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# Celiac Disease

# History

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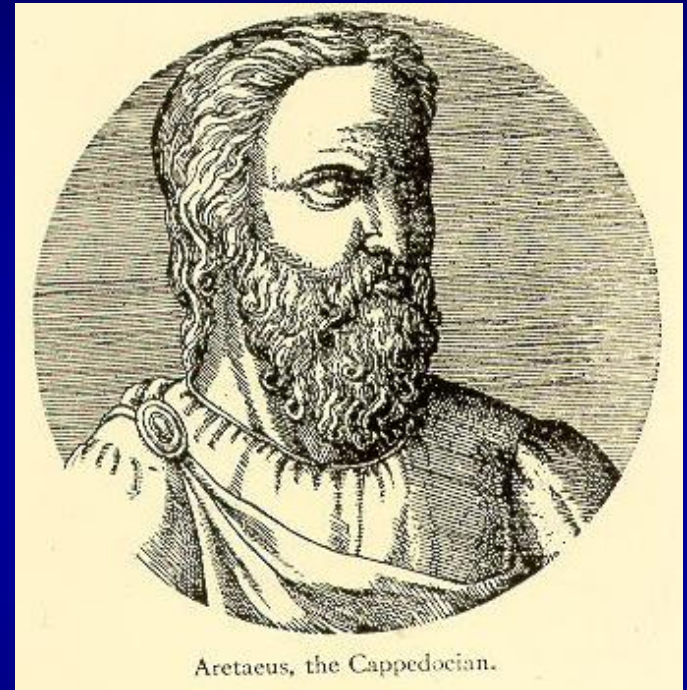
- Aretaeus (2<sup>nd</sup> Century AD) from Cappadocia:

First to describe this entity

- Samuel Gee 1888:

First described the disease in a report entitled  
report entitled

"On the Coeliac Affection"



# Celiac Disease

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- Willem K Dicke:
  - Recognized an association between the consumption of bread and cereals and relapsing diarrhea.
  - This observation was corroborated when, during periods of food shortage in the Second World War, the symptoms of his patients improved once bread was replaced by unconventional, non-cereal containing foods; this finding confirmed the usefulness of earlier, empirical diets that used pure fruit, potatoes, banana, milk, or meat

# Celiac Disease and Diabetes

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- 5 % of patients with type 1 diabetes will develop celiac disease
- Only a minority of type 1 diabetes patients with celiac disease present with typical GI symptoms of food intolerance, food avoidance, gastrointestinal discomfort, and diarrhea.
- More common initial findings include
  - Unpredictable blood glucose measurements
  - Recurrent episodes of hypoglycemia
  - Poor glycemic control
  - Growth failure

Because of erratic intestinal absorption of nutrients

# Gluten-containing diet

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- Wheat
- Rye
- Barley



# Epidemiology

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- Primarily affects whites of northern European ancestry.
- In the at-risk groups, the prevalence of celiac disease was
  - 1:22 in first-degree relatives
  - 1:39 in second-degree relatives
  - 1:56 in symptomatic patients



•1:300 to 1:500 in most countries.

# Pathogenesis



- Genetic factors
  - Frequent intrafamilial occurrence
  - HLA-DQ2 and/or DQ8 gene locus (36%)
  - An association was found with chromosome 15q26 (which contains a type I diabetes susceptibility locus)
  - Non-HLA locus appears to be inherited as an autosomal recessive trait

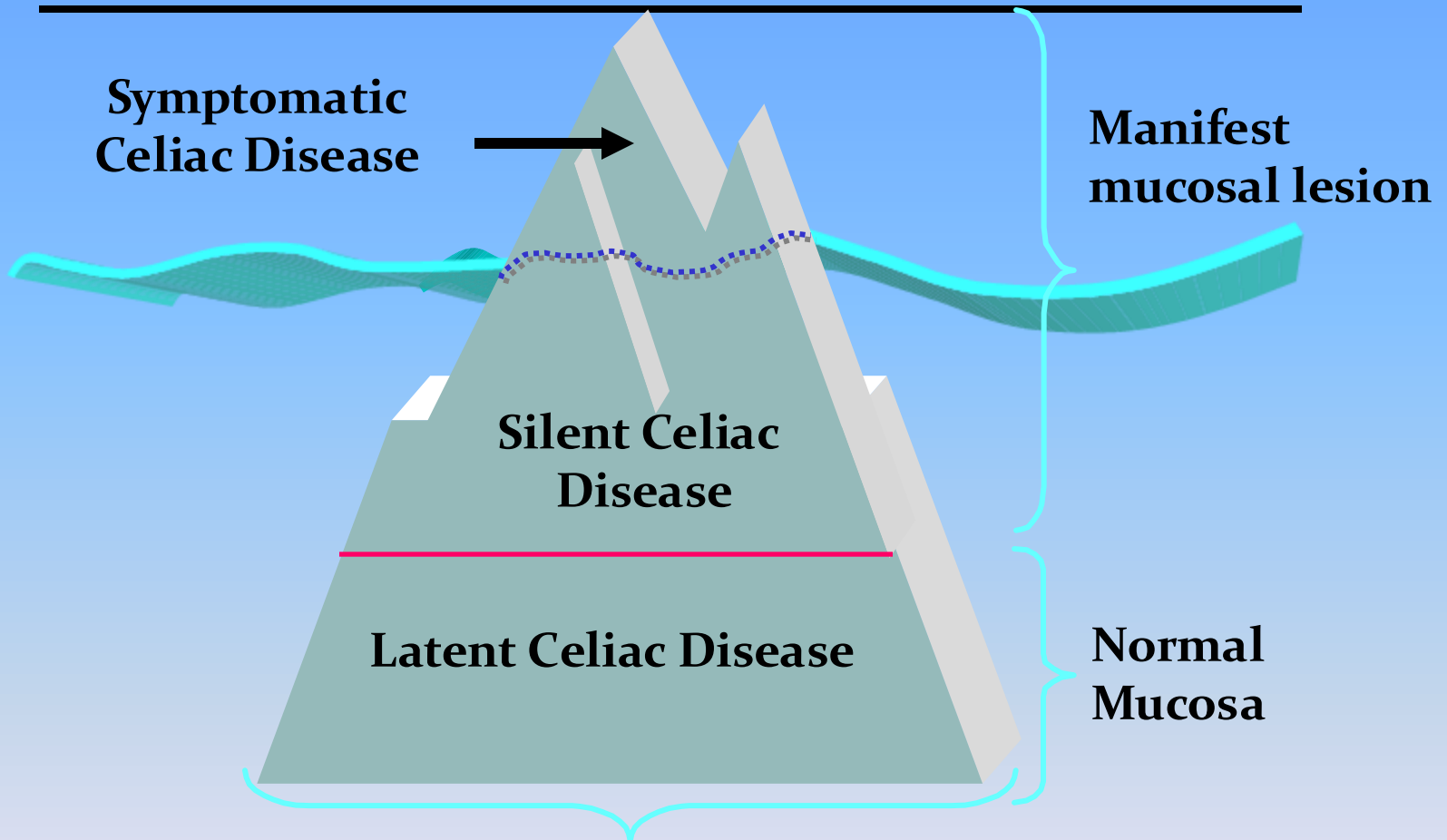


# Classifications

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- Classic disease
- Latent celiac disease
- Potential celiac disease

# The Celiac Iceberg



**Genetic susceptibility: - DQ<sub>2</sub>, DQ<sub>8</sub>**  
**Positive serology**

# Classic celiac disease

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- Three features:
  - Villous atrophy
  - Symptoms of malabsorption such as steatorrhea, weight loss or other signs of nutrient or vitamin deficiency
  - Resolution of the mucosal lesions and symptoms upon withdrawal of gluten-containing foods

# Latent celiac disease

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- Diagnosed at childhood; the patient recovered completely with a gluten-free diet, remaining "silent" even when a normal diet is adopted.
- A normal mucosa was diagnosed at an earlier occasion while ingesting a normal diet, but celiac disease developed later

# Potential celiac disease

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- Never had a biopsy consistent with celiac disease, but show immunologic abnormalities characteristic for the disorder

No true prevalence study till now !



Image © 2005 EarthSat  
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Pointer 31°04'15.20" N 37°10'29.07" E

Streaming ||| ||| ||| ||| ||| ||| ||| ||| 100%

# Clinical Manifestation

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- Classically a disease of infants
- Majority 10 – 40 years of age
- Symptoms
  - Diarrhea with bulky, foul-smelling, floating stools due to steatorrhea, flatulence, and meteorism.
  - Growth failure in children
  - Weight loss
  - Anemia
  - Neurologic disorders from deficiencies of B vitamins
  - Osteopenia from deficiency of vitamin D and calcium.

# Clinical Manifestation

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- Subclinical disease
  - Asymptomatic
  - Non-specific symptoms
  - Fatigue
  - Mood changes
  - Borderline iron deficiency
  - B12 deficiency
  - unexplained elevations in serumaminotransferases



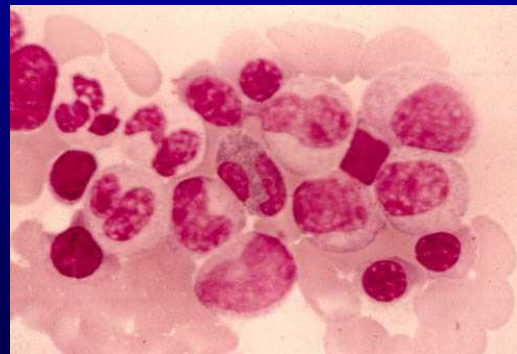
# Clinical Manifestation

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- Neuropsychiatric disease
  - Ataxia
  - Depression
  - Anxiety
  - Epilepsy
  - Idiopathic ataxia
  - Headache

# Clinical Manifestation

- Arthritis
  - 41 % in patients on a regular diet
  - 22 % in those on a gluten-free diet
- Iron deficiency
  - 6 % of patients with iron deficiency anemia have CD
- Metabolic bone disease
- Hyposplenism



# Associated conditions

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- Dermatitis herpetiformis
  - Pruritic papulovesicles over the external surface of the extremities and on the trunk.
  - Biopsy: granular IgA deposits along the subepidermal basement membrane.
  - 24% of CD have DH
  - 85% of DH have CD



# Dermatitis Herpetiformis

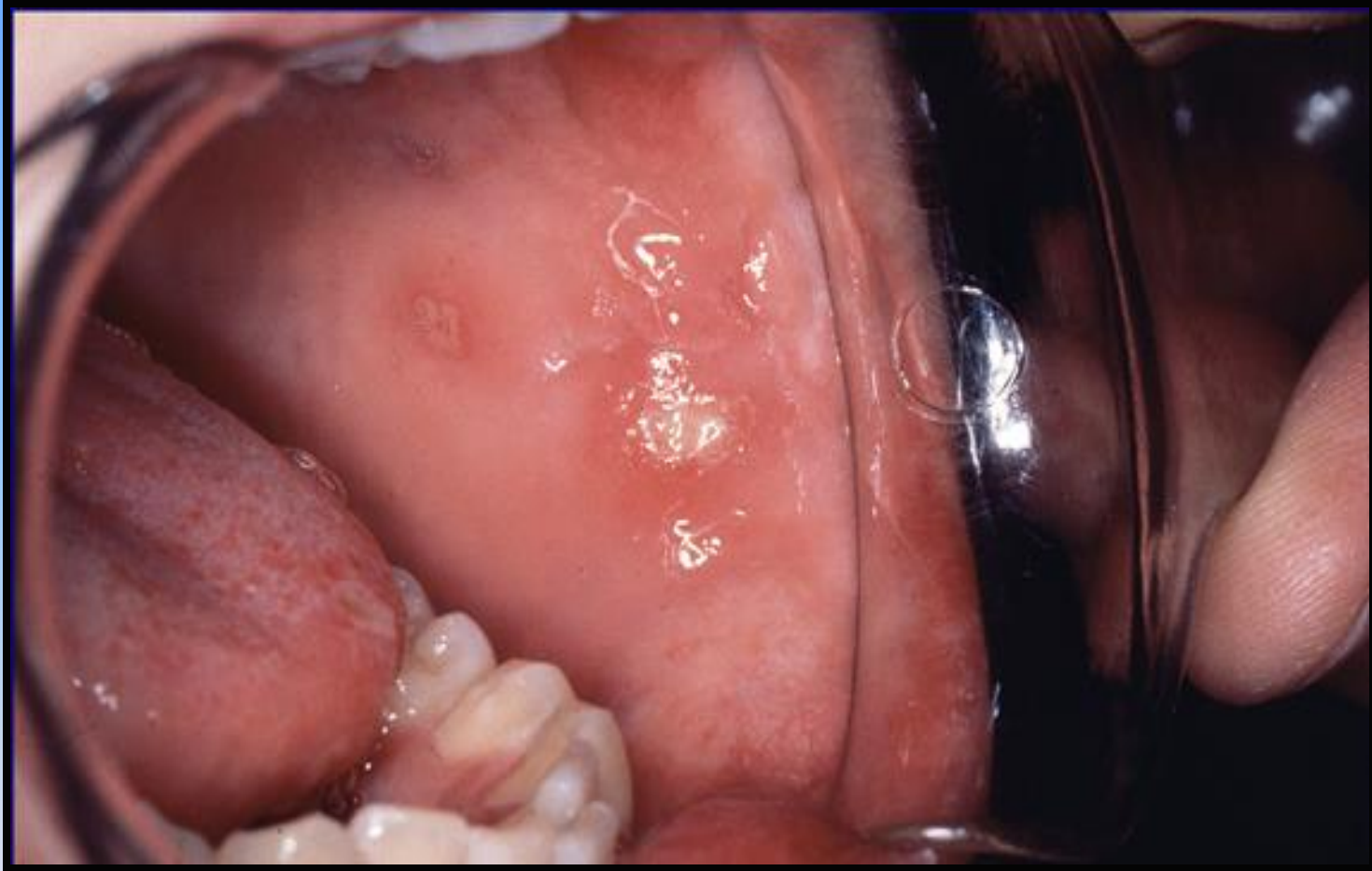
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- Erythematous macule > urticarial papule > tense vesicles
- Severe pruritus
- Symmetric distribution
- 90% no GI symptoms
- 75% villous atrophy
- Gluten sensitive

Garioch JJ, et al. *Br J Dermatol.* 1994;131:822-6.  
Fry L. *Baillieres Clin Gastroenterol.* 1995;9:371-93.  
Reunala T, et al. *Br J Dermatol.* 1997;136-315-8.

# Recurrent Aphthous Stomatitis



*By permission of C. Mulder, Amsterdam (Netherlands)*

# Associated conditions

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- Diabetes mellitus
  - Closely associated with type 1 diabetes mellitus
  - 2.6 and 7.8 % of adults with type 1 diabetes have CD
  - Type 1 diabetes and celiac disease share the genetic loci HLA-DR3, HLA-DQ2, and the IDDM3 locus on chromosome 15q26



# Associated conditions

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- Selective IgA deficiency
- Down syndrome
- Thyroid disease
- Infertility
- Myocarditis and cardiomyopathy
- Liver disease



# **Prevalence of Celiac Disease is Higher in Other Autoimmune Conditions**

|                                    |            |
|------------------------------------|------------|
| Type 1 Diabetes Mellitus:          | 3.5 - 10%  |
| Thyroiditis:                       | 4 - 8%     |
| Arthritis:                         | 1.5 - 7.5% |
| Autoimmune liver diseases:         | 6 - 8%     |
| Sjögren's syndrome:                | 2 - 15%    |
| Idiopathic dilated cardiomyopathy: | 5.7%       |
| IgA nephropathy:                   | 3.6%       |



# Genetic Disorders

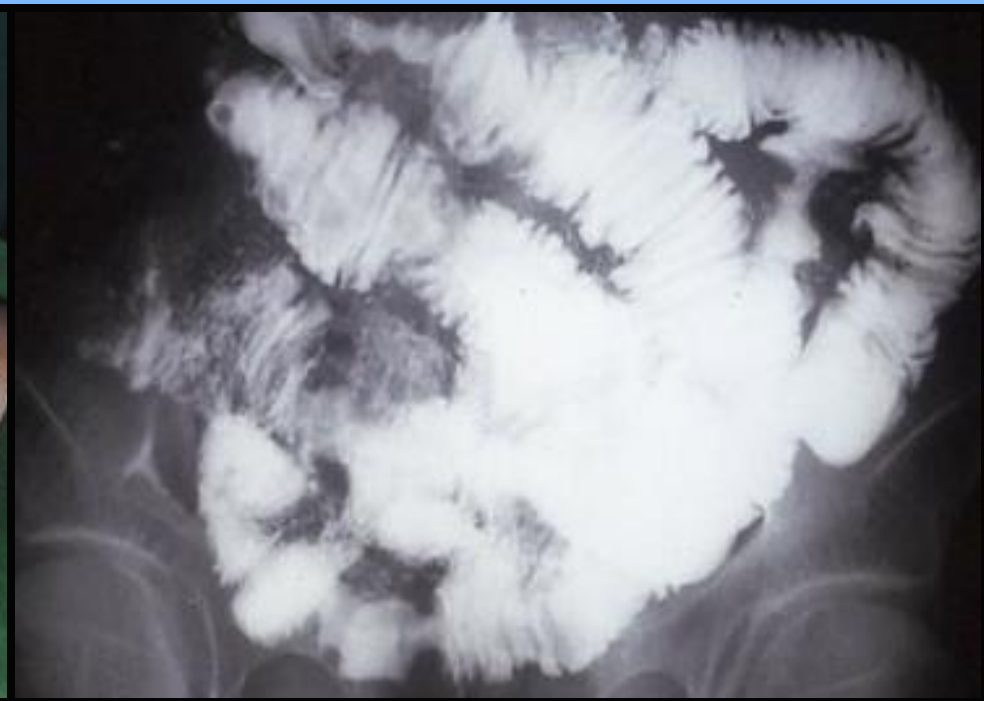
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- **Down Syndrome: 4-19%**
- **Turner Syndrome: 4-8%**
- **Williams Syndrome: 8.2%**
- **IgA Deficiency: 2-3% Can complicate serologic screening**

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- The importance of recognizing Celiac:
    - The danger of malignancy.
    - The presence of unsuspected nutritional deficiencies.
    - The association with low-birth weight infants in affected mothers.
    - The occurrence of autoimmune disorders.

# Intestinal Lymphoma

## ~~Celiac Disease Complicated by Enteropathy-Associated T-cell Lymphoma (EATL)~~



*By permission of G. Holmes, Derby (UK)*

# Who should be screened for Celiac ?

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- Those with gastrointestinal symptoms including:
  - Chronic diarrhea
  - Malabsorption
  - Weight loss
  - Abdominal distension.
- Individuals without other explanations for signs and symptoms:
  - Persistent elevation in serum aminotransferases
  - Short stature
  - Delayed puberty
  - Iron-deficiency anemia
  - Recurrent fetal loss
  - Infertility.

# Who should be screened for Celiac ?

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- Those at high risk for celiac disease including:
  - Patients with type 1 diabetes mellitus
  - Autoimmune endocrinopathies
  - First-and second-degree relatives of individuals with celiac disease
  - Turner, Down, or Williams syndromes.
- Selective refractory cases:
  - Irritable bowel syndrome
  - Persistent aphthous stomatitis
  - Autoimmune diseases
  - Peripheral neuropathy
  - Cerebellar ataxia
  - Dental enamel hypoplasia

# Antibodies Testing

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|  | Sensitivity | Specificity |
|--|-------------|-------------|
| IgA endomysial antibodies              | 85-98%      | 97-100%     |
| IgA tissue transglutaminase antibodies | 90-98%      | 95-97%      |
| IgA antigliadin antibodies             | 80-90%      | 85-95%      |
| IgG antigliadin antibodies             | 75-85%      | 75-90%      |



# Small bowel biopsy

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- Mucosal inflammation
- Villous atrophy
- Crypt hyperplasia

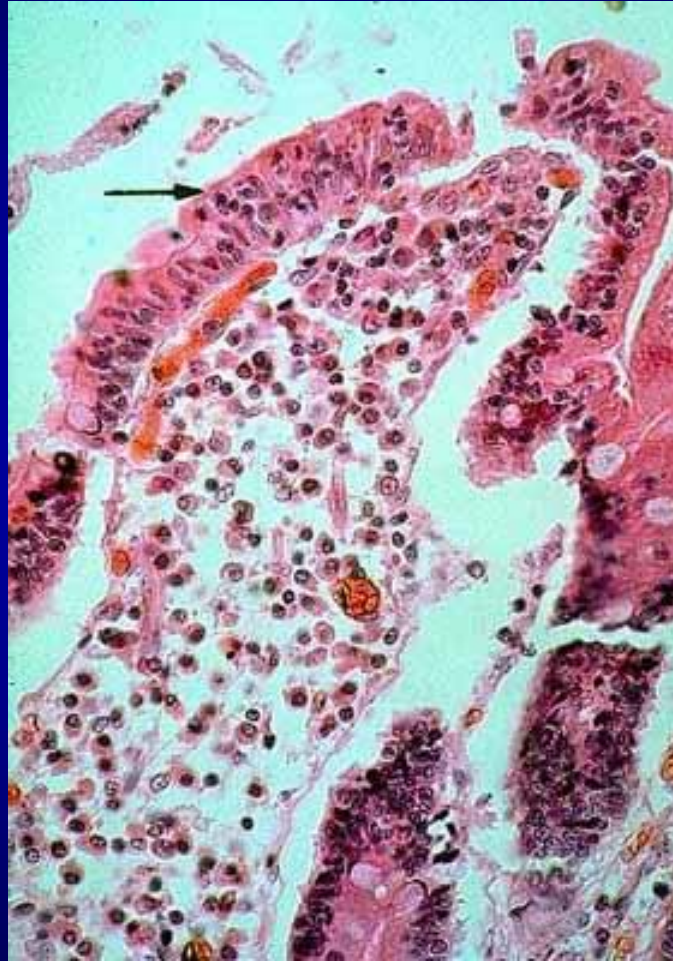


- Biopsy should be repeated after 3-6 months on Gluten-free diet









# Management

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- Consultation with a skilled dietitian
- Education about the disease
- Life long adherence to a gluten-free diet
- Identification and treatment of nutritional deficiencies
- Access to an advocacy group
- Continuous long-term follow-up by a multidisciplinary team



