Dietary Management of Paediatric Food Allergy

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# Most Common Allergens Relative to Peak Age of Food Sensitivity

[Hannuksela, 1983]

<table>
<thead>
<tr>
<th>Years</th>
<th>Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>Milk, Soy, Egg, Fish, Pea, Banana,</td>
</tr>
<tr>
<td>2-7</td>
<td>Egg, Fish, Nuts, Apple, Pear, Plum, Carrot,</td>
</tr>
<tr>
<td></td>
<td>Celery, Tomato, Spices</td>
</tr>
<tr>
<td>Over 7</td>
<td>Fish, Nuts, Apple, Pear, Plum, Carrot, Cel</td>
</tr>
<tr>
<td></td>
<td>ery, Tomato, Spices</td>
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</tbody>
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Development of Tolerance
[Sampson et al, 1989]

To Specific Foods:

• **After 1 year:**
  – 26% decrease in allergy to:
    • Milk
    • Egg
    • Soy
    • Peanut
    • Wheat
  – 2% decrease in allergy to other foods

• **Allergy to some foods more often than others persists into adulthood:**
  – Peanut
  – Shellfish
  – Soy
  – Tree nuts
  – Fish
Development of Tolerance

Incidence:
After 1 year:
- 25% of infants lost all food allergy symptoms

• After 2 years
  - 9% more infants lost food allergies
Prognosis

- Most infants will outgrow milk allergy by 3 years of age, but may become intolerant to other foods
- About 25% will develop respiratory allergies

[Study: Bishop et al 1990]

- Age at which milk was tolerated by milk-allergic children:
  - 28% by 2 years of age
  - 56% by 4 years of age
  - 78% by 6 years of age

- Additional observations of children studied:
  - 50% were also allergic to egg and soy
  - 30% to peanut
Cow’s Milk Allergy (CMA) as a model for food allergy in children

- Associated with a variety of different medical conditions
- Mechanisms responsible are not all understood
- Include IgE-mediated and non-IgE mediated reactions
- Known collectively as CMA
Symptoms and Mechanisms Responsible for CMA

IgE-mediated reactions include classical allergy symptoms:
- Urticaria (hives) - Exacerbation of eczema
- Wheezing - Cough

Non-IgE-mediated reactions include:
- Colic - Abdominal pain
- Nausea - Vomiting
- Diarrhea

• Children with IgE-mediated allergy with eczema may experience only gastrointestinal symptoms on challenge
Suggested Classification Scheme for CMA

[Hill et al, 1986]

Group 1: Immediate Reactors
- Reaction within 45 minutes after milk ingestion
- Symptoms include urticaria, angioedema, exacerbation of eczema, cough, wheeze, vomiting
- Skin test positive (STP) to CMA
- Elevated IgE to CMA by RAST or ELISA
IgE-mediated Reaction

Typical scenario of first reaction to cow’s milk or other food allergen:
• Infant refuses to take more after first taste
• Cries as if in pain
• Swelling of lips, tongue, and mucous membranes of throat in 1-2 minutes
• May be followed by laryngeal edema (throat constriction)
IgE-mediated Reaction continued

- May be accompanied by wheezing
- Occasionally urticaria spreads over entire body
- In severe cases shock may occur
- Usually spontaneous recovery in 15-60 minutes
- Infant appears exhausted after reaction
Suggested Classification Scheme for CMA

Group 2: Intermediate Reactors
- Reaction 45 minutes to 20 hours after milk ingestion
- Symptoms include vomiting, diarrhea
- Skin test negative to cow’s milk allergens
- Insignificant elevation of IgE to cow’s milk in RAST or ELISA
Suggested Classification Scheme for CMA

Group 3: Late Reactors

- Reaction more than 20 hours after milk ingestion
- Symptoms include diarrhea, colic, with or without wheezing, with or without exacerbation of eczema
- Those with eczema skin test positive to cow’s milk allergens
- Insignificant elevation of IgE to cow’s milk in RAST or ELISA
Cow’s Milk Antigens

- More than 25 proteins in cow’s milk can induce antibody production in humans
- $\beta$-lactoglobulin (in whey), casein, and bovine serum albumin are the most important antigens
- Clinical reactions have occurred to all the major cow’s milk antigens
- Some are heat-stable: allergic persons cannot tolerate boiled milk
- Some are heat-labile: allergic people can tolerate boiled milk
Milk Antigens from Other Species

Goat Milk
• Many goat’s milk proteins cross-react with cow’s milk proteins
• The majority of children allergic to cow’s milk are or will become allergic to goat’s milk
• Goat’s milk is deficient in folate

Mare’s Milk
• Fewer proteins are similar to cow’s milk proteins
• In research studies, most milk allergic children tolerated mare’s milk (25 children +CMA; 1 + Mare milk)
Lactose Intolerance

- Caused by a deficiency in the enzyme (lactase) that digests milk sugar (lactose)
- Is not the same as milk allergy
- Milk proteins can be tolerated
- Foods and beverages free from lactose need not be avoided
Symptoms of Lactose Intolerance

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

1. **Congenital alactasia**: *evident from birth*
   - Rare inherited condition

2. **Idiopathic lactase deficiency**: *natural attrition*
   - 80% of the world’s adult population have some degree of lactose intolerance, which usually appears in adolescence
   - There is normal lactase production in childhood

3. **Secondary lactase deficiency**: *temporary condition*
   - Common in early childhood often as a result of digestive tract infection
   - Lactase returns to normal levels after cell injury resolves
Management of Lactose Intolerance

• Only the milk sugar, lactose, needs to be avoided
• Milk proteins are tolerated
• Lactose occurs in the whey (liquid) fraction of milk
• Milk products free from lactose and free from whey are safe
• These foods include:
  – Milk treated with lactase (Lactaid®; Lacteeze®)
  – Hard cheeses (whey is removed; casein remains and is fermented to form cheese)
  – Many people tolerate yogurt, where lactose is broken down by bacterial enzymes
Tests for Food Allergies

• There is no single laboratory test that will diagnose food allergy
• All tests must be confirmed by elimination and challenge
• Tests in common use include:
  – Skin prick
  – Patch tests
  – Blood tests for elevated food-specific IgE (RAST; ELISA)
• In research studies
  – Elevated serum cationic protein
  – Basophil histamine release
Recent Research Studies on Diagnosis of Food Allergy in Infants

(Saarinen et al 2001)

- 6209 unselected infants followed from birth for development of cow’s milk allergy: 118 positive by challenge (1.9%) at 6.9 months

- Four tests used:
  - Skin test
  - Patch test
  - Elevated IgE to cow’s milk proteins (RAST)
  - Elevated eosinophil serum cationic protein

- Conclusions:
  - No single test or combination of all four tests could predict the challenge outcome acceptably
  - A negative response to all four tests does not rule out the possibility of cow’s milk allergy
Diagnosis of Food Allergy in the Infant: Elimination and Challenge

• Reliable diagnosis is based on elimination and challenge:
  – All sources of suspect foods are eliminated from the infant’s diet, and from the mother’s diet if the child is breast-fed
  – Symptoms of allergy in the infant resolve
  – Identical symptoms occur during food challenge
  – Symptoms again disappear on elimination of all sources of the suspect food
  – In suspected CMA, lactose intolerance must be ruled out
Identification of Food Allergies:
Stage 1: Food and Symptom Record

For a 5-7 day period, record the child’s:

- Intake of all:
  - Foods
  - Infant formulae
  - Supplements

- Include the **time** at which each was taken, **amount** taken, and **ingredients**

- The **intensity** of the child’s symptoms rated on a scale of 0 - 4

- **What time** the symptoms occur

- **How long** they last
Stage 2: Elimination Diet

Based on:
- Detailed medical history
- Analysis of exposure diary
- Any previous allergy tests
- Foods suspected by the parents or guardian

• Formulate diet to exclude all suspect allergens and intolerance triggers
• Provide excluded nutrients from alternative sources
## 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
Selective Elimination Diets

• Certain conditions tend to be associated with specific food components
• Suspect food components are those that are probable triggers or mediators of symptoms
• Examples:
  – Eczema: Highly allergenic foods
  – Migraine: Biogenic amines
  – Urticaria/angioedema: Histamine
  – Chronic diarrhea: Disaccharides
  – Asthma: Cyclo-oxygenase inhibitors; Sulphites
  – ADHD: Artificial food colours (e.g. tartrazine)
Food Allergy and Eczema

• Representative study (Burks et al 1998):
  – 165 children with eczema
  – Mean age 4 years
  – 7 foods accounted for 89% of positive challenges
    Milk   Egg   Peanut   Soy
    Wheat  Fish  Tree nuts
  – 27% of subjects also exhibited gastrointestinal symptoms
  – Other studies show similar results
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Atopic Eczema/Dermatitis Syndrome: (AEDS)

• Food allergy has a role in at least 20% of AEDS in children under 4 years.
• In IgE-mediated cow’s milk allergy with AEDS, resolution of CMA occurs in 90% by 4 years of age, but AEDS may persist.
• Non-IgE-mediated CMA usually resolves by 1 year.
• 45% develop sensitivity to other foods at the same time.
• Reactions to aeroallergens develop in:
  – up to 28% by 3 years
  – up to 80% by puberty
Basic Hypoallergenic Elimination Diet

- Only listed foods are allowed
- No vitamin supplements or non-essential medications

- **GRAINS:**
  - White rice
  - Tapioca

- **FRUITS:**
  - Pears; pear juice
  - Cranberries; cranberry juice

- **VEGETABLES:**
  - Squash (all varieties)
  - Carrots
  - Parsnips
  - Lettuce

- **MEAT:**
  - Lamb
  - Wild game
  - Turkey
Basic Hypoallergenic Elimination Diet

- **MEAT**: Lentils
  **SUBSTITUTES**: Split pea
  Garbanzo beans (chick peas)

- **FLAVOURINGS**: Sea salt

- **BEVERAGES**: Distilled water in glass containers

- **OILS**: Canola oil
  Olive oil
  Safflower oil

- **OTHER**: Agar-agar (Make jelly dessert s)
Duration of the Elimination Diet

• A selective elimination diet with nutritionally equivalent substitutes is followed for four weeks
  – Four weeks seems to be optimum for remission of symptoms and for elicitation of symptoms on challenge
• The “Basic Hypoallergenic (few foods) Diet” is nutritionally inadequate and should not be followed for longer than 10 to 14 days
Expected Results of Elimination Diet

• Symptoms sometimes worsen on days 2-4 of elimination

• By day 5-7 symptomatic improvement is experienced

• Symptoms disappear after 10-14 days of exclusion
Challenge

• Use incremental dose challenge (SIDC) to each eliminated food in its purest form to determine:
  – Immediate reaction
  – Delayed reaction
  – Degree of tolerance (dosage)

• Do not test any food suspected to have caused a severe or an anaphylactic reaction except under medical supervision in a facility equipped for resuscitation
Challenge

- The basic elimination diet, or therapeutic diet, continues during this phase.
- Challenge the breast-fed infant through mother’s milk as previously described.
- Add foods causing no adverse reaction when all tests in a single food category have been tested.
  - e.g. Add milk when all tests in the “milk category” have been completed.
Diagnosis of Food Allergy in the Infant Stage 3: Challenge

• Challenge is implemented two to four weeks after elimination of all suspect food allergens
  – Before feeding, smear the food on the infant’s cheek and observe for reddening
  – Place a drop of the food on outer border of infant’s bottom lip; observe for 20 minutes for reddening, irritation
  – Place a drop on the infant’s tongue and monitor for symptoms for an hour
Incremental Dose Challenge

**Day 1:**

- **Morning:** Give a small quantity of the test food
  
  Wait four hours, monitoring for adverse reaction; if no symptoms:

- **Afternoon:** Give double the quantity of test food eaten in the morning.

- Wait four hours, monitoring for any adverse reactions; if no symptoms:

- **Evening:** Give double the quantity of test food eaten in the afternoon
Incremental Dose Challenge

Day 2:

• Do not give any of the test food
  – Continue the elimination diet

• Monitor for any adverse reactions during the night and day. This may be due to a delayed reaction to the test food

• If an adverse reaction to the test food occurs at any time during the test: *STOP*.
  – Do not continue the test food

• Wait 48 hours *after all symptoms have subsided* before testing another food
Incremental Dose Challenge

Day 3:

- *If no adverse reactions* have been experienced proceed to a new food

- **If the results of Day 1 and/or Day 2 are unclear:**
  - Repeat Day 1, using the same food, the same test protocol, but larger doses of the test food

Day 4:

- Monitor for delayed reactions as on Day 2
Management of Food Allergy
Stage 4: Maintenance Diet

• The ideal feeding regimen for an allergic baby is mother’s breast milk devoid of all of mother’s and infant’s food allergens
• If baby is allergic to milk, protein hydrolysate infant formulae may be tolerated; however they are expensive and bitter-tasting
• Some hydrolysate formulae can induce anaphylaxis because of large molecular weight peptides
Infant Formulae

- Many infant formulas are casein-predominant and others are whey-predominant
  - Cow’s milk allergic infant should not be given either type
- Partially hydrolysed whey formula (Good Start®) contains milk allergens and should not be used in the management of established cow’s milk allergy
- Soy protein allergy is most commonly seen in children with cow’s milk protein allergy
  - Soy-based formula is not recommended for milk-allergic babies
Infant Formulae

- Extensively hydrolysed casein formulae (e.g. Enfalac Nutramigen®, Alimentum®, Enfalac Pregestamil®) are usually tolerated
- Some infants with skin and respiratory IgE-mediated CMA may have serious reactions to them
- Elemental formulae (Neocate [USA and UK]; Profylac® [Europe]) may be tolerated
- No cow’s milk hydrolysate formula should be considered completely safe for all children with IgE-mediated CMA
- Introduction should be conducted with caution, using incremental dose challenge and diluted formula
Management of CMA as a Model

• Elimination of all milk and all foods containing cow’s milk proteins
• Children allergic to bovine serum albumin may not tolerate beef; initially eliminate all sources of beef
• Breast milk of mothers following a diet devoid of cow’s milk protein is the ideal food
• In the small number of infants intolerant to lactose, breast milk may have to be pre-treated with lactase enzyme. Breast-feeding should not be discontinued.
Hidden Sources of Cow’s Milk Antigens

- Casein is used as a food emulsifier
- Whey is used as a food fortifier
- Margarines may contain whey and/or casein
- Many prepared and processed foods contain milk proteins and may not have ingredient labels;

  Examples:
  - Breads
  - Cereals
  - Pastas
  - Soups
  - Frozen chips
  - Gravy and sauce mixes
  - Sausages
  - Canned meats
  - Desert toppings
Hidden Sources of Cow’s Milk Antigens

- Foods containing “flavouring” may contain lactalbumin
- “Lactose” may contain $\alpha$-lactalbumin and $\beta$-lactoglobulin
- Leather may be sprayed with casein after it has been tanned
- Casein may be found in a number of non-food items e.g.
  - Artists’ paints
  - Cosmetics
  - Photoetching chemicals
  - Insect spray
  - Paper coating
  - Pet food
  - Contraceptive foams
  - Home permanents
  - Industrial glue
  - Leather finishes
  - Particle board
General Guidelines for Maintenance Diets

- Avoid all sources of the allergen
- Become familiar with terms that indicate the presence of the allergen in manufactured foods
- Contact the manufacturer if unsure of ingredients
- Make quite sure that all the nutrients in the excluded food(s) are replaced by appropriate substitutes
- Consult a registered dietitian for information and supervision of the child’s diet
Examples of Products and Ingredients Indicating the Presence of Milk

**Milk and milk products**
- Milk
- Cheese
- Cottage cheese
- Yoghurt
- Butter
- Buttermilk
- Ice cream
- Sherbet
- Cream
- Curd

**Terms on food labels**
- Casein
- Caseinate
- Whey
- Lactalbumin
- Lactoglobulin
- Milk solids
- Lactose
- Lactulose
Important Nutrients in Milk

• **Important Macronutrients:**
  – Proteins
  – Fats
  – Carbohydrate

• **Important Micro-nutrients**
  – Calcium - Riboflavin
  – Phosphorus - Pantothenic acid
  – Vitamin D - Vitamin A
  – Vitamin B12 - Vitamin E
  – Potassium

• (vitamin D and A are added as fortification).
# Rechallenge Schedule

<table>
<thead>
<tr>
<th>FOOD</th>
<th>RECHALLENGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg</td>
<td>After 12 to 18 months of avoidance.</td>
</tr>
<tr>
<td>Milk</td>
<td>If response is still positive: every 2 to 3 years</td>
</tr>
<tr>
<td>Wheat</td>
<td>If response is still positive: every 2 years</td>
</tr>
<tr>
<td>Soy</td>
<td>After 1 year of avoidance.</td>
</tr>
<tr>
<td>Peanut</td>
<td>After 3 years of avoidance.</td>
</tr>
<tr>
<td>Shellfish</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>If response is still positive: every 2 to 3 years</td>
</tr>
<tr>
<td>Nuts</td>
<td></td>
</tr>
<tr>
<td>Seeds</td>
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*RECHALLENGE ONLY UNDER CLOSE MEDICAL SUPERVISION IF FOOD SUSPECTED TO CAUSE ASTHMA OR ANAPHYLAXIS*