

Food Allergies



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How Common Are Food Allergies?

- **Perceived:**
 - 25 - 30% of parents believe their children have at least one food allergy
 - 33% of adults believe they have food allergies
- **Actual:**
 - 2 - 8% of children <3 - 6 years have verifiable food allergies
 - 1 - 2% of general population have verifiable food allergies
 - May be higher in selected groups

Why is there such a large discrepancy between true and perceived food allergies?



Challenge of Diagnosing Adverse Food Reactions

12 y/o boy with diffuse diarrhea and abdominal pain after eating a hamburger at a fast food joint.



- 1. Allergic reaction to sesame seed on bun**
- 2. Food poisoning (*E. coli*)**
- 3. Acute viral gastroenteritis (coincidence)**
- 4. Latex from glove of kitchen worker**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- What additional information would you want to know to help distinguish between various causes of adverse reactions to foods?**

Infant “Life Cycle”

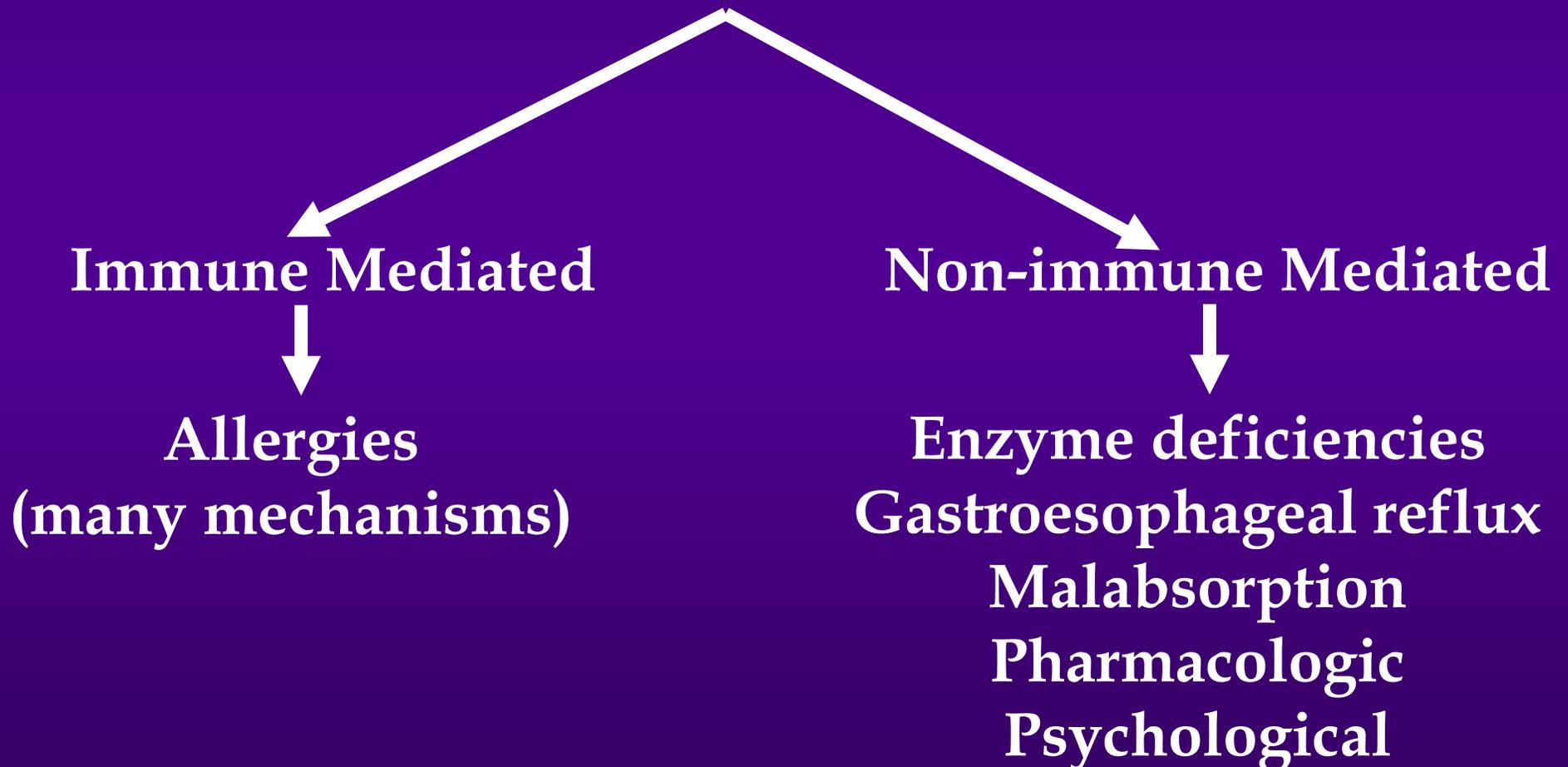


- Feeding & eating are large parts of a infant's life
- Parents will focus first on food as a cause of any problem, whether real or perceived

Some Definitions

- **Adverse food reaction**
 - Any untoward reaction to food or food additive
- **Food Intolerance**
 - Adverse physiologic response to a food or food additive
- **Food allergy**
 - Adverse food reaction due to specific immunologic response

Adverse Reactions to Foods



Possible Causative Factors

- **Food Factors**
 - Something about food, would happen to all or most people who eat the food
- **Host Factors**
 - Something about the person, doesn't happen to most others who eat the food
- **Unknown Factors**
 - Idiosyncratic – can't explain why



Adverse Reaction to Foods

Case Reports – Food Factor

- 17 y/o with impaired motor function/reflexes, disinhibition, disorientation and sedation after 6 cans of beer.

- **DRUNK!**



Case Report

Food Factor - Infant

- **4 month old infant on powdered formula**
- **Mom is illiterate**
- **Child presents with lethargy and seizures. Testing reveals sodium = 113**
- **Water intoxication (dilutional hyponatremia) due to improper mixing of powdered formula**

Adverse Food Reactions

Food Factors

- **Pharmacological**
 - Intrinsic to food
 - Due to preparation
- **Toxic**
 - Exogenous – bacteria, viral, parasitic
 - Endogenous – “poisoning”
- **Additives or contaminants**

Adverse Reaction to Foods

Case Report – Host Factor

- 15 year old complains she is “so fat”
- Exam shows cachectic female
- BMI = 15

- Anorexia



Case Report

Host Factor - Infant

- **3 month old on cow's milk formula develops worsening eczema. Also has mild wheezing with colds**
- **Changed to extensively hydrolyzed formula – improvement in both skin and wheezing**
- **Milk protein allergy**

Adverse Food Reactions

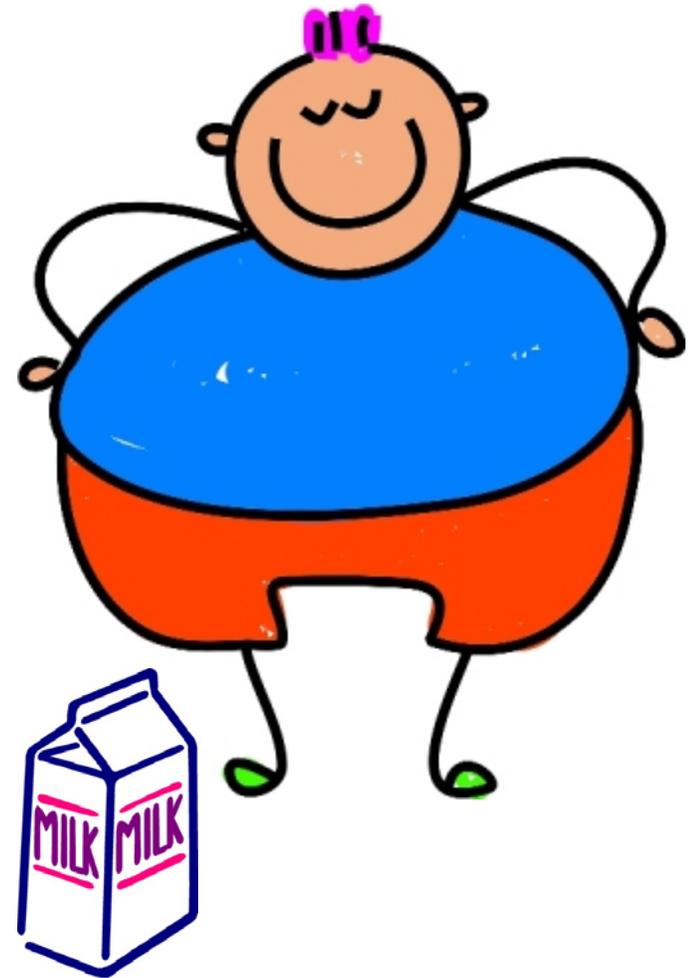
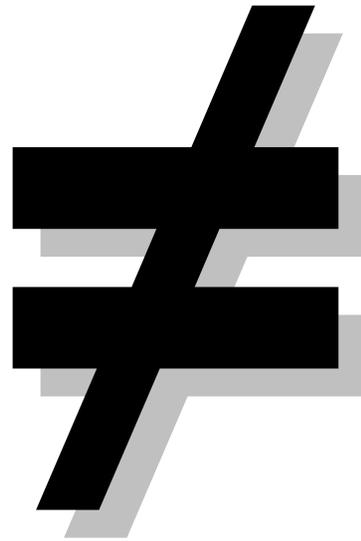
Host Factors

- **Enzyme deficiencies**
 - Lactase deficiency
 - Other oligosaccharidase deficiencies
 - G6PD deficiency
 - + Hemolytic anemia (Fava beans, others)
- **Psychogenic (eating disorders)**
- **Functional**
- **Immunologic**

Immune System

- **A major function of the immune system is to differentiate ‘self’ from ‘non-self’**
 - **For example – recognizing a bacteria as ‘non-self’ and killing the bacteria**

A Cow Is Different From A Person



Food Allergy

The Dilemma

Food is a foreign substance and may therefore stimulate an immune response designed to repel it, but food must be tolerated so it can be processed and absorbed by the gastrointestinal tract for nutrition.

Immune System

- A major function of the immune system is to differentiate ‘self’ from ‘non-self’
 - Also to distinguish between “harmful” and “harmless” foreign substances
 - + Eliminate harmful substances
 - + Ignore harmless substances

Food Allergy

Oral Tolerance

A combination of physiologic and active immunologic mechanisms which allow for the processing and absorption of food for nutrition without generating a detrimental immune response.

Nutrition for Allergists

- **Every food can be divided into 3 components:**
 - **Proteins**
 - **Carbohydrates**
 - **Fats**

Component Intolerances

Major Pediatric

- **Protein**
 - Allergic (immunologic) reactions
- **Carbohydrates**
 - Enzyme (disaccharidase) deficiencies
- **Fats**
 - Exocrine pancreatic / gallbladder deficiencies
- **Other GI diseases may result in intolerance of all components**

Food Allergy

The Big 8 (5*)

- **Children***
 - egg, milk, peanut, soy, fish, wheat
- **Adults**
 - nuts, peanuts, fish, shellfish
- **These 8 (5*) foods account for ~>90% of all food allergies**

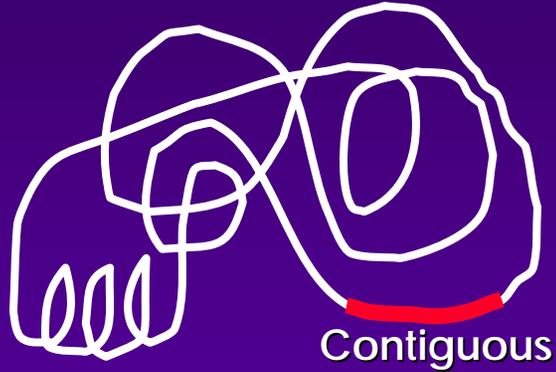
Major Proteins in Food Allergy in Infants

- **Cow's milk**
- **Soy**
- **If breast feeding – anything mom is eating**

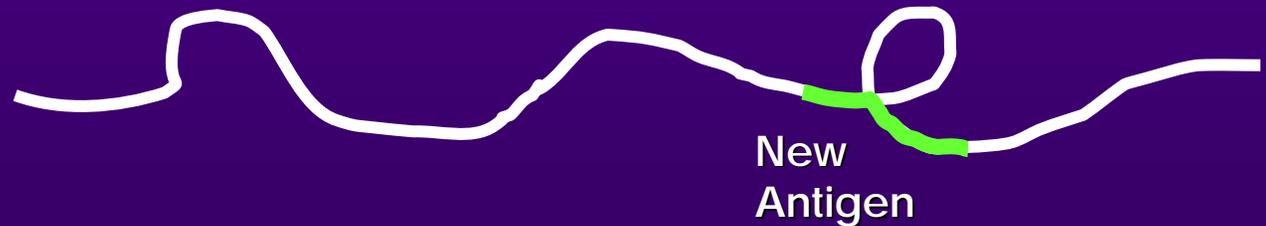
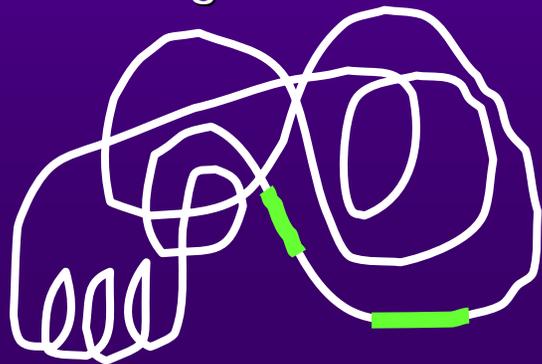
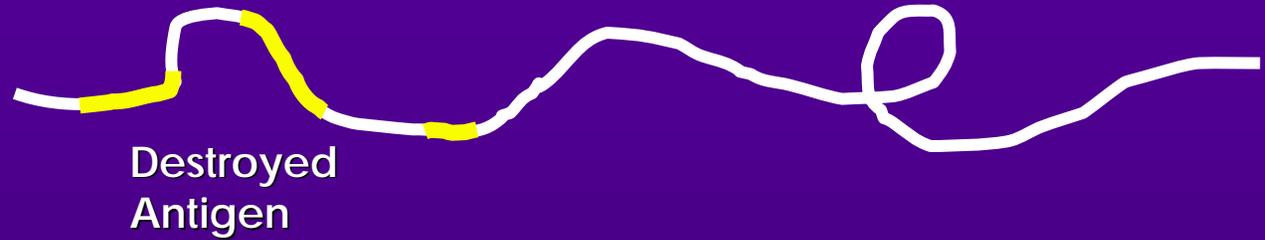
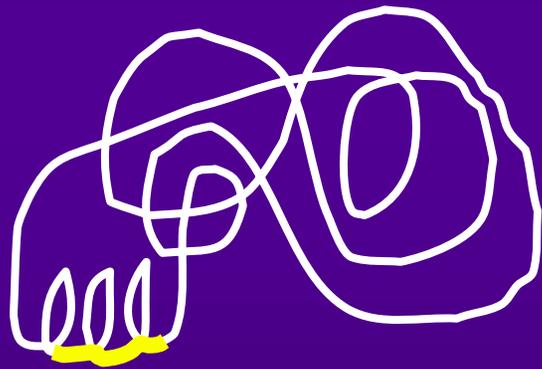
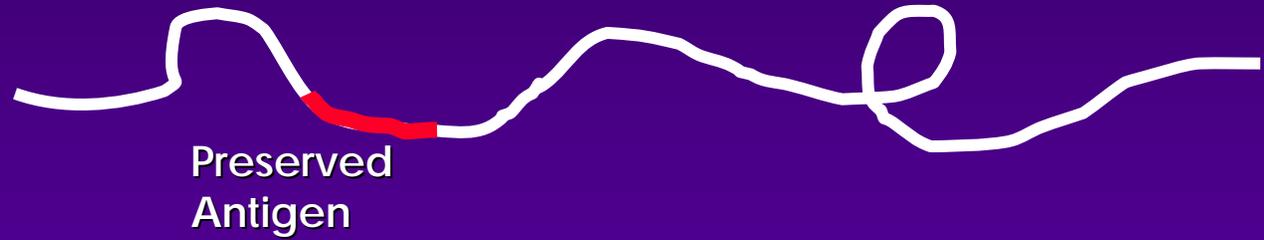
Eggsplain This

- **2 year old develops generalized flushing and hives within minutes after eating one fork-full of scrambled eggs**
 - **Similar reactions to mayonnaise, raw egg touching the skin**
- **Can eat ‘unlimited’ cookies and cakes and pasta with egg as an ingredient**

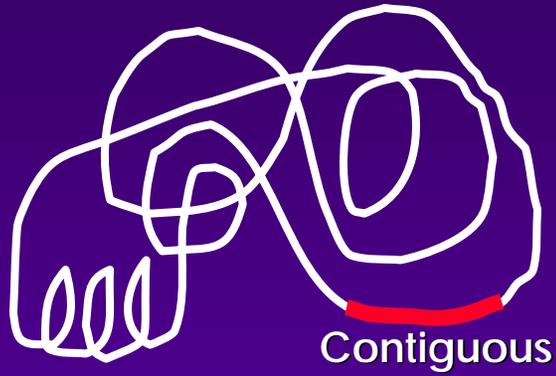
Native Antigen (food)



Processed Antigen (cooked food)



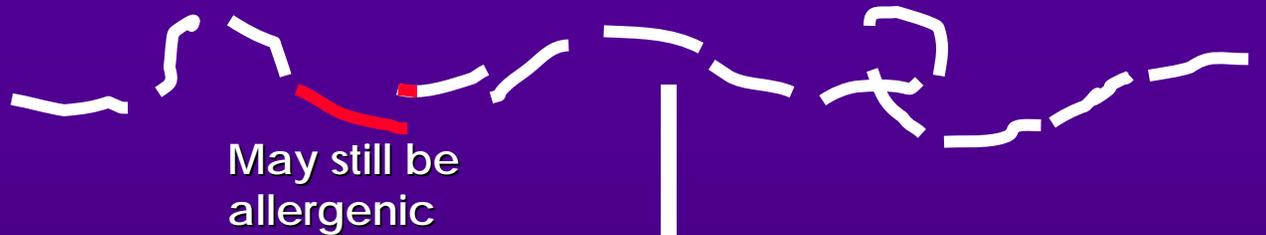
Native Antigen



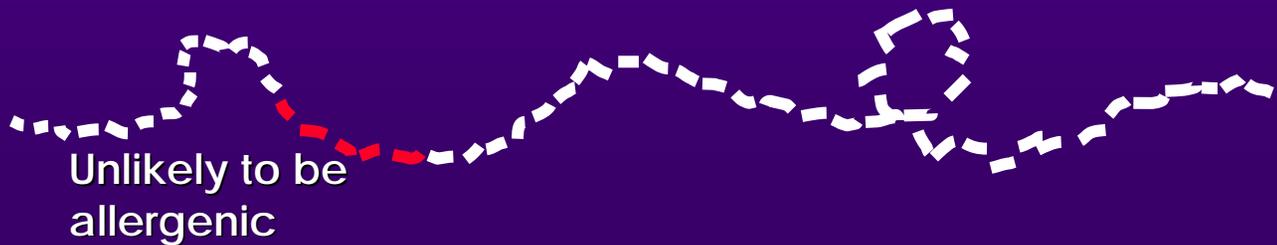
Processed Antigen



Partially Hydrolyzed



Extensively Hydrolyzed



Food Allergy Symptoms

- **Anaphylaxis – life threatening symptoms**
- **Skin**
- **Respiratory Tract**
- **Gastrointestinal**
- **Other**
 - **Cardiovascular, central nervous system**

Respiratory Symptoms

Danger Signs

- **Symptoms of upper respiratory tract**
 - Stridor (like croup)
 - Voice change (soft, hoarse, high pitched, none)
 - Difficulty swallowing, drooling, distress (cyanosis)
 - Sensation of lump in throat, food stuck in throat, itch/pain in throat, tight throat
- **Symptoms of lower respiratory tract**
 - Wheezing (like asthma)
 - Coughing, shortness of breath, distress (cyanosis)
 - Sensation of squeezing or tightness in chest

Auto-injectable Epinephrine

- **Any person who has had a life-threatening, or potentially life-threatening (systemic) reaction to a food should be prescribed auto-injectable epinephrine.**
- **Complete avoidance of that food**
 - **In any form**
 - **In any quantity**

EpiPen



Twinject



Food Allergy

Common Skin Problems

- **Urticaria (hives) / angioedema**
- **Atopic dermatitis / eczema**
- **Dermatitis herpetiformis**
 - **Celiac disease**

Urticaria (Hives)



Angioedema



Atopic Dermatitis (Eczema)







Dermatitis Herpetiformis (Celiac Disease)



***Dermatitis Herpetiformis
(Celiac Disease)***



Celiac Disease

- **Immune-mediated sensitivity to gluten**
 - Wheat, barley and rye
 - Anti-tissue transglutimase IgA, anti-gliadin IgA/IgG, not IgE
- **GI \pm extra-intestinal \pm no symptoms**
 - Varied presentation
- **Genetic susceptibility**
 - HLA DQ2 and/or DQ8 in 98%

Food Allergy

Common Respiratory Problems

- **Rhinitis & conjunctivitis**
 - “Hayfever”- like symptoms
- **Laryngeal edema**
 - Throat swelling
- **Asthma**

Laryngeal Edema Due to Allergic Reaction



Laryngeal Edema Due to Allergic Reaction



Food Allergy

Common Gastrointestinal Problems

- **Nausea / vomiting / diarrhea / pain**
- **Colitis / enterocolitis**
 - **Blood in stools**
- **Eosinophilic gastroenteritis**
 - **Diarrhea, failure to thrive**
- **Celiac disease**
 - **Diarrhea, failure to thrive, non-GI symptoms**
- **?Chronic constipation in infants**
- **?Infantile colic**

Why are Infants Different?

- **Limited diversity of foods**
 - Mostly formula and breast milk, “first stage”
- **Limited accidental exposures**
 - Eat what parents give them
- **Limited differential diagnosis**
 - Many GI diseases present at older age
- **Limited alternative food options**
 - Many foods are not age appropriate

Infant Formula Types (in terms of Allergenicity)

- **Milk protein based (standard)**
- **Soy protein based**
- **Partially Hydrolyzed**
- **Extensively Hydrolyzed**
- **Elemental (amino acid)**

Milk Protein Based (standard)

- **Protein Source: nonfat milk (casein & whey)**
- **Indications: normal GI tract, most healthy infants**
- **Lactose containing**

Similac Advance

Enfamil Lipil

Store brands (Wyeth)

Soy Protein Based

- Protein source: Soy protein isolate
- Indications: Known milk allergy
- **Not hypoallergenic**
- **Lactose free**

- Prosobee Lipil (MJN)
- Isomil Advance (Ross)
- Good Start Soy (partially hydrolyzed)
(Nestles)

Partially Hydrolyzed (milk based)

- **Protein source: 100% whey or predominant whey based**
- **Indications: reflux, delayed gastric emptying, mild feeding intolerance**
- **Not hypoallergenic**
- **Lactose containing**
 - **Good Start Supreme (100% whey) (Nestles)**
 - **GentleEase (predominant whey & casein) (MJN)**

Extensively Hydrolyzed

- **Protein Source: Casein Hydrolysate + Amino Acids**
- **Indications: milk/soy allergies, disorders of digestion, absorption and metabolism**
- **Hypoallergenic**
- **Lactose free**
 - **Nutramigen (5% MCT oil) (MJN)**
 - **Alimentum (33% MCT oil) (Ross)**
 - **Pregestimil (55% MCT oil) (MJN)**

Elemental

- Protein source: free amino acids
- Indications: severe allergies, malabsorption syndromes, GI disease
- Hypoallergenic
- Lactose Free
 - Elecare (33% MCT oil) (Ross)
 - Neocate Infant (5% MCT oil) (Nutricia)

“Hypoallergenic” Formula

- **AAP definition**
 - **95% confidence that at least 90% of children with cows milk allergy will tolerate the Partially Hydrolyzed formula**
 - **Nutramigen**
 - **Alimentum**
 - **Pregestimil**

More about Soy Formulas

- **Soy protein formulas are no less allergenic than cows milk protein formulas**
- **Most infants/children with IgE mediated cow's milk allergy (86%) can tolerate soy based formula**
- **But among those non-IgE mediated cow's milk allergy almost 50% react to soy and require an extensively hydrolyzed formula**

Potential Allergenicity of Hydrolysates

- **Residual proteins in the hydrolysates may cause adverse symptoms in highly allergic patients**
- **For this subset of patients, treatment with an Amino Acid based formula is required**
- **Neocate Infant**
- **Elecare**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- What additional information do you want?**

What To Ask - I

- **Other symptoms?**
 - Skin, respiratory
- **Specific GI symptoms**
 - Gas/distension, diarrhea, emesis
 - Details of diarrhea – blood, fatty, white blood cells, eosinophils
- **Time of onset between eating and symptoms**
 - Immediate, several hours, day

What To Ask - II

- **Reproducibility / Consistency**
 - Symptoms present every time food eaten
 - Symptoms absent if food is not eaten
- **How much food needed to trigger symptom**
 - A few drops or a large quantity
- **Progression over time**
 - Getting worse or getting better
- **Response to changes in diet**
 - Predictable or random

What To Ask - III

- **Family history**
- **Fever, sick contacts?**
- **Growth parameters?**
- **Other symptoms**
 - **Developmental delay, recurrent infections,**

History Suggesting Allergy

- **Fairly immediate onset of symptoms**
 - Usually minutes, occasionally 1-2 hours, rarely several hours
- **Non-GI symptoms (skin, respiratory)**
 - But can be only GI
- **Happens each time food is eaten**
- **Symptoms do not occur if food is not eaten**
- **Very small amounts can trigger symptoms**

History Suggesting Non-Allergy

- **Delayed onset of symptoms**
 - Day or days
- **Only occurs with large quantities or “cumulative” effect over days**
- **Occurs when food is stopped**
- **Doesn’t occur each time food is eaten**
- **Atypical symptoms (“hyper”, bruising, fever, etc).**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Symptoms seem to be worse between 4pm to 9pm every day, and are better in the morning
- Initially on Similac for 3 weeks, changed to Isomil for 3 weeks, then to Good Start for 4 weeks, then to Nutramigen for 2 weeks and the symptoms resolved
- How likely is this to be a food allergy?
- What is most likely diagnosis?

Infant Case Report

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• Why did this baby get better?

• 3 week + 3 weeks + 4 weeks + 2 weeks = 12 weeks!

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Taking Enfamil[®], and when switched formula to Similac[®], symptoms resolved.**
- How likely is this to be a milk protein allergy?**
- What is the formula that should be used in these cases?**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Symptoms occur about 3-4 hours after meals, just prior to next feeding. Mom wants to try rice milk.**
- How likely is this to be a food allergy?**
- What about rice milk?**

What's The Difference Between Rice Milk and Coca Cola?



One is essentially sugar water with negligible other nutrients and has no place in the diet of infants

The other is a carbonated soda

Other Types of Milk?

- **Rice Milk**
 - Good source of Calcium (when enriched)
 - Low in protein
 - Low in fat
 - Low in most other nutrients
- **Goat's Milk**
 - >50% proteins cross react
 - Not acceptable alternative

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Child has eczema which worsens after meals**
- Very strong family history of allergic diseases**
- Mom switched to rice milk for a week, and symptoms improved**

- How likely is this to be a food allergy?**
- What formulas are options for this child?**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Other symptoms include frequent emesis**
- Changed from cow's milk to soy to elemental formula and threw up all. Throws up Pedialyte**
- How likely is this to be a food allergy?**
- What is most likely diagnosis?**

The Burp Gone Bad



Gastroesophageal Reflux

Gastroesophageal Reflux

Symptoms

- Vomiting (emesis, spitting up, wet burp)
- Irritability
- Arching
 - Sandifer syndrome
- Poor weight gain
- Dysphagia, anemia, hematemesis if severe
- Can be associated with respiratory symptoms
 - Cough, asthma, pneumonia, aspiration, croup, ears
 - ALTE (apparent life threatening event)
- NO skin

Gastroesophageal Reflux Incidence

- **50% of infants ages 0-3 months regurgitate at least once daily**
- **5% by age 12 months**
- **Over 3 years old, 1.5-8.2% have significant GERD**
- **Rarely is primarily due to food allergies and should not respond to formula changes**

Infant Case Report

3 month old baby boy is currently being fed with a commercial baby formula. He presents with irritability associated with feedings.

- Problems started after rotavirus diarrhea. Since then has lots of gas and loose stools.**
- No skin or respiratory sx's, no emesis**
- How likely is this to be a food allergy?**
- What is most likely diagnosis?**

Lactase Deficiency

- **Lactase** is enzyme found in brush border of small intestine, on tips of microvilli → cleaves **lactose**
 - Lactose – disaccharide (glucose + galactose), carbohydrate in cow's milk
 - Undigested lactose: osmotic load and substrate for large bowel bacteria → volatile fatty acids and gases

Lactase Deficiency

- **Congenital lactase deficiency is very rare.**
- **Primary lactase deficiency usually presents >3 years, usually later**
- **May have transient lactase deficiency after an acute GI disease (i.e. viral gastroenteritis)**
 - **“Shearing off” of tips of microvilli.**
 - **May take several weeks, or longer, to grow back**

Lactase Deficiency

Symptoms

- **Abdominal distension**
- **Flatulence**
- **Abdominal cramping**
- **Diarrhea**
- **Irritability, crying, weight loss if severe**
- **Dose dependent**
- **NO vomiting**
- **NO skin rash or respiratory symptoms**

Food Allergy--Diagnosis

- **History**
 - food diaries
- **Elimination Diets**
- **Allergy Testing**
- **Food Challenges**
 - double blind placebo controlled
 - other

A Matter of Degree

- A 1 year old child presents with a food RAST of 0.36 kU/L
 - Reference range is <0.35 to >100 kU/L
- Is the patient allergic to the food at a RAST level of 0.36?
- How about ~~0.36~~?

Predictive Values for CAP RAST for Children with Suspected Food Allergy

Food Protein	90% Spec. (kU_A/L)	PPV %	95% NPV (kU_A/L)	90% NPV (kU_A/L)
Egg	7 (2*)	98	-	0.6
Milk	15 (5*)	95	0.8	1
Peanut	14	95	Best NPV = 85% @ 0.35	Best NPV = 85% @ 0.35
Fish	20	100	0.9	5
Soy	30	73	2	5
Wheat	26	74	5	9

* = ≤ 2 year old

Interpreting RAST's - Examples

- **5 yr old with egg RAST = 2 kU/L: 50%PPV**
- **5 mo old with egg RAST = 2 kU/L: 95% PPV**
- **Normal: 75% PPV for wheat: RAST = 26 kU/L**
- **Eczema: 75% PPV for wheat: RAST = 100 kU/L**
- **H/O peanut rxn: 50% react @ RAST = 2 kU/L**
- **No peanut rxn: 50% react @ RAST = 5 kU/L**

Interpreting RAST's

- **Few foods for which there are RAST's that accurately predict clinical reactivity**
 - Milk, egg, fish, peanuts, (tree nut, soy, wheat)
 - Even these not 100% accurate
- **Other foods – no data or poor correlation**
- **Clinical correlation is essential**
 - Use to confirm/negate suspected reaction
 - Use as a guide to challenges or de-challenges

Ten Steps to Treating Food Allergies

1. Avoidance
2. Avoidance
3. Avoidance
4. Avoidance
5. Avoidance
6. Avoidance
7. Avoidance
8. Avoidance
9. Avoidance
10. Avoidance
11. Everything else

Avoidance

- **Avoid every form of the food**
 - For example: milk, Lactaid milk, ice cream, cheese, cottage cheese, cream cheese, sour cream, yogurt, milk chocolate, etc.
- **Avoid any quantity of food**
 - No amount is safe (especially if severe)
 - “Processed in plant that contains....”
- **Avoid all the time**
 - Home, school, field trips, restaurants, friends, relatives, etc.

Infant Case Report

3 month old baby is being fed with breast milk supplemented with cow's milk formula.

- Diagnosed with atopic dermatitis and early asthma**
- Allergy test is positive for milk**
- Mom decides to switch to only breast feeding and stop formula**

- What should you advise mom regarding her diet?**

Sensitization via Breast Milk

~70-80% of peanut allergic individuals have reactions to peanuts on first known exposure

- **“Occult” sensitization occurs via breast milk**
- **Peanut protein detected in ~50%**
 - **Un-degraded major allergens Ara 1 & Ara 2**
 - **average peak 200 ng/ml**
- **Rapid appearance (1-3 hours), peak (2-3 hours) and disappearance (3-4 hours)**
 - **time course is varied in individuals**
 - **similar findings with egg (ovalbumin), milk (β -lactoglobulin) and wheat (gliadin)**

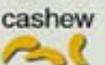
Case Study

- **A 1 year old has severe cow's milk allergy. Mom wants to try goats milk**
- **A 3 year old has anaphylaxis to chicken eggs. Parents ask if duck or goose eggs are OK**
- **A 15 month old child has wheat allergy. Family read that millet, quinoa, amaranth, teff, spelt, emmer, einkorn and Kamut[©] are OK for wheat allergic individuals**

Species

- **Cow's milk cross reacts with goat, sheep, (horse OK!)**
- **Chicken eggs cross react with turkey, duck, goose and seagull**
- **Wheat cross reacts with other "wheats" such as spelt, Kamut[©], emmer, einkorn**

Clinical Cross Reactivity

If Allergic to:	Risk of Reaction to at Least One:	Risk:
A legume* peanut 	Other legumes peas  lentils  beans 	5% 
A tree nut walnut 	Other tree nuts brazil  cashew  hazelnut 	37% 
A fish* salmon 	Other fish swordfish  sole 	50% 
A shellfish shrimp 	Other shellfish crab  lobster 	75% 
A grain* wheat 	Other grains barley  rye 	20% 
Cow's milk* 	Beef hamburger 	10% 
Cow's milk* 	Goat's milk goat 	92% 

If Allergic to:	Risk of Reaction to at Least One:	Risk:
Cow's milk* 	Mare's milk horse 	4% 
Pollen birch  ragweed 	Fruits/vegetables apple  peach  honeydew 	55% 
Peach* 	Other Rosaceae apple  plum  pear  cherry 	55% 
Melon* cantaloupe 	Other fruits watermelon  banana  avocado 	92% 
Latex* latex glove 	Fruits kiwi  banana  avocado 	35% 
Fruits kiwi  avocado  banana 	Latex latex glove 	11% 

Food Allergy--Natural History

- ***Most young children will outgrow most food allergies***
 - type of food
 - severity of reaction
 - immune mechanism
- ***Some older children / adults may lose sensitivity over time***
 - re-exposure to food
- ***Some allergies are “forever”***

Food Allergy--Prevention

- **Can food allergies be “prevented” or only postponed” or nothing at all?**
- **Areas to consider:**
 - Identifying “high-risk” families
 - What can mom do during pregnancy?
 - Should breast feed or bottle feed?
 - If breast feeding, what can mom do with her own diet while she is breast feeding?
 - How long should child be breast fed?
 - If formula started, what formula(s) should be used?
 - When can foods other than formula be started, and in what order should they be introduced?

An Ounce of Prevention

- **A 23 year old female has a 6 month and a 23 month old who both have eczema and are severely allergic to cow's milk, egg and wheat. She is now 3 month pregnant.**
- **What dietary recommendations can you give to mom?**

- **Identify High Risk Infant**

- Pre- or early post-birth

- Clinical, atopic family, cord blood IgE

- **Avoid Infant Exposure to**

- **Food Allergens**

- + In pregnancy
- + In breast milk
- + In Infant diet

- Not recommended (peanuts?, seafood?)

- Possibly (peanuts + seafood + other?)

- Breast feed at least 4-6 months

- Supplement with hypoallergenic formula

- * Extensively hydrolyzed or amino acid

- * Partially hydrolyzed formulas

- Delay solids until 6 months

- * Add least allergenic 1st

- Add new food biweekly or monthly (cows milk @ 9-12 mo; egg @ 1 yr; peanuts, nuts, fish @ 3 yrs)

- **Non-Specific Adjuvants**

- No smoking pre-/post-pregnancy

- Reduce exposure to pollutants



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*“... and since you're a lactose intolerant borderline diabetic
I think you should cut out the milk and cookies.”*