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Letter to the Editor

Rifampicin in the Treatment of Reactions in Leprosy

The article of Steenbergen and Pfaltzgraff (*Lepr. Rev.* (1975) **46**, 115-118) provides evidence that rifampicin may aggravate Type I reactions and the drug therefore should be contraindicated in borderline-tuberculoid leprosy with neuropathy. The authors conclude: ". . . Type II reactions . . . do not seem to be at all exacerbated by the use of rifampicin, but rather to be somewhat suppressed." We wonder if such statements arise from an over-enthusiasm in the early days of a new and potent anti-leprosy drug. Waters *et al.*, (1967) warned: "Indeed nearly every effective new drug introduced for the treatment of leprosy has been claimed to give a lower incidence of ENL than does DDS. Subsequently these claims are usually abandoned."

The real influence of rifampicin on Type II reactions is not yet fully established. Leiker and Kamp (1970) found that 5 of their 7 patients developed reactions. In one patient, with BL leprosy, rifampicin had to be discontinued because of severe ulnar neuritis. Rees *et al.* (1970) mentioned that 2 out of 6 lepromatous patients developed ENL during a 4.5 months course of rifampicin. Of the 20 patients Wilkinson *et al.* (1972) described, one developed mild ENL; in another patient the drug had to be withdrawn because of a more serious Type II reaction.

Papers on rifampicin treatment were presented at the International Colloquium on the Chemotherapy of Leprosy, Borstel, 1974. If we tabulate the data of these rifampicin trials on lepromatous (LL and BL) patients, in which exact numbers of reactional states during therapy were given, the following results are obtained:

	No. patients	No. reactions	Reactions (%)	Mean treatment period
Rifampicin monotherapy	62	22	35	6 months
Rifampicin + Isoprodian	124	51	41	8.5 months
Rifampicin + other drugs	80	33	41	9 months
Total	266	106	40	8 months

There is no significant difference in the frequency of reactions between rifampicin monotherapy and rifampicin in combination with other drugs. However, the 9 patients who were recorded to have been withdrawn from their drug regimen because of severe reactions were all in the rifampicin + Isoprodian trials. Terencio de las Aguas (1975) found that his patients on rifampicin alone developed reactional episodes at a frequency of 0.08 per treatment month, whereas in the

group on rifampicin + Isoprodian this was 0.41 per month. On the other hand Gatti (1975) recognized more reactions during monotherapy than with combined therapy. An interesting paper was presented by Vomstein (1975) who studied the effect of rifampicin + Isoprodian on patients with initial reactions. Most of his 31 cases improved, although some remained thalidomide dependant. Three cases had to be withdrawn because of the intensity of their reactions.

We gave rifampicin (450-600 mg daily) to 4 male African LL patients *during* persistent Type II reactions. Three patients also received Isoprodian. In all 4 patients, although "covered" by prednisolone, the reactional state deteriorated. In fact their reaction with severe, sometimes necrotizing, ENL plus neuritis was so violent as to warrant stopping the newly introduced therapy. We had the impression that rifampicin in combination with Isoprodian gave more severe reactions than did rifampicin alone. Within 10 days of withdrawal the reactional episodes had subsided.

Type I reactions are believed to be a change in cell mediated immunity (Waters *et al.,* 1971). Rifampicin is reported to have suppressive properties on human lymphocytes stimulated *in vitro* with phytohaemagglutinin or PPD-tuberculin (Nilsson, 1971). Therefore one would assume that rifampicin could have a favourable effect on Type I reactions. The findings of Steenbergen *et al.* do not bear this out.

Type II reactions on the other hand are the clinical manifestation of an Arthus phenomenon (Waters *et al.,* 1971). Therefore rifampicin with its potent bactericidal capacities, releasing enormous quantities of free antigen, could have a deterimental influence on Type II reactions. This theory is supported by our findings, although our few cases are too limited for definite conclusions to be drawn. More controlled clinical studies are indicated to elucidate this problem. Until such trials have been completed, pronouncements on the favourable effect of rifampicin on Type II reactions should be considered with scepticism.

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