action has led to the suggestion that a place may exist for their use in combination with anticancer drugs. Certainly many tumours have hypoxic areas with cells poorly accessible to drugs and of low mitotic activity; in such cases environmental modification might well affect responses to treatment.


Yaws again

"There is now little clinical interest in yaws and opportunities for the study of its pathology are already probably extinct." This statement1 by an acknowledged authority seemed true in 1967, but yaws is now returning in several countries from which it had disappeared after the successful campaigns by WHO and UNICEF.2 A timely reminder of the widespread suffering caused by yaws, and of the vociferous welcome accorded by its victims to the doctors whose injections of arsenic and bismuth made the multiple raspberry-like protuberances disappear as if by magic, is provided by a recent article in Tropical Doctor.3 Another recent publication is a book placing yaws in its historical context in pathology in Africa.4 Hackett’s account5 should send readers to their neglected textbooks of tropical medicine6 6 to read of the clinical presentations of a disease likely to increase in prevalence.

Skin departments in Western hospitals are unlikely to witness an influx of patients suffering from the florid lesions of early yaws, yet the late manifestations may pose problems of differential diagnosis? to patients from countries where the disease has been, or will probably be, common.

The reappearance of yaws may reopen unresolved debates about the relations between yaws and non-veneral syphilis9 10 and also between such non-veneral infections as bejel, njorera, dichuchua, and Hibbers11 ('the Scottish yaws'), and South American pinta, caused by Spirochaeta carateum. Perhaps the newer medical schools in Nigeria, Malaysia, Fiji, and Brazil will rise to the challenge and investigate afresh such problems as subclinical infections, latency, the influence of environmental factors on clinical patterns, the significance of returning or persisting serological changes, and the nature and degree of cross-immunity.

Yaws was (and is again) a disease mainly affecting sparsely clothed children living in rural areas of high temperature and high humidity within the tropics. Infection is by direct inoculation of the causative organism, Sp pertenues, through the abraded skin, perhaps deposited by a sucking fly. After an incubation period of a few weeks the initial lesion ("the mother yaw") appears at the site of inoculation: this may be an exudative papilloma, or a group of dry papules, or a localised maculopapular rash.

Within a few weeks a more generalised rash consisting of scores of excrescences makes its appearance, each element being covered with a yellowish film replete with the organisms. The general health may be but little affected, but the picture of unrelied misery cannot be forgotten. During the next five years further polymorphic rashes appear from time to time—annular, circinate, serpiginous, or corymiform—interspersed with periods of quiescence. In warm, moist sites they tend to be condlomatous. The palmar and plantar skin may become hyperkeratotic and fissured, and infective lesions may arise in the fissures. In the long bones there may be osteitis and periostitis.12

After these periods of clinical activity the lesions usually resolve spontaneously. Next comes a silent phase before the appearance of late lesions, such as hyperkeratotic plaques, rupia-like or gummatous skin ulcerations, osteitis (sometime with the production of "sabre tibia"), destructive ulceration of the nose (gangosa), hypertrophic osteitis of the facial bones (goundou), and scarring and cicatricial contractions. Juxta-articular nodules,13 depigmentation of typical treponemal distribution,14 considerable hyperkeratosis of palms15 and soles ("crab yaws") are frequent sequels, with prepatellar bursitis and ganglion. When ainhum occurs in the young, framboesial plantar hyperkeratosis may be an aetiological factor.16 Many of these protean manifestations have their counterparts in other treponematoses, and their clinical differentiation is not usually helped by serological tests.17

The treatment of active yaws, early and late, was simplified18 when the old remedies (rubbing the ulcers with "bluestone" (copper sulphate) or intravenous arsenic and intramuscular bismuth subgallate or salicylate) gave place to a single intramuscular injection of 12 MU of penicillin G in oil gelled with 2% aluminium monostearate. This treatment cured the florid lesions of early yaws with dramatic rapidity and prevented relapse for at least two years. Where whole populations were considered to be contacts, half doses were given to all persons without lesions.

But all the early hopes of eradication founded because of inadequate facilities for effective follow-up, the potential infectivity of late lesions, and the lack of precision in the definition of radical cure.1 A single infectious relapse may become the index case of a localised epidemic of old-time florid yaws: such foci are now appearing in areas where eradication campaigns appeared to have been successful.

Granulocytopenia and septicaemia

Patients with severe granulocytopenia easily acquire Gram-negative septicaemia. This complication is justifiably feared: apart from fever the physical signs are few, but if it is treated early and appropriately it may rapidly progress to circulatory collapse and death.

Prevention might seem the best policy, but isolation and reversed barrier nursing have little to offer, since the organisms responsible are almost invariably endogenous. Sterilisation of the bowel with non-absorbable antibiotics probably delays the onset of infection and is widely practised,1 but even so many patients with severe granulocytopenia eventually become infected.

These infections progress so fast that there is no time to wait for results of bacteriological investigations, and treatment with antibiotics should be started as soon as specimens have been taken. Indeed many units dealing with patients with granulocytopenia recommend treatment of every fever of 38°C (or higher) that persists for more than two hours. Such a policy means that some transfusion or drug reactions will be treated inappropriately with antibiotics, which should be stopped as soon as infection is excluded.

The choice of antibiotics is empirical but not blind. The likely organisms are Escherichia coli, Klebsiella spp, or Pseudomonas aeruginosa. In patients with persistent granulocytopenia recovery is almost twice as likely if the organism is susceptible to two of the antibiotics administered rather than only one.2 Probably the most favoured regimen is gentamicin and carbenicillin. A system of bacteriological surveillance which provides information about the patients' own flora and local drug resistances will be a valuable guide to the use of the newer aminoglycosides tobramycin and amikacin. Cephalothin is indicated if infection with Klebsiella is suspected.3

One of the most important factors determining the chances of recovery is a spontaneous rise in the granulocyte count. Love et al2 found a recovery rate of 93%, in patients whose granulocyte counts rose by as little as 100 x 10^9/L over the first 14 days of treatment compared with only 55% in those in whom the count remained unchanged. These statistics suggest that white-cell transfusions might be life saving. Should white cells be as freely available as red cells and platelets? The answer is logistic. The daily turnover of granulocytes in a non-infected adult is 1.2 x 10^11, with the mature neutrophil spending on average six hours in the circulation.4 During infections the turnover is greatly increased. Even to replace the normal daily requirement would mean transfusing the granulocytes from 80 units of fresh donor blood. Given these figures, white-cell transfusions might be expected to have little practical value. Nevertheless, despite earlier controversy,5 controlled trials have shown that daily infusions of 2 x 10^10 granulocytes are effective in controlling Gram-negative septicaemias in patients with initial granulocyte counts of less than 500 x 10^9/L.4-8

Sufficient granulocytes can be obtained from a donor in about four hours using filtration leucapheresis or continuous-flow centrifugation. Discontinuous-flow centrifugation is somewhat less efficient. Granulocytes from any of these sources are equally effective, but those produced by filtration cause more transfusion reactions.6 To make granulocyte infusions available for every infection in which they might be beneficial would require a vast investment in both machinery and manpower. Furthermore, granulocytes are highly antigenic and share antigens with platelets. One controlled trial of prophylactic granulocyte transfusions in acute non-lymphocytic leukaemia showed no benefit over controls and a high incidence of alloimmunisation producing resistance to platelet transfusions.10 In theory such reactions could be avoided by the use of granulocytes matched for HLA compatibility, but this would create even greater logistic problems, far beyond present resources.

In practice most units, and especially those with the most experience of granulocyte transfusions, find that they are needed only rarely. They can be beneficial in patients with prolonged aplasia and inadequate response to initial antibiotics, and these patients should be identified as soon as possible; granulocyte transfusions are not necessary for the majority of patients, whose marrows may soon be expected to show signs of recovery.


Pancreatic transplantation

Treatment of insulin-dependent diabetes is meant not only to save life but also to achieve the best possible “control” of the blood glucose. Even with the best modern insulin regimens and new techniques of monitoring diabetic control, however, considerable fluctuations still occur in blood glucose concentrations. Better results can be obtained with continuous subcutaneous infusion of insulin,1 but both this technique and the use of the large and expensive artificial pancreas are still experimental. In theory, at least, the most effective solution to these problems should be pancreatic transplantation —last reviewed in 1976.2 Now a recent conference in California has been reported in a supplement of Diabetes.5