

Practice Parameter: Algorithmic Management of Food Allergy



Indian Academy of Pediatrics – Allergy and Applied Immunology Chapter

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Introduction

Food allergy is becoming a major health issue with increasing incidence and complexities. The most common food allergens include milk, egg, peanut, tree nuts, shell fish, fish, wheat, sesame & soy.

Food Allergy can be classified as:

- **Immune Mediated well known as ‘Food Allergy’ or ‘Food hypersensitivity’**
i.e. IgE Mediated; so, a “Classical Food Allergy” or Non-IgE Mediated which primarily affect the gut and cause subacute or chronic symptoms.
- **Non-Immune Mediated well known as ‘Food Intolerance’** e.g. Lactose Intolerance

A ‘true’ food allergy is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food while ‘food mimics’ or ‘adverse reactions to food’ are classified as:

1. Psychological
2. Organic
3. Toxic (Microbiological pharmacological)
4. Non-toxic (also termed as food intolerance or nonallergic food hypersensitivity).

1. **Psychological or Behavioural reactions** to food include food refusal, food fixation, abnormal parental feeding practises, onset after a specific trigger and presence of anticipatory gagging.

Example: A one-year-old child with poor growth and no obvious signs of true food allergy but history of recurrent vomiting especially after food or milk, we should rule out the above psychological reasons for this patient.

2. Organic or Anatomical problems:

- Pyloric Stenosis
- Hiatus Hernia
- Hirschsprung's Disease
- Tracheoesophageal fistula
- Irritable bowel syndrome
- Gastrointestinal ulcers
- Gastrointestinal cancers

Example: Frey's syndrome or auriculotemporal gustatory sweating has been reported to occur with orange juice, tomato, onion and certain non-chocolate candies and snack foods.

3. Toxic reactions from food may be inflicted by any ingredient in the particular food item.

Example: Bacterial toxins spoil food that may result in nausea and vomiting. Other examples are stated in given **Table 1**.

Table 1: Toxic reactions from food

Sr. No.	Toxin	Food item/ Effect
1	Salmonella, staphylococcus	Food spoilage
2	Cyanogenic glycosides	Kernel of almonds, apricots, cassava
3	Fungal aflatoxins	Peanut, apple juice
4	Trichothecenes	Wheat
5	Atropine	Mushroom
6	Ochratoxin	Various grains
7	Glucosinolates	Brassicaceous vegetables, e.g. cabbage
8	Pyrrolizidine alkaloids	Comfrey
9	Haemagglutinins	Beans
10	Solanine	Potatoes (raw) and related plants
11	Seafood toxins	Spoilt fish, especially scombroid fish
12	Tetrodotoxin	Puffer fish
13	Saxitoxins	Clams, oysters
14	Neurotoxin (lathyrism)	Chickling Vetch / grass pea
15	Nitrates	Green vegetables, e.g. spinach

4. Food intolerance: The well-known example is Lactose Intolerance. So, this category is all about enzyme deficiencies; Presenting as symptoms of intolerance on the ingestion of respective food.

Table 2 lists the same. Food intolerances are often categorised under 'Non-immune Mediated Food Allergy'.

Table 2: Enzyme deficiencies

Sr. No.	Deficiency/ Intolerance	Food item
1	Lactase deficiency	Lactose (milk)
2	Fructose intolerance	Fructose, especially fruit juices
3	Sucrose intolerance	Sucrose and starch
4	Alcohol intolerance	Alcohol
5	Sulphite intolerance	Sulphite preservatives
6	G6PD deficiency	Fava (broad) beans
7	Pancreatic insufficiency	Fatty food
8	Galactosaemia	Lactose and galactose (milk&legumes)
9	Phenylketonuria	Phenylalanine (high protein foods) and aspartame sweetener

The ‘true’ Food allergy is divided as per the mechanism of symptoms through disability and repeatability as IgE mediated and non-IgE mediated. A third category can be seen as mixed IgE and non-IgE mediated food allergy. (**Table 3**)

Table 3: Examples of non-IgE and mixed IgE and non-IgE mediated food allergies

Non-IgE mediated food allergy	Mixed IgE and non-IgE mediated food allergy
i. Contact dermatitis ii. Food protein-induced enterocolitis syndrome (FPIES) iii. Food protein-induced allergic proctitis and proctocolitis iv. Food protein-induced enteropathy v. Dermatitis herpetiformis vi. Heiner syndrome vii. Coeliac disease (may also be considered an auto-immune condition)	1. Exacerbation of atopic eczema 2. Eosinophilic oesophagitis 3. Eosinophilic gastritis/enteritis 4. Exacerbation of asthma

The European Academy of Allergy and Clinical Immunology (EAACI) food allergy guidelines focus solely on **IgE mediated food allergy**, as defined by:

1. Typical symptoms (**Table 4**)
2. Evidence of IgE sensitization.

Table 4: Examples of symptoms of IgE-mediated food allergy

Organ or System	Symptoms and signs
I. Skin	1. Urticaria 2. Angio-oedema 3. Pruritus 4. Flushing 5. Erythema in the predilection sites of eczema 6. Ear or palm itching
II. Gastro-intestinal	1. Oral/pharyngeal pruritus 2. Oral/pharyngeal swelling 3. Vomiting 4. Nausea 5. Abdominal cramps 6. Diarrhoea 7. Abdominal pain
III. Ocular	1. Conjunctival erythema 2. Pruritus 3. Lacrimation
IV. Cardiovascular	1. Pallor 2. Cold sweats 3. Heart palpitations 4. Pre-syncope / Syncope 5. Tachycardia 6. Hypotension 7. Shock
V. Respiratory	1) Rhinitis (rhinorrhoea, sneezing, nasal obstruction, pruritus) 2) Hoarseness 3) Stridor/laryngeal oedema 4) Cough 5) Dyspnoea 6) Chest tightness 7) Wheezing 8) Cyanosis
VI. Neurological	1. Anxiety 2. 'Feeling of impending doom' 3. Change in behaviour 4. Irritability 5. Apathy 6. Lethargy 7. Seizures 8. Syncope/Loss of consciousness
VII. Other	1. Uterine contractions resulting in abdominal pain and bleeding 2. Shivering

How to identify a IgE-mediated food allergy and why is it important?

IgE mediated food allergy can lead to severe, life-threatening reactions like anaphylaxis, and requires strict allergen avoidance. A detailed clinical history is the most crucial step in diagnosis, guiding further evaluation and testing. Let us now see how to approach the diagnosis of food allergy.

Diagnostic Tools in Food Allergy

1. Clinical History
2. Physical Examination
3. Allergy Testing:
 - Skin Prick Testing (SPT)
 - Blood Specific IgE Testing
 - Component-Resolved Diagnostics (CRD)
 - Oral Food Challenge (OFC) – *Gold Standard*

Importance of a Food Allergy Diary

Helps establish:

- Temporal relationship
- Reproducibility of symptoms
- Differentiation between IgE-mediated, non-IgE, and intolerance
- Avoids unnecessary food restrictions
- Aids in safe dietary practices

What to Record in a Food Diary?

- Name and quantity of suspected food
- Time of symptom onset after ingestion
- Detailed symptoms observed (by patient and witnesses)
- Reproducibility – did symptoms recur on repeated exposure?
- Symptom relief on food avoidance
- Location of the reaction (home, school, restaurant, etc.)
- Co-factors: exercise, stress, sleep deprivation, alcohol
- Treatment given and response

Skin Prick Testing (SPT) & Serum Specific IgE Testing

These are primary diagnostic tools used to evaluate sensitization to suspected food allergens. However, they must be interpreted in the context of clinical history to assess the likelihood of true food allergy.

When to Use These Tests

- For suspected IgE-mediated food allergies
- For identifying cross-reactive allergens
- Avoid in non-IgE mediated conditions like:
 - FPIES (Food Protein-Induced Enterocolitis Syndrome)
 - EoE (Eosinophilic Esophagitis)

Over-testing can lead to overdiagnosis and unnecessary food restrictions.

Skin Prick Test (SPT)

- A bioassay that detects allergen-specific IgE on cutaneous mast cells.
 - Not a measure of reaction severity — a person can react even with a negative test.
 - An increasing wheal size indicates a higher risk, not necessarily a severe reaction.
 - High Sensitivity, Low Specificity as seen in Table 5.
 - Best used with strong clinical history to increase diagnostic accuracy.
 - SPT is to be avoided in chronic urticaria and atopic dermatitis as this may give false positive results.
- In such cases, specific IgE testing is preferred (see Below).

Table 5: Diagnostic Accuracy

Feature	SPT & Specific IgE
Sensitivity	High
Specificity	Low
Positive Predictive Value (PPV)	Low–Moderate (↑ with high levels)
Negative Predictive Value (NPV)	High (with proper technique)

Serum Specific IgE

- Blood test measuring circulating allergen-specific IgE antibodies.
- Types of methods in Specific IgE testing include:
 1. FEIA (Fluorescence Enzyme Immunoassay): Preferred method
 2. Chemiluminescence Enzyme Immunoassay
 3. Radio-Allergosorbent Assay Technique (RAST): Not to be used due to radiation exposure.
- Can be used when SPT is contraindicated, such as:
 - Recent anaphylaxis
 - Current antihistamine use
 - Extensive eczema
 - Uncontrolled asthma
 - Cardiovascular disease
 - Pregnancy
 - Poor skin condition

SPT and Specific IgE have low to moderate PPV which can be improved with a very high wheal size/ specific IgE level as seen in Table 6. These values are however, not absolute and vary with age. A strong history is needed before advising the patient on allergen avoidance or allowing them to consume the suspected allergen.

Table 7 shows the comparison between SPT or specific IgE test. It is important to understand the final decision on the choice of the test depends on a good clinical history by the allergist/ clinician.

Table 6: Predictive Cut-off Examples (Not Absolute!)

Food	SPT Wheal $\geq$ (mm)	Specific IgE Level $\geq$ (kUA/L)	Approx. PPV (~95%)
Egg	8	7	Yes
Peanut	8	14	Yes
Milk	8	15	Yes
Wheat	8	26	Yes
Soy	8	30	Yes

Table 7: Comparison of Skin Prick Test (SPT) vs. Serum Specific IgE

Parameter	Skin Prick Test (SPT)	Serum Specific IgE
Age Consideration	May be less reactive in infants	Easier to perform in very young children
Influencing Factors	Affected by antihistamines, skin condition	Affected by age, total IgE, lab standards
NPV (Negative Predictive Value)	>95% (Very high)	>90%
PPV (Positive Predictive Value)	~50% (depends on cut-off & population)	~50% (improves with higher levels)
Sensitivity	>90% (High)	~70–90%
Specificity	~50–60% (Moderate)	~50–60%
Speed of Results	Immediate (15–20 mins)	Delayed (lab-dependent; 1–2 days)
Utility	Best for ruling out allergy (high NPV)	Useful adjunct; consider component testing (CRD)

Prick-to-Prick Testing

- Used for labile allergens (e.g., fruits/vegetables) where commercial extracts are unavailable.
- Less standardized but increases test relevance in certain foods (e.g., banana, apple, kiwi).

When to Escalate?

- If clinical history is strong but SPT/specific IgE is negative or inconclusive, consider:
 - Component-Resolved Diagnostics (CRD)
 - Oral Food Challenge (OFC) — *Gold Standard*

Component Resolved Diagnostics (CRD)

CRD is an advanced blood test that detects IgE antibodies to specific individual allergenic proteins (components) rather than the whole food.

It provides greater precision than traditional specific IgE tests, which may react to non-allergenic parts of foods and lead to overdiagnosis.

Why Use CRD?

- Differentiates between true allergy and cross-reactivity
- Predicts the severity and persistence of food allergies
- Helps guide:
 - Oral Food Challenge (OFC)
 - Oral Immunotherapy (OIT)
 - Safe food choices

A set of case scenarios will help in better correlation of these diagnostic tools in allergy.

Scenario 1: Egg Allergy & Baked Egg Tolerance:

A 3-year-old child develops hives within 5 minutes of consuming scrambled eggs, but tolerates baked goods (e.g., muffins). There are no other systemic symptoms (like breathlessness, choking sensation, vomiting, diarrhoea, dizziness or loss of consciousness). These hives have occurred in the past and respond to anti-histamines within 10 minutes.

When they visit the allergy specialist, it is deduced that there is a good temporal correlation and reproducibility of these symptoms. Also, these symptoms have not amounted to a severe allergic reaction or anaphylaxis. SPT to egg white is positive and the allergist counsels about the emergency action plan.

However, what is unclear here is the absence of symptoms on consuming baked egg. This is where we apply CRD test (as seen in **Figure 1**). A single plex CRD report has revealed the following:

CRD Components:

Component	Protein Type	Clinical Significance
Gal d 1 (Ovomucoid)	Heat-stable	Persistent, higher-risk allergy
Gal d 2 (Ovalbumin)	Heat-labile	Often tolerates baked egg

CRD Result:

- **High IgE to Gal d 2**
- **Low/Negative IgE to Gal d 1**

On follow up, the allergist counsels the parents that the patient is likely to tolerate baked egg in the form of muffins or cakes after a **negative OFC**. They are also informed that they should

continue to give baked egg which will accelerate the tolerance development to the scrambled egg preparation (which is less cooked and has more egg protein exposure) in the future.

However, a large amount of baked egg may also lead to a severe reaction like the scrambled egg preparation wherein they should follow the emergency action plan.

Scenario 2: Pollen-Food Syndrome vs True Nut Allergy

A 10-year-old, with birch pollen allergy (presenting as allergic rhinitis) complains of mouth itching 5-10 minutes after eating apples & hazelnuts. The family is concerned and visit the allergist. After a thorough history taking and positive SPT to hazelnut and apple, the allergist informs them that these symptoms could be an oral allergy syndrome or less likely due to a true food allergy.

As shown in **Figure 1**, to confirm this diagnosis, a CRD panel is sent. The report is as follows:

CRD Components:

Hazelnut Component	Associated With	Risk
Cor a 1 (PR-10)	Birch pollen cross-reactivity	Mild symptoms
Cor a 9 / Cor a 14	True hazelnut allergy	Severe reactions/anaphylaxis
Mal d 1 (PR-10)	Birch pollen cross-reactivity	Mild symptoms
Bet v 1 (PR-10)	Birch pollen	Allergic rhino-conjunctivitis

CRD Result:

- Positive to Cor a 1, Mal d 1 & Bet v 1
- Negative to Cor a 9 and Cor a 14

The allergist informs them that it is a Pollen-Food Allergy Syndrome (PFAS) due to the cross reactivity between hazelnut and birch pollen and apples and birch pollen. It is likely safe to eat hazelnuts and cooked apples as these will cause mild oral symptoms and not a systemic allergy.

Clinical Benefits of CRD

- Differentiates **genuine allergy vs cross-reactivity**
- Guides **OFC & dietary decisions**
- Helps **stratify anaphylaxis risk**
- Supports **personalized treatment plans**
- Monitors **tolerance development** or **disease persistence**
- Especially helpful in **complex or polysensitized patients**

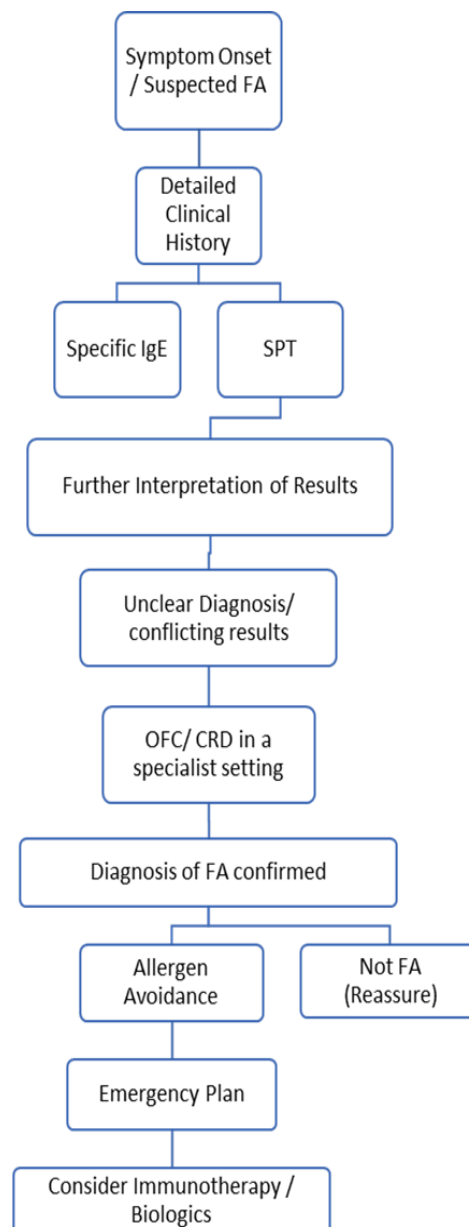


Figure 1: Diagnostic Tools in Food Allergy

Oral Food Challenge (OFC)

What is OFC?

- Gold standard for diagnosing IgE and Non-IgE mediated food allergies
- Used when history and test results are inconclusive
- Always done in a controlled clinical setting with emergency precautions

Clinical Applications

1. Confirm or exclude a food allergy diagnosis
2. Monitor for resolution of an existing FA
3. Identify threshold dose that causes symptoms
4. Aid in planning treatment or dietary expansion

Table 8: Types of Food Challenges

Type	Description	Bias Level
Open Challenge	- Simple & quick - Patient and doctor both know the food	High
Single-Blind Placebo-Controlled (SBPCFC)	- Observer knows, patient doesn't	Moderate
Double-Blind Placebo-Controlled (DBPCFC)	- Gold standard - Neither patient nor observer know the food	None

Note: DBPCFC is mainly used in research settings due to complexity.

Inclusion Criteria

- Inconclusive test results with suggestive history
- Need to confirm or exclude diagnosis
- Participation in scientific trials
- Assessing tolerance development

Exclusion Criteria

- Repeated confirmed anaphylaxis
- Very high SPT/specific IgE values ($\geq 95\%$ PPV)
- Clear diagnosis already established

Pre-Challenge Considerations

- Nutritional importance of the food
- Patient and caregiver preferences & anxiety
- Previous reaction severity
- Parental understanding of procedure & risks

Advantages

- Reduces fear & dietary restrictions if negative
- Identifies safe exposure threshold
- May support tolerance induction
- Improves quality of life

Disadvantages

- Risk of severe allergic reaction

- Time-consuming
- Requires trained staff & emergency setup

Table 9 summarizes all the diagnostic modalities and their applications. This is a quick reference chart for clinicians when they come across allergy patients. It is wise to counsel patients with complex allergies about the emergency action plan (see below) and basic management (shown in table 7) before referring them to the allergy specialist.

Table 9: Allergy investigations at a glance

Investigation	Purpose	When to use	Notes
Specific IgE	To detect IgE antibodies in blood	Suspected IgE-mediated FA	Easy to access but can overestimate FA
SPT	To detect immediate hypersensitivity	Done by trained personnel	Needs 5–7-day antihistamine washout
CRD	Detect reaction to specific allergen components	When specific IgE/SPT unclear / multiple allergens	Use for peanut, milk, egg, etc.
OFC	Confirm diagnosis	When diagnosis uncertain or before reintroduction	Gold standard; hospital setup essential

Management of Food Allergy

1. Allergen Avoidance

- Cornerstone of FA management
- Requires strict avoidance of identified allergens
- Read food labels and avoid cross-contamination
- Patients and caregivers must be vigilant in home, school, travel, and dining settings

2. Medications

For Mild to Moderate Reactions:

- Oral antihistamines (e.g., cetirizine, loratadine)
 - Help manage symptoms like rash, itching, mild swelling
 - Not effective for preventing anaphylaxis

For Severe Reactions (Anaphylaxis):

- Intramuscular (IM) Adrenaline is the gold standard
 - Must be given into the anterolateral thigh

- Should be administered immediately at the first signs of anaphylaxis

3. Emergency Preparedness

- **Education** is critical:
 - Recognize early signs of anaphylaxis (e.g., difficulty breathing, throat tightness, drop in BP)
 - Train in administration of IM adrenaline
- Provide a personalized **Emergency Action Plan (EAP)** to:
 - Patients and parents
 - Schools, daycares, and caregivers

4. Adrenaline Delivery in India

- Epinephrine auto-injectors are not yet authorized for routine use in India and thus indigenous syringe adrenaline is prescribed to the patients
- Current recommendation:
 - Use syringe + adrenaline ampoule
 - Pre-filled, labelled kits with instructions
 - Caregivers must be trained to draw and administer in emergencies

Table 10& 11 show the treatment modalities & practical tips in the Indian scenario for FA management.

Table 10: Treatment options for Food Allergy

Strategy	When to use	Notes
Avoidance	All confirmed cases	Label reading, school info essential
Emergency Plan	All IgE-mediated cases	Include written plan, demonstration
Immunotherapy (OIT)	Select food allergens (peanut, milk)	Only under specialist care
Biologics (Omalizumab)	Severe/multiple allergies	Specialist setting

Table 11: Practical Food Allergy Management Tips in the Indian Scenario

Tip	Details
Allergen education	Provide visual aids, ingredient names in local languages
Label reading	Teach patients to identify allergen synonyms
Emergency kit	Include adrenaline ampoule, syringe, antihistamines, instructions
School coordination	Written action plan, trained staff, allergen-free meal policy
Family awareness	Educate extended family and domestic help
Periodic review	Reassess diagnosis, update management plans annually

Advances in Diagnosis, Management and Prevention of Food Allergy

1. Diagnostic Innovations

Basophil Activation Test (BAT)

- A functional assay using flow cytometry
- Measures activation markers (e.g., CD63, CD203c) on basophils after exposure to allergens
- Useful in ambiguous cases where specific IgE or SPT results are inconclusive

2. Emerging Therapies

a) Oral Food Immunotherapy (OIT)

- Gradual introduction of increasing doses of the allergenic food under medical supervision
- Aims to induce desensitization and potentially long-term tolerance
- Requires careful patient selection and well-equipped allergy centres

b) Biologics (e.g., Omalizumab)

- Anti-IgE monoclonal antibody
- Can be used alone or as an adjunct to OIT
- Beneficial in patients with severe multi-food allergies

3. New Anaphylaxis Rescue Options

Nasal Adrenaline Spray

- Recently approved by the US-FDA for anaphylaxis
- Non-invasive, needle-free delivery

4. Prevention Strategies

a. Early Allergen Introduction

- Landmark studies (e.g., LEAP, EAT) show that early introduction of common allergens (e.g., peanut, egg) around 4–6 months of age reduces FA incidence
- Applies particularly to high-risk infants (e.g., with eczema or family history)

b. Indian Dietary Practices

- The diverse and traditional Indian diet, with early exposure to a variety of spices and lentils, may contribute to a lower prevalence of FA in India
- Continued breastfeeding and home-cooked meals may also be protective

Food Allergy: Quick Summary

1. **Diagnosis requires a detailed history**, supported by tests like SPT, specific IgE, CRD, and OFC.
2. **CRD helps differentiate between true allergy and cross-reactivity**, especially useful in cases like egg allergy and pollen-food syndrome.
3. **OFC remains the gold standard** for diagnosing and monitoring FA but must be done in controlled settings due to the risk of severe reactions.
4. **Management includes strict allergen avoidance, antihistamines for mild reactions, and intramuscular adrenaline for anaphylaxis.**
5. **Newer approaches** include Basophil Activation Test (BAT), Oral Immunotherapy (OIT), and biologics.
6. **Prevention through early allergen introduction (4–6 months of age)** has been shown to reduce FA incidence, with Indian diets possibly playing a protective role.

Suggested Reading

- American Academy of Allergy, Asthma & Immunology (AAAAI) guidelines
- Australasian of Clinical Immunology & Allergy (ASCIA) guidelines
- British Society for Allergy & Clinical Immunology (BSACI) guidelines
- European Academy of Allergy & Clinical Immunology (EAACI) guidelines
- Allergy for the clinician. PK Vedanthan, Harold Nelson, Shripad Agashe, PA Mahesh, Rohit Katial