Letter to the Editor

Madam,

It has been reported that during second quarterly meeting of IADVL, Kerala branch which was held at Kottayam on 12th December 1982, "all the participants warned the danger of developed mycobacterial resistance" for rifampicin pulse-therapy in leprosy and concluded that it should not be followed in "our" patients (IADVL Journal 1982 Vol. 48 No. 6). I would like to clarify this point as this has very important bearing on our leprosy control programme which are already facing the two most important problems like resistance and persistence in a mycobacterial population especially in multibacillary leprosy cases by using dapsone as a monotherapy. It is well known that dapsone resistance in leprosy is due to genetic mutants which are already present in an untreated multibacillary case which are already resistant to dapsone, rifampicin, clofazimine, ethionamide, prothionamide and any other drugs which are effective on M. Leprae. If any of these drugs are used alone, these emergence of resistant strains to that drug is expected. This phenomena is not inductive but selective. The present recommendation of WHO as well as Indian Association of Leprologists * to use multidrug therapy under supervision aims at (1) reducing pool of infection in the community, (2) treating already existing dapsone resistant cases, (3) preventing emergence of resistant strains, (4) reducing total period of treatment for better compliance. Rifampicin being a strong bactericidal drug and known to kill large number of bacilli in a single dose of 600 mg, a minimum dose can be administered under supervision once a month even under most difficult situations. When this is administered with two other drugs (even prothionamide/ethionamide may also be tried as a fourth drug), emergence of resistant strains is practically impossible.

In the absence of an effective drug against persisters, it is expected that at least multidrug therapy may reduce population of persisters. Hence without much of speculations, it is high time to realize gravity of problems and rationale behind this multidrug therapy and give benefit to needy patients.

It is hoped that the Kerala branch of IADVL will revise its stand as early as possible.

Dr. C. R. Revankar.

* Subject to approval.

Madam,

Thank you very much for your letter dated 2—5—'83 requesting me to reply to the comments made by Dr. Ganapati regarding our view against PULSE therapy with Rifampicin in Leprosy. I want to make it clear that none of us was against using this drug in leprosy. The difference of opinion was mainly on its use in leprosy as intermittent (PULSE) therapy.

I do agree that this form of 'PULSE' therapy has been recommended recently by various authors. Since it is the view of some of the members of our branch, I do not want to go in detail about this controversy. I will let you know at the earliest the suggestion made by senior members of our branch in response to the comments by Dr. Ganapati. The following is strictly my personal view on PULSE therapy.

Any antibiotic whether bacteriostatic or bactericidal in its action, if given only intermittently in a bacterial infection there is always more chance for that bacteria to develop resistance to that drug. This is a well known fact in antibiotic therapy. This need not be evident as an immediate effect but one can expect it to develop after years. I don't think Mycobacterium leprae will be an exemption to this general rule. In leprosy we are dealing with an organism having a long multiplication time. Even though a single dose of 600 mg of rifampicin can kill a large number of bacilli, in intermittent therapy, there will be a period when there is only a low level of the drug in the blood and tissues. In this type of frequent exposures of these bacilli, to intermittent therapy, there will be a period when there is only a low level of the drug in the blood and tissues. This type of frequent exposures of these bacilli to sub lethal doses, render them more susceptible to develop 'resistance' to rifampicin. 'PULSE' therapy with rifampicin is a recent introduction in chemotherapy of leprosy. Though not a problem at present, the possibility of development of 'resistance' should be kept in mind by everybody who is using this drug in intermittent therapy. Further, it is well documented that the chances for development of serious complications are more by intermittent therapy, than by continuous therapy with rifampicin. I do agree with Dr. Ganapati's statement that 'supervisability of administration of drug' will be easy by intermittent therapy. But at the same time, remember, Mycobacterium leprae also finds it easy to become resistant if rifampicin is given intermittently. It is always wise to use this most effective drug against leprosy – rifampicin only by continuous therapy. To me, the so called 'PULSE' therapy in leprosy with rifampicin is unscientific, unjustifiable, unethical and unsafe mode of treatment. "If you want to kill the snake kill it then and there with a violent hit. It is DANGEROUS to let it go hurt".

Thank you,

Dr. K. Pavithran,
Asst. Professor,
Skin & VD,
Medical College,
KOTTAYAM.

Dear Madam,

I read with great concern the report of Dr. K. Pavithran, Secretary, IADVL, Kerala branch (Indian Journal of Dermatology, Venereology and Leprology, Volume 48 No. 6 November to December 1982 pp 375-376). It is reported that at the second quarterly meeting of the branch at Kottayam "all the participants warned on the danger of developing mycobacterial resistance by PULSE therapy in leprosy and concluded that it should not be followed in our patients". It is presumed that the "pulse therapy" referred to pertains to the administration of the Rifampicin (RFP) in doses of 600mg at monthly intervals. I have to state that pulse therapy with RFP has been advocated essentially taking to consideration the following facts :–

1. RFP is a very powerful bactericidal drug against M. Leprae with 99.9% kill rate.
2. RFP is not given as monotherapy but is administered along with two other effective antileprosy drugs, for sufficiently long periods.
3. There is no evidence to believe that excessive administration of RFP offers any added benefit (response of M tuberculosis and M. Leprae to the same drug like RFP may not be comparable).
4. Considering field logistics and supervisability of administration, intermittent therapy is more practicable under prevailing conditions in India.
5. Development of "adaptive resistance" by M. Leprae to intermittent exposure to RFP is not proved and is unlikely according to most experts.

I want readers to note that according to the recommendation by the Indian Association of Leprologists wherever infrastructure would permit a supervised administration of RFP for 21 days preceding pulse therapy is preferable.

The statement by Dr. George, Additional Director of Health Services, Kerala that we would not rather be "worrying" about dapsone resistance which is not yet a problem in Kerala" implies a sense of complacency which is not justified by figures emerging from field studies elsewhere in India. It is not known whether Dr. George has made his statements on the basis of any field studies conducted in Kerala. Drug resistance with reference to any disease especially in leprosy should be viewed as a latent public health problem in all parts of India and it may not be wise to wait for clinical expressions of this phenomenon to arise to realise the gravity of the problem.

Dr. George has rightly referred to treatment of more cases as very important. I would like to know what specific field schedules of treatment of leprosy he would recommend in Kerala in the light of our current knowledge about newer drugs in the control of leprosy.