PSEUDOEXACERBATION OF LEPROSY DUE TO THE DIAMINO-DIPHENYL-SULFONES [1]

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Among the incidents observed during our experience with sulfone therapy there is one which, because of its significance and its importance, may be considered as one of the most demonstrative proofs of the activity of these drugs. This is the phenomenon which, for lack of a better term, we have called "pseudoexacerbation" of leprosy.

It is known that during the initial stages of sulfone treatment a certain proportion of patients (12% to 15% in our cases) show a slight to moderate exacerbation of the symptoms. This condition appears in the form of an aggravation of the preexisting cutaneous elements, with the appearance of new ones of the same aspect and nature. In pseudoexacerbation, which is the subject of this paper, there is also an aggravation of the cutaneous symptoms but in a quite different way. Like the ordinary exacerbation referred to, this condition is also seen in the first months, when the patient has received around 200 to 300 cc. of promin solution or 100 to 120 capsules of diasone, rarely later; but the clinical aspect and the nature of the skin lesions are different from those of the preexisting elements.

There is an acute outbreak of well-defined, infiltrated, erythematous patches, some of them with a tendency to a brownish (*ferruginoso*) color; nodular and papular lesions surround the patches; and the patient frequently shows edema of the hands and feet. If the case is of the lepromatous form, as most of them are, the original lesions of that type are masked or replaced by those of the new eruption, though the latter sometimes coexist with them. The condition develops without any prodromal manifestations, and it has very little effect on the general condition of the patient.

The morphological aspect of the exacerbation is, therefore, similar to that of a reacting tuberculoid eruption, whether

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typical or of the "intermediate" or "borderline" form. The difference is that the true tuberculoid reaction appears either in patients of the incharacteristic form of the disease, transforming them to the tuberculoid form, or in previously tuberculoid cases, intensifying that process. The exacerbation due to the sulfones appears in any of the three types, but especially in the lepromatous; and in such cases the tuberculoid-looking lesions of the eruption are observed together with the typical lepromatous ones.

The really interesting feature of these cases of pseudoexacerbation is the structural picture of the eruption lesions. Biopsy of these elements reveals a picture consisting predominantly of epithelioid cells arranged in nodular fashion, with or without giant cells. This condition, together with the presence of foci of more or less intense edema, resembles on the whole the aspect of the reacting variety of tuberculoid type; and the resemblance also extends to the bacteriological findings. It is not uncommon, on the other hand, to observe lepromatous cases in exacerbation in which the histologic picture is truly a mixed one, with coexistence of the tuberculoid and the lepromatous processes in the same biopsy specimen or in different ones taken at the same time. These cases perhaps represent transitional stages between one and the other of the two polar processes.

These reactions, which apparently aggravate the cutaneous condition of the patient, actually signify a considerable improvement. They transform cases of the malignant form, incapable of defense against the germ, into a condition in which there is a defense by means of the tissue response characteristic of the benign forms.

Our records of these pseudoexacerbations comprise 68 lepromatous cases, but we believe there have been many more which have escaped observation. The patients tend not to come up for examination, lest the treatment be suspended. Actually our practice is, on the contrary, to increase the dosage to the maximum in this condition, as long as no contraindications appear.

The clinical histories of many of these cases show how important it is to bear in mind the phenomenon of mutation of type when studying the classification of the different clinical forms of leprosy. We have recorded several cases which (*a*) entered the hospital with incharacteristic lesions, (*b*) suddenly changed to the reacting tuberculoid condition, (*c*) later regressed to the initial indeterminate form, and finally (*d*) underwent conversion to the lepromatous type and remained so for several

years, with repeated attacks of erythema nodosum. Since the institution of sulfone therapy, cases of that kind have presented new acute reactions, this time of a sort typical of the reactional tuberculoid form, as regards both the clinical manifestations and the structural changes.

The exacerbations due to the action of the sulfones follow, in general, the course of the spontaneous outbreaks of the reactional tuberculoid type. This was observed in 17 of our 68 lepromatous cases, in which the new lesions completely replaced those of the original form. In the others the reacting elements and the lepromata coexisted, at least for a time; in some of them the former disappeared completely while the latter continued their ordinary evolution.

It is a remarkable feature of this condition in these lepromatous cases that the alteration of the capacity of the tissue to react, as shown by the appearance of elements which morphologically and structurally are tuberculoid, is not also evidenced by the results of the Mitsuda test. That test gives the same results as before the exacerbation. Tested with Dharmendra antigen after the exacerbation, 66 of our 68 cases remained negative; only 2 became definitely positive.

It seems to us that this partial or total substitution of lepromatous tissue by tuberculoid is highly significant of the activity of the sulfones, leading to the conclusion that, apart from their bacteriostatic action, these substances have a certain capacity of stimulating the reticulo-endothelial system.