

Mrs Shihaam Cader, Chief Dietitian, Red Cross War Memorial Children's Hospital, Cape Town Correspondence to: Mrs Shihaam Cader, e-mail: Shihaam.Cader@westerncape.gov.za

The management of food allergies can be challenging for both the health professional and the family alike. Food allergies are not common in an unselected population but are found to occur more frequently in high risk allergy groups. Interpretation of investigations together with a thorough history-taking will guide the team to optimal diagnosis. Elimination diets are only to be advised thereafter by an experienced dietitian to ensure nutritional adequacy. Reintroduction of foods through a stepwise approach is recommended not only to include the tolerated food allergens back into the diet but also to liberalise it and facilitate adherence thereto.

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Introduction

Food allergy is a complex clinical setting which can result in misdiagnosis and mismanagement with unnecessary avoidance of foods making the daily food intake challenging for families.

The prevalence of food allergies in South Africa seems to be on the increase in high risk groups. In a recent randomised prospective study, 100 children (age 6 months – 10 years) were selected from a dermatology clinic to determine the prevalence of food allergy. The total group showed 66% of the selected children to be sensitised to one food. Of the total group, 68 children had an open oral food challenge (OFC) which demonstrated a 42% prevalence with a true allergy. The most common food allergens found were peanuts (26%), eggs (24%) and cow's milk (2%).1 Early onset, < 6 months of age, of atopic dermatitis was also shown to be a risk factor for the development of food allergy (66%) compared to children older than 1 year (42%).1 The severity of the allergic condition was related to a higher risk of developing one or more food allergies. Of this group those with SCORAD (atopic dermatitis severity) scores of > 40 had a higher prevalence of one or more food allergies (50%) compared to those with lower SCORAD score (30%).1 The prevalence reported in this study, however, was performed in a selected group with a high risk for food allergy. The South African Food Sensitisation and Allergy (SAFSA) study reviewed an unselected group of 1-3 year old children showing a prevalence of 11.6% lower sensitisation to common food allergens, defined by a skin prick test (SPT) > 1 mm, compared to those having a higher sensitisation with SPT > 7 mm (4.2%). Food challenge proven tests thereafter showed prevalence of 1.4% egg allergy and 1.1% peanut allergy.²

Food allergy is classified as either Immunoglobulin E (IgE)- mediated, non-IgE mediated or a mixed combination of both. The diagnostic approach to food allergy is a combination of allergy focused diet history together with investigations such as SPT, specific food IgE levels (sIgE) and OFC. Only then can elimination diets be recommended based on these outcomes.²⁻⁵

The cornerstone of managing food allergy is avoiding the "culprit" foods in the diet. The dietitian's role is not to only advise on elimination diets, but also to advise on suitable alternatives to ensure nutritional adequacy of the diet.³

Those children with more than one type of food allergy are at higher risk of growth faltering and micronutrient deficiencies due to limitations in the variety of food choices. Other areas that a dietitian would require nutritional input for those with any food allergies are³:

- Alternative infant formula or milk substitutes for infants not breastfed and complementary feeding to prevent unnecessary food avoidance
- 2. Guidance on elimination diets for breastfeeding mothers, where applicable
- 3. Information related to lifestyle or social activities such as eating out
- Psychological aspects related to food such as anxiety and fear of reactions in other settings
- 5. Guidance on reintroduction of foods

Allergy focused diet history

The purpose of an allergy focussed diet history (Table 1) aims to determine whether there is an association between the ingestion of

certain foods and volunteered symptoms. Detailed information on each of these components will serve to direct the medical team to further diagnostic testing to support an optimal final diagnosis. It should consist of aspects related to timing of ingestion of food in relation to symptoms, age at the time of adverse reaction(s), amount of food, co-existing medical conditions and whether a given reaction is reproducible or not.⁴

Table1: Allergy focussed diet history in children – key points^{4,6}

- 1. Clinical history linked to allergens and symptoms:
- · Personal history of atopy
- · Family history of atopy
- · Food avoided and why
- Reactions to food:
 - Type of symptoms (e.g.: urticarial, angioedema, vomiting, atopic dermatitis, oral itching, difficulty in breathing)
 - · Age at first symptom(s)
 - · Reactions speed onset of symptom(s)
 - Duration of symptom(s)
 - Frequency of occurrence
 - Setting or place where reaction occurred
 - Reproducibility of symptoms
 - Dose of food
 - Infant feeding history*
 - Did the condition require immediate medical attention
- 2. Other extrinsic factors that could result in an adverse immunological response OR enhance or precipitate the allergic reaction to food include among others:
- Infection
- Medication
- · Exercise before or after ingesting a food allergen
- Hormonal
- · Cross reactivity to an inhalant and food allergens

Diagnosis of food allergy

The combination of SPT and slgE levels together with a history can help direct the diagnosis. Nevertheless, these types of tests only determine whether there is an IgE mediated type of food allergy. Commercial or fresh extracts should always been used for SPTs. The wheal diameter is measured to determine the response of the reaction. Antihistamines should be discontinued 3-5 days prior to testing.6 Immunoassays for specific IgE levels are reliable and reproducible but costly. There are no diagnostic cut-off values for slgE.7 However, the higher lgE levels recorded the greater the likelihood of the presence of a clinical allergic response. Of cardinal importance is the correlation of the test results (high or low) to the history and clinical findings. There are published decision cut-off points with 95% positive predictive value (PPV) available, done in a specific population (Table 2).6 These values therefore are used only to guide the process of determining the final diagnosis in combination with the clinical history.

If these tests are found to be negative, they only confirm the likely absence of IgE mediated allergy but do not exclude the possibility of a non-IgE mediated allergy as reported in delayed gastrointestinal tract symptoms.

Certain protein components (slgE levels) can be measured to determine if allergens are heat stable like ovomucoid and casein protein or to show severity of allergy like Arah2 in peanuts. A study

done in 100 children (6m-10years) to investigate whether Arah2 was a good marker for severity of peanut allergy, reported that 92% of children with raised Arah2 (slgE levels) were truly allergic compared to the asymptomatic sensitive group.8 Within the same study group, ovomucoid was also shown to be a good marker of true allergy to egg compared to the sensitisation group.9

Exclusion diets can also be used as a diagnostic tool whereby a suspected food is removed for a period of 4–6 weeks. This is usually recommended in non-IgE mediated type of food allergy or when reported to have delayed reaction beyond 2–3 days. ¹⁰ The OFC test is the gold standard of diagnosing food allergy particular in the IgE mediated allergy with an immediate reaction. It can also be used for those children who have developed tolerance after periods of elimination. ^{10,11} All OFCs need to be done in a setting equipped with resuscitation equipment. Vital signs and symptoms need to be monitored with every incremental dose given every 15–20 minutes. The final dose is usually the age appropriate portion size. If OFC outcome is successful, i.e. no allergic reaction to the tested food, the individual is to continue ingesting the food item at that final dose for at least twice a week to maintain tolerance. ^{2,10}

Management of food allergy

The primary treatment is strict avoidance of the identified offending food(s). Dietary counselling should ensure that daily nutritional requirements are met to avoid major nutritional deficiencies. Individuals with more than one food allergy usually have more nutritional challenges. Offending foods such as cow's milk, eggs and peanuts can result in major nutritional deficiencies.⁵

Regular growth monitoring is required to determine the nutritional intervention. Those with severe cow's milk allergy and poor nutritional status would need a suitable alternative product that meets daily protein and micronutrients needs. However, those children with good nutritional status and eating solids well would be able to have an alternative such as rice or oat milk as part of their daily intake.^{2.5}

Dietitians should provide clear guidelines on the management of elimination diets that include how to read food labels and identify hidden allergens. Education to include ways on how to address challenges in different settings such as schools and children parties should also be provided.

Cow's milk protein allergy

Cow's milk protein allergy (CMPA) is common in the first 3 years of life. The main proteins in cow's milk are casein (80%) and whey (20%). Casein is a heat-stable whereas whey is heat-labile protein. Those with intolerance to whey are able to tolerate baked form of cow's milk products. 12,13

All forms of cow's milk are to be avoided in confirmed CMPA. Following a strict cow's milk elimination diet can be challenging for families as hidden allergens are found in many different food items. Education related to reading labels should include awareness that cow's milk protein differs to lactose intolerance and that items listed as 'lactose free' are not allowed in the diet. Infants are generally affected by CMPA as it provides a major food group during this

^{*}A detailed diet history during infancy is required to determine trend, if events occurred with the onset of solids or change in milk intake.



stage of life. Mothers who are breastfeeding should be encouraged to continue and only in exceptional cases of severe forms of CMPA would the mother be expected to eliminate offending foods.2 Milk alternatives available would depend on severity of the reaction, religion and cultural considerations, cost, and palatability.2 An example would be that certain infant formula, particularly those with hydrolysed protein, have not been certified as halal in South Africa.

Hypoallergenic formulae are defined as formula proven to be tolerated by 90% of subjects with CMPA. They have also been defined as having the majority of its peptides size being < 1.5kDa. Extensively hydrolysed and amino acid based formulae meet this definition making these formulae the feed of choice for the dietary management of CMPA. Due to the high cost of these products, they are specifically recommended for severe life threatening forms of CMPA and severe growth faltering.¹³ Partially hydrolysed infant formulae marketed in the country as hypoallergenic do not meet this definition and therefore are not recommended for management of CMPA.2,7,11

Soya based infant formula can be considered as alternatives only if clinically proven tolerance to soya protein is available. These formulae are perceived to have better taste and are a more cost effective option. Fears of harmful side effects of phytoestrogens have not been proven in human studies.² No other mammalian milks are recommended due to the cross reactivity of CMP to goat, sheep and buffalo milk. In addition the latter are not nutritionally complete as sole infant formulae.2

Plant based milk products such as rice and oat milk are only recommended if the daily food intake is adequate in protein and micronutrients.² Calcium and vitamin D supplementation is required for children who are not receiving another form of milk substitution or with poor dietary intake of calcium and vitamin D rich foods.5

Milk ladder

Children who outgrow CMPA tend to tolerate baked milk products before fresh whole cow's milk because the high temperatures of baking alter the allergenicity. 12,13 It has been shown that 75% of CMPA children (age range 2.1 - 17.3 years) were able to tolerate baked CMP. Those who had reacted had an increase SPT wheal diameter with increased levels of specific cow's milk and casein IgE levels.¹² Available guidelines recommend that milder reactions, with low SPT and IgE levels, and those who have had no reaction to CMP during the last 6 months can commence on small amounts of baked milk products at home. 12 A milk ladder has been devised as a guideline for the reintroduction of milk products starting with baked milk products and ultimately ending with fresh whole cow's milk. This process should be followed under the guidance of experienced dietitians to advise on how to commence the process in a stepwise approach. Each step of the milk ladder varies between the form of milk product, quantities and content/recipe of a given product.13

Egg protein allergy

Egg allergy presents commonly in infancy and occurs with other food allergens such as CMPA and peanuts. 14,15 The white component of the egg is the main protein causing egg allergy, and consists of

ovomucoid, ovalbumin, ovotransferrin and lysozyme. Some children may also react to egg yolk protein, apha-livetin. 14,15

All forms of egg products need to be avoided initially unless the safety of ingesting baked egg is established. Even though ingestion of raw or uncooked egg may trigger more severe reaction than baked egg, the latter should only be advised by an experienced allergy team. OFC can be done to determine whether baked egg products could be included in the diet. 14,15

Education involves reading labels to identify hidden allergens such as ovalbumin and ovomucoid. Food labels with key words found in baked food items would not need to be avoided if there is tolerance of baked food items.

Egg ladder

Most children with egg allergy "grow out" of it in early life. As the allergy resolves over time, many children may tolerate baked forms of egg products. Similar to the milk ladder, recommendations for those with milder reaction to egg can be trialled with baked egg products at home. However, those children with a history of severe reactions would need to be managed under clinical observation together with repeat SPT and IgE levels determinations. Available guidelines explain a process of different phases for the reintroduction starting with baked forms, followed by lightly cooked and finally fresh whole egg.14,15

There are of course children who do take longer to outgrow their egg allergies, like those with high specific IgE levels to ovomucoid protein. Nevertheless, those with tolerance to baked egg are more likely to outgrow their egg allergy at an earlier age. 14,15

Peanut allergy

Peanut allergy is common in children and can cause severe allergic reactions such as anaphylaxis.16 Peanuts are a member of the legume family and is related to soya bean, lentils, garden peas and chickpeas.16

Like in any other food allergy, avoidance of all forms of peanuts is required in peanut allergy individuals. Reading labels of common foods such as cereals and breads is important to look for hidden allergens. Packaging stating "may contain traces' are an indication that there is cross contamination of peanuts in the manufacturing process. There are individuals with severe form of peanut allergy who react to trace amounts of peanuts and as such these foods would need to be avoided.

Action plans and guidelines should be provided by the medical team and are vital for individuals with a severe form of food allergy such as peanut allergy, particularly if it results in an anaphylaxis reaction.

Monitoring and follow-up assessments

Patients need to be reviewed at regular intervals to ensure adherence to a prescribed elimination diet. After a period of elimination, children would need to be further reviewed as to whether they have developed tolerance to the offending food(s).

In broad frequency terms, infants or younger children with milk, soya and egg allergy should be reviewed every 6-12 months and



older children every 1–2 years with respect to sensitisations to food allergy.²

Ongoing evaluation and monitoring is an essential part of the child's overall management. The key factors to review with each visit include:

1) Growth monitoring:

There are many risk factors that could contribute to impaired growth in children with food allergy such as the early onset of an allergic condition, delay in diagnosis of food allergy, delay in initiation of an appropriate elimination diet and having multiple food allergies. If a certain food item plays a central role in the diet, like an infant formula or if unnecessary foods are eliminated, these can further negatively impact on growth.⁵

- Nutritional adequacy to ensure that all macronutrient and micronutrient needs are met.
- Adherence to any elimination diets and identification of any other triggers with the use of a food diary.
- 4) Lifestyle and psychological aspects3:
 - Children with food allergies, particularly multiple food allergies are to a large extent also limited in participating in social activities. For settings such as parties, holidays, school meals and restaurants, a child would require detailed advice on how to face these challenges without feeling excluded.
 - Anxiety and fear amongst families with children who have severe forms of food allergies are often associated with unnecessary avoidance practices which, in themselves, lead to inadequate dietary intake.
 - Young picky eaters are also likely to develop dietary inadequacies due to their avoiding multiple foods since late infancy due to fear of reactions.
 - Reintroduction of foods after proven tolerance of a food allergen can also bring anxiety for children especially if they clearly recall severe reactions and are advised to eat foods eliminated for long periods of time. Therefore, OFC in a clinical setting is recommended for the reintroduction of a given offending food.

Case study

Child LJ presented at age of 11 months with a history of atopic dermatitis before the age of 6 months. The mother had been eliminating certain foods, namely cow's milk products, eggs and soya bean products due to his condition worsening when ingesting these specific foods. She reported reactions to soya bean, eggs, cow's milk and lentils which she had been avoiding for the last 5 months. Prior to these exclusions from the diet, her child had been on exclusive breastfeeding followed by solid introduction at the age of 6 months. She stopped breastfeeding at the age of 10 months and only gave clear liquids, such as rooibos tea, water, fruit juice, as choice of fluids.

The child had normal weight trend (along 0 Z score line) for first 4 months of age but growth faltered thereafter by crossing Z scores at age of 7 months. The child's weight trend continued between -2 and -3 Z score until the point of intervention by the allergy team at age of 13 months. The child's length at 13 months of age plotted between -2 and -3 Z score line (Figures 1 and 2, respectively).

The following events were reported by the mother with potentially different food allergies:

- 1. Cow's milk products: The patient had more than one exposure to different forms of cow's milk products at different times between 6–10 months of age. The reactions were all the same, involving immediate swelling and rash on his face and body within few minutes of ingestion. These reactions occurred with 4 different standard cow's milk-based infant formula (including lactose free and partially hydrolysed formula) and yoghurt. Each cow's milk exposure varied with small and large volumes.
- Soya products: At 10 months of age the child received soya based infant formula given in small amounts of 50 mls at 2 different occasions whereupon he developed an immediate reaction but less severe compared to previous reactions observed with cow's milk
- 3. Egg products: At around 10 months of age the child ate a boiled egg and had an immediate severe reaction.

Table 2: Skin prick tests and specific IgE levels of offending foods and decision cut off points⁶

	Skin Prick Test (SPT)			Specific IgE levels (sIgE)	
	Results pertaining to case study		Decision cut-off points	Results pertaining to case study	Decision cut-points for
	SPT 1	SPT 2 (6 months after elimination diet)	(95%PPV) ⁶	slgE levels (ku/L)	slgE levels(ku/L) (95%PPV) ⁶
Cow's milk • Commercial extract • Fresh	5 mm 6 mm	9 mm 9 mm	< 2 yr: 6 mm > 2 yr: 8 mm	Cow's milk > 100 Casein > 100 a-lactalbumin 0.69 (heat labile)	< 1 yr: 5 > 2 yr: 15
Soya Commercial extract fresh	2 mm 2 mm	N/D		Soya 4.32	30
EggCommercial egg whiteFresh	5 mm 5 mm	12 mm 10 mm	< 2 yr: 5 mm > 2 yr: 7 mm	Egg white > 100 Ovomucoid > 100 (heat stable)	< 2 yr: 2 > 2 yr: 7
Peanuts Commercial extract fresh	6 mm 3 mm		< 2 yr: 4 mm > 2 yr: 8 mm	Peanuts > 100 Arah2 58.3	14
Lentils	N/D	N/D		Lentils 97.6	

^{*}N/D = not determined



4. Peanuts: The mother reported to have never given him any form of peanuts. However, she reported a possible reaction after he ate lentil soup with the family on one occasion.

All other food groups had been included in the diet including fish and wheat uneventfully. A dietary history given by the mother indicated an overall balanced daily intake but inadequate in calories and protein as well micronutrients, such as calcium and vitamin D.

The following investigations had been done by the medical team (Table 2).

Other medical and environmental factors, such as infections at the time of the reactions, were also considered and ruled out. No family history of atopy was reported.

Treatment plan

Based on the investigations and clinical history the child was provided with an elimination diet for strict avoidance of cow's milk, eggs, peanuts and legumes. He received an open oral soya milk challenge after his low response to SPT for soya. He was able to tolerate the soya milk prescribed which was included in his diet as an allowed milk substitute.

The mother-child pair came for regular follow-up visits to monitor the child's compliance to the elimination diet, growth parameters and review whether he had developed tolerance over time. He had improved his linear growth and weight trend since implementation of the elimination diet and appropriate supplementation from the age of 13 months to present (Figure 1 and 2).

After 2-3 months of the elimination diet an open food challenge for baked egg and baked cow's milk was planned, separately. Each of

these open OFCs was successful demonstrating tolerance of the food items tested. The mother was thereafter to continue only avoiding fresh egg, fresh cow's milk and peanuts. Lentils were reintroduced by the mother prior to any further investigations which the infant tolerated and the mother advised to continue.

No severe adverse reactions occurred during the first 6 months of the elimination diet. The child started play school and the mother returned to work. Anxiety was felt by all family members and at school due to fear of adverse events in the absence of the mother. Clear guidance around different settings, such as school, was provided to ensure compliance to the elimination diet and to minimise any related risks.

SPT were repeated 6 months after following the elimination diet in order to determine whether the child was ready for an open OFC for fresh egg or fresh cow's milk. However, raised SPT reactions were observed at the time. A year later while on elimination diet, he had an accidental cow's milk exposure in the form of yoghurt provided by another family member. A severe reaction ensued and the medical team opted to not do any further investigations for another 6 months. He continued with the elimination diet of fresh egg, fresh cow's milk and peanuts uneventfully to date.

Conclusion

A thorough assessment for diagnosing food allergy(ies) requires good clinical-dietary history to help guide interpretation of related investigations in order to reach optimal diagnosis. Dietary support is required to help families follow a given elimination diet without affecting daily nutritional needs and to maintain a good quality of life. Alternate forms of allergens can be considered as part of the

Weight-for-age BOYS

Birth to 2 years (z-scores)



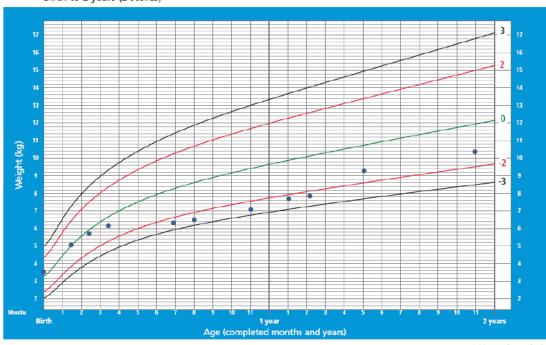


Figure 1: Weight for age chart

WHO Child Growth Standards

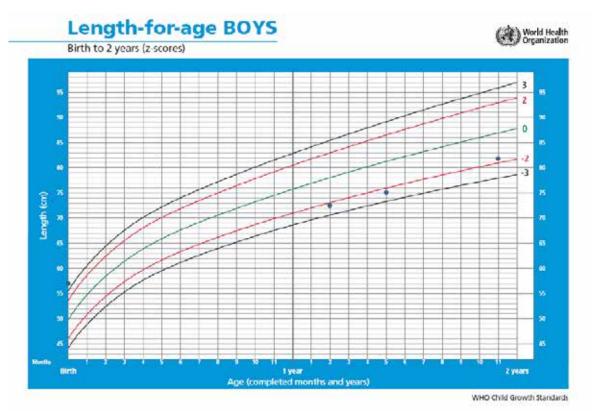


Figure 2: Length for age chart

process of reintroduction done by an experienced dietitian(s). Most children will outgrow food allergy by 5–6years. However, those with severe peanut, tree nut and seafood allergy may have a longer term of elimination.

References:

- Gray C, Levin ME. Food allergy in atopic dermatitis: How, when and why do we test? Current Allergy & clinical immunology. 2014;27(2):82-86.
- Levin ME, Gray CL, Goddard E, et al. South Africa food allergy consensus document 2014. SAMJ. 2015;105(1):62-65.
- Venter C, Laitinen K, Vlieg-Boerstra B. Nutritional aspects in diagnosis and management of food hypersensitivity – the dietitian role. Journal of allergy. 2012. Article 269376. Available at: http://dx.doi.org/10.1155/2012/269376
- Skypala IJ, Venter C, Meyer R, et al. The development of standardised dietary tool to support diagnosis of food allergy. Clinical and Translational Allergy. 2015;1-9. doi: 10.1186/s13601-015-0050-2
- Giovanni M, D'Auria E, Caffarelli C, et al. Nutritional management and follow up of infants and children with food allergy: Italian Society Position statement. Italian Journal of Pediatrics. 2014:40:1-9.
- Van der Spuy DA, Terblanche AJ, Karabus S, et al. Diagnosis of food allergy: History, examination and invivo and in vitro tests. SAMJ. 2015;105(1):69-70.

- Lloyd M. Interpretation of IgE-mediated allergy tests (RAST). Current allergy & clinical immunology. 2015;28(2):100-3.
- Gray CL, Levin ME, DuToit G. Which test is best for diagnosing peanut allergy in SA children with atopic dermatitis? SAMJ. 2016;106(2):214-20.
- Gray CL, Levin ME. Egg sensitisation, allergy and component patterns in Africa children with atopic dermatitis. Pediatric allergy immunology. 2016;27(7):709-15.
- Lang A, Manjra Al, Terblanche AJ, et al. Exclusion diets and challenges in the diagnosis of food allergy. SAMJ 2015;105(1):67-8.
- Lang AC, Van der Spuy DA, Goddard E, et al. Elimination diets and dietary interventions for management of food allergies. SAMJ. 2015;105(1):71-2.
- 12. Luyt D, Ball H, Makwana N, et al. BSACI milk allergy guideline. Clinical and Experimental Allergy. 2014;44:642-72.
- Venter C, Brown T, Shah N, et al. Diagnosis and management of non-IgE mediated cow's milk allergy in infancy- UK primary care practical guide. Clinical and Translational allergy 2013;3(23):1-11.
- Tan JW, Joshi P. Egg allergy: an update. Journal of paediatrics and child health. 2014;50:11-5.
- Clark AT, Skypala I, Leech SC, et al. British Society for Allergy and clinical Immunology guidelines for management of egg allergy. Clinical and Experimental Allergy. 2010;40:1116-29.
- Brough HA, Turner PJ, Wright T, et al. Dietary management of peanut and tree nut allergy: what exactly should patients avoid? Clinical and experimental allergy. 2014;45:859-71.