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## POSSIBLE CHEMOTHERAPY OF RIFAMPICIN-RESISTANT LEPROSY

The emergence of secondary rifampicin resistance in multibacillary leprosy is well documented (1, 2). Although only 24 cases of confirmed rifampicin-resistant leprosy have been reported so far, others have occurred in different countries (3, 4). From an epidemiological point of view, patients harbouring rifampicin-resistant *M. leprae* are of great importance because of their potential ability to transmit such organisms in the community. The majority of the documented rifampicin-resistant patients are also resistant to dapsone, because rifampicin was added to the treatment of these patients only after they had relapsed from dapsone monotherapy. Consequently, neither rifampicin nor dapsone should be prescribed to rifampicin-resistant cases of leprosy. Furthermore, in order to interrupt as soon as possible the transmission of rifampicin-resistant *M. leprae* within the population and minimize the risk of relapse, the strategy for the treatment of rifampicin-resistant leprosy should be different from the treatment of rifampicin-susceptible patients.

Only patients with documented rifampicin resistance should be considered for retreatment with drugs other than the standard regimen recommended by WHO Study Group i.e. rifampicin, dapsone and clofazimine (5). Documented rifampicin resistance means that the bacilli harvested from the patient's skin biopsy have been inoculated into the foot pads of mice, direct drug sensitivity test has been performed according to standard procedures (1, 2, 6) and has demonstrated unequivocal *M. leprae* rifampicin resistance.

The new regimen to be prescribed may include drugs like ofloxacin (7), clarithromycin (8, 9), minocycline (8, 10) and clofazimine. The first three compounds display powerful bactericidal activities against *M. leprae* and have never been employed in any leprosy control programme whereas clofazimine-resistant leprosy has not yet been convincingly demonstrated (6). The important issue is that the drugs must be given in combination for enough period of time, otherwise one may repeat the similar mistake of misusing

rifampicin in the past. The most potent regimen could be: ofloxacin 400 mg + clarithromycin 500 mg + minocycline 100 mg + clofazimine 100 mg, daily, supervised for four to eight weeks; followed by minocycline 100 mg + clofazimine 50 mg, daily, self-administered, for six months; and then, clofazimine 50 mg daily alone until skin smear negativity or for life. If not acceptable, clofazimine may be replaced by minocycline in the last phase of treatment.

Serious consideration must be given to the possible sideeffects and toxicity of all above mentioned drugs. Ofloxacin and minocycline should not be prescribed to children under the age of 15 and to pregnant women. In addition, vertigo and skin sensitization may be induced by minocycline, whereas gastric disturbances, liver toxicity and loss of hearing may complicate the administration of clarithromycin. Thus, the administration of all retreatment drugs should be carefully monitored and, whenever possible, the patients should be hospitalized during the initial phase of treatment.

Patients in whom rifampicin resistance may be suspected are mainly those who relapse after having been treated with rifampicin which has not been combined with dapsone and clofazimine as recommended by WHO and ILEP. In order to confirm rifampicin resistance, the ILEP Medical Commission has arranged several reference laboratories for testing the rifampicin susceptibility of *M. leprae* in the mouse footpad system. Medical personnel who wish to verify their suspected rifampicin-resistant patients may contact any of the laboratories at the following addresses (updated June 2002):

- Professor Jarlier, Faculté de Médecine Pitié-Salpêtrière, 91 boulevard de l'Hôpital, 75634 Paris cedex 13, France. Fax: +33 (1) 40 77 95 96
- Mr James L Krahenbuhl, Laboratory Research Branch, G W Long Hansen's Disease Centre, Louisiana State University, PO Box 25072, Baton Rouge LA 70894 USA. Fax: +1 225 346 5786. E-mail: jkrahel@lsu.edu.

- Mr Stewart Cole, Unité de Génétique Moléculaire Bactérienne, Institut Pasteur, 28 Rue Docteur Roux, 75724 Paris Cedex 15, France. Fax: +33 (1) 40 61 35 83. E-mail: stcole@lsu.edu

ILEP Members may contact these individuals directly.

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*The original text was produced by Professor J Grosset.*

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