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The ultrastructural characteristics of the capillary walls in human nasal mucosa

Kensuke Watanabe and Isamu Watanabe, Tokyo, Japan

SUMMARY

The fine structure of the capillaries of the human nasal mucosa was observed with the electron microscope. It was revealed that the capillaries in superficial nasal mucosa had fenestrae in one area and open endothelial junctions in other area, and some sections showed only continuous endothelium. Large sections were put on mesh sized 1 mm diameter and 100 of capillaries was examined and expressed in percent. The numbers of capillaires were in the order of discontinuous type (17%) < fenestrated type (31%) < continuous type (52%) in the anterior tip of the inferior turbinate, while the distribution ratio in the posterior area was in the order of discontinuous type (8%) < continuous type (25%) < fenestrated type (67%).

In serial sections, some sections of the same capillary revealed the presence of fenestrae or open endothelial junctions, while other sections only showed continuous endothelium. Therefore these three types of capillaries were considered to be the same capillary and different areas were observed. And our data roughly showed the rate of area of fenestrae or open junctions to the continuous area.

The capillaries which observed in the posterior portion had smooth surfaces inside the capillary lumen, but the capillaries in anterior nasal mucosa had many projections and folds inside the capillary lumen. The large pinocytotic vacuoles were enclosed by folds and projections. In the deep portion of nasal mucosa, all capillaries were of the continuous type. These continuous capillaries had thick endothelium although the capillaries in the superficial portion had attenuated endothelium. From the morphological point of view, the permeability of the capillary in the superficial nasal mucosa was high both in the arterior and posterior area compared with other organs. In particular, the open endothelial junctions and endothelial folds which were shown to exist much more in the anterior nasal mucosa than the posterior in our observation revealed large molecules passage through capillary wall.

Under ordinary circumstances, the nose is the first defensive line against the ambient air which has unphysiological temperature and humidity and furthermore contains microorganisms and allergens. In particular, the anterior nasal cavity is charged by these influences. The epithelium of the anterior third is nonciliated, and farther back on the turbinate and septum the epithelium becomes ciliated (Proctor et al., 1973; Hilding, 1963; Mygind, 1975; Lenz, 1973; Watanabe et al., 1978). The capillary formation in the anterior third of nasal cavity may be also different from that in the posterior area.

Accordingly, the authors thought that it would be very interesting to study the morphological difference of the capillary between the anterior area of the nose and the posterior area. Moreover, it would be also very interesting to study the morphological difference of the capillaries between the nasal mucosa and in other organs in order to examine not only the defensive mechanism of nose against the ambient air but also the process of absorption of antibiotics, hormone, vaccine and insulin from the local region, of which administration has been widely applied via nasal mucosa in recent years (Waldman et al., 1968; Fink et al., 1974; Baumann et al., 1976).

MATERIALS AND METHOD

The nasal mucosa of five normal volunteers were used. With a local anesthesia (0.5% procaine 0.5 ml), biopsies were taken with small forceps from the two areas of nasal mucosa; anterior tip and posterior area (two centimeters behind the anterior edge) of the inferior turbinate.

These small blocks were fixed at 4°C for two hours in 2% glutaraldehyde with 0.1 M cacodylate buffer, PH 7.4, then washed three times in 0.1 M cacodylate buffer (PH 7.4) containing 8% saccharose. They were postfixed for one hour at 4°C in 2% OsO_4 with 0.1 M cacodylate buffer, PH 7.4, and then dehydrated with ethanol and embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead to enhance contrast for electron microscopy.

RESULTS

Anterior tip of the inferior turbinate: In the superficial lamina propria of the mucosa, the fenestrated capillaries were observed. The capillary endothelium of the anterior tip of the inferior turbinate was characterized by extremely atten-

Table 1

	superficial portion of nasal mucosa		deep portion of nasal mucosa		arround nasal gland	
	anterior area	posterior area	anterior area	posterior area	anterior area	posterior area
continuous type	52(%)	25(%)	100(%)	100(%)	95(%)	70(%)
fenestrated type	31	67	0	0	5	30
discontinuous type	17	8	0	0	0	0
	100(%)	100(%)	100(%)	100(%)	100(%)	100(%)

Large sections were put on mesh sized 1 mm diameter, and 100 of capillaries per each portion was examined and expressed in percent. (%).

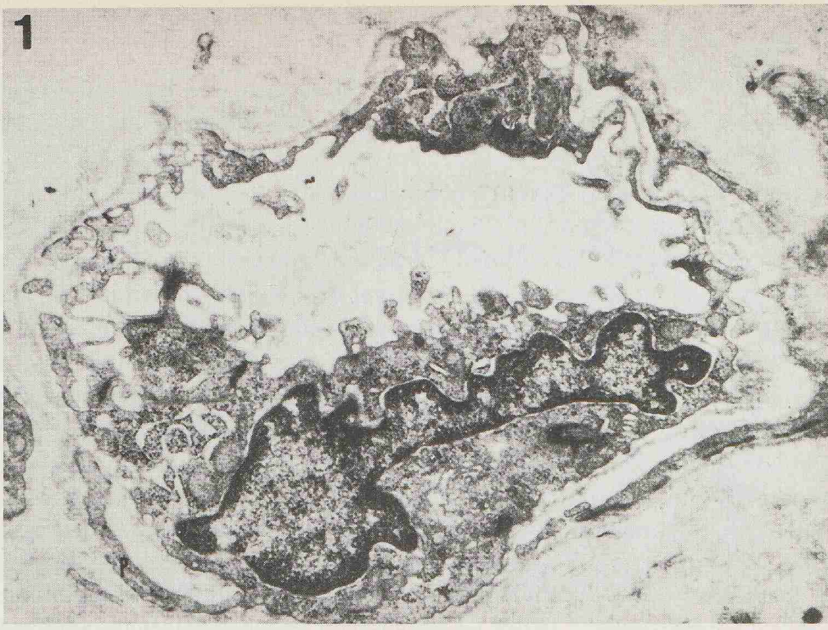

Figure 1. The continuous capillary of the anterior tip of the inferior turbinate is characterized by extremely attenuated endothelium. The endothelium is supported by sparse perictes. *P*: perictes, × 17,500

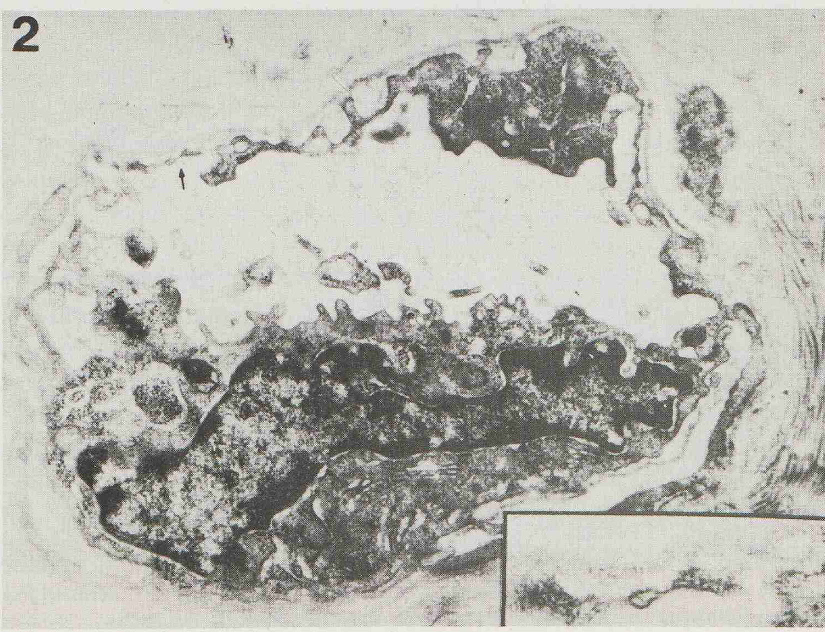

Figure 2. The fenestrated capillary of the anterior tip of the inferior turbinate. The number of fenestrae (arrow) is few and endothelium is charaterized by many projections to the capillary lumen. Figures 1 and 2 are serial sections. × 17,500 insert: High magnification of the arrow portion. × 45,000

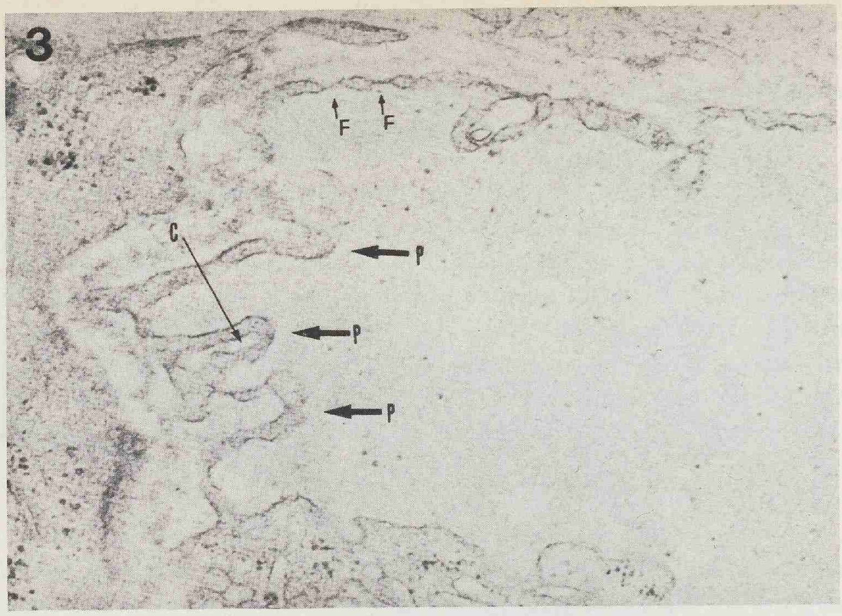

Figure 3. Large capacity (arrow C) are enclosed by the endothelium projected (arrow P) to the inside the vessel. *F*: fenestra × 45,500

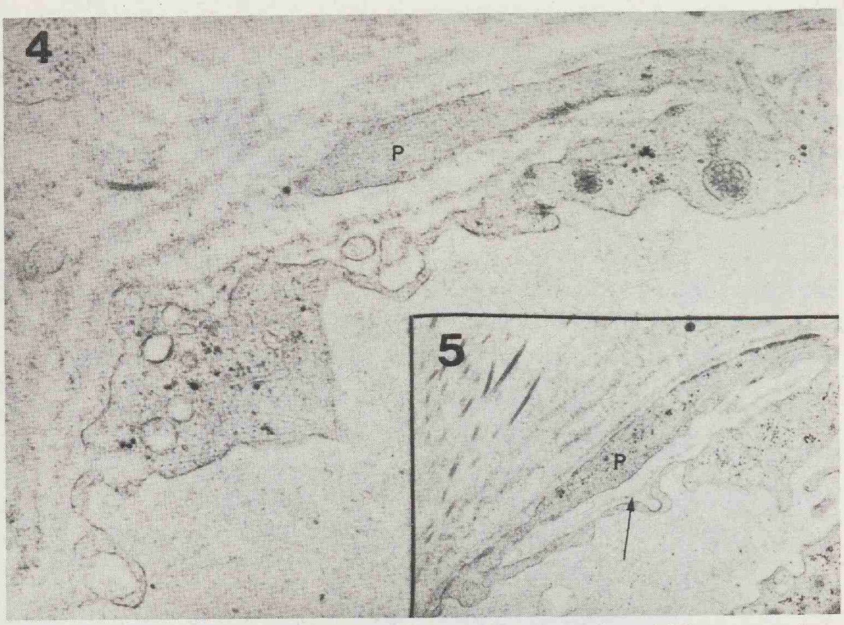

Figure 4. May be pre-stage of Figure 5. Endothelium projected (*P*) seems to form lumen following the accretion of the tip to the endothelium. × 12,000

Figure 5. The endothelium projected to the interstitium, resulted in a large lumen outside the vessel. Basement membrane is observed in enclosed lumen (arrow). × 10.000

uated endothelium which were devoid of usual complement of cell organelles (Figure 1). The endothelium was supported by spares pericytes. Among 100 capillaries observed.52 were estimated as continuous without fenestrae (Table 1). The number of fenestrated capillaries was at 31% and with lower incidence of fenestrae (Figure 2, arrow) than the capillaries in the posterior nasal mucosa. Figure 1 and Figure 2 were serial sections. Therefore some sections of the same capillary revealed the presence of fenestrae, while other sections only showed continuous endothelium. It means that the fenestrae occured in very small patches in the endothelium of nasal capillaries. The capillary endothelium was characterized by many endothelial projections to the capillary lumen (Figure 3, arrow P). The large capacities (arrow C) enclosed by these projections were still unclear whether they originate in the vessel or out of the vessel, but these large capacities showed the transportation of intra- or extra-vascular substances through the capillary wall. The large projections in the direction of interstitium were observed in some capillaries (Figure 4, P). A large transport from outside to inside the vessel could be attained if a large capacity was formed following the accretion of the tip of this projection to the endothelium (Figure 5). Because the basement membrane (Figure 5, arrow) was present in the enclosed lumen, this capacity might be derived from the extravascular portion. The open endothelial junctions were observed at the rate as high as 17% (Figure 6a, 6b and 7) and more frequently observed than in the posterior area. The borders of the endothelial cells were clearly delineated. Between profiles of cell borders, there were large gaps which permitted blood plasma to have direct access to the subendothelial space. The basement membrane was distinctly observed in most cases but with partly unclear areas in some cases, and even a substance of large molecular weight could freely pass through if the basement membrane is absent. Discontinuous capillaries had fenestrae (Figure 6b and Figure 7, arrow F), therefore the open endothelial junctions appeared in a very small area of the endothelium in the fenestrated capillaries.

In the deep portion of lamina propria of the mucosa, only continuous capillaries were observed (Figure 8). Neither fenestrated nor open endothelial junctions were observed. The number of capillaries in the deep portion was fewer than that in the superficial portion. There was no attenuated area in the endothelium similar to the capillary in the skeletal muscles (Bennett et al., 1959; Bruns and Palade, 1968). The endothelium was supported by developed pericytes (Figure 8, P), and the basement membrane (Figure 8, arrow B) enclosed the endothelium and pericytes.

The capillaries that enclosed the acini of the mixed nasal glands were both fenestrated and continuous. The fenestrated ones were very few, and most capillaries were continuous type. The lumen of capillary was extremely narrow in general with many projections (Figure 9).

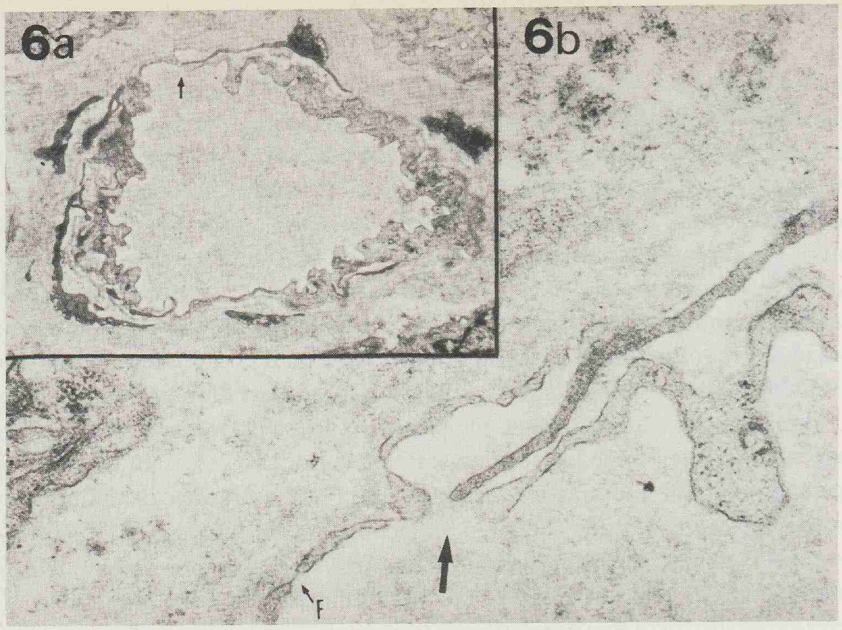

Figure 6a. The open endothelial junction (arrow) is observed. × 9,000

Figure 6b. High magnification of the arrow portion.
F: fenestra × 35,000

Figure 7. The borders of the endothelial cells are clearly delineated.
arrow F: fenestra × 30,000

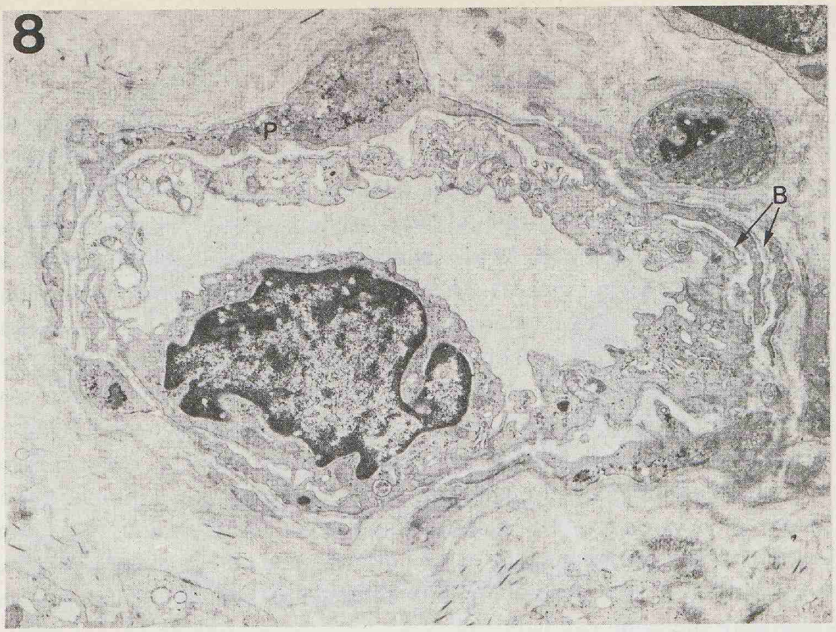

Figure 8. Continuous capillary in the deep lamina propria of the mucosa, enclosed by well developed pericyte (*P*).
P: perycite; *B*: basement membrane × 9,000

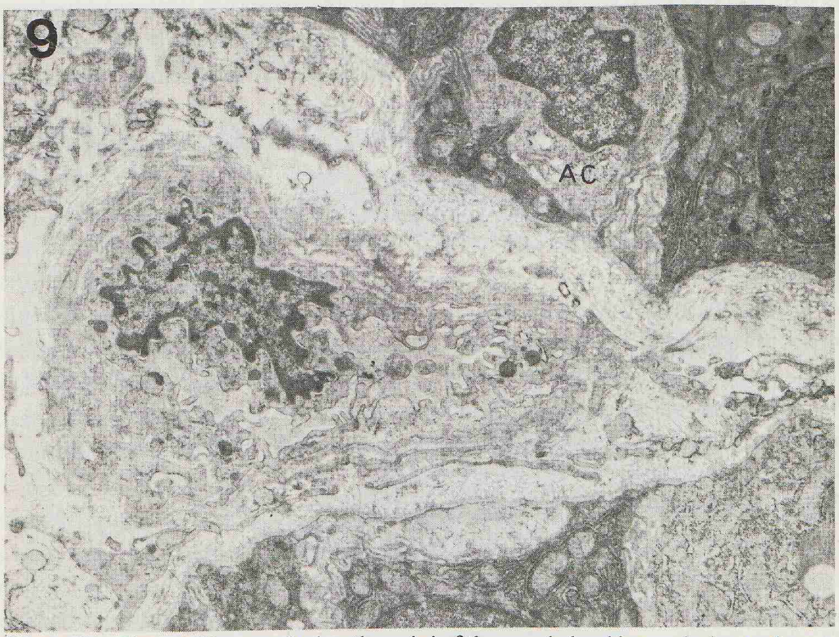

Figure 9. The capillary enclosing the acini of the nasal gland is regularly continuous type. Lumen is generally narrow, and the endothelium is characterized by many projections to the capillary lumen. *AC*: acina cell × 7,500

Posterior area of the inferior turbinate:
Among 100 capillaries observed 67 had fenestrae, 25 had no fenestrae and 8 had open endothelial junctions. The fenestrated capillaries were characterized by smooth surface inside the capillary lumen (Figure 10). The endothelium was supported by sparse pericytes. Continuous capillaries (Figure 11) also characterized by few endothelial projections to the capillary lumen, similar to the fenestrated type in the posterior nasal mucosa. Therefore in the posterior nasal mucosa some sections of the same capillary showed the presence of fenestrae, while other sections showed continuous endothelium. But the fenestrae occured in wider area in the capillary endothelium of the posterior nasal mucosa than of the anterior nasal mucosa. The morphological findings of the capillary in the deep portion of lamina propria of the mucosa were similar to those in the anterior tip. The capillaries around nasal gland were continuous type and fenestrated type. Although almost all capillaries in the anterior tip around nasal gland were continuous type, about 30% of them were fenestrated type in the posterior area (Table 1). It was not clear in this study that the fenestrated capillary enclosed the nasal gland and continuous one were the same capillary.

DISCUSSION

Electron microscopic studies have shown that the structure of capillaries varies from region to region (Bennett et al., 1959). The capillaries are classified into three principal classes. The continuous capillaries constitue the most widespread group. They are found in skeletal muscles (Bennett et al., 1959; Bruns and Palade, 1968), lung (Bennett et al., 1959) and nervous system (Dempsey and Wislocki, '55; Reese and Karnovsky, 1967; Luse, 1956). The fenestrated capillaries have been demonstrated in kidney (Yamada, 1955), endocrine gland (Trier, 1958) and intestinal villi (Clementi and Palade, 1969). The discontinuous capillaries or sinusoids are found in liver (Bennett et al., 1959; Hampton, 1958), spleen (Weiss, 1957) and bone marrow (Bennett et al., 1959). Mayerson et al. (1960) indicated that the permeability increased in the order of capillaries of continuous capillary < fenestrated capillary < discountinuous capillary. It was revealed that the capillaries in superficial nasal mucosa had fenestrae in one area and open endothelial junctions in other area, and some sections showed only continuous endothelium from this study.

Schoefl (1964) reported that after injury the newly regenerated capillaries were abnormally permeable and highly fragile and were morphologicallly estimated as discontinuous type. The anterior is most easily influenced by unphysiological temperature and humidity, microorganisms, allergens, etc., and thus is easily affected by injury. From this point of view the open endothelial junctions observed in the present study might be considered to be the regenerated capillaries emphasized by Schoefl. On the other hand, Schoefl reported that the new

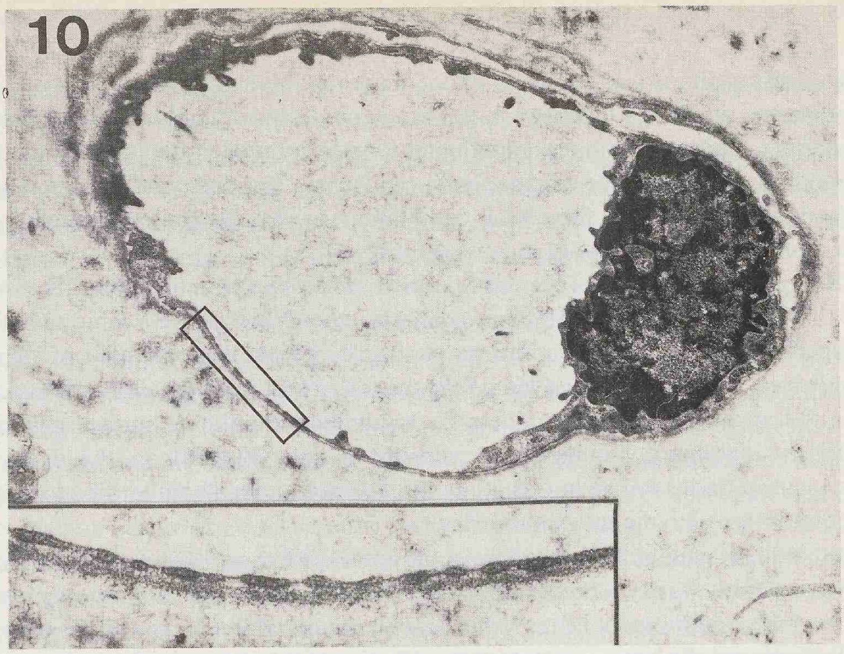

Figure 10. The fenestrated capillary in the posterior area of the inferior turbinate is characterized by smooth surface in side the capillary lumen and more fenestrae than anterior capillary. × 10,000
insert: High magnification of the square area.
Many fenestrae were observed. × 45,000

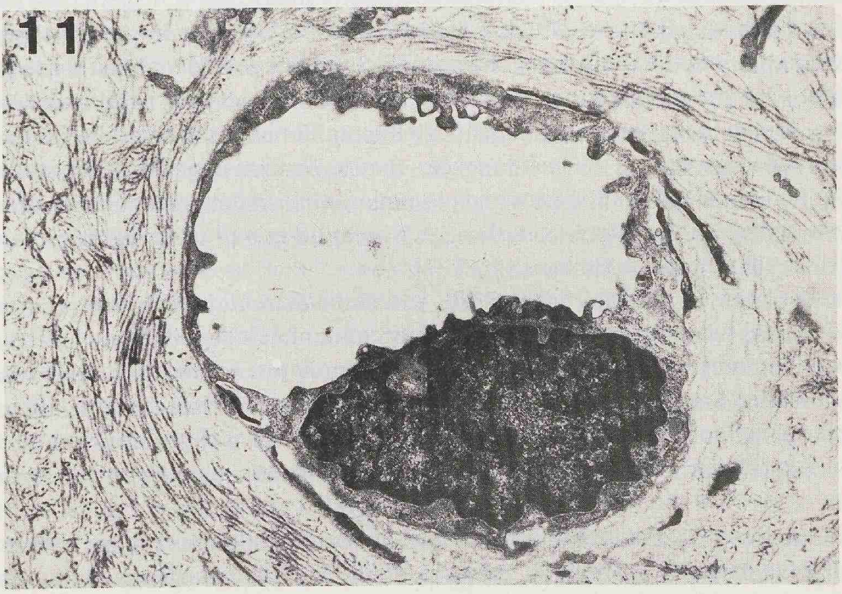

Figure 11. This capillary had no fenestrae in the posterior area. × 10,000

regenarate capillary was deficient of basement membrane; however, most of discontinuous capillaries observed in this study possessed a basement membrane. Therefore, perhaps the open endothelial junctions noted in the nasal mucosa should not be considered as regenerate capillaries. The open endothelial junctions may only signify a functional condition. Anyway, the capillary which has open junctions must have high permeability.

Although the endothelia of lymphatic capillaries possess structures that are similar to those found in discontinuous capillaries, the former possess some specific characteristics which serve for differentiating them from the endothelia of blood capillaries. Leak and Burke (1966, 1968) suggested that the lymphatic capillaries had the anchoring filaments along the abluminal endothelial surface and no definitive basement membrane. According to their suggestions, the discontinuous capillaries found in this study are distinctly considered as blood capillaries and not as lymphatic capallaries.

In the walls of capillaries, especially in the anterior of nasal cavity, many projections and folds were observed in the superficial lamina propria of the mucosa. These folds and projections may shift large amounts of fluid acros the capillary wall. Moreover, the large projection in the direction of the interstitium was observed specifically in the capillaries of the anterior nasal mucosa. The large capacities which were enclosed by these projections were transported from outside to inside the capillaries. As the epithelium is nonciliated in the anterior nares mucous flow rate in this region is low (Hilding, 1963). Many particles which are deposited in the anterior nares remain for a long time and have many chance to penetrate into the submucosa. Particles which penetrate into the submucosa are efficiently transported into the capillary by these projections. It is considered that the transportation from outside to inside the capillaries in the anterior nasal mucosa is more than in the posterior area. Although the capillaries in the anterior area have fewer fenestrae than in the posterior area, they have more open endothelial junctions and more endothelial folds and projections than in the posterior area. More large molecules, therefore, pass through the capillary wall in the anterior nasal mucosa than in the posterior.

Cauna (1969, 1970) reported that the basement membrane that enclosed the endothelial tube of nasal mucosa frequently contained fine pores. In our observation, fine pores were observed in the basement membrane. Whether these were artifacts due to the fixation or not is, however, still unclear. Basement membrane can act as a filter, retarding the passage of particles, molecules or ions above a certain size (Bennett, 1963). Thus, if the basement membrane is absent, the serum may easily flow out into the extracapillary space.

The capillaries in the deeper portion were continuous type and supported by a well-developed layer of pericytes (Cauna, 1970). Therefore, the permeability may be lower than that of the superficial capillary. Additionally, the number of capillaries in this portion is sparse.

Jackson and Burson (1970) reported that the nasal mucosa was approximately 10 times as permeable to the pertechnate ion as middle ear mucosa, and nasal mucosa was also permeable to protein with the physiological technique employed. From the present study, the capillary permeability existing in the superficial nasal mucosa can be said to be very high although there are some morphological differences according to the portion of the nasal cavity.

ZUSAMMENFASSUNG

Die feine Struktur Kapillarröhrchen menschlichen Nasenschleimhautes wurde mit dem elektronischen Mikroskop beobachtet. Es wurde offenbar gemacht, dass die Kapillarröhrchen auf oberflächlichem Nasenschleimhaute die Fenestrae in einer Zone und die offene endotheliale Knotenpunkten in anderer Zone haben, und dass einige Teile derjenigen nur die ununterbrochene endotheliale Schichten haben. Die grössere Exemplare wurden auf einer Masche mit 1 mm Durchmesser gesetzt. Ein hundert Kapillarröhrchen wurden beobachtet und mit Prozent ausgedrückt. Die Nummer dieser Kapillarröhrchen waren in der zunehmende Ordnung von dem unterbrochenen Typ (17%) < dem fenestrierten Typ (31%) < und dem ununterbrochenen Typ (52%) in der vorderen Spitze der Untermuschel, während das Verbreitungsverhältnis dieser Muscheln in der hinteren Zone war in der Zunehmende Ordnung von dem unterbrochenen Typ (8%) < dem ununterbrochenen Typ (25%) < und dem fenestrierten Typ (67%).

In der Kettenexemplaren konnte es in einiger Teilen derselben Kapillarröhrchen offenbar gemacht werden, dass es die Fenestrae oder offene endotheliale Knotenpunkten gab, während andere Teilen nur die ununterbrochenen endothelialen Schichten zeigten. Daher wurde es angenommen, dass diese drei unterschiedlichen Typen der Kapillarröhrchen von derselben Kapillarröhrchen hergeleitet worden seien und dass nur die unterschiedliche Teilen beobachtet worden sein sollten. Unsere Ergebnisse zeigten im algemeinen die Verhältnisse der fenestrierten Teilen zu den ununterbrochenen Teilen oder diejenige zu den offenen Knotenpunkten. Die in den hinteren Zonen beobachtete Kapillarröhrchen hatten glatte Oberflache in dem Lumen der Kapillarröhrchen, aber hatten die in dem vorderen Naschenschleimhaute befindliche Kapillarröhrchen viele Fortsätze und Falten in den Lumen der Kapillarröhrchen. Die grosse pinozytotischen Vakuolen wurden mit den vielen Falten und Fortsätzen eingeschlossen. In den tiefen Teilen der Nasenschleimhaute waren alle Kapillarröhrchen von dem ununterbrochenen Typ. Diese ununterbrochene Kapillarröhrchen hatten dicke endotheliale Schichten, obgleich die Kapillarröhrchen in der oberflächlichen Teilen die attenuierte endothelialen Schichten hatten.

Aus dem morphologischen Standpunt wurde as bemerkt, dass die Permeabilität der in den oberflächlichen Nasenschleimhaute befindlichen Kapillarröhrchen hoher in beide den vorderen und hinteren Teilen als diejenige anderer Organen.

Besonders wurde es offenbar gemacht, dass die offene endotheliale Knotenpunkte und die endotheliale Falten, die sich in unseren Beobachtungen in der vorderen Nasenschleimhaute mehr als in der Hinteren befanden, grosse molekulare Durchgänge durch die Kapillarwände hatten.

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Kensuke Watanabe, M.D.
Dept. of Otolaryngology,
Tokyo Medical & Dental Univ.
1-5-45, Yushima Bunkyo-ku, Tokyo, Japan