CLINICAL PRACTICE GUIDELINES

FOOD ALLERGY

DIAGNOSIS AND MANAGEMENT

2nd EDITION (2026)

ACADEMY OF MEDICINE SINGAPORE

COLLEGE OF PAEDIATRICS AND CHILD HEALTH, SINGAPORE

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EXECUTIVE SUMMARY OF RECOMMENDATIONS

Details of recommendations can be found in the main text.

- **R** = Key Recommendation
- **GPP** = Good Practice Point

CHAPTER 1: DIAGNOSIS OF FOOD ALLERGY

R 1.1 We strongly recommend that in patients with suspected food allergy, a detailed allergy-focused clinical history should be taken as the first step of the diagnostic evaluation. [EM1-1]

R 1.2 We strongly recommend that in patients with a history suggestive of IgE-mediated food allergy, skin prick test (SPT) and/or measurement of food-specific IgE (sIgE) should be performed as first line tests to support diagnosis. [EM1-1]

R 1.3 We strongly recommend that patients with a history of suspected IgE-mediated food allergy be referred to an allergist where component-resolved diagnostic tests may be performed in selected patients in addition to SPT and/or sIgE to further support diagnosis or in preparation for an oral food challenge. [EM1-1]

R 1.4 We strongly recommend that a medically supervised oral food challenge (OFC) be considered to confirm or exclude food allergy in patients if diagnosis remains unclear after initial evaluation, incorporating shared decision-making with patients. [EM1-1]

CHAPTER 2: NON-IgE MEDIATED FOOD ALLERGIES

GPP 2.1 We recommend that severe acute Food Protein-Induced Enterocolitis Syndrome (FPIES) be treated as a medical emergency, and the priority should be haemodynamic support with aggressive fluid resuscitation. [EM2-1]

GPP 2.2 For patients presenting with mild symptoms, a trial of oral rehydration may be attempted. [EM2-1]

R 2.3 We conditionally recommend ondansetron to be considered as an adjunctive therapy in patients ≥6 months of age with acute FPIES reactions. [EM2-2]

GPP 2.4 Intramuscular adrenaline is ineffective and should not be used to treat acute FPIES reactions. [EM2-3]

CHAPTER 3: MANAGEMENT OF FOOD ALLERGY

Cow's Milk Allergy (CMA)

R 3.1 We strongly recommend using extensively hydrolysed cow's milk formula (eHF-CM) or soy formula (SF)* as first choice, and an amino acid-based formula (AAF) as second choice in infants with cow's milk allergy who need a breastmilk alternative. [EM3-1]

*When initiating SF, clinicians should discuss with caregivers the low but possible risk of concomitant soy allergy, particularly in infants with no prior soy exposure.

R 3.2 We conditionally recommend that hydrolysed rice formula (HRF) can be considered as an alternative first choice formula (if available) in infants with cow's milk allergy. [EM3-1]

R 3.3 We strongly recommend against using partially hydrolysed cow's milk formula and mammalian milks (goat/sheep) in children with cow's milk allergy (both IgE and non-IgE-mediated) due to high risk of allergic reactions. [EM3-1]

GPP 3.4 In children (≥ 2 years old) and adults diagnosed with cow's milk allergy who need a milk substitute, fortified plant-based beverages (e.g. soy, coconut, rice, oat, quinoa, almond, cashew, pea) can be used. They should not be used as a substitute for formula milk in infants < 1 year old. [EM3-1]

R 3.5 We strongly recommend against routine maternal cow's milk dietary elimination for breastfed infants with IgE-mediated cow's milk allergy, unless the infant is symptomatic whilst being exclusively breastfed. If a trial of maternal cow's milk elimination is required, this should only occur for an initial period of 2 to 4 weeks, followed by reintroduction into the maternal diet to establish diagnosis. [EM3-2]

GPP 3.6 In breastfed infants with suspected Food Protein-Induced Allergic Proctocolitis (FPIAP) (non-IgE-mediated CMA), a trial of maternal cow's milk elimination should be considered. If a trial of maternal cow's milk elimination is required, this should only occur for an initial period of 2 to 4 weeks, followed by reintroduction into the maternal diet to establish diagnosis. [EM3-2]

GPP 3.7 In breastfed infants with suspected FPIES (non-IgE-mediated CMA), routine maternal cow's milk elimination in a breastfeeding mother is not recommended unless the infant is symptomatic while exclusively breastfed. [EM3-2]

GPP 3.8 If maternal cow's milk dietary elimination is required, vitamin D and calcium supplementation should be advised and referral to a dietitian for nutritional counselling can be considered for the mother. [EM3-2]

R 3.9 We strongly recommend that patients with cow's milk allergies should be assessed for tolerance to baked milk products. If tolerated, regular consumption of baked milk products should be recommended. [EM3-3]

Egg Allergy

R 3.10 We strongly recommend that Measles, Mumps and Rubella (MMR) or Measles, Mumps, Rubella and Varicella (MMRV) or influenza vaccine be given in primary care to patients with egg allergy of any severity, with routine precautions. [EM3-4]

R 3.11 We strongly recommend against split dosing, prior allergy testing to vaccines or eggs, prior allergy specialist review or an extended observation post-administration of MMR, MMRV or influenza vaccines in patients with egg allergy. [EM3-4]

R 3.12 We strongly recommend that patients with egg allergy who require Yellow Fever vaccination should be referred to an allergy specialist for assessment and supervised administration. [EM3-4]

R 3.13 We strongly recommend that patients with egg allergies should be assessed for tolerance to baked egg products. If tolerated, regular consumption of baked egg products should be recommended. [EM3-5]

GPP 3.14 Lysozyme (muramidase)-containing expectorants and mucolytics should not be used in patients with egg allergy as they are derived from eggs. [EM3-6]

Peanut Allergy

R 3.15 We conditionally recommend referring peanut-allergic patients to an allergist to for evaluation of potential tree nut co-allergy and to facilitate introduction of untried tree nuts. Blanket avoidance of tree nuts in patients with peanut allergies is not recommended. [EM3-7]

Tree Nut Allergy

R 3.16 We conditionally recommend allergist referral for tree nut-allergic patients to screen for additional tree nut allergies, to facilitate the introduction of untried tree nuts. Blanket avoidance of all tree nuts in patients with a specific tree nut allergy is not recommended. [EM3-8]

Wheat Allergy

GPP 3.17 Patients with wheat allergies may consume rice, millet, corn and quinoa as alternative grains. [EM3-9]

GPP 3.18 We suggest that patients with wheat allergies consult an allergist with regards to consumption of rye, barley and oat, if not already introduced and tolerated, due to risk of cross-reactivity. [EM3-9]

Fish Allergy

GPP 3.19 We recommend that patients with a fish allergy may continue to eat the types of fish that they can tolerate. An allergist may be consulted before introducing new types of fish. [EM3-10]

Shellfish Allergy

GPP 3.20 We recommend that patients with shellfish allergy may continue to eat the types of shellfish that they can tolerate. An allergist may be consulted before introducing new types of shellfish. [EM3-11]

CHAPTER 4: MANAGEMENT OF ACUTE FOOD-INDUCED ALLERGIC REACTIONS

R 4.1 We strongly recommend using non-sedating H1 antihistamines to treat patients experiencing mild allergic reactions, such as urticaria, angioedema, or oral itch. [EM4-1]

GPP 4.2 Medications are not routinely recommended to prevent allergic reactions from occurring in individuals with established IgE-mediated food allergies. [EM4-2]

R 4.3 We strongly recommend that patients suspected of having food-related anaphylaxis be treated as an emergency with the immediate administration of intramuscular adrenaline as the first-line intervention. [EM4-3]

R 4.4 We strongly recommend administering additional doses of intramuscular adrenaline every 5 to 15 minutes based on the patient's clinical response, for those who do not show improvement while awaiting transfer to an emergency facility. [EM4-3]

GPP 4.5 We recommend that the following treatments be administered as adjunctive measures to intramuscular adrenaline if clinically indicated:

- High-flow supplemental oxygen for hypoxia/respiratory distress
- Intravenous fluids for hypotension/shock
- Inhaled beta-2-agonists for bronchoconstriction
- Non-sedating antihistamines for cutaneous symptoms. [EM4-3]

R 4.6 We conditionally recommend against the routine use of glucocorticoids for the prevention of biphasic anaphylaxis. [EM4-3]

R 4.7 We strongly recommend the prescription of adrenaline autoinjectors for individuals with a history of food-induced anaphylaxis. [EM4-4]

GPP 4.8 We suggest that adrenaline autoinjectors may be considered for individuals with a history of mild-to-moderate allergic reactions to foods, particularly if there are additional risk factors for anaphylaxis. Risk factors include, but are not limited to:

- Unstable or moderate-to-severe persistent asthma
- Previous reaction to trace amounts of food allergens
- Allergies to peanuts or tree nuts
- History of risk-taking behaviour
- Limited/ remote access to medical care
- Underlying systemic mastocytosis
- Oral immunotherapy for food allergy
- Inability to avoid further exposure to the allergen consistently. [EM4-4]

CHAPTER 5: NUTRITIONAL COUNSELLING AND EVALUATION

GPP 5.1 We recommend regular growth monitoring and nutritional counselling for all children with food allergies. [EM5-1]

GPP 5.2 Referral to a dietitian should be made for children with food allergies who present with poor growth or suspected malnutrition, including obesity. Other considerations for a comprehensive nutrition consultation with the dietitian include patients with:

- Cow's milk allergy
- Multiple (>2) concurrent food allergies, especially those excluding major staples such as cow's milk, egg, and wheat
- Elimination diet without appropriate nutritional substitutes
- Delayed weaning progression in infants and/or difficulties transiting to more textured foods, high child and/or parental anxiety around feeding
- History of multiple accidental exposures or anaphylaxis indicating an inability to manage food avoidance
- Additional dietary restrictions such as vegetarianism or personal food beliefs. [EM5-1]

GPP 5.3 Targeted nutritional biomarkers for micronutrient assessment should be considered after evaluating dietary intake, food eliminated, growth patterns and physical signs. [EM5-1]

GPP 5.4 Vitamin and mineral supplementation in children with food allergies should be guided by both the evaluation of nutritional biomarkers and the assessment of dietary intake. [EM5-1]

CHAPTER 6: MANAGEMENT OF FOOD ALLERGIES IN SCHOOLS, PRE-SCHOOLS AND CHILDCARE FACILITIES

GPP 6.1 Schools and childcare centres should have at least one, or more if possible, member of staff trained in the prevention, recognition and management of allergic reactions [EM6-1]

GPP 6.2 Parents of students with a diagnosed food allergy should provide the school or childcare centre with an up-to-date allergy action plan. [EM6-1]

CHAPTER 7: NATURAL HISTORY OF FOOD ALLERGY

GPP 7.1 We recommend that all patients with food allergies should be reviewed regularly by an allergist to reassess allergy status. Children younger than 5 years old should have at least yearly monitoring of food allergies. [EM7-1]

GPP 7.2 We recommend that SPT and food-specific or component resolved IgE should be performed regularly, as a declining trend of sIgE level, and size of SPT wheal is a good prognostic marker for development of tolerance. [EM7-1]

GPP 7.3 We recommend that patients with a trend of declining sIgE and/or SPT wheal size and no recent clinical reactions, should be re-evaluated for possible natural resolution, by an allergist, to enable reintroduction of tolerated food. [EM7-1]

GPP 7.4 The use of egg and milk ladders for reintroduction of egg and milk, in patients with mild egg and milk allergies, can be considered. This should be done under guidance of an allergist as appropriate patient selection and preparation is essential to minimise the risk of anaphylaxis. [EM7-1]

CHAPTER 8: ORAL IMMUNOTHERAPHY FOR FOOD ALLERGY

R 8.1 We strongly recommend offering oral immunotherapy (OIT) under specialist supervision to children with persistent IgE-mediated peanut allergy to achieve desensitisation (increase the amount of peanut tolerated while on therapy), in centres with expertise and infrastructure in OIT. Informed shared decision making is key in patient's choice to take up OIT. [EM8-1, 8-2, 8-3]

R 8.2 We conditionally recommend offering OIT under specialist supervision to children with persistent IgE-mediated hen's egg, cow's milk, tree nut and wheat allergy to achieve desensitisation (increase the amount of allergen tolerated while on therapy), in centres with expertise and infrastructure in OIT. [EM8-1, 8-2, 8-3]

R 8.3 We conditionally recommend OIT be offered as a treatment option for adults. [EM8-1, 8-2, 8-3]

GPP 8.4 OIT should be discussed with, and provided by, a specialist in allergy who is experienced in providing OIT to patients. [EM8-1]

GPP 8.5 Uncontrolled asthma is an absolute contraindication to OIT. Asthma must be controlled before beginning OIT and proactively managed during OIT. [EM8-1]

GPP 8.6 Given the potentially higher risk of anaphylaxis during OIT, carrying an adrenaline autoinjector is good practice. [EM8-1]

CHAPTER 9: ATOPIC DERMATITIS IN FOOD ALLERGY

R 9.1 We strongly recommend against the routine use of food allergy tests to screen for food allergy in atopic dermatitis (AD) patients in view of the high rates of food sensitisation (i.e. false positive). [EM9.1]

R 9.2 We strongly recommend food allergy evaluation by an allergy specialist in young patients (less than 2 years old) with severe and refractory AD despite optimisation of, and adherence to, conventional therapy and where there are concerns of food reactions. [EM9-2]

GPP 9.3 We recommend referral to an allergy specialist for young infants with severe AD, whose timely introduction of solids and allergenic foods may be delayed due to parental concerns. [EM9-3]

R 9.4 We strongly recommend against long-term untargeted elimination of foods in AD patients, as it is detrimental to a patient's health and quality of life. [EM9-3, 9-4]

GPP 9.5 We recommend against the use of patch tests to diagnose food allergy in AD patients. [EM9-2]

CHAPTER 10: UNPROVEN AND DISPROVED TESTS AND TREATMENTS

GPP 10.1 Unproven/disproved tests should not be used in the diagnosis of food allergy. The tests include:

- ALCAT - Antigen leucocyte antibody test
- Food specific IgG antibodies
- Intradermal skin tests
- Atopy patch test
- Neutralisation provocation tests
- Applied kinesiology
- Bioresonance
- Hair analysis [EM10-1]

GPP 10.2 Unproven/disproved modalities should not be used in the treatment of food allergy. These modalities include:

- Neutralisation provocation tests
- Bioresonance
- Rotational diet [EM10-1]

FOREWORD BY CHAIR, SECTION OF PAEDIATRIC ALLERGY AND IMMUNOLOGY, CPCHS

Food allergy represents a growing public health challenge worldwide as well as in Singapore, with significant implications for patients, families, and the healthcare system. Accurate diagnosis and effective management are essential not only to reduce the risk of severe allergic reactions but also to improve quality of life and alleviate the burden of uncertainty that many individuals face daily.

This guideline has been developed to provide clinicians with evidence-based recommendations on the diagnosis and management of food allergy. It emphasises the importance of early recognition, standardised diagnostic approaches, and individualised management strategies that balance safety with nutritional adequacy.

By integrating the latest scientific knowledge with practical guidance, this document aims to support healthcare providers in delivering consistent, high-quality care. It also underscores the need for multidisciplinary collaboration, patient education, and ongoing research to address gaps in understanding and treatment.

We hope this guideline will serve as a trusted resource, fostering better outcomes for patients and advancing the field of allergy care. Ultimately, our goal is to empower clinicians and communities to work together in reducing the impact of food allergy and improving the lives of those affected.

PROFESSOR ANNE GOH ENG NEO

Chair
Section of Paediatric Allergy and Immunology
College of Paediatrics & Child Health, Singapore (CPCHS)
Academy of Medicine, Singapore
Mar 2026

FOREWORD BY PRESIDENT, COLLEGE OF PAEDIATRICS & CHILD HEALTH, SINGAPORE

Food allergies are an increasingly serious global health concern, affecting approximately 8% of children worldwide. In Singapore, recent studies show that food allergies affect up to 5% of our paediatric population, with cow's milk, eggs, and peanuts being the most common allergens. Food-induced anaphylaxis rates are also rising sharply, having nearly tripled over the past decade.

These trends highlight the urgent need for robust, evidence-based clinical practices in food allergy management. A standardised approach – spanning accurate diagnosis, emergency management, and long-term care – helps us avoid the serious consequences of inconsistent practices. These consequences include delayed diagnoses and inappropriate dietary restrictions that can impair a child's growth and development. Standardised practice also ensures that every patient receives optimal, consistent care regardless of where they seek treatment.

Two elements of this document deserve particular attention. The Allergy Action Plan provides essential clarity to school caregivers managing life-threatening anaphylaxis. The section on Unproven and Disproved Tests and Treatments offers crucial protection for anxious families against unhelpful and potentially harmful interventions.

I extend my sincere thanks to the expert team whose dedication and hard work made this document possible. Their efforts align with the College's mission to champion the highest standards of paediatric care in Singapore. I congratulate them on producing this comprehensive and invaluable resource that will undoubtedly improve outcomes for children with food allergies across our healthcare system.

ASSOCIATE PROFESSOR CHUA MEI CHIEN
President
College of Paediatrics & Child Health, Singapore
Academy of Medicine, Singapore
Mar 2026

PREFACE BY CLINICAL PRACTICE GUIDELINES CO-LEADS

Food allergy is an increasingly recognised public health concern in Singapore.[1] Local studies estimate a prevalence of approximately 2.9% to 4.0% based on self-reported data, comparable to other Asian populations.[2-4] Food allergies are immune-mediated adverse reactions to food that can manifest across a spectrum of severity, ranging from mild cutaneous symptoms to life-threatening anaphylaxis.[5, 6] The most common food allergens in Singapore include hen's egg, cow's milk, peanut, tree nuts, shellfish, wheat, fish and soy, with hen's egg allergy being particularly common among young children.

Accurate diagnosis and effective management are essential to reduce the risk of severe allergic reactions and to improve quality of life. Food allergies impose a substantial burden on patients and families, including dietary restrictions, social limitations, anxiety related to food consumption, and the need for constant vigilance to avoid allergens. The psychosocial impact extends beyond affected individuals to families, schools, and social environments, highlighting the importance of coordinated, evidence-based care.[7-9]

Singapore's diverse population and cultural practices also give rise to unique allergenic exposures and clinical presentations that necessitate locally relevant guidance. These include bird's nest allergy, galacto-oligosaccharide (GOS) allergy associated with certain powdered milk formulas, and shellfish allergy related to tropomyosin cross-reactivity.[10-12] Such patterns underscore the need for clinical guidance that reflects Singapore's epidemiology, cultural context, and healthcare environment.

The first Academy of Medicine, Singapore–Ministry of Health (AMS–MOH) Clinical Practice Guidelines on Food Allergy were published in 2010.[13] Since then, the field of food allergy has advanced considerably, particularly in areas such as allergy prevention, diagnostic approaches, and emerging therapeutic options. These developments necessitate an updated set of evidence-based recommendations.

This revised guideline provides comprehensive, evidence-based recommendations to support healthcare professionals in the recognition, diagnosis, and management of food allergy across all age groups in Singapore. The recommendations have been developed with careful consideration of the local healthcare context, including resource availability, cultural acceptability, and implementation within Singapore's healthcare and educational systems. The workgroup comprised multidisciplinary representatives from multiple institutions and sectors, ensuring that the recommendations are relevant, balanced, and applicable across clinical settings.

As the understanding of food allergy continues to evolve, this guideline aims to support consistent, evidence-based practice and ultimately improve patient outcomes and quality of life for individuals living with food allergy in Singapore.

ACKNOWLEDGEMENTS

The Clinical Practice Guideline (CPG) Workgroup extends its sincere gratitude to the Academy of Medicine Singapore (AMS) for its funding support, which enabled the essential GRADE training and writing assistance required for the development of these Clinical Practice Guidelines. While this CPG was commissioned by the College of Paediatrics and Child Health, Singapore (CPCHS), the CPG workgroup maintained complete independence in the guideline development process, ensuring that the content reflects evidence-based recommendations free from external influence. We are particularly grateful to Ms Pearl Yap, Secretariat of CPCHS, whose steadfast administrative support and dedication proved invaluable throughout the entire CPG development process.

The CPG Workgroup wishes to acknowledge the Evidence to Practice Division of the Agency for Care Effectiveness (ACE), Ministry of Health, Singapore, for their expert guidance in applying the GRADE framework, their technical expertise in evidence synthesis, and their invaluable advice on CPG development methodology and processes. Their support significantly enhanced the rigour and quality of our work.

We extend our sincere thanks to Ms Yasmin Lynda Munro, Senior Medical Librarian, Lee Kong Chian School of Medicine, for her invaluable assistance and expertise in conducting the comprehensive literature search and review.

We extend our heartfelt appreciation to our distinguished international reviewers, Dr Sakura Sato and Dr Leung Sze Yin, Agnes, who generously contributed their time and expertise to review our CPG. Their critical insights and thoughtful comments have substantially strengthened the final recommendations.

This guideline has also received formal endorsement from the College of Family Physicians Singapore (CFPS) and the Chapter of Family Medicine Physicians, Academy of Medicine, Singapore. We would like to thank the members for reviewing and providing feedback on this guideline.

These guidelines were also reviewed by SPEAK (Singapore Parents of Eczema and Allergy Kids) to ensure that the perspectives of patients and caregivers were appropriately represented. SPEAK supports the dissemination and implementation of these guidelines to promote evidence-based care for individuals with food allergy and their families.

We also sincerely thank all healthcare professionals, patients, caregivers and members of the public who participated in the public consultation process. Their thoughtful feedback and constructive comments helped to refine and strengthen the final guideline.

The CPG Workgroup gratefully acknowledges the institutional support provided by the various organisations and agencies that our workgroup members represent. This institutional backing enabled our members to dedicate the necessary time and resources to this important work. We particularly recognise that all workgroup members contributed substantial personal time and effort to this CPG without specific remuneration, demonstrating their unwavering commitment to improving the diagnosis and management of food allergies for the benefit of children and families in Singapore and beyond.

The collaborative spirit and dedication of all contributors have made this comprehensive guideline possible, and we trust it will serve as a valuable resource for healthcare professionals caring for patients with food allergies.

A/PROF Elizabeth Tham and **DR Kok Wee Chong**

CPG WORKGROUP CO-LEADS
[JUNE 2026]

CLINICAL PRACTICE GUIDELINE DEVELOPMENT

PRIMARY OBJECTIVE

The primary objectives of these guidelines are to:

1. Provide updated, evidence-based clinical practices suitable for use in the Singapore context.
2. Promote effective healthcare for patients with food allergies across all age groups through application of these evidence-based clinical practices.

These guidelines were written to provide healthcare professionals with evidence-based recommendations to support them in the diagnosis and management of food allergies and food-induced allergic reactions in the Singapore healthcare setting. Furthermore, guidance on how medical professionals can work together with parents, caregivers, teachers and other school personnels to manage children with food allergies is also provided.

TARGET POPULATION

The target population covered by these guidelines is patients of all ages with food allergies. Where appropriate, some of the guidelines may focus on children or breastfeeding mothers as food allergies tend to develop in early childhood.

TARGET USERS

The target users of the guidelines are all professionals caring for patients with food allergies in Singapore (e.g., general practitioners, paediatricians, allergists, nurses, dietitian), as well as parents, educators, caregivers, and school personnel. The intent is for the guidelines to be used to inform clinical decisions and standards of care. This full guideline document will therefore have an accompanying executive summary.

GUIDELINE WORKGROUP COMPOSITION

These guidelines were produced by a multi-disciplinary workgroup appointed by the College of Paediatrics and Child Health, Singapore (CPCHS). The 21-member core workgroup comprised paediatricians, allergists, family physician, dietitian, and academics specialising in allergy research. The workgroup members represented public (i.e., KK Women's and Children's Hospital (KKH), National University Hospital (NUH), Tan Tock Seng Hospital (TTSH)) and private healthcare sectors, and academia (i.e. National University of Singapore). All workgroup members were sent terms of reference and submitted declarations of potential conflicts of interest prior to participation and upon finalisation of these guidelines. A complete list of all workgroup members, their professional affiliations and their roles in the clinical practice guidelines (CPG) can be found in Appendix 1. None of the workgroup members had any relevant conflicts of interests which would impact the development of the guidelines.

GUIDELINE DEVELOPMENT AND METHODOLOGY

Recommendations were made after systematic reviews of the literature pertinent to the clinical questions. Key words from PICO (Population, Intervention, Comparator, Outcome) or PEO (Population, Exposure, Outcome) clinical questions were used in searches on the following electronic databases:

- PubMed, Embase, Medline, Cochrane Library, CINAHL.
- Grey literature databases were not used.

The search time period was set as 2000 to 2023 but sources from 2024 were also included in many of the searches to include more updated guidelines and publications. Additionally, sources from before year 2000 were included in Chapter 10 as the many of the tests and treatments in that chapter did not have more recent publications.

Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology was used to evaluate existing literature, rate the evidence and develop recommendations. Strong recommendations are

phrased as "We strongly recommend..." and indicate high confidence that the desirable effects of an intervention clearly outweigh the undesirable effects (or vice versa). In such situations, most patients should receive (or avoid) the intervention, and the recommendation can generally be adopted as policy in most healthcare settings. Conditional recommendations are phrased as "We conditionally recommend...". These are issued when the desirable effects probably outweigh the undesirable effects but there is uncertainty regarding the balance of effects, variability in patient values and preferences, or considerations related to resource use or feasibility. In these situations, different choices may be appropriate for different patients, and shared decision-making between clinicians and patients is important. The strength of each recommendation reflects the certainty of evidence as well as considerations of the balance of benefits and harms, patient values and preferences, and resource implications.

Where formal recommendations were not appropriate, Good Practice Points (GPPs) were issued instead. GPPs were developed using the same GRADE principles and were applied when a statement addresses a necessary healthcare practice and the net benefit or harm is unequivocal. They were also used when the available evidence is difficult or inappropriate to summarise quantitatively — for instance, when collecting and summarising such evidence would be a poor use of the guideline panel's limited time, energy, or resources. In addition, GPPs require a well-documented rationale that clearly and explicitly connects the indirect evidence, and the resulting statement must be clear and actionable.

The entire workgroup then assessed the key R and GPP statements using a RAND/UCLA method consensus survey, and they were revised until all finalised statements achieved group consensus. The final draft of the guideline underwent external review by two independent experts who had no involvement in its development. Each reviewer evaluated the document for clinical accuracy, completeness of evidence interpretation, consistency of recommendations with current standards of care, and clarity of presentation. Feedback was provided as detailed qualitative comments. The guideline development group systematically reviewed this feedback and revised the CPG accordingly, ensuring that amendments remained aligned with the underlying evidence base prior to finalisation. The list of external reviewers is provided in **Appendix 1**.

A public consultation exercise was also conducted over a 1-month period to seek feedback for the final draft guideline; feedback received was also considered in the formation of the final guideline. These guidelines are valid for a period of 5 years, after which it is strongly recommended that a scoping review be conducted to evaluate for newer literature that might inform any significant changes in the recommendations. The workgroup will monitor for significant new evidence throughout the validity period, and where warranted, updates to specific recommendations may be issued in the form of addendums prior to the scheduled five-year review.

GUIDELINE IMPLEMENTATION

Plans for Dissemination

The final complete guidelines, executive summary of recommendations, and all appendices will be made available on the CPCHS, Academy of Medicine Singapore's website for free download by the public.

News of the completed guidelines will be disseminated, and the guidelines will be promoted via the following approaches:

- Formal launch of the guidelines at the 14th Singapore Paediatric and Perinatal Annual Congress (SiPPAC), which is the main annual paediatric conference in Singapore, widely attended by paediatricians and healthcare professionals from both public and private sectors, as well as from the region and further afield.
- Email broadcasts to all relevant stakeholders in the allergy community through dissemination by the respective workgroup members who represent various disciplines and organisations within Singapore.
- Email broadcasts to primary care healthcare professionals through CPCHS, the Chapter of Family Medicine Physicians, AMS and College of Family Physicians Singapore (CFPS).
- Emails to local reviewers and individuals who gave feedback during the public consultation process.

- Publication of the guidelines in the Annals, Academy of Medicine Singapore, which is a widely read, peer-reviewed, leading medical journal.

Potential Facilitators and Barriers to Implementation

Features which facilitate the implementation of the guidelines include the following:

- Special consideration to the local context, including but not limited to the availability of interventions and resources, cultural acceptability and local healthcare and educational systems.
- Specific attention given to local literature where available to evaluate evidence for relevant clinical questions as they apply to Singapore.
- The heterogenous composition of the workgroup with representatives from several sectors and institutions across the country, which allowed for recommendations to be considered from multiple perspectives and applied across disciplines and sectors.
- The intentional incorporation of public consultation with feedback on the content of the guidelines.

Potential barriers towards implementation of the guidelines include the following:

- Resource limitations (including, but not limited to, trained professionals, manpower, financial resources) within healthcare and educational organisations in the provision of care as per the guideline recommendations
- The time required to change established clinical processes, if needed, to match the recommendations described in the guidelines
- Limited availability of local literature specific to food allergy, especially for the majority of interventions examined
- The guideline is very comprehensive and hence its length may be a barrier to readability and prioritisation in implementation

Whilst all guidelines make recommendations towards best practice, enforcing the use of guidelines is limited unless additional efforts are made to do so nationally.

Cost-effectiveness was considered in all recommendations made in the guidelines, especially for those that involved a change from current clinical practices and with respect to provision of interventions. Availability of these interventions within the local context was also considered where applicable.

Suggestions for Implementation

Implementation of the recommendations laid out by these guidelines would be under the purview of each relevant organisation (e.g., healthcare, educational or community agency). It is expected that the majority of the recommendations are in keeping with current practices, however, where differences in practice are present, the reason for these should be reviewed and addressed where possible.

Guideline Evaluation

Feedback will be actively sought by end-users of the guidelines from various organisations. This will include information on the acceptability and applicability of the recommendations and barriers, if any, to implementation of the recommendations.

Specific points for future audits and evaluations include the following:

- Quantifying changes in knowledge related to food allergy and the given recommendations among target users of the guidelines
- Adherence to recommendations within various professions and specific topics (e.g., investigations performed following a diagnosis of food allergy by physicians)

- Examining the use of complementary and alternative medicine among individuals with food allergy and adherence to the published recommendations.

Appendices

- **Appendix 1:** Guideline Development Group and External Reviewers
- **Appendix 2:** Allergy Action Plan

Supplements

- **Supplement 1**: Evidence Matrices [EM]

Abbreviations

AAF	Amino Acid Formula
AD	Atopic Dermatitis
ALCAT	Antigen Leukocyte Antibody Test
BMI	Body Mass Index
CM	Cow's Milk
CMA	Cow's Milk Allergy
CRD	Component Resolved Diagnostic
CPG	Clinical Practice Guidelines
EAACI	European Academy of Allergy and Clinical Immunology
eHF-CM	Extensively Hydrolysed Formula – Cow's Milk
EoE	Eosinophilic Esophagitis
EPIT	Epicutaneous Immunotherapy
FDEIA	Food-dependent Exercise-Induced Anaphylaxis
FPE	Food Protein-Induced Enteropathy
FPIAP	Food Protein-Induced Allergic Proctocolitis
FPIES	Food Protein-Induced Enterocolitis Syndrome
FS	Food Sensitisation
GOS	Galacto-oligosaccharide
HDM	House Dust Mite
HRF	Hydrolysed Rice Formula
IgE	Immunoglobulin E
IM	Intramuscular
IV	Intravenous
MMR	Measles, Mumps and Rubella
MMRV	Measles, Mumps, Rubella and Varicella
NIAID	National Institute of Allergy and Infectious Diseases
OAS	Oral Allergy Syndrome
OFC	Oral Food Challenge
OIT	Oral Immunotherapy

SF	Soy Formula
sIgE	Specific Immunoglobulin E
SLIT	Sublingual Immunotherapy
SPT	Skin Prick Test
WAO	World Allergy Organisation
YFV	Yellow Fever Vaccine

INTRODUCTION TO FOOD ALLERGY

Food allergies often present in early childhood and are a growing health concern in Singapore, mirroring global trends.[1] They are associated with concomitant atopic conditions, with eczema being the highest risk factor for food allergy. Food allergies also cause significant, and likely under-reported, psychological stress for both children and their caregivers, leading to poorer quality of life.[7-9] In severe cases, food-related anaphylaxis may also be fatal. Therefore, proper recognition and management of food allergies is critical for patient safety and well-being.

EPIDEMIOLOGY

The most common allergens in Singapore are hen's eggs, cow's milk, peanut, tree nuts, shellfish, wheat, fish and soy, with hen's egg allergy having the highest incidence in Singapore, particularly in young children. The gold standard for diagnosing food allergies is a double-blind, placebo-controlled food challenge. However, they are logistically intensive, costly and impractical on a large scale. Thus, the true prevalence of food allergies is difficult to determine and is presently unknown in Singapore. The HealthNuts study in Melbourne found that more than 10% of one-year old infants had challenge-proven food allergy, representing one of the highest reported prevalence rates globally.[14] Challenge-proven food allergy prevalence data and trends in Asia are limited and heterogenous, ranging from 1% among children aged three to seven years in Thailand to 3.8% and 7.7% of one- and two-year-old children in China respectively.[4]

Surrogate diagnostic methods such as self-reported history, skin prick testing or food-specific IgE testing, while more accessible, often lead to over-reporting of food allergies. Food allergy prevalence studies based on self-reported questionnaires in Asian countries, including South Korea, Japan, Hong Kong and Taiwan, have reported rates ranging from 3.4% to 7.0%.[4] Data from Singapore's GUSTO study indicate that the prevalence of IgE-mediated self-reported food allergies ranged from 2.9% to 4%, with greatest prevalence during infancy.[2, 3] A separate study, which analysed data based on convincing history alone, estimated the prevalence of cow's milk and hen's egg to be 0.5% and 1.8% in children 11-30 months respectively and peanut to be 0.64% in children 4-6 years old.[15] More robust studies are currently underway to better estimate the prevalence of food allergies in Singapore.

CLINICAL FEATURES OF FOOD ALLERGY

Food allergy is an immune-mediated adverse reaction to food products. It can be broadly classified into immediate (IgE mediated), delayed (cell mediated) and mixed (IgE and non-IgE mediated).[16, 17] IgE mediated food allergies are the most common and typically acute in onset with symptoms ranging from cutaneous reactions to anaphylaxis. Cutaneous symptoms are the most common and include urticaria (hives), angioedema, dermatographism, and itch. Gastrointestinal symptoms such as abdominal pain, vomiting and diarrhoea are also common in children. Respiratory involvement includes nasal congestion, sneezing, cough, hoarseness of voice, difficult or noisy breathing, wheeze and subjective throat tightness (or globus sensation), and may progress toward more severe reactions. Cardiovascular involvement includes dizziness, collapse and hypotension.[5] Importantly, anaphylaxis is a rapid onset, severe, systemic hypersensitivity reaction, characterised by potentially life-threatening airway problems or circulatory involvement.[6] It represents the most severe presentation of acute systemic allergic reactions and is a medical emergency.

Other types of food allergies include non-IgE mediated allergies such as food-protein induced enteropathies, enterocolitis syndrome or allergic proctocolitis, which present with delayed gastrointestinal symptoms.[18] Mixed type food allergies, like atopic dermatitis or eosinophilic gastrointestinal disorders, may involve both IgE and non-IgE components. However, the underlying pathophysiological mechanisms of non-IgE mediated and mixed type food allergies are not well understood.[16]

UNIQUE FOOD ALLERGENS

Allergens are traditionally considered proteins or glycoproteins whereas carbohydrate moieties were thought to be non-immunogenic due to widespread conservation across mammalian species resulting in general tolerance to these carbohydrate structures. However, emerging evidence suggests that cross-reactive carbohydrate determinants present in food products such as bird's nest or red meat can also be sources of allergens.[19, 20]

Bird's nest allergy

Edible bird's nests, considered delicacies with medicinal value in Asia, are constructed from hardened saliva regurgitated by the male Chinese swiftlet (*Collocalia spp*), a small bird native to the Southeast Asian region.[11] They are usually double boiled with rock sugar to make soup. Even though bird's nest allergy was a well-recognised clinical entity in Singapore in the early 2000s, it is no longer a common food allergy in today's changing dietary landscape.[10] The reason for this decline is largely unknown but awareness of this specific food allergy remains important given its cultural context. Allergic symptoms that occur after the consumption of bird's nest are typically IgE mediated reactions, such as angioedema, wheezing, urticaria and abdominal cramps.[11] Studies suggest that the putative major allergen in bird's nest is the carbohydrate moiety on a 66-kDa glycoprotein whose exact structure remains to be elucidated.[19]

Galacto-oligosaccharide (GOS) allergy

GOS allergy is an emerging IgE mediated food allergy to a pure carbohydrate allergen, with most cases reported in the last decade. GOS are non-digestible, heat-stable, 2-6 units long oligosaccharides, found in several commercially available powdered milk formula for infants, children and pregnant/lactating mothers. It was developed as prebiotics to promote the growth of *Lactobacilli* and *Bifidobacterium* in the gut, maintaining a healthy digestive system. GOS allergy typically presents in older children (more than 5 years old) and adults who are known to be cow's milk tolerant but suddenly develop anaphylaxis after ingesting GOS containing formula milk or products.[12] Reports of GOS allergy have been confined to Asian countries such as Japan, Singapore, Malaysia and Thailand. GOS allergy is likely to arise from cross-reactive IgE antibodies. The putative primary sensitisers for GOS have been identified as dust mite *Blomia tropicalis* in Singapore and the sea squirt for oyster shuckers in Japan.[21, 22]

OTHER PHENOTYPES OF FOOD ALLERGY

Other rare food allergy phenotypes with severe presentations include food dependent exercise-induced anaphylaxis (FDEIA), oral allergy syndrome and oral mite anaphylaxis. These rare food allergy phenotypes are often underdiagnosed due to limited awareness of these entities.

Food-dependent exercise-induced anaphylaxis (FDEIA)

FDEIA represents a unique clinical phenomenon whereby individuals are able to exercise or tolerate specific foods separately without experiencing any allergic reactions. However, reactions occur when individuals exercise within 4 hours of consumption of specific trigger foods or when specific foods are consumed shortly after exercise. A correlation between increased intensity or duration of exercise and increased risk of allergic reactions has been observed.[23, 24]

FDEIA most commonly has its onset during adulthood though it can sometimes also occur in childhood and adolescence.[24] Many common food allergens have been implicated in FDEIA, including grains, shellfish, egg, cow's milk, peanuts, tree nuts and most commonly, wheat. Clinical manifestations can range from mild cutaneous reactions to anaphylaxis.[24] Notably, anaphylactic reactions in FDEIA tend to be more severe compared to typical IgE-mediated food induced anaphylaxis, with frequent involvement of both the cardiovascular and respiratory systems. For medical practitioners, it is important to note that management of FDEIA involves the same emergent care as for other causes of anaphylaxis, particularly with intramuscular adrenaline.[24]

The identification of culprit foods and avoiding their consumption before and after exercise is critical in the management of FDEIA. Patients should be advised to avoid consuming the implicated foods 4 hours before and after exercise as well as avoid cofactors such as NSAIDs and alcohol. However, management of FDEIA should be tailored according to the severity of symptoms, feasibility of allergen avoidance, presence of co-factors and the patient's desire to continue exercise.

Oral Allergy Syndrome (OAS) - Shellfish and house dust mite (HDM)

OAS is characterised by IgE-mediated immediate symptoms restricted to the oral mucosa which may include itching, stinging, and throat tightness.[25] A unique feature in the clinical manifestation of shellfish allergy in Asia is the presence of a milder form with reactions localised to the oral mucosa due to cross-reactivity with house dust mites (HDM) allergens.[26] Patients usually have a history of allergic rhinitis or HDM sensitisation while having negative or low-positive skin prick tests and/or sIgE blood tests to shellfish.[27]

The major allergen in shellfish allergy is tropomyosin, a protein involved in muscle contraction in invertebrates that is also found in HDM, cockroaches and various insects.[26] In warm and humid tropical climates where HDM thrive, there is a high prevalence of HDM allergy and IgE sensitisation in the population. Inhaled tropomyosins from HDMs thus act as the primary sensitiser for shellfish allergy, with IgE cross-reactivity to shellfish tropomyosin, leading to oral allergy syndrome.[26] This same mechanism also underlies allergic reactions seen with eating insect protein-based foods.[28]

Oral mite anaphylaxis (Pancake Syndrome)

Oral mite anaphylaxis is a syndrome characterised by severe allergic reactions occurring in atopic patients shortly after the intake of foods made with mite contaminated flour. The most common symptoms of oral mite anaphylaxis include breathlessness, facial and laryngeal angioedema, wheezing and wheals.[29] Food made with wheat and corn flour, especially pancakes, are most commonly implicated in oral mite anaphylaxis, hence it is also known as pancake syndrome. Diagnosis is made based on the presence of suggestive symptoms occurring after the intake of foods prepared with flour, *in vivo* or *in vitro* demonstration of IgE-mediated sensitisation to mite allergens, a positive skin test with extract of the suspected flour, negative skin tests and clinical tolerance to uncontaminated wheat. Microscopic identification of mites or testing for presence of mite allergens in the suspected flour could be performed where possible.[29]

SUMMARY

In conclusion, food allergies represent a complex and evolving clinical challenge in Singapore. The increasing prevalence of food allergies, coupled with their potential for severe and life-threatening reactions, underscores the importance of accurate diagnosis, appropriate management, and comprehensive patient education. Healthcare practitioners must maintain heightened awareness of both typical presentations and rarer phenotypes such as food-dependent exercise-induced anaphylaxis and oral mite anaphylaxis. As our understanding of food allergies continues to evolve, particularly regarding non-protein allergens and cross-reactive mechanisms, robust epidemiological studies and standardised diagnostic approaches will be essential to improve patient outcomes and quality of life. This clinical practice guideline aims to provide evidence-based recommendations to support healthcare professionals in the recognition, diagnosis, and management of food allergies across all age groups in the Singapore healthcare setting.

The primary prevention of food allergy, including strategies such as early introduction of allergenic foods and other antenatal and postnatal interventions, is beyond the scope of these guidelines. Clinicians are directed to the *Consensus Statement on the Primary Prevention of Allergy in At-Risk Infants* (Academy of Medicine Singapore, College of Paediatrics and Child Health Singapore, and College of Obstetricians and Gynaecologists Singapore, December 2019), and its accompanying *Addendum Guidelines on the Primary Prevention of Allergy in At-Risk Infants* (September 2024), for detailed guidance on this topic.

CHAPTER 1: DIAGNOSIS OF FOOD ALLERGY

R 1.1 ***We strongly recommend that in patients with suspected food allergy, a detailed allergy-focused clinical history should be taken as the first step of the diagnostic evaluation. [EM1-1]***

An allergy-focused clinical and dietary history is the first step in the food allergy diagnostic pathway. (Figure 1.1) The clinical history allows the provider to identify the mechanism of food allergy (i.e. IgE or non-IgE-mediated), to select the allergens to be tested, and to guide the interpretation of the test results.

A clear history of the symptoms experienced, temporal relationship to allergen exposure, and response to treatment is essential. Clinical history should always be accompanied by a detailed dietary history. This should include questions on the patient's usual dietary patterns, particularly whether the implicated allergen had previously been tolerated, any cessation of allergen intake prior to the reaction, and any continued consumption of the allergen without incident after the initial allergic reaction.[30]

Other essential components of the clinical history include ascertaining the presence of other allergic co-morbidities, tolerance to co- or cross-reacting foods, possible occupational exposure to allergens, co-factors, and family history of allergic disease.

A detailed allergy-focused clinical history allows the physician to estimate the likelihood (pre-test probability) that a patient has an IgE-mediated food allergy and guides the selection of appropriate allergy tests and their interpretation to determine the post-test probability for clinical decision-making. A history of regular consumption of age-appropriate portions of the specific food in its relevant form without any allergic symptoms rules out food allergy without the need for testing.

An allergy-focused dietary history supplemented with assessment of growth patterns (such as serial records of height, weight and body mass index (BMI) over time) will also be able to identify over- and undernutrition, potential macro- and micronutrient deficiencies, and identify concerns about development, feeding skills and aversive feeding patterns.[31]

R 1.2 ***We strongly recommend that in patients with a history suggestive of IgE-mediated food allergy, skin prick test (SPT) and/or measurement of food-specific IgE (sIgE) should be performed as first line tests to support diagnosis. [EM1-1]***

R 1.3 ***We strongly recommend that patients with a history of suspected IgE-mediated food allergy be referred to an allergist where component-resolved diagnostic tests may be performed in selected patients in addition to SPT and/or sIgE to further support diagnosis or in preparation for an oral food challenge. [EM1-1]***

Following a detailed allergy-focused history, confirmation of the presence of allergen-specific IgE should be sought to support the diagnosis of an IgE-mediated food allergy. This can be achieved through performing skin prick tests (SPTs) and/or specific IgEs (sIgE) to allergen extracts or individual allergen components (component-resolved diagnostic (CRD) tests).

A systematic review of the literature supports the above tests, which are currently validated to support the diagnosis of IgE-mediated food allergy. SPTs and sIgEs are relatively inexpensive, widely available and are recommended as the first-line tests for evaluation of food allergies. If clinical history is unclear, or the results of SPT and/or sIgEs are not sufficient to support the diagnosis, or are conflicting with the history, sIgE to allergen components (CRDs) may be performed to aid in confirmation of the diagnosis.

The sensitivity, specificity and predictive value of these tests vary between allergens and different populations, and interpretation is specific to the food allergen, geographical location, and the individual being tested.[32] For example, a positive SPT/sIgE alone, in the absence of a suggestive clinical history of a reaction to the food allergen, or known exposure to the food – also known as food sensitisation, is not diagnostic of clinical food allergy. These

tests should, therefore, be performed by a trained allergy specialist to allow accurate interpretation of the test results in the context of a supporting clinical history, established cut-offs and confirmation via an oral food challenge (OFC) if required.

R 1.4 ***We strongly recommend that a medically supervised oral food challenge (OFC) be considered to confirm or exclude food allergy in patients if diagnosis remains unclear after initial evaluation, incorporating shared decision-making with patients. [EM1-1]***

A good clinical history and validated allergy diagnostic tests (SPTs, sIgEs and CRDs) may be sufficient in most cases to achieve a robust diagnosis of food allergy. However, an OFC may be required in some cases where diagnosis may still be uncertain. These may include instances such as:

a) The patient reports clinical symptoms but no sIgE sensitisation has been demonstrated.
b) IgE sensitisation has been demonstrated but the patient's current status of tolerance is unknown, and avoidance is ongoing.
c) To confirm that the allergy has been outgrown, in patients who have been strictly avoiding the food.

1.1 ORAL FOOD CHALLENGE (OFC)

1.1.1 Pre-Challenge Assessment

A thorough pre-challenge assessment is essential to maximise both the safety and diagnostic value of the OFC. The patient should be in a stable state of health at the time of the challenge. Where possible, the trigger food should be excluded from the diet for at least two weeks beforehand, and any co-existing atopic conditions such as asthma or eczema should be well-controlled prior to proceeding. The challenge should be deferred if the patient is acutely unwell, or if underlying allergic disease is in an unstable phase, as this may compromise both safety and the interpretation of results.

Certain medical conditions increase the risk of a severe or difficult-to-treat reaction and should be considered contraindications or relative contraindications to proceeding. These include significant cardiovascular disease, severe chronic lung disease, and pregnancy.

A careful medication review is an important part of pre-challenge preparation. Several drug classes can mask or attenuate allergic symptoms, potentially leading to false-negative results or delayed recognition of a reaction. These include antihistamines, medications with antihistaminic properties, bronchodilators, and biologic agents such as anti-IgE therapies. As a practical guide, symptom-suppressing medications should ideally be withheld for a period of five half-lives before the challenge is undertaken.

1.1.2 Challenge Setting and Personnel

OFCs are high-risk procedures and should thus be performed only under the supervision of a trained allergy specialist, by medical personnel trained in the recognition and management of anaphylaxis, and in a facility equipped to provide resuscitation and advanced life support.

1.1.3 Dosing Schedule

OFCs are conducted using a stepwise incremental dosing approach, where the amount of food protein administered is gradually increased over the course of the challenge. In lower-risk clinical scenarios where the patient is unlikely to react at very small doses, the initial steps may be consolidated, yielding a shorter protocol.

An adequate interval between doses is important to allow sufficient time for any reaction to manifest before the next dose is given. In clinical practice, an interval of 15 to 30 minutes between doses is generally recommended. Longer intervals may be warranted in patients with a history of more severe reactions, or where symptoms appear to be evolving rather than resolving at the time the next dose is due.

The maximum dose administered should be equivalent to a normal age-appropriate serving of the food in question. Reaching this threshold without a reaction is required before a challenge can be considered negative.

1.1.4 Stopping Criteria

Clear and pre-specified stopping criteria are essential to ensure both the safety and diagnostic accuracy of the OFC. These guidelines recommend following the updated AAAAI-EAACI PRACTALL 2024 stopping criteria, which use a traffic-light framework to guide decision-making during a challenge.[33]

1.1.5 Post-Challenge Observation and Discharge

All patients should be observed for a minimum of one to two hours following completion of the challenge, even if no reaction has occurred. Where the clinical history suggests a risk of delayed reactions, or where the patient has experienced symptoms during the challenge, a longer observation period of up to four hours is advisable. Patients who have had a significant systemic reaction requiring treatment should be admitted for overnight observation.

The above provides a brief overview of clinical OFC conduct in tertiary allergy specialty settings for reference purposes. The detailed conduct of OFCs — including specific dosing protocols for individual allergens, management of non-IgE-mediated conditions such as FPIES and eosinophilic oesophagitis, and research-grade double-blind placebo-controlled methodology — is beyond the scope of these guidelines.

As OFCs are inherently risky, the decision to proceed with an OFC should incorporate a shared decision-making framework. This is a collaborative process where clinicians and patients (or their caregivers) work together to make healthcare decisions while considering the best available clinical evidence and the patient's values, goals, and preferences.

The primary physician should counsel the patient and/or parents/legal guardians (for minors) regarding the indications, risks, and alternatives of undertaking an OFC. Patients' and parents' expectations and preferences, such as willingness to continue regular consumption of the trigger food after passing a challenge, should be carefully considered in the decision.

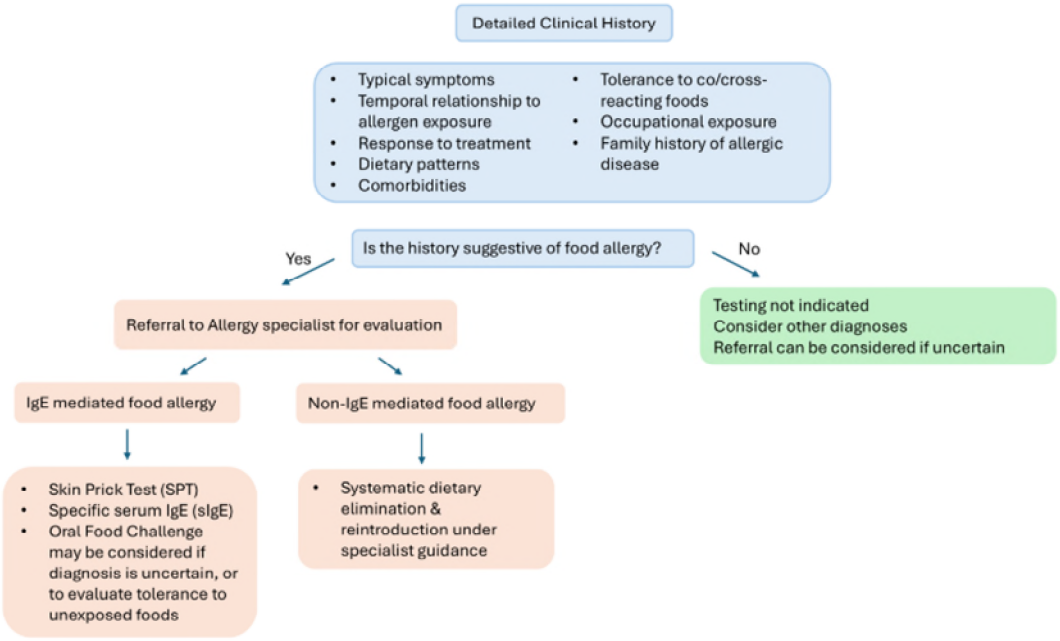

Figure 1.1: Evaluation and Diagnosis of Food Allergy

CHAPTER 2: NON-IgE MEDIATED FOOD ALLERGIES

Studies have shown that food allergy can be non-IgE-mediated and this group of conditions predominantly affect the gastrointestinal tract. The most well-defined non-IgE-mediated food allergies include food protein-induced enterocolitis syndrome (FPIES), eosinophilic esophagitis (EoE), food protein-induced enteropathy (FPE) and food protein-induced allergic proctocolitis (FPIAP).

Non-IgE-mediated reactions are typically delayed with symptom onset occurring several hours to days following exposure to the trigger food. (Table 2.1) With the exception of EoE, diagnosis is clinical and based on reproducible reactions upon re-exposure to the trigger food and exclusion of other differentials.[34]

Given the lack of standardised diagnostic tests and symptom overlap with common childhood disorders like gastrointestinal reflux and infective gastroenteritis, a systematic approach to dietary elimination followed by supervised reintroduction is recommended to avoid overdiagnosis and unnecessary food avoidance in children and breastfeeding mothers.

Table 2.1: Overview of non-IgE-mediated food allergies (adapted from Meyer et al. 2025)[34]

	FPIAP	FPE	FPIES	EoE
Main Symptom(s)	Blood in stools	Faltering growth Diarrhoea	Repetitive Vomiting	Dysphagia Feeding difficulties Faltering growth
Other Symptoms	Loose stools Mucus in stools Painful flatus Anal excoriation	Abdominal pain Hypoalbuminemia	Pallor Lethargy Diarrhoea Floppiness Hypotension Hypothermia	Abdominal pain Vomiting
Age of Onset	<3 months	<1 year	<2 years Adults (less common)	Any age
Common Food Triggers	Cow's milk (most common) Occasionally soy, egg, wheat	Cow's milk (most common) Occasionally soy, egg, wheat	Cow's milk, rice, fish, egg Sometimes fruit, vegetables	Cow's milk, wheat, egg, legumes
IgE Test	No			
Patch Test	No			
Confirming natural tolerance	Home reintroduction	Home reintroduction	Supervised oral food challenge	Home reintroduction

The diagnosis of non-IgE mediated food allergy (FPIAP, FPE) is based on:

1. Exclusion of other differentials (e.g. infections, gastrointestinal disorders, bleeding disorders etc).
2. Trial of strict dietary elimination (under the guidance of physician and dietitian) resulting in resolution of symptoms.
3. Symptoms recurrence with allergen re-introduction.

For EoE, a histological diagnosis is additionally required to confirm the diagnosis.

2.1 FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME (FPIES)

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated food allergy characterised by delayed gastrointestinal symptoms following ingestion of a food trigger. The two main phenotypes are acute and chronic

FPIES. Acute FPIES typically presents as protracted vomiting one to four hours after ingestion of the culprit food, is often associated with pallor, lethargy and/or diarrhoea with symptoms resolving within 24 hours.[35] Severe cases can progress to acidaemia, haemodynamic instability and shock. Chronic FPIES mainly affects formula-fed infants although there are case reports of chronic FPIES developing in exclusively breastfed infants.[36] These patients typically present with intermittent vomiting, diarrhoea and failure to thrive. These symptoms resolve with elimination of the food trigger, but subsequent exposure induces an acute FPIES reaction.

A subset of patients with FPIES develop positive skin prick test and/or sIgE to the FPIES food trigger, referred to as atypical FPIES, and this appears to predict a more persistent disease and increased risk of conversion to an IgE-mediated phenotype over time.[37]

Cumulative incidence rates based on studies from the United States, Israel, Spain, Australia and Japan are between 0.15 and 0.7%.[36, 38-42] Food triggers appear to vary geographically, likely due to differences in feeding practices. While almost any food can be a FPIES trigger, cow's milk (CM) appears to be the most common allergen worldwide.[36] Soy-induced and combined soy/CM-induced FPIES has been reported in 25-50% of cases in the United States but appears to be uncommon locally in Singapore. Other triggers that have been reported include rice, oat, fish, shellfish and egg.[43] Patients who have more than one FPIES trigger have also been reported with varying rates (15-69%) depending on the country.

FPIES presents when the trigger food is introduced into the diet which would explain why CM and soy-induced FPIES tend to present earlier (<6 months) compared to solid food-induced FPIES (6-12 months). Interestingly, there are increasing reports of adults presenting with FPIES-like symptoms to food previously tolerated with shellfish being the most common trigger in this age group.[44]

Age of tolerance development varies by type of food and presence of specific-IgE to the trigger food. The majority of infantile FPIES resolves by school age while a history of severe reactions, having multiple food triggers and adult-onset FPIES predict a more persistent form of disease.[37, 39] Patients with FPIES should be reviewed by an allergy specialist at regular intervals, with reassessment via OFC recommended approximately 12–18 months after the last reaction to evaluate for disease resolution.

Long-term management involves dietary elimination of the trigger food while ensuring adequate nutrition and normal growth. Patients with CM and/or soy-induced FPIES should avoid all forms of these foods, including baked and processed forms unless already tolerated in the diet, and referral to specialist care prior to introduction is recommended.[35] Routine maternal dietary elimination of the food trigger while breastfeeding is not recommended if the infant is asymptomatic while being exclusively breastfed.[35]

2.1.1 Diagnosis

There is currently no definitive diagnostic test for FPIES. Diagnosis is based on a clinical history of typical signs and symptoms following exposure to the trigger food with resolution following its removal and exclusion of other potential causes. (Table 2.2) The combination of nonspecific symptoms, lack of diagnostic tools and unusual food triggers often result in delayed diagnosis. Revised diagnostic criteria for patients suspected of having acute FPIES may aid in making a diagnosis.[35] (Table 2.3) If the diagnosis remains unclear, oral food challenges (OFCs) should be performed by trained specialists to confirm diagnosis. OFCs may also be undertaken to allow for introduction of other high-risk foods and to assess for eventual tolerance to the trigger food. Patients suspected of having FPIES should be referred to an allergy specialist for further evaluation and management.

Table 2.2: Differential diagnosis of FPIES

Allergic Disorders	Gastrointestinal Disorders	Infection/Others
Anaphylaxis Food protein-induced enteropathy	Gastrointestinal reflux disease Coeliac disease Lactose intolerance	Infectious gastroenteritis Sepsis Inborn errors of metabolism

Eosinophilic gastroenteropathies	Immune enteropathies (e.g. inflammatory bowel disease) Necrotizing enterocolitis Anatomical obstruction (e.g. malrotation, intussusception, Hirschsprung disease, pyloric stenosis)	Neurologic disorders (e.g. cyclic vomiting) Food aversion

Table 2.3: Revised diagnostic criteria for acute FPIES (adapted from Nowak-Wegrzyn et al. JACI 2017)[35]

Major Criterion	Minor Criteria
Vomiting 1-4h after ingestion of the suspect food and absence of IgE-mediated symptoms	1. A second (or more) episode of repetitive vomiting after ingestion of the same suspect food. 2. Repetitive vomiting 1-4h after eating a different food. 3. Extreme lethargy with any suspected reaction. 4. Marked pallor with any suspected reaction. 5. Need for emergency department visit with any suspected reaction. 6. Need for intravenous fluid support with any suspected reaction. 7. Diarrhoea within 24h 8. Hypotension 9. Hypothermia
A diagnosis of acute FPIES is made if the patient meets the major criterion and ≥3 minor criteria.	

2.1.2 Emergency Management of Acute FPIES Reaction

Management of the acute FPIES reaction is centred around appropriate fluid rehydration and should be tailored to the severity of symptoms. (Table 2.4)

Table 2.4: Management of acute FPIES based on severity classification (adapted from Nowak-wegrzyn et al. JACI 2017)[35]

Mild 1-2 episodes of vomiting No lethargy	**Moderate** ≥3 episodes of vomiting Mild lethargy	**Severe** ≥3 episodes of vomiting Severe lethargy or hypotonia
Oral rehydration Consider IM ondansetron	Administer IM ondansetron 0.15 mg/kg/dose (max 16 mg/dose) if >6 months old Consider IV fluids	Administer normal saline bolus 20 ml/kg. Repeat boluses may be required as necessary. Administer IV ondansetron 0.15 mg/kg/dose (max 16 mg/dose) if ≥6 months old Consider administering IV methylprednisolone 1 mg/kg (max 16 mg/dose)

GPP 2.1 ***We recommend that severe acute Food protein-induced enterocolitis syndrome (FPIES) be treated as a medical emergency, and the priority should be haemodynamic support with aggressive fluid resuscitation. [EM2-1]***

GPP 2.2 ***For patients presenting with mild symptoms, a trial of oral rehydration may be attempted. [EM2-1]***

The severity of acute FPIES reactions can range from mild-moderate to severe and management is mainly supportive with appropriate fluid resuscitation.[35] Progressive symptoms can lead to dehydration and haemodynamic instability with hypovolemic shock reported in up to 15% of patients.[37] These patients must be managed as a medical emergency with aggressive fluid resuscitation and vasopressors for hypotension not responsive to fluid resuscitation. For patients presenting with mild symptoms, a trial of oral rehydration may be attempted. (Table 2.4)

R 2.3 ***We conditionally recommend ondansetron to be considered as an adjunctive therapy in patients ≥6 months of age with acute FPIES reactions. [EM2-2]***

Ondansetron appears to reduce frequency of vomiting and hospitalisation in acute FPIES with minimal adverse effects based on retrospective cohort studies.[35, 45, 46] Intravascular/intramuscular ondansetron 0.15 mg/kg/dose (max 16 mg/dose) may be considered in patients ≥6 months of age. Ondansetron must be avoided in infants <6 months of age (due to lack of safety data) and in patients with heart defects/arrhythmias (due to the risk of prolonged QT).

GPP 2.4 ***Intramuscular adrenaline is ineffective and should not be used to treat acute FPIES reactions. [EM2-3]***

Given that FPIES is a non-IgE mediated food allergy and adrenaline has no effect on emesis, intramuscular adrenaline is not indicated in the management of acute FPIES reactions.[35, 47] However, some patients with FPIES may also have co-existing IgE-mediated allergy to the same or different food triggers. In such cases, if the clinical presentation is consistent with anaphylaxis rather than — or in addition to — a typical FPIES reaction, intramuscular adrenaline should be administered accordingly.

CHAPTER 3: MANAGEMENT OF FOOD ALLERGY

An individual with a confirmed food allergy should avoid the triggering allergen to minimise allergic symptoms and reactions. It is important to educate patients and caregivers on how to avoid food allergens. This involves reading ingredient labels, being mindful of concealed food allergens, verifying food choices when dining at restaurants and schools, and preventing cross-contamination.

Patients can continue to eat foods that they have previously introduced and tolerated. Eliminating foods that are regularly consumed and tolerated is unnecessary and can have a detrimental effect on the patient's nutritional intake.

Most breastfeeding mothers whose infants have a food allergy do not need to avoid the offending food themselves, except in rare cases where the infant is symptomatic while being exclusively breastfed.[48]

3.1 COW'S MILK ALLERGY

3.1.1 Milk alternatives for patients with cow's milk allergy (CMA)

Infants with cow's milk allergy (CMA) are typically sensitised to specific components of cow's milk proteins such as whey and casein. Specialised milk replacement formulas developed as hypoallergenic alternatives for these patients undergo processing methods that either remove allergenic proteins or hydrolyse them into smaller peptides, which significantly reduces their potential to trigger allergic reactions.[49] There are 4 main milk alternatives that are currently being used in the management of infants with CMA.

Extensively hydrolysed formula (eHF-CM) is derived from cow's milk proteins that are subject to thermal and enzymatic breakdown, followed by ultrafiltration to remove large protein fragments. These formulas can be casein- or whey-based. They are well tolerated in at least 95% of infants with CMA and are nutritionally adequate. However, they may still trigger allergic reactions in a minority of patients who are highly sensitised.

Unlike eHF-CM, amino acid formula (AAF), also known as elemental formula, is not derived from cow's milk and is composed of individual amino acids rather than proteins or peptides. This further reduction in allergenicity of the formula is particularly beneficial for patients who are at higher risk of severe allergic reactions or those who are unable to tolerate eHF-CM.

Soy formula (SF) is made from soy protein isolates and is typically fortified with iron. It is lactose-free and does not contain cow's milk-specific proteins. As it is nutritionally adequate and readily available, it is commonly used as a replacement option for patients with CMA. It is effective in most CMA cases, although approximately 10% of infants with CMA may also react to soy.[50, 51] Data from Singapore suggest a low rate of concomitant soy allergy (<5%) among children with IgE-mediated CMA.[52]

Hydrolysed rice formula (HRF) is a plant-based hypoallergenic formula fortified with amino acids, processed similarly to eHF-CM. Several clinical trials have demonstrated its safety and efficacy in infants with CMA, including those with concomitant soy allergy.[53] However, its high cost and limited availability pose challenges, and data on its use in non-IgE-mediated CMA remains limited.

In view of the limitations of each type of cow's milk alternative, we make the following recommendations.

R 3.1 ***We strongly recommend using extensively hydrolysed cow's milk formula (eHF-CM) or soy formula (SF)* as first choice, and an amino acid-based formula (AAF) as second choice in infants with cow's milk allergy who need a breastmilk alternative. [EM3-1]***

**When initiating SF, clinicians should discuss with caregivers the low but possible risk of concomitant soy allergy, particularly in infants with no prior soy exposure.*

Extensively hydrolysed cow's milk formula and soy-based formula are recommended as the first choice due to its proven safety and efficacy while supporting nutrition and growth.[48, 54-58] SF offers additional benefits, including better palatability, greater accessibility and lower cost, compared to eHF-CM, making it a practical alternative in the Singapore setting. Although soy formula contains phytoestrogens, phytates and aluminium, long-term safety studies have shown no adverse effects on endocrine or reproductive function and do not pose any risk of aluminium toxicity in humans.[59] Concomitant soy allergy, while uncommon in the local context, should be considered particularly in infants who have not previously been exposed to soy.

AAF is recommended as the second choice and is reserved for selected cases of severe or complex CMA, due to its higher cost, palatability and limited availability (requires prescription).[48, 54-57] It may be indicated in CMA patients[56, 60] with:

- Persistent symptoms or allergic reactions despite being on eHF-CM
- Faltering growth/ failure to thrive
- Multiple food allergies requiring extensive food elimination
- Severe cow's milk allergy/FPIES unlikely to tolerate eHF-CM
- Eosinophilic oesophagitis/eosinophilic gastrointestinal disease
- Presence of allergic symptoms while exclusively breastfed

R 3.2 ***We conditionally recommend that hydrolysed rice formula (HRF) can be considered as an alternative first choice formula (if available) in infants with cow's milk allergy. [EM3-1]***

HRF can be considered as an alternative first choice (if available) due to its safety, acceptability and palatability, especially in a rice-consuming population like Singapore.[54, 61] However, its high cost and limited accessibility remain a barrier locally. It is not recommended in non-IgE-mediated cow's milk allergy due to limited data on safety and efficacy in these patients. In infants with cow's milk protein-induced enterocolitis syndrome (FPIES) whose tolerance to rice is unknown, it is advisable to avoid using HRF until further evaluation, as rice is a known potential trigger of FPIES in some patients.

R 3.3 ***We strongly recommend against using partially hydrolysed cow's milk formula and mammalian milks (goat/sheep) in children with cow's milk allergy (both IgE and non-IgE-mediated) due to high risk of allergic reactions. [EM3-1]***

Partially hydrolysed formulas and mammalian milks are not recommended due to high risks of allergic reactions including anaphylaxis, and lack of efficacy in CMA management.[62-65] Patients with CMA should avoid partially hydrolysed formulas as they are only partially broken down and contain significant amount of intact cow's milk protein. Mammalian milk such as goat and sheep milk should also be avoided as they have a high degree of protein homology with cow's milk.[63, 64] Additionally, some mammalian milk products may pose nutritional and hygiene inadequacy concerns if not processed adequately.[48, 56, 57, 66]

GPP 3.4 ***In children (≥ 2 years old) and adults diagnosed with cow's milk allergy who need a milk substitute, fortified plant-based beverages (e.g. soy, coconut, rice, oat, quinoa, almond, cashew, pea) can be used. They should not be used as a substitute for formula milk in infants < 1 year old. [EM3-1]***

Fortified plant-based beverages (e.g. soy, coconut, rice, oat, quinoa, almond, cashew, pea) can be used as milk substitutes in children over 2 years old and adults.[66] There is insufficient evidence to evaluate the potential harm versus benefit, but they are widely available and culturally acceptable. Nutritional adequacy and allergy to specific ingredients must be considered prior to consumption. These beverages are inappropriate for infants under 1 year old as they are nutritionally inadequate to support normal growth and development and should not be used as a substitute for formula milk.[56, 66, 67]

For children between 1-2 years old, plant-based beverages[66] may be considered under these specific conditions:

- Eats a diverse, age-appropriate solid food diet that includes a variety from each food group
- Obtains at least 2/3 of their daily energy requirements from solid foods
- Consumes ≤2 servings/day of milk substitutes (1 serving = 240 ml)
- Has an adequate dietary intake of protein, fat and essential micronutrients
- Eats age-appropriate food textures and consistencies
- Has no feeding difficulties
- Has no known micronutrient deficiencies

3.1.2 Maternal cow's milk dietary elimination in breastfed infants with cow's milk allergy

R 3.5 ***We strongly recommend against routine maternal cow's milk dietary elimination for breastfed infants with IgE-mediated cow's milk allergy, unless the infant is symptomatic whilst being exclusively breastfed. If a trial of maternal cow's milk elimination is required, this should only occur for an initial period of 2 to 4 weeks, followed by reintroduction into the maternal diet to establish diagnosis. [EM3-2]***

Breastfeeding remains the optimal nutritional source for infants and should be actively supported. Evidence has shown that >99% of infants with IgE-mediated CMA will tolerate breastmilk from a mother who consumes cow's milk in her diet.[68] The concentration of cow's milk proteins such as ß-lactoglobulin detected in human breastmilk is very low (in nanogram/millilitre), and is unlikely to elicit an allergic reaction in most infants.[56, 69] Hence, maternal dietary exclusion of cow's milk is generally unnecessary, unless the infant is symptomatic while being exclusively breastfed.[48, 56, 68, 70]

The potential harm associated with maternal cow's milk elimination during breastfeeding in infants with CMA outweighs the benefits. These include a reduction in immune-enhancing components in breastmilk, potential maternal nutrient deficiencies, and a negative impact on the well-being of the mother and family.[68]

GPP 3.6 ***In breastfed infants with suspected food protein-induced allergic proctocolitis (FPIAP) (non-IgE-mediated CMA), a trial of maternal cow's milk elimination should be considered. If a trial of maternal cow's milk elimination is required, this should only occur for an initial period of 2 to 4 weeks, followed by reintroduction into the maternal diet to establish diagnosis. [EM3-2]***

In FPIAP (non-IgE-mediated CMA), a trial of maternal cow's milk elimination is recommended only when the clinical history is strongly suggestive of CMA. If a trial of maternal cow's milk elimination is undertaken, it should be limited to an initial period of 2 to 4 weeks (to assess for symptom improvement or resolution), followed by reintroduction into the maternal diet (to evaluate for symptom recurrence).[68, 70, 71] Continued maternal cow's milk elimination is only justified if there is symptom resolution upon elimination and symptom recurrence following reintroduction of cow's milk in the maternal diet.

GPP 3.7 ***In breastfed infants with suspected FPIES (non-IgE-mediated CMA), routine maternal cow's milk elimination in a breastfeeding mother is not recommended unless the infant is symptomatic while exclusively breastfed. [EM3-2]***

In FPIES (non-IgE-mediated CMA), only about 5% of CMA infants exhibit symptoms while being exclusively breastfed.[42, 70] However, the quantity of cow's milk or dairy products consumed in the maternal diet during breastfeeding may influence the infant's reaction threshold. Thus, routine maternal cow's milk exclusion in breastfeeding mothers is not recommended unless the infant is symptomatic while being exclusively breastfed, to prevent unnecessary nutritional and psychosocial burden.

GPP 3.8 ***If maternal cow's milk dietary elimination is required, vitamin D and calcium supplementation should be advised and referral to a dietitian for nutritional counselling can be considered for the mother. [EM3-2]***

If maternal cow's milk dietary elimination is necessary, it may significantly impact the mother's nutritional status, particularly calcium and vitamin D intake, which are essential for bone health and overall well-being. Therefore, supplementation with calcium and vitamin D should be advised to prevent micronutrient deficiencies.[72] Referral to a dietitian for nutritional counselling can further support the mother in maintaining a balanced diet and ensuring nutritional adequacy during the elimination period.

3.1.3 Incorporating baked milk products in the management of CMA

R 3.9 ***We strongly recommend that patients with cow's milk allergies should be assessed for tolerance to baked milk products. If tolerated, regular consumption of baked milk products should be recommended. [EM3-3]***

The majority (70-80%) of patients with CMA are able to tolerate baked milk products.[56, 66, 73-75] The baking process typically involves high heat (e.g. 180°C for 30 minutes), which denatures heat-labile milk proteins and disrupts conformational epitopes, thereby significantly reducing their allergenicity. The addition of wheat or grain matrix in baked goods creates a 'matrix effect', which further decreases the allergenicity by limiting the interaction of cow's milk proteins with the gastrointestinal immune system.[73, 76]

As cow's milk is ubiquitous in our diet, complete avoidance can be challenging and may impose significant dietary restrictions, negatively affecting the psychosocial well-being and quality of life of affected individuals and their families.[77] When tolerated, incorporating baked milk products such as muffins in the diet can facilitate dietary liberalisation, improve nutritional status and quality of life, and potentially reduce parental anxiety.[75, 78] Hence we recommend that patients with CMA be assessed for tolerance to baked milk products, following risk assessment and shared decision making between patient and allergist.

It is important to recognise that baked milk products are not uniformly equivalent in allergenicity as the degree of heating, the food matrix, and the proportion of milk within a recipe all influence the final allergenic content. Patients who tolerate one form of baked milk may not necessarily tolerate another, and clinicians should counsel families accordingly. It should also be noted that an individual's reaction threshold is not static — intercurrent illness, exercise, concurrent medications, and other cofactors may temporarily lower the threshold for reactivity, increasing the risk of a reaction even to previously tolerated foods. Families should be made aware of this variability. Primary care physicians may consider referring the child to an allergist to provide this counselling if deemed appropriate.

Current evidence is insufficient to conclude that the consumption of baked milk products accelerates the resolution of CMA, as existing evidence consists primarily of observational studies with significant heterogeneity, and one randomised controlled trial.[77-79] Nevertheless, the ability to tolerate baked milk may serve as a useful clinical marker for a more transient phenotype of CMA.[74]

Milk ladders are used to introduce less allergenic forms of baked milk in very small quantities with gradual staged reintroduction of more allergenic forms of milk to assess existing tolerance to less allergenic forms of milk in low-risk patients.

It is important to note that adverse reactions can occur, including life-threatening reactions.[80, 81] For this reason, home based reintroduction should be performed under guidance of an allergist, with careful patient selection of low-risk children with previously mild reactions. For higher-risk patients, reintroduction of the allergen should be done in the hospital in the form of a supervised oral food challenge. It should be emphasised that milk ladders are not a form of oral immunotherapy and should not be used as such.

3.2 EGG ALLERGY

3.2.1 Vaccination in patients with egg allergy

R 3.10 ***We strongly recommend that Measles, Mumps and Rubella (MMR) or Measles, Mumps, Rubella and Varicella (MMRV) or influenza vaccine be given in primary care to patients with egg allergy of any severity, with routine precautions. [EM3-4]***

Presence of egg allergy does not increase the risk of allergic reactions or anaphylaxis to the Measles, Mumps and Rubella (MMR), Measles, Mumps, Rubella and Varicella (MMRV) or influenza vaccines.[82-86]

The MMR or MMRV vaccine is propagated using chick embryo fibroblast cells and contains either negligible or non-detectable traces of egg protein (in picograms), which are insufficient to elicit allergic reactions in egg-allergic individuals.[87, 88] Multiple large-scale studies have demonstrated that the vaccine can be safely administered to egg-allergic individuals in primary care settings.[83, 89-92] Allergic reactions to MMR or MMRV vaccines are rare and are more likely to be attributed to excipients such as gelatine rather than egg proteins.[87]

Most influenza vaccines are produced using embryonated chicken eggs and may contain residual egg proteins, particularly ovalbumin.[89, 93, 94] However, recent randomised trials and prospective studies involving H1N1 and seasonal influenza vaccines, where the residual egg ovalbumin content is restricted to ≤1 µg/dose, have consistently shown that influenza vaccines can be administered safely to individuals with egg allergy without any additional precautions.[84-86, 95] A meta-analysis of 28 studies, 5 involving 4,315 egg-allergic individuals (including 656 with previous history of egg anaphylaxis), found no serious adverse events following influenza vaccination. Most of the current influenza vaccines contain very low amounts of ovalbumin (<0.12 µg/ml) and are deemed safe for intramuscular administration in both primary care and schools, even in patients with prior history of anaphylaxis to egg.[87, 89, 90, 96-99] The intranasal live attenuated influenza vaccine (LAIV) is also grown in hen's egg and therefore, contains trace amounts of egg protein. The ovalbumin content of LAIV is very low (<0.12 µg/ml) and has demonstrated a favourable safety profile in egg-allergic children, allowing it to be safely administered in any setting, including primary care and schools.[84, 85, 89, 90]

R 3.11 ***We strongly recommend against split dosing, prior allergy testing to vaccines or eggs, prior allergy specialist review or an extended observation post-administration of MMR, MMRV or influenza vaccines in patients with egg allergy. [EM3-4]***

Current evidence shows that split dosing, prior allergy testing to vaccines or eggs, prior allergist review or an extended observation period post-administration of MMR, MMRV or influenza vaccines in patients with egg allergy does not reduce the risk of adverse reactions, and therefore, these practices are not necessary.[87-90, 92, 97]

R 3.12 ***We strongly recommend that patients with egg allergy who require Yellow Fever vaccination should be referred to an allergy specialist for assessment and supervised administration. [EM3-4]***

The Yellow Fever Vaccine (YFV) is a live-attenuated vaccine cultured in hen's eggs and contains higher levels of residual egg protein compared to influenza vaccines.[100] Although rare, cases of anaphylaxis following yellow fever vaccination in individuals with egg allergy have been reported.[88, 101] Therefore, several international consensus guidelines recommend that egg-allergic patients who require yellow fever vaccination be referred to an allergy specialist for assessment and supervised administration, ideally at least 2 months prior to travel to endemic regions.[88-90, 92] Further evaluation with vaccine skin testing (e.g. skin prick test, intradermal test), single/graded dosing or desensitisation may be considered in these patients.[87, 90, 91, 102]

3.2.2 Incorporating baked egg products in the management of egg allergy

R 3.13 ***We strongly recommend that patients with egg allergies should be assessed for tolerance to baked egg products. If tolerated, regular consumption of baked egg products should be recommended. [EM3-5]***

The majority (70-80%) of patients with egg allergy can tolerate baked egg products.[103-105] The baking process utilises high heat (e.g. 180°C for 30 minutes), which denatures heat-labile proteins, resulting in loss of conformational epitopes and a subsequent reduction in egg protein allergenicity. The addition of a wheat or grain matrix in baked goods creates a 'matrix effect,' which further reduces the allergenicity by limiting the exposure of egg proteins to the immune system in the gastrointestinal tract.[106-108]

Since eggs are ubiquitous in our diet, strict avoidance of all forms of egg can impose significant dietary restrictions and adversely impact the quality of life for both patients and their families. The incorporation of baked egg products such as muffins into the diet facilitates dietary liberalisation, improves nutritional status and quality of life, and may reduce parental anxiety.[78, 90, 109] Hence we recommend that patients with egg allergies be assessed for tolerance to baked egg products, following risk assessment and shared decision making between patient and allergist.

It is important to recognise that baked egg products are not uniformly equivalent in allergenicity as the degree of heating, the food matrix, and the proportion of egg within a recipe all influence the final allergenic content. Patients who tolerate one form of baked egg may not necessarily tolerate another, and clinicians should counsel families accordingly. It should also be noted that an individual's reaction threshold is not static — intercurrent illness, exercise, concurrent medications, and other cofactors may temporarily lower the threshold for reactivity, increasing the risk of a reaction even to previously tolerated foods. Families should be made aware of this variability. Primary care physicians may consider referring the child to an allergist to provide this counselling if deemed appropriate.

Currently, there is insufficient evidence to conclude that the consumption of baked egg products accelerates the resolution of egg allergy, as most supporting data are derived from observational studies with high heterogeneity. However, tolerance to baked egg may serve as a useful marker for distinguishing between transient and persistent phenotypes of egg allergy.[75-77, 109, 110]

Egg ladders are used to introduce less allergenic forms of baked egg in very small quantities with gradual staged reintroduction of more allergenic forms of egg to assess existing tolerance to less allergenic forms of egg in low-risk patients.

It is important to note that adverse reactions can occur, including life-threatening reactions.[80, 111, 112] For this reason, home based reintroduction should be performed under guidance of an allergist, with careful patient selection of low-risk children with previously mild reactions. For higher-risk patients, reintroduction of the allergen should be done in the hospital in the form of a supervised oral food challenge. It should be emphasised that egg ladders are not a form of oral immunotherapy and should not be used as such.

3.2.3 Avoidance of lysozyme-containing expectorant/mucolytics in egg-allergic patients

GPP 3.14 ***Lysozyme (muramidase)-containing expectorants and mucolytics should not be used in patients with egg allergy as they are derived from eggs. [EM3-6]***

Lysozyme (N-acetyl muramidase) is an enzyme with bactericidal properties and purported expectorant and mucolytic effects. Since 1989, lysozyme-containing products such as Leftose, Neuflo, Neuzyme and Lyzyme have been available over the counter and used by doctors in Singapore. However, published evidence has not demonstrated the efficacy of lysozyme compared to placebo. As a result, the Health Sciences Authority (HSA) has

de-registered lysozyme-containing products as therapeutic products in Singapore in 2018.[113] However, lysozyme continues to be available for use as a health supplement due to its acceptable safety profile.

Lysozyme, which is derived from hen's egg white, has been reported to trigger allergic reactions including anaphylaxis in patients with egg allergies.[114, 115] Therefore, its use is not recommended in patients with known egg allergy.[116, 117]

3.2.4 Cross-reactivity between hen's eggs and eggs from other bird species

Skin test reactivity to eggs from other bird species (particularly quail and duck) is frequently observed in children with hen's egg allergy.[118] Due to the potential for cross-reactivity, it is generally recommended that individuals who are avoiding hen's egg, should also avoid eggs from other avian species, such as duck, goose and quail.[64, 119]

3.3 PEANUT AND TREE NUT ALLERGY

R 3.15 ***We conditionally recommend referring peanut-allergic patients to an allergist to for evaluation of potential tree nut co-allergy and to facilitate introduction of untried tree nuts. Blanket avoidance of tree nuts in patients with peanut allergies is not recommended. [EM3-7]***

R 3.16 ***We conditionally recommend allergist referral for tree nut-allergic patients to screen for additional tree nut allergies, to facilitate the introduction of untried tree nuts. Blanket avoidance of all tree nuts in patients with a specific tree nut allergy is not recommended. [EM3-8]***

The term tree nuts refers to nuts other than peanut and includes – almond, hazelnut, cashew, pistachio, walnut, pecan, Brazil nut, and macadamia. Nut allergies tend to be long-lived and nut avoidance advice is the cornerstone of management.

Historically, the approach to nut allergy was strict blanket avoidance of all nuts in peanut and tree nut allergic patients. Although avoiding all nuts simplifies the management and may decrease the risk of reactions secondary to cross-contact or misidentification, it has pitfalls. Unnecessary dietary restriction resulting from strict nut avoidance may reduce quality of life and lead to the development of new nut allergies. The rate of multiple nut allergies has been shown to increase with age, from 2% at 2 years to 47% at 14 years.[120-123]

20-86% of patients with peanut allergy are sensitised to tree nuts, however only 20-61% have a true tree nut allergy.[124-139] 61-97% of patients with tree nut allergy can be sensitised to multiple tree nuts, and 48-86% are allergic to more than 1 tree nut. However, very few individuals are allergic to all tree nuts.[131-133, 136] Most cashew- and walnut-allergic patients are also allergic to pistachio and pecan, respectively, while almost all pistachio- and pecan-allergic patients are also allergic to cashew and walnut, respectively.[131, 133, 136, 140] There also appears to be a walnut-pecan-hazelnut-macadamia cluster.[131, 136, 140]

SPT and serum sIgE have a good negative predictive value but poor positive predictive value, potentially resulting in false-positive results. Component resolved diagnostics (CRD) can improve diagnostic accuracy, however an oral food challenge (OFC) remains the gold standard for diagnosing food allergies. An individualised evaluation performed by an allergy specialist can guide introduction of individual nuts into the diet, which can reduce dietary restriction and may prevent the development of additional tree nut allergy.

Highly refined nut oils contain extremely small levels of protein and can be safely eaten by most people with nut allergy. Cold-pressed, expelled or extruded nut oils should be avoided as they may contain significant amount of protein. Additionally, coconut, chestnut, water chestnut, gingko nut, nut meg and pine nut do not belong to the same family as peanut or tree nuts despite having the word 'nut' in their name. Consequently, they do not need to be avoided, unless an individual is also allergic to them.

3.4 WHEAT ALLERGY

GPP 3.17 ***Patients with wheat allergies may consume rice, millet, corn and quinoa as alternative grains. [EM3-9]***

Grains are an important dietary source and exclusion of all cereals is not warranted in patients with a primary IgE-mediated wheat allergy.[64] Rice, millet, corn, quinoa, sorghum, teff and amaranth are well-tolerated in patients with wheat allergy and can be consumed as alternative grains.[64, 141, 142]

GPP 3.18 ***We suggest that patients with wheat allergies consult an allergist with regards to consumption of rye, barley and oat, if not already introduced and tolerated, due to risk of cross-reactivity. [EM3-9]***

Wheat allergic patients may react to taxonomically similar gluten-containing grains, particularly rye and barley. The risk of reaction is moderate for rye and barley,[142-144] and lower for oat,[145, 146] especially when selecting oats that have been processed without wheat contamination. Given the likelihood of cross-sensitisation and the limited predictive values of SPT and sIgE levels, patients may benefit from specialist guidance, including food challenge, to assess clinical tolerance prior to introduction.

3.5 FISH ALLERGY

GPP 3.19 ***We recommend that patients with a fish allergy may continue to eat the types of fish that they can tolerate. An allergist may be consulted before introducing new types of fish. [EM3-10]***

Due to the presence of pan-allergens such as parvalbumin, patients with fish allergies have an approximate 50% risk of cross-reaction to other types of fish.[64, 147, 148] Additionally, the difficulty of accurate fish identification in real life puts the patient at risk of allergic reaction. On the other hand, it is important to open up dietary options as fish-allergic patients are often able to consume certain fish particularly canned fish.[149-153] In a retrospective review of Singaporean children with fish allergy, 75% of patients were able to tolerate at least 1 other species of fish.[154] Thus patients may benefit from specialist guidance and assessment of clinical phenotype, with investigations on the type of fish that may be safely introduced (if any).

Additionally, some patients with fish allergy report reactions to fish oil supplements, however, there is significant heterogeneity in commercial product and patient phenotype.[154] Hence patients with fish allergy seeking omega-3 supplementation should either choose fish protein-free alternatives or consult an allergy specialist before initiating fish oil supplements.

3.6 SHELLFISH ALLERGY

GPP 3.20 ***We recommend that patients with shellfish allergy may continue to eat the types of shellfish that they can tolerate. An allergist may be consulted before introducing new types of shellfish. [EM3-11]***

Shellfish include crustacean (e.g. shrimp, crab, crayfish, lobster) and mollusc (e.g. oyster, clam, mussel, scallop, limpet, cockle, abalone, snail, octopus, squid). Since crustaceans are closely related to mites (house dust mite) and insects (cockroach), there is a major risk of cross-sensitisation and clinical cross-reactivity due to the presence of common allergens.[26, 155, 156] Cross-reactivity is also highly likely within the crustacean group, and lower between crustacean and mollusc.[157-159] Since there is clinical heterogeneity, some patients may be able to tolerate certain shellfish.[64, 147, 160] Patients with shellfish allergy interested in exploring dietary options may benefit from specialist review and guidance.

CHAPTER 4: MANAGEMENT OF ACUTE FOOD-INDUCED ALLERGIC REACTIONS

Acute food-induced allergic reactions can range from mild symptoms, such as oral pruritus or urticaria, to severe, rapidly progressing anaphylaxis involving respiratory and cardiovascular compromise. This chapter provides an overview of information concerning the management of acute food-induced IgE-mediated allergic reactions in the context of primary care.

4.1 MILD ALLERGIC REACTIONS

R 4.1 ***We strongly recommend using non-sedating H1 antihistamines to treat patients experiencing mild allergic reactions, such as urticaria, angioedema, or oral itch. [EM4-1]***

Oral H1 antihistamines are the recommended treatment for mild allergic reactions, such as urticaria, mild angioedema, and oral itch, which are primarily mediated by histamine release from mast cells during an allergic reaction. Non-sedating, newer-generation H1 antihistamines (e.g. loratadine, cetirizine) are preferred because they cross the blood-brain barrier to a lesser extent and are therefore associated with a lower incidence of drowsiness. First-generation H1 antihistamines (e.g. diphenhydramine, chlorpheniramine) also have prominent anticholinergic effects, which may pose a problem for children and the elderly, and are contraindicated in children below 2 years of age.[161]

GPP 4.2 ***Medications are not routinely recommended to prevent allergic reactions from occurring in individuals with established IgE-mediated food allergies. [EM4-2]***

Allergen avoidance remains the foremost strategy for managing established food allergies. Patients should be counselled to practise strict allergen avoidance unless advised otherwise by an allergist.

The evidence base supporting the prophylactic use of antihistamines and glucocorticoids in individuals with established IgE-mediated food allergies is lacking. Pre-treatment with these medications is not expected to prevent allergic reactions reliably and may mask the true severity of an allergic reaction, potentially leading to the delayed recognition and treatment of anaphylaxis.

Omalizumab, a monoclonal anti-IgE antibody, has emerged as a treatment option for patients with IgE-mediated food allergies. Omalizumab can be used in individuals aged 1 year and older to help reduce the risk of allergic reactions resulting from accidental exposure to foods to which they are allergic. Patients should continue avoiding all foods to which they are allergic to while receiving omalizumab treatment. The suitability of using omalizumab should be decided in consultation with an allergist.[162]

4.2 ANAPHYLAXIS

Anaphylaxis is a severe and potentially life-threatening acute IgE-mediated allergic reaction and constitutes a medical emergency. Favourable outcomes are contingent on early recognition and institution of appropriate treatment. Food-induced anaphylaxis may be diagnosed based on the rapid development of severe symptoms suggestive of an allergic reaction after ingestion of a suspected allergen, typically affecting multiple organ systems in rapid succession or simultaneously (Table 4.1).[6] Most cases of food-induced anaphylaxis occur within minutes to two hours after exposure to the allergen. Exceptions to this include FDEIA and α-Gal syndrome, which may manifest several hours after ingestion. Management of anaphylaxis is detailed below with a summary provided in Figure 4.1.

Table 4.1: World Allergy Organization Anaphylaxis 2020 Diagnostic Criteria		
Anaphylaxis is highly likely when any one of the following two criteria are fulfilled:		
1	Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both, and at least one of the following:	a) Respiratory compromise
		b) Reduced blood pressure or associated symptoms of end-organ dysfunction
		c) Severe gastrointestinal symptoms
2	Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement	

R 4.3 ***We strongly recommend that patients suspected of having food-related anaphylaxis be treated as an emergency with the immediate administration of intramuscular adrenaline as the first-line intervention. [EM4-3]***

R 4.4 ***We strongly recommend administering additional doses of intramuscular adrenaline every 5 to 15 minutes based on the patient's clinical response, for those who do not show improvement while awaiting transfer to an emergency facility. [EM4-3]***

Adrenaline is the first line and most critical treatment for food-induced anaphylaxis and should be administered promptly. Adrenaline mitigates the pathophysiologic cascade of anaphylaxis by causing vasoconstriction, increasing cardiac output, relaxing bronchial smooth muscle, and reducing the release of mast cell mediators. Pre-hospital adrenaline administration, either in a clinic or as self-injection using an autoinjector, is associated with improved patient outcomes.[163]

Intramuscular injection of adrenaline into the mid-anterolateral thigh is the recommended route as it gives higher plasma adrenaline levels.[164] The recommended dose for healthcare professionals is 0.01 mg/kg of body weight, to a maximum total dose of 0.5 mg, and may be simplified as shown in Table 4.2. Dosing should be repeated every five to fifteen minutes if there is no improvement whilst awaiting transfer to an emergency facility. Adrenaline administered by the intramuscular route is generally well tolerated. This contrasts with the intravenous route, where potentially fatal arrhythmias can occur with bolus adrenaline administration. Where an adrenaline autoinjector is available, it may be used as an alternative. The recommended autoinjector dose is 0.15 mg for children weighing 7.5 kg to less than 25 kg; 0.3 mg for children weighing 25 kg and above, and at least 0.3 mg for adolescents and adults. **Table 4.2: Recommended doses for intramuscular adrenaline as per the World Allergy Organization Anaphylaxis Guidance 2020[6]**

Weight/Age (if weight is not available)	Dose of 1 mg/mL (1:1000) adrenaline
< 10kg (or infants < 1 year)	0.01 mg/kg (0.01 mL/kg)
10kg - <25 kg (or children aged 1 - 5 years)	0.15 mg (0.15 mL)
25 kg to <50 kg (or children aged 6 - 12 years)	0.3 mg (0.3 mL)
>50 kg (or teenagers and adults)	0.5 mg (0.5 mL)

GPP 4.5 ***We recommend that the following treatments be administered as adjunctive measures to intramuscular adrenaline if clinically indicated:***

- ***High-flow supplemental oxygen for hypoxia/respiratory distress***
- ***Intravenous fluids for hypotension/shock***
- ***Inhaled beta-2-agonists for bronchoconstriction***
- ***Non-sedating antihistamines for cutaneous symptoms. [EM4-3]***

Adjunctive therapies play an important supportive role in managing symptoms and preventing end-organ damage in anaphylaxis, but they should not delay or replace the administration of adrenaline. Supplemental oxygen therapy should be provided to patients experiencing hypoxia or respiratory distress, and intravenous fluid resuscitation should be started for those showing signs of shock. Antihistamines can help alleviate skin symptoms such as hives and itching. Inhaled bronchodilators, such as salbutamol, are helpful in relieving bronchoconstriction.

R 4.6 ***We conditionally recommend against the routine use of glucocorticoids for the prevention of biphasic anaphylaxis. [EM4-3]***

The evidence supporting the use of steroids in the management of anaphylaxis is limited and inconclusive. Steroids have traditionally been administered with the aim of preventing biphasic reactions, but this practice is largely based on clinical consensus rather than robust data. Systematic reviews have found no clear evidence that corticosteroids reduce the incidence of biphasic anaphylaxis or improve clinical outcomes in the acute setting.[165] Furthermore, the delayed onset of action of steroids limits their utility in treating the immediate life-threatening features of anaphylaxis. Intramuscular adrenaline remains the first-line treatment for anaphylaxis, and corticosteroids, if used, should be considered adjunctive and reserved for specific scenarios such as coexisting asthma or persistent symptoms.

R 4.7 ***We strongly recommend the prescription of adrenaline autoinjectors for individuals with a history of food-induced anaphylaxis. [EM4-4]***

Adrenaline autoinjectors are single-use devices that deliver a fixed dose of intramuscular adrenaline and are designed for rapid administration into the mid-anterolateral thigh. Individuals with a history of food-induced anaphylaxis should be prescribed at least one adrenaline autoinjector. Provision of a second autoinjector may be considered, particularly for individuals with a history of severe or refractory reactions or where emergency medical access may be delayed.

The European Academy of Allergy and Clinical Immunology (EAACI) 2021 update task force suggests prescribing 0.15 mg adrenaline autoinjectors for children from 7.5 kg to <25 kg, 0.3 mg adrenaline autoinjectors for children from 25 kg and above, and at least 0.3 mg adrenaline autoinjectors for adolescents and adults at risk of anaphylaxis.[166] Patients should still attend a medical facility for observation and possible further treatment after self-administering adrenaline.

All patients and caregivers should receive structured education on allergen avoidance, recognition of early anaphylactic symptoms, and correct use of the autoinjector, including practical training and periodic reinforcement. This should include provision of a written anaphylaxis action plan (Appendix 2), which should clearly outline symptom recognition, emergency action steps and instructions to seek emergency care.

GPP 4.8 ***We suggest that adrenaline autoinjectors may be considered for individuals with a history of mild-to-moderate allergic reactions to foods, particularly if there are additional risk factors for anaphylaxis. Risk factors include, but are not limited to:***

- ***Unstable or moderate-to-severe persistent asthma***
- ***Previous reaction to trace amounts of food allergens***
- ***Allergies to peanuts or tree nuts***
- ***History of risk-taking behaviour***

- *Limited/ remote access to medical care*
- *Underlying systemic mastocytosis*
- *Oral immunotherapy for food allergy*
- *Inability to avoid further exposure to the allergen consistently. [EM4-4]*

Adrenaline autoinjectors may also be prescribed for individuals with food allergies who have not experienced anaphylaxis but are at a higher risk for severe reactions.[166] Clinical judgment should be used to weigh individual risk factors, the likelihood of allergen exposure, and the preferences of the patient or caregiver when deciding whether to prescribe an autoinjector. Relative indications for prescribing are stated in GPP4.8. These include having moderate to severe persistent asthma or lacking reliable access to emergency medical care. Additionally, individuals who engage in higher risk-taking behaviours may also benefit from being prescribed an autoinjector.

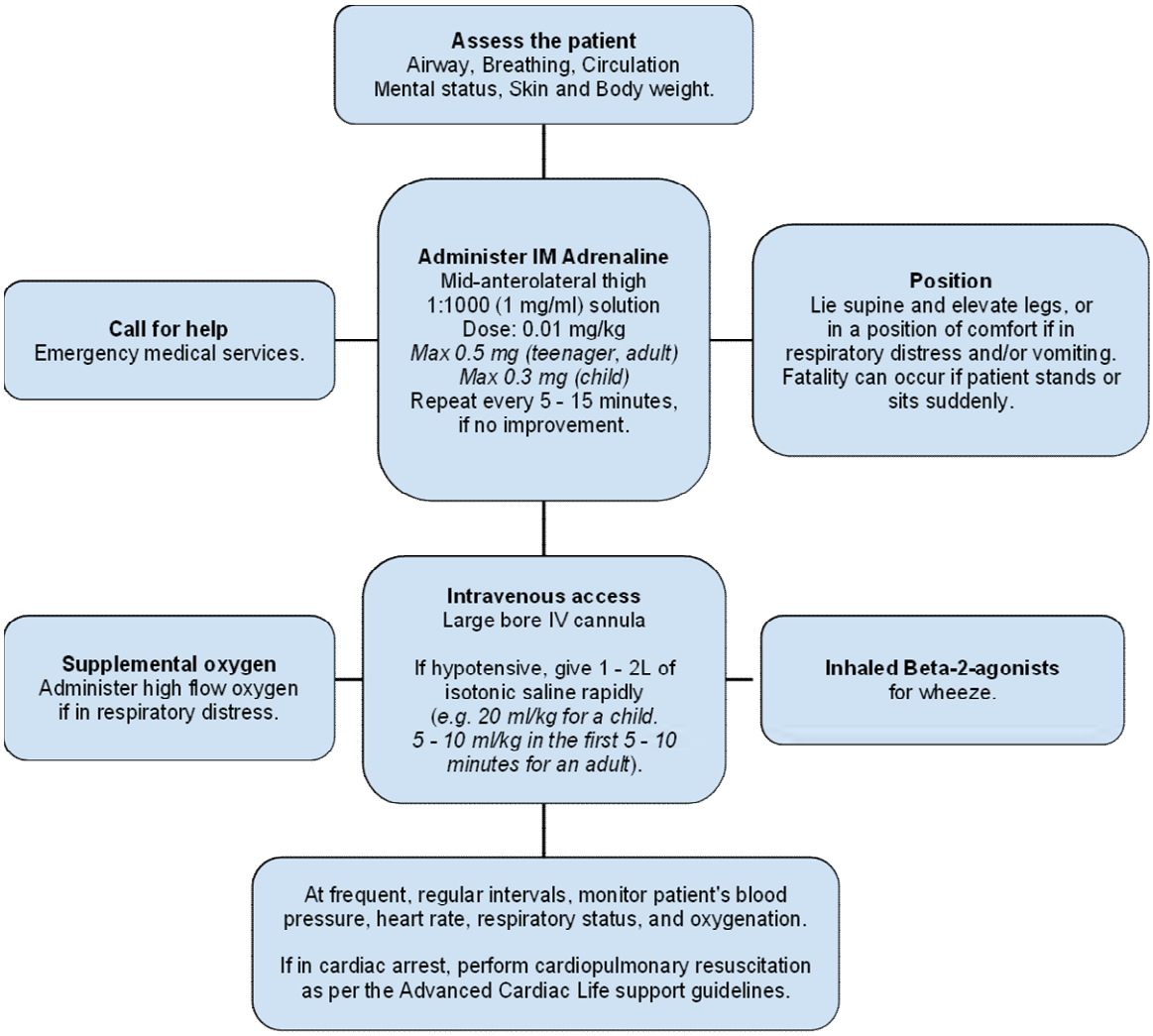

Figure 4.1: Management of Anaphylaxis in the Primary Care Setting (adapted from World Allergy Organization Anaphylaxis Guidance 2020)[6]

CHAPTER 5: NUTRITIONAL COUNSELLING AND EVALUATION

Children with food allergies are at higher risk of nutritional inadequacy and deficiencies, feeding problems and faltering growth. Many food allergy guidelines state growth monitoring and evaluation of nutritional status as an essential aspect of food allergy management.[48, 91, 167, 168] Risk of nutritional issues increases with the number of food allergens eliminated, especially cow's milk.[66] Prolonged elimination diets involving multiple and major food groups should be avoided, unless necessary, due to the detrimental effects such as nutritional deficiencies, impaired growth, long term effects on eating behaviours and quality of life (QoL).[169]

Regular surveillance of nutritional status and QoL should be performed as the risk of suboptimal nutritional intake increases with prolonged elimination. This is especially crucial during early childhood, which is a critical period of growth and neurodevelopment.

Personalised interventions from a dietitian in patients with food allergies can improve growth, nutrition, dietary diversity, feeding behaviours, oral motor skills and mental health and wellbeing of the child and family.[170] Feeding difficulties are also common in children with food allergies, often resulting from negative associations with eating such as vomiting or discomfort, parental anxiety and textural or sensory aversions, especially in children with co-existing conditions such as eczema, reflux or neurodevelopmental concerns.[171, 172] Regular nutrition assessment and monitoring by the dietitian allows for early identification of these nutritional issues and enables timely interventions such as dietary supplementation, adjustment of elimination diet or multidisciplinary management. Multidisciplinary care may involve psychologists to address the psychosocial impact and quality-of-life concerns associated with chronic food allergy management as well as speech or occupational therapists to address feeding difficulties.

GPP 5.1 ***We recommend regular growth monitoring and nutritional counselling for all children with food allergies. [EM5-1]***

Healthcare professionals should regularly review growth measures such as weight, length or height and head circumference (in children under 2 years) or body mass index (as age-appropriate) on appropriate growth charts and track growth velocity as well as any significant changes in growth percentiles over time.[168, 173, 174]

Nutrition counselling should be provided by a dietitian with expertise in food allergy and include education on label reading, avoidance strategies and appropriate substitutions to maintain a nutritionally adequate diet despite the necessary food exclusions.

For young infants and children, other key aspects to address include dietary diversity, weaning progression, development of normal feeding skills, nutrition support during breast-feeding when maternal dietary elimination is required and appropriate choice of supplemental formulas. Early recognition and timely referral for feeding therapy by an occupational or speech therapist is recommended for concerns of feeding difficulties, refusal, or aversions to limit associated nutritional risks.[169]

GPP 5.2 ***Referral to a dietitian should be made for children with food allergies who present with poor growth or suspected malnutrition, including obesity. Other considerations for a comprehensive nutrition consultation with the dietitian include patients with:***

- ***Cow's milk allergy***
- ***Multiple (>2) concurrent food allergies, especially those excluding major staples such as cow's milk, egg, and wheat***
- ***Elimination diet without appropriate nutritional substitutes***
- ***Delayed weaning progression in infants and/or difficulties transiting to more textured foods, high child and/or parental anxiety around feeding***
- ***History of multiple accidental exposures or anaphylaxis indicating an inability to manage food avoidance***

- *Additional dietary restrictions such as vegetarianism or personal food beliefs. [EM5-1]*

Cow's milk allergy presents significant dietary challenges due to the nutritional importance of milk especially in infancy and early childhood. A number of studies have shown that children with cow's milk allergy have lower weight-for-height Z-scores, stunting or a shorter stature as well as being associated with wasting and underweight.[175-177] Dietitians would be able to support breastfeeding mothers with a maternal elimination diet, selecting appropriate infant formula and planning nutritionally adequate diets for infants and children.[170, 172]

Children with multiple food allergies, especially those involving major food groups such as egg, milk and wheat, are at increased risk of nutrient deficiencies and poor growth.[169, 170] A systematic review showed that avoidance of 2 or more allergens reduced longitudinal growth parameters in all types of food allergies studied.[178] Additionally, micronutrient deficiencies are linked to the elimination of specific foods, a lack of nutritionally appropriate, allergen-free replacements and increased nutrient demand.[169] As such, studies have shown that children who received nutrition counselling and monitoring from a dietitian are at significantly lower risk of such nutrient deficiencies, particularly calcium and vitamin D.[48, 170, 172, 178]

Families dealing with food allergies often experience elevated anxiety related to the risk of anaphylaxis, especially in newly diagnosed patients, children with prior severe reactions or emergency visits, and patients with accidental exposures especially in daycare or school settings.[172] This anxiety could lead to fear of introducing new foods, avoidance of safe foods and unnecessary dietary restrictions such as delayed introduction of complementary foods.[170, 172] Dietetic consultation could help to build confidence through education on food labels, allergen avoidance strategies and safe food preparation, clarifying misconceptions and providing guidance for the safe introduction of new foods.[179]

GPP 5.3 ***Targeted nutritional biomarkers for micronutrient assessment should be considered after evaluating dietary intake, food eliminated, growth patterns and physical signs. [EM5-1]***

To mitigate the risk of nutritional deficiencies and poor growth, regular dietary monitoring is essential to ensure that nutritional needs are met over time. There are no specific guidelines on the routine measurement of serum biomarkers for micronutrients in food allergic children and testing should be guided by clinical assessment and diet history. A detailed diet history which includes the type and number of foods eliminated, duration of elimination and diet quality should be taken and assessed together with clinical symptoms and growth trends.[179] The core nutritional biomarkers in food allergic children include:

- Bone profile: 25-hydroxy vitamin D, calcium, phosphate and alkaline phosphatase
- Iron studies: Serum iron, ferritin, transferrin saturation
- Vitamin B12 and folate
- Serum zinc (especially in the presence of growth failure and/or severe eczema)

The most common vitamin and mineral deficiencies in children with food allergies are vitamin D, calcium, iron, zinc and B vitamins.[180-186] The frequency for monitoring of nutritional biomarkers is guided by the degree of deficiency, amount of supplementation prescribed, any introduction of additional food substitutes, new symptoms, and medical history.[169, 170, 173, 179] Most guidelines highlight the importance of regular monitoring of calcium and vitamin D status in children with cow's milk allergy, especially in those older than 1 year of age, not taking suitable formula milk alternatives or poor growth.[71, 187]

GPP 5.3 ***Vitamin and mineral supplementation in children with food allergies should be guided by both the evaluation of nutritional biomarkers and the assessment of dietary intake. [EM5-1]***

There is no evidence for routine vitamin and mineral supplementation in children with food allergies. Supplementation should be specific to the identified nutritional deficiency and tailored to the child's age, dietary intake and laboratory findings.[180, 188] Supplementation should be accompanied by ongoing nutritional counselling and growth monitoring, with dose adjustments as needed based on clinical response and dietary changes.

Calcium and vitamin D supplementation should be considered for children with cow's milk allergy when dietary intake is insufficient, even in the absence of laboratory testing for deficiency. This recommendation is based on the high risk of deficiency and adverse bone health outcomes in children with cow's milk allergy, especially those who do not consume adequate fortified milk substitutes.[183, 189] Multivitamin supplementation can be provided in age-appropriate doses if multiple micronutrient gaps are identified or in cases of highly restrictive diet or picky eating and poor dietary variety.[169, 170, 186, 189]

Clinicians are also advised to have a high index of suspicion and provide zinc supplements to patients with gastrointestinal and dermatologic manifestations suggestive of zinc deficiency, regardless of serum zinc levels.[190] In the presence of clinical signs such as growth faltering, stunting, severe dermatitis or delayed wound healing and dietary risk factors, empiric zinc supplementation is appropriate. Typical paediatric dosing is 10–15 mg elemental zinc daily for children aged 6 months to 12 years, for 3–6 months and reassessment of clinical response and dietary intake.[191]

CHAPTER 6: MANAGEMENT OF FOOD ALLERGIES IN SCHOOLS, PRE-SCHOOLS AND CHILDCARE FACILITIES

Children with food allergies live with the daily risk of allergic reactions that range from mild to potentially life-threatening. Reducing the risk of allergen exposure and managing allergic reactions when they occur is a central part of allergy management. Having a food allergy can impact quality of life, limit participation in day-to-day activities and adversely affect nutrition and growth.

Given that children are expected to spend significant amounts of time in schools, pre-schools and childcare settings, a comprehensive approach involving the patient, family, school staff, community and the medical team is necessary to create a safe and inclusive school environment for food allergic children.

GPP 6.1 ***Schools and childcare centres should have at least one, or more if possible, member of staff trained in the prevention, recognition and management of allergic reactions [EM6-1].***

A median of 375 allergic reactions occur per 100 000 students per year, with 3-20% of these reactions happening in childcare centres or schools. Fatal allergic reactions, although rare, have also occurred in schools and are reported to be associated with a delay in administering intramuscular adrenaline.[192-194]

International studies have shown that teachers and school personnel have limited knowledge, skills, and confidence related to the prevention and treatment of allergic reactions.[195] Training has been reported to be associated with short-term improvements in allergy-related test scores or knowledge, confidence and self-efficacy among teachers and school personnel.[192, 195, 196] While more research is required to understand the effect of training on long-term improvements, there is evidence that many school personnel find it helpful and necessary to receive food allergy training.[197-199]

Allergy training programs should be designed, reviewed and regularly updated by healthcare professionals with expertise in food allergy.[192, 200, 201] School staff training should include the recognition and management of allergic reactions as well as guidance in the implementation of practical strategies to reduce the risk of accidental exposures to known allergens. Published guidelines recommend risk minimisation strategies such as limiting the use of food during lessons, clear food labelling, proper hand washing and cleaning of surfaces that come into contact with food to prevent cross-contamination. If childcare centres or schools implement these strategies and/or site-wide protocols, they should be done in such a way as to promote inclusion. Policies that isolate patients are discouraged as they put food allergic children at higher risk of bullying and social isolation.

GPP 6.2 ***Parents of students with a diagnosed food allergy should provide the school or childcare centre with an up-to-date allergy action plan. [EM6-1]***

Allergy action plans (Appendix 2) are emergency care plans that outline the recommended emergency response to a suspected allergic reaction. The document may be personalised with the student's name, emergency contact information and allergen triggers. Studies suggest that provision of allergy action plans may help reduce frequency of allergic reactions or adrenaline use in students.[192]

Allergy action plans should be completed by a registered medical practitioner and updated regularly or with any changes in allergy status. Allergy Action plans should be provided by parents/students to their schools, and emergency response in the event of an allergic reaction should follow each individual school's internal workflows. [192, 200, 201]

CHAPTER 7: NATURAL HISTORY OF FOOD ALLERGY

GPP 7.1 ***We recommend that all patients with food allergies should be reviewed regularly by an allergist to reassess allergy status. Children younger than 5 years old should have at least yearly monitoring of food allergies. [EM7-1]***

7.1 Natural Resolution and Follow-up

The rate and timing of natural resolution vary depending upon the specific food and may occur as late as adolescence. The National Institute of Allergy and Infectious Diseases (NIAID) guidelines recommend yearly monitoring of egg, milk, soy and wheat allergies and 2-3 yearly monitoring of peanut, tree nuts, shellfish and fish allergies.[91]

Children younger than 5 years old should have at least yearly monitoring of food allergies, especially of egg, milk, soy, wheat and peanut allergies. If the food allergy is not outgrown by 5 years of age, monitoring may be extended to once every 2-3 years.[202]

7.2 Egg and Milk Allergies

Egg and milk allergies are associated with a high rate of resolution of up to 80%. The median age of natural resolution varies according to geographical region - studies of egg-allergic patients in Australia and Japan found 73-89% outgrew their allergies by 6 years of age, and a local Singaporean retrospective review found 81.8% of milk-allergic children outgrew their allergies by 6 years of age.[52, 203, 204] Prognostic factors associated with higher likelihood of natural resolution include the ability to tolerate baked egg and baked milk products, and lower initial sIgE level at baseline.

7.3 Peanut and Tree Nuts Allergies

The rate of resolution of peanut allergy is 25-30% by 6-10 years of age in various cohorts, while resolution of tree nut allergy is only around 10%.[205, 206]

7.4 Soy and Wheat Allergies

Soy and wheat allergies are associated with high rates of resolution, with 69% of soy allergies resolving by 10 years of age and 65% of wheat allergies by 12 years of age. High peak wheat or soy IgE levels of >50 kU/L at baseline are associated with persistent allergies.[207, 208]

7.5 Sesame Allergy

The rate of resolution of sesame allergy was 20-30% in 2 Israeli-based cohorts.[209, 210]

7.6 Fish and Shellfish Allergies

Fish and shellfish allergies are generally more likely to be persistent. A retrospective review of fish-allergic Singaporean children found a 25.9% rate of resolution by median age of 60 months.[154] A follow-up study of challenge proven Thai prawn-allergic patients found that 46% passed a repeat challenge at 10 years, however this study was significantly biased by a high attrition rate as challenges could only be repeated in only 37% of the original cohort.[211]

GPP 7.2 ***We recommend that SPT and food-specific or component resolved IgE should be performed regularly, as a declining trend of sIgE level, and size of SPT wheal is a good prognostic marker for development of tolerance. [EM7-1]***

GPP 7.3 ***We recommend that patients with a trend of declining sIgE and/or SPT wheal size and no recent clinical reactions, should be re-evaluated for possible natural resolution, by an allergist, to enable reintroduction of tolerated food. [EM7-1]***

Clinical factors associated with persistent food allergy include high initial or peak sIgE levels, history of severe atopic dermatitis (especially early onset), multiple food allergies, and severe anaphylactic reactions.[212] A decrease in sIgE levels over time, particularly in the first 4 years of life, is significantly associated with the development of natural tolerance. A decline in SPT wheal size is also associated with development of tolerance, albeit to a lesser degree. Borderline SPTs (wheal size of 3-5 mm) may persist even after clinical tolerance has developed.[91]

Confirming resolution of food allergy requires reintroduction of the food into the diet as loss of sensitisation alone does not guarantee tolerance, and low levels of sIgE or small SPT wheals may be persistent even after tolerance develops. Since reintroduction is associated with risk of food allergic reactions, including risk of anaphylaxis, this should be done under the guidance of an allergist.[91]

GPP 7.4 ***The use of egg and milk ladders for reintroduction of egg and milk, in patients with mild egg and milk allergies, can be considered. This should be done under guidance of an allergist as appropriate patient selection and preparation is essential to minimise the risk of anaphylaxis. [EM7-1]***

Egg and milk ladders are used to introduce less allergenic forms of baked egg and milk in very small quantities (grain or pea-sized amount), with gradual staged reintroduction of more allergenic forms of egg and milk to assess existing tolerance to less allergenic forms of the food allergen in low-risk patients.

It is important to note that 40-80% of children experience adverse reactions on the egg and milk ladder, including a low rate of anaphylaxis events.[80, 81, 111, 112] For this reason, home based reintroduction should be performed under guidance of an allergist, with careful patient selection of low-risk children with previously mild reactions. For higher-risk patients, reintroduction of the allergen should be done in the hospital in the form of a supervised oral food challenge. It should be emphasised that egg and milk ladders are not a form of oral immunotherapy and should not be used as such.

CHAPTER 8: ORAL IMMUNOTHERAPY FOR FOOD ALLERGY

Up until recently, the standard management of food allergy has been strict allergen avoidance and emergency treatment of allergic reactions when they occur. Unfortunately, accidental exposures are inevitable, and food allergic individuals are constantly at risk of allergic reactions, including anaphylaxis.

Food allergen immunotherapy is an emerging therapeutic option for food allergy with oral immunotherapy (OIT) being increasingly used in clinical practice. OIT involves the daily consumption of an allergen, typically starting at very low doses and gradually increasing over weeks to months until a maintenance dose is achieved and continued for months to years. OIT, in its current form, aims to induce desensitisation to the food allergen which is defined as a temporary increase in reaction dose threshold that is maintained through continuous exposure to the allergen. It is not a cure as cessation of therapy usually results in a drop in this reaction dose threshold. Hence, patients who achieve desensitisation may be protected against accidental reactions if the same cautious eating behaviours (allergen avoidance) and regular OIT dosing are continued.

R 8.1 ***We strongly recommend offering oral immunotherapy (OIT) under specialist supervision to children with persistent IgE-mediated peanut allergy to achieve desensitisation (increase the amount of peanut tolerated while on therapy), in centres with expertise and infrastructure in OIT. Informed shared decision making is key in patient's choice to take up OIT. [EM8-1, 8-2, 8-3]***

R 8.2 ***We conditionally recommend offering OIT under specialist supervision to children with persistent IgE-mediated hen's egg, cow's milk, tree nut and wheat allergy to achieve desensitisation (increase the amount of allergen tolerated while on therapy), in centres with expertise and infrastructure in OIT. [EM8-1, 8-2, 8-3]***

Food allergies can be outgrown in childhood. When weighed against the costs and risks of OIT, a 'watch and wait' approach is a reasonable alternative, especially in younger children whose clinical and biochemical profiles suggest they may naturally outgrow the allergy. However, once children reach primary school age and beyond, the likelihood of outgrowing food allergies diminishes significantly compared to toddlers. Thus, a child aged five years and above, or those with very high baseline and up-trending allergen specific antibodies (sIgEs), are more likely to have a persistent allergy.

Recent meta-analyses consistently demonstrated the efficacy of OIT in achieving desensitisation for peanut allergies, with high certainty of evidence.[48, 213-218] These benefits also included improvement in quality of life.[218] The same meta-analyses demonstrated that OIT could achieve desensitisation for hen's egg and cow's milk allergies, with very low to moderate certainty of evidence. One meta-analysis also included a randomised controlled trial on wheat OIT, with evidence of benefit, albeit with low certainty.

R 8.3 ***We conditionally recommend OIT be offered as a treatment option for adults. [EM8-1, 8-2, 8-3]***

While most clinical evidence comes from the paediatric population, there is no evidence to show that OIT is not effective in adults. However, adult patients may require more individualised approaches due to potentially different risk factors, comorbidities, and lifestyle considerations. The decision to proceed with OIT in adults should involve careful evaluation of the patient's medical history, health status, and the ability to comply with the treatment protocol.

GPP 8.4 ***OIT should be discussed with, and provided by, a specialist in allergy who is experienced in providing OIT to patients. [EM8-1]***

The specialised management of food allergies falls under the responsibility of allergy specialists. Since OIT is a relatively new treatment option for food allergies, it should remain within the domain of trained specialists. Given the significant costs, risks and uncertainties associated with OIT, the decision to undertake OIT must be made through a shared decision-making process between the patient/family and an allergy specialist.

This process requires a comprehensive discussion of the indication for OIT, alternative treatments, logistics, costs, and an exploration of potential barriers and facilitators of treatment success, all tailored to each patient and family. Potential risks include allergic reactions or anaphylaxis, eosinophilic esophagitis and failure to achieve desensitisation or sustained unresponsiveness. Consequently, OIT should only be administered under the supervision of an experienced allergy specialist, with dose increments performed in a medical facility equipped to manage severe allergic reactions.

GPP 8.5 ***Uncontrolled asthma is an absolute contraindication to OIT. Asthma must be controlled before beginning OIT and proactively managed during OIT. [EM8-1]***

Evidence shows that uncontrolled asthma increases the risk of mortality in patients with food allergies. Primary studies in OIT generally exclude patients with uncontrolled asthma, as OIT can trigger allergic reactions, including asthma attacks. [218-221] Therefore, the decision to initiate OIT should include a recent assessment of asthma control. Asthma should remain well-controlled before commencing. During OIT, proactive asthma management should include:

- Regular assessment of asthma control
- Adjustment of asthma medications as needed
- Provision of asthma action plan
- Coordination of care between the allergist and other healthcare providers managing the patient's asthma.

GPP 8.6 ***Given the potentially higher risk of anaphylaxis during OIT, carrying an adrenaline autoinjector is good practice. [EM8-1]***

Adverse effects (allergic reactions) during OIT are common. Although most are mild, the risk of requiring adrenaline to treat anaphylaxis is significantly higher compared to no intervention (relative risk of 8.45 for cow's milk and 2.96 for peanut).[213] As such, patients must carry adrenaline autoinjector(s) with them at all times. Patients and caregivers should also be trained in recognising and managing allergic reactions and anaphylaxis, including the appropriate use of adrenaline autoinjectors.

Food allergen immunotherapy is a rapidly evolving field, and the recommendations in this chapter reflect the best available evidence at the time of writing. Research continues to expand our understanding of OIT across several fronts, including the optimal timing of initiation, the feasibility of starting OIT in preschool-aged children, and the prospect of achieving sustained unresponsiveness or remission — outcomes that go beyond desensitisation. The scope of OIT is also broadening, with promising data emerging for tree nut allergy, particularly cashew and walnut. The role of adjunctive biologics, particularly omalizumab, is also an active area of investigation, with emerging evidence suggesting it may improve the safety and efficacy of OIT. Alternative immunotherapy approaches, including sublingual immunotherapy (SLIT) and epicutaneous immunotherapy (EPIT), are also under active study and may offer improved safety profiles, though their efficacy relative to OIT has yet to be fully established. Given the pace of development in this field, clinicians and patients should remain attentive to emerging evidence, and all decisions regarding immunotherapy should continue to be made through a shared decision-making process.

CHAPTER 9: ATOPIC DERMATITIS IN FOOD ALLERGY

Food allergy (FA) is closely associated with atopic dermatitis (AD), and the prevalence of food allergy amongst AD patients ranges between 9.4 – 32.7%.[222-224] Risk factors for food allergy in AD include:

1. Young age:[225]
   a. The highest rates of food allergy are found in AD patients aged 0 – 2 years.
   b. Infants with early onset eczema were shown to be six times more likely to have an egg allergy and 11 times more likely to have a peanut allergy by 12 months.
2. Greater severity of AD:
   a. The rates of food allergy increase significantly with worsening AD severity.[226, 227]

It is however noteworthy that a large majority of patients with AD do not have a concomitant food allergy, especially if the AD is of mild to moderate severity and of older age at onset. Optimisation and adherence to the prescribed skin care regime alone is usually sufficient to achieve AD control in these patients. If AD control remains poor despite this, then an allergist can be consulted to assess for concomitant food allergies.

R 9.1 ***We strongly recommend against the routine use of food allergy tests to screen for food allergy in atopic dermatitis (AD) patients in view of the high rates of food sensitisation (i.e. false positive). [EM9.1]***

Food sensitisation (FS) refers to patients with a positive SPT or raised serum sIgE to a food allergen, but without a clinical reaction when the food is ingested. These cases are not truly food allergic and may represent false-positive test results. FS rates in AD patients can be as high as 60%, which are significantly higher than true food allergy rates.[227, 228] Interpretation of allergy tests and diagnosis of true food allergy in AD patients can therefore be challenging and should ideally be performed by trained personnel to avoid unnecessary elimination of foods in patients with AD.

It is also important that patients who have been tolerating a particular food without reaction should avoid having that food tested, as a positive food allergy test does not imply a food allergy is present and can instead cause anxiety, unnecessary elimination and even cause loss of tolerance to the food, with food allergy subsequently developing because of prolonged avoidance.[229]

R 9.2 ***We strongly recommend food allergy evaluation by an allergy specialist in young patients (less than 2 years old) with severe and refractory AD despite optimisation of, and adherence to, conventional therapy and where there are concerns of food reactions. [EM9-2]***

GPP 9.3 ***We recommend referral to an allergy specialist for young infants with severe AD, whose timely introduction of solids and allergenic foods may be delayed due to parental concerns. [EM9-3]***

The pathogenesis of food allergy in AD can be explained by the dual allergen exposure hypothesis which states that cutaneous exposure to food antigens, particularly in the setting of an impaired skin barrier such as AD, triggers a TH2 response with consequent food-specific IgE production and clinical food allergy; while oral exposure to a food antigen leads to tolerance.[228, 230] This hypothesis has been supported by landmark trials including Learning Early About Peanut Allergy (LEAP),[231] Enquiring About Tolerance (EAT),[232] Prevention of Egg Allergy with Tiny Amount Intake (PETIT),[233] and Preventing Atopic Dermatitis and Allergies in Children (PreventADALL)[234] that have shown that the early oral introduction of peanut and egg (around age 6 months) prevented the development of these allergies across all infants, especially for those with risk factors (e.g. infantile eczema, other food allergy, family history of atopy).

Although the trials for the other allergenic foods have not shown a significant reduction in food allergy with early introduction, international consensus has been to avoid delaying the introduction of other allergenic foods. Timely oral introduction of food allergens before cutaneous sensitisation in patients with AD may therefore be beneficial for food allergy prevention.[230]

R 9.4 ***We strongly recommend against long-term untargeted elimination of foods in AD patients, as it is detrimental to a patient's health and quality of life. [EM9-3, 9-4]***

If a diagnostic elimination diet is required, it should be limited to only 2-4 weeks while ensuring that AD management is optimised. If there is no significant improvement in the patient's eczema despite the elimination diet, the eliminated foods are unlikely to be a trigger and should be reintroduced into the diet sequentially, every 4 – 7 days.

Prolonged elimination of foods, especially if extensive, can compromise growth and loss of natural tolerance. A dietitian referral should be considered if multiple foods are being eliminated to avoid consequences of poor growth and nutritional deficiencies especially in a young child.

GPP 9.5 ***We recommend against the use of patch tests to diagnose food allergy in AD patients. [EM9-2]***

The foods most often implicated in food allergy amongst patients with AD are eggs, milk and peanuts.[235] Types of food allergy reactions in AD include:

a. IgE-mediated (e.g. acute urticaria/angioedema and anaphylaxis that typically occurs within an hour of exposure)
b. Isolated eczematous delayed reaction (flare of eczema usually after hours, rarely up to 1-2 days)
c. Combination of both[228]

IgE-mediated reactions can be evaluated with the use of SPT or sIgE. However, the positive predictive value of skin prick tests or sIgE for food allergy is low (<60%) in AD patients and hence, a positive test without clinical reaction only indicates FS and may not represent true food allergy. SPT and sIgE are however useful to exclude food allergy as they have a high negative predictive value in AD (>95%).[228, 235, 236] SPT and sIgEs need to be performed appropriately and interpreted with caution to avoid unnecessary elimination of foods which are not true allergens, as this can result in poor growth, nutritional deficiencies and poor quality of life. The gold standard confirmatory test for food allergy is a double-blind placebo-controlled food challenge. However, a double blinded placebo-controlled food challenge is not practical for routine clinical practice and therefore, an open food challenge performed by trained personnel in a supervised setting would be a reasonable alternative.

The diagnosis of a delayed eczematous reaction is typically made if the patient fulfils both:

1. A clear improvement in eczema following a period of elimination (typically 2 – 4 weeks) of the food followed by,
2. A clear worsening in eczema following a period of reintroduction of the food (within 1-2 days).

This limited time trial should ideally be done following optimisation of skin control while on a stable skin care regime to avoid confounders. Such evaluation should only be carried out in patients with severe AD that is not controlled despite optimisation of skin care in view that majority of AD patients do not have a concomitant food allergy.

There is insufficient evidence for the use of patch tests in routine clinical practice to diagnose delayed type food allergies in AD, due to the lack of standardised food concentrations and formulations for accurate diagnosis. There is also no role for intradermal tests in the workup of food allergy due to lack of standardised non-irritating concentrations and the risk of adverse reactions. SPT and sIgE are not indicated in the evaluation of delayed type reaction.

CHAPTER 10: UNPROVEN AND DISPROVED DIAGNOSTIC TESTS AND TREATMENTS

In patients with a suspected food allergy, diagnostic tests and therapies that either have no biological plausibility and/or are unproven/disproved in clinical studies should not be carried out. They are misleading, result in inaccurate diagnosis and inappropriate treatment. Since these tests are still available commercially, patients may seek advice on these tests and therapies. Hence the clinician should be versed in the background of these tests, so that response can be informative and appropriate.

10.1 UNPROVEN DIAGNOSTIC TESTS

GPP 10.1 ***Unproven/disproved tests should not be used in the diagnosis of food allergy. The tests include:***

- ***ALCAT - Antigen leucocyte antibody test***
- ***Food specific IgG antibodies***
- ***Intradermal skin tests***
- ***Atopy patch test***
- ***Neutralisation provocation tests***
- ***Applied kinesiology***
- ***Bioresonance***
- ***Hair analysis [EM10-1]***

10.1.1 ALCAT – Antigen Leucocyte Antibody Test

The ALCAT tests claim to identify immune response to various food antigens by analysing white blood cell changes *in vitro* using microscopy. There are no peer-reviewed publications or any reasonable studies to support a diagnostic value for ALCAT.[237-240]

10.1.2 Food Specific IgG Antibodies

Antigen-specific IgG, and IgG4 values have no role in the diagnosis of IgE mediated and non-IgE mediated food allergy. The presence of these antibodies does not indicate disease. IgG4 is produced in response to tolerance and presence of these antibodies indicate frequency of ingestion and tolerance to foods.[241, 242] Clinical studies have refuted their utility in food intolerance.[242] These serological tests are also not recommended by international professional bodies.[243]

10.1.3 Intradermal Food Allergy Test

Although intradermal allergen testing may be indicated in venom and drug allergy when the skin prick test is negative, it should not be used for the diagnosis of food allergy as it has been proven to lack specificity.[244, 245] There is also the risk of anaphylaxis in a highly allergic patient.

10.1.4 Atopy Patch Test

The atopy patch test involves epicutaneous application of intact food allergens in a diagnostic patch test to evaluate food allergy especially for children with delayed symptoms such as atopic eczema and gastrointestinal symptoms. There are conflicting results in the literature regarding the use of atopy patch tests for diagnosis of food allergy as atopy patch tests often give rise to false positive and false negative results.[246]

Consensus recommendation for management of eosinophilic esophagitis does not recommend the use of food atopy patch testing to guide elimination of food as standardisation and validation of food extracts require further investigation.[247]

10.1.5 Hair Analysis

The premise of this test infers that nutritional deficiencies in hair are due to food allergy/intolerance. There are 2 studies to show that these tests are not reproducible and unable to pick up clinically confirmed allergy.[248, 249]

10.1.6 Applied Kinesiology

This test relies on the concept of applied kinesiology which claims that every organ dysfunction is accompanied by a specific muscle weakness, which enables diseases to be diagnosed through muscle-testing procedures. However, it does not conform to scientific knowledge on pathophysiology or treatment of diseases, and controlled studies have found no differences between the results with test substances (usually food) and placebos.[240, 250-252] A review of all published research on applied kinesiology from 1981 – 1987 concluded that they were not scientifically robust, lacked adequate statistical analyses and so no valid conclusions could be made.[253]

NAMBUDRIPAD'S ALLERGY ELIMINATION TECHNIQUES (NAET)

NAET is an alternative therapy that claims to permanently eliminate allergies and sensitivities through a combination of acupressure, kinesiology, and nutritional therapies. Developed in 1983 by Devi Nambudripad—a chiropractor and acupuncturist—it operates on the belief that allergies are caused by energy blockages or electromagnetic mismatches between a person's body and an allergen. Its proposed mechanism is not biologically plausible and there is no robust clinical evidence supporting its effectiveness for the diagnosis or treatment of food allergy.

10.1.7 Electrodermal Testing

Electrodermal testing was developed as an aid in prescribing homoeopathic remedies but has also been applied to assess an individual's allergic status to foods and aeroallergens. It is based on the observation that small changes in electrical impedance in the skin occur on an acupuncture point in response to substances placed in an electrical circuit.[254] A double-blind randomised study comparing electrodermal testing and skin prick tests concluded that this modality could not be used for the diagnosis of allergies.[255]

10.2 UNPROVEN TREATMENT MODALITIES

Unproven/disproved modalities should not be used in the treatment of food allergy. These modalities include:

- ***Neutralisation provocation tests***
- ***Bioresonance***
- ***Rotational diet [EM10-1]***

10.2.1 Neutralisation Provocation Test

This is a disproved technique that involves either sublingual or intradermal or subcutaneous "provocation" by a test food antigen followed by an observation period of 10-20 minutes after each administration, at which time the wheal response is measured, and any subjective symptoms recorded. Although not part of food allergic symptomatology, symptoms such as drowsiness or headache could also be considered as a positive challenge and therefore infer that the person is "allergic" to the food. The patient is then given a different dose of the antigen until the reaction is "neutralised".[238, 252, 256] Treatment of the food allergy involves regular intradermal or subcutaneous injections of the "neutralising dose" either before or after meals containing the offending food.[238, 252, 256] In double-blind studies of this technique, the frequency of positive responses to the injected extracts appears to be the result of suggestion and chance.[257, 258] As there is no plausible rationale or scientific evidence of effectiveness for this method, it should not be used in the diagnosis or treatment of food allergy. Furthermore, a case report showed that intradermal injections in a provocation-neutralisation protocol given to a patient with

systemic mastocytosis induced a life-threatening anaphylactic episode in this patient, making this procedure potentially dangerous.[259]

10.2.2 Bioresonance

Bioresonance is based on the belief that human beings as well as any substances in the environment, including allergens, emit electromagnetic waves which may be either "good" or "bad". These waves can only be measured by specific "bioresonance devices". The devices used are, however, simply resistance-measuring instruments that cannot measure the electromagnetic waves presumed to be involved. There are also no scientific links between electromagnetic waves and food allergy pathophysiology. The effectiveness or accuracy of these devices has never been shown. Controlled studies also failed to show any diagnostic or therapeutic value in adults with allergic rhinitis or in children with eczema.[260, 261]

10.2.3 Rotational Diet

Rotary diets, or the 4-day rotation diet, are unproven diet therapies most commonly recommended for individuals with positive specific IgG or food immune complex assays, and also in several other situations.[262] It was introduced in the 1930's with the premise that it would help patients avoid cumulative food reactions. There, however, are no published clinical trials evaluating the effectiveness of rotary diets for food allergies.

CONCLUSION

All these modalities have also been listed as unconventional, disproved/unproven tests and treatments by the World Allergy Organisation (WAO),[263] European Academy of Allergy and Clinical Immunology (EAACI),[264] and National Academies of the United States of America.[265]

CHAPTER 11: INDICATIONS FOR REFERRAL TO ALLERGY SPECIALISTS

Primary care physicians play a central role in the recognition and initial management of allergic diseases. However, referral to an allergy specialist is warranted when there is diagnostic uncertainty, severe or recurrent disease, failure of standard therapy, or the need for specialised investigations and advanced management. Early referral may improve diagnostic accuracy, facilitate appropriate risk stratification, and reduce morbidity associated with allergic disorders.

Indications for referral in suspected food allergy include:

- All patients with suspected food allergies, including IgE and non-IgE mediated types, and all forms from mild to severe presentations.
- Infants and children with moderate-to-severe atopic dermatitis associated with suspected food triggers
    - Young infant (below 2 years of age) with severe and refractory AD despite optimisation of, and adherence to, conventional therapy and where there are concerns of food reactions.
    - Young infants with severe AD, whose timely introduction of solids and allergenic foods may be delayed due to parental concerns
- Patients in whom dietary elimination is being considered due to suspected food allergies or intolerance.
- Requirement for supervised oral food challenges.
- Need for assessment and interpretation of allergy investigations, including skin prick testing or specific serum IgE testing.
- Consideration for food immunotherapy.

Tertiary Allergy Referral Centres in Public Healthcare Institutions:

Paediatric:

Division of Allergy, Immunology & Rheumatology, Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital

Allergy Service, Department of Paediatrics, KK Women's and Children's Hospital

Adult:

Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital

Division of Rheumatology and Allergy, National University Hospital

Immunology Hub, Singapore General Hospital

Allergy, General Medicine, Sengkang General Hospital

Rheumatology and Allergy Service, Division of Medicine, Woodlands Hospital

APPENDIX 1: GUIDELINE DEVELOPMENT GROUP AND EXTERNAL REVIEWERS

MAIN WORKGROUP MEMBERS

No.	Name	Subgroup Contribution
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2	**Adj Asst Prof Chong Kok Wee** **(CPG Co-Lead)** Head & Senior Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	1. Management of Food Allergy 2. Non-IgE Mediated Food Allergies 3. Management of Food Allergies in Schools, Pre-schools and Childcare Facilities 4. Nutritional Counselling and Evaluation
3	**Dr Peng Kaitian** Associate Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	Introduction to Food Allergy
4	**Dr Hong Wei Jie, Nicholas** Associate Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	Introduction to Food Allergy
5	**Dr Carmen Riggioni** Clinical Associate Division of Paediatric Allergy, Immunology & Rheumatology Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital	Diagnosis of Food Allergy
6	**Dr Loh Wenyin** Senior Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	1. Non-IgE Mediated Food Allergies 2. Management of Food Allergies in Schools, Pre-schools and Childcare Facilities
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8	**Dr Lynette Tan Liling** Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	Management of Food Allergy
9	**Dr Goh Si Hui** Senior Consultant Allergy Service Department of Paediatrics	Management of Food Allergy

	KK Women's and Children Hospital	
10	**Dr Samuel Lee Shang Ming** Consultant Department of Rheumatology, Allergy and Immunology Tan Tock Seng Hospital	Management of Acute Food-induced Allergic Reactions
11	**Adj A/Prof Bernard Thong Yu Hor** Chairman Medical Board & Senior Consultant Department of Rheumatology, Allergy and Immunology Tan Tock Seng Hospital	Management of Acute Food-induced Allergic Reactions
12	**Ms Chong Yan Fong** Senior Dietitian Department of Nutrition and Dietetics KK Women's and Children Hospital	Nutritional Counselling and Evaluation
13	**Dr Lydia Wong Su Yin** Consultant Division of Paediatric Allergy, Immunology & Rheumatology Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital	Natural History of Food Allergy
14	**Ms Nur Farah Addina Lee Binte Zailan** PhD Student Yong Loo Lin School of Medicine, Department of Paediatrics National University of Singapore	1. Natural History of Food Allergy 2. Atopic Dermatitis in Food Allergy
15	**Dr Soh Jian Yi** Senior Consultant Division of Paediatric Allergy, Immunology & Rheumatology Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital	Oral Immunotherapy in Food Allergy
16	**Dr Pauline Chan Ng Poh Lin** Consultant Division of Paediatric Allergy, Immunology & Rheumatology Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital	Atopic Dermatitis in Food Allergy
17	**Professor Lee Bee Wah** Adjunct Professor Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore	Unproven and Disproved Tests and Treatments
18	**Dr Chiang Wen Chin** Visiting Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	Unproven and Disproved Tests and Treatments
19	**Dr Liew Woei Kang** Visiting Consultant Rheumatology and Immunology Service Department of Paediatric Subspecialties KK Women's and Children Hospital	Unproven and Disproved Tests and Treatments
20	**Clin Prof Anne Goh Eng Neo** Senior Consultant Allergy Service Department of Paediatrics KK Women's and Children Hospital	Unproven and Disproved Tests and Treatments
21	**Prof Hugo Van Bever** Senior Consultant Division of Paediatric Allergy, Immunology & Rheumatology	Unproven and Disproved Tests and Treatments

	Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI), National University Hospital	
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This guideline has also received formal endorsement from the College of Family Physicians Singapore (CFPS) and the Chapter of Family Medicine Physicians (CFPS), Academy of Medicine, Singapore.

APPENDIX 2: ALLERGY ACTION PLAN

ALLERGY ACTION PLAN

PAEDIATRIC

Medications specified on this plan should be administered according to the plan.

This document should be completed by the child's treating healthcare professional. It must not be altered without their permission.

Name: _____ **DOB:** ___/___/___

PHOTO

Allergies: _____

Emergency contact details:

Plan prepared by:

I hereby authorise school staff to administer the medications listed on this plan.

Signed: _____

Parent name: _____

MILD ALLERGIC REACTIONS

- Itching and swelling of lips, face and/or eyes
- Hives or wheals (itchy skin rash)
- Tingling mouth
- Abdominal pain/vomiting/diarrhoea
- Sudden change in behaviour

ACTION

- Stay with the child and call for help
- Take antihistamines: _____ (if vomited, may repeat dose)
- Locate EpiPen (adrenaline auto-injector)
- Contact family/caregiver through emergency contact
- Any other medications: _____

ANAPHYLAXIS (SEVERE/LIFE THREATENING ALLERGIC REACTIONS)

- AIRWAY: Persistent cough, hoarse voice, difficulty swallowing, swollen tongue, throat tightness
- BREATHING: Difficult or noisy breathing, wheeze
- CONSCIOUSNESS: Persistent dizziness, looking pale or floppy, suddenly sleepy, collapse, loss of consciousness
- OTHERS: Severe abdominal pain/persistent vomiting

Only a few symptoms may be present and severity may change quickly.

Anaphylaxis can occur without milder symptoms such as skin symptoms or swelling.

ACTION

- If ANY of the above are present, give EpiPen (adrenaline auto-injector) without delay
- If in doubt, give EpiPen
- Lay flat, elevate legs. If breathing is difficult, child may be allowed to sit but not stand

- Give EpiPen/EpiPen Junior without delay
- Call 995 and say ANAPHYLAXIS ('ANA-FIL-AX-IS')

After giving EpiPen:

- Stay with the child and ensure that they DO NOT stand up
- Contact family/caregiver through emergency contact
- Commence CPR if child is unresponsive and not breathing
- If there is no response after 5 min, give a second EpiPen if available
- Medical observation in hospital is recommended after anaphylaxis

HOW TO GIVE EPIPEN

1. Form fist around EpiPen and pull off BLUE safety cap.

2. Hold thigh firmly and keep the leg still to avoid injuries. Place the ORANGE tip against mid outer thigh (with or without clothing).

3. Push down hard until a 'click' is heard or felt. Hold EpiPen firmly in place for 3 seconds. Remove EpiPen.

Massage injection area for 10 seconds.

ALLERGY ACTION PLAN

ADULT

ASTHMA & ALLERGY ASSOCIATION

Medications specified on this plan should be administered according to the plan.

This document should be completed by the patient's treating healthcare professional. It must not be altered without their permission.

Name: _____ **DOB:** ____/____/____

Allergies: _____

_____

_____

Emergency contact details:

_____

_____

_____

Plan prepared by:

MILD ALLERGIC REACTIONS

- Itching and swelling of lips, face and/or eyes
- Hives or wheals (itchy skin rash)
- Tingling mouth
- Abdominal pain/vomiting/diarrhoea

ACTION

- Stay with the patient and call for help
- Take antihistamines: _____ (if vomited, may repeat dose)
- Locate EpiPen (adrenaline auto-injector)
- Contact family/caregiver through emergency contact
- Any other medications: _____

ANAPHYLAXIS (SEVERE/LIFE THREATENING ALLERGIC REACTIONS)

- AIRWAY: Persistent cough, hoarse voice, difficulty swallowing, swollen tongue, throat tightness
  BREATHING: Difficult or noisy breathing, wheeze
- CONSCIOUSNESS: Persistent dizziness, suddenly sleepy, collapse, loss of consciousness
- OTHERS: Severe abdominal pain/persistent vomiting

Only a few symptoms may be present and severity may change quickly.

Anaphylaxis can occur without milder symptoms such as skin symptoms or swelling.

ACTION

- If ANY of the above are present, give EpiPen (adrenaline auto-injector) without delay
- If in doubt, give EpiPen
- Lay flat, elevate legs. If breathing is difficult, patient may be allowed to sit but not stand

- Give EpiPen without delay
- Call 995 and say ANAPHYLAXIS ('ANA-FIL-AX-IS')

After giving EpiPen:

- Stay with the patient and ensure that they DO NOT stand up
- Contact family/caregiver through emergency contact
- Commence CPR if patient is unresponsive and not breathing
- If there is no response after 5 min, give a second EpiPen if available
- Medical observation in hospital is recommended after anaphylaxis

HOW TO GIVE EPIPEN

Form fist around EpiPen and pull off BLUE safety cap.

Hold thigh firmly and keep the leg still to avoid injuries. Place the ORANGE tip against mid outer thigh (with or without clothing).

Push down hard until a 'click' is heard or felt. Hold EpiPen firmly in place for 3 seconds. Remove EpiPen.

Massage injection area for 10 seconds.

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