Leprosy: is the strategy wrong?

Authoritative opinion claims that there has been a failure to provide treatment for most of the world leprosy patients and to control the spread of the disease. But sulphones provide a cheap and practical form of treatment and also prevent transmission of leprosy, writes C. L. Crawford, of the Department of Anatomy and Embryology, University College, London.

IN 1873 the Norwegian Armauer Hansen found bacteria in the tissues of leprosy patients and thus established the infectious nature of the disease. Today the World Health Organisation (WHO) estimates there are 10.8 million people with the disease, of whom only about 18% are receiving any treatment. Although information is limited it also concludes (*Bull. Wld. Hlth. Org.*, **46**, 523; 1972) that there has not been any improvement in controlling the spread of the disease over the past five years. The British Leprosy Relief Association (LEPRA) claim that there are as many as 20 million patients. Browne and Davey, two of the most experienced leprologists, (writing this year in *Leprosy Review*), conclude that existing methods have failed to reduce the incidence of the disease, and Ambrose (*Nature*, **248**, 370; 1974) states that leprosy is increasing in South Asia.

Leprologists stress the unknown facts about the disease; the bacteria cannot be cultivated so a vaccine cannot be developed, and the mode of transmission and the incubation period are unknown. Faced with this lack of knowledge and the pessimism of authoritative opinion, the outlook seems hopeless both for success in preventing the spread of the disease and for the patient's chances of obtaining treatment. But the efficacy of the sulphone in providing a cheap and practical form of treatment and in prevention has been grossly neglected.

The difficulty in culturing *Mycobacterium leprae* could, in fact, be seen as a potential advantage in an attack on the disease. *Mycobacterium leprae* is confined to humans and must therefore exist outside the body only for very short periods. There is no known animal reservoir of infection or vector to spread the disease and transmission takes place only between humans. Probably only a proportion of leprosy patients are responsible for

Leprosy patients, Vadhavasalur, India. (Picture by The Leprosy Mission).

transmitting the disease. This multi-bacillary or lepromatous group may be as low as 10% in some parts of the world and constitutes the reservoir of infection. Also only one in ten of the exposed population, at the most, acquire the disease even in the absence of control measures. If transmission could be interrupted in susceptible people, the disease would decline, as indeed it did in Norway in the last century by a policy of segregation. Also, once eradicated from any country it has never returned. A vaccine is not essential for eradication as the disease has already disappeared from many countries. The transmission of yaws has been successfully interrupted without the bacteria being cultivated or a vaccine developed, by treating patients with penicillin.

The sulphones are the main drugs used in the treatment of leprosy. The experimental multiplication of *M. leprae* in mice is inhibited if *M. leprae* from patients who have received more

than three months of sulphone treatment are injected, suggesting that such bacteria are no longer viable. It may thus be that patients with leprosy are no longer infectious after a few months of treatment, and sulphones may have an important role in preventing the spread of the disease as well as in treatment. Sulphones have been used for the past 25 years and it is essential to determine if they have had any effect in preventing transmission of leprosy.

Any successful preventative measure against leprosy will be shown by a fall in the number of new cases or in the incidence rate; the total number of cases (or 'prevalence' rate) will change much more slowly, because of the inclusion of patients who are already crippled. If the majority are of this type, the prevalence may hardly change at all over a period of years, even though transmission may have been completely interrupted, because leprosy patients can live a long time.

The life expectancy of untreated lepromatous leprosy in Hansen's time was about 10 years; now, with sulphones, it is the same as in the general population. Thus, the 'prevalence' may actually rise in a community treated with sulphones. It is therefore very surprising that the WHO should attempt to draw conclusions about the spread of the disease from the figure of 10.8 million, which is a prevalence estimate. No attempt has been made to obtain information about incidence rates, and even the estimate of the total number of cases is based on very questionable assumptions. Of the 10.8 million, 2.5 million are actually registered; 0.5 million of these are cured or arrested. In each country, to make allowance for unknown cases, a percentage of the registered cases was calculated depending on the efficiency of case finding. This varied between 25% and 300% of the registered cases. This total was added to the 2.5 million registered cases to make up the total of 10.8 million. There must, however, be doubts about the value of figures arrived in such a haphazard way. Where accurate figures of leprosy patients are available, as in Rumania, Cyprus and Libya, it has been shown that the WHO has exaggerated the true figure by from 10 to 50 times. In commenting on the WHO errors in the Cyprus figures, the Cyprus Director-General of Health emphasised that all the patients were old ones and no new cases had occurred in 1970, thus confirming the danger of drawing conclusions about the spread of the disease from prevalence figures. Countries which do have information about incidence rates, such as Okinawa, Hong Kong, New Guinea, Japan and Solomon Islands, Rumania and Cyprus, have all shown a decline. Although their figures will not be completely accurate, they are preferable to the WHO method of assessing the problem.

Most of the countries mentioned have a small leprosy problem. The most accurate information about incidence rates in highly endemic areas has come about in the following way. As no leprosy vaccine is available, BCG vaccine against the similar tubercle bacillus has been used to determine whether it has a protective effect against leprosy. Trials have taken place in Uganda, Burma and New Guinea under the auspices of various research councils, and two trials have also been carried out in India using sulphones for their protective or chemoprophylactic effect by giving them to healthy people. All the trials were controlled by including a group similar in age range which was not protected with BCG or sulphones. At the start of trials the population was sur-

veyed, the leprosy cases were excluded and then new cases were recorded at repeated intervals of between one and two years. Thus, an annual incidence rate can be deduced and the control group will reveal the trend of the disease in these areas, which were deliberately chosen because of the serious leprosy problem.

The results of the BCG trial in Uganda and the two chemoprophylactic trials in India are shown in Tables 1 and 2. All the control groups shows a striking decline in the incidence of leprosy. These two trials took place in communities where sulphones are available to treat patients and, in contrast, the incidence of leprosy in New Guinea did not decline, staying constant at 6 per 1,000 per year from 1964 to 1969; sulphones were not available in this area until late in 1967. Therefore, the most likely explanation of the declining incidence rates is that sulphones given to leprosy patients kill *M. leprae* in a short enough time to interrupt transmission of the disease, thus confirming the experimental findings. The figures for new lepromatous cases are even more dramatic. In two of the areas not a single case was recorded in the controls and in the third the number fell from 11 to 2. Thus, the reservoir of infection has been virtually removed and this makes prospects of eradication bright. The chemotherapeutic and BCG trials were started over ten years ago yet delay in publishing the results fully and in coming to a conclusion about their efficacy has meant that a really effective method of prevention and eradication with sulphones is not being put into practice. If there is still any doubt about the conclusions to be drawn from these trials, these areas

could be resurveyed and the incidence rates recorded in the same age groups as those of ten years ago. There is other evidence based on outpatient incidence rates from two areas of India, Zambia and Uganda and from prevalence rates over a long period in Northern Nigeria, and former French Equatorial Africa (Gabon, Chad, Central African Republic and Congo-Brazzaville). All these have been summarised with my conclusions of the BCG and chemoprophylactic trials previously (*Lancet*, ii 1375, 1971; i, 1186, 1972; *Trop. Doct.*, 3, 137, 1973). Also there is recent evidence of a decline in incidence in Burma and Thailand. Yet Ambrose, Davey and Browne have not mentioned these nor produced any quantitative information to support their own case.

If chemotherapy with sulphones does prevent the spread of the disease then treatment and prevention can be achieved by the same measure, the administration of the drugs to leprosy patients, especially those who are bacteriologically positive. Also by offering to the patients an incentive to attend for treatment, the affected group in the community is automatically brought under supervision, an immense practical advantage over other methods of prevention such as BCG and chemoprophylaxis, which depend on finding healthy contacts of patients. The main sulphone is dapsone which is extremely cheap, costing only 10p a year for each patient, and is easily administered by mouth once a week. Drug resistance is very rare, of the order of 3 per 5,000 lepromatous patients, and it has a wide margin of safety for toxic effects. Thus, mass treatment is practical and economically feasible if given in villages by

Table 1 Annual incidence of leprosy per 1,000 in control and BCG groups in the BCG leprosy trial in Uganda

	Population examined	Control No. with leprosy	Annual incidence	Population examined	Protected with BCG No. with leprosy	Annual incidence
1964	8,071	89	5.5	8,091	18	1.1
1966	9,036	54	3.0	9,052	1	0.05
1968	9,036	31	1.7	9,052	8	0.45

The incidence rate has been halved to give the annual incidence as there is an interval of two years between each survey.

Table 2 Annual incidence of leprosy per 1,000 in Andhra Pradesh, India, in controls and chemoprophylactic groups: A, under 25 years of age; B, over 25 years of age

A						
	Population examined	Controls No. with leprosy	Annual incidence	Population examined	Protected with Sulphones (Dapsone) No. with leprosy	Annual incidence
1965	11,270	54	4.79	11,452	29	2.53
1966	12,124	65	5.36	11,900	14	1.17
1967	12,116	37	3.01	12,157	9	0.74
1968	12,931	36	2.78	12,754	3	0.24
B						
	Population examined	Controls No. with leprosy	Annual incidence	Population examined	Protected with Sulphones (Dapsone) No. with leprosy	Annual incidence
1965	8,104	90	11.10	7,851	91	11.59
1966	7,758	67	8.63	7,758	62	7.95
1967	7,337	38	5.17	7,511	45	5.9
1968	7,311	29	3.9	7,282	34	4.6