Diphtheritic ulceration of the air-passages and its relation to pulmonary phthisis / by John N. Mackenzie.

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DIPHTHERITIC ULCERATION OF THE AIR-PASSAGES AND ITS RELATION TO PULMONARY PHTHISIS.

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There is perhaps no subject in the whole domain of laryngeal pathology which has excited such universal interest and awakened so much animated discussion as the pathological conception of laryngo-tracheal phthisis. The association of ulcerative disease of the upper air-passages with pulmonary consumption has been recognized from an early time, and although nearly a century has elapsed since the publication of Petit's celebrated essay,* the most divergent opinions still prevail concerning the correct interpretation of their reciprocal relationship. The older writers described only one form of ulceration, and busied themselves with the question of a laryngeal tuberculosis in the strict sense of the term, without making those finer histological distinctions which pathological anatomy later developed. The existence of true tubercle as one of the chief, if not the chief etiological factor in the production of what is commonly known as *phthisis laryngea* cannot be gainsaid in the light of recent pathological investigation, and it now only remains to be decided whether all forms of ulceration of the upper air-passages which are encountered in the course of general tuberculosis are to be referred directly to the tubercular diathesis as their primary cause, or whether, on the other hand, there are not some which may be regarded as accidental, owing their origin to influences associated with, but not necessarily dependent upon, the tubercular process.

I propose in this paper to consider a variety of ulceration which has an important bearing on this question, and which, on account of its more frequent localization in the lower portion of the trachea and bronchi, and its usual occurrence in the later stages of pulmonary

* De phthisi laryngea. Montpelier, 1790.

phthisis, comes more within the notice of the pathological anatomist than under the eye of the clinical observer. It is probably due mainly to this fact that it has been overlooked by many of the leading writers on diseases of the throat, notably in England and America, and its existence lost sight of in the discussion of the more engrossing question as to the existence or non-existence of tubercle as a pathological product in phthisis of the windpipe.

This, the so-called *aphthous erosion* of the older writers, was first depicted in the atlases of Cruveilhier* and Albers,† and clearly distinguished from tubercular ulceration by Rokitansky.‡ In his *Lehrbuch der pathologischen Anatomie*, Rokitansky calls attention to round or oval erosions of the mucous membrane, surrounded by a scarlet border and covered with a yellowish slough, which are found during the course of pulmonary phthisis in great numbers in the trachea, and which, after the extrusion of the slough, coalesce and lend to the membrane a sieve-like, worm-eaten appearance. These, which are not to be confounded with tubercular ulceration, are found, according to this distinguished observer, in greatest number on the side of the trachea corresponding to the lung whose disorganization is the more pronounced.

Förster,§ who also clearly recognized this peculiar form of ulceration, whilst admitting its aphthous nature, and pointing significantly to the fact that it may resemble tubercular ulceration so closely as to render an appeal to the microscope necessary to differentiate them, asserts as the result of his observations that the majority of the so-called aphthous erosions of the trachea are in reality tubercular. On the other hand, many authors look upon these ulcers as catarrhal (Louis,‖ Trousseau,¶ Andral,** Hasse,†† Rheiner,‡‡ Rühle,§§ Heinze,‖‖ and others), or, as Rindfleisch¶¶ recently has done, refer them to follicular ulceration; whilst their tubercular nature is maintained

* Livr. 35, Pl. 4, Fig. 3. † II. Taf. 13, Fig. 4.
‡ Lehrbuch d. path. Anat. Bd. III. Wien, 1861. S. 19.
§ Lehrbuch d. pathol. Anat. Jena, 1864. p. 312.
‖ Recherches sur la phthisie. Paris, 1825.
¶ Traité de la phthisie laryngée. Paris, 1827.
** Clinique médicale, Tom. II. Paris, 1829.
†† Spec. patholog. Anat. Leipzig, 1841. I Bd.
‡‡ Virchow's Archiv, V. 1853.
§§ Die Kehlkopfkrankheiten. Berlin, 1861.
‖‖ Die Kehlkopfschwindsucht. Leipzig, 1879.
¶¶ Lehrbuch d. pathol. Gewebelehre, IV. Aufl. Leipzig, 1875.

by Isambert,* Ziegler,† Eppinger,‡ and others. Eppinger, who describes them as *tubercular arrosions*, holds, in the absence of absolute histological proof of direct tubercular infiltration, that they are, notwithstanding, specific tubercular products, and suggests that they may be evoked through the operation of the *monas tuberculosum* of Klebs.

I have adopted the term *diphtheritic ulceration* in conformity with what the histological study of their development has led me to regard as the correct pathology of these lesions. Through the courtesy of my friend and instructor, Dr. Hans Chiari, I examined the respiratory organs of all patients dead of phthisis in the Rudolph and Jewish hospitals of Vienna during a period extending over five months, and published the results of the examination of this abundant material last year in the *Monatsschrift für Ohrenheilkunde*§ in Berlin. I wish to-day to present to you a description of this diphtheritic erosion based upon an analysis of these cases, and to attempt to define as accurately as possible the relations between it and pulmonary phthisis.

Macroscopical Appearances.—Diphtheritic ulceration appears as small, for the most part superficial, irregularly round or oval erosions of the mucous membrane, which vary in size from a pin's-head to a small pea, and which, separate and distinct, stud the surface of the membrane, or, coalescing, form a large ulcer, which spreads in an irregular manner over the mucous surface. Commencing as superficial erosions of the mucous membrane with tolerably well-defined margins, they assume later a more characteristic appearance; their walls become sharp, regular and somewhat elevated, and vary in color from a light reddish shade to a pronounced livid hue. The base is either smooth and red in color, or presents a rough, uneven appearance. It is generally covered with a yellow slough or with a more or less orange-colored exudation. The ulcers are surrounded by a brilliant scarlet border, and the mucous membrane between them is slightly swollen and deeply hyperæmic, thus forming a pathological picture of great beauty. These ulcers, which are always multiple and never single, are most frequently met with, and are by far most abundant, in the lower portion of the trachea and bronchi; in the former the posterior wall

* Annales des maladies de l'oreille, etc. II., 3, p. 162. 1876.

† Volkmanns Vorlesungen, VI. Serie, S. 1305.

‡ Pathol. Anat. des Larynx u. der Trachea. Berlin, 1880.

§ No. 9, 1881. *Ueber die sogenannten aphthösen Substanzverluste auf der Schleimhaut des Larynx, der Trachea u. der Bronchien bei tuberculöser Lungenphthisie.*

seems to be their most frequent seat, though the whole mucous membrane of the trachea may be covered with them. I have seen the trachea in its entire length and circumference, together with the bronchi of both sides, almost completely destroyed and its mucous membrane converted into a gangrenous mass. In my experience they are *never* found in the bronchi of the unaffected lung; but where both lungs are disorganized the bronchi of both sides are studded with them, and in most cases they can be traced directly into the cavities themselves. They are met with less frequently in the larynx and pharynx. In the former they select the laryngeal aspect of the epiglottis, the anterior surface of the arytenoid cartilages and the inter-arytenoid fold as their favorite seats. In the pharynx I have seen them most frequently in the pyriform sinuses, where they sometimes assume a considerable size. Their occurrence here is most probably explained by the accumulation in these cavities of the irritant sputa. In the larynx they lose to a great extent their characteristic appearances and approach more closely the type of simple catarrhal ulceration. They are sometimes found associated with or in the neighborhood of tubercular ulcers, and I have seen them more frequently than tubercular ulceration in the trachea.

Microscopical Appearances.—In the histological examination the diseased structures were with the greatest possible care hardened in Müller's fluid and alcohol and cut into a series of consecutive sections. All were in like manner colored with borax-carmine, and after washing out in absolute alcohol were examined in oil of cloves and Canada balsam.

The sections presented in general the typical picture of circumscribed diphtheritic inflammation of the mucous membrane. At those situations where sloughs were present, the epithelium and upper layers of the mucosa were converted into a finely granular detritus, and the neighboring connective tissue of the mucosa, and also to a great extent the submucosa, highly infiltrated with lymphoid cells. This round-cell infiltration invaded the tissues between the mucous follicles, without, however, involving them in a marked degree in the inflammatory process. The spots where ulceration had already occurred presented in the base and edges of the ulcer likewise a granular detritus, and the surrounding tissues were also the seat of a high grade of round-cell infiltration. Here and there it was possible to recognize transition stages of both the above-described processes, viz. nodules, so to speak, of necrobiotic tissue, in which the

slough had already begun to separate, although adhering closely at several points. The examination of a great many sections showed that *the first stage of the diphtheritic process consisted in a high grade round-celled infiltration of the mucous membrane in its upper layers, with cloudy swelling of the superimposed epithelium.* Distinct miliary tubercles were nowhere to be seen, neither within nor in the neighborhood of the necrobiotic nodules. Sometimes individual nodules coalesced, and especially was this true of the bronchi, so that the membrane over a considerable area presented the above described sloughing of the upper layers of the mucosa. The above anatomical appearances, therefore, leave no room for doubt that these ulcerated areas are the result of a circumscribed superficial diphtheritic inflammation of the mucous membrane—that is to say, an infiltration of its tissues with so rich and rapid cell-proliferation as to eventuate in necrosis and sloughing of the superficial layers.

In view, then, of this interpretation of their nature, what practical conclusions can be drawn concerning the etiology of these lesions? Are they related to the phthisical process in the lungs, and if so, what is the nature of the relationship? The first question I must answer decidedly in the affirmative, since they are most frequently found in connexion with well-pronounced phthisical changes in the lungs; and in regard to the second, it seems impossible to resist the conclusion that the foul contents of the pulmonary caverns, lingering in the bronchi and lower trachea, so irritate the mucous membrane as to cause it to react with diphtheritic inflammation. It may be here remarked that two opinions prevail concerning the part which the sputa play in the production of laryngeal phthisis. Following Louis,* the advocates of the one affirm that the sputa and ulcers stand to each other in the relation of cause and effect, although they differ widely as to the nature of the ulcerative process; some maintaining it to be a simple catarrhal erosion, whilst others regard it as tubercular, evoked through the infection or invasion, as it were, of the superficial layers of the mucosa by the micrococci in the expectorated matter (Ziegler, Eppinger). The champions of the other, and perhaps more popular idea, are equally confirmed in their belief that the sputa play no rôle whatsoever in the destructive changes, and some even

* *Op. cit.* This view was advanced over a century before the time of Louis by Sylvius. (Opera med. *Traj.* ad Rhenum, 1695, p. 692. *Vide* Virchow, Die krankhaften Geschwülste, 2, S. 644–5.)

go so far as to deny the possibility of corrosion of an intact mucous membrane by the contents of the pulmonary caverns (Heinze).

It seems to me that order may be restored to this conflict of opposite opinion, and reconciliation of these widely divergent views be accomplished, by *referring to the corrosive action of the sputa those ulcerations alone which form the subject of this paper.* In examining the problem from this standpoint the influence of the sputa is reduced to definite dimensions, and the error is avoided, on the one hand, of clinging to a doctrine which recent observation has shown to be false, and on the other hand, of overlooking a curious pathological fact which has never been satisfactorily explained.

Passing then to a summary of the evidence upon which the co-relationship between diphtheritic, as contradistinguished from tubercular, ulceration of the air-passages and the corrosive action of the sputa rests, the following facts present themselves in favor of the view expressed above:

α. The predilection of the ulcers for those places which are in constant contact with the sputa, viz. the trachea and the bronchi, and especially the posterior wall of the former, and the laryngeal surface of the epiglottis.

β. The fact that they increase in number as the lungs are approached, and that they are much less common in the upper portion of the trachea and larynx. It was these familiar pathological facts that suggested to Louis the hypothesis which bears his name.

γ. That they may be traced from the bifurcation of the trachea to the division of the bronchial tubes, where in all cases they become visible only in one tube, which is that leading to a cavity. This remarkable distribution of the ulceration in pulmonary phthisis, which I have repeatedly verified by dissection, did not escape the observation of Stokes,* who advanced it in support of Louis' hypothesis.

δ. Their absence in the bronchi of lungs which are not the seat of cavities or advanced phthisical change. This at least has been my experience, and I am unaware that they have been observed by others where the lungs were not the seat of pronounced disorganization.

ε. Their occasional presence in the oesophagus, stomach and intestines, from swallowing the sputa. In one of my cases ulceration was found in the oesophagus and small intestine macro- and microsco-

* Diseases of the Chest. Vol. I, p. 62. Phila., 1837.

pically identical with the diphtheritic ulcers in the larynx. Tubercle was present only in the lungs.

η. Finally, their occasional appearance in suppurative pneumonia (Wunderlich*) and gangrene of the lung.

These lesions, therefore, may be regarded as the result of an *inoculation*, so to speak, of the mucous membrane with the detritus from the broken-down pulmonary tissue, leading to the formation of a loss of substance pathologically distinct from, but possessing some of the external characteristics of the tubercular ulcer. Notwithstanding, however, that these diphtheritic nodules owe their existence to the disintegration in the lung, it does not seem to me justifiable to look upon them, as Eppinger has done, as specific tubercular products, for the following reasons:

First: *That they differ histologically in no respect from the circumscribed diphtheritic ulceration of the mucous membranes of individuals in whom no evidence of tuberculosis exists;* an important point in their differentiation from the well-defined and characteristic anatomical changes of tubercular infiltration and ulceration. In this connexion it may be added that the tubercular process, as shown by Heinze, commences under the epithelium, whereas in the ulcers under review that structure is always first affected.

Secondly: *That well-pronounced circumscribed inflammatory infiltration, resulting in necrobiosis and sloughing, and histologically identical with these diphtheritic lesions, is found, although not as frequently and abundantly, in the mucous membrane of the air-passages, and particularly in that of the trachea, as a secondary complication in diseases other than pulmonary phthisis.* Thus, in circumscribed gangrene of the lung, or as the result of perforation into the trachea of broken-down, sloughing bronchial glands, small, round diphtheritic erosions may be detected in the mucous membrane of the trachea and bronchi, which are the histological analogues of those described above.

Thirdly: *That on other mucous membranes of the body, under similar conditions, namely, as the result of a neighboring, long-standing gangrenous process, or the constant passage over them of an ichorous discharge, ulceration is found, identical in every respect with that described above.* This is true, for instance, of the mucous membrane of the vagina in gangrenous conditions of the uterus. In the anatomical museum of the *Rudolfspital* in Vienna is an instructive preparation of this kind, in which the vagina is studded with these small diph-

* Handbuch d. Pathol. u. Therap. III, 2. Stuttgart, 1856, p. 96.

theritic erosions, the result of gangrene of the *portio vaginalis uteri* from an unknown cause.

The great number of the ulcers, their absence in intense acute and chronic simple catarrh of the pharyngo-bronchial membrane, their characteristic macroscopical appearances, especially their often elevated, livid, irregular edges and sloughing base, and the picture which the microscope reveals, are sufficient to exclude the idea of their catarrhal nature, and strongly militate against the hypothesis which would relegate them to the simple inflammatory condition of the mucous membrane which often ushers in or accompanies the phthisical process in the air-passages.

I think, therefore, in conclusion, that my observations go to show that diphtheritic ulceration of the larynx, trachea and bronchi occurring in the course of pulmonary phthisis is related to the affection in the lung in so far as it is produced by the corrosive action of the sputa; but that in the present state of our knowledge it it is impossible to affirm its specific tubercular nature.