Effect of Platelet-Activating Factor (PAF) on Ciliary Activity

Plastic-activating factor (PAF) is a mediator involved in tissue injury in the process of inflammation and allergic responses. PAF is also considered to be involved in ciliary depression in allergic as well as inflammatory disease of the respiratory tract. However, the mechanism by which PAF could contribute to ciliary depression has remained to be documented. This study was designed to experimentally investigate the influence of PAF on the ciliary activity.

Mucosal samples in the maxillary sinus were obtained from 35 guinea pig Chunchon, Korea Department of Otolaryngology, Hallym University Medical College, Chunchon, Korea Yin-Gyo Jung, MD, Suk-Tae Kang, MD, Jeong-Ha Kim, MD, Cheln-Sang Cho, MD and Hyun-Joon Lim, MD

Mucociliary function is important in non-specific defense mechanisms of the nasal airways. It defends the host by sweeping away inhaled particles such as infectious pathogens, dust, allergens, carcinogenic substance, cellular debris, etc. It has been reported that mucociliary function may not work properly when it is damaged by some pathologic conditions and/or several environmental conditions.

This experiment was undertaken for the purpose of finding out the effects of the repeated instillation of nasal drops upon the mucociliary system.

Macrophages are able to produce significant amount of superoxide when stimulated by PAF. Therefore, an inference has been derived from our study that macrophages might play an important role in PAF-induced tissue injury.

Distribution of Substance P Immunoreactive (SP-IR) Nerve fibers in the Airway Submucosal Gland

SP-IR nerve fibers have been found around the airway submucosal glands of several species of experimental animals and humans. But definite site of SP innervation in glands is still unclear.

Immunohistochemistry combined with electron microscopy was employed to investigate the distribution of SP-IR nerve fibers in the tracheal submucosal gland of cats. SP-IR nerve fibers were found to form network around the glands. Numerous varicosities were detected within the basement membrane of the acini and secretory tubules. All the intra-glandular varicosities showed close spatial contact with serous cells, mucous cells and myoepithelial cells. Our findings suggest that SP-induced mucus secretion from tracheal submucosal glands in cats may be caused not only by glandular contractile response of myoepithelial cells but also by direct stimulation to both serous and mucous cells.
Pituitary Adenylyl Cyclase Activating Peptide (PACAP) is a Sensory Neuropeptide in the Respiratory Tract

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Pituitary adenylate cyclase activating peptide (PACAP) is a VIP-like hypothalamic peptide occurring as two variants, PACAP 27 and the C-terminally extended PACAP 38. Immunoreactive PACAP has been demonstrated in the central nervous system as well as in the enteric nervous system and in the respiratory tract. We have examined the possibility that PACAP occurs in the sensory nervous system of the rat. Immunocytochemistry revealed PACAP in numerous nerve fibers in superficial layers of the dorsal horn of the spinal cord, in few scattered nerve cell bodies of small to medium size in spinal and trigeminal ganglia and in nerve fibers running close to and within the surface epithelium in the nose, the skin, the tongue, the lacrimal and the trachea. In these locations most of the PACAP-immunoreactive nerve fibers were identical with fibers storing substance P and/or calcitonin gene-related peptide (CGRP), the PACAP-immunoreactive fibers constituting a subpopulation. Additional PACAP-immunoreactive fibers, not associated with epithelia, seemed to lack SP and CGRP.

Capsaicin treatment reduced the density of PACAP- and CGRP/SP-immunoreactive fibers in the tissues examined. On the whole, the immunocytochemical results agreed with those obtained by radioimmunoassay for PACAP and CGRP. In situ hybridization revealed labeling of a subpopulation of nerve cell bodies in the trigeminal ganglia. In isolated circular segments from the trachea and pulmonary arteries PACAP caused a concentration-dependent relaxation of precontracted segments.

Nitric Oxide Synthase (NOS) in the Nasal Mucosa

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Nitric oxide (NO) has been postulated as a mediator of endothelium-dependent vasodilation and has been put forward as an important, non-adrenergic, non-cholinergic (NANC) inhibitory neurotransmitter. Neuronal NO is synthesized from the amino acid L-arginine by the enzyme NO synthase which several different constitutive and inducible types have been cloned. NO synthesizing neurons may be visualized by immunocytochemistry using antibodies against NO synthase or by NOS mRNA in situ hybridization.

Material and Methods. Cranial ganglia and specimens from the nasal mucosa were fixed by immersion in a cold mixture of formaldehyde and picric acid in phosphate buffer. They were rinsed in phosphate buffer, frozen on dry ice, sectioned and processed for immunocytochemistry of NO synthases or for NOS mRNA in situ hybridization.

Results. NOSM-positive and NOS2-synthesizing immunoreactive nerve cell bodies were Numerous in the sphenopalatine ganglion. In the nasal mucosa NOS-immunoreactive and diaphorase positive nerve fibers were regularly spared. The fibers were numerous around blood vessels, arteries in particular. Double immunostaining revealed that the NOS-immunoreactive nerve cell bodies and nerve fibers constituted a subpopulation of VIP-containing cells.

Several VIP-like peptides have been discovered in the nasal mucosa. Immunocytochemical studies revealed a rich supply of nerve fibers containing VIP/MEC-like immunoreactivity and moderate supplies of nerve fibers containing helospectin/helodemin and pituitary adenylate cyclase immunoreactivity. The present studies suggest that a subpopulation of the VIP-containing fibers contains NOS-like immunoreactivity. VIP has been put forward as an important mediator of NANC relaxation of smooth muscle in the airways. There is recent evidence that a component of the NANC relaxation is mediated by NO.

Analysis of Antigenic Peptide of Japanese Birch Pollen Allergen

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Allergic rhinitis of birch pollen is common around Northern Europe, North America and Hokkaido in Japan. The major antigenic fragment of European birch (Betula verrucosa) pollen allergen, called Bet v 1, was isolated at M.W.17k dalton. An amino acid sequence of Bet v 1 was already identified.

We tried to identify an antigenic peptide of Japanese-birch (Betula platyphylla var. japonica) pollen allergen using the following methods. IgE binding to this allergen examined by Western blotting method showed the strongest response at M.W.17k dalton. This antigenic fragment was digested by trypsin and then purified by reverse phase HPLC. Lymphocyte proliferative responses (LPR) of a pollenosis patient was proved to be positive to definite fractions of peptides. Amino acid sequences of these peptides were determined by a protein sequencer. A peptide synthesized according to the sequence of the peptide revealed positive LPRs on the patients.

The antigenic peptide of Japanese birch pollen was concluded to correspond to 22nd -33rd amino acids from N terminal of Bet v 1 with 31st amino acid .phenylelalanine, being replaced by isoleucine.

Neurotransmitters for goblet cells in rat nasal mucosa studied by video microscopy

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The epithelial goblet cell is one of the important source of nasal secretions. However, there has been few studies on secretagogues for the epithelial goblet cells. At the last ISIAN, we reported substance P and acetylcholin induced exocytosis in nasal goblet cells. In the present study, we examined the effects of several neuropeptides on exocytosis in those cells.

We employed the video-enhanced differential interference contrast microscopy at a very high magnification(12.000X) to observe secretory responses of the epithelial goblet cells in rat nasal septum mucosa in vitro. Under a differential interference contrast microscope, we can observe the exocytic response of the secretory granules as an abrupt change in brightness of individual granules. We used this optical change as an indication of secretion and examined the capability of neuropeptides (NKA, vasoactive intestinal peptide (VIP), and calcitonin gene-related peptide (CGRP) as secretagogues for goblet cells.

NKA and VIP evidently increased the frequency of exocytosis at 1μM. The responsiveness to 1μM CGRP was not convincingly established. We concluded that NKA and VIP play the role of neurotransmitters for the epithelial goblet cells of rat nasal mucosa.