

'B 663' Possible Anti-inflammatory Action in Lepromatous Leprosy

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In the course of the clinical trial of 'B 663' (Geigy, S. A.) see Barry, V. C., Conalty, M. L. 1965 *Leprosy Review*, this issue reported by Browne and Hogerzeil (1962a, b), it was noted that only two out of the 26 participating patients suffering from lepromatous leprosy developed any symptoms of acute exacerbation while receiving the drug, and in both instances the attack was slight and transient and occurred during the first month of treatment. It is a well-attested observation that in any group of patients suffering from lepromatous leprosy of comparable severity and receiving dapsone in standard doses for a similar period, a much higher proportion would have developed some degree of acute exacerbation. Of the 26 patients, 21 had B 663 for six months, and the remaining five for 12 months: 13 patients received B 663 alone, nine together with dapsone and four with dapsone and ditophal.

(Two patients suffering from bacteriologically positive borderline leprosy are excluded from consideration here, since they are not subject to the same type of acute exacerbation as are patients with lepromatous leprosy. As a matter of interest, however, it may be recorded that neither had any kind of exacerbation during treatment with B 663, but that one of them subsequently developed an acute ulnar neuritis.)

Acute exacerbation on subsequent dapsone therapy

That this group of 26 patients with lepromatous leprosy is typical in respect of liability to exacerbation is shown by the fact that after dapsone had been substituted for B 663, 14 of them developed erythema nodosum leprosum (ENL) and various other manifestations of acute exacerbation. In addition, some patients showed certain features that are frequently though not necessarily associated with such a state; thus, three had acute polyneuritis, one had severe bilateral dactylitis, and one passed through an

acute psychotic episode. It should be added that one patient succumbed to pneumonia during the 13th month of treatment for leprosy.

In the 14 patients affected, the sign of ENL appeared first at various intervals after the change-over to dapsone therapy. In no patient did ENL lesions appear until seven months had elapsed after B 663 therapy had been discontinued. Thus, they appeared after eight to 12 months in five patients; after 13 to 18 months in three; after 19 to 24 months in five, and during the 29th month in one.

To summarize: during treatment with B 663, two patients developed ENL during 186 patient/months (*i.e.* five patients for 12 months, and 21 patients for six months); no patient developed ENL after the first month of such treatment, *i.e.* in 160 patient/months. During treatment with dapsone, 13 patients developed ENL during the next 589 patient/months (*i.e.* 24 patients for 24 months, plus one patient deceased after 13 months), and one patient developed ENL after 29 months.

The two patients who had experienced a transient attack of ENL during the first month of B 663 treatment did not develop any ENL lesions when subsequently taking dapsone.

As in other reported series, there was no constant correlation between the appearance of ENL and the absolute height of the Bacterial Index, or its increase or decrease, or changes in the proportion of normal-staining bacilli (the Morphological Index).

The occurrence of bacterial 'resistance' in five patients after 12 months of B 663 therapy alone, as shown by a more or less sudden increase in the Bacterial Index and the simultaneous reappearance of normal solid-staining rods in the smears at several sites (Browne and Hogerzeil 1962 *c.*), seemed to have no bearing on the incidence of acute exacerbation.

Influence of total dose of B 663

There was no evidence that the five patients who had received B 663 for 12 months were less liable to experience acute exacerbation than the 21 who had received the drug for six months, or that in them the onset of acute exacerbation was postponed by the additional amount of drug they had received. Three of these five experienced ENL of the same severity as the patients who had received the drug for only six months, and the time of onset appeared to be similarly fortuitous.

Clinical features of acute exacerbation

There was nothing in the clinical features of the acute exacerbation in these patients to distinguish them from the general run of such cases in West Africa (Browne 1963). All grades of severity were noted, from the slight and transient, accompanied by no systemic disturbance, to the severe and persistent, characterized by high temperature, general malaise, polyarthralgia, polyadenitis and widespread neuritis in addition to the cutaneous signs of superficial erythema nodosum and deep diffuse panniculitis. Iritis and iridocyclitis were not observed. Three patients had a single short attack, which cleared up either spontaneously within a month, or during temporary withdrawal of dapsone. In three patients, the first attack was more severe, and persisted for from five to 14 months. Ten patients had recurrent attacks spread over 30 months. In one patient in whom the acute exacerbation persisted for 14 months, the skin of the lower part of the posterior aspect of the arms became hard, dark, shiny and tender – part of the picture of progressive lepra reaction.

In spite of the occurrence of ENL in these patients, and the consequent short or prolonged interruption of treatment in many instances, their overall clinical and bacteriological progress has been eminently satisfactory.

DISCUSSION

The incidence and pattern of ENL in this group of 26 patients (reduced to 25 by death) with lepromatous leprosy under treatment with standard doses of dapsone are in keeping with experiences of similar groups in West Africa. The interest lies in the virtual absence of acute exacerbation during previous treatment with B 663, whether or not another drug was being

given concurrently. From subsequent experience, it is apparent that the members of the group were normally prone to exacerbation: they did not experience it while receiving B 663, but did so afterwards.

Since the pathogenesis of acute exacerbation in lepromatous leprosy is still obscure, it is idle at this juncture to speculate on the precise mechanism of B 663 in suppressing the phenomenon.

It is worth recording, however, that the disappearance of morphologically normal bacilli from the skin smears was proceeding at a very satisfactory rate during administration of B 663, and that disintegrating bacilli were present in an ever-increasing proportion of the bacillary load in the dermis and nasal mucosa.

It was not possible, because supplies of the drug were exhausted, to observe the effect of readministration of B 663 on patients who had developed acute exacerbation. Any sustained benefit that might be noted on the established condition would support the suggestion here advanced that B 663 appears somehow to exert a suppressive action on the development of acute exacerbation in lepromatous leprosy.

If it could be shown that patients with lepromatous leprosy under prolonged treatment with B 663, with perhaps the addition of dapsone, make rapid clinical and bacteriological progress and are spared the distress and risks of more or less prolonged episodes of acute exacerbation, with accompanying polyneuritis and ocular complications, then B 663 may well prove to be a drug with a definite and extensive sphere of usefulness in leprosy.

SUMMARY

Erythema nodosum leprosum occurred in only two out of 26 patients whilst they were undergoing treatment for lepromatous leprosy with B 663 (Geigy), and in both cases the condition occurred within the first four weeks of treatment and was slight and transient. When all the patients were subsequently given standard doses of dapsone, however, 14 of them passed through episodes of erythema nodosum leprosum whose clinical features corresponded with those observed in similar groups. It is suggested that B 663 (Geigy) may exert a suppressive effect on the development of acute exacerbation in lepromatous leprosy.

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