

## Original article

## Turnip rape and oilseed rape are new potential food allergens in children with atopic dermatitis

**Background:** When skin prick testing (SPT) young children with atopic dermatitis (AD) for suspected food allergy, we frequently found positive reactions with turnip rape (*Brassica rapa*) and oilseed rape (*Brassica napus*). We performed food challenge to examine whether these children react clinically to turnip rape.

**Methods:** A total of 1887 children were screened with SPTs for sensitization to turnip rape and oilseed rape. Twenty-eight children with clearly positive SPT ( $\geq 5$  mm) were first subjected to labial challenge with turnip rape seeds followed, if negative, by open oral challenge for up to 7 days. Twenty-five children with AD but negative SPT to turnip rape and oilseed rape served as controls.

**Results:** Two-hundred and six (10.9%) children had positive SPT to turnip rape and/or oilseed rape. Twenty-five (89%) of 28 children showed a positive challenge reaction to turnip rape. Seventeen reacted with labial whealing, and eight in oral challenge with facial urticaria, flare-up of AD or abdominal symptoms. All 25 control children remained negative in the labial challenge.

**Conclusions:** Turnip rape and oilseed rape seem to be new important food allergens in young children with AD. The modes of exposure to these allergens and the possible routes of sensitization remain to be established.

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Key words: atopic dermatitis; food hypersensitivity; oilseed rape; turnip rape.

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Accepted for publication 18 May 2005

In western countries young children suffer frequently from food allergy and are often sensitized to multiple foods (1). Cow's milk, egg, wheat, peanut, fish and soy are the main allergenic foods in these children who mostly present with atopic dermatitis (AD) (2, 3). At Tampere University Hospital, for over 10 years, we have routinely performed skin prick test (SPT) screening with a large selection of commonly used foods in infants and young children with AD referred for the investigation of food allergy. Mustard (*Sinapis alba*) has been found to cause food allergies, especially in France (4, 5), which prompted us to include mustard in our SPT series. As the rate of sensitization was high, we included turnip rape (*Brassica rapa*) and oilseed rape (*Brassica napus*), which belong to the same *Brassicaceae* family as mustard, in the SPT series and found again a constant high number of positive SPT reactions.

Allergy to pollens of oilseed rape may occur (6) but, to our knowledge, food allergy to turnip rape or oilseed rape has not been previously described. Both plants are widely used in vegetable oil production. Oilseed rape ranks as the

most commonly grown oilseed crop in Europe and turnip rape is particularly used by Finnish food industry (7).

In the present study we investigated by open food challenge with seeds of turnip rape whether children with positive SPTs to oilseed rape and turnip rape are also clinically reactive to these plants.

## Methods

### Patients

A total of 1887 children under 16 years of age (781 girls and 1106 boys) were screened with turnip rape and oilseed rape SPT during a 2-year period from April 2002 to April 2004. They all had been referred to the Department of Dermatology at Tampere University Hospital for evaluation of food allergy. In these children SPT were positive to cow's milk in 19%, to wheat in 20%, to egg in 31% and to birch pollen in 10%. Most of these children presented with AD and 1337 (70%) of them were below 3 years of age.

Inclusion criteria for the challenge study with turnip rape were that the sensitized children showed in SPT a wheal with a mean diameter of  $\geq 5$  mm to turnip rape or oilseed rape. Twenty-eight children (mean age 4.8 years), whose demographic and clinical characteristics are shown in Table 1, were enrolled in the challenge study. Seventeen of them were allergic to cow's milk and 24 to wheat, as confirmed by open food challenges. The Ethical

**Abbreviations:** AD, atopic dermatitis; SCORAD, AD symptom score; SPT, skin prick test.

Table 1. Demographic and clinical characteristics of the 28 children with positive skin prick test (SPT) reactions to turnip rape and oilseed rape participating in the turnip rape challenge study

| Variables                                        | Value                |
|--------------------------------------------------|----------------------|
| Age, mean (range), years                         | 4.8 (1.0–15.4)       |
| Exclusive breastfeeding, median (range), months  | 4.0 (1.0–5.5)        |
| Atopic heredity: parent or sibling, <i>n</i> (%) | 26 (93)              |
| Personal atopic disorder                         |                      |
| Atopic dermatitis, <i>n</i> (%)                  | 28 (100)             |
| SCORAD, mean (range)                             | 26 (9–60)            |
| Asthma, <i>n</i> (%)                             | 18 (72)              |
| Food allergy                                     |                      |
| Milk, <i>n</i> (%)                               | 17 (61)              |
| Wheat, <i>n</i> (%)                              | 24 (86)              |
| Egg*, <i>n</i> (%)                               | 26 (93)              |
| Total IgE, median (range), kU/l                  | 1150 (26 to >10 000) |
| Sensitization to inhalant allergens              |                      |
| Mugwort, <i>n</i> (%)                            | 15 (54)              |
| Timothy, <i>n</i> (%)                            | 17 (61)              |
| Birch, <i>n</i> (%)                              | 23 (82)              |

\*Based on symptoms and positive SPT and/or specific IgE.

Committee of Tampere University Hospital approved the challenge study and informed consent was obtained from the parents.

### Skin prick tests

Skin prick testing was performed with crushed seeds of turnip rape (*B. rapa* ssp. *oleifera*) and oilseed rape (*B. napus* ssp. *oleifera*) moistened with physiological saline using a commercial one-peak lancet (ALK-Abelló A/S, Hørsholm, Denmark) and prick-prick method (8). The seeds were obtained from a local manufacturer of turnip rape oil (Mildola oy, Kirkkonummi, Finland). Histamine dihydrochloride (10 mg/ml; ALK-Abelló) was used as a positive and saline (Soluprick SQ; ALK-Abelló) as a negative control.

### IgE antibodies to oilseed rape

The IgE antibodies to oilseed rape were measured using ImmunoCAP (Pharmacia CAP System Specific IgE RIA, Uppsala, Sweden) in 28 challenged children. The sera were stored at –20°C before testing. Values ≥0.4 kU/l were considered positive.

### Labial and oral challenge with turnip rape

The turnip rape challenge was open and started with the application of a small amount of oily mass of crushed seeds of turnip rape on the lip (9, 10). If the labial challenge was negative, increasing doses of crushed seeds of turnip rape (10, 10, 30, 100, 300 and 900 mg) were given orally every 20 min. Appearance of wheals or labial swelling or both were regarded as positive. Oral challenges were carried out with turnip rape seeds mixed in an appropriate food tolerated by the child. If negative on the first day, the challenge was continued at home for 6 days by giving 1350 mg of turnip rape daily. The severity of AD was scored at the beginning and at the end of the challenge by SCORAD (11). All gastrointestinal and respiratory symptoms were also registered during the challenge. False-positive irritant reactions in the labial challenge were excluded by challenging lips of 25 children (10 girls and 15 boys) with AD under 10 years of age, but with negative SPT to turnip rape and oilseed rape. All controls had AD, 60% had allergy to cow's milk and 48% to wheat confirmed by food challenge. In addition 60% were sensitized to egg.

### Statistical analysis

Statistical comparison between the groups was made by using permutation test. Correlation coefficients were calculated by the Spearman method.

### Results

Two hundred and six (10.9%) of the 1887 children screened had a clearly positive (≥5 mm) SPT to turnip rape (9.3%) or oilseed rape (9.4%). Eleven percent (149/1337) of the children under 3 years of age were sensitized to turnip rape and/or oilseed rape.

Twenty-five (89%) of the 28 children had a positive and three (11%) had a negative turnip rape challenge (Table 2). The labial challenge was positive in 17 (68%) children showing whealing and/or swelling. In addition, one child got rhinitis. The oral challenge was positive in eight children. Four of the children got immediate symptoms within <3 h and four others during the challenges at home. All 25 control children remained negative in the turnip rape labial challenge.

Table 2. Clinical types of challenge reactions to turnip rape in 25 children

|                                               | Positive challenge tests to turnip rape |                                                                          |                                                                     |
|-----------------------------------------------|-----------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------|
|                                               | Labial ( <i>n</i> = 17)                 | Immediate oral ( <i>n</i> = 4)                                           | Delayed oral ( <i>n</i> = 4)                                        |
| Age, years, mean (range)                      | 4 (1–9)                                 | 4 (1–10)                                                                 | 8 (5–15)                                                            |
| Oilseed rape ImmunoCAP (kU/l), median (range) | 21.6 (0.70 to >100)                     | 23.5 (2.19 to >100)                                                      | 7.3 (0.90–16.30)                                                    |
| Skin prick test, wheal diameter (mm)          |                                         |                                                                          |                                                                     |
| Turnip rape, median (range)                   | 8 (5–23)                                | 7 (6–9)                                                                  | 5 (4–8)                                                             |
| Oilseed rape, median (range)                  | 7 (5–25)                                | 7 (4–12)                                                                 | 5 (4–7)                                                             |
| Challenge                                     |                                         |                                                                          |                                                                     |
| Dose (mg), median (range)                     | Small amount                            | 500 (20–1350)                                                            | 2700 (2700–6750)                                                    |
| Symptoms, <i>n</i>                            | Labial urticaria, 17<br>+ rhinitis, 1   | Facial urticaria, 2<br>Generalised erythema, 1<br>Abdominal complains, 1 | Flare up of AD, 3*<br>Flare up of asthma and abdominal complains, 1 |

\*SCORAD mean (range) change: 24 (11–53) to 31 (11–62).

There was a clear correlation between the size of turnip rape and oilseed rape SPTs [0.69 (95% CI: 0.43–0.95)] in the 28 children challenged with turnip rape (Fig. 1). The SPT results to turnip rape and IgE antibody levels to oilseed rape in challenge-positive and challenge-negative children are given in Fig. 2A and 2B. At the time of challenge SPT reaction to turnip rape and oilseed rape had decreased < 5 mm in two children, whereas in all the

other children SPT was still clearly positive. The first child with a small SPT reaction showed flare up of AD, whereas in the second child the turnip rape challenge was negative. Only one of the 25 control children had IgE antibodies (2.1 kU/l) to oilseed rape. The total IgE was 1510 kU/l (median; 95% CI: 634–1790 kU/l) in the 25 challenge-positive children. In the three challenge-negative children, the total IgE was 26, 27 and 323 kU/l, respectively.

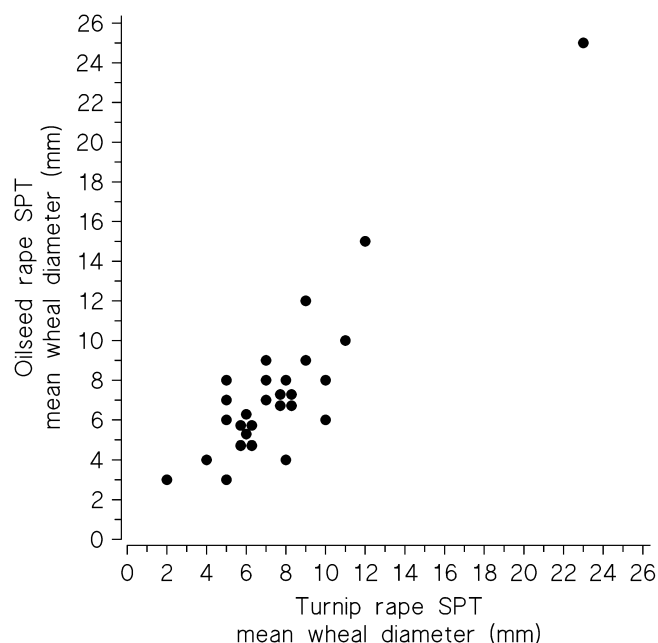


Figure 1. Skin prick test (SPT) reactivity to oilseed rape and turnip rape shows a significant [0.69 (95% CI: 0.43–0.95)] correlation in the 28 challenged children.

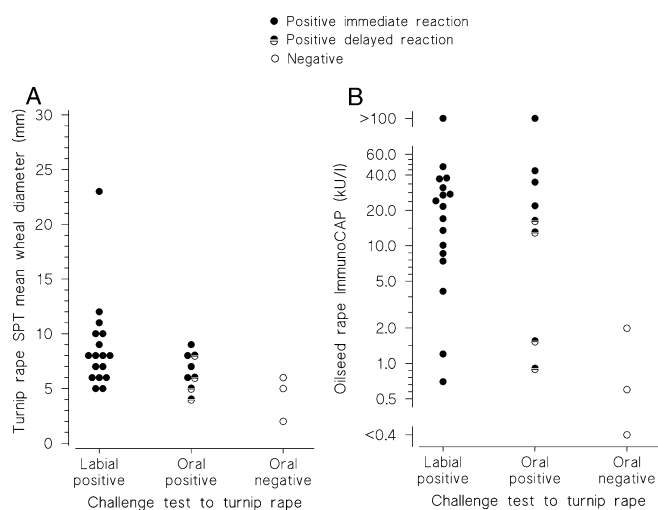


Figure 2. (A) Skin prick test (SPT) reactivity and challenge test; (B) IgE antibody levels to oilseed rape and challenge reactions to turnip rape in 28 children.

## Discussion

In the present study we found as high a prevalence as 11% of positive SPT reactions to turnip rape or oilseed rape in a cohort of 1887 Finnish children examined for suspected food allergy. Twenty-eight children with AD and positive SPTs to turnip rape and oilseed rape and 25 control children with AD and negative SPTs, respectively, participated in the open turnip rape challenge study. Most (89%) of the sensitized children showed positive labial or oral challenge reactions to turnip rape in contrast to none of the SPT-negative control children. The challenge reactions were mostly of immediate type such as labial swelling or facial urticaria. The dose of crushed turnip rape seeds causing positive oral challenge varied from 20 to 1350 mg. The large variation in the cumulative reactive doses correlates well with previous results in peanut and sesame seed challenge studies (12). Three challenge-positive children showed flare up of AD when the oral challenge had lasted for 2–5 days. Similar delayed type challenge reactions have been observed previously with cow's milk and wheat (13–15). When the 25 challenge-positive and three challenge-negative children were compared, the latter had smaller SPT reactions to turnip rape and oilseed rape and also lower IgE antibody levels to oilseed rape, suggesting a lower sensitization level to these plants. There was a tendency that younger children showed larger SPT reactions and immediate type responses to smaller amount of turnip rape seeds than older children, but the numbers of children in the variously reacting challenge groups were small.

Positive labial or oral challenges with turnip rape in the majority of the infants and young children with IgE antibodies to oilseed rape suggest that both of these oilseed plants could be clinically relevant food allergens. The observed high correlation in the SPT reactivity between oilseed rape and turnip rape suggests allergic cross-reactivity, supported also by recent finding of highly homologous 2S albumin allergens in both of them (T.J. Puumalainen, unpublished data). Interestingly, in France mustard allergy is now ranked fourth in children's food allergies (4) and a 2S albumin has been identified as a major allergen in mustard (*Sinapis alba*, *Brassica juncea*) (16, 17). Allergy to sesame (*Sesamum indicum*) has been reported to occur, e.g. in Israel and France and

also seeds of this plant contain allergens belonging to the 2S albumin family (18, 19). Even low-grade consumption of mustard or sesame by the Finnish infants and young children seems unlikely because to our knowledge these agents are not added to commercial or home-made baby or children's food. In contrast, turnip oil is commonly used in the Finnish food industry and is included, e.g. in margarine and baby food (20). However, it remains to be settled whether biologically meaningful amounts of allergenic proteins are present in turnip rape or oilseed rape oils. In the present study we performed preliminary SPTs with refined and cold-pressed turnip oil in a few of the challenge-positive children, but all SPTs were negative (data not shown). It may be noted that cold-pressed and refined oils, such as peanut and sesame oil, have been

reported to cause allergic reactions in highly sensitized individuals (12, 21), which implies that extended studies in this field are warranted.

In conclusion, turnip rape and oilseed rape are potentially important allergens in infants and young children. An oral route seems obvious for sensitization, but the food sources and clinical consequences of this new allergy are challenges for future research.

## Acknowledgments

This study was supported by grants from the Tampere University Hospital Research Fund and the Finnish Society of Allergy and Immunology.

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