MECHANISMS AND MANAGEMENT OF FOOD ALLERGY AND INTOLERANCE

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Symptoms of Food Allergy

- Controversy among practitioners because there are no definitive tests for food allergy
- Rhinoconjunctivitis (hayfever), asthma and atopic dermatitis (eczema) generally considered part of the “allergic diathesis”
- Other conditions, especially in the digestive tract and nervous system are considered more “subjective” and many practitioners dismiss them as “fictitious” or psychosomatic
Examples of Allergic Conditions and Symptoms

- **Respiratory Tract**
  - Seasonal or perennial rhinitis (hayfever)
  - Rhinorrhea (runny nose)
  - Allergic conjunctivitis (itchy, watery, reddened eyes)
  - Serous otitis media (earache with effusion)
  - Asthma
  - Laryngeal edema (throat tightening due to swelling of tissues)
Examples of Allergic Conditions and Symptoms

- Skin and Mucous Membranes
  - Atopic dermatitis (eczema)
  - Urticaria (hives)
  - Angioedema (swelling of tissues, especially mouth and face)
  - Pruritus (itching)
  - Contact dermatitis (rash in contact with allergen)
  - Oral allergy syndrome (irritation and swelling of tissues around and inside the mouth)
Examples of Allergic Conditions and Symptoms

- Digestive Tract
  - Diarrhea
  - Constipation
  - Nausea and Vomiting
  - Abdominal bloating and distension
  - Abdominal pain
  - Indigestion (heartburn)
  - Belching
Examples of Allergic Conditions and Symptoms

- **Nervous System**
  - Migraine
  - Other headaches
  - Spots before the eyes
  - Listlessness
  - Hyperactivity
  - Lack of concentration
  - Tension-fatigue syndrome
  - Irritability
  - Chilliness
  - Dizziness
Examples of Allergic Conditions and Symptoms

- Other
  - Urinary frequency
  - Bed-wetting
  - Hoarseness
  - Muscle aches
  - Low-grade fever
  - Excessive sweating
  - Pallor
  - Dark circles around the eyes
Anaphylaxis

- Severe reaction of rapid onset, involving most organ systems, which results in circulatory collapse and drop in blood pressure
- In the most extreme cases the reaction progresses to anaphylactic shock with cardiovascular collapse
- This can be fatal
Anaphylaxis

Usual progress of reaction

- Burning, itching and irritation of mouth and oral tissues and throat
- Nausea, vomiting, abdominal pain, diarrhea
- Feeling of malaise, anxiety, generalized itching, faintness, body feels warm
- Nasal irritation and sneezing, irritated eyes
- Hives, swelling of facial tissues, reddening
- Chest tightness, bronchospasm, hoarseness
- Pulse is rapid, weak, irregular, difficult to detect
- Loss of consciousness
- Death may result from suffocation, cardiac arrhythmia or shock
Anaphylaxis

- Not all symptoms occur in each case
- Symptoms may appear in any order
- The later the onset of symptoms after eating the food, the less severe the reaction
- Severe reactions occur within minutes to up to an hour of ingestion of allergen
- Onset can be delayed for up to two hours
- In majority of cases of fatal anaphylactic reaction to food, patient was asthmatic
- Potential for anaphylaxis increases when patient is receiving desensitization injections and is allergic to wasp and bee venom
Anaphylaxis

- Almost any food can cause an anaphylactic reaction
- Some foods more common than others:
  - Peanut
  - Tree nuts
  - Shellfish
  - Egg
  - Cow’s milk
- In children under three years
  - Cow’s milk
  - Egg
  - Wheat
  - Chicken
Exercise-induced Anaphylaxis

- Usually occurs within two hours of eating the allergenic food
- Onset during physical activity
- Foods suspected to have induced exercise-induced anaphylaxis:
  - Celery
  - Shellfish (shrimp; oysters)
  - Squid
  - Peaches
  - Wheat
Emergency Treatment for Anaphylactic Reaction

- Injectable adrenalin (epinephrine)
- Fast-acting antihistamine (e.g. Benadryl)
- Usually in form of Anakit® or Epipen®
- Transport to hospital immediately
- Second phase of reaction is sometimes fatal, especially in an asthmatic
  - Patient may appear to be recovering, but 2-4 hours later symptoms increase in severity and reaction progresses rapidly
## Food Allergy & Food Intolerance

**DEFINITIONS:** American Academy of Allergy and Immunology Committee on Adverse Reactions to Foods, 1984

<table>
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<th>Food Allergy</th>
<th>Food Intolerance</th>
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<td>“an immunologic reaction resulting from the ingestion of a food or food additive”</td>
<td>“a generic term describing an abnormal physiological response to an ingested food or food additive which is not immunogenic”</td>
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Classification of Adverse Reactions to Foods According to the Pathogenic Mechanisms

Adapted from Wuthrich, 1993

ADVERSE REACTIONS TO FOODS

ALLERGY (Hypersensitivity) Immunological Reactions

Type IV (T-cells)

Type I (IgE)

Type II/III (IgM IgG)

ANAPHYLACTIC REACTIONS

Contact allergy

INTOLERANCE Non-Immunological Reactions

Physiological reactions

Neurogenic

Enzyme Deficiency (Metabolic)

ANAPHYLACTOID REACTIONS
Mechanisms Responsible for Food Allergy

The Hypersensitivity Reactions
The Hypersensitivity Reactions: Antigen Recognition

- The first stage of an immune response is recognition of a “foreign antigen”
- T cell lymphocytes are the “controllers” of the immune response
- T helper cells (CD4+ subclass) identify the foreign protein as a “potential threat”
- Cytokines are released
- The types of cytokines engendered determine the resulting immune response
T-helper Cell Subclasses

- There are two subclasses of T-helper cells
  - Type 1: TH1
  - Type 2: TH2
- Each subclass produces a different set of cytokines
T-Cell Lymphocytes

T-helper cell subtypes

- TH1 triggers the protective response to a pathogen such as a virus or bacterium
  - IgM, IgG, IgA antibodies are produced

- TH2 is responsible for the Type I hypersensitivity reaction (allergy)
  - IgE antibodies are produced
T-Cell Lymphocytes

- **TH1 subclass produces:**
  - Interferon-gamma (IFN-\(\gamma\))
  - Interleukin-2 (IL-2)
  - Tumor necrosis factor alpha (TNF\(\alpha\))

- **TH2 subclass produces:**
  - Interleukin-4 (IL-4)
  - Interleukin-5 (IL-5)
  - Interleukin-6 (IL-6)
  - Interleukin-10 (IL-10)
  - Interleukin-13 (IL-13)
T-Cell Lymphocytes

- Under certain circumstances (e.g., eczema) TH2 cytokines suppress TH1 cell activity.
- This causes a decrease in the level of immune protection against microorganisms.
- As a result, infection by normally harmless skin bacteria can occur.
Conditions That May Induce TH2 Response

- Inherited allergic potential
- Immaturity of the immune system
- Inflammatory conditions in the gut that interfere with the normal antigen processing pathway
- Immaturity of the digestive mucosa leading to hyperpermeability
- Increased uptake of antigens
Type 1 hypersensitivity
- Initial Exposure to Allergen

B-cell lymphocytes differentiate to plasma cells. Plasma cells produce allergen-specific IgE.
Type I hypersensitivity
- IgE Molecules Attach to Leukocyte

Antibody molecules attach to Ig receptors on the surface of mast cells and basophils.

The Fc region of the antibody molecule attaches to the leukocyte, leaving the antigen-binding region free to bind to allergen at a later exposure.
Type 1 hypersensitivity
- Subsequent Exposure to the Same Allergen

Allergen molecules bind to the antigen-binding regions of the attached IgE.

The allergen must be large enough to bridge two adjacent IgE molecules.
Type 1 hypersensitivity
- Intracellular Granules are Released

Complexing of allergen and antibody causes the release of intracellular granules containing inflammatory mediators such as histamine. These immediately act on tissues and produce symptoms of allergy.

Enzymatic action on the cell membrane produces secondary inflammatory mediators.
Mediator Release

ALLERGEN + IgE

MAST CELL

CHANGE IN CELL ENERGY
ADENYLATE CYCLASE-cAMP

CALCIUM ENTERS CELL

DEGRANULATION

Release of Inflammatory Mediators

HISTAMINE
EOSINOPHIL CHEMOTACTIC FACTOR (ECF-A)
NEUTROPHIL CHEMOTACTIC FACTOR (NCF-A)
ENZYMES - PHOPHOLIPASE A2
Action of Inflammatory Mediators on Tissues:

- Histamine

- Vasodilation
- Swelling of tissues
- Increased vascular permeability
  - angioedema (swelling)
  - rhinitis (stuffy nose)
  - rhinorrhea (runny nose)
  - urticaria (hives)
  - otitis media (earache)
- Itching
- Flushing
- Reddening

**Antidote:** *Antihistamines*

Block receptors for histamine on reactive cells
Action of inflammatory mediators:

- Chemotactic Factors of Anaphylaxis

**Eosinophil Chemotactic Factor of Anaphylaxis (ECF-A)**
- Attracts eosinophils to the site of reaction
- Eosinophils contain granules with inflammatory mediators
- Degranulation releases inflammatory mediators
- Augments allergic reaction

**Neutrophil Chemotactic Factor of Anaphylaxis (NCF-A)**
- Attracts neutrophils to site of reaction
- Degranulation releases more inflammatory mediators
- Augments allergic reaction
Action of inflammatory mediators:

- **Enzymes**

  - Act directly on tissues and cause damage
  - Lead to production of kinins
    - Example: bradykinin
  - In conjunction with prostaglandins causes pain

**Phospholipase A2**

- Acts on cell membrane and releases arachidonic acid
- Leads to production of secondary inflammatory mediators by two enzyme pathways:
  - Cyclo-oxygenase to prostaglandins
  - Lipoxygenase to leukotrienes
Secondary Mediator Release

Arachidonic acid

Cyclo-oxygenase

- PROSTAGLANDINS (PG$_2$)
  - PROSTACYCLIN (PGI$_2$)
  - THROMBOXANE (TX)

Lipoxygenase

- LEUKOTRIENES
  - LTA$_4$
    - LTC$_4$
      - LTD$_4$
      - LTE$_4$
  - LTB$_4$
Action of inflammatory mediators:

- **Leukotrienes**

- LTB$_4$ : Chemotaxin:
  - Attracts more leukocytes to reaction site
  - Augments allergic reaction

- LTC$_4$; LTD$_4$; LTE$_4$:
  - Smooth muscle contraction
  - Responsible for bronchospasm of asthma
Action of inflammatory mediators:

- Prostaglandins

- Smooth muscle contraction and relaxation
- Dilation and constriction of blood vessels
- Increase vascular permeability
- Responsible for pain
Type I IgE-mediated Immediate Hypersensitivity: *Summary of Reaction*

- Food allergen cross-links two IgE antibodies on the surface of mast cell
- Mast cells are degranulated and release inflammatory mediators immediately
- Secondary cells of inflammation (eosinophils, neutrophils) are recruited by chemotaxins
Type I IgE-mediated Immediate Hypersensitivity: *Summary of Reaction*

- Results in local symptoms in the gut (abdominal pain; diarrhea)
- Allows increased absorption of the same and other antigens through the gut epithelium
- Leads to systemic effects such as mast cell activation in the lungs (asthma); skin (urticaria and eczema)
- “Whole body response” is *anaphylactic reaction*
Type III Hypersensitivity: Immune complex mediated reaction

- Antigen specific IgM and IgG are formed in response to food
- Antibodies form an immune complex with antigens
- If there are high concentrations of complexes the complement cascade is triggered
- Anaphylatoxins formed by the complement pathway induce release of inflammatory mediators
Type III Hypersensitivity

- Results in an *anaphylactoid reaction*
- Symptoms resemble Type I hypersensitivity but onset is delayed (8-24 hours)
- May be the initial response (e.g. milk allergy)
- May be secondary to a primary IgE-mediated reaction
Antibodies to Foods in Blood Is a Normal Occurrence

- IgM and IgG antibodies are frequently formed against food antigens.
- This is a normal occurrence.
- When food antigens are absorbed, they will complex with their homologous antibodies.
- The immune complexes are usually rapidly cleared from circulation and do not trigger the complement cascade.
- No symptoms occur.
Type IV Hypersensitivity
Cell-mediated delayed reaction

- Involves T-cell lymphocytes and cytotoxic cytokines
- Occurs 24-72 hours after exposure to antigen
  - reaction proceeds only as long as cells are in contact with allergen
- Most evident in skin and mucous membranes (rash and itching)
- Examples:
  - Poison ivy rash
  - Contact dermatitis (nickel, rubber, leather dyes, detergents, cosmetics)
- Reaction to foods in contact with lips, mouth, tongue, and possibly lining of digestive tract
Type IV Delayed Hypersensitivity

- Causes cell-mediated immune damage local to the site of antigen contact with sensitive cells
- Food antigens shown to cause intestinal damage in animal models by this mechanism
- Evidence of cell-mediated immune responses to proteins in cow’s milk allergy
- May be involved in systemic nickel allergy causing atopic dermatitis

> Hypersensitivity reactions are not mutually exclusive and two or more reactions may occur simultaneously or sequentially
Foods Most Frequently Causing Allergy

1. Egg
   » white
   » yolk
2. Cow’s milk
3. Peanut
4. Nuts
5. Shellfish
6. Fin fish
7. Wheat
8. Soy
9. Beef
10. Chicken
11. Citrus fruits
12. Tomato
Additional Factors Involved in Symptoms of Food Sensitivity

1. Increased permeability of the gastrointestinal tract
   - Inflammation:
     - infection
     - allergy
     - autoimmune processes
     - other pathology
   - Immaturity (in infants)
   - Alcohol ingestion

2. Physical exertion
Additional Factors Involved in Symptoms of Food Sensitivity

3. Stress

4. Level of inflammatory mediators released in response to several different foods concomitantly

5. Level of inflammatory mediators released in response to other allergy (e.g. inhalant)
Mechanisms Responsible for Food Intolerances

Biochemical and Physiological Responses
Symptoms of Carbohydrate Intolerance

- Watery loose stool
- Abdominal distention
- Cramping pain in abdomen
- Flatulence
- Vomiting
- Poor weight gain
Symptoms of Carbohydrate Intolerance

- Excoriation of perianal skin and buttocks due to acid (pH less than 6) stool in children. Adults do not consistently experience such a low stool pH.
- Patients complain of abdominal fullness, bloating, and cramping within 5-30 minutes after ingesting carbohydrate.
- Watery diarrhea occurs from 5 minutes to 5 hours after ingestion.
Carbohydrate Intolerance: Causes of Intestinal Symptoms

- Non-hydrolyzed carbohydrates (polysaccharides, oligosaccharides and disaccharides) pass into the large intestine causing:
  - Osmotic imbalance: induces a net fluid secretion into the gut lumen resulting in loose stool
  - Increased bacterial fermentation resulting in production of:
    - organic acids (acetic, lactic, butyric, propionic)
      - increase osmotic imbalance
    - gases such as carbon dioxide and hydrogen
      - cause bloating and flatulence
Carbohydrate Intolerance: Causes of Intestinal Symptoms

- Increased bulk results in increased stool volume
- Increased fluid and acid environment stimulate intestinal motility and accelerate intestinal transit time.
- Increased speed of intestinal transit results in:
  - loose stool since fluid is not absorbed from food
  - secondary malabsorption of fat
Lactose Intolerance

- Lack of lactase reserves makes lactose particularly vulnerable to maldigestion.
- There are three main types of lactose intolerance:
Lactose Intolerance

1. Congenital alactasia
   [Primary lactase deficiency]

   - Very rare
   - Due to inherited autosomal recessive gene
   - Stools are loose from first days of life
   - Condition is permanent
Lactose Intolerance

2. Idiopathic lactase deficiency:
   [Natural attrition after infancy]
   - Wide variation in prevalence among different racial groups
   - Most races except northern Europeans have a 50-100% incidence
   - 80% of the world’s adult population have some degree of lactose intolerance
   - Intolerance usually appears in adolescence
   - There is normal lactase production in childhood
   - Lactase production is not substrate dependent
Lactose Intolerance

3. Secondary Lactase Deficiency

- Results from damage to the lactase-producing brush border cells
- Lactase is depressed earlier than the other disaccharides in intestinal injury such as celiac disease (gluten-sensitive enteropathy) or intestinal infections
- Lactase returns to normal levels after cell injury resolves
- Lactase is the last disaccharidase to return to normal levels after cell damage
Secondary Lactase Deficiency: Characteristics

- Lactase deficiency is by far the most common form of carbohydrate intolerance in childhood and may result from:
  - Viral or bacterial enteritis
  - Gastrointestinal surgery
  - Extensive small intestine resection
  - Cow’s milk protein allergy
  - *Giardiasis*
  - Protein-calorie malnutrition
Sucrase-Isomaltase Deficiency

- Primary deficiency is rare: it is inherited as an autosomal recessive gene.
- Greenland and Canadian Inuit have an unusual incidence of 10% of the population.
- Appears when sucrose enters the child’s diet, usually when solids are introduced.
- Severity of symptoms depends on the quantity of sucrose in the diet.
- In practice sucrose must be avoided.
Sucrase-Isomaltase Deficiency

- Starch is usually tolerated because sufficient maltase often allows hydrolysis of dietary maltose and maltotriose.

- Maltoses (alpha-dextrins) provide only 10-20% of the osmotic activity of sucrose per gram and thus attract less water into the intestinal lumen.
Pharmacologic Agents in Foods

- **Vasoactive amines:**
  - Histamine
  - Tyramine
  - Phenylethylamine
  - Octopamine
  - Serotonin

- **Methylxanthines**
  - Caffeine
  - Theobromine
  - Theophylline
Pharmacologic Agents in Foods

- Pharmacologic properties may be expressed in two ways:
  - Chemical reacts directly with body tissue in a dose-dependent fashion
  - Chemical reacts with a mediator system that acts on the body tissue
Histamine

- Histamine-mediated reactions can be clinically indistinguishable from food allergy
- Histamine sensitivity is becoming recognized as a disease entity quite distinct from allergy
- “Idiopathic” urticaria and angioedema is a common example of histamine sensitivity
- Symptoms are usually controlled with antihistamines
Mechanism of Histamine Sensitivity

- Excess histamine is broken down by two enzyme systems: histamine N-methyltransferase and diamine oxidase.
- Normally degradation of histamine to its inactive metabolites takes place rapidly.
- Prevents prolonged binding of histamine to its receptors.
- Prevents histamine-induced symptoms.
Mechanism of Histamine Sensitivity

Symptoms develop when:

- Excessive amounts of histamine exceed the enzymes’ capacity to break it down
- There is a lowered enzyme capacity for histamine breakdown
- Drugs inhibit enzyme action (e.g. isoniazid)
Sources of Histamine in Foods

1. Histidine can be decarboxylated to histamine by intestinal bacteria
   - can occur in fish [especially tuna, mackerel, bonito, bluefish, and mahi mahi] that have been improperly refrigerated

2. Histamine is produced by microbial action in manufacture of foods such as cheese, wine, beers, vinegar, yeast extract, sauerkraut
Sources of Histamine in Foods

3. Some foods contain high levels of histamine naturally, especially *spinach* and *eggplant*.

4. Some foods may release histamine by a non-immunologically mediated mechanism which is presently unknown. Such foods include:
   - Egg White
   - Shellfish
   - Strawberry
   - Alcohol (Ethanol)
   - Tomato
   - Citrus Fruits
Tyramine sensitivity

- **Symptoms:**
  - Sharp rise in blood pressure
  - Headache

- **Caused by:**
  - Vasoconstriction induced by dietary tyramine
    - Directly because of lack of tyramine breakdown in the intestine, liver, or arterial walls
    - Indirectly via secretion of epinephrine or norepinephrine, which is normally kept at unreactive levels by MAO-A
Tyramine: Mechanism of Action

- **Mechanism of action:**
  - Low levels of monoamine oxidase (MAO) enzymes

- **Other conditions related to excess tyramine:**
  - Monamine oxidase inhibiting drugs (e.g., Antidepressants such as parnate; Nardil)

- **Clinical conditions induced by tyramine:**
  - Urticaria
  - Migraine headaches
Tyramine in Foods

- Formed by microbial action in food preparation, e.g.:
  - Cheese
  - Wine
  - Yeast extract
  - Vinegar

- Small amounts occur naturally in some foods:
  - Chicken liver
  - Avocado
  - Banana
  - Plum
  - Tomato
  - Eggplant
Characteristics common to persons sensitive to food additives:

- History of asthma and rhinitis - sometimes with urticaria and angioedema
- Aspirin sensitive
Additives Most Frequently Causing Intolerances

- Tartrazine (and other artificial colors)
- Sulfites
- Preservatives:
  - Benzoates
  - Sorbates
- Monosodium glutamate (MSG)
- Nitrates and nitrites
Symptoms of Tartrazine Sensitivity

- Asthma
- Urticaria
- Angioedema
- Nausea
- Migraine headaches
- Some evidence of neurological and behavioral reactions
Postulated mechanisms to explain Tartrazine Sensitivity

1. Inhibition of the cyclo-oxygenase pathway of arachidonic acid breakdown.

2. Histamine release from mast cells
Allergic Response: Secondary Mediator Release

Arachidonic acid

Cyclo-oxygenase
- PROSTAGLANDINS (PG2)
  - PROSTACYCLIN (PGI2)
  - THROMBOXANE (TX)

Lipoxygenase
- LEUKOTRIENES
  - LTA4
  - LTC4
  - LTD4
  - LTE4

PROSTAGLANDINS (PG2)
PROSTACYCLIN (PGI2)
THROMBOXANE (TX)
Foods Frequently Containing Tartrazine

- Soft drinks
- Liqueurs and cordials
- Candy and confectionery
- Ready-to-eat cereals
- Jams and jellies
- Ice cream, sherbet, milk shakes
- Commercial gravies and soup mixes
- Flavor packets
- Pickles, relish, salad dressings
- Prepared baked goods
- Smoked fish and fish products
Foods Frequently Containing Tartrazine

- Snack foods
- Meal replacements
- Any food containing “artificial color” may contain tartrazine unless it is labeled “tartrazine free”

Non-food items:
- Medications (prescription and OTC)
- Vitamin and mineral supplements
- Toiletries and cosmetics
Sulfite Sensitivity

- Most common in asthmatics
- Steroid-dependent asthmatics are most at risk
- Adverse reactions to sulfites is estimated to be as high as 1% of the U.S. population
- Sulfite sensitivity in non-asthmatics is considered to be quite rare
- Symptoms occur in most organ systems:
  - Lungs
  - Gastrointestinal tract
  - Skin and mucous membranes
  - Life-threatening anaphylactic reactions in asthmatics have been recorded, but occur very rarely.
Symptoms Reported in Sulfite Sensitivity

- Severe respiratory reactions: bronchospasm; wheezing; “chest tightness”
- Asthma in asthmatics
- Flushing; “change in body temperature”
- Hypotension (drop in blood pressure)
- Gastrointestinal symptoms (abdominal pain, diarrhea, nausea, vomiting)
- Swallowing difficulty
- Dizziness; loss of consciousness
Symptoms Reported in Sulfite Sensitivity

- Urticaria (hives)
- Angioedema (swelling, especially of the mouth and face)
- Contact dermatitis
- Anaphylaxis (in asthmatics)
- Anaphylactoid reaction (non-asthmatics)
Postulated Mechanisms to explain Sulfite Sensitivity

1. Sulfur dioxide is formed from sulfuric acid when the sulfite dissolves
   - Acts as a direct irritant on hypersensitive airways

2. Sulfite acts as a hapten, combines with a body protein to form a neoantigen that elicits antigen-specific IgE
   - Results in Type I hypersensitivity reaction

3. Enzyme deficiency:
   - Deficiency of sulfite oxidase system which converts sulfite to the inert sulfate
Forms of Sulfites Permitted in Foods

- Sulfites are permitted in the form of:
  - sodium metabisulfite
  - potassium metabisulfite
  - sodium bisulfite
  - potassium bisulfite
  - sodium sulfite
  - sodium dithionite
  - sulfurous acid
  - sulfur dioxide
Forms of Sulfites Permitted in Foods

- Use of sulfites on fresh fruits and vegetables except sliced raw potatoes and raw grapes banned in U.S. since 1986
- Sulfites are not allowed on raw foods in salad bars or for sale in markets, with the above exceptions
- U.S. government regulations require sulfites in excess of 10 ppm in manufactured foods and beverages, including alcoholic beverages, to be listed on labels
- Sulfites are permitted in a wide range of dried, frozen, and processed foods, sweeteners, and snack foods
Sulfite Sensitivity

- There is no evidence that avoiding all sources of dietary sulfites improves asthma
- Exposure to sulfiting agents poses very little risk for individuals who are not sensitive to sulfites
- Sulfites in foods are not denatured by cooking
- Sulfites avidly bind to several substances in foods, such as protein, starch, and sugars. They are not removed by washing
- Sulfates do not cause the same adverse reactions as sulfites. They are inert in the body and need not be avoided by people who are sensitive to sulfites
Benzoate Intolerance
Symptoms

- Reported to induce:
  - Urticaria
  - Angioedema
  - Asthma
  - Rhinitis
  - Purpura (allergic vasculitis)
Benzoates and Parabens:
Use in Foods

- One of the most commonly used food additives worldwide
- Benzoic acid and sodium benzoate (benzoates) are used as antibacterial and antimycotic agents in foods and beverages
- Benzoates are most effective as preserving agents at an acidic pH
- Benzoyl peroxide is used as a bleaching agent, especially in white flour, white bread, and some white Italian cheeses
Benzoates
Naturally occurring

- Benzoates occur widely in nature as simple salts (sodium, potassium), esters, and amides
- Natural benzoates are present at the highest levels in:
  - Cinnamon, Clove, Anise, Nutmeg
  - Prunes
  - Black Tea
  - Berries
    - Especially Raspberry and Cranberry
Benzoates:
Mechanism of Intolerance

- Mechanism of intolerance is unknown
- Has been suggested to involve inhibition of the cyclooxygenase pathway since a significant number of benzoate sensitive people are also sensitive to aspirin
- There may be a similarity in sensitivity to:
  - Tartrazine and other azo dyes
  - Sorbates
  - Salicylates
Monosodium Glutamate (MSG)

- Flavoring common in Chinese cooking and increasingly used to flavor Western foods
- Sensitive individuals report a variety of symptoms that are usually classified as “Chinese Restaurant Syndrome” (also known as Kwok’s syndrome)
Most Frequently Reported Symptoms of Sensitivity to Monosodium Glutamate

- Headache, back of head and neck
- Numbness of face
- Tingling/burning of face and chest
- Tightness in chest
- Rapid heartbeat
- Nausea, diarrhea, stomach ache
- Weakness, balance problems
- Confusion
- Blurred vision
- Chills, shakes, perspiration
- Difficulty breathing
- Asthma in asthmatics
Experts are widely divided on the subject of MSG sensitivity.

One review “led to the conclusion that ‘Chinese Restaurant Syndrome’ is an anecdote applied to a variety of postprandial illnesses.”

Some clinicians have estimated that the prevalence of “Chinese Restaurant Syndrome” may be as high 1.8% of the adult population.
Proposed Mechanism of Action of MSG

- MSG is the sodium salt of glutamic acid
- Glutamic ions are the active ingredients in MSG
- Human plasma glutamate levels after a dose of MSG (0.1 g/kg body weight) can increase to levels greater than 15 times the basal concentration rate in one hour
- Glutamate acts as a precursor for the neurotransmitter acetylcholine (as well as a number of other physiological chemicals in the body)
Proposed Mechanism of Action of MSG: Acetylcholine toxicity

- Acetylcholine reaches toxic levels in a very short period of time
- Acts on the brain and central nervous system
- Symptoms ascribed to MSG sensitivity may be caused by excessive levels of neurotransmitters such as acetylcholine
- However, correlation between plasma levels and symptoms has not been shown
Characteristics of MSG Sensitivity

- Vitamin B6 (pyridoxine) deficiency may occur in some MSG sensitive people.
- Alcohol may increase the rate of absorption of MSG and increase the severity and rate of onset of symptoms.
- Symptoms usually occur about 30 minutes after eating a meal high in MSG.
- Asthma occurs 1 to 2 hours after MSG ingestion, and even as long as 12 hours later.
Sources of MSG

Present in many flavoring mixtures:
- Accent
- Zest
- Gourmet powder
- Glutavenene
- Glutacyl
- Chinese seasoning
- Subu
- Vetsin
- Ajinomoto
- Kombu extract
- Mei-jing
- Wei-jing
- RL-50
- Hydrolyzed vegetable protein (HVP)
- Hydrolyzed plant protein (HPP)
- “Natural flavor” (may be HVP)
Sources of MSG

- Used as a flavoring in foods, especially in Chinese cooking, in canned foods (e.g. soups), and restaurant meals
- Some sensitive individuals will also react to monopotassium glutamate
- Several foods, such as tomato, mushrooms, and cheese contain natural glutamates
Nitrate and Nitrite Sensitivity

- Nitrates and nitrites are used in foods as preservatives.
- Particularly protective against *Clostridium botulinum*.
- Impart flavor and color to manufactured foods, especially meat.

**Symptoms**

- Reports of headache in sensitive individuals.
Nitrates and Nitrites in Foods

- Labels list sodium nitrate, potassium nitrate, sodium nitrite, and potassium nitrite in manufactured foods.
- Present at high levels in processed meats:
  - Pepperoni
  - Hot dog wiener
  - Bologna
  - Bacon
  - Smoked fish
  - Frankfurters
  - Salami
  - Other luncheon meats
  - Ham
  - Some imported cheeses
Nitrates occur naturally in plants: the major source is nitrate-containing fertilizers.

Some species of plants tend to accumulate nitrates more than others:

- Spinach
- Beets
- Radishes
- Turnip greens
- Celery
- Lettuce
- Collards
- Eggplant
Factors Contributing to Food Intolerance

- Combination of certain foods
- Functional state of G.I. tract
- Frequency of administration (accumulated dosage)
- Enhanced absorption:
  - increased permeability of intestinal tract
  - concomitant ingestion of alcohol
- Stress
- Infection
- Level of allergens: e.g. inhalants and foods