Filariasis in India

Over a third of the world's population who are at risk for lymphatic filarial infection live in India. There are 22 million carriers of microfilariae (mf) in India and a further 16 million have symptoms and signs of filariasis. Bancroftian filariasis due to *Wuchereria bancrofti* is the predominant type accounting for 98% of cases and is distributed widely in India. Malayan filariasis caused by *Brugia malayi* is limited to a few pockets of Kerala, Assam and Orissa, where more than 90 million people are at risk. Bancroftian filariasis is transmitted by *Culex quinquefasciatus* (a ubiquitous mosquito breeding in polluted water) while Malayan filariasis is transmitted by Monsonioid mosquitoes which breed in aquatic weeds (*Pistia, Eichhornia* and *Salvinia*).

The majority of mf carriers are asymptomatic and most patients suffering from chronic filariasis do not show mf on blood examination. The acute and chronic manifestations of the disease are somewhat different. In the acute stages, Bancroftian filariasis in males presents with acute epididymo-orchitis and funiculitis. These manifestations do not occur in Malayan filariasis. A common feature of both the acute and chronic stages is filarial fever with lymphadenitis with or without lymphangitis. In chronic Bancroftian filariasis, a hydrocoele often occurs in males but is uncommon in the Malayan form. Lymphoedema is the predominant sign of Malayan filariasis in both sexes.

Bancroftian filariasis occurs more commonly in males, but both sexes are equally afflicted with Malayan filariasis. Geographical variations in the clinical presentation of Bancroftian filariasis have been recorded. Recent studies on the natural history of the disease by clinical grading of lymphoedema indicate that the progression from its early stages to elephantiasis is faster in Bancroftian filariasis—about 9 years in Bancroftian and 14 years in Malayan filariasis.

Night blood smear examination still remains the only practical method for the definite diagnosis of mf carriers. The test, though simple, is not sensitive enough to detect low mf count carriers (an estimated 30% to 35% are missed). It also does not usually detect patients with chronic filariasis and occult filariasis (see also pp. 7-9). Membrane filtration, a more sensitive test, is not suitable for mass diagnosis as it requires venepuncture. To avoid night blood examination, the day-time diethylcarbamazine (DEC) provocative test has been used. An adult dose of 150 mg DEC and smear taken after 45 minutes to detect mf gives the best result. The mf density in the peripheral blood is about 30% lower following day-time DEC compared to night blood examination.

Immunodiagnostic tests have been developed for antibody and antigen detection. Several antigens both from homologous and heterologous sources derived from different stages and components of the parasite have been used for antibody detection. The passive haemagglutination test for antibody, and the ELISA for antigen in blood and urine and antibody detection have also been employed. However, immunodiagnostic tests even with the use of monoclonal antibodies pose problems of specificity due to cross-reactivity with other intestinal nematodes. Species-specific monoclonal antibodies for detection of Malayan filariasis antigen have been produced recently.
techniques particularly for detection of antigens in body fluids seem to be promising and need to be tested in the field. Recently developed DNA probes for Bancroftian and Malayan filariasis do not show any advantage over routine morphological diagnosis, since they require the presence of intact mf (no circulating parasite DNA has been detected in peripheral blood) and night blood examination. A skin test using **Dirofilaria immitis** adult antigens has not been found suitable for case detection and skin tests using larval and adult **Brugia malayi** antigens showed a high false positivity rate in persons with intestinal nematode worms.

Carriers of mf need to be treated with DEC (6 mg/kg/day for 12 days). Parasite clearance occurs in 80% to 85% of cases with a single course, but two or more courses are necessary for parasite clearance in the rest. Though DEC is primarily microfilaricidal, it is also known to have an action against the adult parasite. Both selective treatment of mf carriers and mass therapy of a target population are useful measures to reduce the parasite load in the community; the choice of method depends on the prevalence of disease and the size of the population. Low dose mass therapy by community members has been found useful in Indonesia. DEC-medicated salt has been used to control this disease, but there are certain practical constraints, as alternative sources of salt are preferred by the population. DEC produces side-effects which can affect the earning capacity of people in rural areas and this results in its lower acceptance. Ivermectin, a semi-synthetic macrolide antibiotic found useful in the treatment of Onchocerciasis, was recently tried in W. bancrofti. A single dose resulted in parasite clearance in 5 to 12 days. However, in most cases the parasite reappeared within 6 months. Most patients (98%) complained of fever and other side-effects. Clinical trials of this drug on B. malayi in south India are now in progress. Testing of several other compounds for their filaricidal activity has met with little success.

The exact cause of acute filarial fever episodes is not clear. Acute secondary infections particularly with streptococci have been suggested as a cause but a significant rise in antistreptolysin O titres has not been observed. Those harbouring a septic focus such as dental caries, fungal infections etc. suffer from more frequent attacks of fever, which makes treatment of the primary focus essential. Reinfection and immune reactions may also be the cause of filarial fever. The role of DEC in the management of filarial attacks is not clearly understood. Preliminary observations indicate that DEC aggravates acute manifestations and should be given within two weeks of the improvement of symptoms. Antibiotics, anti-inflammatory drugs and antihistamines along with antipyretics are useful in the acute stages. Repeat courses of DEC, however, are known to reduce the frequency of filarial fever attacks. Conservative management with these repeated courses and other supportive measures such as frusemide, heat therapy, the use of crepe bandages and elevation of the feet have been found to result in a reduction of lymphoedema in Malayan filariasis. The degree of reduction was 70% in early cases of lymphoedema and 36% in patients with elephantiasis. However, similar management in patients with Bancroftian filariasis resulted in only a 27% reduction. Some patients (19% with Malayan and 39% with Bancroftian filariasis) showed an increase in volume despite treatment. The reasons for the differing degrees of response are still not understood. Cases which do not respond to conservative management can be treated by one of several surgical procedures but the recurrence of oedema is a major problem. Lymphovenous anastomoses have been developed for the management of chronic lymphoedema and this method is promising as it has shown a 90% success rate. Recent advances in lymphoscintigraphy help locate the site and degree of blockage and may be useful in the management of these patients.

The control of filariasis has received a low priority in our national health policy. Though large populations exposed to the risk of infection live in rural areas,
the national programme covers the urban population. It should be possible to prevent this disease easily as (i) man is the only definitive host, (ii) DEC is an effective therapeutic agent, and (iii) vectors breed in confined habitats that can be controlled by integrated methods such as environmental management and chemotherapy.

REFERENCES

Growth Hormone and its Substitutes

Human cadaveric pituitary growth hormone, the first of its type, was initially used in clinical trials in children with classical growth hormone deficiency. The treatment was started only when the diagnosis of growth hormone deficiency was established by either a reduced spontaneous growth hormone secretion or a decreased secretion following various stimulation tests. Doubts were raised about the treatment in 1985 when Creutzfeldt-Jacob disease (CJD), a slow virus disease affecting the central nervous system, was detected in 4 patients in the USA and UK who had received this treatment. Later the product was banned in most countries following confirmation of a strong association between the transmission of the agent causing CJD and treatment with human pituitary growth hormone.

By the early 1980s recombinant DNA technology had revolutionized the understanding of and the ability to control the production of proteins. Efforts were made to produce synthetic growth hormone using a specific strain of *Escherichia coli* as a host and a vector plasmid containing the appropriate information. The first biosynthetic growth hormone thus produced was identical to pituitary growth hormone except for an additional methionine residue at the N-terminal. No toxic or mutagenic effects were detected, and fermentation and other procedures resulted in a highly purified preparation. Clinical studies in Japan, West Germany and other countries demonstrated that this preparation when administered subcutaneously or intramuscularly to patients with growth hormone deficiency produced a height velocity of about 8 cm per year in a dose of 0.5 IU per kg body weight per week. Another recombinant growth hormone without the methionine residue was also developed. Clinical trials showed that the gain in height velocity was comparable and the preparation was less antigenic than the methionyl growth hormone.