Non-IgE-mediated immune adverse reactions to foods

Philippe Eigenmann

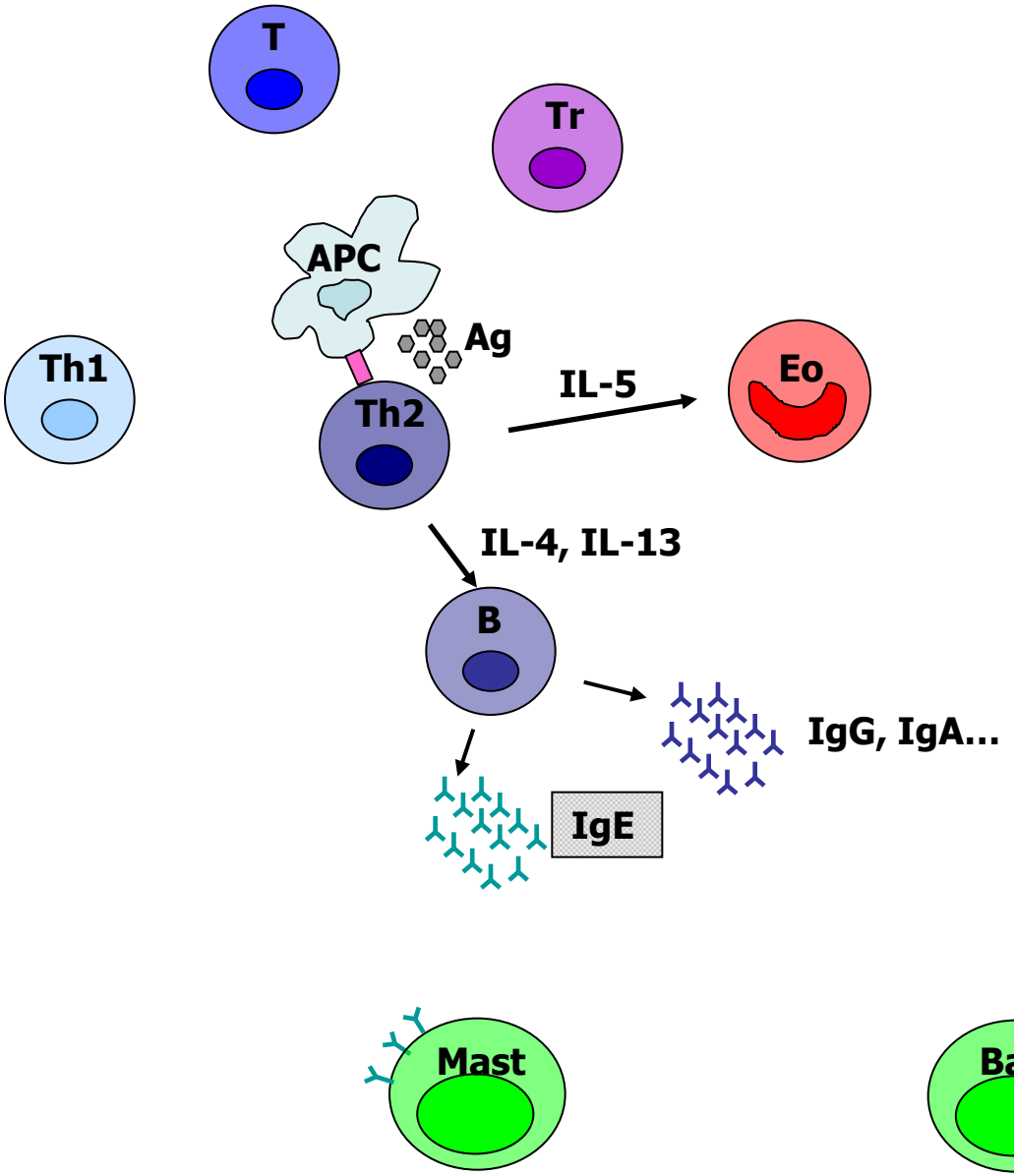
Head, Pediatric Allergy Unit

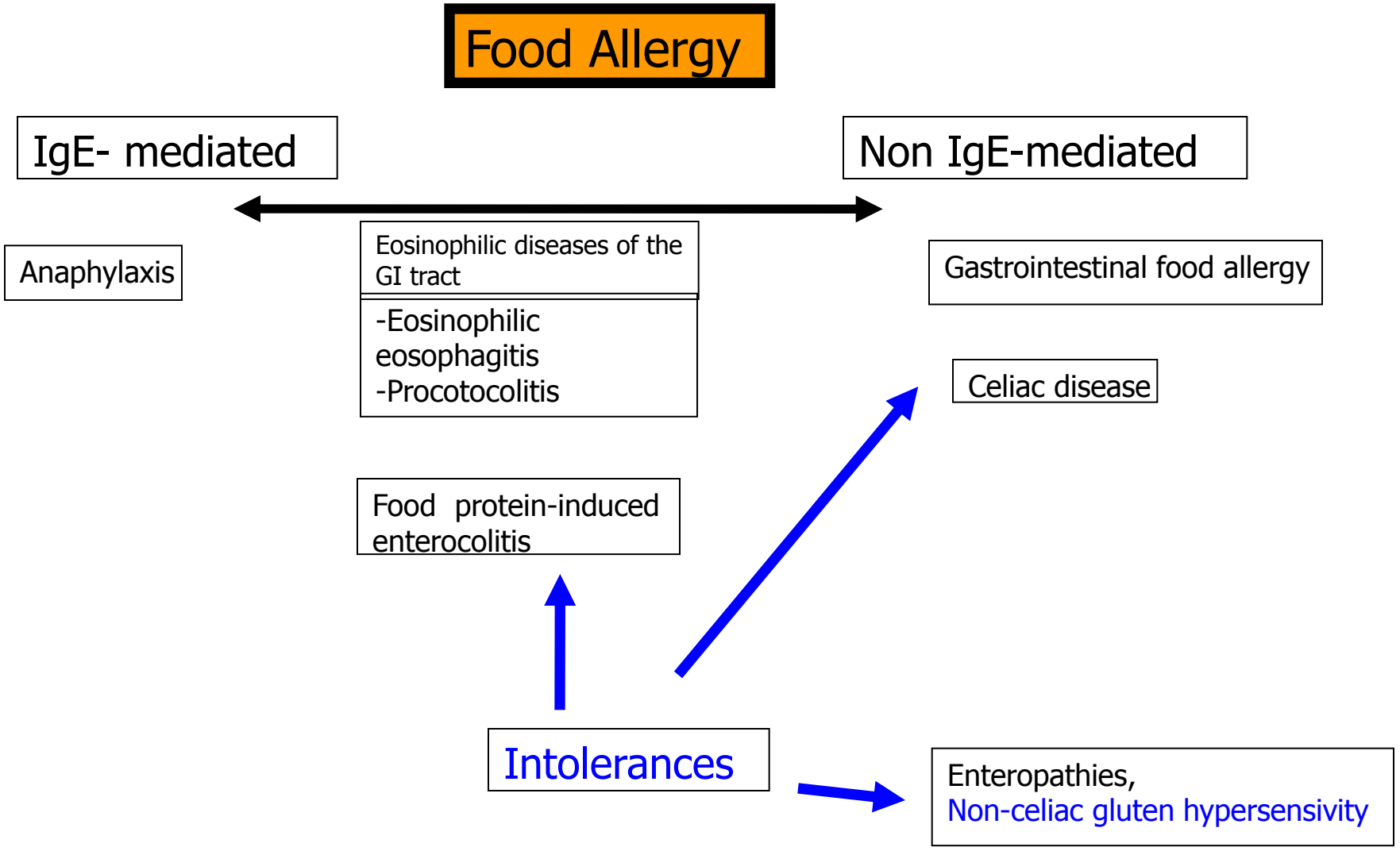
UNIVERSITÉ DE GENÈVE

HUG
Hôpitaux
Universitaires
Genève

I declare no relevant conflict of interest in relation to this presentation.

- **Objectives**:
  - Classification of non IgE-mediated food allergy (clinical, diagnostic criteria)
  - Description of the most frequent non-IgE-mediated food allergies
    - Eosinophilic esophagitis
    - Food-protein induced enterocolitis syndrome (FPEIS)
    - Wheat-associated food hypersensitivities


T
Tr
APC
Ag
Th1
Th2
IL-5
Eo
IL-4, IL-13
B
IgG, IgA...
IgE
Mast
Baso



Adapted from Rothenberg ME, JACI 2004;113:11

Symptoms from the history

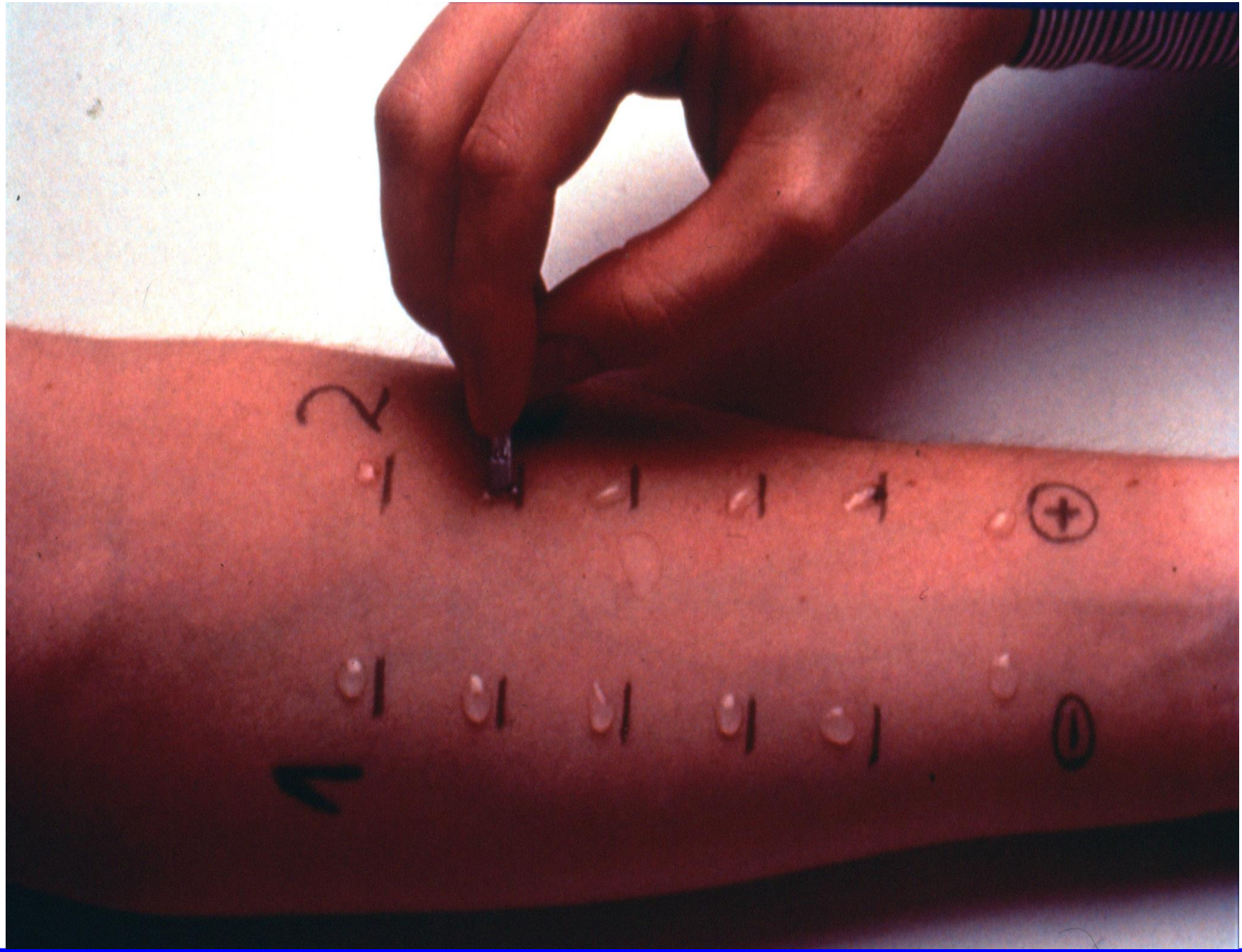
IgE-mediated

- Skin:
  -urticaria, atopic dermatitis
- Respiratory:
  -asthma, throat edema, rhinitis
- GI:
  -diarrhea, vomiting, oral allergy syndrom
- Anaphylaxis

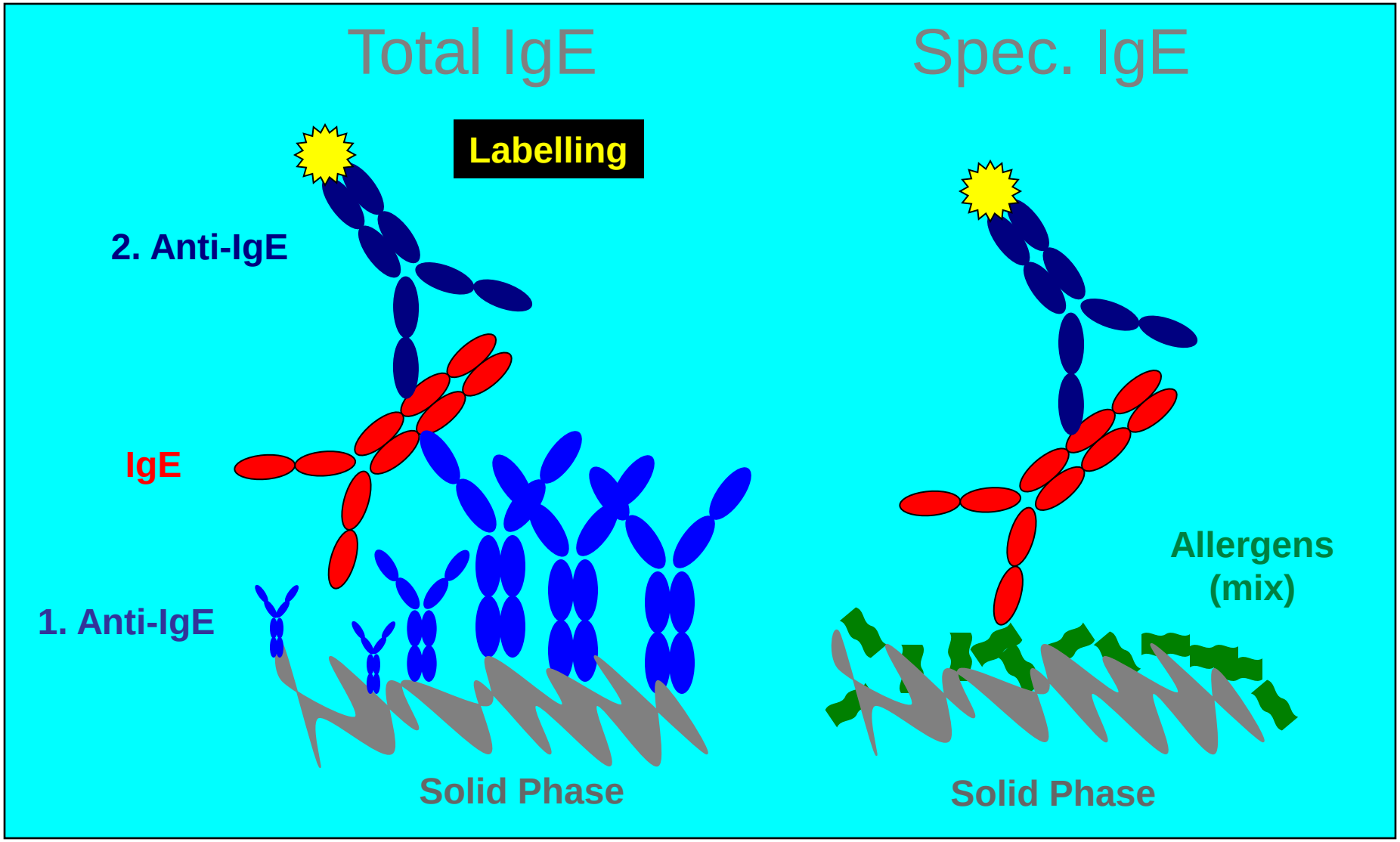
non-IgE

- GI:
  -vomiting, diarrhea, abdominal pain, malabsorption
- Skin:
  -atopic dermatitis
- Others?

- The diagnosis of (IgE-mediated) food allergy
- Non-IgE mediated food allergy
- Food protein-induced enterocolitis (FPIES)
- FODMAPS or other food-related syndromes



Principles of IgE measurement



Food challenges

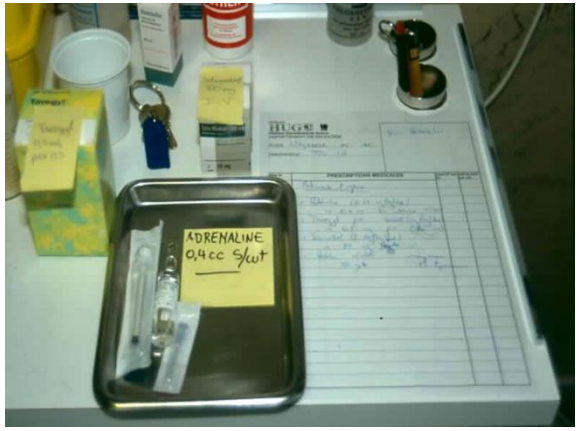
- Open food challenge
  Progressive feeding with the tested food

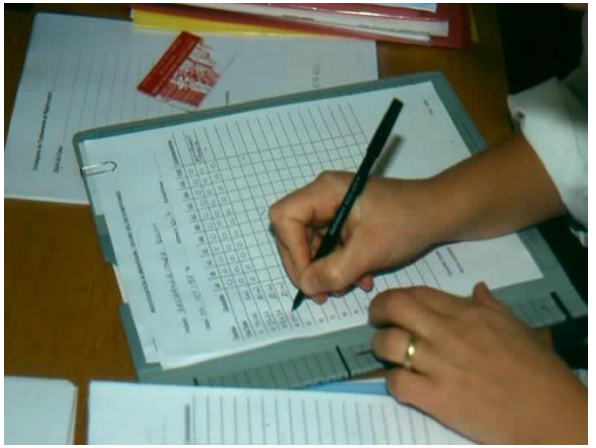
- Single-blinded food challenge
  The patient (and parents) are not aware of the food tested

- Double-blind, placebo-controlled food challenge
  The patient and the investigator are not aware of the food tested


bibi


bibi


ADRENALINE
0,4cc S/cut

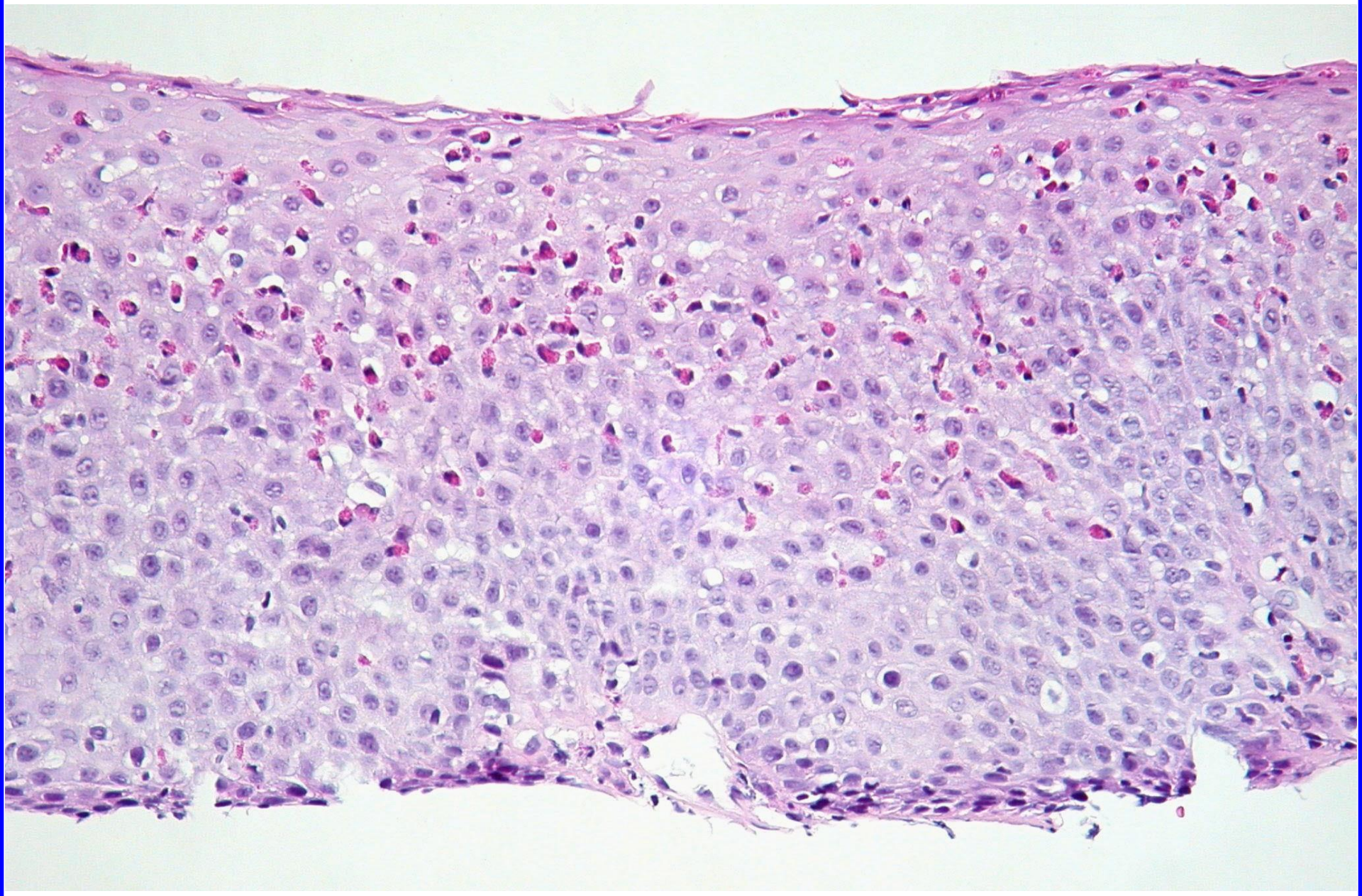


- The diagnosis of (IgE-mediated) food allergy
- Non-IgE mediated food allergy
- Food protein-induced enterocolitis (FPIES)
- FODMAPS or other food-related syndromes

Allergic eosinophilic gastroenteritis/esophagitis

- Symptoms: Abdominal pain, nausea, reflux, diarrhea, dysphagia.
- Laboratory: positive SPT or sp IgE Abs (40%), biopsy: eosinophilic infiltration in the lower oesophagus.
- Allergens: cow's milk, soy, wheat
- Outcome: ?

Kelly *et al.* Gastroenterol 1995;109:1503
Furuta *et al.* Gastroenterology 2007;133:1342



Symptoms according to age

Table 1. Presenting Symptoms among 103 Pediatric Patients with Eosinophilic Esophagitis.*

Symptom	Median Age (Interquartile Range)	No. (%)
Feeding disorder	2.0 (1.2–6.2)	14 (13.6)
Vomiting	8.1 (3.5–12.3)	27 (26.2)
Abdominal pain	12.0 (9.6–15.2)	27 (26.2)
Dysphagia	13.4 (10.0–16.7)	28 (27.2)
Food impaction	16.8 (13.7–19.6)	7 (6.8)

Noel and Rothenberg, NEJM 2004;352:940

A 1 month elemental diet improves EE in children and adolescents

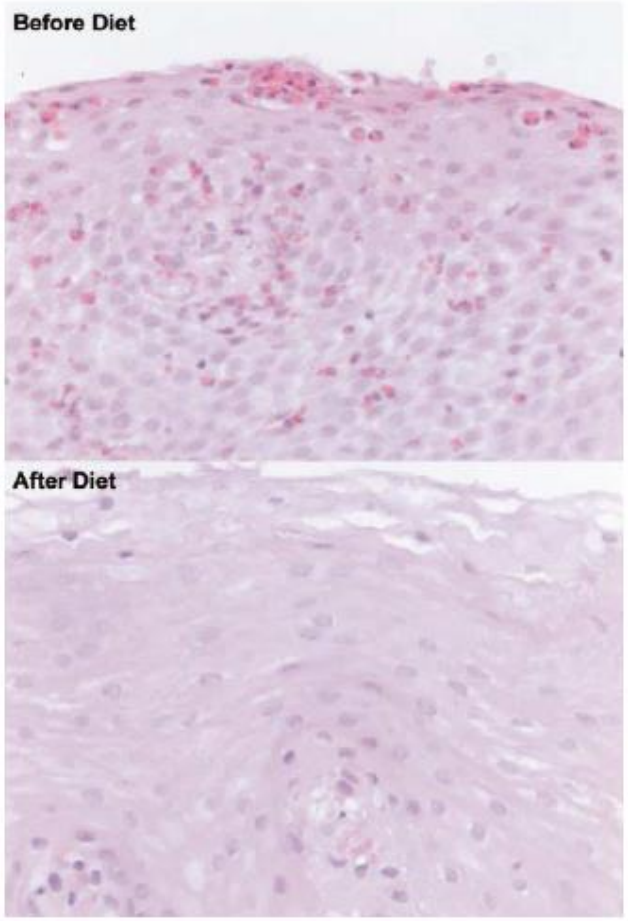


Table 2. Number of Patients With Symptoms Before (Prediet) and After 1 Month of Treatment With Elemental Diet (Postdiet)

	Prediet	Postdiet	*p*
Eosinophils/HPF	33.7 ± 10.3	1.0 ± 0.6	<0.01
Abdominal pain	40	2	<0.01
Vomiting	36	1	<0.01
Heartburn	27	2	<0.01
Water brash	11	1	<0.01
Globus	9	1	<0.01
Dysphagia	7	0	<0.01
Chest pain	4	0	0.04
Night cough	5	1	0.1
Irritability	3	0	0.08

HPF = microscopic high-powered field, equivalent to 40×.

Markowitz, Am J Gastroenterol 2003;98:777

- The diagnosis of (IgE-mediated) food allergy
- Non-IgE mediated food allergy
- Food protein-induced enterocolitis (FPIES)
- FODMAPS, gluten, or other food-related syndromes

Food-induced enterocolitis

- Originally infants
- Symptoms: profuse vomiting (and/or diarrhea) within 2-24 hours.
- Laboratory: rise in polymorphonuclear cells (> 3'500 /mm^3), negative SPT or sp IgE Abs
- Allergens: cow's milk, soy, (but also chicken, turkey, crustaceans, grains…)
- Outcome: usually favorable after 2-3 years?

Sicherer *et al.*, J Pediatr 1998;133:214
Caubet *et al* J Allergy Clin Immunol 2014

Clinical features and resolution of food protein–induced enterocolitis syndrome: 10-year experience

Jean Christoph Caubet, MD,[a,b]* Lara Simone Ford, MD, MPH,[a,c]* Laura Sickles, BA,[a,d] Kirsi M. Järvinen, MD, PhD,[a,e] Scott H. Sicherer, MD,[a] Hugh A. Sampson, MD,[a] and Anna Nowak-Węgrzyn, MD[a] *New York and Albany, NY, Geneva, Switzerland, Westmead, Australia, and Philadelphia, Pa*

(J Allergy Clin Immunol 2014;134:382-9.)

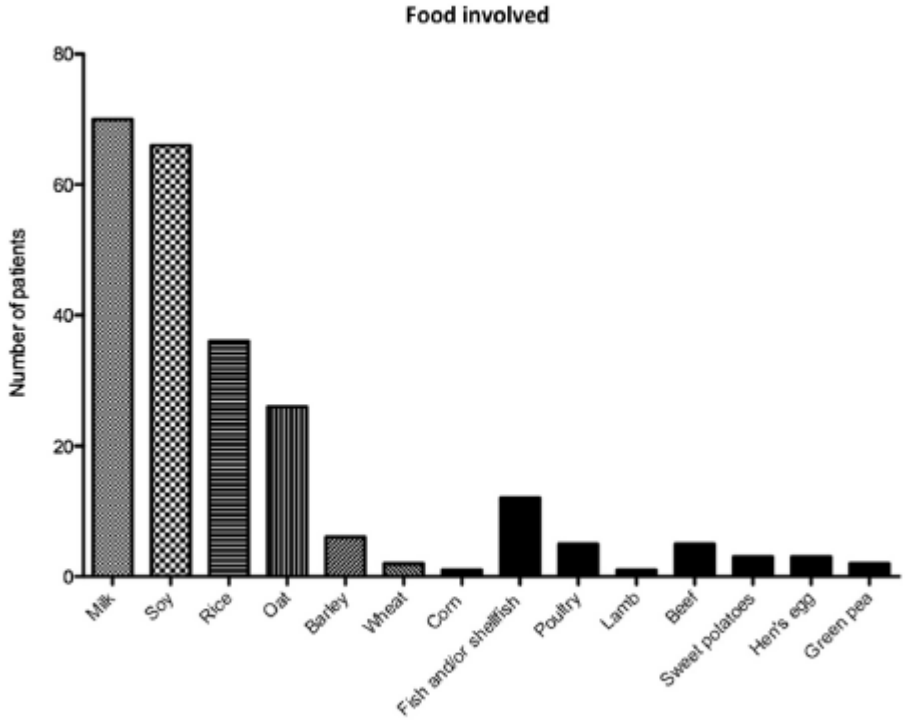
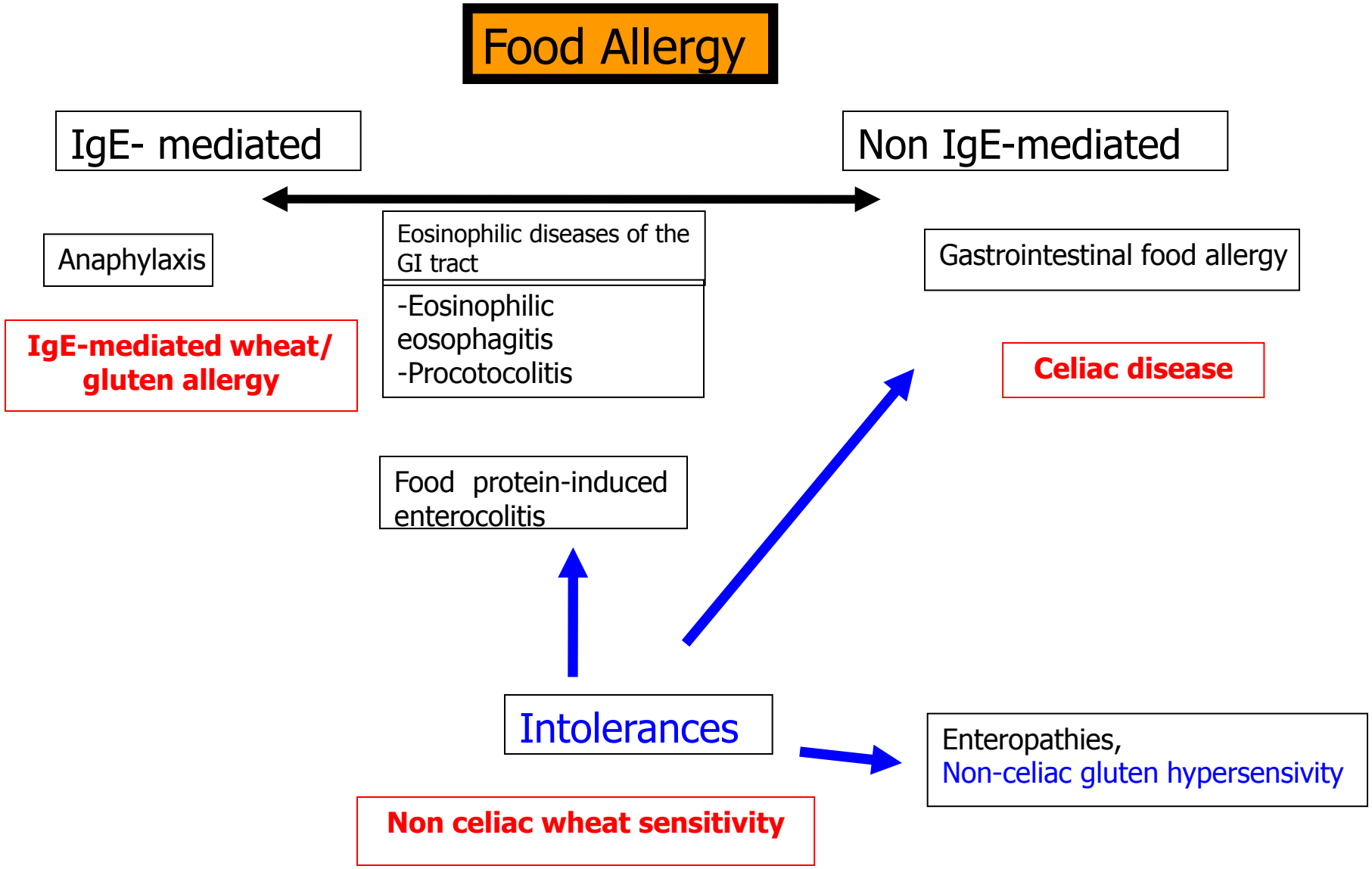


FIG 1. FPIES food triggers.

- The diagnosis of (IgE-mediated) food allergy
- Non-IgE mediated food allergy
- Food protein-induced enterocolitis (FPIES)
- FODMAPS, gluten, or other food-related syndromes



Adapted from Rothenberg ME, JACI 2004;113:11

Sapone et al. BMC Medicine 2012, 10:13
http://www.biomedcentral.com/1741-7015/10/13

BMC Medicine

OPINION Open Access

Spectrum of gluten-related disorders: consensus on new nomenclature and classification

Anna Sapone[1,2], Julio C Bai[3], Carolina Ciacci[4], Jernej Dolinsek[5], Peter HR Green[6], Marios Hadjivassiliou[7], Katri Kaukinen[8], Kamran Rostami[9], David S Sanders[10], Michael Schumann[11], Reiner Ullrich[11], Danilo Villalta[12], Umberto Volta[13], Carlo Catassi[1,14] and Alessio Fasano[1*]

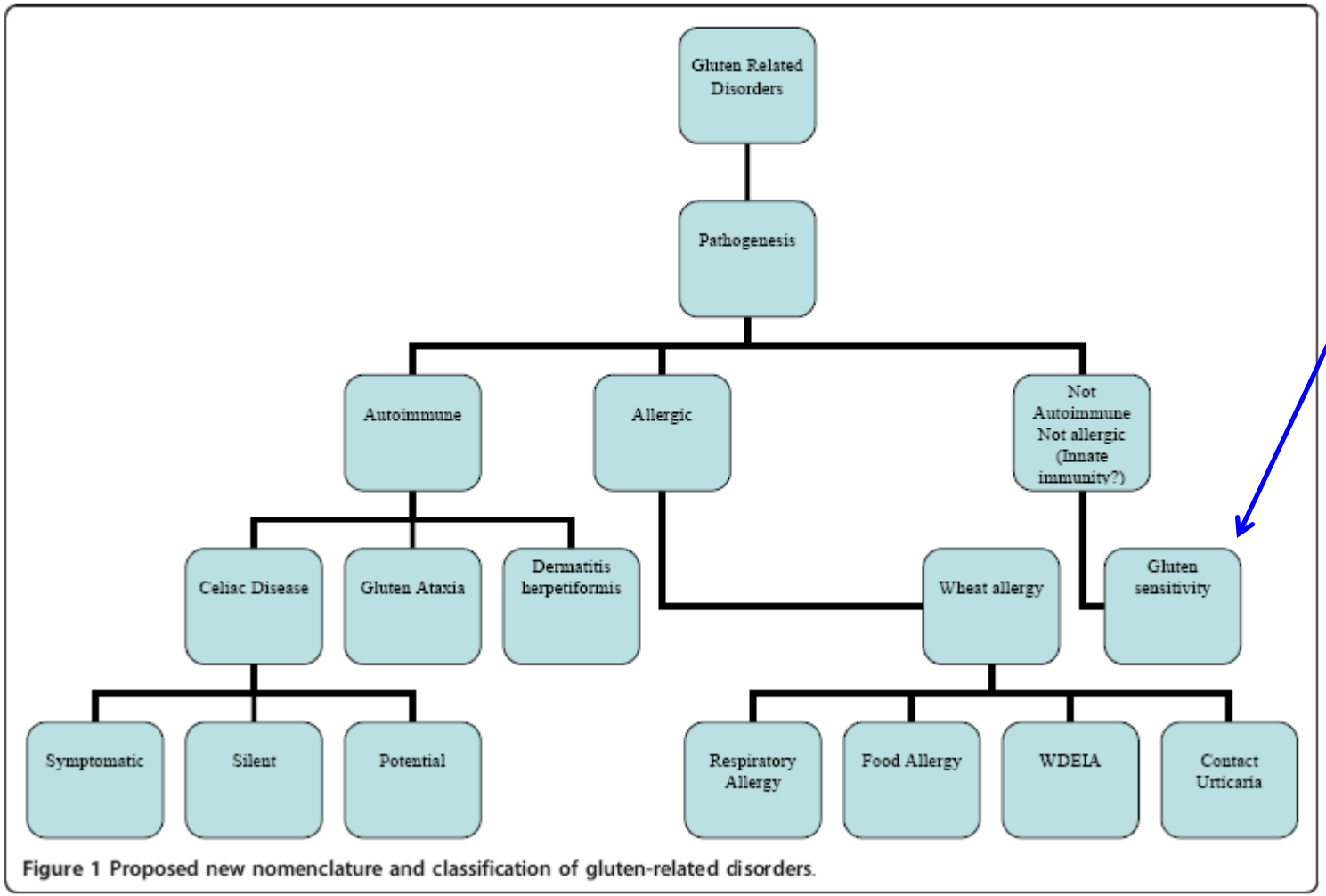


Figure 1 Proposed new nomenclature and classification of gluten-related disorders.

6% in a celiac clinic (1/3 had chronic fatigue)

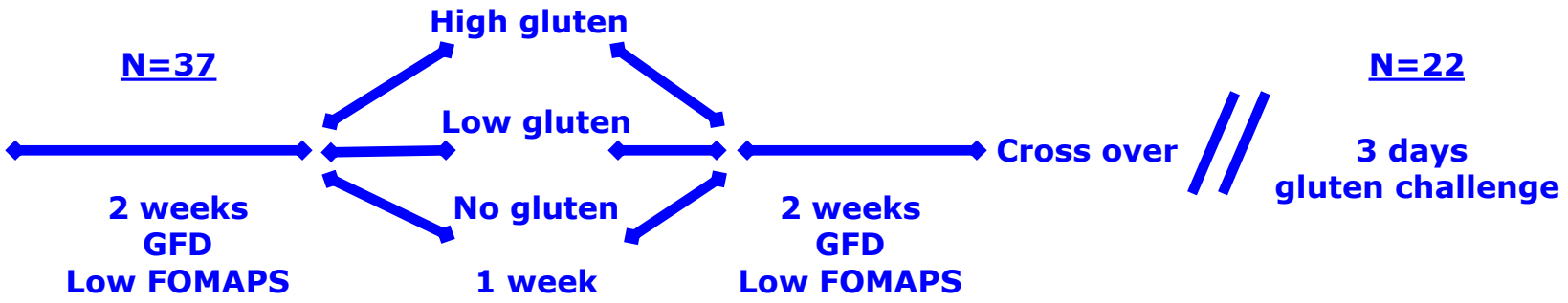
Sapone et al. BMC Medicine 2012, 10:13

GASTROENTEROLOGY 2013;145:320–328

No Effects of Gluten in Patients With Self-Reported Non-Celiac Gluten Sensitivity After Dietary Reduction of Fermentable, Poorly Absorbed, Short-Chain Carbohydrates

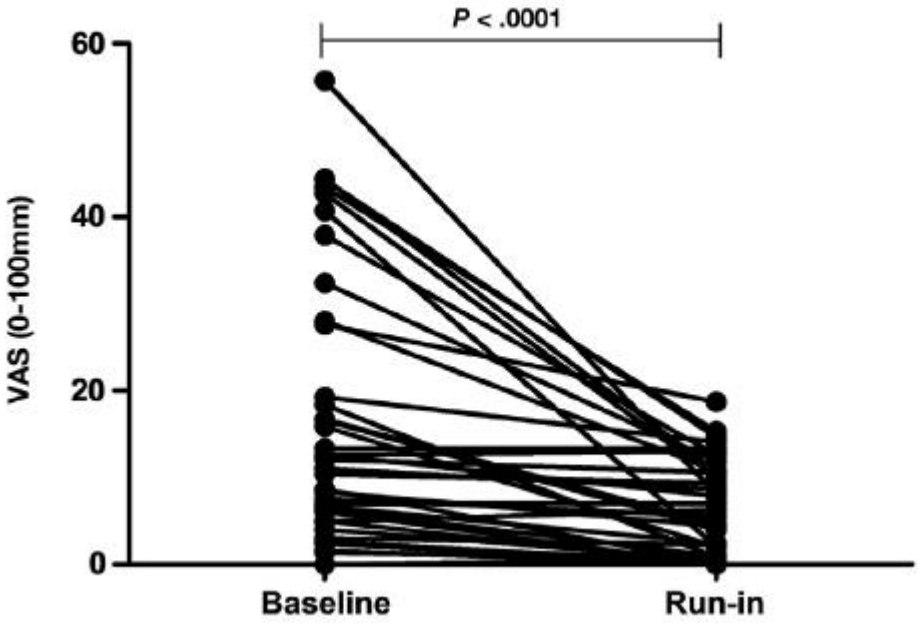
JESSICA R. BIESIEKIERSKI,[1,2] SIMONE L. PETERS,[2] EVAN D. NEWNHAM,[1] OURANIA ROSELLA,[2] JANE G. MUIR,[2] and PETER R. GIBSON[2]

[1]Department of Gastroenterology, Eastern Health Clinical School, Monash University, Box Hill, Victoria, Australia and [2]Department of Gastroenterology, Central Clinical School, Monash University, The Alfred Hospital, Melbourne, Victoria, Australia

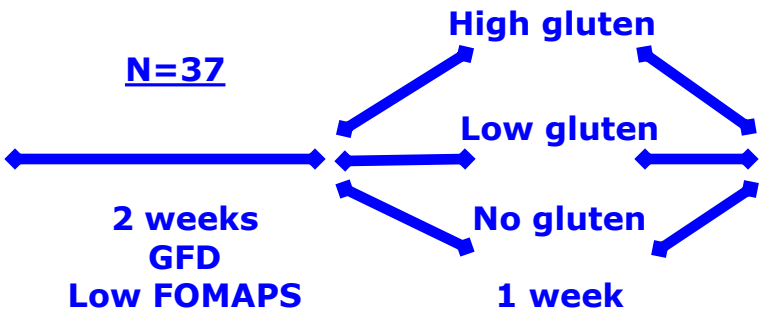


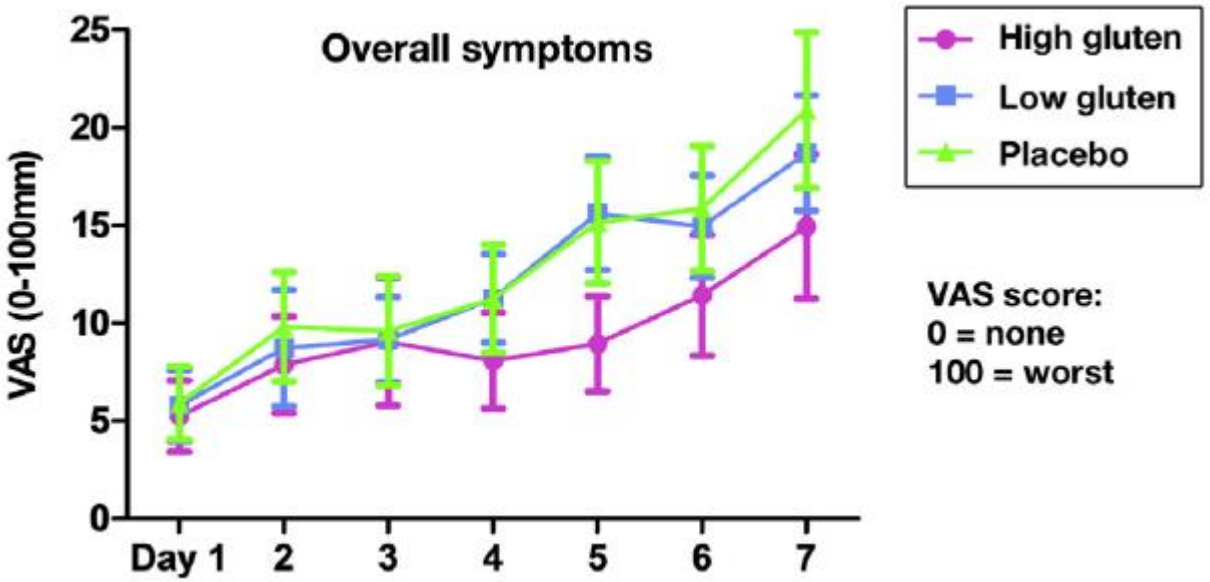
N=37

2 weeks
GFD
Low FOMAPS

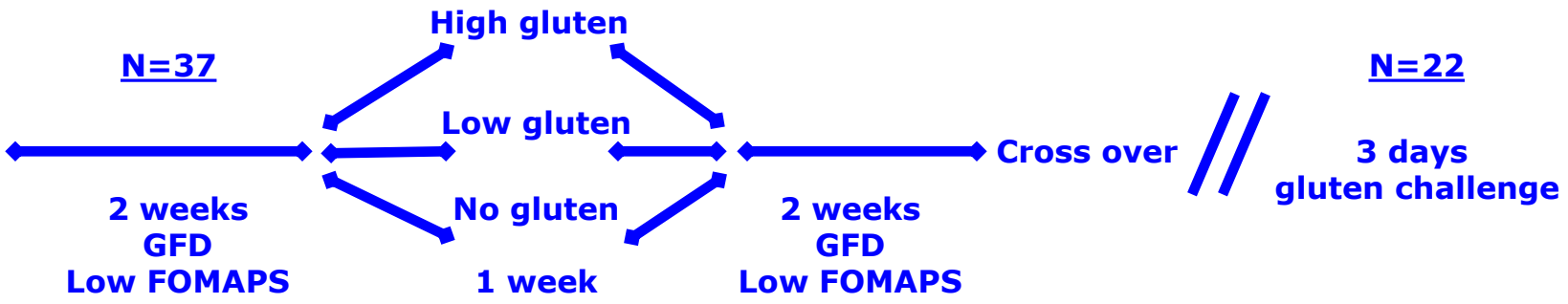


GASTROENTEROLOGY 2013;145:320–328





GASTROENTEROLOGY 2013;145:320–328



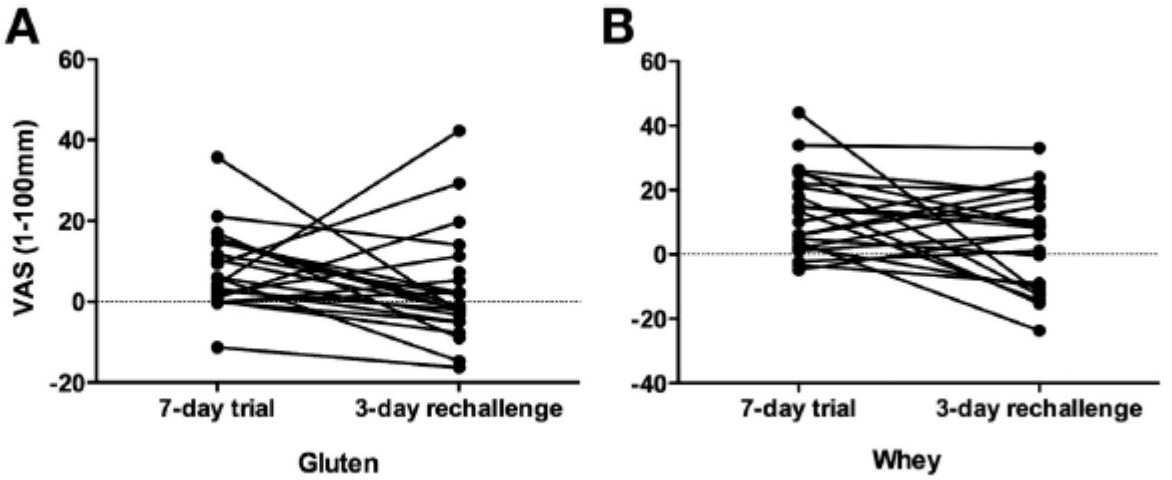


Figure 3. Reproducibility in change in overall symptom severity for (*A*) gluten (16 g/d) and (*B*) whey (16 g/d) treatment arms. The 7-day trial used mean data from the 7-day treatment period and the 3-day rechallenge used data from the third day of the 3-day treatment period.

GASTROENTEROLOGY 2013;145:320–328

Perspectives in relation to allergenicity assessment

- The link between the disease and the food, and the pathogenic mechanism is not always warranted.
  - How does this translate with allergenicity assessment?
  - How can we overcome this hurdle?