

Facial thermography during nasal provocation tests with histamine and allergen

Seppey M, Hessler C, Bruchez M, Savary M, Pécoud A. Facial thermography during nasal provocation tests with histamine and allergen. Allergy 1993; 48: 314–318. © Munksgaard 1993.

Changes of skin temperature (T°) of the nose area during nasal provocation tests with histamine and allergen were followed by means of an infrared thermography camera. By a colimator system in which temperatures measured on a given surface can be integrated and averaged, thermography allows the continuous and quantitative recording of the temperature during the whole procedure in a completely noninvasive way. In 10 normal subjects, increasing doses of histamine induced a dose-dependent rise of the nose external temperature. No significant change was observed with the vehicle solution. In six subjects allergic to grass pollen, the nebulization of increasing concentrations of a pollen extract induced a dose-dependent rise in T° . The T° rise observed after histamine or allergen corresponded to a marked nasal obstruction. The nebulization of the highest dose of the pollen extract did not induce any T° rise in six nonallergic subjects. The continuous recording of the skin temperature by a noninvasive method might yield additional information on the vascular changes rapidly occurring during nasal challenges.

M. Seppey¹, C. Hessler², M. Bruchez¹,
M. Savary³, A. Pécoud¹

Divisions of ¹Immunology and Clinical Allergy,
²Radiology and ³Ear, Nose and Throat, Centre
Hospitalier Universitaire Vaudois, CH-1011
Lausanne, Switzerland

Key words: allergen; histamine; nasal
provocation test; thermography; vascular
response.

Prof. A. Pécoud
Policlinique Médicale Universitaire
19, Rue César-Roux
CH-1005 Lausanne
Switzerland

Accepted for publication 28 September 1992

Nasal provocation tests (NPTs) with allergens are increasingly used in experimental allergy: compared with bronchial challenges, they are less troublesome for patients, and mediators and cells taking part in the allergic reaction can be harvested more easily. The nasal congestion which results in nasal obstruction is a clinically important component of the response to histamine or allergen. Since it is somehow related to the nasal mucosal blood flow (NMBF), much effort has been made to quantify the modifications of the NMBF during provocation tests with histamine or allergens (5). The different methods of determining NMBF have resulted in conflicting results: for instance, NMBF after a challenge with allergen has been found to be increased by the laser Doppler velocimetry technique and decreased by the Xenon washout technique (8, 12).

The blood flow through an organ is a major contribution to the thermal state of that organ. Moreover, the heat loss of any organ is particularly dependent on the blood passing through it, i.e. on the local vasomotor state. This thermal exchange can be measured on the skin by infrared thermography. By this method, we have recorded continuously the skin temperature of the face after NPT. The aim of this preliminary study was to define a noninvasive, specific, and accurate method of investigation of nasal vascular response to various stimuli.

Material and methods

Patients and subjects

A total of 22 subjects entered the study. A) Ten healthy, normal, nonatopic volunteers (10 men, mean age 31, range 24–49) underwent NPT with histamine; the rhinoscopic examination was normal in all of them, and none had taken any medication for several weeks before NPT. B) Six subjects (four men, two women, mean age 32, range 26–37) with a history of hay fever caused by hypersensitivity to grass pollen (positive history and skin prick tests) underwent NPT with an extract of grass pollen; NPT was performed in winter, i.e. at a time when the subjects had no nasal obstruction or other symptoms and did not take any medication. C) Six subjects (three men, three women, mean age 29, range 21–40) were selected as nonallergic controls to undergo NPT with allergen (grass pollen): none had suffered from hay fever and all had negative skin tests for grass pollen. All patients and volunteers gave written consent. The study was approved by the ethics committee of the local hospital.

Thermography

The thermography camera (AGA Thermovision® 680, Lidingö, Sweden) is placed at a distance of 1 m

from the subject's face, continuously recording the infrared radiations emitted by the face. Before use, the system is calibrated by means of an infrared reference source, heated to a given temperature (AGA model 22) and placed near the subject's face. This provides a constant reference temperature and allows the conversion of colorimetric data into temperature degrees. To quantify the results, one aims a surface integrator (rectangular colimator) at the central part of the face; the temperatures recorded within the surface of the rectangle are averaged and transmitted for continuous recording to an on-line computer (Radiometer Servograph, Pen Drive RE A 310, Copenhagen, Denmark).

All NPTs with thermographic recording were performed in a specially air-conditioned room with strictly controlled temperature (20°C) and relative humidity (50%). An effort was made to keep the air movement of the room as small as possible. The patient was kept still, resting comfortably in an arm-chair with a headrest.

Provoking agents

Histamine chloride was used at increasing concentrations (0.03, 0.06, 0.12, 0.50, 1.00, 2.00, and 2.50 mg/ml), diluted in normal saline. The allergen extract was a mixture of four grass pollens ("four grass mix", Pharmedal, Pharmacia, Uppsala, Sweden), commercially available under the form of a lyophilized extract which was reconstituted the day of the NPT in a diluent containing 4 mg/ml phenol and 0.3 mg/ml human albumin. The allergen extract was administered at increasing concentrations from 10^2 to 10^5 biologic units/ml (BU/ml). Histamine and allergens were nebulized into the nose by a disposable metered-dose nebulizer, calibrated to deliver $100 \pm 10 \mu\text{l}$ per puff. All solutions (diluent and provoking agents) were preheated at 30°C before nebulization.

NPT procedure

Before NPT, subjects rested in the air-conditioned room for 30 min to achieve a steady skin temperature. The nasal patency was estimated by the technique of the Nasal Inspiratory Peak Flow Rate (NIPFR) (Clement Clark, London, UK) (25). This method, which was preferred to rhinomanometry because of the latter's methodological drawbacks (interference with skin temperature recording), is suitable for objective measurement of nasal patency (7). Subjects were asked to breathe through the nose as long as possible. Mouth breathing occurred, of course, when complete nasal obstruction was present.

After the base-line temperature was recorded,

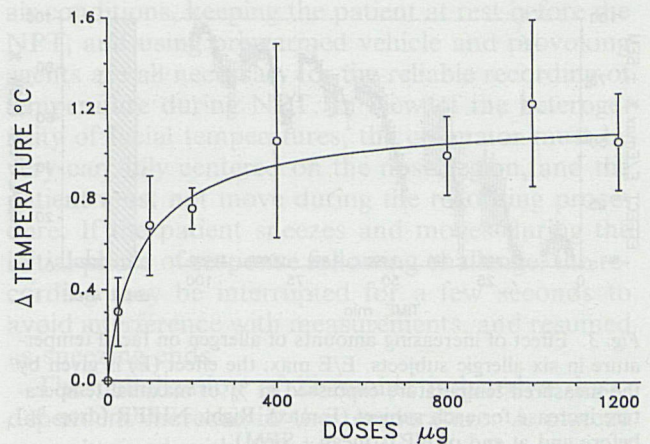


Fig. 1. Effect of increasing doses of histamine on facial temperature; mean $\pm$ SEM of 10 subjects.

400 μl of the vehicle solution (diluent) was nebulized into the nose, equally divided into both nostrils (two puffs per nostril). Continuous thermographic recording started immediately thereafter. After 15 min, the first concentration of histamine (or allergen) was nebulized in the same way, followed every 15 min by increasing concentrations of the provoking agent. Throughout the NPT, no measurement of the NIPFR could be made because of the interference between the pressure on the skin caused by the face mask and the thermographic image; therefore, NIPFR was determined at the end of the NPT, i.e. when the subject complained of a blocked nose. NIPFR drop was defined for a patient as a percentage fall from the formula: $\text{NIPF postchallenge} / \text{NIPF prechallenge} \times 100 (\%)$. In another series of experiments, a single dose of 400 μg histamine was nebulized in order to follow the time course of the temperature changes.

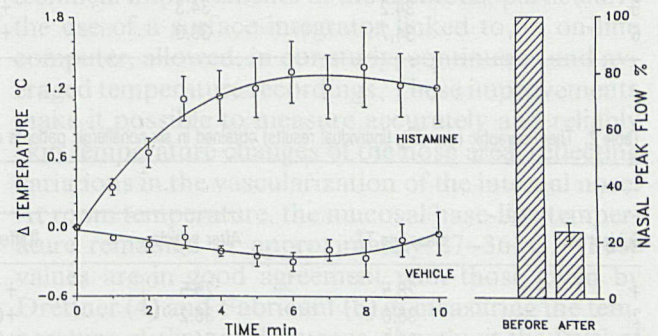


Fig. 2. Effect of 400 μg histamine (upper curve) and of the vehicle solution (lower curve) on facial temperature (mean $\pm$ SEM of 10 subjects). Right: NIPFR (drop %) before and after challenge (mean $\pm$ SEM).

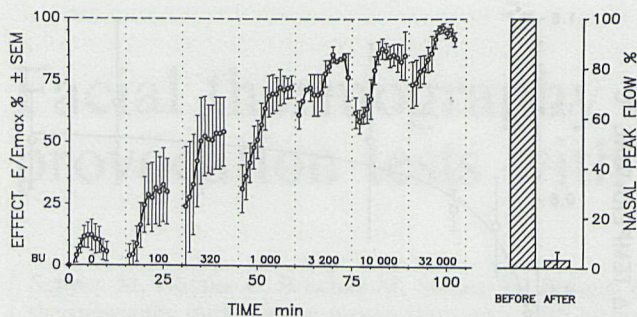


Fig. 3. Effect of increasing amounts of allergen on facial temperature in six allergic subjects. E/E max: the effect (E) is given by the measured temperature expressed in % of maximal temperature increase for each subject (E max). Right: NIPFR (drop %) before and at end of NPT (mean $\pm$ SEM).

Results

NPT with histamine

Increasing amounts of histamine nebulized in 10 normal subjects showed a clear dose-response curve with a maximum effect in all at the dose of 400 μ g histamine (Fig. 1). The time course of the temperature rise, following one single dose of 400 μ g (maximal dose) in the same subjects, in another experiment, peaked at 6 min (Fig. 2). No subject showed any significant rise in temperature following challenge with the vehicle solution (internal control) (Fig. 2). The nebulization of 400 μ g of histamine was followed by a marked nasal obstruction (75% drop in the NIPFR).

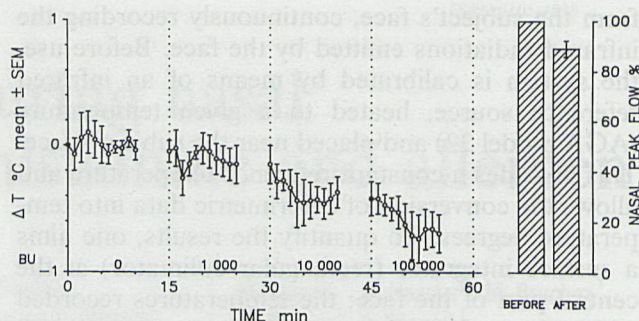


Fig. 4. Effect of increasing amounts of allergen on facial temperature in six nonallergic subjects. Right: NIPFR drop % before and at end of challenge (mean $\pm$ SEM).

NPT with allergen

When we challenged patients allergic to grass pollen with increasing concentrations of this allergen, the continuous recording of the skin showed a rise of temperature (Fig. 3). The time course of the reaction is plotted with the stepwise increase of the allergen concentrations. After challenge, the mean fall of NIPFR was 95% in correlation with the skin temperature rise. The individual base-line temperatures and the highest temperatures recorded after allergen nebulization are shown in Table 1; a rise in temperature was observed in all six patients, the two patients with the lowest base-line temperatures showing the highest increases.

In order to test the specificity of the effect induced by the allergen, six nonallergic subjects underwent a

Table 1. Thermographic recording (individual results) in six patients allergic to grass pollen and challenged with this allergen

Subject No.	Base-line T°	Maximal T° measured			
		After vehicle	(Difference)	After allergen	(Conc.) (Difference)
1	28.2	28.7	+0.5	33.3	(10 000 BU) +5.1
2	26.9	26.9	0.0	33.5	(32 000 BU) +8.6
3	33.0	33.7	+0.7	34.8	(10 000 BU) +1.8
4	34.3	34.5	+0.2	35.2	(1000 BU) +0.9
5	34.2	34.3	+0.1	35.1	(32 000 BU) +0.9
6	34.7	35.0	+0.3	36.6	(32 000 BU) +1.9

Table 2. Thermographic recording (individual results) obtained in six nonallergic patients challenged with a grass pollen extract

Subject No.	Base-line T°	Maximal or minimal T° measured			
		After vehicle	(Difference)	After allergen	(Conc.) (Difference)
1	28.5	29.5	+1.0	27.4	(100 000 BU) -1.1
2	36.0	36.2	+0.2	35.8	(100 000 BU) -0.2
3	34.0	34.1	+0.1	33.2	(100 000 BU) -0.8
4	34.1	34.1	0.0	33.0	(100 000 BU) -1.1
5	33.2	33.4	+0.2	32.4	(100 000 BU) -0.8
6	33.4	33.5	+0.1	32.0	(100 000 BU) -1.4

similar NPT with the same extract of grass pollen (Table 2, Fig. 4). There was a tendency for the temperature to decrease during the procedure. No significant drop in the NIPFR was measured after the highest concentration of allergen.

The symptoms induced by NPT with histamine or allergen were limited to the nose, lasted less than 2 h, and did not require any medication. No bleeding was reported.

Discussion

Thermographic recording of skin temperature is used for the routine diagnosis of skin and breast tumors and for angiologic investigations (15, 24). The camera records the infrared radiation emitted by the skin, which is directly proportional to the skin temperature. Skin temperature depends on two groups of factors, namely internal and ambient factors (10, 11, 15, 17, 24). The environmental settings of our measurement being virtually constant, the changes of temperature recorded were therefore due only to internal factors.

Heat production by the skin depends on several factors, i.e. skin metabolism, local perspiration, arterial blood temperature, tissue conduction, and blood convection. The first three factors mentioned are of virtually no importance in our study: in a temperate room with no air movement, heat loss by perspiration is constant, as is local arterial blood temperature, and does not contribute to heat changes. Similarly, skin metabolism produces only a small amount of heat and does not vary.

Thus, the skin temperature gradient appears to vary mostly according to tissue conduction and blood convection. In tissue conduction, the skin temperature is influenced by a heat transfer from the underlying organs, and thus depends on the thermal conductivity of the subcutaneous tissues. This phenomenon is widely used to detect breast cancer by infrared thermography.

Blood convection is the other chief factor of skin temperature change. It reflects the direct vascular heat transfer to the skin from an internal structure; in our study, the target organ, the internal nose. The heat transfer of any organ is then particularly dependent on the amount of the blood passing through it, i.e. on the local vasomotor state.

There is great heterogeneity in the temperatures measured on the face. The coldest part is the nasal pyramid because of its constant cooling by breathing air at room temperature; the warmest is found at the internal angle of the eyes where the blood vessels are close to the surface (21). Because of the rapidly occurring changes in face temperature, it is crucial to standardize the test conditions as much as possible: working in a room with strictly controlled

air conditions, keeping the patient at rest before the NPT, and using prewarmed vehicle and provoking agents are all necessary for the reliable recording of temperature during NPT. In view of the heterogeneity of facial temperatures, the colimator must be very carefully centered on the nose region, and the patient must not move during the recording procedure. If the patient sneezes and moves during the initial phase of response following challenge, the recording may be interrupted for a few seconds to avoid interference with measurements, and resumed as sneezing ends.

The nebulization of histamine induced a dose-dependent increase in the temperature. A plateau was obtained with 400 µg, a dose on the order of magnitude of the estimated histamine content in nasal mast cells and basophils (18). In many other studies, this dose has been shown to induce marked nasal congestion (2, 3, 16, 20, 23). In the present study, this dose also induced a marked degree of nasal obstruction, as determined by the NIPFR. The temperature increase was clearly related to histamine since the vehicle solution did not induce any change in the temperature.

A similar increase in temperature was obtained in the six allergic patients challenged by an allergen extract. The increase in temperature was also dose-dependent, and NPT resulted in a complete nasal obstruction, as determined by NIPFR. The increase in temperature was specific to the allergic reaction since a slight but significant decrease in the nasal temperature was recorded in nonallergic subjects challenged with the same pollen extract. This effect was probably due to the repeated nebulization (four times) of the allergen extract which was prewarmed at 30°C only. No obstruction was measured in the nonallergic subjects.

Our results extend preliminary data obtained by Phipatanakul et al. (19) and Kus et al. (14). In these studies, the recording of the skin temperature during NPT had also shown an increase in temperature after histamine and allergen challenges. However, technical improvements in the methods, particularly the use of a surface integrator linked to an on-line computer, allowed, in our study, continuous and averaged temperature recordings. These improvements make it possible to measure accurately and reliably skin temperature changes of the nose area, reflecting variations in the vascularization of the internal nose. At room temperature, the mucosal base-line temperature remained at approximately 27–36°C. These values are in good agreement with those given by Drettner (4) and Fabricant (6) in measuring the temperature of the nasal mucosa directly at the level of the inferior turbinate.

In vasomotor and allergic rhinitis, nasal blockage is one of the main symptoms. Major pathophysio-

logic changes occur in the blood vessels as venocongestion of the sinusoids and mucosal edema. Several methods have been used to measure blood flow after nasal challenge (1, 8, 9, 12, 13, 22), but the results are inconsistent and somewhat conflicting. Thus, the different components of the vascular response have not yet been clarified, and further research is necessary.

The rapidity of the temperature changes observed during NPT (less than 2 min after utilization of histamine) suggests that variation in NMBF is a key factor in skin temperature.

Thermography reflects the overall response of the NMBF, by a noninvasive method. In addition, the continuous and dynamic follow-up of the modifications occurring during NPT should avoid the potential bias of a single measurement at a given time of the reaction. Thus, thermography may provide information on the nasal vascular response, helping us to understand the pathophysiologic mechanism. Further studies are in progress, aiming at a better characterization of the thermogenic response observed during NPT.

References

1. BENDE M, ELNER A, OHLIN P. The effect of provoked allergic reaction and histamine on nasal mucosal blood flow in humans. *Acta Otolaryngol* 1984; 97: 99-104.
2. CORRADO OJ, GOULD CAL, KASSAB JY, DAVIES RJ. Nasal response of rhinitic and non-rhinitic subjects to histamine and methacholine: a comparative study. *Thorax* 1986; 41: 863-8.
3. CORRADO OJ, OLLIER S, PHILLIPS MJ, THOMAS JM, DAVIES RJ. Histamine and allergen induced changes in nasal airways resistance measured by anterior rhinomanometry: reproducibility of the technique and the effect of topically administered antihistaminic and anti-allergic drugs. *Br J Clin Pharmacol* 1987; 24: 283-92.
4. DRETTNER B. Vascular reactions of the human nasal mucosa on exposure to cold. *Acta Otolaryngol* 1961; Suppl. 166: 35-40.
5. DRUCE HM. Measurement of nasal mucosal blood flow. *J Allergy Clin Immunol* 1988; 81: 505-8.
6. FABRICANT ND. The topical temperature of clinically normal nasal and pharyngeal mucous membranes. *Arch Otolaryngol* 1957; 66: 275.
7. GLEESON MJ, YOULTEN LJF, SHELTON DM, SIDLAK MZ, EISER NM, WENGRAF CL. Assessment of nasal airway patency: a comparison of four methods. *Clin Otolaryngol* 1986; 11: 99-107.
8. HOLMBERG K, BAKE B, PIPKORN U. Nasal mucosal blood flow after intranasal allergen challenge. *J Allergy Clin Immunol* 1988; 81: 541-7.
9. HOLMBERG K, BAKE B, PIPKORN U. Mucosal blood flow in the human nose following local challenge with histamine. *Allergy* 1989; 44: 45-51.
10. HOUDAS Y, VAN DEN BUSSCHE F, DELVOYE AM. Les facteurs de la température cutanée: application aux explorations thermographiques. Paris: La Nouvelle Presse Médicale, 1975; 4: 38-47.
11. HOUDAS Y, RING EJF. Human body temperature. Its measurement and regulation. New York: Plenum Press, 1982: 59-77.
12. JULIUSSON S, BENDE M. Allergic reaction of the human nasal mucosa studied with laser Doppler flowmetry. *Clin Allergy* 1987; 17: 301-5.
13. KONNO A, TOGAWA K, NISHIHARA S. Participation of vascular reflex in mucosal swelling in nasal allergy. *Acta Otolaryngol* 1982; 94: 131-40.
14. KUS J, KRAKOWKA P. The effectiveness of nasal provocation tests for the diagnosis of atopic bronchial asthma. *Allergol Immunopathol* 1983; 11: 233-41.
15. LAWSON RN. Thermography: a new tool in the investigation of breast cancer. *Can Serv Med* 1957; 13: 517-18.
16. MYGIND N, SECHER C, KIRKEGAARD J. Role of histamine and antihistamines in the nose. *Eur J Respir Dis* 1983; 64: 16-20.
17. NORMELL LA. Recording of normal and impaired cutaneous thermoregulatory vasomotor responses by infra-red thermography: a methodological study. *Scand J Clin Lab Invest* 1974; Suppl. 138: 3-24.
18. OHTSUKA H, OKUDA M. Important factors in the nasal manifestation of allergy. *Arch Otorhinolaryngol* 1981; 233: 227-35.
19. PHIPATANAKUL CS, SLAVIN RG. Use of thermography in clinical allergy. *J Allergy Clin Immunol* 1972; 50: 264-75.
20. SECHER C, KIRKEGAARD J, BORUM P, MAANSSON A, OSTERHAMMEL P, MYGIND N. Significance of H₁ and H₂ receptors in the human nose; rationale for topical use of combined antihistamine preparations. *J Allergy Clin Immunol* 1982; 70: 211-18.
21. SEPPEY M, PÉCOUD A. Can thermography be used in nasal provocation tests? *ACI News* 1990; 2: 16-17.
22. TANIMOTO H, OKUDA M, YAGI T, OHTSUKA H. Measurement of the blood flow of the nasal mucosa by the hydrogen clearance method. *Rhinology* 1983; 21: 59-65.
23. TONNESEN P, MYGIND N. Nasal challenge with serotonin and histamine in normal persons. *Allergy* 1985; 40: 350-3.
24. WINSOR T, WINSOR D. The noninvasive laboratory - history and future of thermography. *Angiology* 1985; 2: 341-53.
25. YOULTEN LJF. Nasal airway patency measurement in the assessment of rhinitis therapy. *Arb Paul Ehrlich Inst Bundesamt. Sera Impfstoffe Frankf A M* 1983; 78: 111-13.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.