Parasympathetic control of blood circulation and secretion in the nasal mucosa

Anders Änggård, Stockholm, Sweden.

SUMMARY

The effects of selective parasympathetic nerve activation on the secretory response and the vascular exchange and capacitance sections in the cat nasal mucosa were studied. The vascular events were investigated by measuring the local disappearance of ^{125}I- and changes in gross pulse rate from ^{131}I- labelled serum albumin as monitored over the nose. A frequency-dependent increase in nasal secretion and local blood content occurred in the range 0.5-12 imp/sec: an increase in disappearance rate was observed at the same time. This indicates that the vascular and secretory responses are activated simultaneously. The secretory responses, but not the vascular events, were shown to be blocked by atropine. The results thus show that the postganglionic parasympathetic mediator of nasal secretion is cholinergic, whereas the vasodilatation appears to be due to a different mechanism, which is not sensitieve to atropine. The beneficial effect of some antihistamines in vasomotor rhinitis may thus be due to their anticholinergic properties.

RHINOLOGISTS are often confronted by patients suffering from nasal obstruction, rhinorrhea and sneezing in varying combinations. In many of these patients there is no history or demonstrable evidence of allergy to support the diagnosis of an allergic rhinitis. In some cases the symptoms are assumed to result from increased parasympathetic activity to the nasal mucosa and the term "Vasomotor rhinitis" was suggested by Malcomson (1958) to describe this condition. However, it is still not known whether increased parasympathetic activity results in concomitant increases in secretion and nasal obstruction.

Thus it has been suggested that a Vidian neurectomy should be reserved for those cases where watery rhinorrhea is the primary symptom (Goolding-Wood, 1970). However, this operation may be equally successful where nasal obstruction is the dominant feature (Gregson, 1970). As regards the medical treatment of vasomotor rhinitis antihistamines are widely employed. However, their mechanism of action in this disorder is not yet clear. The parasympathetic control of the vascular and aecretory events in the nasal mucosa is therefore of interest from a theoretical as well as from a clinical point of view.

The aim of the present study was to investigate the vascular responses in the

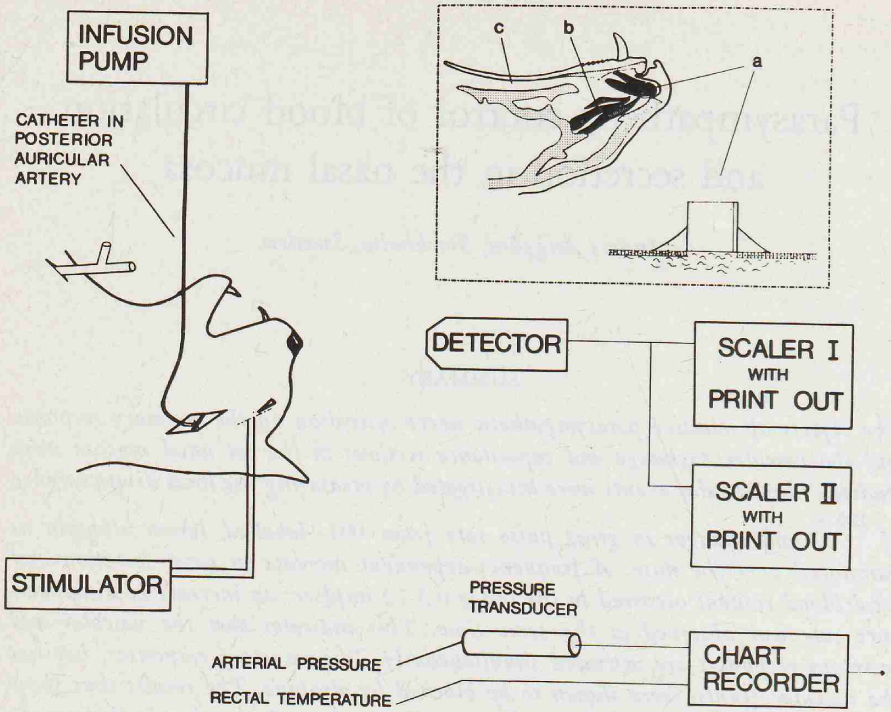

Figure 1. Drawing showing experimental procedure. The lead shields masking the nasal cavities are not shown. Inset represents sagittal section of the head of the cat and the application technique with the polyethylene tube fixed over the de-epithelized area on the inferior concha (a), middle concha (b), nasopharynx (c).

exchange and capacitance vessels of the cat nasal mucosa following selective parasympathetic nerve activation, and to investigate whether a secretory response is accompanied by an increased local blood content of the nasal mucosa.

The frequency response relations for these effects were studied using graded parasympathetic stimulation. A pharmacological analysis of the responses was also made. Parasympathetic stimulation was carried out by stimulating the Vidian nerve with monophasic square wave pulses with a duration of 1 msec and an intensity of 8 V.

A superior cervical ganglionectomy had been performed 1-2 weeks previously and thus the Vidian nerve was purely parasympathetic. The vascular events in the exchange vessels were followed by measuring the disappearance rate of ^{125}-I from a local depot in the nasal mucosa. The epithelium was removed from a small area of the maxilloturbinal mucosa and a small polyethylene tube was applied and fixed over the exposed area with an adhesive (Fig. 1). Thus an open well was created with the subepithelial tissues in the bottom. One hour later the tracer solution was placed in the well. The disappearance of the depot was monitored by

an external scintillation detector connected to two recording channels and secured in a fixed relation to the nose. Radioactivity was counted for periods of 40 sec. The disappearance rate (k-value), which represents the fractional elimination of the depot per minute, was later calculated for each time interval using a computer. Changes in local blood content in the nose were studied separately or simultaneously with the disappearance measurements, by measuring changes in gross pulse rate from intravenously administered I^{131}-labelled serum albumin monitored over the nose. A 5 cm thick lead shield fitting tightly around the head and the nose of the cat had a narrow slit over the right side of the nose and shielded the detector from the rest of the cat. Gross pulse rate from the intravenously administered I^{131}-albumin was measured as described above. When both tracers were used the pulse rates in both recording channels were determined separately. Appropriate corrections were made for the overhearing of I^{131} in the I^{125} channel (for further details see Änggård and Edwall, 1974).

Nasal secretion was estimated by inspection of the well formed by the polyethylene tube and used in the disappearance measurements. Through an operation microscope it was possible to observe the accumulation of secretion and grade it as slight (+), noticeable +, obvious ++ or rich +++.

In a few experiments the secretion was measured quantitatively. In such cases the epithelium in the bottom of the well was not removed, and the volume required to fill the well was measured. The secretion during the stimulation period was then measured in relation to this volume.

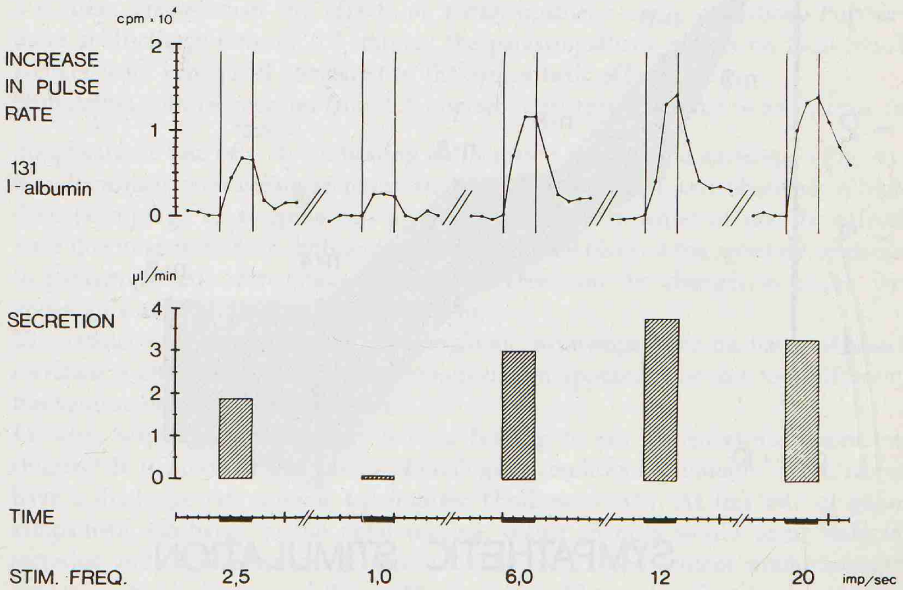

Figure 2. Influence of graded parasympathetic nerve stimulation on the secretory response, and the gross pulse rate of ^{131}I-albumin measured over the right nasal cavity.

RESULTS

Parasympathetic stimulation with frequencies from 0.5 or 1.0 imp/sec regularly resulted in a slight watery secretion (Fig. 2). Above 2.5 imp/sec secretion was very rich. Frequency dependent secretion was seen from 0.5 - 12 imp/sec together with simultaneous increases in local blood volume.

When these effects of parasympathetic stimulation on local blood content are compared with the results obtained in similar experiments where the effects of graded stimulation of the sympathetic fibres were studied (Fig. 3) (Ängqård and Edwall, 1974), the maximal effects following sympathetic nerve stimulation were

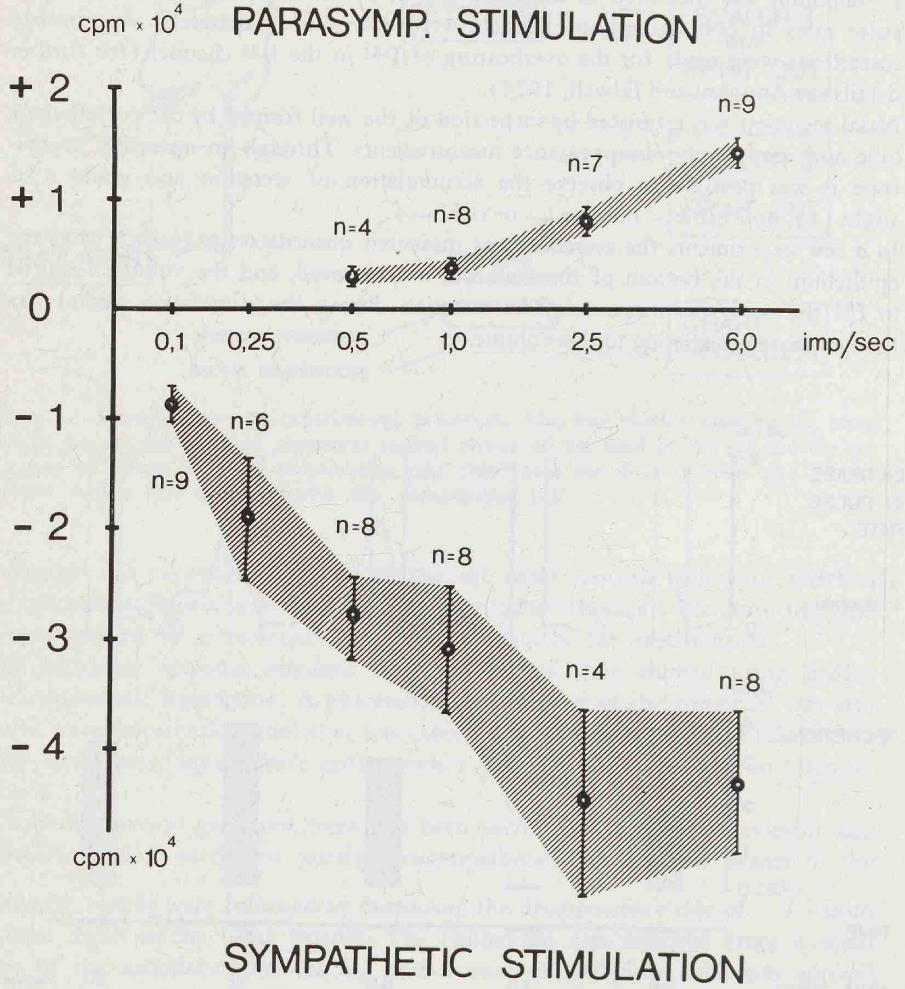

Figure 3. Influence of parasympathetic and sympathetic nerve stimulation on the gross pulse rate of ^{131}I-albumin measured over the right nasal cavity. Mean, S.E.M. and number of observations are shown.

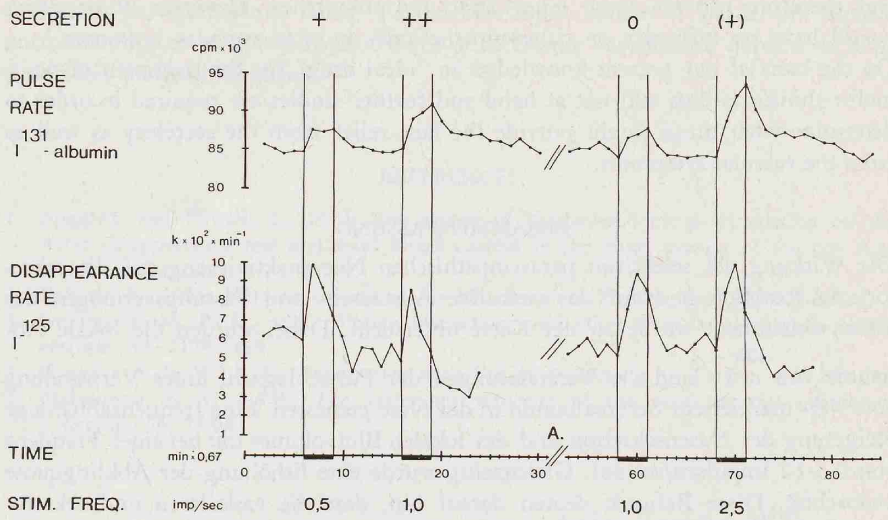

Figure 4. Influence of parasympathetic nerve stimulation on tracer disappearance rate of $^{125}I^-$ and the gross pulse rate of ^{131}I-albumin measured over the right nasal cavity. The secretory response is indicated above the curves. None 0. Slight (+). Noticeable +. Obvious + +. Cat 2.4 kg. (A). Intra-arterial infusion of atropine 1 mg/kg.

3-4 times greater than the effects of parasympathetic nerve activation. Furthermore at discharge rates of 0.5 imp/sec the parasympathetic effects on local blood content were very small compared to the sympathetic effects.

Stimulation with frequencies from 0.5 imp/sec consistently resulted in an increase in disappearance rate of $^{125}I^-$ indicating an increased tissue-blood exchange (Fig. 4). Simultaneously increases in secretion and local blood content were observed. A high dose (1 mg/kg) of atropine was given to investigate whether or not the effects were due to activation of cholinergic fibres. Atropine blocked the secretory response to parasympathetic stimulation, but had no effect on the changes in tracer disappearance rate or on local blood content.

The results thus show that the postganglionic parasympathetic mediator of nasal secretion is cholinergic, whereas the vasodilatation appears to be due to a different mechanism, not sensitive to atropine.

In what way do these findings have a bearing to our patient with vasomotor rhinitis? It is probable that under physiological conditions autonomic nerve fibres have a discharge rate around 1-2 imp/sec (Folkow, 1955). At this rate of parasympathetic discharge to the nasal mucosa, major changes would occur only in secretion and capillary exchange function. The local blood content would increase only to a minor degree and the nasal patency would not therefore be appreciably altered. Of the drugs commonly used to treat vasomotor rhinitis some antihistamines might be expected to block nasal secretion by virtue of their anticholinergic action

and therefore provide some relief from the rhinorrhea. However, these drugs would have no influence on parasympathetically induced vascular responses.
On the basis of our present knowledge an "ideal drug" for the treatment of vasomotor rhinitis is thus still not at hand and further studies are required in order to determine what drugs might provide the best relief from the secretory as well as from the vascular symptoms.

ZUSAMMENFASSUNG

Die Wirkung der selektiven parasympathischen Nervenaktivierung auf die sekretorische Reaktion und auf das vaskuläre Austausch- und Fassungsvermögen der Nasenschleimhaut wurde an der Katze untersucht. Dabei wurden die lokale Abnahme von ^{125}I- und die Veränderungen der Pulsschlagzahl unter Verwendung von ^{131}I- markiertem Serumalbumin in der Nase gemessen. Eine frequenzabhängige Steigerung der Nasensekretion und des lokalen Blutvolumes trat bei einer Frequenz von 0.5-12 Impulsen/sec auf. Gleichzeitig wurde eine Erhöhung der Abklingquote beobachtet. Diese Befunde deuten darauf hin, dass die vaskulären und sekretorischen Reaktionen gleichzeitig aktiviert werden. Die sekretorischen Reaktionen konnten durch Atropin gehemmt werden, nicht jedoch die vaskulären. Die Ergebnisse lassen erkennen, dass der postganglionäre parasympathische Euberträger cholinerg ist, wohingegen die Vasodilatation von einem anderen, durch Atropin nicht beeinflussbaren Mechanismus gesteuert wird. Die günstiger Wirkung einiger Antihistaminika bei der vasomotorischen Rhinitis kann daher möglicherweise auf deren anticholinergischen Eigenschaften beruhen.

RÉSUMÉ

L'auteur a étudié, au niveau de la muqueuse nasale du chat, les effets d'une stimulation élective des fibres nerveuses parasympathiques sur les activités sécrétoire et vasomotrice locales.
L'activité sécrétoire est appréciée grâce à l'observation visuelle sous microscope de la quantité approximative de mucus accumulé dans un tube en polyéthylène dont une section est appliquée contre la muqueuse.
L'activité vasomotrice est explorée par la mesure du degré de résorption d'une petite quantité d'I ^{125} déposée à la surface d'une zone de muqueuse désépithélialisée et par la mesure du volume sanguin estimé au niveau de la muqueuse à l'aide de sérumalbumine marquée à l'I ^{131}, introduite par voie intraveineuse.
L'augmentation de la sécrétion et du volume sanguin contenu dans la muqueuse est observée pour des fréquences de stimulation comprises entre 0,5 et 12 impulsions/seconde. Une augmentation de la capacité de résorption au sein de la muqueuse est observée au même moment.
Ces constatations démontrent que les activités sécrétoire et vasomotrice de la muqueuse nasale sont stimulées simultanément. La réponse sécrétoire est seule inhibée par l'atropine. Les résultats indiquent donc que le médiateur parasympathique postganglionnaire de la sécrétion nasale est de nature cholinergique tandis que la vasodilatation paraît résulter d'un mécanisme différent qui n'est pas

influencé par l'atropine. Ainsi, l'effet bénéfique obtenu à l'aide de certains antihistaminiques au cours du traitement de la rhinite vasomotrice dépend de leurs propriétés anticholinergiques.

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Anders Änggård, M. D.
Department of Otolaryngology
Karolinska Sjukhuset
S-104 01 Stockholm 60
Sweden