In Reply to the Letter to the Editor by Ramam & Srivastava

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Sir,

We thank Drs Ramam & Srivastava for their comment. Dapsone must still be regarded as a safe preparation; however, dapsone hypersensitivity syndrome (DS) cannot be considered an uncommon adverse effect. Frequency fell from 12% in 1949 (1) to $<0.5\%$ in 1981 (2). In 1986, a worldwide postal survey among leprosy centres (3) showed that 19.2% of them had recently encountered cases of DS with an estimated frequency of 0–2%. The last reported series have shown frequencies of 0.27% (1986, 4645 patients) (4), 24% (1992, 37 patients) (5), 1.3% (1994, 700 patients) (6) and 1.58% (2001, 252 patients) (7). However, some centres treating large numbers of patients with dapsone apparently have experienced very few cases. Risk level seems not to be related to the treated basal disease, malnutrition (8), or multi-drug therapy (3, 4) but to starting on full dapsone dosage and probably to a small average body weight population (4) and genetically determined differences in drug detoxification capacity.

For diseases other than leprosy, low initial doses and a gradual induction period have been recommended for decades by investigators and by the dapsone package insert. For leprosy, in spite of a lack of consensus since the early 1980s (1), some leprologists still advise starting with low doses in order to decrease incidence and severity of DS, assuming the standard WHO recommended dose of 100 mg only after 4 weeks (4).

Re-introduction of dapsone following DS usually precipitates a recurrence but only when the same dose is applied. In a series of 51 patients (9) treated with lower doses for desensitization, most of them showed none (43%), or only one recurrence (15.6%). In another series of 14 patients (10) treated with even lower initial doses, no recurrence was found in 92.8% of them. We disagree that this matter and the success of the procedure are unclear, regarding the literature. Already in 1949–1951, permanent desensitization was found to be possible in the vast majority of cases (9).

Mild reactions to dapsone, as in our patient, are not uncommon and have been reported previously (9). In fact, forehead or upper limbs are characteristic areas of onset, the rash either remaining confined to those areas or being widely disseminated (11). Rash confined for 1 week before severe widespread has also been reported (2). Early investigators noted that the DS was less severe when lower starting doses were used (1) and with immediate withdrawal after onset of the first signs of DS. The presence of both circumstances in our patient can explain the mild clinical expression and the quick recovery.

Since the earliest reports, the skin rash of DS has been well known to clinically resemble infectious mononucleosis (3, 11), in DS being the first sign, in the viral disease following a prodromic period. In our patient, the absence of a prodromic period of fever, adenopathy and catarrh preceding the rash, and the lack of lymphocytosis with atypical cells and affectation of the trunk, do not suggest such viral disease. In fact, onset with desquamating lesions confined to the face and the upper arms, followed by eosinophilia and lymphadenopathy, without fever and affectation of the trunk, strongly suggests the onset of DS. To our knowledge, other kinds of viral exanthems do not

correspond with the clinical and evolutive findings reported in this patient.

Lastly, considering the potential gravity of DS, we agree that a careful re-introduction of dapsone could be a valid therapeutic option only in as much as the treatment is absolutely needed and the hypersensitivity reaction is not severe, early, or manifest at very low dosages.

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