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FOOD INTOLERANCE

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OBJECTIVES
- Understand what is meant by a food intolerance (FI)
- Understand how food additives can lead to a FI response
- Appreciate why gut dysbiosis increases the likelihood of a FI
- Learn how to manage food intolerances

“What is food to one man may be fierce poison to another”

Lucretius circa 75BC
(Roman Poet)

Adverse Food Reactions – a battle of definitions
- Food allergy (2% of population)
- False food allergy
- Food intolerance (20%)
- Food sensitivity
- Food aversion

A battle of definitions
- Food allergy – adverse reaction to food where immune system is involved
- False food allergy – Non-immunological mast cell stimulation through foods
- Food intolerance – Any adverse reaction to food where the involvement of the immune system is unproven
- Food sensitivity – umbrella term for food allergy, food intolerance etc. (non-psychological)
- Food aversion – avoidance of food for psychological reasons
  - (Brostoff J and Gamlin L. Food allergy and intolerance. 1998; p. 80)
False Food Allergy
Direct mast cell triggering to release histamine through lectins, peptides etc.

False food allergy
- Lectins - Legume family: peanuts, beans, peas and lentils (histamine release through lectins)
- Peptides binding to mast cells: in egg white, strawberries, crustacean shellfish such as prawns, shrimp, crabs, lobster, tomatoes, fish, pork, alcohol and chocolate
- Proteinase: Pineapple and papaya
- Unknown mechanism: Buckwheat, sunflower seeds, mango and mustard

Food Allergy - IgE
- In classical allergy, IgE is produced in response to an otherwise innocuous antigen, such as a food molecule
- IgE antibodies are usually found on the surface of mast cells

Food allergy – anaphylaxis
- Typically:
  - Immediate within 15 minutes
  - Potentially very severe reaction
  - To tiny amounts of a certain food, eg. nuts.

Food Intolerance
Food Intolerance

- Prevalence – very difficult to assess
- Probable range 10-25 % of population
- Any age
- Reaction can occur hours to days later
- Enzyme deficiency (genetic mutation) or immune responses caused by food specific IgG antibodies due to leaky gut.
- Wide range of symptoms affecting many parts of body/organ systems:
  - (Brostoff J and Gamlin L. Food allergy and intolerance. 1998)

Food Addiction/Withdrawal Phenomenon

- Balance between food antigen and IgG Ab complexes.
- Less antigen means large complexes therefore more inflammation
- Therefore – food craving => eat and get small complexes, less reaction
- If avoid 4-6 weeks, less antigen and antibody – less craving and reaction gone.

Food Intolerances and craving

- Somewhat surprising to find that patients with food intolerances often (50%) crave the foods they are intolerant of. eaten frequently
- Opiates – endorphins
- Exorphins: foods broken down through digestive enzymes can mimic endorphins.
  - In laboratory, these have been produced from milk, wheat, maize and barley, using human digestive enzymes.
  - Human effect antagonized by naloxone
  - Effects: addictive – euphoric
  - Speculate: withdrawal symptoms
  - (Brostoff J, Gamlin L, Food allergy and intolerance, 1998; p. 250ff)

Food Intolerance

Majority develop because of:
- Poor digestion
- Dysbiosis
- Candidiasis
- Parasites
- Intestinal infections
- Poorly balanced diet
- Alcohol consumption
- Effects of drugs and medications

Symptoms and Signs of Food Intolerance in Children

- asthma, eczema, recurrent otitis media, ADHD +/-, behavioural and learning problems, fatigue, abdominal pain
- Most common offending foods are:
  - eggs, milk, nuts, soy, fish, corn and wheat
Common substances involved in non-immune mechanisms of FI

- Lactose and other disaccharides
- Biogenic amines (histamine and tyramine)
- Salicylates
- Preservatives such as sulfites, benzoates, BHT/BHA
- MSG
- Artificial Colouring especially tartrazine

Janice Vickerstaff Joneja, PhD: Dietary Management of Food Allergies and Intolerances

Plus Common Foods Like:

- Gluten: wheat, oats, barley, rye, triticale
  => gliadinomorphin
- Cow’s Milk: protein casein
  => Casomorphin
- Fish, nuts, seafood, soy
  (American College of Allergy, Asthma and Immunology)

Tyramine Intolerance

- Vasoactive amine

Those sensitive are:
- taking certain medications,
- suffer from migraine headaches,
- suffer from chronic urticaria

Tyramine Intolerance Symptoms

- Pruritis
- Feeling hot
- Flushing of skin
- Sweating
- Chills
- Clamminess
- Lightheadedness
- Hives

Natural Sources of Tyramine

- Aged cheeses, avocado, banana, beer, wine, chicken liver, eggplant, fermented beverages, raspberry, red plum, tomato, vinegar and pickles, wines (esp red), yeast extract, broadbeans, sauerkraut
Migraine – tyramine

- Normally, tyramine ingested in the diet is metabolized by monoamine oxidase in the gut and liver and conjugated by enzymes.
- Patients with dietary migraine have a presumed deficiency in monoamine oxidase and conjugating enzymes, permitting tyramine to be absorbed from the gut into the circulation.
- A vasoconstrictor effect may result, primarily by release of norepinephrine from sympathetic nerve endings.


Histamine Intolerance

- Produced by action of histidine decarboxylase (HDC) on aa histidine
- HDC made by bacteria in the large bowel
- Extrinsic histamine: fish and shellfish guts (2x q20min) => not allergy
- Cheese, alcohol, vinegar, sauerkraut, soy sauce, processed meats (all microbial fermentation products).
- Citrus fruits, strawberry, raspberry, tomatoes, apricot, cherry, plums, eggplant, pumpkin all have histamine present naturally.

How much histamine is excessive?

- Threshold depends on:
  - Genetic origin – defect in catabolism HMT (histamine methyltransferase) and DAO (diamine oxidase)
  - Disease –cirrhosis, viral liver diseases
  - Physiological conditions
  - Medications – first pass liver

Symptoms of Histamine Excess

- Pruritis (skin, eyes, ears, nose)
- Urticaria
- Angioedema
- Hypotension
- Tachycardia
- “Panic attack”
- Chest pain
- Nasal congestion
- Coryza
- Headache
- Fatigue, confusion, irritability
- Abdominal pain

Management

- Reduce histamine-releasing events
- Avoid consumption of histamine-containing and histamine releasing foods and food additives

Salicylate Intolerance

- 5% of population
- 25% of persons sensitive to ASA also react adversely to azo dye tartrazine.
- Depends on dose
- No strong link between ASA sensitivity and salicylate sensitivity
- Found in fruit, veg, herbs, spices and condiments, nuts and seeds.
- Depends on method of farming, type and length of storage.
Salicylate Intolerance

- Unknown exact mechanism of action
- “drug-like effect” on nasal membranes and skin

Salicylate Intolerance Symptoms

- Puritis, rash, hives
- SOB, cough, wheezing
- HA, fatigue, hyperactivity
- Lack of concentration
- Sinusitis, congestion
- Stomach upset
- Swellings of hands, feet and face
- ?ADHD, ADD (Feingold Association)

Management Suggestions

- Avoid unripened fruit and veg
- All fruit and veg should be ripe and thickly peeled
- Avoid outer leaves of leafy veg
- Food lists

Benzoate Intolerance

- Benzoic acid (BA) and sodium benzoate are used to prevent spoilage by microorganisms
- Occur naturally in foods: most berries, prunes, tea, cinnamon, nutmeg, clove and anise, cherry bark and cassia bark.
- Go to liver => + glycine => excreted 100% as hippuric acid
- Benzoyl peroxide used for bleaching =>BA

Benzoate builds up in the gut lumen

- Occurs when
  - Liver detoxication mech. is compromised,
  - Deficiency in pantothenic acid or glycine

  CAUSING: intestinal dysbiosis and weakened mucosal epithelium

Benzoate Intolerance

- Persons sensitive to ASA or suffer from atopic allergies are particularly vulnerable to benzoate sensitivity
- Symptoms: asthma, urticaria, angioedema, headaches, (possible erythema multiforme)
Management

Avoid:
- Natural sources of benzoic acid, processed foods, bleached flour, products containing hydrolysed lecithin: margarine, salad and cooking oils, frozen desserts, chocolate, baked goods.

Sulfite Intolerance

Sulfiting agents are used to:
- Prevent oxidation and browning of light-colored fruits and vegetables such as apples and potatoes
- Prevent black spots on shrimp and lobster
- Control microbial growth in fermenting beverages such as wine
- Prevent decomposition by hindering the growth of bacteria
- Preserve flavor
- Prevent spoilage
- Bleach food starches
- Stabilize and maintain the potency of medications

Sulfite Intolerance

Sulfur dioxide, sodium bisulfite, sodium (hydrogen) sulphite, sodium metabisulphite, and other sulphites - applied to:
- Dried fruit usually treated with sulphur dioxide – no need for labelling (if no SO2 – ‘unsulphured’)
- Also used in alcoholic drinks (not labeled), potatoes, apples, coconut, grape juice, some vinegars, frozen pizza dough, fish, glace fruits, restaurant/take-away foods, packaged foods.
- occur naturally
  - (Brostoff J, Gamlin L. Food allergy and intolerance. p. 313.)

Sulfite Toxicology

1% of population
- Sulfites + water = SO2 (irritates airways)
- hapten eliciting IgE response
- sulfite oxidase deficiency prevents sulfate formation from sulfite.
- Symptoms of sulfite sensitivity include bronchospasm, wheezing, chest tightness, flushing, hypotension, N/V/D, dysphagia, dizziness, LOC
- urticaria, angioedema, abdominal pain, seizures and anaphylactic shock resulting in death

Sulfite Intolerance

- Sulfites can trigger asthma
- In steroid-dependent asthmatic children, the prevalence has been found to be 20%.
- Reactions to sulfites can vary from mild to severe and even fatal bronchospasm in about 5% to 10% of patients with asthma.
- Sensitivity to sulfites is found more often in women than in men

Management

- give asthmatics a food list
- molybdenum deficiency (200 micrograms/d)
- Vit B12 (1-3 grams/day)
- avoid cabbage, garlic, onions, eggs, legumes and brussel sprouts.
Monosodium Glutamate – MSG

Synonyms:
- Sodium glutamate,
- MSG,
- L-glutamic acid,
- monosodium salt
- Hydrolyzed vegetable protein
- Autolyzed yeast
- Whey protein

Monosodium glutamate is added to many foods as a flavor enhancer.
- It is ubiquitous in processed foods,
- It is found in frozen foods, canned soups, salad dressings, processed meats, sauces, and snack foods.
- Occurs naturally in tomato, mushrooms and cheese

MSG Intolerance
- Some asthmatics may have serious reactions to MSG
- Headaches generally appear within 15-60 minutes after ingesting relatively large amounts of MSG.
- MSG is a potent vasoconstrictor, and a vascular basis for the symptoms appears most likely.

MSG Symptoms
- The term Chinese restaurant syndrome was coined after a report associated Chinese food with headache and a group of symptoms, including flushing, paresthesias, sweating, palpitations, weakness and facial swelling, neck ache, blurred vision, N/V, tachycardia, rigors, asthma, depression, irritability, slurred speech, water retention, paranoia.

Management
- Educate Asthmatics
- Ask, ask, ask
- Trisalts
- Check labels
- Vit B6

Tartrazine Intolerance
- Tartrazine (Yellow No. 5) is an approved azo dye present in many food products and even drugs (!)
- Tartrazine sensitivity is most frequently manifested by urticaria and asthma.
- Mechanism of action unknown
Tartrazine Intolerance

- Cross-sensitivity in aspirin-sensitive and NSAID-sensitive patients may also occur.
- Azo dyes in general have been implicated in accentuating hyperkinetic syndromes in children.


Management

- Hyperactivity in children => 6-week open trial of a diet free of synthetic food coloring.
- Behavioral improvement with the diet
- Less irritable and restless, corrected sleep disturbance.
- Therefore avoid commercial pre-made foods


Aspartame

- Marketed under the popular names NutraSweet, Equal, Spoonful and Equal-measure.
- Found in many sugar-free candies, gums and soft drinks
- Aspartame is made up of three chemicals, aspartic acid, phenylalanine and methanol
- Digestion: methanol $\rightarrow$ formaldehyde

Aspartame and migraine

- migraine, epilepsy, and neuropsychiatric problems.
- ‘The evidence is in favor of aspartame as a significant trigger of headaches in migraine, especially when the exposure is prolonged.’


For food intolerance:

1) Elimination of offending foods.
2) Intestinal health with optimal detoxication function achieved through an excellent diet and corrective measures where imbalances exist.
The Immune Barrier

- Throughout length of small intestine => GALT or MALT => sIgA => (def or high antigenic load)
- Gut is the largest immune organ containing over 60% of the cell mass of the immune system
- Complex relationship between intestinal hyperpermeability and adverse food reactions => increasing IgG1 and 4

Honor thy symbionts

- ability to break down otherwise indigestable plant polysaccharides, biotransformation of conjugated bile acids, degradation of dietary oxalates, and synthesis of certain vitamins.
- so we become tolerant of a wide variety of microbial antigens.
- appears to reduce allergic responses to food or environmental antigens.
- [Jian Xu and Jeffrey I. Gordon; Honor thy symbionts. PNAS; 2003; 10452–10459.]

“Welcome to - the leaky gut”

Contribution to gut dysbiosis - hypochlorhydria

- Reduced stomach acid
- ?significance of PPIs/antacids
- Leads to reduced breakdown of proteins in stomach (→ ?allergy/intolerance)
- Failure to inactivate yeast (→ ?fungal type dysbiosis)
- failure to inactivate pathogenic bacteria (→ ? bacterial type dysbiosis – small bowel bacterial overgrowth)

Causes of small intestinal bacterial overgrowth (SIBO)

- Hypochlorhydria or drug induced hypoacidity
- Crohn’s disease
- Diabetes (20-40% of Diabetics with chronic diarrhoea)
- SLE, Scleroderma
- Chronic pancreatitis
- Giardiasis and other parasitic infections
- Malnutrition
- Reduced motility in elderly patients, weight loss in elderly (significant problem)
Other causes of gut dysbiosis

- Antibiotic use (NB. Single course of antibiotics probably not enough to cause significant gut dysbiosis)
- Radiation treatment
- Surgery
- Stress
- Alcohol

Types of ‘gut dysbiosis’

- **Bacterial dysbiosis** (e.g. bacterial overgrowth in small or large intestine)
- Parasitic infections
- Fungal type dysbiosis (controversial!)

Gut Dysbiosis

Signs and Symptoms

- “IBS-like”, bloating, flatulence, D/C, undigested food in stools, food sensitivities, dyspepsia, fatigue, rashes, myalgias, arthralgias
- compromised digestion and absorption
- vit B, iron and calcium deficiencies

Treatment and Prevention:

- Look at diet (sugar intake?)
- prescribe probiotics with antibiotics

The 4 R approach

- **Remove**: bacteria, viruses, fungi, parasite, allergens and toxins
- **Replace**: pancreatic enzymes, HCl, intrinsic factor
- **Reinoculate**: probiotics
- **Repair**: prebiotics, diet, supplements

How to diagnose food intolerance?

Complete list of reliable laboratory tests for food intolerance

- 
- 
- 
-
Only reliable test for food intolerance

**Elimination diet and reintroduction**
- Caveat: not for ‘true’ food allergies, because of the risk of anaphylactic reactions
- Phenomenon of ‘masking’ and ‘unmasking’

Unreliable laboratory tests or investigations for food intolerance
- RAST, Skin prick does not work in food intolerance (non-immunologic)
- ‘Alternative blood tests’ probably not reliable
- ‘Fringe medicine tests’ very problematic (kinesiology, VEGA, etc.)
- BUT – IgG subclasses can be helpful

Management of Food Intolerance
- Elimination diet – one or multiple foods
- Rotation diet
- Confirm with provocation

Management of Food Intolerance
- Eliminate/avoidance => desensitize the body => withdrawal first
- Abduction model *(Claudia Miller)*
- 4-5 day Rotation diet of very unusual foods 30 days later or eliminate longer if reaction still
- **Note:** 1 teaspoon of unbuffered powdered vit C in a glass of water OR Alka Seltzer Gold
Common Foods

Food intolerance in IBS

- Elimination diet relieved symptoms.
- Milk, wheat, eggs and coffee were most frequently identified to cause symptom exacerbation in IBS.

Exclusion diet and IBS- Manchester

- Diet excluding all foods to which they had raised IgG antibodies
- Relaxing the diet led to a 24% greater deterioration in symptoms in those on the true diet (p = 0.003).

Table 1. Frequency of foods excluded from the diet (n of patients)

<table>
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<th>Food</th>
<th>Treatment group</th>
<th>Sham group</th>
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<td>Corn</td>
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<tr>
<td>Yeast</td>
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Food intolerance and RA

- elimination diet excluding milk, eggs, cereals and food additives
- Percentage of patients with severe pain decreased from 40% day and 44% night to 14% (day) and 0% (night) after 6 weeks. The number of painful joints was reduced from 20 to 14 after 6 weeks. There was significant decrease in the length of morning stiffness and increase in grip strength.
- ⅓ of patients described themselves as ‘better’ or ‘much better’.
- Average weight loss due to the diet was over 4.5 kgs.

* (Darlington, LG, Ramsey NW, Mansfield JR. Placebo-controlled, blind study of dietary manipulation therapy in rheumatoid arthritis. Lancet, February 1, 1986; 256:8)

Migraine

- Migraine patients reporting a particular food or drink as a precipitant varies from 7% to as high as 44%.
- prevalence of diet-related migraine varied with race: diet-related migraine prevalence was higher in white patients (61%) than in black patients (35%)
- Most commonly implicated foods are chocolate, cheese, citrus fruit, and alcoholic drinks.

Migraine – food intolerance

- Double-blind trial of an elimination diet in 88 patients treated with a diet that eliminates all but a few sensitizing food antigens.
- 93% with severe frequent migraine responded and were free of headaches.
- The diet consisted of lamb or chicken, rice or potato, banana or apple, Brassica, water, and vitamin supplements.
- **Cow’s milk and cheese** caused headaches in most of the patients in the study, but none of the patients complained of headaches after substituting goat’s milk cheese.


Summary food intolerance

- Probably quite common (20% of population)
- Multiple symptoms in many organs/organ systems that often are considered ‘psychogenic’
- Because of delayed reaction, ‘masking’, and even food craving, often not clear what the offending foods are
- Difficulties in making the diagnosis (controversial)
- Only reliable test exclusion diet and reintroduction (but perhaps IgG)
- However: diagnosis and treatment also possible with a rotation diet.