CORRESPONDENCE

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TUBERCULOID CHANGES IN THE VISCERA

To the EDITOR:

I wish to offer my congratulations on recent issues of the JOURNAL, which I believe contain important contributions to the knowledge of leprosy. Perhaps I feel especially interested in them on account of the articles dealing with the tuberculoid and necrotic tissue-changes in nerve and skin lesions, a matter that has occupied my mind from the time of my first dealings with the problems of this disease.

In 1889 chance brought me a case in which there was marked necrosis of the nerves; this case I reported in the *Verhandlungen der Deutschen Dermatolog. Gesellschaft* (VI Congress, Wien, p. 503). The recent reports of Wade, Muir, and Lowe on this subject, published in the JOURNAL, extend the work of other authors and confirm my view that the condition was due to leprosy and not to tuberculosis. But at that time this view was heretical, necrosis being considered the special domain of tuberculosis.

The findings in that case, along with those in three others seen earlier in postmortem work in Hawaii, led me to demonstrate microscopic slides of these changes at the dermatological congress held in Strassburg in 1898. By a curious and happy coincidence Jadassohn, Blaschko and Glück also presented at that meeting evidence of tuberculoid conditions in leprous skin, for which they too claimed the influence of leprosy alone, without the assistance of tuberculosis. In the paper that I read then I presented the theory that the differences between the two types of leprosy are solely dependent on the reciprocal state of the host and the invader.

There is another phase of the question of tuberculoid leprosy that is still worth further study, that of visceral leprosy in its miliary

tuberculoid form. I saw that condition in 11 out of 17 postmortems that I performed in Honolulu in the middle of the eighties of the last century. These postmortems were done under difficulties, but plenty of material for study was obtained and the alcohol-fixed tissues were in good condition when I brought them to Neisser's clinic in Breslau in 1887. Having been unable to infect rabbits with the material I held this condition to be a manifestation of leprosy, and contrary to the opinions of Hansen, Neisser and Leloir I could not agree that it was a combination with tuberculosis [Zur Frage der visceralen Lepra. Vortrag bei dem IV Deutschen Dermatologen Kongress, Breslau, 1894. *Verhandlungen der Deutschen Dermatolog. Gesellschaft* (1894) 441]. Danielssen and Boeck saw a good deal of this very extraordinary form of visceral leprosy.

I now consider that tuberculoid visceral leprosy is an indication that a certain degree of immunity has been acquired by the infected organism. In the early stages of a case of nodular leprosy there is little resistance, then it tends gradually to the mixed form, and finally, when years have elapsed and the patient has reached a certain stage of immunity, these tuberculoid lesions in the viscera prepare the final stage.

Would it not be feasible to start an inquiry in the JOURNAL on this subject of miliary visceral leprosy, with regard to its prevalence in different centers, races, and climates, and its occurrence in either of the two types of leprosy, calling special attention to its liability to be confounded with tuberculosis and therefore ignored? It might be of importance to inquire whether the changes in question are more likely to be found in old cases in which the nodular form of the disease has been overcome.

Klopstockstrasse 18 PROF. DR. ED. ARNING.
Hamburg, Germany

Comment by Dr. H. P. Lie, Bergen, Norway:

I quite agree with Professor Arning's proposal that a re-examination regarding the relations between visceral leprosy and tuberculosis ought now to be undertaken. In view of the prevalence of tuberculosis it is, without doubt, quite certain that the two infections are often met with together, and it cannot be thought that leprosy is capable of immunizing one from tuberculosis even if it may have some influence on the form and appearance of the tuberculosis. Arning's findings were at one time thoroughly discussed, but it was of course impossible to arrive at any definite conclusions then.

In Norway leprosy in the internal organs has often been combined with tuberculosis, though much more rarely now than formerly. In the course of

years I have made a number of experiments, both by cultivation and inoculation, with material from the lung, spleen, intestines, liver and lymph nodes from cases in which there were changes that presented similarity with one or another form of tuberculosis. In all these cases I have succeeded in finding tubercle bacilli.

The question now raised, however, is whether the same conditions exist in these circumstances in all races, in all lands and in all climates, or whether there are places where conditions are such regarding leprosy and its similarity to tuberculosis that the two may be confounded if thorough examinations be not carried out.

It goes without saying that these examinations in all cases must be based on cultivation tests and inoculations in animals that are most susceptible to tuberculosis. The large centers for leprosy research are, of course, so equipped that these examinations can be undertaken with scientific reliability, and I presume it is at those places that there are the best opportunities for making postmortem examinations. During such examinations attention should, of course, be especially directed to cases which present the picture of tuberculoid leprosy in the skin or nerves.

Comment by Dr. N. E. Wayson, until recently in Honolulu, Hawaii:

With regard to Professor Arning's query, I can only say that I have not seen the condition that he describes, to wit, a miliary tuberculoid form of leprosy. In all the cases which I have seen at necropsy in which there were definite focal granulomata in the viscera I have found tuberculous infection in one or more locations.

I have been informed by the physicians on duty at Kalaupapa that a very large percentage of deaths of patients at that institution result from tuberculosis, but so far as I know there has been no systematic study of these cases to determine by bacteriological methods the presence of the tubercle bacillus. I am sorry that I am unable to contribute more materially to the subject brought up by this query.

Comment by Drs. S. H. Black and O. E. Denney, Carville, La.:

Professor Arning, in his postmortem examinations of lepers in the Hawaiian Islands about fifty years ago, encountered visceral leprosy in 11 out of 17 autopsies, as evidenced by the presence of macroscopic, palpable, solid, semiglobular masses, found to contain bacilli, singly and in groups, and which material did not infect rabbits. It is inferred that he desires, not an academic discussion of his report, but a description of visceral leprosy as met in various countries in more recent times.

In the last fifteen years 176 autopsies have been performed in this hospital by various pathologists. After gross inspection of the organs, histologic examination has been made routinely from the commonly examined viscera (and on occasion of all tissues) by means of sections stained with hematoxylin and eosin and by the Ziehl-Neelsen technique. In not one of these autopsies has the pathologist encountered macroscopic lesions of the viscera which were interpreted as being unmistakably leprous. In a small number of cases nodular lesions were encountered and diagnosed, macroscopically, as tuberculous because of the appearance of the lesions and the clinical knowledge of the presence of tuberculosis supplemented by laboratory confirmation.

Since the macroscopic lesions described by Arning have not been encountered here in a series ten times as large as his, one may conclude that in this country leprosy does not manifest itself in the manner described by him. This is not completely satisfactory, since the population of this hospital is cosmopolitan and has represented nearly every leprous center.

Were it assumed, with Hansen and others, that Arning's Hawaiian cases were leprosy and tuberculosis combined, it would seem that in 176 autopsies the pathologists of this hospital should have encountered some atypical visceral nodules resembling those reported by him. Fortunately, tuberculosis is not an outstanding contributing factor to the morbidity or mortality in this hospital; only 45 deaths of the total of 258 in fifteen years were attributed to tuberculosis as the causative or contributing factor. This reduces numerically the probability of our encountering atypical nodular tuberculous lesions.

Concerning our findings of visceral leprosy, granulomata have been found in nearly all body-tissues excepting the central nervous system. However, such lesions have been microscopic in size; rarely has the pathologist ventured the diagnosis of leprosy of a viscus from gross inspection. The final histologic diagnosis of leprosy of a viscus has been made only when supported by the finding of numerous acid-fast bacilli, singly and in globus formation. In the approximate order of relative frequence, leprosy has been seen in the deeper tissues as follows: lymph nodes, peripheral nerves, testes, liver, kidney, spleen, ovaries, lung, adrenal, pancreas, intestine, bone (excluding atrophy and secondary infections), and muscle.

The concurrence of tuberculosis and leprosy in a single viscus has rarely been satisfactorily demonstrated in this hospital, though photomicrographs that might be submitted show typical discrete leprous and tuberculous foci in the same lung. It has not been rare, however, to find tuberculosis in one viscus and leprosy in another of the same patient.

Comment by Dr. John Lowe, Calcutta:

I am afraid that I cannot contribute any information of value regarding the occurrence of tuberculoid changes in the viscera in leprosy. Most of our pathological work in India is based on biopsy specimens. It is very difficult to get autopsy material of cases which would be likely to show tuberculoid changes, because in India tuberculoid changes are seen almost exclusively in those less severe forms of leprosy which do not cause death. I have, however, obtained from the Calcutta police morgue autopsy material from cases of nerve leprosy showing tuberculoid lesions in the skin and the nerves, but I have not detected in these cases similar lesions in the viscera. Since my experience is confined to only three or four cases, I am afraid that little weight can be given to my findings in this respect.

Comment by Dr. G. A. Ryrie, Sungei Buloh, F. M. S.:

With regard to the incidence of visceral tuberculoid lesions (if any) of leprosy, I fear that I can contribute nothing. Except under special circumstances I do an autopsy in every case of death here, but as a rule this is confined to naked eye examination of the viscera. Muir has described a number of cases of "leprosy of the lung," but in no case was an autopsy done. Personally I

have never seen clinically a case that could be so diagnosed, and in about two hundred autopsies performed have seen nothing that could suggest it. However, the question raised by Professor Arning should be investigated thoroughly in order to settle it once and for all.

Comment by Dr. H. W. Wade, Culion, P. I.

Since the latter part of 1921 a large number (nearly 2,500) of autopsies have been performed at Culion by several pathologists, in various degrees of thoroughness. Only a minority of these cases have been investigated intensively —there is far too much of this material for that—and most of them have been done on the basis on which routine autopsies are made in the ordinary general hospital, at the request of the clinicians to check their diagnoses. However, the pathologists have naturally been alert to observe anything unusual in the viscera ordinarily examined, and histological examination of the principal organs has usually been made.

Speaking for myself, I have always been interested in the question of the existence of lesions like those pictured by Danielssen and Boeck in their atlas and described by Arning, and have long since been of the same opinion as most of the European workers, that they must have been due to tuberculosis. It has seemed to me significant that, so far as I am aware, nothing of the kind has been described as due to leprosy since more familiarity with the etiology of tuberculosis was gained than existed in the middle of the eighties—though it is to be admitted that that very familiarity might lead one to ascribe to tuberculosis lesions that could be of other origin.

Be that as it may, the fact remains that at Culion we have encountered nothing in the viscera that resembled tuberculous lesions that could not be ascribed, both grossly and microscopically, to that infection, and only exceptionally have lesions been encountered that could be suspected of being of tuberculoid leprous nature so far as we know such lesions. It is true that in only a few instances have guinea-pigs been inoculated (direct culture work would usually be unsatisfactory with unrefrigerated autopsy material in this climate), but those animals that have been inoculated have all become tuberculous. Despite special interest in the tuberculoid condition in leprosy, I am as yet unconvinced that it occurs in the visceral organs, but agree that special efforts should be made in different regions to settle the question definitely.