

CELIAC DISEASE

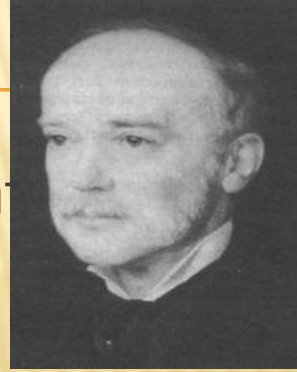


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DEFINITIONS

- small intestinal malabsorption of nutrients after the ingestion of wheat gluten or related proteins from rye and barley
- villous atrophy of the small intestinal mucosa
- prompt clinical and histologic improvement following strict adherence to a gluten-free diet
- clinical and histologic relapse when gluten is reintroduced

History of Celiac Disease



- Described by Dr. Samuel Gee in a 1888 report entitled “On the Coeliac Affection” – anemia, cachexia, diarrhea and development delay in children. (Term “coeliac” derived from Greek word koiliakaos – abdominal)

- Similar description of a chronic, malabsorptive disorder by Aretaeus from Cappadochia (now Turkey) in 2nd century



- 1940s - Dutch paediatrician Dr Willem Karel Dicke noticed clinical improvement of his patients during the Dutch famine (during which flour was scarce). Dicke noticed that the shortage of bread led to a significant drop in the death rate among children affected by coeliac disease from greater than 35% to essentially zero

EPIDEMIOLOGY

Environmental factors

- **Gliadins (wheat) , secalins (rye) , hordeins (barley) , avenins (oats)**

Genetic factors

- **5 – 15% of first degree relatives**
- **75% concordance in identical twins**
- **HLA DQ2 / DQ8 □ *Absence excludes the diagnosis of celiac***

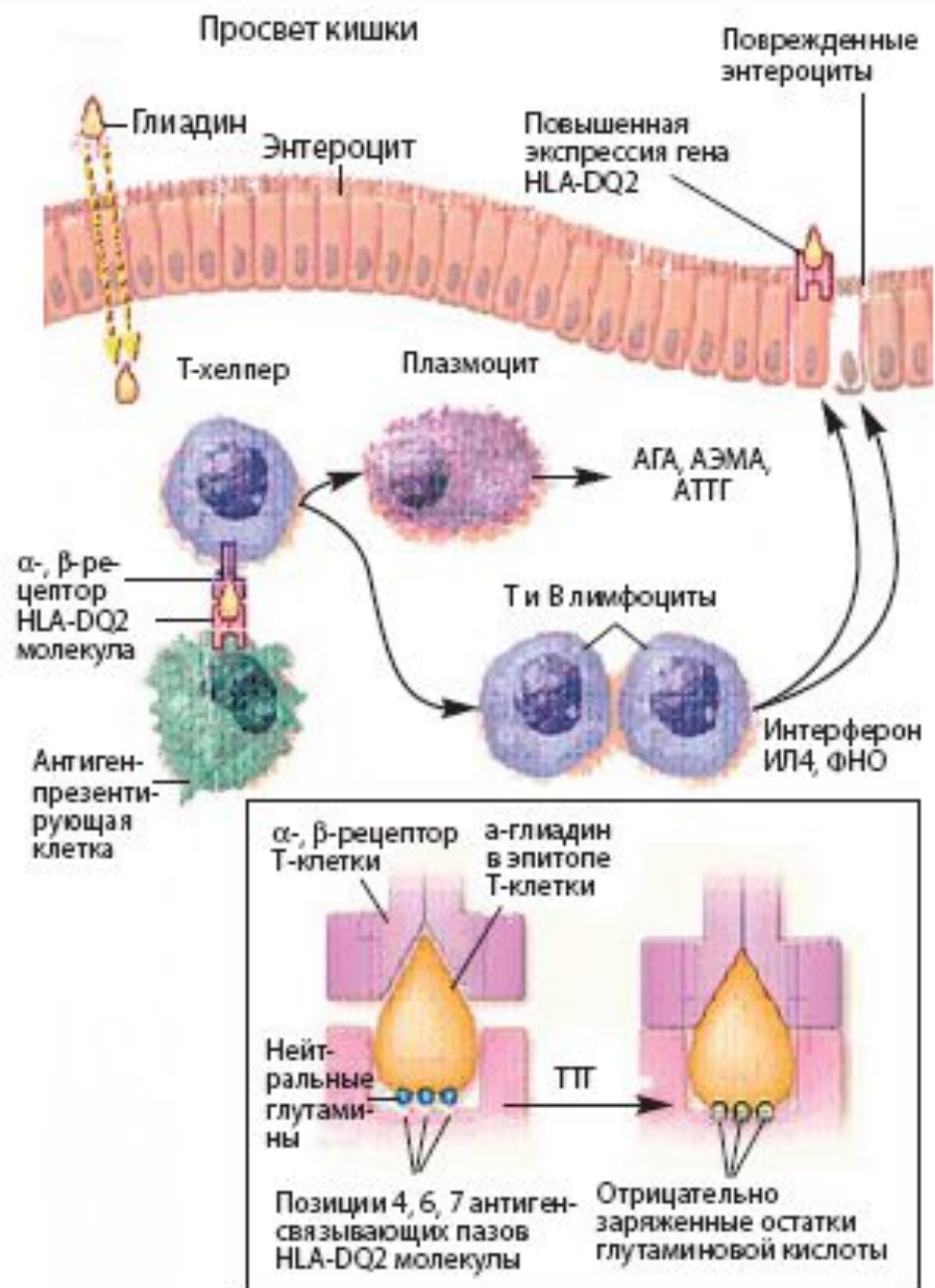
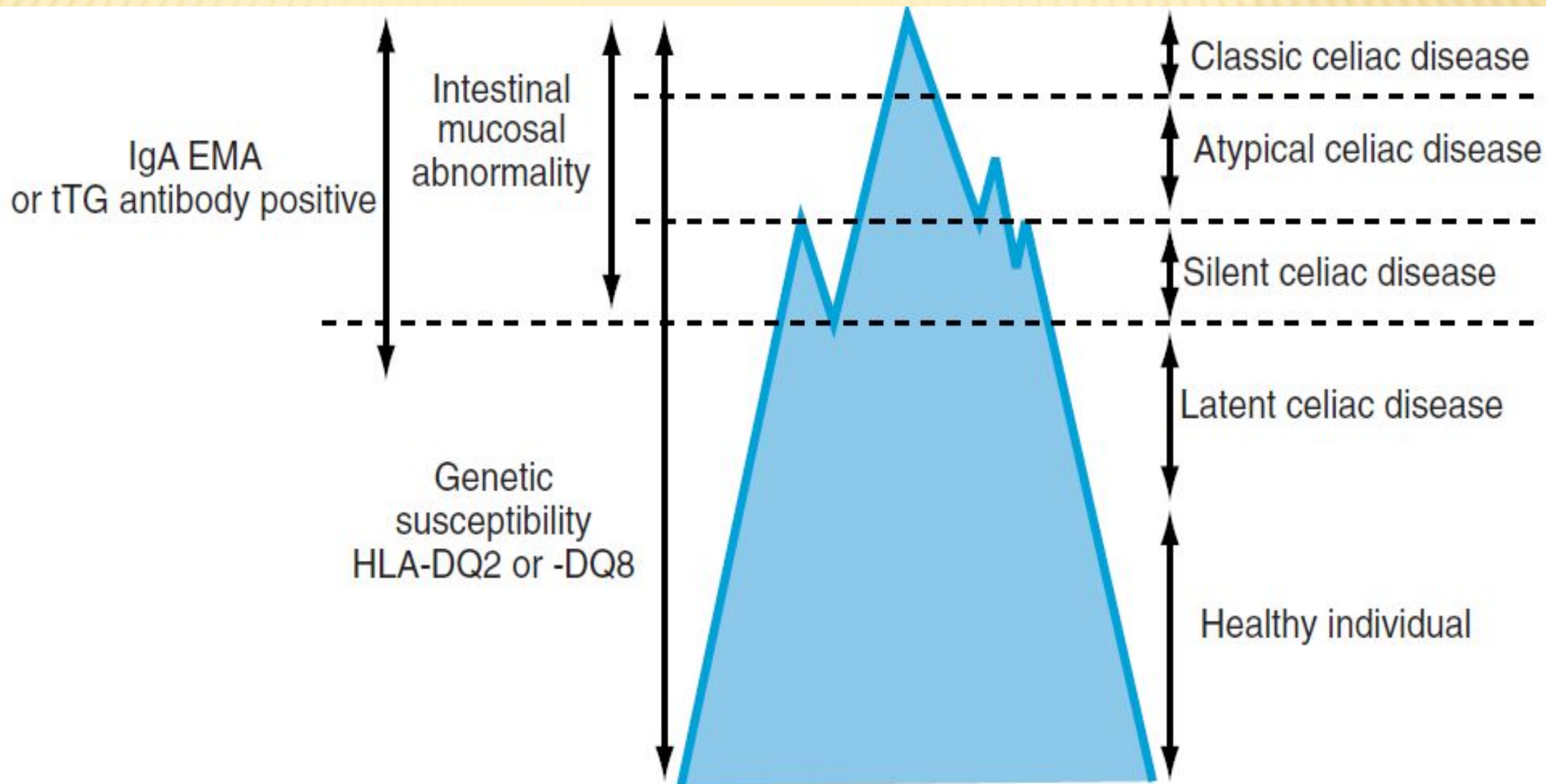


Рис. 1. Схема патогенеза глютенчувствительной целиакии

Serologic Tests for Untreated Celiac Disease

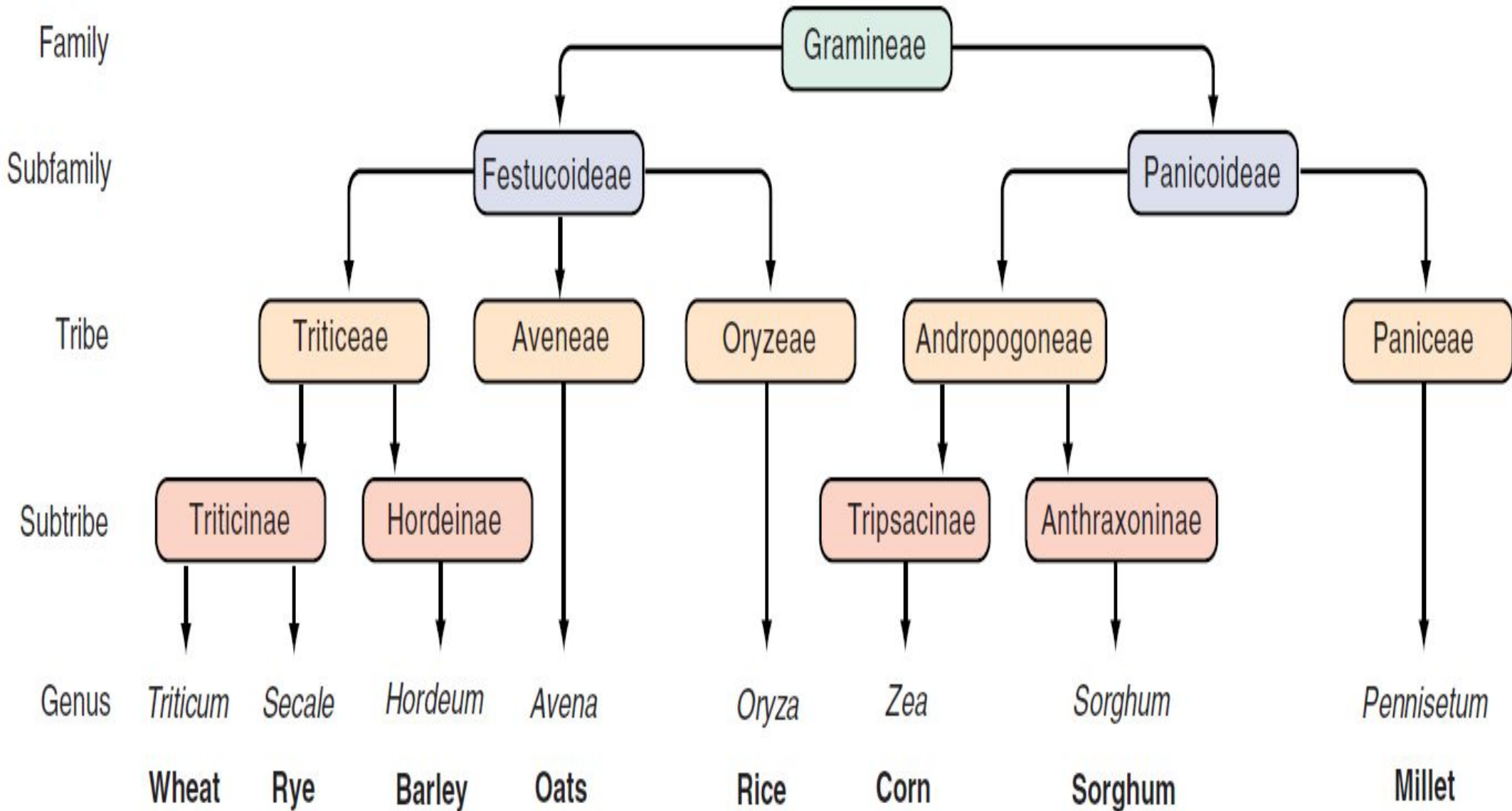
SEROLOGIC TEST	SENSITIVITY* (%)	SPECIFICITY* (%)	POSITIVE PREDICTIVE VALUE (%)	NEGATIVE PREDICTIVE VALUE (%)
Immunoglobulin A Endomysial Antibody				
Indirect immunofluorescence assay	85-98	97-100	98-100	80-95
Guinea pig tTG [†] ELISA	95-98	94-95	91-95	96-98
Human tTG [‡] ELISA	95-100	97-100	80-95	100
Antigliadin Antibodies (AGAs)				
IgA	75-90	82-95	28-100	65-100
IgG	69-85	73-90	20-95	41-88

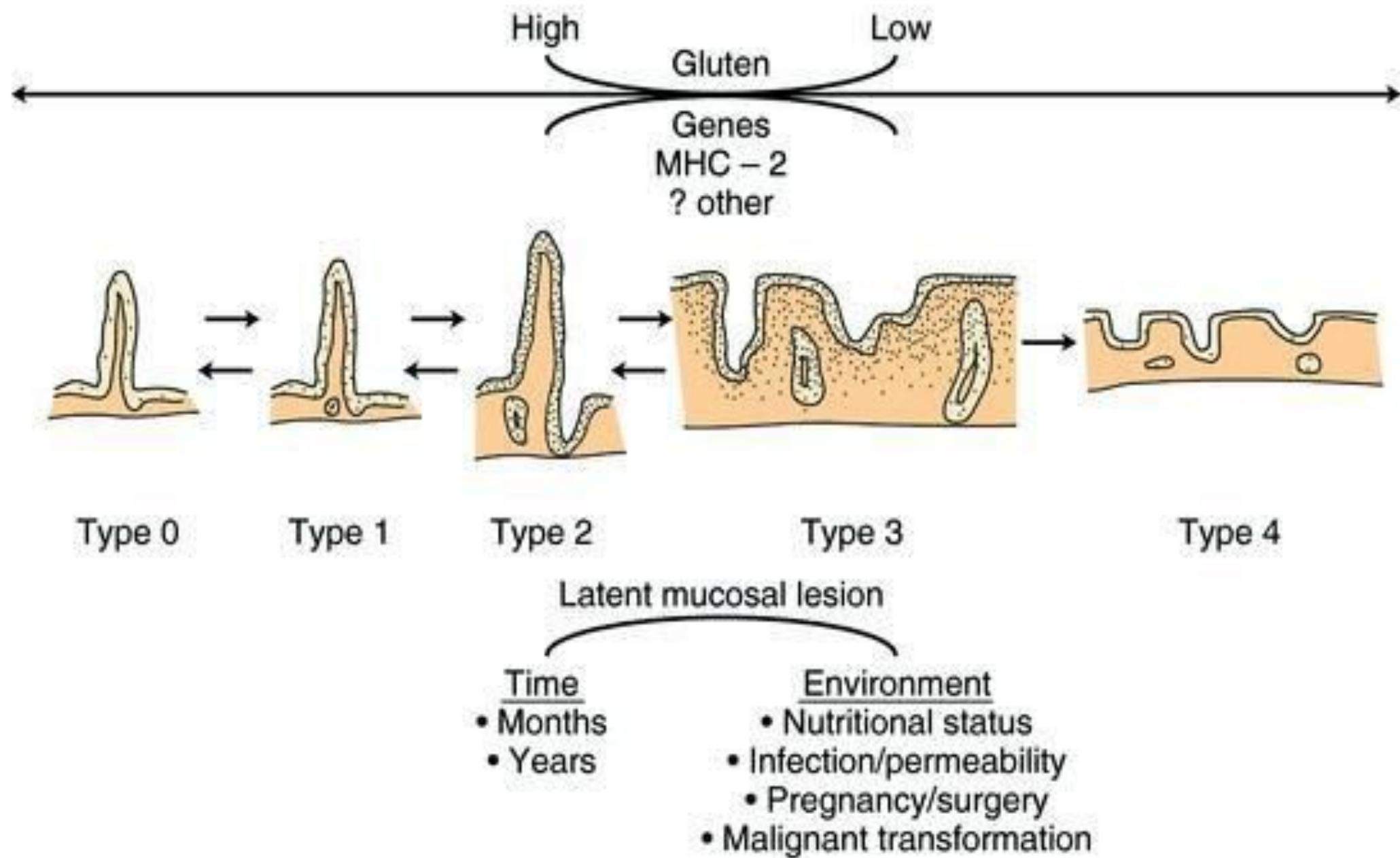
The Celiac Iceberg



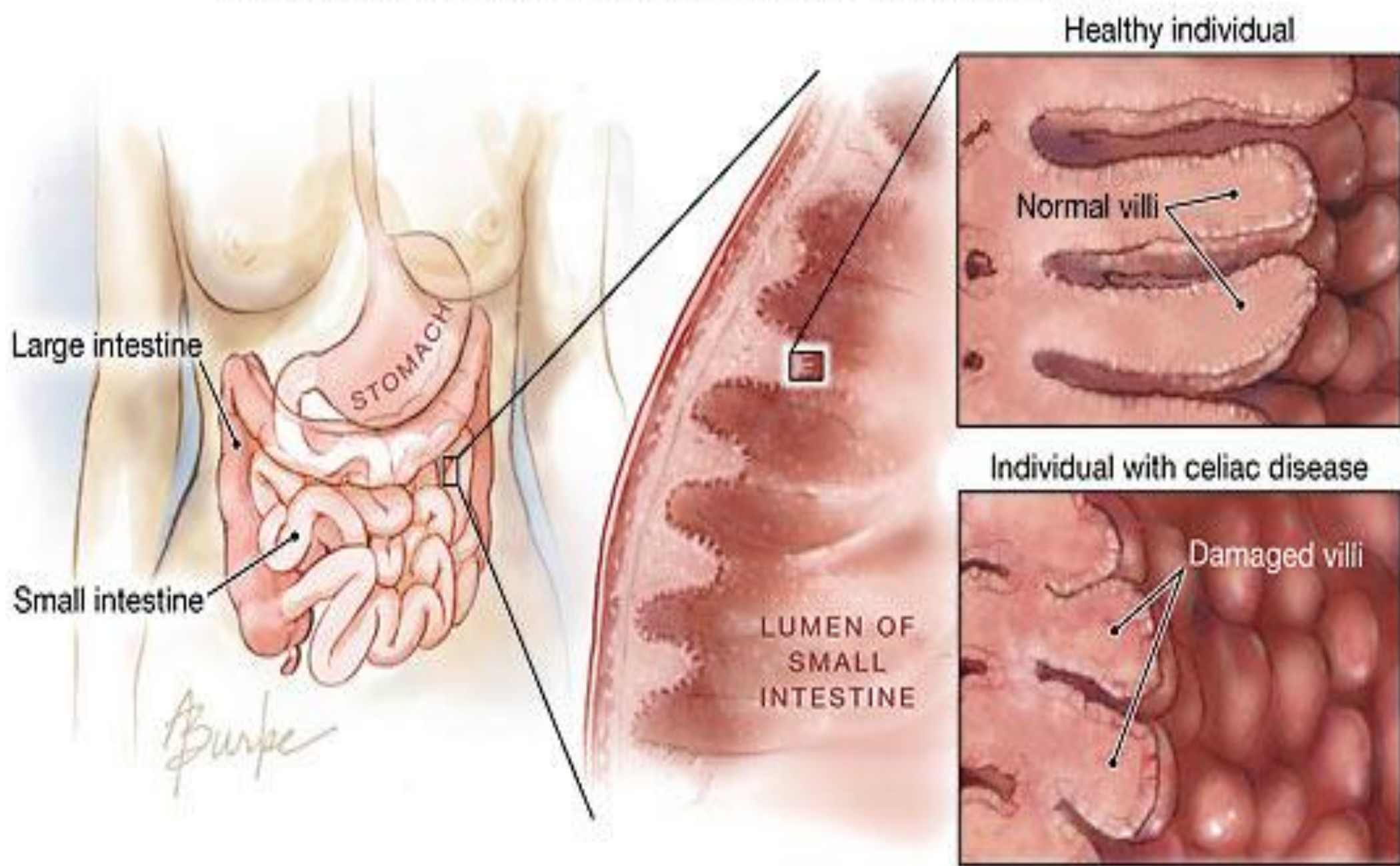
The Prevalence of Celiac Disease

Country	Prevalence
Italy	1:200
Hungary	1:85
Scandinavian	1:99
Brazil	1:281
Germany	1:500
U.S.A	1:500
England	1:77
<i>Israel</i>	1:157

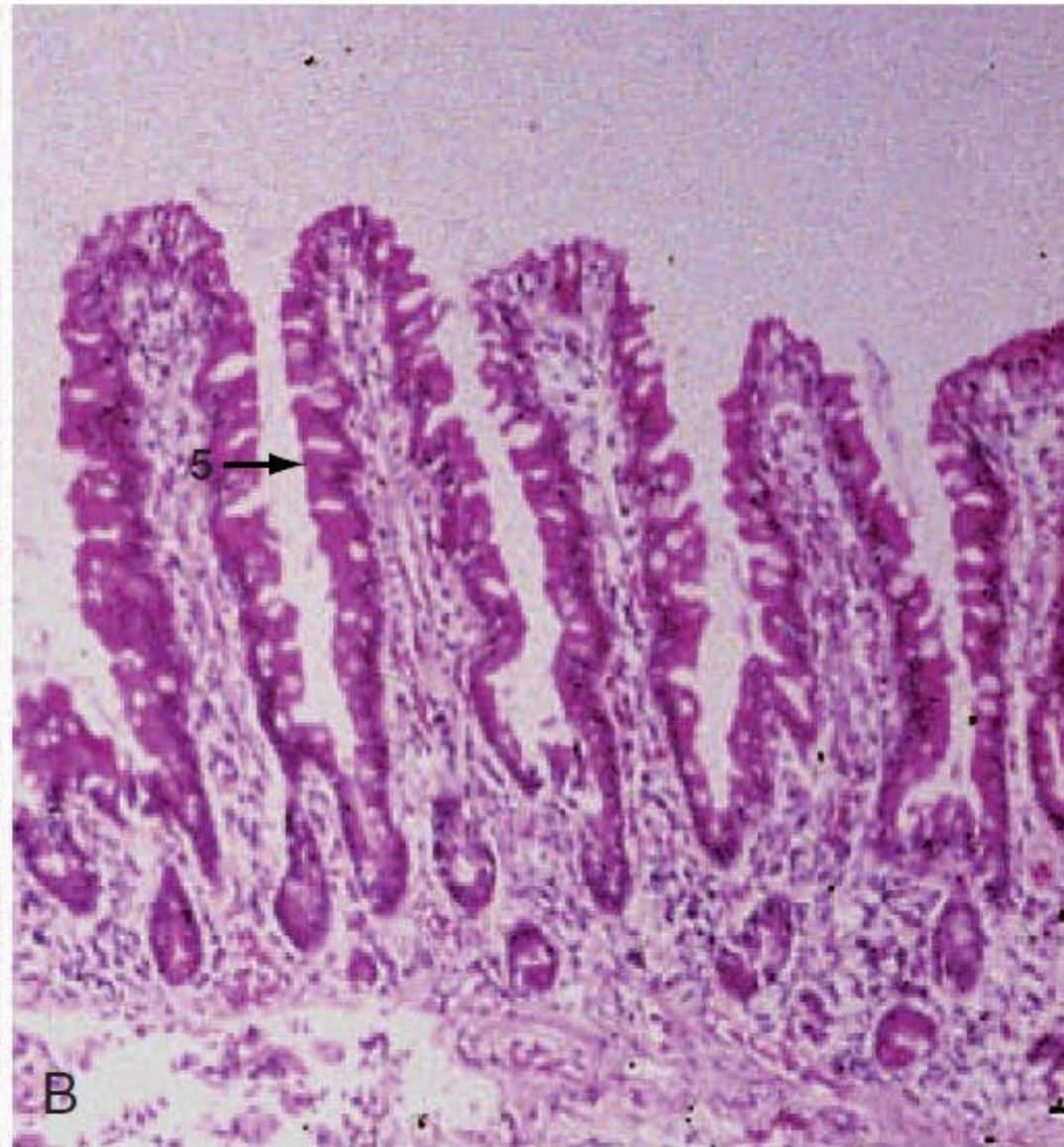
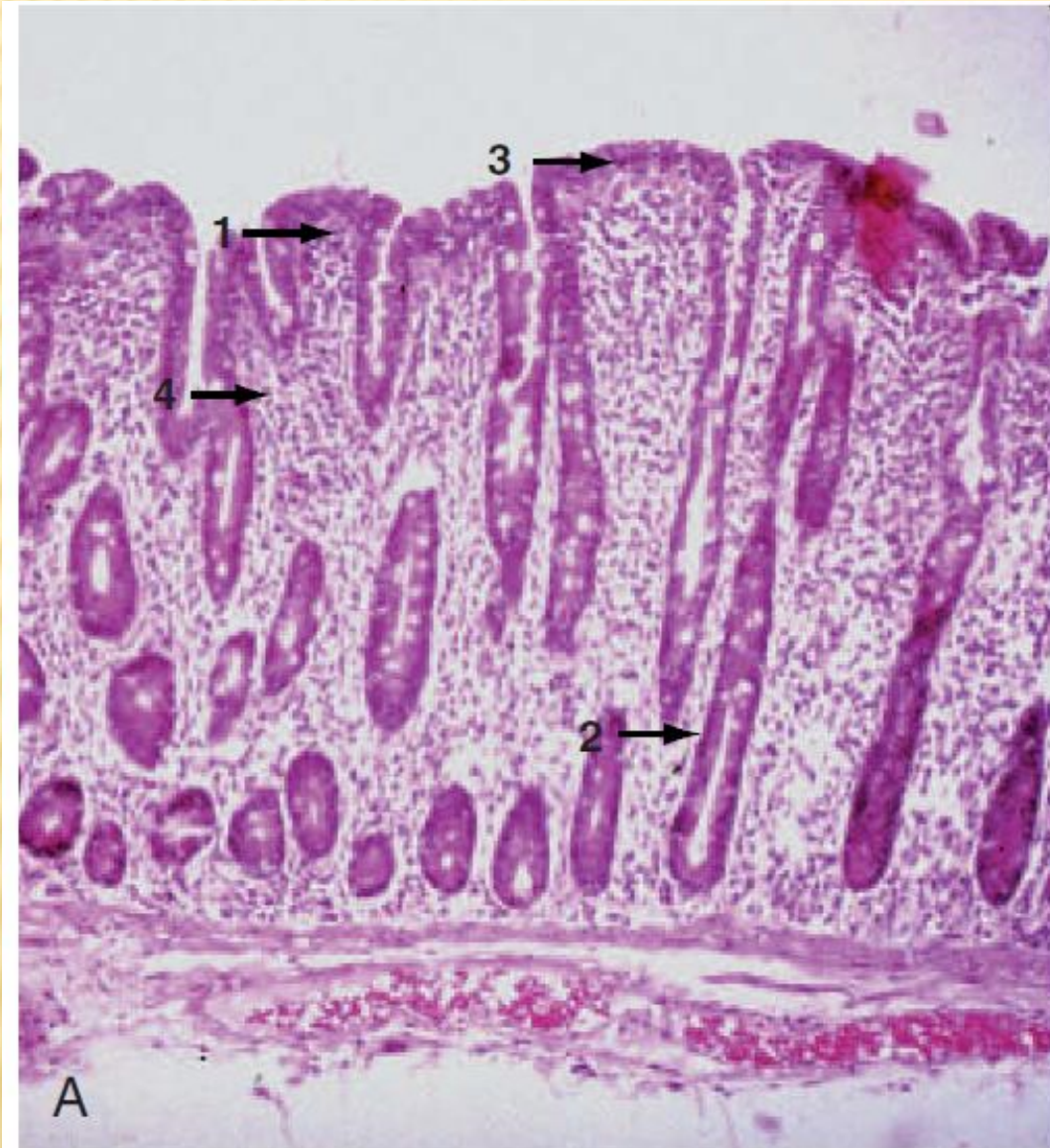




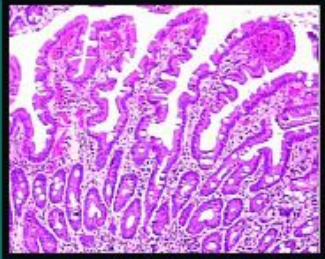
Appearance of Healthy Intestinal Villi and Villi in Celiac Disease



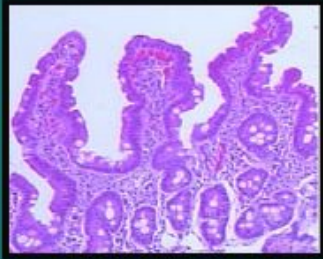
Mucosal Pathology in Celiac Disease



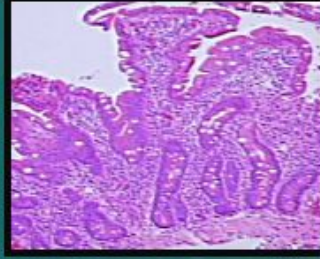
Modified Marsh Score



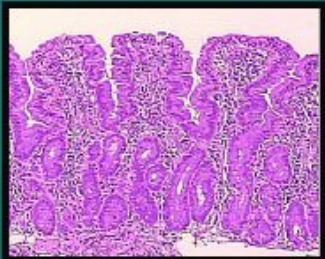
Normal 0



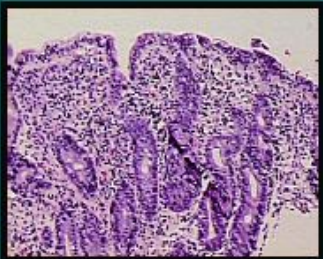
Infiltrative 1



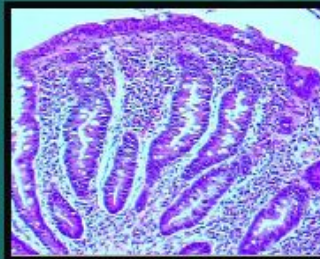
Hyperplastic 2



Partial atrophy 3a



Subtotal atrophy 3b



Total atrophy 3c

Marsh grade	Histological features
0	Normal mucosa
1	Increased number of intra-epithelial lymphocytes, usually exceeding 20 per 100 enterocytes
2	Proliferation of the crypts of Lieberkuhn
3	Variable villous atrophy
3a	Partial villous atrophy
3b	Subtotal villous atrophy
3c	Total villous atrophy
4	Hypoplasia of the small bowel architecture

Clinical Manifestation

- Abdominal pain
- Diarrhea, constipation
- Gassiness, distention, bloating
- Anorexia
- Poor weight gain, FTT
- Irritability, lethargy
- Anemia, fatigue
- Vitamin deficiencies
- Muscle wasting
- Osteopenia
- Short stature
- Recurrent abortions / infertility
- Delayed puberty
- Dental enamel hypoplasia
- Dermatitis Herpetiformis
- Aphthous ulcers



Как проявляется целиакия у взрослых:

Неврологический аппарат

Раздражительность, тревожность

Ротовая полость

Изъязвления в углах рта
Травмы в полости рта

Желудочно-кишечный тракт

Диарея и запоры
Спазмы и абдоминальный отёк
Рвота
Зловонный кал

Кожа

Герпетиформный дерматит

Двигательный аппарат

Боли в суставах
Остеопороз

Системные симптомы

Анемия
Потеря веса
Задержка жидкостей
Склонность к кровотечениям

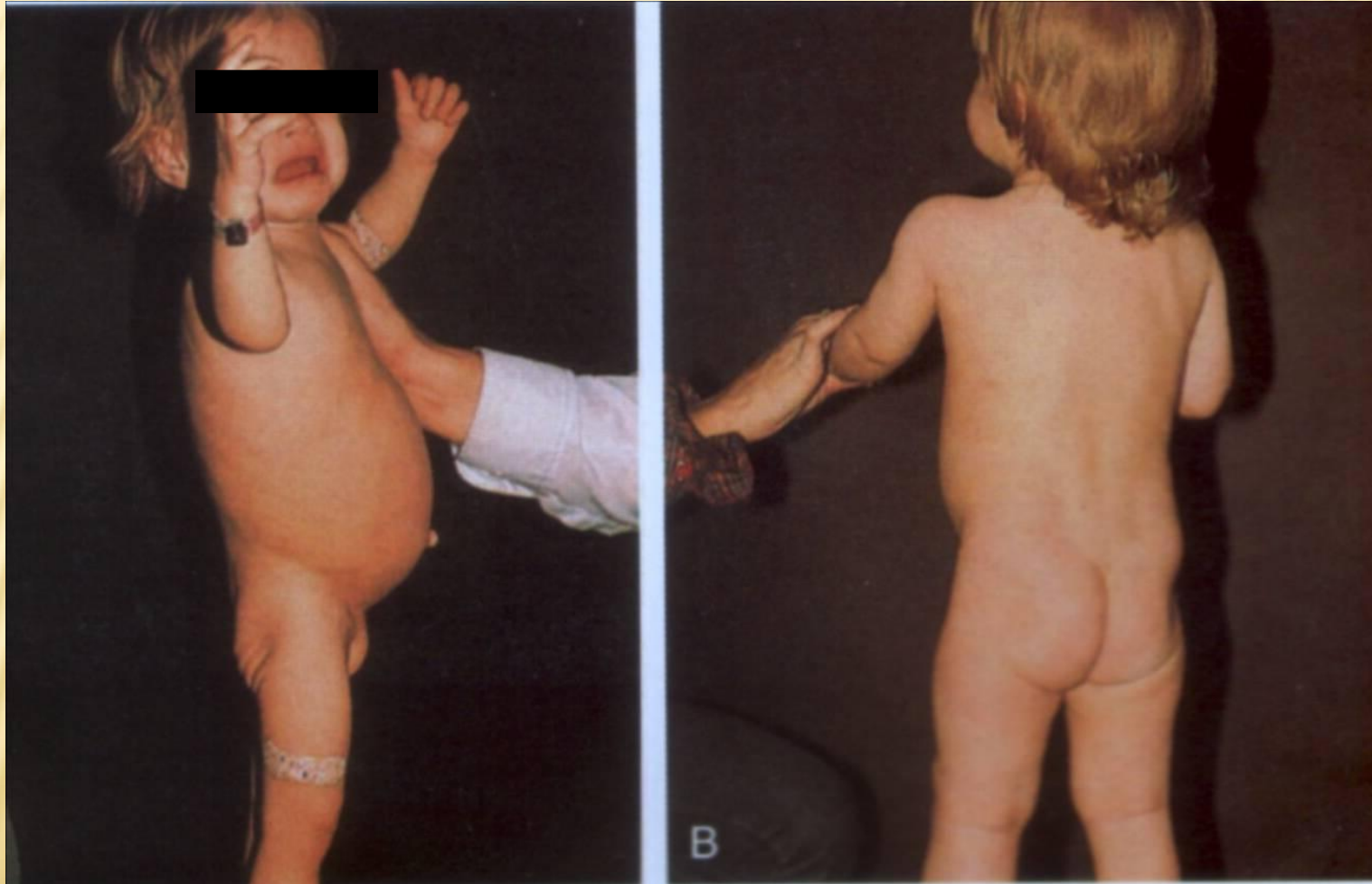




Extraintestinal Manifestations of Celiac Disease

MANIFESTATION	PROBABLE CAUSE(S)
Cutaneous	
Ecchymoses and petechiae	Vitamin K deficiency; rarely, thrombocytopenia
Edema	Hypoproteinemia
Dermatitis herpetiformis	Unknown
Follicular hyperkeratosis and dermatitis	Vitamin A malabsorption, vitamin B complex malabsorption
Endocrinologic	
Amenorrhea, infertility, impotence	Malnutrition, hypothalamic-pituitary dysfunction
Secondary hyperparathyroidism	Calcium and/or vitamin D malabsorption causing hypocalcemia
Hematologic	
Anemia	Iron, folate, vitamin B ₁₂ , or pyridoxine deficiency
Hemorrhage	Vitamin K deficiency; rarely, thrombocytopenia due to folate deficiency
Thrombocytosis, Howell-Jolly bodies	Hyposplenism
Hepatic	
Elevated liver biochemical test levels	Unknown
Muscular	
Atrophy	Malnutrition due to malabsorption
Tetany	Calcium, vitamin D, and/or magnesium malabsorption
Weakness	Generalized muscle atrophy, hypokalemia
Neurologic	
Peripheral neuropathy	Deficiencies of vitamins such as vitamin B ₁₂ and thiamine
Ataxia	Cerebellar and posterior column damage
Demyelinating central nervous system lesions	Unknown
Seizures	Unknown
Skeletal	
Osteopenia	Malabsorption of calcium and vitamin D
Osteoarthropathy	Unknown
Pathologic fractures	Osteopenia

GLUTEN DIET AFTER GFD FOR 10 WEEKS



Population at Risk for Celiac Disease

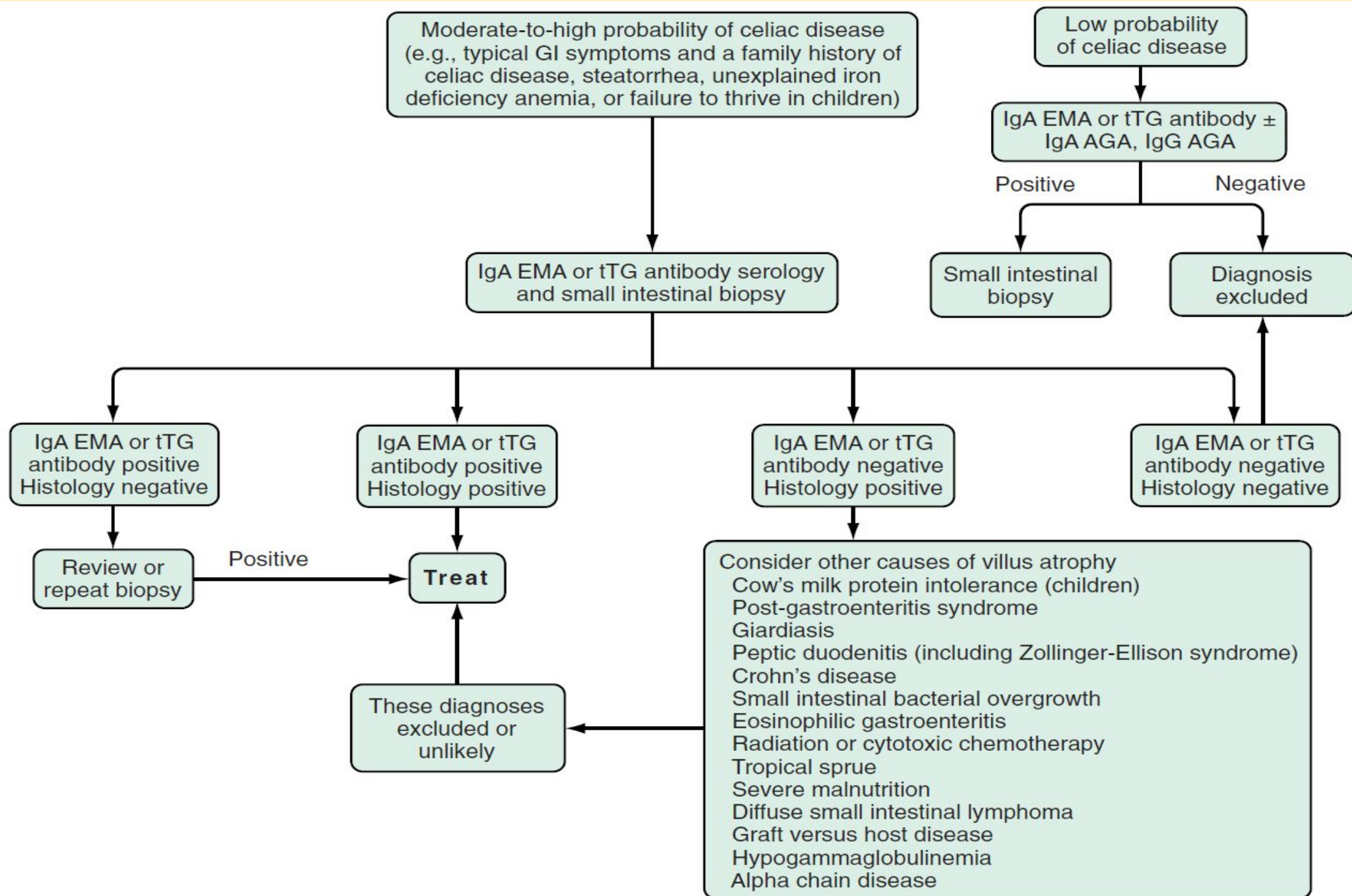
- First Degree relatives
- Chromosomal abnormalities
 - Trisomy 21
 - Turner syndrome
 - Williams syndrome
- Autoimmune disorders (DM I, Hashimoto, Graves...)

Disorders Associated with Celiac Disease

- Dermatitis herpetiformis (100 %)
- Diabetes mellitus type 1 (5-10 %)
- Down syndrome (7-19%)
- Immunoglobulin A deficiency (7%)
- Inflammatory bowel disease
- Microscopic colitis
- Hypothyroidism or hyperthyroidism
- Immunoglobulin A mesangial nephropathy
- Idiopathic pulmonary hemosiderosis
- Recurrent pericarditis
- Rheumatoid arthritis
- Sarcoidosis
- Epilepsy with cerebral calcification
- Fibrosing alveolitis
- Bird-fancier's lung

DIAGNOSIS

- ❑ Small intestine biopsy AND improvement of histological finding after gluten-free diet (GFD)
 - ❑ Increase in IEL
 - ❑ Villi disappearance or reduced height
 - ❑ Cellular cuboidal appearance
 - ❑ Increase in lymphocytes, plasma cells in the lamina propria
- ❑ Changes may be seen in: Crohn's disease, Tropical sprue, Milk protein allergy, Lymphoma, Bacterial overgrowth etc.
- ❑ Autoantibodies should also disappear after GFD



The Importance of Early Diagnosis

- 1. Osteoporosis**
- 2. Decreased height**
- 3. Malignancy (lymphoma)**
- 4. Autoimmune diseases**

Maternal Celiac Disease

- ❑ **Intrauterine growth retardation**
- ❑ **Abortion**
- ❑ **Poor outcome of pregnancy**

Paternal Celiac Disease :

- ❑ **Low birth weight**

THERAPY

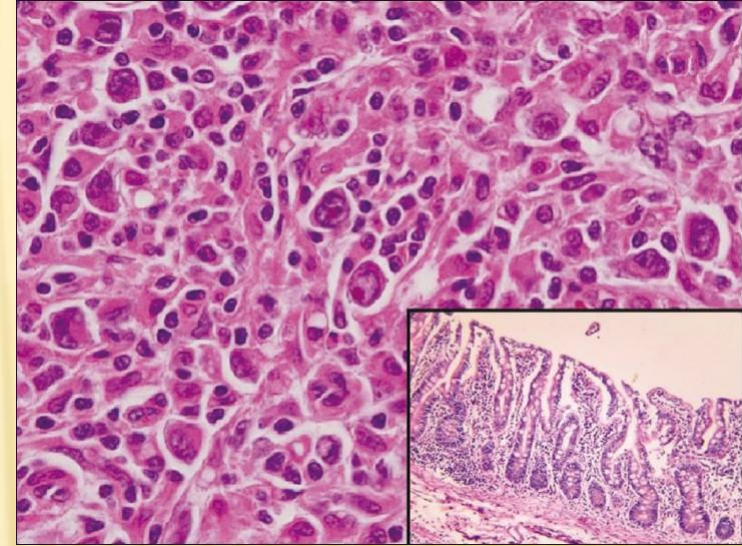
- ❑ Gluten free diet!!
- ❑ Oat up to 40 Gr is permitted
- ❑ Biopsy finding and symptoms with improve
- ❑ Failure to respond
 - ❑ Are you adherent with GFD??
 - ❑ Refractory celiac disease
 - ❑ Allergy to other proteins
 - ❑ Response to corticosteroids
 - ❑ True refractory sprue ❑ t-cell lymphoma



COMPLICATIONS

❑ **Cancer**

- ❑ T Cell lymphoma
 - ❑ sudden loss of response to GFD
 - ❑ initial non-response to GFD
- ❑ Small bowel carcinoma as well
- ❑ Ulcerations along the small intestine
- ❑ Collagen deposition beneath the basement membrane – collagenous sprue



MANAGEMENT OF CELIAC DISEASE

- ▣ **C**onsultation with a skilled dietitian
- ▣ **E**ducation about the disease
- ▣ **L**ifelong adherence to a gluten-free diet
- ▣ **I**dentification and treatment of nutritional deficiencies
- ▣ **A**ccess to an advocacy group
- ▣ **C**ontinuous long-term follow-up by a multidisciplinary team



