CORRESPONDENCE

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DIMORPHOUS LEPROSY

To the Editor:

I have been following, with some interest, the discussions which have centered around what has been spoken of as "atypical macular cases in Africa" [The Journal **28** (1960) 66-67 (editorial)].

This discussion has been centered, very largely, around the matter of terminology, and the general impression that I have gained is that it is considered that this variety of macular case is more common in Africa than elsewhere. As I, along with Dr. Khanolkar, have been responsible for introducing the phrase "dimorphous leprosy," perhaps I should endeavor to try, once again, to explain what this term means to us, for there seems to be a certain misconception with regard to the exact localization of this group in relation to the international classifications of leprosy which have been generally accepted since the Havana and Madrid congresses.

In the first place, let me emphasize that I am not in the least concerned with regard to what term is used for a particular type of clinical lesion; nor am I so obtuse as to want to retain a term or a conception which is contrary to the observed facts.

Perhaps it might be helpful if I were to remind readers of the history of this word "dimorphous." Some ten years ago Khanolkar and I were discussing the whole question of tissue reaction in leprosy, particularly in relation to the host-parasite response, and we set down in tabular form the knowledge which we possessed at the time, and which was generally based on the classification which had been worked out at the Havana congress, accepting the conception of the polar nature of leprosy, which I think can be briefly described as comprising, at one pole, that form of the disease which shows no adequate tissue response, and because of the absence of this response the parasite (*M. leprae*) overcomes the tissues of the host and disseminates widely in the form of lepromatous leprosy; whereas, at the other pole, the tissue response is so marked that the tissues are able to "contain" the parasites within themselves, so that the disease spreads with difficulty, and, in the great majority of such instances, leprosy becomes spontaneously healed.

We then sat down and worked out what we considered was the clinical and histopathological picture in the various clinical forms of what we then considered tuberculoid and lepromatous leprosy, with an intermediate form—borderline—between tuberculoid and lepromatous in in-

filtrated cases. When we came to the macular cases we felt that there was a considerable area of disagreement as to just what the conception of the macular case was in leprosy. Incidentally, in this connection I give, from a standard textbook of dermatology (Sequeira's Diseases of the Skin, 6th edition, 1956, p. 27), the definition of "macule": "Macules are circumscribed, non-elevated, alterations in the colour of the skin of any size or shape. Examples: the eruptions of scarlet fever, macular syphilide, the port-wine mark." This term "macule" therefore applies to any group of flat lesions in leprosy.

If one turns now to the consideration of macular lesions in leprosy of the nature of what was described in the Cairo classification as "simple macular leprosy," a little observation will reveal three distinct forms of macules as (1) corresponding to what the Indian leprologists refer to in general as maculoanesthetic lesions in leprosy; (2) that form of leprosy which is essentially lepromatous, but by routine methods of examination the bacilli are difficult or almost impossible to find; and (3) that form of macule which presents neither of these characteristics, but some of the characteristics of both. From our clinical observations, it seemed to us that these various clinical manifestations of macular lesions can be divided as follows: (*a*) those macules which are essentially maculoanesthetic and show the three essential clinical signs: (1) the macules are single, or countable (not more than four to six), (2) the edges are distinct and well-marked, and (3) their distribution is asymmetrical. In this connection, it may be said that on correlating the clinical and histopathological pictures in these cases, we found that in the active form of these lesions the histology was essentially "tuberculoid," and could come under the definition which was used by Wade, many years ago, as "pretuberculoid." The evolution of the maculoanesthetic lesion has been adequately described by Khanolkar in the textbook "Leprosy in Theory and Practice" (pp. 84-85); and in my earlier textbook, "A Practical Textbook of Leprosy," will be found a good photographic example of the maculoanesthetic lesion (Fig. 28, p. 46), and the essential histology of the nerves in the dermis (Fig. 12, p. 30).

On the other hand, I think it is generally accepted that there is a clinical form of macule which is exactly opposite to that which we find in the maculoanesthetic or pretuberculoid macule, in that the macules are (i) multiple, tend to be small, (ii) with vague or indefinite edges, and (iii) symmetrically distributed. The histopathology of these macules, when correlated with the clinical picture, is also different from that shown in the maculoanesthetic lesion, in that the cellular distribution is diffuse, chiefly round-celled and histiocytic, and the nerves show no invasion, there is some increase in the Schwann cells, with the round-celled infiltration around the affected nerve, and not in the nerve, and in which *M. leprae* can be demonstrated within the nerve but not gen-

erally in the dermal tissues. It can be said that neither the preleproma-tous macule nor the maculoanesthetic lesion is excessively common, for it is seldom that the reaction of the tissues of the body in relation to *M. leprae* is clear-cut.

It was this realization that caused Khanolkar and me to work out theoretically what the clinical and histopathological pictures should be if neither the tissues (the host) nor the bacilli (the parasite) were in ascendancy. Interestingly enough, some months after Khanolkar and I had discussed this question, Dr. Gass of Vellore showed me a section and I made the remark, "That is what I have been looking for"; and I saw, under the microscope, that type of histopathology which we expected would be seen in this form of macular leprosy, which showed neither lepromatous features nor tuberculoid features, but in which there were the lepromatous element and the tuberculoid element in the same section. I then made inquiries as to the clinical form of the disease and found that, clinically, the features showed a mixture of what appeared to be a tuberculoid response, that is, there were anesthetic macules (maculoanesthetic) with clear-cut edges, and interspersed among these were smaller macules with fuzzy indefinite edges, and the lesions were symmetrically distributed (essentially a lepromatous response). I think Dr. Ross Innes is as near correct as is possible when he refers to the term "dimorphous" as two-shaped, except that the term "spot" is hardly applicable, for "spot" gives the idea of something small, whereas a macule in dermatology can be large or small; the chief feature is the fact that it is flat, that is, nonelevated. I wish we leprologists would adhere strictly to dermatological nomenclature in our description of clinical lesions in leprosy.

It was from this starting point that the whole conception of the dimorphous macular lesion developed. Since that date I have studied histopathologically sections from many parts of the world; I have examined many hundreds, if not thousands, of macular cases and, generally speaking, can say that in those cases in which the lesions were active the histopathology was essentially of a similar nature to that which we had worked out on theoretical grounds. I may say further that when I examine a histopathological specimen I have no idea from where the biopsy material is sent; it may have come from Africa, it may have come from any part of the world—to me it is only a number. And having adopted this practice for the past twenty years, I can say with some confidence that all cases in which there is activity of the lesions, the histopathological picture has, by and large, been correlated with that form of clinical leprosy which I expected.

It is quite futile to discuss the question of terminology, and to maintain that one's terminology is better than someone else's. All that one is trying to convey is that, clinically and histopathologically, the host-parasite response in macular leprosy is of a similar nature, but of less

degree to that seen in infiltrated leprosy, and if there is a stage in which the tissue response is neither tuberculoid nor lepromatous in infiltrated lesions—"borderline," although I dislike the term for it is not a borderline but a zone through which I believe all leprosy passes—so there is in macular and neuritic lesions. It is our belief that if macular lesions were examined critically, the clinical features and the histopathology described separately, the general conclusion would be that they too fall into the above three categories, which present what is essentially lepromatous on one side, and that which is essentially tuberculoid on the other, with an intermediate form which shows two-shaped lesions.

If the consensus is that these types of lesions should be designated as "indeterminate," I have no objection to that term, because they are indeterminate, that is, neither the tuberculoid component nor the lepromatous component has established itself enough to gain the ascendancy. But if we are going to use the term "indeterminate" for this type of lesion, let us not confuse this term with those lesions which are truly indeterminate, or, to use a preferable term "undifferentiated"—that is, so early that neither the clinical nor the histopathological picture has declared itself—or with those macules which are essentially clinically, histopathologically, and immunologically lepromatous (bacteriologically negative on routine examination). If this were understood, then there would be no point of dispute.

I, therefore, beg that we may look upon leprosy in its clinical form in relation to the host-parasite response and endeavor to elucidate the clinical aspects of the disease in relation to its histopathology. Both Khanolkar and I would welcome independent observations following the lines indicated in this letter.

I may say, in passing, that it seems to me logical to conclude that this host-tissue response in its various manifestations will be seen, not only in macular lesions and infiltrated lesions, but also in neuritic lesions. If this, then, is the case, one should be able to recognize, histopathologically, tuberculoid neuritic lesions (relatively uncommon), dimorphous neuritic lesions (the commonest of neuritic lesions), and lepromatous neuritic lesions. These have not as yet been described, although I believe that we may have come across an example of a lepromatous neuritic lesion. It must be admitted, however, that the place of neuritic lesions in the classification of leprosy can only be determined by other than clinical methods, and, therefore, I have suggested that the neuritic lesions should be placed in the indeterminate group.

With reference to the transformation of tuberculoid leprosy into lepromatous, it entirely depends on one's individual definition of what a tuberculoid lesion really is. I am willing to concede that my definition of the established tuberculoid, or as it has been called, "the truly polar

tuberculoid lesion," may be too narrow, and is seldom seen in the light colored skin, but more often in the darker skin; and in order to be so classified should show the following features: clinically, the lesions should be single, or countable, with clear-cut edges, and asymmetrically distributed, and the histopathology should show a marked tuberculoid structure in which, in the dermis, the tuberculoid foci are so intense that they have coalesced and all nerve filaments have been completely destroyed, and the granuloma extends up to the dermis, without a separation of a subepidermal relatively clear zone.

There is an aspect of the tuberculoid picture, however, which is puzzling me and which we are endeavoring to study, and that is what I have termed the reactional tuberculoid lesions, in which the lesions have all the features of tuberculoid leprosy except that they are numerous and symmetrical, and, histopathologically, have tuberculoid features except that there is some separation, although not consistently, of a relatively free subepidermal zone. It is this group of lesions which we are trying to elucidate, both clinically and histopathologically, and until we have further evidence it is difficult for me to decide just how frequently the established tuberculoid lesion occurs which does not transform to lepromatous leprosy. This lesion does occur, for when I have discussed these matters with Latin-American writers, and pointed out the type of lesion which one does not expect to see transform to lepromatous leprosy, there has been general agreement that they do not so transform.

Interestingly enough, we have had evidence that the general conception which has been forced upon us, that is, that practically all leprosy passes through a dimorphous phase, is supported by the fact that not infrequently when lepromatous leprosy begins to subside, the previous dimorphous features which were suppressed as the result of the ascendancy of the *M. leprae* begin to show themselves, both clinically and histopathologically. The best example of this was in an article by Dr. Relvich, with which he sent me biopsy specimens from macular lesions, and which I described independently as dimorphous. Then he wrote to me and said, "How can this be, for these cases were originally lepromatous cases?" In discussing these matters with my colleagues from time to time, whether they come from India or Africa or elsewhere, and in discussing the conception of leprosy in relation to the host-parasite response, and endeavoring to demonstrate the fact that there is a correlation between the clinical picture and the histopathological picture in every aspect of this tissue response, there is general agreement as to the basis upon which we have developed our conception of leprosy. Therefore, it seems to me that a great deal of time is wasted on the matter of terminology, and it would be well if we examined our cases on the basis herein indicated, to see whether we cannot, in the great majority of instances, relate leprosy in its clinical manifestations to its immunological response, as shown by histopathology, and if this

is done, then the matter of a detailed, and more scientific, terminology is of secondary importance, and could be agreed upon with little difficulty.

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