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TRACHEITIS AND BRONCHITIS LEPROSA [1]

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Among the many points in dispute with regard to leprosy is that of involvement of the air passages by the disease. All who have written on the subject are in agreement that the upper parts of the air passage may be very frequently and severely affected, down to and including the larynx, the latter being involved in practically all cases of nodular leprosy of some duration. But here agreement ceases. Leprosy of the lungs especially is in dispute; but this matter I cannot discuss fully here, as the scope of this paper is limited to a discussion of the occurrence of leprotic changes in the trachea and bronchi.

Danielssen and Boeck, in their fundamental work "Om Spedalskhed," published in 1847, mentioned discrete, fairly hard, yellowish-brown nodules, which rarely become larger than a pea, in the trachea and the larger bronchial branches. They also stated that the deeper jugular and bronchial lymph nodes may swell and become as large as a hen's egg, sometimes hard and at other times filled with a soft mass, partly yellowish white in color and partly almost black. However, on close study of the sketches accompanying this work I am not convinced that they are of leprous nature; it seems more probable that they are tuberculous, or a mixture of tuberculosis and leprosy. However this may be, judging by the literature it seems that the changes described by these writers in the trachea or bronchial branches have not been found by more recent observers. As a matter of fact, nothing more is heard of the subject until 1888, when Bonome described a clinical picture of a leper which he called "bronchopneumonia tuberculosa chronica" with "peribronchitis indurativa" or "cirrhosis fibrosa nodosa." The windpipe and the mucous membrane of the great bronchi are described as being infiltrated, and there was swelling of the peritracheal and bronchial lymph nodes. The caliber of the bronchi was normal with the exception of some smooth-

[1] Published in shorter form, in the Norwegian language, in *Medisinsk Revue* (1935) No. 9.

walled ectasies. As nothing was said with regard to the microscopic condition, or the inoculation of animals, we are unable to form any definite conclusion as to the nature of these changes. However, I am inclined to think that they were tuberculous.

Ten years later, in 1898, Brutzer described a case of considerable interest from the leprosarium in Riga. A patient with nodular leprosy, who for eighteen months had been obliged to use a tracheal cannula on account of stenosis of the larynx, presented at postmortem a considerable thickening of the tracheal mucous membrane below the cannula. The mucous membrane was thickened (up to 5 mm.), and the tracheal lumen was only 8 mm. in diameter. The changes in the trachea decreased in severity downward, but even at the bifurcation they were quite considerable. These changes seemed to be of more recent date than the leprous changes in the larynx itself, which had decreased considerably. Enormous masses of leprosy bacilli were found in the bronchial mucosa, and also in the swollen peritracheal lymph nodes. Only a few bacilli were found in the bronchial mucosa, and none at all in the bronchial nodes.

On several occasions in the nineties of the last century I personally found leprosy bacilli—though in most cases in small numbers—in the peritracheal and bronchial nodes and also in the peribronchial connective tissue of the smaller bronchi, but with no macroscopic changes in the trachea or the bronchial mucosa. Consequently I concluded that the leprosy bacilli were able to penetrate these mucous membranes without causing any changes or reaction in them. To this question I will revert shortly.

Among the cases of lung leprosy that were described by Babes in 1901 there are two in which are mentioned leprotic bronchitis and "leprotic" gangrenous bronchial cavities, surrounded by necrotic foci or interstitial desquamating pneumonia. No mention is made of the trachea. I am of the opinion that Babes' conclusions cannot be accepted, at any rate entirely. The changes are far too multifarious and incongruous, and the bacterial flora is far too varied and rich. Since the time of Babes' publications, more than a generation ago, nothing further has appeared regarding the changes described by him.

CASE REPORTS

In this report I am presenting certain cases which I have observed personally in more recent years, when there was less confusion in this matter than there had been among the older workers.

CASE 1.—A woman, 67 years of age, admitted in 1921 to Pleiestiftelsen No. 1 with pronounced nodular leprosy which had broken out after an incubation time of at least 15 years. The disease progressed steadily, and in 1924 tracheotomy had to be performed on account of stenosis of the larynx. She died suddenly seven years later, from lung embolism.

Postmortem examination.—The mucous membrane in the trachea and the larger bronchi were found to be several millimeters in thickness, and the lumena much smaller than normal. The mucosa presented a curious uneven appearance, but there were no nodules or ulcerations; the color was fairly dark (Plate 39, fig. 1).

Microscopic examination.—Only here and there are found remains of epithelium. The mucosa consists in great part of leprotic tissue (Plate 39, fig. 3), with numerous leprosy bacilli, mostly in small bunches (Plate 39, fig. 4). The bacilli decrease in number with depth, but some are found here and there in the perichondrium and even in the cartilage cells. Outside of the cartilage, bacilli are found in the small lymph nodes (Plate 39, fig. 3). Several are also seen in the nerves of the mucous membrane, but outside of the cartilaginous rings it is practically impossible to find any. In no place have these bacilli brought about any reaction on the part of the nerve tissue.

In the finer bronchi the mucous membrane is more normal, though here, also, the epithelium often presents pathological changes. Here and there are also to be seen free desquamated pigment-bearing cells, some of which contain bacilli, and some bacilli are found free in the lumen of the bronchi.

CASE 2.—A seaman, 27 years of age, admitted in 1918 with signs of primary nodular leprosy. Despite thorough treatment for several years the disease progressed fairly steadily, and in 1929 tracheotomy had to be performed on account of stenosis of the larynx. Dyspnea decreased for some months, after which the patient was troubled with respiratory difficulties and marked secretion of thick mucus from the trachea. This condition persisted, with short remissions, until during a violent coughing attack, in 1932, he brought up through the tracheal cannula a pea-sized lump consisting of granulation tissue with masses of leprosy bacilli, without surface epithelium. After a period of considerable relief breathing difficulties again developed, chiefly on account of great masses of thick mucus in the trachea. The disease as a whole steadily advanced, ulcerations and suppurations occurred, and the patient died of sepsis in a high degree of marasmus. During the last week he lay quite apathetic, with much mucous secretion and a gangrenous stench emanating from the tracheal cannula.

Postmortem examination.—There were found, among other things, string-like pleural adhesions, and in the cavities, mostly on the right side, cloudy fluid, with an easily removed fibrous coating posteriorly on the right lung. The lower lobe of the right lung was almost entirely firmer than normal and practically

without air, the cut surface grayish; in the upper part an irregular cavity, of hazelnut size, with black ragged walls and dark, foul-smelling content. A number of smaller broncho-pneumonic foci were found in other parts of the lungs. The hilus glands were somewhat enlarged, but neither here nor in the lungs themselves was there anything that looked like tuberculosis. A scarred stenosis in the larynx. In the trachea and bronchi a quantity of thick mucus, in part dark. The mucosa was somewhat dark, and unevenly thickened with protrusions that, here and there, resembled small grayish warts (Plate 39, fig. 2). These changes extended far down in the bronchi, and corresponding to them were enlarged lymph nodes along the trachea and the larger bronchi, the biggest about the size of a small oval plum. The cut surfaces were grayish, with a sprinkling of yellow here and there; no tubercules or caseous parts could be found.

Microscopic examination.—The epithelium in the trachea and larger bronchi presents marked and curious changes (Plate 40, fig. 5). There is nothing to remind one of the usual covering of this region; the epithelium resembles to a high degree that of the skin. There is no perceptible horny layer, but the cells on the surface are quite flat (Plate 40, fig. 6), and here and there are found small epithelial islands which on casual examination suggest the pearls of flat epithelial cells such as can be found in the cancroids of the skin. Most pronounced, however, are the cells corresponding to those in the stratum spinosum of the skin (Plate 40, fig. 7). The basal-cell layer is somewhat irregular; the cells are rarely typically cylindrical, but often longish, with pointed ends, and often slanting. The epithelium in its entirety sends out irregular pegs down into the leprous infiltration of the thickened submucosa, but no infiltrating growth of epithelium can be discovered.

A few leprosy bacilli are to be found in the epithelium, partly between and partly in the cells, but in the connective tissue beneath the epithelium are enormous masses of bacilli, mostly in parts nearest the epithelium in the above-mentioned protrusions of the mucosa (Plate 40, fig. 8). The number of bacilli decreases with depth, but they are seen here and there in the perichondrium and the cartilage cells. Outside of the cartilage the bacilli are almost exclusively found in the lymphoid nodules. The nerves of the mucosa also contain bacilli, but with no reaction on the part of the tissue. Here, also, the numbers decrease towards the center, until in the nerves on the outside of the cartilage there are practically none.

In the medium-sized and finer bronchi, particularly in the latter, the epithelium presents a more normal appearance, but even here it is partly broken off or fluffed out with desquamating cells. Here, again, bacilli are found in the mucosa, but in far smaller numbers than in the upper portions of the tract.

The gangrenous part of the lung has a rich and varied bacterial flora, but no definite leprosy bacilli and only a very few pneumococci. In the small broncho-pneumonic foci there are, among other bacteria, a number of leprosy bacilli, either free in the lumen of the bronchi or, more often, in loose epithelial cells or pigmented mononuclear cells. In the peritracheal and bronchial lymph nodes there are many bacilli, partly in large groups and very often together with pigment masses in the cells.

CASE 3—.M. M., born 1899, fisherman of leprous family, admitted to Pleiestiftelsen No. 1 in 1922 with nodular leprosy of two years' duration. This condition steadily advanced to a pronounced ulcerating form. In 1931 tracheotomy was performed on account of stenosis of the larynx. Considerable amyloid degeneration developed in the inner organs, and he died, uremic, April 16, 1935.

Postmortem examination.—Some hypostasis was found in the lungs, and in the apices some small grayish scars; otherwise nothing abnormal. The larynx showed a considerably scarred stenosis, due to a previously ulcerated nodule. Some mucus in the trachea and bronchi, but no nodules or ulcerations. The mucous membrane presented a normal appearance.

Microscopical examination.—The epithelium of the tracheal mucosa is fairly normal, but both in it and on its surface are a few leprosy bacilli, without any reactive phenomena. Beneath the epithelium bacilli are also present in several places, again without reaction. At a single point above the bifurcation there are small leprous globi in the epithelial cells as well as between them, and under the epithelium a mass of bacilli with only a very slight reaction on the part of the tissue. Here, also, the number decreases rapidly with depth.

Bacilli are also found in the somewhat swollen peritracheal lymph nodes, but the presence of a great number of vacuolated lepra cells without bacilli points decisively to the fact that the leprous process in these nodes was partly of longer duration than in the mucous membrane.

DISCUSSION

The cases here discussed prove that leprosy bacilli can settle and thrive in the trachea and the mucous membrane of the bronchi. They occur in these tissues perhaps more frequently, at any rate as far as nodular leprosy is concerned, than has hitherto been believed, for their presence there does not always give rise to changes that can be observed macroscopically, as is seen in Case 3. But that they may bring about visible changes, which may be very striking, is evident from the first two cases presented. However, in each of these three cases there was a condition which must not be overlooked; namely, that the patient had worn a tracheal cannula for several years.

It will be recalled that Brutzer's case, which was the first undoubted case of leprous tracheitis reported, was that of a patient who had gone about with a tracheal cannula for eighteen months. My Case 1 is exactly like that one, although Brutzer makes no mention of difficulty of breathing after tracheotomy. Breathing difficulties are common in patients who have worn cannulas for long periods. The mucous membrane is irritated, probably by the air which enters directly without passing the upper wind passages where it is warmed and purified, and in consequence secretes a thick mucus which quickly

dries and adheres to the surface in large or small crusts. Various measures are used to relieve this condition; the crusts may be loosened by introducing a feather, which produces violent coughing and thus removal of the crusts; inhalation of steam is also made use of; and some patients find that lukewarm salad oil helps to loosen the crusts.

It is evident that by these means irritation of the mucosa cannot be avoided, and a vicious circle arises which may make the patient's existence extremely unpleasant. This was the case with both of my first patients, especially Case 2, who for several years never had many peaceful hours, day or night. He especially asked for oil to be continuously dripped in, together with inhalation of vapour; these he asserted were the only things that gave any relief.

That such a severe and prolonged traumatic effect cannot but injure the mucous membrane to a high degree is evident. It seems justified to conclude that the mucous membrane of the trachea and bronchi, which under normal conditions must be considered as having a certain amount of reactionary power toward the leprosy bacilli, thereby lose their immunity, as it were, and become the seat of a flourishing growth of the bacilli. The fact that leprous tracheitis has not heretofore been reported in any patient who has not been subjected to tracheotomy must be looked upon as supporting this assumption. From the processes that occur in the nerves and skin we have ample evidence of the part that trauma plays in the localization of leprosy bacilli. That no actual tracheitis or bronchitis was found in the third case, but merely a few microscopic changes, despite the fact that tracheotomy had been performed, is simply explained by the fact that this patient belonged to the fortunate few who experienced no breathing difficulties after tracheotomy, and was therefore spared the traumatic attacks on the mucous membrane that the other two patients underwent. As the number of these cases of leprotic tracheitis and bronchitis described is as yet very small, it is important that this matter be thoroughly investigated in the future.

As far as the striking and curious changes of the epithelium in Case 2 are concerned, I have been unable to find any similar case in the literature at my disposal.[2] It can scarcely be a malignant tumor, even if at first glance its appearance may suggest such a formation. As far as I can see it must be looked upon as a metaplastic

[2] I am indebted to Professor Harbits for references to the literature.

change caused by the changed conditions that exist after tracheotomy, and to measures taken to relieve the patients, but the question arises whether a continuation of this process could not have resulted in a malignant neoplasm. The piece of leprotic tissue that the patient coughed up could scarcely have been a part of the papillomatous mucosa, for as epithelium was completely lacking it was probably a piece of the granulation tissue which may now and then be seen forming at the lower end of a cannula, caused by irritation of the mucous membrane during coughing.

With regard to the source of the leprosy bacilli that settle in the mucous membrane and bring about tracheitis and bronchitis, it seems entirely probable that they originate from the leprotic upper parts of the air passages, and not from the blood. Leprosy bacilli can, of course, easily be aspirated from ulcerations in the larynx by forced inhalation, or even quite mechanically, and may also be carried down by the methods used to relieve the distress of tracheotomized patients. The fact that the leprotic process decreases in intensity downward in the air passages also indicates that the leprotic changes originate in the larynx rather than through bacillary emboli.

The findings in Case 3 prove decisively that leprosy bacilli can enter the mucous membrane of the air passages without producing any reaction on the part of the tissue, when the upper protective epithelial layer is missing. Herein lies the explanation of why it is so extremely difficult—almost impossible—to determine with certainty the seat of the primary affection in leprosy, in contrast to the condition as regards syphilis and tuberculosis.

The leprotic affection of the nerves in the trachea and bronchi is also of considerable interest, and has not, as far as I am aware, been recorded previously. It points strongly to the fact that the nerve infection originates in the most peripheral nerve branches and then advances, more or less rapidly, towards the center along the nerves. There is no reason to assume that conditions should be otherwise in the skin, and consequently this finding in the nerves of the trachea supports the assumption that nerve leprosy is due to an ascending leprotic neuritis.

CONCLUSIONS

1. Under certain conditions leprous changes of considerable degree may be found in trachea and bronchi.

2. Traumatic actions of various kinds seem to produce, or at least to promote, these leprous changes.

3. Leprosy bacilli may pass through the mucous membrane of the trachea and bronchi without producing macroscopic changes. This fact suggests an explanation for the rare occurrence of the so-called leprotic chancre, if it is found at all.

ADDENDUM

This article was sent to press at about the time the one by Tajiri on the subject of leprotic changes in the lung [THE JOURNAL 3 (1935) 467] was published, and several weeks before it was seen. Tajiri does not mention the conditions of the trachea and the bronchial mucosa here described, but his microscopic findings in the bronchi seem to be in keeping with mine.

DESCRIPTION OF PLATES

PLATE 39.

FIG. 1. Trachea of Case 1. (2/3 natural size.)

FIG. 2. Trachea of Case 2. (2/3 natural size.)

FIG. 3. Photomicrograph of trachea, Case 1, showing changes in the mucosa and the neighboring small lymph node in which bacilli were found. About 5.5 ×.

FIG. 4. Leprosy bacilli in the mucous membrane of the trachea, Case 1. About 1300 ×.

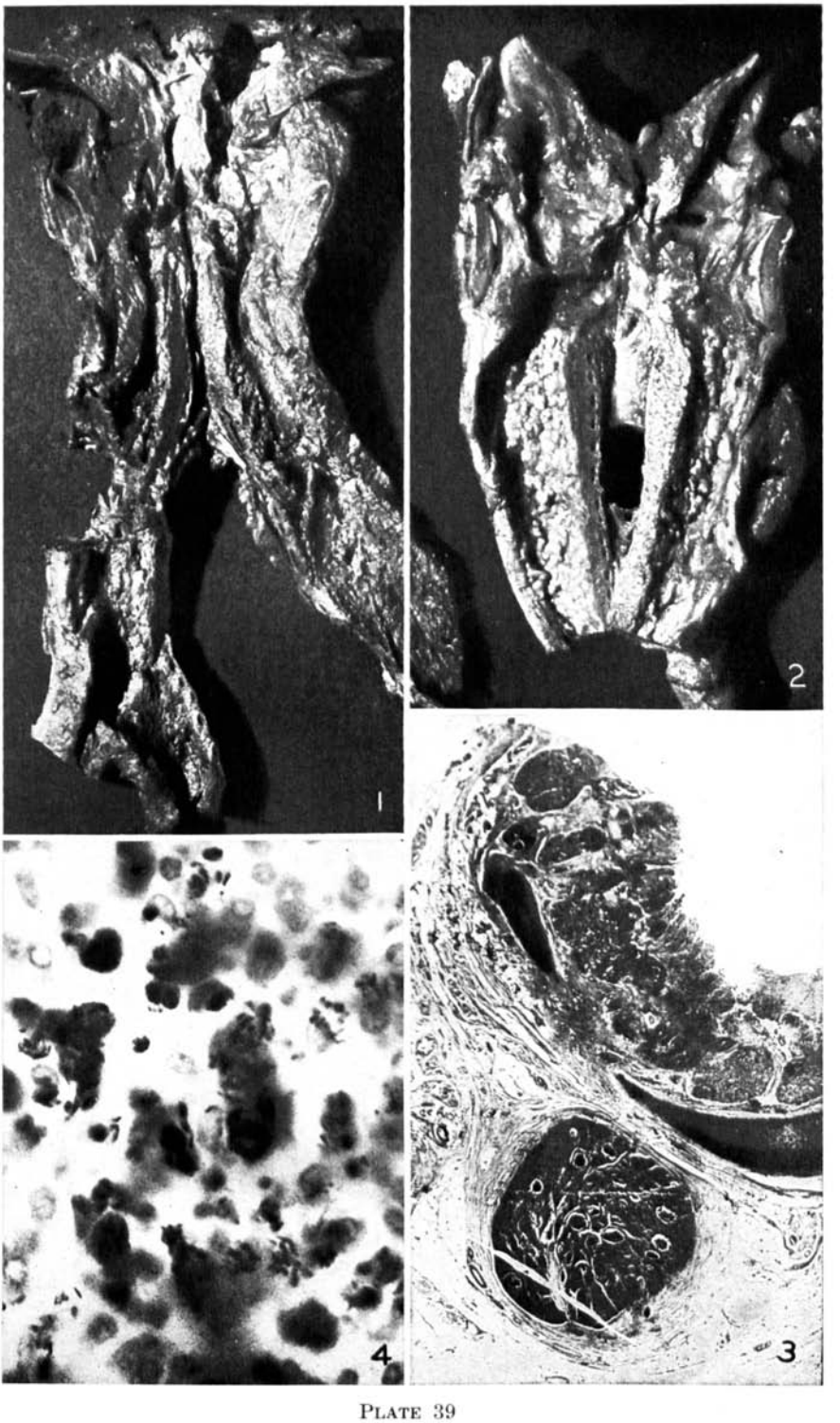

PLATE 39

PLATE 40

FIG. 5. Showing, besides changes more or less similar to those in Fig. 3, the remarkable metaplastic changes in the epithelium. Photomicrograph of trachea, Case 2. About 7×.

FIG. 6. Showing the metaplasia of the epithelium. Photomicrograph of trachea, Case 2. About 70×.

FIG. 7. Showing the stratum spinosum of the metaplastic epithelium. Photomicrograph of trachea, Case 2. About 850×.

FIG. 8. Leprosy bacilli in the mucous membrane of the trachea, Case 2. About 540×.

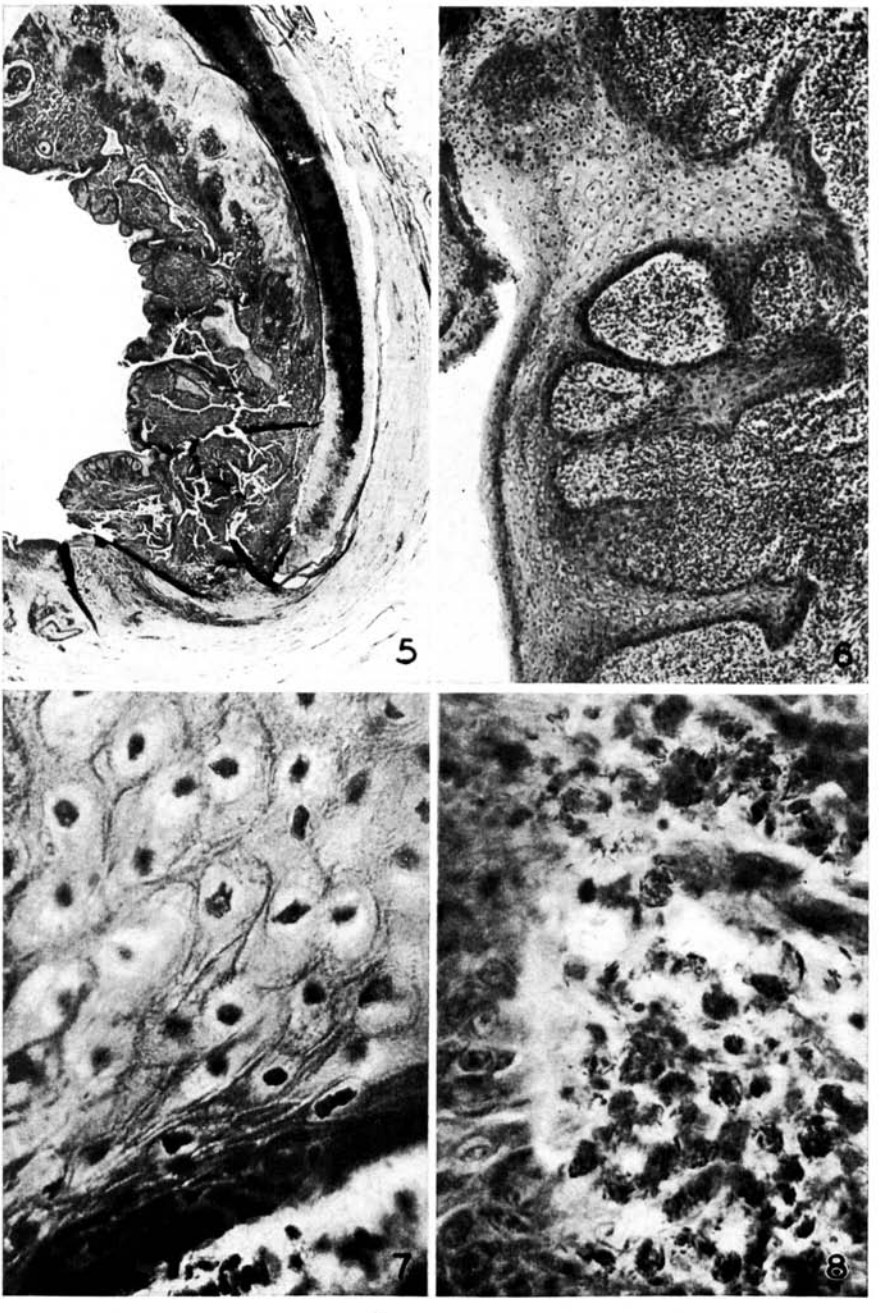

PLATE 40