GNB

Pathology lecture

2019

Pathology and mechanisms of malabsorption

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Objectives

Upon completion of this lecture the students will:

1. Understand that the malabsorption is caused by either abnormal digestion or small intestinal mucosal disease
2. Know that malabsorption can affect many organ systems (alimentary tract, hematopoietic system, musculoskeletal system, endocrine system, epidermis, nervous system)
3. Know the following aspects of celiac disease:
    a. definition
    b. pathogenesis
    c. clinical features
    d. pathology (gross and microscopic features)
    e. complications (T-cell lymphoma and GI tract carcinoma)
4. Know the cause and types of Lactose intolerance

Malabsorption Syndrome

Inability of the intestine to absorb nutrients adequately into the blood stream

Impairment can be of single or multiple nutrients depending on the abnormality

Physiology

– The main purpose of the gastrointestinal tract is to digests and absorbs nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, minerals and electrolytes.

Mechanisms and Causes of Malabsorption Syndrome

1. Inadequate digestion

2. Deficient bile salt

3. Primary mucosal abnormalities

4. Inadequate small intestine

5. Lymphatic obstruction

Mechanisms and Causes of Malabsorption Syndrome

Inadequate digestion
- Postgastrectomy
- Deficiency of pancreatic lipase
- Chronic pancreatitis
- Cystic fibrosis
- Pancreatic resection
- Zollinger-Ellison syndrome

Deficient bile salt
- Obstructive jaundice
- Bacterial overgrowth
- Stasis in blind loops, [illegible]cula
- Fistulas
- Hypomotility states (diabetes)
- Terminal ileal resection
- Crohns' disease
- Precipitation of bile salts (neomycin)

Primary mucosal abnormalities
- Celiac disease
- Tropical sprue
- Whipple's disease
- Amyloidosis
- [illegible]adiation enteritis
- Abetalipoproteinemia
- Giardiasis

Inadequate small intestine
- Intestinal resection
- Crohn's disease
- Mesenteric vascular disease with infarction
- Jejunoileal bypass

Lymphatic obstruction
- Intestinal lymphangiectasia
- Malignant lymphoma
- Macroglobulinemia

Pathophysiology

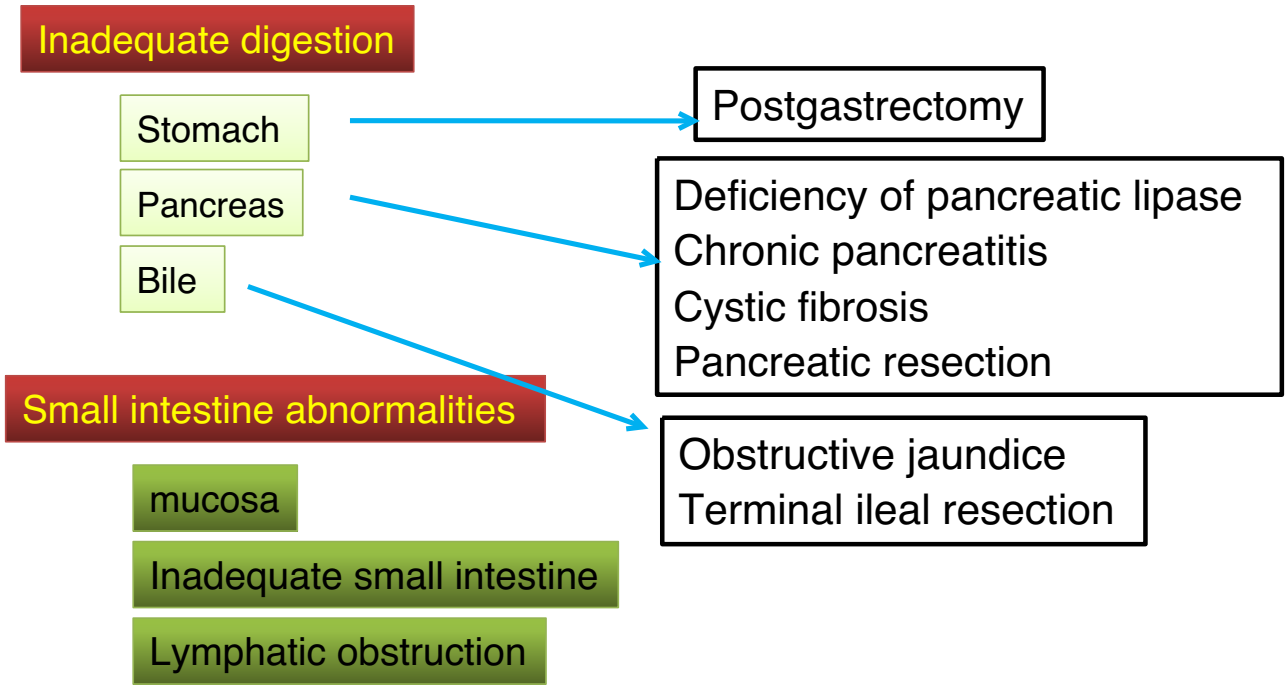
Inadequate digestion

Or

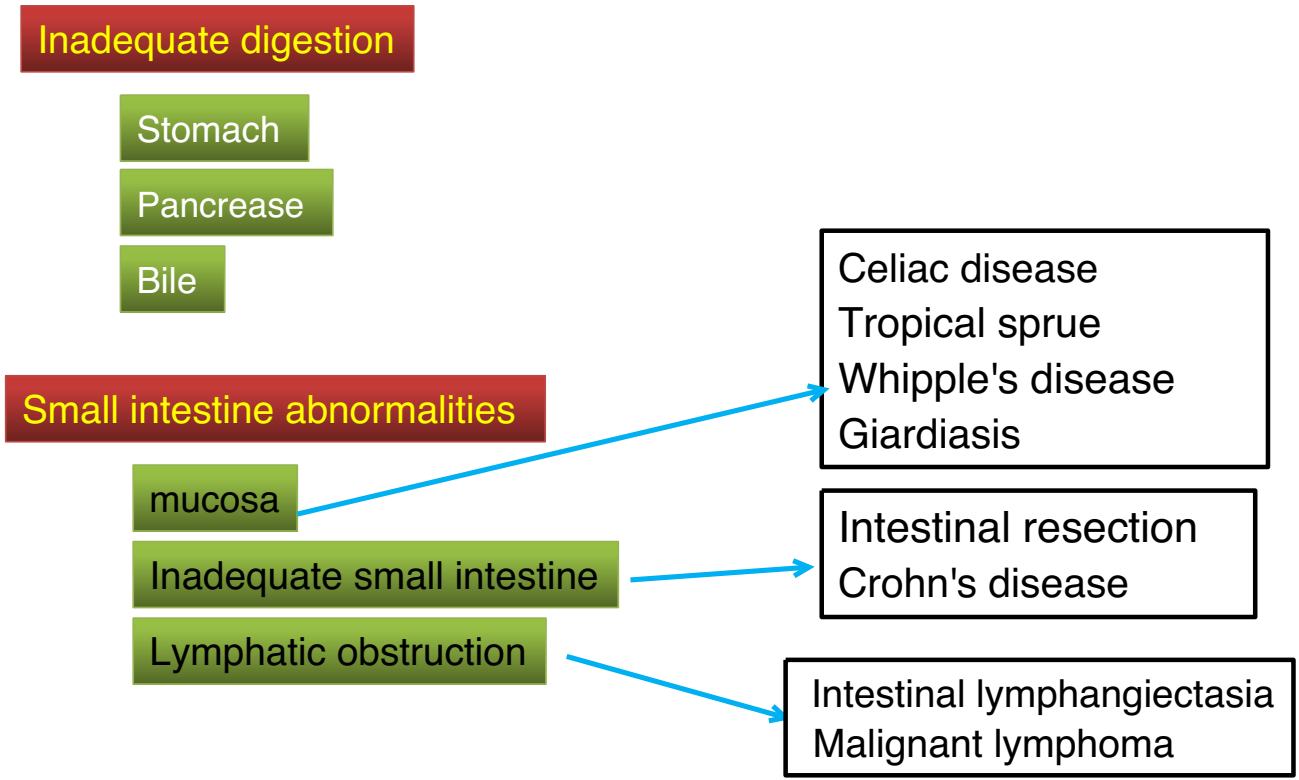
Small intestine abnormalities

= Malabsorption

Pathophysiology



Pathophysiology



Know that malabsorption can affect many organ systems

Malabsorption Syndrome

Clinical features

1. There is increased fecal excretion of fat (steatorrhea) and the systemic effects of deficiency of vitamins, minerals, protein and carbohydrates.

Steatorrhea is passage of soft, yellowish, greasy stools containing an increased amount of fat

2. Growth retardation and failure to thrive in children
3. Weight loss despite increased oral intake of nutrients

Systemic effects of the malabsorption syndromes

- Weight loss and anorexia
- Abdominal distension and borborygmi (increased bowel sounds)
- Diarrhoea (loose, bulky stools)
- Steatorrhoea—malabsorption of fat, producing pale, foul-smelling stools that characteristically float in water
- Muscle wasting

Know that malabsorption can affect many organ systems

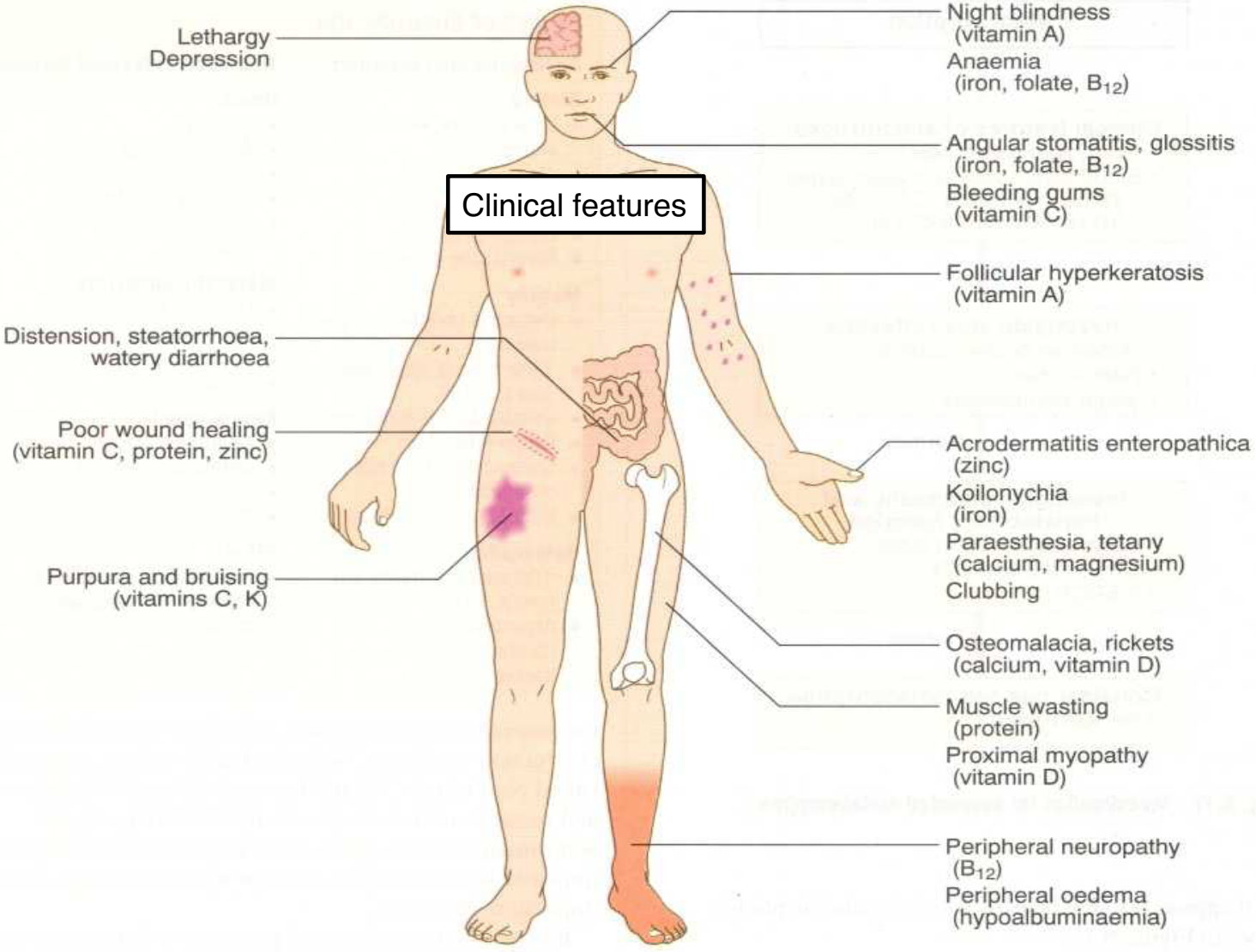
Malabsorption Syndrome

Clinical features

Depend on the deficient nutrient

- Protein → Swelling or oedema
- B12, folic acid and iron deficiency → Anaemias (fatigue and weakness)
- vitamin D, calcium → Muscle cramp; Osteomalacia and osteoporosis
- vitamin K and other coagulation factor → Bleeding tendencies

Know that malabsorption can affect many organ systems



Diagnosis

There is no specific test for malabsorption.

Investigation is guided by symptoms and signs.

1. Fecal fat study to diagnose steatorrhoea
2. Blood tests

3. Endoscopy

Biopsy of small bowel

Malabsorption Syndrome

Celiac disease

An immune reaction to gliadin fraction of the wheat protein gluten

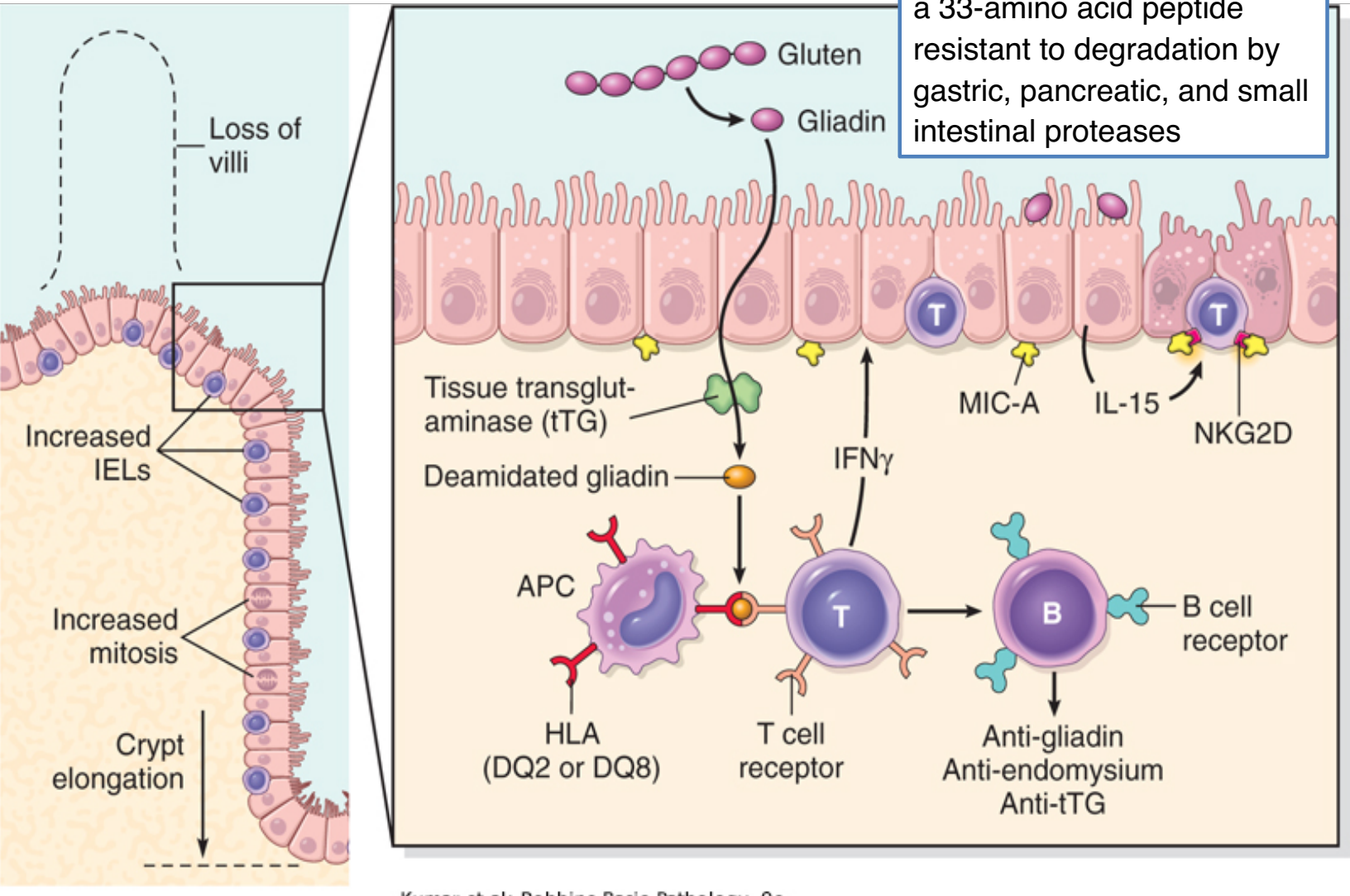
Usually diagnosed in childhood – mid adult.

Patients have raised antibodies to gluten autoantibodies

Highly specific association with class II HLA-DQ2 or HLA-DQ8 alleles.

Celiac disease

a 33-amino acid peptide resistant to degradation by gastric, pancreatic, and small intestinal proteases



Clinical features

Celiac disease

Typical presentation
GI symptoms that characteristically appear at age 9-24 months. Symptoms begin at various times after the introduction of foods that contain gluten.

A relationship between the age of onset and the type of presentation;

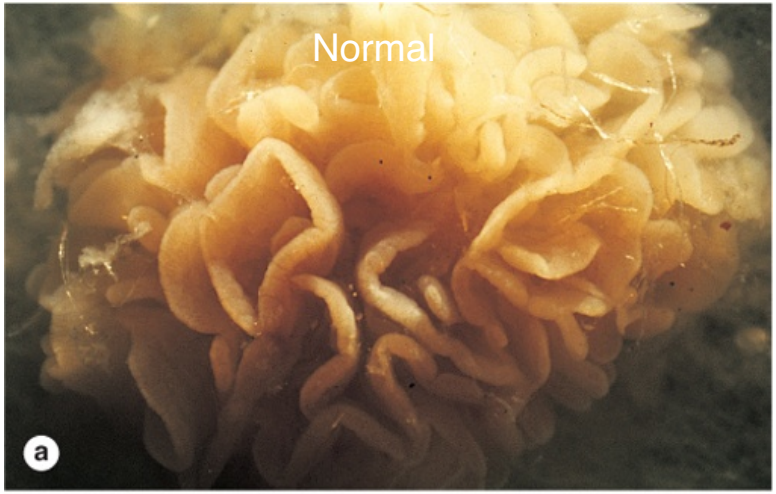
Infants and toddlers….GI symptoms and failure to thrive

Childhood……minor GI symptoms, inadequate rate of weight gain,

Young adults……anemia is the most common form of presentation.

Adults and elderly……GI symptoms are more prevalent

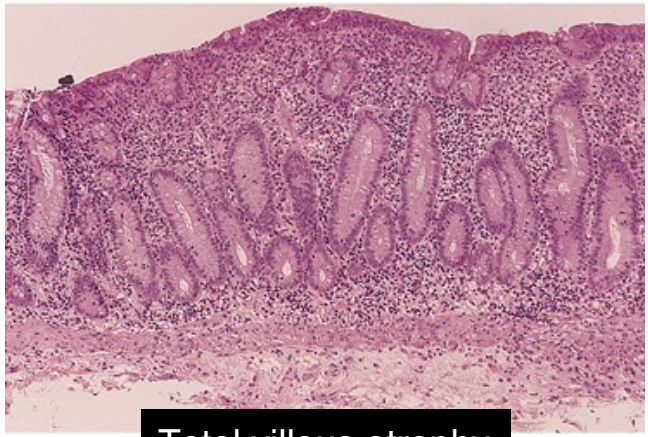
Endoscopy



Celiac Disease

Histology

- Mucosa is flattened with marked villous atrophy
- Increased intraepithelial lymphocytosis
- Crypt elongation



Celiac Disease

Diagnosis

Clinical documentations of malabsorption.

Stool ……↕…… Fat

Serology is +ve for IgA to tissue transglutaminase or IgG to deamidated gliadin or anti-endomysial antibodies

Small intestine biopsy demonstrate villous atrophy.

Improvement of symptom and mucosal histology on gluten withdrawal from diet.

wheat, barley, flour
Other grains, such as rice and corn flour, do not have such an effect.

Celiac Disease

Complications

Osteopenia , osteoporosis

Infertility in women

Short stature, delayed puberty, anemia,

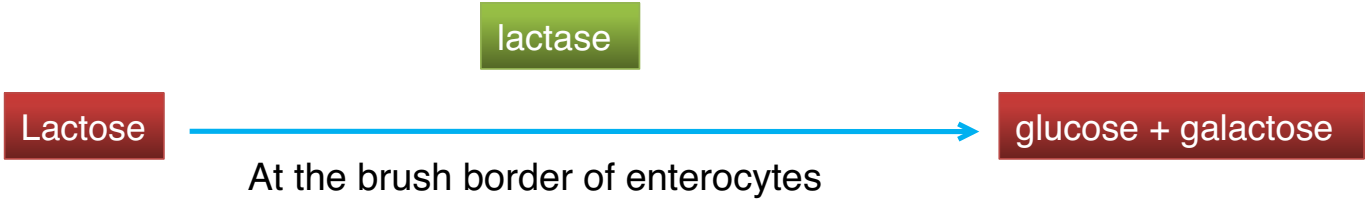
Malignancies: [intestinal T-cell lymphoma]

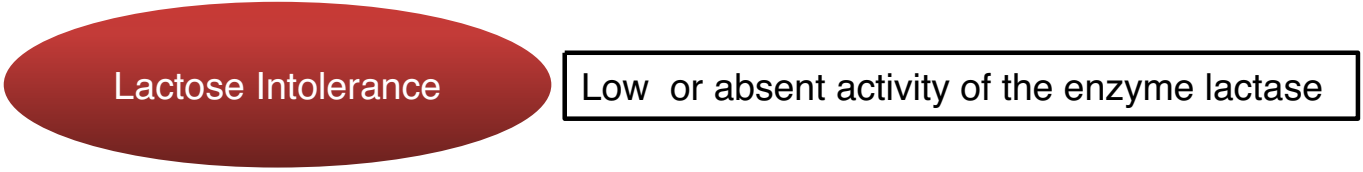
10 to 15% risk of developing GI lymphoma.

Lactose Intolerance

Lactose Intolerance

Pathophysiology





Lactose Intolerance causes

Inherited lactase deficiency

Congenital lactase deficiency

extremely rare

Childhood-onset and adult-onset lactase deficiency

common

Genetically programmed progressive loss of the activity of the small intestinal enzyme lactase.

Acquired lactase deficiency

Transient

Secondary lactase deficiency due to intestinal mucosal injury by an infectious, allergic, or inflammatory process

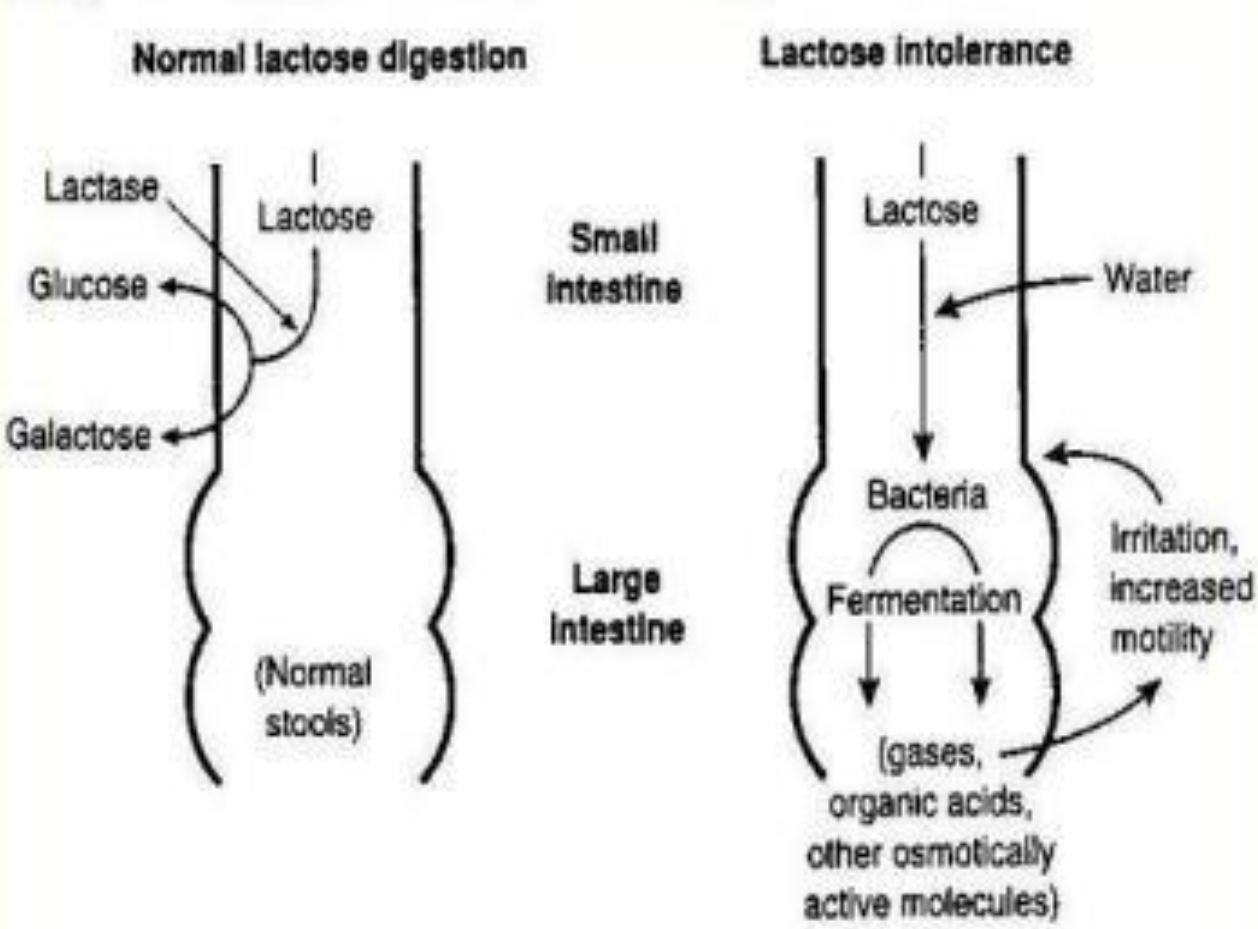
Gastroenteritis: Infectious diarrhea, particularly viral gastroenteritis in younger children, may damage the intestinal mucosa enough to reduce the quantity of the lactase enzyme

Clinical

Bloating, abdominal discomfort, and flatulence

……1 hour to a few hours after ingestion of milk products

Lactose Intolerance



Lactose Intolerance

Diagnosis

Empirical treatment with a lactose-free diet, which results in resolution of symptoms;

Hydrogen breath test

Hydrogen breath test .

- An oral dose of lactose is administered
- The sole source of H2 is bacterial fermentation;
- Unabsorbed lactose makes its way to colonic bacteria, resulting in excess breath H2.
- Increased exhaled H2 after lactose ingestion suggests lactose malabsorption.

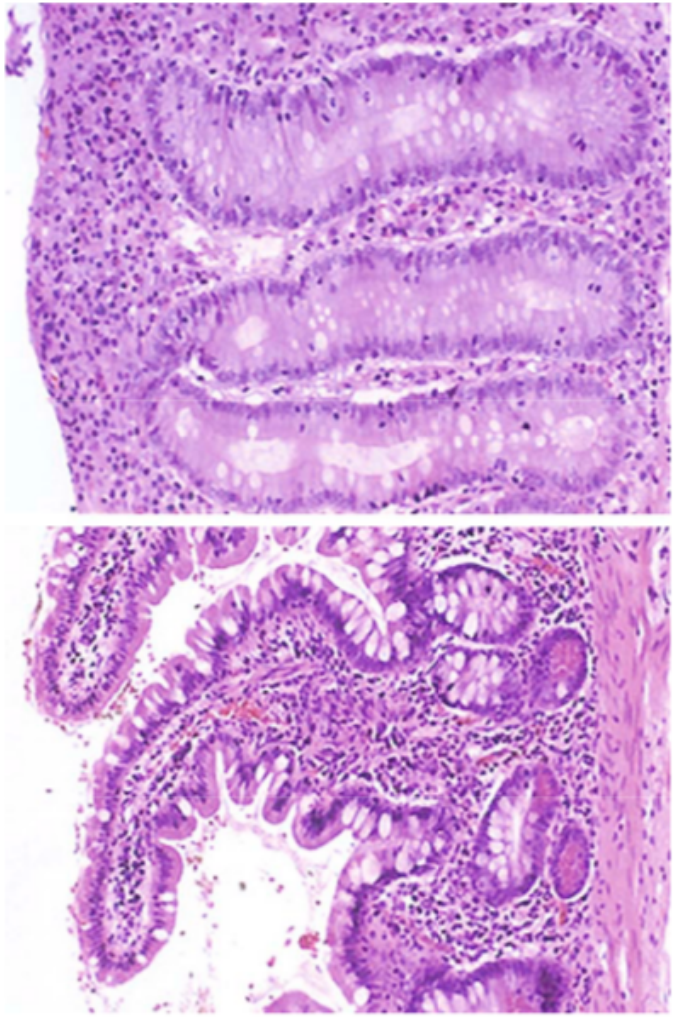
A 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance

Lactose Intolerance summary

- Deficiency/absence of the enzyme lactase in the brush border of the intestinal mucosa → maldigestion and malabsorption of lactose
- Unabsorbed lactose draws water in the intestinal lumen
- In the colon, lactose is metabolized by bacteria to organic acid, CO_2 and H_2; acid is an irritant and exerts an osmotic effect
- Causes diarrhea, gaseousness, bloating and abdominal cramps

Questions

A 33-year-old man with a 5-yea history of chronic diarrhea has recently lost 6 kg and become chronically fatigued. A biopsy specimen of his jejunum (top) is compared with a normal jejunal biopsy specimen. After a change in diet, he improves.



Q1. What is your diagnosis?

The flattening with atrophy of the villi, the loss of goblet cells, and the chronic inflammation are features of celiac disease (nontropical sprue or gluten-sensitive enteropathy).

Q2.

Q3.

Testing for antiendomysial antibodies (directed against transglutaminase in epithelial cells), antigliadin antibodies, and antireticulin antibodies may be helpful.

Q4. What skin condition can accompany this disease ?

Gluten (found in wheat, rye, or barley flour) contains the gliadin protein that binds to epithelial cells; cytotoxic T cell injury directed against gliadin-modified cells leads to cell loss. The removal of gluten (gliadin) from the diet removes the antigenic stimulus to the T cells, and the epithelium is eventually restored.

Dermatitis herpetiformis, with sub-basilar skin blistering and associated IgA deposition, may occur with this condition.

Question

- A 23-year-old woman from Hong Kong who is living in Zurich has had bouts of explosive, watery diarrhea with abdominal bloating since her arrival 6 months ago. Her stool has no occult blood, ova, parasites, or bacterial pathogens. Her laboratory findings are shown.

Vitamin B_{12}
450 pg/mL (nl 200–800 pg/mL)

Folate
11 ng/mL (nl >1.9 ng/mL)

Antiendomysial antibody (EMA)
Negative

Quantitative stool fat, 72 hours
3 gm (within normal limits)

D-xylose absorption
35% excretion in 5 hours (within normal limits)

Bile salts
Normal

Hydrogen breath test
Increased early peak

1. What is your diagnosis?

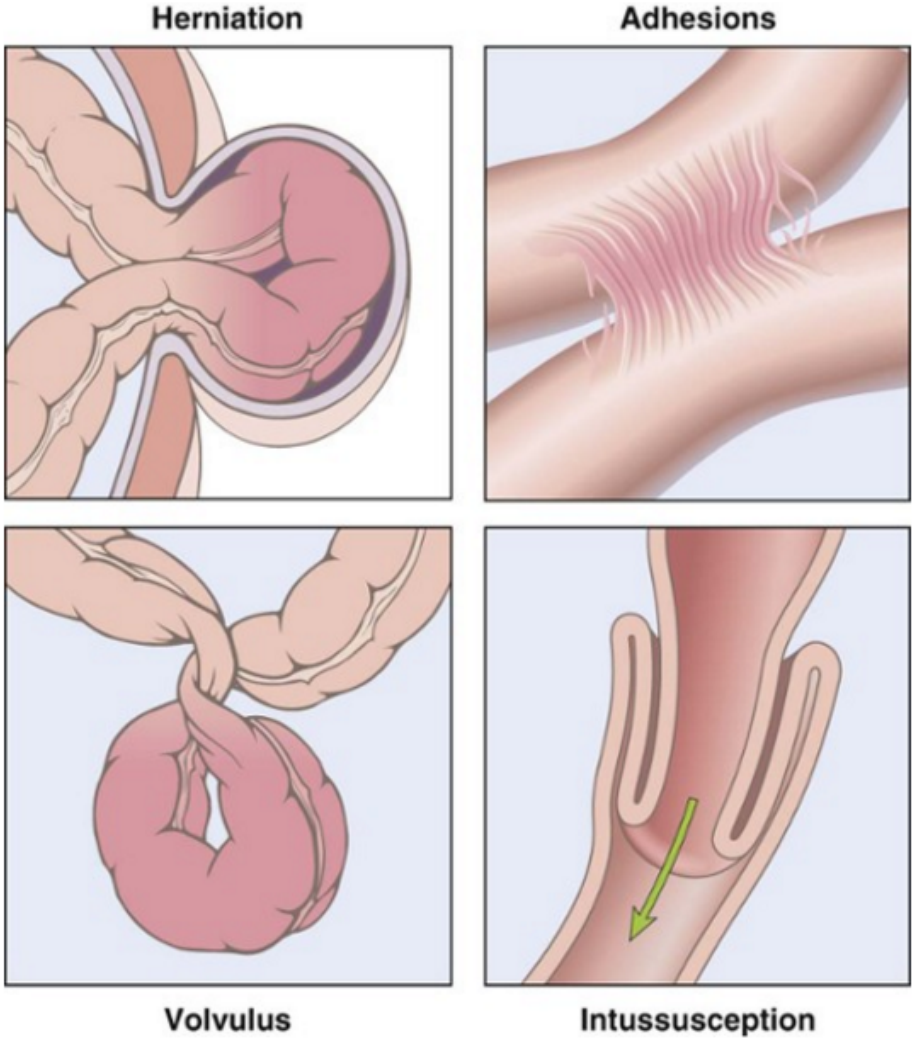
lactase deficiency. Disaccharidases are secreted from apical enterocytes, with infants expressing more than adults. Europeans typically have more lactase expression than Asians do.

2. What is the pathogenesis?

When disaccharides are not absorbed, gut bacteria have increasing substrate to ferment, which produces hydrogen that is absorbed and exhaled. It is the bacterial overgrowth and osmotic diarrhea that cause the unpleasant symptoms.

3. How can this be treated?

Avoiding foods containing lactose sugar include dairy products will reduce the symptoms.


Herniation
Adhesions
Volvulus
Intussusception