

Gerhard Henrik Armauer Hansen

What did He See and When?

William H. Feldman, D.V.M.¹

Gerhard Henrik Armauer Hansen was truly an extraordinary person, about whom there exists for most physicians and medical scientists an abysmal lack of information. This, despite the fact that he was the first to associate a specific microorganism with a chronic, infectious disease. The disease was leprosy, long known in Hansen's native Norway and other Scandinavian countries. The minute "rods," "sticks," or "bacillary forms" that he described as associated with the dermal lesions of leprosy were, in fact, the microorganisms known now as *Mycobacterium leprae*.

Hansen was born in Bergen in 1841. His parents had ten sons, five daughters, and "very few resources." Hansen had to earn the money to support himself during his school years (²). In 1868, he was appointed assistant physician at the Bergen hospital for leprosy (Lungegaardshospitalet). The physician in charge was Dr. D. C. Danielsen, the distinguished dermatologist and founder of scientific leprology. Hansen was strongly influenced by Doctor Danielsen and actually became very fond of his chief, despite the friction that often seemed to exist between them (⁵). Hansen was a frequent visitor in the Danielsen home, and at the age of 32 he married Danielsen's daughter Fanny. The marriage ended tragically after only nine months, when the young wife died of pulmonary tuberculosis. It is of interest to note that at the age of 17, Danielsen became a victim of tuberculosis of the hip, which confined him to bed for several years (¹⁰). Four of his sons also contracted tuberculosis and died as a consequence of the infection (⁵).

Two years after the death of his first wife, Hansen remarried. From this union,

one child, Daniel Cornelius Armauer Hansen, was born. He eventually became a leprologist (⁵).

HANSEN'S RESEARCH IN LEPROSY

Hansen's laboratory, unlike those of his well-financed German and French contemporaries, Koch, Neisser, Pasteur, and Roux, was that of an humble, modest man whose personal wants were few. He had a broad interest in the biologic sciences, and contributed significant publications in zoology and marine biology (⁸). His interminable enthusiasm for the attack on the mysteries of leprosy eventually became a self-sacrificing dedication throughout his professional life. In addition to his epochal studies on the etiology of leprosy, he made contributions concerning the epidemiology, prevention, and institutional management of the disease (³).

The Discovery²

The prevalence of leprosy in Norway in the mid-19th century was relatively high. The number of known cases was said to be nearly 3,000, or 17 cases per 10,000 population (⁵). This figure is probably inaccurate because of faulty diagnoses, but among inhabitants of the coastal areas of the Norwegian western provinces leprosy was of particularly frequent occurrence.

Hansen's final triumphs in his search for definitive evidence to support his concepts regarding the etiology of leprosy are best appreciated if one reflects on the status of bacteriology in the pre-Koch and pre-Pasteur era. Proof that diseases could be

¹Chief, Laboratory Research in Pulmonary Diseases, Dept. of Medicine and Surgery, Veterans Administration, Washington, D. C. 20420.

²A carefully documented account of Hansen's early observations regarding the presence in leprosy tissue of rod-like or bacillary objects has been prepared by Fite and Wade (⁴).

caused by living germs that could be seen only with a microscope had not been established. Dyes and methods for staining microorganisms were little known. It should be noted that Hansen's observations were made many years before Koch announced the discovery, in 1882, of the tubercle bacillus. Furthermore, any original ideas Hansen had regarding the infective nature of the cause of leprosy were strenuously, and often violently, opposed by Danielssen, who maintained that leprosy was either humoral or hereditary, but definitely not contagious (3).

Danielssen and Hansen shared an enthusiasm for pathologic anatomy, and each performed many necropsies on the bodies of victims of leprosy who died in Norwegian leprosy hospitals. The meticulous dissections practiced by each of these men and the abundance of material, obtained by necropsies over a long period of time, provided a wealth of information that constituted evidence, first presumptive, but eventually convincing, that leprosy was a contagious disease, caused by a specific bacterial parasite. In an attempt to demonstrate the infective character of leprosy, Hansen inoculated rabbits and cats (3), and later (1891), monkeys (8) with tissues from patients with the disease. These experiments all failed, however, to indicate that the infection had been transmitted.

Both Danielssen and Hansen were interested in *in vivo* experimental attempts to transmit leprosy from one person to another. It is related that over a period of many years, Danielssen made these attempts on himself and several of the servants and patients in the hospital where he served. On one occasion Hansen also revealed excessive enthusiasm for *in vivo* experimentation (11). In 1879, without the recipient's consent, he inoculated leprosy material from one patient into the conjunctival sclera of another affected with the anesthetic form of leprosy. The results of the experiment were negative, but his zest for vivisection was disastrous for Hansen. As a consequence of his indiscretion, he lost his position at the leprosy hospital.

Nevertheless he was allowed to continue as Chief Medical Officer for Leprosy in Norway.

Had Danielssen not been so arbitrary, and had he been less cynical, he might well have shared with Hansen the honor of discovering *M. leprae*. Danielssen was well aware of the small "brown" or "yellowish," grossly discernible "granular masses" associated with leprosy nodules, and he considered them characteristic of the disease. It is unlikely that he thought these masses

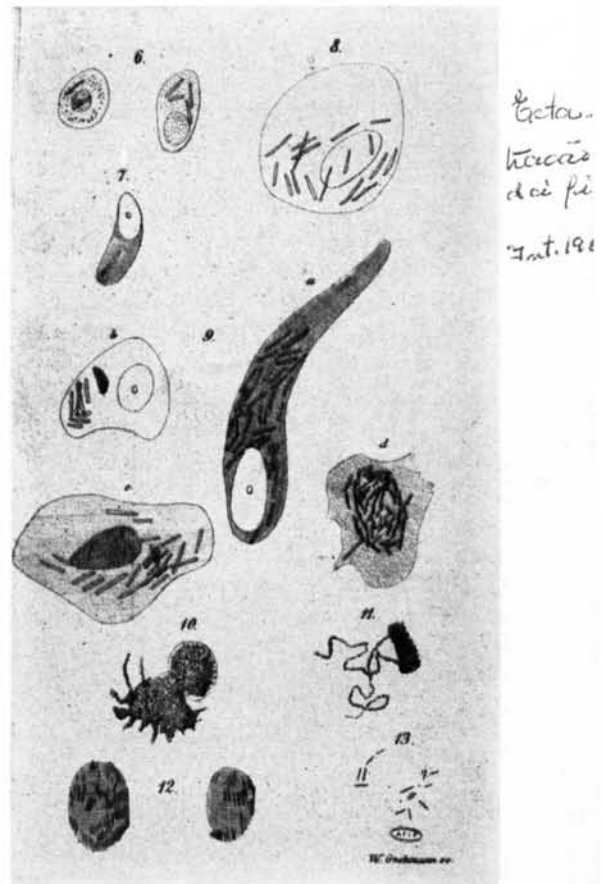


Fig. 1. From the Atlas on Leprosy by Danielssen & Boeck, entitled "Om Spedalskhed," published in Bergen in 1847. The photomicrograph shown represents a congealed accumulation of many monocytic or histiocytic cells containing numerous rod-like substances. Such cells were later designated by Virchow as "lepra cells," and by Neisser as "globi." Structures similar to the picture shown were referred to by Danielssen and by Hansen as "brown nodules" or "granules." Magnification $\times 300$.

had etiologic significance. This would have been particularly true after the great Rudolf Virchow visited Danielssen in Bergen in 1859 and saw the "brown granules." Virchow was not impressed. In fact, he pooh-poohed Danielssen's concept and considered the nodules as "mere clumps of degenerated fat." (9)³

In 1869, Hansen recorded the occurrence of brown nodules or elements in "all leprosy proliferations in advanced stages," which "bear a striking likeness to bacteria in certain stages of development." (3) In his 1874 address before the Medical Society of Christiania (Oslo), Hansen stressed that his evidence proving leprosy to be a specific contagion was indirect and presumptive. He did say, however, that "There are to be found in every leprosy tubercle extirpated from a living individual—and I have examined a great number of them—small staff-like bodies, much resembling bacteria, lying within the cells; not in all, but in many of them. . . ." (3,7)

In support of Hansen's observations of "rods," "sticks," or "bacillary forms" in leprosy tissues, is a report by H. V. Carter, who was a Surgeon Major of the British Army, stationed in India. Carter visited Hansen in Bergen in September 1873, and wrote that "by Doctor Hansen's kindness I have myself seen the minute organisms (a species of Bacterium) which are present in living leprosy matter taken from the interior of a 'tubercle.'" (1)

THE HANSEN-NEISSER DISPUTATION

In 1879, five years after the publication of Hansen's observations establishing the presence in leprosy tissue of microscopic bacillary objects, a 24-year-old research microbiologist from Breslau, Germany, came to Norway. During a two-months' sojourn, he and a companion visited most of the hospitals concerned with leprosy and observed many patients. In addition, their Norwegian hosts provided the visitors with generous amounts of leprosy material for

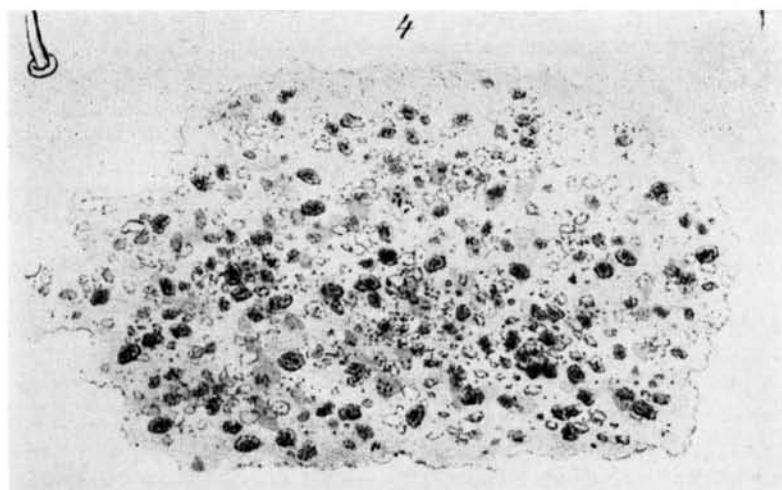
microscopy. The visitor was Albert Neisser, who had recently discovered the gonococcus. Upon returning to Breslau, Neisser used staining methods proposed by Weigert and by Koch. Subsequently, he reported that there were revealed "everywhere bacilli in large numbers, in all 14 pieces of skin and nodules." Bacilli were also observed in the liver, spleen, lymph nodes, and cornea, and most abundantly in the testis (2). Thus began the so-called Hansen-Neisser controversy, as Neisser protested that it was he who first provided a detailed description of the leprosy organism (4,11).

Obviously the explanation for Neisser's success in demonstrating the bacilli was the availability of stains not obtainable by Hansen. Hansen was aware of the necessity of suitable dyes if the rod-like objects he saw in tissue cells were to be properly displayed in microscopic preparations. If he could have stained his preparations by the method subsequently used by Neisser, the validity of Hansen's observations probably would have been firmly established more than a decade before Neisser visited Norway in 1879.

Fite and Wade, after a critical review (4) of the Hansen-Neisser controversy, concluded that the rod-like bodies, observed in leprosy tissue and described by Hansen, were truly *Mycobacterium leprae*. These authors stated that Neisser's observations, although made several years after Hansen's report of 1874, "were the first convincing ones of the bacilli themselves, and the first satisfactory evidence of their relationship to the lesions of leprosy." (4) This was a noteworthy contribution, since Neisser succeeded in "confirming and extending Hansen's observations." (4)

Despite the Hansen-Neisser controversy concerning priority in establishing the bacterial nature of leprosy, the incontrovertible fact is that both protagonists contributed significantly to the emergence of important information, information that finally identified leprosy as a chronic, infectious, bacterial disease, the pathogenesis of which was unlike that of any other infection of man known then or recognized since!

³Years later, reversing his previous conclusion, Virchow designated these brown nodules or granules "lepra cells." Neisser named them "globi."



*Catalepticae
e dea fig.
Int. 1966:34*

FIG. 2. In the several objects shown, a few to many rod-like substances are present intracellularly. It is presumed that the various drawings were made by Hansen and were used to illustrate some of his publications in support of his belief that rod-like items were related in some manner to the pathogenesis of leprosy. Magnification unknown. (From "Hansen, G. H. A.—*Virchow's Arch.* 79:32-42, 1880.")

Like many of his countrymen, Hansen had a keen sense of humor and a spirit of humility. During the latter part of the 19th century, he attended many international medical congresses as the official representative of Norway. Concerning the Leprosy Conference in Berlin in 1897,⁴ he stated, "I noted for the first time that I was a famous man." Initially, he was displeased with the deference shown him, but as the days passed, the homage became familiar, and he wrote, "I began to like it," and added, "This is dangerous."⁶

In a tribute to Hansen in 1925, Dr. I. Kobro, a Norwegian physician, wrote: "What characterized Hansen scientifically was the pathological-anatomical basis for his scientific view, the correctness of the results of his investigations, his thorough theoretical schooling, and above all, the penetrating knowledge that dominated all he published."⁸⁵

As a final comment, it is opportune to mention that despite the fact that leprosy has been recognized for centuries and has been studied assiduously in several parts of the world for many decades since the time

of Hansen's discovery, as of now the disease may be categorized as a most frustrating enigma. Perhaps at the end of the sessions that have just begun, new enthusiasms will have been engendered and new ideas spawned that will finally extract secrets from *M. leprae* that have previously remained inviolate.

REFERENCES

1. CARTER, H. V. Report on leprosy and leper asylums in Norway. Presented to the Secretary of State for India in Council. November 1873. London, Her Majesty's Stationary Office, 1874.
2. CZAPLEWSKI, Albert Neisser und die Entdeckung des Leprabazillus. *Arch. Dermat. u. Syph.* 124 (1917-1918) 513-530.
3. [EDITORIAL]. Hansen (1841-1912)—Lifetime Student of Leprosy. *J. American Med. Assoc.* 184 (1963) 890-891.
4. FITE, GEORGE L. and WADE, H. W. The contribution of Neisser to the establishment of the Hansen bacillus as the etiologic agent of leprosy and the so-called Hansen-Neisser controversy. *Internat. J. Leprosy* 23 (1955) 418-428.
5. GONZALEZ PRENDES, M. A. Gerhard Henrik Armauer Hansen. *Leprosy Rev.* 31 (1964) 127-147.
6. HANSEN, G. ARMAUER. *Livserindringer og Betragtninger* (In English, *Memoirs and Reflections*), Kristiania: Forlagt H.

⁴The Berlin Conference referred to was the First International Congress of Leprosy.

⁵The original was in the present tense.

- Aschehout & Co. (W. Nygaard) (1910) 142 pp. (The unpublished English translation was made at the request of Dr. G. W. McCoy.)
7. HANSEN, G. A. Indberetning til det norske medicinske Selskap i Christiania om en med Understøttelse av Selkabet foretagne Reise for at anstille Undersøgelser angaaende Spedalskhedens Aarsager. Norsk Mag. f. Laegeved. **9** (1874) 1-88. Spedalskhedens Aarsager. pp. 76-79; *translated*: Causes of leprosy. Internat. J. Leprosy **23** (1955) 307-310.
 8. KOBRO, I. Gerhard Henrik Armauer Hansen. Ann. Med. Hist. **7** (1925) 127-132.
 9. LILLINGSTON, CLAUDE. Centenary of leper hospital in Bergen. Brit. Med. J. (June 15, 1957) 1416.
 10. MELSOM, REIDAR. The guiding principles of the campaign against leprosy in Norway during the last hundred years. Mem. Vth Congr. Internac. Lepra, Havana, April 1948, 693-702.
 11. VOGELSANG, TH. M. The Hansen-Neisser controversy, 1879-1880. Internat. J. Leprosy **31** (1963) 74-80.

Dr. Binford. Thank you, Dr. Feldman. You have presented the challenge for others to take up the work that Hansen started 91 years ago.

In the announcement sent to you last fall concerning participation in this meeting, it was said that at this conference microbiologists, biochemists and scientists from other disciplines, not working directly on leprosy, would be invited to meet with investigators now engaged in leprosy research. There would be an objective appraisal of present approaches, and, hopefully, new ways for

attacking unsolved problems would be offered. The program of this conference consists therefore, of the presentation of present current approaches by investigators working on leprosy and the presentation of possible new approaches by scientists not working directly on the disease. The program of this conference therefore now takes on an aspect entirely different from what we have had earlier this morning. We have allowed considerable time for discussion, and hope that discussion will be free. The entire meeting is being recorded on tape.