Review Article

PRACTICAL MANAGEMENT OF FOOD ALLERGY

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ABSTRACT
Food allergy is on the increase, particularly in Africa and Asia. Significant regional variations in the key food allergens are determined by diet and inhalant allergy cross-reactivities. A good clinical history, supported by appropriate validated *in vivo* and *in vitro* tests, is the bedrock of diagnosis. Clinicians should be aware of potential hidden allergens in food substitutions. Accurate food labelling for key allergens by manufacturers is required but may not be readily available.

Keywords: food allergy; practical management; key food allergens; inhalant allergy cross-reactivities

INTRODUCTION

Food allergy has become more common over the past 30 years. Previously, anaphylaxis was rare in clinical hospital practice; currently, our hospital's Emergency Department sees 1–2 new patients per week. In parallel with this trend there has been an increase in patients presenting with symptoms of non-IgE-mediated food intolerance. Differentiating between food allergy and food intolerance is important for both the management of patients and their education. Misinformation concerning food allergies propagated by some media needs to be counteracted. Correct diagnosis of food allergy and intolerance is essential to ensure that patients receive the most appropriate management and do not restrict their diet unnecessarily as a result of misbeliefs and inaccurate information.

HISTORY OF FOOD ALLERGY

Problems with foods have long been recognised. Food intolerance and/or allergy was first described by Hippocrates in the 4th century BC with regard to reactions to cheese and wine. Richard III of England is said to have suffered from strawberry-induced urticaria, although the evidence for this is extremely weak. The first scientific account of food allergy, however, was that by Oscar Menderson Schoss in 1912: he described the first use of skin-prick testing (SPT) in order to confirm egg allergy.[1]

INCREASING PROBLEM OF FOOD ALLERGY

The prevalence of both food allergy and food intolerance has increased over the past 30 years.[2] The causes of this are debated but include socio-economic changes (decrease in parasitic infections – hygiene hypothesis) and dietary changes (increased consumption of processed foods and the popularisation of previous 'luxury' foods such as peanuts). It is expected that as the African and Asian economies grow, rates of food allergy will increase to those levels seen in Australia, Europe and the United States.[3] Good comparative data are, however, lacking.

A condition that has been recognised increasingly over the past two decades – as a possible food-related condition – is eosinophilic enteritis, most commonly presenting as eosinophilic oesophagitis with dysphagia and, if untreated, strictures.[4]

DIFFERENCE BETWEEN FOOD ALLERGY AND INTOLERANCE

Media misreporting of food-related problems informed by a failure to distinguish between true food allergy, mediated by IgE and, occasionally, T cells and food intolerance – for example, irritable bowel syndrome (IBS) – has led to a widespread public belief that any problem with food is due to 'allergy'. A number of studies over many years have shown that the incidence of medically confirmed true food allergy is far lower than that reported by the general public.[5] It is essential that healthcare professionals take care to ensure that patients understand the difference, as the risks from true food allergy are very different from those of food intolerance, and the treatment will therefore also differ.

CLINICAL CONSULTATION FOR SUSPECTED FOOD ALLERGY

The key to the diagnosis of food reactions lies *not* in the testing, but it *is* about history-taking. The tests should be used to confirm a patient's clinical history. The history must be comprehensive and include details of the reaction, its timing in relation to food and the nature of the food or foods involved. Difficulties arise when a patient arrives at the clinic with preconceptions about the food trigger and has therefore ignored other potential causes. Composite foods, such as takeaway food, where ingredients

are not known or available, present a particular problem. Where possible, the clinician should request lists of ingredients: the patient could, for instance, use a cellphone to photograph the ingredients listed on packets in supermarkets and shops. The internet may be a source of ingredients contained in products from major manufacturers. Hidden allergens may be the culprit: these include such ingredients as lupin flour, organic food colourings (cochineal/carmine), mustard, celery and anisakis (a parasite found in raw/marinated fish).[6]

A case in point involves a patient presenting with a reaction to a dressed salad. By a process of elimination it had to be the salad dressing, but the patient had difficulty in believing this, as he had had no problems with other oil and vinegar dressings. It transpired that he had used a craft-made oil-and-vinegar dressing and, on subsequent investigation, the ingredients included chopped red peppers. Skin testing to the dressing and to red peppers was positive.

Another case of anaphylaxis to imported ice-cream cones was reported; that reaction could be attributed to lupin flour used as a wheat substitute. Lupin flour is also used as a wheat substitute in gluten-free products. Lupin may cross-react with peanut and cause allergic reactions in peanut-allergic individuals.[7]

Food substitution may also be responsible for unexpected allergic reactions. Vietnamese river cobbler (*Bassia*) is often substituted (without declaration) for more expensive white fish such as cod and haddock, but it is allergenically different. Patients who know they can eat cod are mystified when they sometimes have severe reactions to 'cod' when they eat out.

A further example of food substitution commonly encountered in South Africa is to be found in basil pesto. Here, more expensive pine nuts are substituted with cashew nuts, macadamia nuts or sunflower seeds.

The clinician should also explore potential co-factors such as exercise, alcohol intake and non-steroidal anti-inflammatories, antacids or acid-suppressing medications (H2-blockers, proton pump inhibitors), all of which alter gut permeability and allergen digestion, and allow whole unprocessed allergen to enter the circulation. The severity of the reactions may be enhanced by the consumption of drugs that inhibit the breakdown of bradykinin.[8]

A common misconception by patients – and often endorsed by doctors – is that waking with angioedema in the morning is related to food eaten during the previous evening. However, this is most unlikely as IgE-mediated reactions will usually occur within minutes – with an outside range of 4–6 hours (although it is extremely unlikely to be more than 1–2 hours). Most early-morning angioedema is attributable to other causes, exacerbated by the drop in blood pH during the night when renal function is decreased.

By the end of the consultation, the clinician should have a clear idea whether the reaction(s) are IgE-mediated or not, whether tests are appropriate and, if so, which. For non-IgE-mediated reactions testing may still be appropriate to reinforce the 'not an allergy' message.

SUB-TYPES OF IGE-MEDIATED FOOD ALLERGY

Essentially, any protein-containing food is capable of causing an IgE-mediated allergy. Molecular studies or allergen components are now able to identify the key allergens in most problematic foods and identify the homology between similarly functioning proteins in different plant and animal genera.

STORAGE PROTEINS

So-called 'storage proteins' in fruits and nuts tend to be heat-stable and are therefore not destroyed either by cooking or by processing. These allergens tend to be those most commonly associated with severe anaphylactic reactions. The most common storage protein sensitisations in South Africa are those to peanut storage proteins, specifically *Ara h 2, 6, 1* and *3*.[9]

LIPID-TRANSFER PROTEINS (LTPS)

This class of plant proteins can cause limited oral allergy-type symptoms, but some may cause anaphylaxis. Management is often difficult but defaults to the most serious perceived risk, so it is usually appropriate to consider a supply of adrenaline for self-injection.

ORAL ALLERGY SYNDROME (OAS) (PROFILINS, PR-10)

Reactions to widely shared profilins and PR-10 proteins are invariably mild and limited to the mouth. These proteins are usually rapidly destroyed by heating or short bursts (15 seconds on full power) from microwaves. Because of their wide distribution, patients allergic to one PR-10-containing food may over time develop reactions to other PR-10 containing foods.

ALPHA-GAL (GALACTOSE-ALPHA-1,3-GALACTOSE)

This allergic reactivity is unusual in that the allergen is a carbohydrate and the route of sensitisation is usually via tick bites. This sensitisation may lead to a reactivity to red meats (beef, lamb, venison). In areas where there is a high frequency of tick bites this cause of severe food allergy should be considered. Patients typically present with a delayed reaction (approximately 4–6 hours after exposure), which may include abdominal symptoms, urticaria and even anaphylaxis after eating red meat.[10]

FOOD-DEPENDENT, EXERCISE-INDUCED ANAPHYLAXIS

Severe allergic reactions to food are described when the food is consumed and immediately preceded or followed by exercise. If the food is consumed without exercise, then no reaction occurs. It is thought that changes in intestinal permeability and the effectiveness of digestion during exercise accounts for this. The most commonly associated foods are wheat (particularly that associated with specific IgE to omega-5-gliadin or LTP) and shellfish (prawn – mainly in Japan).[11] 'Exercise' may be as simple as walking; it lowers the threshold for consuming food and increases the severity of reactions, although wheat-dependent exercise-induced anaphylaxis can be induced at rest in susceptible individuals, surprising though this may seem![12]

Aspirin and alcohol can have similar effects and may potentiate exercise-induced symptoms. Recognition of the importance of

co-factors is crucial. This is because neither the clinician nor the patient will otherwise be able to identify why a patient has reactions, as the reactions will appear to be random and not linked to foods.[13]

EOSINOPHILIC OESOPHAGITIS (ENTERITIS)

Eosinophilic oesophagitis is a mixed IgE/cell-mediated reaction. It usually presents with dysphagia in young people. Biopsies will confirm the excess of eosinophils. A widespread involvement of the small and large intestines may lead to more generalised abdominal symptoms and mimic inflammatory bowel disease. Specific IgE tests to foods may be positive, but are a poor guide to avoidance.

DIAGNOSIS OF FOOD ALLERGY

History is the mainstay of food-allergy diagnosis. Testing of any type is confirmatory and used to stratify risk. The presence of a specific IgE does not automatically equate to clinical allergy, but simply indicates sensitisation or non-specific cross-reactivity. For example, patients with grass-pollen allergy (hay fever) frequently have a specific IgE to wheat, but have no clinical symptoms when they consume wheat-based foods. IgE to house-dust mite (HDM) may cause cross-reactive antibodies to shrimp. The recognition of sensitisation without clinical symptoms is becoming more important with the increasing using of micro-array systems for detecting specific IgE (Immuno-Solid-phase Allergen Chip – ISAC). Any positive result must be interpreted in the context of the clinical history and not the other way round.

The purpose of testing is to confirm allergies suspected on history or to refute allergies suspected by the patient. The gold standard remains SPT, although, depending on circumstances, *in vitro* testing can be used, but it may not give equivalent results. SPT requires skilled operators using a standardised technique. Operator competency should therefore be audited at regular intervals. Both a positive control (histamine solution) and a negative control (saline) are mandatory in all tests. If more than one site on the body is used, then controls must be reapplied owing to variations in mast-cell distribution. Skin-prick tests are preferentially performed on the flexor surface of the forearm, but in small children the back is sometimes used.

Commercially produced solutions of food allergens can be used. However, processing them may destroy heat-labile allergens. Standardisation is variable and is usually based on protein nitrogen content rather than allergenic protein content. Prick-prick testing using fresh foods, or foods 'as eaten' is better but the allergen content will usually be higher than that in commercial solutions, which increases the risk of large local and/or systemic reactions. Where the reaction has occurred to a composite food, asking the patient to bring it in for inspection and testing is helpful. Patients will remember only the headline ingredient, but the clinician should look at all its constituents. An SPT should be undertaken with caution in patients who have had severe systemic symptoms to foods and the person performing the skin-prick test should have appropriate training in the management of anaphylaxis. They should also have access to resuscitation equipment and immediate medical back-up. Long-acting antihistamines should be discontinued for at least a week prior to testing; it may be possible to omit short-acting antihistamines for 72 hours. The histamine control will determine whether the effect has worn off.

SPTs are read at 15 minutes after application. There must be a reasonable positive control (> 3 mm) and no reaction to the negative control. For patients with obvious dermatographism, a positive result is one that is at least 2 mm greater than the negative control.

Specific IgE testing ('RAST' tests) may be used as an alternative: where, for example, an SPT facility is not available, where there is no commercial SPT solution or where SPT is either contra-indicated or where the patient is taking antihistamines that cannot be stopped. Extensive dermatitis or dermatographism renders reliable SPT difficult and/or impossible. Specific IgE tests are expensive and should be confined to the key allergens required. Blanket screening is *not* supported by laboratories. The use of specific IgE testing is appropriate for identifying key molecular allergens that identify sub-types of food allergy and help to stratify risk – for example, the use of peanut recombinant proteins *Ara h2, Ara h 6, Ara h1* and *Ara h3* serves to identify storage protein allergy, whereas *Ara h8* identifies oral allergy and *Ara h9* identifies LTP allergy.[9]

Non-specific reactions may occur due to cross-reactive carbohydrate determinants (CCDs), present in a wide range of foods. This type of reactivity appears to be common in South Africa and is postulated to be due to high pollen sensitisation levels. These do not cause clinical problems, as is often seen with peanut. An allergen-specific IgE to CCD is available to help identify these cross-reactivities.[14] There is evidence that the inhibition of such CCDs enhances the accuracy of *in vitro* diagnostic tests.[15]

Microarrays (ISAC) are superficially attractive because they can screen against large panels of allergens with relatively small blood samples (very useful in small children). However, the agreement with standard ImmunoCap tests and with SPT can be poor, because a limited selection of known allergenic components are present in these panels and they may miss significant allergies. Their role is therefore limited to second-line investigations in patients with multiple sensitisations where multiple allergen cross-reactivities are suspected. They may be of most value in searching for a cause in idiopathic anaphylaxis where the history gives no diagnostic clues. However, detailed history-taking together with a review of food ingredients is still paramount.

Basophil activation tests (BAT/CAST) have gained popularity in helping clinicians to decide when to perform a food challenge.[16] These tests are widely available in South Africa, in contrast to the paucity of trained clinicians or allergologists who are able to perform food challenges. It is important to remember that the sensitivity of BAT is not comparable to SPT or allergen-specific IgE, but the specificity is better than these methods in predicting clinical reactions. However, BAT tests at an international

level have not yet been fully standardised.[17,18] Multi-centre international studies are underway to explore the role of these tests in predicting tolerance in food allergy.

Finally, it should be mentioned that food-challenge testing is still the only method of definitively confirming or excluding food allergy.

LOCAL FACTORS IN SOUTH AFRICA

Patterns of food-allergic reactivity in different parts of the world depend largely on dietary intake and the pattern of inhalant allergies. PR-10 allergy is rare in South Africa, but oral allergy syndrome (OAS) to raw nuts, melon, watermelon, avocado, cucumber and raw carrots as a result of profilin allergy is relatively common. LTP allergy is reported frequently and the symptoms may range from OAS to severe anaphylaxis.[14] LTP allergy may also be associated with exercise-induced anaphylaxis; moreover, it may be difficult to diagnose, as different species of the same plant (eg peanut) may have different concentrations of LTP and therefore vary in their allergenicity. This also seems to apply to the LTP content of beer, where patients with LTP allergy report tolerance to some alcoholic beverages and reactions to others – which is presumably related to the LTP concentration.[19] Alcohol may also play a role as a co-factor in reactions. Anaphylaxis to fruits such as peach and apricot attributable to LTP allergy have also been reported. The main sensitiser to LTP in the South African setting is presumed to be plane tree pollen, which originates in a tree that is widely planted in the South African urban environment.

Tree nut allergy in South Africa may include hazelnut, cashew, pistachio, macadamia, almond (rarely) and walnut, and peanut allergy is common.[20] Allergy to brazil nut and other exotic nuts is rare, but cases are increasingly being reported as more of these nuts are being included in patients' diets.

Sesame is an emerging allergen globally: it is the ninth most important food allergen in the United States.[21] A recent population-based survey in the United States demonstrated a patient-reported sesame allergy prevalence of 0,49% and a proven IgE-mediated allergy prevalence of 0,23%. Sesame allergy has been described in South Africa, but its true prevalence is unknown. Unpublished ISAC component data collected from a large private laboratory in South Africa (January to December 2018) indicate that the prevalence of sensitisation to *Ses i 1*, a major sesame component, was 0,7% of all patients who received an ISAC test during that year (the 100th most frequent component sensitisation reported on ISAC) (personal communication).

Soy allergy is often over-reported, as CCD cross-reactivity is commonly seen in patients diagnosed with soy allergy. Many patients are asymptomatically sensitised to the soy storage proteins *Gly m5* and *m6*. Delayed-type soy allergy cross-reacting with cow's milk has been reported.

Alpha-gal allergy causes urticaria, abdominal pain and anaphylaxis, and has been described in KwaZulu-Natal, the Eastern Cape and Limpopo provinces. Recent studies have also indicated a high level of asymptomatic sensitisation to alpha-gal in the Eastern Cape province.[22] Primary meat allergy resulting from allergy to serum albumins is described and patients may be symptomatic to a variety of red meats, including venison.[22]

While wheat 'allergy' is deemed to be common, this is not supported by evidence of an IgE mechanism, and therefore it falls into the category of intolerance. Patient awareness and self-reported reactions to wheat and gluten are on the increase; this is fuelled by the global marketing of gluten-free products and free access to information on the internet. Coeliac disease is underdiagnosed in South Africa; identified cases usually have European ancestry (English, Irish or Scandinavian).

Seafood allergy is relatively common in South Africa, but may be challenging to make the diagnosis, because patients often react to local fish and shellfish species, no commercial allergens being available.[23,24]

MANAGEMENT OF FOOD ALLERGY AND INTOLERANCE

The key to management is the accurate distinction between true food allergy and food intolerance, where mechanisms other than IgE are involved. For IgE-mediated reactions, the risk must be stratified, a process that may be assisted by identifying the target allergens. Allergy to storage proteins tends to be more likely to cause anaphylaxis. Assessing the risk should include an assessment of the ease of avoidance and the likelihood of exposure to hidden or undeclared allergens.

In this regard, food-labelling standards are crucial, provided that they are enforced. South Africa currently requires only egg, cow's milk, gluten and peanuts to be stipulated on food labels. Takeaway and street food outlets are the hardest to police. In the United Kingdom, there have been a number of successful prosecutions of food outlets which have provided incorrect or misleading information on food allergen content, leading to fatal outcomes. Notwithstanding these limitations, it is essential that patients with true food allergies receive detailed and correct information from trained dieticians on avoiding allergens, including the sources of hidden allergens.

Where there is a risk of further severe reactions, all patients should be given a clear allergy management plan; this should include information about how to treat mild, moderate and severe reactions. Treatment packs *for adults* should include a long-acting, non-sedating antihistamine with rapid onset of action (two cetirizine tablets, 20 mg, chewed), prednisolone (20 g po stat) and adrenaline for self-injection (adrenaline auto injector (AAI)). Prednisolone is given mainly to reduce the *de novo* synthesis of mediators and its effect is therefore slow. Dosing for *children* should follow appropriate paediatric guidelines.

Repeated supply interruptions have occurred for all major AAIs marketed in the United Kingdom (Epipen, Jext, Emerade). A locally produced adrenaline injector for South Africa is in development. Patients should have two matching AAIs, with a dose appropriate to their age/weight, and they should be trained

in how to use the AAI that they carry. One manufacturer in the United Kingdom suggested that the dose for an adult should be 500 mcg. However, this is based on Resuscitation Council Guidelines for the management of anaphylaxis by healthcare professionals and not for self-administration by patients. The recommended dose of 300 mcg for adults has been used over many years and appears to be safe and effective. However, those with significantly raised BMIs (> 35 kg/m^2) may benefit from a larger dose. Needle length may be an issue: *in vitro* work has shown that in obese patients the injection does not reach muscle and therefore absorption may be erratic.[25] However, none of the available devices have needles long enough to overcome this issue fully in the morbidly obese.

Immunotherapy for food allergens, particularly peanut, is being trialled in children, but to date the results have not been clear-cut, quality of life (QoL) does not seem to be improved, and there may be an increase in allergic and anaphylactic reactions compared to avoidance or placebo.[26] Palforzia (AR101) is an oral immunotherapy product that has recently been licensed for peanut allergy in the United States, although it is not deemed curative.[27] It is likely that safe and effective immunotherapy will need to await the use of recombinant allergen-based vaccines, rather than consumption of whole peanut. Recent studies have called into question the issue of strict peanut avoidance in small children, with early introduction possibly being helpful in preventing the development of allergy.[28]

The management of eosinophilic oesophagitis is usually undertaken with swallowed steroid asthma sprays. Dietary management should be trialled, irrespective of allergy test results, using a 4- or 6-food-elimination diet (milk, soy, eggs, wheat, peanuts/tree nuts and seafood), or one in which an allergen is targeted. However, this may not be effective, and if there is no improvement, then dietary restriction should be relaxed.

For food intolerance, pragmatic avoidance is required, and nutritional adequacy should be checked by a registered dietician. Intolerances usually cause gastrointestinal symptoms. Those with food intolerances may tolerate small quantities of the food but experience increasing symptoms as the dose is increased. This is in contrast to IgE-mediated allergy, where even small quantities of food may cause systemic effects. There is no harm in avoiding gluten-containing foods, other than the expense of the alternatives; but avoidance should be discouraged where there is no evidence that gluten is responsible for symptoms. For those with irritable bowel-type symptoms, a trial of the FODMAP diet (Fermentable Oligo-, Di-, Mono-saccharides and Polyols, short-chain carbohydrates that are poorly absorbed in the small intestine) is worth considering, again with the support of a dietician to ensure that nutritional needs are met. Unnecessarily avoiding foods, especially in early childhood, may alter immunological tolerance and has the potential to increase the risk of subsequent reactions. It is now known that changes to diet – for example the elimination of wheat – have a profound effect on the intestinal microbiome. The significance of these changes to a person's health and immune function remains to be explored.

FURTHER PROSPECTS FOR TREATMENT

A greater understanding of the molecular nature of allergens and their cross-reactivity is likely to improve our understanding of food allergy and to enable to target treatments, including immunotherapy, better. Similarly, the development of a better understanding of the role of the microbiome in the development of food allergy and food intolerance holds the promise of prevention.

DECLARATION OF CONFLICT OF INTEREST
The authors declare no conflict of interest.

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REFERENCES:

1. Wuthrich B. History of food allergy. Chem Immunol Allergy 2014;100:109–-119.
2. Prescott SL, Pawankar R, Allen KJ, Campbell DE, et al. A global survey of changing patterns of food allergy burden in children. World Allergy Organ J 2013;6(1):21.
3. Tang ML, Mullins RJ. Food allergy: Is prevalence increasing? Intern Med J 2017;47(3):256–61.
4. Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. Gastroenterology 2018;154(2):319–332.e3.
5. Altman DR, Chiaramonte LT. Public perception of food allergy. J Allergy Clin Immunol. 1996;97(6):1247–1251.
6. Skypala IJ. Food-induced anaphylaxis: Role of hidden allergens and cofactors. Front Immunol 2019;10(673).
7. Moneret-Vautrin DA, Guerin L, Kanny G, Flabbee J, et al. Cross-allergenicity of peanut and lupine: The risk of lupine allergy in patients allergic to peanuts. J Allergy Clin Immunol 1999;104(4 Pt 1):883–888.
8. Versluis A, Van Os-Medendorp H, Kruizinga AG, Blom WM, et al. Cofactors in allergic reactions to food: Physical exercise and alcohol are the most important. Immun Inflamm Dis 2016;4(4):392–400.
9. Borres MP, Karabus S. What is new in allergy and component testing? Curr Allergy Clin Immunol 2018;31:131–136.
10. Gray CL, Van Zyl A, Strauss L. Midnight anaphylaxis to red meat in patients with alpha-gal sensitisation: A recent discovery in the food allergy world and a case report from South Africa – guest review. Curr Allergy Clin Immunol J 2016;29(2):102–104.
11. Salcedo G, Sanchez-Monge R, Diaz-Perales A, Garcia-Casado G, Barber D. Plant non-specific lipid transfer proteins as food and pollen allergens. Clin Exp Allergy 2004;34(9):1336–1341.
12. Christensen MJ, Eller E, Mortz CG, Brockow K, Bindslev-Jensen C. Exercise lowers threshold and increases severity, but wheat-dependent, exercise-induced anaphylaxis can be elicited at test. J Allergy Clin Immunol Pract 2018;6(2):514–520.
13. Christensen MJ, Eller E, Mortz CG, Brockow K, Bindslev-Jensen C. Wheat-dependent cofactor-augmented anaphylaxis: A prospective study of exercise, aspirin, and alcohol efficacy as cofactors. J Allergy Clin Immunol Pract 2019;7(1):114–121.
14. Pentz A, Green RJ. Advances in the diagnosis and management of allergic disease: Applications to South African practice. S Afr Med J 2014;104(11):794.
15. Aberer W, Holzweber F, Hemmer W, Koch L, et al. Inhibition of cross-reactive carbohydrate determinants (CCDs) enhances the accuracy of in vitro allergy diagnosis. Allergol Select 2017;1(2):141–149.

16. Ruinemans-Koerts J, Schmidt-Hieltjes Y, Jansen A, Savelkoul HFJ, et la. The Basophil Activation Test reduces the need for a food challenge test in children suspected of IgE-mediated cow's milk allergy. Clin Exp Allergy 2019;49(3):350–356.
17. Hemmings O, Kwok M, McKendry R, Santos AF. Basophil Activation Test: Old and new applications in allergy. Curr Allergy Asthma Rep 2018;18(12):77.
18. Hoffmann HJ, Santos AF, Mayorga C, Nopp A, et al. The clinical utility of basophil activation testing in diagnosis and monitoring of allergic disease. Allergy 2015;70(11):1393–1405.
19. Quercia O, Zoccatelli G, Stefanini G, Mistrello G, et al. Allergy to beer in LTP-sensitized patients: Beers are not all the same. Allergy 2012;67:1186–1189.
20. Karabus S. One tough nut to crack! A case of anaphylaxis to almond and an update on immunotherapy for food allergy. Curr Allergy Clin Immunol 2019;32(3):154–162.
21. Warren CM, Chadha AS, Sicherer SH, Jiang J, Gupta RS. Prevalence and severity of sesame allergy in the United States. JAMA Netw Open 2019;2(8):e199144.
22. Wilson JM, Platts-Mills TAE. Red meat allergy in children and adults. Curr Opin Allergy Clin Immunol 2019;19(3):229–235.
23. Sharp M, Lopata A. Fish allergy: In review. Clin Rev Allergy Immunol 2013;46.
24. Lopata A, Jeebhay M. Allergy and asthma to indigenous seafood species in South Africa. Curr Allergy Clin Immunol 2007;20:196–200.
25. Song TT. Epinephrine needle length in autoinjectors and why it matters. J Allergy Clin Immunol Pract 2018;6(4):1264–1265.
26. Chu DK, Wood RA, French S, Fiocchi A, et al. Oral immunotherapy for peanut allergy (PACE): A systematic review and meta-analysis of efficacy and safety. Lancet 2019;393(10187):2222–2232.
27. FDA approves first drug for treatment of peanut allergy for children. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children.
28. Chan ES, Abrams EM, Hildebrand KJ, Watson W. Early introduction of foods to prevent food allergy. Allergy Asthma Clin Immunol 2018; 14 (Suppl.2) 57–64.