

# Celery allergy associated with birch and mugwort pollinosis

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Skin prick tests (SPT) with various celery, carrot and potato preparations (raw, cooked, cooking water of each vegetable and allergen extracts) as well as specific IgE determinations by RAST to celery mix, celeriac (or root celery), stick celery and heated celery extracts were performed in 70 patients with positive prick or intracutaneous tests to birch and/or mugwort pollens and celery (extract and/or raw). 94% of the patients showed positive prick tests to raw celeriac, 36% to cooked celeriac and 8/13 to cooking water. Celery-birch positive patients ( $n = 13$ ) showed negative or low RASTs to heated celery extracts and to stick celery. By contrast, in the celery-mugwort sensitive patients ( $n = 6$ ) the celery RASTs with heated celery extracts remained clearly positive and high RAST values to stick celery could be found. Celery-birch-mugwort-association ( $n = 22$ ) favoured more positive results with relatively high values of RAST to celeriac. The results of homologous and heterologous RAST inhibition experiments with birch, mugwort, unheated and heated celery (100°C) carried out in nine celery-RAST positive sera are also discussed.

*Key words:* birch pollen; celery; mugwort pollen; food hypersensitivity; RAST; RAST inhibition.

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## CLINICAL ASPECTS

Modern cooking which includes an increased use of vegetables has made celery a frequent food allergen which ingestion may induce various immediate allergic reactions from contact urticaria to anaphylactic shock. Associated birch and/or mugwort pollinosis is often observed, indicating a cross-sensitivity between vegetables or other plant antigens and pollens. The well-known fact that some patients experience reactions by eating raw celeriac only, whereas others also react to cooked celery, could be explained by the celery-birch association to thermolabile and the celery-mugwort association to thermostable allergens. The exact nature of allergens involved is still to be determined.

The observation that celery intake can induce hypersensitivity reaction was made already over 60 years ago in our clinic (6). Since then several clinical and experimental studies have been carried out by various groups demonstrating many patterns of association of food hypersensitivity and pollen allergy (1, 2, 5, 9, 11, 12, 13, 15, 16). In Switzerland celery is a very important allergen, responsible in the raw or cooked

form or even as spice, for various IgE-mediated allergic reactions from a contact urticaria of the lips and mouth to a life-threatening anaphylactic shock (15). Most of the patients experience reaction from eating raw celery only; however, in others also cooked celery may cause serious IgE-mediated reactions.

Pollinosis with mugwort and/or birch pollen skin sensitization as well as associated carrot

and spices allergy is quite often seen in these celery allergic patients (celery-carrot-mugwort-spice-syndrome) (8, 9, 13, 16). On the other hand, in birch pollen-sensitive individuals apples and other fruits (stone fruit) can often induce allergic manifestations when eaten fresh (2, 3, 5), whereas cooked fruits are perfectly tolerated, proving the existence of thermolabile allergens. Finally, some patients had adverse reactions to celeriac (or root cellery) but tolerated stick celery (8).

The purpose of this investigation was to study whether the sensitization to fresh celery was related to a birch pollen allergy by common thermolabile allergens and the sensitization to cooked celery was associated with a sensitivity to mugwort pollen by partially identical thermostable allergens. The association pattern of a sensitivity to celeriac and stick celery was also assessed.

MATERIAL AND METHODS

Seventy patients (47F, 23M), mean age 31 years (27-53) with positive skin tests to birch pollen, mugwort pollen and celery entered our study from January 1987 to July 1987. Twelve other patients including six subjects with isolated grass pollinosis were chosen as controls.

Skin prick tests (SPT) were performed with a SPT needle (Stallerpoint, Stallergènes Lab., Fresnes, France), on the volar side of the forearm, using commercially available allergens in glycerol (Alyostal Stallergènes) of birch and

mugwort pollens (biologically standardized in 100 IR = index de réactivité) and celery extract in a concentration of 1:20 w/v. Aqueous celery extract was also tested intracutaneously (ICT) at 1:1,000 w/v concentration.

Fresh (raw) and cooked vegetables (celeriac, carrot, potato) were used for modified prick tests (MSPT) in which a fine needle used for ICT was put into the vegetable immediately before the SPT, as described by Pepys (10). In 13 patients SPT was also performed with the cooking water of each vegetable. Middle-sized vegetables (carrot, celery, potato) were boiled separately 30 min in 400 ml tap water until well cooked.

Twelve patients, six non-atopics and six with hay fever to grass pollens but not to birch or mugwort, were tested as controls with all the above mentioned vegetables and cooking water.

The SPT and MSPT were read after 15 min and the results assessed relating the wheal area to that induced by histamine dihydrochloride (10 mg/ml [Pharmacia]). A wheal of at least 3 mm (average diameter) was considered as positive in presence of a negative control test with glycerol solution with 0.5 % Phenol (Stallergènes).

Specific IgE to celery (f85) were determined in serum samples of all 70 patients by Phadebas RAST (Pharmacia, Sweden) following the instructions of the manufacturer. With a positive result (obtained in 41 patients) RAST was per-

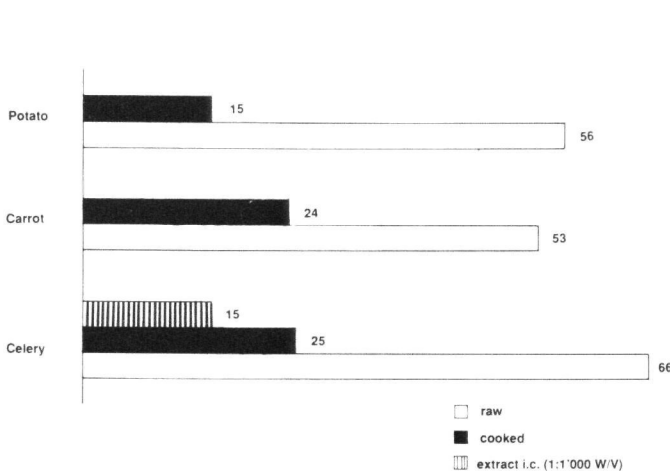


Fig. 1. Number of cases with positive modified prick tests with potato, carrot and celery (cooked and raw) and with positive intracutaneous test with celery extract (n = 70).

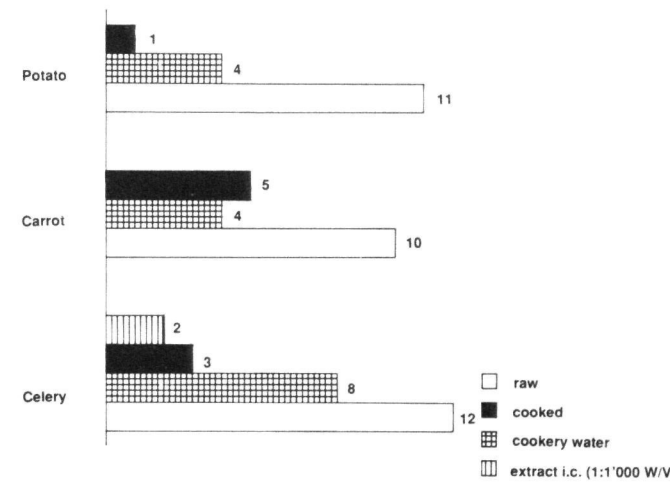


Fig. 2. Number of cases with positive modified prick tests with raw and cooked vegetables and their cooking water (n = 13).

formed to birch (t3) and mugwort pollen (w6), to non-heated (0°) and heated (60°-80°-100°C) celery extracts and to celeriac and stick celery.

RAST discs with extracts of heated celery, celeriac and stick celery were prepared by coupling 250 µl extract to 100 CNBr-activated filter paper discs. No significant non-specific IgE binding to the discs was observed in sera with IgE levels up to 3,000 kU/l. All other allergen discs were obtained from Pharmacia Diagnostics AB, Uppsala.

RAST inhibition experiments were performed in nine patient sera in the following way. Equal volumes of serum, diluted in phosphate buffered saline to a RAST activity of approx. 5,000 cpm, and serial dilutions of an extract were incubated at + 4°C overnight. The serum extract mixture was then analysed in RAST as described for Phadebas RAST. The results were expressed as percent binding and calculated according to the formula:

$$\% \text{ binding} = \frac{(\text{serum} + \text{extract}) \cdot \text{cpm}}{(\text{serum} + \text{buffer}) \cdot \text{cpm}} \times 100.$$

A background value of 200 cpm was subtracted from each test result before calculations.

A 30 % or more decrease in binding was regarded as a significant inhibition.

RESULTS

Modified prick tests with vegetables

According to the design of the study all 70 atopics presented at least one positive skin test to celery: 66 of them (94 %) reacted in modified prick test to raw celeriac, 25 (36 %) to cooked celeriac and 15 (22 %) in ICT to the standardized commercially available celery extract (Fig. 1). Fifty-three (70 %) patients had positive modified prick tests to raw and 24 (34 %) to

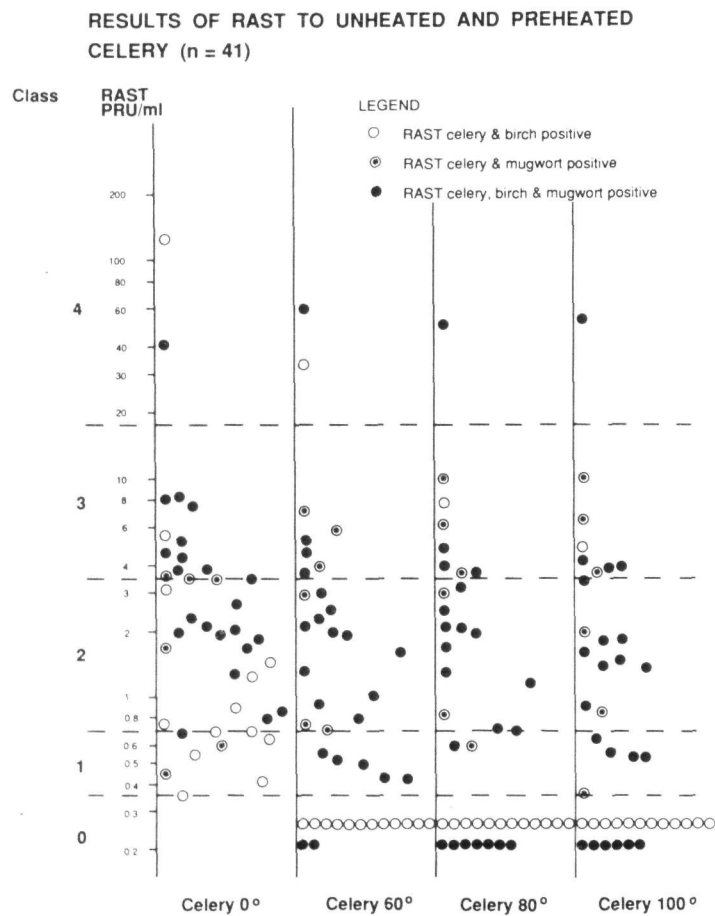


Fig. 3. Results of RAST to unheated (0°) and heated(60°, 80°, 100°) celery extracts (n = 41) (○ = celery-birch RAST positive sera; ⊙ = celery-mugwort RAST positive sera; ● = celery-birch-mugwort RAST positive sera).

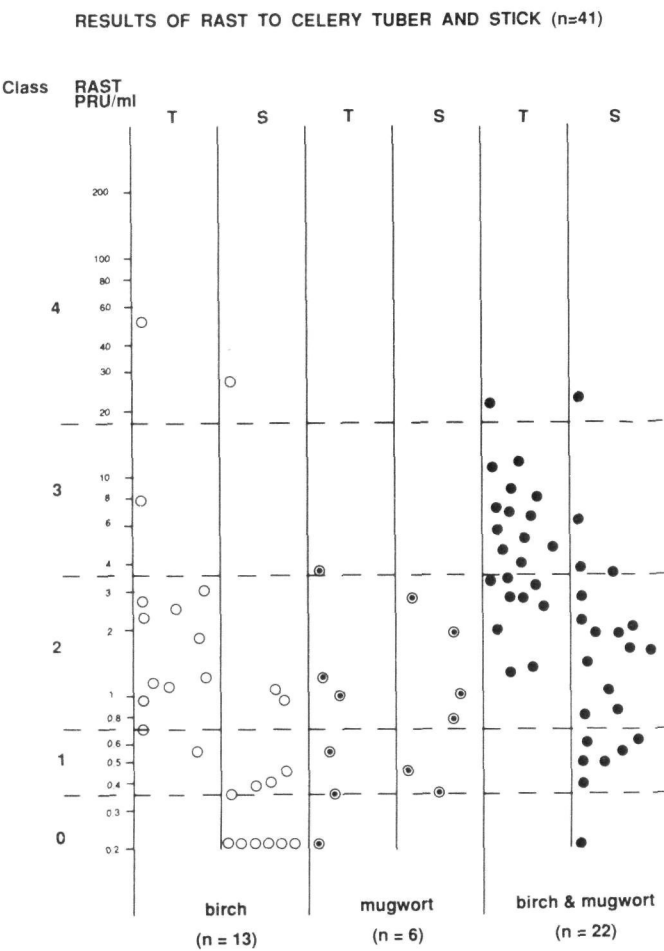


Fig. 4. Results of RAST to stick celery (S) and root (T) (n = 41) (○, ⊙, ● = same significance as in Fig. 3.).

Table 1

Data of patients whose sera were used for homologous and heterologous RAST inhibition experiments

| Patients         | Diagnosis   | RAST Class (PRU/ml) |            |              |
|------------------|-------------|---------------------|------------|--------------|
|                  |             | Celery (f85)        | Birch (t3) | Mugwort (w6) |
| 1. G.A., 1945, M | AB, FA      | 3(15.6 )            | 4(290.0)   | 0            |
| 2. S.B., 1935, F | PR, FA      | 2( 1.8 )            | 4( 28.0)   | 0            |
| 3. S.W., 1938, M | PR, FA      | 2( 1.1 )            | 3( 14.0)   | 0            |
| 4. D.D., 1965, M | FA          | 2( 0.27)            | 0          | 3(19.0 )     |
| 5. Z.E., 1947, F | AD, FA      | 2( 0.86:            | 0          | 2( 0.95)     |
| 6. E.B., 1969, F | PR + PA, FA | 2( 0.48)            | 0          | 2( 2.1 )     |
| 7. V.G., 1935, M | AD, FA      | 4(96.0 )            | 3( 22.0)   | 4(57.0 )     |
| 8. I.J., 1962, F | PR, FA      | 3( 2.7 )            | 3( 11.0)   | 4(21.0 )     |
| 9. S.A., 1970, M | AB, FA      | 3(14.0 )            | 4(149.0)   | 2( 1.8 )     |

M = male, F = female, AB = asthma bronchiale, PR = pollen rhinitis, PA = pollen asthma, AD = atopic dermatitis, FA = food allergy.

cooked carrot. Raw potatoes gave 56 (80 %) and cooked potatoes 15 (21 %) positive skin tests, but only one patient reported adverse reactions after ingestion of cooked potatoes.

In 13 patients additional prick tests with the cooking water of each vegetable gave 8 positive tests to celery, 5 to carrot and 4 to potato cooking water (Fig.2), whereas all the controls had negative skin tests to the tested vegetables and to their cooking water.

RAST to celery

In celery-birch allergic patients (n = 14; represented as ○ in Fig.3) the RAST activity to

heated celery extracts became negative, except in one case with extremely high sensitization (class 4, respectively 125 PRU/ml) to raw celery (0°) in whom the RAST decreased to class 3, respectively 5 PRU/ml to heated celery (100°). In the celery-mugwort sensitive patients (n = 6; ⊙) the celery RASTs with heated celery extracts remained clearly positive or even appeared to increase in some patients.

In celery-birch positive patients a low or negative RAST to stick celery in comparison with celeriac was generally found, while the celery-mugwort allergic patients had higher RAST values to stick celery than to celeriac (Fig.4). Celery-birch-mugwort association (n = 21; ●)

RESULTS OF RAST INHIBITION EXPERIMENTS

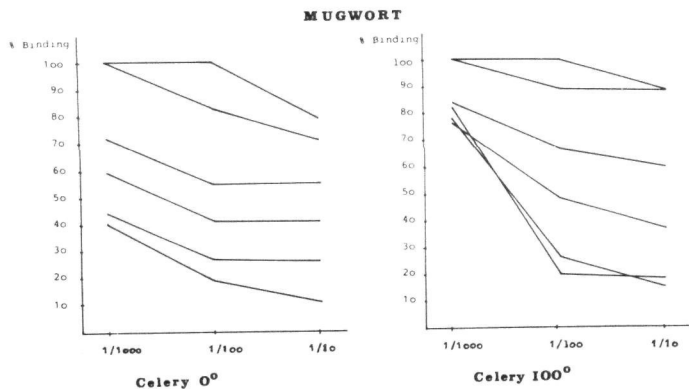


Fig. 5. Results of RAST inhibition experiments (mugwort RAST, inhibition by celery 0° and 100°).

RESULTS OF RAST INHIBITION EXPERIMENTS

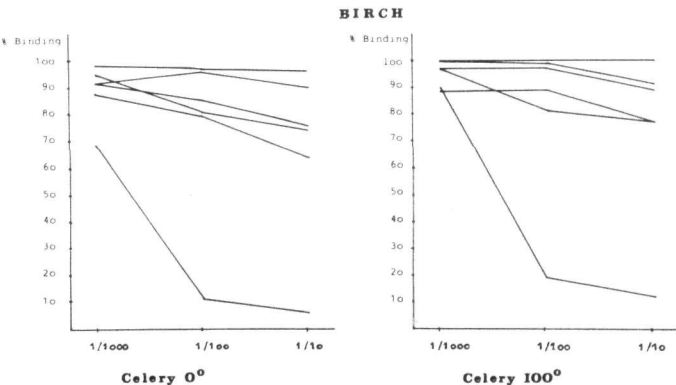


Fig. 6. Results of RAST inhibition experiments (birch RAST, inhibition by celery 0° and 100°).

favoured more positive results with relatively high values of RAST to celeriac.

RAST inhibition experiments

The data of the patients who were clinically sensitive to celery (urticaria, angio-edema or anaphylactic shock), most of them also to fresh fruits, vegetables and spices, are shown in Tables 1 and 2. The diagnosis of food allergy was based on a clear anamnesis (observed clinical symptoms after eating the specific food) and on a strong positive MSPT (+ + or + + +) with the raw and/or cooked vegetables or spices.

With exception of one serum, which showed 90 % RAST inhibition to birch, only one weakly significant (35 %) inhibition (celery 0° only) of the IgE binding to birch disc by celery 0° and 100° (Fig. 5) was obtained. Great variations (10–80 %) of inhibition were seen in RAST to mugwort when patient serum was preincubated with celery 0° and celery 100° extract (Fig. 6); however, 5/6 sera showed significant (> 30 %) inhibition with celery 0° and 4/6 with celery 100°.

Preincubation of birch-positive sera with mugwort extract did not inhibit the birch RAST. Similarly, with one exception, birch

pollen extract did not inhibit the mugwort RAST.

Birch pollen extracts inhibited the reaction of birch/celery-positive sera to celery 0° and celery 100° discs and mugwort pollen extracts inhibited the reaction of mugwort/celery-positive sera to the same allergens. Both birch and mugwort pollen extracts, with one exception, inhibited the positive RAST reactions of birch/mugwort/ celery-positive sera.

DISCUSSION

The association between hypersensitivity to celery/carrot and mugwort/birch pollen allergy could be confirmed in the present study, clearly pointing to the problem of the close relationship between sensitization to pollen and other plant allergens. Several workers (3, 4, 14) have proved the existence of common epitopes on fruit, vegetable and pollen antigens as well as structural similarities between various spices of the same family.

No correlation between the results of the skin test to cooked vegetable and to its cooking water could be noted. However, all patients with positive cooking water test reacted, generally more strongly, in modified prick test to the raw vegetable. This occurs probably because of the elution of certain soluble (but thermostable) allergens during the cooking process.

The RAST results to non-heated and heated (60°, 80°, 100°C) celery extracts in the present investigation confirm our hypothesis of a celery-birch association of thermolabile and a celery-mugwort association of thermostable allergens, the nature of which still needs to be determined (14). The results of our heterologous RAST inhibition experiments using celery-positive sera support the presence of birch and mugwort-associated allergens. Birch-allergen could inhibit a celery-positive RAST in sera with a combined birch and celery positivity and vice versa for mugwort. The celery RAST of sera positive to both pollens and celery were inhibited by both pollens. The thermolability of the birch-associated celery allergens was not so obvious in the RAST in-

Table 2

Symptoms of food allergy and food eliciting symptoms (all skin tests with the respective food showed + + or + + + positive reactions)

| Patients | Symptoms  | Foods                                            |
|----------|-----------|--------------------------------------------------|
| 1.       | KU,Rh     | celery, carrot, apple, fennel                    |
| 2.       | KU,Rh     | celery, carrot, apple                            |
| 3.       | KU,QO     | celery, apple, hazelnut                          |
| 4.       | FIA,AU    | celery, parsley, different spices                |
| 5.       | AKU,QO    | celery, diferent spices                          |
| 6.       | ASh,QO    | celery, carrot, curry                            |
| 7.       | QO,LO,AU  | celery, different vegetables and spices          |
| 8.       | QO,AU,FIA | celery, spices                                   |
| 9.       | QO,KU     | celery, carrot, apple, paprika, different spices |

KU = contact-urticaria, Rh = rhinitis (after eating food), QO = Quincke-oedema, FIA = food-induced anaphylaxis, AU = acute urticaria, AS = anaphylactic shock, LO = larynx-oedema.

hibition experiments, probably for quantitative reasons; a large excess of extract was added.

Further studies are needed, such as determination of IgE binding antigens by immunoblot analysis (14), which would provide better information about the molecular distribution of the antigens shared by different botanically unrelated species. This knowledge may in turn improve our understanding of associated pollen allergy and food hypersensitivity, thus helping us to a better diagnosis and management of the patient.

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