such studies will have to be based on newly arising clinical cases.
2. The main objective of work of the sort proposed is the identification of risk factors whose modification or use may contribute to the control of the disease.
3. The factors studied should cover all the attributes likely to be relevant to the onset of leprosy in the groups under study, i.e., probably need to include a wider range of constitutional and environmental variables, including information on intercurrent diseases, than has generally been the case so far. Because the incidence of leprosy is low, projects of this sort require very large numbers and long follow-up periods, which need to be related to the endemicity of leprosy in the study areas.
4. Strict attention must be paid to the development and use of standardized criteria and procedures so that the results of different studies may usefully be compared.
5. Clear distinctions must be drawn between case-finding (the detection of established as well as new cases) and incidence, in order to avoid possible confusion (especially in the early stages of a prospective study) as to whether incidence is really changing or not.
6. In addition to observational studies, opportunities afforded by on-going field surveys for epidemiometric model building and computer simulations of onset and natural history should be utilized.
7. Population-based studies of the sort suggested are likely to pay dividends in other ways, by providing sampling frames for the collection of biological material, the conduct of clinical trials, and for a range of other purposes.
8. Field research programs should take full account of the medical requirements of all diagnosed leprosy patients.
9. The need for large study populations presents problems, especially in countries where skilled and semiskilled manpower and other resources are limited. However, the experiences and achievements of groups who have attempted large scale studies make it clear that these can be carried out. In addition, individual investigators or small teams who can carry out well-planned epidemiological studies of particular problems, especially where exceptional conditions or opportunities exist, should be encouraged.

INTERNATIONAL COORDINATION; VOLUNTARY AGENCIES

The role that international bodies such as the World Health Organization and voluntary agencies can play in contributing to the general coordination and comparability of large-scale, long-duration studies and of smaller undertakings requires special emphasis.

COMMITTEE 6: THERAPY

Members

J. Languillon (Chairman)
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"It has been said that it is now a practical proposition to control leprosy in this generation and eradicate it during the next. All that has to be done is to ensure that an adequate number of the correct pills pass down the throat of patients for a significant length of time" (13).

TREATMENT OF UNCOMPLICATED LEPROSY

Diaminodiphenylsulfone (DDS). The parent sulfone, DDS, continues to hold sway as the drug of choice in the management of uncomplicated leprosy; its low cost and the infrequency of the emergence of sulfone re-
sistant cases, when given in conventional
doses, are its special features. Its slow bac-
teriostatic action and the consequent
necessity to administer it over long periods
of time and its inability to quickly clear the
body of bacilli are some of its inherent
drawbacks.
Under DDS therapy, even after the
complete disintegration of bacilli in the
skin, intact bacilli have been reported to be
still present in smooth muscle and superfi-
cially located striated muscle (1), liver,
bone marrow and lymph nodes. This may
perhaps explain why relapses tend to occur
even while the patient continues on the
drug.
Unanimity has not been reached with re-
gard to the optimum effective dose of
DDS, frequency of administration of the
drug, its relationship to the occurrence of
reactive states and continuation of treat-
ment after attainment of the inactive state,
but the committee recommends treatment
of lepromatous cases for life.
Other drugs. Less effective bacteriostatic
agents such as thiambutosine, streptomycin
and thiosemicarbazone are used less fre-
quently in the treatment of leprosy.
Long-acting sulfonamides. These have
the advantage of weekly administration by
mouth. Some leprologists claim to have ob-
tained good results with these drugs par-
ticularly in tuberculoid forms of the disease
and its complicating neuritis. However,
since serious and even fatal complications
have followed the use of these drugs in the
treatment of other diseases, the drugs
should be used with caution in mass leprosy
campaigns.
Clofazimine. A notable advance in the
therapy of leprosy was the demonstration of
the activity of clofazimine against M.
leprae. The drug has bacteriostatic as well
as anti-inflammatory properties.

The initial reports of Browne bearing out
the anti-inflammatory properties of clo-
fozimine (\textsuperscript{1}) were followed by the demonstra-
tion of the antmycobacterial activity by
Petit et al.\textsuperscript{(2)} in the human, and by Shepard
\textsuperscript{(3)} in the mouse foot pad. The extensive
clinical and experimental studies of Ross
and his colleagues established the efficacy
of clofazimine in sulfone-resistant cases.
Clofazimine has established its value in the
treatment of lepromatous leprosy but its
high cost and the easy availability of the
safe, effective and cheap DDS militate
against its use in the treatment of uncom-
pli cated lepromatous leprosy.
Diacetildiaminodiphenylsulfone (DADDS).
An initial short-term trial with this drug in
the Philippines \textsuperscript{(4)} and a subsequent lon-
gitudinal clinical trial in New Guinea \textsuperscript{(5)}
and Micronesia \textsuperscript{(6)} have yielded satisfac-
tory results. Although the initial reports re-
garding scheduled therapy in underde-
veloped areas are encouraging, the possibil-
ity of the emergence of sulfone resistance,
ocurrence of relapses and the possible
danger that this preparation may perpetuate
a reactive state in cases in which the drug
has triggered such a state have to be borne
in mind.
Rifampicin. The newest entrant into the
therapy of leprosy is a very potent antibio-
tic. Rees and his colleagues, after establish-
ing its efficacy in mouse foot pad infection
with M. leprae, used the drug in active and
sulfone-resistant lepromatous cases \textsuperscript{(7)} and
found it effective. It is expected that the
rapid killing of M. leprae will prevent the
slow release of intracellular antigens of M.
leprae and thus eliminate or markedly re-
duce the incidence of complications of im-
munocomplex deposition such as RNL. Al-
though no toxic effects have been reported
by these workers, there have been conflict-
ing reports about its hepatotoxicity and the
occurrence of thrombocytopenia \textsuperscript{(8)}. In
view of its high cost and limited availabil-
ity, it would be wise to restrict its use to
selected cases.

\textbf{COMBINED THERAPY}
Concurrent administration of drugs such as
thiambutosine, long-acting sulfonamide,
thiosemicarbazone, clofazimine and rifam-
picin along with DDS have been tried in the
treatment of leprosy with a view to obtain-
ing a synergistic effect and also to prevent
the development of sulfone resistance. The
results of the trials are not uniform—some
found the combined treatment better than
DDS alone, while others did not notice any
substantial difference.

\textbf{TREATMENT OF COMPLICATIONS
ASSOCIATED WITH LEPROSY
Reactions in leprosy.} With the advent of
sulfone therapy, the incidence of the reac-
tive states has been on the increase with the manifestations becoming more severe and serious.

The first major breakthrough in the management of reactive states in lepromatous leprosy was the introduction of corticosteroids (1). Although this drug dramatically relieves the agony of severe reactions, the attendant undesirable side effects and drug dependence pose serious therapeutic problems.

The indication for the use of corticosteroids in the management of the distressing complications associated with leprosy has declined with the introduction of thalidomide (2). The effectiveness of thalidomide in controlling the acute exacerbations in lepromatous leprosy has been confirmed. In dimorphous and RTL reactions, it is reported to be much less effective. The major drawback of this drug is its teratogenic effect when administered to pregnant women.

While the consensus of opinion among workers is that the drug produces a spectacular effect in acute lepra reaction, there is no unanimity regarding the effect of the drug in neuritis, ocular and joint manifestations. In many instances these complications respond more readily to corticosteroid therapy, possibly because of its more generalized anti-inflammatory effect.

In recurrent lepra reaction, a maintenance dose of 50 mg to 100 mg/day of thalidomide is reported to keep the reaction under control. Further experience with the drug has shown that under its protective cover, steroid-dependent cases can be weaned from steroids and sulfone-sensitive cases continued on treatment with DDS.

With Browne’s report of a possible anti-inflammatory action of clofazimine in lepromatous leprosy, a new era of hope opened up for lepromatous patients who were subjects of recurrent necrotizing reaction. The controlled clinical trials of Karat et al (3) confirmed the beneficial effects of the drug in lepra reaction. Similar reports have also appeared from Hastings, Warren and Trautman and many others. However, the beneficial effect of clofazimine takes as long as 8-12 weeks and sometimes high dosages, to become manifest and hence in severe cases with necrotizing lesions it will be necessary to combine clofazimine with corticosteroids or thalidomide until the acute phase is controlled. The significant improvements in the general health of these severely ill patients have been well documented.

While it is not effective in quickly controlling the acute reactive states, clofazimine has been observed to suppress not only the recurrent reactive episodes, but also permits withdrawal of steroid in steroid-dependent cases. Also it increases a tolerance to DDS in sulfone-sensitive cases while simultaneously exerting a beneficial effect on the disease process. Long-term studies are necessary to determine whether once the reactive states are controlled and the patient is able to take DDS in adequate doses, clofazimine can be withdrawn. It is a matter for serious consideration whether this drug could be safely used in cases of recurrent severe lepra reaction with overt renal involvement.

SULFONE RESISTANCE

The occurrence of drug resistance, one of the anticipated outcomes of chemotherapy, has now been well established in lepromatous cases (4) on DDS therapy. Inadequate dosage and irregular treatment appear to be contributing factors. This condition poses serious therapeutic problems. Clofazimine and rifampicin either alone or in combination with DDS (or other drugs such as thiambutoxime and ethionamide) have been found to be effective in the management of these cases. However, emphasis should be laid on the prevention of this clinical state by adequate DDS therapy.

CHEMOPROPHYLAXIS IN LEPROSY

Chemoprophylaxis using DDS orally (5) and DADDS (6) has been found to yield satisfactory results. The value of chemoprophylaxis in the prevention of the development of lepromatous leprosy, its duration, the optimum dose and the frequency of administration are yet to be determined.

REFERENCES

2. Karat, A. B. A., Jeevanrajan, A.
Despite substantial and sometimes even striking gains in many fields of leprology, progress in leprosy control has not kept pace—mainly because of the present unavailability of an ideal drug or specific vaccine. Control continues to focus on the patient or those more prone to develop leprosy. The population at higher risk is known, but the means to protect it are not yet available or still under study, and active drugs are badly needed to make a greater impact on the load of infectiousness. Hopefully, the preparation of a specific vaccine and/or the obtaining of favorable results in chemoprophylaxis can make primary prevention possible. The prevalence and duration of leprosy, plus its unique characteristics and socio-economic implications, call for special priority in public health programs and in research.

Because there have been no major breakthroughs necessitating special changes in the guidelines and methodology of leprosy control, the relevant reports prepared by the Committee of Leprosy Control (Rio, 1963) and by the WHO Expert Committee on Leprosy (1966 and 1970) are generally valid today. Therefore our attention will be focused only on certain aspects of control which need more emphasis or represent an addition to the previous guidelines.

There are definite indications that where