Rhinology, XVI, 203–213, 1978

Quantitative histology of the normal sphenoidal sinus

Chr. Mogensen and M. Tos, Copenhagen, Denmark

SUMMARY

From 32 normal sphenoidal sinuses in 16 patients the mucosa was removed at autopsy, stained by the PAS-alcian blue whole mount method, and the density of goblet cells as well as of mucous glands was determined.

The median density of goblet cells was 6200 cells per mm^2, without statistically significant differences between the walls. The median density of glands was very low, 0.06 gland/mm^2, highest in the anterior wall which has 0.1 gland/mm^2 and lowest in the posterior wall which has 0.05 gland/mm^2. The total gland count was less than 50 in 94% of the sinuses, 51–80 in 4%. The glands were small, tubulo-acinous. Hence, the production of mucus by the glands is entirely negligible in relation to that of the goblet cells.

The object of this study was to determine the density of mucus-producing elements – goblet cells and mucous glands – in the mucous membrane of the sphenoidal sinuses and to collect further and more exact data concerning the nature and mucus-producing ability of the mucosa.

The literature on the histology and histopathology of the sphenoidal sinuses is very scanty, perhaps because diseases of the sphenoidal sinuses are rare and if present rarely diagnosed.

At the beginning of the 3rd foetal month there grows backward from the postero-superior end of the nasal cavity a small cul-de-sac which represents the primordium of the sphenoidal sinus. It grows but slowly, and at birth it is 4 mm in height, 2 mm in width, and 2 mm in length (Peter, 1925). During the first years of life it slowly grows downward, reaching the sphenoidal bone by the fifth year. It is not known whether the primordium of the sinus contains mucous elements.

In adults the sphenoidal mucosa is the thinnest and most delicate of all respiratory tract membranes and is rather loosely attached to the bone (Eggston and Wolff, 1947). It is lined with pseudostratified, columnar, ciliated epithelium with few goblet cells (Latta and Schall, 1934). Very little is known about its

mucous glands: according to Eggston and Wolff (1947) there are usually no sero-mucous glands in the sphenoidal sinuses, though exceptionally there may be one or two close to its ostium. Messerklinger (1967a) found transport of secretion in the sphenoidal sinus direct to the ostium, unlike the findings in the frontal sinuses (Messerklinger 1967b).

Hajek (1926) summed up the pathology of the sphenoidal sinuses on the basis of autopsy findings. Acute infection of the mucosa often accompanied acute infections of other paranasal sinuses, manifesting itself as oedema, epithelial defects, and haemorrhage in the mucosa. Chronic infections were uncommon autopsy findings, and therefore histopathological descriptions were deficient (Hajek, 1926). In the description of the pathology, no mention is made of the mucous elements, and in more recent literature we have been unable to find more detailed descriptions of the histology and histopathology of the sphenoidal mucosa.

In connection with our serial quantitative studies of the histology and histopathology of the mucous membranes in the nasal sinuses, we felt that the mucosa of the sphenoidal sinuses too merited a more exact investigation, although its clinical importance is apparently inferior to that of the other sinuses. Quantitative histology affords a possibility of comparing mucus production in the various nasal sinuses and of setting up some normality criteria for the density of goblet cells and glands.

MATERIAL AND METHODS

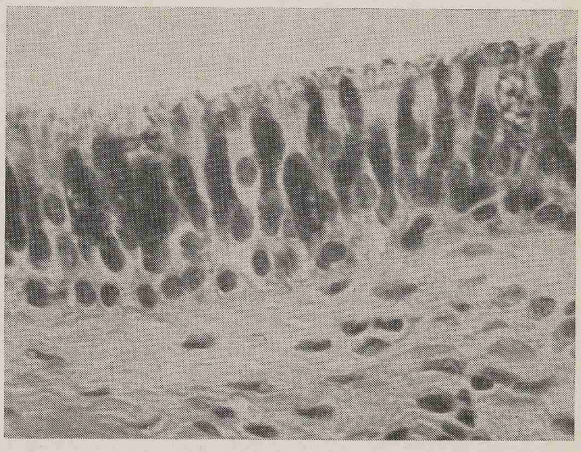
From 16 patients who had died of malignant or cardiovascular diseases and had shown no signs of acute or chronic diseases of the nose or nasal sinuses, the mucosa of both sphenoidal sinuses was removed, through the clivus and sella turcica, after the right and left sinus had been divided *a priori* into six walls: (1) Superior wall along the sella turcica to the ostium, (2) inferior, (3) anterior, including the ostium which is situated superiorly in the anterior wall, (4) posterior wall, (5) medial wall along the intersphenoidal septum, and (6) lateral wall. The area of mucosa in each wall measured a maximum of 150 mm^2. The entire mucosa was stained by the whole mount method (Tos, 1970), cleared in anise oil, and embedded in a chamber with anise oil-colophonium sealed with paraffin. From each locality a representative piece of mucosa was cut into sections and stained by a combined PAS-alcian blue and haematoxylin-eosin method. Goblet cells were counted in 27 sinuses, in 12 patients in both, and in 3 patients in only one sinus. In Reichardt's projection microscope, magnification $\times 500$, a maximum of 5 counts were made in 0.01768 mm^2 large fields in each wall. Thereafter, the median density in each wall and in each sinus was calculated. Owing to epithelial defects occurring in the course

of detaching and preparing the mucous membrane, the goblet cells could not be counted in all walls of all sinuses.

Glands were counted in all 32 sphenoidal sinuses in a magnification of ×50 in the stereomicroscope. In each wall the glands were counted in 3–12 fields of 4 mm^2, and the mean density in each wall was calculated.

RESULTS

The epithelium was everywhere pseudostratified, columnar, with ciliated cells and goblet cells (Figure 1a). In thickness it ranged from 25–45 μ, and its basement membrane was thinner than in the nose. The lamina propria consisted of loose fibrous tissue with blood vessels, in places seromucous glands without having an actual glandular layer. In all, the mucosa was 0.2–0.7 mm thick, and there were no definite differences in epithelial or mucosal thickness between the various walls.



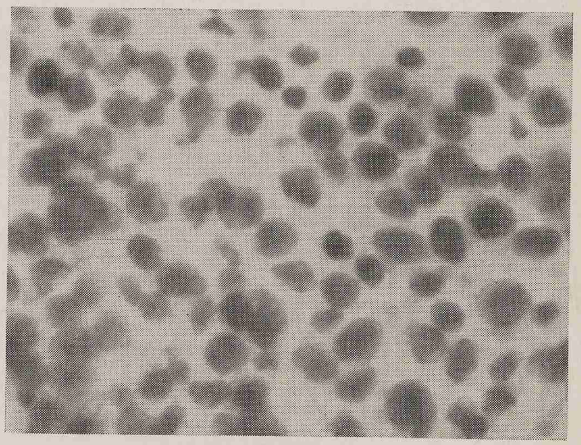


Figure 1.
a. Respiratory epithelium. PAS-alcian blue-haematoxylin-eosin section ×500.

b. Goblet cells in whole mount ×500.

GOBLET CELL DENSITY

On whole mounts the goblet cells presented as round to oval, blue, sharply demarcated patches, usually of a diameter from 5 to 10 μ (Figure 1b). They were observed throughout the epithelium, but – as elsewhere in the respiratory tract – of an irregular distribution. The smallest number of goblet cells per 0.01786 mm^2 field was 25 cells/field, the largest 206. The lowest median of 5 counts in a locality was 33 cells corresponding to 1900 cells per mm^2, the highest 174 cells corresponding to 9800 cells per mm^2.

The interindividual median density in the various walls in all sinuses (Figure 2) was highest in the inferior wall, lowest in the posterior wall. However, the difference in density between these two walls was not statistically significant ($p > 0.05$) (Mann-Whitney test).

There were no statistically significant differences ($p > 0.05$) in median density in the individual walls between the right and left sinus (Figure 3). The inter-

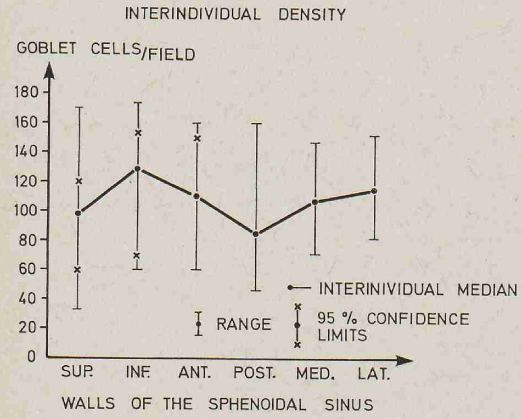


Figure 2.
Interindividual median density of goblet cells in different walls of the sphenoidal sinus.

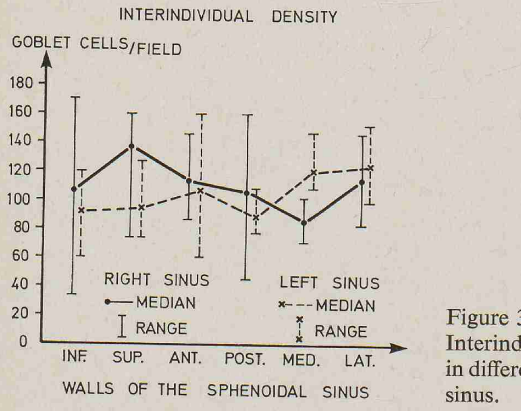


Figure 3.
Interindividual median density of goblet cells in different walls of the right and left sphenoidal sinus.

individual median density of all medians on the right was 113 cells/field, on the left 104 cells/field, which is not a statistically significant difference ($p > 0.05$). The interindividual median density of all counts was 109 cells/field, corresponding to 6200 cells per mm^2.

The individual median density in each patient showed a range of 26–140 cells/field. In the patient with the lowest range limit, however, the goblet cells were counted in only one locality because of epithelial defects. Therefore, the lowest range limit can only be acccepted with great reserve. The next lowest range limit was 60 cells/field.

GLANDS

Size and shape: The glands were flat, about 100–200 μ in thickness. They were round, having a diameter of 0.3–0.5 mm, or oval having a longer diameter of 0.3–0.6 mm and a shorter diameter of 0.2–0.4 mm (Figure 4). The area was 0.06–0.24 mm^2. The volume of the gland mass was 0.006–0.048 mm^3. In one patient (Case 14) there were a few large glands having an area of 0.8 mm^2 with dilated ducts and tubules.

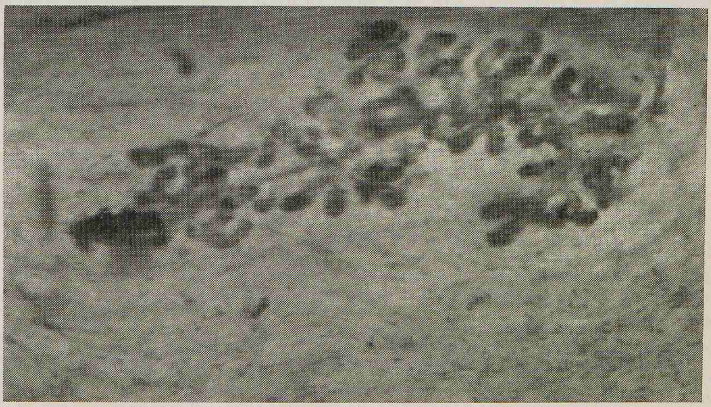


Figure 4. Gland in sphenoidal sinus seen in whole-mount ×100.

Excretory ducts were very short, lined with cuboidal epithelium and divided into two lateral ducts sending out several tubules with acini at their ends. Tubules as well as acini were either predominantly mucous, predominantly serous, or seromucous. Case 14 had several glands with distended tubules and acini filled with mucus. In some of these tubules the secretory epithelium was active and the tubules were lined exclusively with distended mucous cells. In others the tubules consisted of very flat epithelium, presumably with no secretory activity. These phenomena possibly represent hyperactivity and degeneration of the glands respectively.

Distribution: Glands were found in all 32 sinuses studied, although in the great majority they were few. In 31% of the sinuses glands were found in all 6 walls, in 22% in only five walls, in 18% in four, and in 28% in three walls. Most often it was the lateral wall which was devoid of glands (Table 1). In all, 25% of the 183 walls studied showed no glands.

Table 1. Number of sphenoidal sinuses without glands in different walls.

walls of sinus	number of walls investigated	sinuses without glands	
		no.	%
superior	32	8	25
inferior	30	8	27
anterior	31	4	13
posterior	30	7	23
medial	30	9	30
lateral	30	10	33
total	183	46	25

By conventional histological study of sections from each wall glands were found in only 20% of those walls in which the whole-mount method had revealed glands. Thus, due to the low density and small total number of glands numerous sections are required to find merely one gland. This explains divergences in the literature concerning the occurrence of glands in the sphenoidal sinuses.
The total median area of mucosa studied per sinus was 275 mm^2, range 48–700 mm^2. Within this area 3–10 glands were found in 53% of the sinuses, 11–20 in 16%, 21–30 in 16%, 31–50 in 10%, and 51–80 glands in 6%. As a rule, these glands were situated singly. True, there were areas having several glands accumulated, especially in the superior and anterior walls, but considering such a small number of glands scattered over several different walls of the sinus and over a relatively large area, this cannot be called grouping.

Density of glands: The interindividual median density was highest, 0.1 gland/mm^2, in the anterior wall, next highest, 0.8 gland/mm^2, in the inferior wall, and lowest, 0.05 gland/mm^2, in the posterior wall. In the remaining three walls the median density was 0.06 gland/mm^2 (Figure 5). The 95% confidence limits were 0–0.15 gland/mm^2, while the range was fairly wide. There was a statistically significant difference in density ($p < 0.08$, Mann-Whitney test) between the anterior wall having the highest and the posterior wall having the lowest density, while differences between other walls mutually and in relation to the anterior wall were not statistically significant ($p > 0.05$).
No significant differences in density between the right and left sinus were found.

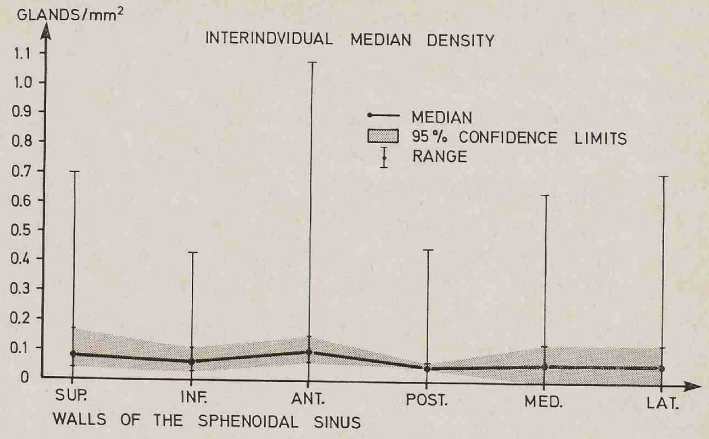


Figure 5. Interindividual median density of glands in different walls of the sphenoidal sinus.

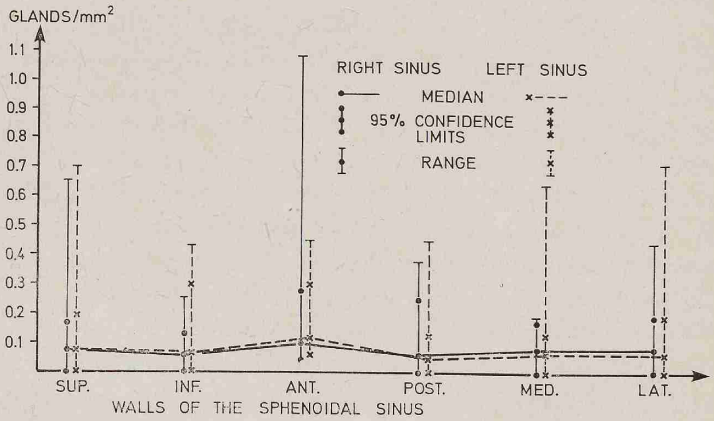


Figure 6. Interindividual density of glands in different walls of the right and left sphenoidal sinus.

Table 2. Individual median density of glands in the right and left sphenoidal sinus, and in both sinuses together.

case no.	left sinus	right sinus	both sinuses	case no.	left sinus	right sinus	both sinuses
1	0.09	0.06	0.06	9	0	0.06	0.06
2	0.04	0.03	0.04	10	0.05	0.03	0.05
3	0	0.06	0.06	11	0.05	0.04	0.05
4	0.06	0.12	0.09	12	0.1	0.06	0.08
5	0.03	0.06	0.05	13	0.22	0.06	0.12
6	0.03	0.1	0.03	14	0.13	0.43	0.25
7	0.11	0.13	0.13	15	0.08	0.2	0.1
8	0.06	0.05	0.06	16	0.12	0.13	0.13
median					0.06	0.06	0.06

This applied when testing each wall (Figure 6) as well as the individual medians of density in the right and left sinus (Table 2).

Individual density: In the great majority of patients the individual median density was very low, without major differences between the left and right sinus (Table 2). In Case 14 the density was essentially higher on the left than on the right, there being 80 glands on the right and 16 on the left. In Case 13 this was reversed, there being 56 glands on the right and 8 on the left.

Table 3. Number of sphenoidal sinuses in which glands were not found in one, two or three walls.

walls without glands	no. of sinuses	%
one	7	22
two	6	18
three	9	28
total	22	69

Relation between density of glands and of goblet cells: In Case 14 with a high gland density on the left, there was a median density of 110 cells per field, in Case 13 with a high gland density on the right also a fairly high goblet cell density, viz. 143 cells/field. On the whole, however, there was no significant correlation between the gland and goblet cell density.

DISCUSSION AND CONCLUSION

Naumann (1964) wrote that among the nasal sinuses the sphenoid is "oddman out" where diagnosis is concerned. This is true also of its histology and histopathology, and in the literature we have not been able to find any publication affording a possibility of comparing the findings described. Similarly, little is known about abnormalities of the sphenoidal mucosa.

The median density of goblet cells is the same as in the frontal sinus (Tos et al., 1978), but essentially lower than in the maxillary antra where it is 9700 cells/mm^2 (Mogensen and Tos, 1977). Interindividual differences are fairly marked, but not greater than elsewhere in the respiratory tract.

The median density of glands is extremely low, and the total gland count, less than 80, is so small that the mucus production of the glands is completely negligible as compared with that of the goblet cells.

Thus, the total mucus production in the normal sphenoidal sinuses is very slight, and the mucociliary clearance demonstrated by Messerklinger (1967a) is effected almost exclusively by the mucus of the goblet cells. This is in conformity with the low physiological requirement of mucus in the sphenoidal

sinus, where no air current is present and a more effective clearance not needed. As the mucus-producing capacity of the glands is extremely slight, there will not, in catarrhal disease states, occur a sudden and violent increase of mucus production as in the nose. This, combined with the favourable situation and size of the orifice, perhaps explains why the sphenoidal sinus rarely gives rise to symptoms in disease states of the nose and paranasal sinuses.

Gland density may be analysed in three ways: (1) We preferred – as previously in the nose (Tos and Mogensen, 1976) – to count glands in 3–12 four mm^2 fields in each wall and calculate the mean density of each wall as well as the median density for each sinus, representing the median density of all six walls. This showed an interindividual median density for all sinuses of 0.06 gland/mm^2. As there was only one or a few glands in each wall, we could count all glands by placing the counting fields in sites where the glands were present and in a suitable number of sites where no glands were present. Thereby, we could also calculate the total number of glands in each sinus. (2) By directly measuring the total mucosal area in the sinus and calculating, on the basis of the total number of glands, the individual median density, which gives an interindividual median density of 0.045 gland/mm^2. Such a calculation is the most accurate one, but can only be done in organs with relatively few glands, never in the nose which has about 50,000 glands. Another condition is that the entire or almost entire mucosa is removed. (3) By the third method, calculating on the basis of the total number of glands and of the area of all counting fields the mean density for each sinus, the interindividual density was 0.09 gland/mm^2. Differences between the three methods are small, and the first method, on which the study was based, showed a density between the other two.

In no sinus did the objective examination show grossly abnormal mucosa. Microscopic examination also showed no striking differences in density, vascular dilatation, or round-cell infiltration. Besides, perusal of the case records afforded no positive information about a history of sinusitis or nasal allergy. However, this does not exclude that some sinuses have been exposed to pathological actions at some time of life.

We found a larger number of glands in the anterior and superior walls, i.e. in the areas closest to the ostium of the sinus. This is in agreement with the findings in the maxillary antrum, where the density is highest in the medial wall (Mogensen and Tos, 1977) and frontal sinus where it is highest in the inferior part (Tos et al., 1978). The explanation of this phenomenon is embryological: In the trachea (Tos, 1966), nose (Tos and Poulsen, 1975), rhinopharynx (Tos, 1977), and Eustachian tube (Tos, 1970) gland formation starts in the 11th foetal week in a given part of the organ whence it gradually spreads to the entire mucosa. In the nose the gland spread reaches the middle of the meatus medius by the 15th week, whereupon it can spread to the primordia of the

maxillary antra, ethmoids, and frontal sinuses. To the primordium of the sphenoidal sinuses, supero-posterioly in the nose, the glands spread from the rhinopharynx in the 16th week (Tos and Poulsen, 1975). Owing to the asymmetrical postnatal growth of sinuses and to the fact that new glands do not form after birth, the gland density may be expected to be highest around the orifices.

ZUSAMMENFASSUNG

Von 32 normalen Keilbeinhöhlen von 16 Patienten wurde die Schleimhaut ausgenommen, nach PAS-Alzianblaumethoden der Ganzpräparate gefärbt und die Dichte der Becherzellen und mukösen Drüsen bestimmt. Mediandichte der Becherzellen war 6200 Zellen per mm^2, ohne signifikante Unterschiede zwischen der verschiedenen Wändern. Mediandichte der Drüsen war sehr klein, 0.06 Drüsen per mm^2, am grössten auf der vorderen Wand mit 0.1 Drüsen per mm^2, am kleinsten auf der hinten Wand. Im ganzen wurden bei 94% der Keilbeinhöhlen weniger als 50 Drüsen gefunden, bei 4% zwischen 51 und 80 Drüsen. Die Drüsen waren klein, tubuloacinös. Die Bildung des Schleims von Drüsen ist ganz negligabel in Verhältniss zur Becherzellen.

REFERENCES

1. Eggston, A. A. and Wolff, D., 1947: Histopathology of the Ear, Nose and Throat. Baltimore: Willian & Wilkins, p. 536.
2. Hajek, M., 1926: Pathology and treatment of the inflammatory diseases of the nasal accessory sinuses. St. Louis: C. V. Mosby Co., p. 78.
3. Latta, J. S. and Schall, R. F., 1934: The histology of the epithelium of the paranasal sinuses under various conditions. Ann. Otol. Rhinol. Laryng., St. Louis 43, 945.
4. Messerklinger, W., 1967a: Über die Drainage der menschlichen Nasennebenhöhlen unter normalen und pathologischen Bedingungen. Mtschr. Ohrenheilk. 101, 313.
5. Messerklinger, W., 1967b: Ist in allen menschlichen Stirnhöhlen das Prinzip des Sekrettransportes gleich? Arch. klin. ex. Ohr.-Nas-KehlkHeilk., 189, 317.
6. Mogensen, Chr., and Tos, M., 1977: Quantitative histology of the maxillary sinus. Rhinology 15, 129.
7. Naumann, H. H., 1964: Banale Entzündungen der Nase und ihrer Nebenhöhlen. In: Hals-Nasen-Ohrenheilkunde, v. J. Berendes, R. Link, F. Zöllner. Stuttgart, Thieme, Bd 1, p. 198.
8. Peter, K., 1925: Vergleichende Anatomie und Entwicklungsgeschichte der Nase. In: Handbuch der Hals-Nasen-Ohrenheilkunde, v. Denker, A., Kahler, O., Berlin, Springer, vol. 1, pt. 1. p. 126.
9. Tos, M., 1970: Mucous glands of the trachea in children. Quantitative studies. Anat. Anx. 126, 146.
10. Tos, M., 1970: Development of mucous glands in the human Eustachian tube. Acta Otolaryng. 70, 340.
11. Tos, M., 1966: Development of the tracheal glands in man. Acta Path. Microbiol. Scand. Suppl. 185, 1.
12. Tos, M., 1977: Mucous glands in the developing human rhinopharynx. Laryngoscope, 87, 987.
13. Tos, M. and Poulsen J., 1975: Mucous glands in the developing human nose. Arch. Otolaryng. 101, 367.

14. Tos, M. and Mogensen, Chr., 1976: Density of mucous glands in normal adult nasal septum. Arch. Oto-Rhinol-Laryng. 214, 125.
15. Tos, M., Mogensen, Chr. and Novotny, Z., 1978: Quantitative Histology of the normal frontal sinus especially the density of goblet cells and mucous glands. Arch. Otolaryng. In print.

Chr. Mogensen, M.D.
M. Tos, M.D.
E.N.T. University Clinic
The Gentofte Hospital
Copenhagen, Denmark.