Coeliac Disease

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What is gluten

- Complex of water insoluble proteins from wheat, rye, barley.

Definition

- Chronic immune mediated enteropathy
- Genetically predisposed individuals
- Precipitated by exposure to gluten

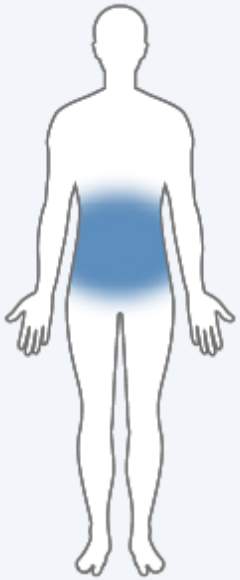
Varied Presentations

- This may account for the reason why the diagnosis is missed so often.

Clinical presentation

- Diarrhoea /Steatorrhoea / Bloating / Flatulence / Weight loss
- Abdominal cramping and pain after cereals
- Failure to thrive and short stature
- Iron deficiency anaemia

Classical manifestation

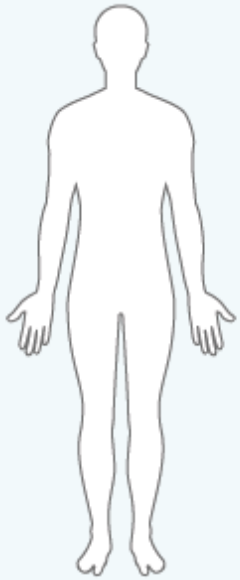


- Chronic diarrhoea
- Poor appetite
- Weight loss
- Abdominal distension
- Poor nutritional status
- Coeliac crisis

Non-classical form

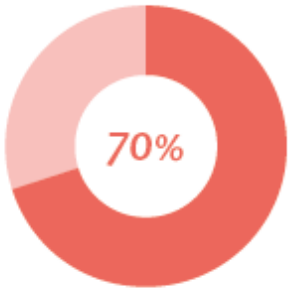
- Recurrent abdominal pain
- Bloating
- Diarrhoea or constipation
- Persistent iron deficiency
- Chronic fatigue
- Hypertransaminasemia
- Short stature
- Dermatitis herpetiformis
- Nutritional deficiencies
- Arthralgia or arthritis
- Alopecia
- Recurrent stomatitis
- Defects in dental enamel

Subclinical CD



- Displays no clinical manifestations, and is most commonly identified via screening programmes
- Although disease is asymptomatic, damage to the intestine still occurs

CD is still largely underdiagnosed



of cases escape diagnosis and treatment, on average

Types of coeliac disease

- Classical disease: Malabsorption, diarrhoea, steatorrhoea, weightloss, nutritional deficiencies
- Non-classical coeliac disease: Anaemia,fatigue, abdominal bloating, osteoporosis, infertility
- Asymptomatic/silent coeliac disease: positive antibodies and villous atrophy

Types of coeliac disease

- Potential coeliac disease: positive serology and normal villous morphology.
- Non-responsive coeliac disease: ongoing or recurrent symptoms despite 6-12months of a strict gluten free diet.
- Noncoeliac gluten sensitivity: Symptoms or signs that develop after gluten ingestion in a patient where coeliac disease was excluded.

Genetics

- HLA-DQ2 /DQ8 haplotypes
  - Gluten derived gliadin peptides activate mucosal T lymphocytes

Epidemiology

- Western (adults):
  - Europe:Adults 1-2.4% prevalence
  - USA : 0.7%
- Africa (children): 1.9% prevalence
  - Children with diabetes: 10.2%

Properties of wheat

- 4 main proteins
  - Prolamins (gliadins)
  - Glutenins
  - Globulins
  - Albumins
- Gluten = Prolamins and glutenins
- Oats contain the same prolamine amino acid sequences as wheat, however in a lower concentration.

MECHANISMS

Wheat gluten is a complex mixture of proteins named gliadins and glutenins

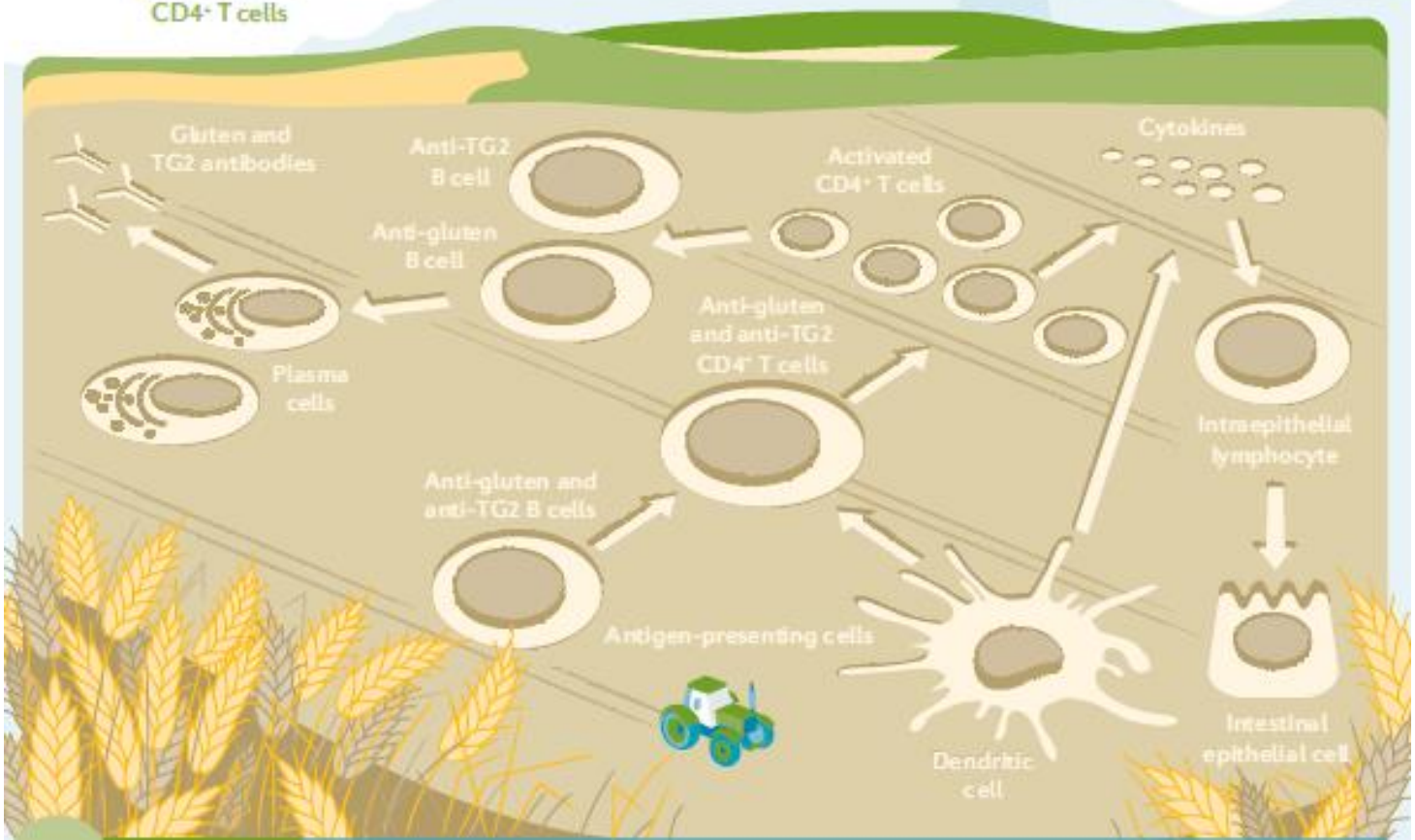
Gliadins and glutenins are resistant to gastrointestinal proteolytic processing, leading to the generation of long gluten peptides

Gluten peptides are deamidated by transglutaminase 2 (TG2), which enhances the binding affinity of gluten peptides to HLA-DQ2 and HLA-DQ8

Activated $CD4^+$ T cells induce production of anti-gluten and anti-TG2 antibodies

Cytokines, such as IL-15, activate intraepithelial lymphocytes to kill intestinal epithelial cells, thus contributing to enteropathy

Gluten peptides presented by HLA on antigen-presenting cells activate gluten-specific $CD4^+$ T cells



Gluten and babies

- Gluten exposure between 4-6months of age reduced the risk of coeliac disease as compared to earlier exposure.
- Recurrent rotavirus infection
- H.pylori colonisation is inversely associated

Manifestation	Probable Cause(s)
CUTANEOUS	
Ecchymoses and petechiae	Vitamin K deficiency; rarely, thrombocytopenia
Edema	Hypoproteinemia
Dermatitis herpetiformis	Epidermal (type 3) tTG autoimmunity
Follicular hyperkeratosis and dermatitis	Vitamin A malabsorption, vitamin B complex malabsorption
ENDOCRINOLOGIC	
Short stature, delayed puberty	Malnutrition, hypothalamic-pituitary dysfunction
Amenorrhea, infertility, impotence	Malnutrition, hypothalamic-pituitary dysfunction, immune dysfunction
Secondary hyperparathyroidism	Calcium and/or vitamin D malabsorption with hypocalcemia
HEMATOLOGIC	
Anemia	Iron, folate, or vitamin B_{12}, deficiency
Hemorrhage	Vitamin K deficiency; rarely, thrombocytopenia due to folate deficiency
Thrombocytosis, Howell-Jolly bodies	Hyposplenism
HEPATIC	
Elevated liver biochemical test levels	Lymphocytic hepatitis
Autoimmune hepatitis	Autoimmunity

MUSCULAR	
Atrophy	Malnutrition due to malabsorption
Weakness	Generalized muscle atrophy, hypokalemia
NEUROLOGIC	
Peripheral neuropathy	Deficiencies of vitamin B_{12} and thiamine; immune-based neurologic dysfunction
Ataxia	Cerebellar and posterior column damage
Demyelinating CNS lesions	Immune-based neurologic dysfunction
Seizures	Unknown
SKELETAL	
Osteopenia, osteomalacia, and osteoporosis	Malabsorption of calcium and vitamin D, secondary hyperparathyroidism, chronic inflammation
Osteoarthropathy	Unknown
Pathologic fractures	Osteopenia and osteoporosis

Coeliac Crisis

- Life threatening
- Diarrhoea leading to severe dehydration, metabolic disturbances and renal impairment.

Diagnosis

- Symptoms
- Serology
- Histology

Coeliac Serology

- Must be taken from an untreated patient before initiation of gluten free diet.
- IgA
- Tissue transglutaminase IgG, (tTg)
- Endomysium antibodies IgG
- Deaminated gliadin peptide
- Anti gliadin antibodies (nonspecific – no longer used)

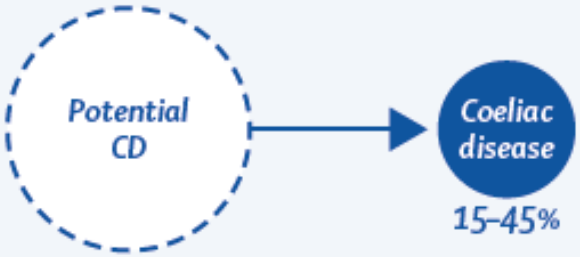
Serology

Serology markers include:

- **IgA anti-transglutaminase 2 (TG2) antibodies.** In people on a gluten-containing diet, IgA class anti-TG2 is highly sensitive and specific for active CD (>95%)
- **IgA anti-endomysial antibodies (EMA).** This second-level test is nearly 100% specific for CD

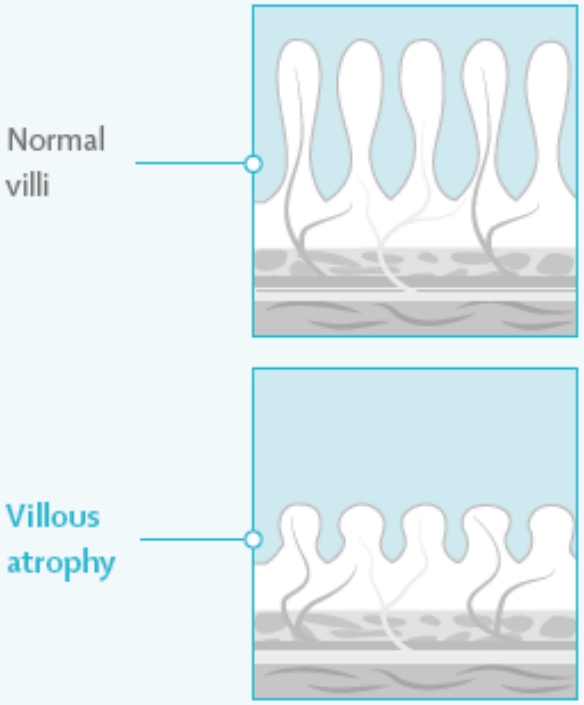
Potential CD

- Positive serology without villous atrophy can be classed as "potential CD"
- **Progression from potential CD to CD occurs in 15% to 45% of cases**



Biopsy

Histological marker: villous atrophy



- **The biopsy can be skipped** in children with an IgA anti-TG2 level >10 times the normal upper limit, and a positive IgA-EMA on a separate blood sample according to European diagnostic guidelines

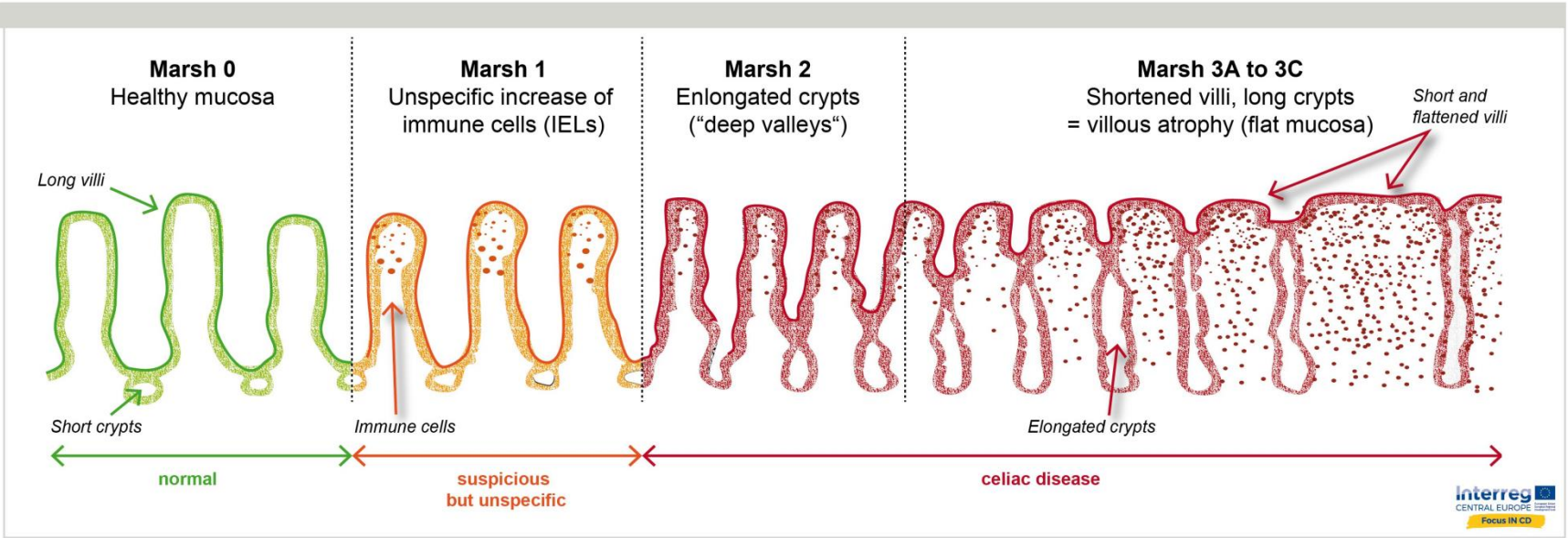
Coeliac serology

- Important Points
  - Total IgA must be measured
  - Main diagnostic antibodies are IgA based TTG and deaminated AGA
  - If IgA deficient then we can use IgG bases TTG and AGA

Pathology

- Characterised by flattening of small intestinal mucosa with
  - absence of villi,
  - Elongation of crypts that open onto flat surface.
  - Thin mucosa
  - Cytoplasmic basophilia, infiltrates of plasma cells and lymphocytes.
  - Increase in lysosomes, reduction in ribosomes.
  - Intraepithelial lymphocytes

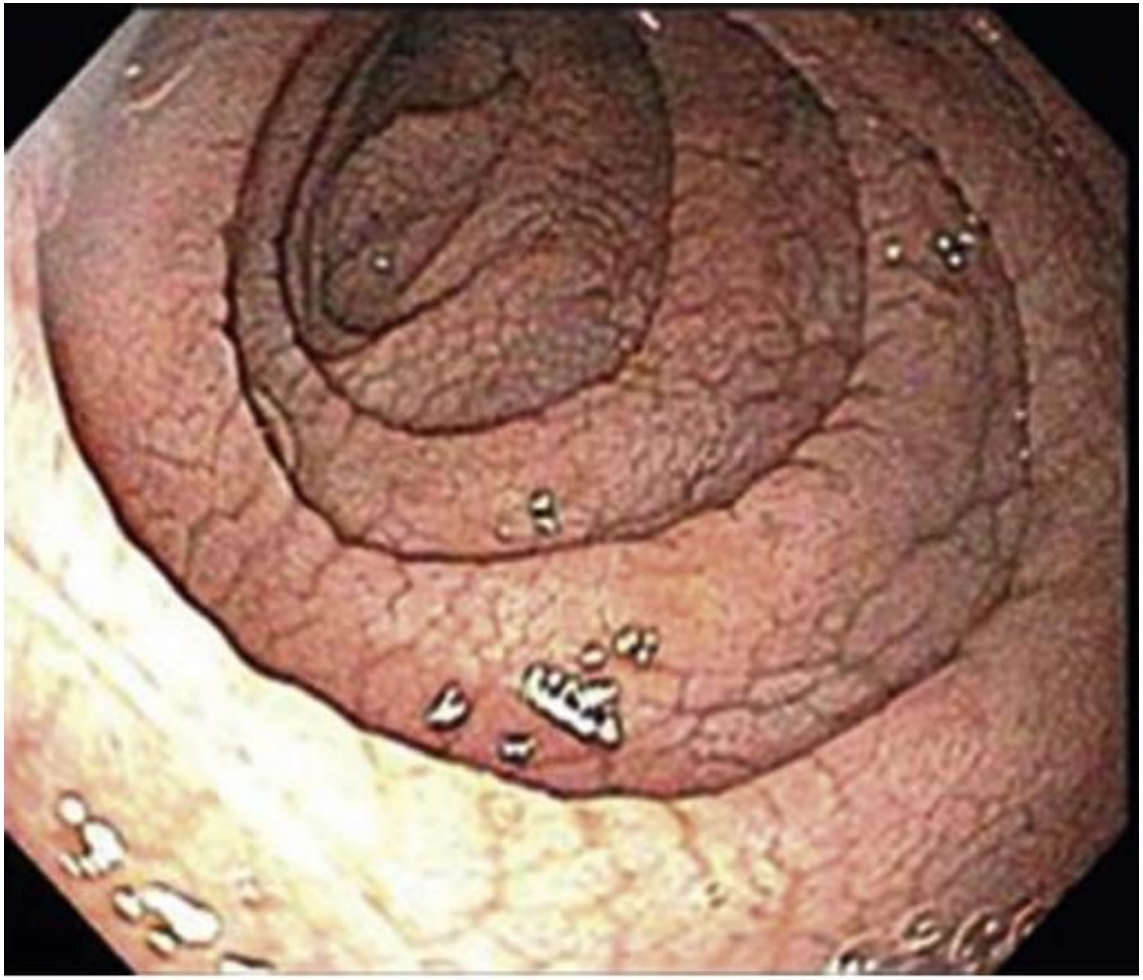
Q-March Classification



Pathology

- The proximal small intestine is almost always more severely affected
- “Ultra-short coeliac disease involves the duodenal bulb only.

Scalloping/absence of duodenal folds



Small intestinal biopsies

- 4-6 Biopsies from 2nd and 3rd parts of duodenum

- Differential for scalloping
  - Eosinophilic enteritis
  - Giardiasis
  - Amyloidosis
  - Tropical sprue
  - HIV enteropathy

Gluten Challenge

- Used in patients who have been on gluten free diet without confirmation of diagnosis
- Avoid in patients who develop severe symptoms after gluten ingestion.

- Increase slowly until consuming 1-2 slices of bread daily.

Differential diagnosis

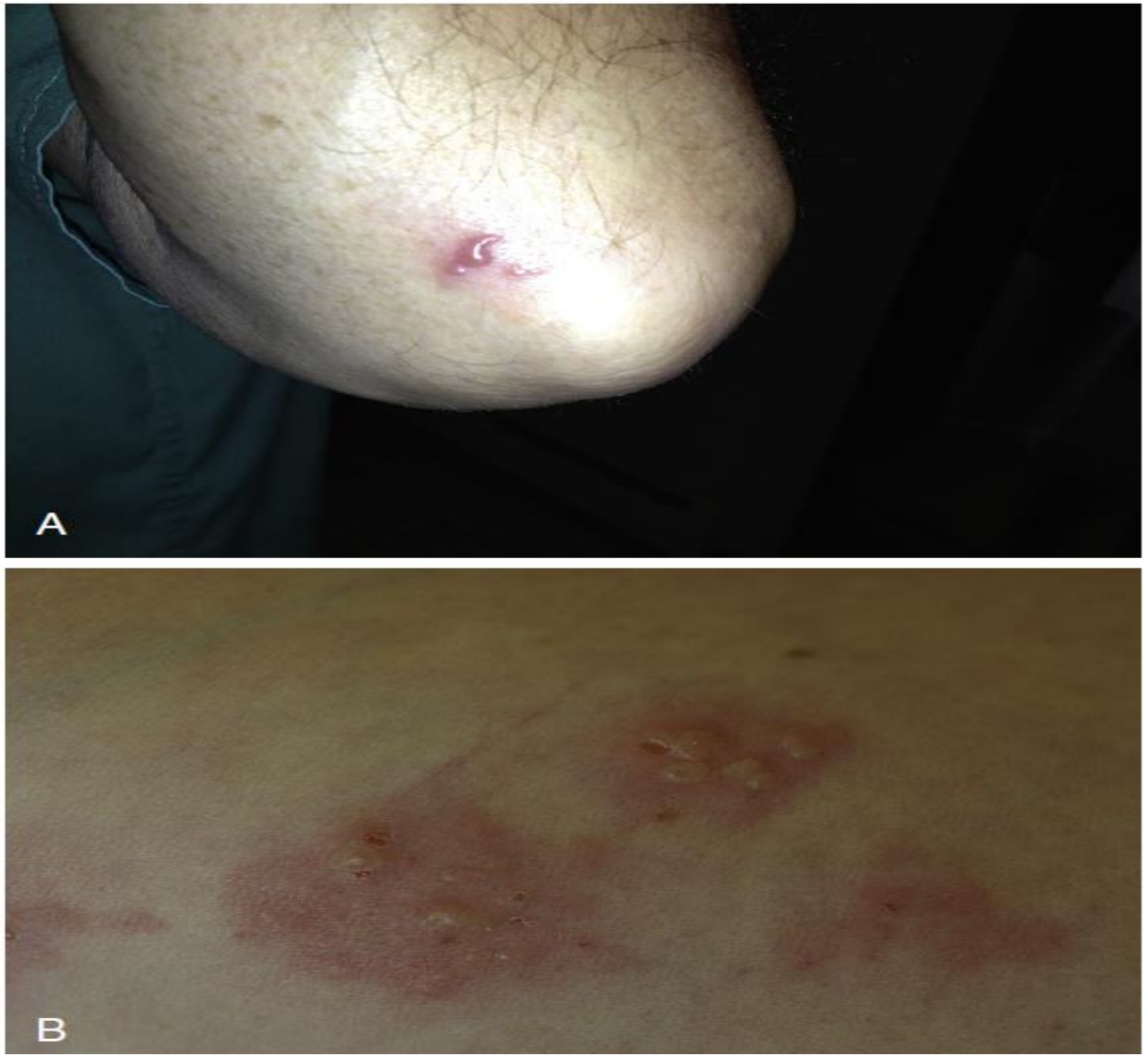
- Malabsorbtion
  - Pancreatic disease
  - Cholestatic liver disease
  - SIBO
  - Terminal ileal disease
- Lactose intolerance
- Infectious
  - Mycobacterium Avium
  - Giardia
  - Parasites
- Whipple disease
- IBS
- Microscopic colitis

Diseases associated with Coeliac disease

ASSOCIATED CONDITIONS

Addison disease
Autoimmune hemolytic anemia
Autoimmune liver diseases
Bird-fancier's lung
Cavitary lung disease
Cystic fibrosis
Dermatitis herpetiformis
Diabetes mellitus type 1
Down syndrome
Epilepsy with cerebral calcification
Fibrosing alveolitis
Hypothyroidism or hyperthyroidism
Idiopathic pulmonary hemosiderosis
Immune thrombocytopenic purpura
Immunoglobulin (Ig)A deficiency
Iridocyclitis or choroiditis
Macroamylasemia
Microscopic colitis
Recurrent pericarditis
Sarcoidosis
Sjögren syndrome

Dermatitis Herpetiformis



Treatment

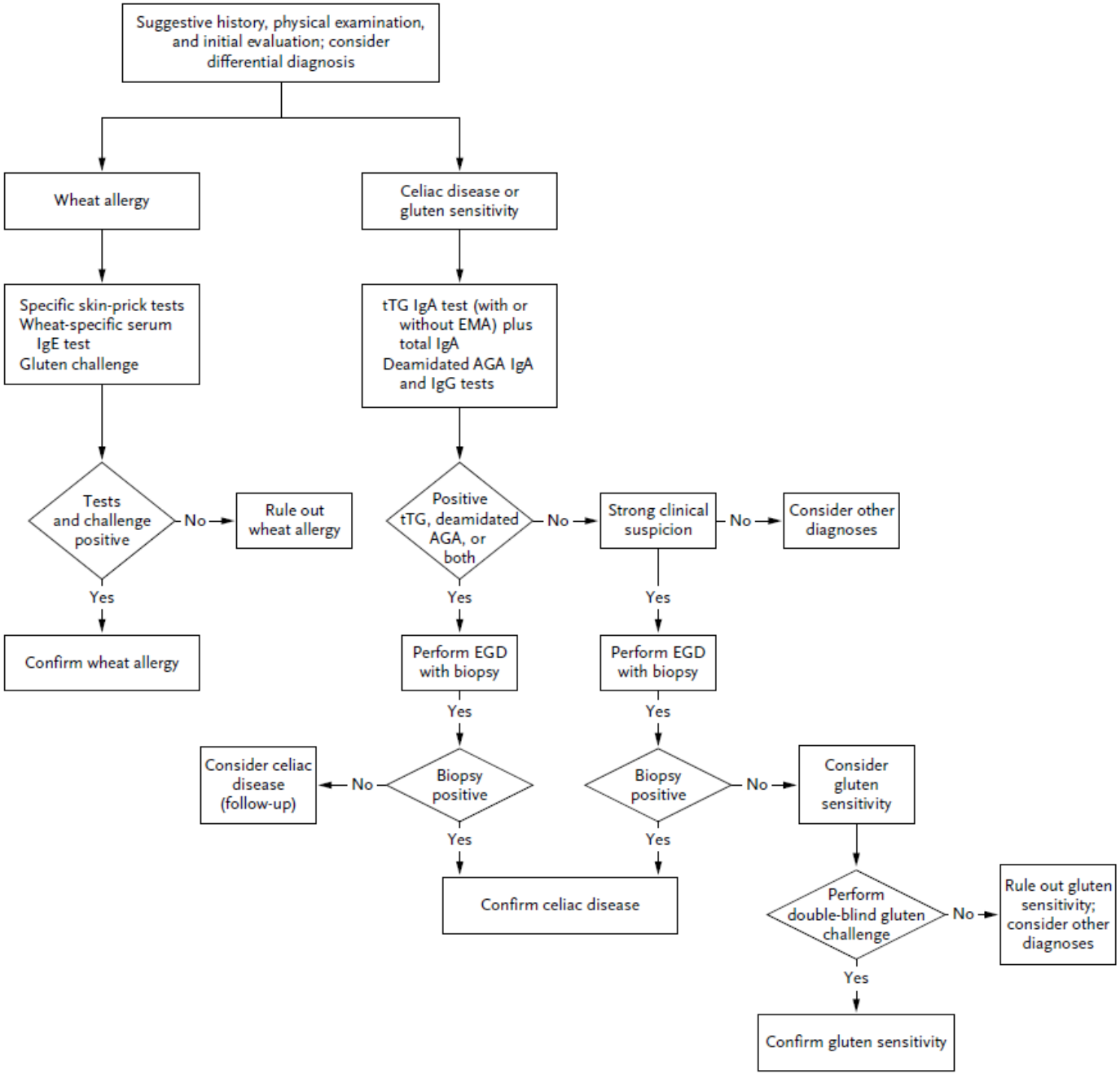
- Gluten free diet
- Supplement
  - VIT D
  - VIT B12
  - Folate
  - VIT K
  - Calcium
- Glucorticoids – reseved for coeliac crisis and refractory coeliac disease

Monitoring

- Bone mineral density one year after therapy
- Repeat biopsies to confirm mucosal healing 2 years after therapy

Complications

- Ulcerative jejunoileitis
- Enteropathy Associated T Cell Lymphoma (EATL)
- Non-Hodgkin lymphoma


Suggestive history, physical examination, and initial evaluation; consider differential diagnosis
Wheat allergy
Celiac disease or gluten sensitivity
Specific skin-prick tests
Wheat-specific serum IgE test
Gluten challenge
tTG IgA test (with or without EMA) plus total IgA
Deamidated AGA IgA and IgG tests
Tests and challenge positive
No
Rule out wheat allergy
Yes
Confirm wheat allergy
Positive tTG, deamidated AGA, or both
No
Strong clinical suspicion
No
Consider other diagnoses
Yes
Yes
Perform EGD with biopsy
Perform EGD with biopsy
Yes
Yes
Consider celiac disease (follow-up)
No
Biopsy positive
Biopsy positive
No
Consider gluten sensitivity
Yes
Yes
Confirm celiac disease
Perform double-blind gluten challenge
No
Rule out gluten sensitivity; consider other diagnoses
Yes
Confirm gluten sensitivity

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