Prevention of Food Allergy

From Pre-conception to Early Post-Natal Life

Does Atopic Disease Start in Foetal Life?

[Jones et al 2000]

- Foetal cytokines are skewed to the Th2 type of response
- Suggested that this may guard against rejection of the “foreign” Foetus by the mother’s immune system
- IgE occurs from as early as 11 weeks gestation and can be detected in cord blood

Does Atopic Disease Start in foetal Life? (continued)

- At birth neonates have low INF-γ and tend to produce the cytokines associated with Th2 response, especially IL-4
- So why do all neonates not have allergy?

Does Atopic Disease Start in foetal Life? (continued)

- New research indicates that the immune system of the mother may play a very important role
- IgG crosses the placenta; IgE does not
- Certain sub-types of IgG (IgG1; IgG3) can inhibit IgE response
- Suggested that IgG anti-IgE antibodies suppress the Th2 response

Does Atopic Disease Start in Foetal Life? (continued)

- IgG1 and IgG3 are the more "protective" subtypes of IgG
- IgG1 and IgG3 tend to be lower than normal in allergic mothers
- In allergic mothers, IgE and IgG4 are abundant
- In mothers with allergy and asthma, IgE is high at the foetal/maternal interface
- Foetus of allergic mother may thus be primed to respond to antigen with IgE production

Significance in Practice

- Allergenic molecules demonstrated to cross the placenta and sensitize the foetus in utero
- Evidence that low dose exposure to food antigens tolerises
- Exposure to small quantities of food antigens from mother's diet thought to tolerize the foetus, by means of IgG1 and IgG3, within a "protected environment"

Significance in Practice continued

- Atopic mother's immune system may dictate the response of the foetus to antigens in utero
- The allergic mother may be incapable of providing sufficient IgG1 and IgG3 to downregulate foetal IgE
- However – there is no convincing evidence that sensitization to specific food allergens is initiated prenatally
- Current directive: the atopic mother should strictly avoid her own allergens

The Neonate: Conditions That Predispose to Th2 Response

- Inherited allergic potential (maternal and paternal)
- Intrauterine environment
- Immaturity of the infant's immune system 
- Hyperpermeablilty of the immature digestive mucosa
- Inflammatory conditions in the infant gut (infection or allergy) that interfere with the normal antigen processing pathway
- Increased uptake of antigens

Current Areas of Investigation to Reduce Risk of Allergy

Science to Practice

Fatty Acids and Allergy

- Theory:
  - Linoleic acid (ω-6 FA) is a precursor of arachidonic acid
  - Arachidonic acid is the precursor of secondary inflammatory mediators, especially of the pro-inflammatory prostaglandin E_2 (PGE_2)
  - PGE_2 has a strong inhibitory effect on IFN-γ and increases IL-4; thus promoting the Th2 (allergy) response

Fatty Acids and Allergy

- α-linolenic acid, EPA and DCHA are ω-3 fatty acids
- Are precursors to prostaglandins of the 3 series (PGE_3), which are less inflammatory than the 2 series
- Will tend to inhibit Th2 and thus promote Th1 (protective) activity
- Thus will down-regulate the allergic response
- Increased intake of fish should reduce allergy
- Old-fashioned idea of taking cod liver oil should help prevent allergy

Fatty Acids and Allergy

Omega-6 Fatty acids

↓

Arachidonic acid

↓

Prostaglandin PGE_2

↓

Inhibits IFNγ (associated with Th1 response)
Allows up-regulation (increase) in IL-4 (Th2 response)

↓

ALLERGIC REACTION PROMOTED

Omega-3 Fatty acids

↓

EPA
DCHA

↓

Prostaglandin PGE_3

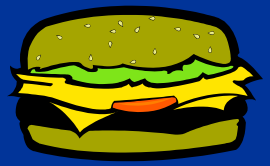
↓

PGE_2 is reduced
IFN-γ is not inhibited

↓

ALLERGIC REACTION REDUCED

Sources of ω-6 and ω-3 Fatty Acids



- ω-6 Fatty Acid Sources:
  - Meats, especially red meat
  - Milk and milk products, including butter, cheese, yogurt

- ω-3 Fatty Acids
  - α-linolenic acid:
    - Canola oil; Soy oil; Wheat germ oil;
  - Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DCHA):
    - Fish, especially oily fish
    - Salmon; Trout; Mackerel; Halibut
    - Cod and Halibut liver oils

Conflict of Results

[Duchen et al 2000; n=120]

- Lower levels of long-chain ω-3 fatty acids in mature breast milk of mothers of atopic as compared to non-atopic infants (atopy measured during first 18 months)

[Stoney et al 2004 (n=620)]

- Higher levels of long-chain ω-3 fatty acids in colostrum of mothers of infants sensitized to foods (cow's milk; egg; peanut: STP +)) at 6 months of age compared to those of non-sensitized infants
- Breast milk fatty acid profile was the same in atopic and non-atopic mothers:
- FA in breast milk results from maternal diet

Vitamin Supplementation and Risk of Allergy

[Milner et al 2004 (n = >8,000)]

- Vitamin supplementation in the first 6 months associated with:
  - Higher risk for asthma in black infants
  - Higher risk for food allergies in formula-fed infants
- Vitamin supplementation at 3 years of age associated with:
  - Increased risk for food allergies but not asthma
  - In both breast-fed and formula-fed children

Vitamin Supplementation and Risk of Allergy (continued)

[Matheu et al 2003 (murine study)]

- Early vitamin D supplementation augmented allergen-induced Th2 response, with production of:
  - IL-4
  - IL-13
  - IgE
- Vitamin D supplementation tends to downregulate Th1 response, with beneficial effects on development of Th1-mediated conditions such as:
  - Airway eosinophilia
  - Type 1 diabetes mellitus

Epicutaneous Exposure to Food Allergens

[Hsieh et al 2003 (murine study)]

- Patch administration of ovalbumin induced:
  - High level of ovalbumin-specific IgE
  - Elevated plasma histamine levels
  - Histological changes in intestine and lung tissue
  - Th2-predominant cellular immune response in lungs after oral challenge
- Significance of epicutaneous exposure to allergens as a result of skin testing?

Role of Micro-organisms in Preventing Food Allergy

- Commensal gut microflora might suppress Th2 response by promoting:
  - Th1 response
  - Protective SIgA production
  - TGF-ß production
- In mouse food anaphylaxis, lactobacillus:
  - Induced IL-12 production
  - Suppressed IgE-response
  - Suppressed anaphylaxis

Probiotics in Prevention of Food Allergy

Human study [Kalliomaki et al 2001]

- Mothers given lactobacillus GG antenatally
- Infants given oral lactobacillus for 6 months post-natally
- Treated group reduced risk of eczema at 2 years
- No difference in treatment and control groups:
  - Total IgE
  - Specific IgE to food allergens
  - Skin-prick tests

Summary of Current Research
1. Identification of Risk Categories

- High risk:
  - Atopic mother
- Moderate risk:
  - Atopic father
  - Atopic sibling(s)
- Low risk:
  - No family history of allergy

Summary of Current Research

2. Preventive Measures

- High risk:
  - Identify mother's allergens
  - Maternal avoidance of her own allergens from preconception onwards
  - In addition, starting about two weeks prior to delivery mother avoids most highly allergenic foods throughout lactation
    - Peanuts
    - Tree nuts
    - Shellfish
    - Fish
    - Eggs
    - Milk proteins
  - Degree of avoidance of eggs and milk remains controversial

Summary of Current Research

2. Preventive Measures (continued)

- Moderate risk
  - No need to restrict mother's diet prior to, or during most of her pregnancy
  - Starting two weeks prior to delivery, mother avoids the most highly allergenic foods and continues throughout early lactation
    - Peanuts
    - Tree nuts
    - Shellfish
    - Fish
    - Eggs
    - Milk proteins
  - Degree of avoidance of eggs and milk remains controversial

Summary of Current Research
2. Preventive Measures (continued)

- Low Risk:
  - Good nutrition practices for mother from preconception onwards
  - Good nutrition practices for early infant feeding
  - Breast-feeding is the best possible source of nutrition and protection
  - Allergen avoidance is unnecessary unless the infant demonstrates signs of allergy

Summary of Current Research
2. Preventive Measures (continued)

- Low Risk:
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Routes of Allergen Exposure in Infancy

- Food Allergens:
  - Placenta pre-natally (relatively uncommon and not proven)
  - Breast milk during lactation
  - Infant formulae
  - Via the skin e.g. in eczema creams and ointments; skin prick tests
  - Solid foods
  - Covertly by caretakers
- Inhaled Allergens
  - Dust and dust mites; Pollens; Molds
  - Tobacco smoke
- Contact and inhalation
  - Animal danders; Dust and dust mites

Measures to Reduce Food Allergy in Infants with Symptoms of Allergy or at High Risk Because of Genetic Background

1. Exclusive breast-feeding for the first 6 months
2. Total maternal avoidance of:
   - any food inducing allergy symptoms in the infant
   - any food inducing allergy symptoms in mother

   - eggs
   - cow's milk and dairy products
   - peanuts
   - nuts
   - shellfish

   } As a preventive measure initially if not avoided in above categories {clinicians disagree about this}

Measures to Reduce Food Allergy in Infants (continued)

3. Colostrum as soon after birth as possible
4. Avoid infant formulae in the newborn nursery: NO exposure to formulae in the hospital
5. Avoid small supplemental feedings of infant formulae at widely spaced intervals
6. If formula is unavoidable introduce in incremental doses over a 3-4 week period

Measures to Reduce Food Allergy in Infants (continued)

7. Introduce solid foods after 6 months starting with the least allergenic. Use incremental dose introduction to promote oral tolerance
8. Delay the most allergenic foods until after 12 months:
   - cow's milk
   - eggs
   - peanuts
   - nuts
   - shellfish
   - fish
   - beef
   - chicken
   - soy
   - wheat
   - citrus fruits
   - tomatoes

Adding Solid Foods

- Aim: To induce tolerance and avoid sensitization
- Method: Incremental dose introduction of foods

Day 1:

Morning (breakfast):

½ teaspoon of food

Wait four hours. If no reaction:

Noon (lunch):

1 teaspoon of food

Wait four hours. If no reaction:

Evening (dinner):

2 teaspoons of food

Adding Solid Foods (continued)

Day 2:

Monitor for delayed reactions.

Give none of the new food.

Day 3:

Morning (breakfast):

2 tablespoons of food

Wait four hours. If no reaction:

Noon (lunch):

¼ cup of food

Wait four hours. If no reaction:

Evening (dinner):

As much of the food as baby wants

Adding Solid Foods (continued)

Day 4:

- Monitor for delayed reactions. Give none of the new food

No adverse reactions experienced during the four day introduction period:

- the food can be considered **safe** and included in the diet

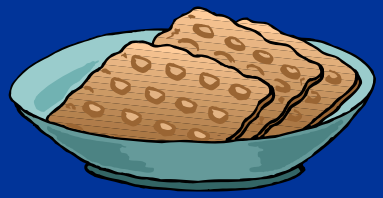
Adverse reaction occurs at any time during the test period:

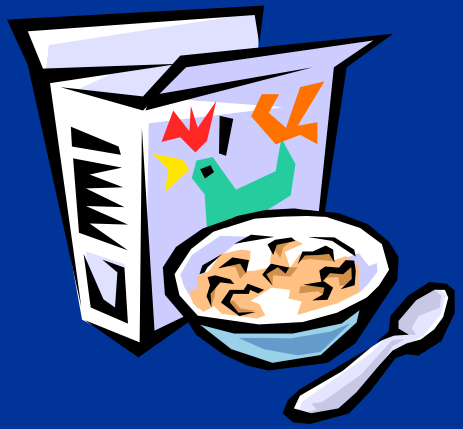
- **STOP**
- do not give any more of the test food

- Wait at least two months before testing that food again
- Wait 48 hours after all symptoms have subsided before starting to introduce another new food

Sequence of Adding Solid Foods for the Allergic Baby

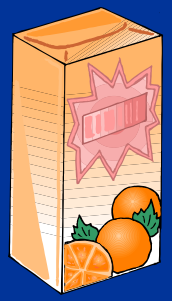
- Cereals:
  - At 6 months:
    - Rice
    - Tapioca
    - Arrowroot
    - Millet
    - Quinoa
    - Amaranth
  - After 9 months:
    - Barley
    - Oats
  - After 12 months:
    - Corn
    - Wheat





Sequence of Adding Solid Foods for the Allergic Baby

- Fruit and Juices:
  - At 6 months (cooked at first):
    - Pear
    - Apricot
    - Peach
    - Plum
    - Grape
    - Apple
    - Banana
  - after 12 months:
    - Citrus fruits
    - Berries
    - Tomato



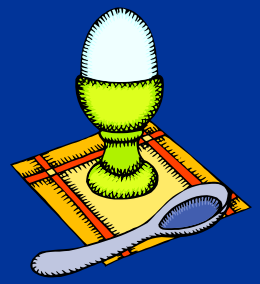
Sequence of Adding Solid Foods for the Allergic Baby

- Vegetables
  - At 6 months (cooked at first):
    - Sweet potato
    - Squashes
    - Parsnip
    - Broccoli
    - Yam
    - Turnip
    - Carrot
    - Cauliflower
  - After 12 months:
    - Legumes (peas, beans, lentils)
    - Spinach

Sequence of Adding Solid Foods (continued)

- Meat:
  - At six months:
    - lamb
    - turkey
  - after 9 months:
    - veal
  - after 12 months:
    - chicken
    - beef
    - pork

- Eggs:
  - after 12 months:
    - test yolk first
    - white later



Sequence of Adding Solid Foods (continued)

- Milk and Milk Products
  - At or after 12 months:
    - Start with full cream milk, full cream yogurt, or equivalent
- After 12 months:
  - Fin fish (not shellfish)
- After 2 years
  - Shellfish
  - Peanuts
  - Tree nuts
  - Seeds
  - Chocolate