ON THE BACILLUS OF LEPROSY.¹

BY

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THE pathology of tubercular leprosy (Elephantiasis Græcorum) is intimately associated with two discoveries. The first series of observations, which defined the group of diseases amongst which leprosy is now classed, were chiefly concerned with the cell-growth that is invariably found in the tubercles. The second series, which were initiated by the investigations of Armauer Hansen in Norway, are concerned with an organism, presumably foreign to the human body, which is found in the cells of leprosy tissues—the so-called *Bacillus lepræ*.

With the cell-growth of leprosy I shall not attempt to deal in this paper. It has been frequently and well described in the numerous memoirs, monographs, and text-books of pathology that have been published during the last decennium. Comparatively little has been added to our knowledge of the ordinary pathological histology of

¹ The research which is reported on in this paper forms part of a series of investigations on the parasites of the human skin, towards which a grant has been made by the Scientific Grants Committee of the British Medical Association.

the disease since the description given by Virchow in the second volume of his work on 'Tumours,' published nearly twenty years ago. It is well known that that eminent pathologist grouped together syphilis, lupus, and leprosy, as forming a class of granulation tumours; these three diseases having in common, destruction of tissue and the formation of groups of cells which bear a resemblance more or less marked to granulation cells.

Of the two appearances, the destruction of fibrous tissue and the grouping of cells, the greatest weight has been assigned to the latter, the cell of leprous tissue being supposed to be intimately associated with the development of the disease.

The first notice of the bacillus of leprosy is contained in a report made to the Medical Society of Christiania in 1874 by Hansen. In his paper on the subject in the 'Quarterly Journal of Microscopical Science,'¹ this report is referred to as containing the statement that he had "often, indeed generally, found, when seeking for them in the leprous tubercles, small rod-shaped bodies in the cells of the swelling."

The date of this report fixes that of the first publication of the discovery, and assigns it indisputably to Hansen.

With commendable caution Hansen was slow to assign too much importance to the appearances which he had observed, and in his paper in the 'Quarterly Journal of Microscopical Science' (published simultaneously in French and German), we still find him hesitating to regard the bacilli as the cause of leprosy. Having failed to inoculate rabbits by introducing portions of the leprous growths under the skin of the animals, he considered the failure was adverse to the supposition that the bacteria are the real virus. His paper is illustrated by a plate giving drawings of the organisms.

The existence of bacilli in lepra-cells has been confirmed by Neisser, Cornil and Suchard, Koebner, and others. It only remains now to extend the investigation,

¹ New series, vol. xx, 1880.

so far as the presence of these organisms is concerned, to a larger number of cases of leprosy, taken from widely separated countries. In considering the question of the connection of the disease with the presence of the parasite, it becomes important to know whether the bacilli are found in all cases and in patients in all parts of the world, and it is on these points that the evidence I now place before the Society chiefly bears.

In the summer of 1882 my friend Dr. Manson, of Amoy, brought me leprosy tissue from China, from three cases which had been under his observation.

CASE 1.—The leprosy had been known to exist for three to four years, and was a case of mixed anæsthetic and tubercular leprosy. There were tubercles on the face, anæsthesia, and muscular atrophy of the hands and arms, and swelling, bronzing, and anæsthesia of the feet and legs. I examined a tubercle which was excised from the face.

CASE 2.—The leprosy had been known to exist for five to six years. There was leontiasis of the face, anæsthesia, bronzing, and swelling of the legs, feet, arms, and hands.

CASE 3.—The leprosy, which was of the anæsthetic and annular type, had existed for three years, the patient being a male, æt. 24. A small, round, slightly elevated, dusky-red patch on the abdomen, which had existed for only nineteen days, was excised in its entirety.

Dr. Manson placed the excised portions of tissue in alcohol immediately after he removed them from the living patients. He brought them with him to England and I received them from his own hands. From the time that they were removed from the patients until the time when their preparation for microscopic observation was completed, the possibility of the development of organisms in the tissues was excluded.

I was also favoured with leprosy tissue from the West Indies by Dr. John D. Hillis, F.R.C.S., medical superintendent of the General Leper Asylum, British Guiana, the author of an able and instructive work on West Indian Leprosy. Portions of skin with the tubercle were excised

from the face and right pinna of a black native, æt. 27, affected four years with pure tuberculated lepra. The tissue was taken from the living subject, placed immediately in alcohol, and then in absolute alcohol. They were received by me in alcohol in a well closed bottle.

I shall pass very briefly over the methods by which I endeavoured to show the presence of bacilli in these leprous tissues. They consisted simply in attempts to follow closely the methods which have been published by Koch and Ehrlich. These attempts, for reasons which I can hardly understand, were at first not very successful, then came a stage during which I found it comparatively easy to show the bacilli but found it impracticable to make permanent preparations. Latterly, and for some months past, I have found it easy to show the bacilli and not difficult to make permanent preparations. These improvements in preparation were partly due to greater experience in manipulation, and partly to modifications in the method of operating. The *technique* of this kind of work is, according to my experience, still very imperfectly developed. Whilst the demonstration of bacteria in fluids, as the bacilli of tubercle in sputum for example, is so easy that any intelligent person can be taught to succeed in it in a very short time, the demonstration of organisms in tissues preserved in alcohol, is in many instances by no means easy and in many cases fails. A certain method, applicable to all cases in which organisms are present in solid tissues, and of easy application, is yet to be discovered. As my own efforts in this direction are still progressive in their results, I think it better to reserve anything I may have to contribute on this part of the subject for future publication. In the meantime I may state that the demonstration of the bacilli of leprosy by staining with gentian violet and methylaniline violet, and fuchsine as recommended by Professor Ehrlich for tubercle bacilli, will not be found difficult by anyone who is familiar with work of this kind.

The bacilli described by Hansen were found in the skin

of the three Chinese lepers and in the skin sent me from the West Indies. They were also found in the epiglottis of a leper who died in Australia. This patient was born in New South Wales and was the son of an English father and an Irish mother. I am indebted to my friend Dr. Maclaurin, of Sydney, for sending me the larynx, and to Dr. Cox, of Sydney, for notes of the case.

Of the three portions of skin from three different patients brought me by Dr. Manson, I possess permanent preparations of one only. But bacilli were also observed in the skin from the other two cases.

My description is based on the case of Chinese leprosy, of which I have been able to preserve specimens, and on the specimens of Demerara leprosy.

When a vertical section through the skin of a leprous nodule, prepared for the demonstration of bacilli, is bleached to a certain degree, all the tissues of the cutis become colourless, and the leper cells alone are stained. These stand out boldly, deeply stained with methylaniline violet, if that dye has been used, whilst the surrounding connective tissue does not show a trace of staining. Such a section is suited for observing the size and form of the leper cells. The whole cell is coloured uniformly and no nucleus is visible. If the connective tissue amidst which the cells lie is carefully examined, no bacilli are found in the bundles or in the interfascicular spaces (so much at least has been the result of a careful and repeated examination of my sections prepared from these cases).

If the bleaching process is carried a degree further, bacilli are seen in some of the cells—those in which the decolorisation is most advanced—whilst the other cells are still seen as deeply-stained masses. The longer the bleaching is continued the greater the number of cells which are seen to contain bacilli, until a point is reached at which the bacilli themselves become faint.

In a section in which the bleaching has so far advanced as to show many bacilli, the organisms may be seen grouped within the contour of a lepra cell, or they may

be seen singly or in small numbers apparently lying free in the tissues. I am disposed to believe that the latter appearance is deceptive. In the more deeply-stained sections no individual bacilli are observed, cells alone retaining the dye. Some of these cells are indeed very small, many of them, especially in parts in which the leprous infiltration is beginning, being as small as white blood-corpuscles. It is probably due to the small number of bacilli contained in these minute cells that the appearance of apparently isolated bacilli in more completely bleached sections is due.

In the parts of the skin not affected with the leprous infiltration no bacilli were observed.

During the preparation and study of a large number of sections I have come on two appearances (both hitherto, so far as I am aware, undescribed) of the greatest significance.

It has been remarked by more than one observer that when the epidermis is entire in non-ulcerated leprous tubercles no bacilli are found in the epidermis. Cornil and Suchard,¹ for example, use the following words:—“A remarkable peculiarity which we have observed in all our preparations is that the different layers of the epidermis do not contain any microbe, the epidermic covering forming a varnish impermeable to the special parasite of leprosy. We shall return to this point in studying the conditions of this malady compared with the contagion of other cutaneous affections;” and, again, they state further, “that the epidermic layers although thinned are free from parasites. This epidermic layer opposes itself, so long as it is preserved, to the external diffusion of the parasite, and forms a barrier to it which renders contagion very difficult. The site of the parasite is deep. The contrary is the case in most parasitic affections of the skin which are specially contagious, such as eruptive fevers—smallpox, for example, and erysipelas.”

¹ “Note sur le Siége des Parasites de la Lèpre,” *Annales de Dermatologie, &c.*, 2me série, vol. ii, p. 655.

I have found in one of my sections bacilli in the epidermis. Whilst the tissue was deeply stained the appearance was observed of small cells, which retained the aniline colour, being scattered through the epidermis at different points. After the section had remained some time in oil of cloves I was able to observe that the colour of these cells was due to their containing bacilli. The size of the cells was that of white blood-corpuscles. I made a camera drawing of the preparation, and Mr. Thurston, to whom I am much indebted for the care he has taken in preparing the plates which accompany this paper, made an independent camera drawing of the same preparation. The position and number of the bacilli in the two drawings corresponded. A reference to the drawing on the plate renders it unnecessary for me to describe them further. The epidermis surrounding these cells was quite uncoloured, of normal thickness and texture. The leprous infiltration of the section was chiefly in the deeper part of the corium, the papillary layers being intact, and containing very few bacilli.

I believe that the bacilli in the epidermis in this section were contained in white blood-corpuscles which had passed into the epidermis, but I am prepared to admit that this view is open to discussion.¹

The other appearance was again found in a solitary instance. In this section, also, the leprous infiltration was in the thicker and deeper layer of the cutis, the papillary layer being entire and containing very few bacilli. In the papillary layer, midway between the epidermis and the leprous infiltration, a lymphatic vessel was seen lying parallel to the epidermis, and containing two lymph-corpuscles in its lumen. In both of the corpuscles bacilli could be seen, but in one of them more distinctly and in greater number than in the other. Part of the lymphatic vessel, containing the corpuscle in which the

¹ Although since the above was written I have examined many sections in which the staining was perfect, I have not again met with a similar appearance (July 18th).

bacilli were most numerous, is shown in the drawing (Pl. XII, fig. 1).

The accuracy of the observation was again tested by Mr. Thurston and myself making independent camera drawings which almost exactly corresponded. The only point in which my observation differed from that of Mr. Thurston is that, in Mr. Thurston's drawing a bacillus is lying free in the lumen of the vessel close to the corpuscle; I included this bacillus in the corpuscle. The difference probably depends on the respective focuses used in making the drawings.

This seems the place for me to call attention to three facts, and to the theory which I believe they support.

It has been frequently observed that the smaller cells of leprous infiltration resemble white blood-corpuscles, and in their size and appearance I have found no difference between them and the ordinary small cell-infiltration with which we are familiar in many pathological conditions of the skin.

It has been stated above that in the epidermis, cells similar in size to white blood-corpuscles, have been found containing bacilli, and in the lymphatic vessel a lymph-corpuscle has also been found containing the organisms.

To my mind these appearances suggest the theory that the lymph-corpuscles are one of the media by which the bacilli are carried from one part of the body to another. The fact that the infected lymph-corpuscle has been found in a lymphatic vessel, although as yet, so far as I know, unique, enables us to understand how the disease is carried from the skin to internal organs. Although the fact in support of this theory is yet isolated, it will be granted that it renders it a highly plausible one.

The groups of bacilli found on the borders of the lymphatic vessel in the section which I have described, are in all probability due to the fact that lymph-corpuscles had passed from the vessel into the adjacent connective tissue. In any case it is clear that they had an intimate relation to

the vessel, because the surrounding connective tissue and the papillary layer were free from organisms.

Some experiments were made with the view of ascertaining whether it is possible to show in the healthy skin organisms similar to those found in leprosy. With this view, sections of healthy skin from the female breast and the leg of a man, and sections from an epitheliomatous tumour of the vulva, and from the skin of several patients who had died of scarlet fever, were submitted to the same process by which the bacilli of leprosy were demonstrated, and in no instance were any such organisms observed. Further, in the leprous tubercle itself the connective tissue of the healthy skin, adjacent to the infiltration, showed no bacilli. We are therefore warranted in concluding that the organisms found in the cells of leprosy have an intimate connection with the disease.

During the progress of this investigation, whilst already engaged in preparing this paper, I received from Sydney the larynx of a man who died of leprosy in the Liverpool Asylum of New South Wales. I have received a detailed account of the case, drawn up by Dr. Cox, of Sydney. The case will be published hereafter when my examination of the larynx is more complete. At present I am only desirous of placing on record the size and appearance of the bacilli in a case of leprosy having its origin in Australia. The patient had been affected with genuine tubercular leprosy for six years at the time Dr. Cox drew up the notes. An addendum to his report states that the patient died two months afterwards from suffocation, a result which will astonish no one who examines the larynx which I have received. Sections have been prepared from a small portion of the greatly thickened epiglottis, and they show bacilli of the same appearance as those found in the cases which I have already described.

The evidence of the association of a bacillus with the leprous infiltration at present stands thus :—It has been found in Norwegian leprosy by Hansen and other Norwegian observers; it has been found by Cornil and

Suchard in specimens taken from the leper asylum of Grenada, and from a patient under treatment in Paris ; it has been found by Koebner in a patient who had contracted the disease in South America ; by Majocchi and Pellizzari in two patients from the Island of Elba ; and I have now found it in skin excised from patients in China, in the West Indies, and in the larynx of a leper who was born, and died, in Australia. The intimate association, therefore, of the parasite with the disease seems indisputable.

I am not prepared to lay too much stress on the size, form, or appearance of bacilli as indicating identity of kind, but anyone who compares the drawings that have been published of the lepra bacilli with each other must be struck with the similarity in these respects which the organisms seen by different observers have to each other. The drawings by Hansen,¹ Neisser,² Cornil and Suchard,³ and of Majocchi and Pellizzari⁴ all closely resemble each other. The question of size is a somewhat difficult one. Foreign observers are in the habit of indicating size by the numbers of the eye-pieces and objectives which they use in making their drawings. It has been my object in preparing this paper to lay before the Society something which, in England at least, will be considered more definite.

I have been fortunate in securing the assistance of Mr. Edgar Thurston, who is highly competent in the difficult task of drawing minute organisms to scale. The plates which he has prepared show the bacilli in Chinese leprosy, in West Indian leprosy, and in Australian leprosy, as magnified by a fixed number of diameters ; and in order to afford standards of comparison, drawings have been made of the bacilli of tubercle, of the bacilli found in sections of a putrid sheep's cornea, and of the bacilli

¹ Loc. cit.

² 'Virchow's Archiv,' vol. 84.

³ Loc. cit.

⁴ 'Studiî Ematologici nei Leprosi,' Florence, 1882.

which formed a large part of the scum of cold mutton infusion. A comparison of these drawings will show that so far as regards the size of the various bacilli, erroneous statements have been made.

It will be noticed that the bacilli in the epiglottis of the Australian leper, while they are of the same length as the bacilli in the other leper specimens, appear more slender. This is probably due to the fact that the larynx from Australia had been for a considerable time in alcohol before the tissues were examined.

The bacilli are generally found single but occasionally they are found of the double length, the protoplasm of two rods being contained in one sheath, a distinct space being seen between the rods.

The existence of bacilli in the blood of leprous patients has been affirmed and denied. Koebner and Majocchi and Pellizzari state that they have found them in the blood. My own observations on this point are very limited. I have on several occasions examined the blood of two lepers, both of them of English descent, who had contracted the disease in Hindostan. In one of them, an advanced case of the disease, leper cells were observed in the blood freshly drawn from a finger affected with the infiltration. In some of these cells, examined fresh in the serum, appearances were noted which were highly suggestive of bacilli. I should not, however, have felt warranted in affirming their existence had it not been that one of these cells, whilst under observation, was ruptured by the pressure of the cover glass and a number of bacilli were set free, the distinctive form being easily observed. In the other case, a less advanced example of the malady, leper cells were also on several occasions observed in the blood, and on one occasion two rods were observed free in the serum.

Postscript (June 6th, 1883).—Since the above paper was sent to the secretary of the society I have examined, as a member of a committee appointed by the Clinical

Society, tissues excised from leprous tubercles in the arm of a boy who had acquired the disease in Hindostan. Bacilli were found in numbers in the excised skin.

In this case I detected, for the first time, bacilli in the blood-vessels of the tubercles, and I have since found the parasites in blood-vessels in another case.

The bacilli in this East Indian case were of the same size and form, and exhibited the same peculiarities, in regard to the action of aniline dyes, as those found in West Indian and Chinese leprosy.

I have also, since the paper was written, obtained preparations in which bacilli stained by fuchsine were seen to be beaded or filled with spores, thus showing a resemblance in another point to the tubercle bacilli.¹ Indeed, with the discovery of spores in the rods the similarity as regards shape, size, and apparent structure appears complete; a fact that becomes more important when we consider that the bacilli in both diseases have the remarkable quality of retaining the fuchsine stain after the bleaching action of dilute nitric acid has removed it from the surrounding elements and tissues.

In the present state of our knowledge of micro-organisms I deprecate drawing any hasty conclusions from this resemblance, but the fact is worthy of being recorded and of receiving attention.

¹ The demonstration of spores in the rods appears to be entirely a question of definition and illumination. I have fuchsine preparations in which nearly all the bacilli appear beaded.

DESCRIPTION OF THE PLATES XII AND XIII.

The Bacillus of Leprosy (GEORGE THIN, M.D.).

PLATE XII.

Fig. 1.—Vertical section through a tubercle in West Indian leprosy. (The leprous infiltration in the corium, below the part shown in the drawing, was dense.) The drawing shows part of a lymphatic vessel, containing an infected lymph-corpuscule, in the papillary layer of the cutis. *a*, The highly pigmented rete mucosum of the negro skin. (The individual cells of the rete are not drawn.) *b*, The papillary layer of the cutis; *c*, a group of bacilli close to the wall of the lymphatic vessel, the cell in which they were contained (as the author believes) not being visible on account of the extent to which the bleaching has been carried; *d*, a lymph corpuscule containing bacilli, lying free in the lumen of a lymphatic vessel. $\times 1230$ diameters.

Fig. 2.—Vertical section through a tubercle in Chinese leprosy, showing bacilli in the unbroken epidermis. *a*, The horny layer of the epidermis; *b*, group of three bacilli, corresponding to one cell; *c*, deep surface of the epidermis; *d*, papillary layer of the cutis. $\times 950$ diameters.

Fig. 3.—Vertical section through a tubercle, under a low magnifying power in order to show the disposition of the leprous infiltration. *a*, The epidermis; *b*, the papillary layer of the cutis; *c*, a hair; *d*, the leprous infiltration. The cells are seen deeply stained with the aniline dye. $\times 75$ diameters.

PLATE XIII.

Fig. 1.—Showing bacilli in the leprous infiltration of a tubercle in Chinese leprosy. The contours of some of the cells are seen with the bacilli in the cells. Amongst the bacilli which appear to be lying free, the arrangement in groups in most instances indicates the position of cells in which they are contained, the cells being no longer visible. $\times 1100$ diameters.

Fig. 2.—Showing the bacilli in the leprous infiltration in a tubercle in West Indian leprosy. $\times 1100$ diameters.

Fig. 3.—Bacilli from West Indian leprosy, stained with fuchsine, and showing a beaded (spore) appearance. (Compare with Figs. 4 and 5, which show bacilli of tubercle, drawn from a preparation of Mr. Thurston's.)

(Figures 4, 5, 6, and 7 are introduced to afford objects of comparison with the bacilli of leprosy.)

Fig. 4.—Bacilli of tubercle, very highly magnified. $\times 2350$ diameters.

(Figures 5, 6, and 7 are drawn with the same magnifying power as the bacilli of leprosy in Figs. 1 and 2.)

Fig. 5.—Bacilli of tubercle. $\times 1100$ diameters.

Fig. 6.—Bacilli in a section of a putrid sheep's cornea. $\times 1100$ diameters.

Fig. 7.—Bacilli from scum on cold mutton infusion. $\times 1100$ diameters.

Fig. 8.—Bacilli of leprosy in the epiglottis. (Australian case.) $\times 1100$ diameters.

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 8.

Fig. 5.

Fig. 4.

Fig. 7.

Fig. 6.