Mucous elements in the nose

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SUMMARY

A review of studies of the nasal mucous elements by whole-mount methods. Goblet cell development is described till the 30th week of gestation, by which density is still very small. Density must increase towards and after birth. Som problems concerning intraepithelial, anterior nasal as well as Bowman's glands are discussed. The development of the small sero-mucous glands is described and their distribution and density discussed.

THERE are goblet cells and intra-epithelial glands in the epithelium of the respiratory region and serous anterior nasal glands and small seromucous glands in the lamina propria. In the olfactory region there are serous Bowman's glands. Over the past two years we have been studying the mucous elements with complete-preparation techniques, the principle of which is to stain the whole mucous membrane and then clear it with aniseed oil. We used the PAS method which stains the mucous elements red, the PAS-alcian blue method which stains them blue and the osmium method which stains all the epithelial elements, serous glands, vessels and nerves brown (Tos, 1966).
The aim of this paper is to summarize results so far and to point out possible ways in which the study of mucous elements can be continued using the complete-preparation techniques.

GOBLET CELLS

It has often been reported that the number of goblet cells is elevated or reduced under pathological conditions (Hajek, 1905; Oppikofer, 1907; Hansel, 1930; Eggston and Wolff, 1947; and other authors), but we do not know the normal distribution and density of goblet cells in the nose. During studies on the embryology of goblet cells, Poulsen and Tos (1975) came across several interesting situations which may modify the distribution and density of goblet cells in children and adults: the cells start to develop in the 13th week — in front in the vestibule of the nose. In the weeks which follow they spread backwards, particularly along the floor of the nose and the lower margin of the septum, and in the 16th week they meet a goblet cell front which has also spread along the

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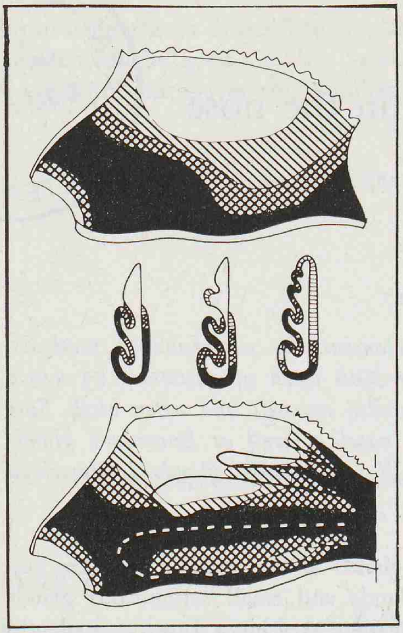


Figure 1. Verschiedene Dichtezonen der Becherzellen in der 30. Woche. Grösste Dichte ist schwarz.

floor of the nose from the soft palate. From the 17th to 23rd week, they spread backwards along the meatus and from there to the conchae. A similar distribution takes place from behind, from the nasopharynx. In the 30th week goblet cells are found throughout the respiratory region, which at the lateral wall includes the hindmost two-thirds of the superiod meatus, the posterior half of the concha media and the hindmost third of the concha superior (Figure 1).

The density of the goblet cells alters continually during development, partly as a result of further new formation, and partly as a result of the growth of the mucosal area (Figure 2) (Tos and Poulsen, 1975). Thus, in the 30th week the density of goblet cells in the nose varies (Figure 1): on the septum is a zone of highest density — consisting of the vestibule and continuing to the front quarter and the whole of the lower margin of the septum. Further above is a zone of medium density and right above (at the border with the olfactory region) the density is still very low. The situation is somewhat similar in the lateral wall (Figure 1).

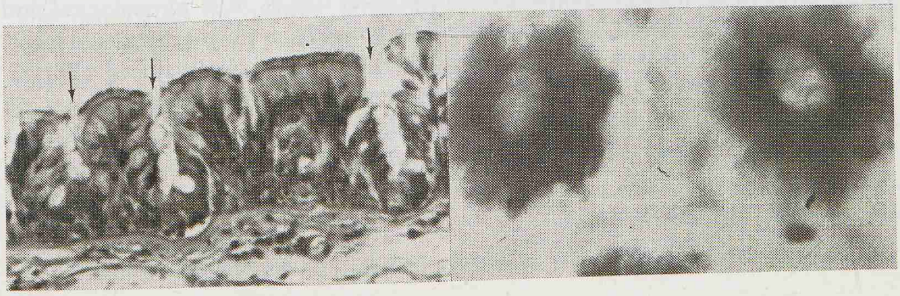
In the 30th week the overall density is still very low compared with that in the adult nose, where it is 5700 cells per mm^2 in the anterior three-quarters of the septum and 6700 cells per mm^2 in the hindmost quarter. Thus, the density must increase markedly towards and after birth, particularly in those areas where it is very low in premature babies. In order to put to good use the uniformity of goblet-cell distribution and density found in foetuses, the quantitative studies of the density must be continued using material from newborn babies, children and adults.

Figure 2. Grosse Dichte mit Grupierung der Becherzellen im Vestibulum septi in der 15. Woche. Hinten (links) und oben kleinere Dichte x 400.

INTRA-EPITHELIAL GLANDS

The intra-epithelial glands are situated in the epithelium and consist of 20-50 mucous cells arranged radially around a small lumen (Figure 3). These glands were described in the nose in the last century (Zarniko, 1894; Boenninghaus, 1895; Goerke, 1897; Okada, 1898); they were thought to be pathological structures, being found in particular in the presence of nasal polyps. However, Oppikofer (1907) found them in most normal nose and so they were later considered to be a normal constituent of the nasal mucosa. Messerkliner (1958) demonstrated experimentally that they are unstable structures which can develop within an hour of injecting pilocarpine, only to disappear again after half-an-hour. During quantitative studies on intra-epithelial glands in other organs, we (Ellefsen and

Figure 3. Intraepitheliale Drüsen im Schnitt (a), im Ganzpräparat (b) x 500.



Tos, 1972) found only one trachea containing intra-epithelial glands out of 20 adult tracheas which we studied systematically. They were very irregularly distributed and arranged in small islets, where they were very dense. They were regarded as pathological and stable formations. We found intra-epithelial glands in all 10 normal adult Eustachian tubes we studied (Tos and Bak-Pedersen, 1972); however, they were extremely irregular in distribution and they varied considerably in number — from a few to 50 in three tubes, between 200 and 400 in five tubes and 1500 and 2500 glands in two tubes.

In systematic studies on 50 noses stained with PAS-alcian blue from foetuses and premature infants, I found no intra-epithelial glands. This indicates that they are not a normal constituent of the mucosa, but they are produced by some previous pathological effect.

In the normal adult noses studied, we found a very irregular distribution of intra-epithelial glands — they would be highly concentrated in one region and completely absent from another. However, the intra-epithelial glands account for an insignificant proportion of total mucus production, the mucus-producing capacity of the individual gland being very small compared to the capacity of a subepithelial seromucous gland. Quantitative studies are needed to define their number and density.

ANTERIOR NASAL GLANDS

Bojsen-Møller (1965) was the first to describe the anterior nasal glands in humans. These glands have ducts 2-20 mm in length which open into the vestibule of the nose and which drain the serous acini from the tuberculum septi and from the area in front of the foremost pole of the concha inferior. As a result of counting the orifices in the vestibule of the nose, Bojsen-Møller considers that there are 50-80 such glands on the septum and 50-80 in the lateral wall. They do not develop in the same way as the small seromucous glands (Tos and Poulsen, 1975). They begin to develop in the 11th week with the down-growth of solid cylinders into the depth of the lamina propria, where they bend, grow backwards and begin to devide several times. In the 12th, 13th and 14th weeks one or two new glands are formed, but I was not able to find any more recently-developed anterior glands. Until the 17th week they are very clearly visible in complete-preparations; they appear as long strands deep in the propria (Figure 4). However, I could only find 20-30 such glands. In my opinion, they play a very little part in overall mucus production, they are of little physiological and pathophysiological significance and they are probably a phylogenetic rudiment: in some mammals, such as rabbits, rats and apes, they are well-developed (Bojsen-Møller, 1964) and account for the major portion of the entire glandular mass. In humans there are few of them and their glandular mass is small and insignificant in relation to the other seromucous glands, of which there are several thousand.

SMALL SEROMUCOUS GLANDS

These glands are tubulo-alveolar and their orifices are distributed throughout the

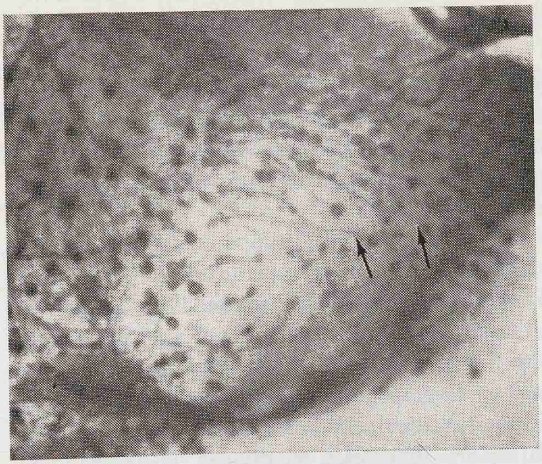


Figure 4. Vordere Teil des Septums in der 17. Woche. Anteriore Drüsen (Pfeile) mit langen Gangen und viele kleine sero-Muköse Drüsen inswischen x 20.

entire respiratory region. Their ducts are short and usually develop vertically down into the lamina propria where the glandular mass is distributed. Brunner (1942) reviewed the pathology of the glands, but Naumann (1964) wrote that the pathology of the glands continues to be "a sealed book" presumably because their anatomy is still unresolved. There are quite conflicting views as to their distribution: they are most dense throughout the conchae (Eggston and Wolff, 1947), on the medial side of the concha inferior (Kubo, 1907; Wagemann, 1964) and on the tuberculum septi (Brunner, 1942); their density decreases towards the posterior pole of the concha inferior (Oppikofer, 1907) and no glands are found above the vestibule of the nose or behind the conchae (Schiefferdecker, 1900).

The small seromucous glands [studied using complete-preparation techniques (Tos and Poulsen, 1975)] start to develop in the 13th week in front in the nasal vestibule (Figure 4). The glands spread to the other regions very much like the goblet cells, that is to say they spread from front to back along the lower part of the septum, along the floor of the nose and along the meatus. In the 17th week they also start to spread from the back to the front from the naso-pharynx, running towards the roof of the nose and the concha suprema. The conchae are filled from the meatus, and by the 23rd week the glands have spread throughout the respiratory region.

The density of the glands varies throughout their development. The density has been measured in front, in the middle and posteriorly on the septum in 50 foetuses and premature infants (Tos and Mogensen, 1976). The density increases throughout development and in the 23rd week there are 28 glands per mm^2 in front, 20 per mm^2 in the middle and 18 glands per mm^2 behind. This indicates that there is vigorous formation of new glands up to the 23rd week. The density in a newborn infant (Figure 5) was 27 glands per mm^2 in front on the septum, and 23-24 glands per mm^2 in the middle and behind, which indicates that new glands are also formed after the 23rd week. A density of 7—9 glands per mm^2

was found in a normal adult nose; this varied somewhat from region to region, with lower density posteriorly.

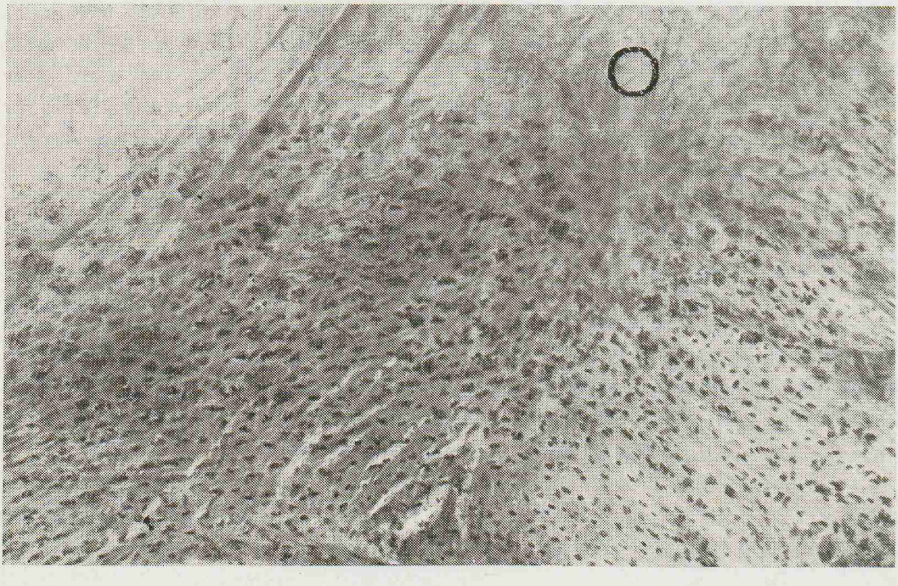
The glandular orifices are regularly distributed; there are neither zones with a high concentration of orifices nor zones completely without glandular orifices (Figure 5). However, the differences between the density in different regions hinted at here must be studied quantitatively using a large amount of normal material.

The distribution of the glandular mass in the lamina propria is particularly complicated and difficult to study since the stain is not capable of penetrating the thick, compact nasal mucosa. However, embryological studies can give some indication of the distribution: the earliest glands grow vertically deep down into the lamina propria and start to divide deep down. There they form a coherent glandular layer. Glands which start to develop later on when the lamina propria has become thicker and more solid, and particularly once blood vessels have been formed, cannot grow downwards before they start to divide. Their glandular mass therefore develops superficially in the lamina propria. Therefore, two glandular layers are likely to be found in material from adults — the superficial layer and the deep layer.

BOWMAN'S GLANDS

The Bowman's glands are situated in the olfactory region. They are small and

Figure 5. Hinterer oberer Teil des Septums bei Neugeborenen. Regelmässig verteilte kleines sero-mukösen Drüsen. Unten grosse, oben kleinere Dichte, im Regio olfactoria (o) kleine PAS-alzianblau positive Drüsen x 15.



tubular. Since they are serous, they cannot be stained with PAS and alcian blue (Figure 5) and they are difficult to study by complete-preparation techniques. They start to develop in the 15th week in the roof of the olfactory region and in subsequent weeks they spread over the entire olfactory region. In an 18-week-old foetus stained with osmium, a density of 25 glands per mm^2 was found; this is rather higher than the density of small seromucous glands at the same age.

RÉSUMÉ

L'auteur présente une revue des travaux concernant les éléments sécrétoires observés sur des préparations de muqueuse nasale examinée dans son entièreté. Le développement des cellules caliciformes de l'épithélium est décrit jusqu'à la 30è semaine de la gestation. A cette période, la densité des cellules est encore assez faible; elle augmente jusqu'à la naissance et après celle-ci. Divers problèmes sont discutés, se rapportant aux glandes intraépithéliales, aux glandes antérieures du nez, aux glandes des Bowman. Le développement des glands séro-muqueuses réparties dans le chorion de la muqueuse de type respiratoire est décrit; leur distribution et leur densité sont discutées.

ZUSAMMENFASSUNG

Übersicht über Studien der mukösen Elemente in der Nase mit Ganzpräparatmethoden. Die Entwicklung der Becherzellen bis zur 30. Woche, wo die Dichte noch sehr gering ist, wird beschrieben. Die Dichte muss gegen die und nach der Geburt stark steigen. Einige Probleme betreffend intraepitheliale, anteriore nasale sowie Bowmansche Drüsen werden diskutiert. Die Entwicklung der kleinen seromukösen Drüsen wird beschrieben, und die Verbreitung und Dichte derselben diskutiert.

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