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Histochemical detection of lymphatic drainage pathways in the middle nasal meatus*

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SUMMARY

Following extensive middle meatal antrostomy, even without manipulation inside the maxillary sinus, a reactive edema of the maxillary sinus mucosa may be subsequently detected. A presumptive correlation has been established between this particular mucosal reaction and insufficient maxillary lymphatic drainage. Histochemical examination of the lymphatic drainage pathways was carried out on surgical specimens. During the performance of surgical maxillary fenestrations, 80 surgical specimens of the middle nasal meatus were obtained including adjacent parts of the medial maxillary wall. The specimens were subjected to visualisation of lymphatic vessels based on the histochemical detection of 5'-nucleotidase according to Werner (1993). Both the nasal and the maxillary sinus mucosa showed a distinct superficial and deep longitudinal lymphatic capillary network (15 - 200µ ∅) with an orientation towards the natural maxillary sinus ostium. The density of the network increased from cranial to caudal, from dorsal to ventral and reached maximum density at the natural maxillary ostium. Lymphatic vessels of the maxillary sinus mucosa were thin but numerous in comparison to nasal vessels. The maxillary lymphatic capillary network showed direct connections to the nasal vessels, not only along the mucosal folds of the primary maxillary sinus ostium, but also in most cases (57 %) transmurally through the natural bony gaps of the uncinate process.
Grünwald's theory (1910) which states that lymphatic drainage of the maxillary sinus is established exclusively along the mucosal pane through the natural ostium was disproved. Maxillary mucosal congestion subsequent to extensive middle meatal antrostomy may be explained by ablation of the intramural and transmural lymphatic drainage pathways.

Key words: paranasal sinuses, middle meatal antrostomy, lymphatic drainage, sinus surgery, wound healing.

INTRODUCTION

During the course of normal wound healing following extensive middle meatal antrostomy, even without manipulation inside the maxillary sinus, a specific reaction of the bland maxillary sinus mucosa is often seen. Normally the secondary mucosal reaction consists of polypoid swelling which only subsides very slowly, or often incompletely (Fig. 1). Regardless of the healing process in neighbouring sinus cavities, the maxillary mucosal edema may persist and give rise to superinfection, in turn jeopardising general healing. Based on systematic photo documentation of paranasal wound healing, we speculated that the postoperative mucosal swelling may represent a secondary lymphatic edema caused by the ablation of draining lymph vessels during major maxillary fenestration (Hosemann et al. l991b, c). In order to prove this assumption we analysed surgical specimens obtained during extensive maxillary antrostomy by histochemical visualisation of the lymphatic vessels. The histochemical detection of lymphatic vessels was based on an increased activity of 5'-nucleotidase in the endothelial cells of lymphatic capillaries, in contrast to blood capillaries which reveal a significantly lower activity (Werner 1993). By analysing the lymphatic drainage pathways of the middle nasal meatus we lay the foundation for possible changes in future strategies and techniques for maxillary antrostomy, with the goal of preventing secondary mucosal alterations.

METHODS

Fifty-six patients were subjected to endoscopic endonasal surgery for chronic paranasal sinusistis. The surgical technique was based on Wigand (1989). During routine, extensive fenest-

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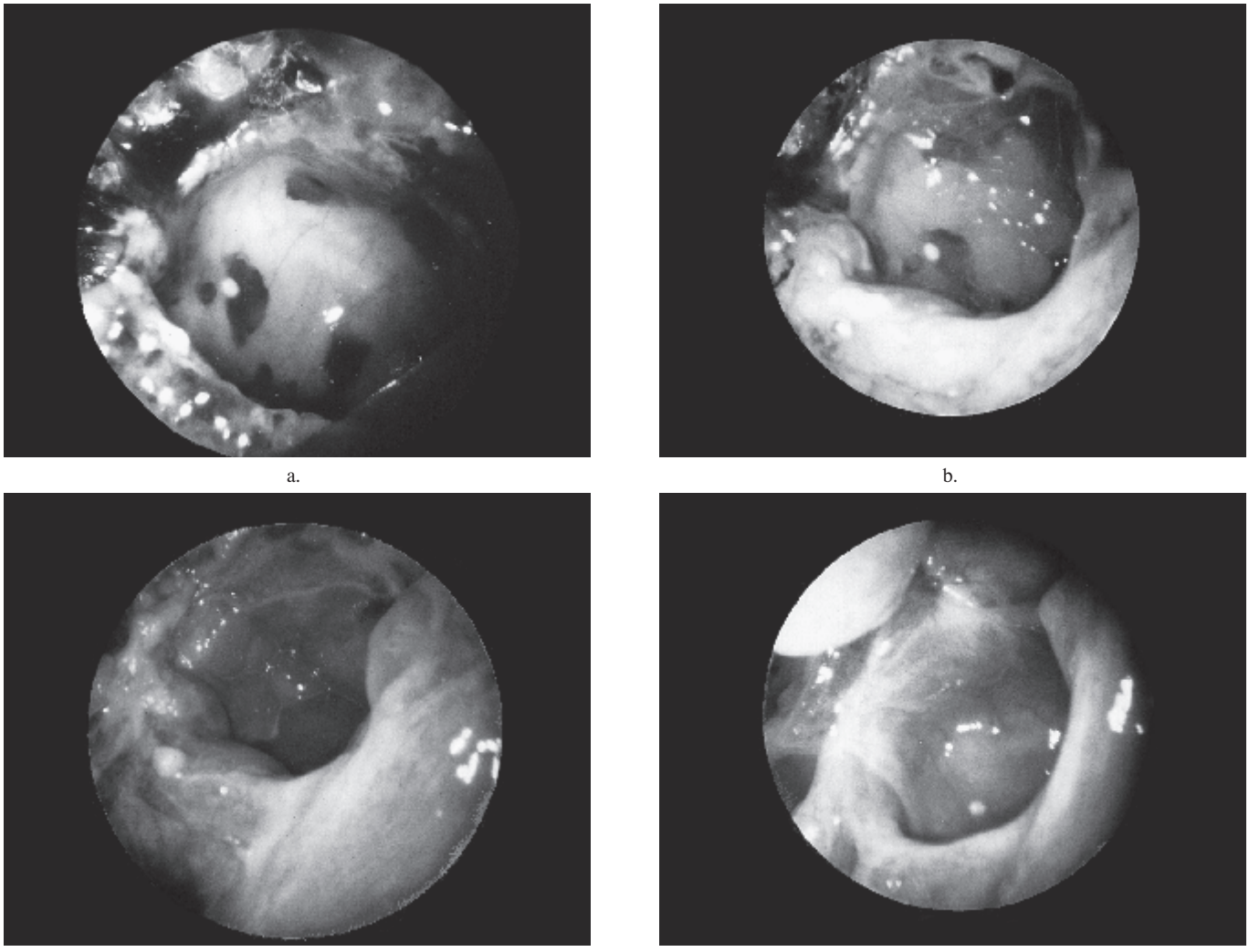
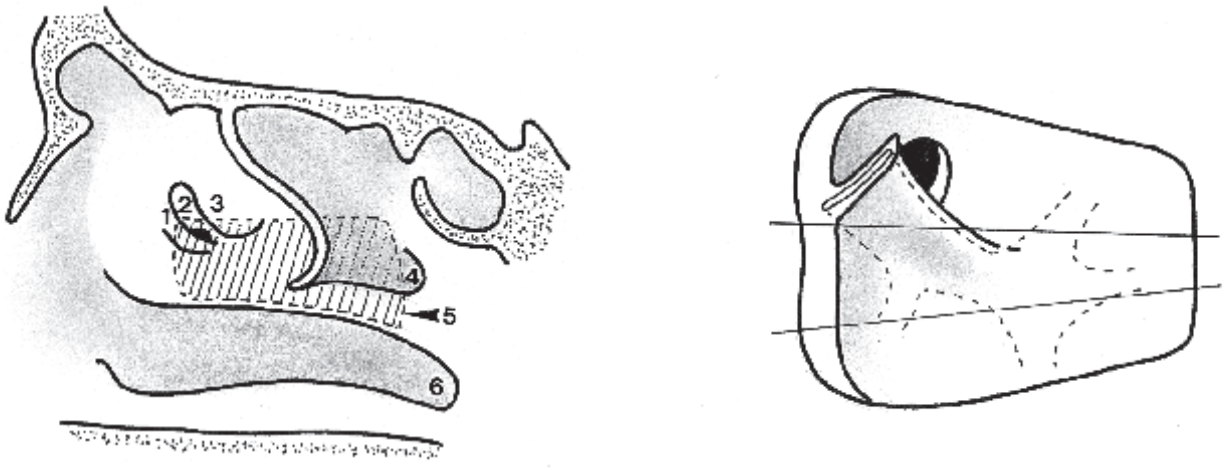


a. b.

c. d.

Figure 1. Secondary reaction (lymphatic edema) of the maxillary sinus mucosa following middle meatal antrostomy (Hosemann et al., 1991b).
a. On the left side a large naso-antral window is created resecting the anterior and posterior fontanelles. Using a 70° angled telescope, the maxillary sinus mucosa can be seen in its normal state on the 5th postoperative day.
b. On the 13th postoperative day an increasing secondary swelling of the maxillary sinus is observed (70° telescope).
c. The mucosal reaction reaches a maximum on the 27th postoperative day (70° telescope).
d. On the 55th day the polypoid edema in most areas is replaced by a homogenous thickening of the mucosa (70° telescope).



a. b.

Figure 2. a. Drawing of the lateral nasal wall, right side. For a better overview, parts of the middle turbinate have been resected. The hatch-marked area represents a maximum middle meatal antrostomy of the maxillary sinus. 1: uncinate process 2: ethmoidal infundibulum 3: ethmoidal bulla 4: dorsal attachment of the middle turbinate 5: outline of maximum middle meatal antrostomy 6: Inferior turbinate.
b. Drawing of a maximum specimen gained by middle meatal antrostomy. The specimen contains the natural maxillary ostium and parts of the uncinate process. The horizontal cutting plane for serial sections for histochemistry purposes is also outlined.

ration of the maxillary sinus in the middle nasal meatus a maximum surgical specimen was obtained consisting of the anterior and posterior fontanelle together with the natural maxillary ostium where possible. We examined 73 surgical specimens consisting of the middle nasal meatus and adjacent parts of the medial maxillary wall. In 5 other cases we were only able to remove the uncinate process by infundibulotomy. During the course of excision of the specimens mentioned above, sometimes a compromise with respect to completeness had to be made. In order to overcome this problem, we examined two additional fresh cadaver specimens (14 hours post mortem) which included the entire middle nasal meatus. The histological specimens were immediately frozen in liquid nitrogen after excision. The frozen tissue was carefully cut into horizontal serial sections (10 μ thick) using a cryostat. The sections were subjected to histochemical visualisation of the lymphatic vessels according to Werner (1993). Detection of lymphatic capillaries is based on the increased activity of the enzyme 5'-nucleotidase located in the *tunica media*, and especially in the endothelia of lymphatic vessels. Blood vessels reveal relatively low enzyme activity, if any at all. The sections were incubated in a histochemical medium containing AMP as a substrate of 5'-nucleotidase (Sigma, Deisenhofen/Germany). The release of phosphate transformed lead nitrate into lead phosphate (Merck, Darmstadt/Germany) in the medium. The addition of ammonium sulphide resulted in the formation of lead sulphide causing a dark brownish-black precipitate. Nuclear counterstaining was done using hematoxylin (Sigma, Deisenhofen/Germany). Control experiments were done both by incubation without AMP, and by inhibition of 5'-nucleotidase using methylene blue-5'-adenosindiphosphate (Sigma, Deisenhofen/Germany).

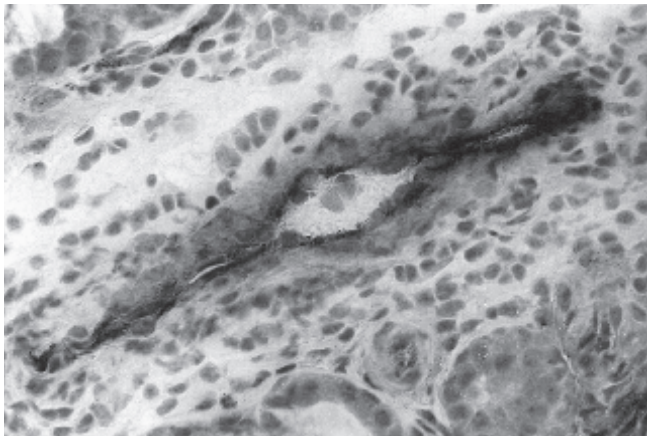


Figure 3. Histochemical visualisation of a lymphatic capillary in the maxillary sinus mucosa based on the detection of 5'-nucleotidase in lymphatic endothelia. In general, lymphatic vessels are mostly collapsed revealing a line-like pattern of brownish-black lead sulphide deposits (x 140).

Evaluation of the histochemical sections was carried out under the light microscope. The density of lymphatic vessels was estimated individually with the help of an optical measuring device. Counting vessels automatically using an image analysing system turned out to be impossible due to unclarity caused by unspecific staining of bony tissue. Identified lymph vessels were traced by analysis of serial sections examining the multidimensional course of lymphatic drainage pathways. In total, 28,000 histochemical sections were evaluated.

RESULTS

Lymphatic vessels were marked by dark brown precipitation. Lymphatic capillaries were mostly collapsed appearing under light microscopy as irregular brownish-black lines. Bony tissue showed a flat, broad distribution of a similar, but more intense colour. Both the mucosa of the middle nasal meatus and the maxillary sinus mucosa revealed, in general, a distinct superficial and a deep, underlying network of lymphatic vessels. The superficial capillaries were situated near the epithelial basal membrane. Around mucosal glands the horizontal pattern of the vessel distribution changed and the capillaries were found to be associated with individual gland tubes. Elsewhere, close proximity to larger blood vessels (arterioles) could be seen. The superficial lymphatic network was centred around the natural maxillary sinus ostium. The orientation of the deep vessels was less obvious. Both individual networks were connected by vertical lymphatic vessels. The connecting vessels were more conspicuous in the deeper tissue planes.

The individual lymphatic vessels showed a diameter between 15 and 200 μ. Superficial subepithelial vessels revealed a smaller diameter compared to deep-lying lymphatic capillaries neighbouring bony tissue. Lymphatic vessels of the maxillary sinus were more numerous, but mostly thinner compared to capillaries of the nasal cavity. The density of lymphatic capillaries increased twofold in the deep tissue planes. However, density showed individual variations not only in different, but also in the same specimens. In general, the maximum density was seen in the inferior and anterior parts (around the primary maxillary sinus ostium) of both the maxillary sinus mucosa and the middle nasal meatus. Lymphatic vessels in the area of the upper dorsal fontanelle of the middle nasal meatus were comparatively rare.

The density of lymphatic vessels was roughly estimated as “high” in 56 of 67 (84%) analysable specimens. Six specimens (9%) showed an overall reduced amount of lymphatic capillaries, and the remaining 5 tissue samples (7%) were rated as low. In 38 of 67 tissue samples (57%) lymphatic vessels were detected passing transmurally from the maxillary mucosa, through bony gaps of the uncinate process, directly into the opposite mucosal side of the middle nasal meatus, separate from the natural ostium. An additional 15 specimens (22%) showed a vertical orientation of lymphatic vessels in basal parts of the mucosa without unequivocal evidence of direct connection with the opposite mucosa in serial sections. In 14 specimens (21%) the distribution of lymphatic vessels was strictly confined to each mucosal plane (maxillary mucosa and nasal mucosa of the middle meatus) with the only communication between both sides being along the mucosa of the natural maxillary ostium. Six specimens showed artefacts and were not suitable for evaluation.

The density of lymphatic capillaries was strikingly high in the samples of the uncinate process and showed an increase along

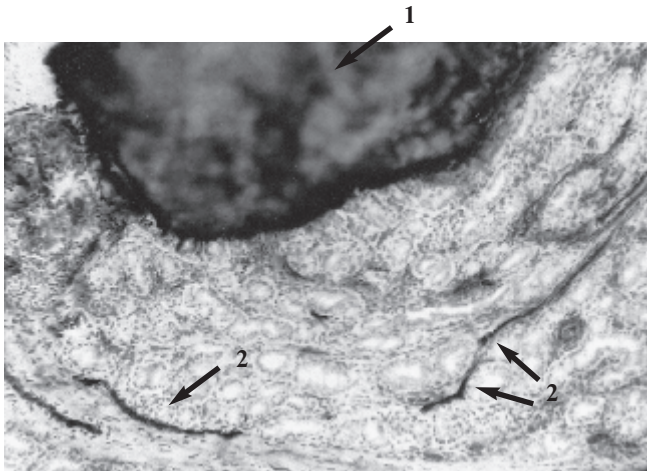


Figure 4a. Lymphatic drainage pathways of the maxillary sinus mucosa. Horizontal cutting face of the natural maxillary ostium demonstrating the fusion of the maxillary and nasal mucosa around the bony edge (1: part of the uncinate process). Bone tissue reveals an intense planar black staining. Lymphatic vessels (2) run parallel to the mucosa from the maxillary sinus to the middle nasal meatus (× 580).

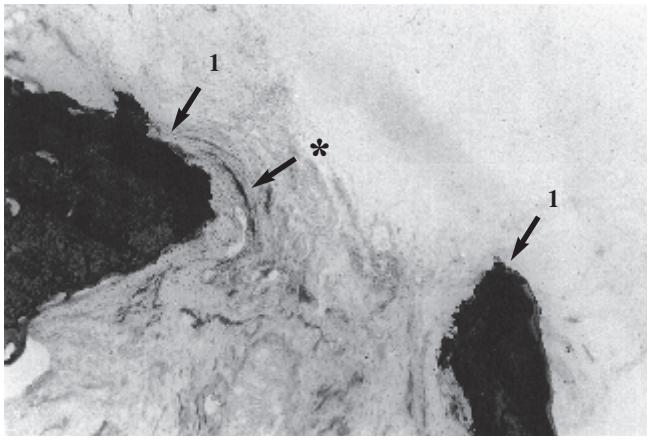


Figure 4b. Cutting face of two sections of the uncinate process (1) bound together by connective tissue. A transmural lymphatic vessel is shown in the bony gap(*). The vessel connects the maxillary sinus transmurally with the nasal mucosa in the area of the middle nasal meatus (×140).

the process, revealing a maximum density inferiorly and posteriorly. The posterior-inferior two thirds of the uncinate process near the natural maxillary ostium showed lymphatic vessels passing through bony gaps of the process connecting the mucosa of the front side with the mucosa of the ethmoidal infundibulum. Around the natural ostium the density of lymphatic vessels increased significantly. On both sides the vessels were arranged around the ostium in a radiating pattern. Connecting vessels passed around the ostial edge along the mucosal plane.

The density and distribution of lymphatic capillaries were very similar in the cadaver specimens. Again, maximum density was seen in the anterior and inferior sections of the middle meatus and in the adjacent parts of the maxillary mucosa bordering on the natural ostium. Density was reduced to a minimum in the posterior and superior parts of the middle meatus and the adjacent maxillary sinus.

DISCUSSION

Between the uncinate process with its tiny bony exophytes, and the inferior turbinate and the lacrimal and palatine bone, there are certain areas in the middle nasal meatus devoid of bony support structures known as fontanelles. In these areas the mucosa of the maxillary sinus is directly adjacent to the nasal mucosa and is separated only by a thin sheet of connective tissue. The anterior fontanelle is situated inferior to the uncinate process, posterior to the anterior ethmoidal process of the inferior concha, and anterior to a variable bony link between dorsal ramifications of the uncinate process and the inferior turbinate. The posterior fontanelle is bound anteriorly by the dorsal uncinate process and posteriorly by the palatine bone or the posterior ethmoidal process of the inferior turbinate (Hajek 1926, Lang 1988). In the literature there are different recommendations for fenestration of the maxillary sinus in the middle nasal meatus. Some surgeons prefer to enlarge the natural ostium at the expense of the anterior fontanelle. Others perform a fenestration where primarily the posterior fontanelle is resected. Advantages and disadvantages of the different surgical techniques are discussed in detail with respect to mucociliary clearance (Hilding 1941). However, the effect on maxillary lymphatic drainage is almost totally neglected. The current investigation of lymphatic vessels was initiated as a result of the observation of secondary mucosal reactions in the maxillary sinus following extensive middle meatal antrostomy (Hosemann et al. 1991b). Opinions have differed on the concept of lymphatic drainage of the maxillary mucosa since the beginning of this century. Grünwald stated in 1910 that lymphatic pathways are generally restricted to the mucosal planes and do not pass directly through the sinus walls. In this case, maxillary lymphatic drainage is assumed to occur exclusively along the mucosa via the natural ostium. In the middle nasal meatus the lymphatic capillaries build up a dense network which radiates out from the natural ostium (Grünwald 1910). A similar view is also held by Kihara (1933). In contrast, André (1905) is of the opinion that lymphatic vessels additionally leave the maxillary sinus remote from the natural ostium through its bony walls (quoted by Grünwald 1910). Using dye injections, Mann (1980) identified a lymphatic drainage pathway of the maxillary sinus through the posterior sinus wall into the nasopharynx. Animal experiments using rabbits presented evidence supporting the theories of both Grünwald and André (Hosemann et al. 1991c, Mullin and Ryder 1921).

The current investigation supplements the histochemical studies by Werner (1993). We preferred using histochemistry for detection of lymphatic vessels because of the higher specificity compared to other methods, as well as for logistical reasons (Barsky et al. 1983, Bollinger et al. 1981, Castenholz 1985, Werner et al. 1987). In summary, we have shown the existence of a superficial and a deep network of lymphatic capillaries. The majority of specimens (57%) showed transmural lymphatic drainage of the maxillary sinus with connecting vessels in the fontanelles of the middle nasal meatus. These findings support the model proposed by André (1905). Thus, we maintain that

extensive maxillary antrostomy in the middle nasal meatus leads to an ablation not only of the mucosal lymphatic vessels around the natural ostium, but also destroys the transmural drainage pathways. Animal experiments have shown that lymphatic vessels of the paranasal mucosa regenerate very slowly, if at all (Hosemann et al. 1981a). Based on this fact, we may interpret the observed mucosal reactions of the maxillary sinus mucosa following antrostomy as secondary lymphatic edema.

Lymphatic vessels are relatively scarce in the posterior and superior sections of the middle meatus. Due to this fact, the natural ostium of the maxillary sinus should be enlarged into the posterior nasal fontanelle rather than the anterior one during middle meatal antrostomy. There should be no circumferential damage to the mucosa of the natural ostium in order not to interfere with both mucociliary and lymphatic drainage.
In general, secondary maxillary ostia naturally increase in number with age (Myerson 1932). Intercurrent local inflammation is thought to play an important role in pathogenesis. Traversing lymphatic vessels may facilitate transmural putrid infection and hereby may contribute to the size and topography of the secondary ostia.

REFERENCES

1. André: Contribution à l'étude des lymphatiques du nez et des fosses nasales (1905) Thèse de Paris 1905 (quoted by Grünwald 1910)
2. Barsky SH, Togo S, Baker A, Liotta LA, Siegal GP (1983) Use of anti-basement membrane antibodies to distinguish blood vessel capillaries from lymphatic capillaries. Am J Surg Pathol 7: 667-677
3. Bollinger A, Jager K, Sgier F, Seglias J (1982) Fluorescence microlymphography. Circulation 64: 1195-1200
4. Castenholz A (1985) The demonstration of Lymphatics in casts and fixed tissue with the scanning electron microscope. In: A Bollinger, H Partsch H, JHN Wolfe (Eds.) The initial lymphatics: new methods and findings. Thieme, Stuttgart, Germany, pp 75-83
5. Grünwald L (1910) Die Lymphgefässe der Nebenhöhlen der Nase. Arch Laryng Rhin 23: 1-5
6. Hajek M (19263 Pathologie und Therapie der entzündlichen Erkrankungen der Nebenhöhlen der Nase. 5th ed. F Deuticke, Leipzig, Wien, Austria, pp 11-13
7. Hilding AC (1941) Experimental sinus surgery: effects of operative windows on normal sinuses. Ann Otol Rhinol Laryngol 50: 379-392
8. Hosemann W, Göde U, Langer F, Röckelein G, Wigand ME (199la) Experimentelle Untersuchungen zur Wundheilung in den Nasennebenhöhlen. I. Ein Modell respiratorischer Wunden in der Kaninchenkieferhöhle. HNO 39: 8-12
9. Hosemann W, Dunker I, Göde U, Wigand ME (199lb) Experimentelle Untersuchungen zur Wundheilung in den Nasennebenhöhlen. III. Endoskopie und Histologie des Operationsgebietes nach einer endonasalen Siebbeinausräumung. HNO 39: 111-115
10. Hosemann W, Wigand ME, Göde U, Fänger F, Dunker I (199lc) Normal wound healing of the paranasal sinuses: clinical and experimental investigations. Eur Arch Otorhinolaryngol 248: 390-394
11. Kihara T (1933) Beiträge zur Anatomie des Lymphgefässsystems der Wirbeltiere und des Menschen (Japaner). Nr. 16 Die feinere Verteilung der Lymphgefässe in der Nasenschleimhaut des Menschen. Folia anat jap 11: 247-255
12. Lang J (1988) Klinische Anatomie der Nase, Nasenhöle und Nebenhöhlen. Thieme, Stuttgart, Germany
13. Mann W (1980) Die Lymphdrainage der Kieferhöhle. Laryngol Rhinol Otol 59: 782-785
14. Mullin WV, Ryder CT (1921) Studies on the lymph drainage of the accesssory nasal sinuses. Laryngoscope 31: 158-178
15. Myerson MC (1932) The natural orifice of the maxillary sinus. Arch Otolaryngol 15: 80-91
16. Werner JA, Schunke M, Tillmann B (1987) Histochemical visualization of lymphatic capillaries in the rat: a comparison of methods demonstrated at the posterior pharyngeal surface. Arch Histol Jap 50: 505-514
17. Werner JA (1993) Untersuchungen zum Lymphgefässsystem des Aerodigestivtraktes im Kopf-Hals-Bereich. Habilitationsschrift, Medizinische Fakultät Kiel
18. Wigand ME (1990) Endoscopic surgery of the paranasal sinuses and anterior skull base. Thieme, Stuttgart, Germany

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