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ATROPHIC RHINITIS IN ITS HISTORICAL, ETIOLOGICAL AND HISTOLOGICAL ASPECTS.*

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The interest which has arisen among rhinologists to arrive at a better understanding of the lesions of atrophic rhinitis in their correlation with the clinical symptoms is the excuse for my including in this paper an exhausting but not an exhaustive review of its modern history.

The point of view from which I start is to attempt by a process of induction to lay before you and bring into prominence those facts in it which lead to the conclusion that there is some common underlying lesion which binds together the allied clinical phenomena of the different varieties of atrophic rhinitis and to indicate that affiliation with other lesions which points to the same conclusion. That lesion I believe to be a periostitis of the thin scroll bones—a common enough process, but a lesion in a unique situation. Nowhere else in the body have we thin plates of cancellous bone between two layers of fibrous periosteum. Nowhere else in the body have we thin sheets of cartilage between two layers of perichondrium. In hypertrophic rhinitis, or better in all chronic rhinitis, we have a periostitis. In all sinus affections we have a periostitis. These being the allied local lesions with which we have to do, this being the unique bone configuration with which

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we are confronted, I turn to the account of the work done on atrophic rhinitis chiefly in modern times. After that with your permission, I will take up some of the results of my own objective study of the histology of the lesion.

HISTORY.

There is no doubt that the history of atrophic rhinitis may be traced back to the remotest antiquity in the history of civilization, especially that variety of it associated with crusts and a foul odor. It seems likely that the reference in the Talmud to a polyp in the nose causing a bad smell, to which I have referred elsewhere¹ is an indication of its occurrence among the early Jews. The Hindu Susruta spoke of it under the name of Putinaska, as one of the thirty-one diseases of the nose. While in the medicine of the Greeks I have noted no indication of the existence of ozena, as we understand it, there is a reference in Celsus to the fact that the Greeks themselves gave the name of ozena to the literature of medicine, and he recognized that "it is hardly possible to cure this disease." He recommended its treatment, in some cases, by the application of the actual cautery, but he also employed other methods. Galen recognized it, as indeed did the post-Galenic writers, the Arabians and the physicians of the Renaissance. It may be found spoken of by Fabricius ab Acquapendente, who modified the procedure of Celsus by inserting a metal speculum in the nose, and by putting the hot iron in that, which imparted heat to the tissues without actual cauterization. This modification was adopted by later writers.

However, it is impossible always to know just how closely ancient diagnosis and differentiation corresponded with our own. That in individual cases it must have been faulty, we realize from the fact that in quite modern times we are able to note the absence of a differentiation which has become essential to our present intelligent study of the disease. I therefore hasten on to that period.

In 1866, Weber,² who had devoted himself largely to the study of the ear, contributed an article to one of the reference handbooks of surgery on nasal disease, from which it is quite apparent that atrophic rhinitis as we know it—non-syphilitic—without the presence of a foreign body, was undifferentiated at this time.

Zaufal,³ in 1874, claimed that the ozena present in some cases of catarrh is associated with a congenital deficiency in the development of the inferior turbinated bone. This idea that it is connected with a congenital bone-defect was many years subse-

quently (1898) expanded in the work of Meisser⁴ to the conception that it is due to an abnormal wideness of the nasal fossae, which is congenital. Alexander quotes Sauvages⁵ as having claimed, in 1763, that it is due to the nose being too narrow. Hopmann⁶ again, in 1893, had claimed the nasal fossae are congenitally too short. As recently as 1908 he has reiterated⁷ his belief in the shortening of the septum as an indication that a congenital conformation of the nasal fossae is the cause of ozena. Exactly how this condition referred to by Hopmann should have an influence on nasal affections is not very clear, nor is the idea attributed to Sauvages very suggestive, but the too great roominess of the nasal chambers, at first thought, would seem a more plausible explanation, as a greater volume of air contained in them would provide for the evaporation of a greater amount of moisture and so tend to crust-formation. But as a matter of fact, it soon appears on reflection that this rests upon erroneous conceptions. The air is a moving current, and there can be but little difference in the evaporation coefficient whether the same volume of air passes through a small chamber or a large one. In fact, so far as there is provision for evaporation the advantage lies with the normal nose as compared to the larger chambers supposedly attendant on the beginning of the atrophic process, inasmuch as the air current is more closely in contact with the mucosa and can carry away the moisture somewhat more rapidly. As a matter of fact the inception of these ideas rested upon a very insecure basis. Little has been learned of the etiology by observers using modern methods of examination and still less by students of nasal histology. The same may be said of the idea of Michel,⁸ in 1876, that atrophic rhinitis is essentially a disease of the accessory sinuses. This is still a prominent feature in discussions on the etiology of accessory sinus disease. It also rested, especially at that time, upon insufficient differentiation. Indeed its prominence as an etiological factor in the minds of rhinologists of the present day may be said to be due to an inadequate separation of the various kinds of ozena from one another and to the inadequate separation of different kinds of atrophic processes in the nose from one another. Crusts may form from sinus disease as well as from an atrophy of the nasal mucosa. There may be an ozena and an atrophic process which has extended to the mucosa of the accessory sinuses. Elsewhere I have recently referred to the modern history of the accessory sinus disease in its relationship to atrophic rhinitis⁹ and I will not refer to it here again except incidentally.

There is an atrophy of age and atrophy following nasal operations. As in almost every domain of medicine history here takes account of the differentiation of phenomena in the course of the discussion of theory and the acquisition of our knowledge of facts. Hartmann, in 1878,¹⁰ as a result of post-mortem examinations had already refuted Michel's idea as to the genesis of ozena in the accessory sinuses. He was inclined to accept Zaufal's theory. Tissier, in 1894, claimed it to be a bone disease of the ethmoid labyrinth in the embryo and the infant. The accessory sinuses are thus affected in his view as a continuation of a congenital condition, the secretions forming a favorable medium for the growth of bacteria. Gerber, in 1900, examined the question of nasal anomalies in their relation to the etiology of ozena and came to the conclusion that the roominess of the fossae and a depressed nasal arch (chamaeprosopia and platyrrhinia) often combined with syphilis, are predisposing factors. In later years there has been a recrudescence of the belief that ozena is due to a necrosing ethmoiditis¹¹ and again the ethmoid and sphenoid cavities have been vigorously attacked.

In the early work of B. Fraenkel,¹¹ in 1876, may be noted the first attempt to separate cases of true ozena from those of syphilitic ozena. While he thus erected the typical atrophic rhinitis with ozena into a separate entity, he failed to indicate that it was dependent also upon a bone change, as is the ozena of a syphilitic nose. His idea that it was a specific change in the secretions was a natural prelude to the belief which soon arose that this depended upon some specific form of bacterial life. Loewenberg¹⁵ described in 1885 a bacterium constantly found in the secretions of ozena and this has been many times confirmed by other observers since then. Klamman,¹⁶ Thost,¹⁷ Seifert,¹⁸ Strauch,¹⁹ Valentine,²⁰ Hajek,²¹ Reimann,²² Abel,²³ Struebling,²⁴ and others contributed to the bacteriology of ozena within a few years after Loewenberg's paper; but the etiological importance of these bacteria, in spite of much recent literature as to other germs, has not been accepted as preponderating in the causation of atrophic rhinitis, and it can not be said that bacteriology so far has materially elucidated the mystery of the etiology and pathology of the disease. These writers for the most part looked upon micro-organisms with a mental magnification borrowed from the high contagionist craze of the day. For them the bacterium was the primal factor in the disease. Naturally this left the atrophic bone-change even more completely unprovided for than did the subsequent sinus theory of

Gruenwald and his followers, to which I have referred as starting with Michel. Fraenkel divided nasal catarrhs into hyperplastic and atrophic, regarding the latter as a sequel of the former. He also admitted the influence of various dyscrasias as etiological factors. More than thirty years later he had the satisfaction of reminding²⁵ his colleagues that this early classification is fundamentally to-day the basis of differentiation of intra-nasal inflammations. In 1879 Eugen Fraenkel²⁶ studied sections of the atrophic nasal mucosa under the microscope and noted changes in the epithelium, though he asserted that it is destroyed and replaced by other cells. He remarked on the few acinous glands to be observed. He believed there was always an underlying dyscrasia of tuberculosis or of syphilis. He believed there were always deep lesions of the mucosa and of the bone. In the same year Gottstein,²⁷ though believing in its systemic nature, recognized ozena as a constant symptom of that stage of a chronic rhinitis in which it has come to an atrophy of the mucosa and the glands in it. The vitiation of the secretions from this cause he proposed to treat by the use of intra-nasal tampons of cotton left in the nose for twenty-four hours or more. Hermann Krause,²⁸ in 1881, described microscopic appearances in two cases of ozena and noted the presence of evidences of fat and fatty acids in the secretions of the mucosa, fibrosis of the stroma and blood vessels, and the relative increase of lymphoid cells. The destruction of glands he believed to be due to limitation of the blood-supply and the fibrosis of the blood vessels. These ideas were many of them introduced in America by Bosworth in several excellent papers,²⁹ in 1882, and in his "Treatise of the Diseases of the Nose and Throat." He believed atrophic rhinitis with ozena was usually the sequence of a purulent rhinitis in childhood. Bruegelmann,³⁰ in 1884, looked upon the nature of ozena as a suppuration of the nasal turbinated bones. He thought the increased dimensions of the nasal chambers an anomaly of development, and he believed that this and a scrofulous diathesis are predisposing factors in the etiology.

Zuckerkindl brought the discussion to its more useful channels in refuting the fallacies of the theories dependent on a congenital bone-defect or abnormality, and in suggesting that the changes in the bone are apparently the result of an intra-vitam inflammatory process, but it was a number of years before this view became the prevailing one. Many papers were written in support of the view that it is due to a congenital conformation of the nasal fossae. These are reviewed in the paper of Meisser (l. c.) and the later one

of Alexander. The paper of Cholewa and Cordes³¹ is to be mentioned as claiming that the essential lesion is a bone lesion, but a peculiar one, not of an inflammatory nature. As for the changes observed in the mucous membrane itself, these have been variously described as primary and as secondary to a bone lesion by numerous observers, among whom we may name Habermann³² in 1886, Schoenemann³³ in 1902, Oppikofer³⁴ in 1907 as representative of opinions expressed at isolated times. The whole question is exhaustively reviewed by Alexander.³⁵

John N. Mackenzie,³⁶ in 1884, expressed the belief that there is always a hypertrophic stage to atrophic rhinitis. Moure³⁷ declared himself a sharer in the belief of Gottstein that the essential lesion in atrophic rhinitis lies in the glands. Habermann (l. c.) also accepted this view. The involvement of the serous and mucous glands is well established in present-day nasal histology, but it has never been generally accepted as a satisfactory exposition of the whole process or of its etiology.

Luc³⁸ and Bronner,³⁹ in 1887-8, again drew attention to the apparent association of ozena and accessory sinus disease. Gruenwald⁴⁰ advocated this idea in his book on nasal suppuration, and that other lesions also were the cause of it, such as adenoid vegetation, etc. Luc,⁴¹ in 1888, reported three cases of tracheal ozena, and a discussion as to priority in the observation of the affection arose with Massei. Zarniko⁴² and others asserted that tracheal ozena may exist without a nasal lesion. Potiquet⁴³ contributed a number of papers to the earlier discussions of atrophic rhinitis by modern rhinologists.

I have already referred to the literature of the microbial theories of the etiology of ozena. The similarity of the bacillus found by Loewenberg, Abel and Paulsen in ozenatous cases with the bacillus of Frisch, and of both with the bacillus of Friedlaender led to much discussion as to the connection of ozena, scleroma and pneumonia.⁴⁴ While most observers confirmed the early reports of various bacterial forms found in the secretions of ozena, no one was able to demonstrate the presence of any of them in the sub-epithelial tissue of the mucosa itself and some of the reputed specific forms were found in normal noses or in noses not the site of atrophic rhinitis. Perez⁴⁵ not only discovered a cocco-bacillus as the cause of ozena, but found it also in a dog, and, injected into rabbits, it caused gradual atrophy of the turbinated bones. He suggests that it is acquired by man from the dog. Hajek⁴⁶ who made investigations on the bacterial contents of the nose, expressed

his belief that the organisms found in ozenatous cases had little or nothing to do with the etiology of the disease. He believed that atrophic rhinitis had always a preliminary stage of hypertrophy. In the discussion on his paper, in 1887, in which he asserted this and that the Friedlaender bacillus often found in the nose played a secondary part even in pneumonia, he was opposed by Weichselbaum, Paltauf and Roth.

Siebenmann,⁴⁷ who was a collaborator with Meisser in the examination of cranial form as a factor in the etiology of ozena, made a careful study of the histology of atrophic rhinitis, but he, as many other writers, laid a stress upon the specificity of the metaplasia of the epithelium of the surface which would not have been the case if such work had been controlled sufficiently by the examination of this element in normal noses and in other pathological conditions, since in adult life there is always much of it to be noted. Cozzolino⁴⁸ believed the lesion first begins as a keratosis of the surface epithelium and becomes secondarily bone disease. There was a tendency with many others, as with Rethi⁴⁹ for example, to consider the ozena as something specific and aside from the anatomical lesions of atrophic rhinitis.

I have noted that from time to time authors had incidentally remarked on the connection of tuberculosis and ozena, owing to their having a common basis in malnutrition. Theisen,⁵⁰ in 1904, made it the subject of a paper. Broeckaert⁵¹ contributed to the study of its histology the expression of his opinion that the disease was due to a toxin produced by a parasyphilitic or a paratuberculous systemic infection. These terms came into use about this time, and their exact pathological significance is still enshrouded in mystery. Frese⁵² was of the opinion that most of the cases are of syphilitic origin. Sobernheim,⁵³ in 1909, reported that seventeen cases of typical ozena gave a negative Wassermann reaction, adding another proof to the view that the nasal affection may exist without any syphilitic antecedent. A number of others testified to the same effect. It was spoken of as a larval tuberculosis.⁵⁴ Schoenemann,⁵⁵ in 1909, traced a connection between the occurrence of eczema and that of ozena. From time to time various authors have suggested that ozena is a trophoneurosis.⁵⁶

Freitel⁵⁷ made an attempt to determine the age at which ozena first shows itself and concluded that in the great majority of cases it was in the school age of children that it developed, 4 to 14 years. In all treatises on the subject since the affection was first differ-

entiated by B. Fraenkel, the preponderance of the female sex in the cases affected by it was noted.

The treatment of atrophic rhinitis, especially of its chief symptom, ozena, has been varied. Going back to the time of its differentiation, we have already noted that tampons were recommended by Gottstein, and in the earlier history of rhinology this was a common form of treatment for all nasal affections, the linen or other absorbent tampon being saturated with various medicaments. Cauterization, we have seen, was also recommended by the ancients for what they called ozena, and in 1884-5 it was recommended⁵⁸ again as a therapeutic agent in its modern differentiation. In most of the writers on the subject recommendation for treatment included thorough cleansing and the application subsequently of some stimulating medicament, like thymol, aristol, turpentine, ichthyol, etc. Braun, Laker and Demme⁵⁹ recommended (1891) vibratory massage. This was employed by others either by hand or by electrically driven machinery. Faradism was also used,⁶⁰ also the electrolytic application of chlorid of copper⁶¹ and submucous electrolysis.⁶² Dionisio⁶³ employed various forms of photo-therapy in ozena and in the same year (1903) Casassa⁶⁴ reported on the therapeutical use of radium.

Brindel⁶⁵ in 1902 inaugurated the treatment of ozena by the injection of paraffin under the atrophied mucosa and this method of treatment has persisted to the present time, it being strongly recommended by Hutter⁶⁶ ten years later. Broeckaert,⁶⁷ who adopted the idea promptly, subsequently supplemented it by more vigorous measures. It was practiced by Fliess⁶⁸ and by many other rhinologists for a time after this, until the report of an embolus of the retinal artery in two or three cases of the injection of paraffin in the skin of the nose discouraged for a while frequent resort to it. On the strength of his belief that atrophic rhinitis with ozena was the result of a disease of those cavities, Broeckaert,⁶⁹ in 1905, in addition to the use of paraffin proposed to operate radically on the ethmoidal sinuses and to curette the sphenoid. He removed the middle turbinate, allowing the inferior to remain, reinforcing it with paraffin injections and injections of it also into the septal walls and floor of the nose. He proposed also to destroy the nasosinusal wall of the antrum, but not to curette the latter unless it was diseased. He claimed the injection of paraffin was efficient not only as a prothesis filling out the large spaces, but as a stimulant modifying the nutrition of the mucosa. Guyot⁷⁰ employed suction of the nasal chambers by mechanical methods in the treatment of

ozena. A number of cases were treated with injection of anti-diphtheric serum because diphtheroid bacilli were found in the crusts, chiefly by Italians.⁷¹ Skillern and Holmes⁷² used vaccines made from the pure culture of the Abel bacillus. Emulsions of the culture of the lactic acid bacillus have been used by many in the treatment of ozena.⁷⁴ Foy,⁷⁵ in 1911, claimed considerable benefit can be attained by the patients being taught to breathe persistently and properly through the nose. Ozena has been treated with hot air, dry or moist.⁷⁶

In the January number of Semon's *Centralblatt fuer Laryngologic*, 1912, there is a very valuable review of the literature of ozena during the years 1909, 1910, 1911, by Alexander. Among the points to which he gives prominence is the inequality in the distribution of cases geographically, racially and socially, its incidences as to sex and age. He drew attention to the fact that while the Wassermann reaction in his own experience and in that of others had given negative results in cases of ozena, he had himself seen a typical case of ozena, the offspring of a syphilitic father, the sister of a congenitally syphilitic brother, and in her case the Wassermann reaction was also negative. He also drew attention to the fact that while ozenatous subjects rarely contract syphilis, such cases have been reported by Fraenkel and Sobernheim (l. c.) and others, and that the question of the relationship of true ozena to syphilis is not by any means settled. It may be remarked that the subject is much embarrassed by the confusion which still reigns as to the clinical differentiation of the cases. With syphilitic ozena on the one hand and atrophic rhinitis on the other, without crusts or odor, it is difficult for an author to keep constantly in view the typical cases of atrophic rhinitis with ozena. The confusion is increased by the introduction of the consideration of accessory sinus disease attended by intra-nasal crust formation. In this excellent review it can be plainly seen that with the exception of the therapy, which is always new, optimistic and futile, there has been scarcely a question raised in the literature of the subject during the three-year period with which it is concerned that had not been thoroughly discussed in the former three decades in discussions of the phenomena presented by ozena.

ETIOLOGY.

Most modern observers who have devoted themselves to the histology of the lesions of atrophic rhinitis believe it is primarily a bone disease. In the consideration of the etiology various predisposing factors have been urged, some of them with considerable

plausibility, others with none. General systemic malnutrition in children, sometimes dependent on syphilis, seems warranted from the number of cases observable in this class often seen in two or three children of the same parents. Sex quite evidently is a determining factor, as a very large majority of the cases occur in females. Puberty also is clinically observed to have a determining influence on the advent of the symptoms.

These factors are observable in the apparent etiology of those cases of chronic rhinitis with crust-formation and the typical ozonic odor. In regard to the latter, while we speak of a typical ozonic odor it seems probable, from the state of opinion as to the bacteriology of the disease, that there is no specificity about it. Large numbers of bacterial forms, swarming in a lipo-proteid excretion of the mucous surfaces, set up chemical changes in which the volatile and non-volatile fat derivatives are concerned, which give rise to the odor.

While space forbids a discussion of the many theories advanced in regard to the etiology, it may be well to say that syphilis, long regarded as an etiological factor from the point of view of heredity has recently been investigated in its relationship to ozena by the Wassermann reaction. Negative results were almost uniformly obtained when complement fixation was tested for in the serum of the blood of ozenatous subjects. How far this can be regarded as conclusive in negation of the idea of a syphilitic hereditary factor in the etiology of true ozena it is too early yet to decide.

Excluding the cases of active tertiary nasal syphilis, as we do in modern rhinology in speaking of ozena, there is little warrant for the belief that hereditary syphilis has more to do with the etiology of atrophic rhinitis than that the syphilitic dyscrasia, like the tuberculous dyscrasia, is the cause of a lowered state of general vitality. Like tuberculosis, atrophic rhinitis is the disease of poverty. It occurs in the well-to-do just as phthisis does, but it is a disease of malnutrition, the usual cause of which, as we know, is poverty.

There is an affiliation of atrophic rhinitis with accessory sinus disease by virtue of the fact that the process itself occasionally extends to the mucosa of these cavities. There are also certain cases in which a chronic discharge from the posterior ethmoidal and sphenoidal sinuses exists with crust formation. In the former category of cases surgical treatment of the sinus accomplishes nothing, in the latter category of cases eradication of the sinus affection cures the ozena. In the majority of cases of atrophic

rhinitis with ozena the sinuses are not involved in any way, even in advanced stages. Frequently the openings of the sphenoidal sinus can be perceived by anterior rhinoscopy, owing to advanced atrophy, and the mucous membrane may be seen to be free of crust or other discharge.

Atrophic rhinitis sometimes exists in one nostril, when there is marked deviation of the septum. The concavity on the one side shows abundant crusts and an atrophic mucosa. Straightening of the septum regularly cures the condition. Atrophic rhinitis not infrequently follows extensive operative destruction of intra-nasal structure. These undisputed phenomena lend some plausibility to the theories and observations advancing, as an etiological predisposing factor, the congenital roominess of the nasal chambers. The arguments and facts usually adduced in support of such theories have not sufficed to convince the majority of rhinological observers of their tenability. Finally a certain amount of atrophy, without crusts, is the physiological accompaniment of old age. There is plainly a shrinking of both bone and mucosa.

There is hardly any histological lesion which could serve as a common cause for changes in the mucosa of all these cases except that of a bone lesion which has interfered with the nutrition of the soft parts. The bone itself is affected in them all, and while there is no satisfactory evidence in the bone itself of inflammatory action, the process is manifestly associated with a pre-existing chronic inflammation of the mucosa in a sufficient number to suppose that in these at least the bone atrophy is due to it. An analogous bone lesion may be supposed to exist in the other cases. It must be confessed, after all is said, that the etiology and even the succession of histological changes is far from satisfactorily understood or accurately known.

PATHOLOGY.

In this form of nasal inflammation the epithelial metaplasia is more marked than in the hypertrophic form and it is constantly present. Even in fairly normal nasal chambers the cylindrical epithelium is in places frequently replaced by flattened cells. In atrophic rhinitis this is universal. Yet so far as I know there is no stickle cell-formation such as is sometimes seen in the epithelial metaplasia of other morbid processes. There is a tendency to cornification of the surface layers.

There is beneath the epithelium an infiltration of the stroma with a relatively much increased number of round cells. These are marked around the ducts of the acinous glands. There is a

steady encroachment on the epithelial structures of the glands by these round cells and a lowly organized fibrous connective tissue which finally all but destroys all traces of glandular structure. The same may be said for the blood vessels. Whether cavernous sinuses in these cases have ever been much developed at puberty or not is a question. At any rate the blood vessel walls have been to a large extent obliterated by the fibrous and the round-cell infiltration. That in this process of cell degeneration there is the production of considerable fatty detritus is probably true, but to the extent one would infer from the accounts of some observers is certainly not my experience. This proteid decomposition evidently finds its way to the surface with the copious discharge of serum which takes the place of the normal viscid fluid of the glands, and there its rapid evaporation leaves behind in the form of crusts a lipid proteid precipitate which rapidly ferments and is split up into fatty acids by various bacteria. A large number of these have been found and several have been described as specific in the disease, but neither the bacilli of Loewenberg, Perez, Pes-Gradenigo, nor the diphtheroid bacillus, all of which have been urged as etiological factors, have been accepted as of any significance in the causation of the lesions. It seems probable that in the sense that there is an antecedent hyperplasia of the periosteum in atrophic rhinitis, we may say that hypertrophy is followed by atrophy in certain cases of nasal inflammation, but it seems quite certain that while this pre-existing periosteal hyperplasia may be present in the larger number of cases of typical atrophic rhinitis with ozena, this is the only element in the mucosa which is affected by preliminary hyperplasia. That this is always affected primarily must also be acknowledged as more or less hypothetical. Nevertheless the most significant change in structure is the thickening of the periosteal layer. Inasmuch as the distribution of nutrient arteries to bone and to mucosa lie in this element of the mucosa, inasmuch as it seems to be a fibrosis which ultimately destroys the glands and the blood vessels of the mucosa itself, it is a fair conjecture that it is in the periosteum and the perichondrium—for the septal cartilage also becomes thin and even in places absorbed—we must seek for the root of the changes which give this nasal disease unique characteristics.

The histological features of the disease seem to justify us in calling it a fibrosis, but the clinical features which accompany them justify us rather in calling it a mystery. There is no analogue to it elsewhere in the body. This gives us a clue to its essential na-

ture. There is no other region in the body where we have a very thin plate of bone covered on both sides by a vascular secreting mucous membrane and separated from the bone on each side by a thin layer of periosteum which carries its nutrient blood-vessels. Often present in early childhood, associated with puberty in women, the symptoms ceasing for the most part after middle life, not beginning, except in the rarest cases, after adolescence, apparently not necessarily preceded by a condition of chronic inflammation or by hypertrophy, conceiving of it as initially a fibrosis of the layers of connective tissue next the bone and cartilage is a matter of some difficulty,—yet, after all, that seems the most reasonable hypothesis purely from a histological standpoint.

In order to understand the essential lesions of the stroma of the mucous membrane in atrophic rhinitis, I must repeat somewhat the remarks I have made in a recent series¹⁷ of articles on the contractile elements in the connective tissue.

Looking for the first time at the picture presented by sections of the nasal mucosa of animals, stained by the Weigert formula or one of its modifications, the observer is struck with the abundance of elastic fibers. Their profusion at first seems not to be more pronounced, on the average, in one locality than in another, but it soon becomes evident that, aside from their great abundance in the walls of the large blood-vessels, the most constant and the most richly supplied locality is the periosteum and the deeper layers of the stroma intimately associated with it. Thick interlacing bundles are always demonstrable, running, in an irregular way, parallel with the planes of the bone. Everywhere the blue-black threads run through the middle layers of the stroma, always either parallel or obliquely to the surface. Nearly always demonstrable is a special layer of fibers situated in the stroma just under the epithelium at varying distances from it, but in such relation to it and in such arrangement that one cannot fail to perceive that it subserves a special physiological need, somewhat apart from the general tonicity the widely scattered fibers elsewhere would give the mucosa.

The persistence of this layer of wavy fibers just under the epithelial line is not infrequently noted in a mucosa considerably altered by hypertrophy. It is a layer indefinite in extent and somewhat inconstantly seen in the normal mucosa in the human infant and in animals. It is well to draw attention to the fact that never in the free stroma do the elastic fibers run in planes vertical to the surface or vertical to the periosteum, but always obliquely to them, except for the sub-epithelial fibers just spoken of, and the elastic

fibers of the periosteum itself which run in more or less horizontal directions in relation to the surface and the bone.

Recently an article by Duerck⁷⁸ has drawn attention to straight telegraph-wire like fibers revealed in connective tissue generally and in arterial walls by some of the Weigert stains for nerve sheath demonstrations. He seems to think these had not been previously demonstrated in the walls of the arteries. While they may not have been especially emphasized in the work of Koelliker and Ebner, from which he quotes, they certainly are a more or less familiar phenomenon to histologists and may be demonstrated with the hemotoxylon-resorcin stain as modified by Hart. It is not unusual to see these fibers, or fibers at least morphologically similar to them, in the connective tissue of turbinated bodies of infants, and they are seen also in those of the monkey.

Breugelman⁷⁹ who used the 'hemotoxylon eisenlack' stain for sections of the penis also demonstrated them there. We may imagine they furnish in the walls of the arteries and elsewhere that form of elasticity lent to a lady's corset by the whalebone stays, but it is not at all certain that their straightness, their "telegraph wire" appearance may not be due to their being ordinary elastic wavy fibers stretched out straight by traction or by virtue of their position.

The distribution of elastic tissue around the gland acini is not very marked, or apparently in such a mechanical arrangement as to work in the most efficient manner in expelling the contents. While it is true that in some cases it is demonstrable in the material from animals, such is not uniformly the case. One gains the impression that such expulsion of mucus from the glands as may occur from the contractile action of the tissues, arises more from the general elasticity of the stroma than from a special network around the glands. Although the description of Schiefferdecker⁸⁰ is not very accurate, it seems to me, I repeat what he says. Backward from the *vestibuli nasi* "with the beginning of the glands, the elastic fibers, especially in the deeper parts of the stroma, become more slender, but are nevertheless still thick; they surround the glands and, singular to say, reach a greater thickness exactly at those places which lie between the epithelium and the glands, so that this part appears as the characteristic continuation of the network hitherto penetrating the whole stroma."* Now while this may be

*Schiefferdecker has had the same experience with the apparent capriciousness of elastic tissue stains, and he also is not disposed to trust the results of tinctorial reactions. It seems to me we are justified in supposing that there are variations of chemical and tinctorial reactions which do not influence elasticity, but it is also possible that a functional demand may temporarily effect a chemical and hence a tinctorial change and also

the character of the elastic fiber arrangement bordering on the vestibule, in the deeper portions of the nose such is not the case. The same author subsequently speaks of the glands of the deeper parts of the nose being surrounded by a *membrana propria*. It is true, as will subsequently appear in a discussion of pathological conditions, that one can observe appearances, as if the base of the gland-cells exuded a homogeneous substance which forms a sort of an incomplete and irregular hull to a gland acinus; but it is very difficult to be sure that this, in the material from animals, is not simply a slightly more dense arrangement of connective-tissue fibrils. Among these, as I have said, may frequently be traced the elastic fiber of the stroma, but there is no specific peri-glandular network of fibers taking the Weigert stain, nor is there anything which can be called a *membrana propria*.

In the walls of the nasal blood-vessels I am not aware there is any exceptional feature to the distribution of the elastic fiber. In the endothelium of the single-walled capillary the occasional appearance of a purple stain may be thought to argue for an elasticity which is more evident, judging from the stains, as the thickness of the walls increases. The intima of the venous sinuses is very thick, and the longitudinal elastic fibers always stand out as sharp landmarks in sections of the erectile tissue colored with Weigert's stain. It also mingles freely with the external coats of the venous sinuses. The arterial vessels present no especial feature in this regard.

What I wish to dwell on especially is the condition of the elastic fiber itself in the presumably normal material, as distinguished from the elastic fiber and the elastin noted in the material from the nasal mucosa of adults removed in the course of clinical work. Normally the elastic fiber is indefinitely long, slender, branching, usually with finely drawn-out ends interlacing everywhere with other fibers. Just where and how they are anchored to other cells is not very clear. The transverse measurement of the elastic fiber varies greatly in different localities. In the nasal mucosa it is of smaller caliber as seen in the infant and in the monkey. It ranges from a hardly perceptible line, as viewed with the o. im. 1/12 obj., up to perhaps two microns. Koelliker, speaking of the elastic

a change in elasticity. In other words, elasticity being an expression of energy, it may vary in the tissues, just as muscular energy varies without betraying itself in structure to our powers of vision. This falls in very well with a recent remark of von Hansemann (*Deszendenz und Pathologie*, Berlin, 1909) whose ideas on the mutability of tissue-form for more than a decade have been known under the name of "anaplasia." "In man slightly differentiated connective tissue is extraordinarily variable in its occurrence and everywhere adapts itself in form and position to temporary demands made by normal and pathological states."

fiber in general, says it ranges up to six microns in diameter or even to twice or thrice that. In the nose when it exceeds two or three microns it is usually associated in the loose stroma with pathological conditions and itself presents various departures from what I conceive is its normal condition. In my notes I have spoken of this normal condition as "efficient looking," meaning thereby they were arranged in such a way as, supposing they were capable of contraction, their shortening would lead to a condensation of the tissues in which they lie. This was to distinguish them from swollen fibers with abrupt ends, broken into sections, granular, sometimes betraying their former state of continuity only by a row of granules into which they had disintegrated in the course of disease,—perhaps at times they break up into this state of discontinuity as a result of the technic of fixation, hardening and staining. Great clouds of elastin granules are thus seen crowding some fields. In the normal mucosa when such clouds exist they are more or less homogeneous, the granules for the most part not being resolved by the highest powers of the microscope.

So far as my own convictions go, there can scarcely be a doubt of the origin of the elastin and the elastic fiber as an exudate of the cells in adult tissue, even when the fiber is efficient looking. In normal tissue it is organized into a fiber by a precisely working machine, but when the stimulus is over-great, as in hypertrophic conditions, the fibers are thick and swollen, with abrupt ends, often broken into sections or a row of granules, but frequently existing as a cloud of coarsely granular material in the stroma. Such granules are seen inside of cells, especially at the free surface of gland cells. Up to a certain point this disorderly condition of the elastin corresponds to the extent and the degree of the hypertrophy, and then a change sets in.

I cannot here enter into an exhaustive discussion of all the changes in the nasal mucosa supervening upon an hypertrophic rhinitis. I must, however, trace in outline the course of events which can be gathered only from a composite mental impression of the moving picture of morbid processes after years of observation. The static conditions conventionally looked upon as the "pathology" of disease is a sterile way of studying vital problems. Morbid tissue, like normal tissue, is a living thing, moving along the path in which it is guided by the laws of living matter and by, in this locality, the preponderating influence of the environment. At hardly any given moment is the condition exactly what it subsequently becomes. The only constant thing is change. I am com-

pelled then, in attempting to place the changes in the so-called elastin in the proper light, to be a little discursive. There is a growing tendency, for which we must be profoundly grateful, to treat of pathology not as something dead and immovable, but as of something living and mobile, a process and not a state. In chronic inflammation of the nasal mucosa the static conception of it is entirely unintelligible. We must conceive of it as a process in which changes are slowly advancing as the result of age, heredity and environment.

There may be changes in the nasal mucosa as the result of a chronic rhinitis which has not perceptibly increased or diminished the bulk of the tissue. Hypertrophy and atrophy are gross and inexact terms, but they are so fixed in rhinological usage that it is impossible, at least inconvenient, to break away from them. So notwithstanding the protest I make in what I have to say it will be more convenient to start from a basis furnished by some of the conventional divisions of atrophic rhinitis, of no value in themselves except as indicating some of the causes underlying the process.

It often happens that atrophy supervenes upon states of the mucosa whose condition of chronic inflammation has caused symptoms so trifling as not to betray it. It is occasionally the case that edematous polypi (especially in asthmatic and hay-fever cases) spring from a mucosa in which previous inflammatory changes have been insignificant, and the same may be said of atrophic rhinitis. Nevertheless it is true that a periosteal lesion without any antecedent hypertrophy of the mucosa may be the first step in the pathological process which leads to an atrophic rhinitis. Such is a fact, I believe, in those ozenic cases, not too common now that a keener differentiation of diagnosis is exercised, which we recognize as having begun in early childhood, when there may have been a half-suppressed syphilitic inheritance, or some other systemic deep-lying vice. This also frequently applies to those cases whose symptoms of ozena, with the characteristic crusts and odor, date back to puberty only. There is another class of cases, pseudo-ozenic we may call them, which have foul decomposing crusts without the specific odor, and associated with sinus supuration. In both these categories there is an antecedent periosteal lesion. In the first, the true ozenic cases, there is a periosteal lesion due to some unknown systemic cause which has blocked the nutrient arteries of the superjacent soft parts. Such is also the condition *mutatis mutandis* in the other category just mentioned.

The suppurative inflammation of the mucosa of the sinuses has spread through the periosteum to the bone. One bone change we may say is endogenic, the other is exogenic, and the results (true ozena and pseudo-ozena) may be differentiated by careful clinical observation. There is still a third class of atrophy in addition to that succeeding hypertrophy. I refer to the atrophy of age. The bone shrinks, the epithelium is atypical, the venous sinuses are fewer and smaller, the racemose mucous glands are suppressed, while from the single-tubed serous glands of Bowman in the upper regions of the nose and from direct transudation a watery fluid flows and drips, often so inopportune, from the nose of age.

There is always some edema or serous infiltration accompanying atrophy even in the very last stages. In the end the connective tissue cells have taken on an embryonic type with branching processes, and such mesh of fibrils as still exist is crowded with the small leucocytes and their naked nuclei. At this stage the elastic tissue in the walls of the radical arteries and veins, even that of the intima, has become disorganized and partially absorbed. The glands, all but perhaps some traces of their ducts, have disappeared and the stroma of the turbinates is little better than granulation tissue.

To summarize then: In the newborn infant the elastin material exists in the nasal mucosa, so far as selective stains reveal its presence, in the form of a fine net-work of fiber and no coarse granular material or swollen fibers. Later in life the latter appear and in hypertrophy are prominent in the landscape of the sections. As changes go on to atrophy of any kind or to edema, the useless non-efficient material is absorbed first and the fine fibers last, perhaps themselves passing through a stage of disorganization. I think there can be no doubt that in adult tissue the granular elastin has an intra-cellular origin, and it is probable that even some of it thrown out in inflammation may be organized into efficient fibers, but for the most part this attempt at organization is incomplete and imperfect. Like the callus thrown out from bone, it must be looked upon as a process of repair and regeneration. The material carries with it imperfectly the heredity of early embryonic life, the tendency to tissue-formation. It is quite impossible to account for the appearances on the supposition that all the disorganized material has had its origin in the degeneration of pre-existing normal fibrils.

In taking up the question of the presence of the smooth muscle cell in the stroma of the nasal mucosa, so interesting from many

points of view of a general nature, the special histological questions concerning it have hitherto aroused interest only in one respect. Is it a fact that separate smooth muscle cells or limited bundles of cells lie free in the loose stroma of the erectile tissue of the turbinate bodies, or are they always closely connected with the coats of the large blood-vessels? Zuckerkandl⁸¹ and Herzfeld⁸² maintain the latter view, and their position may be regarded as summed up in the words of Herzfeld: "The erectile tissue of the nasal mucosa is rich in organic musculature. This, however, does not lie free in the connective tissue of the erectile bodies, but forms as in all other parts of the body the middle tunic of the arteries and veins, and lies closely pressed around the walls of the lacunae of the erectile tissue."

Students of rhinology became familiar with the view of Zuckerkandl, which is of the same tenor, many years ago. While muscle cells had been described in the stroma of erectile tissue elsewhere, the *corpus cavernosum* of the penis, the nipples, etc., the scalp, the skin of many animals, for many years no one ventured to assert in the face of Zuckerkandl's authority their presence in the stroma of the nasal erectile bodies. I had been indisposed to accept the views of Zuckerkandl chiefly for physiological reasons and from the clinical study of the nasal mucosa. Owing to the difficulties of differentiation and the unsatisfactory technic in vogue before Mallory's recent introduction of his connective tissue stains have added so much to the more exact study of cellular relations, it was difficult to acquire sufficient assurance to refuse an assent to an authority so weighty as that of Zuckerkandl. It is true that Schieferdecker⁸³ has asserted of late years that muscle fibers do lie free in the stroma, but the confirmation of the assertion was a difficult matter, and it still remains a disputable matter. The difficulties are not wholly technical nor entirely those of personal opinion, but, in the question are involved some fundamental principles of histology, of embryogenesis and of other matters of by no means inconsiderable interest in general biology.

The relation of the smooth muscle cell to the racemose glands in the nasal mucosa differs somewhat from that which obtains in the skin since, according to Koelliker,⁸⁴ in the connective tissue net-work around the skin glands, there is mingled with it elastic fibers, fat cells and often muscle cells. It is true that muscle cells can often be made out in connection with the racemose glands of the mucosa, but in health with regularity only around the ducts of the glands, and here they are seen even closer up under the sur-

face epithelium at their mouths,—the only situation immediately under the surface epithelium, so far as I have been able to observe, where the muscle cell can be demonstrated in the nasal mucosa. We usually have the mouth of the duct at the bottom of a deep sulcus in the mucosa, so that the muscle cell as a matter of fact does not even here usually approach very closely to the surface. Further it may be noted in this connection that frequently blood-vessels of considerable caliber (fifty microns estimated in one observation in my notes) have no encircling muscle coat when they lie close under the surface epithelium. It will be remembered that I described as normally existing close under the epithelium a special horizontal layer of elastic fibers, and we may readily believe that these are more serviceable in obtaining a smooth surface on contraction than muscle fibers would be in that situation, while deeper in the stroma a musculature is required to supplement the obliquely arranged elastic fibers. For efficiency in respiration and in olfaction a smooth nasal surface would be very desirable, but for proper drainage it is imperative. I shall not attempt a complete description of the musculature of the blood-vessels further than to say the deep veins and sinuses and deep vessels of even very small caliber are supplied with well-developed muscle cells in their coats, both longitudinal and transverse; in the superficial vessels, as I have just intimated, the character of the coats is that of large and small capillaries.

One cannot have constantly before one's eyes the difficulty of distinguishing the indifferent cell from the differentiated muscle cell in the connective tissue without the growth of a conviction that out of the former may arise the latter in answer to some functional demand, increasing in importance as one approaches the vascular layers. In another respect it may quite as rationally, even from my observations, be argued that the muscle cells have split off primarily from those of the vessel coats, by mitosis, in the development of the bulk of the erectile bodies which takes place at puberty. This might easily occur and the muscle cells might be isolated at considerable distances by the proliferation and interposition of the different connective tissue cells of the loose stroma. In the calf, and in the human infant before birth, especially in the latter where the embryonic type of cell prevails, the isolation of the muscle cell, if I am to trust my own notes, is even more conclusively to be observed than in the human adult. To be sure there is no reason why the genesis of the stroma muscle cells may not be ascribed to both sources, i. e., to their original embryonic differ-

entiation in the tissue and to their derivation under certain conditions from the musculature of the blood vessels. The question of the mutation of the indifferent adult connective tissue cell into a muscle cell is quite another matter, and will find little support from some observers. Nevertheless, while I admit that my observations are susceptible of an orthodox interpretation in this instance, I am disposed to exclude the possibility of such a metamorphosis, especially in the disturbances of chronic inflammation. In other articles⁸⁵ I have dwelt sufficiently upon the evidence of a metamorphosis of epithelial cells into cells exhibiting the fibrils of connective tissue under the stimuli of chronic inflammation. Here, as in the tonsils, chronic inflammation certainly induces an appearance of metaplasia which has forced itself on my attention. The branching connective tissue cell is much more closely related embryologically to the muscle cell than to the epithelial cell, and how much resistance this view of their functional and morphological mutability may receive I do not know.

This brings me to the fate of the smooth muscle-cell in plainly pathological states of the nasal mucosa. I have explained at great length the difficulty one must experience in saying where normal nasal structure in the adult becomes abnormal. A very wide neutral territory must be pictured as existing between the two. With the elastic tissue we have seen that when we emerge out of that neutral debatable strip into the clearly pathological domains of edematous infiltration and of atrophic change, we have found a very marked diminution not only in the efficient coaptation of the elastic granules and the configuration of the fibers which occurs early in the course of hyperplastic change, but we have found a marked diminution in the quantity of elastin, organized and disorganized, everywhere in the tissue. Clinically, in the viscid mucus which clogs the gland acini in atrophic rhinitis, we recognize an increased demand for the function of an actively contracting cell around the acinus. Comparing sections differently stained of the same tissue in atrophic rhinitis we at once note in the penultimate stage that the muscle cells have offered a markedly greater resistance to degeneration and absorption than has the elastic fiber. I have pointed out that in the normal tissue the smooth muscle cell, or something resembling it, is seen around the mouth of the racemose gland ducts but not around the acinus. In the primary changes in the glands in the course of chronic hypertrophy the muscle cell is noted also wrapped around the acini in such a way as to suggest that it is there in answer to a functional demand for the expulsion of a

thickened mucus, or possibly to take the place of the elastic tissue which has ceased in the stroma to transmit its pressure to the glandular structures. Passing on to fairly well advanced atrophic conditions, stages in which there has been marked destruction of the venous sinuses and the glands by the encroachment of low-grade fibrous tissue and the obliteration of these structures, we note that the muscle cell in the walls of the arterioles and venous sinuses most affected is assuming the irregular nucleus form and branching cell body of the indifferent connective tissue cell. At least, from my point of view this is what seems to take place, though I cannot deny the validity of the description which narrates the history of the process in another fashion, viz., that this indifferent connective tissue cell replaces the muscle cell.

A careful study of the cell forms in the stroma of these moderately advanced cases of atrophy in comparison with hypertrophy will reveal comparatively very many more cells, entirely isolated from the neighborhood of any blood-vessel, which have assumed or preserved the morphology of the smooth muscle cell than in normal or hypertrophic mucosa. It is true, a perfect picture of the muscle cell form is not obtained in the technic I have used, and the criticism is unavoidable that pressure has moulded indifferent connective tissue cells into the rounded ribbon or spindle-like form of the muscle cell with a cylindrical nucleus; but I am sure if they were wound around a blood-vessel there would be no hesitation on the part of any histologist in classifying them as smooth muscle cells. In the later or last stage of atrophy of the mucosa all muscle cell forms have disappeared, the stroma has been reduced almost to the condition of granulation tissue made up of round cells in a feeble mesh of star-shaped branching cells with long processes, resembling the embryonic type of cell, and numbers of single-walled capillaries.

The structural changes wrought in the mucosa are evidenced in the vitiation of the secretions. The absorption of bone and cartilage are responsible for a change in the external configuration of the nose when the disease has begun in early childhood, before the facial bones are fully developed. Whether it has begun in childhood or at puberty, the roominess of the nasal chambers is dependent upon atrophy of the scroll bones and of the mucosa covering them.

How to account for the disappearance of the crusts and the secretions in those cases in which it occurs after middle life, remains a subject for histological research. A restoration of the glands and

blood-vessels anatomically seems biologically improbable, yet there is a return to a secretion on the surface of such a nature that its evaporation is not rapid enough to prevent it from carrying away with it those non-volatile ingredients which formerly were left behind as crusts of dried secretion.

The atrophy of age is of the same structural nature, so far as the glands and blood-vessels and the periosteum are concerned, and it seems probable that in those cases which recover from their terrible affliction of foul-smelling nasal crusts, the senile stage of the mucosa is reached and its condition suffices to remove the trouble. In this view then we may believe that a fibrosis of unknown origin in the periosteum and perichondrium induces, by shutting off the proper nutrition of the tissues, a state of vicious lipid-proteid metabolism in the mucosa, the waste products of which washed out with the serum and lymph of the tissues produce the crusts on the surface. These vary with the concentration of the solid constituents of the secretions. Sometimes they are not sufficiently concentrated to remain as a deposit on the surface. We may thus account for cases of atrophy without crusts or excessive odor. The approach of age slows down the activity of all metabolic processes and tends thus automatically to cure the ozena of atrophic rhinitis and leave behind only the structural atrophy. I am fully aware, at the present state of our knowledge, how likely this hypothesis is to prove insufficient on critical analysis or even erroneous when more complete objective knowledge is attained.

To summarize the histological pathology of atrophic rhinitis, we may say that owing either to antecedent intra-nasal inflammation, or to a constitutional dyscrasia, or to the physiological change of age, or to all three, thickening of the fibrous elements in the periosteum or perichondrium is followed by consequences which are manifested through the effects of local malnutrition due to interference with the blood and perhaps the lymph supply of the mucous membrane and the bone it covers. These are: 1. The metaplasia and cornification of the surface epithelium. 2. Round-cell infiltration. 3. Destruction of the blood vessels. 4. Destruction of the glands. 5. Destruction of the elastic fibers. 6. Absorption of the bone, especially of the inferior turbinate. 7. Destruction of the smooth muscle fibers in the stroma. 8. These structures, to some extent, replaced by round-cell infiltration and by lowly organized fibrous connective tissue sometimes approaching the embryonic type. 9. While these changes are going on there is excretion or transudation to the surface of lipo-proteids, derived from tissue-waste and

perverted gland function, which form a stinking, viscid secretion and crusts in which bacteria plentifully multiply. 10. Finally, this destructive metabolism ceases with the advent of old age. The foul secretions and crusts disappear, and the surface is moistened by a serous exudate which dilutes the remaining gland secretion sufficiently to secure its drainage. Thus nature brings about a cure difficult or impossible for man to accomplish.

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