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Armauer Hansen—The Man and His Work[1]

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The story of Armauer Hansen's discovery of the leprosy bacillus is exciting in itself and far-reaching in its consequences. As in a classical drama the unities of time, place, and action are observed and the unfolding of the tale is severely logical.

One of the hallmarks of first class research work is that the problems investigated are of real importance. A hundred years ago, leprosy was an important endemic disease in Norway. In some districts of western Norway over 2.5% of the population suffered from leprosy, the incidence of the disease had increased markedly from 1800 to 1850, and it presented society with an acute problem.

Armauer Hansen graduated from the medical school at the University of Oslo in 1866 and began his work at the Leprosy Hospital in Bergen in 1868 ([19]). His immediate superior, Doctor Danielssen, who was in charge of the hospital was the leading authority in the field. In 1847, Danielssen and Boeck published their celebrated work *On Leprosy* ([1]). This book was, from an international point of view, the first major scientific work on leprosy and it led to Bergen's becoming a center for leprosy research.

It was here that Armauer Hansen began his work with this disease. He endeavored to acquire fresh knowledge about leprosy, especially as regards the cause of the disease so as to establish a better basis for dealing with it.

On reading the four papers he published from 1869 to 1874, I was struck by his academic learning and his insistence on following a strictly logical line of argument based on his own careful observations. This presents a glaring contrast to the discussion that raged in Norway at that time about leprosy. It was heated, clouded by imprecise arguments, but also studded with firmly held and very different views on the nature of the disease. Some were of the opinion that the disease arose of itself, "spontaneously," others that it was due to bad living conditions, others again that its cause was a "miasma," that is an infectious element that arose from the soil. By far the greater majority thought that the disease was hereditary, and Danielssen held this opinion till his dying day ([19]).

Drognat-Landré wrote a treatise in 1869 on the basis of his epidemiological studies in Dutch Guiana ([2]). He found that careful investigations of Europeans who got leprosy in Surinam strongly indicated that their illness was caused by infectious contact with leprosy patients. We know that this work made a strong impression on Armauer Hansen, but obviously not on the contemporary medical world. On this he wrote in 1872: "In case it should be of general interest, I am happy to state that it was Drognat-Landré's book that made me aware that our research had not paid sufficient attention to the question of infection" ([6, 14]).

In his first two papers published in 1869 and 1870([4, 5]), Armauer Hansen described the results of his anatomical and clinical investigations of leprosy. On the basis of these he drew the conclusion that leprosy was a "specific disease," that is a distinct, well-defined disease and therefore probably with a definite cause. He wrote, "My view of the disease has slowly become clarified, as is only reasonable," but his conclusion as regards the cause—infection, heredity, or something else—was still, "One can produce examples that support one view and examples that support another, and others that support a third view, yet none of them is convincing."

In 1871 and 1872 he traveled around in the districts of western Norway where leprosy was most frequent and carefully investigated 69 families who suffered from leprosy. He applied strict logic to the various arguments and found that heredity could not account for the observations he had made. But the positive aspect is more in-

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FIG. 1. Isolated farm in western Norway.

teresting: how did he arrive at the conclusion that the disease must be infectious?

Through studies of leprosy patients who lived on isolated farms and in whose families no other cases occurred, he discovered that these patients had always previously been in contact with leprosy cases ([7]). Figure 1 shows an isolated farm in western Norway. They are often found on a small area of flat ground surrounded by steep cliffs, and we must go a long way further along the fjord before we come to the next farm. It is evident that contact between the inhabitants must be strongly affected by such geographical conditions, and the argument is quite strong.

He further described two cases of newcomers to leprous districts from nonleprous areas who contracted the disease. He found that both had been in contact with leprosy patients before they became ill.

In large families he found one segment without leprosy, while others who had moved and come into contact with leprosy patients got the disease, and he wrote, "this excludes heredity."

He also made use of statistics. In 1856 a national leprosy registry was established in Norway with annual precise registration of all patients ([15]). The various enumerations before 1850 are difficult to compare, but we know for sure that the number of leprosy patients increased greatly from around 1800 to 1850. The number was roughly the same in the period from 1850 to 1860. After 1860 there was a rapidly diminishing number of new cases.

In the 1850's four new leprosy hospitals were built, so that a high proportion of the patients with nodular disease were now admitted to hospitals. Armauer Hansen perceived a connection between these events and wrote ([7]): "The evacuation from the districts by reason of admissions to the hospitals is of significance for the diminished number of new patients."

However, the decrease in the number of new cases varied from place to place. He investigated whether this corresponded to the rate of admission to hospital. Figure 2 shows data from his 1874 paper ([7]). The black dots are from a region where an estimated 20% of all leprosy patients were admitted to a hospital in the three recorded periods. The crosses show data from another region where admission to a hospital was not introduced until later—very few were admitted in the period from 1856 to 1860, while 20% of the patients were admitted in the next two periods. The upper

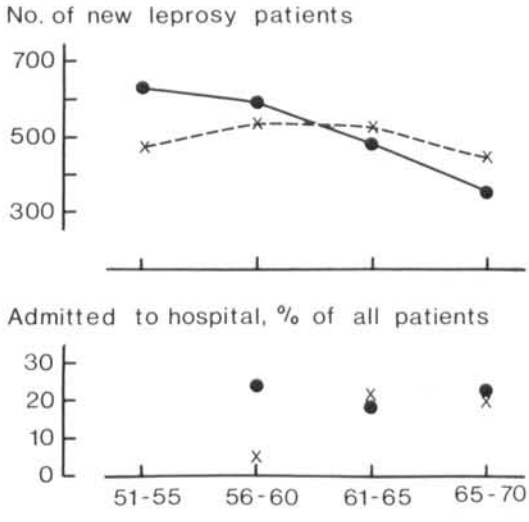

FIG. 2. Number of new leprosy patients in two regions of western Norway in relation to admissions to hospital. To illustrate that there was a delay before fewer new cases occurred in the region where admission to a hospital was introduced later. Data from (7).

curves show the number of new cases in these two regions. He demonstrated therefore that in regions where admission to a hospital was introduced later, there was a delay before fewer new cases occurred, and these conditions were made plain in the course of a 15 year period. His conclusion from this was, "This is too short a period to show an effect on something which is hereditary, but it is, on the other hand, in very good agreement with infection" (7).

The idea that a disease could be infectious was not new. What is impressive about Armauer Hansen's approach is that he rejected the foggy explanations that were current at the time in relation to leprosy and that he attempted to arrive at an explanation of the disease by fresh personal investigations. As we have seen, he was led by clear logical reasoning to conclude that the disease could not be hereditary, but that it must be infectious. His view then conflicted fundamentally with that of his immediate superior. Doctor Danielssen must have been an unusual character; he maintained his own view, but allowed the junior colleague to press on with his.

So began the work of searching for the bacillus. How long it lasted we do not know, but he first made a series of attempts to find it in the blood, always with a negative result. His means were simple and he must have had a great capacity for self-criticism. He wrote down what he saw. He saw fungi, he saw bacteria, and he was aware that this had nothing to do with what he was searching for. He then moved on to the investigation of leprous nodules. His first observation was (7), "Where there is a superficial ulceration of the nodules with formation of a scab, a great number of bacteria are always to be found in and under the scabs." He was again aware that this is not what he was searching for; these were irrelevant bacteria present because of the ulceration. "I have therefore constantly chosen nodules covered by unimpaired skin." And eventually success crowned his efforts. On February 28, 1873, he examined a boy with many leprous nodules on his face. He removed one nodule from a nostril. He cut through it, carefully scraped the edge of the cut with a knife, rubbed the stuff onto a glass slide, and wrote (7): "If one examines the specimens without adding anything, one can here and there perceive rod-like bodies either at rest or in slightly oscillating motion; when the cells are preserved whole, their number is low. If one now adds a drop of water to the specimen, the rods show livelier movement and little by little more and more rods appear. The cells swell considerably in water, and if one looks through strong lenses, one perceives in many cells, besides granules, also rod-like bodies, which do not take part in the dancing movements of the granules but swing rather slowly from one side to the other; to some extent one finds the rods together in bundles, crossing one another at very acute angles. If one now moves the coverslip so that a great number of the swollen cells burst, the number of rods in the specimen becomes exceedingly large, and they move in very lively fashion."

At the Armauer Hansen Institute in Addis Ababa we carried out the experiment again, exactly as he described it. We added distilled water to the specimen, the cells swelled up and burst, and the rods streamed out, just as he described it. Professor Arnesen, of Ullevål Hospital in Oslo, assisted me in photographing this experiment, in an attempt to illustrate the conditions that Armauer Hansen faced.

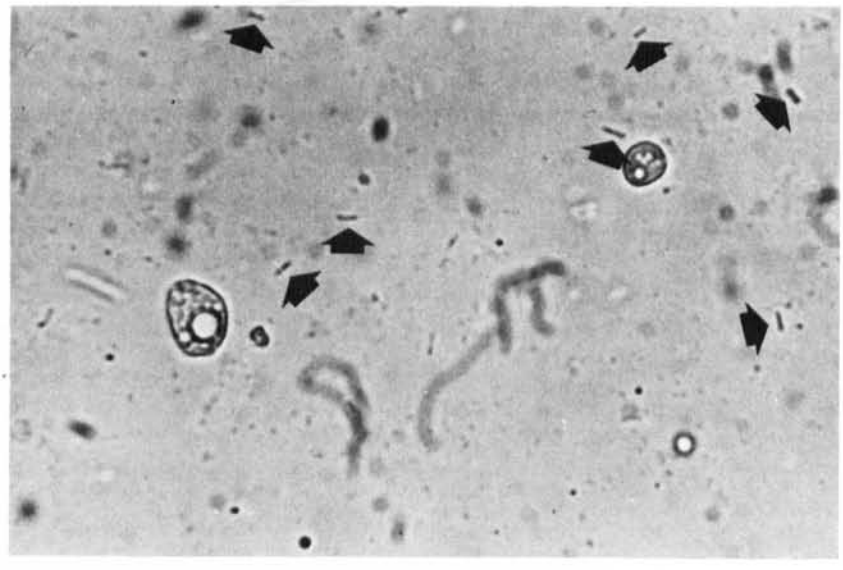

FIG. 3. Unstained leprosy bacilli prepared as described by Armauer Hansen [7]. Several rods are clearly seen (arrows), and many appear more faintly.

But the attempt really does Armauer Hansen little justice for he had only a simple microscope, no electric light, and he was searching for something of unknown appearance. Figure 3 shows the unstained preparation where we can see a great deal of matter from the cells. We can see several rods clearly, and also suspect the presence of many more. The rods are easier to recognize in the microscope when they move. Figure 4 shows the specimen after modern staining where the acid-fast bacilli stand out in quite a different way!

After having read his papers and repeated his classic experiment, I am free from doubt. He knew that he had seen rods

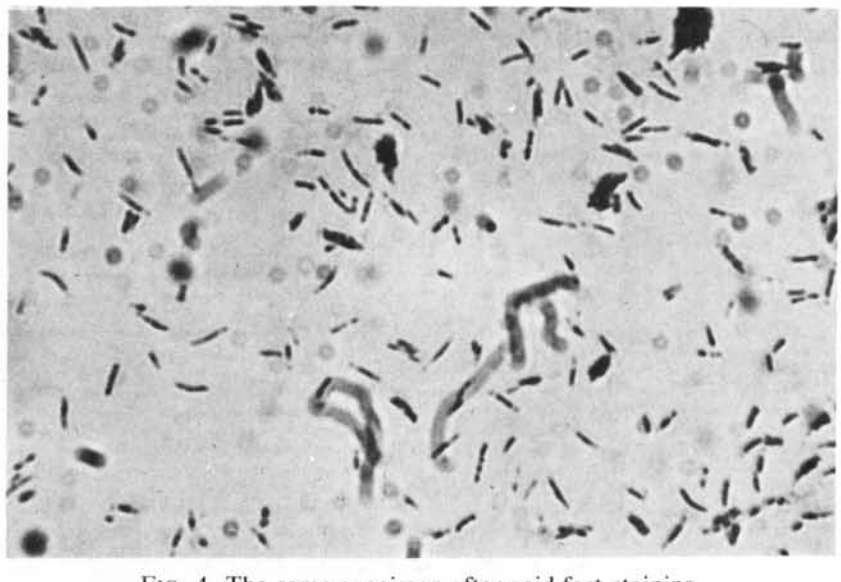

FIG. 4. The same specimen after acid-fast staining.

within the cells from leprous nodules, he described what he had seen, and his observation and description were correct. On the basis of his epidemiological studies he developed a completely clear view that the disease was infectious.

It was an epoch-making discovery. Armauer Hansen had demonstrated that leprosy must be a chronic, infectious disease, and this was the first time that a bacillus had been connected with such a disease.

For Armauer Hansen the scientific milieu in Bergen must have played an important role. Danielssen and Boeck's treatise in 1847 was the first major scientific work on leprosy. The milieu was active, determined to acquire fresh knowledge about the disease by means of personal observations. This must have provided a stimulus and support. It was a good school but probably became a hard—even merciless—one after Armauer Hansen had formed a view about the disease which was fundamentally different from that of Danielssen.

As a medical student, Armauer Hansen was greatly influenced by Emanuel Winge, his tutor in pathology ([19]). Winge had an open mind and the ability to perceive fresh explanations of vital problems, and he especially taught his pupils the latest in medicine. We have seen that Armauer Hansen attached great importance to his epidemiologic studies. He studied each individual case carefully, especially the relationship to other leprosy patients, and it was this process that provided him with the strongest arguments supporting the infectious nature of the disease. I believe that Homan and Hartwig's work in Kragerö in south Norway must have played a major part in making him attach so much importance to this method of procedure. They carried out their work during the great dysentery epidemic in 1859 and with typhoid in 1864. On the basis of careful epidemiologic studies, they concluded that these diseases must be transmitted each by its own specific infectious agent ([12, 13]). And in 1869, Winge and Heiberg described to The Medical Society in Oslo their findings in a man who died of septicemia. On his cardiac valves they observed long chains of microbes which they described as "long, infiltrating threads consisting of beadshaped bodies." Sixty years later they were identified as streptococci by further examination of the preserved heart ([10]).

The idea that a living infectious agent could be the cause of a disease was therefore current when Armauer Hansen started his work, but most of those who worked with leprosy were averse to it. Today it is taken for granted that infectious diseases are due to bacteria, viruses, fungi, etc., but at that time such was not the case. Methods to stain bacteria were in their infancy and primitive. In 1869 Davaine had proved that the anthrax bacillus was the cause of anthrax in humans ([14, 18]). This was the first case in which it was proved that a bacillus could induce a disease in humans. In 1873 Armauer Hansen discovered the leprosy bacillus, and Obermeyer published his account of the spirochaete which was the cause of relapsing fever. It was in 1882 that Robert Koch first described the tubercle bacillus, and later in the 1880's a long series of bacteria were described that caused disease in humans. This brings Armauer Hansen's work into proper relief—it was indeed epoch-making.

Armauer Hansen has been criticized for his long-lasting caution in stating that the rods were the cause of the disease. In their comments on his 1880 paper ([8]) on the leprosy bacillus, Fite and Wade for instance state ([3]): "If this sounds like a weak article, it is because it is weak. Little new is recorded, and that inadequately. There is no evidence of more than a trivial amount of fresh work. We can but wonder whether, between 1874 and 1879, Hansen had really appreciated the importance of his observations."

As we have seen, Armauer Hansen developed a completely clear view that leprosy is an infectious disease in his 1874 paper. He also described his microscopic observations in detail, and it is obvious that they were correct. The crucial question then was whether the rod-shaped bodies were the direct cause of the disease, and to prove it.

In his famous work of 1840 Henle ([11]) had defined the conditions that must be satisfied to prove that a microbe is the cause of a disease: 1) it must always be possible to find the microbe in connection with the disease; 2) it must be possible to isolate

and study the microbe outside the animal organism; and 3) the microbe must be able to induce the disease it induced under natural conditions when, after cultivation, it is again injected into an animal. These requirements were reformulated by Koch in 1882 after he had discovered the tubercle bacillus, and they later became known as Koch's postulates.

We know quite a lot about Armauer Hansen's intense work from 1874 to 1880 ([19]). He tried to grow the bacillus *in vitro* and made a series of inoculations attempting to transmit the disease. These are obviously experiments attempting to satisfy Henle's postulates. We also know his academic background in natural science and strict requirements for substantiation before he drew his conclusions. His longtime collaborator, Dr. Looft, later told Professor Vogelsang specifically that Armauer Hansen knew Henle's postulates ([20]). To me, it is thus only reasonable that Armauer Hansen was very cautious in asserting that the rods were the direct cause of the disease.

You are all certainly aware that Armauer Hansen worked with a particularly difficult microorganism. He had seen the bacillus in unstained material in 1873, and shortly afterwards he was able to stain it with osmic acid. Its acid-fast nature was demonstrated by Neisser and Ehrlich in Germany about 1880 ([16]) on the basis of material they obtained in Bergen, and this was a major step forward. Further basic advances in the knowledge of the pathogenic microbe required the fulfillment of Koch's postulates. The first of these that ". . . the presence of the microbe in connection with the disease must always be demonstrable" was also satisfied in Bergen when the bacillus was demonstrated in patients with "maculo anesthetic leprosy" ([9]). It is evident today that leprosy bacilli may be found in all lesions diagnosed as leprosy by competent clinicians, but this may require hours of search through serial sections in tuberculoid cases.

Armauer Hansen carried out a long series of experiments involving cultivation and inoculation, all with negative results. A beginning was, I suppose, first made at satisfying the other two postulates in 1960 when Shepard demonstrated a limited multiplication of *Mycobacterium leprae* in the foot pad of normal mice ([17]).

The second part of Armauer Hansen's lifework was his efforts to bring the disease under control. He had proved that the disease was infectious, and for him this provided a basis for a rationally based fight against it. If one could reduce the number of bacilli scattered around among the population, if one could reduce the likelihood of infection, the disease was bound to recede. With the facilities then available this could only be achieved by isolating the patients, especially those who spread the greatest number of bacilli. As early as 1874 he stated ([7]), "The patients with nodules are the most dangerous—they ought to be isolated, preferably at the earliest possible opportunity."

As chief medical officer for leprosy, he drafted a proposal for the legislative amendments necessary to provide a legal basis for isolation of patients as a step in prevention of the disease. The first enactment appeared in 1877, entitled "An act relating to the care, and support of impoverished leprosy patients, etc." It applied only to the impoverished leprosy patients for whom the authorities had to provide. It prohibited the system of communal relief under which leprosy patients were often made to travel from one farm to another in a particular district, staying and being maintained for a short period at each place. They must have had a pitiable existence, and the system was almost ideal for disseminating the disease. The Act put a stop to this state of affairs. Further, it provided that they be isolated, preferably in hospitals. If this was not practicable, they were to be provided for under conditions approved by the local health authorities. The next enactment of 1885 was more comprehensive. It introduced isolation of all leprosy patients and, if necessary forcible internment in public institutions. Leprosy patients were nevertheless permitted to live at home if they observed the prescribed precautions. Nor did the Act require the separation of married couples who wished to live together. The Act gave rise to violent conflict and opposition. It seems, however, that it was administered in a humane manner, and the resentment gradually melted away. Later, correspond-

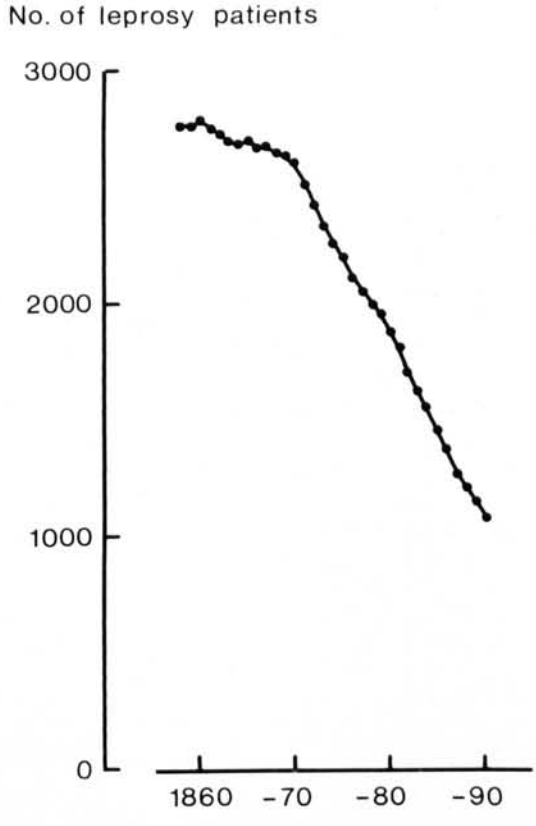

FIG. 5. Number of leprosy patients in Norway 1857-1890. Data from ([9]), page 145.

ing principles have been applied in Norwegian statutes relating to other infectious diseases, for example in the Tuberculosis Act.

Leprosy control is the major concern of all who work with this disease; here preventive medicine is especially important. When Armauer Hansen proved that the disease was caused by infection, he attained a new, rational basis for its control. At that time isolation was the only means available. He made use of it, and taking the conditions with which he was faced into account, I am of the opinion that this was justified and correct.

The significance of isolation for the decline of leprosy in Norway has been amply discussed and will be discussed for years to come. The bend of the frequency curve (Fig. 5) is striking and corresponds to a rather sudden hospitalization of a major part of the leprosy population. Socioeconomic factors have also played their role, especially the gradual increase in living standards, diminution of domestic overcrowding, and higher standards of hygiene.

The special geographic conditions in the fjords of western Norway have presumably also contributed to the effect. Figure 6

FIG. 6. Local community in Sognefjord in western Norway.

shows a typical local community. People lived close together under the mountains with frequent personal contact, most of them having only sporadic contacts with other communities. Under such conditions I would presume that the absence of one lepromatous patient means a radically diminished risk of infection for many people.

Today the situation is entirely different in leprosy control programs. Early case finding and good case holding with adequate drug therapy are strong measures to reduce the infectiousness of leprosy patients. It is thus no longer justifiable to isolate them; they should live in society with and on the same terms as the rest of us.

Armauer Hansen is unique in Norwegian medicine.

We are a small nation, and Norway's contribution to new and vital knowledge must be small when measured on a global scale. Today we honor the memory of Armauer Hansen. His contribution was very great even by such a standard.

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