

# Peptide containing nerves in the nasal mucosa

R. Uddman, L. Malm and F. Sundler, Malmö, Sweden

## SUMMARY

*Numerous nerve fibres containing vasoactive intestinal peptide (VIP), substance P (SP) or immunoreactive avian pancreatic polypeptide (APP) occur in the nasal mucosa of several mammals, including man. Generally, the nerve fibres are distributed around small blood vessels and seromucous glands. In addition, SP containing fibres can be seen in the nasal epithelium.*

*The pterygopalatine ganglion contains acetylcholinesterase (AChE) positive nerve cell bodies together with VIP and SP containing ones. After exposure to colchicine it could be shown that the VIP and SP containing nerve cell bodies also were positive for AChE.*

*VIP and SP are potent mediators of atropine resistant vasodilatation in the mucosa. The physiological effects of APP are not known.*

The rapid progress in peptide chemistry, radioimmunology and immunohistochemistry has led to the detection of several different types of peptide containing neuronal systems in both the central and peripheral nervous system (Hökfelt et al., 1980). The findings indicate that the autonomic nervous system is composed not only of adrenergic and cholinergic neurones but also of a variety of peptidergic neurones. In the upper respiratory tract nerves containing vasoactive intestinal peptide (VIP), substance P (SP) or immunoreactive avian pancreatic polypeptide (APP) are fairly numerous.

In the nasal mucosa VIP fibres are mainly found around blood vessels and seromucous glands (Figure 1a) (Uddman et al., 1978; Uddman et al., 1980a). VIP given intraarterially, close to the nose, evokes a dilatation of nasal resistance and capacitance vessels (Malm et al., 1980). Electrical stimulation of the Vidian nerve, within certain frequencies, also evokes a vasodilatation which is atropine resistant. During this electrical stimulation there is a frequency-dependent increase of VIP in nasal venous blood (Uddman et al., 1980b). It is therefore conceivable that VIP acts as a neurotransmitter in the nasal mucosa mediating the wellknown atropine resistant vasodilatation.

Substance P is a peptide with potent vasodilatory and secretory actions. In the nasal mucosa substance P containing nerve fibres surround blood vessels and se-

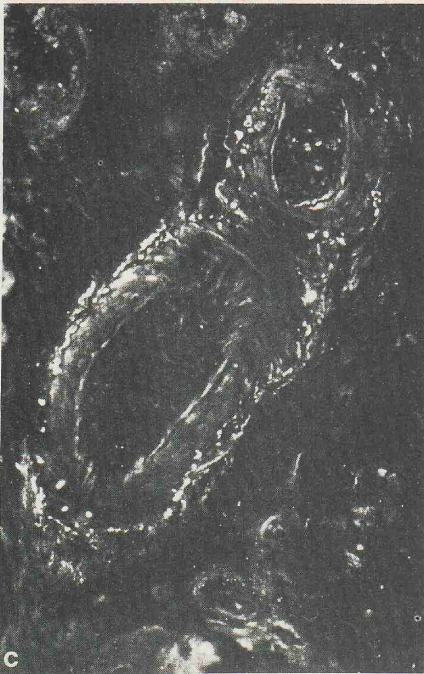
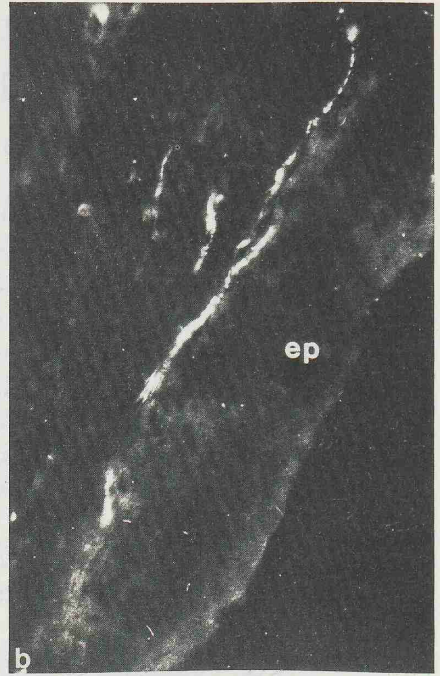


Figure 1. Cat nasal mucosa. a. VIP-immunoreactive nerve fibres are numerous around small blood vessels and glandular acini (X 150). b. SP-immunoreactive nerve fibres in the subepithelial layer of the nasal mucosa. ep = epithelium. (X 300). c. APP-immunoreactive nerve fibres around blood vessels (X 200).

romucous glands. In addition, substance P fibres are seen in the subepithelial layer (Figure 1b) and sometimes within the epithelium. Substance P fibres are numerous in tissues known to receive a heavy sensory innervation such as the skin (Hökfelt et al., 1975) and the tooth pulp (Olgart et al., 1977) and there is some evidence that substance P fibres in such tissues may represent the peripheral ramifications of primary sensory neurones. Although the bulk of SP fibres are located around blood vessels and acini of seromucous glands it is possible that some of the fibres, notably those occurring close to or within the nasal epithelium, may have a sensory function.

In the nasal mucosa numerous nerve fibres containing immunoreactive APP surround blood vessels and seromucous glands (Figure 1c) (Uddman et al., 1980c). So far, the origin of the fibres, the exact chemical structure of this peptide and its physiological effects are unknown.

In the pterygopalatine ganglion there are numerous nerve cell bodies containing acetylcholinesterase. After exposure to colchicine, known to block intraneuronal transport, the number of nerve cell bodies containing acetylcholinesterase increase to the extent that virtually all cell bodies contain demonstrable enzyme activity. By immunohistochemistry it can be shown that the pterygopalatine ganglion also harbours numerous nerve cell bodies containing VIP and a few nerve cell bodies containing substance P (Figure 2) (Uddman, 1980d).

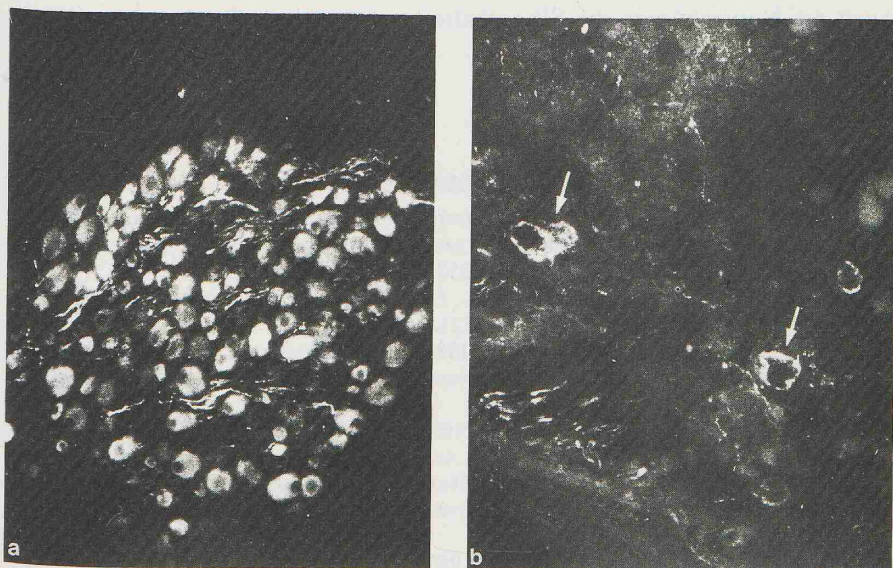


Figure 2. Cat pterygopalatine ganglion 6 h after local application of colchicine. a. Numerous nerve cell bodies displaying VIP immunoreactivity of varying intensity (X 200). b. A few cell bodies display SP immunoreactivity (arrows). Some coarse fibres in the lower left corner (X 300).

Sequential staining reveals that also these nerve cell bodies contain acetylcholinesterase. The findings therefore imply that acetylcholine may coexist with VIP and substance P in a proportion of the neurones and if this coexistence is present also in the nerve terminals, these neurones may operate with more than one transmitter.

#### ZUSAMMENFASSUNG

Nervenfasern, die vasoaktive intestinale Peptide (VIP), Substanz P (SP) oder immunoreaktive avian pankreatische Polypeptide (AAP) enthalten, weisen in der Schleimhaut der Nase von vielen Säugetieren, den Menschen einbegriffen, ein häufiges Vorkommen auf. Gewöhnlich befinden sich die Nervenfasern ringsum kleine Blutgefäße und seromuköse Drüsen. Ausserdem können Fasern, die SP enthalten, in dem Epithel der Nase beobachtet werden.

VIP und SP sind starke Vermittler von atropinresistenter Gefässerweiterung in der Schleimhaut der Nase. Die physiologische Rolle des APP-immunoreaktiven Materials ist nicht bekannt.

In dem Ganglion pterygopalatinum wurden acetylcholinesterase-(AChE-) positive Nervenzellkörper sowie auch solche mit VIP oder SP beobachtet. Auf Einwirkung von Colchicin reagiert das Ganglion mit einer Anreicherung von VIP und AChE in praktisch sämtlichen Zellkörpern, was auf ein gleichzeitiges Vorkommen von Acetylcholin und VIP in manchen Neuronen zurückgeführt werden kann. Auch die Nervenkörper, die SP enthalten, werden nach Colchicineinwirkung AChE-positiv.

#### REFERENCES

1. Hökfelt, T., Kellerth, J. O., Nilsson, G. and Pernow, B., 1975: Experimental immunohistochemical studies on the localisation and distribution of substance P in cat primary sensory neurones, *Brain Res.* 100, 235-252.
2. Hökfelt, T., Johansson, O., Ljungdahl, A., Lundberg, J. M. and Schultzberg, M., 1980: Peptidergic neurons, *Nature*, 284, 515-521.
3. Malm, L., Sundler, F. and Uddman, R., 1980: Effects of vasoactive intestinal polypeptide (VIP) on resistance and capacitance vessels in the nasal mucosa, *Acta Otolaryngol. (Stockh.)*, 90, 304-308.
4. Olgart, L., Gazelius, B., Brodin, E. and Nilsson, G., 1977: Release of substance P-like immunoreactivity from the dental pulp, *Acta Physiol. Scand.* 101, 510-512.
5. Uddman, R., Alumets, J., Densert, O., Håkanson, R. and Sundler, F., 1978: Occurrence and distribution of VIP nerves in the nasal mucosa and tracheobronchial wall, *Acta Otolaryngol. (Stockh.)*, 86, 443-448.
6. Uddman, R., Malm, L. and Sundler, F., 1980a: The origin of vasoactive intestinal polypeptide (VIP) nerves in the feline nasal mucosa, *Acta Otolaryngol.* 89, 152-156.
7. Uddman, R., Malm, L., Fahrenkrug, J. and Sundler, F., 1980b: VIP increases in nasal venous blood after stimulation of the Vidian nerve. *Acta Otolaryngol. (Stockh.)*, 91, 135-138.

8. Uddman, R., Håkanson, R. and Sundler, F., 1980c: Immunoreactive avian pancreatic polypeptide occurs in nerves of the mammalian nasal mucosa and Eustachian tube, *ORL* 42, 242-247.
9. Uddman, R., 1980d: Vasoactive intestinal polypeptide distribution and possible role in the upper respiratory and digestive regions, Thesis.

Rolf Uddman, M.D.  
Lars Malm, M.D.  
Dept. of Otolaryngology  
Malmö General Hospital  
Malmö  
Sweden.

Frank Sundler, M.D.  
Dept. of Histology  
University of Lund  
Lund  
Sweden.