

the serum sample was preincubated with pollen extracts from *Lolium perenne*, *Olea europaea*, *Artemisia vulgaris*, *Parietaria judaica* and *Platanus acerifolia*. (Figure 1).

Oral challenge test with raw cardoon produced pruritus in mouth and lips swelling 30 min after the ingestion whereas oral challenge with cooked cardoon did not produce any kind of symptomatology.

We report a case of cardoon allergy confirmed by positive results in in vivo and in vitro tests. Our patient had personal antecedents of rhinoconjunctivitis and asthma due to inhalation of various pollens: *Lolium perenne*, *Olea europaea*, *Artemisia vulgaris*, *Parietaria judaica* and *Platanus acerifolia*. The symptomatology due to cardoon ingestion had taken place several years after the pollen allergy status began. We demonstrated the existence of serologic cross-reactivity among proteins from cardoon and some others from the pollens against which the patient was sensitised.

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Different clinical presentation of *Anisakis simplex* associated urticaria is dependent on the frequency of raw fish intake

To the Editor:

The fish nematode *Anisakis simplex*(A.s.) has widely been implicated in urticaria, angio-oedema and anaphylaxis, both as a hidden food allergen as well as in acute parasitism.^{1,2} Gastro-allergic Anisakiasis (GAA) has been described as an acute allergic reaction like urticaria, angio-oedema or anaphylaxis accompanying the penetration of the live larvae of A.s. through the gastric mucosa.³ This entity has been associated with fish-eating habits, where raw fish intake is a risk factor. Patients with these IgE-mediated symptoms tolerate well-cooked fish with non-viable A.s., because excretory-secretory proteins are responsible for the allergic reaction, released only by the live larvae. It has been postulated that the urticarial reaction is accompanied by an inflammatory reaction in the gastric mucosa that helps the host to get rid of the larvae. Furthermore, all patients with GAA have detectable specific antibodies of all isotypes from the first day, thus confirming previous episodes of acute parasitism, mainly without clinically allergic symptoms.⁴ The immunologic primary response corresponds thus to at least one previous episode of Anisakiasis with subclinical or only light symptoms.

Chronic urticaria has also been associated with A.s. sensitisation and possible dietary measures have been proposed.⁵ In order to evaluate if dietary habits could be involved in the different clinical presentation (acute versus chronic urticaria) related to A.s. parasitism, we analysed

eating habits in three clinical groups. We studied 32 patients with GAA and acute urticaria, and 75 chronic urticaria patients with detectable specific IgE > 1.5 kU/l (CAP-PHADIA) against A.s.: CU+. The control group consisted of 25 patients with chronic urticaria without sensitisation against A.s. (CU-). Patients with GAA and CU+ displayed a positive skin prick test against A.s. and CU- patients had a negative skin prick test and no detectable serum specific IgE against A.s. Patients were interviewed about the overall frequency of fish intake per week and the frequency of raw fish intake per month.

No significant differences were stated for gender, age or overall frequency of fish consumption. Median specific IgE against A.s. was lower in CU+ (6.8; IQR 4.1–23 kU/l) than in GAA (40.2; IQR 19.7–80.1 kU/l; $p < 0.0001$), probably owing to the longer time interval from the last parasitic episode.⁴ Whereas, as expected, the habit of consuming raw fish was associated with sensitisation against A.s. as shown by previous episodes of acute parasitism in both groups of A.s. sensitisation associated urticaria, GAA and CU+ showed an association with a different frequency of raw fish intake (Figure 1). This fact gains significance because of the further difference in the frequency of raw fish intake between both A.s. sensitisation associated urticaria groups and the control group: Patients with GAA eat raw fish with a higher frequency than patients with CU+, whereas the frequency of raw fish eating was higher in both groups compared with the group of CU-.

In our preliminary estimation, the frequency of raw fish intake is considered equivalent to the risk of acute parasitism. Whereas a high risk of parasitism leads, after an unknown number of previous subclinical parasitic episodes, finally to an acute urticaria in GAA, our results show evidence that an existing, but lower, frequency of raw

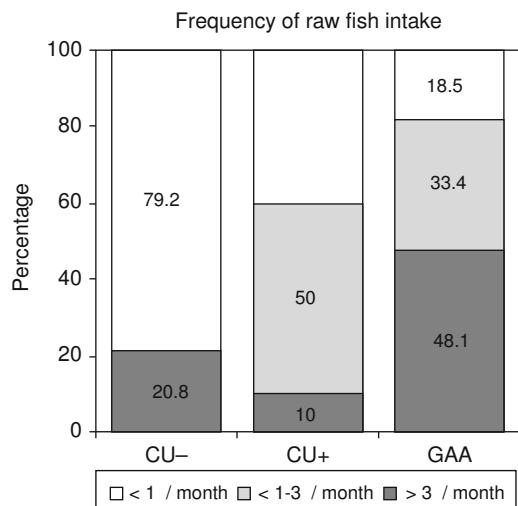


Figure 1 Frequency of raw fish intake (anchovies in vinegar sauce) in chronic urticaria without sensitisation (CU–), chronic urticaria associated to *Anisakis simplex* sensitisation (UC+) and gastro-allergic Anisakiasis (GAA). Percentages are given for statistically significant differences at $p < 0.0001$ (Chi-square test by SPSS 15.0).

fish intake, i.e. of parasitic episodes, is associated with a chronic urticarial reaction by an as yet unknown mechanism. The dose and exposure characteristics of allergens, for example, have been implicated in different immunoglobulin isotype production.⁶ In parasite models, chronic stimulation by parasite antigens is associated with higher IL-10 production and thus a differential IgG4 isotype production.⁷ In this respect, we have previously shown that serum-specific IgG4 against *A.s.* is present in all GAA patients, but only in a subgroup of CU+ patients with a better prognosis in those who have detectable IgG4.^{5,8}

As the overall frequency of fish intake was not associated with the difference between acute or chronic urticaria in *A.s.* sensitised patients, this study also supports the idea that fish that is not eaten raw or undercooked does not pose a risk for the appearance of urticaria.⁹ Future studies about the possible differential sensitisation profile against major allergens, such as Ani s 1, Ani s 4 or Ani s 5 in the different groups of urticaria could possibly be helpful in clarifying dietary recommendations.¹⁰

This preliminary study has not taken into account other possible risk factors with respect to fish-eating habits, like the preference of intake of different fish species or the cooking habits, which will be addressed in future studies.

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