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MANAGEMENT AND TREATMENT OF TROPICAL DISEASES

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BEE AND WASP STINGS

Bee stings and wasp stings are relatively common in the tropics. The effects are very similar to those following spider bites, including on rare occasions, general symptoms and haemoglobinuria. In addition, victims may be allergic from previous bee or wasp stings; a subsequent sting, even a single one, can result in rapid collapse with death in 10–30 minutes. This rapid collapse is mainly caused by oedema of the throat and bronchospasm arresting respiration.

Bees have a barbed sting which is left behind together with the venom sac. Wasp stings are not barbed and are therefore not left behind. In treatment the bee sting should be removed. It is a tiny black shaft with the white poison sac attached to its free end. It should not be grasped by forceps or fingers; this would express more venom from the sac. The sting should be scraped from the flesh with the finger or the blade of a knife. Local antiseptic is then applied. Pethidine may be needed for pain. Adrenaline is indicated for general symptoms; if these persist, an intravenous drip of hydrocortisone will be needed. People who are allergic to bee or wasp stings can be desensitised but this is usually temporary unless maintenance desensitising injections each month are continued indefinitely.

JELLYFISH STINGS

Jellyfish have myriads of microscopic stinging capsules called nematocysts on their tentacles. When touched, these capsules extrude a sting which can inject venom. However, only a small number of jellyfish have stings which can penetrate intact human skin. These few are the dangerous jellyfish which are confined to tropical waters. The most dangerous of all is the Cubomedusus or box-jellyfish, sometimes called sea-wasp. It has a cuboidal body or float, one to three inches in diameter, and a lash of several tentacles growing from each of the four body corners. It is translucent and difficult to see in the water. Physalia or the Portuguese man-o-war jellyfish has an easily visible coloured float from which numerous minor tentacles hang, together with a single main tentacle which can be over 10 feet long. Although it has an evil reputation, severe poisoning seldom follows the stings of the Portuguese man-o-war; fatal stings are extremely rare. In contrast, several deaths following stings by the box-jelly, Chironex fleckeri, have been recorded in Australian waters.
Death is due to rapid collapse within a few minutes of the sting; these rapid deaths appear to be due more to heart failure than to respiratory failure. Another smaller cubomedusan causes the Irukandji sting, so-named after an Australian aboriginal tribe. Local symptoms are minimal but after 10-20 minutes, violent generalised pains ensue, with restlessness and sweating. These symptoms may continue for one or two days.

Stings by most jelly-fish other than box-jellies cause only local weal with tingling and discomfort, usually lasting a few hours. Only a small proportion (about 10-20 per cent) of the nematocysts discharge their stings and venom, and this has important implications for treatment. Local effects following box-jelly stings can be more serious and necrosis of the skin may occur.

Methylated spirits (or any other alcohol) should be applied to the stung parts to kill the undischarged nematocysts. If no alcohol is available, dry sand or any dry powder should be thrown on the sting and then the tentacles and slime should be scraped off. Dry sand is better than wet sand. The sting should not be rubbed with wet hands, cloth, and so on, as this will spread and aggravate the sting. After the spirits have dried, calamine lotion is a suitable local application. In severe cases with rapid collapse, the victim should be laid on his back, methylated spirits poured on the sting, and tourniquets put on affected limbs. If breathing stops, mouth-to-nose artificial respiration should be given; if the heart stops, closed-chest cardiac massage should be carried out.

A potent sea-wasp antivenom has recently been produced at the Commonwealth Serum Laboratories, Australia. In human victims of Chironex fleckeri stings this antivenom was followed by a dramatic reduction in local tissue reaction. From experimental findings it is considered that active immunisation of man may be feasible.

44-Sprue

S.J. BAKER AND V.I. MATHAN

Tropical sprue, as it is known today, may be defined as a primary malabsorption syndrome, probably of mixed, though as yet unknown, aetiology, occurring among residents in the tropics or people who
have visited the tropics. By using the word ‘primary’ we exclude from
the definition such conditions as giardiasis, strongyloidiasis, capil-
lariasis, tuberculosis, Crohn’s disease, Whipple’s disease, coeliac
disease and anatomical lesions of the intestine such as diverticul-
osis, fistulae, blind loops etc. Whatever the precise aetiology of
tropical sprue, there is damage to the gastrointestinal tract which
results in both malabsorption of food and increased faecal losses of
fluid, electrolytes, protein and probably other substances. Clinically
the disease may manifest itself in all degrees of severity from the
mild, almost asymptomatic case to the patient severely ill with gross
emaciation, severe diarrhoea and multiple deficiency states. Although
commonest in the 20–40 age group, it may occur in people of any age
including young children.

The disease has a peculiar and interesting distribution. It is known
to occur in many parts of the tropics including India, Pakistan,
Ceylon, Burma, Singapore, Malaysia, China, Hong Kong, Indonesia,
Borneo, the Philippines, Northern Australia, Fiji, the Middle East,
Central America, and some islands of the Carribean especially Haiti
and Puerto Rico, but it has not been found in Central or Southern
Africa. It used to be said that the disease only affected Caucasians,
but this is one of the classical myths of tropical medicine. In fact it
occurs widely among the local inhabitants in endemic form and in
India, Burma and Pakistan, it sometimes occurs in epidemic form.

A study of the natural history of the disease shows that in untreated
cases the mortality may be as high as 30 per cent. The clinical course
is characterised by frequent remissions and relapses. Even without
treatment spontaneous cure is common—a fact which makes the
evaluation of any line of therapy extremely difficult.

Since it may be of multiple aetiology, to describe the treatment of
sprue at the present stage of our knowledge, is like describing the
treatment of ‘colitis’ before the various forms of colitis were differ-
entiated and specific remedies found. Nevertheless certain general
principles are applicable to all cases.

SYMPOMATIC TREATMENT

Control of the diarrhoea is important to reduce fluid and electrolyte
losses. Drugs such as opium, codein, belladonna, kaolin or bismuth
may be given by mouth, and atropine and codein by injection. The
most effective combination for adults is one of opium and bella-
donna either in capsule or tablet form containing:

- opium 60 mg
- extract belladonna 15 mg

or in the form of a mixture containing

- tincture opium 0.6 ml
- tincture belladonna 0.6 ml
- chloroform water to 15 ml

These may be given 1–4 times daily. The mixture is harder to
carry around, but has the advantage that fractional doses can easily
be employed. The intelligent patient should be instructed to adjust
the dose so that they have only one formed stool per day. Belladonna
should be given to elderly males with caution because of the risk of
inducing urinary retention.

Codein 30–60 mg by mouth or by injection may be given 4-hourly.
For children, the dose is 0.5 mg per kg body weight. This is also a
valuable drug, but not so effective as belladonna and opium. Bismuth
salicylate 1–2 g in a suitable mixture can be given 4-hourly. For
children under 5 the dose should be 0.5 g. Kaoelin 5–20 g in a suitable
mixture can also be given 4-hourly or even more frequently. For
children under 5 the dose is 1–5 g.

Vomiting is rarely severe, but may occasionally be a problem.
When this is so, patients should be treated with anti-emetics and, if
necessary, continuous gastric suction and intravenous fluid replace-
ment. The most suitable antiemetic drug is prochlorperazine (stena-
til) 12.5–25 mg given intramuscularly and repeated at 4–6 hourly
intervals as necessary. The related chlorpromazine (10–50 mg) is
also a powerful antiemetic, but must be used with care since it is
more likely to produce hypotension and this may be dangerous in
patients who are already hypotensive.

FLUID AND ELECTROLYTE REPLACEMENT

Fluid and electrolyte disturbances are most severe in the early phases
of the disease or during acute exacerbations in chronic cases. If
untreated these are an important cause of mortality. In milder cases
and where there is little or no vomiting, dehydration can be corrected
by oral therapy either with electrolyte solutions containing sodium
140 m Eq per litre (8.3 g sodium chloride per litre) and potassium
27 m Eq per litre (10 ml of potassium mixture—see later) with glucose and flavouring, or in the home by fruit juices or, where available, tender coconut water.

In more severe cases intravenous replacement therapy must be instituted. The indications for parenteral therapy are the presence of (i) vomiting.
(ii) severe dehydration.
(iii) a thin rapid pulse, and a low or falling blood pressure.
(iv) a continuing negative fluid balance in spite of oral replacement therapy—usually due to continuing severe diarrhoea.
(v) acidosis, manifested clinically by rapid deep respirations.

The amount of fluid to be given must be judged by the size of the patient, the extent of dehydration and measurement of continuing fluid losses. An accurate fluid balance record, including faecal losses, is of the utmost importance in planning the fluid requirements. The amount given in any 24 hour period must make up any existing deficit, cover measurable fluid losses and allow at least one litre extra (in the adult) to cover insensible losses. The commonest error in therapy is to give too little fluid, but care must also be taken not to overload the patient by giving too much.

Since the patient is dehydrated due to loss of gastrointestinal secretions, the initial fluid deficit should be made up by the administration of "normal" saline (0.85 per cent) or 5 per cent glucose in saline, and not just glucose and water. Similarly in replacement of further losses caused by vomiting and/or diarrhoea, normal saline should be employed. Urinary losses and insensible losses should be made up by the use of 1 part of normal saline to 2 parts of 5 per cent glucose in water.

Diarrhoeal stool contains a lot of potassium, so dehydrated patients will also have hypokalaemia. With the dehydration and loss of body base, there will also be a greater or less degree of metabolic acidosis. These patients may therefore need both added potassium and alkali. Whenever possible, serum electrolyte and bicarbonate concentrations, and blood pH should be measured and therapy tailored accordingly. When facilities are not available, the physician must make an intelligent guess at the appropriate therapy.

Potassium salts may be given either orally or parenterally. Since potassium given orally may be nauseating, if the deficit is large, it is better to give intravenous therapy. The amount needed may vary from 2 or 3 to 25 or more grams of potassium chloride. The aim should
be to restore and maintain the serum potassium concentration at a normal level. If there are no facilities for estimating serum potassium, changes in E.C.G. pattern can provide some guide to therapy. It is better to err on the side of giving too little potassium, and to give it orally, rather than to run the risk of inducing hyperkalaemia. An adult with diarrhoea and moderate dehydration can safely be given 13 m Eq of potassium 6-hourly, either by mouth or by the parenteral route, provided there is a reasonable urine output. This dose can be continued until hydration is restored. A reasonably simple but palatable preparation of potassium is the following:

- Potassium acetate: 0.5 g
- Potassium bicarbonate: 0.5 g
- Potassium citrate: 0.5 g
- Water: 5 ml

Each 5 ml contains 13.5 m Eq of potassium.

Tablets and particularly enteric coated tablets of potassium should not be given because of the risk of producing intestinal ulceration.

Obvious acidosis is only found in the more severe cases and can be treated by giving sodium lactate or sodium bicarbonate intravenously. Sodium lactate is usually made in 1/6, 1/3 or full molar strengths—the latter is sclerosing to veins, and must therefore be given directly into one of the large veins, femoral or subclavian. In an adult, 500 cc of 1/6 molar lactate (82 m Eq) raises the plasma bicarbonate 2-4 m Eq per litre. Where acidosis is very severe (plasma bicarbonate less than 10 m Eq per litre), intravenous sodium bicarbonate (200 ml of an 8.4% solution—1 m Eq per cc) is preferable to lactate for initial therapy because it provides immediately available base. However it is difficult to prepare in sterile form and is, therefore, not recommended for routine therapy. Where the plasma bicarbonate cannot be estimated, alkali in the form of 1–3 g of sodium bicarbonate can be given 3 times a day by mouth, if acidosis is suspected.

Unlike the situation in non-tropical sprue, calcium deficiency is seldom seen. When it does occur, it most often presents as unexplained tetany. Such cases are readily treated by the parenteral administration of calcium gluconate (10 cc of 10 per cent solution) followed by oral calcium gluconate 1 g 3 times daily.

It is probable that in some of the more severely affected cases magnesium deficiency may also be present, though this has never been fully documented. In adults with severe sodium and potassium deficiency, it may therefore be also worth while giving magnesium
sulphate, 2 cc of 50 per cent solution by intramuscular injection 12-hourly.

TREATMENT OF ANAEMIA

Mild cases of short duration may have no anaemia, but in chronic cases anaemia is common. It is most often due to a combined deficiency of iron and folic acid and/or vitamin B12. Morphological examination of blood and bone marrow will usually indicate whether the anaemia is due to iron, or folate-vitamin B12 deficiency, or a combination of both. Measurement of serum iron, serum vitamin B12 and serum and red cell folate levels may help further to delineate the cause of the anaemia, but such estimations are not essential for the planning of treatment.

If the patient is severely anaemic (P.C.V. of 10 or less) and especially if there are signs of circulatory overload present, such as cardiac enlargement, triple cardiac rhythm, jugular venous engorgement, crepitations in the lung bases or tender enlargement of the liver, treatment of the anaemia is urgent, and is best carried out by giving a partial exchange transfusion of 2 units of blood. Fifty to one hundred cc of blood is withdrawn from one arm, through a wide bore needle (15 gauge), and then an infusion of compatible whole blood, or preferably packed cells, is started through a wide bore needle (15 gauge) into a vein on the other arm. The rate of administration of the blood is arranged to match the rate of withdrawal. The total volume withdrawn should always be 50–100 cc greater than the volume administered. In this way the haemoglobin level can be raised quickly without producing circulatory overload. If signs of cardiac decompensation are present, preliminary rapid digitalisation and the administration of diuretics may be beneficial. In very ill patients severe pyrogenic or allergic reactions may have serious consequences. One hundred mg of hydrocortisone should be given intravenously prior to the exchange transfusion together with all other precautions to reduce the incidence of such reactions.

Patients with a less severe grade of anaemia should be treated by the appropriate haematin(s). For iron deficiency 1 tablet of ferrous sulphate (200 mg) should be given twice or thrice a day. In rare cases, where the patient does not tolerate oral iron, or where there is no response to this dose, it may be necessary to give it by the parenteral route in the form of iron dextran complex, or saccharated oxide.
of iron. Although there is a theoretical possibility of malabsorption of iron, this is seldom if ever so severe as to prevent a response to therapeutic amounts of oral iron.

Megaloblastic anaemia may be due to either folate or vitamin B12 deficiency, or a combination of both deficiencies. Daily therapy with small doses of either vitamin B12 1 µg, or folate acid 200 µg, is useful for distinguishing the two deficiencies, but for routine treatment such doses are unnecessary and difficult to use. In ordinary practice vitamin B12 deficiency can be adequately treated by the intramuscular injection of 100 µg of cyanocobalamin once a week, and folate acid deficiency by 1 tablet of 5 mg of folate acid (pteroylglutamic acid) daily. If there is doubt about the nature of the deficiency causing the megaloblastosis, it is better to give both vitamins. Vitamin B12 should be given by injection because of the high incidence of vitamin B12 malabsorption, but folate acid absorption from a 5 mg dose is always satisfactory so that it is unnecessary to give this by injection.

The duration of treatment for anemia in the first instance should be for 3 months. At the end of this time treatment can be stopped, and the patient kept under observation for several years for possible relapse. If such relapse should occur treatment will have to be resumed. However such patients should preferably be investigated to determine the precise nature and cause of the recurring deficiency state and be treated appropriately. Most often such relapses will be found to be associated with continuing malabsorption of vitamin B12, either due to the presence of complete gastric atrophy, or a continuing ileal lesion preventing vitamin B12 absorption even in the presence of added intrinsic factor. The latter lesion may sometimes be cured by antibiotics.

OTHER VITAMIN DEFICIENCIES

Clinical manifestations of other vitamin deficiencies may be present and should be treated appropriately. Vitamin A deficiency is common and manifests chiefly as night blindness, Bitot's spots, xerosis conjunctivae and in the most severe form keratomalacia. When keratomalacia is present, water miscible vitamin A palmitate should be given by intramuscular injection (adults 100,000 units, children 25-50,000 units depending on size). This single injection provides enough for at least 2 weeks. In subjects with keratomalacia, the oil
soluble form should not be used for injection, as it is very slowly absorbed from the site of injection and may fail to raise the serum level or reverse the eye changes. After initial parenteral therapy, and in patients with milder forms of deficiency, oral vitamin A may be given, preferably in the water miscible form, 5–10,000 units daily for 3–4 weeks.

Signs of thiamine, riboflavin and nicotinic acid deficiency may also occur. These are best treated with a vitamin B complex preparation, since deficiencies are usually multiple. This can be given by mouth, but if the patient is very ill, it is better given by injection.

FOLIC ACID

It has been the experience in some parts of the world, that administration of folic acid brings about rapid improvement in the condition of the patient, and in some cases cure of the disease. In south Indian subjects with sprue, the authors have not been able to demonstrate any consistent improvement in intestinal function following folic acid therapy, and in these patients, folate deficiency appears to be a secondary phenomenon, rather than the cause of the disease.

Irrespective of the role of folate therapy in bringing about a healing of the intestinal lesion, since folate deficiency is extremely common, it is reasonable to give all patients folic acid, 1 tablet of 5 mg, daily, even in the absence of megaloblastic anaemia. Where folic acid deficiency exists, such treatment will bring about a dramatic improvement in the patient’s feeling of well-being, a disappearance of glossitis and a haematological response.

If folic acid is given to a patient with vitamin B12 deficiency, there is some danger of precipitating neurological damage. This risk can be abolished by the concomitant administration of vitamin B12, or the measurement of serum vitamin B12 levels at, say, 3 monthly intervals. Alternatively a careful watch should be kept on the patient, and the patient warned to report immediately should he develop any neurological symptoms.

ANTIBIOTICS

In some cases the administration of a broad spectrum antibiotic produces a marked decrease in stool volume, a diminution of steator-
rhea and an improvement in xylose and vitamin B12 absorption. The most widely used antibiotic has been tetracycline (250 mg 4 times a day). The results of short term antibiotic therapy have been variable, but the best results have been found in Caucasian subjects from Hong Kong, Singapore, Puerto Rico and south India. In Indians in south India the results of short term antibiotic treatment have been less satisfactory. The reasons for these differences are not clear. In a group of patients from Puerto Rico long term tetracycline therapy for 4-6 months has been shown to be associated with marked improvement or cure. Similar long term therapy has also been tried in a small number of Indian patients with encouraging results, and is worth trying as a routine in all subjects with chronic sprue that do not respond to other measures.

ADRENOCORTICAL STEROIDS

In general adrenal corticosteroids have no place in the treatment of tropical sprue. However the urinary excretion of 17-oxo and oxogenic steroids is often greatly reduced, and severely ill patients may develop an Addisonian-like adrenal crisis. In such cases use of adrenocortical steroids may be life saving. Initially hydrocortisone should be given intravenously 100 mg 4-8 hourly, or dexamethasone intramuscularly 4 mg 4-8 hourly. When the patient is able to take oral medication, prednisone by mouth can be substituted for the parenteral therapy. An oral dose of 15 mg 6-hourly can be given initially and tapered off gradually as the condition improves.

DIET

A great deal has been written about different diets advocated for patients with sprue. However there seems to be no particular virtue in most of these. A high fat diet may not be acceptable, but there is little evidence that a low fat diet is beneficial. Some patients have very low lactose levels in their jejunal mucosa and in some of these, symptoms may be exacerbated by drinking milk. If this occurs milk should be restricted. In general, the authors’ practice is to allow patients to continue their usual diet. Where there is marked hypoproteinaemia, a high protein diet or protein supplements, may be of value in aiding the more rapid restoration of the body protein pool. When there is marked anorexia and/or vomiting, only a fluid diet may be acceptable and in very severe cases all oral feeding may have
to be suspended for a time. Although tropical sprue is to be distinguished from gluten induced enteropathy (coeliac disease) some cases of tropical sprue appear to have an acquired sensitivity to wheat gluten. Such patients may benefit from temporary exclusion of gluten from the diet, however once they are better they do not relapse on reintroduction of gluten.

OTHER COMPLICATIONS
Apart from deficiency states, the commonest complication of tropical sprue is secondary infection, most often of the respiratory tract—pneumonia or bronchopneumonia. When patients are severely ill, the usual manifestations of infection such as fever and rise in pulse rate may not be present, and careful search should always be made for signs of infection. When present, infections should be vigorously treated with appropriate antibiotics—if possible with bacteriological control and antibiotic sensitivity testing.

Abdominal distension is a common symptom and sign of many cases of sprue. Sometimes this may be very marked and be associated with copious vomiting, loud prolonged borborygmi and colicky abdominal pain. Such patients may be mistakenly diagnosed as suffering from acute intestinal obstruction. This diagnosis may appear to be further substantiated by the radiological finding of multiple fluid levels in dilated loops of small intestine. If the patient’s history suggests a diagnosis of sprue, conservative treatment of the pseudo-obstructive state should be instituted with continuous intestinal suction and parenteral fluid replacement. This will usually result in a return of intestinal function within 3-4 days. Needless to say the reverse situation of an organic intestinal stricture resembling tropical sprue may also occur and needs constantly to be kept in mind. The differential diagnosis will usually depend on adequate radiological examination of the small intestine after the acute attack has subsided.

Occasionally, in severely ill patients, a state of paralytic ileus develops, with absence of intestinal peristalsis, distension of the abdomen and the accumulation of fluid in the intestine. Such patients should be treated by the classical therapy for paralytic ileus, namely continuous intestinal suction and parenteral fluid administration, together with vigorous replacement therapy to make good existing deficiencies. In particular paralytic ileus is often associated with potassium deficiency and may in fact be caused by it.
Disorders of the nervous system may occasionally develop as a result of deficiency states. Peripheral neuritis occurs in a small proportion of cases and usually responds to treatment with vitamin B complex. This is best given by injection, 1-2 ml daily. Rarely subacute combined degeneration of the cord is found. This responds to treatment with vitamin B12, 100 μg by injection twice a week. In both conditions, physiotherapy with re-educational exercises may be helpful in the more severely affected individuals.

CHANGE OF RESIDENCE
It has been said that an expatriate who is suffering from sprue should be sent home and should not return to the tropics. There is no clear cut evidence that recovery from the disease is any quicker if such a person is repatriated than if he is kept in the tropics. There is also no firm ground for advising such people against returning to the tropics.

PROPHYLAXIS
There is no known prophylaxis against the disease. Some have advocated the prophylactic use of folic acid but the efficacy of this has yet to be evaluated.

CONCLUSION
In summary the treatment of tropical sprue should consist of:
1. Control of diarrhoea (and vomiting).
2. Correction of fluid and electrolyte disorders.
3. Treatment of anaemia and correction of other deficiencies.
4. Folic acid
5. In refractory cases prolonged therapy with tetracycline.

In each case treatment must be tailored to fit the needs of the individual patient. In mild cases this can readily be done, but in severe cases planning of therapy may tax all the laboratory facilities and clinical skill of even the best hospitals and the most experienced physicians. Further developments in therapy must await an increased knowledge and understanding of this syndrome.

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