case. In the secondary forms treatment can be discontinued as the mucosa recovers and lactase reappears.

Summary and Conclusions

Malabsorption syndromes are common in the tropics; the causes have a definite geographical distribution. Protein-calorie malnutrition is the commonest and often most difficult differential diagnosis. Common causes in temperate regions (e.g., adult coeliac disease and coeliac disease) seem to be less common, but there is evidence that this is merely because they have not been properly looked for. In Africa chronic calcified pancreatic disease is undoubtedly a more common cause than in most temperate areas, and in the Far East tropical sprue accounts for many cases. Recent demonstration of disaccharide deficiencies—either primary or secondary—in several parts of the tropics may lead to the more adequate treatment of some cases of diarrhoea and malabsorption. It is most important to exclude other causes, such as those commonly seen in temperate zones, for only by systematic exclusion will it become clear which are the truly common causes in any locality.

A full clinical history and examination, together with a simple haematological, biochemical, and radiological examination, will allow a reasonable diagnosis in some cases. Careful macroscopic inspection of the stool is of very great importance, though malabsorption may be present without gross abnormalities. In many cases it is impossible to arrive at the exact cause of the syndrome unless the diagnostic facilities of a large hospital are available. Treatment is often simple and can easily be maintained at up-country stations when the diagnosis has been made. It is essential to consider the entire differential diagnosis in every case.

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Nitrites and Nitrates in the Treatment of Ischaemic Heart Disease

Ischaemic heart disease or coronary failure results when the supply of oxygenated blood through the coronary arteries is inadequate to meet the demands of cardiac muscle. Occlusive disease of the coronary vessels is nearly always the result of atherosclerosis. This is a disorder affecting large arteries in which fatty deposits and fibrous nodules narrow the lumen of the artery, reduce the potential blood flow, and predispose to intravascular thrombosis and the clinical syndrome of angina of effort.

At rest there is little difference between the rate of coronary blood flow in the normal subject and in the patient with coronary artery disease. However, a normal individual can increase his coronary blood flow severalfold, but the patient with coronary artery disease is unable to do so, and indeed may not even be able to increase the resting blood flow at all.

The normal coronary circulation delivers more blood to the myocardium on demand, and the strongest physiological stimulus to coronary vasodilatation is hypoxia. Angina of effort develops only when there is severe myocardial hypoxia as a result of inadequate perfusion, and, under these circumstances, the affected coronary vessels are already under the maximum physiological stimulus to dilate.

Nitroglycerin and Nitrates

The drug that betters this physiological dilating mechanism does not exist. However, the beneficial effects of nitroglycerin (glyceryl trinitrate) in angina of effort are undoubted, and indeed have been known for over 100 years, but this is not the result of coronary vasodilatation.

The basic pharmacological property of nitrates is to relax smooth muscle, and it is the effect on vascular smooth muscle that is particularly relevant to the patient with ischaemic heart disease. The major effect of nitrates is on the small postcapillary vessels. As a result of relaxation of the smooth muscle of these vessels the mean systemic arterial blood pressure falls, and this reduces the oxygen requirements of the heart usually to a level which can be adequately supported by the unaltered coronary blood flow. While it is true that nitroglycerin dilates the coronary arteries of normal human beings, it does not increase the coronary blood flow in patients whose vessels are damaged by atheroma, and whose vessels are already maximally dilated as a result of local tissue hypoxia. It is therefore misleading to call nitroglycerin and other similar drugs coronary vasodilators. It is also unlikely that these drugs will stimulate the development of a collateral circulation, and, indeed, proof of any beneficial effect in promoting the development of such collateral vessels in patients with coronary artery disease is lacking.

Long-acting Compounds

The effects of nitroglycerin and amyl nitrite, though beneficial for the acute attack of angina, are short-lived, and attempts have been made to produce drugs with a prolonged action. Many preparations have been marketed claiming to be long-acting coronary vasodilators, but not only do they have no vasodilating effect on the diseased coronary arteries but none has been shown to have any greater effect on angina of effort than a placebo.

The problems of assessing these drugs are great. Objective evaluation of changes in the coronary circulation is difficult. Coronary arteriography cannot give the conclusive evidence, as even if an increase in the calibre of coronary arteries is demonstrated this does not prove that there is an increase in blood flow, as the smaller arterioles cannot be visualized, and these are the vessels that regulate blood flow. If isotope studies of coronary blood flow demonstrate an increase, this does not indicate that the increase in flow is to the ischaemic area. Indeed, this is unlikely, as the diseased vessel is probably not able to dilate further. The electrocardiogram is often used as an objective measure of the patient's exercise tolerance, but even this has pitfalls, as repetitive tests are executed with decreasing effort and anxiety.

These objective methods do not measure angina. Angina is a syndrome which cannot be measured objectively. Subjective methods are therefore essential to the clinical assessment of therapeutic agents, and only the controlled trial can determine the efficacy of a new drug.

A large proportion of patients with angina improve on placebo therapy. The knowledge that they are involved in a test of a potentially effective treatment reduces the incidence of angina in 30% of cases. Anxiety stimulates the sympathetic innervation of the heart and brings about the release of endogenous noradrenaline, which increases the oxygen requirement of the heart by increasing cardiac work and metabolism. Any drug given with enthusiasm will allay anxiety, and will therefore improve the patient's symptoms. It is thus essential that
trials of these drugs should be controlled. Such trials that have been controlled have demonstrated that long-acting nitrates are of no more value than a placebo.

As none of the long-acting preparations can be recommended for the treatment of coronary artery disease, practitioners would do well to devote their therapeutic energy to more rewarding methods of treatment, such as inducing their patients to lose weight, avoid heavy meals, and stop smoking. Propranolol, the beta adrenergic antagonist, is the only drug that has been demonstrated to have a long-term beneficial effect in some patients with angina, and this drug should be given a trial in patients with refractory coronary artery disease.

Fertility After Oral Contraceptives

Q.—What evidence is there that a woman is more fertile after a course of oral contraceptive drugs? Does this apply to nulliparous women as well as to those who have borne children?

A.—The progestational steroids were first used clinically not as oral contraceptives but as fertility-increasing agents. They were known to inhibit ovulation, but were given not for this purpose but for the rebound ovulation which occurred when they were withdrawn. This piece of speculation has been confirmed by subsequent experience.

C. Tietze found that the conception rate on discontinuing mechanical contraception was 34% in the first menstrual cycle. This was confirmed by J. W. Goldzieher and his colleagues, who also found that their patients giving up oral contraceptives had a 66% conception rate in the first cycle. In Britain an 80% conception rate within two months of stopping oral contraception has been recorded.

Some workers have explained these figures on the basis that women taking oral contraceptives are more fertile. This has not been established quantitatively, and in any case this view is incompatible with the observation that increased rebound fertility may be easily induced in a wide variety of animals in the laboratory.

We publish below a selection of questions and answers of general interest.

References


Reiter's Disease

Q.—What are the modern views on the treatment and prognosis of Reiter's disease?

A.—The aetiology of Reiter's disease is still unknown and treatment remains, therefore, empirical. The natural history of the untreated condition is very variable, and this makes it difficult to assess the value and effects of any therapy employed. It is usual to advise rest for the joints, and in anything but a mild attack admission to hospital has many advantages. The urethritis is usually indistinguishable from that of non-specific urethritis, and treatment of this with tetracycline, 250 mg. six-hourly for 5 to 14 days, is generally given. The joint pain and discomfort can be controlled with suitable analgesics. Soluble aspirin, 600 mg. every six hours, is sometimes sufficient, but in other cases phenylbutazone, 200 mg. twice daily, is required. Corticosteroid hormones are rarely indicated except in very intractable cases.

The conjunctivitis rarely requires active treatment, but if uveitis should occur it needs urgent treatment with atropine and prednisolone drops, and this is best undertaken in collaboration with an ophthalmologist. The erosions of the mucous membranes do not call for local treatment apart from strict cleanliness.

The same applies to the less common skin manifestations of keratoderma blennorrhagica. Nevertheless, if these lesions are particularly troublesome healing can be influenced by local applications of fluocinolone acetonide cream under occlusive plastic dressings.

The patient should be kept at rest whilst the arthritis is active and the joints should be put through the full range of active and passive movements each day to prevent stiffness. Active physiotherapy may be useful when the arthritis has subsided. The progress of the disease can be followed by regular clinical examinations and repeated tests of the erythrocyte sedimentation rate, whose level is usually closely related to the activity of the arthritis.

Reiter's disease is a relapsing condition, and further acute attacks can be expected in a proportion of cases. The disease also progresses insidiously despite treatment and produces lesions of the sacroiliac joints, stiffness of the spine, deformities of the feet, plantar fasciitis, and recurrent attacks of uveitis. Many patients at this stage have chronic prostatitis and a small number may develop rare cardiovascular complications—such as defects in the conduction mechanism or aortic incompetence. The prognosis should therefore be very guarded, and prolonged follow-up of all cases is desirable.

References


Oxygen Diffusion

Q.—The thickness of the alveolar-capillary membrane is stated to be a factor in the rate of diffusion of oxygen from the alveoli to the blood. What is the evidence to support this statement?

A.—Any membrane must supply some impedance to the diffusion of gases through it, and if the membrane has a uniform structure the extent to which gaseous diffusion is restricted must depend on the thickness of the membrane. The practical questions are: (1) how great is the impediment to gaseous diffusion provided by the normal alveolar-capillary membrane; and (2) how important is the diffusion barrier in conditions of thickening of the alveolar membrane?

It is now generally agreed that the normal alveolar membrane provides virtually no appreciable impediment to the diffusion of oxygen from alveoli to blood. Nevertheless, Hamman and Rich described a syndrome of "acute diffuse interstitial fibrosis of the lungs" in which there was desaturation of the arterial blood associated with gross thickening of the alveolar lining membranes. Since then similar functional defects have been recognized in other conditions (e.g., scleroderma). It was tempting to suppose that the thickened membrane was responsible for the hypoaemia, especially since this could be overcome by increasing the inspired oxygen tension. The absence of hypercapnia could reasonably be ascribed to the greater diffusibility of carbon dioxide in the aqueous phase.

Impaired oxygen transfer with normal ventilation is not, however, necessarily due to a diffusion defect, because the functional defect can be exactly simulated by a mismatching of blood to alveolar gas. If blood perfuses regions of the lung which are poorly ventilated, it may emerge relatively unsaturated with oxygen, though with a normal carbon-dioxide content.

No methods at present available can distinguish between inequalities of ventilation and perfusion and low diffusing capacity. However, most people think that a thickened alveolar membrane is probably considerably less important in most cases than ventilation/perfusion abnormalities.

References


Anti-gas-gangrene Serum

Q.—Should anti-gas-gangrene serum be given prophylactically to footballers with extensive lacerations—for example, from stud injuries?

A.—No point will be served by giving anti-gas-gangrene serum with extensive lacerations, since the serum is not bactericidal but only antitoxic, acting against the toxin produced by the Clostridium welchii. The treatment of such lacerations is best achieved by adequate débridement and the administration of antibiotics when necessary.