

The Variegated Clinical Pattern of Leprosy

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It falls to my lot to make a cursory, didactic and rather superficial presentation of the clinical entity known as leprosy, and to introduce workers in other disciplines to the bewildering variety of lesions comprised within the term. My chief aim will be to emphasize as far as may be at present possible the pathologic principles underlying these diverse manifestations. In so doing, we shall become acquainted with some of the descriptive terms in everyday use by leprologists, often (be it admitted) employed in a special or restricted sense.

Leprosy may be regarded as a clinical symptom-complex which is the result of infection by the presumably causative organism (*M. leprae*), and a tissue response to that infection that varies within the widest possible limits.

THE HOST-PARASITE RELATION IN LEPROSY

The most helpful way to approach the study of leprosy as a disease is to consider the infecting parasite and the receptive host, and the prolonged and complicated interplay between a parasite that appears to vary in antigenic possibilities between one country and another, and a host whose basic responsiveness to invasion may either locally delimit the inoculation or else raise no barrier to the multiplication of *M. leprae* and their widespread dissemination.

The outstanding clinical features of this relation are two-fold: first, *M. leprae* may either multiply in unrestrained fashion and produce a diffuse and bulky granuloma in the skin and upper respiratory mucosa, or may be so rare as to be detected only with great difficulty. Secondly, the varied features of local tissue hypersensitivity may be superadded to both of these two extreme pathologic manifestations of leprosy, early

in tuberculoid disease and later in lepromatous, producing in either case characteristic lesions in the tissues affected.

The causative organism appears to have a predilection not only for the skin and the upper respiratory mucosa, but also for the peripheral nerves. Leprosy is a serious disease mainly by reason of its capacity to interrupt nerve pathways and destroy fibers mediating nerve impulses in the limbs and face. The sheer volume of the ebullient granuloma in lepromatous leprosy may disfigure the victim and disturb the functions of the skin and nasal mucosa, and the vigorous allergic reaction to paucibacillary infection in tuberculoid disease may produce unsightly skin lesions and damage adjacent structures by local extension and consecutive fibrosis; but it is *par excellence* the destruction of nerve fibers in all the major forms of leprosy that constitutes the main pathologic problem of the disease and exacts the most serious toll of human suffering, physical and mental. The conventional picture of leprosy—the unrecognizably human form disfigured by the leonine face, and suffering from ulcerating and foreshortened digits—is the end-result of extensive granulomatous infiltration of the skin coupled with damage to the peripheral nerves. The ulceration of the extremities is nonspecific, and is of the same order as that occurring in congenital indifference to pain, Morvan's disease, Dejerine Sotta's syndrome, primary amyloidosis of nerves, and damage to peripheral nerve pathways from many causes; i.e., it is essentially due to repeated unappreciated trauma to insensitive tissues.

If, however, the disease complex called leprosy is characterized by these serious manifestations or sequelae, it is most fortunate that the victim is not continually subjected, as in many other infections, to the local and systemic effects of endo- or exo-toxins. The enormous parasitization of

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the dermis, with an inconceivably high concentration of *M. leprae* per unit volume of tissue, is possible only because living leprosy mycobacteria produce no systemic toxic phenomena and evoke no inflammatory response in patients with lepromatous disease. As a general rule and up to a point, the more *M. leprae* a person harbors, the less noticeable is the clinical evidence of the disease.

CLASSIFICATION

Without entering into the minutiae of the vexed and controversial realm of classification, it may be indicated that the so-called "polar" types represent extremes of tissue sensitivity to mycobacterial antigens. On the one hand, there is the paucibacillary infection, with a more or less vigorous tissue response tending to limit and eventually to overcome the invasion, if we may use a teleologic expression. By reason of the typical histologic picture associated with it, whatever precise form its clinical manifestation may assume, this type of infection is referred to as "tuberculoid." The individual lesions generally show a variable elevation above the surrounding skin, and hence attract the descriptive appellation of "major" or "minor" or "intermediate" grade. Some may be truly macular, and some fall into the maculo-anesthetic group of Indian leprologists.

On the other hand, there is the unrestrained multiplication of *M. leprae* mainly within reticulo-endothelial cells, suffering no limitations except those imposed by some little-understood need for proximity to the surface of the body, e.g., the superficial layers of the dermis and the nasal mucosa. This is the "lepromatous" type, characterized by hypopigmented macules, nodules, and diffuse infiltration of the skin.

Early leprosy lesions of the skin that are as yet of equivocal or uncertain polarity, are called "indeterminate."

Between the two extremes of typical "polar" tuberculoid leprosy and typical "polar" lepromatous leprosy, there is a broad intermediate zone in which all possible gradations of tissue sensitivity and tissue reactivity occur, the lesions of some pa-

tients partaking of features characteristic of either extreme. They have the worst of both worlds. While the polar types in the individual are stable and "determined," patients in the broad intermediate zone tend to be relatively unstable immunologically.

Examples of lesions of the major types are shown in Figures 1-6.



FIG. 1. Minor tuberculoid lesion.



FIG. 2. Macular tuberculoid lesion.



FIG. 3. Reactional tuberculoid lesions.



FIG. 4. Macular lepromatous leprosy.

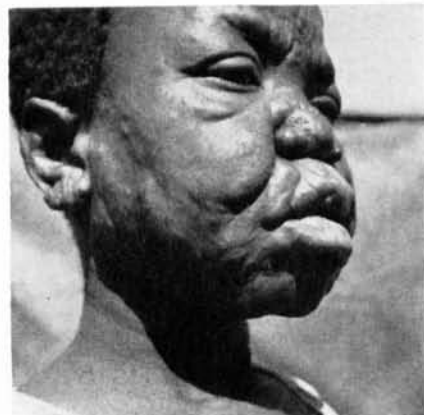


FIG. 5. Nodular and diffuse lepromatous leprosy.

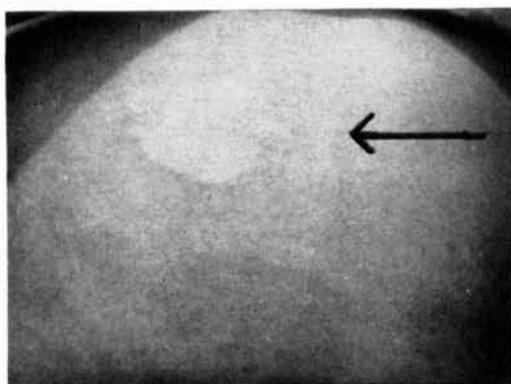


FIG. 6. Plaque in indeterminate leprosy.

COURSE

A high but variable proportion of cases classified as "indeterminate" or "minor tuberculoid" will regress spontaneously without any treatment and eventually disappear. The rest tend to indolent progression, with consequent involvement of the

peripheral nerves.

The typical course of borderline leprosy is toward early peripheral nerve damage and gradual extension of the skin lesions, often as the result of repeated exacerbation. The tendency is for the condition to degenerate toward the lepromatous.

The typical course of the majority of cases of lepromatous leprosy among the deeply pigmented races, is from the macular through the nodular to the diffuse, with peripheral nerve involvement rather late, i.e., three to four years after the first sign in the skin.

EXACERBATION

All types of leprosy except the indeterminate are subject to exacerbation, which may be followed by fibrosis and resolution in tuberculoid leprosy, or become serious and persistent in lepromatous leprosy, interrupting treatment temporarily or permanently.

In all types of leprosy, the local skin lesions may individually or collectively participate in episodes of acute exacerbation or "reaction," but in lepromatous leprosy the exacerbation may be heralded or accompanied by an erythema nodosum called erythema nodosum leprosum because of its rather special features.

The serious aspects of exacerbation concern not only the skin, but more especially the nerves, and (in lepromatous disease) both nerves and eyes. In the course of exacerbation in any type of progressive leprosy, the main peripheral nerve trunks may be acutely involved, either locally, focally or generally; this polyneuritis may be transient or persistent, or recurrent, clearing up completely or entailing irreversible damage. In the acute exacerbation of lepromatous disease, iridocyclitis (presumably allergic) may suddenly supervene.

This rapid introduction to the main clinical features of the disease entity known as leprosy will have achieved its purpose if it provides a pathologic basis for our forthcoming discussions.

Acknowledgments. My thanks are due to Dr. S. O. Egwuatu, Chief Medical Officer, Ministry of Health, Eastern Nigeria, for permission to publish this article.

Dr. Binford. Thank you, Dr. Browne, for bringing us this fascinating spectrum of leprosy. Those of you who have not been able to work in a leprosy hospital, or see leprosy patients, can realize from Dr. Browne's presentation why people who come into contact with the disease become so intrigued with it. Leprosy is not a static disease but has a variety of patterns.

We are calling the next speaker our "key note speaker." To this conference we have invited scientists from universities who have been studying problems in the metabolism of microbial organisms. For many years Dr. Robert G. Cochrane has been trying to get leprosy research into universities so that investigators can see this disease from various angles and go into it more deeply than is possible for physicians or other scientists working in various out of the way places where the disease exists. Dr. Cochrane has for many years stimulated leprosy research in universities. He is

currently the adviser on leprosy to the Minister of Health in London. At present he is Acting President of the International Leprosy Association, carrying on for Dr. José M. M. Fernández, the President, who is now incapacitated by illness.¹ Dr. Cochrane was formerly technical adviser to the American Leprosy Missions. Some years ago he was Professor of Medicine and Director of the Christian Medical College at Vellore, India. I am glad to show you this book which has recently been published, the second edition of "Leprosy in Theory and Practice," edited by Dr. Cochrane and Dr. T. F. Davey. This book has 41 collaborators; 7 of these collaborators are with us today. This book provides a very wide coverage of opinions, skills, and talents in leprosy. Dr. Cochrane will now give the key note address of this conference.

¹Following the death of Dr. Fernández (see pg. 399) Dr. Cochrane was elected President on 30 September 1965.