

# INTERNATIONAL JOURNAL OF LEPROSY

PUBLISHED AS THE OFFICIAL ORGAN OF THE  
INTERNATIONAL LEPROSY ASSOCIATION  
WITH THE AID OF THE LEONARD WOOD MEMORIAL

Postal Address: P. O. Box 606, Manila, Philippine Islands.

Office at the School of Hygiene and Public Health

Entered at the Post Office at Manila, P. I., as second-class matter.

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VOL. 2

OCTOBER-DECEMBER, 1934

No. 4

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## EDITORIALS

*Editorials are written by members of the Editorial Board, and opinions expressed are those of the writers. Any statement that does not meet with agreement will be of service if it but stimulates discussion, to facilitate which the Correspondence section is maintained.*

### ARMAUER HANSEN AND THE LEPROSY BACILLUS

Two years ago the fiftieth anniversary of the discovery of the bacillus of tuberculosis by Robert Koch was celebrated. It is now sixty years since Armauer Hansen, in 1874, first made public his finding of the leprosy bacillus. This was a matter of sufficient importance, not only with respect to leprosy in particular but also to medical biology in general, to merit more than passing mention.

Opinions regarding the nature and causes of leprosy have, during the course of time, varied greatly. From ancient times most people have looked upon it as an infectious disease, but there have also been times when this view has been in abeyance. This was particularly the case in Europe at the end of the Middle Ages, when the disease decreased greatly in that area as a whole and totally disappeared in certain countries there. In Norway, however, after a considerable improvement in the 16th century, it again increased and in the 19th century attained probably a greater intensity and extension than

it ever had before. This, of course, aroused the greatest interest, and discussions regarding the nature and cause of the disease became very lively, at times heated. This was particularly the case after the publication of Danielssen and Boeck's epochal work "Om Spedalskhed" (On Leprosy) in 1847. These two pioneers of modern scientific investigation of leprosy considered, in agreement with the general opinion at that time, that the disease was non-infectious, but they were of the opinion that it most frequently broke out in consequence of unfavorable living conditions, or, occasionally, broke out spontaneously from some unknown cause. When the disease had once appeared they believed that it spread in a family through heredity. In their opinion the nature of the disease consisted of an unfavorable blood mixture, a *dyscrasia sanguinis*, which was characterised by an unfavorable accumulation of albumen in the blood. The blood tried to free itself of this albumen and deposited it in the skin, wherefrom nodular leprosy resulted, or else into the nervous system, which caused the symptoms characteristic of nervous or anesthetic leprosy.

Danielssen and Boeck's authority was such that the greater number of men shared their opinion. Nevertheless there were others, such as Hjorth, who denied that leprosy was hereditary and maintained that it always arose spontaneously. Holmsen also disagreed with the hereditary view of the disease, and was of the opinion that it was due to a miasma that existed in certain places—the special leprous localities—according to which idea leprosy would be a specific disease. Lochmann was also of the opinion that leprosy was specific, but maintained that it most often spread by heredity and only in rare cases through infection. Such were the varied and uncertain opinions regarding leprosy when young Armauer Hansen, at the end of the sixties, began to work on leprosy as assistant to chief physician Danielssen at Lungegaard's Hospital, in Bergen.

In attempting to unravel the difficult questions presented Hansen soon became aware of the striking similarity between syphilis and leprosy, and maintained that on the basis of what was known about the former one could draw certain conclusions with regard to the latter disease. By thorough and ingenious analysis of syphilis he arrived at the conclusion that it is infectious, not hereditary. The term *hereditary* syphilis is quite erroneously used for *congenital* syphilis, the latter only signifying that infection has taken place *in*

*utero*. Further, he concluded that heredity was the criterion for non-specificity and infectivity was that for specificity of a disease; if one could decide on the question regarding heredity or infectivity in a disease one would thereby solve the problem of specificity or non-specificity. In accordance with this argument syphilis, to Hansen, was a specific disease.

How was it with leprosy, which presented so many similarities to syphilis? Hansen directed his attention to the question of heredity versus infectivity in leprosy, and commenced a thorough study of the occurrence of the disease in Norway and the conditions under which it occurred. These examinations were so extensive that it would be impracticable to discuss them in detail here. The results arrived at are to be found in his report on the matter to the Norwegian Medical Society in Christiania, 1874.<sup>1</sup>

I consider this report as Hansen's masterpiece. It contains all of his epochal ideas regarding leprosy, even though they be cautiously phrased and not always completely and clearly worked out. Regarding the causes of leprosy in Norway he stated: "Even if I have been unable to furnish definite proof in any direction, I have pointed out a number of phenomena in this disease which are explained naturally under the assumption of infection, but must on the other hand remain inexplicable under the assumption of heredity. Thus leprosy, according to my assumption, comes under the category of specific diseases that are infectious but not hereditary, as are specific diseases in general." In order to test his assumption that leprosy was an infectious and specific disease, he tried to communicate it to animals, and inoculated twelve rabbits with leprous material, but the results were all negative.

It now remained for him to discover a specific agency against the disease. However, the first examinations in this direction here in Norway were carried out before his time, for Danielssen had touched upon this matter in the forties. He first thought that there must be a "chemical moment" which not only accelerated the forming of the special cells in leprosy, but also altered the normal tissue. These special cells are described in the aforementioned work by him and Boeck as oblong cells with a fairly thick membrane, larger than

<sup>1</sup>The full name of the work is: "Indberetning til Det norske medicinske Selskap i Christiania om en med Understøttelse av Selskabet foretagne Reise for at anstille Undersøgelser angaaende Spedalskhedens Aarsager. Christiania, 1874."

the usual inflammatory round cells. The most characteristic feature was the large, only slightly transparent nuclei (kernels) that filled the entire cells, making them of a fairly dark greyish color, and that contained several deep brown, pigmented particles. These cells which Danielssen described at that time we meet later on in the literature on leprosy, partly as the so-called Virchow's lepra cells, partly as Hansen's brown elements or Neisser's leprous globi. Danielssen was inclined to believe that these cells contained a particular element peculiar to leprosy and made several attempts to prove this, but without success. When Virchow was in Bergen to study leprosy, in 1859, Danielssen showed him these findings. Virchow was of the opinion that the changes observed were due to fatty degeneration, and this idea was accepted by Danielssen.

As a dermatologist Danielssen was also greatly interested in the skin diseases caused by fungi, and published a study of them. It was therefore quite natural that he also searched for fungi in leprosy, but he did not find anything certain.

However, the new bacterial era, founded by Pasteur, appealed strongly to most investigators, particularly the new generation, because of his demonstration of the great importance of fungi and bacteria in disease. The perspectives which opened up for the solving of many problems in medicine led to the search for microorganisms in practically all diseases.

Hansen said: "During this fungus-mad period, as *Cohnheim* called it, my examinations were also directed along that line." For material he used both the blood and leprous nodules. He did not succeed in finding any bacteria in the blood, and the cultures which he made from it under cover-glasses, with all the precautions known at that time, presented after some days numerous leptothrix fibres and zooglear groups, but no free rod-shaped bacteria. In examining leprous nodules only those with unbroken epidermis were used, as ulcerated or encrusted nodules always contain much contamination. The tissue was removed with scissors disinfected in alcohol. In such tissues were found, besides tissue-debris of various sorts, rather large cells and large and small brown elements (cf. Danielssen's findings). "Without adding anything," Hansen said, "one can find here and there rod-shaped bodies, either at rest or in slight oscillating movement. When the cells are whole, unbroken,

their numbers are slight, but by adding a drop of water to the preparation the rods become more lively and little by little more rods appear, the older the nodule the more numerous the rods. The cells, but not the brown elements, swell considerably in water and if one examines them under a strong lens one discovers in many of them, besides granules, also rod-shaped bodies that do not take part in the dancing movements of the granules but oscillate more slowly from side to side. At times one will find the rods together in bunches, crossing each other at very sharp angles. If one now moves the cover-glass, whereby a great mass of the swollen cells burst, the number of rods in the preparation becomes exceedingly great, and they move about in very lively fashion. The size varies greatly from 0.006 to 0.0015 mm. . . . When a piece of a fresh nodule is picked to pieces in a drop of 1 per cent osmic acid, or if the nodule is preserved in osmic acid and examined one or two days later (if longer than this the preparations become less favorable on account of deep coloration) the rods lying in the cells are more intensely colored by the osmic acid than the other contents of the cells and are much more easily made out than in the fresh preparation. In some cells one finds bunches of rods, and some cells are as it were packed with them. If brown elements happen to be in the preparation then these become dark brown to black. If we tap the cover-glass slightly, so that the cells break, a mass of rods appear in the preparation."

Hansen summed up his findings in the following manner: "That rod-shaped bodies are to be found in leprous nodules, and that for the most part at any rate they lie in the cells, must be looked upon as certain in view of what has been stated, but whether these rods are bacteria, and the large brown element perhaps cells that encircle zooglear masses, is another matter." He emphasized the striking similarity between the brown elements in leprous nodules and Klebs' illustrations of zooglear masses in the first number of *Zeitschrift für experimentelle Pathologie und Pharmacie*. As further support for his supposition of the bacterial nature of the rods he stated that the brown elements, and at least many of the rods, were not affected by potash lye in fresh preparations, and that they were colored by osmic acid to the same intensity as bacteria and zooglea. This, in a nutshell, is the most important of what Hansen said about his first findings of rods in leprosy. The work was published, as mentioned, in 1874, but these findings were made during the previous year and

consequently Hansen himself maintained that the discovery of the leprosy bacillus must be reckoned as from 1873.

From what has been cited here it will be seen that Hansen, to begin with, was somewhat doubtful regarding the character of the rods that he found, and it is entirely in keeping with his scientific reliability and critical character that he expressed himself with great caution regarding his findings. One must not lose sight of the fact that he was dealing with a chronic disease, and that at that time it was a quite new and unexpected idea that such a disease could be caused by bacteria. It was not until nearly ten years later that the discovery of the bacillus of tuberculosis was announced by Robert Koch.

After the first findings here discussed Hansen carried on with energy his study of the nature of the rods discovered, and proved that in nodular leprosy they were to be found in all undoubtedly leprous skin nodules, in the spleen, the liver, and particularly the lymph nodes, but were never found in healthy individuals. He therefore gradually arrived at the definite conclusion that these rods were the cause of leprosy. He often demonstrated his bacilli to interested persons, but these demonstrations were not infrequently met by ironical smiles. However, the numbers of those who came to believe in the bacillus and its importance grew steadily, and when the methods for staining acid-fast bacilli were discovered the numbers of doubters became negligible.

For us Norwegians, Armauer Hansen's countrymen, he stands as an illustrious example of the true investigator of nature. With a personality characterized by geniality, he represented the sober-minded scientific worker, with a capacity to examine critically the methods which he used and the conclusions to which his findings led him. If whosoever may essay to solve the difficult questions that still remain in leprosy will bear in mind this characteristic of the discoverer of the leprosy bacillus they will save themselves and others the embarrassments and disappointments that so often result from incomplete investigations and hastily-drawn conclusions.

H. P. LIE.