

Food Allergy Diagnosis & MANAGEMENT



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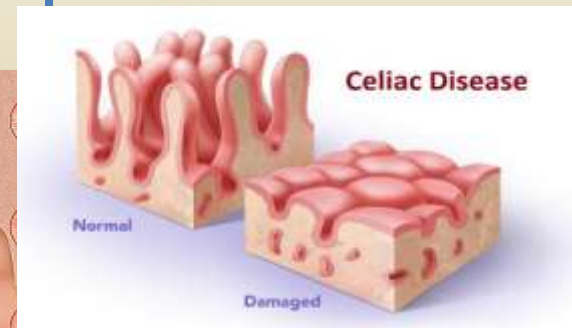
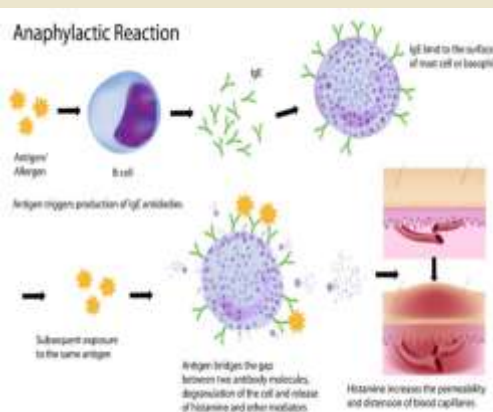
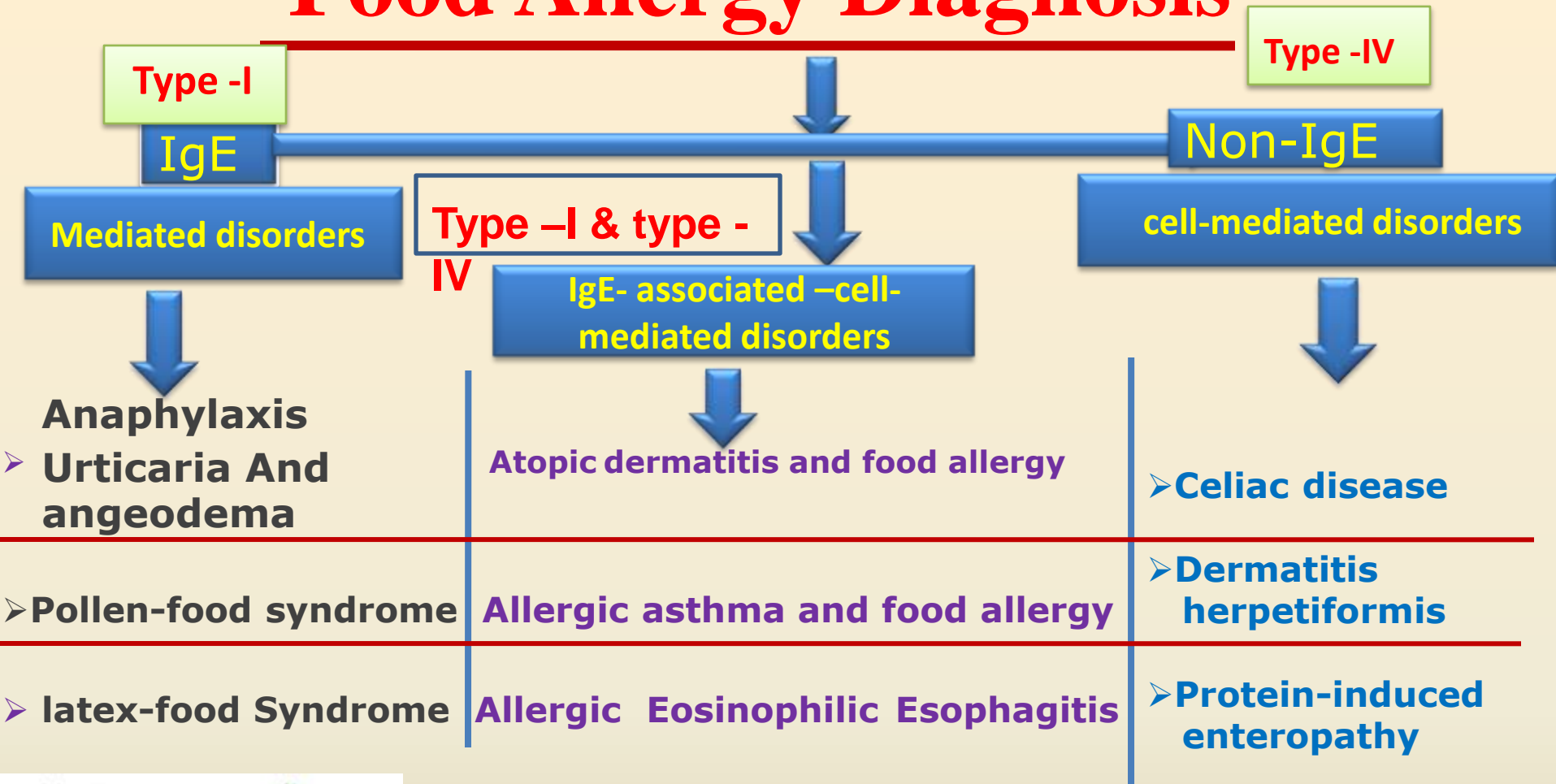
ALLERGY –IMMUNOTHERAPIST

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Food Allergy Diagnosis



Foods Involved

- More than 170 foods reported to cause IgE-mediated reactions
- 90% of food allergy in children from milk, egg, peanut, soy, wheat
- 85% of food allergy in adults from peanut, tree nuts, fish, shellfish
- Incidence varies by country, depends on exposure, genetics , and mode of food preparation

What makes Food Allergic ? IgE binding sites (EPITOPS)

Food allergy in adults

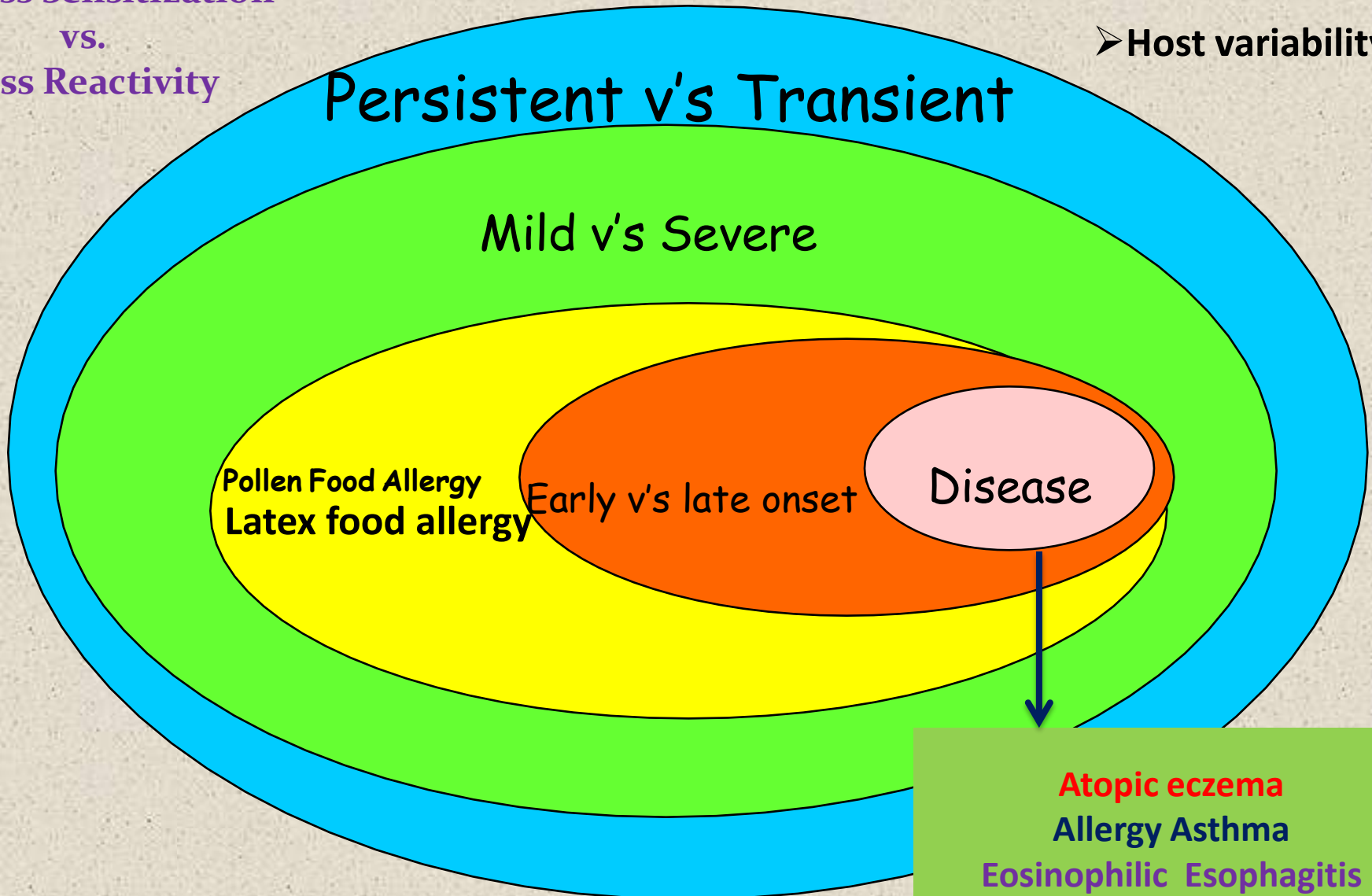


- *Fish*
- *Shellfish*
- *Nuts/seeds*
- *Peanuts*
- *Sesame*

Food Allergy Phenotypes

Cross Sensitization
vs.
Cross Reactivity

➤ Host variability



HISTORY

- Description of symptoms
- Time between ingestion of food and onset of symptoms
- Minimum quantity of food required to elicit symptoms

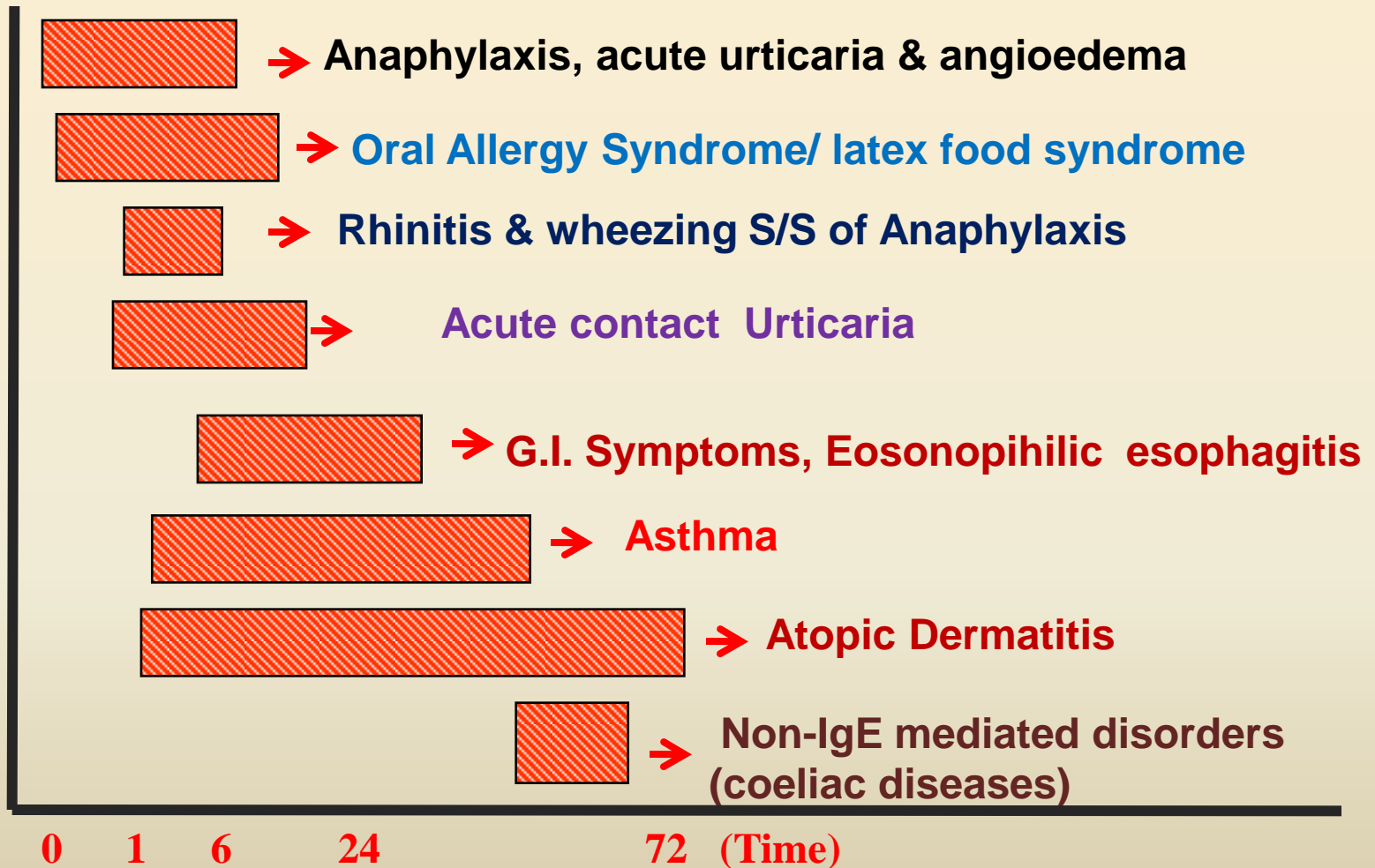
ANIMAL ORIGIN

- Milk
- Egg
- Fish
- Meat
- Poultry
- Sea foods

VEGETABLE ORIGIN

- Nuts & seeds
- Fruits & vegetables
- Herbs & spices
- Grains products
- Drinks such as :
Wine, Beer Tea, cola, etc.

FOOD ALLERGY DIAGNOSIS



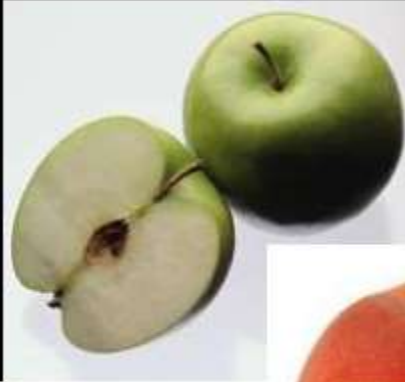
Oral Food Challenge (OFC) is Gold Standard

- Time consuming
- Risky
- Hospitalization/intensive care

Egg



Apple



Celeriac



Cod



Peach



Hazelnut



Peanut

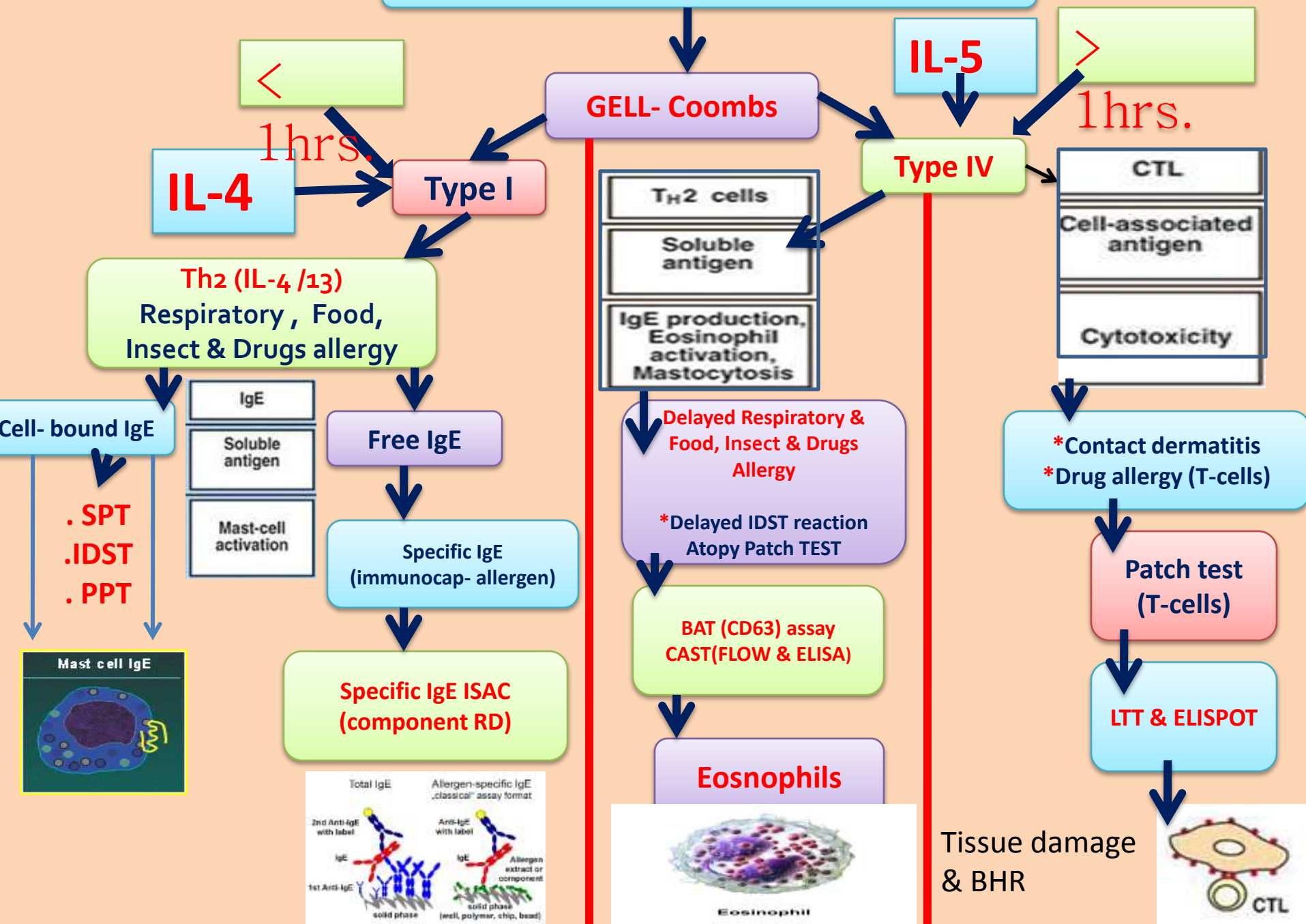
Shrimp



Milk



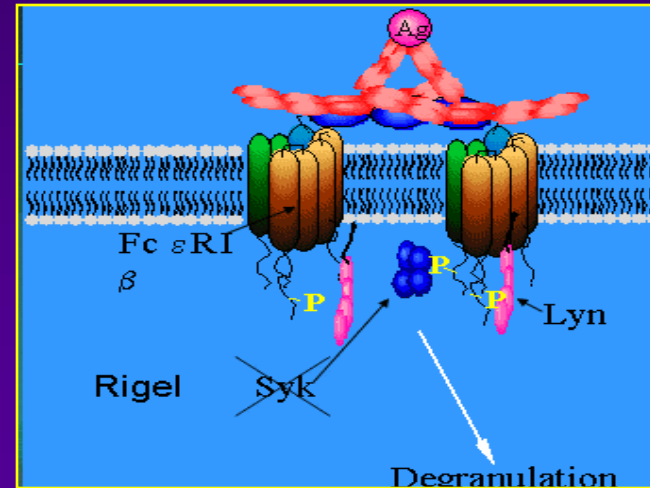
ALLERGY DIAGNOSIS



Food Allergy--Testing

- Skin tests
 - Diameter of skin wheal / flare
- RAST or similar
 - Quantity of food-specific IgE

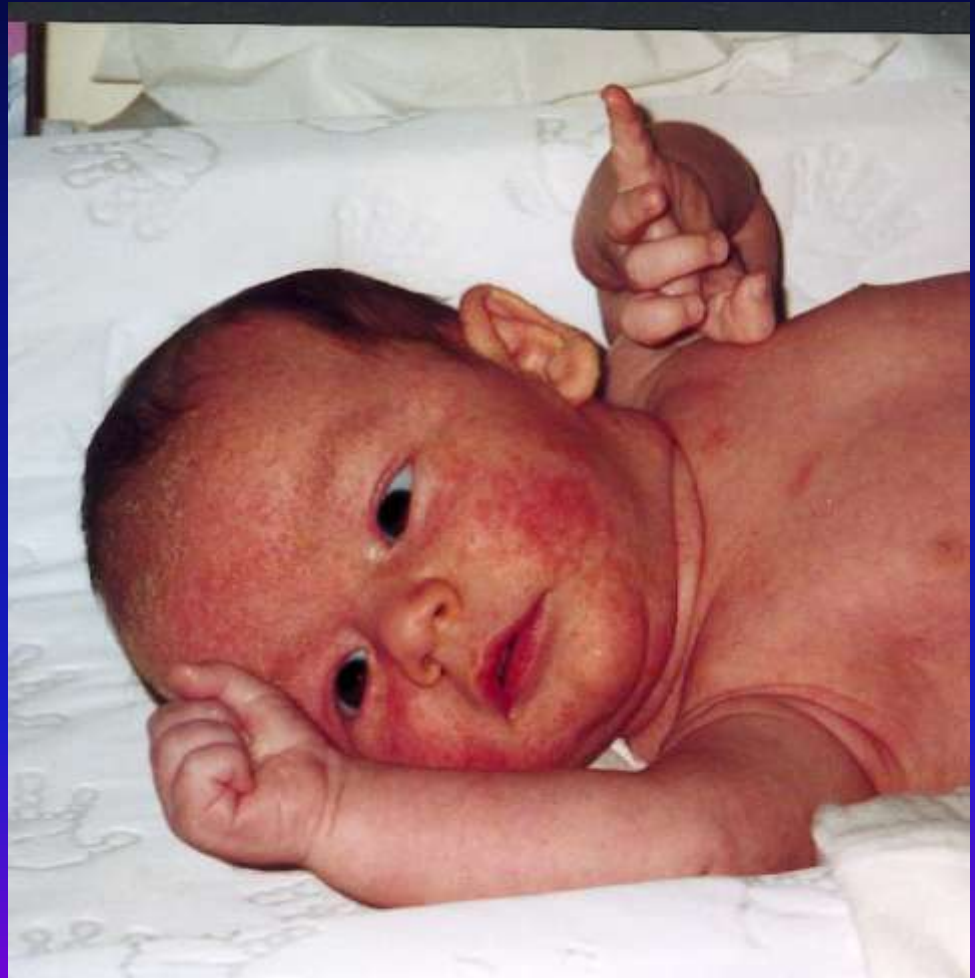
* CRD (Component Resolved Diagnosis)



< 0.1 → → → → → → → → → → >100
(no allergy) (highest allergy)

Case: Atopic Dermatitis

- 2 month old male**
with irritability,
eczematous rash
- exclusively breast fed
 - regular maternal diet
 - no apparent correlation with mother's diet
 - mother has mild AR



Results of Studies

- **Prick Skin Tests**

- milk: 8/12
- egg: 2/4
- peanut: 0/2
- soy: negative
- wheat: 4/15
- histamine: 5/10
- saline: 0/2

- **Food-IgE [kU/L]**

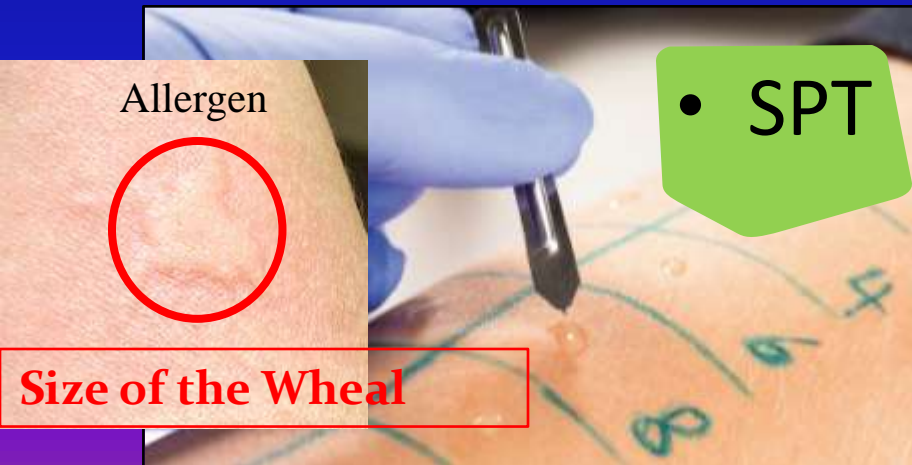
- milk: 6.1
- egg: 0.8
- peanut: <0.35
- soy: <0.35
- wheat: 4.1

Your next step:

- A. Eliminate egg, milk & wheat from mother
- B. Eliminate milk & wheat from mother
- C. Eliminate milk from mother
- D. Start hypoallergenic formula

Range for specific IgE test results

IgE level (kU/l)	Allergen specific IgE level
< 0,1	Below detectable levels
0.35 – 0.69	Low
0.70 – 3.49	Moderate
3.50 – 17.49	High
17.50 – 49.99	Very high
50 - 100	Very high
>100	Extremely high



Performance characteristics of ImmunoCAP[®] at cut-off 0.35 kU/L



immunoCAp
specific IgE

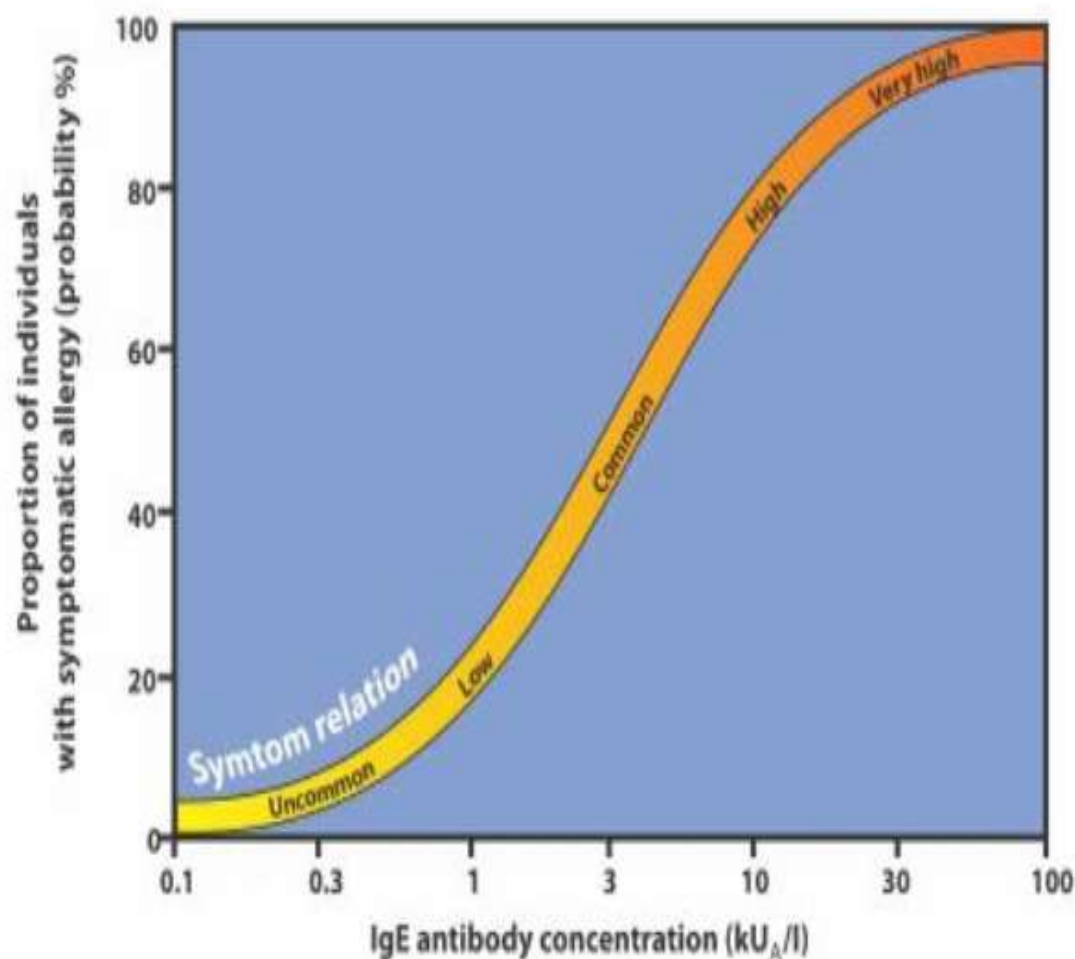
	Egg	Milk	Peanut	Soy	Wheat	Fish
No. pts pos/neg	145/51	95/101	136/60	34/162	23/173	52/144
sensitivity	98	100	97	94	96	94
specificity	45	30	38	25	20	65
Positive Predictive value	84	57	78	21	14	49
Negative Predictive value	88	100	85	95	97	97

Normal values

ImmunoCAP Allergen : $< 0.1 \text{ kU}_A/\text{l}$

ImmunoCAP Phadiatop/Allergen mix : $< 0.35 \text{ KU}_A/\text{l}$

The higher the level of Specific IgE antibodies, i.e. sensitization, the higher the risk for symptomatic allergy



Factors to consider for a final diagnosis :

- Age
- Degree of atopy
- Allergen load
- Type of sensitizing allergens
- Previous symptoms
- Other triggering factors

Interpreting RAST's - Examples

Age

(Specific IgE)

- 5 yr old with egg RAST = 2 kU/L: 50% PPV
- 5 mo old with egg RAST = 2 kU/L: 95% PPV

Disease

- Normal: 75% PPV for wheat: RAST = 26 kU/L
- Eczema: 75% PPV for wheat: RAST = 100 kU/L

History

- H/O peanut rxn: 50% react @ RAST = 2 kU/L
- No peanut rxn: 50% react @ RAST = 5 kU/L



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**



Predictive Values for CAP RAST

for Children with AD

(Specific IgE)

Food Protein	95% PPV (kU_A/L)	90% PPV (kU_A/L)	95% NPV (kU_A/L)	90% NPV (kU_A/L)
Egg	6	2	-	0.6
Milk	32	23	0.8	1
Peanut	15	9	Best NPV = 85% @ 0.35	Best NPV = 85% @ 0.35
Fish	20	9.5	0.9	5
Soy	Best PPV = 50% @ 65	-	2	5
Wheat	Best PPV = 75% @ 100	-	5	79

95% Predictive Decision Levels

Allergen	Decision Pt (kUA/L)	PPV	Sens.	Spec.
Egg	7	98%	61%	98%
(≤ 2 yrs of age)+	2	95%		
Milk	15	95%	57%	94%
(≤ 1yr of age)++	5	95%		
Peanut	14	100%	57%	100%
Soy	30	73%	44%	94%
Wheat	26	74%	61%	92%
Tree nuts+++	15	95%	----	----

+ Boyano MT, et al. *Clin Exp Allergy* 2001; 31:1464-9.

++ Garcia-Ara C, et al. *JACI* 2001; 107:185-90.

+++ Clark AT, Ewan P. *Clin Exp Allergy* 2003; 33:1041-45.

Sampson *JACI* 2001; 107:891-96.

Size Of SPT With 100% Likelihood Of Positive Open Challenge

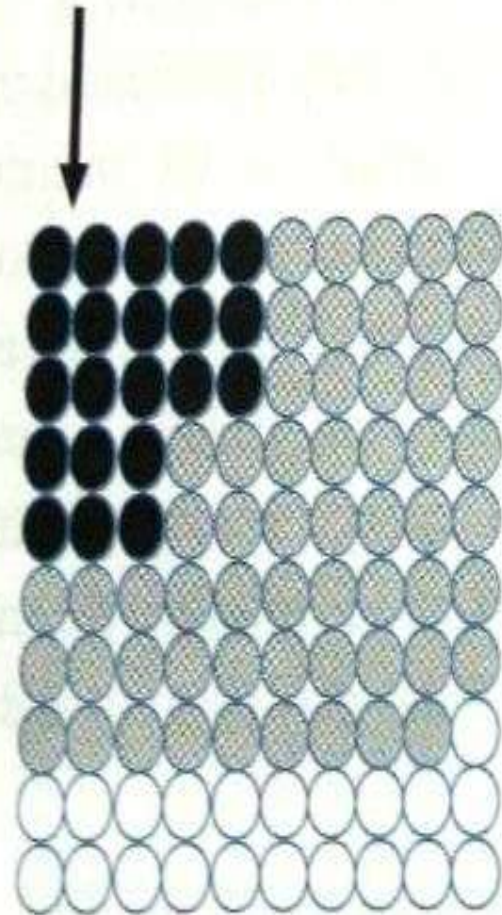
- PPV of positive SPT - <50% vs DBPCFC
NPV of negative SPT - >95% vs DBPCFC

	Milk	Egg	Peanut
Children 0-2yrs	≥6mm	≥5mm	≥4mm
Children all ages	≥8mm	≥7mm	≥8mm



• SPT

SPT ≥ 8 mm = "diagnostic" of peanut allergy



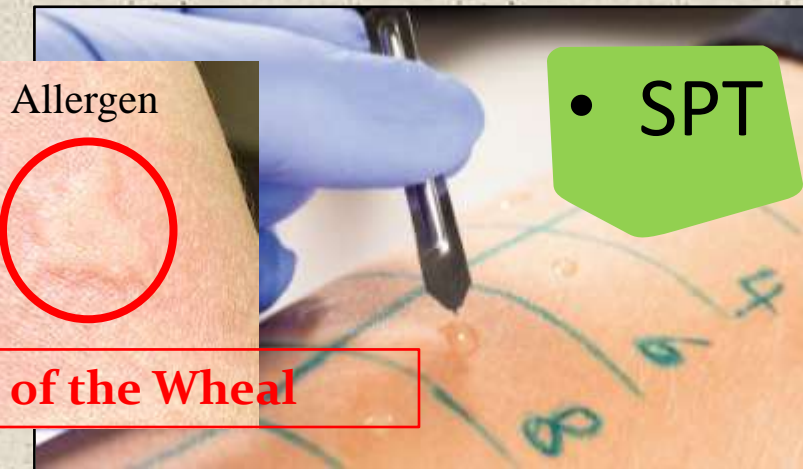
SPT 3 to 7 mm =
IMMUNOLOGICAL GREY ZONE

SPT < 3 mm = very unlikely to
be peanut allergy

Sensitivity, specificity, NPV and PPV for specific cut-off levels

	Sensitivity %	Specificity %	Odds Ratio	95% CI	PPV	NPV
SPT > 5mm	91	50	9.7	2.3–43.6	88	57
SPT > 8mm	77	81	14.2	3.1–73	94	46
IgE > 7 kU/L	81	50	4.3	1.2–16.3	82	40
IgE > 15 kU/L	49	69	2.1	0.6–7.8	86	25
Combination 1	64	80	7.1	1.6–35.9	93	34
Combination 2	62	88	11.4	2.2–79.8	95	37

Combination 1: SPT > 5 mm and IgE >7; Combination 2: SPT > 8 mm and IgE >7



immunoCAP
specific IgE



50% and 95% Predictive Value have been Established for Food Specific-IgE and SPT

TABLE II. Tests to assess the likelihood of obtaining a positive or negative OFC in children

Food	Serum food-IgE (kIU/L) [†]		SPT wheal (mm) [†]	
	~95% Positive	~50% Negative [†]	~95% Positive	~50% Negative [†]
Cow's milk	$\geq 15^{16}$ ≥ 5 if younger than 1 year ¹³²	$\leq 2^{23}$	$\geq 8^{21}$	
Egg white	$\geq 7^{16}$ ≥ 2 if younger than 2 years ¹³³	$\leq 2^{23}$	$\geq 7^{21}$	$\leq 3^{22}$
Peanut	$\geq 14^{16}$	≤ 2 with and ≤ 5 without history of peanut reaction ²⁴	$\geq 8^{17,21}$	$\leq 3^{17}$
Fish	$\geq 20^{16}$			

Allergen



• SPT

immunoCAP
specific IgE



Size of the Wheal

AD and Milk Allergy

Milk PST – 8/12 mm
Milk-IgE – 6.1 kU_A/L

**2 weeks after
initiating a
milk-free diet**

**1/3 of infants with
atopic dermatitis
have food allergies**



MILK – 30 PROTEINS

- **80 % Casein**
- **20% whey -**
 - **β Lactoglobulin**
 - **α Lactoglobulin**
 - **Bovine serum – globulin & albumin**



- **β - Lactoglobulin is principal protein in Whey Component (61%) in Cow's Milk but is absent in human milk.**

Intact protein formula/hydrolyzed protein Formula & Extensively hydrolyzed protein formula

Native Protein



Free Amino Acid
Formulas

individual
amino acids

Intact Protein Formula



Hydrolyzed Protein Formula



Extensively Hydrolyzed Protein Formula



Hypoallergenic Formulas

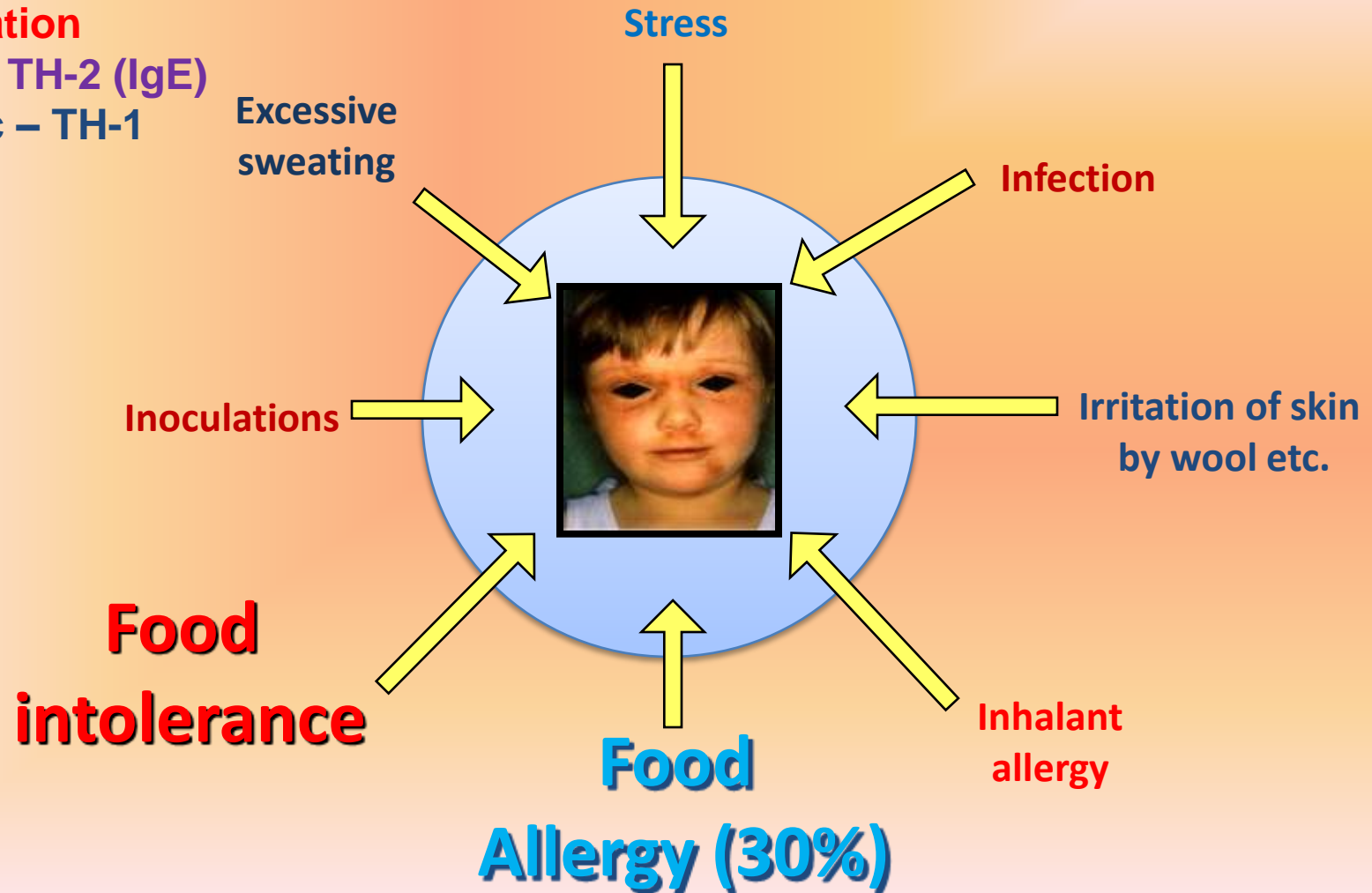
- **Partially hydrolyzed whey**
 - Good Start
- **Partially hydrolyzed casein/whey**
 - Gentlease
- **Partially hydrolyzed soy**
 - Good Start Soy
- **Extensively hydrolyzed casein**
 - Alimentum
 - Nutramigen
 - Pregestimil
- **Extensively hydrolyzed whey**
 - Peptamen
- **Elemental (free amino acid)**
 - EleCare
 - Neocate
 - E028 Splash
 - Pediatric Vivonex
 - Tolerex
- **Mixed amino acid + hydrolysate**
 - Pepdite (aa + soy/pork)
 - Peptinex (aa + casein)

Precipitation & Exacerbation Of Atopic Dermatitis



Complicating factors in atopic dermatitis

Biphasic inflammation

- Acute – TH-2 (IgE)
- Chronic – TH-1



Where is Role of Component-Resolved Diagnostics (CRD)?

	RAMU		SHAMU	
3 months	Eczema		Eczema	
6 m SPT to egg	+3		+4	
3 y SPT to peanut	+4		+5	
Treatment	Diet, no egg or peanut		Diet, no egg or peanut	
Symptoms, peanut	Never eaten		Never eaten	
IgE to peanut (10 y)	61 kU/l		45 kU/l	
Food challenge (10 y)	No symptoms		Urticaria, severe, stomach-ache, rinitis, cough	

Same same - but different?

What makes Food Allergic ? IgE binding sites (epitops)

Proteins - 20 families (0.26%)

Cupin family of Proteins

Vicillins
(Peanut, soyabean)

Prolamin family of Proteins

Albumin
(Mustard seed, Tree nuts)

PR-10 (Pathogenesis related) Proteins

The oral allergy syndrome
(Celery Carrot)

Animal Food Allergens

The Tropomyosins
(Crustaceans & Mollusks)

Legumins
(Almond, Cashew nut)

Lipid Transfer Proteins
(Peach, Lettuce)



The parvalbumins
(Fish, Edible frogs)

Multiple families
(Egg & Milk allergens)



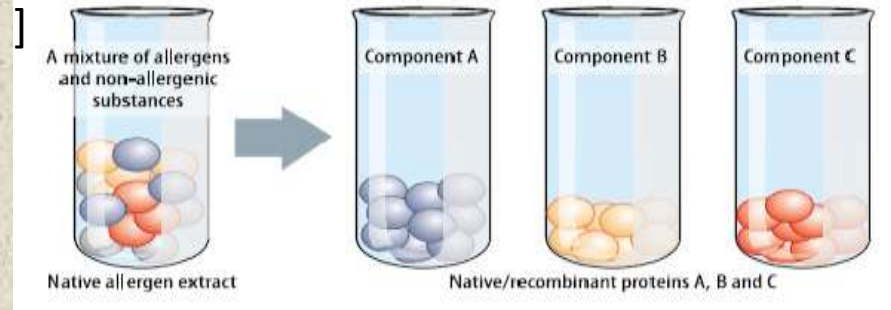
Arachis hypogaea – peanut



General reasons why molecular allergy (MA) is applied to diagnostic methods (IgE testing)

Role Of Component-resolved Diagnostics (CRD)

A science that make it feasible to quantify IgE antibodies to specific allergen proteins on a molecular allergologic level



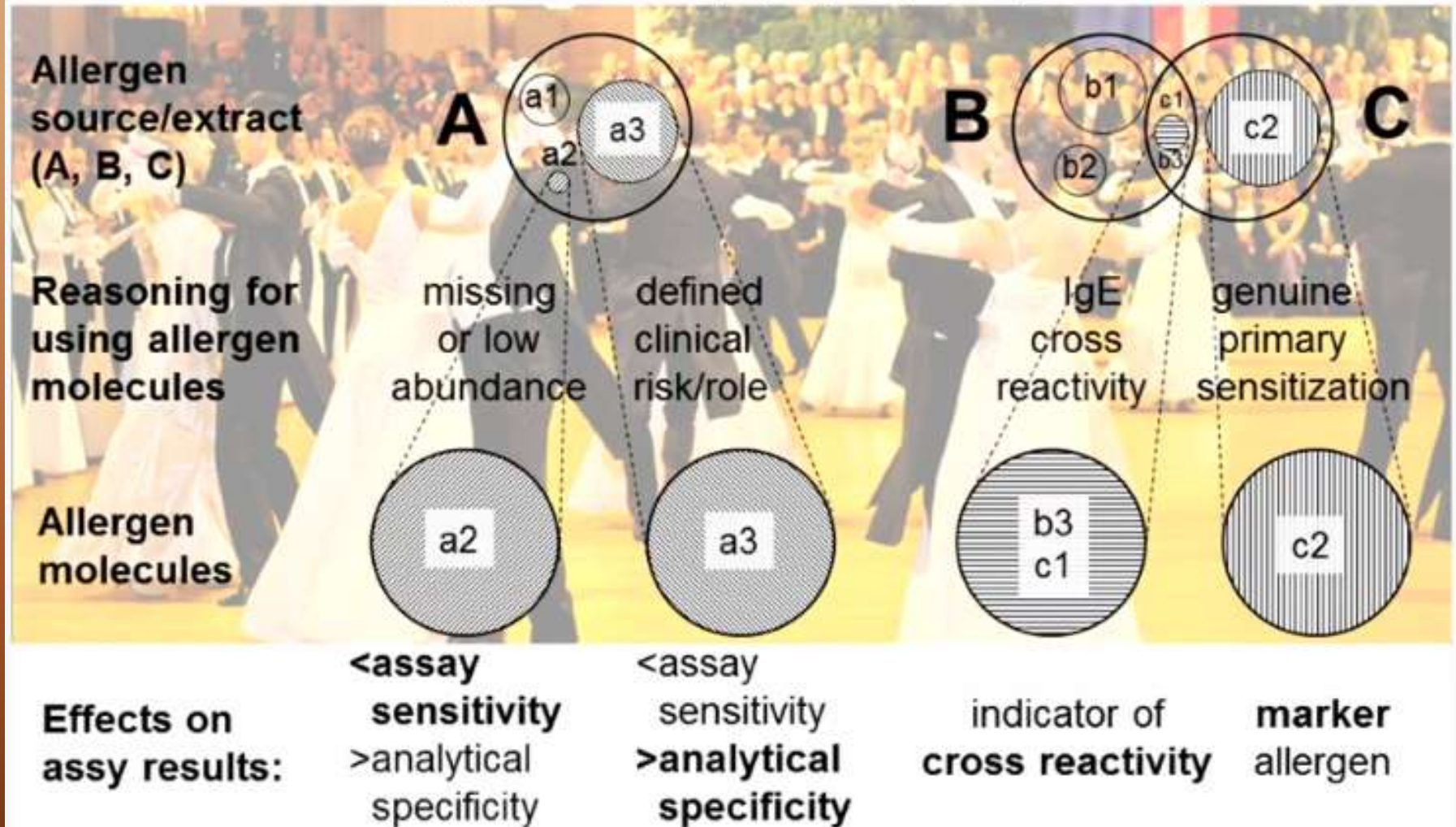
Whole Allergen Components, (Individual Allergenic Epitopes Molecules)

CRD have been introduced in order to increase the probability of

- True Food/aero-allergens & insects Allergy diagnosis
- Identify patients at high risk of reactions
- Identify patients more prone to persistent disease

General reasons why molecular allergy (MA) is applied to diagnostic methods (IgE testing)

Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, Ollert M et al.
Pediatr Allergy Immunol 2016;27(Suppl.23):1-250 (free access)



Marker allergens

```
graph TD; A[Marker allergens] --> B["„Species-specific“ marker allergens"]; A --> C[Cross-reactive marker allergens]; A --> D[Prediction of symptoms]; B --> E[Genuine sensitization against a certain allergen source]; C --> F[Cross-sensitization];
```

„Species-specific“ marker allergens

Genuine sensitization against a certain allergen source

Cross-reactive marker allergens

Cross-sensitization

Prediction of symptoms

***“Rule of thumb”*: How to use MA**

Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, Ollert M et al.
Pediatr Allergy Immunol 2016;27(Suppl.23):1-250 (free access)

- Suspected allergen from family with **broad cross-reactivity?** i.e.
 - PR-10,
 - nsLTP
 - profilin
 - polcalcin
 - albumin
 - parvalbumin
 - tropomyosin
- Test specific IgE only to **one representative** member, i.e.
 - i.e. Bet v 1
 - Pru p 3
 - Phl p 12 or Bet v 2
 - Phl p 7 or Bet v 4
 - Fel d 2
 - Gad c 1
 - Pen a 1

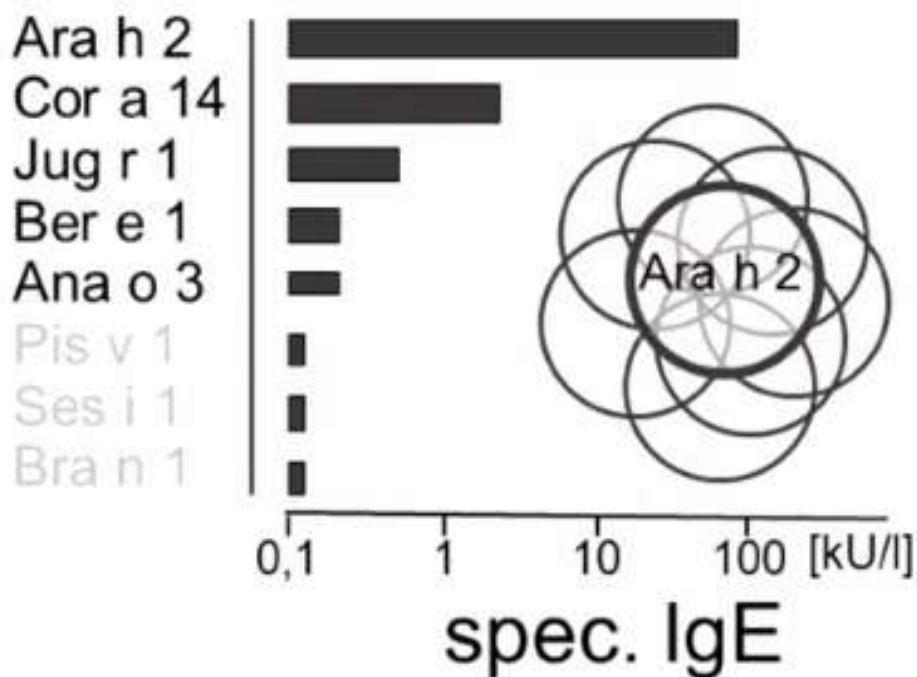


***“Rule of thumb”*: How to use IgE tests in MA**

Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, Ollert M et al.
Pediatr Allergy Immunol 2016;27(Suppl.23):1-250 (free access)

- Allergen from family with **limited cross-reactivity?** (seed storage proteins, lipocalins)

2S albumins



- test suspicious member(s) and related ones*
- hierarchy indicates primary sensitizer
- *if negative, cross-reactivity is unlikely

Vegetable Origin

Rule of Thumb



- A.** Profilin and PR10 proteins
- o Highly cross reactive (PR 10 especially to Birch)
 - o Often associated with less severe reactions e.g. OAS
- B.** nsLTP's and Storage Proteins (**highly reactive**)
- o Associated with more severe reactions
 - o More heat/digestive enzyme resistant and therefore can be more often associated with OAS and well as digestive problems



Vegetable Origin

Storage proteins

Storage proteins

- Proteins found in seeds
- Often stable and heat resistant
- Often associated with systemic and severe reactions (Anaphylaxis)

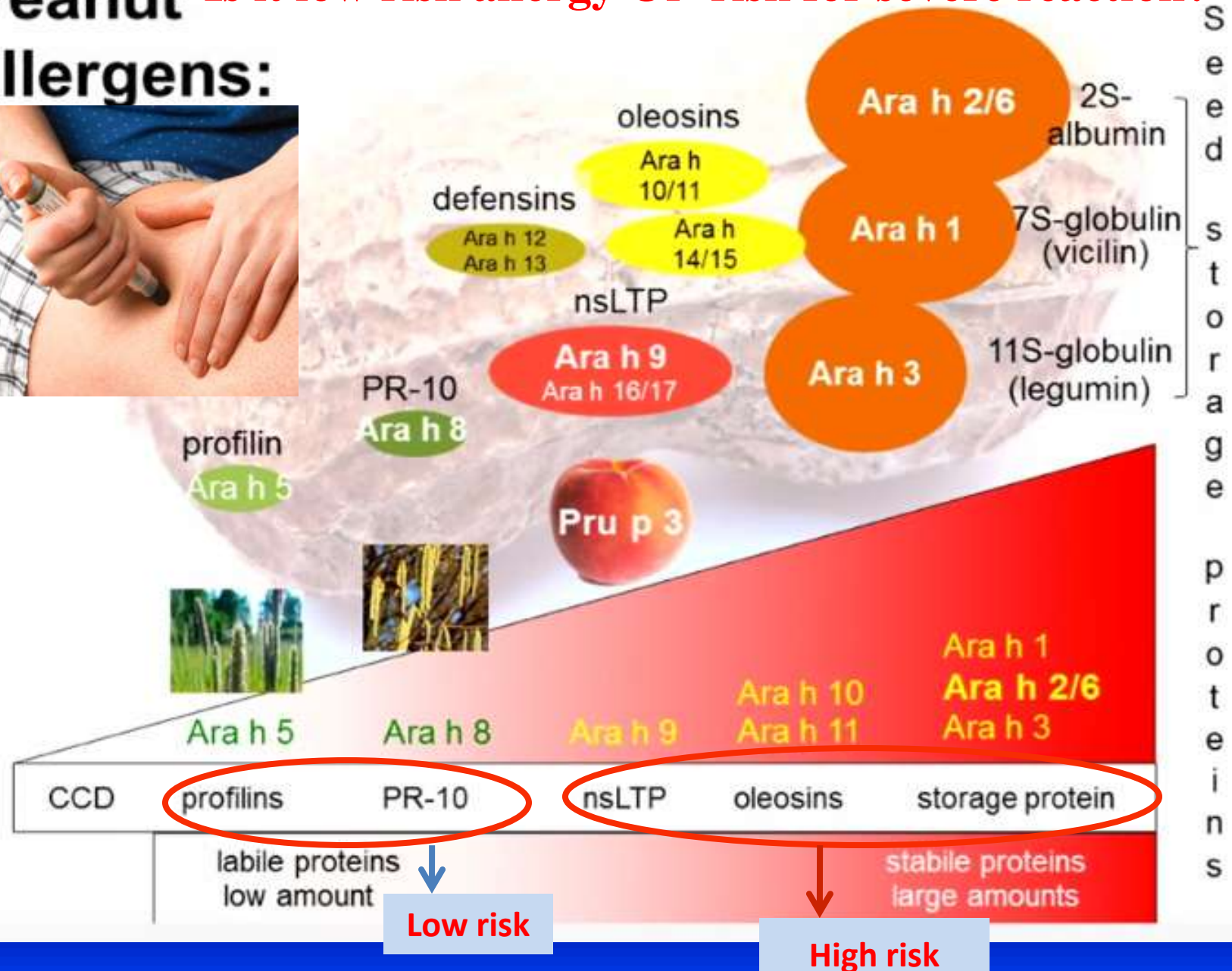
- Legumes
- Nuts
- Grains and seeds



2 S albumin, Ara h 2	Gliadins
7 S globulin, Ses i 3	Alpha amylase inhibitors
11 S globulin, Gly m 6	Vicilin, Jug r 2

Peanut allergens: Is it low risk allergy Or risk for severe reaction?

Peanut allergens:



H/O Urticaria & S/S of Anaphylaxis After Eating Nut Mix.

Is it low risk allergy Or risk for severe reaction?

Avoid Peanuts or All Nuts

SPT - > 6mm. Wheal Size
specific IgE to peanut, 58kU/l,

Ara h 1 4.8 kU/l All other nuts <0.1 kU/l

Ara h 2 93kU/l

Ara h 3 4 kU/l

Ara h 8 <0.1 kU/l

Ara h 9 + (LTP)
Ara h 1,2,3 +/-
Ara h 8 - (PR10)

Ara h 9 -
Ara h 1,2,3 +
Ara h 8 -

Ara h 9 -
Ara h 1,2,3 -
Ara h 8 +

Primary sensitization
Risk of severe reactions

Secondary sensitization
Cross-reactivity with birch
pollen
Local reactions (OAS)

Molecular based Sp. IgE



Assessment of peanut allergy (High risk)

Peanut (SPT/specific IgE) + Ara h 2

Peanut: neg
Ara h 2: neg

Low risk for severe reactions to peanut

Further testing:
In geographical areas where birch is common consider testing for Ara h 8

Peanut: pos
Ara h 2: neg

Risk for severe reactions to peanut

Further testing:
Risk grading:

Ara h 1	● ● ●
Ara h 3	● ● ●
Ara h 9	● ● ●
Ara h 8	● ●
CCD	●

Peanut: pos
Ara h 2: pos

High risk for severe reactions to peanut

Inj-Adrenaline



Epipen®



Peanut allergen Components

RAMU



SHAMU



IgE to peanut (10 y)

61 kU/l

45 kU/l

IgE to Ara h 2

< 0.35 kU/l

35 kU/l

IgE to Ara h 8

62 kU/l

3.5 kU/l

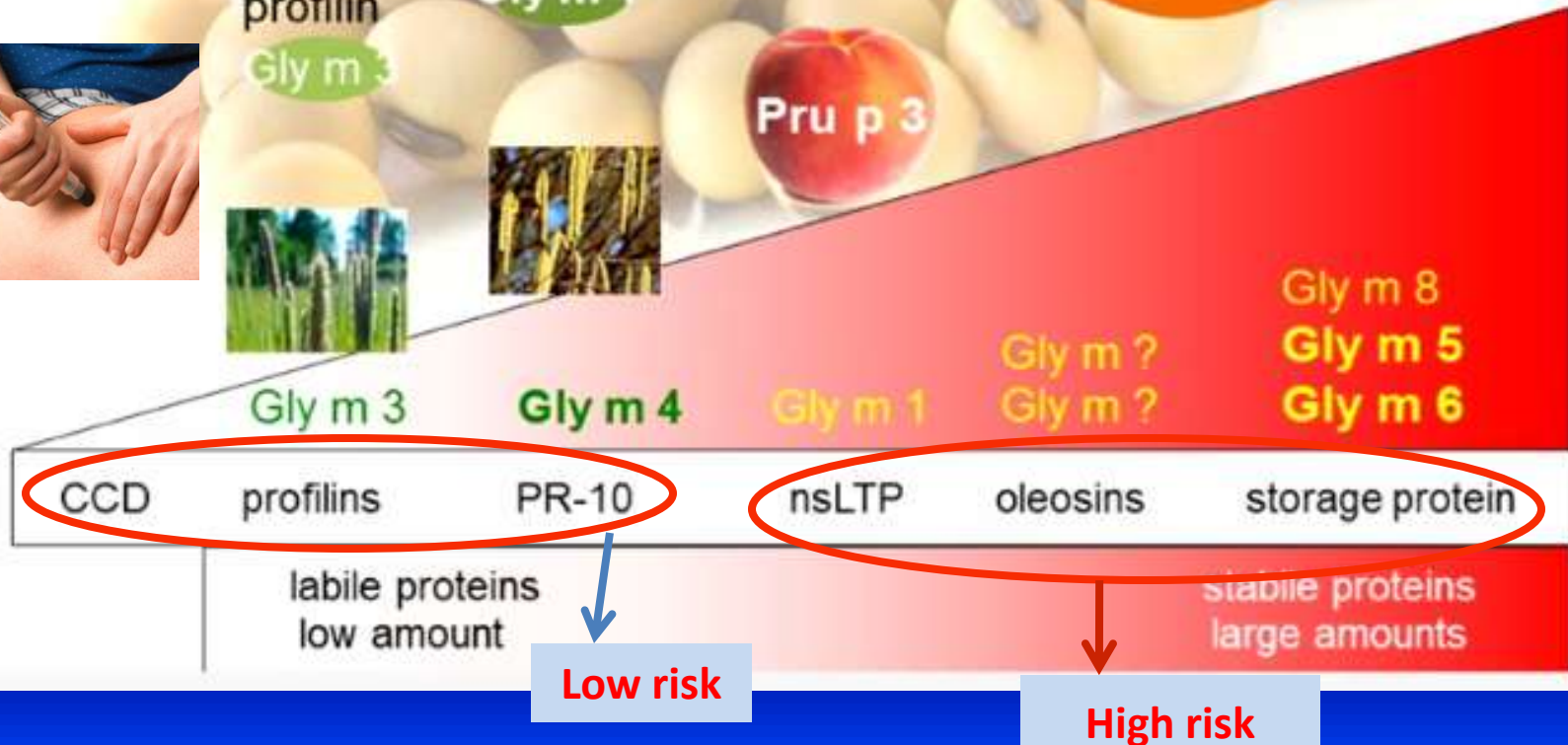
Food challenge
(10y)

No symptoms

Urticaria, severe,
stomach-ache,
rinitis, cough

Soy allergens: Is it low risk allergy Or risk for severe reaction?

Test with
ImmunoCAP[®]
Allergen Soybean
+ Gly m 8 + Gly
m 5/Gly m 6



S
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Suspicion of soy allergy/ Risk for severe reactions?

- Test with ImmunoCAP □ Allergen Soybean + Gly m 8+Gly m 4 + Gly m

Soybean: neg
Gly m 4: neg
Gly m 5/Gly m 6:
neg

Soybean: pos or neg
Gly m 4: pos
Gly m 5/Gly m 6: neg

Soybean: pos
Gly m 8: pos or neg
Gly m 5/Gly m 6:
pos



If patient is pollen- allergic:

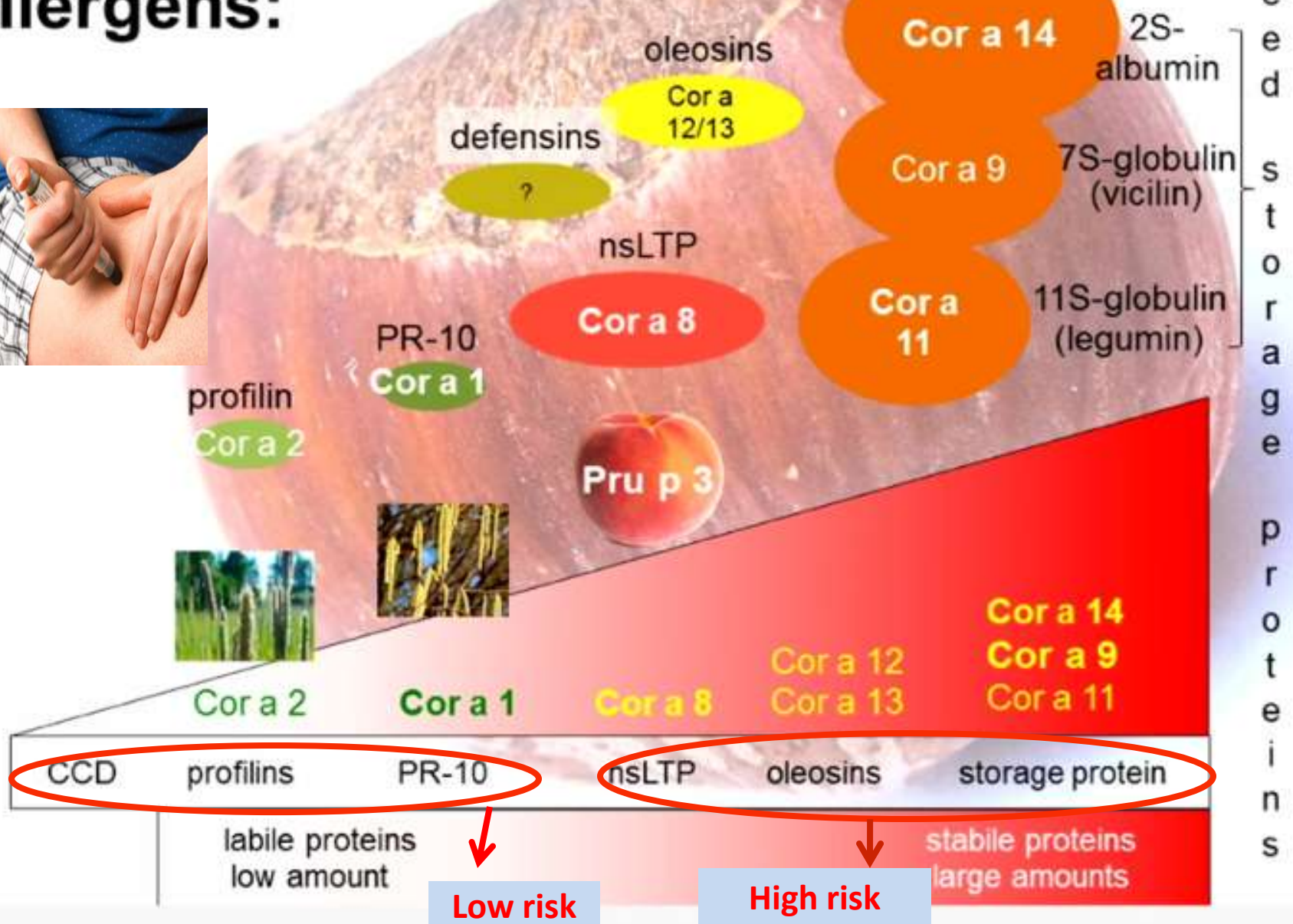
**Risk for reactions to soy
- predominantly OAS
but sometimes severe**

**Risk for severe
reactions to soy**

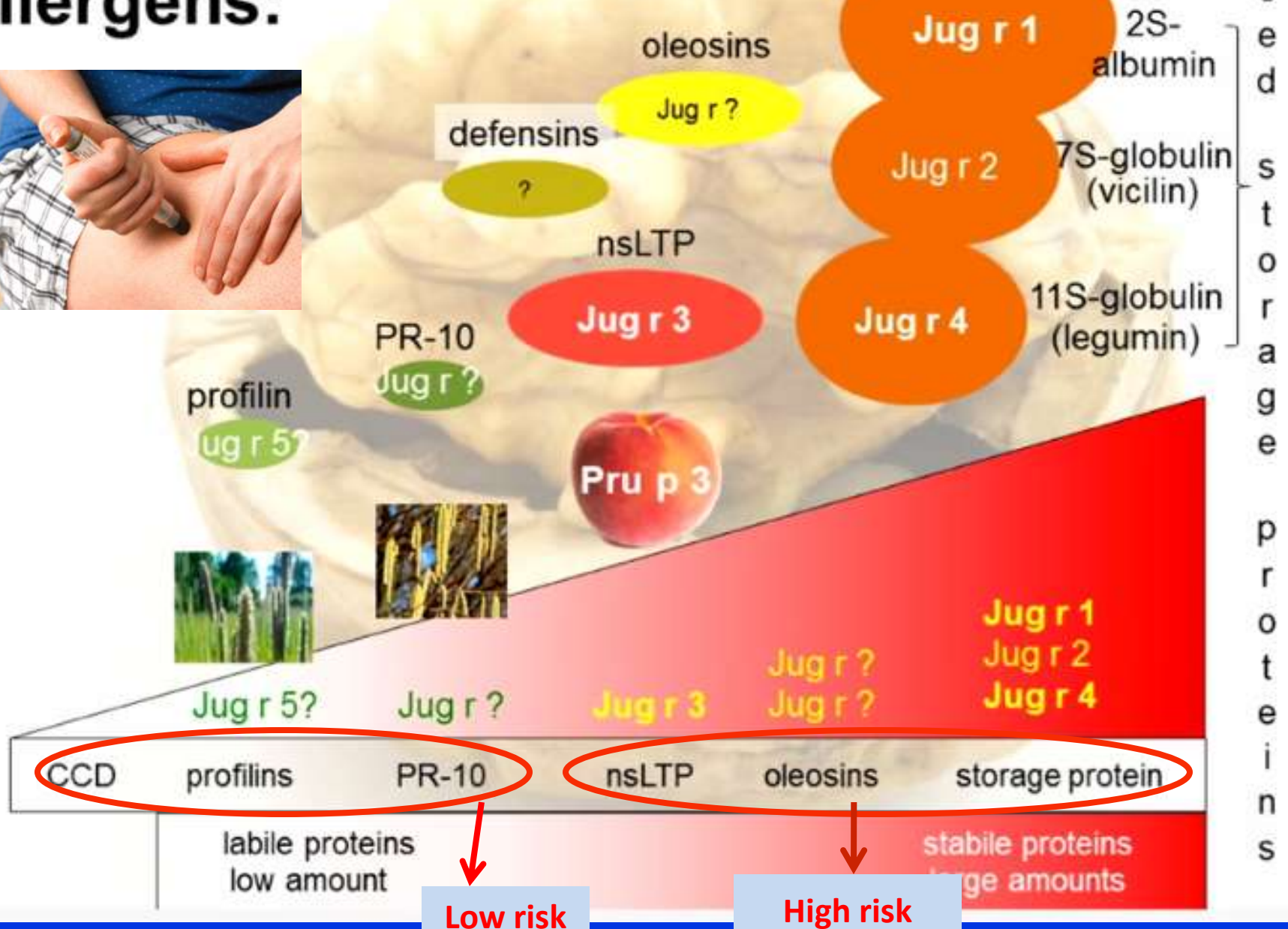
Mittag JACI 2004, Ballmer-Weber JACI 2007, Kleine-Tebbe JACI 2002, Treudler JInVACI 2008
Van Zuuren Allergy 2010, Kosma Acta Paediatr 2011

Hazelnut allergens:

Is it low risk allergy Or risk for severe reaction?



Walnut allergens: Is it low risk allergy Or risk for severe reaction?



EGG – 40 Proteins

- One of the most common allergies in infants and young children
- Common clinical decision - reintroducing cooked egg back into the diet

Major Egg Allergen Components¹

Gal d 1	Ovomucoid	11 %	→ High risk
Gal d 2	Ovalbumin	54%	
Gal d 3	Conalbumin	25%	
Gal d 4	Lysozyme	12%	



1, Bernhisel-Broadbent et al J Clin Allergy Immunol 1994;93;1047-59

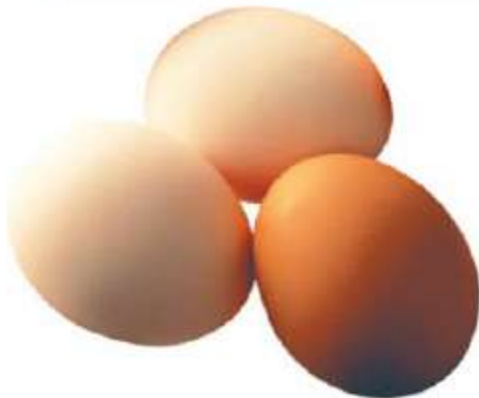
(Respiratory Allergy – Significant)

Assessment of egg allergy (High risk)

Egg white (SPT/specific IgE) + Ovomucoid

Egg white: neg
Ovomucoid: neg

Low risk for clinical
reactions to egg



Egg white: pos
Ovomucoid: neg

Risk for clinical
reactions to egg

Absence of
IgE antibodies to
ovomucoid indicates
tolerance to
ingestion to baked
egg

Egg white: pos
Ovomucoid: pos

High risk for clinical
reactions to egg

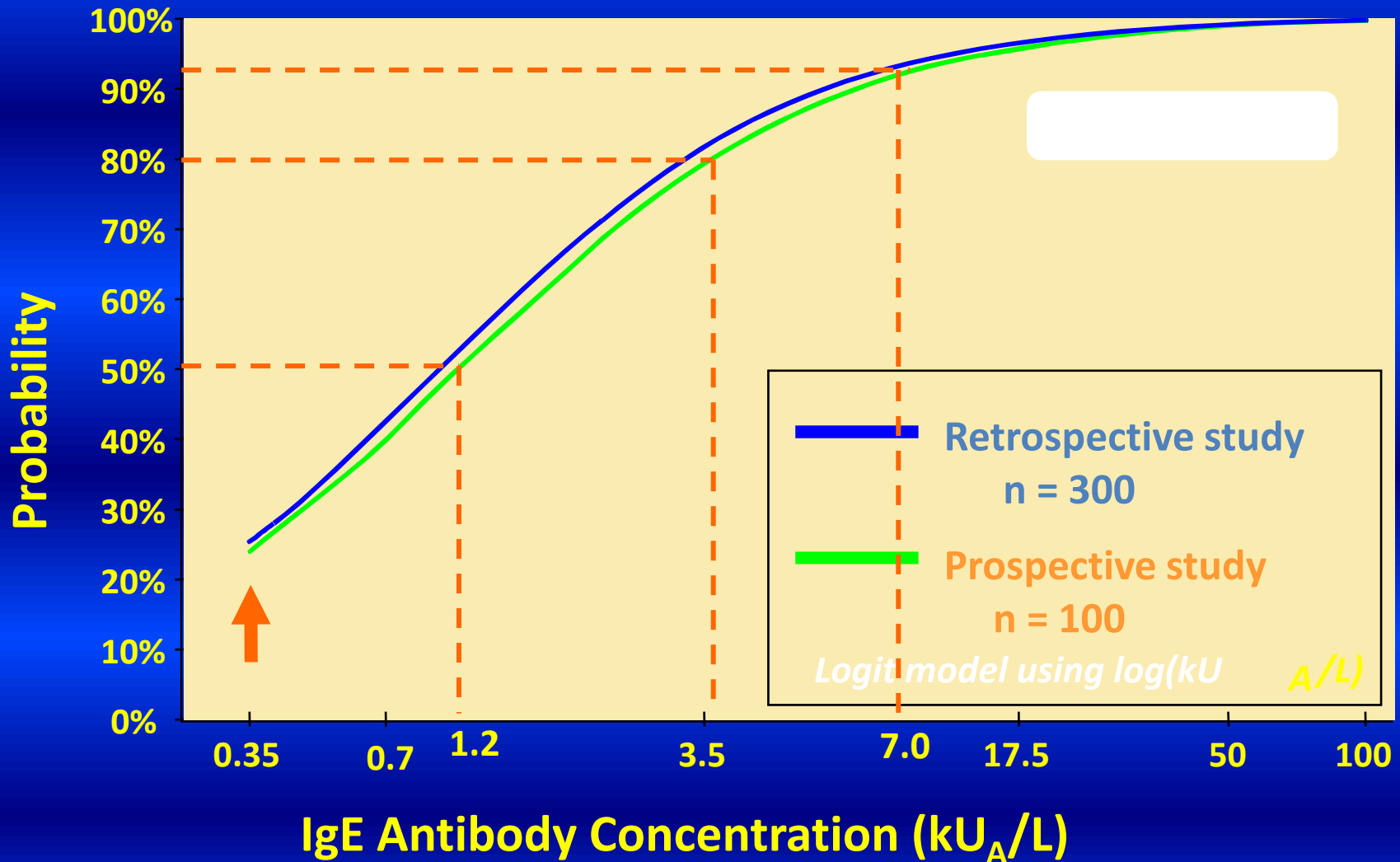
Increased risk for
persistent egg
allergy



EpiPen®



Probability of Reacting to Egg





Wheat allergy



Wheat

- Among the 6 foods responsible for most food allergic reactions in children
- Extensive cross-reactions to grasses and fruits
- What components are important?
- Omega-5 gliadin
- Linked Clinically to Exercised Induced Anaphylaxis¹²



¹Palosuo et al J Allergy Clin Immunol 1999;103:912-7

² Ito et al Allergy 2008 63:1536 - 1542

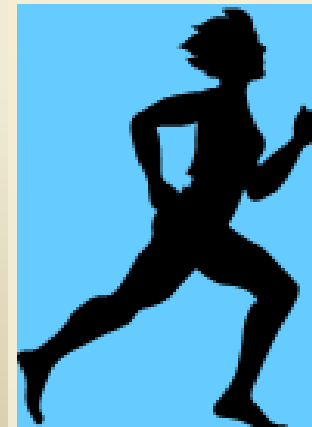
➤ **ALBUMEN INDUCED – BAKER'S ASTHMA**



Exercise-induced Anaphylaxis

16 year old athlete developed hives and fainted on two separate occasions, while running, 2 hours after lunch. She had a tuna salad sandwich with celery. She has eaten this same sandwich since without symptoms but not within 6 hours of running

- Usually occurs within two hours of eating allergenic food
- Onset during physical activity
- Foods most frequently reported to have exercise-induced anaphylaxis:
 - Wheat (omega-5-gliadin) and other grains
 - Celery and other vegetables
 - Shellfish (shrimp; oysters)
 - Chicken
 - Squid
 - Peaches and other fruits
 - Nuts especially hazelnut
 - Peanuts and soy beans
- May be associated with aspirin ingestion





Shellfish Reaction **Tropomyosin**



25 year old man who has eaten shellfish and fish his whole life, with absolutely no problem at all. Last month, he ate fish/shellfish for dinner (6pm) and went home feeling fine. That night (around 11pm) he began itching and flushing, and felt abdominal discomfort.

Cofactor- . NSADIS/Beta blocker /ACE-I
Alcohol
Exercise



Fish allergy: parvalbumin and beyond

Animal Origin

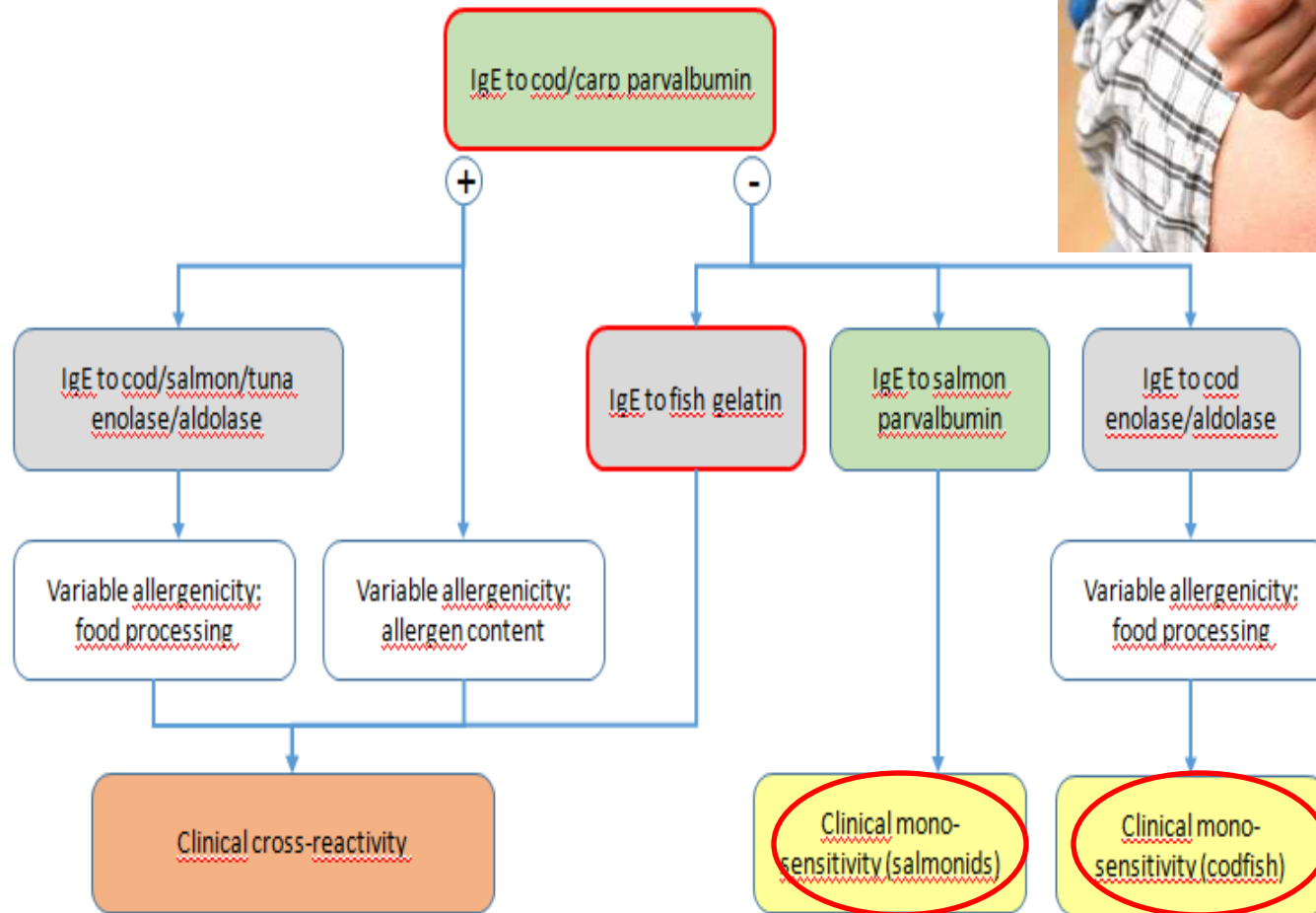
Fish Allergy: Parvalbumin/Shellfish:Tropomyosin

- A class of highly conserved Protein
- Physically associated with actin and myosin in muscle Fibres
- Heat stable
- Found in most edible parts of crustaceans
- Dust mite
- Cockroach
- Crustacean
- IgE- mediated alpha gal food allergy
 - (Beef/pork & lamb)
 - Egg- ovomucoid





fish allergens for IgE-diagnosis































Epipen




























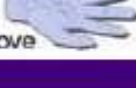

IgE- mediated alpha-gal food allergy (Beef /pork &lamb)

- H/O urticaria or anaphylactic reaction
- Delayed onset (3-6 hrs after ingestion)
- Positive specific IgE alpha gal (sugar moiety)
- Sensitization by TICK BITE



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% 

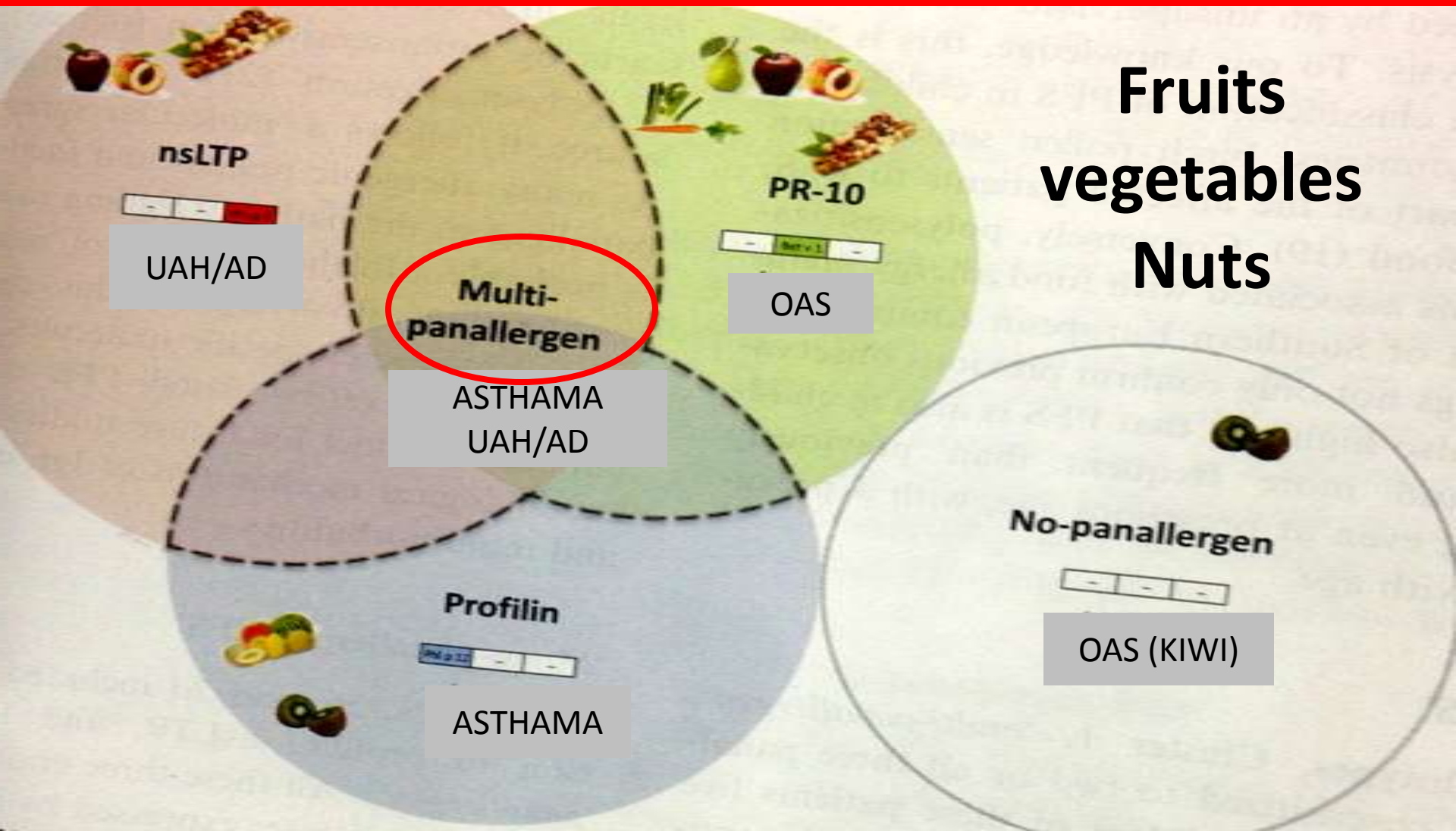
If Allergic to:	Risk of Reaction to at Least One:	Risk:
Cow's milk* 	Mare's milk horse 	4% 
Pollen birch  ragweed 	Fruits/vegetables apple  peach  honeydew 	55% 
Peach* 	Other Rosaceae plum  pear  cherry 	55% 
Melon* cantaloupe 	Other fruits watermelon  banana  avocado 	92% 
Latex* latex glove 	Fruits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

Cross sensitization vs. cross reactivity

Sicherer S, JACI. 2000;108:881.

Pollen food allergy

15 year old boy has itchy lips and throat when eating fresh apples, but not apple pie. He has itchy eyes, sneezing, runny nose each Spring.



Vegetable Profilin's

Origin *Bet v 2-homologous allergens*

Profilins

- Highly cross-reactive, present in most plants
- Seldom associated with clinical symptoms but may cause demonstrable or even severe reactions in a small minority of patients

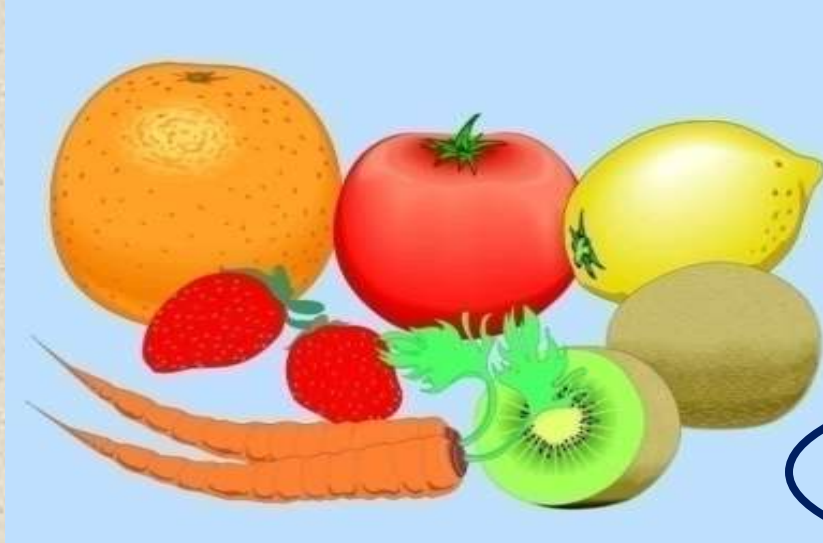
- Tree pollen
- Fruits
- Vegetables
- Nuts
- Grass Pollen
- Weed Pollen



Bet v 2	Phl p 12
Pru p 4	Hev b 8

Profilins in Plants – OAS (fruits)

MELON, WATERMELON, TOMATO, BANANA, PINEAPPLE AND ORANGE



In vivo:

SPT (wheal/flare in mm):

histamine: 4/6

birch pollen: 8/20

In vitro:

Total IgE 90 kU/l

Spec. IgE

Bet v 1 18 kU_A/l (20%)

Profilin (i.e. Phl p 12) =
5 kU_A/l (>2%)

Melon 0.5 kU_A/l (0.2%)

Profilins are proteins usually unstable to heat and acid present in pollens and plant foods

Sensitization to pollen profilin occurs through the respiratory tract

Vegetable Origin PR-10 proteins

Bet v 1-homologous allergens

PR-10 proteins, Bet v 1 homologue

- Heat labile protein
- Often associated with local symptoms (local Anaphylaxis)
- Often associated with allergic reactions to fruits and vegetables in northern Europe

- Tree pollen
- Fruits
- Vegetables
- Nuts



Bet v1	Pr u p 1
Cor a 1	Ara h 8
Mal d 1	Gly m 4

Vegetable Origin LTPs

non-specific Lipid Transfer Proteins

LTP, lipid transfer protein

- Stable to digestion and heat
- Often associated with allergic reactions to fruits and vegetables in southern Europe
- Often associated with systemic and severe reactions in addition to OAS (Anaphylaxis)

- Fruits
- Vegetables
- Nuts
- Weed pollen



Pru p 3	Ole e 7
Cor a 8	Ara h 9
Par j 2	Art v 3

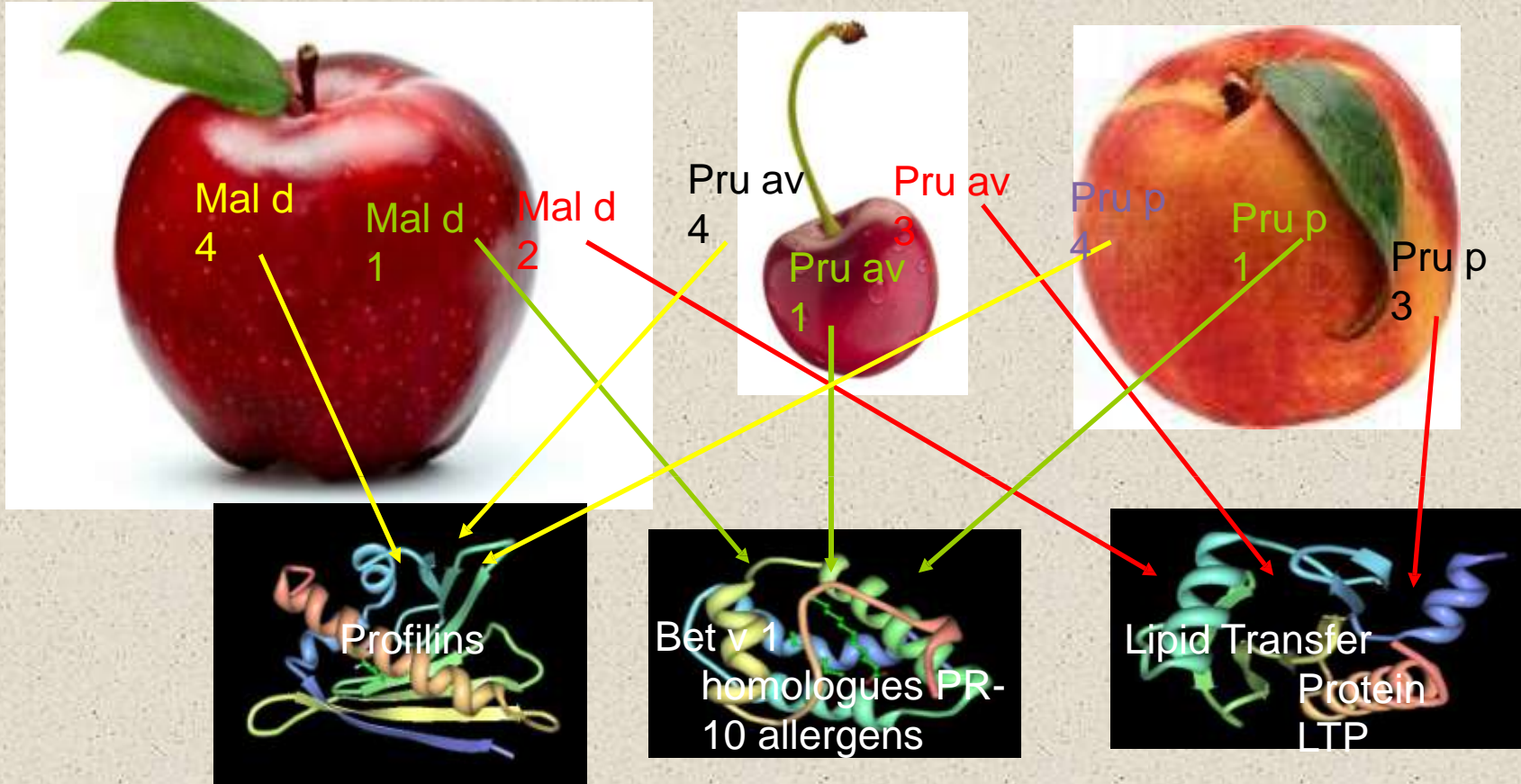
Lipid Transfer Protein (LTP) in plants

Present in Rosaceae, tree nuts, peanut, maize, mustard, asparagus, grapes, mulberry, cabbage, dates, orange, fig, kiwi, lupine, fennel, celery, tomato, eggplant, lettuce, chestnut and pineapple

LTPs are a family of stable proteins that resist heating and enzymatic digestion, and may give Systemic Reactions



ALLERGENIC PROTEIN EPITOPES



Potential to cause symptoms or severe reactions

POLLEN -FOOD ALLERGY

Fruits/vegetables /Nuts

Bet v (Pr 10), Grass POLLEN ALLERGEN

OAS

*Unique
allergens*

(Profilin) Phl p 12

*Moderately cross-
reactive*

Grass and tree

Pru p 3 (LTP)

Highly cross-reactive

Grass tree & weeds

Profilin, LTP

*OAS + moderate to
severe SAR and
asthma*

*Level of cross-
reactivity*

*Anaphylaxis
(UAH/ad severe
asthma)*

**Most allergen sources contain representatives of all
three types(multi pan allergen)**

POLLEN FOOD ALLERGY

History suggestive of pollen-food syndrome

Fruits/vegetables /Nuts

• SPT – + Ve Pollen

Sp IgE Peanut 91 kU/l

Ara h 1 <0.35

Ara h 2 <0.35

Ara h 3 <0.35

Ara h 8 121 kU/l

Not confirmed by SPT with fresh material and/or specific IgE

Oral Challenge

Confirmed by SPT with fresh material and/or specific IgE

Clinical Features

Clinical Features

Prick Prick Test

for fresh fruits and vegetables
(Unstable & Labile Allergen)



OAS

Both Labile and stable allergens are suspect

IgE to Bet v 1 Positive

IgE to Bet v1- 2 Pos

Sensitization To Bet v1-like Allergens

Sensitization to both Bet v1-like allergens and profilin

NO ORAL CHALLENGE

NO ORAL CHALLENGE

NO ADRENALINE

NO ADRENALINE

Symptomatic / anaphylaxis

Profilin

LTP

Systemic Reactions

Stable Allergen are suspect

IgE to LTP positive

IgE to seed storage protein positive

Sensitization To LTP (Pru p 3)

Sensitization to Storage Protein

Evaluate for potential cross-reactivities

Evaluate for potential Cross-reactivities

NO ORAL CHALLENGE

NO ORAL CHALLENGE

CARRY ADRENALINE

CARRY ADRENALINE

Asero R. et al Int.Arch.Allergy Immunol Bohle 2005
B, Allergy 2007



Latex-Fruit Syndrome

Some fruits contain **cross-reacting proteins** with latex

- Banana
- Avocado pear
- Strawberry
- Guava
- Citrus fruit
- Peach
- Mango
- Watermelon
- Cherry

Signs of allergic reactions

- **Pruritus**
- **Tightness in the throat**
- **Breathing difficulty**
- **Hives**

Inj-Adrenline



In one study, 86 % (49 of 57) of fruit-allergic patients were also allergic to latex compared with 4 % (2 of 50) of controls.

Latex-Fruit Syndrome

Specific Allergy Test and Specific Allergic Diseases

Latex Allergy

Immediate

(Latex: Ricinus(sis) + Mercapto Benzothiazole etc.)

Suspect

1. Anaphylaxis
2. Contact Dermatitis
3. Contact urticaria

Diagnosis:-

1. SKIN TEST
2. USE TEST
3. SERUM TEST

Latex Allergy

Late Reaction

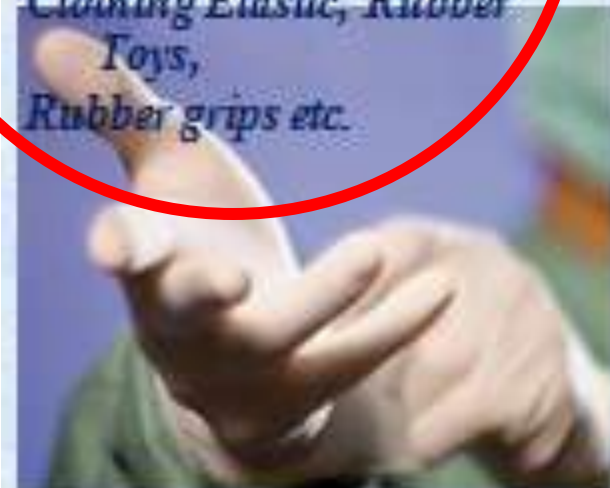
(Latex: Braxilensis) + Mercapto Benzothiazole etc.

H/O

Gloves, Balloons & Condoms
Bandages, Body Bottle Teats,
Baby Dummies, Rubber bands,
Clothing Elastic, Rubber Toys,
Rubber grips etc.



Inj-Adrenaline



IgE- associated -cell-mediated disorders

Case: 7 year-old girl

Consultation for regular control of eczema, rhinitis and food allergy

Personal history

- Eczema since childhood and uses steroid ointments
- Allergic rhinitis against birch (Tree pollen)
- Oral itching when eating peanuts and tree nuts
- The parents want to know if it is ok if their daughter eats peanuts & tree nuts because recently no reactions to small amounts.

IgE (allergen extract)

(Molecular based)

Hazelnut (f17): 78 kU_A/l

Cora14-13kU/L

Peanut (f13): 0.40 kU_A/l

Arh-2 <0.35 kU/L

→ **Can we answer the parent's question?**

Hazelnut-high risk

IgE-associated -cell-mediated disorders

Case: 2 year-old boy

Consultation for regular control of food allergy

History

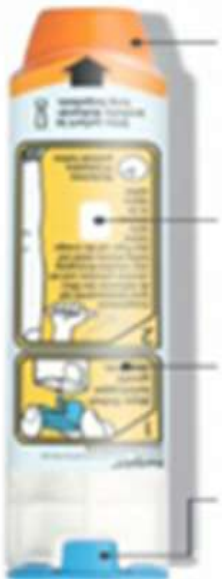
- Has eczema and milk / egg allergy
- Pasta with egg gave general urticaria which led to an ER visit
- Licking of ice cream gave rash around mouth.

How severe is this boy's allergy? -Egg-High Risk

Milk <0.35kU/L

Egg white	f1	13 kU _A /l
Ovomucoid	f233	10.8 kU _A /l

Inj-Adrenaline



IgE- associated -cell-mediated disorders

Case: 2,5 year-old girl

*Consultation for regular control of food allergy
+ asthma?*

History

- Has egg allergy, no eczema and suspicion of asthma.
- Is sensitised to cat and gets rashes when close to cat.
- Egg allergy diagnosed for the first time at 11 m of age. Urticaria and edema.
- Avoiding egg without mistakes

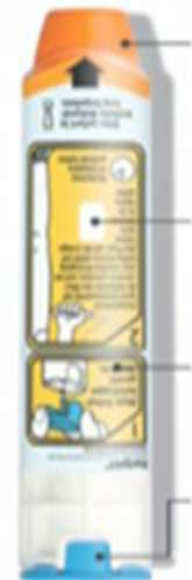
Can egg be introduced now into the diet?

Egg white	+ve	0.50 kU_A/l
Ovomucoid	-ve	0.1 kU_A/l

Inj-Adrenline



Ans:- cooked egg in to the diet





The diagnosis of food allergy associated with asthma is not easy...

... nevertheless consider food allergy when:

- a. asthma symptoms start early in life
- b. asthma associated with AD
- c. asthma is difficult to manage
- d. history indicates relation between asthma and meals
- e. in CMA

Baena-Cagnani CE. Role of food allergy in asthma in childhood.
Curr Opin Allergy Clin Immunol 2001;1: 145-9.

**Multiple food allergies associated
with asthma hospitalizations**
Food allergy is associated with severe asthma

Wang J. Food allergen sensitisation in inner-city children with
asthma J Allergy Clin Immunol 2005;115:1076-80



IgE- associated -cell-mediated disorders

9 yo boy with 4 mo history of vomiting, abdominal pain, weight loss, difficulty swallowing food. Endoscopy reveals eosinophilic infiltration of esophageal mucosa and strictures.

32 year old woman, who complains of chronic abdominal discomfort, diarrhea, bloating, and constipation. She is convinced that food allergies are causing her symptoms, so requests food allergy testing.



Eosinophilic esophagitis

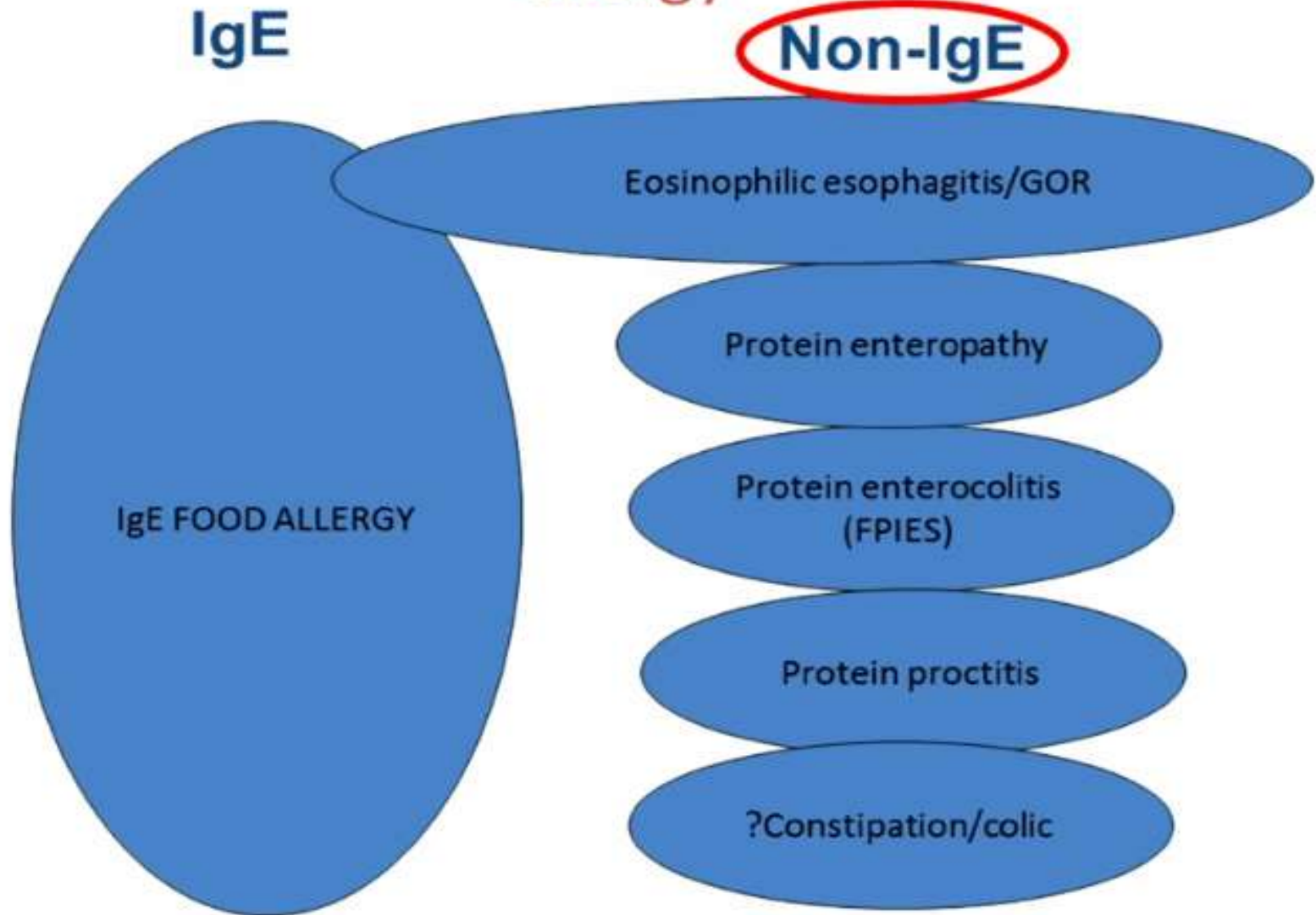
Clinical manifestation	Age	Allergen	Clinical features	Histology
Eosinophilic esophagitis	Early infancy – ANY AGE	Cow's milk (most common) Others (soy, egg, wheat)	Vomiting Diarrhoea FTT <u>Food impaction</u> Dysphagia Feed refusal Abdo/chest pain	<ul style="list-style-type: none"> • Usually • Panesophagitis • Unresponsive to PPIs • >15 eosinophils/HPF

Red flags for endoscopy to rule out EoE

- food sticking, choking during eating
- meat needs to be diced or pureed
- Slow eating/washing down meal with fluids

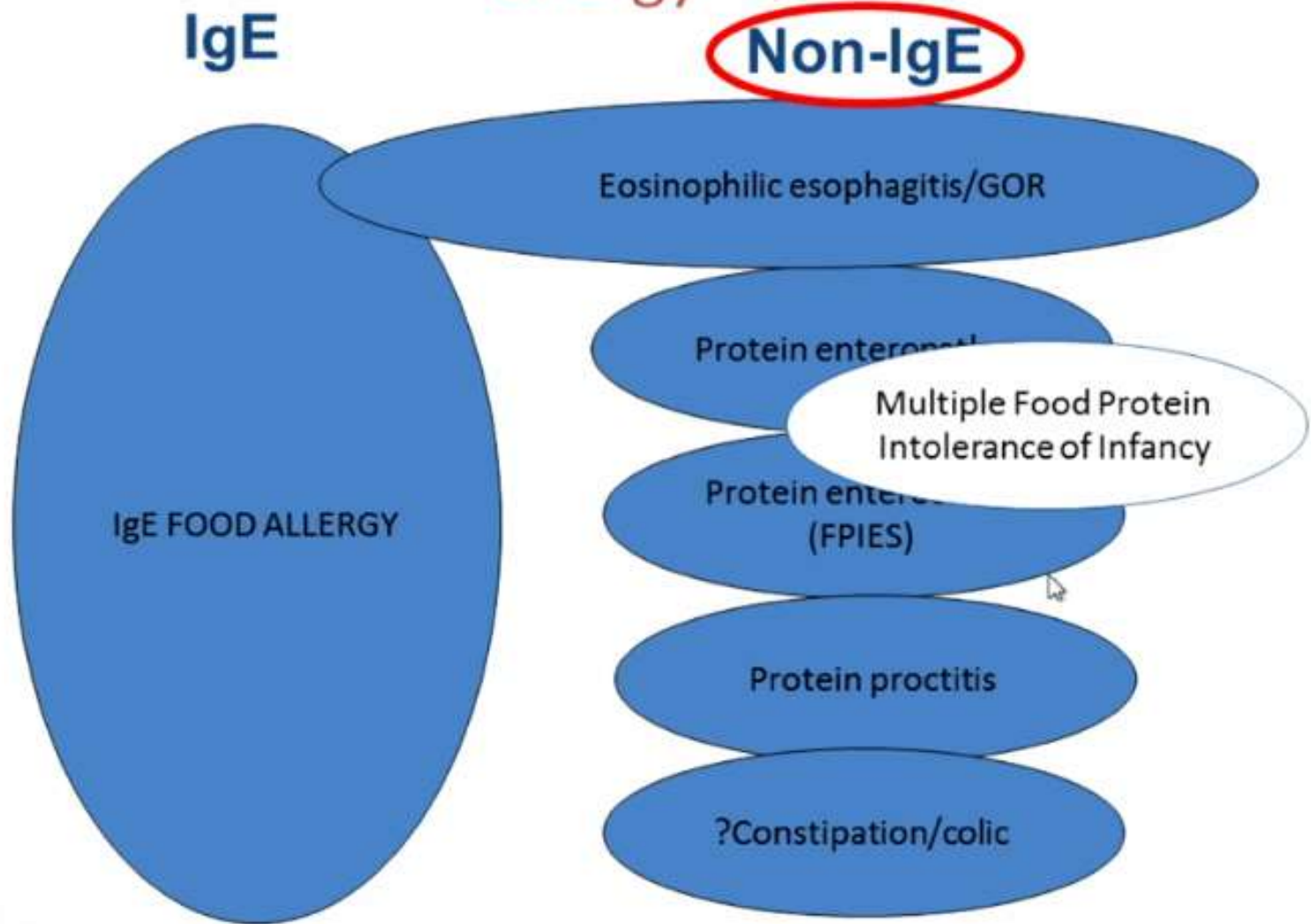
Non-IgE-Mediated Allergies

Gastrointestinal manifestations of food allergy



Non-IgE-Mediated Allergies

Gastrointestinal manifestations of food allergy



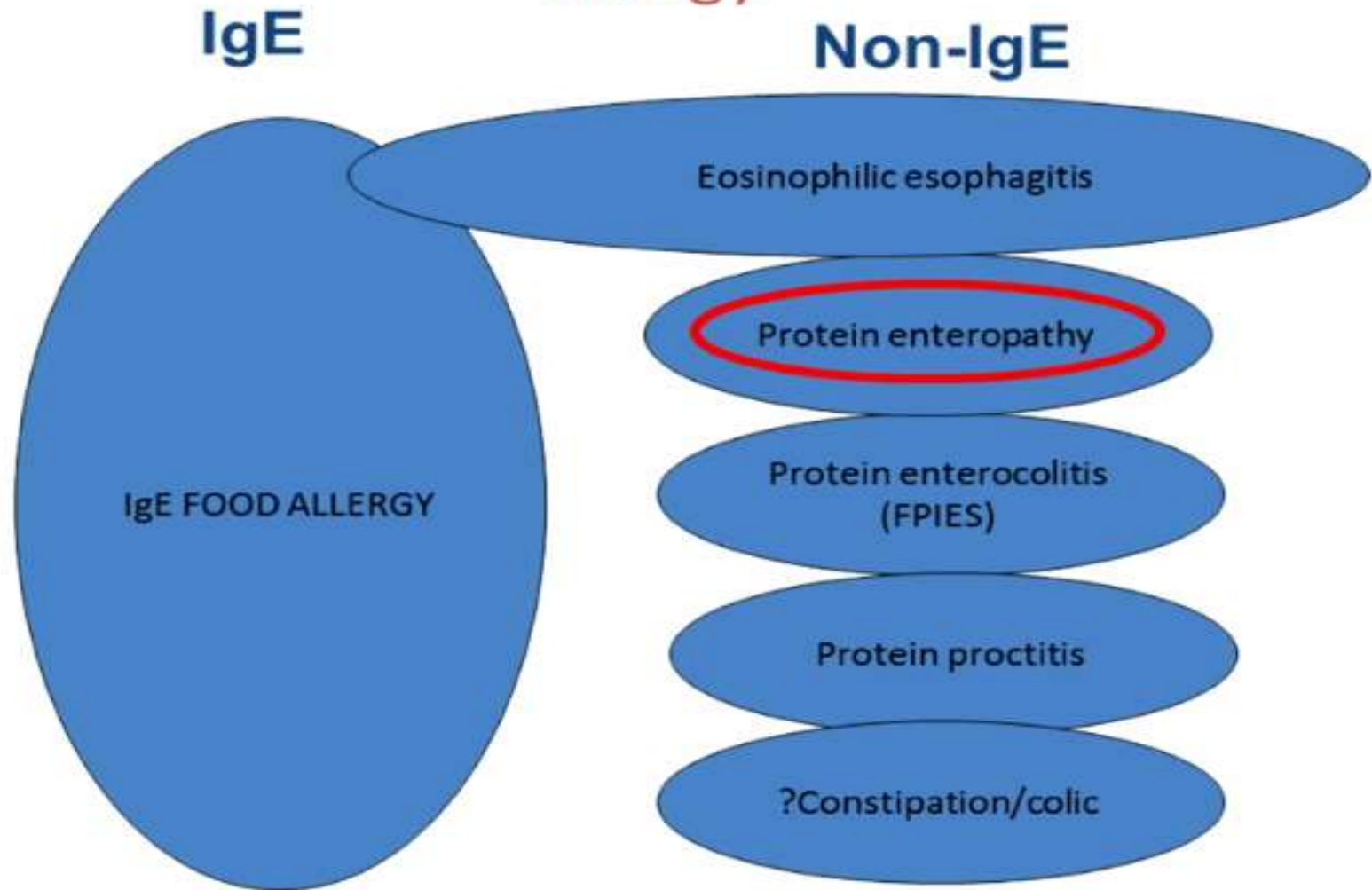
Non-IgE-Mediated Allergies

Gastroesophageal reflux

Clinical manifestation	Age	Allergen	Differential Diagnosis	Histology
<ul style="list-style-type: none">• Vomiting• FTT	Early infancy ANY AGE	<u>Cow's milk</u> (most common) <u>Others (soy)</u>	<ul style="list-style-type: none">• Physiological• EoE• Ladd's band• Malrotation• Coeliac disease	Often normal Non-specific inflammations Erosions


Non-IgE-Mediated Allergies

Gastrointestinal manifestations of food allergy



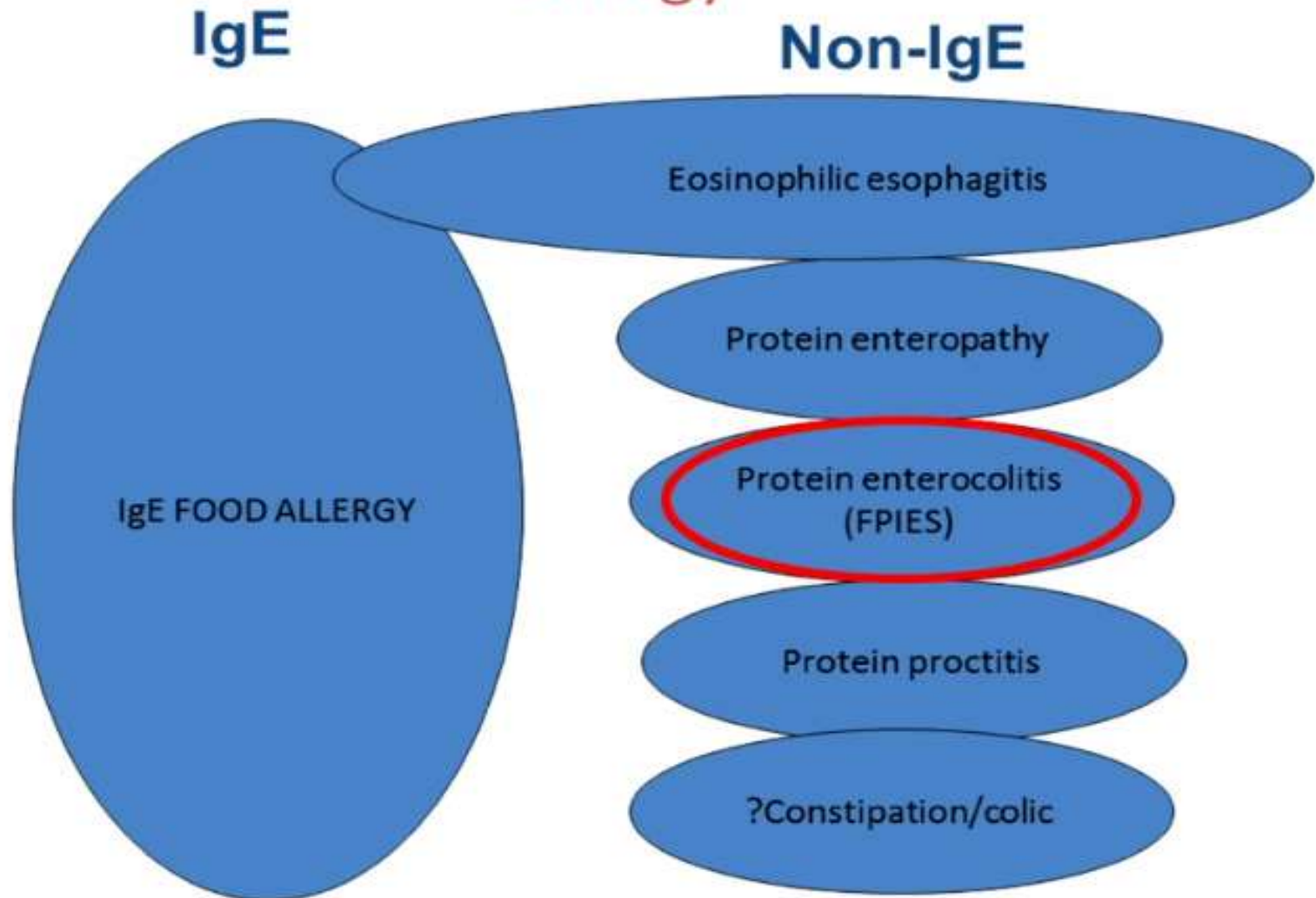
Non-IgE-Mediated Allergies

Protein-induced Enteropathy

Clinical features	Age	Allergen	Differential Diagnosis	Histology
<ul style="list-style-type: none"> • Vomiting • Diarrhoea • Anaemia • FTT • Constipation • Protein-losing enteropathy 	<p>Early infancy</p> <p><u>Coeliac disease</u> – ANY AGE</p>	<p><u>Cow's milk</u> (most common)</p> <p>Others (<u>soy</u>, <u>wheat</u>)</p>	<ul style="list-style-type: none"> • Lactose intolerance • Giardiasis • Autoimmune enteropathies • Immune deficiencies 	<p>Endoscopy/biopsy – patchy villous atrophy with lymphocytic cellular infiltrate</p> 

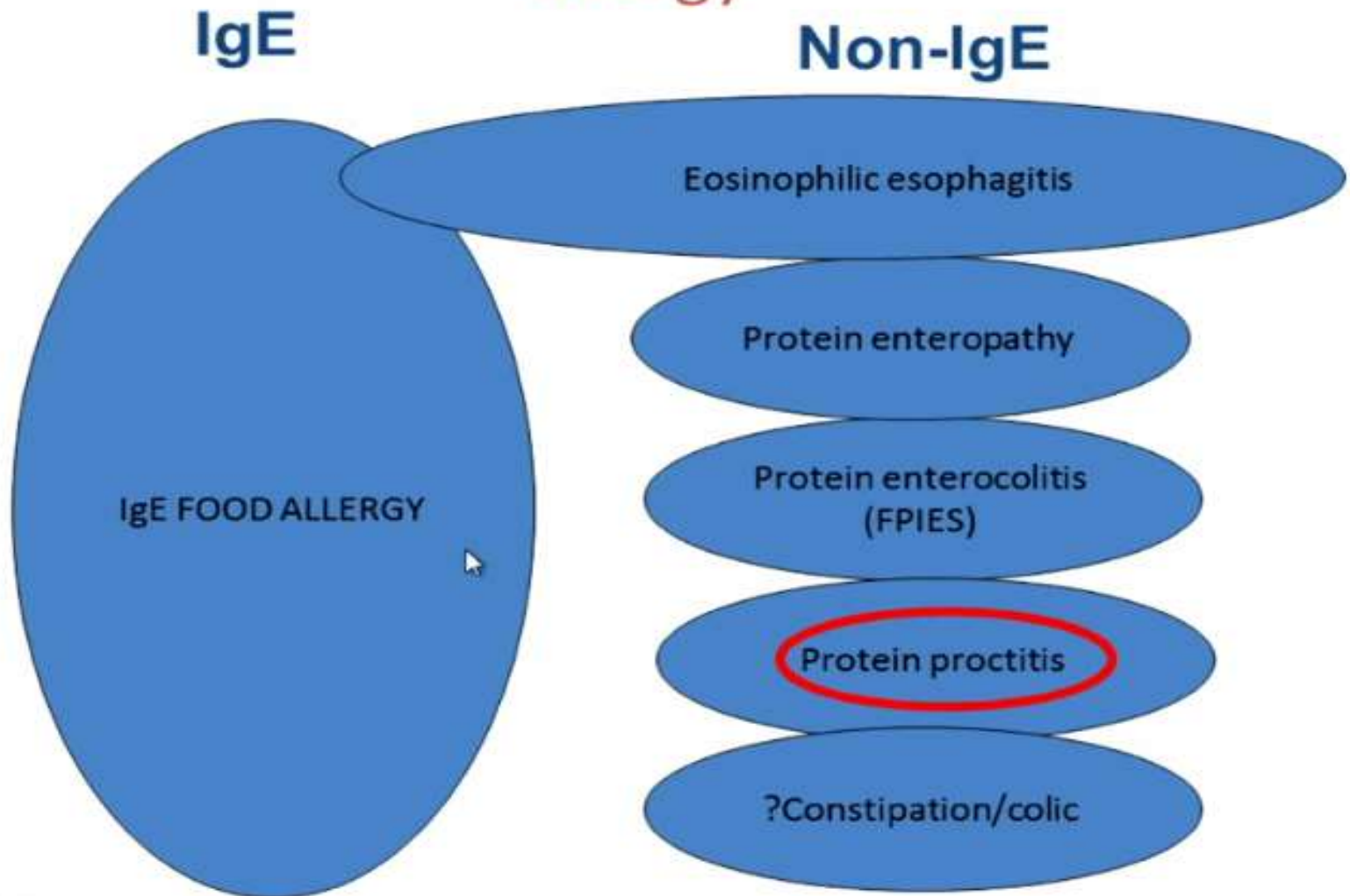
Non-IgE-Mediated Allergies

Gastrointestinal manifestations of food allergy

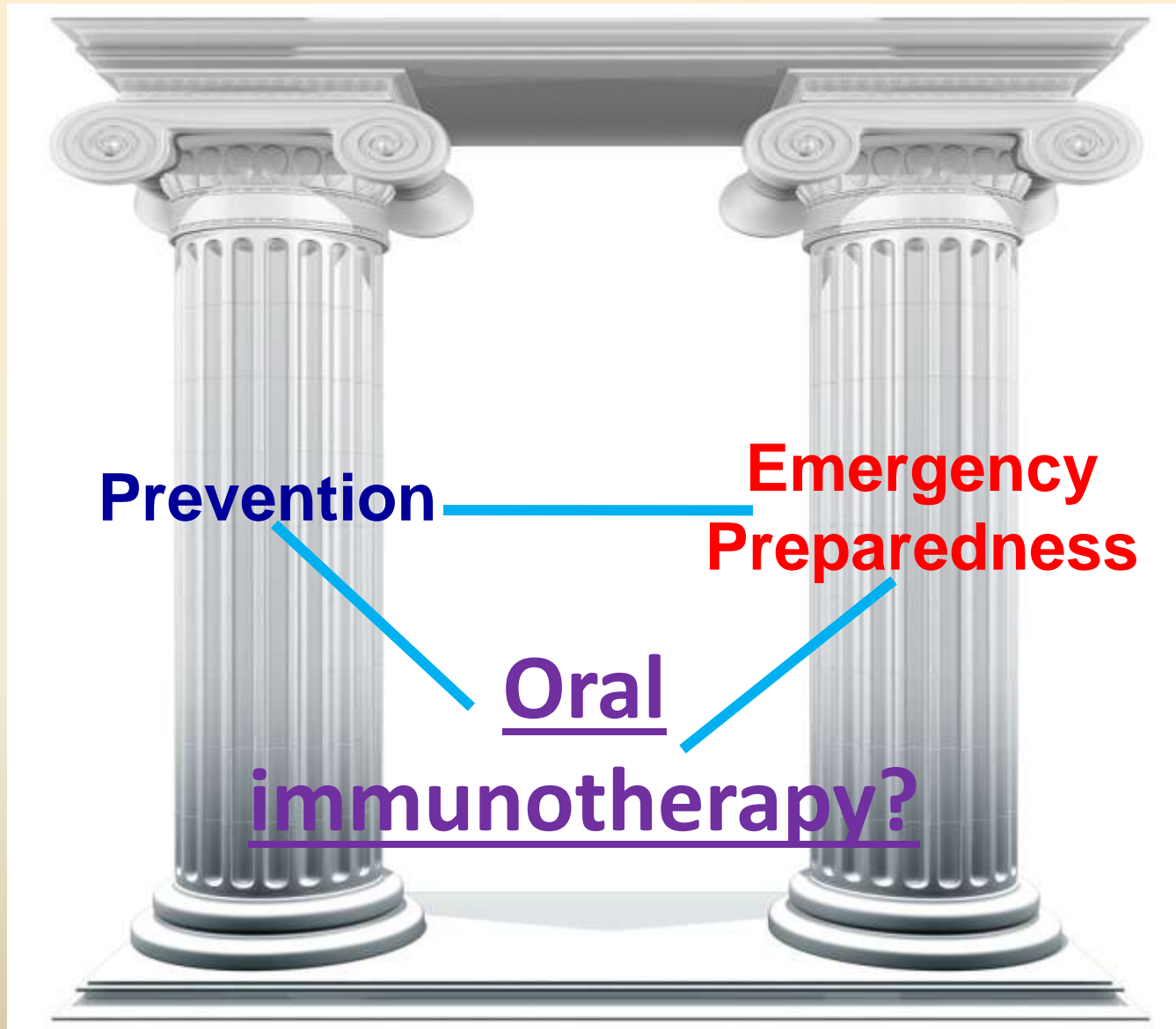


Non-IgE-Mediated Allergies

Gastrointestinal manifestations of food allergy



Pillars of Food Allergy Management



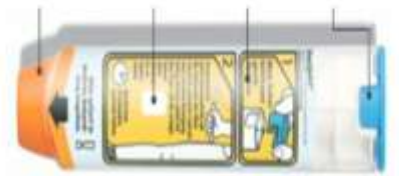
These must be applied at all times and in all settings

Teach Food Allergy Basics

Timing
Anaphylaxis
Epinephrine



Let them know that
symptoms can
progress quickly.
Tell them about
anaphylaxis and
how prompt
treatment with
epinephrine is key.



Jext®



Emerade®



(Munoz-Furlong et al. Nutrition Guide To Food Allergies. FAAN. 2005)

(Sampson, HA, Hospital Practice, 2000)

(Food Allergy Practice Parameter. Annals of Allergy, Asthma & Immunology. 2

Food Allergy Fatal and Near Fatal Anaphylaxis

- *Most away from the home*
- *Unintentional ingestion with known food allergy*
- *Majority are peanut & tree nut*
- *Asthma is a significant risk factor*
- *Adolescents and young adults are at greatest risk*
 - *70% of mortalities between ages 12 and 21*
- *Delayed or lack of administration of epinephrine*
 - *88% of fatalities*

These facts provide an excellent teaching tool.

They demonstrate that food allergies need to be taken seriously and that simple measures can decrease risk.

(Bock JACI 2001;107:191)

(Bock JACI 2007;119:4:1016-18)

(Sampson et al. JACI 2006;117:391-7)

(CDC, *Voluntary Guidelines for Managing Food Allergies*. 2013)



Food Allergy Management must be Implemented in all Settings (how to use epipen auto injector - Inj-Adrenaline)



Home



School



Restaurants



Parties and Play Dates



Alternative Care Givers

Administering an Epi-pen

(Inj-Adrenaline)
(0.3 to 0.5ml X IM)



❖ Remove grey activation cap



❖ Jab black end into outer thigh

- Use enough force to make a bruise
- This can be done through clothing



❖ Hold 15 seconds



❖ Keep patient lying down



Epinephrine:

Contraindications/Considerations

- **No contraindication if treatment for anaphylaxis**
 - Caution with cardiac issues, arrhythmias, uncontrolled hypertension or hyperthyroidism, aortic aneurysm, recent intracranial surgery and patients on sympathomimetics, TCAs, MAO inhibitors
 - Beta blockers decrease response to epinephrine
- Discuss with comanaging medical teams and coordinate patient centered approach*

(NIAID 6.3.3)

(Anaphylaxis Practice Parameters. JACI.2005)

(Sicherer and Simons. Pediatrics. 2007; 119;638-646)

Epinephrine: Considerations with asthma

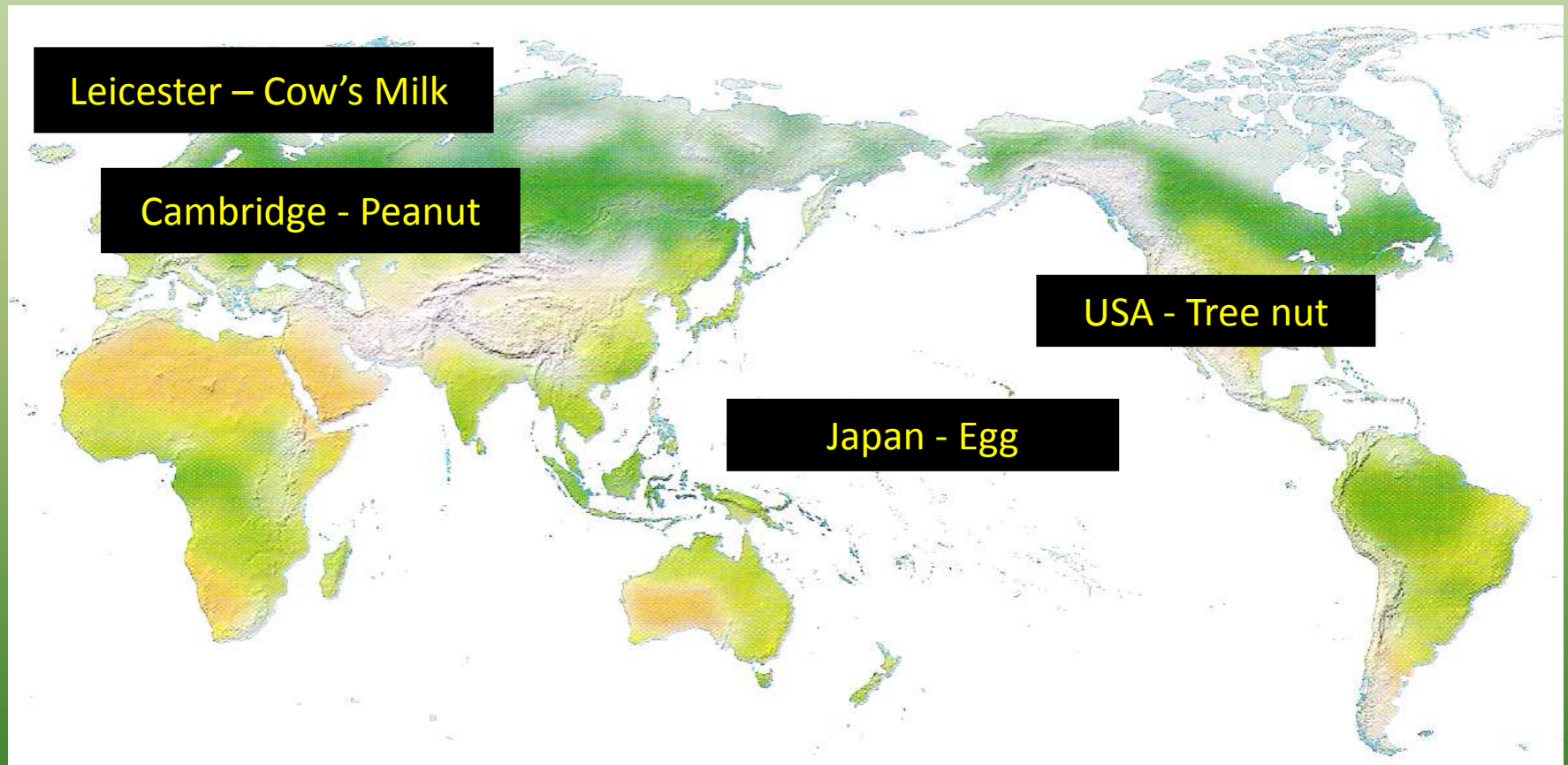
- *If Ever Any Concern That A Food Allergic Reaction Has Triggered An Asthma Attack Then Treat With Epinephrine First*

.Delays In Epinephrine Use Are Associated With Increased Risk Of Death

Oral Immunotherapy(OIT)



The future – Oral desensitisation



Peanut oral immunotherapy

PN OIT: Experience to date

- Treatment period 2010-2016, ongoing
- >700 peanut allergic patients treated
- Patients from all New England states, NY, NJ, Maryland, Ohio, Canada
- Safety issues addressed and acceptable adverse affect profile
- 92% successfully desensitized – consuming 3-10 peanuts daily

OIT With Other Foods

- Milk- Depending on severity of allergy-milk drops or baked milk desensitization (with milk-containing muffins)
- Egg Protocols- Similar as for milk-egg protein drops, baked egg
- Tree nuts-Cashew ~ 30 patients treated successfully to date, Walnut – just started
- In the future-other tree nuts, sesame

Baked Milk and Egg Containing Diet in Managing Milk and Egg Allergy

- Cooking/heating can change the protein structure of food altering recognition by immune system
- Studies report 70% of milk and egg allergic children can tolerate baked milk or egg
- By eating regularly baked milk/egg, can help desensitize to straight milk/egg
- Should be performed in controlled clinical setting

Sublingual immunotherapy (SLIT) for foods

- SLIT studies have shown some efficacy for hazelnut, peanut, cow's milk and other foods
- SLIT appears to be associated with fewer systemic side effects than OIT
- However, OIT is more effective for desensitization as shown in studies using milk and peanut

New Therapies for Food Allergies

- **Anti-IgE (omalizumab, Xolair®)**
- **Immunotherapy**
 - modified antigens
 - immunomodulators
- **DNA vaccines**
 - murine models
 - parenteral
 - Oral
- **Oral Desensitization**
 - Milk, egg, hazelnut, peanut, kiwi

Omalizumab (Anti-IgE) and food allergy

- Researchers conclude that peanut **OIT** in **combination with Omalizumab** allows for rapid, effective desensitization in the majority of peanut allergic patients, including those with high peanut-specific IgE levels **Omalizumab aids fast oral desensitization for peanut allergy**

➔ Successful management of severe **cow's milk** allergy with omalizumab treatment and CD-sens monitoring



Other treatments

Recombinant food allergen vaccines

1) *Peanut Patch-EPIT* (Epicutaneous immunotherapy)

- Success in phase 2 trials (50% of patients could tolerate 10 x dose with treatment)
- Phase 3 trials underway-Company : DBV Technologies

2) *Peanut protein in capsules*-Using standardized pharmaceutical grade food allergens

- CODIT TM “characterized oral desensitization immunotherapy” Company: Aimmune

Summary

- Understand different food allergy conditions
- Risk Factors: possibly low vitamin D, delayed introduction of allergenic foods, hygiene hypothesis , Co-factors NSAIDS,ALCOHAL, EXERCISES etc.
- Primary prevention: LEAP study, hypoallergenic formula
- Oral immunotherapy gaining more acceptance and can be performed safely and effectively in private practice/treatment center

Thanks

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TRAINING IN ALLERGY TESTING AND IMMUNOTHERAPY

ORGANIZED BY

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email : pc_kathuria@yahoo.com, Website : www.nationalskinallergycentre.in, www.nationalallergycentre.in

Three Day Training program in clinical history taking, skin prick tests (SPT, SIDT, PPT, APT, SAPT, PCK Technique), IgE measurements and Interpretations, allergen-immunotherapy (Combined cluster immunotherapy & anti-IgE (Omalizumab) therapy) SLIT, SCIT, RIT, ORAL DESENSITIZATION, DRUGS DESENSITIZATION, ASPIRIN DESENSITIZATION and Anaphylaxis will be organized by NATIONAL ALLERGY CENTRE under the guidance of National Experts. **THE TRAINING WILL PROVIDE OPPORTUNITY FOR HANDS ON TRAINING AND CLINICAL MANAGEMENT OF ALLERGIC DISEASES WITH FREE ADVISE FOR FURTHER SIX MONTHS.** Medical graduates/post graduates interested may apply with their curriculum vitae and certificates for consideration to Course Director Training, NATIONAL ALLERGY CENTRE, for further consideration.



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