

## THE CLASSIFICATION OF LEPROSY.

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To endeavour to set down one's views on the classification of leprosy is no easy task. I welcome, however, this opportunity to discuss the present international classification in the light of the Cairo Conference (1938) nomenclature, and of the more recent work of the South American leprologists.

The classification recommended by the Cairo Conference represented the best agreed description of the various types of leprosy, but most members considered that it was essentially an

interim attempt and expected that certain doubtful points would be clarified at a subsequent international gathering. Owing to the war no such representative meeting has yet been possible.

Since 1938 much work has been done especially along the line of histopathology, and it can be fairly claimed that we have a much clearer idea concerning tissue resistance in leprosy. The South American classification is a step in the right direction in that they have based their classification on a pathological concept, and linked up with the only test that we have which indicates an effective tissue response—the Lepromin Test.

In studying leprosy one cannot help realising that there are quite definitely two polar forms, the one which exhibits frank and successful tissue defence, and the other in which the body seems quite incapable of setting up any tissue defence at all. The former type is characterised by its histological structure, which in the sub-types shows only minor differences. In this form the characterised picture is the epithelioid focus, consisting of epithelioid cells and, in the more marked examples, of giant cells. In all these nerve invasion is marked and the lepromin test is consistently and usually strongly positive. This form is essentially "Neural" because it is accompanied by gross nerve involvement which frequently, in the more marked instances, leads to nerve destruction with consequent deformity. At the other end of the scale is a type of leprosy in which the organism seems to have gained complete control and is characterised by the phagocyte macrophage known as the lepra cell which, in the more advanced cases, undergoes vacuolation (the foamy cell). Lepromatous leprosy, as this type is correctly called, represents the defeat of tissue defence and the parasitisation of the whole reticulo-endothelial system by *M. leprae*.

I am personally of opinion that effective tissue defence, as represented in tuberculoid leprosy, when once established cannot be broken down, and so far as is known it is not possible to stimulate a defensive process of this nature if it is absent; in other words I do not subscribe to the view that true tuberculoid leprosy ever becomes lepromatous or vice-versa.

In between these two 'polar' forms is a no man's land which is inadequately or completely uncharted. The translation of the symposium of the S. American classification only hints at the extent of this uncharted area, and tends to use the term "uncharacteristic" in rather a confusing manner. For instance, it includes in the term "uncharacteristic" the slight non-specific inflammatory change of the early macule, and apparently does not clearly differentiate this from the relatively large, and most important, and yet confusing, group of cases which lie mid-way between

true tuberculoid on the one hand and leproma on the other. It would have been better to follow the suggestion first put forward by Pardo-Costello and Tiant, and divide the uncharacteristic lesions into :

- (a) Non-specific. In this category are all macules which show a simple non-specific inflammatory tissue reaction.
  - (b) Border-line. That confusing group which is neither tuberculoid nor leproma and often shows gross ulceration with a strong tendency to become leproma. In order to clarify the matter and define my terms I suggest the following classification :
    - I. Macular leprosy.
      - (a) Neural macular leprosy.
        - Lepromin usually positive—may be negative.
      - (b) Prelepromatous macular leprosy—Lepromin negative.
    - II. Tuberculoid leprosy.
      - (b) Major tuberculoid
      - (a) Minor tuberculoid
- III. Lepromatous leprosy—Lepromin always negative.
- IV. Uncharacteristic or Border-line cases.
  - (a) Atypical tuberculoid.
  - (b) True intermediate forms.
  - (c) Sarcoidal.
  - (d) Atypical leproma.
- v. Neural anaesthetic or pure neural leprosy. Lepromin usually negative.
- vi. Residual lesions, previous type. Lepromin positive or negative according to the type to which the case previously belonged.

Types I and IV are transitional in that they can change into one or other of the true types—tuberculoid or leproma. Types II and III are characterised by the great tendency to remain true to form and, I believe, never change. Type V usually remains true to type, but occasionally may become lepromatous.

The following is a description of the various types and subtypes.

#### I. MACULAR LEPROSY.

It is generally agreed that frequently the initial lesions in leprosy are of the nature of macules. These macules clinically and histologically can be divided into two varieties : the neural which shows nerve involvement, and the prelepromatous which shows no neural signs.

##### (a) *The Neural Macule.*

As these lesions are true macules in the dermatological sense,\*

\*A small discoloured patch or spot on the skin, not elevated above the general surface.

it seems more reasonable to confine the term neuro-macular to this sub-type of leprosy, rather than include the raised infiltrated lesions of tuberculoid leprosy in this classification. These macules clinically are characterised by a definite, though not raised edge. In other words there is a well marked demarcation between affected and non-affected skin. Histologically the macule shows a tendency to the focalisation of the round cell around hair follicles and vessels in the corium, and definite invasion of round cells in the nerves in the corium. Clinically the macules, except those on the face, show loss of sensibility, particularly thermal sense, and tactile sensation may be absent when the macules are found on the extremities. In about 60% the lepromin test is positive.

(b) *The Prelepromatous Macule.*

These macules occur usually in children under 15, although they may be seen occasionally in adults. The macules are, I believe, precursors of lepromatous leprosy and have been referred to as incipient lesions. They exhibit all the features of lepromatous leprosy in appearance, in distribution and in size, but bacilli cannot be found on standard methods of examination. They are characterised by their vague, indefinite edge, no loss of sensation, and the lepromin test is invariably negative. Histologically they show a diffuse round celled infiltration with numerous macrophages, no nerve involvement and no definite concentration of the cellular reaction around hair follicles and vessels in the corium. The cellular reaction is of a non-specific inflammatory nature, and the difference between the two varieties of macules is in the distribution of the round cells, and in the presence or absence of nerve involvement.

## II. TUBERCULOID LEPROSY.

I believe that the S. American workers are correct when they describe tuberculoid leprosy as one of the polar forms. Personally I contend that tuberculoid leprosy does not become lepromatous, and that it is a manifestation of active and effective tissue defence. Once this defence has been stimulated it cannot be broken down. Space does not permit of the discussion as to how this defence is produced. It is however essential if one maintains the thesis, that tuberculoid leprosy does not become leproma to define the term "Tuberculoid." By tuberculoid I mean that form of leprosy which shows itself in clinical lesions which are infiltrated, and the periphery of which is well defined; they are associated with enlargement of the supplying cutaneous nerve branches and with enlargement and sometimes abscess formation of larger nerves such as the ulnar, great auricular, etc.; there is a positive, usually strongly positive, lepromin and characteristic histological picture

the main features of which are as follows :—

(a) Granulomatous infiltration immediately under the epidermis with non-cellular sub-epidermal zone.

(b) Epithelioid and giant cells, with focalisation of the granuloma around hair follicles and vessels in the corium. In the reactive phase the focalisation may not be apparent owing to the massive mobilisation of epithelioid and giant cells; the more reactive the lesion, the less conspicuous are the round cells.

(c) Gross involvement of the nerves in the corium, which may be so affected that their structure is difficult or almost impossible to recognise.

Unless the clinical, immunological and histological picture follows this formal pattern then the lesion is not, in my opinion, typically tuberculoid. I admit the term "tuberculoid" is unsatisfactory, but "allergic" is worse, and it is difficult to coin another phrase which describes the lesion better.

### III. LEPROMATOUS LEPROSY.

This, I agree with the South American is at the other pole, and therefore is a true polar lesion. Lepromatous leprosy represents that form of the disease in which the defence against *M. leprae* is completely broken down and is characterised in the early stage by vague macules with indefinite edges and the presence of bacilli. The appearance, distribution and size of the macules are characteristic. They exhibit no clinical signs of nerve involvement, and differ from the prelepromatous macule in being erythematous, slightly shiny and more numerous, and in being always bacteriologically positive. Once a prelepromatous macule has become bacterioscopically positive it is classified as lepromatous. In addition lepromatous leprosy is, in my opinion, always negative to lepromin, and has the following main, histological features :—

(a) Granuloma is diffusely distributed through the corium. In earlier stages round cells are conspicuous, later these tend to disappear and be replaced by macrophages (*lepra* cells) which, as the condition advances, appear to become vacuolated (foamy cells).

(b) There is always a well marked sub-epidermal zone free from cells.

(c) The nerves in the corium show little or no cellular infiltration, but frequently stand out clearly, due possibly to a mild response to the presence of the bacilli, producing slight oedema of the nerve bundles and proliferation of their perineurium.

As in tuberculoid leprosy so in leproma, one is not justified in diagnosing typical leproma unless the clinical, immunological and histological picture follows this general pattern.

## IV. UNCHARACTERISTIC OR BORDER-LINE CASES.

I would confine the term "uncharacteristic" of the S. American workers entirely to that form of leprosy which shows atypical histological features. Histologically the group falls into four categories: atypical tuberculoid, intermediate, sarcoidal and atypical leproma. Clinically all these give the same general picture, but the nearer a lesion is to a tuberculoid group the more conspicuously does it stand out from the surrounding skin, and the nearer it is to the lepromatous group the more vague are the edges. The periphery, however, never shows the well marked 'whipcord-like' edge of the tuberculoid to which the term 'succulent' used by Wade fits well. The following are the histological features:—

(a) *Atypical tuberculoid*. The physician who does not make a detailed histological examination is very likely to classify this lesion as tuberculoid. The corium is completely invaded by masses of giant and epithelioid cells and round cells are not conspicuous. The granuloma does not extend up to the epidermis but leaves a clear subepidermal zone, and this I consider to be the significant point in making a diagnosis of atypical tuberculoid.

(b) *Intermediate*. This term is used because the histological picture shows the elements of both leproma and tuberculoid leprosy: a clear subepidermal zone in which there are usually numerous enlarged capillaries, a feature of all border-line cases; epithelioid and/or giant cells, and often marked infiltration with round cells, giving an appearance of focalisation; vacuolated lepra cells (foamy cells) and not infrequently giant foamy cells, sometimes in large numbers; gross nerve involvement as in tuberculoid leprosy.

(c) *Sarcoidal*. The histological picture is one in which there is a clear sub-epidermal zone, usually with dilated capillaries. The granuloma consists of solid masses of epithelioid cells with an occasional giant cell, and an entire absence of round cells.

(d) *Atypical leproma*. Clinically this has the general appearance of leproma, but there is no loss of hair on the eyebrows and there is a great tendency to rapid and spontaneous healing. Histologically the picture is similar to leproma, there may be an occasional multinucleated cell, but no true giant cells and the nerves in the corium are unrecognisable owing to their complete invasion and involvement in the granulomatous infiltration. Foamy cells are frequently conspicuous. It is not possible at this stage to estimate the prognostic significance of these lesions. They show, especially those which are nearer leproma, a marked tendency

to behave as leproma and, like them, frequently relapse after first clearing up.

#### V. NEURAL ANAESTHETIC LEPROSY.

This is that type of leprosy which shows polyneuritic changes without skin lesions, the brunt of the attack by the *M. leprae* being confined to the nerves. There is an extensive involvement of the nerve endings in the skin—true peripheral—neuritis, and an interstitial fibrous tissue reaction in the larger nerves such as the ulnar and peroneal. Why the *M. leprae* should concentrate its attack on nerves is inexplicable. It appears that there is no true tissue immunity in this form, firstly because the majority of neural anaesthetic cases (over 60%) are lepromin negative, secondly because if the *M. leprae* overflow from the nerves and attack the skin there is a great tendency for lepromatous leprosy to develop.

#### VI. RESIDUAL LESIONS.

Flattened lesions of tuberculoid leprosy cannot always be definitely recognised from the neural macule, unless the lesion has been very active, when it shows definite scar-tissue, or unless residual tuberculoid foci can be demonstrated on section.

The scope of this paper does not allow of expansion, but I trust that these outlines which modify the Cairo classification are sufficiently clear to indicate a pathological conception which has been built up as a result of a study of S. Indian cases.

In closing I would state that I am in entire agreement with the S. American leprologists in their insistence on the correlation of the clinical, histological and immunological data before definitely classifying a case and giving a prognosis.