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Development of the ciliary epithelium in human nose

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SUMMARY

In 15 foetuses, ranging in age from the 8th to the 23rd menstrual week, the development of ciliated cells in the nose was analysed quantitatively by counting ciliated cells in high power fields.

The formation of ciliated cells is the first step in the differentiation from embryonic to respiratory epithelium, which starts in the 9th menstrual week. The density of ciliated cells increases strongly and reaches a maximum already in the 16th week. It does not further increase in older foetuses and prematures.

Based on the rapid increase in density it is assumed that the differentiation of ciliated cells takes about 2-3 days which is considerably shorter than for goblet cells.

The object of the present study was to gain a little more insight into the process of differentiation of the respiratory epithelium. By means of PAS-alcian blue whole-mount specimens we have earlier studied the developmental stages of the goblet cells (Poulsen and Tos, 1975) and the changes in their density during the prenatal development and growth of the nose (Tos and Poulsen, 1975). We found that the goblet cells start forming, in the 13th menstrual week, anteriorly in the nasal cavity and in the lateral wall of rhinopharynx. Hense they spread to the posterior part of the nose in such a way that differentiation in the anteroposterior and posteroanterior directions join in the mid-nose. In the beginning of their development, in the 15th to the 17th week, the density of goblet cells was relatively high anteriorly in the nose, after which time it fell and remained relatively low in all segments of the nose throughout the entire prenatal period. Also at birth the goblet cell density was 3 to 5 times lower than in the adult nose.

The question is whether the density of ciliated cells is similarly low in the prenatal period and whether the same temporal relations apply for differentiation into ciliated cells as for goblet cells. As differentiation of cells forms part of all reparatory processes of the mucosa this is not only of embryologic but also of general histopathological and clinical interest.

There have apparently been no special studies of the ciliated cells in the foetal nose. Clara (1938) found that the differentiation from embryonic to respiratory epithelium has been completed in the nose by the 4th foetal month. In rhino-

pharynx, Kanagasunteram and Ramsbotham (1968) found that the embryonic-epithelium is thinner in those segments that later on become lined with respiratory epithelium than those that become lined with squamous epithelium. The first ciliated cells were found in a foetus with a crown-rump length (CR-length) of 29 mm, i.e. corresponding to the end of the 9th week (Streeter, 1921). Bang (1964) found goblet cells in the 11st week and a high density anteriorly in the nose in the 17th week.

MATERIAL AND METHOD

The material comprises 15 foetuses ranging in age from the 8th to the 23rd menstrual week. The age was determined on the basis of the CR-length and foot length using Streeter's tables (1921). After fixation, the entire mucosal lining of the nose was dessected free and divided into an anterior, a middle and a posterior part, from which serial sections were cut. They were stained with hematoxylin-eosin and PAS-alcian blue. The nasal septum was further divided into a lower, middle and upper segment, giving a total of 9 localities. In each of the nine localities the number of ciliated cells were determined in 3 sections by counting in high power fields at $\times 400$ magnification. Counting of ciliated cells was performed without immersion at $\times 400$ magnification as well as with immersion at $\times 1000$. Since counting with immersion and maximum magnification afforded the most reliable separation from the neighbouring cells, the result of this counting was used. The length of the individual 5 µ sections, representing the length of the high power field and the counting area, was 450 µ. Median number and range of ciliated cells in each locality of septum, or each segment, could thus be determined. In addition, the condition of the epithelium presence of goblet cells and their number as well as the form and structure of the glands were examined.

RESULTS

The epithelium

In the youngest foetus with a foot length of 6 mm, i.e. corresponding to the middle of the 9th menstrual week, embryonic epithelium consisting of 2–3 layers of round, undifferentiated cells was found in the nose (Fig. 1). The same epithelium was found in the beginning of the 10th week, though posteriorly and anteriorly in the nose beginning transformation into cylindrical cells were seen (Fig. 1a). During the 11th and 12th week this transformation spread to the rest of the nose, at the same time intensifying so that in the 13th week pseudostratified, cylindrical epithelium was found all over septum. In the 11th week beginning formation of glands was observed and in the 13th week formation of goblet cells (Figs. 1b and 1c). In the lateral wall principally the same transformation of the epithelium occurred as on septum, first anteriorly in the meatus and on the lateral wall of the inferior concha, spreading from here to the rest of conchae.

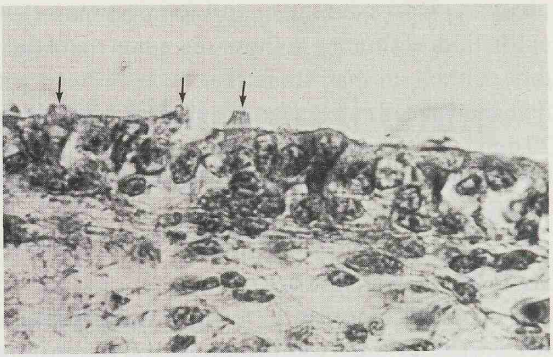
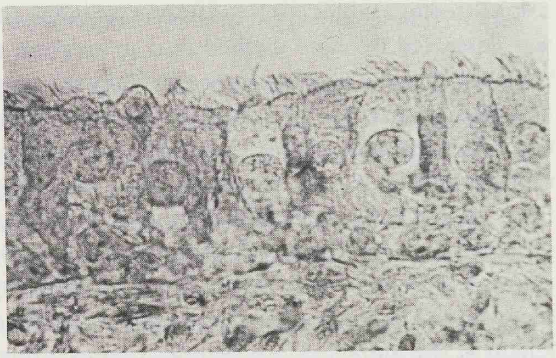
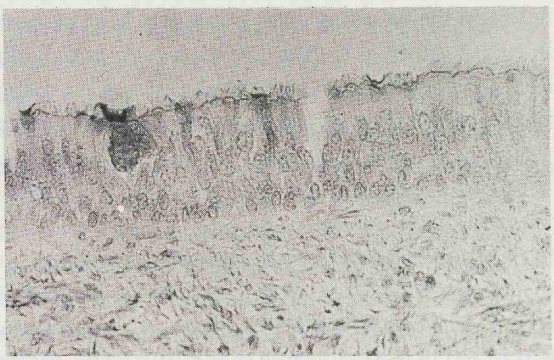


Figure 1.
a. The embryonic epithelium with round cells and without a basal membrane has started transforming into cylindrical cells. A few ciliated cells are seen (arrows). From foetus in the 10th week. Hematoxylin-eosin (× 600).



b. Cylindrical epithelium with ciliated cells. No goblet cells. From foetus in the 14th week (× 600).



c. High, cylindrical epithelium with a few goblet cells. The ciliated cells clearly dominate. From foetus in the 15th week (× 400).

Number of ciliated cells

Already in the 9th week a few ciliated cells with rather short cilia were observed in some sections. During the following weeks the number of ciliated cells increased strongly (Fig. 2), reaching a maximum of 60–70 cells per high power field already in the 16th week. From the 16th week to the 23rd week the number of ciliated cells did not change. There were no significant differences in the number of ciliated cells between the anterior, middle and posterior parts of the nose (Friedmann's test $p > 0.05$).

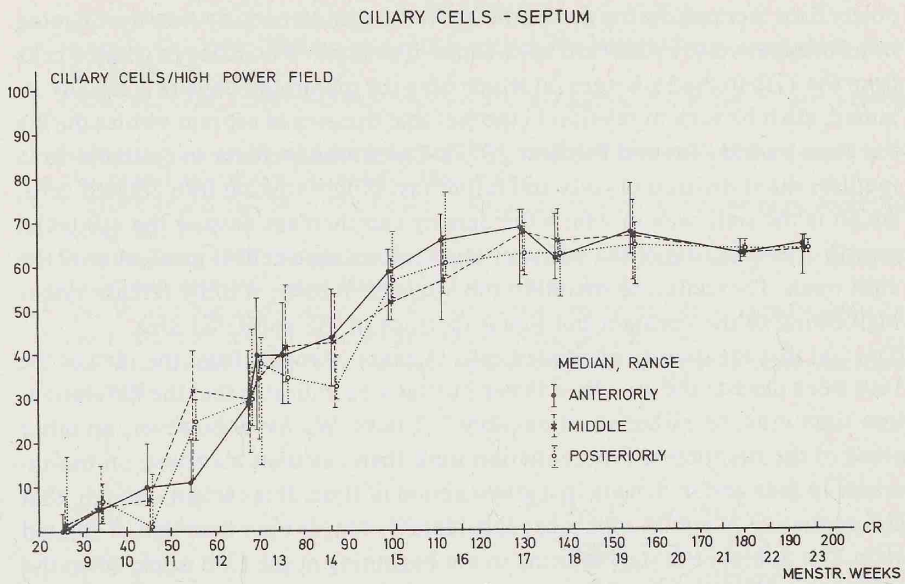


Figure 2. Number of ciliated cells in high power field in different groups.

DISCUSSION

Whereas the changes in the goblet cell density can be exactly determined in selectively stained whole mount specimens, in which the goblet cells are counted in well-defined areas (Tos and Poulsen, 1975), counting of ciliated cells presents certain difficulties when their density is so high that the entire section is covered with cilia. This state is attained already in the 16th week and does not change with increasing age of the foetus. The problem is how to ensure that closely lying cells are counted separately. Comparison of results of counting with and without immersion showed that in sections of foetuses older than the 15th week and of the same length there were 2 to more ciliated cells with immersion than without immersion. An increase in magnification from × 400 to × 1000 thus yielded 4–18% more ciliated cells. A further increase in magnification would probably increase by a few per cent the number of ciliated cells counted per high power field but it would hardly have a major effect on the general conclusion. Scanning electron microscopy, revealing a number of cilia on the surface but without cell borders below the cilia, does not afford a better possibility for quantitating ciliated cells. The study showed that differentiation into ciliated cells is the first step in the differentiation of the embryonic epithelium and that cilia may develop in the nose almost simultaneously with transformation of the round cell to the cylindrical cell. The first ciliated cells appear in the 9th week, both anteriorly and posteriorly, when the epithelium still is predominantly embryonic, and their number per high

power field increase during the following weeks simultaneously with the ongoing transformation into cylindrical epithelium. The marked increase in ciliated cells from the 11th to the 15th week, at which time the maximum density is already attained, must be seen in relation to the fact that the area of septum trebles during the same period (Tos and Poulsen, 1975). The strong increase in epithelial area requires rapid division of cells and rather fast differentiation into ciliated cells, which is the only way in which the density can increase despite the epithelial growth. The intensity of the differentiation into ciliated cells is greatest until the 16th week. Thereafter, to maintain the attained density, it must remain rather high owing to the constant but linear increase in the epithelial area.

The fact that the density of ciliated cells increases strongly from the 11th to the 16th week despite the growth of the epithelial area indicates that the differentiation time must be rather short possibly 2–3 days. We have, however, no other proof of the mentioned differentiation time than calculations based on the increase in area and in density in a given period of time. It is certain, though, that differentiation of goblet cells takes considerably longer time than that of ciliated cells. The goblet cells start forming in the beginning of the 13th week, when the epithelium is cylindrical, pseudostratified and with a considerable density of ciliated cells (Fig. 5). On the basis of quantitative studies of the density it was found that the differentiation of goblet cells in foetuses probably takes approximately 14 days (Tos and Poulsen, 1975). Accordingly, the low density of goblet cells during the developmental stage as compared with that of the ciliated cells may be explained. A rather low density of goblet cells was likewise found in the Eustachian tube of prematures, though the density in children and adults is considerably (Tos and Bak-Pedersen, 1969).

RÉSUMÉ

Chez 15 foetus dont l'âge varie entre 8 et 23 semaines, le développement des cellules ciliées de la muqueuse nasale est analysé par le comptage des cellules à fort grossissement optique.

La formation des cellules ciliées représente la première étape de la différenciation embryonnaire de l'épithélium respiratoire; elle débute au cours de la 9e semaine. La densité des cellules ciliées augmente fortement et atteint un maximum déjà lors de la 16e semaine. Elle n'augmentera plus chez les foetus plus âgés et les enfants prématurés.

Se basant sur la rapidité de l'augmentation de la densité des cellules ciliées, les auteurs concluent que celles-ci se différencient en 2 à 3 jours, c-à-d une durée beaucoup plus courte que pour les cellules mucipares.

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