Drugs against leprosy

Following the disappointing results obtained with dapsone monotherapy, a concerted effort is now being made in India to introduce multidrug therapy in a programme aimed at the eradication of leprosy. Favourable reports have been received from the districts where it has so far been possible to adopt this approach, although long-term follow-up will be necessary before it can be proclaimed a success.

In India about 400 million people live in areas where leprosy is endemic and are therefore exposed to the risk of infection. Prevalence rates of at least 10 per 1000 occur in 76 districts, while in 125 the rate is 5-9 per 1000. The estimated case load is 3 950 000, of which 20% are multibacillary patients. The proportion of deformed patients is about 15% and that of affected children is about the same. There are large variations in prevalence, not only between states but also between districts.

There has been a substantial increase in control activities since the National Leprosy Control Programme was launched in 1954. Good results have been obtained in selected areas but overall the Programme has failed to produce an impact on the incidence of the disease, mainly owing to low coverage and poor compliance of patients on dapsone monotherapy. On 31 March 1986 there were 3 294 000 registered cases. In recent times approximately 500 000 new cases have been detected each year. Currently, over 400 000 cases are released from control annually; this figure is expected to increase greatly as multidrug therapy expands.

The aims

Today's National Leprosy Eradication Programme aims at breaking the chain of disease transmission by providing continuous treatment to all cases as close to their homes as possible, and by educating patients, their families, and the community about leprosy.

Multidrug therapy is the sheet anchor of the eradication programme. The twin objectives are to interrupt transmission and to cure patients. It is also desired to prevent the emergence of drug-resistant strains of the causative organism, *Mycobacterium leprae*. Until recently, virtually the only drug treatment was dapsone monotherapy. This led to a dangerous epidemiological situation in which increasing numbers of patients relapsed with dapsone-resistant leprosy and the resistant strains spread to the contacts of the affected people.

The drugs

The revised strategy recognizes that the simultaneous administration of several different antibacterial drugs will prevent the selection of drug-resistant mutants. The greatest risk of developing resistance exists among multibacillary patients, who

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constitute almost the sole reservoir of infection.

The drug regimens followed for multibacillary (skin smear positive) and paucibacillary (skin smear negative) leprosy patients have been recommended by a working group set up by the government in 1982 and represent a slight modification of those recommended by the World Health Organization. For multibacillary leprosy an initial intensive phase of supervised treatment is given for two weeks with 600 mg rifampicin, 100 mg clofazimine, and 100 mg dapsone daily, followed by monthly supervised doses of 600 mg rifampicin, 300 mg clofazimine, and 100 mg dapsone as well as daily self-administration of 50 mg clofazimine and 100 mg dapsone. The minimum duration of treatment is two years; most patients complete treatment in 3–4 years. For paucibacillary leprosy the treatment lasts only six months and consists of 600 mg rifampicin monthly under supervision and self-administration of 100 mg dapsone daily. The cost of drugs for complications. This vertical approach should not be considered a denial of primary care as the specialized personnel are able to reach the community at the periphery. The decision to have specialized services for leprosy control was taken in view of the intensity of the disease and the need to obtain results quickly and efficiently. However, as the intensity of the problem declines there will be a clear need to integrate multidrug therapy and other aspects of control into the general health services.

Multidrug therapy comprises preparatory, intensive, and maintenance phases. Before being selected for coverage, a district must have, apart from high leprosy endemicity, an adequate infrastructure to deal with leprosy for the entire population, trained personnel who will be able to give effective supervision, and an established base of leprosy control activities ensuring that a minimum of 80% of the estimated cases are identified. In view of financial and infrastructural constraints it is planned to extend multidrug therapy to all the remaining areas of high endemicity in a phased manner during the period 1987–95.

Multidrug therapy was started in two districts in 1982 and has now been extended to 16 districts with a population of 44 million. Of the 530 000 cases dealt with, 17.4% have been multibacillary. Support from the Swedish International Development Agency and other external agencies generally covers additional drug costs, increased mobility, and performance-related cash incentives. Of the 16 districts, five have completed the intensive phase and entered the maintenance phase. During the intensive phase all the leprosy cases on record received multidrug therapy. These five districts account for a population of 9 562 000 and a case load of 219 000. In the

![Multidrug therapy is extremely well tolerated by patients.](image)

Multidrug therapy is extremely well tolerated by patients.

treating a multibacillary patient is US$ 22 for the first year and $ 19 for each of the following years. For paucibacillary leprosy the entire drug cost is less than $ 3.

**Delivery**

Multidrug therapy is essentially carried out by specialized personnel at the primary and referral levels, with the district as the operational unit. Temporary hospitalization facilities are available for the treatment of
remaining districts, multidrug therapy has been in progress for periods ranging from 9 months to 3 years. It has been well accepted by patients, tolerance is good, side-effects are minimal, and the regularity of treatment is excellent.

Encouraging results

As can be seen in the table, in four of the five districts where the intensive phase has been completed there has been a large drop in prevalence rates. Even in the fifth district (Purulia) there has been a substantial drop. Such reductions, ranging from 39% to 80%, were not generally possible under dapsone therapy. On average, 67.2% of registered cases have been on multidrug therapy in the five districts. However, if the district of Purulia is excluded on the ground that the introduction of multidrug therapy among paucibacillary patients was delayed here for operational reasons, coverage rises to 83.1% of registered cases.

During the maintenance period the treatment regimens that were commenced in the intensive phase will continue until the course is completed. New leprosy patients detected during the maintenance period will be put on the appropriate regimen. Cured patients are subjected to annual surveillance for three years following paucibacillary leprosy and for five years after multibacillary leprosy.

The annual rate of detection of new cases in 1986 declined in four districts that had completed the intensive phase by the end of 1985; deformity rates among new cases declined in three of the districts. However, the proportions of multibacillary cases and of children aged 0–14 years among the new cases in 1986 did not differ markedly from those of the two previous years. Up to December 1986 the relapse rates among 16,929 multibacillary and 46,251 paucibacillary cases in which multidrug therapy was successfully completed were 0.06% and 0.07% respectively.

Mammoth task ahead

Even though multidrug therapy extends to only 8% of the cases in the country, the programme is the largest of its kind in the world. With a view to curing all known cases by the turn of the century, it is planned to have introduced multidrug therapy in all 76 districts with prevalences of 10 or more per 1000 by 1990. This will cover about 60% of the cases and is expected to cost approximately US$ 38 million over a period of five years, to be paid largely out of the national budget. In addition, the creation and maintenance of the infrastructure for the leprosy programme costs about $ 31 million every year. It is envisaged that in the following five years all the 125 districts where the prevalence rate is 5–9 per 1000 will also come under multidrug therapy, thus extending coverage to 90% of the cases in the country. The eradication programme has recognized, at least for the initial years, a need for specialized personnel to deal with leprosy in districts of high and moderate endemicity, in view of the severity of the problem and the
importance of properly implementing multidrug therapy.

In districts of low endemicity, where leprosy care is provided by the general health care services, treatment is still based on dapsone monotherapy. However, five such districts have been earmarked for the introduction of timetable and clear goals, and the advantage of administrative flexibility. Resource mobilization is not considered a constraint and there is excellent cooperation between the state governments and the national government. The state governments have laid down an adequate base of infrastructural facilities with assistance from New Delhi.

The programme has received enthusiastic acceptance not only from health personnel but also from the public, as indicated by increased self-reporting of cases in districts where multidrug therapy has been adopted.

Multidrug therapy is extremely well tolerated by patients and the incidence of side-effects is minimal. Attendance at clinics averages 90% as against less than 50% during dapsone monotherapy. It would be premature to comment on the long-term efficacy of multidrug therapy, but the observations made so far by medical officers and patients indicate that relapse following cessation of therapy is quite uncommon. This has also emerged in field studies where patients have been closely followed up. However, further long-term follow-up is needed to confirm these observations.

One of the weaknesses of the eradication programme is that the laboratory services are often inadequate for carrying out the skin smear examination. Laboratory support is vital for the classification of cases as multibacillary or paucibacillary and for deciding when treatment for multibacillary patients should be discontinued. However, misclassification is not of such a degree that it constitutes a serious impediment to the overall effectiveness of multidrug therapy.

The training of personnel has been satisfactory but a clearer understanding by staff of the rationale behind multidrug therapy would strengthen the programme.
Improved medical and referral services for the treatment of reactions and the prevention of deformities through adequate utilization of temporary hospitalization facilities would give patients greater confidence in the value of this therapy.

The real test of multidrug therapy will come when, after most cases have been cured, a specialized service will no longer be sustainable and it will be necessary to integrate the therapy into the general health care system. Preparation for this step should begin soon.

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A combination of favourable factors, including a strong political commitment to deal with leprosy, the availability of multidrug therapy, and an infrastructure capable of delivering the technology, has made the eradication of leprosy in India a distinct possibility in the foreseeable future.

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**Facts about leprosy**

- Leprosy occurs in most parts of Africa, Asia, and Latin America, about 1600 million people being exposed to the disease.
- The World Health Organization estimates that there are 10–12 million leprosy cases in the world, at least a quarter of them having deformities.
- Leprosy is a far more serious problem than the number of cases implies since disfigurement caused by the disease leads to serious psychological, economic and social difficulties for the patients, particularly as a result of the stigma attached to it in many societies.
- For a long time leprosy was treated with dapsone but in recent years the causative bacterium has developed resistance to the drug. Furthermore, dapsone had to be administered for very long periods, and this led to poor compliance by patients.
- Research on the chemotherapy of leprosy has resulted in the technological breakthrough of multidrug therapy, making treatment far more effective and capable of fully combating the resistance problem.
- Although multidrug therapy requires expensive drugs, the treatment periods are much shorter than those needed when dapsone was used.
- For benign paucibacillary leprosy, multidrug therapy continues for six months, and for malignant multifocal leprosy it is given for a minimum of two years. The costs per patient are US $1.60 for the benign condition and $23.20 for each year of treatment of the malignant disease.
- Well-organized health services with appropriately trained personnel are essential when multidrug therapy is used.
- Most countries with a leprosy problem have accepted the principle of multidrug therapy; however, the pace at which it is introduced is rather slow because of the costs and the inadequacy of health services.
- In recent years great progress has been made in the development of a vaccine, currently undergoing field trials in Malawi and Venezuela.