EDITORIAL

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CHEMOTHERAPY OF LEPROSY

Over the last decade or so chemotherapy of leprosy has undergone a traumatic experience. With the introduction of sulphones in the treatment of leprosy it was assumed that control and eradication of leprosy was perhaps round the corner, so long as one could ensure administration of sufficient amount of sulphones to all the leprosy patients. The relative non-toxicity, reasonable efficacy and low price of the sulphones did nothing to change this impression. For almost three decades, therefore, sulphones continued to hold sway as the drug of choice in the management of all forms of leprosy. Until a few years, the only disconcerting feature was the persistence of degenerate, perhaps nonviable, bacilli in the skin. With the passage of time it also became apparent that while bacilli may have disappeared from the skin and the mucous membranes viable, drug-sensitive, bacilli were persisting in different parts of the body such as the skeletal muscles, the dartos, the nerves and the lymphnodes; and relapses in lepromatous form of leprosy even after several years of treatment could be ascribed to the persistence of these bacilli. The most serious set back to the adequacy of sulphone treatment was the progressive emergence of drug-resistant strains in proportions varying from 3% to 20% from different parts of the world which highlighted the need for supplementation or substitution of sulphone therapy.

In the past few years several groups of workers met at different forums such as the W.H.O. meetings, the International Leprosy Congresses, the "Heathrow" meeting to review the whole question of chemotherapy in leprosy. The following points seem to emerge and are being highlighted.

Sulphone :

The parent compound DDS would still need to be given in all except the sulphone resistant patient. There is no question that earlier recommended dosages of 6–10 mg/kg/week ought to be given in full, that there is no need of a "build up," that the dosage has to be administered daily and the practice of periodically interrupting the drug therapy need to be abandoned in an attempt that any further emergence of resistant strains could be prevented. The practice of discontinuing therapy during reactional states, may also have to be given up while measures to control the reactions are being undertaken.

Conventional oral therapy could profitably be supplemented with acedapsone so that even unintentional interruption in therapy would ensure a drug level higher than MIC – under all circumstances.

Based on a status paper presented at a meeting of the Scientific Working Group on Leprosy of the ICMR.

Depending on the form of leprosy the treatment would require to be given for upto patients' life time. In the bacilliferous forms, BL/LL, a combination with other antileprosy drugs seems imperative. The choice for the combination therapy seems to be between rifampicin, clofazimine, thiacetazone, ethionamide and prothionamide. Important considerations in choosing one or other of these drugs are serum concentration/M.I.C. ratio, the cost effectiveness, and the problem of the drug interaction or toxicity.

The problem of drug interaction will preclude the combination of thiacetazone and one of the thionamides while the other drugs can be given in combination. Even though rifampicin tends to lower the serum concentration of dapsone, this does not seriously interfere with the therapeutic effectiveness of the drug.

Rifampicin :

This semisynthetic antibiotic is perhaps the most potent chemotherapeutic agent available in the treatment of leprosy. The morphologic index (MI) seems to come down within a few weeks even when a single large dose has been administered; 5-10 mg/kg body weight seems to be an effective daily dosage. The drug is bactericidal, diffuses readily into nerves and muscles and toxic reactions are uncommon particularly when given in continuous regimes. Liver damage can be serious and the drug should, therefore, be used with caution in alcoholics and those with pre-existing liver damage. With intermittent dosage schedules the toxic effects are more severe and more frequent having been reported to occur in 20-30% of patients with tuberculosis treated with this durg. Five toxicity syndromes have been described-namely 'influenzal', abdominal, respiratory, shock and purpuric. Acute renal failure has also been ascribed to intermittent rifampicin therapy. The most serious limiting factor in case of rifampicin is the cost and therefore different short term therapeutic regimes have been advocated. In our set-up it would seem that rifampicin either cannot be used at all or only a single large dose will have to be employed in combination with sulphones or a drug other than rifampicin would have to be selected.

Clofazimine :

This fat-soluble iminophenazine dye tends to get concentrated preferentially in the lepromatous leprosy lesions. Its bacteriostatic activity is inferior to rifampicin and equivalent to that of sulphones, but the drug has a distinct advantage in being anti-inflammatory at the same time, so that clofazimine can be used in the treatment of reactions also. Since the drug is preferentially concentrated in the tissue, serum concentrations seem to have little relevance and MIC is, therefore, not easy to determine. The mode of action is unclear. The chief handicaps with clofazimine have been the peculiar, often unacceptable, red discoloration of the skin and the high cost factor.

In combination therapy, 100 or even 50 mgm a day would seem to be an adequate dose. With this dosage, the toxicity is minimum and the drug is well accepted. The more serious side effects such as gastrointestinal toxicity have been reported only with prolonged treatment with higher dosages such as 200-300 mg a day, employed in the treatment of reactions.

Thiacetazone :

Thiacetazone is a synthetic compound and possesses an antibacterial activity inferior to clofazimine and dapsone. It also has the disadvantage of cross-reacting with thionamides but has a distinct advantage in being a very cheap drug that can be used in combination with sulphones. In our experience toxic

epidermal necrolysis, at times fatal, has been seen as a result of thiosemicarbazone administration in patients with tuberculosis. We are in the process of adopting this as a second line drug for the treatment of leprosy.

Thionamides

Ethionamide and prothionamide are good bactericidal drugs for M. leprae. Prothionamide is better because of less toxicity. These drugs are related to INH but have no cross resistance to it. In patients who are not given thiosemicarbazone, this could be an effective alternative combination drug in the treatment of leprosy.

The other antitubercular drugs have not been of tremendous value in the treatment of leprosy. Under our own circumstances it would seem that a combination of oral sulphones and an additional injection of acedapsone together with thiosemicarbazone would be feasible and practical for this country and perhaps in many other countries of African and South American continents. Because of its serious toxicity in South East Asia region thiosemicarbazone is not going to be accepted in other countries of Asia. Rifampicin and clofazamine despite their therapeutic superiority over thiosemicarbazone may seem unpracticable because of the cost.

The days of monotherapy with sulphones in the treatment of multibacillary leprosy are over. The need of the hour is to prevent emergence of resistant strains (a) by dual therapy and (b) by giving a single large dose of rifampicin to patients who have been on monotherapy for a long time. Early detection of resistant strains and institution of non-sulphone dual therapy in such patients would be imperative. We will have to act fast. I hope it would not be too late too soon!

L. K. Bhutani, M.D.,
New Delhi

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— *Managing Editor*