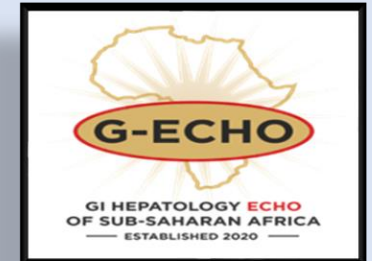


FOOD ALLERGIES



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Supervisor: Prof. Reid Ally



INTRODUCTION

- An adverse food reaction is any untoward reaction that occurs following ingestion of a food or food additive.
- May be the result of a toxic or non-toxic reaction.
- Toxic reactions.
- Non-toxic reaction: Immune mediated/non-immune mediated.

Introduction cont..

- Food intolerances: Enzymatic, pharmacologic, or idiopathic.
- Food allergies: IgE-mediated or non-IgE-mediated.
- 2% -10% of the overall US population have food allergies.
- 8% of children have food allergies.

Introduction cont..

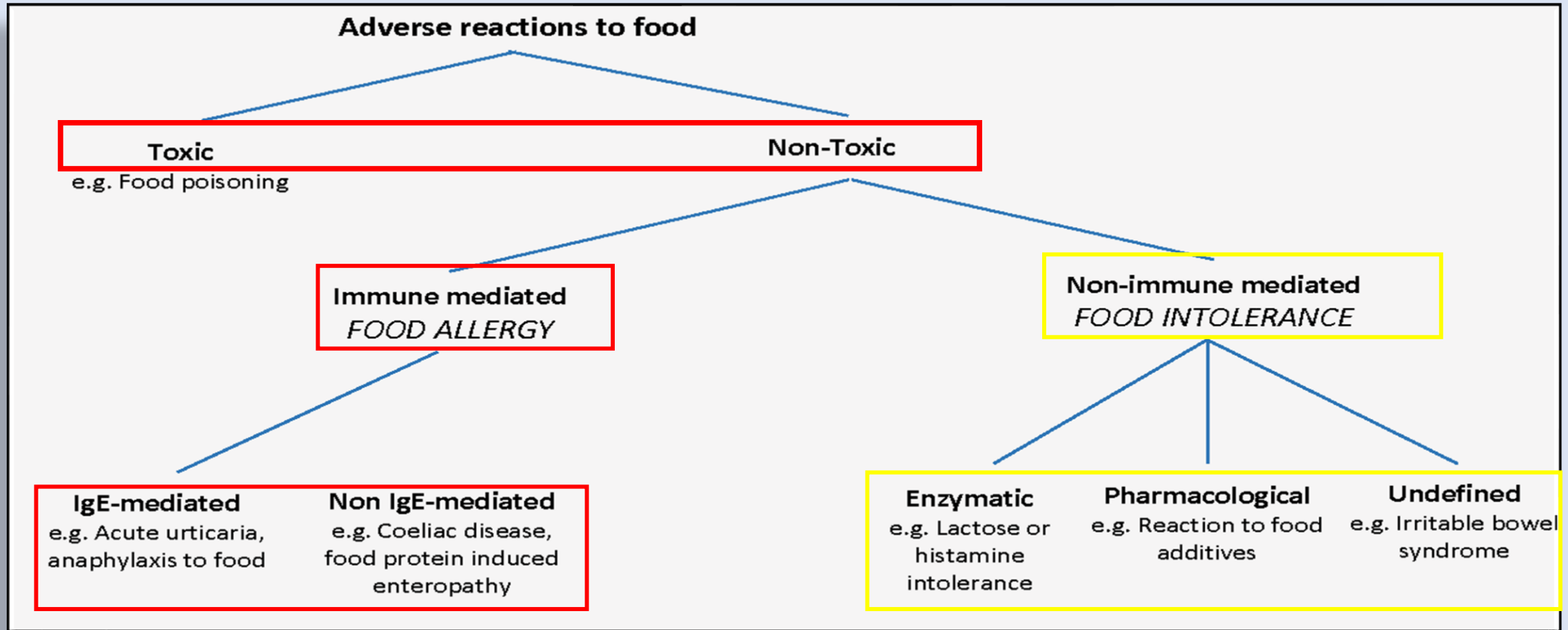


Figure 1: The classification of adverse food reactions, as initially proposed by the EAACI-Position paper on Adverse Reactions to Food^{1,2,3}

Allergens	0-1 year 147 children (%)	1-3 years 359 children (%)	3-15 years 468 children (%)	Adults 287 (%)
Eggs	77.5	69.6	24.3	6.3
Milk	29.2	25.6	7	3.5
Peanut	19.7	37.6	49.3	10.1
Fruit in husk	2.7	4.4	10, 2	15.7
Legumes	0.6	4.4	13.4	5.9
Fish	0.6	5	10	3.1
Prunoïdees	0	0	0	31.3
Lawyer, banana, chestnut, Kiwi	0.6	1.3	5.3	22.6
Apiaceae	0	0	1.7	16.4
Wheat, grain	6.1	6.4	2.7	13.2

Source: (D.-A. Moneret-Vautrin, 2008)

PATHOGENESIS

PHYSIOLOGIC

➤ Block penetration of ingested antigens.

- Epithelial cells.
- Glycocalyx.
- Intestinal microvillus membrane structure.
- Tight junctions.
- Intestinal peristalsis

➤ Break down ingested antigens.

- Salivary amylases and mastication.
- Gastric acid and pepsins.
- Pancreatic enzymes.
- Intestinal enzymes.
- Intestinal epithelial cell lysozyme activity.

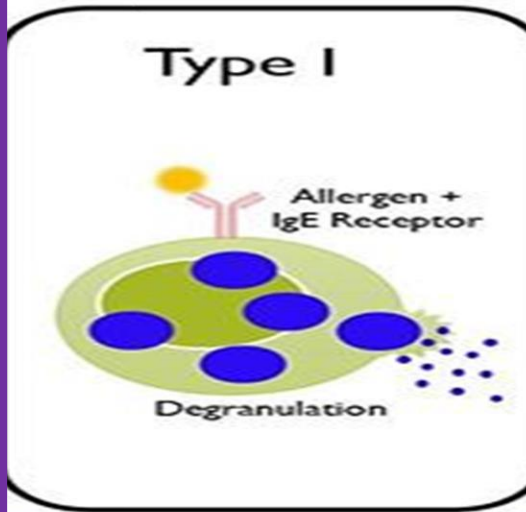
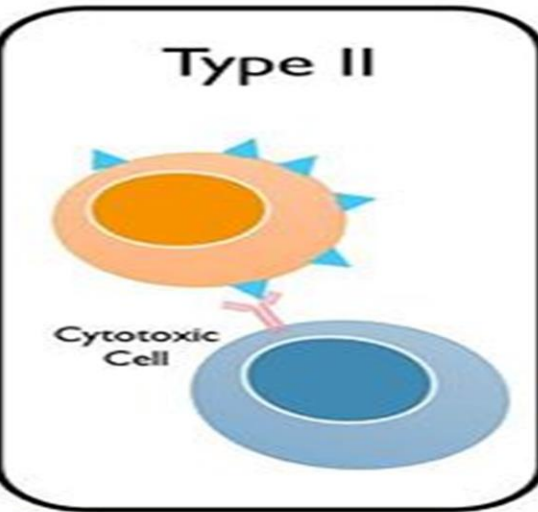
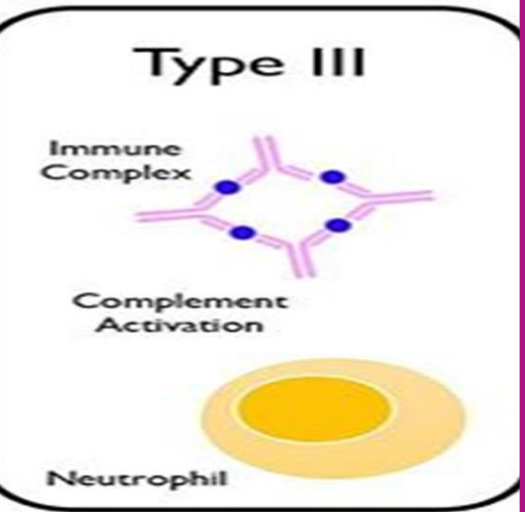
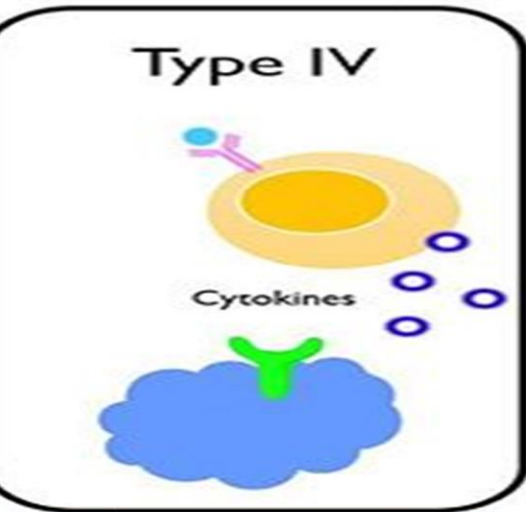
PATHOGENESIS

Immunologic

- Block penetration of ingested antigens.
 - Antigen-specific sIgA in intestinal lumen
- Clear antigens penetrating intestinal barrier.
 - Serum antigen-specific IgA and IgG
- Reticuloendothelial system.

Microbiota

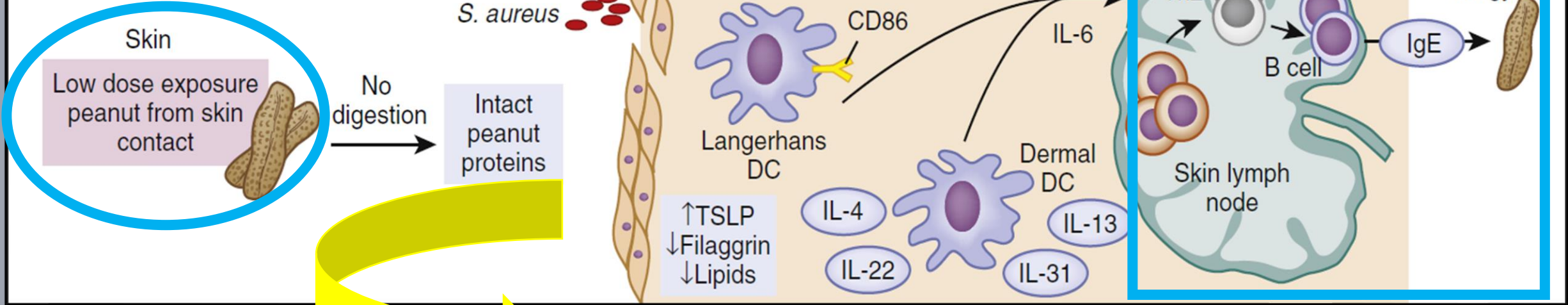
Types of Hypersensitivity Reactions

	Type I	Type II	Type III	Type IV
				
Mediators	IgE-Mediated	IgG or IgM Cytotoxic	Immune Complex-Mediated	T-Cell-Mediated
Onset	Within 1 Hour	Hours to Days	1-3 Weeks	Days to Weeks
Examples	Anaphylaxis	Hemolytic Anemia	Serum Sickness SLE	Rash SJS

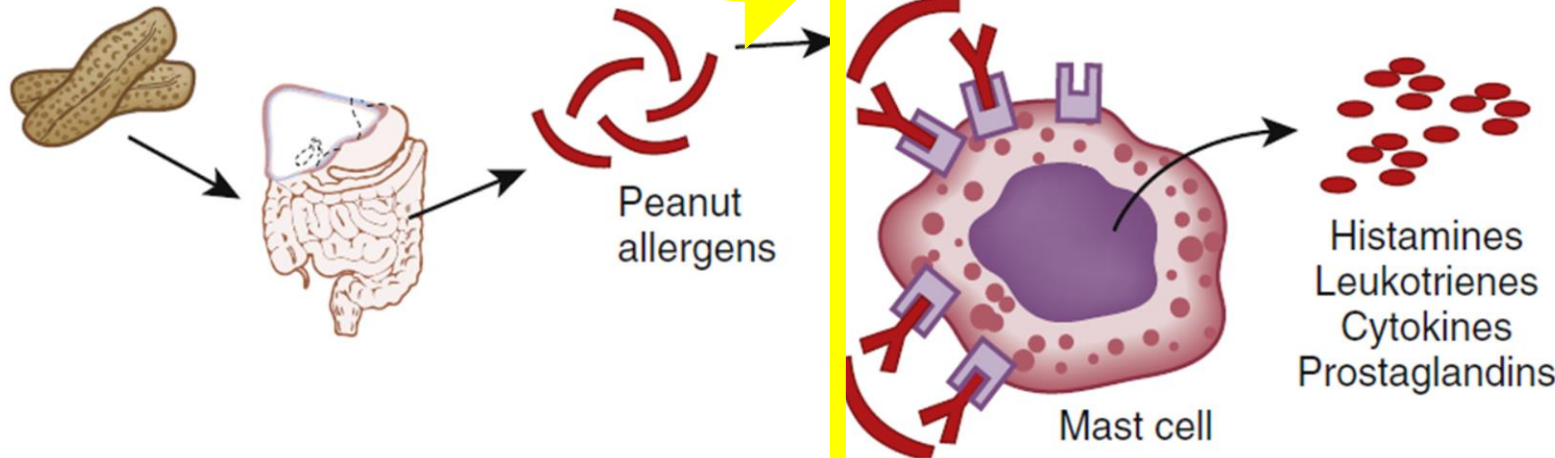
Son JH, Park SY, Cho YS, Chung BY, Kim HO, Park CW. Immediate Hypersensitivity Reactions Induced by Triamcinolone in a Patient with Atopic Dermatitis. J Korean Med Sci. 2018 Mar 19;33(12):e87.

IgE-mediated Food Allergy

Sensitisation



Allergic reaction



Systemic symptoms

- Airway obstruction
- Arrhythmia
- Hives
- Low blood pressure

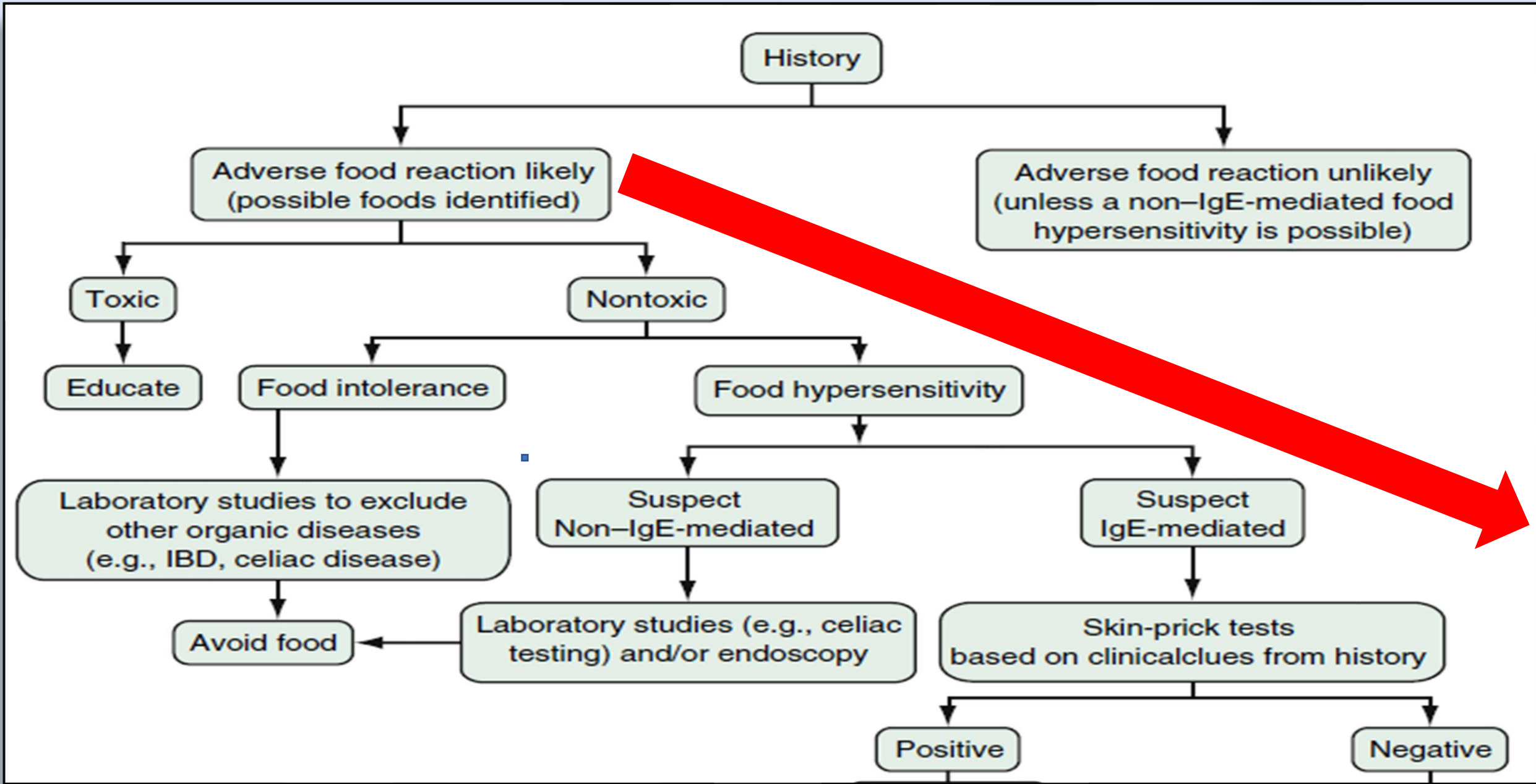
Local symptoms

- Cramping
- Diarrhea
- Itching
- Nausea
- Swelling
- Vomiting

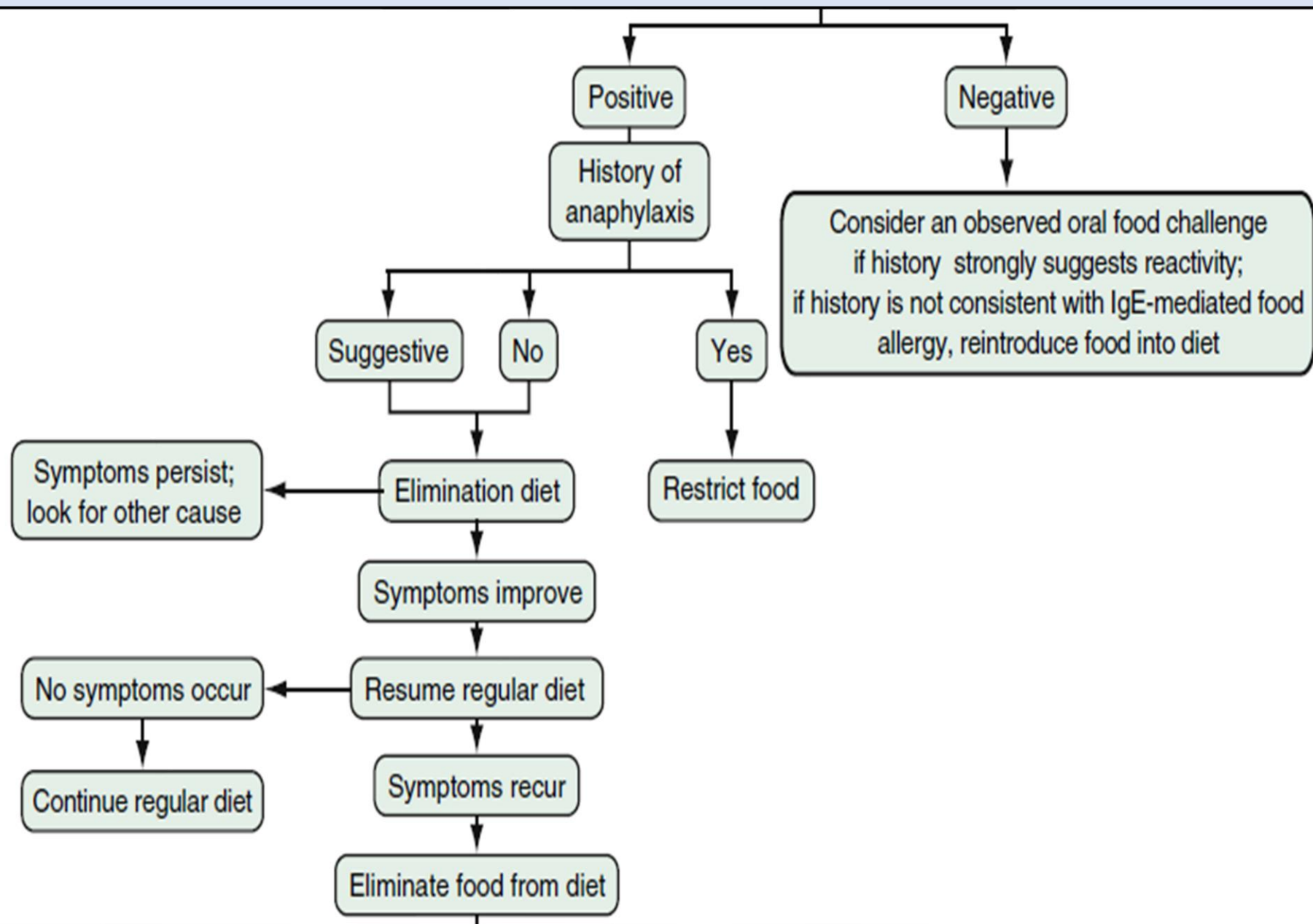
CLINICAL FEATURES

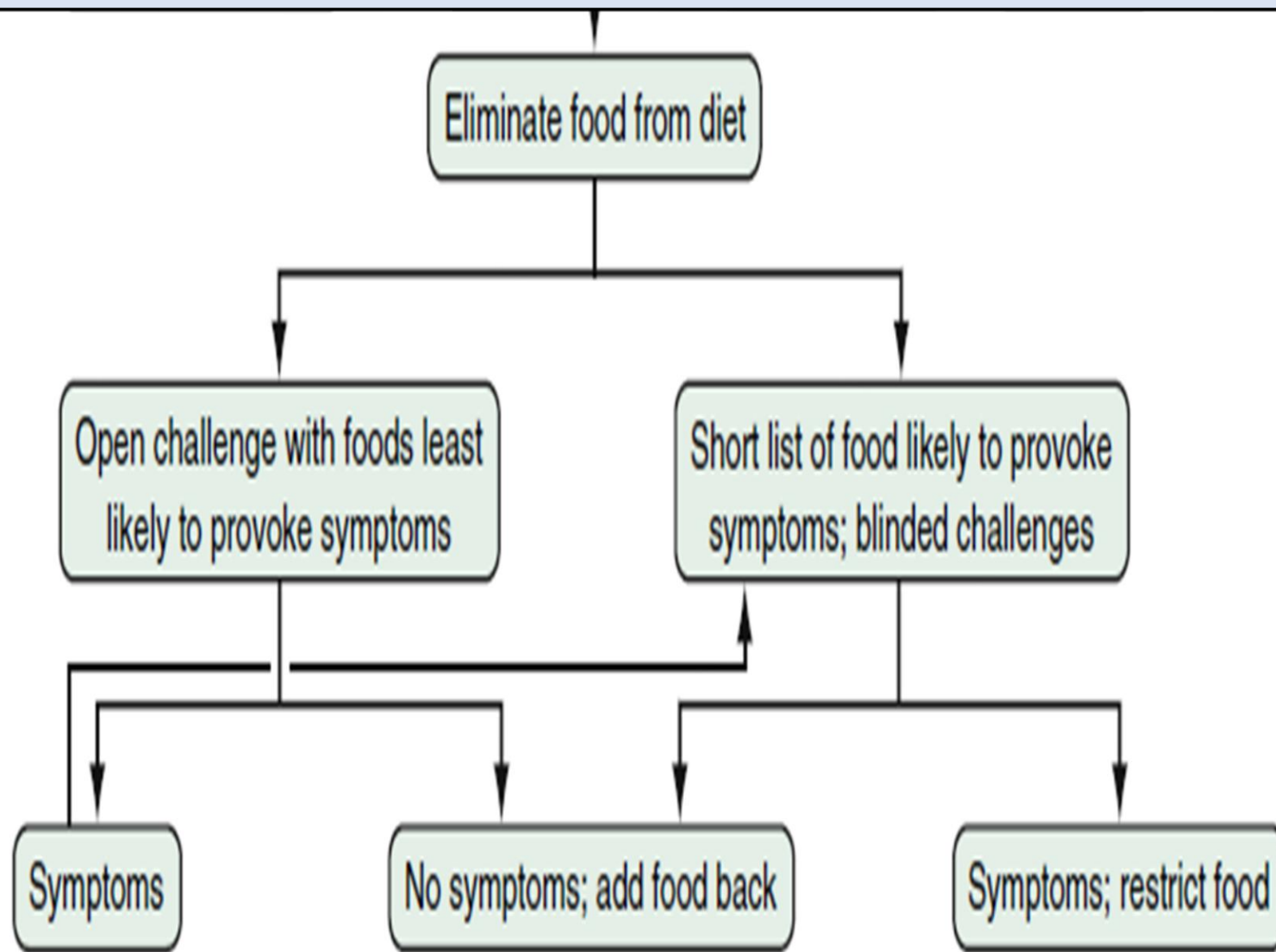
Gastrointestinal Food Allergic Disorders

Disorder	Key Features
IgE-mediated	
Oral allergy	Oral pruritus, mild angioedema of oral cavity
Gastrointestinal immediate hypersensitivity	Acute nausea, vomiting, pain, diarrhea
Mixed IgE and non-IgE-mediated	
Eosinophilic esophagitis	Dysphagia, post-prandial nausea and vomiting, epigastric pain
Eosinophilic gastroenteritis	Vomiting, abdominal pain, diarrhea, malabsorption, and failure to thrive
Non-IgE-mediated	
Food protein-induced enterocolitis	Vomiting, diarrhea, poor growth, lethargy, dehydration
Food protein-induced enteropathy	Malabsorption, emesis, poor growth, diarrhea
Food protein-induced proctocolitis	Bloody diarrhea, mucous in stools, normal growth
Celiac disease	Malabsorption, failure to thrive, diarrhea



Sleisenger, M. H., Feldman, M., Friedman, L. S., & Brandt, L. J. (2021). Sleisenger and Fordtran's gastrointestinal and liver disease: Pathophysiology, diagnosis, management. Philadelphia: Saunders/Elsevier.

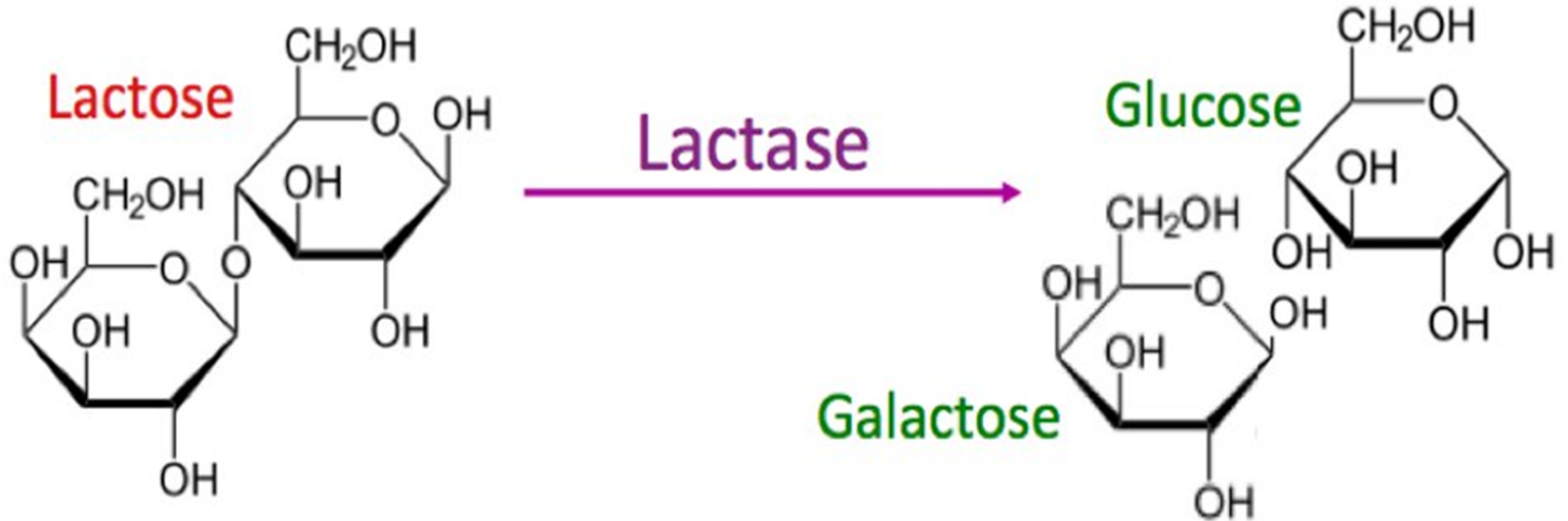


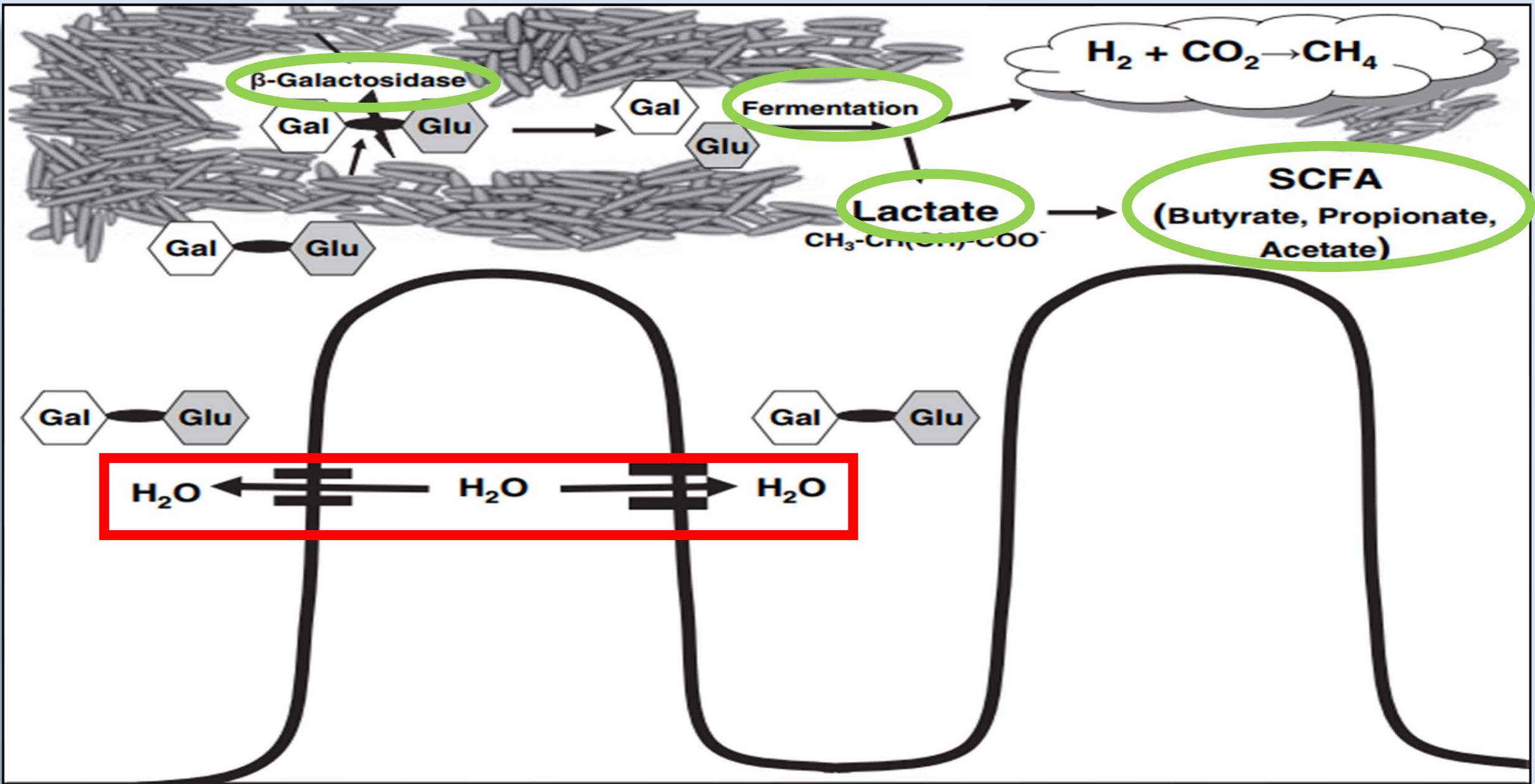


LACTOSE INTOLERANCE

- Lactose is a disaccharide of β -D-galactose and β -D-glucose, $\beta(1,4)$.
- It is digested by enzyme lactase, in the brush border of intestine.
- Lactose intolerance is inability to metabolise lactose.
- Classified as Congenital, Primary and Secondary.

LACTOSE INTOLERANCE

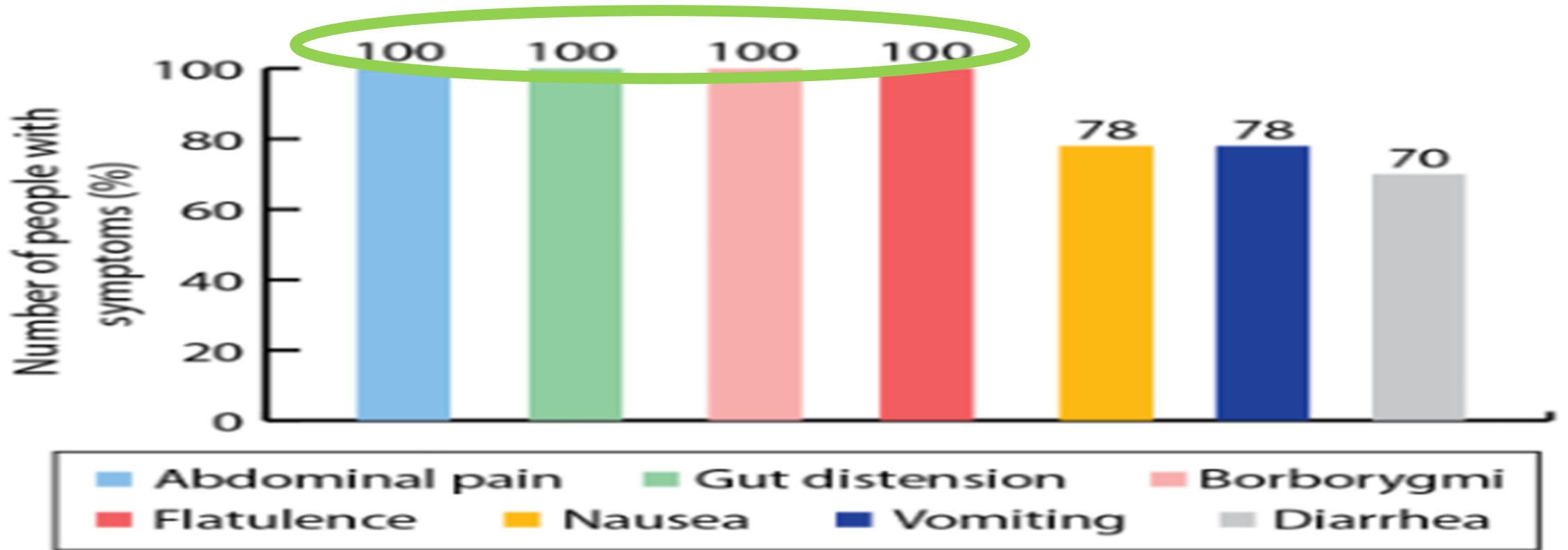




<https://doi.org/10.1111/j.1365-2036.2007.03557>

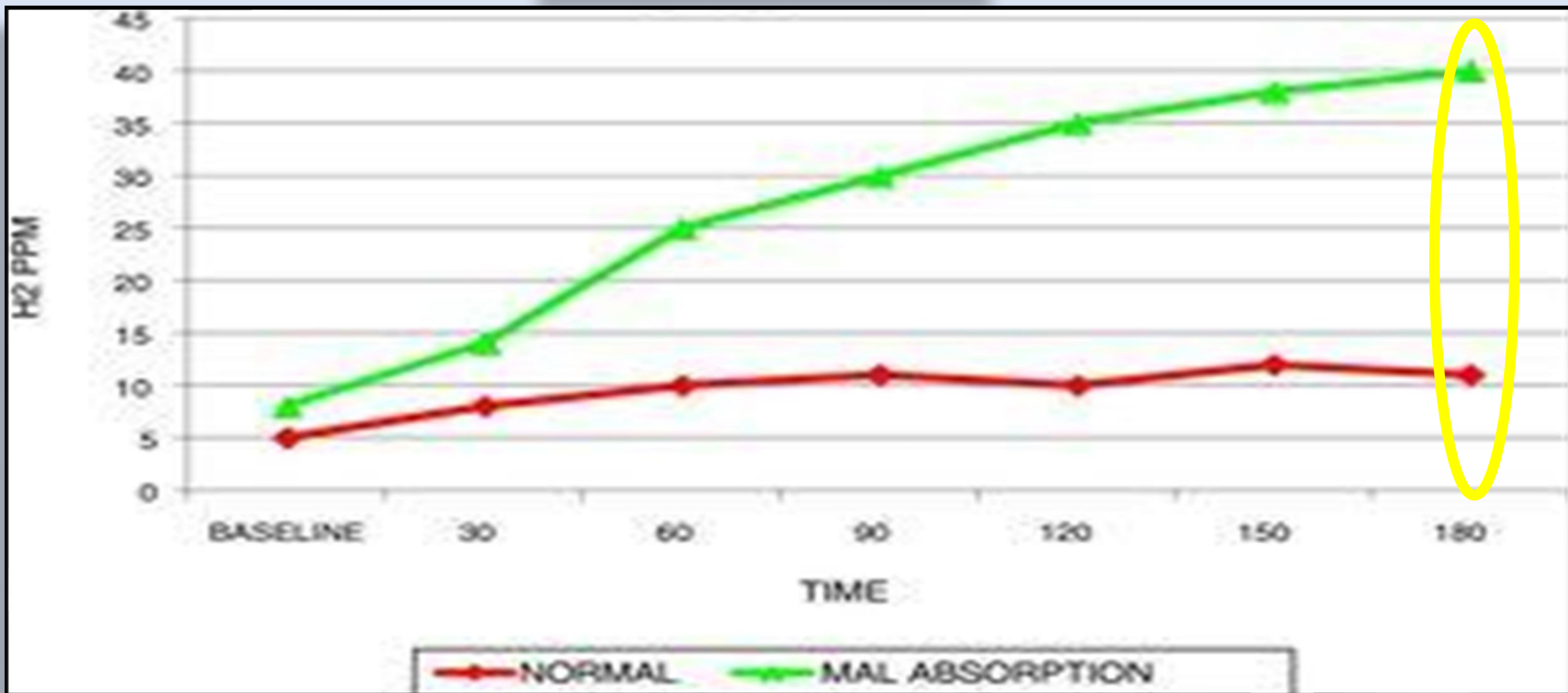
CLINICAL FEATURES

Figure 3: Symptoms reported by individuals at the time of diagnosis of lactose intolerance



<https://doi.org/10.1111/j.1365-2036.2007.03557>

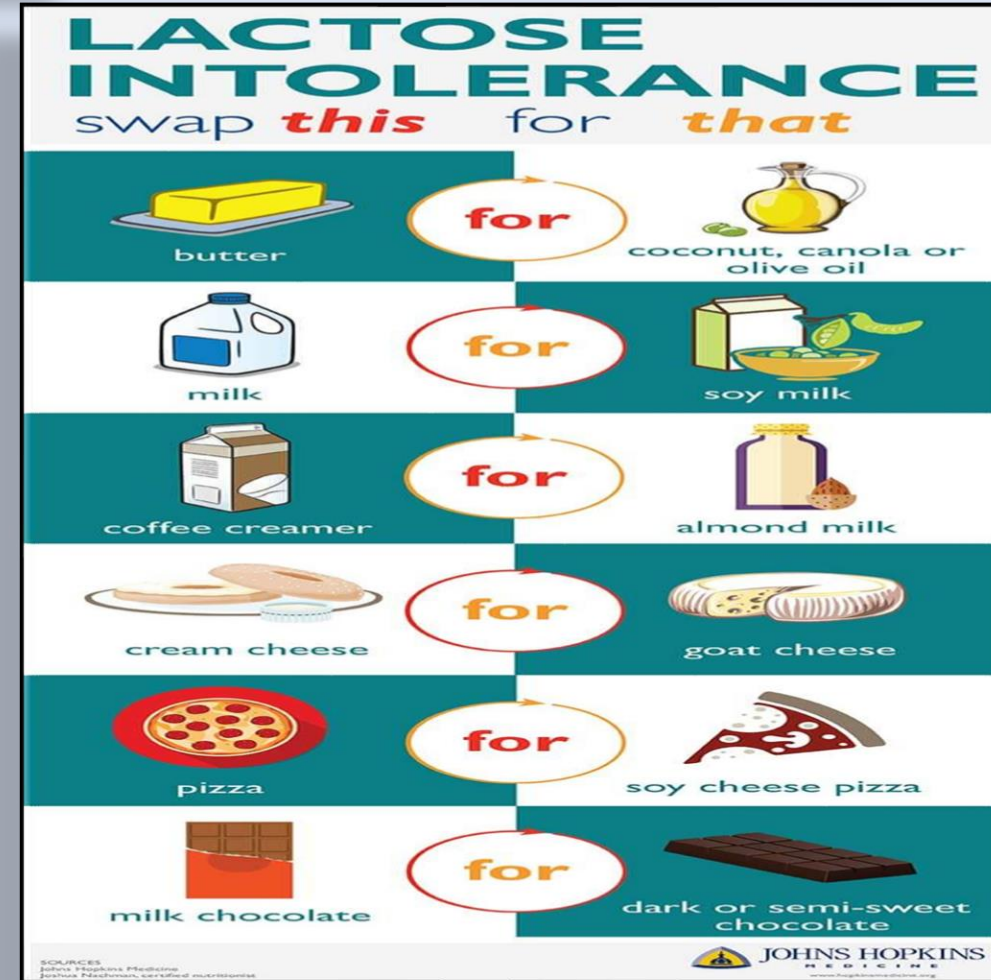
DIAGNOSIS



<https://doi.org/10.1111/j.1365-2036.2007.03557>

MANAGEMENT

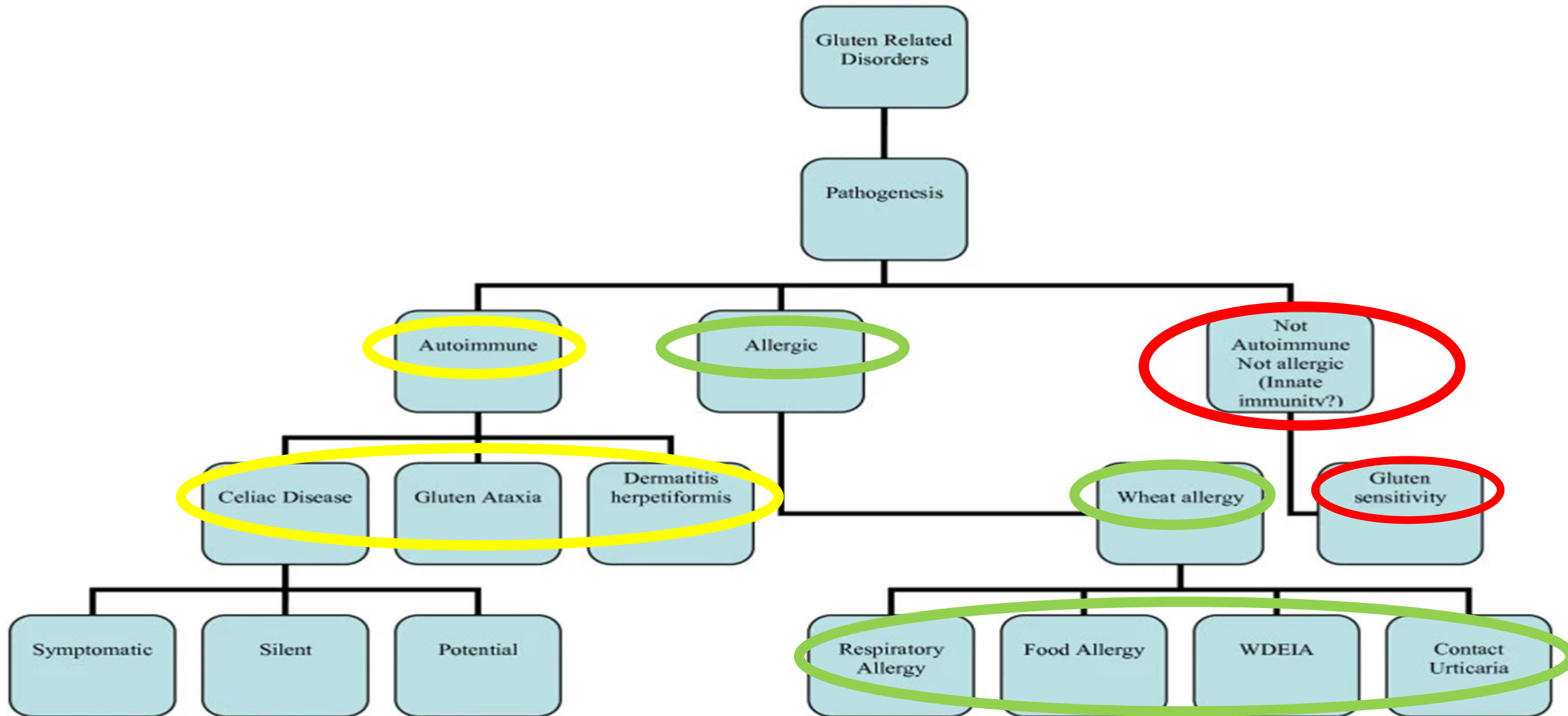
- Dietary management
- Lactase enzyme supplementation therapy



<https://doi.org/10.1111/j.1365-2036.2007.03557>

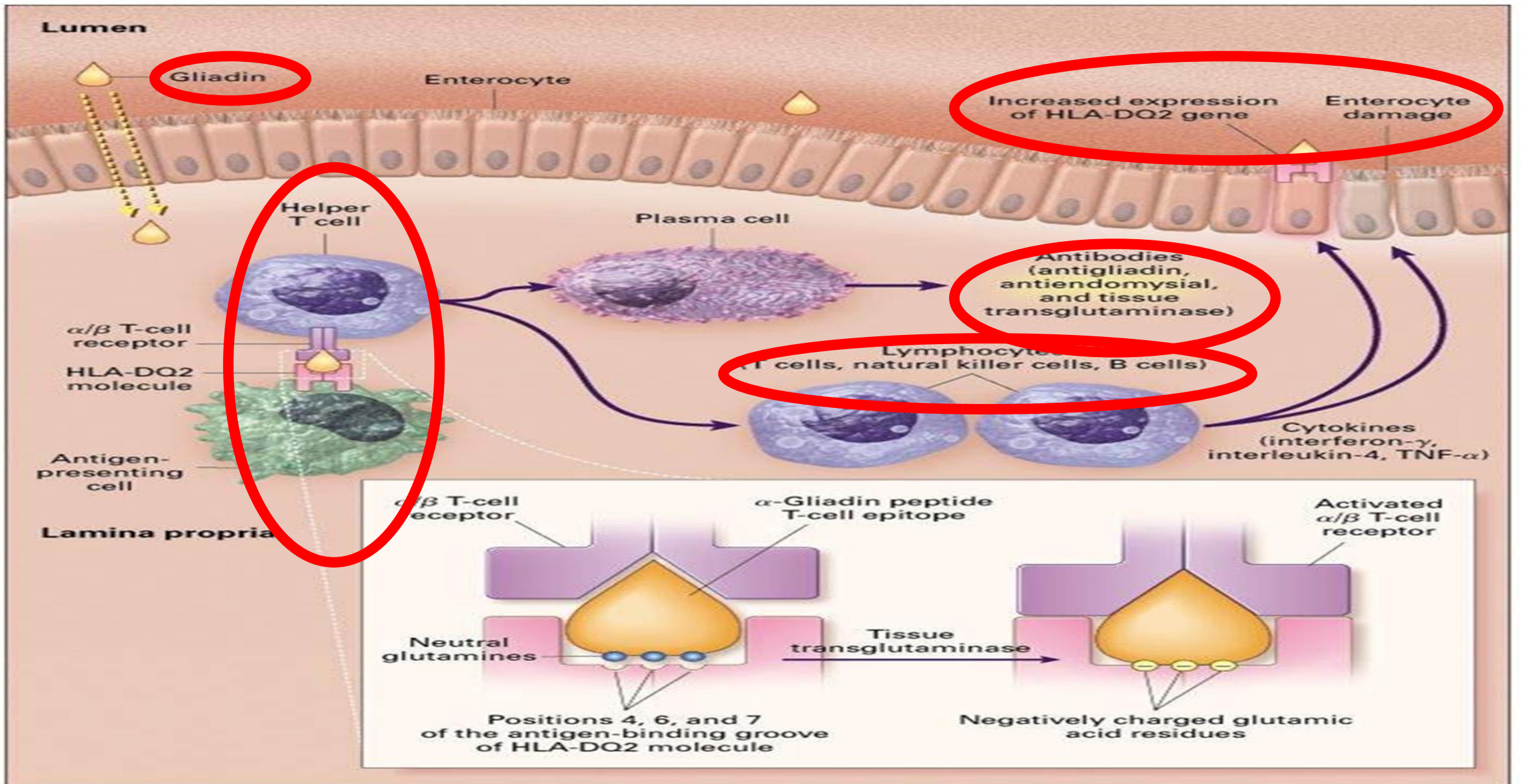
Gluten Related Disorders



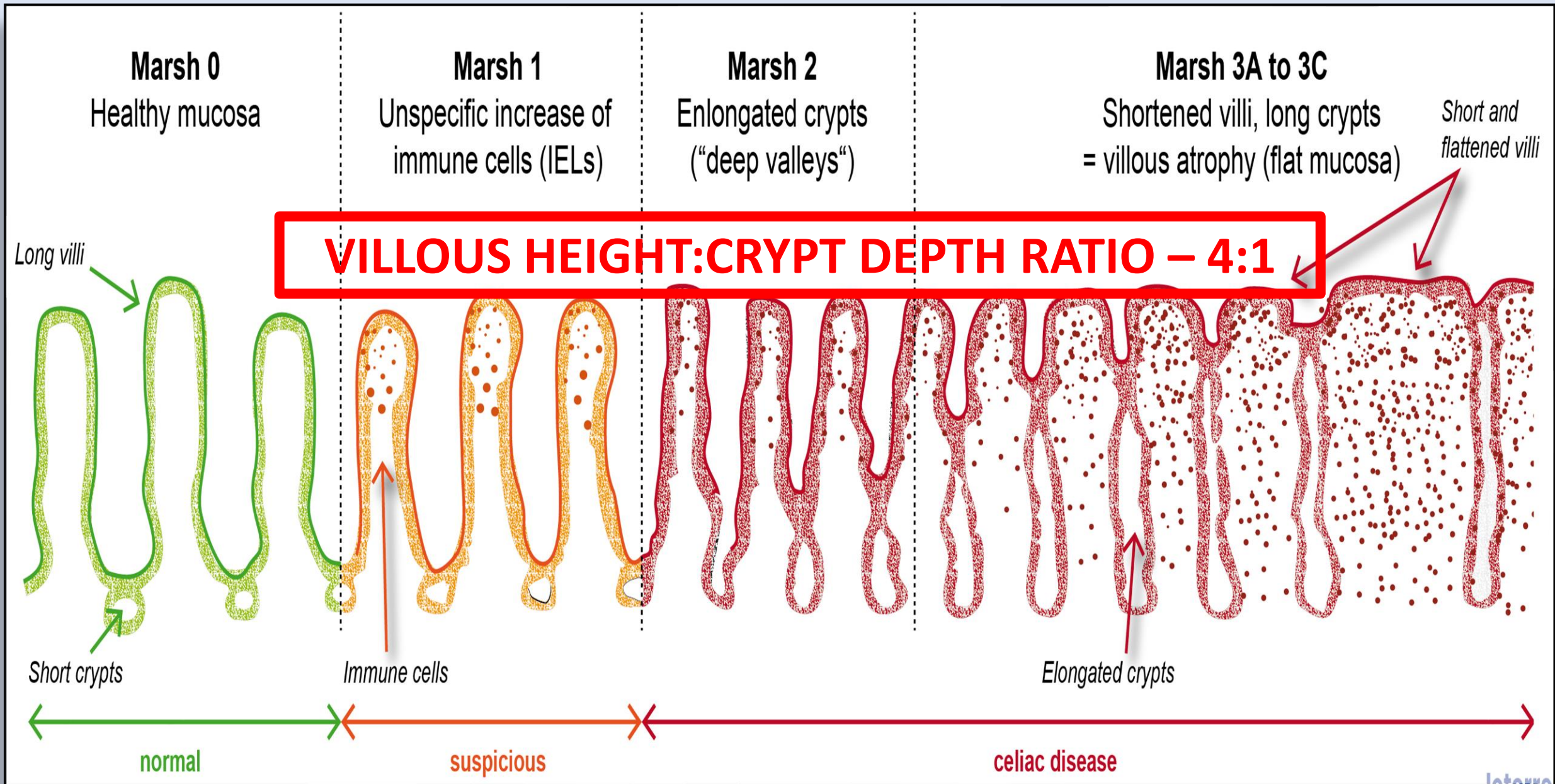


CELIAC DISEASE

- Chronic autoimmune disease of the small intestine triggered by the ingestion of Gluten.
 - Causes intestinal inflammation.
 - Impairs absorption of nutrients.
 - Systemic complications.



<https://bio.davidson.edu/courses/Immunology/Students/spring2006/Mohr/celiac.html>



<https://celiacfacts-onlinecourses.eu/mod/lesson/view.php?id=630&pageid=235>

DIAGNOSIS

- Clinical suspicion
- Serology
- Biopsy
- Therapeutic response

Bloating, gas, abdominal pain

Diarrhea or constipation

Pale, foul-smelling stools

Weight loss

Joint pain

Change in mood—depression, irritability

Extreme fatigue

Menstrual irregularity

Infertility

Oral aphthous ulcers

Tooth discoloration

Itchy skin rash with blisters (dermatitis herpetiformis)

Compiled from the National Institute of Diabetes and Digestive and Kidney Diseases (digestive.niddk.nih.gov/ddiseases/pubs/celiac_ez/) and the Celiac Disease Foundation (www.celiac.org).

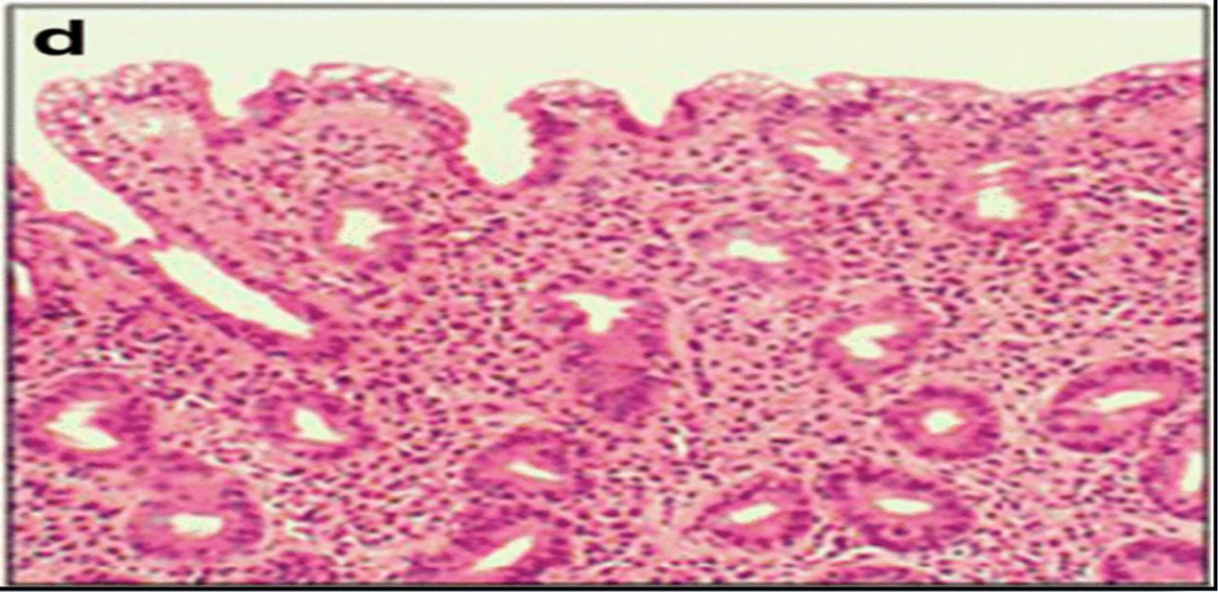
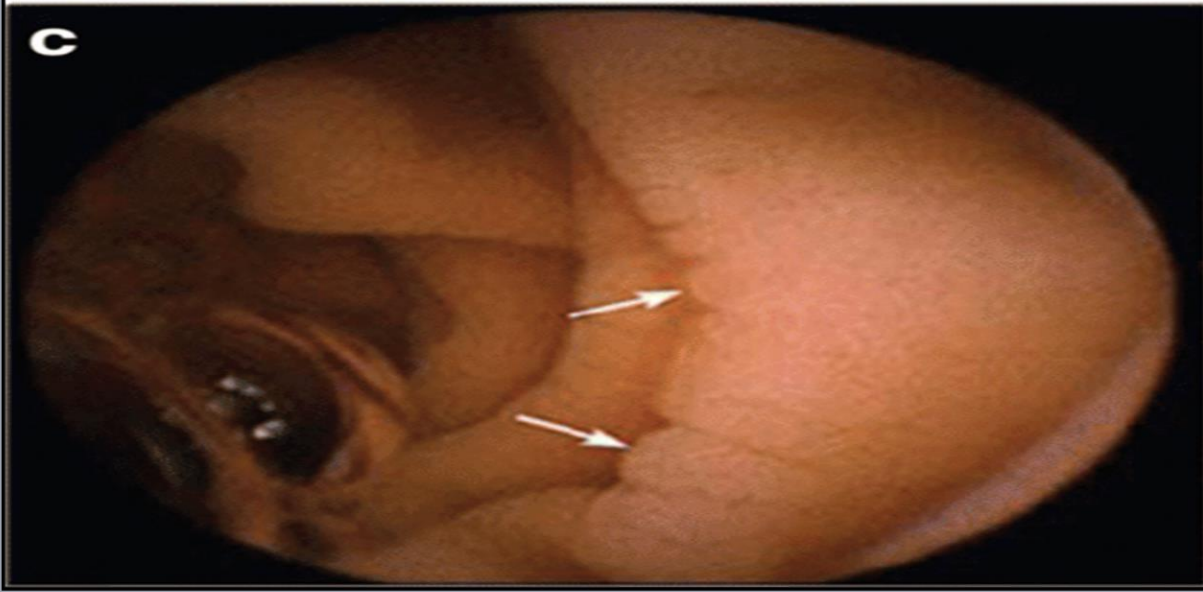
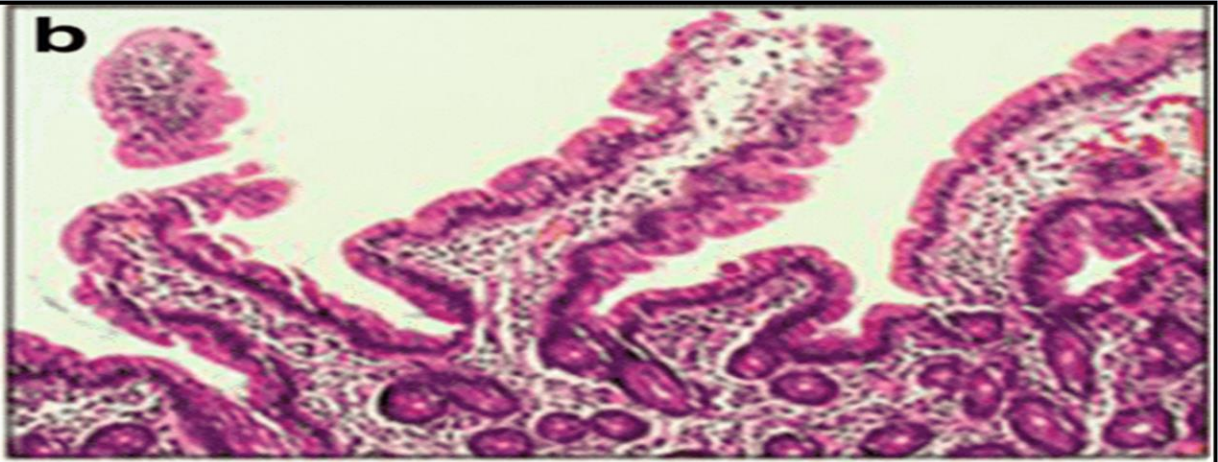
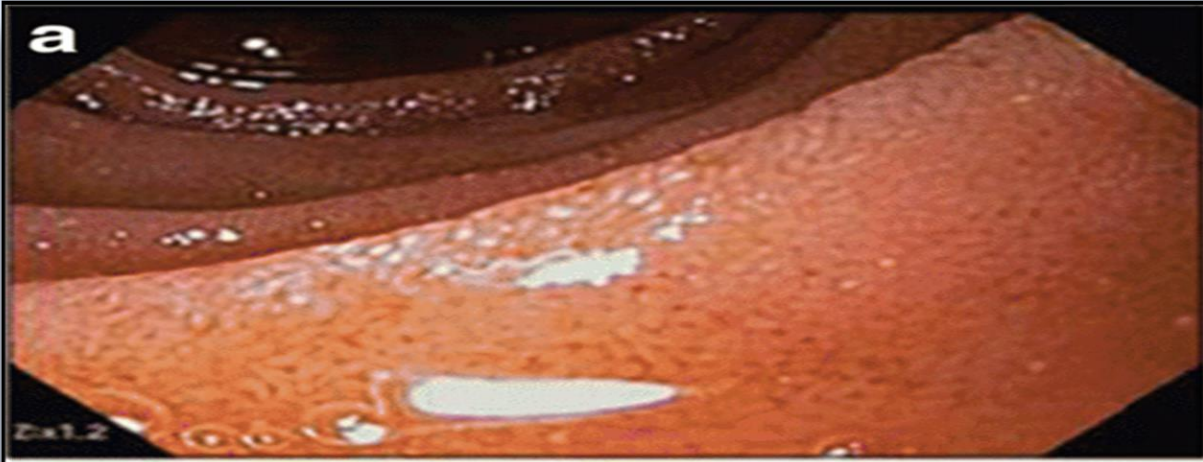
SEROLOGICAL MARKERS

Table 1. Serum Tests for the Diagnosis of Celiac Disease.*

Test	Sensitivity (Range)	Specificity (Range)	Comments
	<i>percent</i>		
IgA anti-tTG antibodies	>95.0 (73.9–100)	>95.0 (77.8–100)	Recommended as first-level screening test
IgG anti-tTG antibodies	Widely variable (12.6–99.3)	Widely variable (86.3–100)	Useful in patients with IgA deficiency
IgA antiendomysial antibodies	>90.0 (82.6–100)	98.2 (94.7–100)	Useful in patients with an uncertain diagnosis
IgG DGP	>90.0 (80.1–98.6)	>90.0 (86.0–96.9)	Useful in patients with IgA deficiency and young children
HLA-DQ2 or HLA-DQ8	91.0 (82.6–97.0)	54.0 (12.0–68.0)	High negative predictive value

* Data are from Husby et al.²⁸ and Giersiepen et al.²⁹ DGP denotes deamidated gliadin peptides, and tTG tissue transglutaminase.

ENDOSCOPIC EVALUATION



McAllister, B.P., Williams, E. & Clarke, K. *Rev Allerg Immunol* 57, 226–243 (2019).

CAUSES OF VILLOUS ATROPHY

Giardiasis

Collagenous sprue

Common-variable immunodeficiency

Autoimmune enteropathy

Radiation enteritis

Whipple's disease

Tuberculosis

Tropical sprue

Eosinophilic gastroenteritis

Human immunodeficiency virus enteropathy

Intestinal lymphoma

Zollinger–Ellison syndrome

Crohn's disease

Intolerance of foods other than gluten (e.g., milk, soy, chicken, tuna)

MANAGEMENT

- Consultation with a skilled dietician.
- Lifelong adherence to a gluten free diet.
- Identification and treatment of nutritional deficiencies/complications.
- Access to an advocacy group.
- Continuous long term follow up by a multidisciplinary team.

THERAPEUTIC RESPONSE

- Clinical remission: Immediate
- Serologic response: Weeks-months
- Mucosal healing: 6-24 months.
- Poor response to GFD

Non-Celiac Gluten Sensitivity (NCGS)

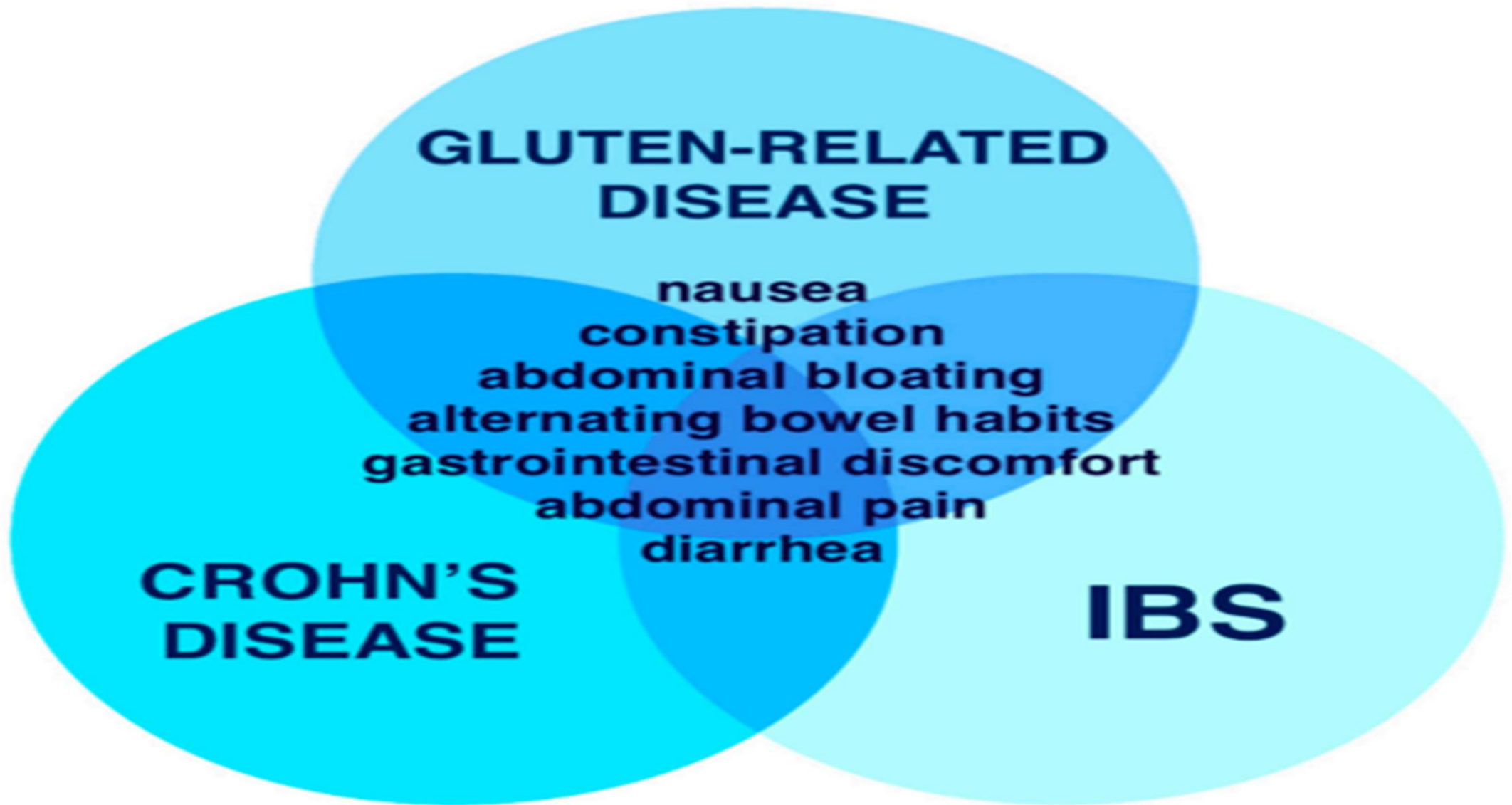
NCGS defined as:

- Symptom - gluten ingestion.
- Absence of celiac specific antibodies.
- Absence - celiac specific histology
- Variable HLA status.
- Resolution of symptom on gluten withdrawal

EPIDEMIOLOGY

- NCGS prevalence 0.6-13%
- Adults > children
- F>M
- M:F RATIO - 1:2.5

Gastrointestinal symptoms	Neurological–psychiatric symptoms	Other symptoms
Abdominal pain	Foggy mind	Eczema
Bloating	Tiredness	Skin rash
Diarrhea	Headache	Joint pain
Constipation	Depression	Muscle pain
Alternating bowel movements	Numbness in arms, legs, and fingers	Oligo- or poly-menorrhoea
Nausea	Hyposthenia	Anemia
Vomiting	Loss of balance	Weight loss
Hematochezia	Disturbed sleep pattern	Weight increase
Anal fissures	Mood swings	Puffiness
		Interstitial cystitis



Roszkowska, A., et al. (2019). "Non-Celiac Gluten Sensitivity: A Review." *Medicina* 55(6): 222

PATHOGENESIS

- Innate immunity dominates in NCGS.
- TLR-key role in innate immunity-upregulated.
- NCGS has increased expression of claudin-4, marker of decreased intestinal permeability.
- Amylase/trypsin inhibitor(ATI)
- FODMAPS

DIAGNOSIS

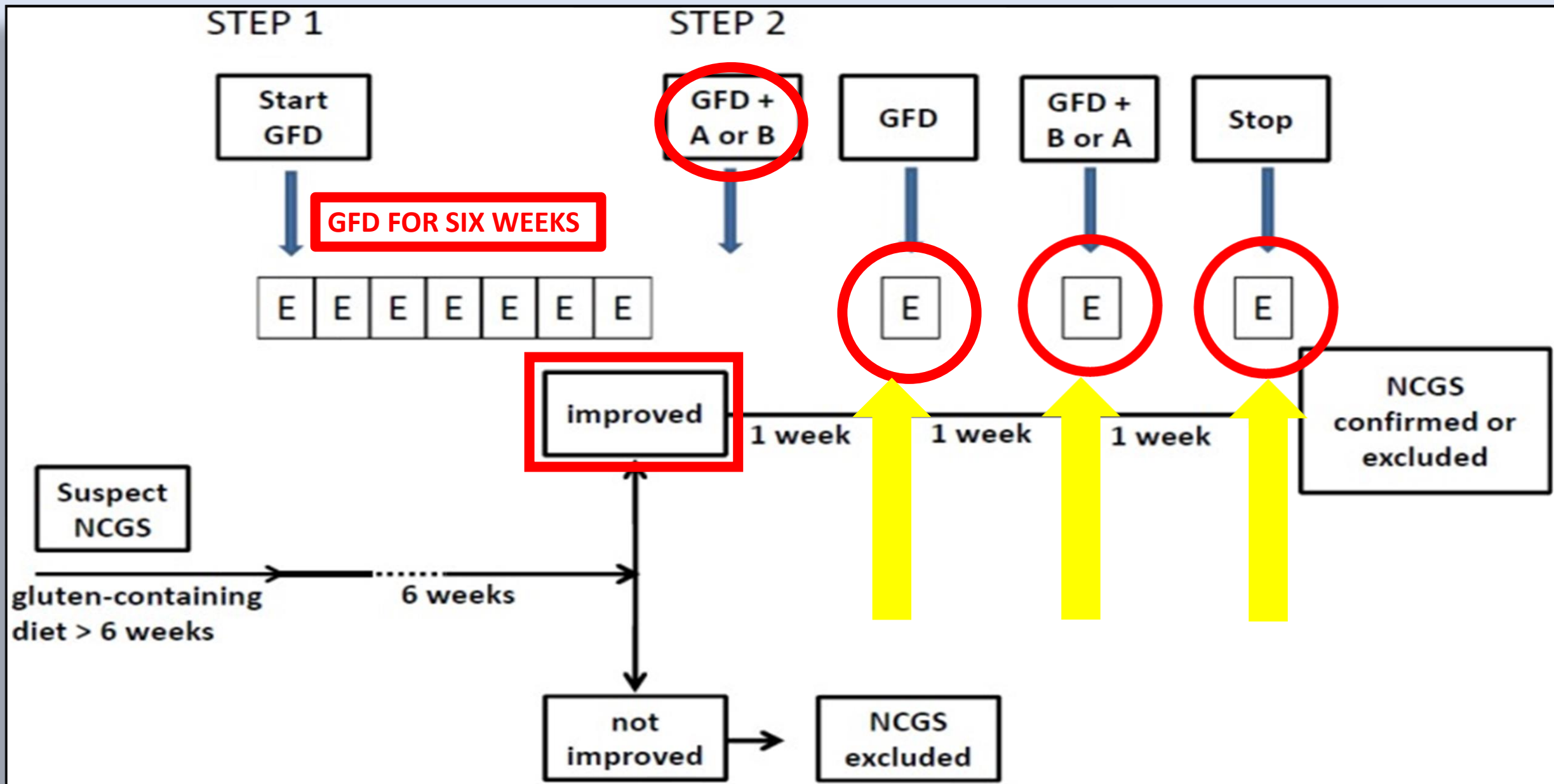
- Primarily diagnosis of exclusion.
- Exclusion of CD histology, serology and HLA.
- Wheat allergy excluded by serum IgE levels.
- Gluten elimination.
- Salerno expert's criteria.

DIAGNOSTIC PROTOCOL

- Clinical response to GFD
- Measuring effect of reintroduction of GCD
- Clinical evaluation - Sx rating scale

Questionnaire used for Step 1 evaluation (the same items are evaluated during Step 2).

Intestinal Symptoms	Baseline	1 Week	2 Week	3 Week	4 Week	5 Week	6 Week
Abdominal pain or discomfort							
Heartburn							
Acid regurgitation							
Bloating							
Nausea and vomiting							
Borborygmus							
Abdominal distension							
Eructation							
Increased flatus							
Decreased passage of stools							
Increased passage of stools							
Loose stools							
Hard stools							
Urgent need for defecation							
Feeling of incomplete evacuation							



	Celiac Disease	NCGS	Wheat Allergy
Prevalence	0.5–1.7%	no population studies	0.5–9% in children
Pathogenesis	autoimmune	non-specific immune response	IgE mediated response
DQ2-DQ8 HLA haplotypes	positive in 95% cases	positive in 50% cases	negative
Serological markers	IgA anti-EMA, IgA anti-tTG, IgG anti-DGP, IgA anti-gliadin	IgA/IgG anti-gliadin in 50% cases	specific IgE antibodies against wheat and gliadin
Duodenal biopsy *	Marsh I to IV with domination of Marsh III and IV	Marsh 0-II, but according to some experts Marsh III might also be in NCGS	Marsh 0-II
Duodenal villi atrophy	present	absent	might be present or absent

* Marsh classification.

CONCLUSION

- Food allergy is treated primarily by dietary avoidance.
- Lactose intolerance not always symptomatic.
- GFD is complex- a skilled dietician essential.
- Overlapping symptoms in Crohn's disease, IBS and gluten-related disease.