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CHANGES IN EPITHELIUM OF THE NASAL MUCOSA DURING ADAPTATION TO HIGH-ALTITUDE CONDITIONS

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Much attention has recently been paid to the adaptation of man and animals in various extremal climatic zones [2, 3, 8]. One such zone is at high altitudes in the mountains [1]. Although the nose plays an important role in maintaining functional unity of the respiratory system [7] and is the first structure exposed to the action of the atmospheric environment, changes in the nasal mucosa under the influence of high mountain altitudes have not been adequately studied.

To study the time course of adaptive morphological changes in the upper respiratory passage at high altitudes, the nasal mucosa of rabbits was investigated by scanning electron microscopy (SEM) during a stay of 1 month in the Pamir Mountains.

EXPERIMENTAL METHOD

Experiments were carried out on 25 male Chinchilla rabbits weighing 2.8-3.5 kg. The animals were taken up to the Anzob Pass (3375 m above sea level) and killed on the 3rd, 7th, 14th, and 30th day of their stay at a high altitude. The nasal mucosa of rabbits killed at an altitude of 810 m above sea level served as the control. An original method was used for fixation, namely injection of 3-5 ml of 2% glutaraldehyde solution in phosphate buffer (pH 7.3) in a single dose immediately after decapitation. After inspection of the nasal cavity, pieces of mucosa measuring 0.5 × 0.5 cm were excised from the middle third of the nasal septum, fixed in 2% glutaraldehyde solution at 4°C for 24 h, postfixed in 1% OsO_4 in phosphate buffer (pH 7.3) for 1 h, dehydrated in acetone, and dried by the critical point method in liquid CO_2 in the chamber suggested by Murakhovskii and Kholanskii [4]. The pieces of tissue

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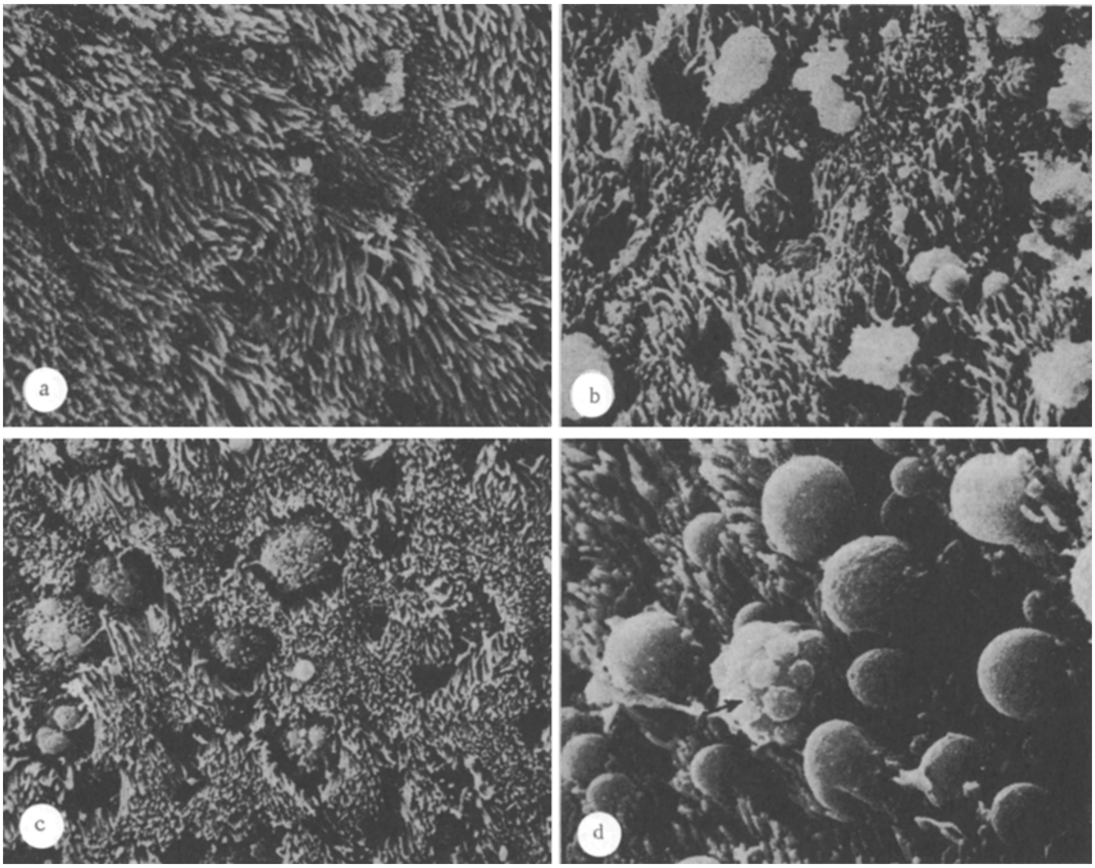

Fig. 1. Ultrastructure of surface of nasal mucosa during adaptation to high mountain altitudes: a) control. 32,250 ×; b) increased secretion of goblet cells. 2800 ×; c) increased number of goblet cells in phase of accumulation of secretion. 2000 ×; d) many piriform evaginations of ciliated cells, with a goblet cell in the presecretory phase in the center (arrow). 4200 ×. Third day. SEM.

were then glued to aluminum holders with colloidal silver paste. The surface of the fragment was sprayed with a layer of gold 25-30 nm thick on an "Eiko IB-3" apparatus and examined in the Hitachi S-500 scanning electron microscope with an accelerating voltage of 20-25 kV.

EXPERIMENTAL RESULTS

After a stay of 3 days at a high altitude the epithelial surface of the nasal mucosa differed considerably from that of the control animals (Fig. 1a). The differences were, first, increased secretory activity of the goblet cells and also of the glands of the lamina propria of the nasal mucosa, the efferent ducts of which open on the surface of the epithelium in the form of funnel-like depressions. Lumps of mucus, with a cloud-like appearance, were distributed on the surface of the ciliated cells, between which the gaping lumen of the secretory goblet cells could be seen (Fig. 1b). A characteristic feature of the different regions of the epithelial surface was that groups of goblet cells were all in the same phase of the secretory cycle, whether it be the phase of accumulation of secretion, when their surface appeared hemispherical and clearly outlined among the background of ciliated cells (Fig. 1c), or the phase of discharge of secretion (Fig. 1b). Another particular feature of the ultrastructural picture of the epithelium was an increase in the number of polymorphic piriform evaginations on the apical surface of the ciliated cells, which projected considerably above the surrounding cilia (Fig. 1d). These piriform evaginations differed in their external appearance from goblet cells overfilled with mucus, for the apical surface of the latter was nodular in appearance on account of secretory granules. The surface of the piriform evaginations of the ciliated cells, on the other hand, was as a rule smooth or slightly undulating. Their diameter at the point of maximal width varied from 1.4 to 4.2 μ. Marked edema of the mucosa was observed, as shown by the clarity of the cell boundaries and the presence of slit-like depressions between the cells. By the 7th day small regions of "baldness" appeared on the surface

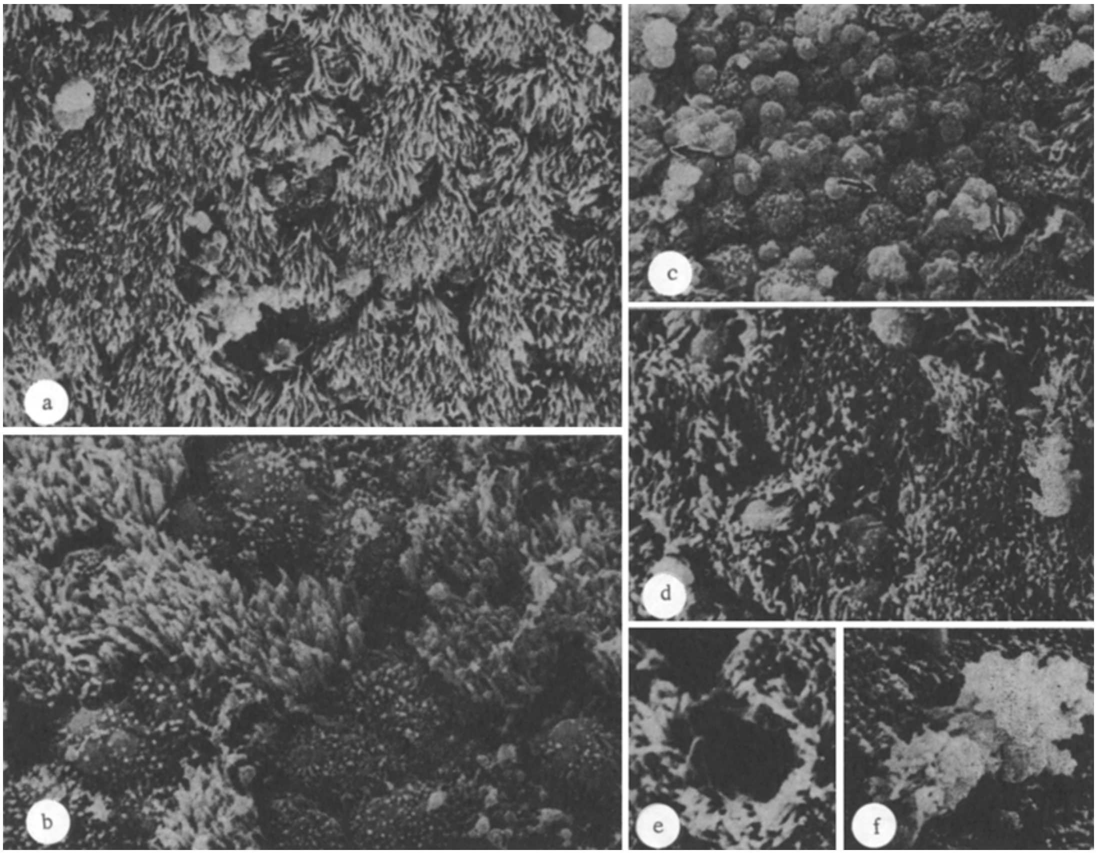

Fig. 2. Ultrastructural changes on surface of nasal mucosa during adaptation to high mountain altitudes: a) small regions of "baldness" of ciliated epithelium. 1600 ×; b) regions of "baldness" formed by groups of goblet cells. 3200 ×; c) wide area of goblet cells in phase of accumulation or discharge of secretion. Widening of intercellular spaces as a result of edema (arrows). 1900 ×; d) discharge of mucus from individual granules of goblet cells (arrows). 3000 ×; e) crater-like depression after discharge of secretion. 4200 ×; f) desquamated ciliated cell surrounded by mucus. 3500 ×. a, b) 7th day; c–f) 14th day. SEM.

of the mucosa as a result of replacement of ciliated cells by goblet cells (Fig. 2a). It was noted that the secretory cycle appeared to become synchronized, when a group of goblet cells could be seen at the stage of accumulation of secretion, and containing a reduced number of microvilli on their surface (Fig. 2b).

The pattern of the mucosa on the 14th day was heterogeneous: Edema was present, the areas of "baldness" were larger, and most of the goblet cells in them were in the presecretory phase or in the phase of secretion (Fig. 2c). Mucus was discharged both by separate granules (Fig. 2d) and from the whole apical surface of the goblet cell. In the latter case, the place of the secreting cell was occupied by a crater-like depression, bounded by the raised edge of the torn plasmalemma (Fig. 2e). Sometimes single desquamated ciliated cells were found (Fig. 2f). Evidence of the activation of repair processes also was given by the fact that many cells with growing cilia could be seen in some areas of "baldness" (Fig. 3a). The following stages of ciliogenesis were accordingly distinguished, being clearly demonstrable by SEM. In the stage of latent ciliogenesis the cells still had no cilia, but they differed from the surrounding nonciliated cells by being covered with microvilli 0.574 ± 0.005 μ long and 0.148 ± 0.005 μ wide, i.e., the same size as on a mature ciliated cell. Next, in the second (initial) stage of ciliogenesis, short cilia arranged in small groups began to appear on the surface of these cells between the microvilli. The ends of these groups of cilia appeared to be fused. In the next (intermediate) stage of cilogenesis the cilia were now dissociated. Their length was half that of fully formed cilia and their free ends had a more regular arrangement. In the final stage of ciliogenesis the cilia attained their maximal size: length 2.950 ± 0.016 μ, width 0.280 ± 0.005 μ.

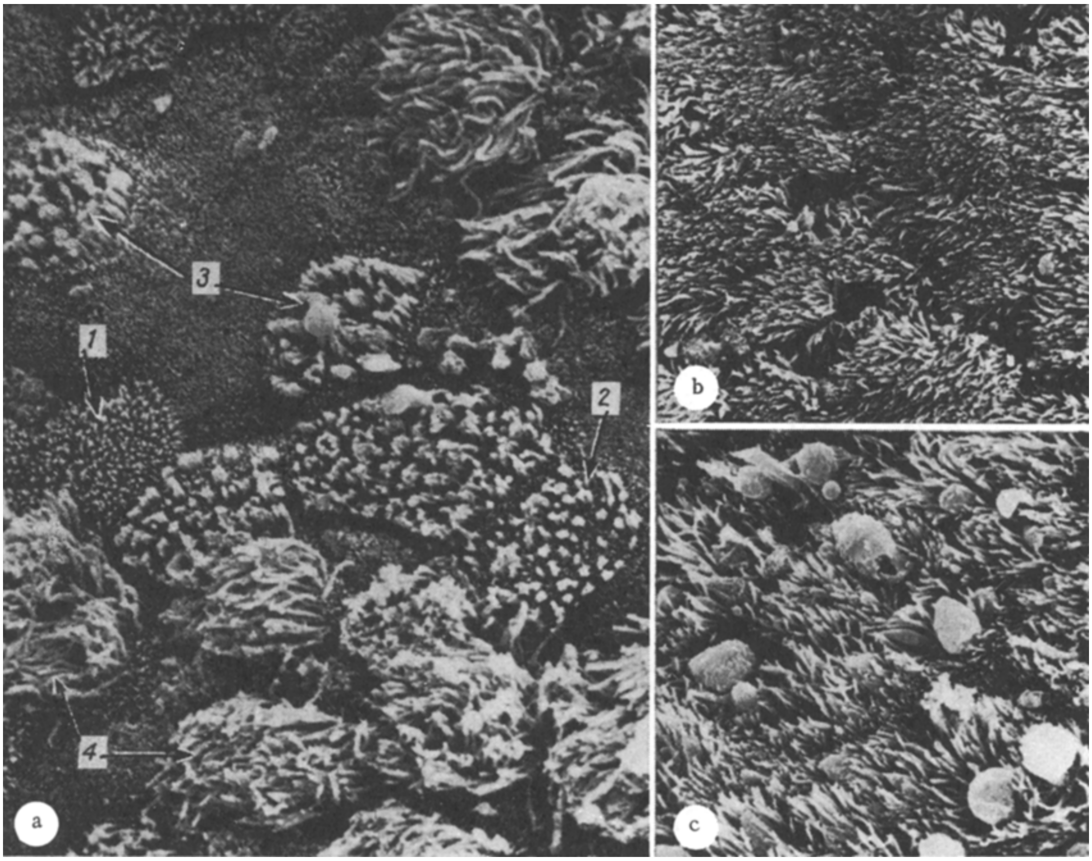

Fig. 3. Ultrastructural changes on surface of nasal mucosa during adaptation to high mountain altitudes: a) different stages of ciliogenesis: 1) stage of latent ciliogenesis, 2) initial stage, 3) intermediate stage, and 4) final stage of ciliogenesis. 3400 ×; b) decrease in number of goblet cells. 1800 ×; c) decrease in number of piriform evaginations of ciliated cells. 2800 ×. a) 14th day; b, c) 30th day. SEM.

After a stay of 1 month at high mountain altitudes the epithelial surface showed a marked reduction in the number of goblet cells (Fig. 3b). However, the pattern observed on the epithelial surface of the nasal mucosa of animals in the plains was still not fully restored. In some regions ciliated cells with single thickened cilia and piriform evaginations on their apical surface could still be seen, although they were fewer in number than in the early stages of adaptation (Fig. 3c). Piriform evaginations on ciliated cells of the nasal mucsoa, an increased number of which was observed as early as on the 3rd day, followed by an appreciable decrease toward the 30th day of adaptation to high altitude conditions, evidently play an important role in the immunologic protection of the animal, and it is also considered that they can secrete immunoglobulins [9]. In the initial stages of adaptation synchronization of the secretory cycle in the various zones of the epithelium was a distinctive feature not normally observed, when goblet cells in the same region are more often in different stages of the secretory cycle. Hyperplasia and hypertrophy of the goblet cells were most marked on the 14th day of adaptation. Cells with growing cilia also are found under normal conditions, for the epithelium of the respiratory passages is constantly being renewed [5]. Activation of repair of the epithelium of the nasal mucosa was most marked after the animals had stayed 2 weeks at a high altitude. Under these circumstances, comparative study by transmission electron microscopy and SEM revealed basal bodies of future cilia [6] in the cytoplasm of cells which had no cilia on their surface, but which were covered by microvilli of the same size as the mature ciliated cell; this stage of development of the ciliated cell was accordingly distinguished as the stage of latent ciliogenesis.

These investigations by SEM thus showed that in the early periods of adaptation to high altitude conditions in the mountain functional stress on the epithelium of the nasal mucosa is observed. This is expressed morphologically as an increase in the number of goblet cells and in their secretion, and also as the appearance of piriform evaginations on the apical surface of the ciliated cells, which evidently play an important role in local immunologic defense. Later activation of repair processes is observed. The changes described above have a tendency to normalization after a stay of 1 month at a high altitude. These results suggest that the changes observed are compensatory and adaptive in character and that adaptation for 1 month is the minimal time necessary for the body to acquire a state of adaptation to extremal high altitude conditions.

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