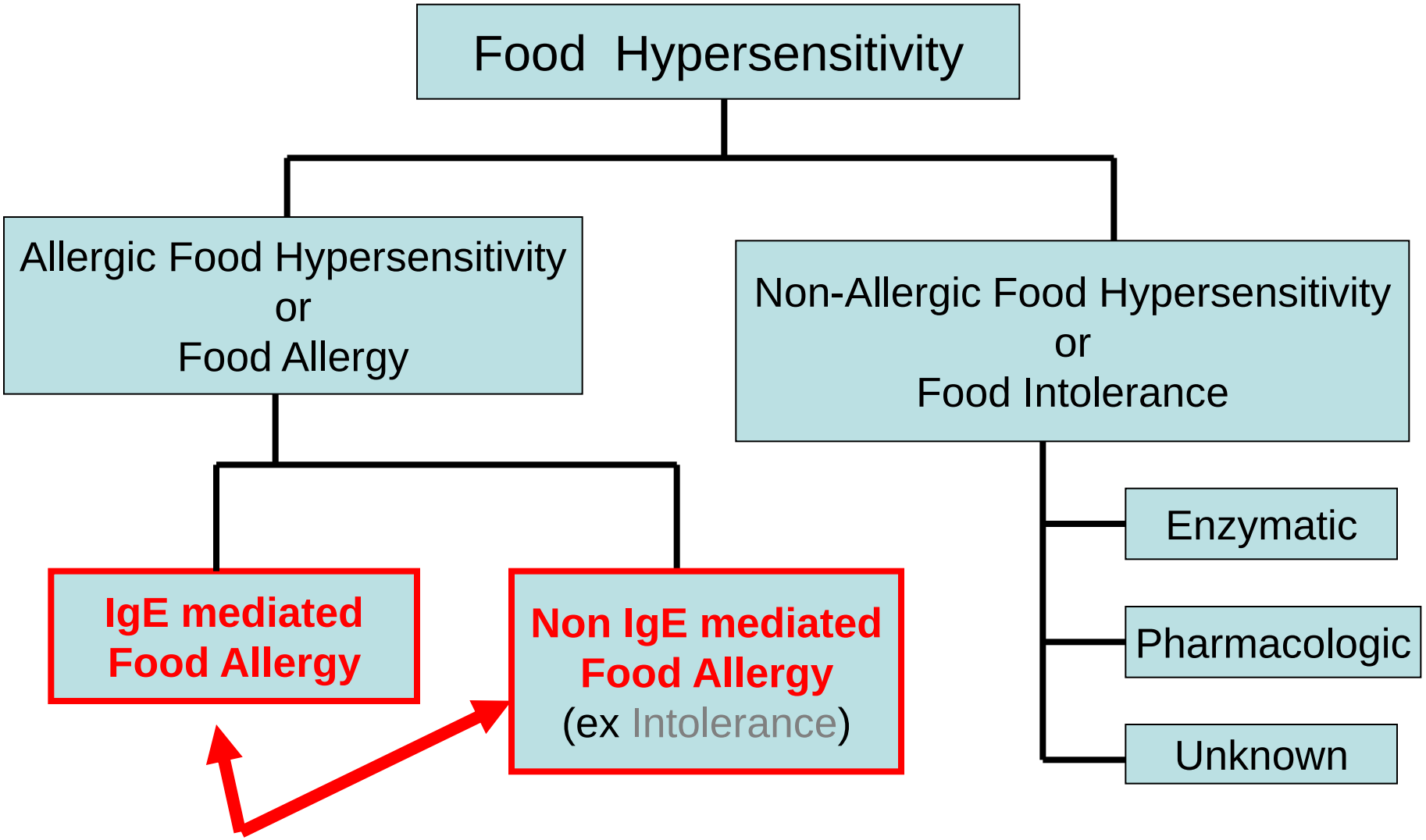
CARREFOURS
DE L'INNOVATION AGRONOMIQUE

Allergies, intolérances et hypersensibilités alimentaires

INRA
SCIENCE & IMPACT

Nomenclature



Johannson SG et al Revised Nomenclature for Allergy for global use October 2003 JACI 2004 ; 114 : 832-6

Clinical patterns of food allergy

IgE-mediated

Non IgE-mediated

Clinical patterns of food allergy

IgE-mediated

Eosinophilic disorders

Non IgE-mediated

Clinical Aspects of Gastrointestinal Food Allergy in Childhood

Scott H. Sicherer

Pediatrics 2003;111;1609-1616

TABLE 1. Named Gastrointestinal Food-Allergic Disorders of Infancy and Childhood

Disorder	Key Symptoms/Signs/Features
IgE antibody mediated, acute onset	Anaphylaxis
Immediate gastrointestinal hypersensitivity	Acute onset nausea, emesis, pain, diarrhea, may follow foods: milk, egg, wheat, soy, peanut, tree nuts, seafood
Oral allergy syndrome	Pruritus, mild edema confined to oral cavity caused by IgE antibodies originally induced by pollen sensitization that react with homologous proteins in certain uncooked fruits/vegetables
IgE antibody associated in some cases/cell mediated, delayed-onset/chronic	EoE
Eosinophilic gastroenteropathies	Symptoms vary upon site(s)/degree of eosinophilic inflammation; esophageal: dysphagia, pain; generalized: ascites, weight loss, protein losing enteropathy, edema, obstruction; multiple foods
Cell-mediated, delayed-onset/chronic	FPIES
Dietary protein enterocolitis	Chronic exposure: emesis, diarrhea, poor growth, lethargy; reexposure after restriction: emesis, diarrhea, hypotension (15%) ≈2 h after ingestion; foods: milk, soy, grains
Dietary protein proctitis	Mucousy, bloody stools; causes: breast milk with maternal cow milk ingestion, cow milk
Dietary protein enteropathy	Malabsorption, edema, emesis, poor growth, usually caused by cow milk
Celiac disease	Malabsorption, diarrhea, response to gluten, HLA-DQ2 associated

Clinical patterns of allergy vary according to food allergens

Food allergens

IgE-mediated		Non IgE-mediated
Milk	Two types of sensitisation	Milk
Egg		Egg
Wheat		Wheat
Soy		Soy
Peanut	IgE-mediated only	-
Tree nuts		-
Kiwi fruit		-
Sesame		-
		-
		-

Clinical patterns of peanut allergy

IgE-mediated

Clinical patterns of milk allergy

IgE-mediated

Eosinophilic disorders

Non IgE-mediated

Clinical patterns of wheat allergy

IgE-mediated

Eosinophilic disorders

Non IgE-mediated

Auto-immune disease **Celiac disease**

Clinical patterns of wheat allergy

IgE-mediated

Eosinophilic disorders

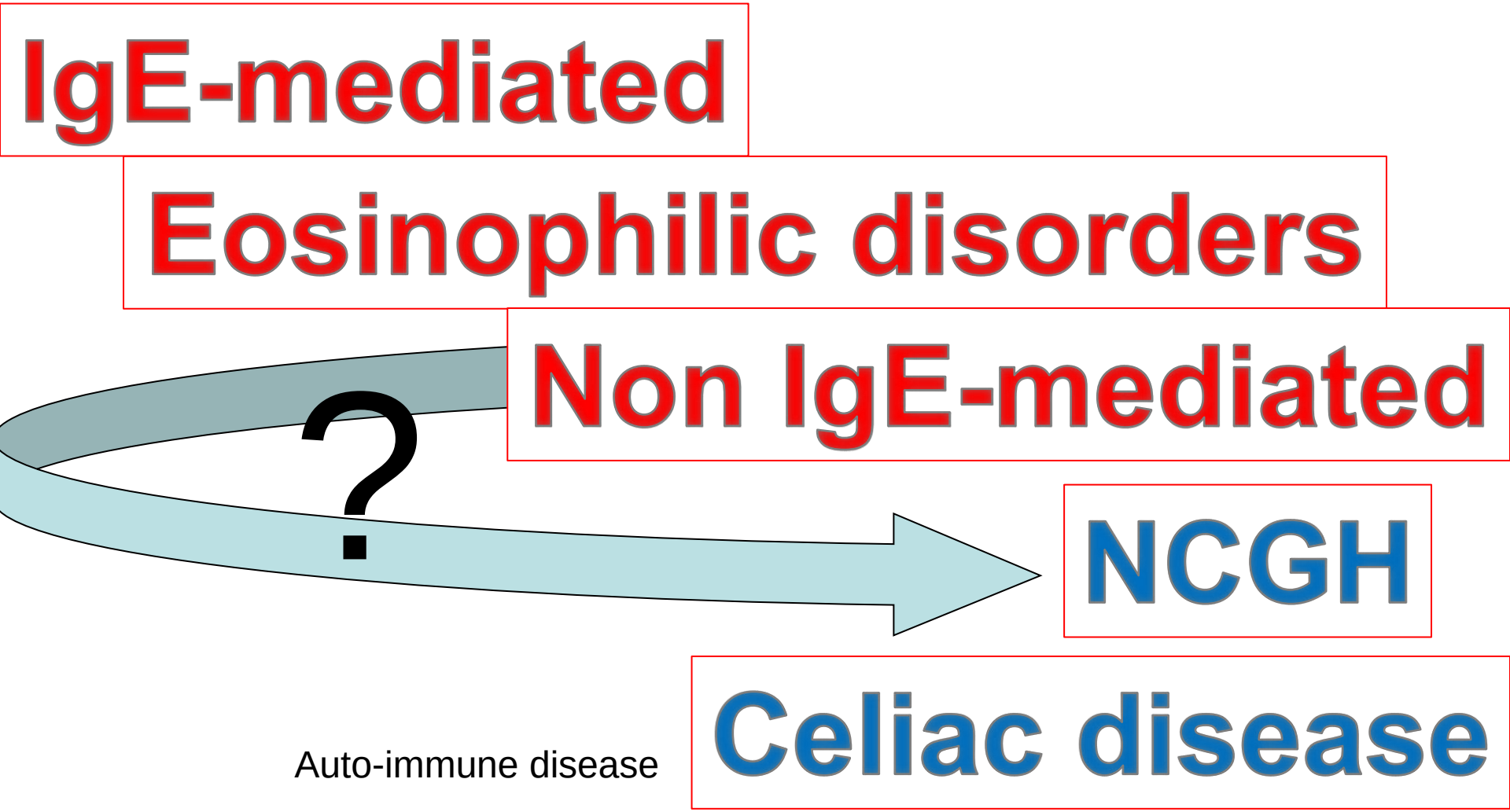
Non IgE-mediated

NCGH

Auto-immune disease

Celiac disease

Clinical patterns of wheat allergy



Clinical patterns of wheat allergy

IgE	Non IgE
Milk	Milk
Egg	Egg
Wheat	Wheat
Soy	Soy
Peanut	
Tree nuts	
Kiwi fruit	
Sesame	

Different from celiac disease

Wheat allergy vs celiac disease

- **Allergic** disease

- **Auto-immune** disease

- **Elimination: wheat**

- **Elimination: gluten**, contained in wheat, barley, rye (not oats)

Different clinical patterns of food allergy may combine in the same patient

Association of different clinical patterns of food allergy

IgE-mediated + **Eosinophilic disorders**

Peanut allergy→ Anaphylaxis

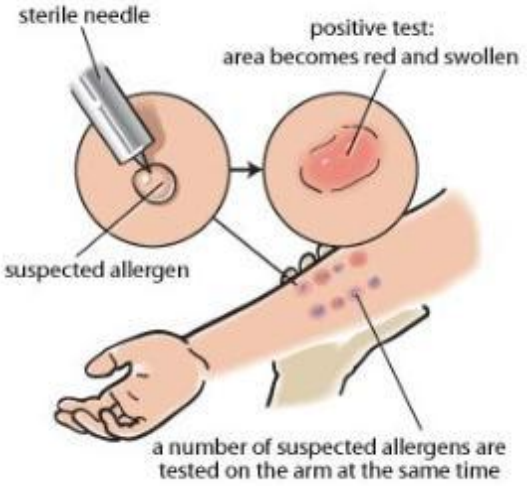
Milk allergy→ EoE

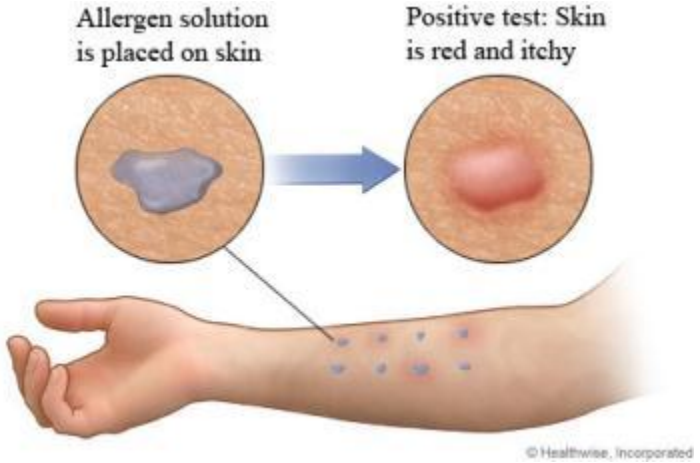
IgE-mediated allergy

- Anaphylaxis
- Angioedema, urticaria,
- Abdominal pain, vomiting, diarrhea
- Rhinitis, asthma
- Positive skin prick test
- Elevated specific IgE

IgE-mediated food allergy

Positive Skin prick tests





Threshold values

Usually <3mm sensitisation, >7mm allergy

IgE-mediated food allergy

Blood specific IgE

Threshold values have been studied for some foods e.g. milk

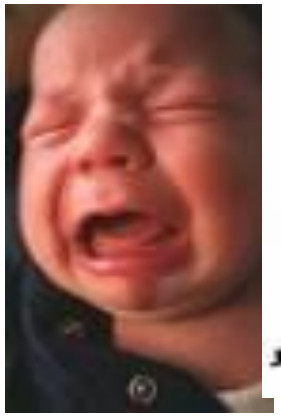
Table 3. IgE threshold values for 95% CI clinical reactivity to milk.

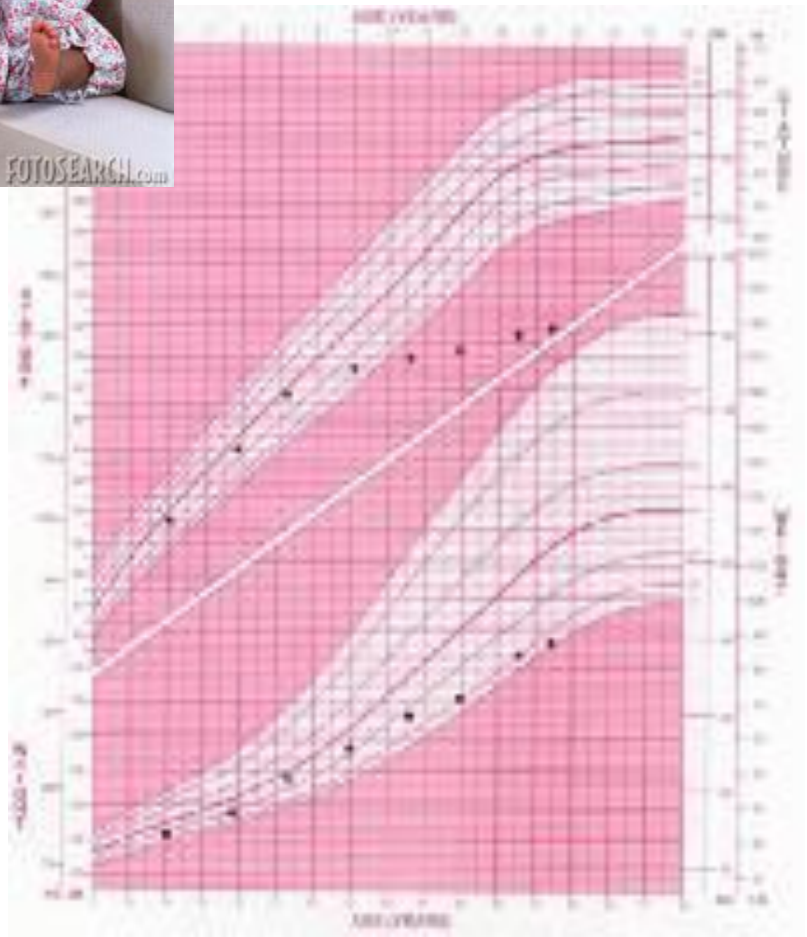
Study (year)	Positive milk challenge				Ref.
Sampson & Ho (1997)	sIgE >32 kU/L (95% specificity) sIgE >15 kU/L (90% specificity)				[19]
	13–18 months	19–24 months	>24 months		
García-Ara *et al.* (2004)	sIgE > 2.7 kU/L	sIgE >9 kU/L	sIgE >24 kU/L		[30]
	Negative milk challenge		Positive milk challenge		
Vassilopoulou *et al.* (2008)	sIgE <3.94 kU/l	SPT wheal <4mm	sIgE >25.4 kU/L	SPT wheal >7.5 mm	[28]
	Negative milk challenge				
	<1 year	*<2 years*	*<4 years*	*<6 years*	
Yavuz *et al.* (2013)	sIgE <2.8 kU/L	sIgE <11.1 kU/L	sIgE <11.7 kU/L	sIgE <13.7 kU/L	[31]

SPT: Skin prick test.

Dupont, Exp Rev Clin Immunol, 2013

Non IgE-mediated food allergy





Non IgE-mediated food allergy

- Also atopic dermatitis

- And respiratory manifestations

Non IgE-mediated enteropathy
(old "intolerance")

- From 0 - 24 months
- Diarrhea (mild to moderate steatorrhea in # 80% of cases)
- Food implicated: milk, cereals, egg, fish
- Poor weight gain
- Diagnosis:
  - Biopsy shows **patchy villous atrophy** with prominent mononuclear round cell infiltrate, few eosinophils,
  - Response to exclusion diet,
  - Challenge test
- Resolved at 2 - 3 years old

Adapted from J Allergy Clin Immunol. 2004; 113:808-809

Non IgE-mediated : food protein-induced enterocolitis syndrome (FPIES)

- Infants <8-12 months, delayed in breast-fed babies
- Symptoms :
  - **Chronic** (milk or soy protein-based formulas) : irritability, anaemia, abdominal distension, failure to thrive
  - **Acute**, **protracted vomiting 1- 3 hours after feeding, bloody diarrhoea (leading to dehydration)**
- Resolved: 50% at 18 months, 90% at 36 months
- **Adults and older children, fish, shellfish** and cereals hypersensitivity → similar syndrome with delayed onset of severe nausea, abdominal cramps and protracted vomiting

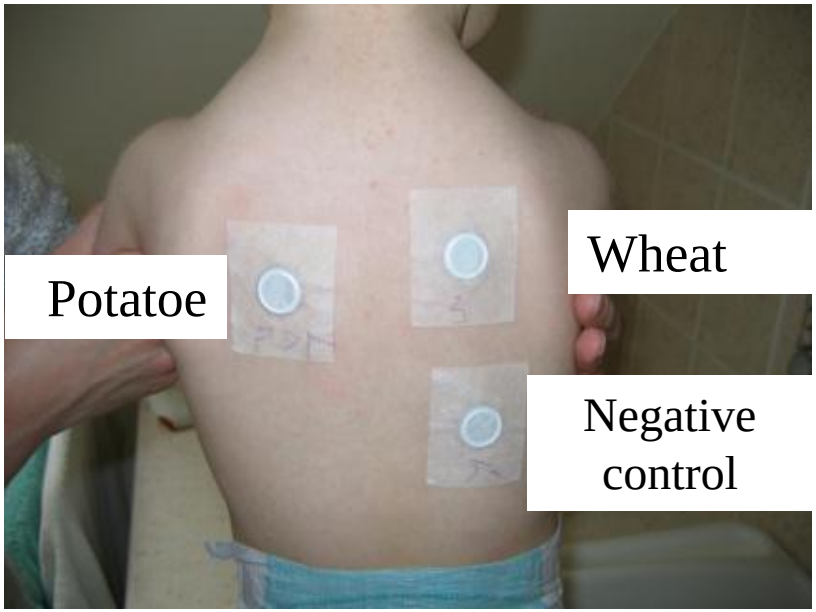
Adapted from J Allergy Clin Immunol. 2004; 113:808-809

Non IgE-mediated food allergy

- Digestive clinical pattern : enteropathy / food protein induced enterocolitis (FPIES)

- Diagnosis:
  - Skin prick test always negative
  - Specific IgE detectable in 1/3 cases (FPIES)
  - Atopy Patch Test : sensitivity and specificity depending on allergen

non IgE : Atopy Patch Tests



Reading at 72 hours

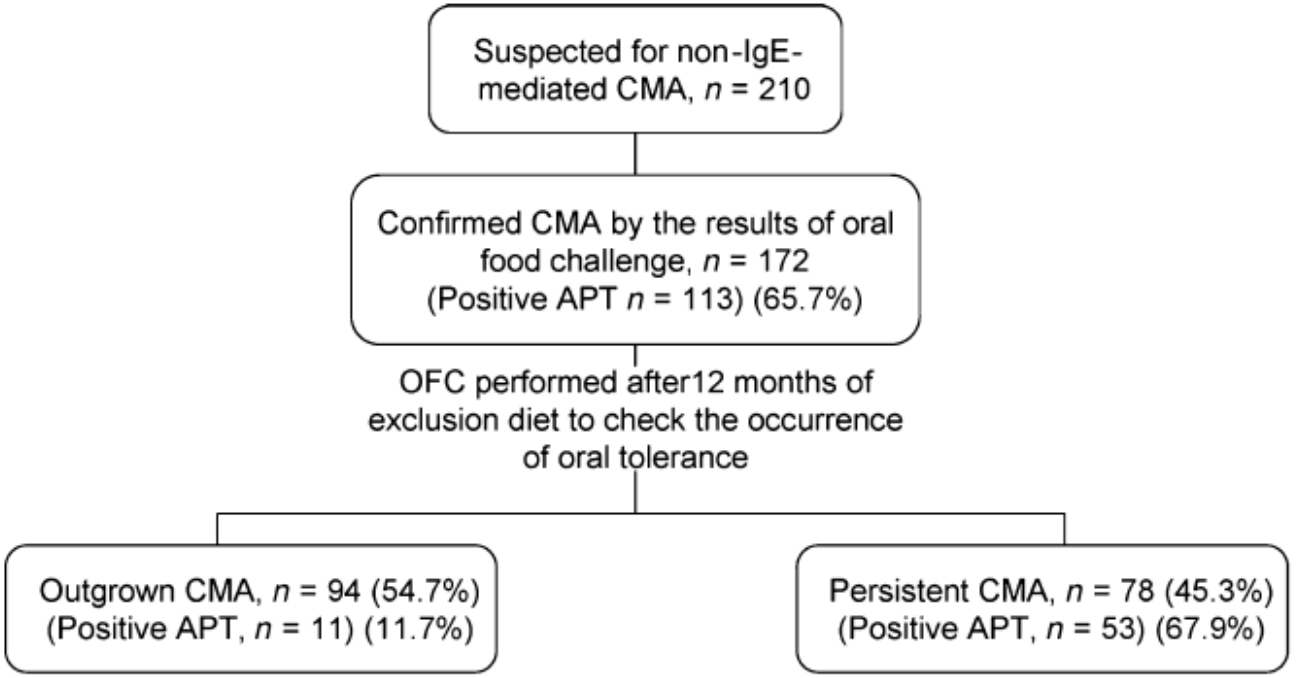
THE ATOPY PATCH TEST FOR DETECTION OF COW'S MILK ALLERGY WITH DIGESTIVE SYMPTOMS

Table. Clinical data, IgE, and skin tests in CMA and non-CMA groups

	CMA group (n = 24)	Non-CMA group (n = 11)	*P* value
Male/female	14/10	6/5	ns
Age (mo)	15.5 ± 13.2	20.8 ± 16	ns
Symptoms (n)			
Gastroesophageal reflux	15	4	ns
Colics	11	4	ns
Diarrhea	13	6	ns
Constipation	3	1	ns
Failure to thrive	3	1	ns
Blood in stools	1	0	ns
Total IgE (KUI/l)	29 ± 58	15 ± 5	ns
Positive milk-specific IgE (n)	3	0	ns
Positive skin prick test	0/6	0/6	ns
Positive APT	19/24	1/11	< .001

- De Boissieu et al, J Pediatr, 2003

Atopy patch tests predict oral tolerance in non-IgE-mediated cow's milk allergy



Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	LR +/–
67.95% (95%CI 56.42–78.07)	88.3% (95% CI 80.03–94.01)	82.81% (95%CI 71.32–91.1)	76.85% (95%CI 67.75–84.43)	5.80/0.36

- Nocerino R et al, Allergy 2012

Eosinophilic esophagitis

Intractable reflux
Failure to thrive

EoE

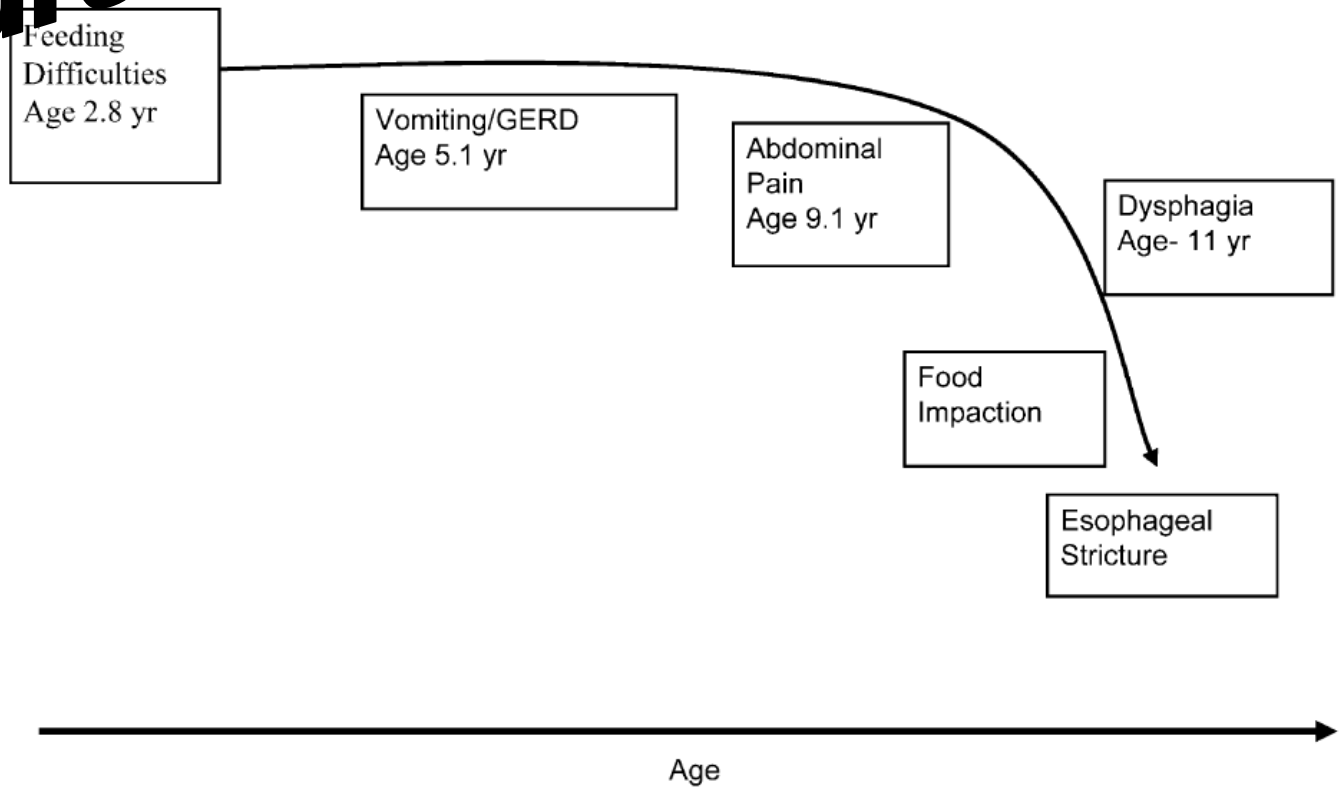
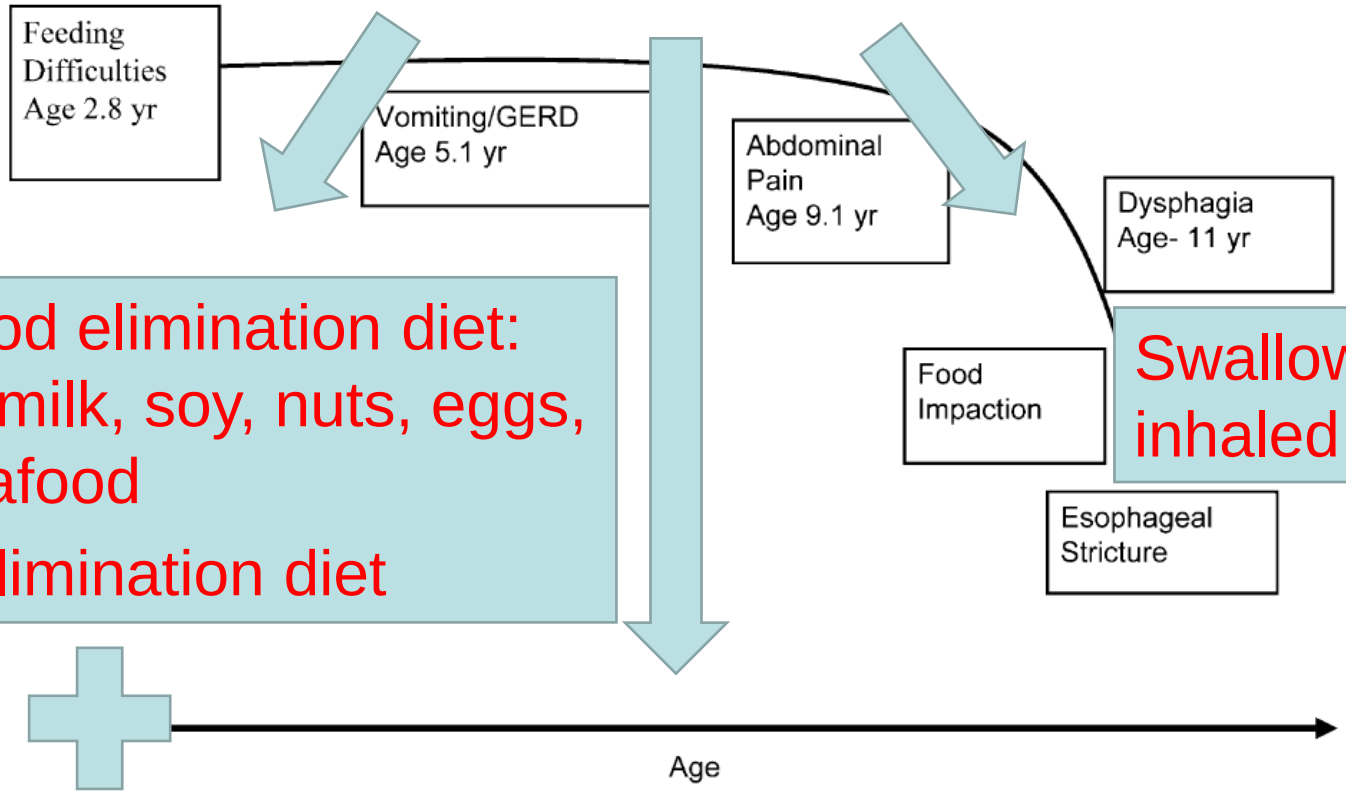


FIG. 3. Potential natural history of eosinophilic esophagitis (mean age of presentation). GERD = gastroesophageal reflux disease.

Spergel et al, JPGN, 2009

EoE



- Six food elimination diet: wheat, milk, soy, nuts, eggs, and seafood
- Milk elimination diet

Swallowing inhaled steroids

FIG. 3. Potential natural history of eosinophilic esophagitis (mean age of presentation). GERD = gastroesophageal reflux disease.

Allergy testing oriented diet

Spergel et al, JPGN, 2009

Diagnosis of allergen during EoE

- Skin prick test almost always negative
- Specific IgE very often detectable
- Patch test often positive

- Orientation of elimination diet, followed by elimination - challenge

Which tools to use?

Depends on clinical pattern

And on the association of different clinical patterns in the same child

Patterns of milk allergy

- Anaphylaxis

Skin prick test	Specific IgE	Atopy patch test
positive	high	Not done

- Enteropathy

Skin prick test	Specific IgE	Atopy patch test
negative	absent	positive

- FPIES

Skin prick test	Specific IgE	Atopy patch test
negative	detectable (1/3)	positive

Patterns of milk allergy

- EoE

➢ Milk

Skin prick test	Specific IgE	Atopy patch test
negative	detectable	negative/positive

- Milk EoE plus wheat & peanut anaphylaxis

➢ Wheat

Skin prick test	Specific IgE	Atopy patch test
positive	high	not done

➢ Peanut

Skin prick test	Specific IgE	Atopy patch test
positive	high	not done

The Great Pla[illegible]ratory, Inc.

William Shaw, Ph.D [illegible]ctor [illegible] 77th Str[illegible] [illegible]49 Fax (913) 341-6207

IgG: NO!!!

Requisition #:

Patient Name:

Patient Age:

Sex:

[illegible] Nam[illegible]

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Comprehens[illegible] [illegible]gy Test — IgG

Dairy	
Casein	1.54
Cheese	1.17
Goat's Milk Cheese	1.93
Milk	2.13
Mozzarella Cheese	1.05
Whey	3.32
Yogurt	3.48
Beans and Peas	
Garbanzo Bean	3.20
Green Bean	1.18
Kidney Bean	1.42
Lima Bean	0.72
Pea	1.05
Pinto Bean	0.84
Soybean	0.82
Fruit	

Corn	1.05
Flax	1.44
Gliadin	1.36
Lentil	0.96
Millet	1.33
Oat	9.58
Rice	0.82
Rye	1.51
Sorghum	2.26
Wheat Gluten	1.39
Wheat	1.04
Fish	
Cod Fish	0.85
Crab	0.70
Halibut	1.01
Lobster	1.52
Salmon	1.99

Conclusion

- Clinical patterns vary with allergen
- Different clinical patterns may be associated in the same child
- Adapt testing to allergen and to clinical pattern
- Always do allergy testing in patients with EoE, in order not to miss associated anaphylaxis