Proposed GA²LEN Standardized Allergen Battery: What About Regional Sensitization Differences?

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Palabras clave: Alergia. Serie de alérgenos. Norte de Portugal. *Plantago lanceolata*. Polen.

In 2009, the Global Asthma and Allergy European Network (GA²LEN) proposed a pan-European standardized allergen battery for clinical practice and research [1]. While *Parietaria* species sensitization is an unquestionable cause of seasonal allergy in Mediterranean countries [2], and as such is included in this battery, *Plantago lanceolata* is widely considered to be a rare, isolated cause of hay fever and/or allergic asthma. This weed tolerates a wide variety of climatic conditions, and thrives in dry environments with low fertility. The Portuguese city of Porto and its surroundings belong, in biogeographic terms, to the Euro-Siberian region, the Cantabrian-Atlantic province, the Galician-Asturian subprovince, and the Galician-Portuguese sector; the climate is Mediterranean (Köppen climate classification, Csb) with a cool summer and substantial winter rainfall. Since a higher-than-expected prevalence of this pollen has been described in climatically similar regions of Spain [3-5], and since not infrequently, we have obtained significant levels of in vitro and in vivo specific immunoglobulin (Ig) E to this allergen, we launched a project designed to estimate the rate of *P lanceolata* sensitization in a sample of inhabitants of Porto and to compare it to the rate of *Parietaria judaica* sensitization. Furthermore, because Ole e 1 and Pla l 1 allergens share common epitopes [6], as a secondary outcome, we decided to investigate whether or not concomitant sensitization might be a consequence of cross-reactivity between these allergen sources. To accomplish this, we reviewed skin prick test (SPT) results performed with a standardized set of aeroallergens by our university hospital allergy department over 2 consecutive years. Patients with positive SPTs to *P Judaica* and/or *P lanceolata* living near Porto were selected. The largest and perpendicular wheal diameter for each allergen was measured and the following value calculated: largest + perpendicular diameter/2; the test was considered positive when this mean value was ≥3 mm and controls showed adequate reactions [1]. Measurements were performed by 2 independent observers and the average of both observations was used. Pollen grains were collected in a Burckhardt trap and counted by a specialized botanist. All data analyses were performed using the SPSS statistical package version 18.0 for Windows (SPSS, Chicago, Illinois, USA).The χ^2 test was used to analyze differences between categorical variables, and independent sample tests were used for continuous variables (the *t* test for normally distributed variables and the Mann-Whitney U test for asymmetrically distributed variables). A *P* value of less than .05 was considered statistically significant.

A total of 1588 patients (628 with pollinosis) were enrolled. Of these, 229 were sensitized to *P lanceolata*, corresponding to a sensitization rate of 14.4% of all patients and 36% of pollen-allergic patients. Sensitization to *P judaica* was detected in 203 patients (sensitization rates of 12.8% and 32%, respectively). No statistically significant differences were observed between the 2 samples for demographic data, sensitization rates, symptoms, mean wheal sizes, or monosensitization rate (Table 1).

During this 2-year period, a pollen count was performed on 662 days. A total of 24 792 grains/mm^3 were collected, of which 696 grains/mm^3 belonged to *P lanceolata*.

The sensitization rate detected for *P lanceolata* was higher than that observed for *P judaica*, although the latter is considered to be a more common cause of weed pollinosis. Since only 38% of individuals sensitized to *P lanceolata* were also sensitized to *Olea europeae*, the higher-than-expected rate of *P lanceolata* sensitization is not fully explained by common

Table. Demographic Characteristics of the Sample and Main Results

	Sensitization to *Plantago lanceolata* (n=229)	Sensitization to *Parietaria judaica* (n=203)	*P*
Male patients, No. (%)	79 (35)	69 (34)	.912[a]
Age, mean (SD), y	36.1 (14.2)	37 (13.4)	.493[b]
Symptoms (No. of patients)	Rhinitis/asthma; (220) urticaria/ angioedema (9)	Rhinitis/asthma; (94) urticaria/ angioedema (9)	.794[a]
Wheal size, median (range), mm	5 (3-24.5)	6 (3-23)	.499[c]
Monosensitization, No. (%)	4 (1.7)	9 (4.4)	.103[a]
Concomitant sensitization to *Olea europaea*, No. (%)	86 (38)	Not applicable	–

[a]χ^2 test.
[b]Independent samples *t* test.
[c]Independent samples Mann-Whitney U test.

epitope cross-reactivity. *P lanceolata* pollen is present in Porto, as proven by the pollen count.

It seems, therefore, that each country, and perhaps even different regions within a country, should adapt the proposed GA²LEN battery so as not to miss clinically relevant sensitizations. *P lanceolata*, for instance, should be included in batteries used in northern Portugal. Considering that climatic changes are occurring with increasing speed, studies such as this one should be performed in different biogeographic regions regularly in order to compile information on local sensitizations and to adapt the content of aeroallergen batteries accordingly.

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Immediate Allergy to Mepivacaine

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Allergic reactions account for less than 1% of all adverse reactions to local anesthetics (LAs) [1]. Delayed-type IV hypersensitivity reactions to LAs from the benzoic acid ester group are the most frequent type of reactions, whereas immediate reactions to amide-type LAs are rare. At present, prick and intradermal tests with LAs are not considered to be useful diagnostic tools, although there have been some recent reports of immunoglobulin (Ig) E– mediated allergic reactions to LAs with positive intradermal tests [2-5].

We report the case of a 47-year-old woman who, 2 months earlier, had undergone carpal tunnel surgery under LA, and had developed itching, erythema, and edema in the puncture area 5 minutes after subcutaneous mepivacaine (Scandinibsa; Inibsa SA, Barcelona, Spain) administration. An ice bag was applied, and symptoms improved within approximately 1 hour. The patient had a previous history of allergy to pollens, mites, crustaceans, and ampicillin. She was referred to our department, and skin tests were carried out. A prick test with mepivacaine 10 mg/mL was negative, but an intradermal test with mepivacaine diluted to 1 mg/mL was positive, with 25 mm of erythema and a 10-mm wheal. This result strongly suggested the involvement of a type I allergic reaction. On the contrary, prick and intradermal tests were negative with bupivacaine 5 mg/mL (Svedocain 0.50%; Inibsa SA), ropivacaine 10 mg/mL (Naropin Polyamp, AstraZeneca Farmaceutica Spain SA, Madrid, Spain), prilocaine diluted to 10 mg/mL (Citanest; Inibsa SA), and lidocaine diluted to 10 mg/mL (Lidocaína 2% iny; B Braun Medical SA, Barcelona, Spain). Finally, a challenge test with articaine/epinephrine (Ultracain; Normon SA, Madrid, Spain) to a cumulative dose of 1.6 mL (64 mg) was well tolerated.

It is widely accepted that skin tests with amide-type LAs are not useful. Nevertheless, several LA allergy cases with positive skin tests have been published in recent years. In some instances, bupivacaine was occasionally tolerated in mepivacaine-allergic patients with a positive intradermal test [4,5], while in others, there were reports of cross-reactivity between mepivacaine, bupivacaine, and lidocaine [2,3]. Articaine is an amide LA containing a thiophene ring different to that found in other amide LAs, which have a phenyl-methylated ring. Accordingly, this LA could be the best choice, but a challenge test is still advisable. Also, immediate allergy to articaine with good tolerance of mepivacaine has previously been reported [6]. We have presented a case of allergy to mepivacaine, proven by skin testing, and subsequent tolerance of Ultracain (articaine 40 mg, epinephrine 10 mcg, sodium

bisulfite 0.5 mg/1 mL). Unfotunately, we were unable to find a marketed product containing articaine without epinephrine for the challenge test. Although some doubts could arise about the negative challenge because of the amount of epinephrine contained in the drug tested, in our opinion, a 10-mcg-dose would appear to be insufficient to slow down an allergic reaction.

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Allergy to Red Caviar

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Palabras clave: Alergia. Caviar Rojo. Huevas. Salmón, Vitelogenina.

Salted fish roes are consumed worldwide and are considered valuable and nutritious appetizers. Beluga caviar is a luxury delicacy that is eaten as a garnish or a spread. Salmon roe (SR), also known as red caviar due to its red-orange hue, is widely consumed since it is considerably cheaper than black caviar, is more versatile, and can be eaten with many different foods. Although SR consumption has increased in recent years, little has been published on allergic reactions to this roe [1-3].

A 56-year-old man presented with oral pruritus, vomiting, chest tightness, and dysphagia within minutes of eating red caviar. He did not report any previous or subsequent symptoms after eating any kind of fish or fish or bird eggs, and he had no past history of allergic disease or atopy.

Protein extracts from SR were prepared by homogenization in phosphate-buffered saline, followed by dialyzation and lyophilization. Skin prick tests to common commercial fish (including hake, trout, salmon, monkfish, sardine, sole, and tuna), crustaceans, molluscs, *Anisakis simplex*, egg yolk, egg white, ovalbumin, and ovomucoid were performed, with negative results. Prick-by-prick tests carried out with SR yielded a wheal of 15×11 mm. Serum-specific immunoglobulin (Ig) E (sIgE) against commercial salmon extract, egg yolk, egg white, ovalbumin, and ovomucoid (Pharmacia CAP system, Pharmacia Diagnostics AB, Uppsala, Sweden) were <0.35kU/L (total IgE, 30 IU/mL). sIgE against SR (enzyme allergosorbent test) was 0.4kU/L. Additional sIgE determinations against extracts from trout roe (TR) and salted hake roe (SHR) revealed values of 0.5 kU/L and 0.4 kU/L, respectively. All extracts were analyzed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) as described by Laemmli [4], with protein bands ranging between 97 kDa and 10 kDa for the SR, TR, and SHR extracts. An SDS-PAGE IgE-immunoblot assay revealed IgE reactivity with 18-kDa and 21-kDa proteins in the SR extract, an 18-kDa protein in the TR extract, and 18-kDa and 30-kDa proteins in the SHR extract (Figure 1A). An SDS-PAGE immunoblot inhibition assay with SR extract as an inhibitor and TR and SHR extracts in solid phase showed complete IgE-binding inhibition (Figure 1B).

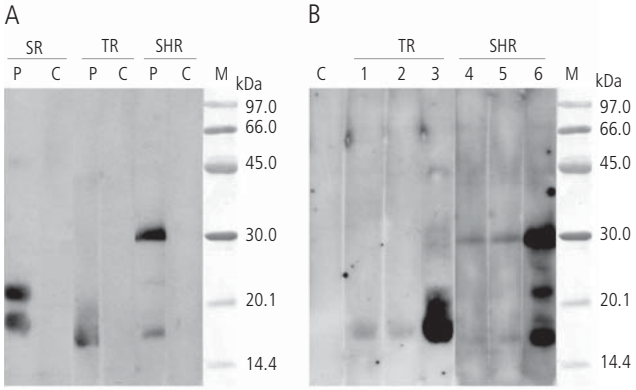

Figure. Immunoglobulin (Ig) E binding of proteins in salmon roe (SR), trout roe (TR), and salted hake roe (SHR) extracts. A, Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) IgE-immunoblotting. B, SDS-PAGE IgE-immunoblot inhibition assays. Lane P, patient serum; Lane C, control serum (pool of sera from nonatopic individuals); Lane 1, patient serum preincubated with TR extract; Lanes 2 and 5, patient serum preincubated with SR extract; Lanes 3 and 6, patient serum preincubated with lamb extract; Lane 4, patient serum incubated with SHR extract; Lane M, molecular mass marker.

The major allergens in hen egg allergy are egg white proteins. In fish roe, however, the main component is yolk, and there is no equivalent to egg white. Fish roe has 3 major yolk proteins: lipovitellin, phosvitin, and ß'-component (ß'-c). Vitellogenin, a precursor of these yolk proteins, is expressed in the blood of sexually mature females of nearly all oviparous animal species. Produced by the liver in response to circulating estrogens, vitellogenin is taken up by growing oocytes and modified to form egg yolk proteins [5]. It is a continuous polypeptide chain, which is degraded into specific yolk proteins by proteolytic splitting [5]. The major allergenic components described in salmonid roes are 2 proteins with the same molecular mass as the SR IgE-binding proteins detected in the present study: lipovitellin (21 kDa) and ß'-c (18 kDa), both subfragments of vitellogenin [3].

Food allergy to SR was first reported in 2002 [1], and vitellogenin was later demonstrated to be a relevant allergen in both red caviar allergy [3] and Beluga caviar allergy [6]. IgE cross-reactivity between SR and other kinds of fish roe such as herring and pollock roe have been described [2] but no reports have demonstrated cross-reactivity with TR or SHR. Although possible cross-reactivity between SR and salmon flesh has been described [2], no significant association has been demonstrated.

We have presented a case of IgE-mediated allergy to SR, and suggest that the relevant allergens are subfragments of vitellogenin such as lipovitellin and ß'-c. Cross-reactivity with TR and SHR has also been demonstrated for the first time.

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Cosmetic Facial Peel-Induced Contact Anaphylaxis: Chestnut Allergy Without Latex-Fruit Syndrome

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Palabras clave: Anafilaxia. Castaña. Urticaria de contacto. Cosméticos.

Contact urticaria is a hypersensitivity reaction triggered by cutaneous contact with specific irritants or allergens. It is clinically characterized as an immediate-type wheal-and-flare reaction occurring within minutes of exposure and is usually rather limited to the contact site. Allergic contact urticaria is a consequence of an immunologic immunoglobulin (Ig) E–mediated hypersensitivity pathomechanism. Under special conditions, such as prolonged contact time or decreased barrier function (ie, eczematous skin, abraded skin, mucosal surfaces), allergic contact urticaria in highly sensitized individuals may progress to generalized urticaria and anaphylaxis with systemic symptoms.

Within 5 minutes of application of a facial peeling mask containing abrasives and chestnut and almond extracts, a 16-year-old female developed wheals, swelling, and redness of the face followed by angioedema and subsequent collapse. Emergency treatment including intravenous fluid replacement, antihistamines, and systemic corticosteroids relieved the symptoms, and the patient was discharged after overnight observation. Two years earlier, the patient had experienced swelling of the face after ingestion of a fresh mango. Similar, although less intense, symptoms had also occurred after consumption of a fresh lychee. All other fruits and vegetables were tolerated without symptoms.

Skin prick tests revealed a ++ reaction to the facial peeling mask, while 5 healthy volunteers did not show any positive reactions. A positive prick test reaction was defined as a + reaction when the wheal diameter was ≥3 to <4 mm, as a ++ reaction when it was ≥4 to <6 mm, and as a +++ reaction when it was ≥6 mm. Prick-to-prick-testing with foods performed according to international standards showed a +++ reaction to chestnut and mango and a ++ reaction to lychee, while no positive reactions were observed for almond or banana. Prick testing with 2 commercially available latex extracts (Allergopharma, Reinbek, Germany; ALK-Abelló, Wedel, Germany) was also negative. In addition, the total serum IgE level was normal and no allergen-specific IgE was detected against chestnut (f299), mango (f91), latex (k82), kiwi (f84), or almond (f20) using the Phadia ImmunoCAP system (Phadia, Freiburg, Germany). After completion of the allergologic work-up the patient was advised to avoid not only consumption of chestnut, mango, and lychee but also cutaneous contact with these foods.

Chestnut (*Castanea sativa*) is a member of the Fagaceae family. In contrast to Asia, the consumption of chestnuts is limited in Central Europe, with cooked preparations being preferred. While chestnut allergy is very rare in Central Europe, chestnut allergy is quite frequent in Korea, where it accounts for up to 3.2% of all food allergies [1]. Most cases of IgE-mediated hypersensitivity to chestnuts have been attributed to the so-called latex-fruit syndrome, in which ingestion of fruits such as avocado, kiwi, banana, and, more rarely, chestnut lead to urticaria and anaphylaxis in latex-sensitized individuals. The latex-fruit syndrome is caused by cross-reactivity between class I chitinases with a hevein-like domain such as Mus a 1 (banana), Pers a 1 (avocado), Cas s 5 (chestnut), and Hev b6.02 (latex hevein) [2,3]. However, chestnut allergy may occur independently of the latex-fruit syndrome, and in these cases Cas s 8, a lipid transfer protein, has been identified as the offending allergen [4].

Our patient developed contact urticaria progressing to anaphylaxis after topical application of a chestnut-containing facial peeling mask. While contact urticaria is frequently observed in food handlers, reports associated with the use of cosmetics are less common. However, with an increasing number of food proteins being included in so-called natural cosmetics, reports of cases may increase [5]. Neither chestnut-induced allergic contact urticaria nor contact anaphylaxis has been previously reported in latex-sensitized or non-latex sensitized individuals. Therefore, to the best of our knowledge, this is the first case of chestnut-induced allergic contact anaphylaxis not linked to the latex-fruit syndrome. Unfortunately, the patient refused to undergo further diagnostic tests and therefore the nature of the offending allergen, which possibly explains concomitant lychee (Litchi chinensis, family Sapindaceae) and mango (*Mangifera indica*, family *Anacardiaceae*) allergy, remains speculative at this point.

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