Gustatory rhinitis: A syndrome of food-induced rhinorrhea

Gordon Raphael, MD, Mindy Hauptschein Raphael, MS, RD, and Michael Kaliner, MD *Bethesda, Md.*

The consumption of certain foods causes watery rhinorrhea (gustatory rhinitis) in many individuals. To examine the underlying mechanisms responsible for this common phenomenon, 12 subjects ingested control foods and positive foods (foods that cause rhinorrhea). Nasal lavages performed 10 minutes after each food challenge were analyzed for albumin and total protein. Positive food challenge, but not control food challenge, induced rhinorrhea in all subjects. Positive food challenge increased albumin (7.8 ± 1.9 to 24.5 ± 7.6 mg/L; $p < 0.025$) and total protein (79 ± 9 to 258 ± 41 mg/L; $p < 0.001$) without altering the ratio of albumin to total protein (albumin percent). Nasal pretreatment with atropine clinically blocked the positive food-induced rhinorrhea and significantly inhibited secretion of both albumin and total protein, again without affecting the albumin percent. Thus, gustatory rhinitis is produced by spicy foods that stimulate atropine-inhibitable muscarinic receptors (probably on submucosal glands), and the syndrome can be treated prophylactically by use of topical atropine. (J ALLERGY CLIN IMMUNOL 1989;83:110-5.)

Food reactions are frequent complaints and often reflect responses that are nonimmunologic in nature. Such reactions may be classified as adverse reactions or intolerances to food.[1] The literature cites IgE-mediated food allergy as one cause of rhinitis[2-6]; however, rhinitis occurs only rarely as an isolated manifestation of food allergy.[1, 7-11]

In contrast to food allergy, there are stimuli or situations that reliably cause rhinitis, including allergic rhinitis caused by inhalant allergens, upper respiratory tract infections, exposure to cold air,[12] assuming the recumbent position,[13] recovering from performing vigorous exercise,[14, 15] and inhaling irritating or noxious gases, dusts, or fumes.[16] In addition, another situation exists that commonly produces rhinorrhea but has received little attention. This syndrome involves the profuse watery rhinorrhea that develops after eating certain foods and is generally unaccompanied by sneezing, congestion, or pruritus. The purpose of this article is to define the phenomenon of food-induced rhinorrhea (gustatory rhinitis), to suggest the pathogenic mechanism involved, and to present evidence that topical atropine will prevent this reaction.

From the Allergic Diseases Section, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md.

Received for publication Jan. 25, 1988.
Accepted for publication June 19, 1988.

Reprint request: Gordon D. Raphael, MD, National Institute of Allergy and Infectious Diseases, Bldg. 10, 11C207, 9000 Rockville Pike, Bethesda, MD 20892.

MATERIAL AND METHODS

Sixty adult subjects were asked to complete a questionnaire about food-related rhinitis symptoms. Seven female and five male subjects between the ages of 21 and 45 years were selected from this group and had food and nasal challenges after informed consent was obtained. No subjects were studied within 3 weeks of recovery from an upper respiratory tract infection, and none of the subjects complained of nasal symptoms at the time of study. No subject took medication (except for regular insulin and thyroid replacement in two subjects) for at least 48 hours before challenge. Atopic subjects were defined as having seasonal symptoms of rhinitis and/or asthma and were skin prick-test positive to relevant aeroallergens. Atopic subjects were studied outside the allergy season when they were asymptomatic. Nonatopic subjects had no allergy symptoms (other than gustatory rhinitis) and were negative to skin tests. Subjects were skin tested to the foods that were implicated by history as provoking gustatory rhinitis.

Food questionnaire

A questionnaire was developed to determine the prevalence of rhinorrhea produced by the consumption of foods and/or beverages. The questionnaire consisted of 127 items that were divided into several broad categories: meats, milk and milk products, fruits and juices, breads and grains, vegetables, fats, nuts and seeds, desserts, spices, and miscellaneous. Responders indicated the frequency with which each item produced rhinorrhea on a scale of 1 (nose never runs), 2 (nose runs sometimes), or 3 (nose runs always).

TABLE I. Foods that produce gustatory rhinitis

Food	Average score	Nose runs sometimes (%) (2)*	Nose runs always (%) (3)*
Hot chili peppers	1.91	36	27
Spicy foods	1.83	63	10
Horseradish	1.80	41	20
Hot and sour soup	1.64	29	18
Red cayenne pepper	1.60	38	11
Tabasco sauce	1.55	36	9
Black pepper	1.46	38	4
Onion	1.29	12	8
Vinegar	1.29	29	0
Mustard	1.21	13	4

*Percent of total population who scored this result.

Reagents

Nasal-challenge solutions consisted of normal saline (0.9% sodium chloride solution, Abbott Laboratories, Chicago, Ill.) and atropine sulfate (Muro Pharmaceutical, Inc., Tewksbury, Mass.).

Foods were commercially obtained or occasionally provided by subjects. Control foods were foods that historically produced no symptoms on ingestion, whereas positive foods were foods that by history reliably caused rhinorrhea. Food skin test materials (food extracts, histamine, and glycerol saline) were obtained from the Extract Laboratory at Walter Reed Army Medical Center (Washington, D.C.).

Challenge methods

Subjects were seated comfortably in an upright position. A soft 8F rubber catheter was atraumatically inserted along the floor of the right nasal cavity and was connected to suction to collect nasal secretions and lavage fluid. In each experiment, four prewashes with normal saline (4 ml each) were performed at 1-minute intervals in order to remove preexisting nasal secretions. A hand-held nebulizer was used to deliver nasal prewashes, saline challenges, atropine treatments, and nasal lavages, and these were applied to the right nasal cavity only. The fourth prewash was collected and served as the baseline. Samples were kept on ice until the end of the experiment at which point they were stored at −70° C for subsequent analysis.

Protocols

Two protocols were used in this study. In the first protocol, subjects had a control nasal challenge with normal saline (0.3 ml), and then, at 10-minute intervals, they ate a control food followed by a positive food. In the second protocol, subjects had the same control food and positive food challenges, the nasal mucosa was treated with 100 μg of atropine (0.3 ml), and the positive food challenge was again repeated. Each nasal challenge, atropine treatment, or food challenge was performed at 10-minute intervals followed by a 4 ml nasal lavage.

Assays

Total protein. Protein in each sample was measured according to the method of Lowry et al.[17] All protein values are expressed in milligrams per liter.

Albumin. Albumin was measured by a specific, competitive ELISA. Human serum albumin (Sigma Chemical Co., St. Louis, Mo.), 0.005 mg/0.1 ml in 0.1 mmol/L of carbonate buffer, pH 9.6, was plated overnight at 4° C in polypropylene microtiter plates. The wells were blocked for 30 minutes at 23° C with goat serum (Gibco Laboratories, Grand Island, N.Y.), diluted 1% in a buffer containing phosphate-buffered saline and 0.05% Tween 80 (Fisher Scientific Co., Fairlawn, N.J.). Standards or samples (0.05 ml) were then added to 0.05 ml of goat antihuman serum albumin-horseradish peroxidase conjugate (Cappel Worthington Biochemicals, Malvern, Pa.), diluted 1/1000 in phosphate-buffered saline with 0.05% Tween 80, and incubated at 23° C for 90 minutes. The plates were developed with an o-phenylenediamine dihydrochloride substrate (Sigma Chemical Co.) and read at 490 nm. The assay range was between 1 to 100 mg/L.

Albumin percent. The albumin percent is calculated by dividing the albumin concentration by the total protein and multiplying by 100%.

Histamine assay. Histamine was measured by a single isotope radioenzyme assay according to the method described by Shaff and Beaven[18] and modified by Dyer et al.[19] The sensitivity of this assay was <1.0 μg/L.

All assay results are recorded as means ± SEM.

Statistics

Student's *t* test for paired sample analysis and Fisher's exact test were used for statistical comparisons.

RESULTS

Food questionnaire

The food questionnaire was distributed to 60 adults (36 female and 24 male subjects) between the ages of 21 and 68 years (median age, 34 years). Approximately 99% of all items on the questionnaires were

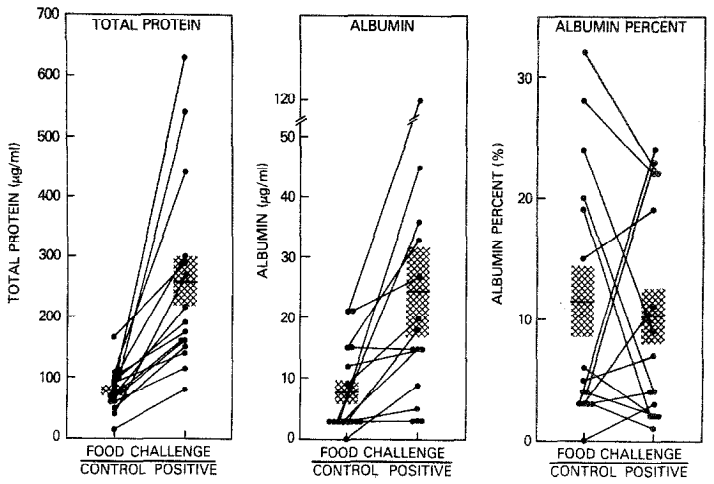

FIG. 1. Total protein, albumin, and the ratio of albumin to total protein (albumin percent) in nasal lavages collected 10 minutes after control food challenge and positive food challenge (n = 15). The means ± SEM are depicted by the *horizontal lines* within the *hatched bars*. Positive food challenge produced significant increases in total protein ($p < 0.005$) and albumin ($p < 0.025$) but not albumin percent.

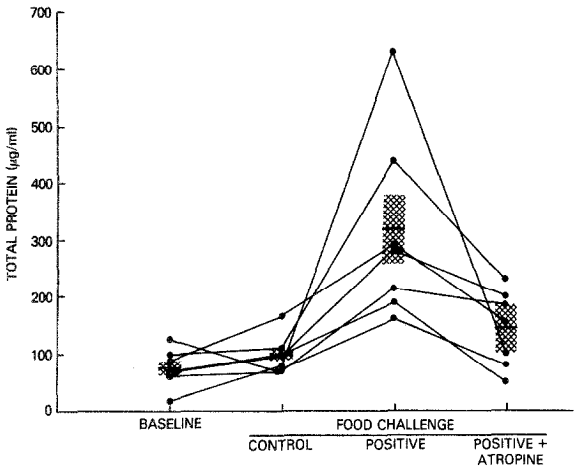

FIG. 2. The effect of atropine on total protein secretion in nasal lavages after food challenge (n = 7). Subjects ingested a control food, a positive food, and then repeated the positive food 10 minutes after topical nasal atropine treatment. The mean ± SEM are depicted by *horizontal lines* within the *hatched bars*. Baseline measurements are obtained from the fourth nasal prewash before the oral food challenges.

completed. Many of the food items (51/127) received scores of 1 (nose never runs). Of the remaining items, most received some scores of 2 and rare scores of 3 (nose runs always). The average scores were heavily weighted toward a score of 1 because most subjects indicated that foods did not generally produce rhinorrhea.

Several food items, however, clearly produced rhinorrhea in this population, and these are listed in Table I. Hot chili peppers, with an average score of 1.91, most frequently caused rhinorrhea (in >60% of all responders). Note that other high-scoring food items, such as spicy foods, red (cayenne) pepper, and tabasco sauce, may share a common component with hot chili peppers.

Nasal and food challenges

Twelve subjects (seven female and five male subjects) participated in nasal and food challenges. The group included six atopic subjects, five nonatopic subjects, and one subject with vasomotor rhinitis. Each subject indicated that the consumption of at least one food item reliably produced rhinorrhea without any other symptoms suggestive of food allergy (such as nasal pruritus or sneezing; anosmia; swelling or pruritus of the lips, tongue, or oropharynx; gastrointestinal symptoms, including nausea, vomiting, or diarrhea; urticaria; or respiratory symptoms). All subjects were skin test negative to the foods used in the food challenges.

Fifteen subjects had a control food challenge with wheat crackers, potato chips, pretzels, hot tea, or gefilte fish balls, followed by a positive food challenge with hot chili peppers, horseradish, or hot and sour soup. Subjects were instructed to maximize exposure of the food within the mouth rather than quickly swallow it.

Control food challenge did not produce any subjective symptoms or clinical signs. Positive food challenge, in contrast, produced bilateral rhinorrhea in all subjects (Table II). There were no complaints of nasal or oropharyngeal pruritus, the urge to sneeze, lip

TABLE II. Symptoms after food challenge

Symptoms	No. of positive/total (%)		
	Control food challenge	Positive food challenge	Positive food challenge after atropine
Rhinorrhea on right	0/15 (0)	15/15 (100)	0/7 (0)*
Rhinorrhea on left	0/15 (0)	15/15 (100)	4/7 (57)
Facial flush	0/15 (0)	10/15 (67)	3/7 (43)
Nasal congestion	0/15 (0)	4/15 (27)	2/7 (29)
Tearing	0/15 (0)	4/15 (27)	0/7 (0)
Perspiration	0/15 (0)	1/15 (7)	1/7 (14)

*Decrease significant at $p < 0.002$.

TABLE III. Nasal lavage net total protein* after repetitive positive food challenge

Subject	Positive food challenge No. 1 (mg/L)	Positive food challenge No. 2 (mg/L)
D. M.	85	465
R. J.	100	160
F. Y.	360	600
D. M.	320	690
Mean ± SEM	216 ± 72	479 ± 115†

*Net total protein is calculated by subtracting baseline protein from the protein in the positive food challenge samples.
†Increase is significant at a $p < 0.05$.

swelling, gastrointestinal symptoms, or pulmonary symptoms throughout the study. Facial flushing developed in about half the subjects but was unassociated with a change in pulse (68 ± 2 beats/min before and 69 ± 2 beats/min after challenge). Postchallenge nasal examination invariably revealed watery secretions with variable amounts of mucus. Mild mucosal edema (on the side containing the nasal catheter) was noted in a few subjects.

Saline challenge in eight subjects resulted in 72.5 ± 13.8 mg/L of protein, whereas control food challenge failed to significantly affect the measurement (61.3 ± 9.0 mg/L). The effect of control food challenge and positive food challenge on nasal protein, albumin, and albumin percent are illustrated in Fig. 1. Positive food challenge significantly increased the total protein in every subject, increasing from a mean of 79 ± 9 mg/L to 258 ± 41 mg/L ($p < 0.005$). The albumin concentration likewise increased from 7.8 ± 1.9 mg/L to 24.5 ± 7.6 mg/L ($p < 0.025$). In contrast, the albumin percent, which represents the ratio of albumin to total protein, decreased from 11.5 ± 2.9% to 10.3 ± 2.3% and was therefore virtually unchanged from control food challenge values.

Previous studies have indicated that muscarinic stimulation with topical methacholine induces nasal secretions that contain proportional increases in both albumin and protein, whereas histamine stimulation elicits secretions that are disproportionately enriched in albumin.[20] Since food-induced secretions corresponded closely to the secretory pattern of cholinergically induced secretions, the effect of topical atropine on gustatory rhinitis was examined. Seven subjects received control food challenges, positive food challenges, and then repeat positive food challenges after receiving topical nasal atropine treatment (Fig. 2). Nasal lavages after control food challenge contained 98.6 ± 11.5 mg/L of protein, whereas positive food challenge dramatically increased the protein to a level of 317.9 ± 58.1 mg/L ($p < 0.001$). Atropine pretreatment reduced this response to 142.8 ± 23.6 mg/L ($p < 0.025$ as compared to no atropine treatment). Atropine also significantly reduced food-induced albumin secretion from 19.1 ± 5.4 mg/L before treatment to 6.7 ± 2.7 mg/L after treatment ($p < 0.05$). The albumin percent, however, was unchanged by atropine treatment and remained at control levels.

To ascertain if two repeated challenges with a pos-

TABLE IV. Histamine (microgram per liter ± SEM) in nasal lavages after food challenge in 15 subjects

Baseline	Control FC	Positive FC	Positive FC after atropine
1.4 ± 0.6	2.5 ± 1.2*	3.4 ± 1.6*	3.6 ± 3.6*

FC, Food challenge.
*No significant difference from baseline.

itive food was capable of eliciting continuous nasal secretion, four subjects had successive challenges with positive foods (Table III). In each instance, both the first and second positive food challenges elicited increased nasal protein secretion compared to baseline. Indeed, in every instance, the second challenge elicited more protein secretion than did the first ($p < 0.05$). Therefore, the ability of atropine to decrease secretion after the second positive food challenge indicates a specific response to muscarinic blockade.

In addition to these laboratory parameters, topical atropine symptomatically eliminated the rhinorrhea on the treated side of the nose (right side). However, atropine did not significantly block rhinorrhea on the contralateral side, facial flushing, congestion, or perspiration (Table II). Atropine treatment, which does not affect baseline protein secretion when it is used by itself, did not produce any adverse symptoms (dry mouth, blurred vision, or difficulty with urination).

Histamine was measured in nasal lavages to explore the possibility that mast cell degranulation may cause or be associated with gustatory rhinitis. Baseline histamine levels were 1.4 ± 0.6 μg/L in 15 subjects. Control food challenge, positive food challenge, and positive food challenge after atropine treatment all failed to cause significant elevations in histamine levels (Table IV), suggesting that gustatory rhinitis does not involve mast cell degranulation.

When data from the experiments above were analyzed by subgroups based on gender or atopic status, no significant differences in clinical symptoms or laboratory parameters were uncovered. It was therefore concluded that gustatory rhinitis does not have a predilection for either atopic individuals or for either sex.

DISCUSSION

Ingestion of hot, spicy foods elicits rhinorrhea caused by stimulation of atropine-inhibitable muscarinic receptors. This phenomenon has been termed "gustatory rhinitis." Gustatory rhinitis is a common phenomenon characterized by the acute onset of watery (and sometimes mucoid) rhinorrhea, precipitated by the ingestion of certain foods. Although most foods do not cause gustatory rhinitis, it is clear that certain foods produce this condition in a large portion of the population.

Gustatory rhinitis differs from allergic rhinitis in several important respects. Symptoms invariably begin within a very few minutes of eating the involved food, and last only as long as the food is eaten. Subjects with gustatory rhinitis do not complain about nasal or oropharyngeal pruritus, even though the food may actually cause a burning sensation in the mouth. In addition, they do not complain about nasal congestion, the urge to sneeze, or conjunctival itching, all of which are characteristic of allergic rhinitis. And finally, skin tests with extracts of implicated foods are consistently negative in subjects with gustatory rhinitis.

Control food challenge produced neither clinical symptoms nor nasal secretions during the study. In contrast, positive food challenge reproducibly produced nasal secretions containing increased protein and albumin, but without changing the albumin percent. This observation suggests that gustatory stimulation induces nasal secretions containing albumin and protein in the same proportion as exists under basal conditions and that increased vascular permeability therefore does not account for the increased proteins. It should be further noted that in addition to subjects complaining of gustatory rhinitis, subjects who deny gustatory rhinitis symptoms also experience the same increases in rhinorrhea and protein secretion after challenge. Preliminary data in subjects with negative histories demonstrated that total protein in nasal lavages increased from 65 ± 15 to 315 ± 38 mg/L after strong gustatory stimuli, results similar to those reported in this article.

It has previously been demonstrated that methacholine nasal challenge stimulates proportional increases in both protein and albumin secretion without changing the overall albumin percent.[20] Prior treatment with atropine blocks methacholine-induced protein and albumin secretion without altering the albumin percent. Both of these results suggest that cho-

linergic stimulation causes secretion of albumin and nonalbumin proteins and that the source of these proteins is glandular.[21] In this study, gustatory stimulation caused secretions resembling secretions induced by methacholine stimulation. The similarity is further supported by the capacity of atropine to suppress both stimuli. These data therefore suggest that gustatory stimulation provokes a muscarinically mediated secretion of glandular proteins that can be inhibited by atropine.

Three lines of evidence indicate that gustatory rhinitis does not involve nasal mast cells or their mediators. (1) The symptoms elicited do not resemble mast cell-related rhinitis symptoms. (2) Atropine prevents the gustatory response but fails to affect histamine-induced rhinorrhea. (3) No increase in nasal histamine can be detected. Thus, it is very unlikely that gustatory stimulation provokes mast cell-mediator release.

The following sequence of events may explain the syndrome of gustatory rhinitis. Certain foods, particularly spicy "hot" foods, contain chemicals (such as capsaicin) that stimulate afferent sensory nerves in the mucosa of the mouth and oropharynx by interacting with chemical or irritant receptors or by eliciting the release of neuropeptides from sensory nerves.[22] A neural reflex arc is initiated that stimulates atropine-inhibitable parasympathetic efferent nerves supplying the nasal mucosa and glands, producing nasal secretion and congestion; the lacrimal glands in the eyes, producing tears; the sweat glands on the head and forehead, producing perspiration; and the vasculature of the head and neck, causing a facial flush.

In subjects who are particularly sensitive to gustatory stimuli and who have suffered from the embarrassment of gustatory rhinitis, there are now two options. They can avoid the provocative foods or they can apply topical nasal atropine prophylactically (once it becomes available). Thus, for people with a passion for spicy foods, there may soon be an effective therapy that will allow them to eat to their heart's (and nose's) content.

REFERENCES

1. American Academy of Allergy and Immunology Committee of Adverse Reactions to Foods. Adverse reactions to foods. Bethesda, Md.: National Institute of Allergy and Infectious Diseases, 1984:52-5. (DHEW publication no. (NIH) 84-2442).
2. Eriksson NE. Food sensitivity reported by patients with asthma and hay fever. Allergy 1978;33:189-96.
3. Ogle KA, Bullock JD. Children with allergic rhinitis and/or bronchial asthma treated with elimination diet. Ann Allergy 1977;39:8-11.
4. Ogle KA, Bullock JD. Children with allergic rhinitis and/or bronchial asthma treated with elimination diet: a five-year follow-up. Ann Allergy 1980;44:273-8.
5. Businco L, Benincori N, Cantani A. The spectrum of food allergy in infancy and childhood. Ann Allergy 1986;57: 213-8.
6. Heiner DC. Food allergy and respiratory disease. Ann Allergy 1983;51:273-4.
7. May CD. Objective clinical and laboratory studies of immediate hypersensitivity reactions to food in asthmatic children. J ALLERGY CLIN IMMUNOL 1976;58:500-15.
8. Hannuksela M, Lahti A. Immediate reactions to fruits and vegetables. Contact Dermatitis 1977;3:79-84.
9. Bock SA, Lee W-Y, Remigio LK, May CD. Studies of hypersensitivity reactions to foods in infants and children. J ALLERGY CLIN IMMUNOL 1978;62:327-34.
10. Bock SA. Adverse reactions to milk from first to 3 years of age [Abstract]. J ALLERGY CLIN IMMUNOL 1987;79:138.
11. Atkins FM, Steinberg SS, Metcalfe DD. Evaluation of immediate adverse reactions to food in adult patient I. Correlation of demographic, laboratory, and prick skin test data with response to controlled oral food challenge. J ALLERGY CLIN IMMUNOL 1985;75:348-55.
12. Togias AG, Naclerio RM, Proud D, et al. Nasal challenge with cold, dry air results in the release of inflammatory mediators: possible mast cell involvement. J Clin Invest 1985;76:1375-81.
13. Cole P, Haight SJ. Posture and nasal patency. Am Rev Respir Dis 1984;129:351-4.
14. Olson LG, Strohl KP. The response of the nasal airway to exercise. Am Rev Respir Dis 1987;135:356-9.
15. Syabbalo AK, Bundgaard A, Widdicombe JG. Effects of exercise on nasal airflow resistance in healthy subjects and in patients with asthma and rhinitis. Bull Eur Physiopathol Respir 1985;21:507-13.
16. Patow CA, Kaliner M. Nasal and cardiopulmonary reflexes. Ear Nose Throat 1984;63:78-81.
17. Lowry OL, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin-phenol reagent. J Biol Chem 1951;193:265-75.
18. Shaff RE, Beaven MA. Increased sensitivity of the enzymatic isotopic assay of histamine: measurement of histamine in plasma and serum. Anal Biochem 1979;94:425-30.
19. Dyer J, Warren K, Merlin S, Metcalfe DD, Kaliner M. Measurement of plasma histamine: description of an improved method and normal values. J ALLERGY CLIN IMMUNOL 1982; 70:82-7.
20. Raphael GD, Druce HM, Wright RH, Kaliner MA. Analysis of nasal mucous membrane vascular permeability. J ALLERGY CLIN IMMUNOL 1986;77:239.
21. Widdicombe JC, Wells UM. Airway secretions. In: Proctor G, Anderson A, eds. The nose: upper airway physiology and the atmospheric environment. Amsterdam: Elsevier Biomedical, 1982:215-44.
22. Lundblad L, Saria A, Lundberg JM, Anggard A. Increased vascular permeability in rat nasal mucosa induced by substance P and stimulation of capsaicin-sensitive trigeminal neurons. Acta Otolaryngol (Stockh) 1983;96:479-84.