—V.V. Pai, M.B.B.S., D.D.V.

Medical Officer

—R. Ganapati, M.B.B.S., D.D.V.

Director
Bombay Leprosy Project
Vidnyan Bhavan
11 V.N. Purav Marg
Sion-Chunabhatti
Bombay 400 002, India

Reprint requests to Dr. Shetty.

REFERENCES

1. CHATTERJEE, B. R. Drug resistance and multi-drug therapy in leprosy. Lepr. India **54** (1983) 402–411.
2. HAFFNER, S. E. and JHELM, U. Increased growth of *Mycobacterium malmoense in vitro* in the presence of isoniazid. Eur. J. Clin. Microbiol. Infect. Dis. **10** (1991) 787–788.
3. MIORNER, H. and OLSSON, B. Improved isolation of mycobacteria other than *M. tuberculosis* on isonazid containing Lowenstein-Jensen medium. Eur. J. Clin. Microbiol. Infect. Dis. **7** (1988) 47–49.

Antileprosy Drugs, Pregnancy and Fetal Outcome

TO THE EDITOR:

In 1982, a World Health Organization (WHO) Study Group devised and recommended multidrug therapy (WHO/MDT) with pulsed doses of rifampin and clofazimine in addition to dapsone for leprosy. There is a lot of controversy regarding the use of these drugs in pregnancy due to the lack of controlled studies. Most of the studies have advocated the use of dapsone and clofazimine ([2, 3, 5, 6]) in pregnancy without serious side effects, including teratogenicity. However, congenital malformations have been reported in 2 out of 56 newborns of leprosy patients treated with dapsone in another study ([4]). The status of rifampin is still more controversial. Experimental studies in mice and rats have shown it to produce spina bifida and cleft palate in doses above 150 mg/kg ([8]). Another report describes 9 malformations in 204 human full-term pregnancies ([7]). In contrast, a surveillance study of Michigan (U.S.A.) Medicaid recipients has shown no major birth defects in 20 newborns exposed to rifampin in the first trimester ([1]). Presently, clofazimine and rifampin are classified in category C: according to their fetal risk as defined by risk factors used by the U.S. Food and Drug Administration (Federal Register 1980; 44:374, 34–67) ([1]).

We have retrospectively studied 5500 leprosy patients over a 19-year period who included 13 female patients (age group 18–30 years) of different subtypes (TT = 1, BT = 3, BL = 6, LL = 3) who had taken these drugs out of ignorance during pregnancy. All of these patients received 100 mg dapsone daily with 600 mg rifampin once monthly. Further, two patients received clofazimine and two patients took intermittent prednisolone throughout their pregnancies. All of these patients had full-term normal deliveries, including twins in one case.

Although our study is an uncontrolled study, it still shows that these drugs can be safely used in pregnancy.

—Puneet Bhargava, M.B.B.S.

Resident House Officer

—Chitar Mal Kuldeep, M.D.

Assistant Professor

—Narender Kumar Mathur, M.D.

Professor and Head
Department of Dermatology, Venereology and Leprology
S.M.S. Medical College and Hospital
Jaipur 302 004, India

Reprint requests to Dr. N. K. Mathur, C-24 Peeyush Path, Bapu Nagar, Jaipur 302 004, India.

REFERENCES

1. BRIGGS, G. G., FREEMAN, R. K. and YAFFE, S. J., EDS. *Drugs in Pregnancy and Lactation.* 4th edn. Baltimore: Williams and Wilkins, 1994, pp.188–189, pp.768–769.

2. DUNCAN, M. E. and PEARSON, J. M. H. The association of pregnancy and leprosy. III. Erythema nodosum leprosum in pregnancy and lactation. Lepr. Rev. **55** (1984) 129–142.
3. KARAT, A. B. Long-term follow-up of clofazimine (Lamprene) in the management of reactive phases of leprosy. Lepr. Rev. **46** Suppl. (1975) 105–109.
4. MAURUS, J. N. Hansen's disease in pregnancy. Obstet. Gynecol. **52** (1978) 22–25.
5. PLOCK, H. and LEIKER, D. L. A long-term trial with clofazimine in reactive lepromatous leprosy. Lepr. Rev. **47** (1976) 25–34.
6. SCHULZ, E. J. Forty-four months' experience in the treatment of leprosy with clofazimine (Lamprene; Geigy). Lepr. Rev. **42** (1972) 178–187.
7. STEEN, J. S. M. and STAINTON-ELLIS, D. M. Rifampicin in pregnancy. Lancet **2** (1977) 604–605.
8. TUCHMANN-DUPLESSIS, H. and MERCIER-PAROL, L. Influence d'un antibiotique, la rifampcine, sur le developpement prenatal des ronguers. C.R. Acad. Sci.(d) **269** (1969) 2147–2149. As cited in: Shepard, T. H. *Catalog of Teratogenic Agents.* 6th edn. Baltimore: Johns Hopkins University Press, 1989, pp. 558–559.

Recurrent Erythema Nodosum Leprosum Precipitated by Antileprosy Drugs

TO THE EDITOR:

Erythema nodosum leprosum (ENL), an inflammatory reaction occurring in patients with lepromatous or borderline lepromatous leprosy ([3, 5]), presents as a group of tender dermal and/or subcutaneous nodules that arise in apparently normal skin. Although ENL occasionally develops in untreated patients ([6]), more than 50% of patients with lepromatous leprosy in South East Asia develop ENL within the first year of administration of sulfones ([9]).

Recently, a lepromatous leprosy patient [bacterial index (BI) of 5+] was referred to us with a severe ENL reaction with necrotic lesions after 4 months of multidrug therapy (MDT). A thorough clinical examination and relevant laboratory investigations were done to rule out other causes of ENL. After stopping MDT, the ENL lesions subsided. The patient, then given dapsone, rifampin and clofazimine individually, developed ENL with dapsone and rifampin while he tolerated clofazimine. In view of the recent advances in antileprosy chemotherapy, he was given individually ofloxacin, minocycline and clarithromycin, and developed ENL lesions within 24 hr of taking ofloxacin and clarithromycin. He has been taking the combination of minocycline and clofazimine for the past year but, unfortunately, neither his BI nor histopathology have shown any improvement.

Lepromatous leprosy is associated with polyclonal B-cell activation ([7]). Several authors have shown that circulating IgM antibodies against phenolic glycolipid-I (PGL-I) are decreased in serum during ENL ([1, 4]). Other authors using suction-induced blister formation on ENL lesions have shown increased levels of IgM antibodies against PGL-I in blister fluid ([2]). It appears that with the onset of bactericidal antileprosy therapy there is disintegration of bacilli and release of antigenic material ([8]). Supporting evidence includes the finding of disintegrated bacilli and foamy macrophages in ENL lesions, the deposition of immune complexes composed of IgM, IgG and complement components of the classical pathway and infiltration of polymorphonuclear leukocytes (neutrophils) ([10]). All of these changes show that bactericidal antileprosy drugs can precipitate ENL in susceptible individuals by the release of antigenic material, and PGL-I is likely the antigenic component of immune complexes in ENL.

—Puneet Bhargava, M.B.B.S.
Resident House Officer

—Chitar Mal Kuldeep, M.D.
Assistant Professor

—Narender Kumar Mathur, M.D.
Professor and Head
Department of Dermatology, Venereology and Leprology
S.M.S. Medical College and Hospital
Jaipur, India

Reprint requests to Dr. N. K. Mathur, C-24 Peeyush Path, Bapu Nagar, Jaipur 302 015, India.