

CLINICAL APPROACH TO ADVERSE REACTIONS TO FOOD ADDITIVES

Adverse reactions to food additives are clearer against a broad background of adverse reactions to food.



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BACKGROUND

Although a newer classification has recently been proposed, the traditional classification, as shown in Fig.1, remains a useful way of illustrating the range of adverse food reactions.

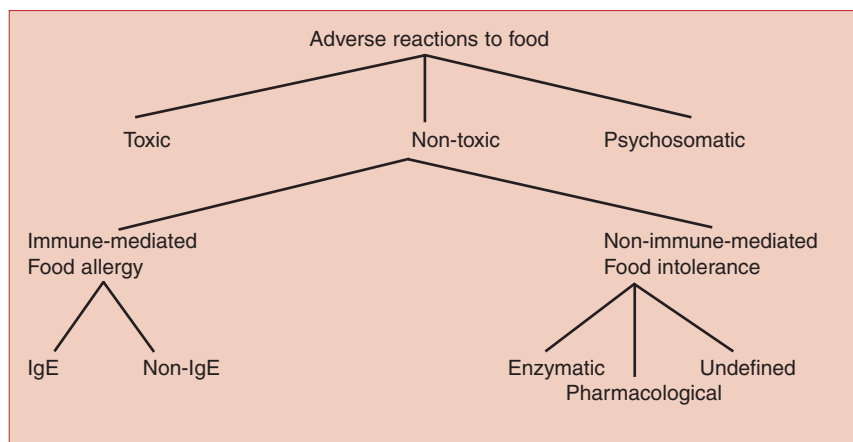


Fig.1. Classification of adverse reactions to foods.

Although in allergy the emphasis has been on immune-mediated reactions, and specifically immediate IgE-mediated reactions, up to 30% of immune-mediated reactions are non-IgE. And we need to appreciate that the number and variety of naturally inherent substances, as well as additives, pose the challenge of developing a wider sense of the causes and mechanisms of adverse reactions.

Examples of toxic reactions include reactions to histamine in scombroid fish poisoning and to bacterial toxins in food poisoning. Although the emphasis of enzymatic reactions has been on lactose, sucrose and fructose intolerance, many additives such as sorbitol may, if ingested in large enough quantities, result in adverse reactions. Rarely mentioned in textbooks are non-immune-mediated adverse reactions, more of a nuisance than a health risk, such as bloating from eating cabbage or onion, abnormal-smelling urine after the ingestion of asparagus, and red urine from beet-root. Pharmacologically active substances can cause significant adverse symptoms; these substances include vasoactive amines such as tyramine, serotonin and histamine, found in cheeses, fish, chocolate, bananas, red wine, citrus fruits, strawberries and other foods. Some individuals experience marked adverse reactions to average intake of caffeine or alcohol.

To compound the difficulty in teasing out a potential cause for a patient's adverse reaction to a food, about 75% of the Western diet is made up of processed foods containing additives and preservatives. Each Westerner consumes an average of 4 - 5 kg of food additives per year. A food additive is any substance not commonly regarded or used as food, which is added to food at any stage to affect its keeping

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quality, texture, consistency, taste, colour, alkalinity or acidity, or to serve any other technological function in relation to food, and includes processing aids.

Important additive triggers of adverse reactions include sodium metabisulphite, sulphur dioxide, sodium benzoate, colourants and occasionally tartrazine and sodium nitrate. Nevertheless, although more than 2 000 additives are in use, most appear not to contribute to adverse reactions. In recent years, as a consequence of consumer pressure, some synthetic chemicals have been replaced by additives derived from allergenic sources, such as casein and caseinate from milk, binders from egg and texturisers or emulsifiers from soy. The additives often inherit the exact allergenicity of the parent compound. Some additives such as the colourant cochineal, derived from insects, may result in immediate IgE-mediated reactions. Other natural preservatives and additives such as yeast, vinegar and alcohol may result in adverse reactions.

The health professional therefore needs to appreciate that a number of mechanisms may contribute to adverse reactions to a processed food; and also that additives as 'hidden allergens' may cause typical immediate IgE-mediated allergic reactions. Importantly, foods and additives found in foods have crossed over into the cosmetics industry. For example, egg and avocado occur in shampoo and milk in skin lotions.

Sorbic acid (typically used in fruit drinks and yoghurt) can cause skin reactions when present in treatments for skin ulcers.

PRESENTATION OF ADVERSE REACTIONS TO ADDITIVES

Around 30% of consumers have claimed to be allergic to or intolerant of a foodstuff, but only in approximately 5 - 8% of cases was there clinical confirmation. Nevertheless, thorough investigation of complaints, although complex and challenging, is necessary.

Certain additives are known to cause the same types of reactions as those caused by IgE-mediated responses (i.e. asthma, urticaria, atopic dermatitis) but in far fewer cases. They may exacerbate asthma, eczema, or symptoms of food allergy. In general, adverse reactions to additives do not have a typical presentation. Moreover, because many of the reactions are not mediated by IgE, diagnosis will require food elimination and oral challenge trials.

Intolerance reactions are in general dose-dependent. For example, an individual may tolerate half a glass but not a full glass of a drink containing sulphur dioxide. Naturally occurring histamine or tyramine in food may have the same effect.

There is a common belief that additives may contribute to or cause hyperactivity. But it is important to note that 'hyperactivity' describes a number of conditions, including true ADHD (attention deficit hyperactivity disorder), but substances such as caffeine may result in hyperactive-like behaviour. But 'hyperactivity' may also flow from chronic conditions that disturb sleep, such as obstructive allergic rhinitis and severe eczema, ironically leading to behaviour that looks like hyperactivity (see below).

ASSESSMENT

History

Obtain a detailed history, perform a complete physical examination, and formulate a suspicion of an allergy, intolerance, toxic reaction or food aversion after ruling out other causes for the symptoms. Diet should only be considered as a cause when more serious

underlying conditions (including psychiatric disease) have been excluded.

Consider the following:

- Are the reactions associated with natural food, processed food or both?
- How much of the food needs to be ingested before reactions occur?
- How soon after ingestion do the reactions occur?
- What are the symptoms?
- Are they always elicited when the same food is ingested?
- Are the reactions typical of an allergy or intolerance?
- Does the patient have any known allergies?
- Do the reactions occur even when the patient is away from home?
- Do the reactions manifest over weekends or holidays?
- Are the reactions associated with exercise or a combination of foods?

'Atypical' or delayed adverse reactions to food which are not type I IgE-dependent reactions, and for which conventional allergy tests are usually unhelpful, are quite common. They can be difficult to diagnose until the diet is systematically investigated. This is doubly true of additive reactions, because of the complexity of processed foods.

Examination

The physical examination is generally unhelpful unless it reveals a topical skin reaction to a topical treatment. Facial marks of atopy, e.g. nasal crease, allergic shiners, or Dennie's lines, may suggest an allergic disposition and a possible immune-mediated reaction, but non-immune-mediated adverse reactions to additives are more commonly associated with atopic individuals. In children, if the predominant complaint is one of hyperactivity, an examination for nasal patency and/or other features of perennial allergic rhinitis should be sought. Particularly prominent allergic shiners, complete or marked nasal obstruction, a high arched hard palate and mouth breathing are all significant features, and especially when associated with snoring, apparent apnoea and upturned bedclothes in the morning, may indicate severe obstructive allergic rhinitis with subsequent sleep deprivation, which may result in either lethargy during the day or paradoxically, hyperactive-like behaviour. In this event, treatment with

topical nasal steroids will be more appropriate than a special diet.

In vivo tests

Commercial skin tests have no role to play in assessing adverse reactions to additives unless these are derived from a known allergen, e.g. egg. However, patients who react to an additive derived from one of the major allergens will most likely have had the food eliminated from the diet already, and only checking for hidden sources of that allergen will be required. Skin prick tests may have some value in the hands of practitioners familiar with this technique, if the history indicates an IgE-mediated mechanism. If the adverse event was life-threatening, testing should be done only in a resuscitative facility.

In vitro tests

Serum-specific IgE

Currently, commercial serum-specific IgE tests, e.g. ImmunoCAP (CAP RAST), have no role to play in assessing adverse reactions to additives unless the additive is derived from a known allergen. Nonetheless, some tests (e.g. total IgE) may assist in differentiating whether the patient has an allergic background.

CAST test (sulphidoleukotriene release test)

At least two laboratories in South Africa offer the CAST test, which tests for sensitivity to a number of additives. However, the CAST test sensitivity and cut-off values are still being investigated for most of the preservatives and, depending on the additive being tested, may be helpful in less than 50% of patients truly affected by an additive. This test is nevertheless a valuable investigative tool in certain circumstances.

Dietary tests

Where the history or tests are unhelpful, a food diary or an elimination challenge diet may be most informative.

Food diary

A food diary (or diet diary) is often an adjunct to the medical history and is less dependent on the patient's memory. The patient keeps a chronological record of all foods eaten over a specified period

of time, including quantity, any symptoms and the time of onset. The diary may reveal relationships between foods and symptoms and is not as dependent on the patient's memory.

Elimination diet

An elimination diet is often used to either diagnose or manage an adverse food reaction. A certain food (or foods) suspected of provoking the reaction is completely eliminated from the diet. It is most useful if symptoms are occurring more than 2 - 3 times a week. This process can take 2 or 3 months, and is generally dietitian-supervised on an outpatient basis. Where preservatives and colourants are suspected, an elimination diet should be considered before expensive screening tests. The diet avoids all the major allergens, preservatives and additives. It is administered for 2 - 3 weeks with a diary card. Cessation of symptoms confirms that a food or additive is indeed responsible for the symptoms. The diet comprises lower allergenic foods and not non-allergenic foods; therefore, occasionally patients are still affected.

After symptoms stop, the food or additive causing the symptoms can be identified by re-introducing the eliminated foods one by one, first unprocessed foods, then the processed foods which the patient ate before the diet. Confirmatory testing either by RAST, skin prick test, CAST or repeat challenge test under controlled conditions can then be considered. Note that a patient may be affected by more than one additive; therefore testing should not be halted prematurely.

DBPCFC (double-blind, placebo-controlled food challenge)

The double-blind, placebo-controlled food challenge has been called the gold standard for the diagnosis of food allergy. It has been used successfully in both children and adults for the last several years to examine a wide variety of food-related complaints. It eliminates psychogenic factors and observer bias. The procedure is labour-intensive but can be modified for an office setting. The DBPCFC may be required to confirm that the implicated additive is in fact responsible for symptoms.

Controversial tests

Research has shown that no complementary or alternative diagnostic procedure can be recommended for allergic diseases, including electrodermal tests (Vega or Best tests), ALCAT, cytotoxic tests, kinesiology, or IgG antibody tests.

Conclusion

The elimination of food additives is difficult as additives are ubiquitous in processed foods. However, it can greatly improve patient quality of life. Patients need to read food product ingredient labels carefully and learn key words, e.g. casein, whey, lactalbumin, and caramel colour. In the case of vague terms such as natural flavourant or high-protein flavour, the patient should contact the manufacturer to determine the source of the additive.

Further reading available on request.

IN A NUTSHELL

The majority of synthetic additives do not cause adverse reactions.

Sulphur dioxide and the sulphites may exacerbate allergic disease.

Natural additives derived from major allergens are becoming a major cause of adverse reactions to additives.

Reported 'allergy' to additives should be approached with scepticism, but a multifaceted and thorough investigation should still be conducted because an additive may cause reactions via a variety of mechanisms.

An elimination diet may be the only useful modality for finding the causative additive.