader a stage further to the visualization of symptoms and signs as forming a clinical picture of a pathological process. Completely revised with many new illustrations."

PYE'S SURGICAL HANDICRAFT

Edited by Hamilton Bailey, F.R.C.S.

New 18th Edition (Ready soon). In Two Volumes.

Vol. 1. About 400 Pages. Illustrated. **Price: About 32/6**

Vol. 2. In Active Preparation. Price to be announced.

"For the newly-appointed house surgeon, the practitioner located in a comparatively rural district, and the ship's surgeon, this book is, and has been for many years, a tried and trusted friend."

THE MEDICAL ANNUAL, 1961

Edited by R. Bodley Scott, F.R.C.P. and R. Milnes Walker, F.R.C.S. (with 42 Contributors)

Subscription Price: 38/6 post free. **After Publication: 42/- (post 1/9)**

"The Medical Annual today is one of the important books of the year."
". . . it is really indispensable to the busy practitioner."
"It remains an extremely useful review of recent progress in most fields of medicine."

OBTAINABLE FROM

DONALD FERRIER

8, 9, 10 & 18 TEVIOT PLACE, EDINBURGH 1

CAL 5325 and 5689