visit overseas; gammaglobulin is given at the rate of 0·2-0·4 ml/kg body weight, corresponding to about 0·5 g and should be given shortly before leaving this country to those requiring it. Who such persons should be is difficult to say; often it is the traveller who requests it.

Schedule for Travel Overseas

To comply with these recommendations for immunization is clearly a formidable procedure and if only because of the time available the schedule must often be altered. A convenient basic course is one modified from that suggested by Roodyn,13 and set out in the Table; it may be adjusted or supplemented by poliomyelitis or tetanus immunization to meet the requirements of the individual, which will vary depending on the time available, the region to be visited, and previous inoculations.

<table>
<thead>
<tr>
<th>Basic Immunization Schedule for Overseas Travel</th>
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<tr>
<td>Attendances</td>
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<td>First</td>
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<td>Second</td>
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<td>(four weeks</td>
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<td>after first)</td>
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<tr>
<td>Third</td>
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<td>(just before departure)</td>
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Miscellaneous Disorders

Persons visiting warm climates not infrequently suffer from skin disorders, of which the commonest are insect bites, prickly heat, and fungus infections.

Most people experience discomfort at the site of mosquito, sandfly, or other insect bites; in some, however, the reaction is more violent with considerable extension of the original lesion. An antihistamine cream may give some relief; the value of diethylphthalate as an insect repellent has already been mentioned. Prickly heat is especially seen in the humid parts of the tropics and may be very uncomfortable affecting all ages, including babies; it is not painful and does not itch—it "pricks," as its name describes. Astringent lotions, of which 1·0000 mercury perchloride is a very cheap example, give some relief. Fungus infections again are especially common in the warm, damp parts of the world—the crutch, groins, axillae, and feet; the old remedy, Whitfield's ointment (compound benzoic acid ointment) is quite as effective as the more recent preparations and much cheaper. Personal hygiene and attempts to keep affected parts dry by, for example, frequent changes of socks into which talcum powder has been sprinkled, also help; no socks at all is even better.

Diarrhoea greatly troubles many people visiting tropical or even temperate countries, the reasons for this being poorly understood. Equally inexplicable is the apparent relief afforded by Enterovioform (iodochlorhydroxyquinoline) which seems to "keep going" so many travellers on such visits. Some people go further and take with them sulphonamide preparations or a tetracycline. Enterovioform and sulphaguanidine are very unlikely to do harm and are to be valued if they make a stay overseas more enjoyable, but the use of tetracycline should be discouraged.

References


Today's Drugs

With the help of expert contributors we print in this section notes on drugs in common use

Lipid Lowering Agents

British Medical Journal, 1972, 2, 642-643

A rise in the serum levels of lipids is associated with increased risk of atherosclerotic vascular disease. There is little evidence that manipulation of serum lipid levels into the normal range prevents the development of ischaemic heart disease or other vascular disease in otherwise healthy individuals. It has recently been suggested that administration of clofibrate to patients with established ischaemic heart disease results in a significant decrease in mortality, especially a decrease in sudden deaths, but whether this is due to a decrease in serum lipids, or to some other action of the drug, is not clear.

General Management of Hyperlipidaemia

Before embarking on drug therapy for hyperlipidaemia it is important that the serum cholesterol, triglyceride, and lipoprotein pattern be defined, since different therapy is appropriate for different patterns of lipid disorder. Secondary causes of hyperlipidaemia such as diabetes and hypothyroidism should be sought and appropriate treatment given.

Diet

The first step in the management of a patient with hyperlipidaemia is a consideration of his diet. Many patients are overweight and weight reduction may lead to a fall in serum...
lipids. Some types of hyperlipidaemia are specifically induced by excess fat or carbohydrate intake, and in such cases the calorie intake should be redistributed. Substitution by unsaturated for saturated fats is particularly important in patients with familial hypercholesterolaemia.

**DRUGS AFFECTING CHOLESTEROL AND BILE SALT ABSORPTION**

**Cholestyramine**

Cholestyramine is an ion-exchange resin which binds bile salts in the bowel, promotes their faecal excretion, and prevents their enterohepatic circulation. These actions lead to greater use of the body stores of cholesterol, the precursor of bile salts and hence the serum cholesterol concentration falls. There is some compensatory increase in cholesterol synthesis but the balance is usually in favour of cholesterol depletion.

Cholestyramine is most effective in patients with high serum levels of both cholesterol and low-density lipoproteins. It may produce falls of up to 30% in both of these factors.

Though cholestyramine is relatively non-toxic, therapeutic doses of 8-16 g per day are unpalatable. Cholestyramine should be taken with or shortly before each meal, mixed with fruit juice. It will bind not only bile salts but also other lipid-soluble drugs—for example, oral anticoagulants which are administered at the same time. Hence, if possible, other drugs should be taken four to six hours later than cholestyramine.

**Neomycin**

It is thought that the strong negative charge of this polybasic antibiotic disrupts the integrity of intestinal micelles which are required for lipid absorption. Its hypolipidaemic action is independent of its action which sterilizes the contents of the gut, and it is mainly of value in patients with high serum cholesterol concentrations. The usual dose is 1-2 g per day. Intestinal absorption of neomycin is poor and, provided renal function is normal, systemic accumulation does not occur. The main risks of this form of therapy are renal damage and damage to the eighth cranial nerve.

**DRUGS AFFECTING LIPOPROTEIN RELEASE OR REMOVAL**

**Clofibrate**

Clofibrate (ethyl-α-p chlorophenoxycisobutyrate or Atromid S) lowers the serum levels of triglyceride-rich, very low-density lipoproteins, and to a lesser extent, cholesterol-rich, low-density lipoproteins. Its mode of action is poorly understood. Clofibrate reduces the rate of secretion of newly synthesized lipoproteins from the liver and also inhibits cholesterol synthesis before the production of mevalonate. Other theories of action include its effect in inhibiting mobilization of free fatty acids and, less likely, its action in displacing thyroxin from plasma binding sites. It is most effective in patients with raised serum triglyceride and cholesterol concentrations, and least effective in patients with familial high serum levels of low-density lipoproteins. Triglyceride levels are lowered by 30 to 40% and cholesterol levels by 15-20%.

In addition, clofibrate lowers the serum level of free fatty acids and reduces plasma fibrinogen levels, platelet stickiness, and platelet turnover. It also enhances plasma fibrinolytic activity. As mentioned above, these additional effects may be responsible for its effectiveness in two recent studies in patients with ischaemic heart disease. In these trials there was a significant reduction in plasma cholesterol, which was maintained over a five-year period, while no such change was seen in the group treated with a placebo (corn oil). Both studies showed a reduction in sudden death in patients presenting with angina. An overall reduction in the incidence of non-fatal myocardial infarction was also found in clofibrate-treated patients who had previously suffered from angina, irrespective of their serum lipid levels.

The usual daily dose of clofibrate is 1.5-2.0 g. Occasionally patients suffer nausea, and transient minor rises in serum aspartate amino transferase (SGOT) are found. In one study myalgia and raised serum creatine phosphokinase levels were found in five out of 60 patients, but this has not been confirmed. Clofibrate reduces the requirements for oral coagulants by an ill-understood mechanism.

**Nicotinic acid**

Like clofibrate, this drug inhibits the release of very low-density lipoproteins and reduces fatty acid turnover. It has a greater effect on serum cholesterol than clofibrate, and there may be, in addition, a direct reduction of cholesterol synthesis.

The therapeutic dose of nicotinic acid is 3-6 g per day. It is best to give the drug initially in the smaller dose at meal times to reduce gastric irritation and minimize the flushing and pruritus which it may provoke. Other side effects are abnormalities of liver function and carbohydrate tolerance; raised serum uric acid levels are occasionally seen.

**D thyroxin**

Thyroid hormones have a complex action on lipid metabolism, increasing cholesterol turnover and increasing lipoprotein synthesis and removal. The overall effect is to lower serum levels of low-density lipoproteins. Dextro-thyroxin is an isomer of the naturally occurring hormone. It produces less increase in heart rate and oxygen consumption for an equivalent cholesterol lowering action than the laevo isomer. Doses of 4-6 mg per day lower serum low-density lipoproteins by about 20%. Higher doses can increase the metabolic rate and even with recommended doses angina may be precipitated. It is usual to use a beta-adrenergic blocking drug with dextro-thyroxin to reduce these peripheral hormonal effects.

**Conclusions**

The treatment of hyperlipidaemic states remains at present a field for the specialist who has facilities for characterization and assessments of the abnormalities. Secondary causes of hyperlipidaemia should always be sought and dietary measures are still the most important single therapeutic manoeuvre.