

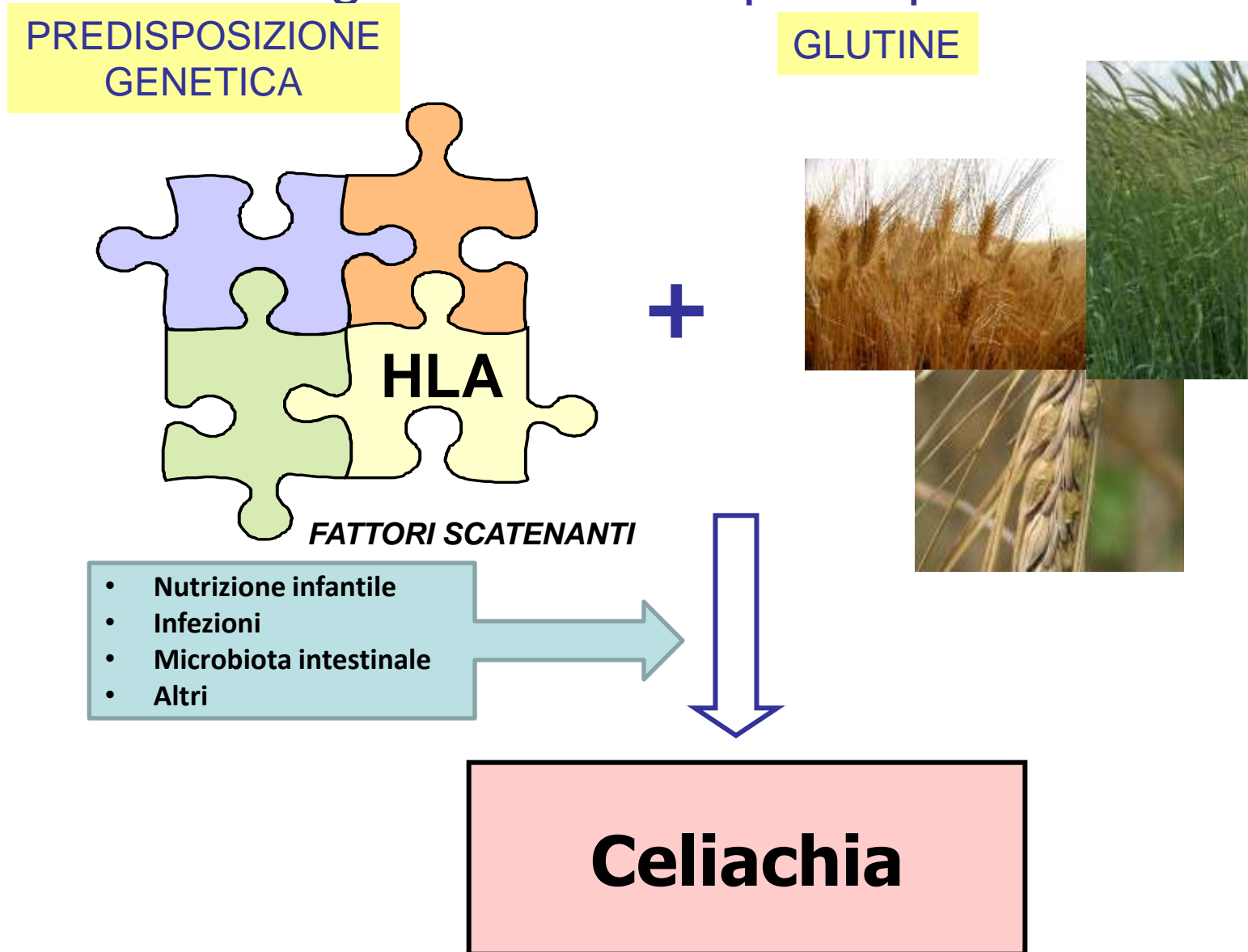
# Celiachia e Sensibilità al Glutine Non Celiaca

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Politecnica delle Marche, Ancona, Italy  
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Hospital, Boston, USA*

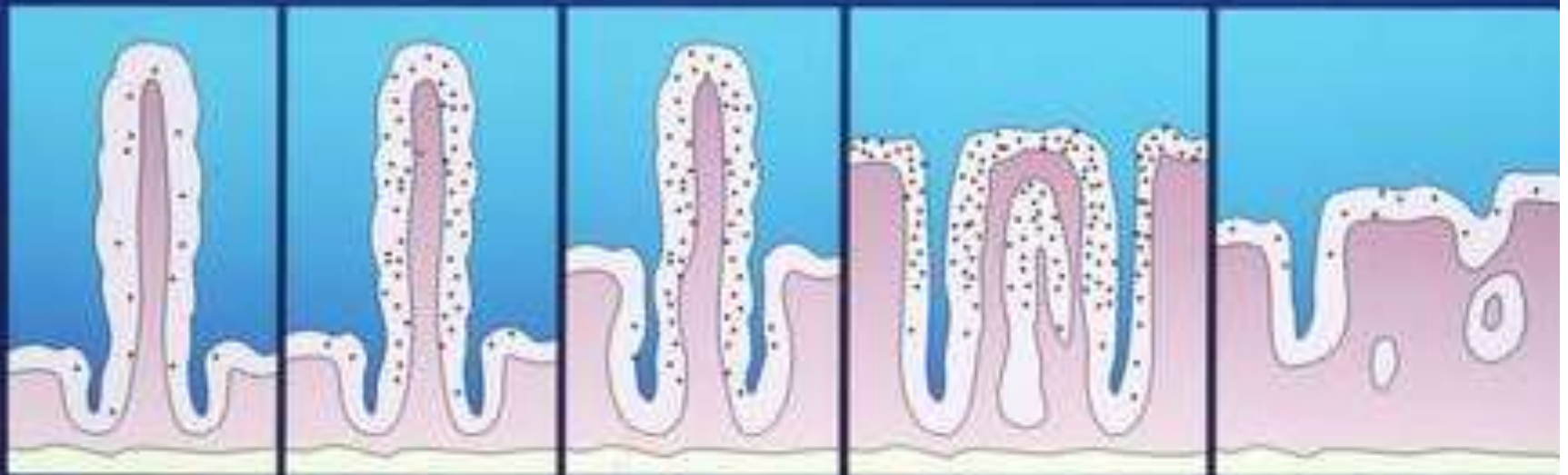


# Celiachia: patologia multisistemica autoimmune causata dalla ingestione di glutine nei soggetti geneticamente predisposti



# Enteropatia celiaca (dal grado 1 a 3c)

## Pathological Spectrum



Normal



I



II



III



IV

Potenziale

Manifesta

# HLA haplotypes and risk of celiac disease

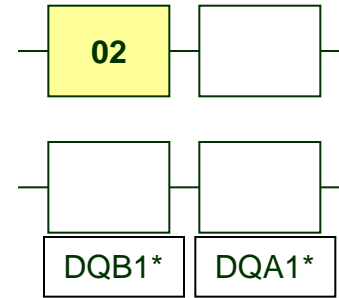
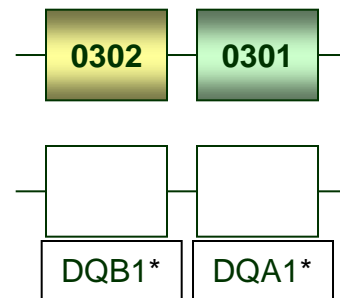
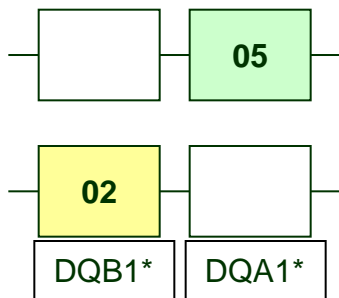
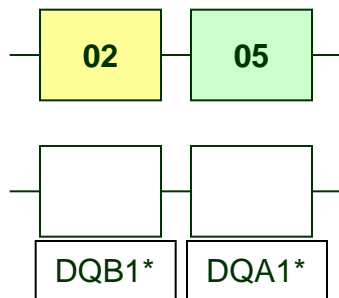
DQ2 *cis*

DQ2 *trans*

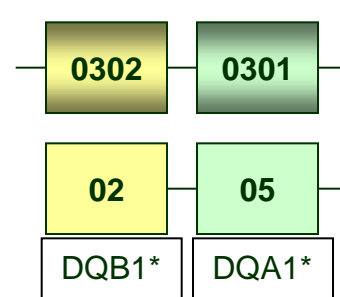
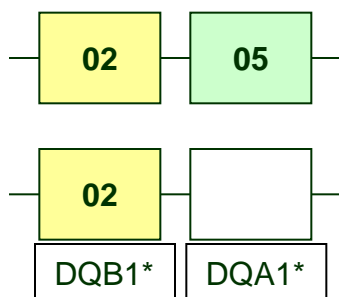
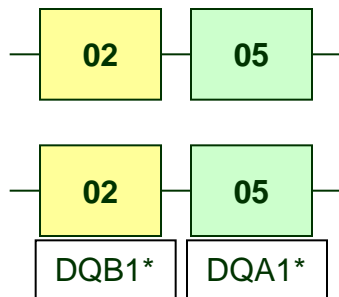
DQ8

Half DQ2

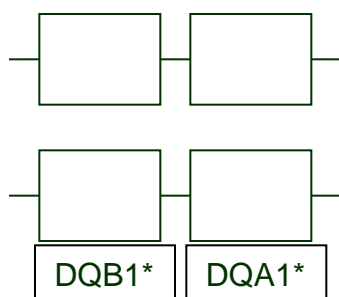
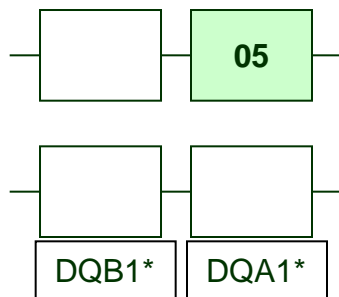
AT  
RISK



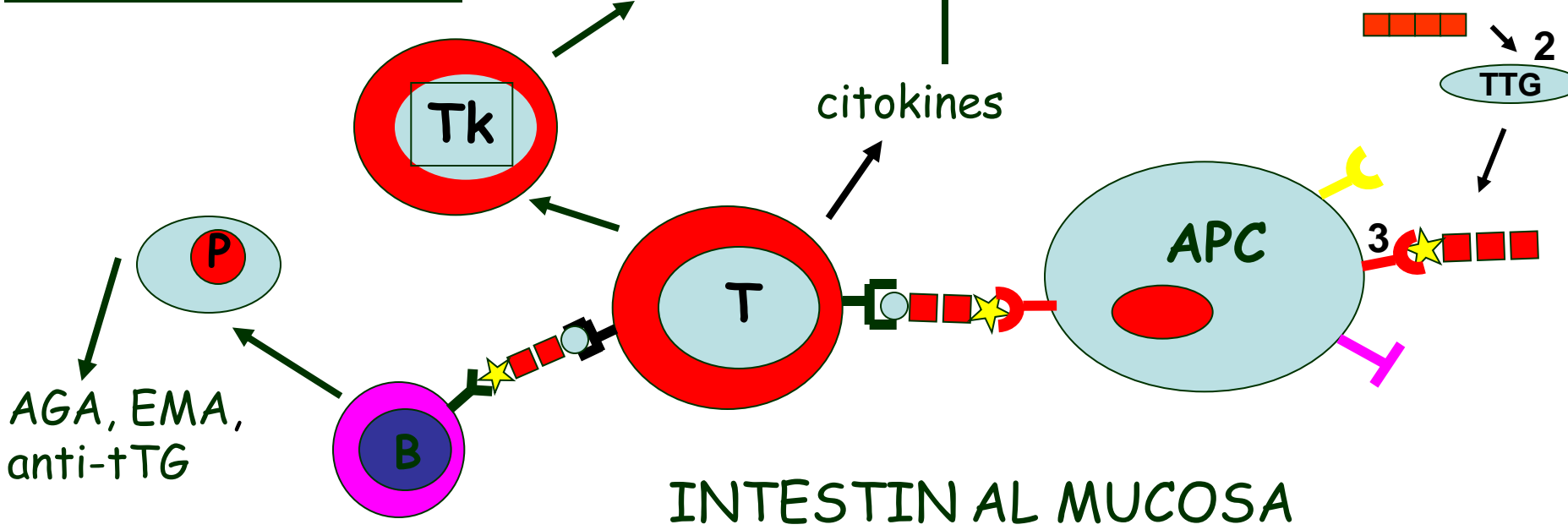
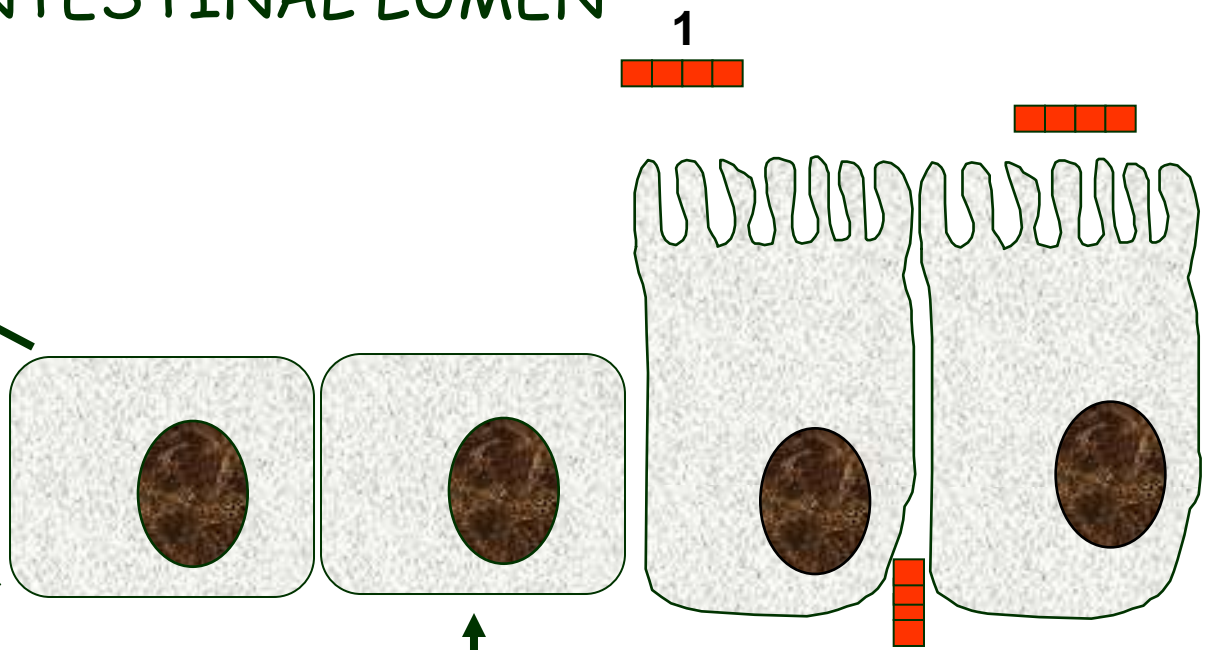
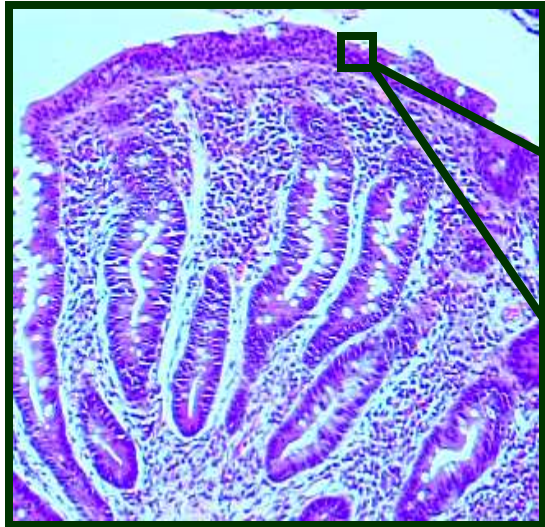
HIGHER  
RISK



VERY  
LOW  
RISK



# INTESTINAL LUMEN



# La celiachia: un “camaleonte” clinico

## General

- Short stature
- Weight loss
- Lassitude/lethargy
- Edema
- Clubbing
- Koilonychia
- Bruising

## Gastrointestinal

- Anorexia, nausea, vomiting
- Glossitis, mouth ulcers
- Abdominal distension and pain
- Flatulence and flatus
- Diarrhea, constipation

## Psychiatric

- Depression
- Anxiety

## Neurological

- Peripheral neuropathy
- Ataxia
- Epilepsy

## Hematologic

- Anemia
- Folic acid and iron deficiency
- Raised mean corpuscular volume
- Hemorrhagic manifestations

## Biochemical

- Reduced serum calcium, raised alkaline phosphatase
- Increased serum aminotransferase levels

## Reproduction

- Infertility
- Recurrent miscarriages

## Musculoskeletal

- Osteomalacia, osteoporosis, bone pain
- Myopathy
- Cramps, tetany, paresthesia

## Renal

- Nocturnal diuresis

## Skin

- Dermatitis herpetiformis
- Pigmentation



# Typical celiac disease



# CD atypical presentations and complications

IRON DEFICIENCY

CHRONIC FATIGUE

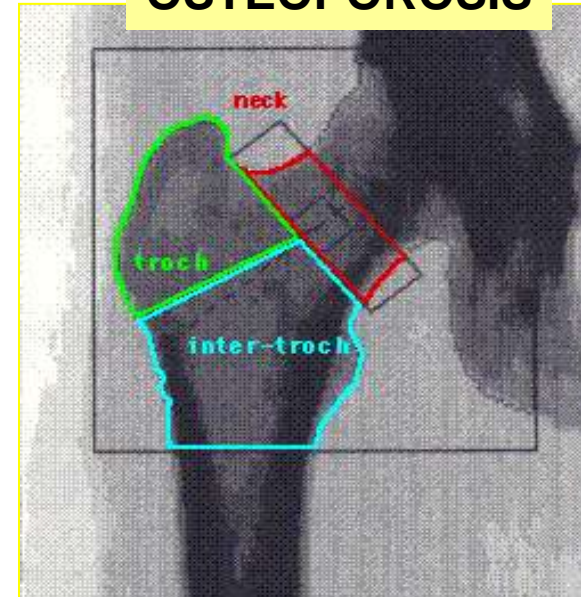
HEPATITIS



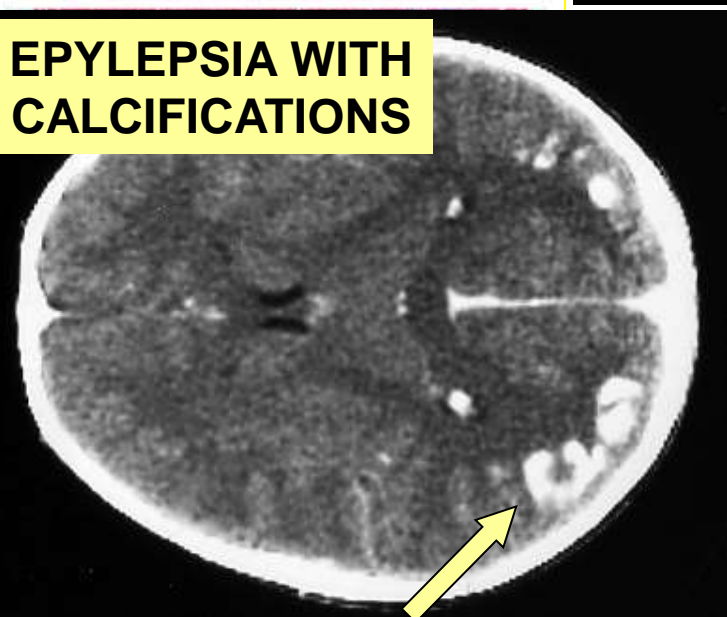
DERMATITIS  
HERPETIFORMIS



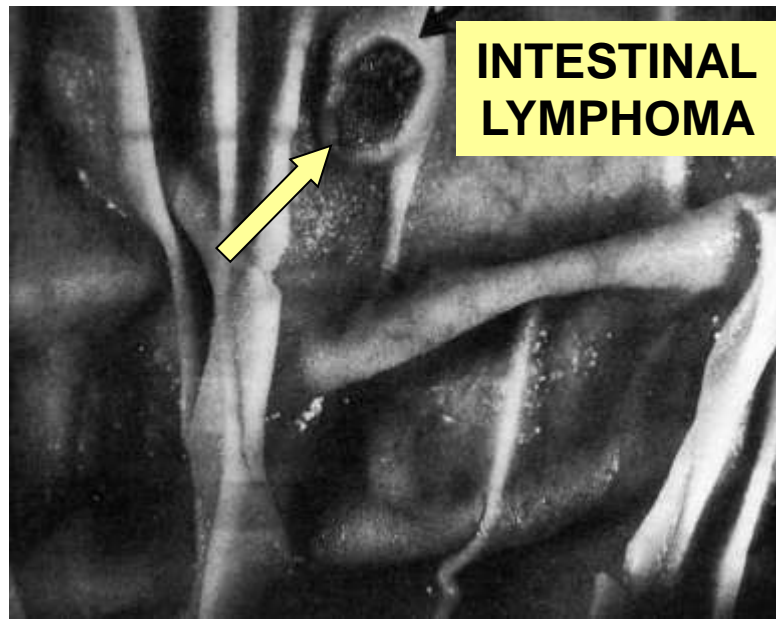
OSTEOPOROSIS



EPILEPSIA WITH  
CALCIFICATIONS



INTESTINAL  
LYMPHOMA





# La celiachia nel 2018: caso clinico

- Ragazzina di 12 aa sovrappeso con anamnesi muta
- Visita biologa nutrizionista: consigliati test intolleranze alimentari
- Positività per molti componenti alimentari incluso il frumento > avvia GFD
- Pediatra non crede ipotesi intolleranze > rimette a dieta libera e consiglia test celiachia
- Anti-tTG IgA positivi ad alto titolo →  
**DIAGNOSI DI CELIACHIA**

CLINICAL PRACTICE

# Celiac Disease

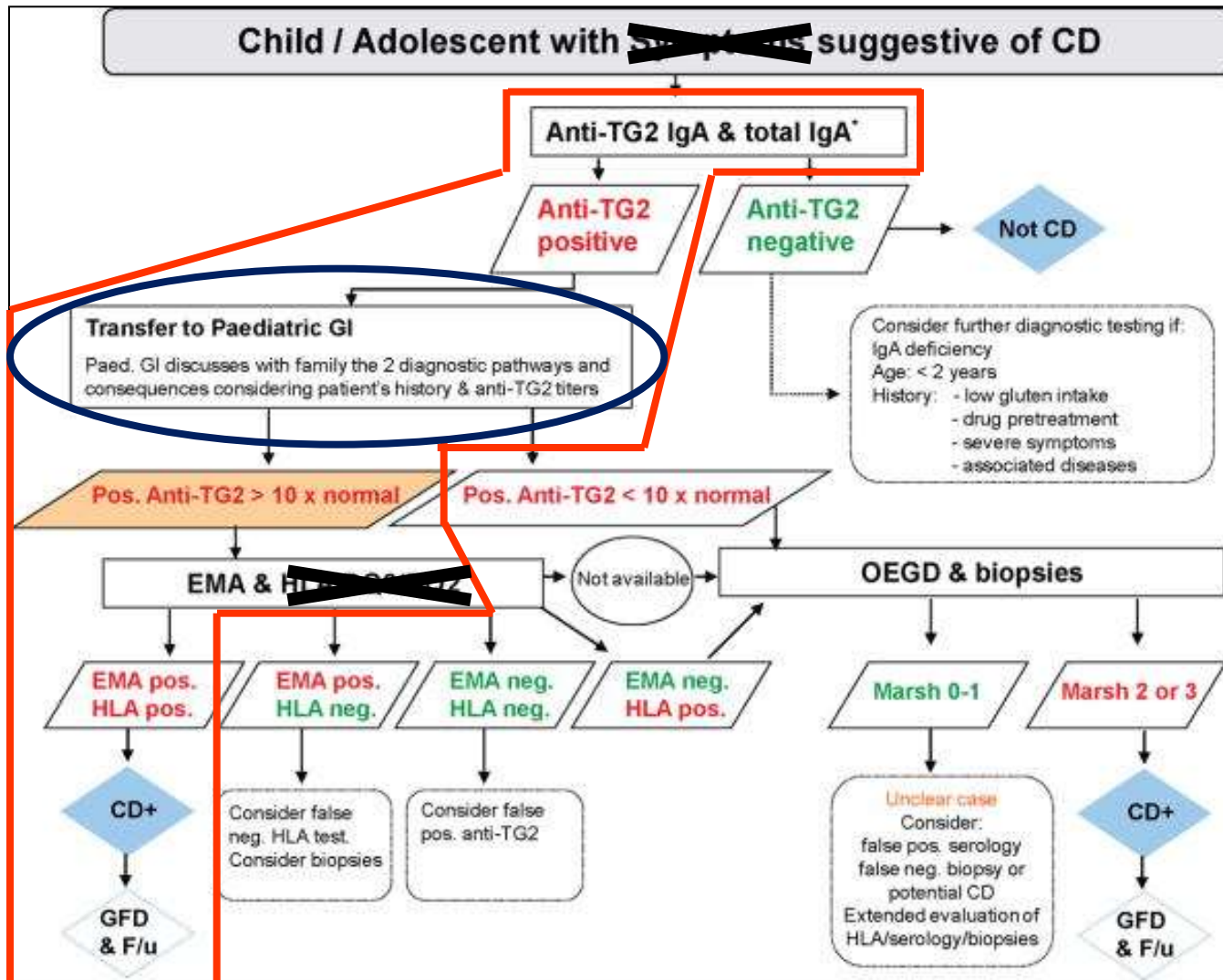
Alessio Fasano, M.D., and Carlo Catassi, M.D., M.P.H.

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

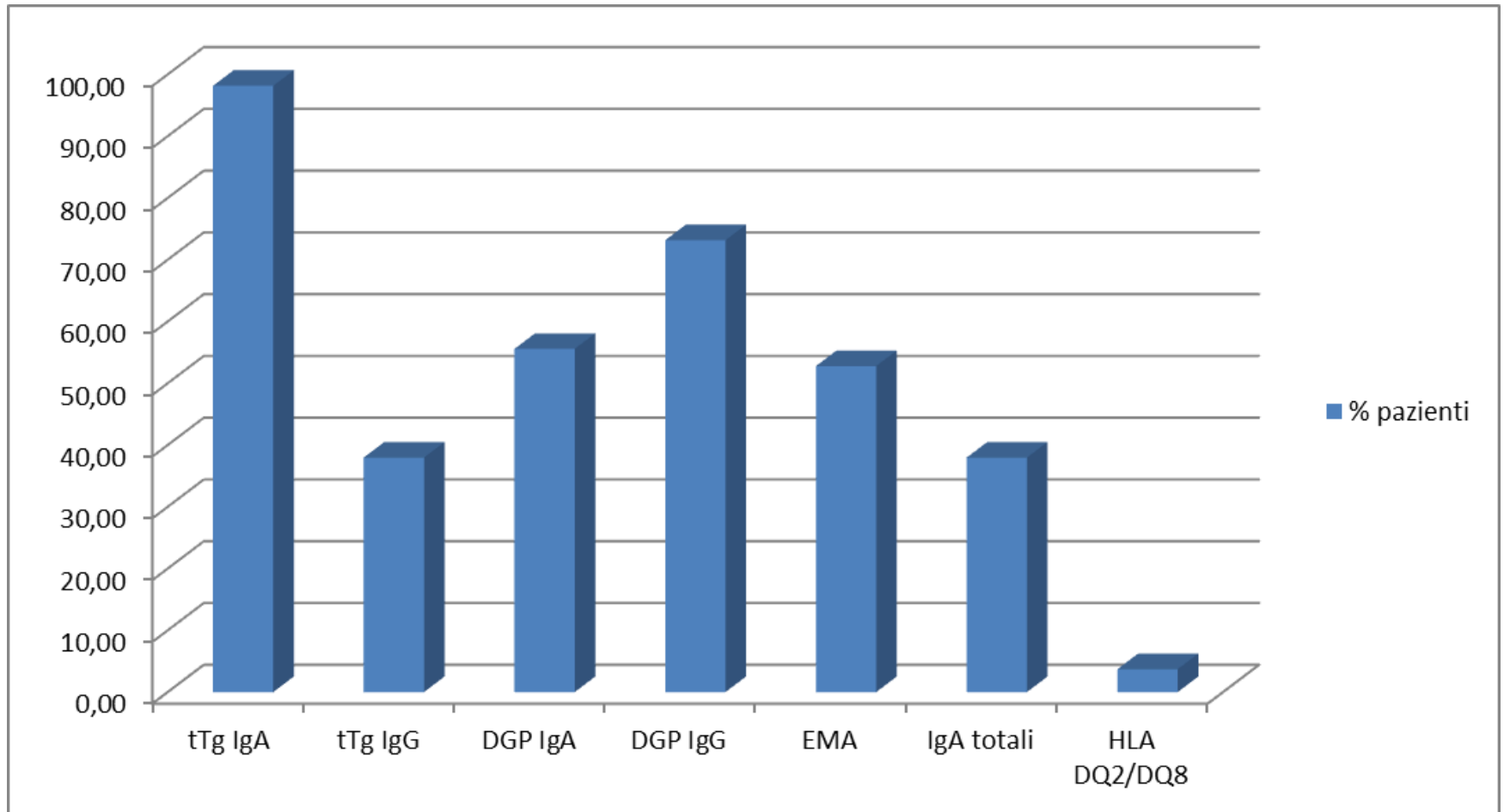
Test	Sensitivity (Range)	Specificity (Range)	Comments
	<i>percent</i>		
IgA anti-tTG antibodies	>95.0 (73.9–100)	>95.0 (77.8–100)	Recommended as first-level screening test
IgG anti-tTG antibodies	Widely variable (12.6–99.3)	Widely variable (86.3–100)	Useful in patients with IgA deficiency
IgA anti-endomysial 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

# European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease

<sup>1</sup>S. Husby, <sup>1</sup>S. Koletzko, <sup>1</sup>I.R. Korponay-Szabó, <sup>5</sup>M.L. Mearin, <sup>11</sup>A. Phillips, <sup>\*</sup>R. Shamir, <sup>2</sup>R. Troncone, <sup>\*\*</sup>K. Giersiepen, <sup>11</sup>D. Branski, <sup>††</sup>C. Catassi, <sup>§§</sup>M. Leigeman, <sup>|||</sup>M. Mäki, <sup>\*\*\*</sup>C. Ribes-Koninckx, <sup>™™</sup>A. Ventura, and <sup>\*\*\*\*</sup>K.P. Zimmer, for the ESPGHAN Working Group on Coeliac Disease Diagnosis, on behalf of the ESPGHAN Gastroenterology Committee



# Gli esami che si richiedono nel sospetto di celiachia



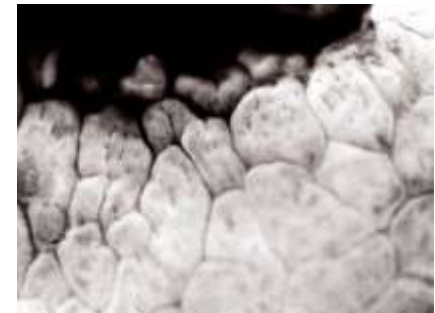
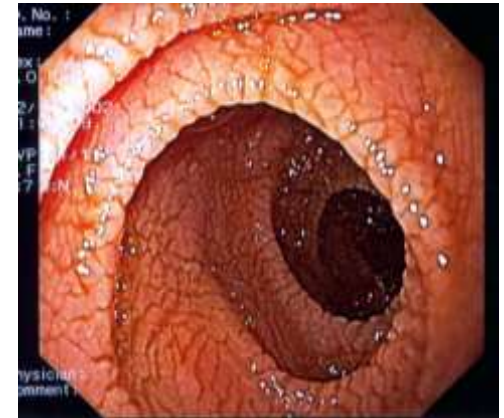
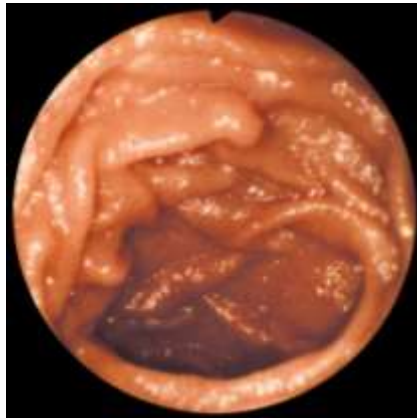


# I costi degli esami per la celiachia (tariffario regione Marche)

La celiachia dopo la diagnosi

# Normal small bowel

# Celiac disease



Gluten

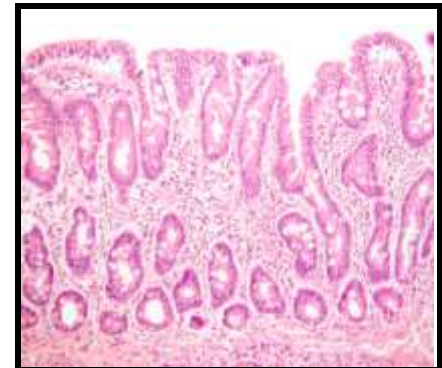
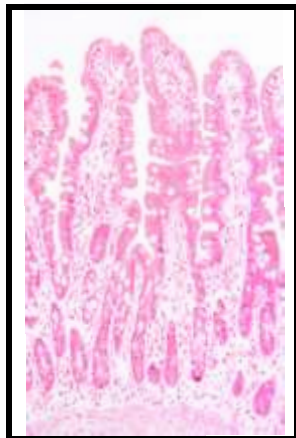


Gluten-free diet



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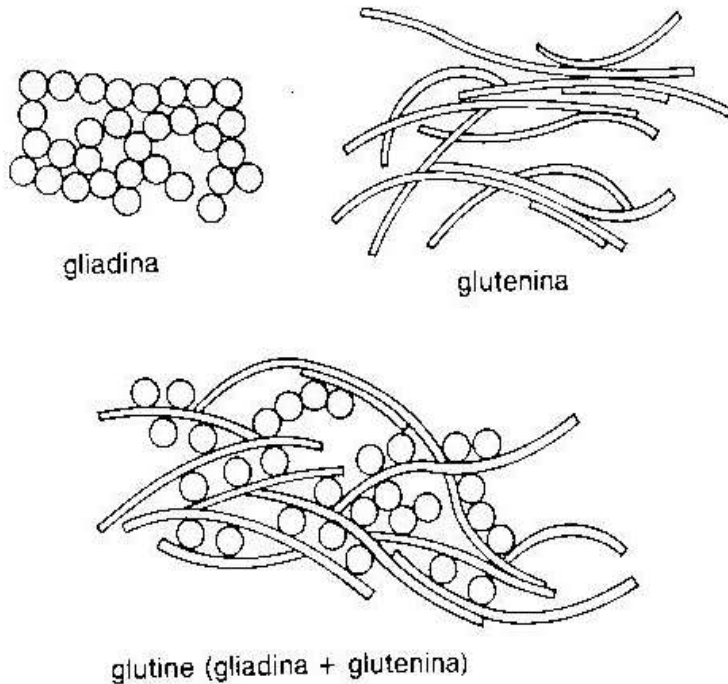


# La dieta senza glutine

- Esclusione dei cereali contenenti glutine: frumento, segale ed orzo
- Libera assunzione di tutti gli altri prodotti naturali: cereali consentiti, legumi, verdura e frutta, carne, pesce, latte e derivati
- Il problema è rappresentato dagli alimenti confezionati



# Gluten is a basic ingredient for food technology



# IL GLUTINE QUESTO SCONOSCIUTO

- Rappresenta la frazione proteica principale nel frumento ed in altri cereali (orzo e segale)
- **Non ha un elevato valore biologico** (povero di lisina e metionina)
- Frazioni tossiche per il celiaco si trovano soprattutto nelle gliadine ma anche nelle glutenine
- Apporto medio di glutine nella dieta europea dell'adulto: circa 15 g al giorno

# I cereali nella dieta celiaca



## *DA EVITARE*

- Frumento
- Orzo
- Segale
- Farro
- Kamut
- Spelta

## *CONCESSI*

- Mais
- Riso
- Miglio
- Amaranto
- Quinoa
- Manioca/tapioca
- Grano saraceno
- Teff

Avena

# Gli alimenti da sostituire con i prodotti “spiga barrata”



- Pane, grissini, crackers, biscotti
- Pasta, semolino
- Pizza
- Farro
- Cous-cous
- Seitan e Fu
- Crusca di frumento
- Amido di frumento (non tutti)
- Pane di segale
- Prodotti a base di orzo
- Birra
- Malto, aceto di malto
- Il “vero” lievito di birra



# Non contengono glutine

- Glutammato
- Sciroppi di glucosio
- Dolcificanti
- Maltodestrine
- Superalcolici

# La piramide alimentare del celiaco



**ATTIVITA' FISICA QUOTIDIANA**

# Problematiche nutrizionali della GFD

- Apporto sub-ottimale di fibre, ferro, folati ed altre vitamine del gruppo B e calcio
- Apporto eccessivo di zuccheri semplici e lipidi ?
- Predisposizione alle patologie dismetaboliche?
- Apporto eccessivo di possibili contaminanti (es. micotossine) ?

# Dove si nasconde il glutine ?

- ❖ **Alimenti commerciali** (salumi, minestre pronte, maionese, salse, etc)
- ❖ In cereali in origine gluten-free a seguito di **contaminazione** durante la semina, molitura, stoccaggio, lavorazione, etc
- ❖ Nei prodotti contenenti **amido di frumento**
- ❖ Al ristorante, in pizzeria, alla mensa, etc



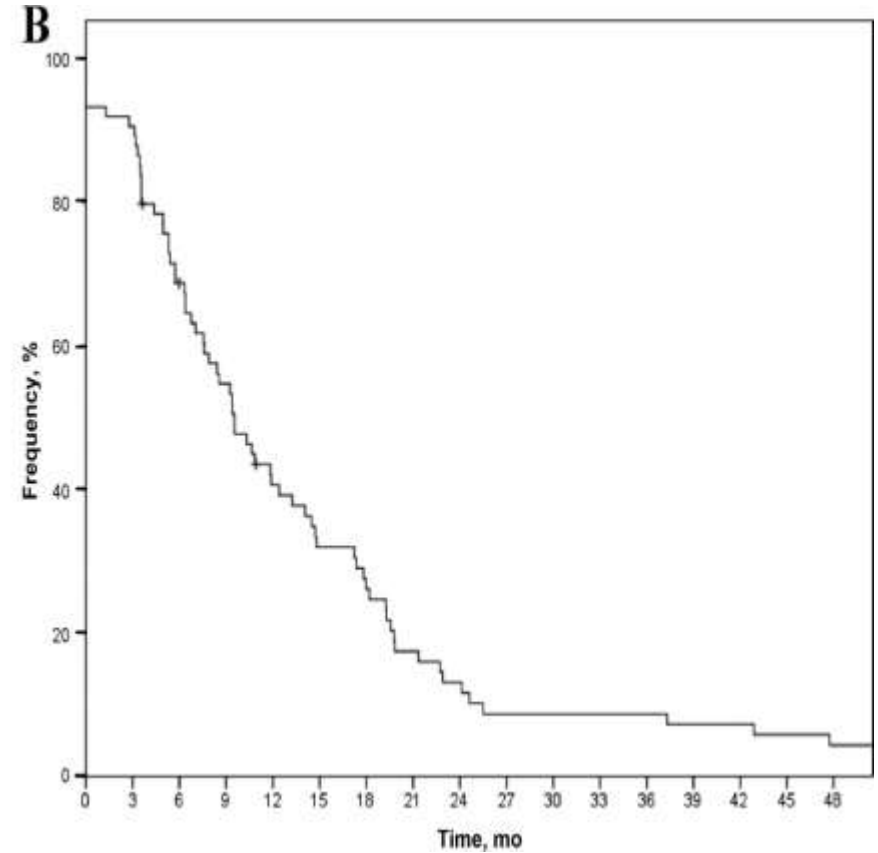
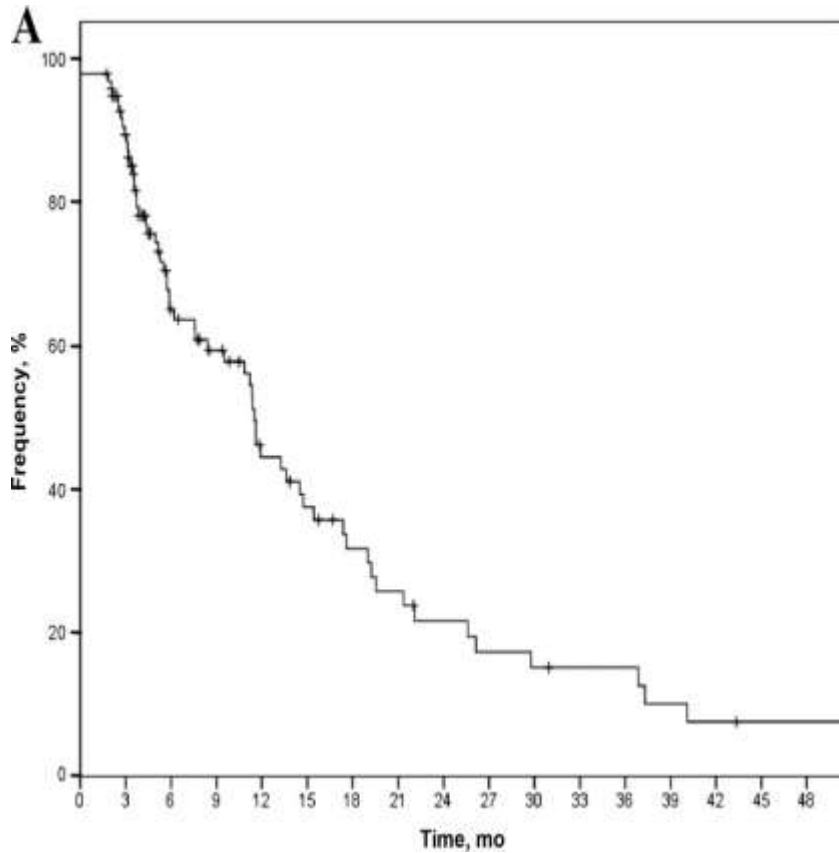
# Contaminazione da glutine: punti-chiave

- La tossicità delle tracce di glutine è dimostrata (DGA = mg 10) ma ulteriori studi su questa tematica sono necessari
- La sensibilità alle dosi minime di glutine varia notevolmente tra pazienti
- L'ingestione di tracce di glutine è una possibile causa di incompleta normalizzazione della mucosa dopo GFD
- Le indagini anticorpali non sono sufficientemente sensibili da svelare minime trasgressioni dietetiche

# Come valutare l'aderenza alla dieta

- Intervista dietetica
- Valutazione clinica
- Marcatori sierologici (TTG)
- GIP fecale e urinario
- Biopsia intestinale

# Cinetica di scomparsa di antiTTG (A) ed EMA (B) in bambini celiaci in GFD



# Timing controlli: dopo 6 mesi dalla diagnosi e poi ogni 12-24 mesi

- Verifica della aderenza alla dieta
- Identificazione di patologie associate (carenza marziale, patologie autoimmuni, osteoporosi)
- Sviluppo di alterazioni metaboliche
- Diagnosi precoce di complicanze

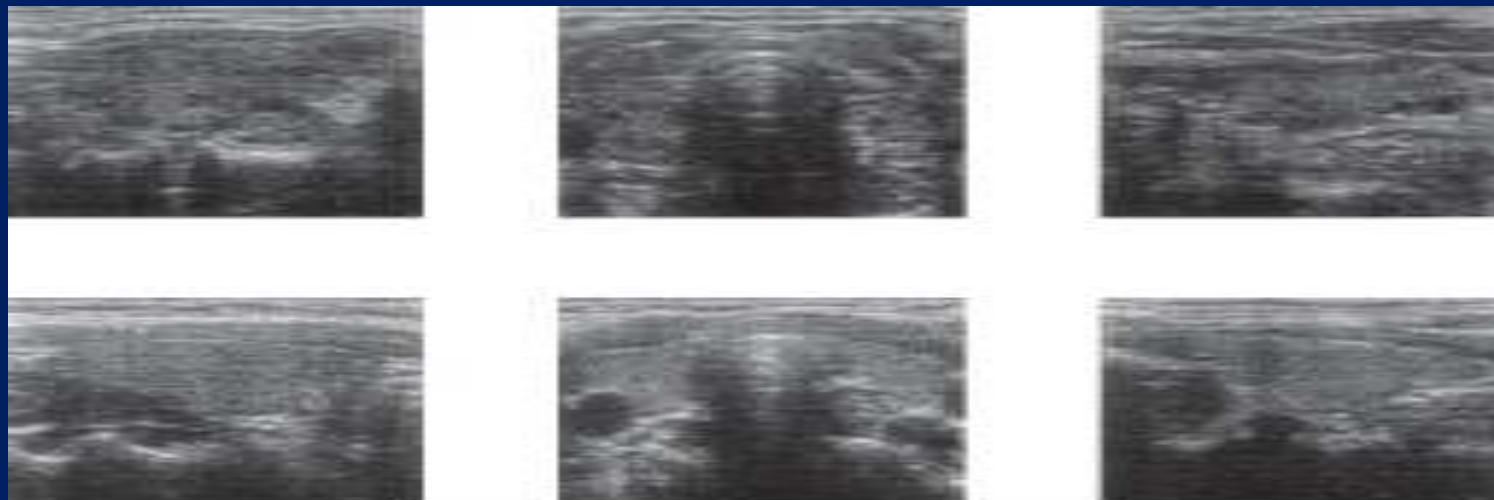
# Thyroid disease and CD

- Autoimmune thyroiditis (AT), hypothyroidism, hyperthyroidism are more common in CD
- AT is often silent at onset
- The increased risk is not entirely corrected by the GFD

**Right lobe**

**Transverse c s**

**Left lobe**



**Hashimoto's**

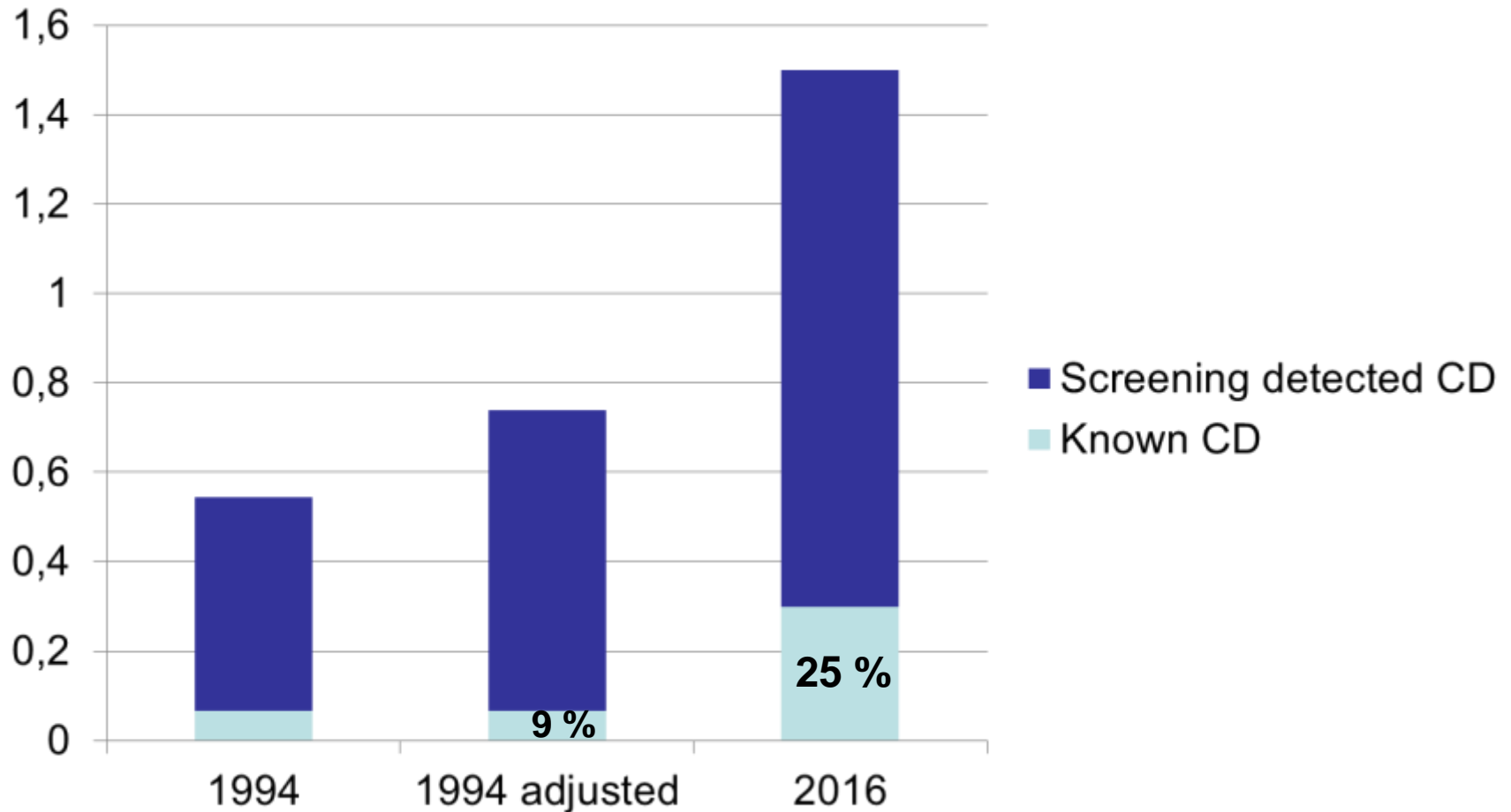
**Normal**

# Esami utili nel corso del follow-up

- Anticorpi anti-tTG IgA
- Metabolismo del ferro
- Colesterolo tot ed HDL, trigliceridi
- TSH, anticorpi anti-tiroide
- Altri autoanticorpi ? **NO**
- Densitometria ossea (adulto)
- Biopsia intestinale (casi selezionati)



# Changes in the celiac iceberg Italy 1994 to 2016



## Disturbi glutine-dipendenti

### Patogenesi autoimmune

- Malattia celiaca
- Atassia da glutine
- Dermatite erpetiforme

### Patogenesi allergica

#### Allergia al grano

- Allergia respiratoria
- Allergia alimentare
- Dermatite da contatto
- Anafilassi indotta da esercizio fisico, grano-dipendente

### Patogenesi NON autoimmune / NON allergica (immunità innata?)

#### Sensibilità al glutine non celiaca

## **Non Celiac Gluten Sensitivity**

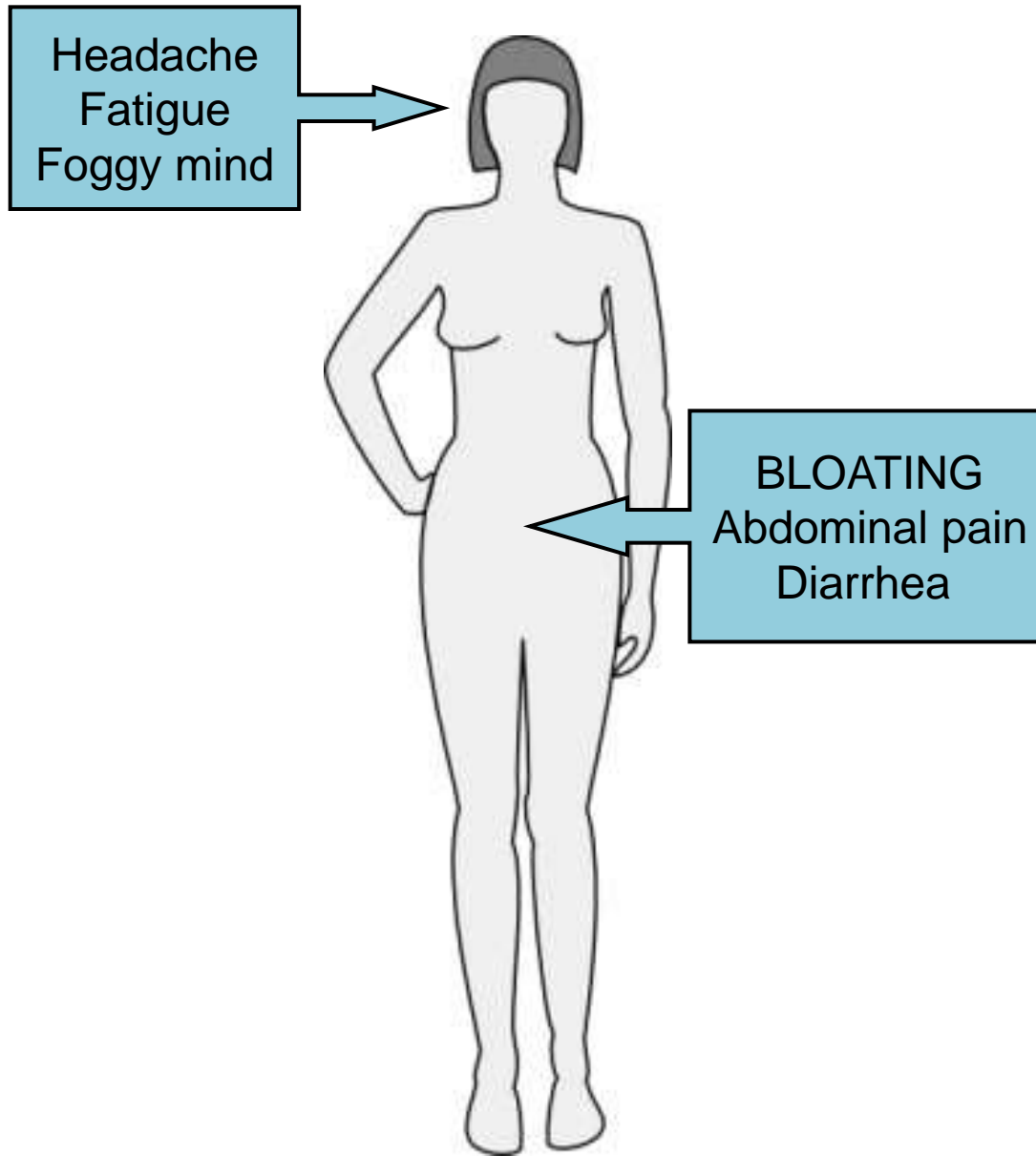
A poorly defined syndrome characterized by a variable combination of intestinal and extra-intestinal symptoms, typically occurring soon after ingestion of gluten-containing foods and disappearing quickly upon their withdrawal, occurring in individuals where both CD and wheat allergy have been excluded

# Clinical manifestations of NCGS

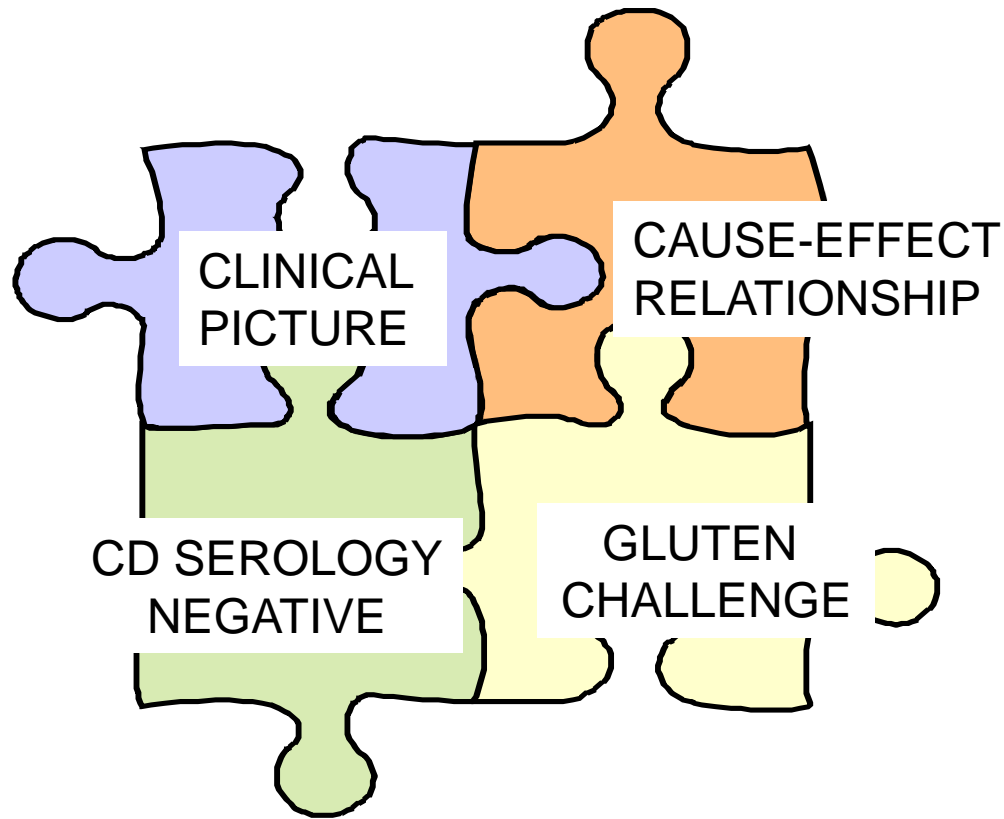
<i>Frequency</i>	<i>Intestinal</i>	<i>Extra-intestinal</i>
<b><i>Very Common</i></b>	Bloating	Lack of wellbeing
	Abdominal pain	Tiredness
<b><i>Common</i></b>	Diarrhea	Headache
	Epigastric pain	Anxiety
	Nausea	Foggy mind
	Aerophagia	Numbness
	GER	Joint/muscle pain
	Aphthous stomatitis	Skin rash/dermatitis
	Alternating bowel habits	
	Constipation	
<b><i>Undetermined</i></b>	Hematochezia	Weight loss
	Anal fissures	Anemia
		Loss of balance
		Depression
		Rhinitis/asthma
		Weight increase
		Interstitial cystitis
		Ingrown hairs
		Oligo or polimenorrhea
		Sensory symptoms
		Disturbed sleep pattern
		Hallucinations
		Mood swings
		Autism
	Schizophrenia	

*The Salerno NCGS diagnostic criteria (Nutrients, 2015)*

# The major clue to the diagnosis of NCGS is the finding of a typical clinical picture

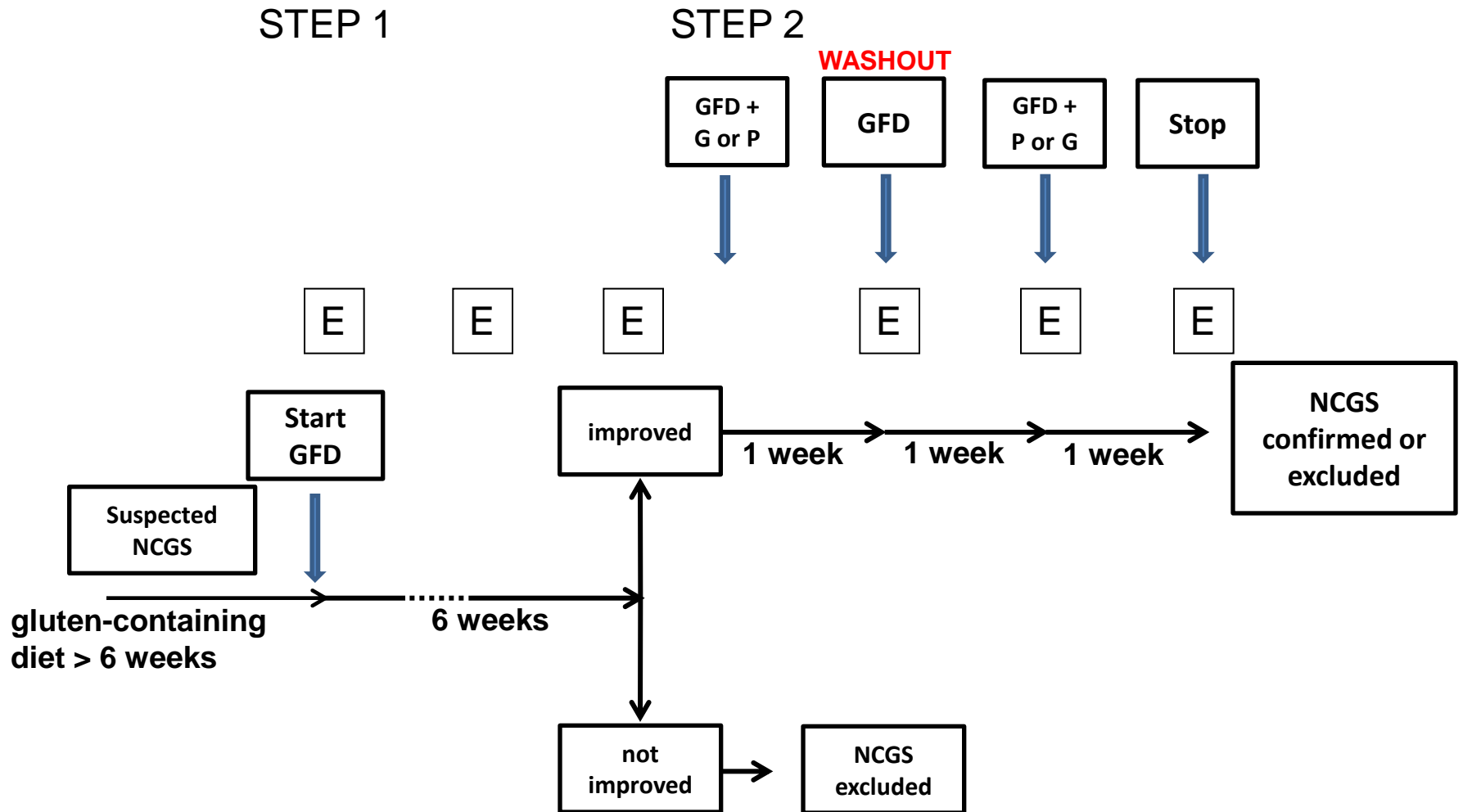


# NCGS: diagnosis is difficult but not impossible





# NCGS diagnosis: the flow diagram



*The Salerno NCGS diagnostic criteria (Nutrients, 2015)*

# Clouds on NCGS

Biomarker?

Definition?

Epidemiology?

Pathophysiology?

Trigger/s?

Complications?

Natural history?

# Wheat Amylase-Trypsin Inhibitors (ATIs)

- part of the natural defense against parasites and insects
- 2-4% of wheat proteins (albumins), daily consumption 0.5-1.5 g
- high bioactivity in modern hexaploid wheat, in rye and barley, lower in older wheat variants, including spelt, emmer and einkorn
- directly engage TLR4–MD2–CD14 complex resulting in the release of proinflammatory innate cytokines

# I FODMAPs questi sconosciuti

Disaccharides  
Lactose

Milk, custard, ice cream  
and yogurt



Monosaccharides  
Free fructose (fructose in excess of glucose)

Apples, pears, mangoes, cherries,  
watermelon, asparagus, sugar snap peas,  
honey, high-fructose corn syrup



Oligosaccharides  
Fructans, galacto-oligosaccharides

Wheat, barley, rye, onion, leek, white part  
of spring onion, garlic, shallots, artichokes,  
beetroot, fennel, peas, chicory, pistachio,  
cashews, legumes, lentils and chickpeas

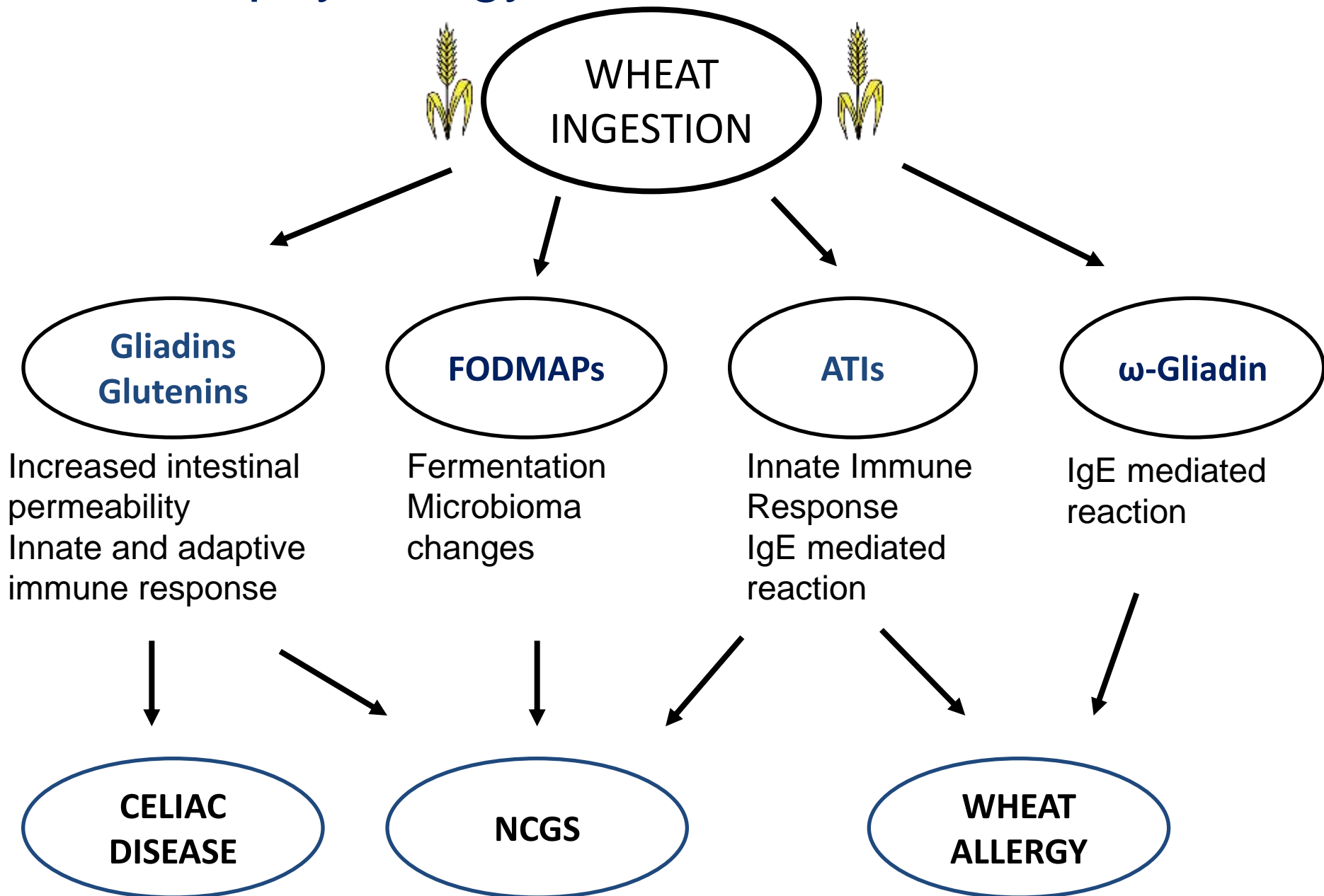


Polyols  
Sorbitol, mannitol, maltitol, xylitol

Apples, pears, apricots,  
cherries, nectarines,  
peaches, plums, watermelon,  
mushrooms, cauliflower,  
sugar free chewing gum/  
mints/sweets

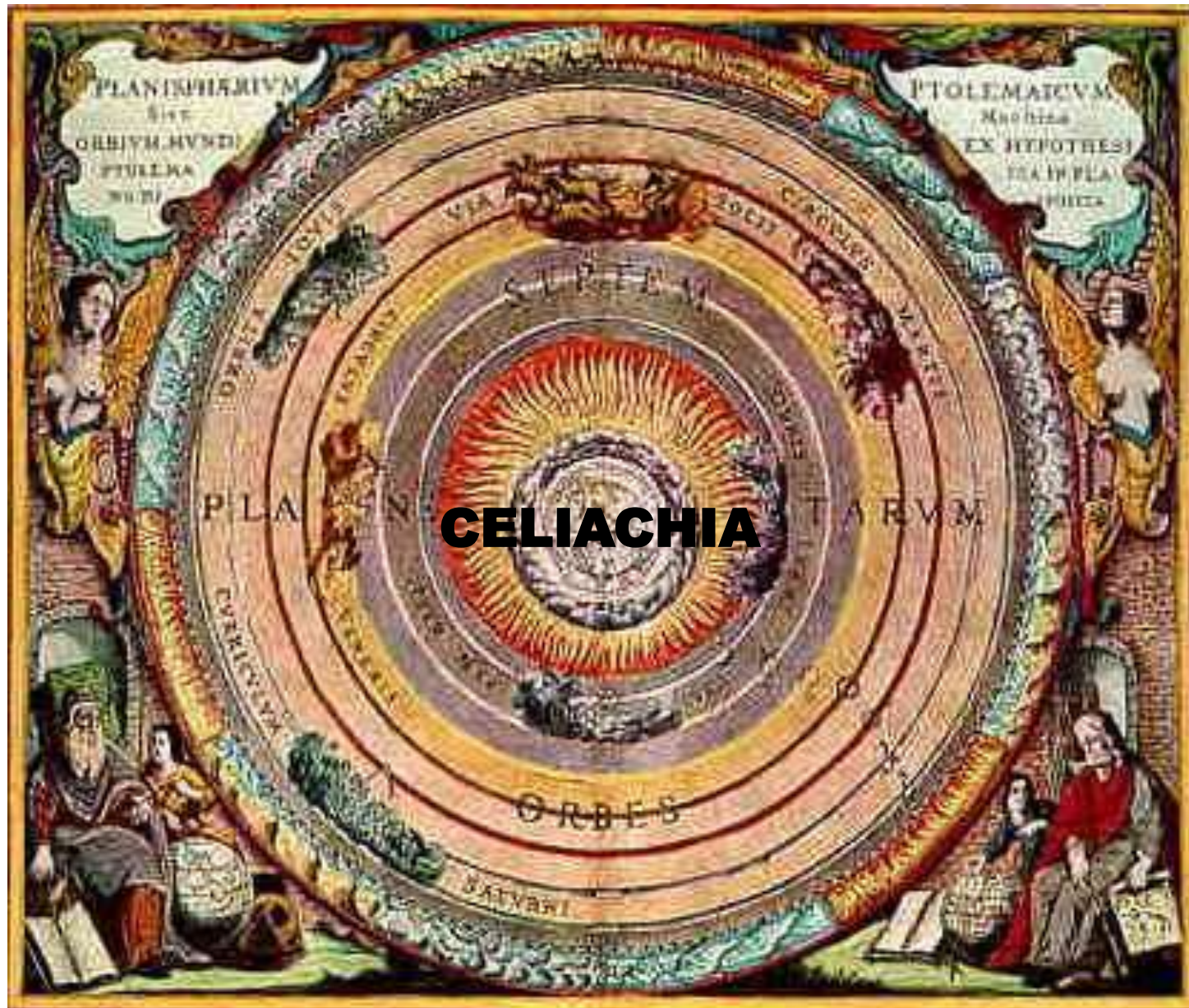


# Pathophysiology of Gluten Related Disorders





*Disordini glutine-indotti: da una visione Tolomaica.....*





*...ad una visione Copernicana*

**Healthy  
population  
(gluten tolerant)**

**autism  
(subgroup)**

**W  
A**

**IBS  
(subgroup)**

**NCGS**

**Celiac  
disease**

**D  
H**

**G  
A**