

Sensitization to propolis in 1255 children undergoing patch testing

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To investigate the frequency and the features of contact sensitization to propolis in children, we patch tested 1255 consecutive children suspected of allergic contact dermatitis with propolis 20% petrolatum over an 8-year period (1995–2002). Positive responses were observed in 5.9% of patch-tested subjects, with a significantly higher frequency in boys than in girls. The dermatitis was localized mainly on the face, hands and limbs. A significant linear increase in the annual frequency of propolis allergy was noted. Confirming literature data, a significant association with balsam of Peru sensitivity was present in children reacting to propolis, linked to the presence of common constituents in the 2 substances. In conclusion, based on our data, we suggest that propolis should not be used in topical products for children because of its high sensitization rate at the paediatric age.

Key words: allergic contact dermatitis; children; patch tests; propolis. © Blackwell Munksgaard, 2004.

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Propolis or bee-glue is a compound with adhesive properties used by bees to seal hive walls and strengthen the borders of the combs as well as the hive entrance. The major source of propolis is the resinous exudates of poplar buds collected by bees. Although its composition changes according to place and time of collection, it normally consists of 30% wax, 55% resins and balsams, 10% essential oils and 5% pollen plus cinnamic alcohol and flavonoids (1–5). By gas chromatography/mass spectrometry, more than 180 propolis constituents have been identified: free aromatic acids (e.g. benzoic, caffeic, cinnamic, coumaric and ferulic acid), benzyl, methylbutenyl, phenylethyl, cinnamyl and other esters of these acids, flavonoids, chalcones and dihydrochalcones, terpenoids, sugars, ketones and alcohols (6). The esters of caffeic acid (phenylethyl caffeate and methylbutenyl caffeate) showed strong sensitizing properties in patients as well as in guinea-pig experiments (1, 6–8). However, other constituents too (e.g. isoferulates, flavonoid aglycones and free aromatic acids) may play a role in propolis allergy, depending on their varying amount in different samples.

Propolis' sensitizing properties explain the numerous reports of allergic contact dermatitis (1, 2, 7, 9–21). Propolis is known as an occupational contact allergen mainly in beekeepers, but also in musicians and manufacturers of stringed musical instruments (1, 10, 14, 16–19). However, most cases of propolis allergy are not occupational (1, 7, 9, 10, 12, 13, 20, 21). This compound is widely used in folk medicine and in the biocosmetic industry for its antiseptic, antimycotic, bacteriostatic, astringent, choleric, spasmolytic, anti-inflammatory and anaesthetic properties. It is marketed in tablets, powders, lotions, ointments, solutions, creams, toothpaste, chewing gum, etc. The increase in contact allergy to propolis over the last 2 decades is due to its rising use in biopharmaceutical and biocosmetic preparations, because natural products are in fashion today. Moreover, they are regarded as harmless, bland and free of side-effects and therefore suitable for children. However, literature data about propolis allergy in the paediatric age are scarce so far (15, 22–24). The aim of this study was to investigate the frequency and the clinical aspects of contact sensitization to propolis in children.

Patients and Methods

From January 1995 to December 2002, a total of 1255 consecutive patients aged 7 months to 12 years, with suspected allergic contact dermatitis, underwent patch tests with our paediatric series of 30 allergens including propolis 20% petrolatum (pet.) (23). The patient population comprised 583 boys and 672 girls. In 442 children, atopic dermatitis (AD) was diagnosed according to the criteria of Hanifin and Rajka. The patch test material, provided by FIRMA (Firenze, Italy), was applied to the healthy skin of the back with Finn Chambers® on Scanpor tape (Epitest, Tuusula, Finland) for 3 days (25). Patch test reactions were evaluated 0.5–3 hr after removal, according to International Contact Dermatitis Research Group guidelines (26).

Statistical analyses were performed using an SPSS (release 10.0 for Windows, SPSS, Chicago, IL, USA) software package. The χ^2 test was used to compare the frequency of positive results in different patient subgroups (male versus female and propolis-positive children versus propolis-negative ones). The χ^2 test was also used to assess a possible time trend in propolis reactivity. A *P* value <0.05 was considered statistically significant.

Results

Of the 1255 children undergoing patch testing, 74 (5.9%) showed positive reactions to propolis, 4 doubtful erythematous responses and 1177 were negative (Table 1). Their mean age ($\pm$ SD) was 5.4 ($\pm$ 2.8) years. They were 46 boys and 28 girls. The frequency of propolis sensitization was significantly higher in boys than in girls (7.9% versus 4.2%). Among propolis-positive patients, 29 (39%) were affected by AD. 18 (24%) children were sensitized to propolis alone, whereas the remaining 56 (76%) showed positive responses also to other haptens of our paediatric series. Among propolis-sensitive children, 9.5% reacted to balsam of Peru (Myroxylon pereirae resin), whereas only 1.8% of propolis-negative subjects showed positive responses to it. This difference was statistically significant. On the contrary, no significant differences in the frequency of sensitization to fragrance mix were observed between

Table 1. Patch test responses to propolis in 1255 subjects with suspected allergic contact dermatitis, according to the intensity of the reactions

Negative	?+	+	++	+++
1177	4	24	36	14

propolis-positive and propolis-negative patients (4.1% versus 6.5%).

Table 1 shows the most frequently involved skin sites in propolis-allergic subjects. The face was most frequently affected, followed in decreasing order by the hands and limbs. Localization to flexural sites of the limbs was present in 24% of cases. As regards skin-site involvement, no significant differences were present between propolis-positive children and a control population, including 587 children sensitized to haptens other than propolis (Table 2). To assess a possible time trend in propolis reactivity, the annual incidence was calculated and compared using the χ^2 test. A significant linear increase in the number of positive responses was observed as shown in Fig. 1.

In about 75% of our study population, patch test reactions were considered relevant, as judged by the history and the response to avoidance of products containing propolis.

Discussion

Since the first description of contact dermatitis due to propolis in a beekeeper in 1915 (27), nearly 250 cases have been observed and published. While formerly remaining an occupational skin disease in beekeepers, allergy to propolis today occurs mainly in people using biocosmetics and biopharmaceutical products, owing to the current fashion of employing these kinds of natural products all over the world.

The sensitization rate to propolis in patients suffering from dermatitis has been reported to vary between 1.2% and 6.6% (3, 6, 11, 28–31). In Czechoslovakia, where propolis is a very popular lay medicine, Macháčková (11) identified 4.2% of 650 patients as being sensitized to propolis 10% pet., whereas in a German study performed in the same years (1988–1990) on 3177 subjects, 1.2% of the tested population was positive to propolis (6). About 12 years later, 1.9% of

Table 2. Skin-site involvement in 74 children sensitized to propolis and 587 children sensitized to haptens other than propolis

Skin site	Propolis (%)	Other haptens (%)
Face	49	39
Hands	24	21
Upper limbs	24	29
Flexural sites of the limbs	24	26
Lower limbs	22	29
Trunk	20	19
Feet	11	7
Widespread	9	8
Neck	4	4

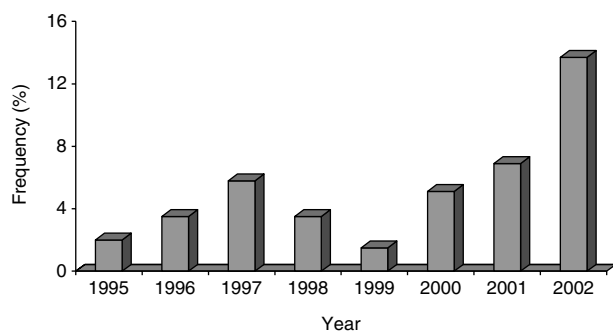


Fig. 1. Frequency (%) of positive responses to propolis by year.

1831 German patients undergoing patch testing reacted to propolis (31). Reider et al. (29) observed a sensitization rate of 6.55% in 433 consecutive patients from Austria, whereas Wöhrle et al. (28) reported a 1.2% frequency of positive responses to propolis in 2660 subjects patch tested in Vienna. Rudzki et al. (3) demonstrated that various propolis samples can cause different sensitization rates. They patch tested 1830 dermatitis patients with 3 propolis samples from various regions of Poland, observing sensitization rates varying from 1.4% to 1.8%. So far, few studies have considered the issue of propolis allergy in children (22–24). Rudzki and Rebandel (22) found positive responses to propolis in 1.3% of 626 patch-tested subjects aged 3–16 years. From 1988 to 1994, 0.7% of children referred to our Allergological Unit for suspected contact dermatitis proved to be allergic to propolis (23). In comparison with these results, we observed a significant increase in propolis sensitization in the subsequent period (1995–2001): 4.8% of 1094 paediatric patients showed positive responses (24). The actual findings confirm this previous work. Collecting data about propolis allergy over an 8-year period, we found a high sensitization rate (5.9%) and a significant linear increase from 1995 (2%) to 2002 (13.7%), reflecting the increasingly and widespread use of natural products for children. Most of the parents of our propolis-allergic patients regarded biocosmetics and biopharmaceutical products as free of side-effects and particularly suitable for their children. After careful questioning, about 75% of them confirmed the actual or past use of natural products or alternative medicine remedies, although they were not aware of their composition in most cases.

A 20% concentration of propolis for patch testing is routinely employed in Italy and has never been reported to provoke irritation (9, 23, 24, 32, 33).

Whereas in adults propolis allergy has been reported to prevail in women (6), we observed a significantly higher frequency of positive responses in boys. As regards skin-site involvement, face dermatitis predominated in our propolis-sensitive children, although no statistically significant differences were noted in comparison with a control population of children sensitized to haptens other than propolis.

A significant association with contact allergy to balsam of Peru was observed in children reacting to propolis with respect to controls (9.5% versus 1.8%), confirming previous literature data (2–6, 8, 10, 30). As propolis shares at least 13 minor constituents with balsam of Peru, pseudo cross-reactions in propolis-sensitive subjects to balsam of Peru are explicable.

In conclusion, our findings reflect the growing popularity and use of propolis at paediatric age. Because of its high sensitizing potential, it is no wonder that, as its use increases, allergic contact dermatitis is observed to a greater extent. We therefore suggest, in agreement with several other authors, that propolis should not be used in topical products for children.

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