Malaria is still a problem in the south of China, especially in the semi-tropical jungle areas bordering southeast Asia. Most cases are of the falciparum type, we were told: the former important vector, *Anopheles minimus*, has been largely exterminated and the problem now is *A. balabacensis*. However, the numbers of cases were said to be falling each year as a result of spraying with D.D.T. and treatment/prophylaxis with chloroquine and primaquine.

Hookworm and filariasis are still public health problems, but again the combination of improvements in sanitation combined with mass treatment programmes are said to be bringing them under control.

Bacterial and Viral Diseases

Of the bacterial and viral diseases, plague, cholera, and smallpox are apparently extinct—a view shared by the W.H.O. Immunization and vaccination programmes, which fall within the scope of the barefoot doctors, seem to be followed with enthusiasm. Every health station, in both town and country areas, maintains records of the vaccination status of children in its area. At present the routine range includes DPT vaccine; measles; poliomyelitis (oral attenuated virus); BCG (given by injection or by mouth, the first dose within three days of birth); smallpox (though as in Britain the vaccination rate is falling); and vaccines against Japanese B encephalitis and meningococcal infection.

Screening Procedures

Though there is still a long way to go, China can claim to have the infectious and parasitic diseases under reasonable control—"we are in the phase of consolidation," was the attitude of the public health authorities. They are confident enough of the position to have started work on the next level of preventive medicine, screening tests for the population.

The decentralization of the medical services has marked advantages for screening campaigns—and certain drawbacks. The commune hospital we visited outside Shanghai, for example, had set out to x-ray the chest of every one of its 23,000 inhabitants once a year, and this was clearly a practicable proposition—but it was far from clear how many other communes would be following the same programme.

There does seem to be a nationwide campaign of screening for cervical cancer (which in China is more common than breast cancer, though we could find no national statistics on incidence). Gynaecology departments in hospitals took every possible opportunity to take cervical smears, and on the communes this was another of the responsibilities of the barefoot doctors. It seemed that the reading of the smears was done in the commune hospital laboratory.

Screening programmes for specific diseases have been started in some parts of China—the tests for oesophageal cancer in the northeast and for nasopharyngeal cancer in the south (see *B.M.J.*, 25 May, p. 429) are examples.

Barefoot Doctors the Key

While the health authorities can retain the enthusiasm of the barefoot doctors their preventive policies can be highly effective at the commune level. Good quality sanitation and immunization can achieve a great deal. The use of these keen but relatively unskilled health workers in screening campaigns is a more speculative venture, and the results will be of great interest.

References

- ¹ *Medicine and Public Health in the People's Republic of China*, ed J. R. Quinn. New York, U.S. Department of Health, Education and Welfare, National Institute of Health, 1973.
- ² Sidel, V. M., and Sidel, R., *Serve the People*, Observations on Medicine in the People's Republic of China. New York, Macy Foundation, 1973.
- ³ Horn, J. S., *Away with all Pests*. New York, Monthly Review Press, 1969.

Today's Treatment

Blood and Neoplastic Diseases

Treatment of Iron Deficiency and Iron Overload

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Iron Deficiency

Current practice in the management of iron-deficiency anaemia can give little cause for satisfaction, since follow-up studies indicate a relapse rate of around 30% in both hospital and general practice series. These disappointing results must reflect either an insufficiently energetic approach to the

identification and removal of the underlying cause, or to inefficiency in supplying replacement iron.

REMOVAL OF UNDERLYING CAUSE

Persistence of the primary cause of negative iron balance will guarantee a relapse after withdrawing iron therapy, and sources of manifest or occult bleeding should be identified, and, where possible, treated medically or surgically. Hormonal therapy for menorrhagia has proved useful and hysterectomy may be indicated near the menopause. Full gastrointestinal investigation is justifiable in all men and postmenopausal women (and in premenopausal women without menorrhagia)

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to detect and treat bleeding lesions, often otherwise asymptomatic. Dietetic instruction, diagnosis and treatment of overt or occult malabsorption syndromes, and discouraging the abuse of aspirin will also make a valuable contribution.

Even with diagnostic enthusiasm and therapeutic ingenuity, however, there remains a residue of patients in whom removal of the underlying cause is impossible; this is usually because the patient's general condition prevents a radical approach—for example, repair of a hiatus hernia in a frail elderly person—or because the lesion is not amenable to surgical treatment, as in extensive hereditary haemorrhagic telangiectasia. There is also an occasional case of gastrointestinal bleeding where no source can be found even after exhaustive investigation. In such patients continuous iron supplementation is the only alternative.

IRON TREATMENT

The only indication for iron treatment is the presence of a demonstrable iron-deficiency state, especially iron-deficiency anaemia. There is no need to treat latent iron-deficiency states since these are unlikely to be associated with symptoms, and iron deficiency complicating polycythaemia vera is also usually left untreated. Nevertheless, prophylactic iron is justifiable in the following circumstances: during pregnancy; after partial or total gastrectomy, where iron deficiency anaemia may be expected in up to 60% of patients; in the management of low birth weight infants—for example, premature babies, twins, and infants after caesarean section; and in some centres, to women blood donors.

Choice of Oral Preparation.

Iron should be given by mouth unless there are good indications to the contrary. There is little to choose between the commonly used preparations: iron absorption from ferrous sulphate, gluconate, fumarate, and succinate is closely similar. The rate of haemoglobin regeneration is not greatly affected by the iron preparation used, and in most patients with iron-deficiency anaemia the time factor is not critical. Choice is thus usually determined by cost and side effects. It is customary to start treatment with ferrous sulphate, 200 mg thrice daily, given after food to minimize gastric intolerance. If side effects arise dosage can be reduced, or a change made to an alternative preparation, remembering that improved tolerance of another tablet is often due to its lower content of elemental iron (see table I). Liquid preparations are useful in children and sometimes succeed in adults with gastric irritation. Some oral preparations contain adjuvant substances which can produce modest increases in iron absorption—for example, ascorbic acid, chelates of iron—but this hardly justifies the additional expense.

TABLE I—Iron content of some commonly used oral iron preparations

Iron Salt	Preparation	Elemental Iron Content (mg/dose)
Ferrous sulphate	Tabs. Ferrous Sulphate Co. B.P.C.	62
	Tabs. Ferrous Sulphate B.P. 200 mg	60
	Feospan 150 mg (slow release)	45
	Ferro-Gradumet 525 mg (slow release)	105
	Slow Fe 160 mg (slow release)	50
Ferrous gluconate	Tabs. Ferrous Gluconate B.P. 300 mg	35
	Tabs. Cerevon 300 mg	35
	Tabs. Fergon	35
Ferrous succinate	Tabs. Ferromyn 100 mg	35
	Caps. Ferromyn	37
	Elixir Ferromyn	37/5 ml
Ferrous fumarate	Tabs. Fersamal	65
	Syrup Fersamal	45/5 ml
	Fersaday 304 mg (slow release)	100

Slow release capsules are now in use on a wide scale and are heavily promoted. These are likely to carry iron past the first part of the duodenum into an area of the gut where conditions for iron absorption are poor; their low incidence of side effects may well reflect the small amounts of iron released, and they too have no clear therapeutic advantage to justify their cost.

Response Rate

A flat reticulocyte curve usually begins four to five days after instituting treatment and lasts for about 10 days; the haemoglobin concentration should rise by about 0.1–0.2 g per 100 ml daily. Treatment should be continued until the haemoglobin level is normal; thereafter, reconstitution of the stores may take several months, since iron absorption is progressively resisted by the gut mucosal cells as iron status improves. Full oral treatment is, therefore, recommended for a further six months. If it has proved impossible to modify the underlying cause of negative iron balance, especially in patients with chronic blood loss, treatment may have to be continued indefinitely. Epithelial tissue changes such as atrophic glossitis and koilonychia are usually improved, though the response is often slow.

Side Effects

Since iron salts are astringent, irritant gastrointestinal side effects may occur, though these can be minimized by giving iron with food. Nausea and epigastric pain are dosage-related; there is a less clear relationship between dose and altered bowel habit, such as constipation or diarrhoea. The incidence of side effects with ferrous sulphate is no greater than with other iron salts if comparable doses of elemental iron are used. A psychological basis for the side effects of iron is undoubtedly present in a few cases, though this has probably been over emphasized in the past. Young mothers should always receive careful instructions to keep iron tablets out of the reach of young children.

Failure to Respond to Oral Iron

Failure to respond to oral iron is a fairly common problem and demands a reappraisal of the clinical situation. Failure to co-operate with treatment, either because of genuine side effects, or more commonly because of lack of interest or intelligence, is the usual reason. Continuing blood loss may be severe enough to outstrip the additional iron provided by therapy, and malabsorption states may prevent adequate absorption even of therapeutic doses of iron, though this is rare. Lastly, the diagnosis of iron-deficiency anaemia may have been incorrect, and the laboratory criteria used to confirm the presence of iron deficiency should be critically reviewed; the usual source of confusion is the presence of a hypochromic anaemia not due to true iron deficiency—for example, anaemia of chronic infection or inflammatory disease, thalassaemia, or a sideroblastic anaemia.

There is no substance in the belief that a complete response to treatment excludes underlying malignancy as a cause for iron-deficiency anaemia.

PARENTERAL IRON TREATMENT

The only real indication for parenteral iron is the failure of oral treatment, for the reasons outlined in the previous section—that is, lack of patient co-operation, side effects from oral treatment, severe blood loss, and resistant malabsorption.

To these might be added (a) the presence of gastrointestinal disease which could be exacerbated by the irritant effect of oral iron—for example, ulcerative colitis—and (b) the need for rapid replacement of the iron stores to support predictable future demands—for example, iron deficiency discovered late in pregnancy, or in preparation for surgery.

Parenteral Preparations

Iron dextran (Imferon) is a high molecular weight compound of ferric hydroxide and dextran, and can be given both intramuscularly and intravenously. Iron sorbitol citric acid (Jectofer) can only be given intramuscularly. Jectofer is not homogeneous and contains a range of molecules of different sizes; nevertheless, the mean molecular weight is low and this allows rapid diffusion and absorption from the injection site, but also excretion in the saliva, and substantial urinary losses of each dose. Around 100 mg of either preparation can be given daily by deep intramuscular injection, and the manufacturer's dosage schedules usually include a supplement for replacement of the iron stores.

Comparative studies of equivalent doses of oral and intramuscular iron have shown no significant increase in haemoglobin response. This may be because the slow rate of diffusion of iron dextran from the injection site achieves a delivery of iron to the marrow no faster than that provided by the oral route; in the case of iron sorbitol, urinary excretion of up to 40% of each dose also results in loss of effective iron reaching the marrow. The need for a rapid cure of the anaemia is thus not a sound indication for iron by the intramuscular route.

Choice of Preparation

At present iron sorbitol is probably preferable to iron dextran, particularly in young patients, unless there is evidence of existing or previous urinary infection. Iron dextran by the intramuscular route is now usually avoided in patients with a long life expectancy, after reports of sarcomata at the injection sites in animals; such lesions have not been clearly described in man, but the possible induction time is unknown and could be prolonged. A summary of the side effects of parenteral preparations is given in table II.

TABLE II—Side effects of intramuscular iron

Side Effects	Iron dextran	Iron-sorbitol-citric acid
Pain	+	+
Skin staining	++	+
Sarcoma	?	—
Flushing	+	—
Nausea and vomiting	+	+
Joint pains	+	—
Fever	+	—
Metallic taste (salivary excretion)	—	+
Exacerbation of pyelonephritis (urinary excretion)	—	+
Blastic crisis in leukaemia	—	+
Haemosiderosis	+	+

Total Dose Infusion of Iron Dextran

Total dose intravenous infusion of iron dextran is now used widely, especially in obstetric practice. While iron administration by this route is rapid and reliable, and the incidence of side effects is low, several disquieting adverse reactions have been reported—especially in allergic subjects. For these reasons, and, since oral iron is harmless, intravenous iron should be used only in selected cases when proper indications exist for its use—that is, where continuing blood loss is likely to be permanent and oral prophylaxis cannot keep pace; when a patient requiring parenteral iron has a small muscle mass, or

a haemostatic defect, contraindicating intramuscular injections; or when reasons of psychological or social pressure make iron treatment by other means impracticable.

Iron Overload

Iron overload may be acquired by absorption of inappropriate quantities of iron from the gut, as in idiopathic haemochromatosis; in various forms of dietary iron excess, including Bantu iron overload; in hepatic cirrhosis and after portacaval anastomosis and in refractory anaemias with hypercellular bone marrow where iron absorption is increased. Iron excess may also be acquired parenterally, usually by repeated blood transfusions for refractory anaemia, but occasionally by uncontrolled parenteral iron treatment. Though the body can slightly augment passive iron losses in states of iron overload, there is no excretory mechanism for iron, and therapeutic removal of the iron becomes necessary to prevent or reverse tissue damage. This can be achieved either by repeated venesections or by long-term administration of iron chelating agents. The former is much more efficient but clearly can be applied only to patients whose marrow function will allow blood regeneration; thus all patients with iron loading associated with chronic refractory anaemia are necessarily excluded, and require chelator treatment. In addition to iron removal, these patients simultaneously need careful supportive management for diabetes, liver failure, and cardiac disease.

VENESECTION TREATMENT IN IDIOPATHIC HAEMOCHROMATOSIS

The removal of 500 ml of blood allows the mobilization of about 250 mg of iron from the tissue stores. Though regeneration of red cells in iron-loaded patients is sufficiently rapid to allow more frequent venesection, it is customary to withdraw 500 ml of blood only once or twice weekly. Since the average iron load in the patient with symptoms is about 20–25 g, this commits the patient to a venesection programme lasting between one and two years. Complete iron depletion is recognized when hypochromic changes appear in the red cells, when the serum iron and total iron-binding capacity indicate iron deficiency, when liver biopsy shows absent stainable iron, and when urinary iron excretion after a test dose of an iron chelator is in the normal range. Reaccumulation of iron can thereafter be prevented by a 500 ml venesection every three–four months. A similar regimen should be instituted in relatives with iron loading.

The mean survival time in these patients is almost doubled by venesection treatment. Improved liver function, a fall in insulin requirement, arrest in pigmentation, and improvement in cardiac function may all be expected; hepatic fibrosis has been reported to regress. Hypogonadism, arthritis, and the incidence of primary carcinoma of the liver appear to be unaffected by iron removal. The outcome is probably related to the severity and duration of iron loading before treatment is begun.

Venesection treatment has been shown to provide definite symptomatic improvement in porphyria cutanea tarda, and is effective in removing the iron overload of alcoholic cirrhosis, though iron loading in the latter is rarely severe enough per se to cause tissue damage.

IRON CHELATOR TREATMENT

In refractory anaemias—when iron overload has been acquired by repeated transfusions, by inappropriate iron treatment, or by excessive intestinal iron absorption—venesection is clearly impracticable, and treatment with chelating agents represents the only available means of removing iron from the body,

though the discrepancy between iron acquired by blood transfusion and the amount capable of being eliminated even with large doses of chelators makes the task a daunting one. Two chelating agents are available—diethylene triamine pentacetic acid (DTPA), usually given by intermittent intravenous infusion, and desferrioxamine, given by subcutaneous or intramuscular injection. The iron excreted varies with body iron stores; depending on iron load, a dose of 1.0 g of des-

ferrioxamine or DTPA will eliminate around 20-30 mg of iron in the urine. In patients requiring regular blood transfusion it may be found convenient to administer a large dose of intravenous DTPA with each transfusion, thus avoiding a separate injection. The clinical benefits to be derived from long-term treatment with chelators, particularly in preventing liver and cardiac damage, are not yet clear and require further evaluation.

Any Questions?

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

Liver Function Tests for Anaesthetists?

Are anaesthetists specially vulnerable to liver disease and would regular liver function tests be of any value?

There are relatively few well-documented instances of anaesthetists developing liver damage following exposure to anaesthetic agents. Anaesthetists and hepatologists argue as to the specificity and true cause of liver changes seen after halothane anaesthetics but the reaction is almost certainly a sensitivity type in that only a very small percentage of people exposed develop evidence of hepatotoxicity. The possible increase in the frequency of abortion and perinatal death in female anaesthetists and operating nurses is unlikely to be related to underlying liver disease. A pilot study on a research basis of liver function changes in anaesthetists under different operating conditions would be of interest and should precede any larger study. It is most unlikely that screening an anaesthetist by regular liver function tests would give a reasonable yield of positive results. This would be so particularly if minor changes in serum enzyme level, which seem to occur not infrequently and without obvious cause, were ignored.

Herpes Zoster in Babies

How common is herpes zoster in the first year of life?

Under one year of age herpes zoster is rare though cases have been reported even in the newborn period. Both chickenpox and herpes zoster are caused by the varicella-zoster virus. The former results from the individual's first exposure to the virus. It is thought that herpes zoster results from a reactivation of latent varicella-zoster. So if an infant develops herpes zoster the first contact with varicella-zoster may have been made during fetal life. I do not know why in childhood—in contrast to adults—pain with herpes zoster is so unusual and postherpetic neuralgia almost never occurs.

Feldman, G. V., *Archives of Disease in Childhood*, 1952, 27, 126.

Inheritance of Fragilitas Ossium

A young man has fragilitas ossium. There is no known family history, but his brother has recently married and is worried that his children might develop the disease. Is there any risk of this happening?

Fragilitas ossium of the osteogenesis imperfecta tarda type is a dominant condition. If no other member of the family shows evidence of the disorder it is likely that the patient has been affected as a result of a fresh mutation and no other

member of the family is at risk except the offspring of the patient. The patient's brother, therefore, has only a very low risk of having children with the disorder, provided he himself shows no evidence of the condition, such as blue sclerotics, or of a history of undue bone fragility.

Salt Supplement in the Tropics

Is extra salt really advisable in hot countries?

The simple answer is no, apart from exceptional circumstances, and generally salt is more likely to do harm than good. The sweat salt loss for an unacclimatized individual is usually about 4.0 g/l., but can range from less than 2g to more than 20 g. The normal European daily dietary salt intake is about 10 g and the renal salt conservation mechanism is so efficient that almost all is immediately available to compensate for sweat losses when required. Reduction in the sweat salt content is a slower process requiring three to four days of severe heat exposure to develop.¹ Salt supplementation may therefore be indicated for an individual suddenly exposed to repeated bouts of moderately hard physical work in a hot climate. After the first few days, however, it should only be needed if the sweat losses necessitate a daily fluid intake of over 5 l.² An excessive salt intake increases the urinary fluid loss and, since the ingestion of fluid is frequently below the optimum in hot countries, the risk of dehydration is enhanced. Almost everyone has heard of stoker's cramp, which is a condition caused by acute salt depletion but is very rarely encountered. The possibility of a less severe, but nevertheless important, degree of salt depletion should however be considered in any individual who is sweating freely and who has anorexia or is suffering from diarrhoea and vomiting as the result of a gastrointestinal upset. Athletes and their trainers frequently seek advice on the need for extra salt when preparing for a competition to be held in a hot climate. The Marathon race and other similar endurance sports certainly cause very high sweat rates even in temperate climates, but the total daily loss is not large and the individuals concerned become largely acclimatized even without exposure to a hot climate. Furthermore, laboratory studies have shown that the ingestion of salt prior to exertion in the heat may actually impair performance, since sweating then occurs less freely with a consequently higher body temperature.³ The athlete who contemplates salt supplementation would be well advised to see whether it is really needed by testing his urine for chlorides using a simple technique such as the Fantus test.

¹ Weiner, J. S., and Van Heyningen, R. E., *British Journal of Industrial Medicine*, 1952, 9, 56.

² Edholm, O. G., et al., 1962, *Army Personnel Research Committee, Report No. A.R.R.C. 61/25*, London, Medical Research Council.

³ Senay, L. C., Jr., *Journal of Applied Physiology*, 1968, 25, 149.