The Celiac Iceberg

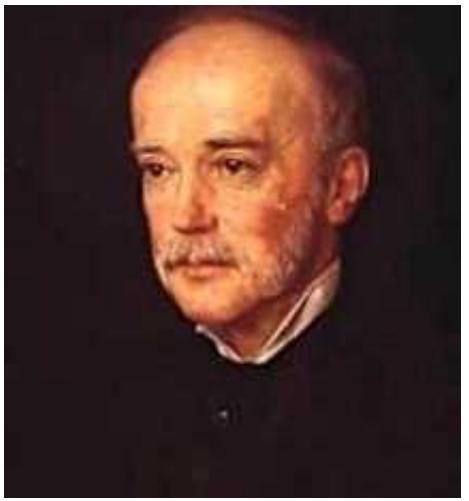
Dr P Mandi

Format

- CD overview
- Epidemiology
- Pathophysiology
- Clinical presentation
- Diagnosis
- Management

Second century A.D. Aretaeus of Cappadocia described a condition called koiliakos (derived from koelia, Greek for abdomen) that caused abdominal pain and diarrhea, referring to patients with the malady as celiacs.

October 5th 1887 Paediatrician Samuel Gee in a lecture to medical students titled "Celiac Affection" constituted the modern "rediscovery" of celiac disease



- 1944: Dutch physician Willem Karel Dicke links celiac disease to wheat. In the Dutch famine of 1944, he observes that the prevalence of celiac disease in children drops to nearly zero due to the shortage o

Photograph of Dicke in a characteristic pose as a close and considerate friend to his patients in his time of Director of the Wilhelmina Children's Hospital, Utrecht.

- 1989
- Immunologist Ludvig Sollid’s group from Oslo narrowedq down the major genetic risk for celiac disease to two versions of the histocompatibility leukocyte antigen (HLA) molecule.

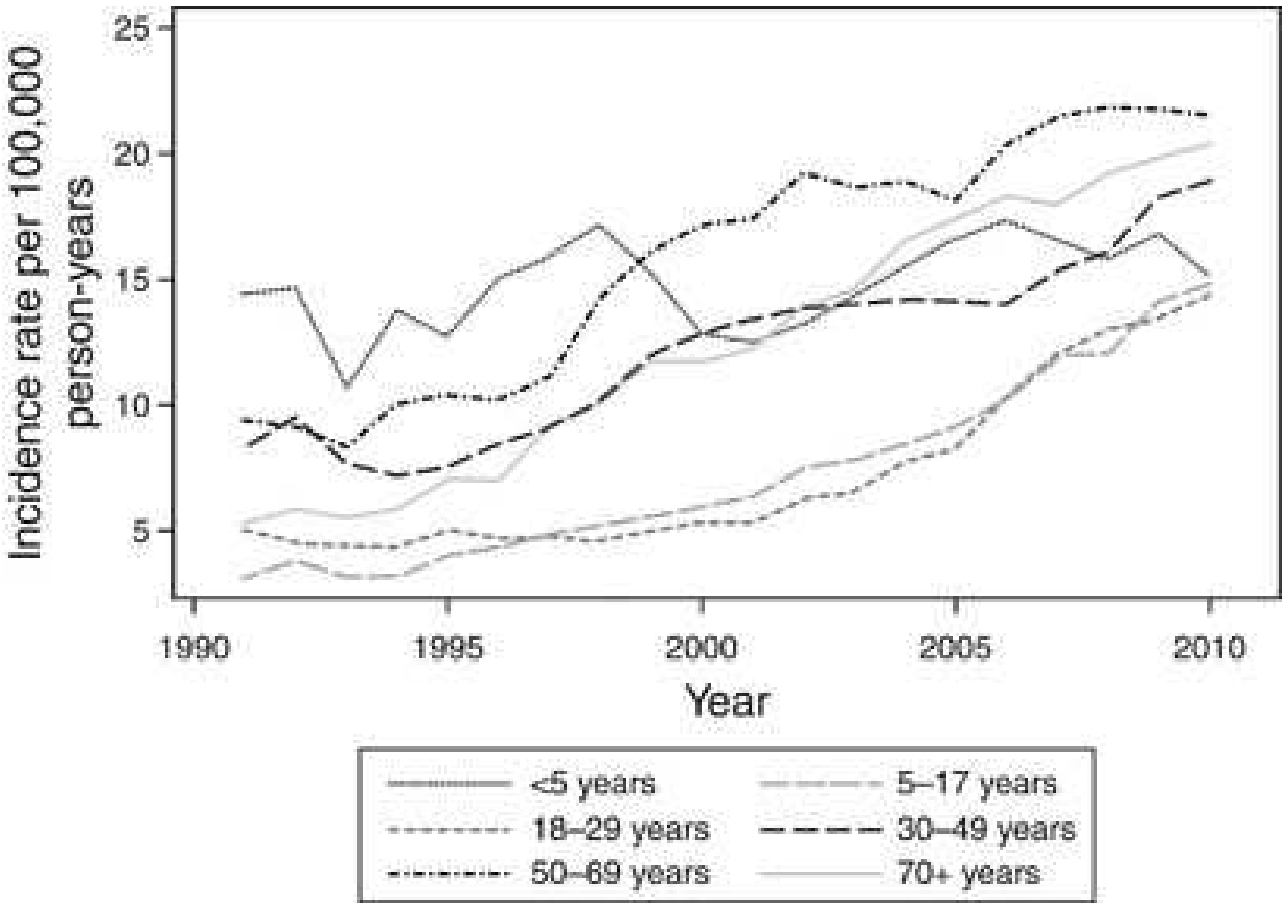
- 1997
- Gastroenterologist Detlef Schuppan, then at the Free University of Berlin, discovered that the autoantibodies of celiac patients are directed against tissue transglutaminase (an enzyme released from the intestine’s cells when gluten passes into the mucosal layer). He introduced a simple blood-screening test for initial diagnosis.

Epidemiology

- In the past CD was considered a rare disorder, affecting individuals of European origin and onset in the early years of life.
- *"The typical child with cd, (is) usually , fair haired, blue-eyed . . . "* Anderson textbook of *Paediatric Gastroenterology 1975*
- *1950's was 1:8,000 & 1:4,000 in England and Wales respectively*

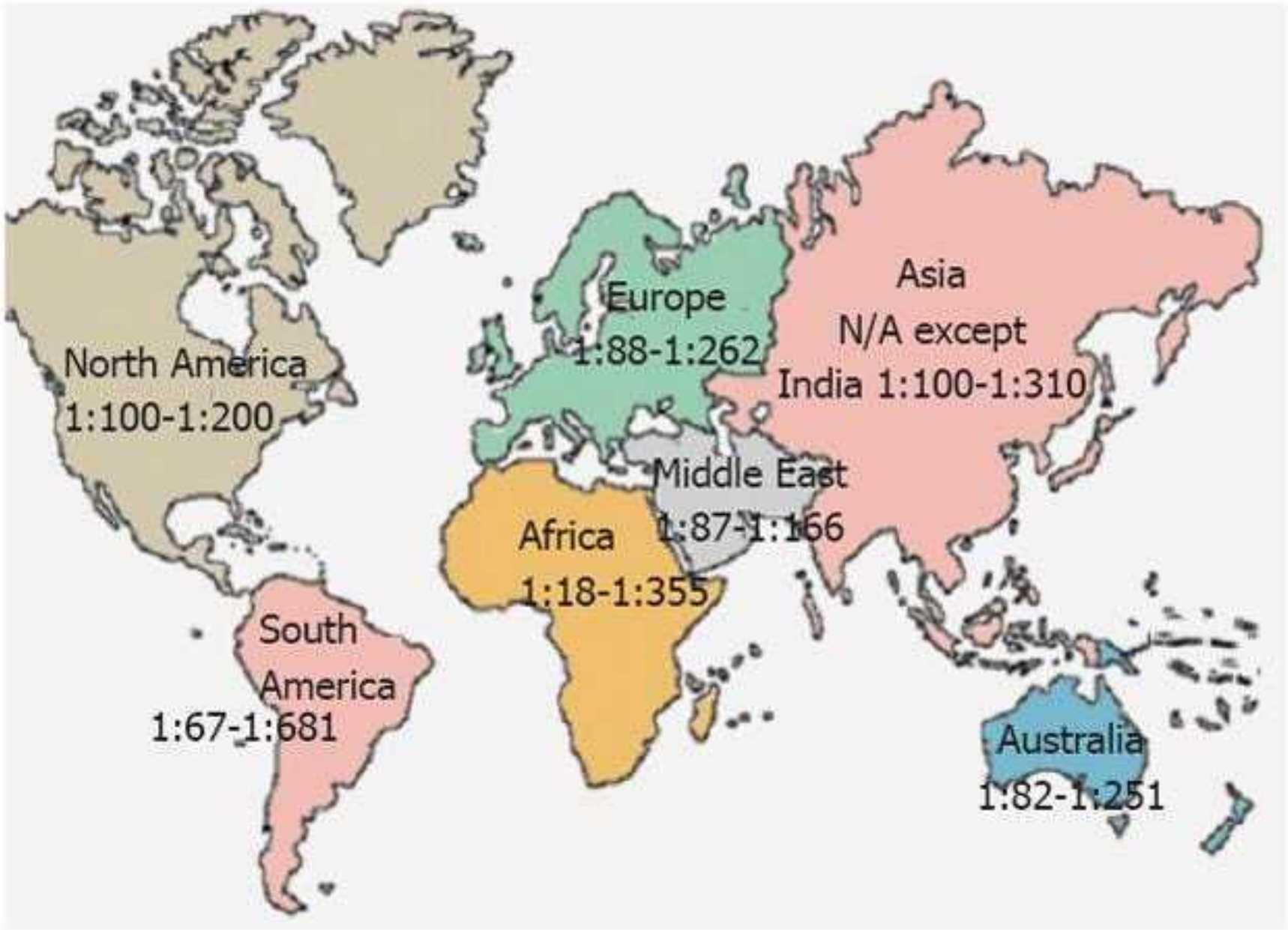
Epidemiology

- With screening, prevalences increased to1% in Europe and North America
- Similarly high values found in at risk groups in Middle East and India
- Highest prevalence among the Saharawi of North Africa ~ 5.6% of general population



Three-year rolling average incidence of celiac disease (CD) in the period 1990–2011, by age group.

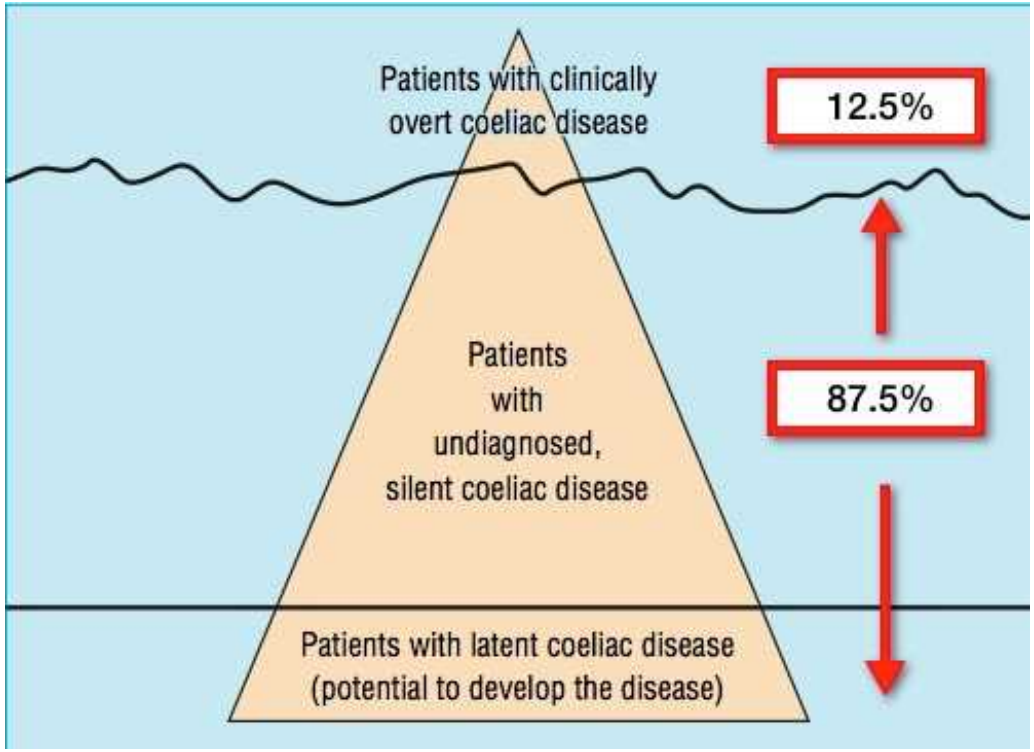
Am J Gastroenterol 2014; 109:757–768

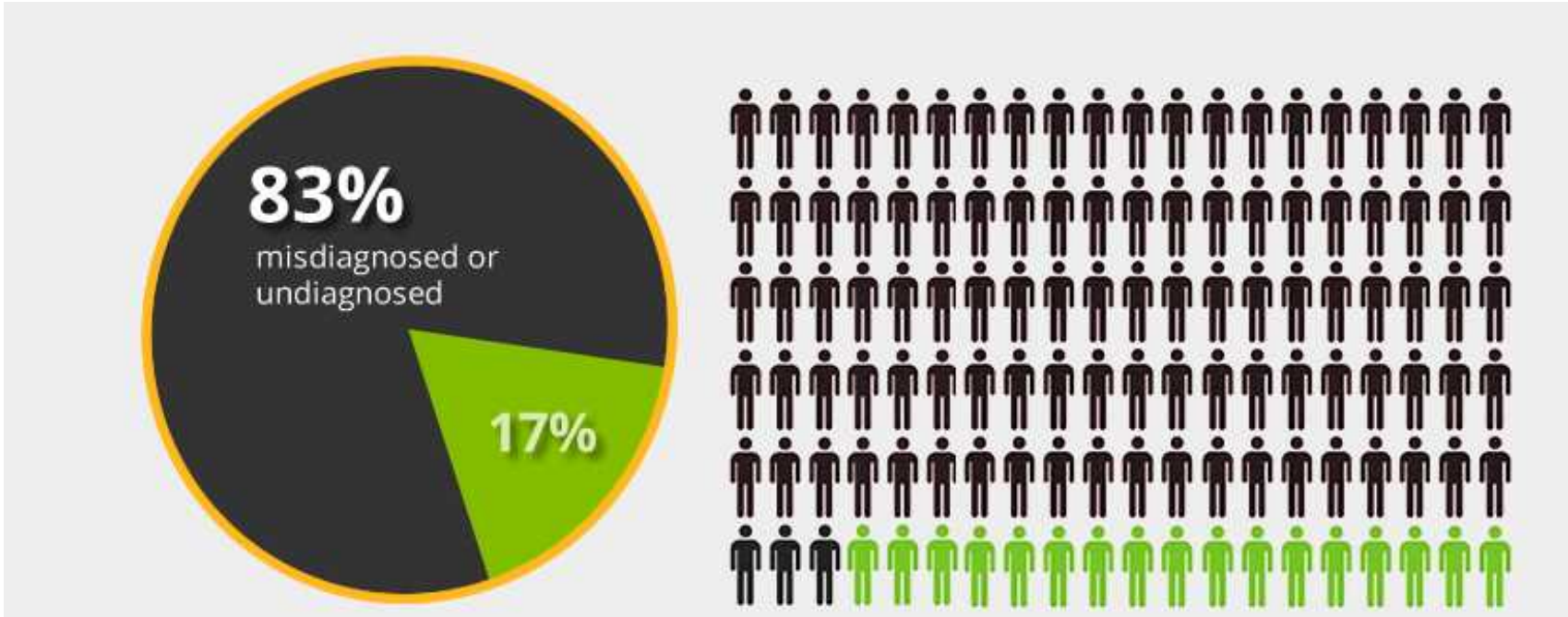


- *World J Gastroenterol. Nov 14, 2012; 18(42): 6036-6059*

- The ratio of typical to silent CD was 1:8. These findings suggested that CD is highly prevalent in the young adult population in Israel.

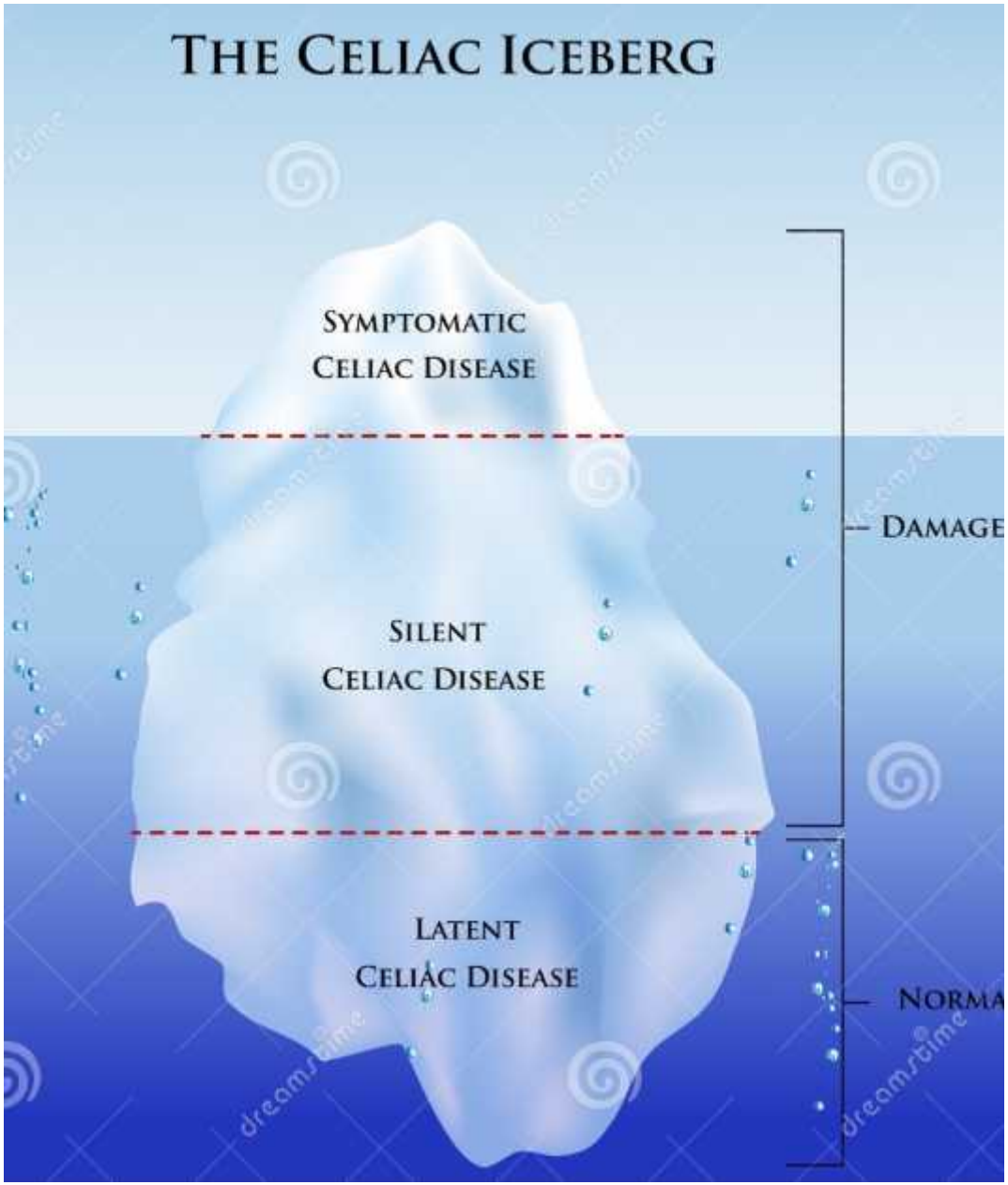
Isr Med Assoc J 2010; 12:266–269.




83%
misdiagnosed or
undiagnosed
17%

- Increased awareness of clinical polymorphisms & more liberal serological testing, will reveal more of the submerged iceberg

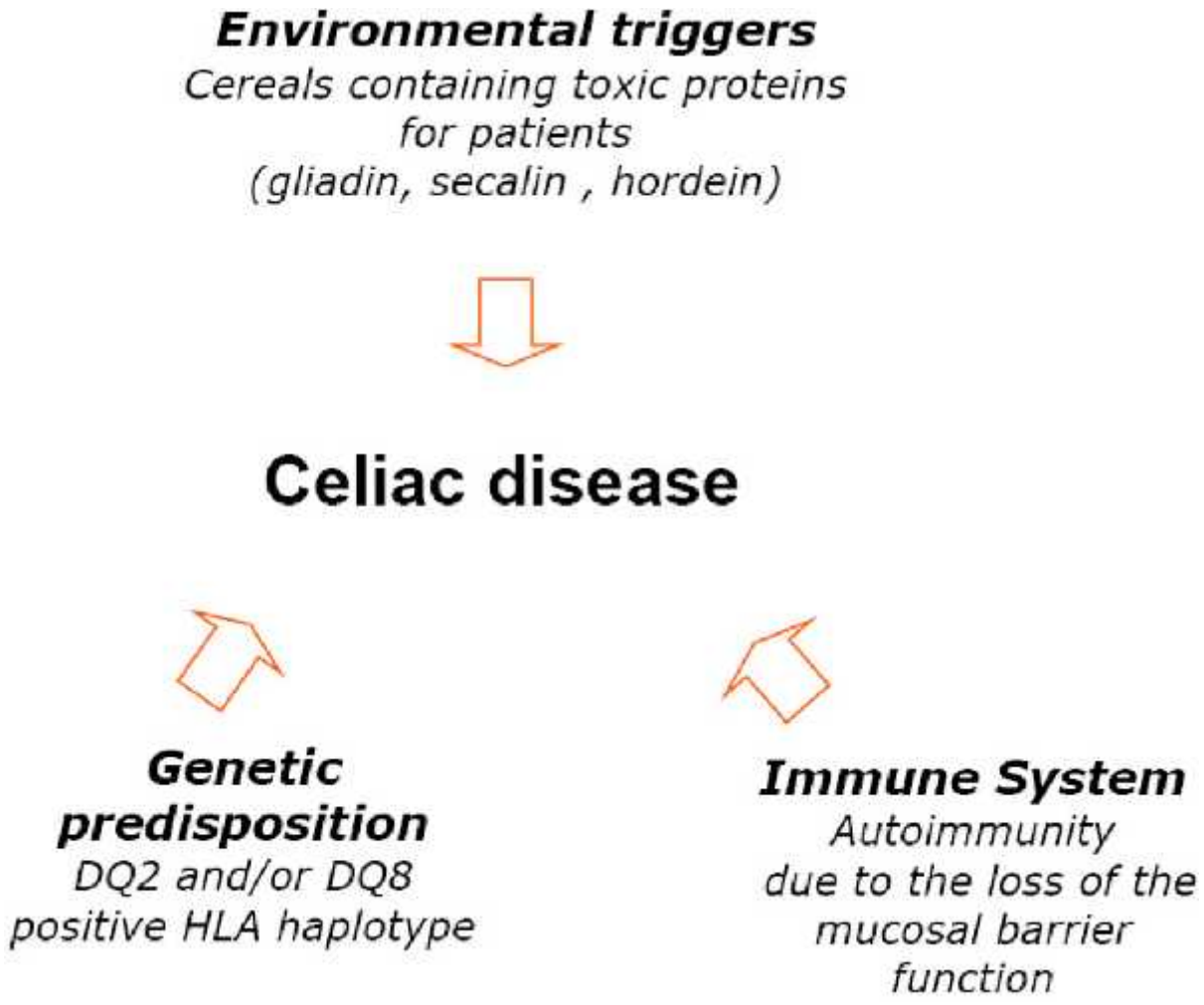
BMJ 1999;318:164-7. , J. Pediatr 2002;140:379-80.



Pathophysiology

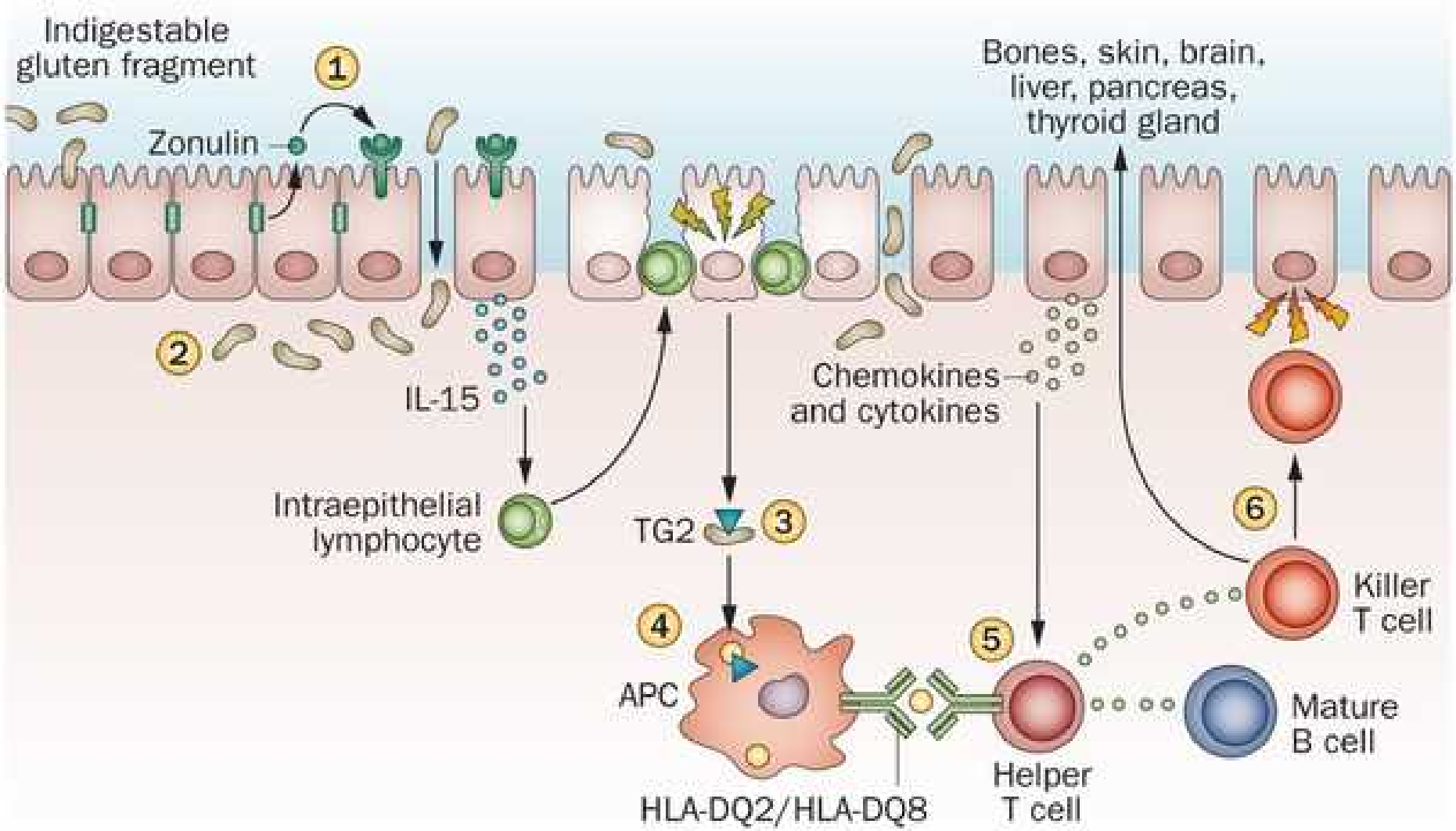
- Immune mediated inflammation of the small intestine
- Requires
    - 1 Host susceptibility HLA-DQ2 or HLA-DQ8
    - Trigger glutein (found in wheat, rye,barley)
    - Autoantigen (IgA tissue transglutaminase)
- Glutein is found in wheat rye and barley

Pathophysiology



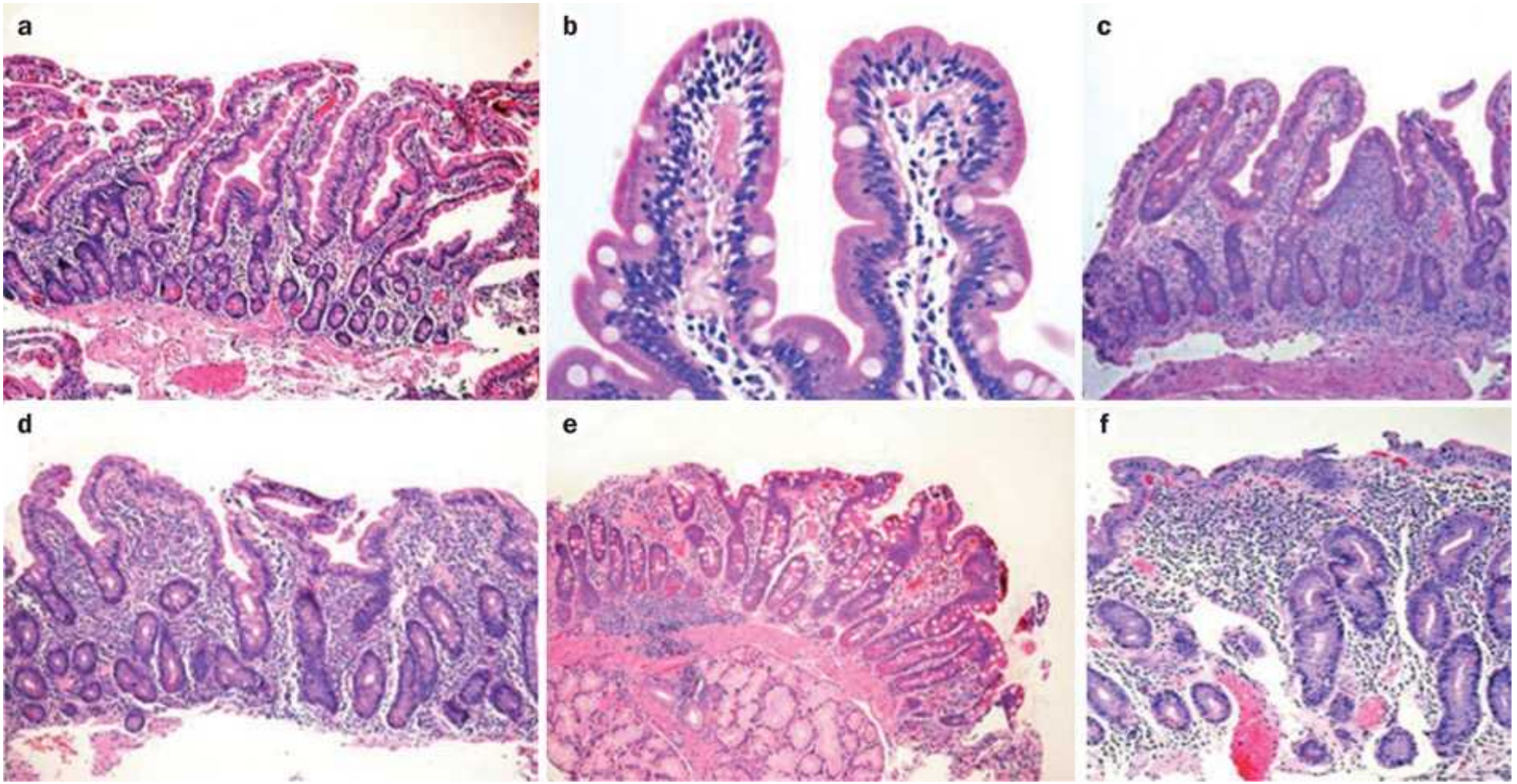
Pathophysiology

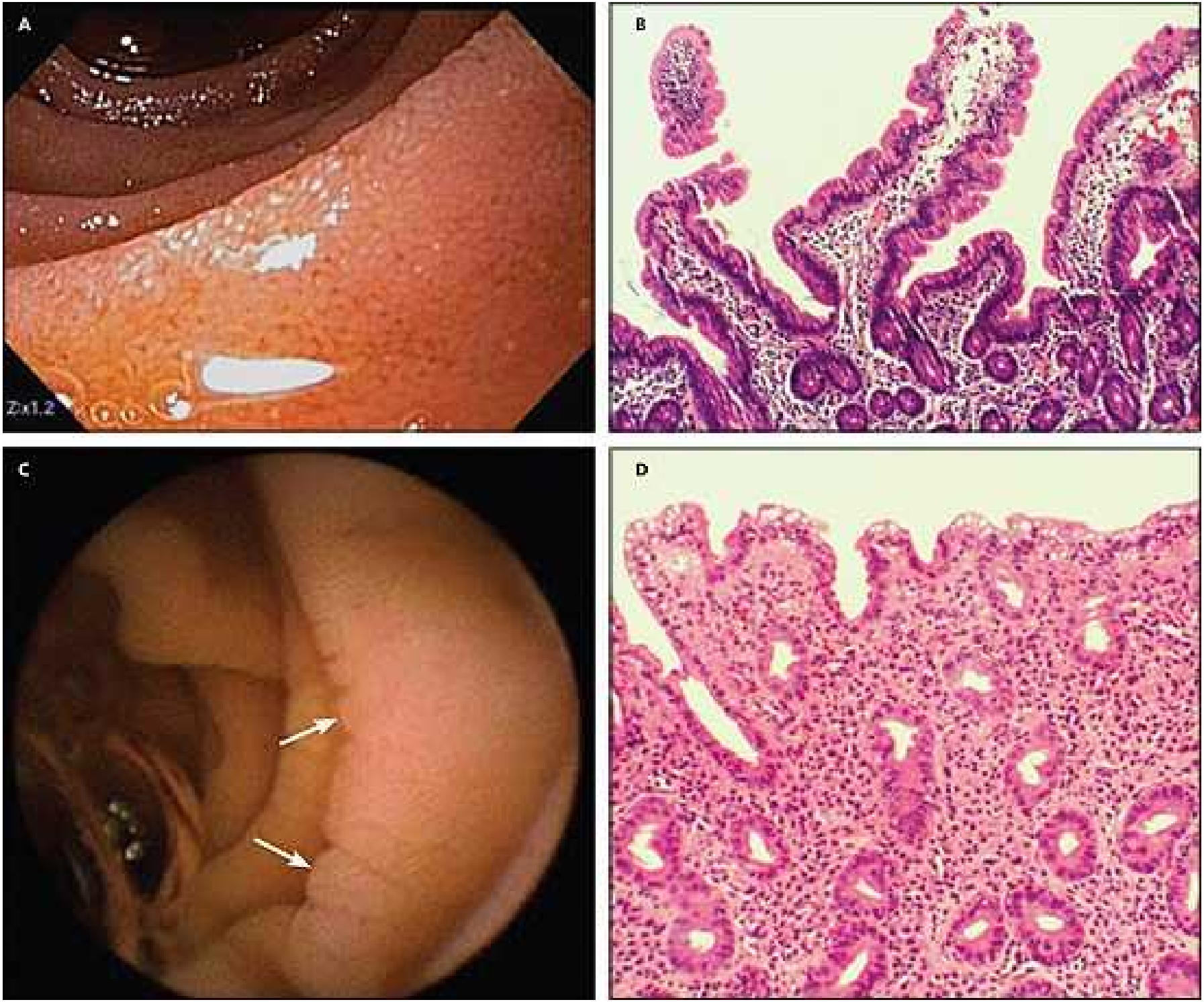
- Ingestion of gluten in genetically predisposed individual triggers autoimmune inflammatory reaction in the SI
- Histologically characterized by T cell infiltrates of epithelium and laminia propria, with crypt cell hyperplasia and leading to progressive villous destruction and 2* decrease in absorptive surface area
- End result global malabsorption of macro and nutrients



Nature Reviews | Gastroenterology & Hepatology

Cereals	Prolamine	Composition Q/P	Toxicity
Wheat	Gliadin	36%/17-23%	+++
Barley	Hordeins	36%/17-23%	++
Rye	Secalins	36%/17-23%	++
Oats	Avenins	High/LowP	+
Maize	Zeins	Low Q, high A,V	-
Millet	?	Low Q, high A,V	-
Rice	?	Low Q, high A,V	-


a
b
c
d
e
f


A
Zx1.2
B
C
D

Histological stages

Modified Marsh classification

- Damage is progressive
- Type 0 : Pre-infiltrative (normal)
- Type 1 (infiltrative lesion)- increased intraepithelial lymphocytosis
- Type 2 (Hyperplastic lesion) - type 1 + hyperplastic crypts
- Type 3 (destructive lesion) - type 2 + progressive villous atrophy 3a, 3b, 3c

Clinical Presentation

- Four possible presentations
- ***Typical:*** characterized mainly by GIT signs and symptoms
- ***Atypical:*** Present with various extraintestinal manifestations and Minimal or absent GIT symptomatology
- ***Silent:*** Asymptomatic but small intestine mucosal damage present and CD autoimmunity detectable on serology
- ***Latent:*** Asymptomatic with normal mucosal morphology. Have genetic compatibility with CD +/- positive autoimmunity. Glutein dependent changes +/- symptoms may appear with time

Typical Celiac disease

- Presents between 6-24 months of age, after introduction of weaning foods containing gluten
- ***Infants and young children:*** Chronic diarrhoea, annorexia vomiting recurrent abd pain, distension, poor weight gain, apathy and irritability
- ***Older children:*** abd pain, nausea, bloating, intermittent diarrhoea and constipation

Extra GIT manifestations

***Strong to moderate evidence*:** Dermatitis herpetiformis, dental hypoplasia, osteopenia, short stature,delayed puberty, IDA

Less strong evidence: Hepatits, Arthritis, epilepsy with occipital calcifications

J Pediatr Gastroenterol Nutr, Vol. 40, No. 1, January 2005

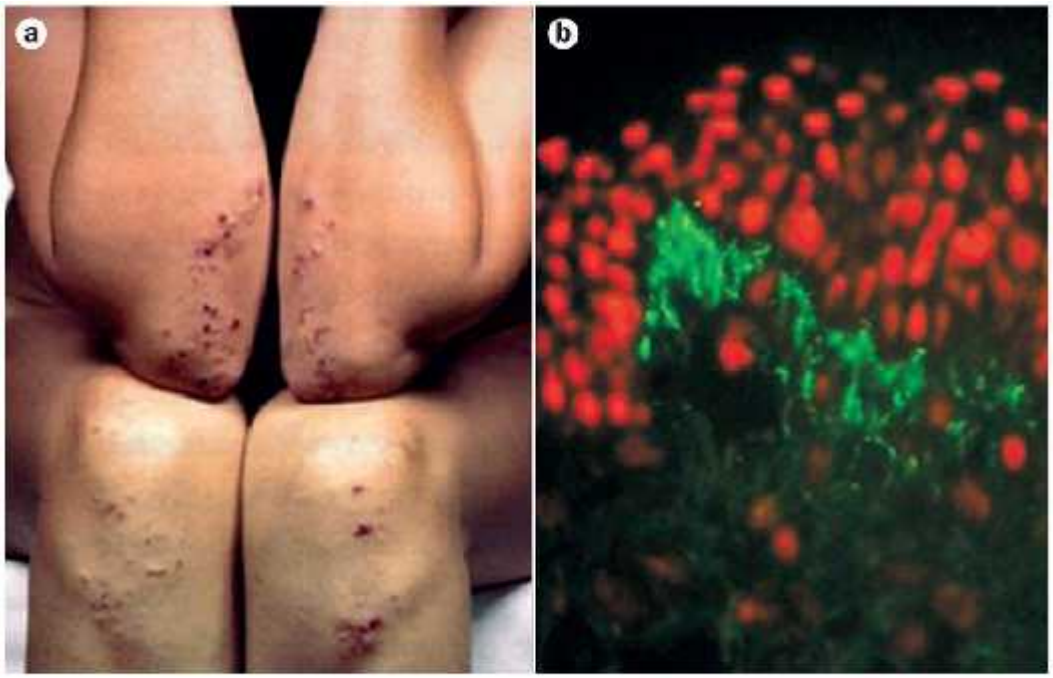
Associated conditions

Type 1 Diabetes.
Autoimmune thyroiditis
Down’s syndrome
Turner’s syndrome
William’s syndrome
Selective Ig A defeciency
1st degree relatives

J Pediatr Gastroenterol Nutr, Vol. 40, No. 1, January 2005

Dermatitis herpetiformis

- Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/J



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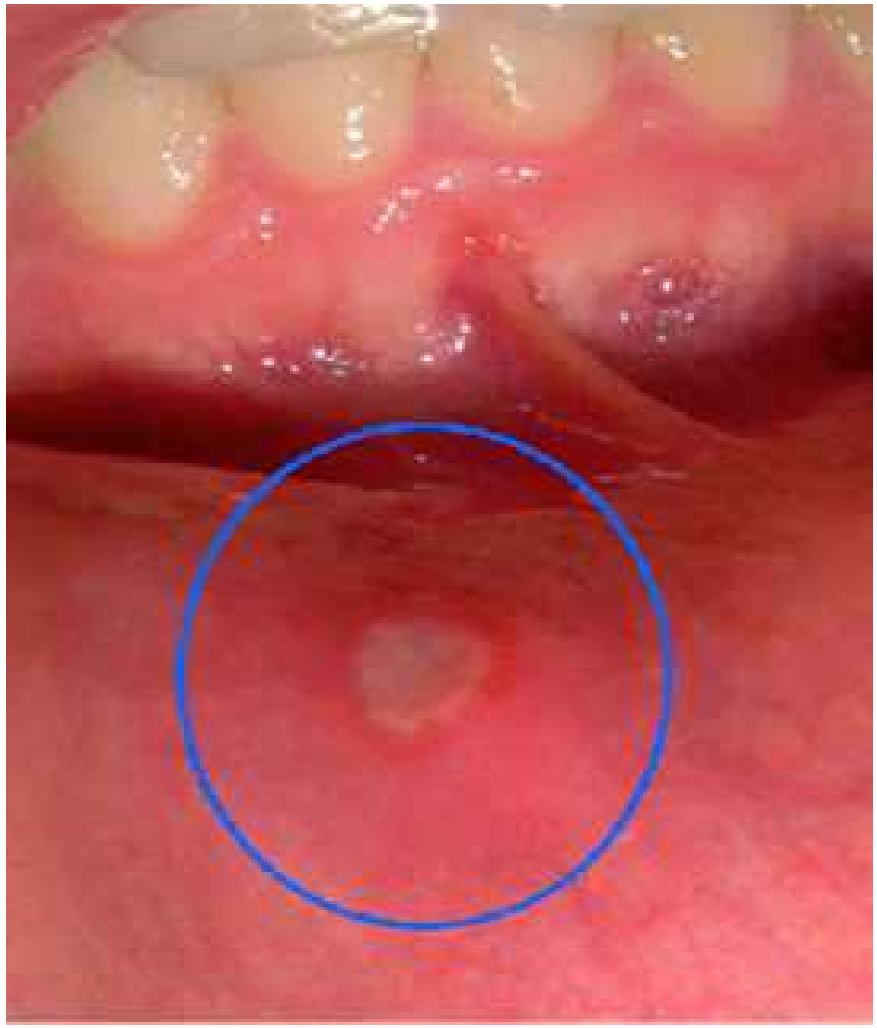
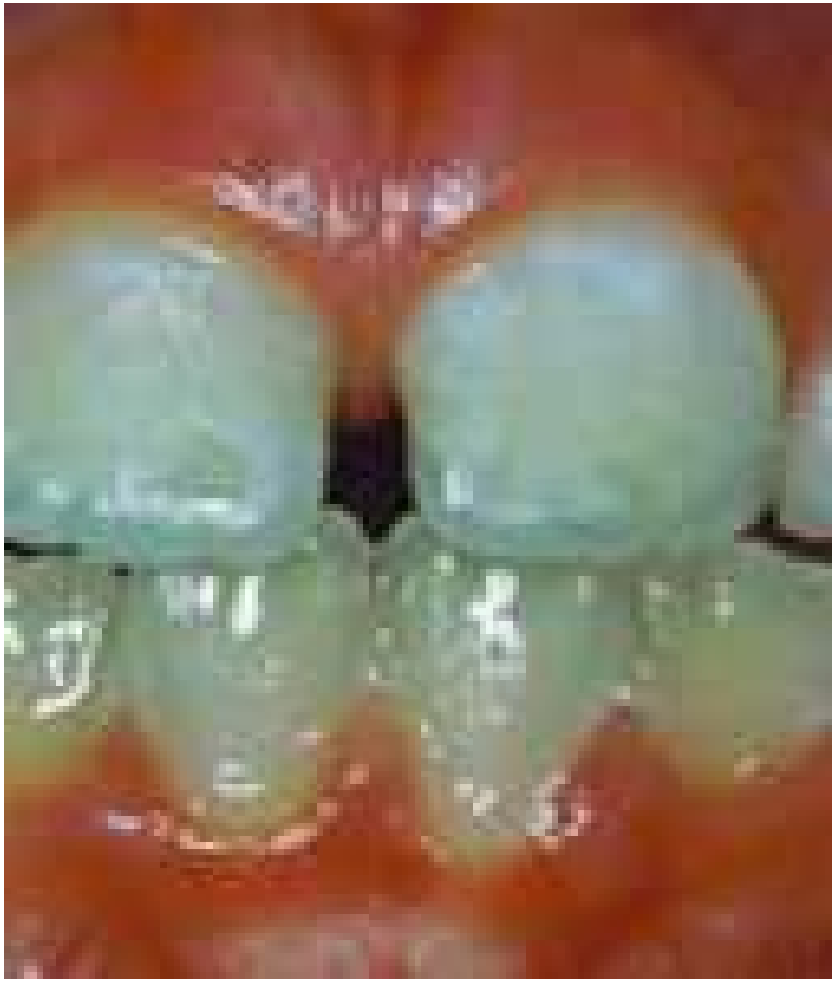
Aphthous ulcers

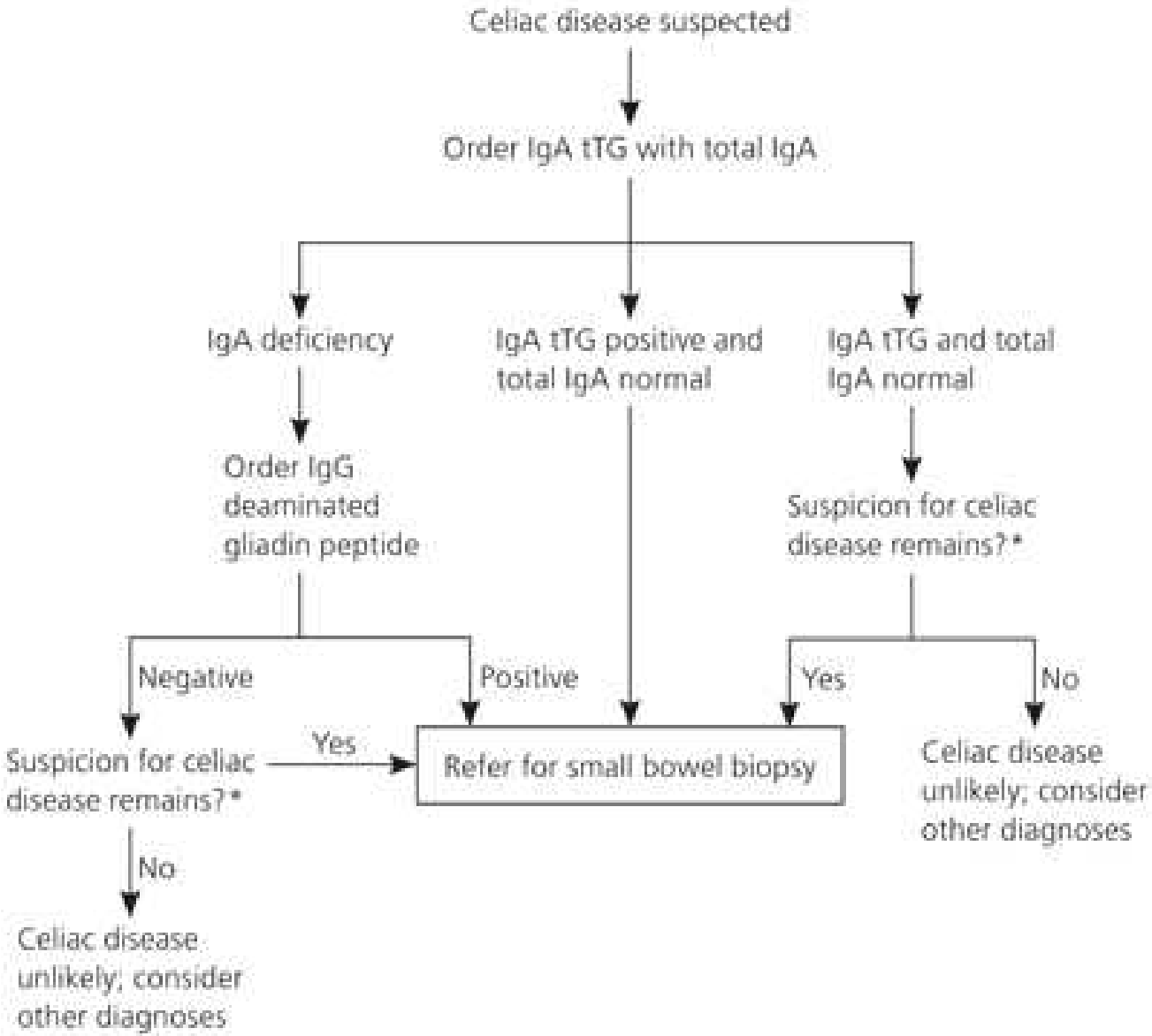


Dental Enamel hypoplasia

- J Oral Pathol Med. 1990;19(6):241-5.




gluten intolerant
Nervous System
mouth sores
malabsorption
constipation
weight loss
Osteoporosis or Bone Loss
Depression or Anxiety
damage to dental enamel
gluten sensitivity
acid reflux
bloating
seizures
iron deficiency
Headaches & Fatigue
small intestine
CELIAC DISEASE
diet
protein complex
Dermatitis Herpetiformis
genetic
autoimmune disease
diarrhea
brain fog


Celiac disease suspected
Order IgA tTG with total IgA
IgA deficiency
IgA tTG positive and total IgA normal
IgA tTG and total IgA normal
Order IgG deaminated gliadin peptide
Suspicion for celiac disease remains?*
Negative
Positive
Yes
No
Suspicion for celiac disease remains?*
Yes
Refer for small bowel biopsy
Celiac disease unlikely; consider other diagnoses
No
Celiac disease unlikely; consider other diagnoses

Differential diagnosis

- SAM/PEM
- Giardiasis
- TB
- HIV enteropathy
- Whipple's disease
- Autoimmune enteropathy
- Crohn's disease
- Food intolerance eg CMA
- Eosinophilic gastroenteritis
- Radiation enteritis

Treatment

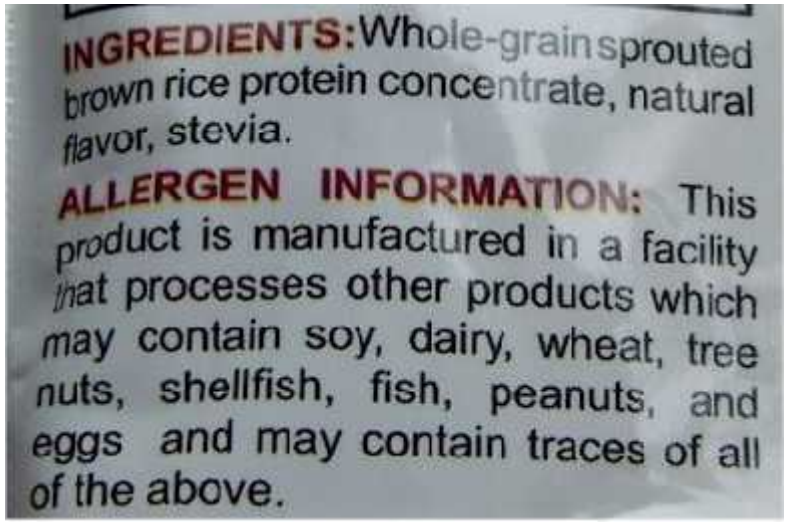
- Lifelong avoidance, GFD is the cornerstone of treatment
- Symptoms resolutions starts occurring in weeks
- Dietary intake of glutein <10gms daily unlikely to cause mucosal reactions

Akobeng AK, Thomas AG. Systematic review: tolerable amount of gluten for people with coeliac disease. Aliment Pharmacol Ther. 2008 Jun 1. 27(11):1044-52

Total Carbohydrate	300g	375g
Dietary Fiber	25g	30g

MADE FRO[illegible] WHOLE WHEAT FLOUR, [illegible]VATER, HIGH FRUCTOSE CORN SYRUP, YEAST, SOYBEAN OIL, WHEAT GLUTEN, UNSULPHURED MOLASSES, CONTAINS 2 PERCENT OR LESS OF: OAT FIBER, SALT, SODIUM STEAROYL LACTYLATE (DOUGH CONDITIONER), CITRIC ACID, CALCIUM PROPIONATE AND SORBIC ACID TO RETARD SPOILAGE, MONO AND DIGLYCERIDES, BUTTER (MILK)*, WHEY*, SOY LECITHIN.
*ADDS A TRIVIAL AMOUNT OF CHOLESTEROL.

- Reading food labels important malt= barley,



INGREDIENTS: Whole-grain sprouted brown rice protein concentrate, natural flavor, stevia.

ALLERGEN INFORMATION: This product is manufactured in a facility that processes other products which may contain soy, dairy, wheat, tree nuts, shellfish, fish, peanuts, and eggs and may contain traces of all of the above.

- Incomplete remission in compliant patients likely due to cross-contamination at milling factories

Reasons for non-compliance

- Cost
- Availability
- Poor palatability
- Poor nutritional counseling
- Poor followup
- poor food labeling
- Socio-cultural, peer pressure
- Transition to adolesence

New therapeutic frontiers

- Enzyme supplementation (bacterial prolyl endopeptidases)
- Correction of intestinal barrier against glutein entry
- Blocking of gliadin presentation to HLA
- tTG inhibitors

J Clin Gastroenterol. 2010 Jan;44(1):4-8

Summary

- CD is a chronic genetically determined inlammatory disorder of the SI driven by glutein ingestion
- Prevalence of 1-5% & increasing
- Varied clinical manifestations
- Diagnosis depends on high risk of suspicion, tTG testing of at-risk patients and endoscopic confirmation
- Treatment is lifelong GFD

Take home message

- CD is in our midst
- For every typical celiac seen there are 7 atypical or silent celiacs (CELIAC ICEBERG)
- Increased awareness of the polymorphisms and more liberalized testing of at-risk patients could significantly reduce mortality and morbidity associated with untreated disease

Thank You