# Food Allergies in Childhood

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# Food Allergies in Childhood

- Approach to diagnosis and management
- Current advice on prevention of allergic disease including food allergy

- Infant feeding advice

# WAO Nomenclature 2003

### Allergy

- Reaction <u>initiated</u> by specific immunological mechanisms
- Intolerance
  - Reaction <u>initiated</u> by NON-immunological mechanisms

### Food Hypersensitivity (All reproducible reactions)



### **Exponential Rise in Food Anaphylaxis**



Liew WK, Williamson E, Tang MLK. J Allergy Clin Immunol 2009;123:434-42

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# Incidence of Food Allergy

- Overall ~ 2 5% of population experience food allergy reactions
- 6% 8% children experience food allergic reactions <sup>2</sup>
- Recent HealthNuts study found more than 10% of 12 month old Melbourne infants have food allergy <sup>1</sup>
- 2% adults experience food allergic reactions <sup>3</sup>

- 1. Osborne N et al. J Allergy Clin Immunology 2011
- 2. Bock et al. Pediatr 1987;79:683-88
- 3. Young et al. Lancet 1994;343:1127-30

	IgE mediated	
Onset of symptoms	< 30 mins - 1hr	
Skin	Erythema Urticaria Angioedema	
Gastrointestinal	Vomiting Diarrhoea Cramps	
Respiratory	Persistent cough, Stridor, Wheeze Hoarse voice	🗲 Anaphylaxis
Cardiovascular	Hypotension Pale, Floppy Infant	

	IgE mediated	Mixed	Non IgE mediated
Onset	< 30 mins - 1hr	1hr → 24hr / 48hr	1hr → 24hr / 48hr
Skin	Erythema, Urticaria Angioedema Eczema	eczema	-
Gut	Vomiting Diarrhoea Cramps	Vomit, Diarrhoea FTT/LOW Abdominal pain GOR	Vomit, Diarrhoea FTT/LOW Abdominal pain
Resp	Persistent Cough, Stridor Wheeze Hoarse voice	_	-
CVS	Hypotension Pale and floppy infant	-	Hypotension Pale and floppy infant

#### 8 major food groups cause >90% food allergy



#### Food Anaphylaxis Admissions Subgroup 1994-1998



Liew WK, Williamson E, Tang MLK. J Allergy Clin Immunol 2009;123:434-42

### Diagnostic Tests for IgE Mediated Food Allergy

- Skin Prick Test
  - Sensitive, inexpensive, simple, rapid
  - Negative predictive value >95%
  - Positive predictive value 50%
- Serum allergen-specific IgE (sIgE)
  - Similar to SPT in sensitivity, specificity, NPV, PPV
  - More expensive, delayed result
- Food challenge
  - Must be supervised
  - Should NOT be performed at home if positive SPT or slgE

Diagnostic Approach to IgE Mediated Food Allergy

- Most important information is the history
- If history suggests food allergy then perform slgE test to that specific food
- Avoid 'screening' slgE testing as a +ve result when the patient has not eaten the food can be difficult to interpret
  - Exception is in a child with food anaphylaxis → slgE testing for common food allergens that have not yet been introduced

### How to interpret slgE test if food not introduced

- +ve test <u>without history of exposure</u> to the food is a poor predictor of allergy
  - Cow's milk, egg  $\rightarrow$  50% not allergic
  - Peanut  $\rightarrow$  60-70% not allergic
- The larger the SPT and the higher the serum sIgE level, the more likely there is clinical allergy
- 95% thresholds (PPV or specificity) can help make a diagnosis of food allergy if no previous exposure

#### \*\* BUT... Size SPT does NOT predict severity of reaction

Pucar et al Clin Exp Allergy 2001;31:40) Spergel et al Ann Allergy Asthma Immunol 2000;85:473) Diagnostic Approach for Delayed Food Allergies

- There are no specific tests for non-IgE mediated or mixed IgE/non-IgE mediated food allergy syndromes
- History is the primary tool for diagnosis
- GI endoscopy and biopsy can support diagnosis

### Management of Food Allergy

- Allergen avoidance is the first line approach
  - Read ingredient labels, 'may contain traces' labelling
  - Alternative foods.... Involve dietician
  - Educate about situations that carry increased risk of accidental exposure.... eg: eating out, parties, friend's home
- Risk minimisation
  - Educate on recognition and treatment of allergic reactions
  - Action plan #
  - Consider provision of adrenaline auto-injector \*
  - Ensure that asthma is well controlled #
  - Annual review with GP or Paediatrician

\* Not relevant for non-IgE or mixed IgE/non-IgE mediated food allergy # May not be relevant for non-IgE or mixed IgE/non-IgE mediated food allergy

#### ACTION PLAN FOR Allergic Reactions

ascia

www.allergy.org.au

#### ASCIA www.allergy.org.au



### Who should have an Adrenaline Autoinjector?



### Can we predict who will have Anaphylaxis?

- Level of specific IgE and SPT size are <u>NOT</u> predictive of severity of reaction
  - → Not prescribed for a large SPT or high slgE
- Risk factors:
  - History of anaphylaxis indicates high risk of subsequent anaphylaxis... but 40% first event
  - Age adolescents and young adults
  - Delayed adrenaline remote geographic location
  - Poorly controlled asthma
  - Allergy to peanut or tree nuts

### **PBS Indications for Adrenaline Auto-injectors**

#### Recommended if...

History of anaphylaxis (and continued risk)

#### May be recommended if...

<u>Generalised allergic reaction</u> PLUS risk factors

- Geographically isolated
- Age adolescence or adult
- Asthma
- Nuts or Stinging insects

## PBS Indications for Epipen/Epipen Jr

#### Not normally recommended for...

- Positive skin prick tests or blood slgE tests in the absence of previous clinical reaction
- Local reactions to insect stings (children & adults)
- Generalised skin rash only to insect stings (children)
- Asthma without history of anaphylaxis or systemic reaction
- Family history of anaphylaxis or allergy

### **Ongoing Management of Food Allergy**

- Annual review by GP or Paediatrician
  - Review diet nutritionally adequate, dietician
  - Accidental ingestion and allergic reactions
  - Education on recognition and emergency treatment of allergic reactions
  - Update Action Plan
  - Review need for adrenaline auto-injector \*
  - Review asthma control
  - Monitor SPT or RAST → consider as test approaches negative to determine if appropriate to challenge \*

\* Not relevant for non-IgE or mixed IgE/non-IgE mediated food allergy

# When to Refer to an Allergist

- Anaphylaxis
- If history does not match SPT / slgE test result
  - Positive history and negative test
  - Positive test (but <95% threshold) and NO history of ingestion</li>
- Non-IgE mediated syndromes
  - FPIES (food protein induced enterocolitis syndrome)
  - Failure to thrive
  - Low protein (protein losing enteropathy)
  - If no response to elimination diet

# **Prevention of Allergic Disease**

- For babies at INCREASED RISK of allergic disease (family history of allergic disease)
  - Breastfeed for at least 6 months
  - Introduce complementary foods from 4-6 months
  - If unable to breastfeed in first 4-6 months, use a hydrolysed formula in place of standard formulas
  - Avoid exposure to cigarette smoke
  - Not recommended: elimination diets during pregnancy or lactation

AAAAI advice: Fleischer D et al. JACI In Practice 2012
 AAP advice: Greer FR et al. Pediatrics 2008;121:183-91.
 ASCIA advice: Prescott SL, Tang MLK. Med J Aust 2005;181:464-7.
 ESPGHAN advice: Agostoni C et al. JPGN 2008;46:99-110.

### Benefits of breastfeeding and breast milk

- Breast feeding helps the **emotional bond** between mother and child and contributes to the emotional development of the infant
- Breast milk is nutritionally complete for infants from 0 to 6 months

   contains all the nutrients a baby needs for growth and
   development & is easily digested
- Breast milk contains a large number of **immune factors** such as immunoglobulins, cytokines, prebiotics etc that assist in gut maturation, physiological development and immunity
  - Breast fed babies have fewer and less severe infections
- Breast feeding may lower risk of developing chronic diseases such as childhood obesity, diabetes, CVD in later life
- Breast milk promotes a healthy gut microbiota
  - Higher numbers of 'good' bacteria, fewer pathogenic bacteria

#### Breast feeding and Prevention of Allergic Disease

- Systematic Reviews fail to show a protective effect for breastfeeding in prevention of allergic disease <sup>1</sup>
- Studies with longer term follow up show increased risk for food allergy, asthma, rhinitis <sup>2-5</sup>
- Methodological issues with breastfeeding studies
  - Not possible to randomise breastfeeding  $\rightarrow$  reverse causation
  - Recall bias in retrospective studies
  - Variable definitions of breastfeeding and allergic outcomes
  - Failure to adjust for confounding factors
    - Risk factors for allergic disease
    - Study population allergic disease risk, breast milk composition
- 1. Yang YW et al. Br J Dermatol 2009;161: 373
- 2. Matheson MC et al. J Allergy Clin Immunol 2007;120: 1051-1057
- 3. Rusconi F et al. Am J Respir Crit Care Med 1999;160: 1617-1622
- 4. Wright AL et al. Thorax 2001;56: 192-197
- 5. Sears MR et al. Lancet 2002;360: 901-907

### **Breast Milk Immune Factors**

#### Anti-microbial compounds

Immunoglobiuines: slgA, SlgG, SlaM Lactoferrin, lactoferrin B and H Lysozyme Lactoperoxidase Nucleotide-hydrolizing Antibodies κ-casein and α-lactalbumin Haptocorrin Mucins Lactadherin Free secretory component Oligosaccharides and prebiotics Fatty acids Maternal leukocytes and Cytokines sCD14 Complement and complement receptors β-defensin-1 **Toll-like receptors** Bifidus factor Tolerance/priming compounds Cytokines: II10 and TGFB Anti-idiotypic antibodies



End point (n end points/total N) Atopic eczema Atopic sensitization Duration of breast-feeding All asthmat Atopic asthmat Nonatopic asthmat Allergic rhinitis and age at introduction of (157/2617),§ (86/960), §(66/1573),§ (371/2593),§ (961/2530),§ (776/2293),§ complementary foods\* HR (95% CI) HR (95% CI) HR (95% CI) OR (95% CI) OR (95% CI) OR (95% CI) Total breast-feeding First third: < 0 mo. 1.91(1.21-3.02)2.95 (1.31-6.66) 1.97 (1.28-3.02) Second third: \$.0-9.5 mo 3.60 (1.67-7.76) Third third: >9.5 mo. 1 P value 003001Wingal and the four states and the four loss 0.79(0.55.116)First third: <5.0 mo 0.72(0.44 - 1.19)1.10(0.54-2.25)Second third: 50:555 me 0.59 (0.41-0.86) 0.57(0.31 - 1.06)0.66(0.50-0.87)i ing ing a stano 1 P value 02 06 02 Other cereals First third: <4.5 mo 1.47 (1.10-1.97) 1.17 (0.88-1.56) Second third: 4.5-5.5 mo Third third: >5.5 mo 1 P value .029 Fish-First third: <6.0 mo 0.68(0.47-0.98)0.71(0.55 - 0.92)Second third: 6.0-9.0 mo 0.63(0.48-0.84)0.64(0.52-0.79)Third third: >9.0 mo .01 P value <.001 100 First third: <8.0 mo 0.61 (0.39-0.94)  $0.46(0.25 \cdot 0.84)$ 0.73 (0.52-1.02) 0.82(0.65 - 1.03)0.55 (0.38-0.81) 0.55 (0.34-0.91) 0.71 (0.59-0.87) Second third: 8.0-11.0 mo 0.72(0.55-0.94)Third third: >11.0 mo 1 04 P value 005 < 001004

TABLE III. Adjusted association between breast-feeding and age at introduction of complementary foods and the risk of asthma, allergic rhinitis, and specific atopic sensitization in 5-year-old children

HR, Hazard ratio; OR, odds ratio.

\*The foods remaining in the last stage of the stepwise model were simultaneously adjusted for the confounding covariates sex of child, siblings, parental asthma, parental rhinitis, hospital of birth, maternal smoking during pregnancy, season of birth, duration of gestation, maternal age, maternal basic education, pets at home by 1 year of age, mode of delivery, and birth weight.

†Asthma, regardless of atopic status.

‡Asthma stratified by atopic sensitization.

\$Number included in the analysis, constituting those with complete information on the exposure and the respective end point.

Maize, rice, millet, and buckwheat.

### Timing of Introduction of Foods and Allergy Risk

• Is there an optimal time for oral tolerance induction?



Prescott et al. Pediatr Allergy Immunol 2008;19:375-80

#### Timing of Introduction of Foods and Allergy Risk

- Delayed introduction of foods after 6-9 months is associated with an increased risk of allergic disease (eczema, asthma, allergic rhinitis) <sup>3-9</sup>
  - Food allergy was not assessed in these studies

- 1. Norris JM et al. JAMA 2003; 290:1713-20; 2. Norris JM et al. JAMA 2005; 293:2343-51
- 3. Alm B et al. Arch Dis Child 2009;94:11-5; 4. Filipiak B et al. J Pediatr 2007;151:352-8;
- 5. Hesselmar B et al. Acta Paediatr 2010;99:1861-7; 6. Kull I et al. Allergy 2006;61:1009-15;
- 7. Snijders BE et al. Pediatrics 2008;122:e115-22; 8. Virtanen SM et al. Br J Nutr 2010;103:266-73;
- 9. Zutavern A et al. Arch Dis Child 2004;89:303-8

# Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy Du Toit et al. JACI 2008

TABLE II. The ratio of the risk of food allergies in the UK compared with Israel

	Peanut		Sesame		Tree nuts		Egg		Milk	
	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	<b>P</b> value	RR (95% CI)	<b>P</b> value	RR (95% CI)	P value
All individuals										
Unadjusted	10.8 (5.2-22.3)	<.001	6.1 (2.5-14.6)	<.001	15.2 (6.6-34.7)	<.001	3.4 (2.1-5.7)	<.001	1.9 (1.4-2.7)	<.001
Adjusted for age group* and sex§	10.4 (4.8-22.2)	<.001	5.3 (2.2-13.0)	<.001	14.0 (6.0-32.5)	<.001	3.1 (1.8-5.2)	<.001	1.7 (1.2-2.4)	.008
Adjusted for age group,* sex,§ food allergy,‡ and atopy†	5.8 (2.8-11.8)	<.001	2.7 (1.1-7.0)	.057	8.4 (3.6-19.5)	<.001	1.8 (1.0-3.1)	.054	1.3 (0.9-1.9)	.33
Primary school										
Unadjusted	17.4 (5.5-55.6)	<.001	6.3 (2.2-18.0)	<.001	17.4 (5.5-55.6)	<.001	4.8 (2.4-9.4)	<.001	1.7 (1.1-2.5)	.012
Adjusted for sex§	16.9 (5.3-53.5)	<.001	6.1 (2.2-17.6)	<.001	16.5 (5.3-51.8)	<.001	4.6 (2.3-9.0)	<.001	1.6 (1.1-2.4)	.046
Adjusted for sex,§ food allergy,‡ and atopy†	9.8 (3.1-30.5)	<.001	3.6 (1.1-12.1)	.045	9.5 (3.0-29.5)	<.001	2.5 (1.3-4.9)	.011	1.2 (0.8-1.9)	.47



# Introducing egg between 4 and 6 months is associated with a reduced risk of egg allergy



Koplin et al JACI 2010

# Introducing egg between 4 and 6 months is associated with a reduced risk of egg allergy

	No.*	Egg allergy (%)	Unad	Unadjusted		Adjusted	
Variable			OR (95% CI)	P value, trend	OR (95% CI)	P value, trend	
Age at introduction of egg (mo) <sup>†</sup>							
4-6	485	5.6	1.0	<001	1.0	<.001	
7-9	933	7.8	1.4 (0.9-2.3)		1.3 (0.8-2.1)		
10-12	730	10.1	1.9 (1.2-3.0)		1.6 (1.0-2.6)		
>12	98	27.6	6.5 (3.6-11.6)		3.4 (1.8-6.5)		
Age at introduction of solids (mo);							
<4	69	4.4	1.0	.70	1.0	.16	
4	354	9.0	2.2 (0.7-7.4)		1.7 (0.5-6.0)		
5	636	8.8	2.1 (0.6-7.0)		1.2 (0.4-4.3)		
6	996	9.4	2.3 (0.7-7.4)		1.2 (0.4-4.2)		
>6	106	5.7	1.3 (0.3-5.5)		0.7 (0.2-3.0)		
Duration of breast-feeding (mo)§							
<1	293	5.5	1.0	.005	1.0	.088	
1-3	311	7.7	1.4 (0.8-2.8)		1.1 (0.5-2.2)		
4-6	328	10.4	2.0 (1.1-3.7)		1.1 (0.6-2.3)		
7-9	285	10.9	2.1 (1.1-4.0)		0.9 (0.5-1.9)		
10-12	312	11.5	2.3 (1.2-4.2)		0.9 (0.4-1.8)		
>12	655	11.0	2.1 (1.2-3.7)		0.7 (0.4-1.4)		

TABLE II. Association between infant dietary	factors and egg	allergy at 1	year of age
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\*Numbers in each analysis differ because of missing data.

†Adjusted OR based on logistic regression model adjusted for family history of allergy, eczema diagnosis before the introduction of egg, and parent-reported reactions to 1 or more foods in the infant.

‡Adjusted OR based on logistic regression model adjusted for family history of allergy, age at introduction of egg, duration of breast-feeding, maternal smoking during pregnancy, parents' country of birth, and eczema diagnosis before the introduction of solids.

\$Adjusted OR based on logistic regression model adjusted for family history of allergy, maternal consumption of egg during breast-feeding, maternal smoking during pregnancy, and eczema diagnosis before ceasing breast-feeding.

#### Koplin et al JACI 2010

# RCT: Effect of egg introduction at 4m vs 8m in infants with eczema on Egg Allergy





**HG 1.** IgE-mediated egg allergy and positive SPT response (+ SPT) to egg at 12 months of age. **A**, Proportion of infants. **B**, RR between the egg and control groups.

Palmer et al JACI 2013



# INFANT FEEDING



#### www.allergy.org.au

#### BREASTFEED FOR AT LEAST 6 MONTHS:

- There are many nutritional and non-nutritional benefits of breastfeeding for both the mother and infant.
- · Breastfeeding is recommended for at least 6 months.
- Breastfeeding can continue beyond 12 months, or for as long as mother and infant wish to continue.

#### **BEFORE 4 MONTHS:**

- If complementary infant formula is required before solid foods are started, a standard cow's milk infant formula may be used (where there is no history of allergic disease in the infant's parents or siblings).
- Infants with a history of allergic disease in the infant's parents or siblings may be placed on a partially hydrolysed formula (usually labeled "HA" or hypo-allergenic). These formulas are not suitable for children who have already developed cow's milk allergy.
- Soy milk and other mammalian milks such as goat milk are not recommended for allergy prevention.

#### FROM 4-6 MONTHS:

- When your child is ready, consider introducing a new food every 2-3 days according to what the family usually eats (regardless of whether the food is thought to be highly allergenic).
- Give one new food at a time so that reactions can be more clearly identified. If a food is tolerated, continue to give this as a part of a varied diet (see Table for examples).
- Breast milk or an appropriate infant formula should remain the main source of milk until 12 months of age, although cow's milk can be used in cooking or with other foods.

#### NOTE:

 There are no particular allergenic foods that need to be avoided

- Some children will develop allergies. If there is any reaction to any food, you should seek medical advice and that food should be avoided until your child is reviewed by a medical practitioner with experience in food allergy.
- Infants who already have eczema are at higher risk of allergies.
   In general this advice applies to these children, however if your child develops a reaction to a food this should be discussed with your doctor (as above).
- If you are uncertain about this advice you should discuss this with your doctor.



#### Australian Government

National Health and Medical Research Council

Department of Health and Ageing

### EAT FOR HEALTH Infant Feeding Guidelines

#### Breastfeeding

### SUMMARY

#### Recommendations

- Encourage, support and promote exclusive breastfeeding to around 6 months of age.
- Continue breastfeeding while introducing appropriate solid foods until 12 months of age and beyond, for as long as the mother and child desire.
- While breastfeeding is recommended for the first 6 to 12 months and beyond, any breastfeeding is beneficial to the infant and mother.



Australian Government

National Health and Medical Research Council

**Department of Health and Ageing** 

### EAT FOR HEALTH Infant Feeding Guidelines

#### The transition to solid foods

SUMMARY

At around the age of 6 months, infants are physiologically and developmentally ready for new foods, textures and modes of feeding, and they need more nutrients than can be provided by breastmilk or formula alone. By 12 months of age, a variety of nutritious foods from the Five Food Groups, as described in the *Australian Guide to Healthy Eating*, is recommended.

#### Recommendations

- Introduce solid foods at around 6 months, to meet the infant's increasing nutritional and developmental needs.
- Foods can be introduced in any order provided iron-rich nutritious foods are included and the texture is suitable for the infant's stage of development. Cow's milk products including full-fat yoghurt, cheese and custard may be given, but not cow's milk as a main drink before 12 months.

# Summary

- Food allergies are increasing particularly in young children
- Diagnosis mainly relies upon history of reaction
  - Allergen-specific IgE test supports diagnosis of IgE mediated food allergy
  - No specific test for non-IgE mediated or mixed forms of food allergy
- Management involves education and provision of action plan
  - Adrenaline autoinjectors may be of benefit in some but not all children
- Limited prevention strategies available at present
  - Primarily aimed at high risk infants
- Current guidelines
  - Breastfeeding for at least 6 months
  - Introduce foods (including allergenic foods) from 4-6 months
  - For <u>high risk infants</u> hydrolysed formula if unable to breastfeed in first 4-6 months of life