

The Whole Body

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- Both immunologic and non-immunologic mechanisms can provoke systemic reactions following food ingestion.
- Histamine is the only mast cell mediator which has been demonstrated to be elevated in the serum as a result of systemic allergic reactions to food.
- In individuals highly sensitive to foods, airborne exposure to food allergens can produce anaphylactic reactions.
- Crossreacting allergens present in some foods and in natural rubber latex can lead to systemic reactions following either latex exposure or food ingestion.

Key words: Anaphylaxis, histamine, tryptase, latex, crossreactivity

Systemic Reactions

There are no widely accepted criteria for deciding when food induced reactions should be classified as a whole body or systemic reactions. Systemic reactions are, probably, best described as reactions simultaneously involving multiple organs, especially reactions which are potentially life-threatening (1, 28). Using this definition both immunologic and non-immunologic mechanisms can provoke systemic reactions following food-ingestion.

Mechanisms in anaphylaxis

The most severe form of systemic reaction produced by foods is anaphylaxis. Anaphylaxis is a reaction resulting from the sudden release of multiple chemical mediators including histamine, prostaglandins, leukotrienes, and others, as a result of events mediated by IgE antibodies (1, 3, 28). The effects of mediators, which are most likely to be life threatening, are edema of the upper airway, severe asthma, and circulatory collapse (3, 7). Either upper airway edema or asthma can produce hypoxia because of obstructed airflow (9, 15, 22, 23). Circulatory collapse is usually the result of a combination of decreased intravascular volume and decreased myocardial contractility (9, 24). Fatal anaphylactic reactions from foods have been

documented in both adults and children (19, 29). While the prevalence of fatal food reactions is unknown, one estimate suggested that more children in the United States die of food induced anaphylaxis than from insect sting anaphylaxis (27). The time of onset of the reaction after food ingestion is variable, but symptoms are typically noted within a few minutes. Initial symptoms are likely to be swelling or itching of the lips, tongue, or throat, nausea and vomiting (27, 29). In some patients, the initial symptoms are rapid loss of consciousness and cyanosis (19, 29). Sampson et al., have pointed out that in some cases of fatal food-induced anaphylaxis, children initially had mild symptoms and were thought to be improving only to have severe symptoms develop up to 2.5 hours later (19).

Thus, food induced anaphylaxis can manifest as uniphasic, biphasic and protracted anaphylaxis as defined by Stark and Sullivan (25). In the six fatal cases reported by Sampson et al., the time from ingestion until death ranged from 95 to 300 minutes (19).

Reports of fatal and near fatal anaphylactic reactions from foods have some consistencies. Previously diagnosed asthma has been present in most reported cases of both adults and children

with fatal or near fatal reactions (19, 29). Disturbingly, most individuals involved in fatal and near fatal reactions were aware of their allergic sensitivity to the food causing the reaction, but inadvertently ingested the food anyway. The foods most frequently associated with severe reactions in the United States have been peanuts, tree nuts, seafoods, eggs and milk (19, 29). In other countries and cultures, different foods may be more frequently associated with severe anaphylactic reactions, presumably because of dietary differences.

Diagnosis of anaphylaxis

The diagnosis of anaphylaxis is based on clinical signs and symptoms, since there are not definitive laboratory tests. One of the most promising laboratory tests for supporting a diagnosis of anaphylaxis is measurement of mast cell tryptase in serum (20, 21). Mast cell tryptase appears to be unique to mast cells and the presence of elevated concentrations of this protein in the serum indicate that substantial mast cell degranulation has occurred.

Tryptase measurements are practical for clinical use. Peak elevation of serum tryptase is found 45 to 60 minutes after the onset of the reaction and serum concentrations may remain elevated for hours (21). Serum samples for tryptase measurements do not require special processing or handling and tryptase concentrations are relatively stable in serum for 48 hours at room temperature (21). While tryptase levels have been reported to be elevated in patients with anaphylaxis induced by various agents, Sampson et al., were not able to detect increased tryptase concentrations in two of their patients with near fatal reactions. Three additional patients with severe food-induced anaphylaxis studied by Sampson et al. also had normal serum tryptase concentrations (19). The failure to find increased tryptase concentrations suggests that either other mechanisms are involved in food-induced reactions or that mast cells may be able to release some mediators while not releasing tryptase. Sampson et al., also measured tumor necrosis factor X in some patients and again no increase in serum concentrations was found. Histamine has been found to be elevated during food-induced allergic reactions, but histamine is elevated for only a brief interval of 10-20 minutes (3, 18).

Natural history

An important question is whether an individual, especially a child, will lose anaphylactic food sensitivity over a period of years. Bock and Atkins were able to follow-up 32 of 46 children who had carefully documented reactions to peanuts 2-14 years previously (4). All subjects continued to have skin test reactivity to peanut. Twenty-four of the subjects, who had accidentally ingested peanut in the preceding five years, reported reactions. Interestingly, Bock and Atkins found that four of the 46 children, demonstrated to be peanut allergic, had died of asthma by the time the families were recontacted for study (49). This finding suggests that the combination of peanut allergy and asthma may indicate a very high risk of death. It also suggests that some fatal asthma attacks may be the result of inadvertent and unrecognized peanut ingestion by sensitive individuals.

In individuals highly sensitive to foods, airborne exposure to food allergens can produce anaphylactic reactions (2, 5).

Airborne allergens and crossreactivity

Some case reports also suggest that airborne exposure to foods can sensitize individuals leading to anaphylaxis the first time the food is ingested (12, 30). While multiple studies have reported crossreacting allergens between foods and pollens, the clinical significance of these crossreactions, in terms of the risk of anaphylaxis, is largely unknown. There is one group of patients in whom crossreactive food allergens have been associated with anaphylactic reactions. Natural rubber latex contains allergens which crossreact with various foods (6, 8, 16, 17). Some patients have had anaphylactic reactions from both latex contact and from ingesting a crossreacting food (6, 8, 16). Given the frequent exposure of many individuals to both natural rubber latex and the crossreacting foods, it is impossible to determine whether these individuals were primarily sensitized by food or by latex. Most affected individuals, however, have been health care workers, suggesting that latex was the primary sensitizer.

Exercise-induced anaphylaxis

An unusual form of food-related anaphylaxis is the syndrome of exercise anaphylaxis which only occurs if the person ingests a particular food prior to exercising (10, 11). Individuals with this syndrome typically have evidence of allergen

specific IgE for the incriminated food, but can eat the food without difficulty provided they do not exercise strenuously within a few hours following ingestion. In a few cases, the only symptom related to the combination of food ingestion and exercise was urticaria or exacerbation of urticaria. The mechanism involved in food-related, exercise induced anaphylaxis are unknown.

Idiopathic anaphylaxis

A study of 102 patients with a diagnosis of idiopathic anaphylaxis demonstrated that 31% of the patients were sensitive to one or more foods when the patients were tested with a battery of 79 food antigens (26). Anaphylaxis was provoked by food challenges in five patients and two other patients had relief of symptoms by food elimination, but refused food challenge. The authors concluded that the episodes of anaphylaxis were not-idiopathic in 7% of their patients (26).

Scombroid fish poisoning

While there are a number of non-immune, systemic reactions to foods, there is only one form of non-immune food reaction which is likely to be confused with anaphylaxis. Scombroid fish poisoning is typically manifested as flushing, especially of the face, neck and upper chest, palpitations, headache, nausea and vomiting within minutes of ingesting the fish (13, 14). Improper storage of some fish results in bacterial conversion of histidine into histamine. Symptoms are thought to be the result of histamine intoxication following ingestion of fish with high levels of histamine (13). The fish most commonly implicated are members of the families, *Scombridae* and *Scomberesocidae*, which include tuna, mackerel, skipjack, and bonito. Some affected individuals have noted that the ingested fish had a strange metallic taste. Symptoms are generally self-limited and responsive to anti-histamine therapy, although severe symptoms have been mentioned (13). Findings which help differentiate scombroid poisoning from seafood allergy include the reports of group outbreaks in which all individuals ingesting the fish are affected and the absence of a prior history of seafood allergy in affected individuals. The clinical suspicion can be verified by measuring histamine concentrations in the fish. Some food poisons can produce symptoms shortly after ingestion, but these symptoms are not typical of allergic symptoms and a history of the food ingested will often

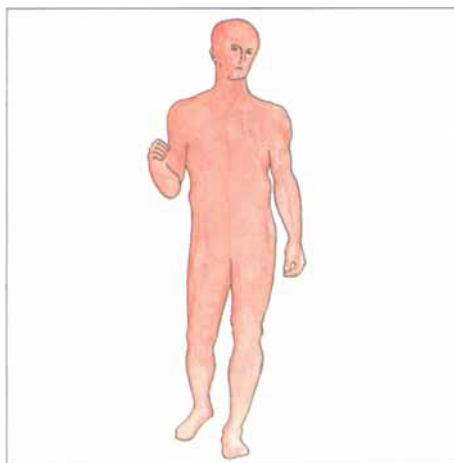
suggest the diagnosis, such as neurologic symptoms after mushroom ingestion.

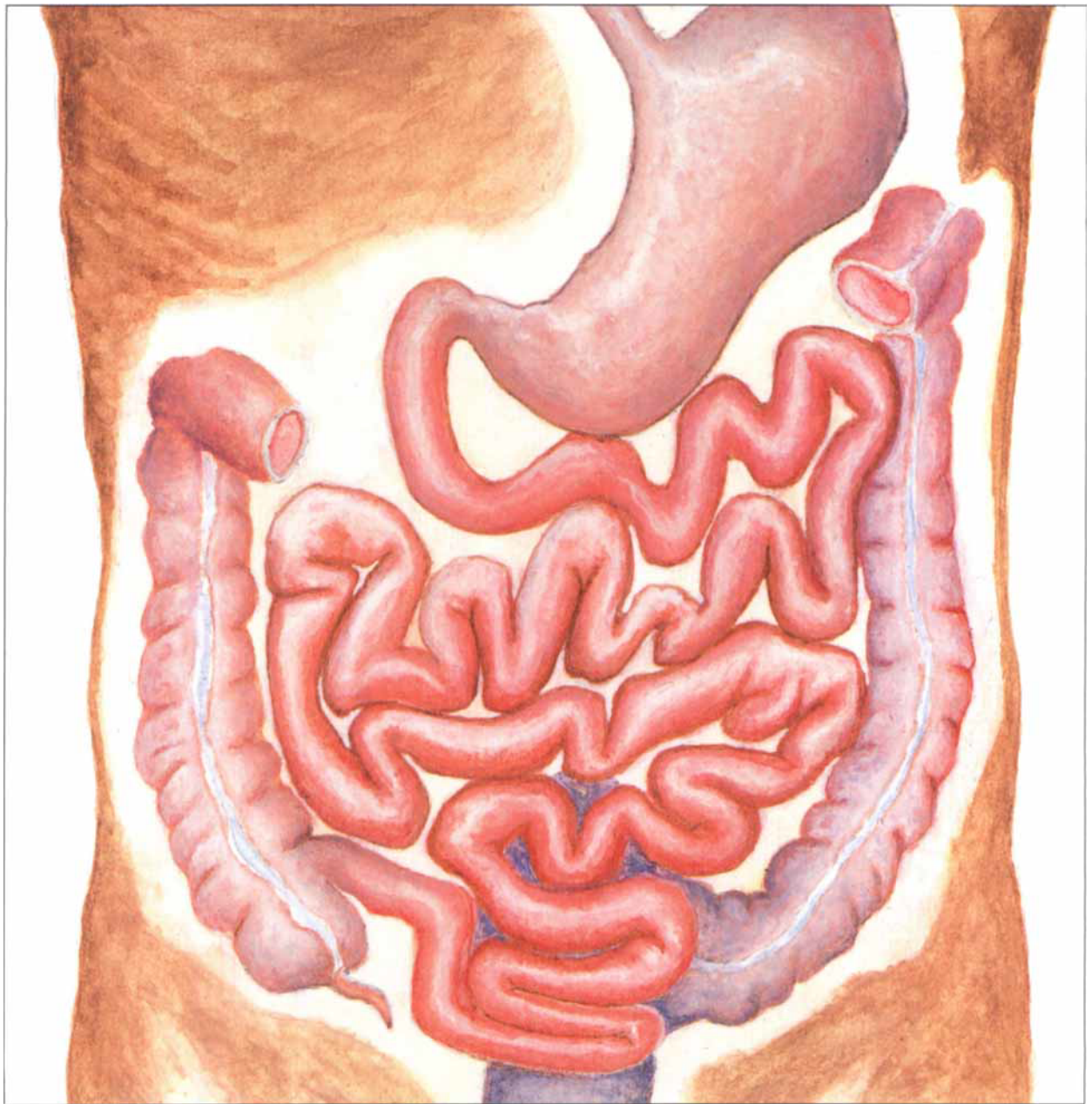
Further work is needed to determine the mechanisms of food induced anaphylaxis and to improve methods for preventing food induced anaphylaxis.

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