HYPERSENSITIVITY REACTION TO DAPSONE

Sir,

I would like to follow on from Dr Mary Joseph's report of four cases of hypersensitivity reaction to dapsone (*Lepr Rev* 1985; **56:** 315–320) by reporting a fatal case due to the same reaction.

The case was in an Indian patient and the diagnosis was based on the history and clinical presentation. The man presented in his early forties with widespread, symmetrical macules over his limbs, face and trunk with early infiltration of his face and some erythema. He was referred to the

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Belgaum Leprosy Hospital by a general medical practitioner who suspected the diagnosis of leprosy. The clinical presentation was of BL leprosy and his skin smears were positive. He denied previous treatment and was commenced on 100 mg of dapsone daily as an outpatient (this was prior to the introduction of multidrug therapy).

He was brought back to the hospital several days later suffering from fever, nausea, malaise and generalized exfoliative dermatitis. The clinical picture was suspicious of a hypersensitivity reaction to dapsone and at this point he admitted to previous treatment with dapsone. This had been prescribed elsewhere one year previously when he had developed a skin rash and jaundice several weeks after commencing dapsone therapy. He had been admitted to hospital on that occasion and a review of his hospital records revealed that the differential diagnosis then was either infective hepatitis or a drug reaction; however the dapsone was stopped and he made a good recovery. He had not taken any dapsone since that time.

On admission this time he was febrile, had generalized lymphadenopathy and an enlarged, tender liver. His liver function tests were abnormal. The dapsone was stopped and in view of his serious clinical condition he was commenced on corticosteroids. His condition rapidly deteriorated over the next 4–5 days when he became markedly jaundiced and showed evidence of acute liver failure and finally died in hepatatic coma despite high-dose corticosteroid therapy. A post-mortem examination was performed which failed to show any pathology other than the hepatic changes.

The man presumably suffered from the so called 'DDS syndrome' described by leprologists at the advent of the dapsone era. Dapsone hypersensitivity reaction was regarded as extremely serious and was not infrequently fatal.[1] However there have been few reports of this reaction in recent years and a review in the *Lancet* in 1981[2] commenting on two cases[3,4] noted that it had virtually disappeared in the previous 20 years. Since then there have been single case reports[5] and now Dr Joseph's recent report describes four cases.

The questions remain to be answered as to how common is this reaction and whether or not its frequency has increased over the last 5 years. It has been suggested that the practice of commencing dapsone therapy at 100 mg daily, as opposed to the lower doses used formerly, has increased the incidence of the reaction;[3] but this is in conflict with the view that the hypersensitivity reaction to dapsone is not related to the dose.[4] The lack of reports of the reaction in recent years can be explained in three ways; the reaction is occurring but is not being recognized, or it is occurring and being recognized but is not being reported, or finally the reaction is extremely rare. It is very important that we establish which of these possible explanations is the right one.

It seems very improbable that Dr Joseph would come across four cases in a short period of time if the condition was extremely rare which suggests that one of the first two explanations may be the right one. If the condition is increasing in frequency it is important that we establish this since the cause may be a preventable one such as an impurity in the dapsone manufacture or a drug interaction associated with the new multidrug therapy.

I suggest that a centralized recording system is set up for the notification of suspected cases of hypersensitivity reactions to dapsone. It would be necessary to enrol treatment centres first rather than simply recording suspected reaction so that a true estimate of the frequency can be made. Cases of suspected reactions or death within 2 months of the commencement of treatment with dapsone should be reported giving details of the dose, manufacturer and batch number of the dapsone tablets prescribed as well as the detailed clinical history of the patient.

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References

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[5] Kromann NP, Vilhelmsen R. The dapsone syndrome. *Arch Dermatol* 1982; **118:** 531–532.