Diagnostic evaluation of food allergy

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Some combination of the following diagnostic tools, although not all of these elements are necessary in every patient:

- History and physical examination
- Prick/puncture skin testing
- In vitro testing
- Gastroenterologic tests
- Elimination diets
- Food challenges

Role of the history in evaluation

The clinical history is an essential component of the evaluation of a patient with possible food allergy.

- Distinguish food allergy from a host of other adverse food reactions
- Distinguish among different types of food allergy
- Identify a possible culprit food

The way in which the pretest probability impacts the interpretation of allergy tests

- ***Patient 1*** *has experienced two severe allergic reactions following the isolated ingestion of scrambled egg, requiring and responding to treatment with epinephrine on both occasions.*

- ***Patient 2*** *has severe atopic dermatitis and eats egg regularly. He has never experienced an apparent acute reaction to egg. However, his mother is aware that food allergy can exacerbate this condition and has therefore requested an allergy evaluation.*

- ***Patient 3*** *has no history of allergic problems, but her parents think she misbehaves more after eating egg.*

Patient 1 has a very high pretest probability of egg allergy, so a *moderately positive test* *is sufficient to validate* the clinical suspicion.

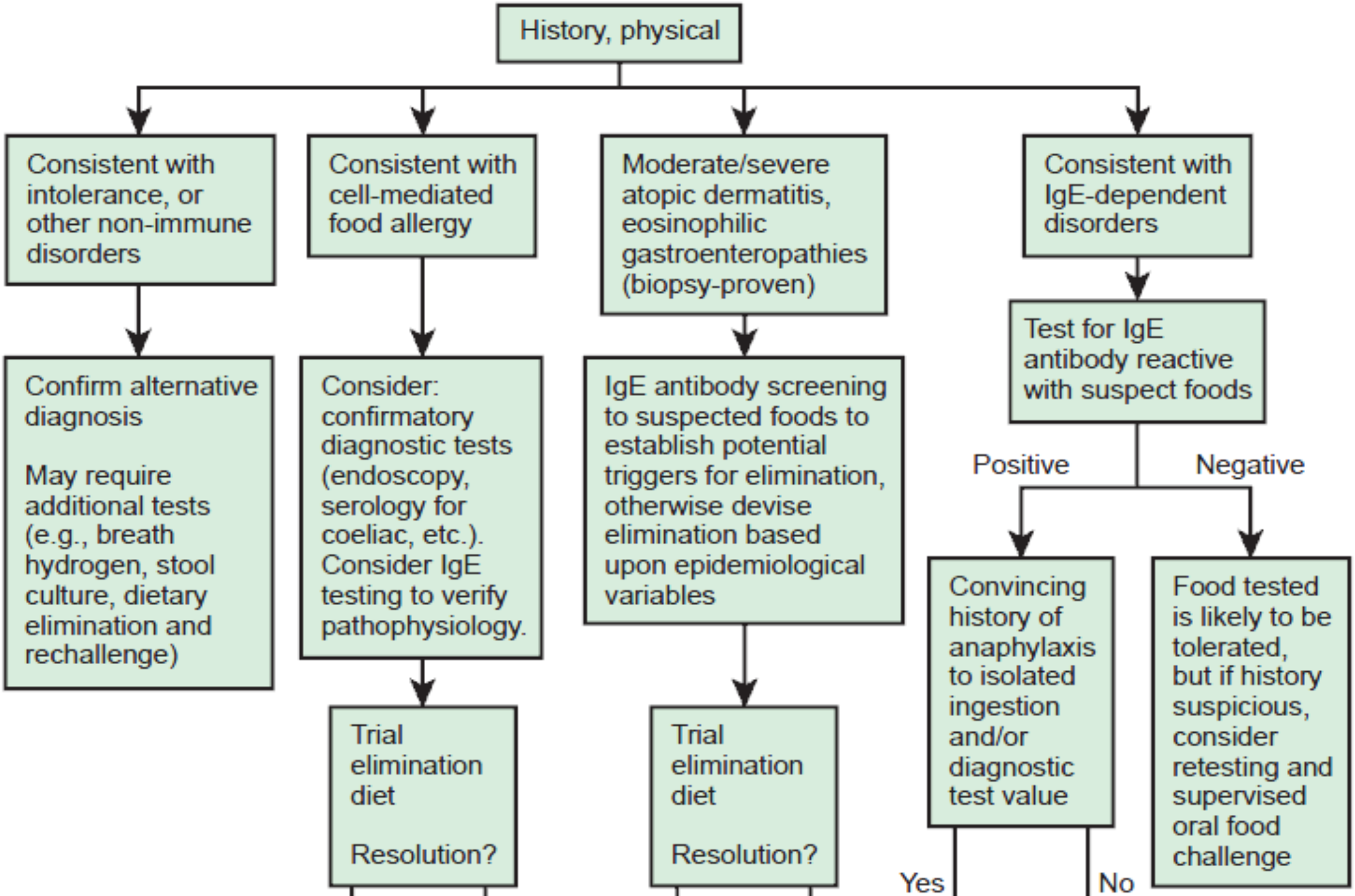
If the in vitro test had been ***negative***, the pediatrician would be correct to ***question the result*** and refer the child to an allergy specialist for further evaluation.

Patient 2 has a *moderate pretest probability* since up to 40 percent of children with moderate to severe atopic dermatitis have underlying food allergy, and egg is a common cause of childhood food allergy.

In this patient, the positive result is suggestive of true allergy, although ***further evaluation*** is needed to demonstrate that egg allergy is contributing to skin inflammation.

Patient 3 has an extremely low pretest probability, and the test result is not sufficiently positive to impact the clinician's initial impression.

This case also illustrates one of the ***disadvantages of performing testing*** in patients whose histories are not consistent with allergic disease, as irrelevant results may confuse the situation.


History, physical
Consistent with intolerance, or other non-immune disorders
Consistent with cell-mediated food allergy
Moderate/severe atopic dermatitis, eosinophilic gastroenteropathies (biopsy-proven)
Consistent with IgE-dependent disorders
Confirm alternative diagnosis
May require additional tests (e.g., breath hydrogen, stool culture, dietary elimination and rechallenge)
Consider: confirmatory diagnostic tests (endoscopy, serology for coeliac, etc.). Consider IgE testing to verify pathophysiology.
IgE antibody screening to suspected foods to establish potential triggers for elimination, otherwise devise elimination based upon epidemiological variables
Test for IgE antibody reactive with suspect foods
Positive
Negative
Trial elimination diet
Resolution?
Trial elimination diet
Resolution?
Convincing history of anaphylaxis to isolated ingestion and/or diagnostic test value
Food tested is likely to be tolerated, but if history suspicious, consider retesting and supervised oral food challenge
Yes
No

Evaluation of a suspected IgE-mediated food allergy

In vitro testing

Radioallergosorbent tests (RASTs)

Fluorescent enzyme immunoassay (FEIA)

Skin tests

prick/puncture

Intradermal

In vitro testing by a generalist is appropriate ***when the pretest probability of food allergy is moderate to high***.

RASTs and ***FEIA*** tests are in vitro assays used to identify *food-specific IgE antibodies* in the serum.

In vitro tests are:

- Widely available
- Unaffected by the presence of antihistamines or other medications
- Useful in patients with severe anaphylaxis in whom skin testing may carry an unacceptable degree of risk
- Useful in patients with dermatologic conditions that may preclude skin testing, such as severe atopic dermatitis and dermographism.

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Although ***higher concentrations*** of food-specific IgE correlate to an ***increased likelihood of a reaction upon ingestion***, an individual patient with a significant food allergy can have a high, medium, low, or even negative in vitro test using these systems.

The prick/puncture (or epicutaneous) skin testing

The test is still valid ***even if the patient is not eating the food***.

It is also highly ***effective for excluding*** IgE-mediated allergy, particularly in a patient *with a low pretest probability*.

Because of the ***low specificity of skin testing***, it should not be used to screen patients for allergy by testing with broad panels of food allergens without regard for clinical history, since this is likely to yield false positive results.

The skin of ***infants*** may be less reactive, yielding *more false-negative results*, although this difference has not been formally studied. Unfortunately, very young children may also have *more systemic reactions* to skin testing.

Skin testing is not usually performed for several weeks after an episode of anaphylaxis, because it has been observed that anaphylaxis can render the skin temporarily nonreactive. The reasons for this refractory period have not been studied, although extensive depletion of surface IgE and/or granule contents within cutaneous mast cells are possible explanations. ***Full restoration of skin reactivity can take two to four weeks***.

To perform prick/puncture skin testing, a source of food allergen is applied to the skin, together with appropriate positive (histamine) and negative (saline) ***controls***.

A skin prick test eliciting a wheal at least 3 millimeters in diameter, after the saline control is subtracted, is considered positive. Anything else is considered negative.

The general sensitivity and ***specificity*** of skin prick testing for the diagnosis of food allergy are often estimated to be greater than 90 and approximately ***50 percent***, respectively.

The larger the wheal, the greater the *likelihood* of clinical allergy.

However, the size of the skin test ***does not correlate with the severity*** of a reaction.

Intradermal skin tests

— Intradermal skin testing should **not** be performed in the evaluation of food allergy, since it does not add to the diagnosis and carries a greater risk of inducing a systemic reaction than does prick skin testing .

Fatalities have been reported with intradermal testing to foods

Determination of Allergen-Specific IgE by Skin Testing vs In Vitro Testing

VARIABLE	SKIN TEST	sIgE ASSAY
Risk of allergic reaction	Yes (especially ID)	NO
Affected by antihistamines	Yes	NO
Affected by corticosteroids	Usually not	NO
A. by extensive dermatitis or dermographism	Yes	NO
Broad selection of antigens	Fewer	Yes

Atopy patch tests

— Atopy patch testing is another type of skin testing that involves the topical application of a food-containing solution to the skin for 48 hours and has shown some promise in the diagnosis of ***non-IgE-mediated food allergy***.

However, there ***are no standardized reagents, application methods, or guidelines for interpretation***, and this type of testing *cannot be recommended outside of research settings*.

Component testing:

The potency of individual proteins in a food may relate to their lability. Ara h 2, for example, is a peanut seed storage protein that is stable. Ara h 8 is a labile protein.

An individual with a strong immune response to Ara h 2 and no response to Ara h 8 might be predicted to have a severe peanut allergy compared with a person with no response to Ara h 2 and a modest response to Ara h 8, even though a positive test to whole peanut extract would be positive in both, possibly with the same result.

Future diagnostic tools for food allergy

Gene-level testing for food allergies

(HLA)-DR and HLA-DQ locus as genetic determinants for peanut allergy

T cell stimulation tests

measuring T cell responses to food allergens