

# ABC OF ALLERGOLOGY

## ADVERSE REACTIONS TO FOOD ADDITIVES

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The role of food additives in allergology has always been controversial. Much publicised studies in the 1970s attributed at least 40% of asthma, eczema, urticaria and rhinitis exacerbations to food additives. Tartrazine became a buzz-word on everyone's lips.



Food additives and particularly preservatives have been around for a very long time and play a most important role in preventing food spoilage and enhancing the appearance of food in stores. The oldest and most commonly used preservatives include salt, vinegar and sugar. Many hundreds of food additives and preservatives are commercially available and used in everyday foods (over 1 500 E numbers are listed). The vast majority are absolutely harmless and these include vitamin C, citric acid and acetic acid. A small number have been repeatedly implicated in adverse reactions by mechanisms often not fully understood, the most problematic being sulphur dioxide, sodium benzoate, sodium nitrite and their derivatives. Monosodium glutamate (MSG) and tartrazine are other culprits whose adverse effects have received much media interest.

Recent clinical studies seem to indicate that certain of these food additives do play an important role as adjuvants in food-related hypersensitivity, triggering 'allergic' diseases such as urticaria, asthma, rhinitis and eczema via mechanisms usually not mediated by IgE. Adverse reactions are often dose-related, may be delayed for up to 24 hours, and occur after prolonged exposure usually to a combination of additives; only certain individuals seem to be sensitive. Current prevalence rates for adverse reactions to food additives range from 0.12% to 2% of the population but are far more likely to be seen in certain groups, particularly in urticaria sufferers, aspirin-intolerant individuals and those with chronic asthma.

### The main culprits

**Sulphites.** These preservatives, including sulphur dioxide, sodium sulphite and potassium metabisulphite, are added to processed foods, juice concentrates, wine and pharmaceutical products. They may induce acute bronchospasm, chronic urticaria and even life-threatening anaphylaxis in some very sensitive individuals.

**Benzoates and parabens.** Sodium benzoate, benzoic acid and methyl-paraben are examples of these antimycotic and antibacterial agents used to prevent food spoilage. They can trigger urticaria, angioedema, asthma, rhinitis and purpura in certain sensitive people. Parabens are more often found in pharmaceuticals and cosmetics and can cause contact dermatitis and urticaria. Benzoates may even occur naturally in certain foods such as cinnamon, tea and berry fruits.



**Monosodium glutamate (MSG),** the controversial flavour enhancer found in Aromat® and Chinese seasoning, has been implicated in the 'Chinese Restaurant' or Kwok's syndrome of flushing, a burning sensation in the chest and neck pain, as well as headache and rapid pulse. Asthma exacerbations have also been independently attributed to MSG.

The food dyes tartrazine and cochineal have been implicated as triggers for urticaria. These food colourants similar in structure to aspirin may trigger acute asthma in about 1 in 1 000 cases. Other implicated food dyes include erythrocin and sunset yellow.

**Nitrates** and sodium nitrite give meat its attractive pink colour. This additive has also been occasionally implicated as a trigger in asthma, urticaria and rhinitis.

### Mechanisms of food-additive-induced reactions

The overwhelming majority of food-additive reactions are not IgE mediated, with many occurring up to 24 hours after challenge hence making IgE (immediate hypersensitivity) reactions unlikely. Some food additives cause direct mast cell and basophil activation with histamine release by mechanisms as yet unexplained. Arachidonic acid lipoxygenase pathway activation as found in aspirin intolerance is thought to be the basis for leukotriene release seen in adverse reactions to tartrazine, sodium benzoate and nitrates (Fig. 1). This pro-inflammatory cysteinyl-leukotriene release that has been well documented in food-additive intolerance would explain the variable timing of reactions seen (up to 24 hours after challenge).

Provocation testing for food-additive intolerance has been difficult to standardise, and results of challenges vary greatly from study to study. It would appear that constant low-dose additive exposure is more likely to trigger reactions than intermittent high-dose exposure. This would explain the low incidence of adverse reactions seen in strict clinical studies where there is usually a week-long washout period followed by 5-day incremental increase in food-additive exposure.

Combinations of additives such as benzoates, sulphites and nitrites seem to trigger reactions more often than exposure to single additives. The route of exposure is vitally important – oral dosages of liquids are more

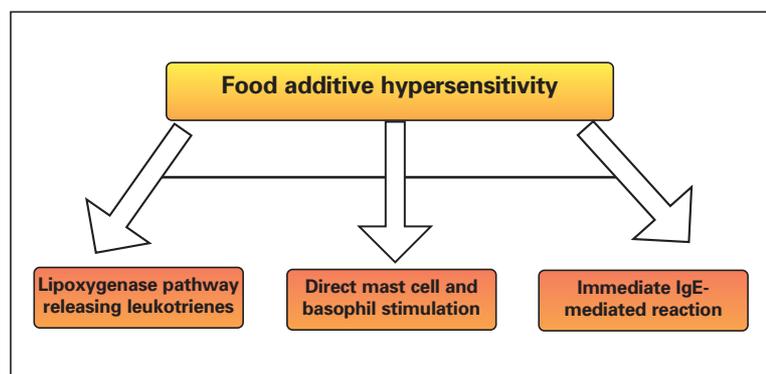


Fig. 1. Potential food additive hypersensitivity mechanisms.

provocative than additives hidden in gelatine capsules (which later dissolve in gastric content). Experts feel that the vehicle in which the additive is concealed may be crucial to the study outcome, e.g. potential adverse reactions to the gelatine capsule are possible. The dose threshold for inducing adverse reactions appears to vary from individual to individual. We know that coexistent illnesses lower the additive reaction threshold. Often small amounts of additive may be tolerated and tolerance seems to vary throughout one's lifetime. The postchallenge observational period is also crucial, for patients should be observed long enough to document all delayed reactions (at least 24 hours or more).

### **Lack of diagnostic tests**

To date, no reliable diagnostic tests for food-additive intolerance have been developed. We know that IgE does not play an important role in these reactions; hence skin-prick testing and RAST testing results have been disappointing. Various IgG ELISA tests and leucocytotoxic tests promoted recently have proved equally disappointing. Direct challenge testing is the only available test with any reliability at present, but here the results vary greatly depending on challenge dose and prevalence of other concomitant disease processes. The cellular allergen stimulation test (CAST) which determines leukotriene release from blood leucocytes has proved to be of variable diagnostic value. But the current CAST positive cut-off points for determining a definite positive result have not been clearly identified. VEGA tests, bio-energy field evaluation and kinesiology provide no diagnostic value for food-additive allergy sufferers and are not recommended.

### **Clinical presentations**

Food-additive intolerance may cause or aggravate a number of allergy-like conditions including chronic urticaria, angioedema, chronic asthma and rhinitis. The findings of studies in the 1970s which suggested very high incidences of food-additive-induced allergic disease have not been repeated in recent studies. Perhaps this is due to a generally lower intake of additives and greater public awareness of the problem. Current studies in asthma suggest up to 22% of sufferers may be sulphite sensitive, while 8% react to benzoates in food with a 20% decline in lung function. Approximately 10% of individuals with chronic urticaria will relapse on a diet containing sodium benzoate and 8% of people with chronic non-allergic rhinitis will deteriorate on a diet that contains a combination of sulphites, benzoates, nitrites, MSG and tartrazine. Tartrazine was recently found to trigger eczema in only 1% of cases suspected of being tartrazine sensitive. The possible role of food additives in causing childhood behavioural problems has largely been dispelled by recent studies. A diet high in refined sugars may well aggravate unruly behaviour in children, but this is on a pharmacological basis ('sugar surge') rather than by any allergic mechanism.

The Melkersson-Rosenthal syndrome is a rare condition involving chronic oro-facial granulomatosis of the lips, peripheral facial paralysis and fissuring of the tongue, seen occasionally in atopic families and triggered by sodium benzoate exposure.

### **Others implicated**

Antioxidants are used to prevent fats and oils from becoming rancid. BHA and BHT have been occasionally implicated as causes for urticaria, rashes and asthma. Emulsifiers and stabilisers such as corn starch and soya extracts are largely harmless unless one is allergic to corn or soya.

Although sweeteners such as aspartame and saccharin have been implicated in urticaria, reactions are usually rare. Complementary practitioners often implicate sugar as a cause of allergies, but sugar does not act as an allergen except in the rare event of it binding to another protein 'hapten' (which may induce allergenicity).

### **Naturally occurring pharmacological agents**

Certain naturally occurring substances in food can trigger adverse pharmacological reactions or 'pseudo-allergic' reactions. These are not true allergies but can closely mimic allergic reactions to the unwary. These substances include natural aspirin-like chemicals such as salicylate and vaso-active amines such as histamine, tyramine, serotonin and phenylethylamine.

Acetyl salicylic acid as found in aspirin can trigger asthma in up to 20% of adult asthmatics. Sodium salicylate also occurs naturally in spices, tea, green apple skins and certain berry fruits. Aspirin-sensitive individuals can theoretically react to this natural salicylate, and possibly also to sodium benzoate and tartrazine, and may present with asthma or urticaria. Aspirin-sensitive people are prone to asthma and urticaria and develop nasal polyps with obstruction of the nose.

Vaso-active amines or 'natural histamine-like substances' may occur in dark-meat fish, mature cheeses and certain over-ripe fruits and vegetables. They can induce pharmacological flushing, headaches, palpitations and cramping. Poorly stored scombroid fish such as 'yellowtail' can cause a similar reaction when the thawed fish flesh releases histamine when eaten.

Other pharmacologically active substances may also mimic allergies.

Caffeine and the methyl-xanthines in tea, coffee and cola cause CNS stimulation, palpitations and nausea.



Ethanol as in alcoholic drinks is a vasodilator and diuretic, and speeds the absorption of other allergens eaten (hence exacerbating allergic reactions to known allergenic foods). Those of Asian descent have a genetic deficiency of the alcohol breakdown enzyme which exacerbates this intolerance.

Capsaicin in peppers, paprika and Tabasco sauce releases pro-inflammatory 'substance P', inducing an oral burning sensation and indigestion.

Myristicin found in nutmeg can induce psychosis, apprehension and chest pains on a pharmacological and non-allergic basis.

Remember that food grown 'organically' conveys no allergy protection and will be just as likely to cause allergies in sensitised individuals.

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### **FURTHER READING**

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