

Microvascular anatomy of the nose

Widdicombe J. Microvascular anatomy of the nose.
Allergy 1997; 52 (suppl 40): 7-11. © Munksgaard 1997.

The microvasculature of the nose consists of: 1) A dense subepithelial network of capillaries, with fenestrations between the endothelial cells. This network provides nutrients to the epithelium and glands, and allows passage of water into the lumen for evaporation and air-conditioning. 2) A system of capacitance vessels or sinuses, which when they distend, block the nasal lumen, and when they empty, open the nasal passages. Changes in their volume will affect the filtering and air-conditioning functions of the nose. 3) Arteriovenous anastomoses which allow rapid passage of blood through the mucosa. They are probably important in air-conditioning, and in the countercurrent mechanisms that tend to keep the brain cool in a hot dry climate. The anatomical interrelationships between these different systems is not well understood, nor is their differential control in terms of actions of mediators and nerves. In neurogenic inflammation sensory nerves are excited and release local mediators such as substance P via axon reflexes. These sensory neuropeptides will cause vasodilatation, vascular congestion and extravasation of liquid from the postcapillary venules, with resultant oedema and exudate. They may also cause secretion from the submucosal glands.

John Widdicombe

Sherrington School of Physiology, UMDS,
St Thomas' Hospital, London, UK

Key words: blood capillaries; capacitance vessels; blood sinuses; arteriovenous anastomosis; countercurrent heat exchange; air-conditioning; temperature control

Professor J. G. Widdicombe,
Sherrington School of Physiology, UMDS,
St Thomas' Hospital, Lambeth Palace Road,
London SE1 7EH, UK

Introduction

The microvasculature of the nasal mucosa differs from that of other parts of the respiratory tract in several ways. It has a highly developed system of capacitance vessels, or blood sinuses, which are absent or far less frequent in the tracheobronchial tree. During congestion these will expand the mucosa and, since the nose is enclosed in bone, the expansion must encroach on the airway lumen, tending to nasal blockage. The nasal vasculature has many arteriovenous anastomoses (AVAs), whereas these seem to be absent in the lower airways. In terms of control, the nasal vasculature shows cyclical changes of congestion, giving rise to the nasal cycle. This has not been demonstrated for the lower airways. These differences in structure and function are related to the role of the nose in filtering and conditioning inspired air, and in the control of body temperature and water content.

Capillaries

The nose, like all parts of the respiratory tract, has a copious system of capillaries just under the epithelium (1-4) (Fig. 1). The density of these capillaries is presumably related to the need to supply

oxygen and nutrients to the highly metabolising epithelium, and for glandular structures in the mucosa (5). In addition they will allow water to escape into the airway lumen and for evaporation to take place in conditioning inspired air. This important function of the nose, compared with lower airways, may explain why the nasal subepithelial capillary walls have fenestrations, usually on the epithelial side of the blood vessel. These fenestrations would allow water to escape readily in response to osmotic gradients. In the lower airways the capillaries are seldom fenestrated, although fenestrations are seen in capillaries underlying neuroepithelial bodies and bronchus-associated lymphoid tissue. Moreover, fenestrations are also normally found in some rodents and in the mucosa of patients with asthma (6).

Capitance vessels

Capitance vessels, or sinuses, are conspicuous in the nasal mucosa of all mammals (Fig. 1). When they distend with blood the mucosa will swell and tend to block the airway lumen, presumably making filtration and possibly air-conditioning more efficient. When they tend to empty of blood the mucosa will shrink and the airflow resistance in the nose will decrease.

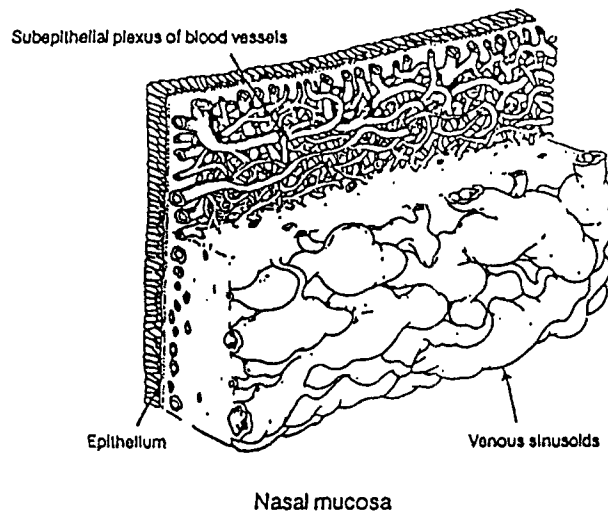


Fig. 1. Diagram of the nasal vascular beds. A major obstructive mechanism of the nasal passages in filling of venous sinusoids (sinuses). The epithelium and the subepithelial plexus of microvessels are actively involved through the plasma exudation process, both in normal mucosal defense and in inflammatory airway diseases, such as rhinitis. From (4).

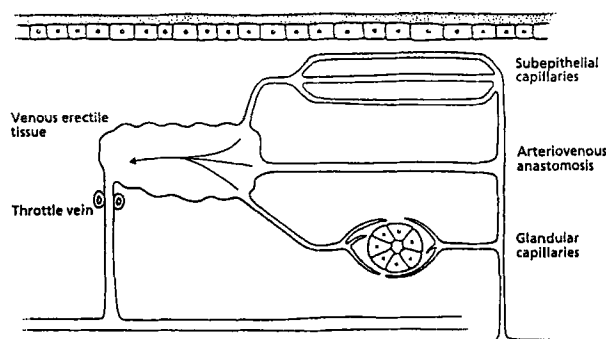


Fig. 2. Diagram of nasal vasculature. The venous sinusoids forming the venous erectile tissue may be filled by the venous drainage from the subepithelial capillaries, arteriovenous anastomoses, and glandular capillaries. The level of filling of the venous erectile tissue may be determined by the activity of throttle veins, by compression of the periosteal veins associated with arterial vasodilation, and by changes in the sympathetic vasoconstrictor tone to the smooth muscle of the venous erectile tissue. From (9).

The sinuses have a thick layer of smooth muscle in their walls, and presumably contraction and relaxation of this muscle will cause changes in blood capacity (2, 3, 7, 8). However, it is also thought that the sinuses may be made to distend by the contraction of the muscle in "throttle veins" at the exit from the sinuses (9) (Fig. 2), or by enlargement of the calibre of AVAs at the entry to the sinuses (see later). There are thus potentially three muscular mechanisms that could change sinus calibre, and little is known about the nervous or humoral control of these systems.

The blood volume of the capacitance vessels

varies cyclically, giving rise to the nasal cycle, whereby the two sides of the nose vary reciprocally in resistance and airflow (9). The effect is nervously mediated.

Postcapillary venules

It is through the walls of postcapillary venules that extravasation of plasma takes place during inflammation of the mucosa, by the opening of gaps in the intercellular junctions between the endothelial cells (10, 11) (Fig. 3). This will lead to an increase in interstitial liquid volume and pressure, and the latter will tend to force plasma-like liquid through into the lumen as exudate (4, 12). The humoral mediators that cause extravasation of plasma are many, and include histamine, bradykinin, various prostaglandins, and sensory neuropeptides such as substance P (SP). It is less clear whether plasma extravasation can be caused only by changes in postcapillary venular pressure. In theory dilatation of resistance vessels such as arterioles should increase postcapillary venular pressure and lead to extravasation, but possibly the presence of agents acting directly on the vessels is also necessary. A mediator such as histamine may therefore have two actions, an increase in the pressure in the postcapillary venules by dilatation of arterioles, and the opening of gaps in the intercellular junctions between the endothelial cells. Some agents, such as β -receptor agonists, can decrease plasma extravasation and, since they cause arteriolar dilatation they must also presumably inhibit the opening of intercellular clefts (12, 13).

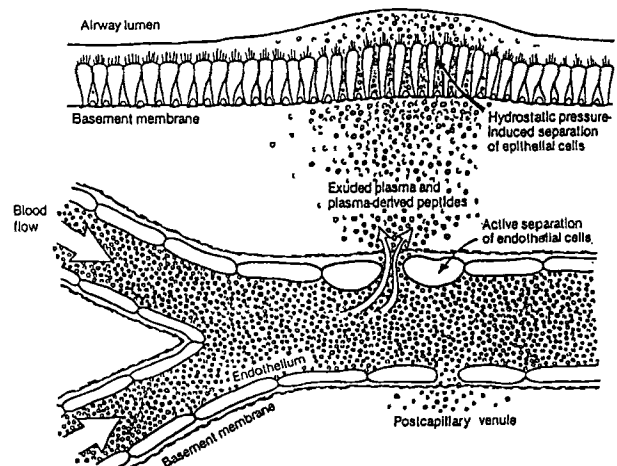


Fig. 3. Scheme illustrating the concept of inflammatory stimulus induced exudation of plasma macromolecules across the vessel wall and the mucosal barrier. Note that the luminal entry of unfiltered exudate can occur across a normal epithelium. From (4).

Arteriovenous anastomoses (AVAs)

The presence of many AVAs in the nasal mucosa has been demonstrated by observing the passage of microspheres through the nasal vasculature, the diameter of the microspheres being chosen so that they cannot traverse capillary networks. As many as 50% of microspheres injected into the arterial input to that of vasculature can be collected on the venous side, and appropriate mediators can be shown to increase the proportion collected, presumably by opening the AVAs (14, 15).

The role of the AVAs is probably related to temperature and water control, as in other parts of the body such as the hands and feet. The nose has important countercurrent exchange mechanisms of two types (16, 17). In a cold climate the inspired air will cool the nasal mucosa at the front of the nose and the venous blood draining backwards from it, and this in turn will cool the arterial input to the nose. The result will be that during expiration the exhaled gas will be of lower temperature than otherwise, so heat will be retained in the body. Exactly the same process can take place in the arms and legs. However, in the case of the nose the process will also tend to retain water in the body since the cold mucosa will lead to condensation, and some of this water may be held in the nose. AVAs would not be necessary for this countercurrent exchange system, and in the hands and feet they close during exposure to cold. However, the second countercurrent system would be aided by the opening of AVAs. This is the response in a hot dry environment when, paradoxically, the nasal mucosa is cooled because evaporative water loss has a larger calorific effect than that due to inspired gas temperature. The cold blood leaving the nose comes into close contact with blood going to the brain, and some species have a specialised organ for this, the carotid rete. As a result the brain temperature is kept a few degrees lower than core body temperature, and this may be an important adaptive feature for animals in hot climates, especially when exercising. The mechanism has been well demonstrated in some species, and is probably present also in man, although this issue is still being debated.

From the above description one would not expect the AVAs to be related to the capacitance vessels, and there is considerable anatomical dispute as to whether they are. They have rarely been described histologically, but their best identification shows that they join arterioles to venules, and have a clear innervation with the nerves containing neuropeptide-Y and presumably also nor-adrenaline (7, 18). However early anatomical descriptions suggested that the AVAs feed directly

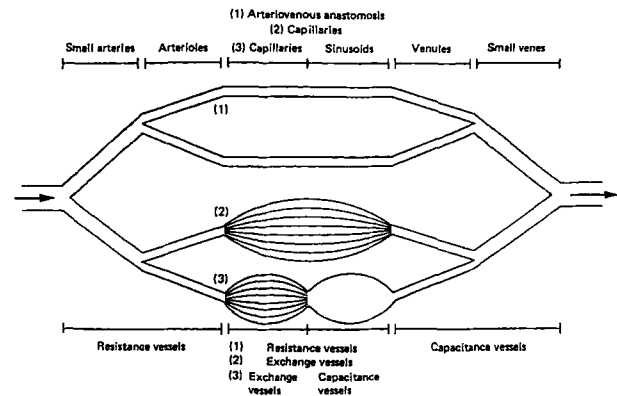


Fig. 4. Diagram of the anatomy (top) and function (bottom) of nasal blood vessels, showing arteriovenous anastomoses bypassing capillaries and sinuses. From (20).

into the blood sinuses and that their opening would engorge the sinuses (9) (Fig. 2). This would mean that when AVAs open in response to a hot environment, the nasal mucosa should also swell. However this does not seem to be the case and hot climates decrease nasal airflow resistance (17, 19). It is more likely that, as in other vascular beds, the AVAs short circuit the sinuses and capillary networks, so that they can induce an increase nasal blood flow without necessarily causing congestion or decongestion (20) (Fig. 4).

The humoral and nervous controls of the three vascular motor systems, arteriolar or resistance vessels, sinuses or capacitance vessels and AVAs, have not been adequately analysed. Most studies have measured total vascular resistance or airflow resistance due to nasal congestion. If it is assumed that nasal airflow resistance represents predominantly the volume of the capacitance vessels, then it can be shown experimentally that this volume can be controlled independently from total nasal vasculature resistance (21). For example, in the dog perfused-nose preparation some mediators (histamine, bradykinin) will cause large changes both in vascular resistance and nasal airflow resistance, others (neurokinins) will cause predominantly a decrease in vascular resistance with little change in airflow resistance, and yet others (prostaglandins) will decrease both vascular resistance and airflow resistance (21) (Fig. 5). The last response is presumably due to the opening of AVAs coupled with decongestion of the nose.

Neurogenic inflammation

The last decade has seen considerable investigation of neurogenic inflammation in the nose. This is the mucosal response to stimulation of sensory nerves, probably with nonmyelinated fibres, in the mucosa. The receptors are activated by a range of

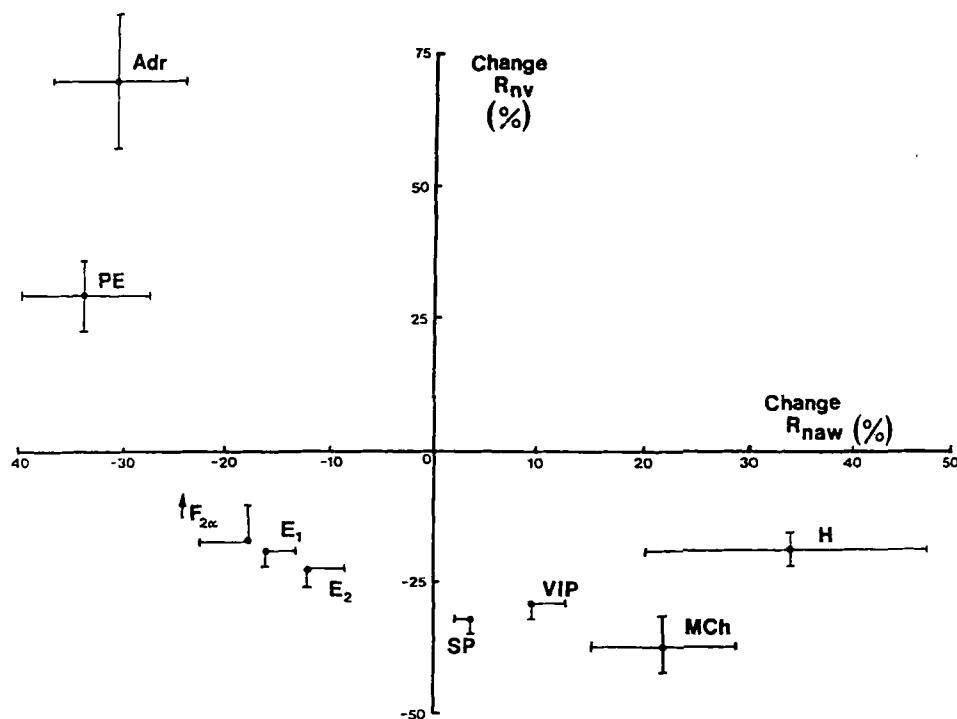


Fig. 5. Relationship between change in nasal vascular resistance (R_{nv} , dilatation downwards) and nasal airflow resistance (R_{naw} , blockage to the right) for the perfused nasal vasculature of the dog. Drugs were injected into the arterial supply of the nose. H, histamine; MCh, methacholine; SP, substance P; VIP, vasoactive intestinal polypeptide; Adr, adrenaline; PE, phenylephrine; $F_{2\alpha}$, E_1 , E_2 , prostaglandins $F_{2\alpha}$, E and E_2 . Note that drugs have widely different actions on vascular and airflow resistances. From (21).

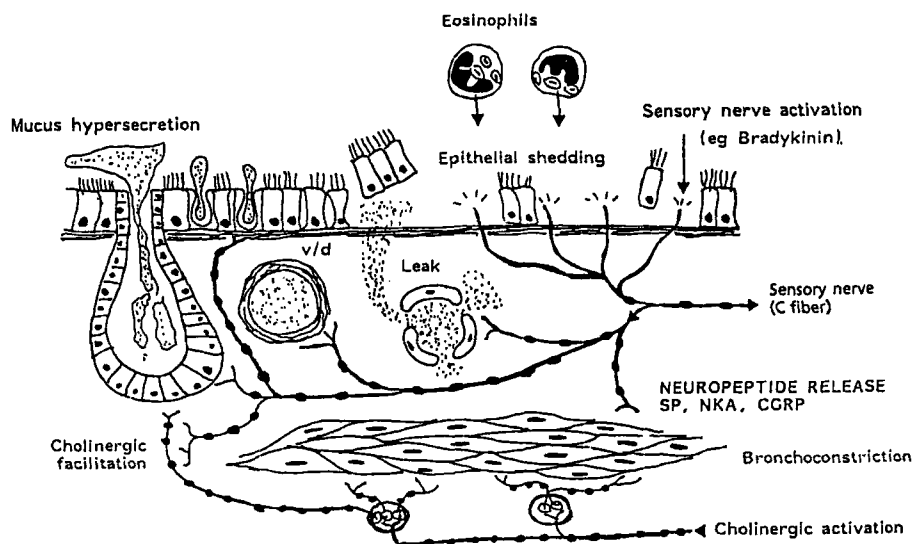


Fig. 6. Possible neurogenic inflammation in asthmatic airways via retrograde release of peptides from sensory nerves via an axon reflex. SP causes vasodilatation, plasma exudation, and mucus secretion, whereas neurokinin A (NKA) causes bronchoconstriction, enhanced cholinergic reflexes, and calcitonin gene-related peptide (CGRP) causes vasodilatation. From (23).

excitants and mediators, including cigarette smoke, capsaicin, histamine, bradykinin and prostaglandins (4, 10, 12, 13, 24, 25). The receptors ramify in the mucosa and when some branches, for example in the epithelium, are activated, action potentials will spread throughout the sensory

receptor complex along all its branches setting up an axon reflex. The branches will release neuropeptides such as SP, neurokinin A and calcitonin gene-related peptide. These mediators will stimulate mucus release from the submucosal glands (26), and also cause vasodilatation and nasal conges-

tion. Thus they presumably dilate resistance arterioles and the capacitance sinuses. The neuropeptides also produce extravasation of plasma from the postcapillary venules, with an increase in interstitial liquid volume or oedema and exudate of plasma-like liquid into the airway lumen (4, 12). This may constitute an important defensive mechanism in the nose.

Conclusions

The nasal vasculature is complex, with components not found in other parts of the respiratory tract. The anatomical connections between these different parts of the vasculature have not been fully determined, but must have an important influence on nasal function. The innervation of the nasal blood vessels includes both sympathetic and parasympathetic components of the autonomic nervous system but these have been studied largely in terms of total nasal blood flow or vascular resistance, and of airflow resistance, and less is known about how they act on different parts of the nasal vasculature. The same consideration applies to many of the studies of mediators. Some can be shown to act strongly on one type of vessel, for example, histamine and SP on postcapillary venules, but even these agents have actions elsewhere. The fact that many inflammatory and neurogenic mediators will be released simultaneously in conditions such as rhinitis vastly complicates the picture when we try to determine relative changes in each of the parts of the nasal vasculature.

References

1. WIDDICOMBE JG. Microvascular anatomy of the airways. In: BUSSE WW, HOLGATE ST, eds. *Asthma and rhinitis*. Boston: Blackwell Scientific Publications, 1995: 722–32.
2. CAUNA N. Blood and nerve supply of the nasal lining. In: PROCTOR DF, ANDERSEN I, eds. *The nose: upper airway physiology and the atmospheric environment*. Amsterdam: Elsevier Biomedical, 1982: 45–69.
3. CAUNA N, HINDERER KH. Fine structure of blood vessels of the human nasal respiratory mucosa. *Ann Otol Rhinol Laryngol* 1969; 78: 865–79.
4. PERSSON CG. Plasma exudation from tracheobronchial microvessels in health and disease; In: BUTLER J, ed. *The bronchial circulation*. New York: Marcel Dekker, 1992: 443–73.
5. WIDDICOMBE JG. Why are the airways so vascular? *Thorax* 1993; 48: 290–5.
6. LAITINEN LA, LAITINEN A. The bronchial circulation. Histology and electron microscopy. In: BUTLER J, ed. *The bronchial circulation*. New York: Marcel Dekker, 1992: 79–98.
7. BARANIUK JN, LUNDGREN JD, OKAYAMA M, GOFF J, MULLOL J, MERIDA M, SHELHAMER JH, KALINER MA. Substance P and neurokinin A in human nasal mucosa. *Am J Respir Cell Mol Biol* 1991; 4: 228–36.
8. WIDDICOMBE JG. Comparison between the vascular beds of upper and lower airways. *Eur Respir J* 1990; 3: 564–71.
9. ECCLES R, BENDE M, WIDDICOMBE JG. Nasal blood vessels. In: MYGIND N, PIPKORN U, eds. *Allergic and vasomotor rhinitis: Pathophysiological aspects*. Copenhagen: Munksgaard, 1987: 63–76.
10. McDONALD DM. The ultrastructure and permeability of tracheobronchial blood vessels in health and disease. *Eur Respir J* 1990; 12 (Suppl): S72S–S85S.
11. McDONALD DM. Neurogenic inflammation in the respiratory tract: Actions of sensory nerve mediators on blood vessels and epithelium of the airway mucosa. *Am Rev Respir Dis* 1987; 136: S65–S71.
12. PERSSON CG. Leakage of macromolecules from the tracheobronchial microcirculation. *Am Rev Respir Dis* 1987; 135: S71–S75.
13. BARNES PJ. Airway NANC nerves and neuropeptides. In: BARNES PJ, RODGER IW, THOMSON NC, eds. *Asthma. Basic mechanisms and clinical management*. London: Academic Press, 1992: 359–89.
14. ÅNGGÅRD A. Capillary and shunt blood flow in the nasal mucosa of the cat. *Acta Otolaryngol (Stockh)* 1974; 78: 418–22.
15. MALM L. Response of resistance and capacitance vessels in feline nasal mucosa to vasoactive agents. *Acta Otolaryngol (Stockh)* 1974; 78: 90–7.
16. COLE P. Upper respiratory airflow. In: PROCTOR DF, ANDERSEN I, eds. *The nose. Upper airway physiology and the atmospheric environment*. Amsterdam: Elsevier Biomedical Press, 1982: 163–89.
17. COLE P. Nasal airflow resistance. In: MATHEW OP, SANT'AMBROGIO G, eds. *Respiratory function of the upper airway*. New York: Marcel Dekker, 1988: 391–414.
18. BARANIUK JN, LUNDGREN JD, GOFF J, MULLOL J, CASTELLINO S, MERIDA M, SHELHAMER JH, KALINER M. Calcitonin gene-related peptide (CGRP) in human nasal mucosa. *Am J Physiol* 1990; 258: L81–L88.
19. ECCLES R. Neurological and pharmacological considerations. In: PROCTOR DF, ANDERSEN I, eds. *The nose: upper airway physiology and the atmospheric environment*. Amsterdam: Elsevier, 1982: 191–214.
20. MYGIND N. *Nasal allergy*. Oxford: Blackwell Scientific Publications, 1978.
21. LUNG MA, PHIPPS RC, WANG JCC, WIDDICOMBE JG. Control of nasal vasculature and airflow resistance in the dog. *J Physiol* 1984; 349: 535–51.
22. BARNES PJ. Airway NANC nerves and neuropeptides. In: BARNES PJ, RODGER IW, THOMSON NC, eds. *Asthma. Basic mechanisms and clinical management*. London: Academic Press, 1992: 359–89.
23. BARNES PJ. Airway neuropeptides. In: BUSSE WW, HOLGATE ST, eds. *Asthma and rhinitis*. Boston: Blackwell Scientific Publications, 1995: 667–85.
24. BARANIUK JN. Neural control of human nasal secretion. *Pulm Pharmacol* 1991; 4: 20–31.