THE HISTOPATHOLOGY OF HYPERTROPHIC RHINITIS IN CHILDREN.

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The chronic inflammations of the intranasal structures in children possess especial interest from the fact that a knowledge of their nature may be expected to furnish the key to several obscure pathologic conditions of later life. Nevertheless, our information regarding the early stages of these affections is extremely meager, and a fruitful field is still here open for investigation.

Without discussing the relation to each other of the various forms of inflammation within the nose, I present the histologic descriptions of three cases of hypertrophic rhinitis in children. As will be seen, they exhibit an essential similarity to each other in both clinical and pathologic characteristics.

Case 1.—The patient, a girl 10 years of age, was brought to the clinic for nasal obstruction of one year's duration. Examination showed a pale, poorly nourished child. The tonsils were slightly larger than normal and there was a small amount of non-obstructive adenoid tissue in the nasopharynx. Glandular enlargement was absent and there was no evidence of rachitis. The lower turbinates on both sides were enlarged and in contact with the septum. The enlargement was shown by the probe to be seated in the tissue covering the bone, the latter being unchanged in size. The consistence was about that which would be found in a normal turbinate. The surface anteriorly was smooth and rounded; posteriorly it was mammillated, particularly on the right. The color of the mucous membrane was much paler than normal. Under cocain a slight shrinking in size was noted. The middle turbinates could be seen with difficulty, but exhibited, so far as could be determined, a similar pale enlargement. There was a moderate amount of thin mucus in the nasal passages.

Histology.—A portion of the lower turbinate on the right was removed with the snare and hardened in Zenker's fluid. Under the microscope, sections show a furrowing of the mucous membrane, which varies in thickness from three or four cell layers on its exposed surface to fifteen or twenty cell layers along the side and bottom of the furrows. The cells are columnar in type and show nothing abnormal in their cytoplasm or nucleus. The epithelium lining the furrows is ciliated, while that on the exposed free surface shows no cilia. In the intercellular spaces are a few scattered polymorphonuclear neutrophils.

Below the mucous membrane is a loose connective tissue extending to the periosteum. The transverse diameter of this connective tissue is from three to four times greater than normal. It appears as an irregular wide-meshed, exceedingly delicate fibrous network, in which are contained scattering clusters of glands, a few thin-walled, more or less tortuous, blood-vessels, here and there a large sinus, together with numbers of free lying cells. The relative proportion of these constituents, varies, as it does normally, in different parts of the sections, the free lying cells being most numerous near the mucous membrane, while the glands are more deeply situated. Furthermore, at the extreme anterior end of the turbinate the reticulum is loosest and the blood-vessels, sinuses, round cells and glands are fewest in number, while a short distance posteriorly the fibrous reticulum is more compact, and these structures are proportionately more numerous.

The free lying cells are most numerous just below the mucous membrane, but are nowhere abundant or gathered to form groups. Those nearest the endothelium of the blood-vessels have the character of the small mononuclear leucocytes of the blood. In the immediate neighborhood plasma cells are found in small numbers, together with cells intermediate in form and staining properties between small mononuclear leucocytes and plasma cells. These two types of cells with the intermediate forms are also found in fair numbers in the immediate neighborhood of the glands and are as well sparingly scattered throughout the whole of the connective tissue. Small numbers of polymorphonuclear neutrophils occur irregularly distributed, together with a few eosinophilic polynuclear leucocytes. A relatively large number of *mastzellen* are found, most numerous near

the mucous membrane. These *mastzellen* are comparatively small, with a few small granules.

The sinuses are sparingly found, chiefly in the central portions of the connective tissue. They are elongated, oval in shape, are lined with endothelium, and contain a varying amount of amorphous granular material, together with, in some cases, red and white blood-corpuscles.

The blood-vessels are few in number, traverse the connective tissue in all directions, and possess a wall of one or two layers of endothelial cells.

The glands are of the ordinary racemose type found in this region and present no noteworthy alteration.

Case 2.—A boy, 10 years of age, pale, poorly nourished, somewhat rachitic. The adenoid and faucial tonsils are slightly enlarged; cervical glands normal. According to the parents' statement, nasal respiration had for some years been frequently interrupted. For the past six months the nose had been completely stopped. Examination showed both lower turbinates greatly enlarged, the left completely filling the nasal passage, the right nearly in contact with the septum. The appearance of the enlargement was similar to that in the preceding case, being pale, smooth, of normal consistence, and shrinking but slightly under cocain. The middle turbinates were seen with difficulty; both were moderately enlarged, and pink, the color contrasting markedly with that of the pale lower turbinates.

Histologic examination.—The mucous membrane is smooth and even, without furrows, and is composed of three to five layers of columnar cells, in which mitotic figures are numerous. The cilia are, in most places intact. A considerable number of polymorphonuclear leucocytes are seen in the intercellular spaces of the mucous membrane. Below the mucous membrane is a loose connective tissue reticulum similar to that in the preceding case. The structure is in general somewhat more compact, the glands are about as numerous, the blood-vessels are much more abundant, as are also the sinuses, while the round cells are conspicuously fewer and are scarcely, if at all, aggregated into groups.

The round cells are chiefly small mononuclear leucocytes, which are found most numerous in the immediate neighborhood of the blood-vessels, many lying in contact with the endothelium of the capillaries. Next in order of frequency are plasma cells scattered irregularly through the connective tissues. Cells intermediate between the small mononuclear leucocytes and the typical plasma cell are found in numbers. *Mastzellen* are conspicuous everywhere and are relatively more numerous than in the preceding case. The sinuses and glands present nothing especially worthy of note. The round-celled infiltration in the neighborhood of the latter is less than in the preceding case. The infiltrating cells are small mononuclear leucocytes, plasma cells, and cells intermediate between them in about equal proportion. Eosinophiles are not found.

Case 3.—A boy, 8 years of age, moderately pale, fairly well nourished, apparently not rachitic. There is moderate enlargement of pharyngeal and faucial tonsils; cervical glands normal; nasal respiration nearly absent on right side, much diminished on left; duration of condition not possible to ascertain with accuracy. Examination showed the right lower turbinate much enlarged and in contact with the septum, pale, smooth, of about normal consistence, shrinking moderately under cocain. The left lower turbinate was also enlarged and pale, though to a less marked degree. The middle turbinates were moderately enlarged, slightly paler than normal. As in the preceding cases, they were decidedly pink by contrast with pale lower turbinates.

Histologic examination.—The mucous membrane covering the lower turbinate presents in general an even outline, dipping down in but one or two places to form a shallow furrow. It is of the columnar type, varying in thickness from three to six cell-layers. Here and there a few cilia are seen in regions where the mucous membrane is thickest, but in most places cilia are absent. Numbers of mitotic figures are observable in the epithelial cells. Many polynuclear neutrophilic leucocytes lie in the intercellular spaces of the epithelium.

Below the epithelium and extending to the periosteum is a loose connective tissue, appearing as an irregular wide-meshed, exceedingly delicate fibrous network, in which are contained scattering clusters of glands, a few thin-walled or less tortuous blood-vessels, here and there a large sinus and many free round cells, largely aggregated into loose groups. The relative proportion of these constituents varies in different parts of the section. In the region corresponding to the extreme anterior end of the lower turbinate the reticulum is loosest and the blood-vessels, sinuses, round cells and glands are fewest, while posteriorly the reticulum is more compact, and the blood-vessels, sinuses, round cells and glands are more abundant. The round cells are chiefly found immediately below the mucous membrane,

aggregated largely into loose groups around the blood-vessels. The cells nearest the endothelium of the blood-vessels have the character of the small mononuclear leucocytes of the blood. In the neighborhood are great numbers of plasma cells, and cells intermediate in form between the leucocytes and plasma cells. There are also found irregularly scattered a considerable number of polynuclear neutrophils and eosinophils. A few *mastzellen* are seen here and there throughout the connective tissue.

The sinuses are elongated, oval in shape, lined with endothelium and are empty except for a varying amount of an amorphous, fine, granular substance. The blood-vessels are irregular in course, traversing the connective tissue in all directions, and containing in addition to the red blood-corpuscles, many lymphocytes and polynuclear neutrophils. The glands are of the ordinary racemose type found in this region and present no noteworthy change. These are surrounded by a varying number of infiltrating cells, chiefly small mononuclear leucocytes, plasma cells and cells intermediate between these forms.

THE PATHOLOGY OF EPIDEMIC CEREBRO-SPINAL MENINGITIS.

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In 1887 Professor Weichselbaum¹ found a peculiar diplococcus which he called *diplococcus intracellularis*, in six cases of cerebrospinal meningitis, whose clinical histories corresponded exactly to that of the epidemic type of this disease, and not at all to that caused by the pneumococcus. He described these cocci as being particularly found within the cells of the exudate, always occurring in the form of a diplococcus with the opposite sides flattened. It grew best at body temperature, not well on blood or potato.

Considerable confusion existed until 1895, when Jäger² published his observations in the cases of ten soldiers dying of the epidemic form of the disease. During this period, up to the time of Jäger's article, a number of articles appeared claiming that either all forms of meningitis were caused by the pneumococcus, and that this was but a localization of the general infection with this germ, or that it was caused by a variety of the pneumococcus. Jäger completely corroborated the work of Weichselbaum, namely, that in the epidemic form the meningococcus, as it is called, is constantly found, and that it has nothing in common with the pneumococcus. In addition to its structural characteristics described by Weichselbaum, Jäger found that it has a fairly visible capsule, grew best on glycerin agar, can be more easily cultivated than the pneumococcus, and unlike the latter, has no effect when injected subcutaneously into animals. When injected into peritoneal or pleural cavities, death occurred in forty-eight hours.

Heubner³ describes ten cases in which he found the meningococcus during life, confirmed its presence in five by autopsy, and obtained pure cultures of the organisms. He experimented upon animals, using the reversed lumbar puncture method, i. e., injecting pure cultures or fluid from cases into the spinal canal of two goats—which he had found to be the most susceptible animal. In one goat death occurred in one and a half days. The autopsy showed a hemorrhagic spinal meningitis. The exudate contained many meningococci confirmed by cultures. The organism was also found in the kidney and liver. A second goat was injected twice with cultures from a mild case, without result, but when some fluid, which had been taken by lumbar puncture from a severe case of the

disease, was used, the animal died in twenty-four hours. The autopsy showed a turbidity of the spinal meninges and an acute hydrocephalus. The presence of meningococci was proven by stained specimens and cultures. This resistance of most animals to the meningococcus compared to the ease with which they are killed by the pneumococcus corresponds to the clinical observations of the greater mortality of sporadic or pneumococci meningitis—89 per cent. as compared to 50 to 39 per cent. in the case of meningococcus meningitis.

Peterson,⁴ during an epidemic in Berlin, found the meningococcus in twenty-three out of twenty-six cases, by lumbar puncture.

Kister⁵ found it in pure cultures in the fluid obtained by puncture in two cases of cerebrospinal meningitis, and studied it bacteriologically. The chief differences which he found were that with Nicolle's modification of Gram's method it retained the stain if the re-agent was allowed to act a short time, but became decolorized if permitted to act for some time. He could not obtain a growth on glycerin-agar.

Urban⁶ succeeded in obtaining the meningococcus in pure culture in five cases of the epidemic form of the disease. He obtained an abundant growth in gelatin and on potato.

Councilman, Mallory and Wright,⁷ in an exhaustive research during an epidemic of meningitis in Boston, collected 111 cases. In thirty-five of the cases in which postmortems were held, the meningococci were found either in cultures or on microscopic examination of the exudate or of the tissues in all but four cases. Of these latter, in one it had been found by lumbar puncture; in a second, there was a mixed infection with tuberculosis; two others were chronic cases. As a rule, the organisms were obtained in cultures more easily when made in the acute than in the chronic cases. Blood serum was found the best medium; very feeble growths on agar were obtained. The organism was always found in the bodies of the polynuclear leucocytes, but never within the nucleus. It was never found outside of the meninges or brain. Mixed infections were not uncommon. The pneumococcus was found seven times, and once Friedlander's bacillus. Typic meningitis in a goat was produced by inoculating directly into the spinal canal. The animal died within twelve hours, and at autopsy a slight fibrinopurulent exudate was found in the meninges of both brain and cord. The average duration of the acute cases in human beings was six and a half days, while twenty-eight and a half days can be considered an average of the chronic cases. They found the most marked lesions at the base of the brain. They were purulent infiltration of the pia arachnoid, especially around the blood-vessels. There was never as much fibrin as in pneumococcus meningitis. In the brain itself there was an increase of the neuroglia cells of the cortex, and infiltration along the second, sixth and eighth cranial nerves. A similar change existed in the spinal nerves and ganglia. The majority of the lung complications were due to the pneumococci, although in one case a thrombus composed of leucocytes filled with meningococci was found.

Hektoen⁸ found the *diplococcus intracellularis* in pure culture in a case of Dr. J. B. Herrick's during an epidemic of the disease. The organism grew well on glycerin-agar and blood serum in the typic manner.

Kamen⁹ studied the organism in a typic case, both in the fluid obtained by lumbar puncture and