some dermal nerves. The old pathologic dictum is, however recalled, to the effect that similar or identical morphology does not constitute proof of identical etiology. In leprosy circles, the presence of acid-fast infiltration of nerves is regarded as so characteristic of leprosy as to be almost absolute proof of such infection being leprosy in origin. There are, however, several theoretical pitfalls possible to this assumption (vide following editorial). These are precisely most possible in the presence of extremely low resistance to the invading pathogen, as is apparently the case in the reported armadillo infection. If this infection is due course accepted as true infection with M. leprae, the pattern and general distribution will in all probability differ from that seen in the human infection.

The question of terminology arises immediately and it is a temptation to call the armadillo infection "lepromatous leprosy." This designation, however, now has a long and tediously acquired clinical and immunopathologic characterization. None of these characteristics have as yet been demonstrated in the armadillo infection, save for the above-noted striking histopathologic similarity and the reported ability of its pathogen to oxidize D-dopa. It is, in fact postulated (?) that in iatrogenic immuno-suppression in the human, tuberculosis may be present in lepromatoid histopathologic patterns of infection. It has, therefore, been suggested that at least for the present, the designation "lepommatoid infection, presumptively by M. leprae" be used.

It is noted that even in Dr. Storny's comprehensive discussion of the armadillo, there is no mention of any acid-fast, naturally occurring infection of this creature. It is, of course, not impossible but would be highly remarkable if this animal is as susceptible to M. leprae as armadillo number eight is reported to be and yet be unaffected by any other acid-fast organism in its natural state. Perhaps information to this effect is as yet inadequate and incomplete. Herein lies one of the many potentials for investigation that these reports open up.

It is hoped that these remarks will not be interpreted as critical of the investigators or as an attempt to lessen their glow of achievement. It is their known competence and demonstrated carefulness that lend hope to the reported findings. It is merely that this path in leprosy research has been so long and tedious and so replete with pitfalls, as the investigators have themselves recognized, that one is aware of the considerable amount of work that they face as they continue their very interesting course. Indeed, it is with this knowledge that we publish these reports with hope of ongoing success and hope of increasing pride in our opportunity to publish.

(O. K. Skinsnes)


M. Leprae and its "Affinity" for Nerves

Ever since the publication of the "Atlas Colorié de Speadakskeid" by Danielssen and Boeck in 1847,1 neural involvement in leprosy has been recognized as a striking characteristic of this disease. It is so remarkable that for many years the clinical classification of the disease was designated by the gradings of the degree of involvement of skin and nerve, as for example L1N2, L2N3, etc. As histopathologic study, correlated with lepromin-originating immunologic understanding of the disease manifestations advanced the immunopathologic basis for classification changed, but appreciation of the diagnostic significance of neural involvement was enhanced. Today demonstration of acid-fast infiltration of cutaneous, or other nerves is regarded as a significant diagnostic feature and no histopathologic description of presumptive leprous skin biopsy is complete if it does not note the status of the cutaneous nerves.

Khanolkar's reported studies on the basis of which he concluded that "All leprosy is neural in its inception, in as much as the spreading of micro-organisms is either in or along nerve fibers in the initial stages. The bacilli are attracted toward the degenerating and regenerating nerve fibers in the cutaneous nerve plexuses. . . . The predilection of children to acquire the disease is explained on the basis of a continuous growth and change in the skin in childhood and the special liability of the cutaneous nerve plexuses to damage." In a subsequent paper he postulated that "The leprosy bacilli multiply in the axoplasm of the nerve fibers, enter the bodies of the Schwann cells and often remain dormant in that sheltered location for long periods of time. Under the stimulus of certain supervening changes . . . the bacilli begin to proliferate in the nerve fibers and appear in large numbers in the intercalated zones, from which they burst out into the endoneural and perineural tissues. There they are taken up by histiocytes which gradually become transformed either into lepra cells or into epithelioid cells depending upon the immunological response of the host to the presence of leprosy bacilli." As far as we know these concepts have not been championed by others. Weddell and Lumsden have each been intrigued by the mechanisms of the neural affinity of M. leprae. In many ways their interest in the pathogenic role of the Schwann cell have been complementary and in opposition to Khanolkar's concept of the extension of M. leprae within the neural axis. Lumsden thus concluded "that the bulk of the bacillary spread and multiplication occur along the columns of Schwann cells enveloping the individual nerve fibers . . . ." With this viewpoint we are at variance.

Despite these studies, the term "neural affinity" is unexplained and, in so far as it implies some selective prodigality of the leprosy bacillus for any or all elements of the peripheral neural structures, may be misleading. Nerves are essentially fixed sign posts in the tissues and their associated Schwann cells are more fixed in location than wandering macrophages moving about in the tissues. It requires a considerable concentration of acid-fast organisms in a tissue before they can be detected by either light or electron microscopy. With their established frequency in Schwann cells, which are favorable for their accumulation and probably also their multiplication, it is not unreasonable that they will be found more readily in this location than in wandering macrophages. The latter need not, therefore, be regarded as less involved in the phagocytosis of these organisms than are the Schwann cells. The situation is somewhat akin to a hound ranging a field—he may do this rapidly and only relatively rarely find something of interest to him, whereas the same hound will almost invariably find any tree which is present and find something about that tree that interests him.

Khanolkar suggested that "from the point or points of entry in the skin the bacilli find their way anywhere under the epidermis, through the intercommunicating superficial lymphatic network." This may well be true and it is possible that this movement may be either transport of free organisms or transport through spaces by engulfing macrophages. In our own observations we have seen, in lepromatous leprosy, seen dilated endothelium-lined spaces lying about and within the perineural fibers of small dermal nerves. Within these one occasionally finds acid-fast organisms in small numbers. The fact that these organisms can be found in this manner under light microscopy suggests that there may be a considerable number actually passing in these channels. Our interpretation has been that these are lymphatic spaces though, admittedly, it
is often difficult or impossible in histopathologic sections to differentiate lymphatics from small venous capillaries. These same nerves also show a pattern of bacillary distribution within their structure. Both this internal distribution pattern and the perineural lymphatic pattern of the presence of organisms is morphologically similar to the pattern of distribution seen when neoplastic cells show neural infiltration, as seen in instances of prostatic carcinoma and of pancreatic carcinomatous cells invading a neural plexus of the abdominal cavity. Similarly striking in analogy has been the pattern of mammary carcinoma cells infiltrating the large nerves of the brachial plexus.

We recall that many anatomists, including Abel, hold that the only true lymphatics of nerve trunks lie outside the perineurium. Others have, however, postulated the presence of lymph-containing spaces between the nerve fibers themselves whether or not such spaces are morphologically delineated by endothelial or other lining. The pattern seen in extensive peripheral nerve infiltration by neoplastic cells is consonant with this possibility. In a considerable number of ulnar and sciatic nerves, which we have examined by serial sections,\(^7\) we have found a remarkably similar pattern of foam cell infiltration throughout the length of several such nerves and acid-fast organisms were demonstrated in some of these cells.

In a previous editorial,\(^3\) we ventured to compare first and second infection types of tuberculosis with lepromatous and tuberculoid leprosy and suggested that in many ways lepromatous leprosy is immunopathologically the equivalent of an ongoing first infection type of disease whereas tuberculoid leprosy, once cellular immunity and hypersensitivity is established, is immunopathologically akin to a second infection type of tuberculosis. It will be recalled that in tuberculosis infection, during the period before the development of cellular immunity and hypersensitivity, there is lymphatic drainage of tubercle bacilli from the infected focus to adjacent lymph nodes and that severe progressive first infection tuberculosis is, in many instances, largely a lymph node disease. A pattern of bacillary distribution within their structure. Both this internal distribution pattern and the perineural lymphatic pattern of the presence of organisms is morphologically similar to the pattern of distribution seen when neoplastic cells show neural infiltration, as seen in instances of prostatic carcinoma and of pancreatic carcinomatous cells invading a neural plexus of the abdominal cavity. Similarly striking in analogy has been the pattern of mammary carcinoma cells infiltrating the large nerves of the brachial plexus.

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\(^3\) Skinsnes, O. K., "First Infection Type" Leprosy, Internat. J. Leprosy 57; pp 310-313 (Editorial).
possibly even armadillo number eight.
This discussion is not intended to vitiate the significance of neural involvement as a helpful criteria in determining whether or not the acid-fast organism causing infection in a given experimental animal is indeed M. leprae. It does suggest caution, however, in regarding this as an absolute criterion until such a time as the nature of a specific affinity of M. leprae for nerves be elucidated and demonstrated as unique, or until such a time as it is shown that markedly susceptible hosts, in the virtual absence of cellular immunity and hypersensitivity, will not, if given a dermal infection, seed their nerves with products of the inoculum either through lymphatic drainage or hemic perfusion. (O. K. Skinnes)