

Pediatric allergy pitfalls: What every physician needs to know



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Disclosures

	Company/Organization	Details
I am a member of an Advisory Board or equivalent with a commercial organization.	CSL-Behring Sanofi-Genzyme Liffey Biotech Immunology CSO	Advisor for development of therapeutic molecule for allergic hypersensitivities
I am a member of a Speaker's Bureau	n/a	
I have received payment from a commercial organization (including gifts or other consideration or 'in kind' compensation).	n/a	

Objectives

Discuss the unique aspects of allergies in children with emphasis on food and drug allergy

Discuss methods for accurate diagnosis

Discuss best management practices for both prevention and treatment

The Case

Scenario

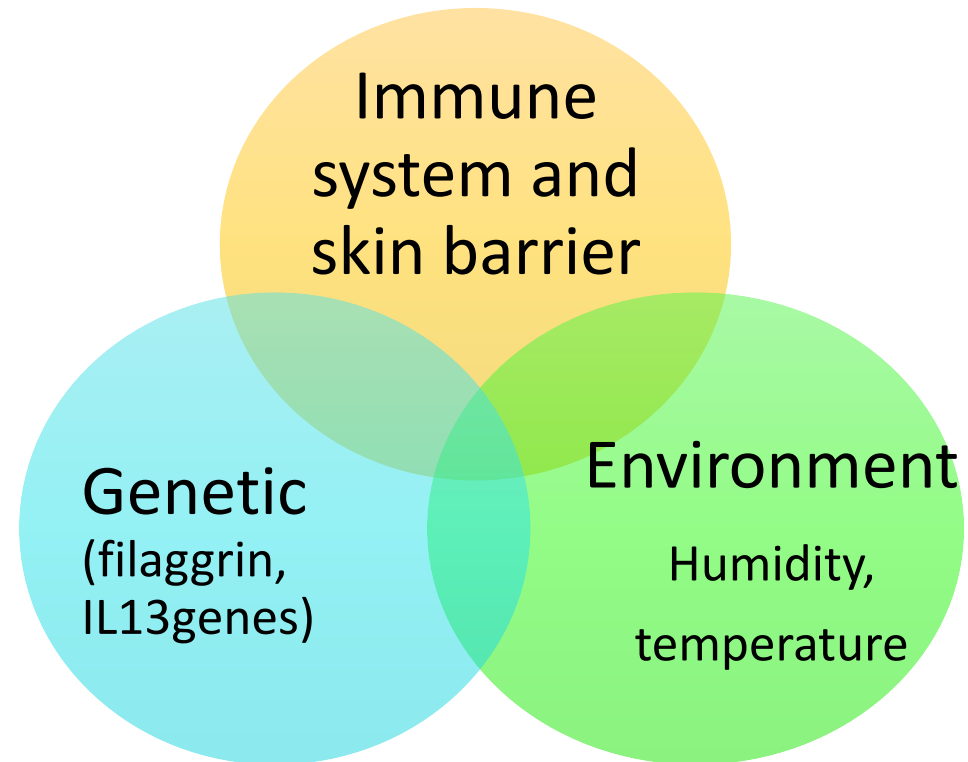
- A mother with a 6 month old comes for advice
- The child has eczema
- Mother wants to know what to do about the eczema and what foods could be causing it.

Responses True/False

- Eczema and food allergy are connected?
- Food avoidance reduces eczema?
- Infants with eczema should have specific antibody testing for foods to help manage their eczema

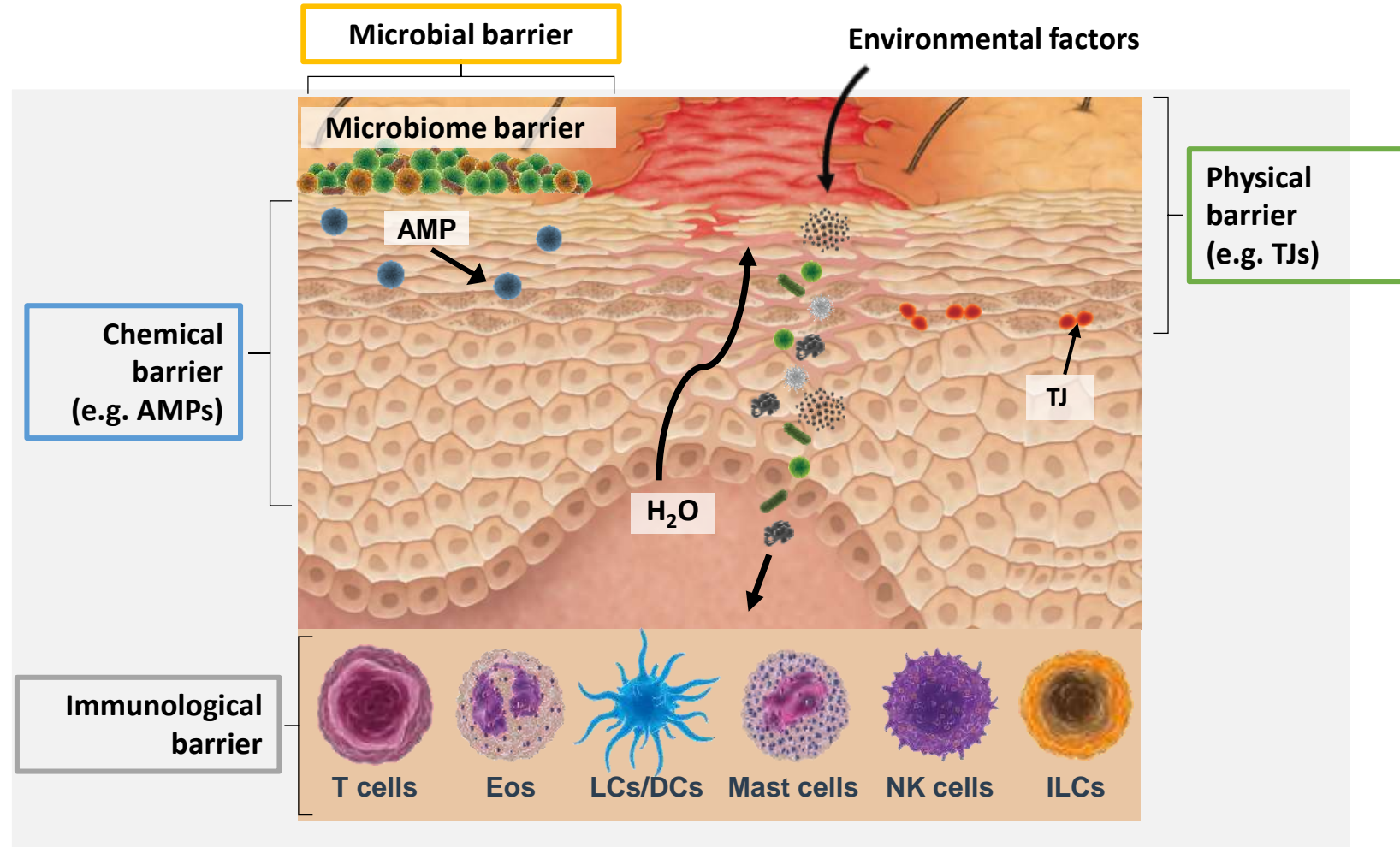
Eczema and food allergy-what is eczema?

- Eczema results from loss of skin barrier function associated with an inappropriate immune responses in the skin to both pathogenic and commensal bacteria.
 - Protect the barrier as evidence suggests that use of skin emollients reduces allergic sensitization



The Skin Barrier Is Composed of Microbial, Physical, Chemical, and Immunological Barriers

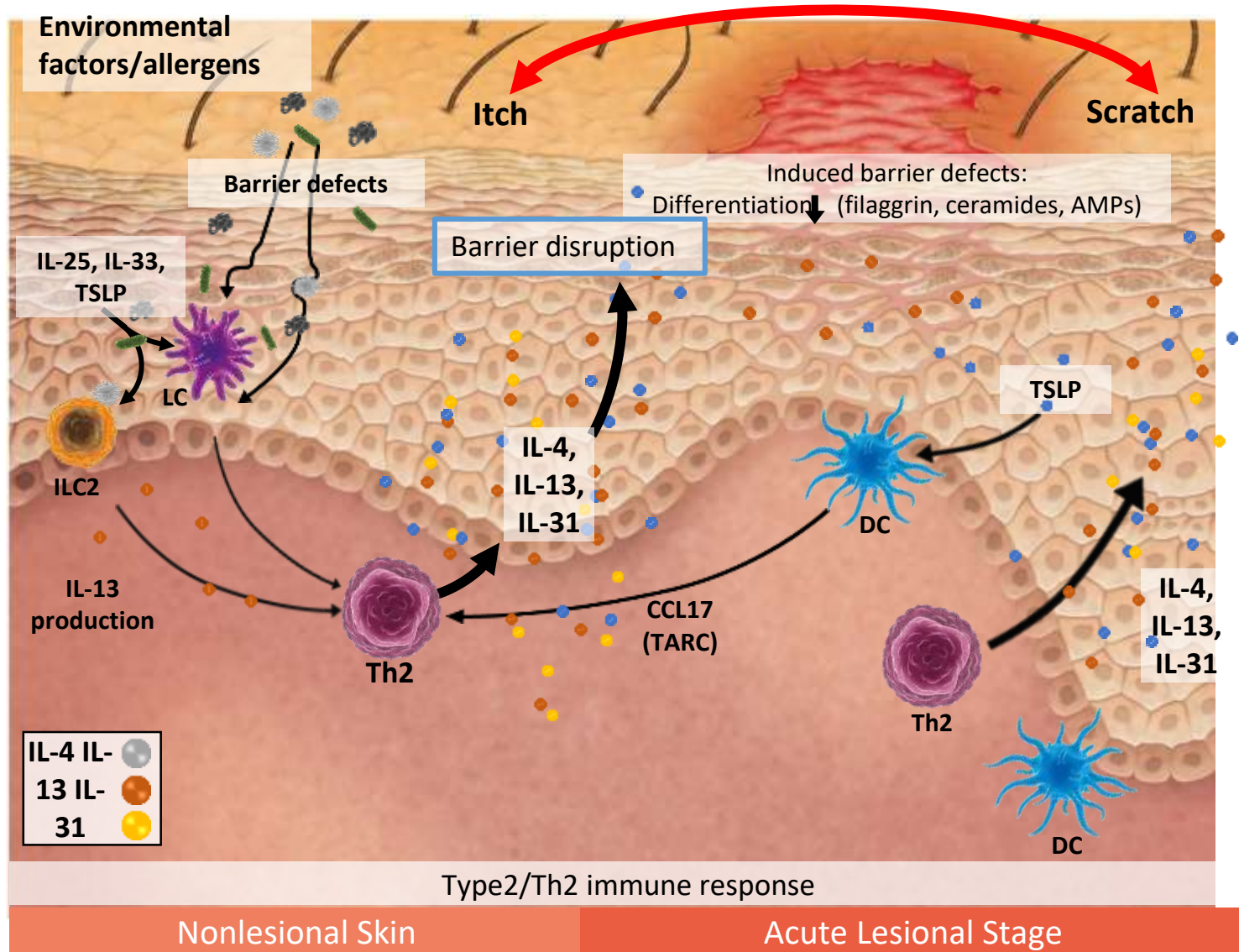
- Epidermal barrier function in AD can be affected by:¹⁻³
 - Commensal dysbiosis³
 - Genetic (e.g. filaggrin) and epigenetic alterations¹
 - Lipid/structure defects¹
 - Inflammation induced by the resident immune cells²
- Barrier disruption allows for entry of environmental factors and further activation of the immune system¹



AMP, antimicrobial peptide; DC, dendritic cell; Eo, eosinophil; ILC, innate lymphoid cell; LC, Langerhans cell; NK, natural killer.

Figure adapted from: Kuo I et al. *J Allergy Clin Immunol* 2013;131:266–278.

In Acute Skin Lesions, Atopic Dermatitis Inflammation Is Associated With Increased Type 2 (including TH2) Cells



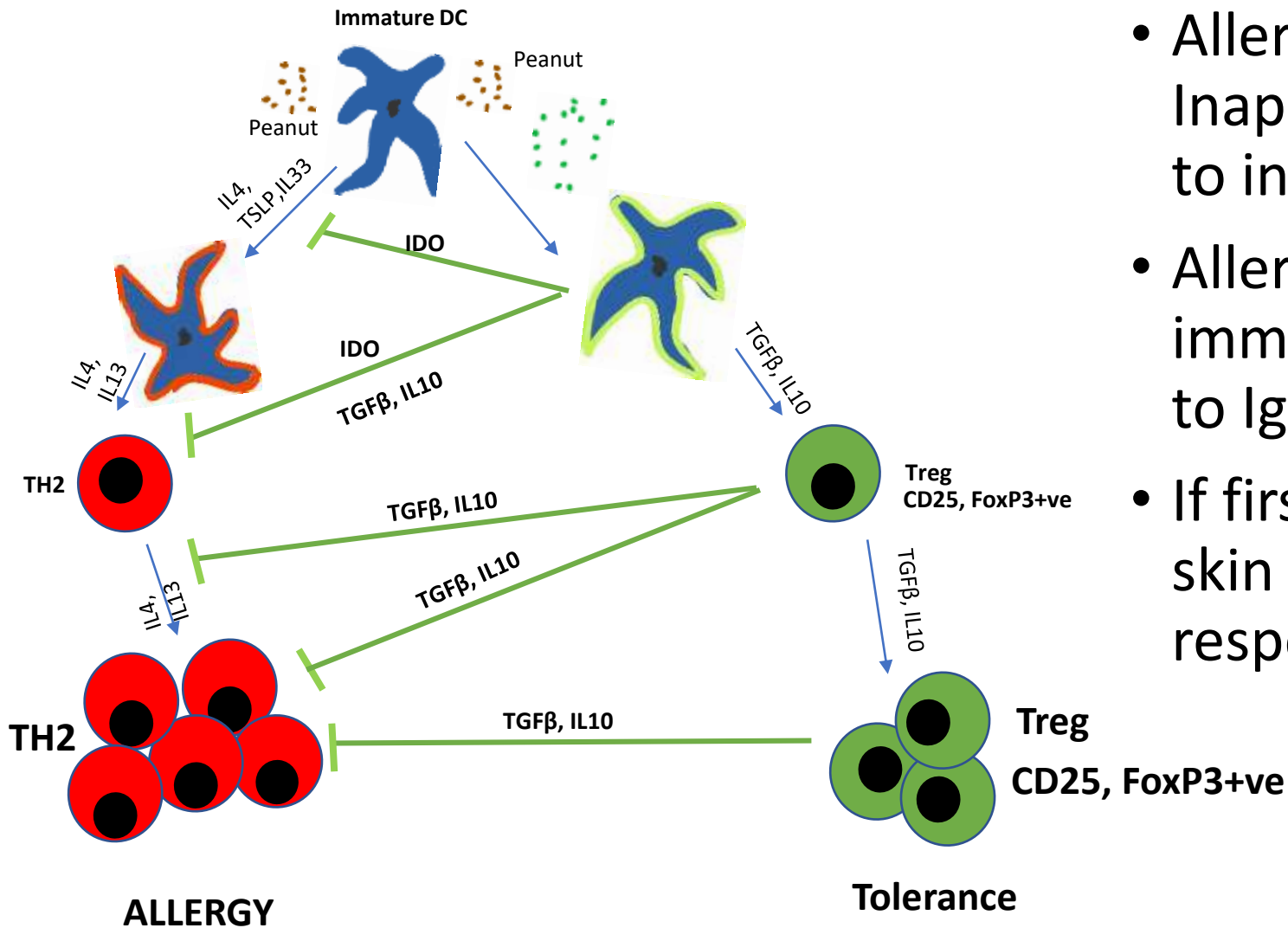
TARC, thymus- and activation-regulated chemokine.
 1. Noda S, Krueger JG, Guttman E. *J Allergy Clin Immunol* 2015;135:324–336. 2. Gandhi NA, Bennett BL, Graham NM et al. *Nat Rev Drug Discov* 2016;15:35–50. 3. Wynn TA. *Nat Rev Immunol* 2015;15:271–282.



- Studies suggest that in infants with severe eczema milk sensitivity may be a component worsening their disease.
- In the vast majority of children food ingestion has no relation to their skin symptoms
- However, sensitization to foods through skin exposure is now believed to be an important “cause” of food allergy in infants.
- WHY?

What does this have to do with food allergy?

Mechanism of food allergy



- Allergy results from Inappropriate immune response to innocuous substances
- Allergen stimulation induces TH2 immunity (IL4 and IL13) leading to IgE formation.
- If first contact occurs in inflamed skin (eczema) the immune response will likely be allergic

Pitfalls and Pearls

Pitfall

- Food allergy causes eczema

- Food avoidance reduces eczema

Pearl

- Eczema increases the risk for skin-mediated sensitization to foods. Emollient therapy and early introduction of foods orally can reduce sensitization.


- In children with SEVERE eczema (ie not responding to aggressive emollient therapy or medical management and compliant) specific foods such as milk are implicated and skin may improve with removal from the diet. Allergy consult first please!

Biggest Pitfall- food specific IgE or IgG testing

Pitfall

- Infants with eczema should have specific IgE testing for foods to help manage their eczema
- Infants with eczema should have specific IgG testing for foods to help manage their eczema

Pearl

- The skin is an immunoreactive organ and sensitization to allergens through the skin is possible.
 - The positive predictive value of specific IgE-testing for the diagnosis of true clinical allergy is less than 20%
- All individuals who eat make IgG to foods  DO NOT FALL FOR THE SCAM

A Recent Case in My Clinic: What are her allergies?

- 17 month old with eczema (severe) since age 4 months.
- Dr ordered blood tests.
- She has never been introduced to
- eggs, milk, peanuts, sesame, tree nuts.
- She has taken other legumes, fish.
- She developed red plaques with shrimp.
- Mother feels maybe some improvement of eczema with removal of foods from the maternal diet.
- Eczema is treated with topical
- corticosteroids and hydration creams.
- She is on soy, rice and breast milk

IgE SPECIFIQUES (ALLERGENES)
 PRÉLEVÉ LE 16/05/12 14:30
 LAIT (VACHE) 3,56
 ARACHIDES 7,52
 B-LACTOGLOBULINE <0,35

DEPARTEMENT CLIN

<u>ANALYSE(S)</u>	<u>RÉSULTAT(S)</u>
<u>IgE SPECIFIQUES (ALLERGENES)</u>	
PRÉLEVÉ LE 16/07/28 10:50	
BLANC D'OEUF	7,70
GRAINES de SESAME	1,26
ARACHIDES	8,82
NOIX DE GRENOBLE	7,44
NOISETTES	1,02
NOIX DU BRESIL	0,48
AMANDES	2,53
PACANES	0,99
NOIX D'ACAJOU	2,25
PISTACHES	3,12
JAUNE D'OEUF	1,17
CHAT SQDAMES	0,50

***** NOTE *****

Veuillez prendre note que seul le nom a

The Case

Scenario

- 4 year old presents with pruritic skin rash on her trunk on day 7/10 of amoxicillin for OM.
- Diagnosed with allergy to penicillin and antibiotic changed to biaxin.
- The next day the rash is worse and she is told to avoid biaxin

True/False

- This child is likely to have an allergy to amoxicillin but not penicillin
- Multiple antibiotic allergies can occur
- Avoidance is an important part of management and she should have a medic alert bracelet for these allergies

Allergies to antibiotics

10-20% of hospitalized patients have “allergy to penicillin” on their chart

In large cohort studies, β -lactam allergy designation increases the risk for adverse events in hospitalized patients

When patients are evaluated for allergy 75-98% of those with “penicillin allergy” tolerate penicillin and other β -lactams.

Patients with a history or “diagnosis” of antibiotic allergy should be reassessed as there is a very high rate of “false” diagnoses.

Allergies to medications in children

Pearl

- The most common cause of rash in children is an acute infectious illness
- In a study where all comers were challenged with amoxicillin 94% of children had negative challenges
- Rashes often worsen over the first few days

Pitfall

- Many children treated with amoxicillin will have rashes
- Very few children with rash have an allergy to amoxicillin-most of those have delayed-type reactions-not IgE-mediated that are specific to the medication used.
- Patients still requiring antibiotics should be warned that the rash may continue or worsen.

How to diagnose allergies to amoxicillin/penicillin in children

Oral provocation test is the gold standard test.

Skin testing and serum IgE testing are less accurate

Children are given a small dose of amoxicillin followed by a large dose.

- No immediate reaction (within 1-4 hrs) suggest no IgE-mediated allergy to penicillin or amoxicillin

Delayed onset rash can occurring and is believed to be antibiotic specific (not related to the entire family)

Many children with delayed onset symptoms will likely out-grow reactions over time and should be reassessed in 2-3 years.

Although still under study-similar results are expected for other antibiotics

The Case

Scenario

- A mother brings her 4 month old infant for routine check up. The child is well with mild-moderate eczema and mother asks about introduction of solids.
- The family history is positive for an older sibling with peanut allergy.
- Mother wants to know about food introduction in this child.

True/False

- Delayed introduction of allergenic food will decrease risk of food allergy in this child.
- Food preparation affects allergenicity of foods.
- Do not introduce peanuts until seen by allergist

Food introduction to infants:

When did feeding and infant become a medical act?

Risk factors for food allergies

- Family history of atopy
- High birth order
- Urban environment
- Allergen avoidance-no pets in the home
- Maternal smoking
- Eczema
- Egg allergy

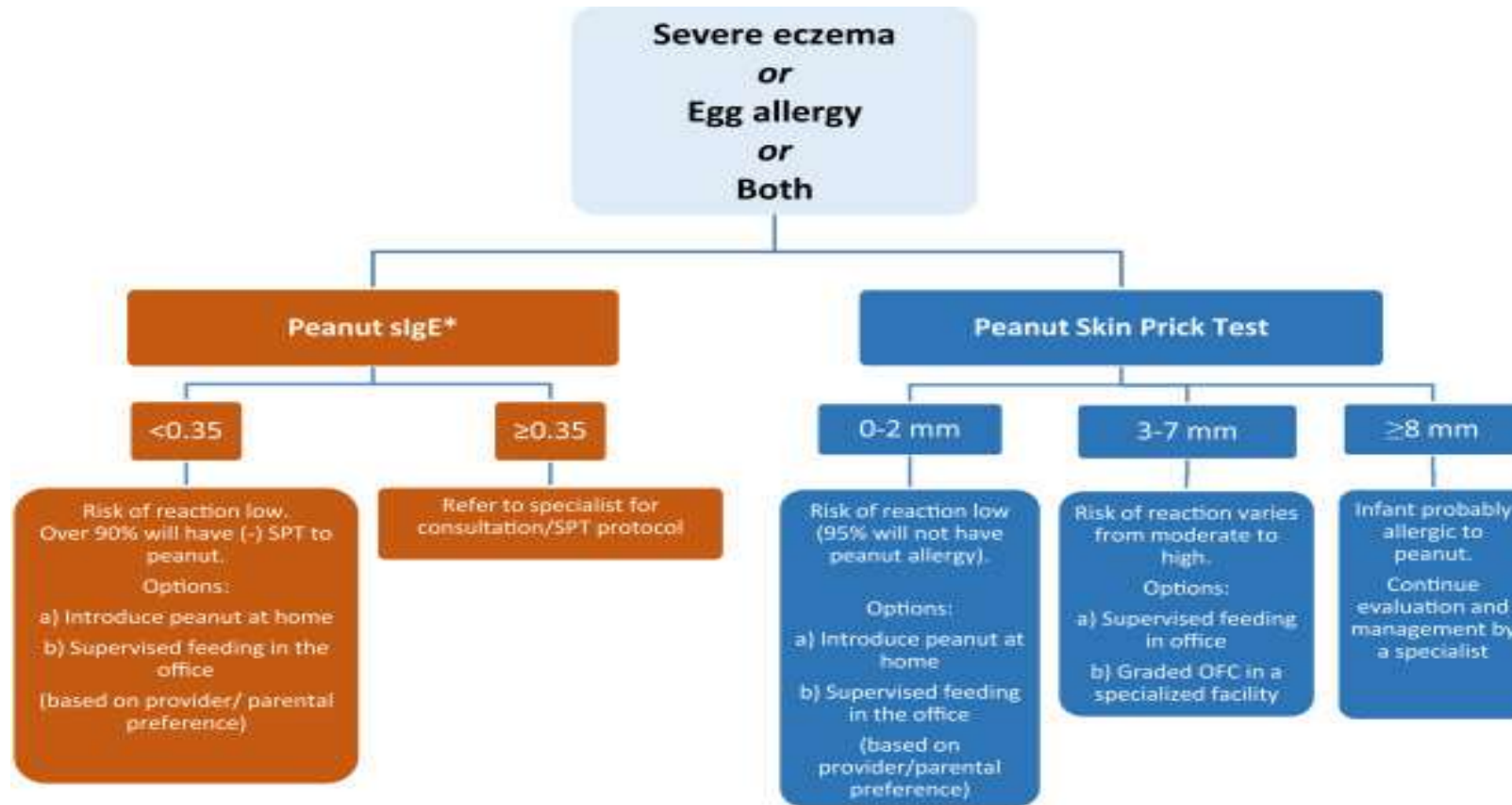


The “Problem”

- Food allergies affect 6-10% of the population
 - Many foods may be implicated although milk, egg, peanut, tree nut, sesame and seafood/fish are more common
- Diagnosis requires either a clear history of reaction plus a positive diagnostic test and/or a positive oral food challenge with objective symptoms.
 - In absence of history SPT has a 30% PPV and IgE blood tests 20%
- Previous recommendations for food introduction in infants shown to increase the frequency of food allergies (peanut) in high risk infants.
 - Only peanut was studied in the landmark trial.

Food Introduction in Infancy

The “Recommendation”



* To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.

Food Introduction in Infancy

The Realities



Best “chance” for allergy prevention occurs early <11months and even earlier.



Predictive values of suggested test show very high false positive rates



The study used to support these recommendations was not designed to “prove” this approach.



Unless access to allergy care is guaranteed, most patients at risk will not be able to apply the guidelines as written.



There are no reports of anaphylactic deaths due to foods in infants.



What about other foods?

Prevention strategies with actual supporting evidence.



Smoking avoidance



Breastfeeding if possible for 4-6 months—low grade evidence studies equivocal



No special diet for pregnant or lactating mother



Emollient therapy for eczematous skin








Introduce foods **without specific restriction** as early as possible.

What foods and how?

- Recommend to introduce eggs using the egg ladder.

Egg ladder

	Cracked eggshell	
	Utensils with raw cake mixture or raw egg	
	Processed meat/burger/sausage	↑
	Teacakes™ Milky Way™ Mars™ Snickers™	
	Crème Egg™ Chewits™	↑
	Hollandaise, Horseradish & Tartar sauces	↑
	Royal™ icing	
	Sorbet & Mousse	
	Mayonnaise/salad cream	↑
	Marshmallow	↑
	Meringue/fresh ice-cream	
	Crème caramel & Crème Brûlée	
	Scrambled egg	↑
	3. ALMOST RAW	↑
	Omelette	
	French Toast	↑
	Quiche	↑
	Yorkshire pudding	
	Fried/hardboiled egg	
	Cooked batter/tempura/breadcrumbs	↑
	Dried & fresh egg pasta & egg noodle	↑
	Pancake	
	2. LIGHTLY COOKED	↑
	Waffle biscuit	↑
	Boudoir™ & Lady's finger™ biscuits	
	Baked sponge/muffin/cake & biscuits	↑
	1. WELL COOKED	↑

Peanuts and nuts

- Introduce early (4-6 months)
- Can use peanuts crushed and mixed into apple sauce-start with $\frac{1}{2}$ peanut and increase as tolerated.
- Same strategy may be used for tree nuts and sesame
- Avoid peanut and nut butters initially as allergen bioavailability is increased in these forms



The Case

Scenario

- 9 month old given peanut butter for the first time
- Within 15 minutes develops perioral hives
- Symptoms resolve without intervention

True/false

- This child has demonstrated an allergy to peanut
- An epipen should be prescribed
- 1/5 children outgrow allergy over time so parents can try to give peanuts again in 2 years
- No other treatments available

Oral Immunotherapy for foods

Pearl

- Oral immunotherapy or desensitization is currently under investigation for children with food allergies.
- Risks include anaphylaxis and significant symptoms occur in most older children
- Many very young children tolerate slow introduction of allergenic foods into the diet even with a history of perioral hives and positive tests.
- Parental compliance is required

Pitfall

- Older children (>age 2 years) at increased risk for anaphylaxis
- Possibility of complete success (ie cure) is about 20% in children studied (older than age 6 years)
- In most children (>80%) increased of tolerant thresholds are achieved after 12 months
- Any attempt to desensitize should be done under supervision of an allergist and resuscitation equipment should be available

Case outcome

Pearl

- Oral desensitization is offered and child begins at $\frac{1}{4}$ peanut crushed in apple sauce.
- 6 months later tolerating peanut butter on toast.
- Skin test remains positive

Pitfall

- Threshold is increased
- Not known if “a cure” has been achieved
- Positive test suggests still sensitized.
- Long term prognosis-not known

Summary

Eczema care is key to decreasing risk for development of allergic sensitization.

Eczema is only rarely worsened by ingestion of specific foods

Complex food introduction needs to occur early and often

Oral food immunotherapy is possible but not for everyone

- Labor intensive and risks are significant

Most rashes are not drug related

Oral drug challenge a key diagnostic tool.

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