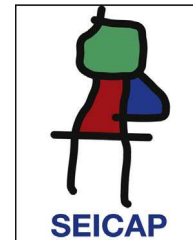




# Allergologia et immunopathologia

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## RESEARCH LETTERS

### Allergy to quince

To the Editor

The **quince**, or *Cydonia oblonga*, is a small deciduous tree which belongs to the Rosaceae family. It is native to warm-temperate southwest Asia in the Caucasus region. In Spain, quince is scarcely harvested in some regions of Andalucía and Valencia. Interestingly, it has been described that quince extracts show immunomodulatory effects with potential therapeutic activity.<sup>1–3</sup> Quince extracts have also been used in fragrances and pastry. To the best of our knowledge there are no previous published reports of quince-monosensitised patients, which highlights the relevance of this case. We describe a case of a 57-year-old woman who ate a self-harvested raw peeled quince which caused an immediate glottic and lingual angio-oedema requiring epinephrine and corticosteroid treatment.

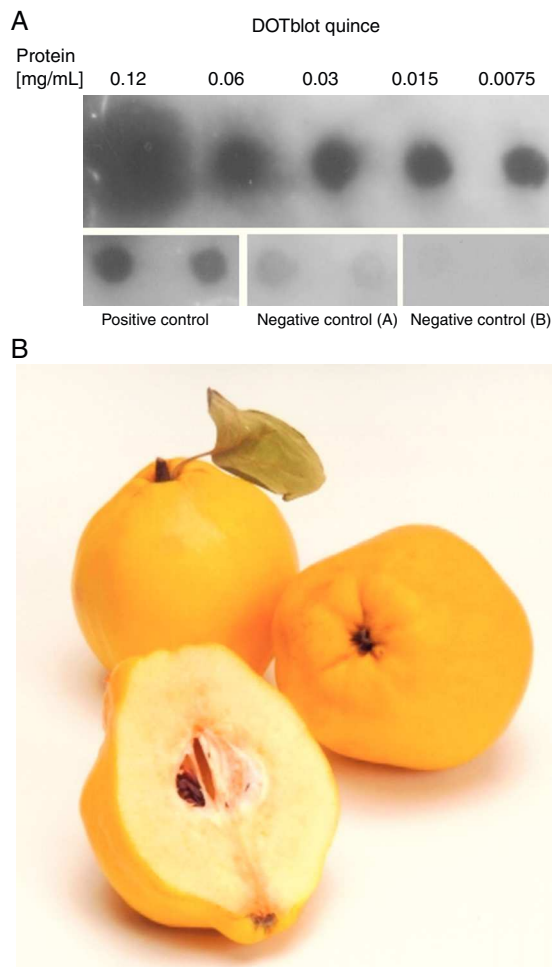
A 57-year-old woman was referred to our outpatient allergy division due to an immediate glottic and lingual angio-oedema after the ingestion of a small piece of a raw peeled and self-harvested quince. She reported complete absence of skin contact to it, as the quince was completely peeled by her husband, due to the development of erythematous pruritic hands immediately after touching the former fruit several times before this reaction. However, her husband had ingested the rest of the quince showing no symptoms. She was transferred to the Emergency Department of our University Hospital where mandatory treatment with intramuscular epinephrine, dexchlorpheniramine and methylprednisolone was subsequently fulfilled. Before the current episode, the patient had previously shown complete tolerance to physical exposition and/or ingestion of quince (both peel and pulp). She reported neither drug coingestion, nor fever or infection coincidental in time with the reaction, and complete absence of atopic background. Additionally, she did not complain about spring-related symptoms nor fruit or vegetable allergy. Moreover, she had never ingested quince jelly. An allergy work-up was performed after informed consent.

Skin-prick-tests (SPT) were performed with the most common aeroallergens in our area, as well as with other Rosaceae family members and profilin, obtaining negative results for all of them. Prick-by-prick testing to quince flesh (raw) showed strongly positive results (wheal equals to the size of histamine wheal and with six atopic patients as

negative controls) while quince peel (raw and boiled) and boiled flesh resulted negative.

The patient blood test showed that the total immunoglobulin E (IgE) concentration was 104 UI/L and specific-IgE to Pru p 3 was 0.0 kU/L (ImmunoCAP System, Thermo Fisher Scientific™). Serum specific IgE analysis was performed using an IgE dot-blot assay (Bio-Rad™, Hercules™, California, USA) according to the manufacturer's instructions (Fig. 1A). Proteins of the quince peel were obtained by homogenisation and solubilisation with phosphate-buffered saline. Insoluble proteins were eliminated by centrifugation and filtration. Soluble proteins were dialysed against water in order to achieve lyophilisation. Then, 50 mg of quince extract was reconstituted in 250 µL of buffer phosphate saline and 0.12, 0.06, 0.03, 0.015 and 0.0075 mg/mL of protein was introduced onto the wells to perform the assay. A polyvinylidene fluoride transfer membrane was used. Serum was applied with a blocking buffer (phosphate buffered saline containing 1% bovine serum albumin and 0.05% Tween, 1:1, v/v). The antibody was a mouse anti-human IgE (Fc) Horseradish peroxidase (HRP) (Southern Biotech™) and the Western Lightning Plus-ECL™ system (PerkinElmer Life and Analytical Sciences™, Shelton, Connecticut, USA) was used as substrate. The patient's serum was positive to quince and negative to *Dermatophagoides pteronyssinus* (Dpt) extract as control. Dpt extract was likewise resuspended in blocking buffer. Serum from a non-allergic patient was used as a negative control (control 1). Other controls were performed using *Dermatophagoides pteronyssinus* extract, the serum from a patient allergic to Dpt (control 2, positive), and the serum from a non-allergic patient (control 3, negative).

As the ingestion of quince is generally scarce, the frequency of allergic reactions subsequent to its ingestion remains elusive, and this likely accounts for its allergenic characteristics.<sup>4</sup> Quince fruit is usually ingested as cooked pastry but not raw, as in this case, so the frequency of the elicited hypersensitivity is unknown (Fig. 1B). Some authors have suggested that Rosaceae fruit allergy without pollinosis is severe<sup>5</sup>; patients suffering from the former fruit hypersensitivity are frequently seen with systemic involvement, mainly anaphylaxis, often without oral allergy syndrome, eliciting up to a 40% of anaphylactic reactions after ingestion.<sup>5</sup> The patient did not have atopic background, which reinforces the odds to develop severe symptoms as stated before. Madrid area is a birch-free



**Figure 1** A. Results of IgE Dot Blot Assay. Responses of serum from our patient to different concentrations of protein from quince (0.12, 0.06, 0.03, 0.015 and 0.0075 mg /mL) are shown (upper image). The response to Dermatophagoides pteronyssinus of serum from a patient who was sensitized to *D. pteronyssinus* extract, which was used as a positive control of the assay, is also shown (positive control). The response to *D. Pteronyssinus* of serum from a non atopic patient is shown (negative control). B. Quince (*Cydonia oblonga*), a member of the Rosaceae family.

region, so PR-10 foods and PR-10 related pollens were not investigated. Besides, the patient did not complain about other PR-10 related foods such as Fabaceae, Apiaceae, Betulaceae, Anacardiaceae, Solanaceae, Asparagaceae or Cucurbitaceae.

Moreover, the patient was advised to strictly avoid quince and quince-containing foods and was instructed in the use of epinephrine autoinjector which was likewise prescribed. Pruritic erythema of the hands after contact with quince is likewise scarcely observed. It is known that those involved in fruit growing, handling and processing, are at risk from topical exposure to develop contact urticaria.<sup>6</sup> Both contact hypersensitivity and non-allergy topical reactions related to fruits could also develop, due to volatile substances that can be irritating to the skin. The former could constitute one of the reasons why this specific reaction has been scantily

reported, as quince is not frequently encountered in supermarkets or groceries. In this exceptional case, self-harvest for self-consumption of the quince made it accessible to hand contact, as the patient did not wear gloves to collect it, possibly triggering a sensitisation which could have led to such a severe reaction, in which *Pru p 3* sensitisation was not involved as previously reported.

We have presented a singular case of an IgE-mediated reaction to quince, in a monosensitized patient. To the best of our knowledge, this is the first case reported in the literature in which monosensitisation to quince showed such a cumbersome reaction after prior sensitisation due to hand contact. An IgE-mediated mechanism was demonstrated both by skin and in vitro tests. Moreover, the patient did not have an atopic background, which reinforces the importance of this case.

Lastly, performing skin prick-by-prick tests with fresh quince (both raw and boiled) in patients with immediate hypersensitivity reactions to this fruit is suitable and recommended, as proven in this case. Further investigation must be carried out in order to clarify the culprit allergens as regards the up-to-date immunomodulatory effects of this fruit.

### Conflicts of interest

There is no known conflict of interests for the authors.

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### Author contributions

DAA and MAM were involved in study design, laboratory assessment, data analysis and writing manuscript.

MJSG, MRR, JBE and DAA were involved in patient follow-up, pharmacologic advisory and writing manuscript.

FP was involved in skilled technical assessment.

### Ethical disclosures

**Confidentiality of data.** The authors declare that no patient data appears in this article.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

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## The Hacettepe Method is an efficient, safe and cost effective method of drug allergy work-up<sup>☆</sup>

To the Editor,

Drug allergy can be life-threatening, as it negatively affects and delays the treatment of diseases. It also increases healthcare costs by causing a shift towards more expensive alternative drugs.

Drug allergy is one of the most common causes of admission to allergy clinics; it is the most common cause of allergological inpatient consultation in the USA, and is the third most common cause of allergology services consultations in Spain, following bronchial asthma and rhinitis.<sup>1,2</sup> However, the number of specialised allergy clinics that address the problem of adult drug allergy is limited in many countries, including Turkey. In addition, waiting for an allergy examination appointment and the performance of drug allergy tests are time consuming. The current gold standard for drug allergy diagnosis and work-up – the oral provocation test (OPT) – takes one day for each drug tested. Different drugs are not usually tested on consecutive days, as a waiting period is necessary (of at least one day) before testing each new drug.

In Turkey there are 70 adult allergy specialists and 22 centres that perform the OPT in adults (data obtained from the Turkish National Society of Allergy and Clinical Immunology). Adverse drug reactions affect 10–20% of hospitalised patients and  $\geq 7\%$  of the general population.<sup>3</sup> Considering that the population of Turkey in 2012 was 75,627,384 and that 75.1% of the population is aged >15 years, the number of adult allergy clinics is not sufficient to effectively treat such a common public-health problem as drug allergy.<sup>4</sup>

Our allergy clinic has a fixed number of two professors and 1–2 fellows who provide patient care. [Table 1](#) shows the total number of patients who were seen at the

outpatient clinic and the number of OPTs performed for the corresponding year.

For the reasons stated above the Hacettepe Method has been used at our clinic since 2002 to perform OPTs simultaneously with multiple drugs (i.e. 2–3 drugs from the same or different groups) on the same day in an effort to identify safe alternatives. Use of the Hacettepe Method has reduced the amount of time, money, and manpower used for diagnostic work-up. OPTs were performed by randomly selecting three drugs the patient was not intolerant to based on anamnesis (paracetamol, codeine, meloxicam, rofecoxib, celecoxib, benzydamine, and azapropazone), and those drugs were tested on the same day; the drugs were administered in 30-min intervals at the following doses: lactose (placebo) 50 mg; paracetamol 500 mg and 750 mg; codeine 20 mg and 30 mg; meloxicam 7.5 mg and 15 mg; rofecoxib 12.5 mg and 25 mg; celecoxib 100 mg and 150 mg; benzydamine 50 mg and 75 mg; and azapropazone 300 mg and 450 mg. Tests were completed when a reaction was observed or when the higher test dose of the third drug was reached.<sup>5</sup> Subsequently, the identical methodology was used for antibiotic and antibiotic-analgesic drug provocation tests.<sup>6,7</sup> We tested 2–3 different groups of antibiotics or antibiotics plus analgesics on the same day.

**Table 1** Number of patients tested at the outpatient clinic and the number of OPTs performed for the corresponding year.

Year	Patients seen at the clinic (n)	OPTs performed (n) <sup>a</sup>
2006	1980	250
2007	3495	300
2008	5261	275
2009	5258	400
2010	5583	375
2011	5744	405
2012	5585	394

<sup>a</sup> Each test included 1–3 drugs.

<sup>☆</sup> This research letter was not funded from any organisation.