

was made to establish which drug class, whether pyrazolones or NSAID, caused the first intolerance episode in these subjects. Patients from this group were used as controls.

ASA was challenged in a single-blind, placebo-controlled fashion (4); the following doses were given 1 h apart: day 1: 50 mg, 125 mg; day 2: 250 mg, 500 mg.

Placebo was given first in each session. Patients were controlled for at least 1 h after the last provocative dose and were newly seen on day 3 in order to detect possible late reactions. Patients gave informed written consent before each challenge session. All subjects who tolerated ASA were strongly recommended to contact us as soon as possible in the case of subsequent NSAID-induced adverse reactions.

Some 3/46 (6%) patients had U/A reactions after ASA administration; all reactions took place on day 1 after the 50- or the 125-mg dose, and were easily controlled by conventional therapy. All positive patients had a clinical history of U/A caused by pyrazolones administration (3/34, 9%); by contrast, ASA was tolerated in all patients with a history of SJS or anaphylaxis reactions ($n=12$).

In the control population, the first adverse reaction was induced by NSAID other than pyrazolones in 34 (87%) cases and by pyrazolones in five (13%) cases. In the remaining six cases, it was not possible to ascertain the causative agent of the first adverse reaction. To date, no patient who tolerated ASA on placebo-controlled challenge has contacted us to report NSAID intolerance.

The present study confirms that most patients with clinical history of adverse skin reactions induced by pyrazolones can take ASA and other NSAID safely (1). However, both the prospective and the retrospective parts of this study show that in about 10% of these patients, particularly those who experienced U/A reactions, pyrazolone intolerance reactions represent the first episode of more general NSAID intolerance. A simple SBPCDC with ASA may prevent potentially severe adverse reactions in these cases; such a test should be recommended in all patients with a history of pyrazolones-induced urticaria.

About 10% of patients with skin reactions to pyrazolones develop general NSAID hypersensitivity.

Key words: adverse reactions; aspirin; NSAID; pyrazolones.

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Pollen exposure and sensitization

SEVERAL pieces of evidence from the literature support the hypothesis that sensitization to aeroallergens depends upon allergen exposure. Following the same track, we compared skin reactivity and prevalence of allergic symptoms in 933 school-children living at high altitude or at sea level in two medium-sized towns. The same team of field-workers performed skin tests at both locations. As expected, due to low mite-allergen exposure, the percentage of children sensitized to mites was much lower in those living at high altitude, especially in children born there (1). Surprisingly, the percentage of children sensitized to grass and mugwort pollens was much higher at high altitude than at sea level. The percentage of skin sensitivity to grass pollen was equal to 21.7% in children born and living at high altitude, whereas it was equal to only 8.5% in children living at sea level. Figures for mugwort sensitivity were 7.6% and 1.0%, respectively. We wondered whether the higher prevalence of sensitization to pollen at high altitude was related to a higher exposure to pollens.

■ Thus, we compared pollen counts in both settings. Pollen grains were trapped with a Burkart apparatus located either in Briançon (French Alps, altitude: 1350 m) or Martigues (near Marseille, southeastern

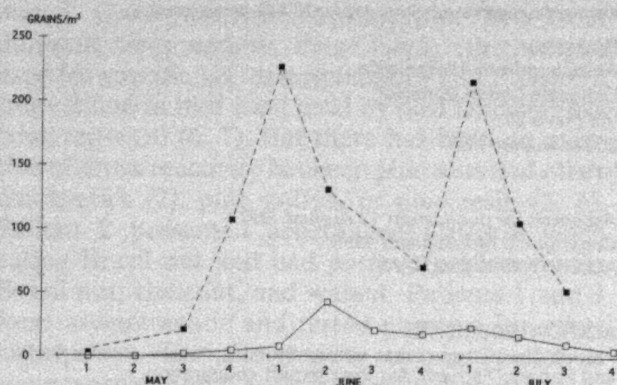


FIGURE 1 Grass pollen counts performed in spring, expressed in number of pollen grains per cubic meter and per week. Solid line and blank squares correspond to counts performed in Briançon (high altitude); dashed line and dark squares to counts performed in Martigues (sea level).

France at sea level). In both locations, the apparatus was placed in town, on the roof of the hospital, at a similar distance from a reliable source of pollens. The apparatuses were calibrated in order to provide the same suction flows. Pollen counts were performed by the same technician, in a blind manner. Results were expressed as number of pollen grains per cubic meter and per week. Comparative pollen counts were performed during only one season.

■ Figs. 1 and 2 display pollen counts measured at both locations. Note that the ordinate scale is different. Cumulated grass pollen counts were much higher in Martigues (sea level) than in Briançon (high altitude). The opposite result was found for mugwort pollen, but counts were much lower than for grass pollens.

The difference in sensitization rate to mugwort is in keeping with differences in pollen counts. In contrast, sensitization to grass pollens was much higher at high altitude despite lower pollen counts. Several hypotheses can be put forward to explain this discrepancy:

- 5) *Difference in sampling techniques.* However, sampling was in the same conditions. Besides, the fact that grass pollen counts were higher at sea level and mugwort pollen counts higher at high altitude does not favor this hypothesis.
- 2) *Difference in reading slides.* Readings were performed in a blind manner by the same investigator.

If we admit that the difference in pollen counts is genuine, there are several hypotheses to explain the discrepancy between grass pollen counts and grass sensitivity:

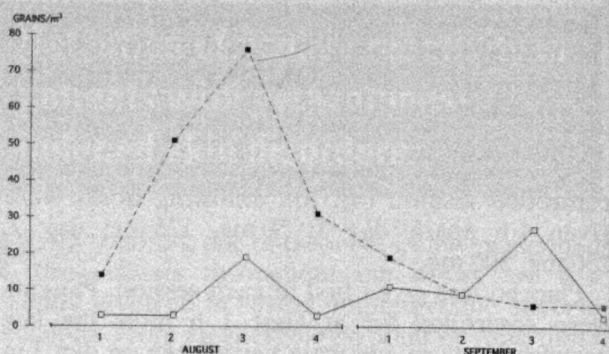


FIGURE 2 Mugwort pollen counts performed in autumn in same locations. Solid line corresponds to counts performed in Martigues (sea level); dashed line to counts performed in Briançon (high altitude).

- 1) Children at high altitude may spend more time outdoors, especially in summertime, and thus have a higher cumulative exposure to pollens.
- 2) In atopic-prone subjects, sensitization could occur according to which allergen is available in the environment. Atopic children living at high altitude cannot become sensitized to house-dust mites because they are very few. Thus, they may be more sensitive to other available allergens. Cvitanović et al. also demonstrated in the Split area (Croatia) an inverse relationship between risk of sensitization to *Parietaria* pollens on one hand, and to house-dust mites on the other hand (2).
- 3) Pollen at high altitude might not carry the same allergenic load as pollen at sea level. Conceivably, pollen at high altitude, because of large and rapid changes in temperature or because of exposure to ozone, may have a higher antigenic content.

Discrepancy was found between sensitization to pollens in schoolchildren living in two communities and pollen counts.

Indeed, it has recently been shown (3) that pollens exposed to pollutants, ozone among others, release more proteins and that ozone-exposed pollen induced greater *in vitro* histamine release from basophils of patients sensitized to this pollen. However, mean air pollutants levels were significantly higher in the coastal city (Martigues) for each of the three gaseous pollutants measured on a routine basis; i.e., SO₂, NO₂, and O₃.

This discussion outlines the need to evaluate both the number of airborne pollens and their

allergenic load in order to perform meaningful comparisons.

Key words: allergy; environment; pollen; sensitization.

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Allergic contact dermatitis to phenylephrine

PHENYLEPHRINE eye-drops are frequently used in ophthalmology as mydriatic agents to obtain maximum pupillary dilation for diagnostic or therapeutic purposes. Phenylephrine is a sympathomimetic drug which mainly stimulates α -adrenergic receptors. Because of its vasoconstrictive effect, it is also used in nasal decongestants, and in otologic and other topical preparations to increase the local activity of topical anesthetic and anti-inflammatory agents. Local complications, such as conjunctival irritation or release of iris pigment into the anterior chamber and corneal edema (1), or systemic side-effects, such as hypertensive crisis from phenylephrine, are rare (2). We report a case of allergic contact dermatitis to phenylephrine contained in eye-drops.

A 69-year-old man regularly developed acute periorbital dermatitis and conjunctivitis after

treatment with multiple ophthalmic preparations for eye diagnostics such as fundoscopic examina-

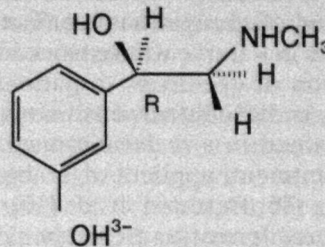


FIGURE 1 Structural formula of (R)-phenylephrine.

tion. He was referred for allergologic investigations. Patch tests were performed with Finn Chambers applied to the patient's back fixed with Fixomull elastic tape (Beiersdorf, Hamburg, Germany). The test included the European Standard series, the drug series, the disinfection and preservative series, ointment bases and emulsifiers, and the series of dental materials. The materials were obtained from Hermal (Reinbek/Hamburg, Germany). In addition, a battery of the patient's own various eye-drops (Novesin[®], Mydriaticum[®], Phenylephrin[®], Methocel[®], and Cyclogyl[®]) was tested (Table 1).

The test patches were removed after 48 h, and readings were performed at 48 and 72 h, according to the recommendations of the ICDRG (International Contact Dermatitis Research Group). The patch tests to Phényléphrine eye-drops (5%) used by the patient were positive (++) on intact skin and strongly positive (+++++) on stripped skin. Patch tests to the other series were negative with the exception of a positive (++) response to the preservative Quaternium-15, a formaldehyde-donating biocide. However, the manufacturer of Phenylephrin 5 "Blache"[®] (Novopharma) confirmed to us that this product does not contain Quaternium-15.

Table 1. Patch test results with the patient's own eye-drops

	Patch test results	
	48 h	72 h
Novesin [®] (0.4%)	Negative	Negative
Mydriaticum [®] (Tropacamide 0.5%)	Negative	Negative
Phenylephrin [®] (Blache 5%)	++	++
Methocel [®] (2%)	Negative	Negative
Cyclogyl [®] (1%)	Negative	Negative

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