King Saud University
College of Medicine
Second year – GIT block

Malabsorption

Lecture 4

430 Pathology Team

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Red: Doctors' and important notes.
Green: Team notes.

Malabsorption Syndrome

Definition: Inability of the intestine to absorb nutrients adequately into the bloodstream

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

Physiology: The main purpose of the gastrointestinal tract is to:

- Digest and absorb nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, and electrolytes.

Mechanisms and Causes of Malabsorption Syndrome: (Don't memorize, just read them)

Inadequate digestion	**Primary mucosal abnormalities** (the digestion is normal but the lining and absorption is damaged)
Postgastrectomy	Celiac disease
Deficiency of pancreatic lipase	Tropical sprue
Chronic pancreatitis	Whipple's disease
Cystic fibrosis	Amyloidosis
Pancreatic resection	Radiation enteritis
Zollinger-Ellison syndrome	Abetalipoproteinemia
Deficient bile salt	Giardiasis
Obstructive jaundice	**Inadequate small intestine**
Bacterial overgrowth	Intestinal resection
Stasis in blind loops, diverticula	Crohn's disease
Fistulas	Mesenteric vascular disease with infarction
Hypomotility states (diabetes)	Jejunoileal bypass
Terminal ileal resection	**Lymphatic obstruction**
Crohns' disease	Intestinal lymphangiectasia
Precipitation of bile salts (neomycin)	Malignant lymphoma
	Macroglobulinemia

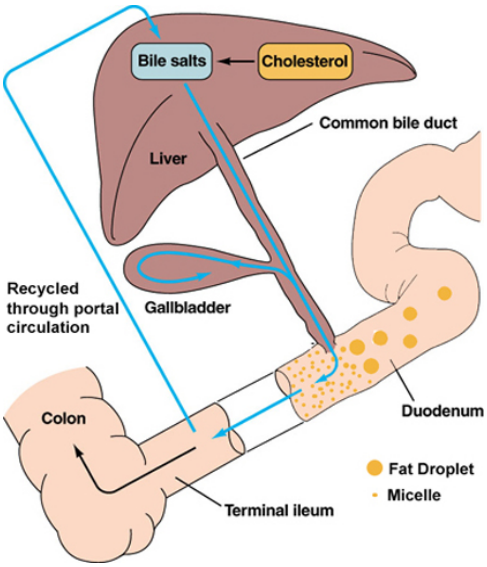
Absorption in the intestine happens through lymphatics and then it gets into the blood stream. So, lymphatic obstruction leads to malabsorption (lymphoma, macroglobulinemia, congenital abnormalities and radiation therapy)

Pathophysiology:

Malabsorption is either caused by inadequate digestion or by Small intestine abnormalities.

1. **Inadequate digestion**
   A. **Stomach** e.g. tumors or Postgastrectomy
   B. **Pancreas:**
   Deficiency of pancreatic lipase
   Chronic pancreatitis
   Cystic fibrosis
   Pancreatic resection

Chronic alcoholism is the most common cause of pancreatic enzyme deficiency and chronic pancreatitis.



C. **Bile:**
   - Obstructive jaundice
   - Terminal ileal resection

Colic, tumor, stone, or fibrosis in the bile duct/tract (anything that can cause obstruction)

Bile is recirculated to liver via the enterohepatic circulation. In the terminal ileum, bile salts are transported into the portal blood by exchange of Na+, where it is carried to the liver to be used again. So by iluem resection, this cycle is interrupted and causes malabsorbtion.

2. **Small intestine abnormalities**
   A. **Mucosa**:
   Celiac disease
   Tropical sprue

people who visit tropical areas usually get gastroenteritis and develop diarrhea and malabsorption. The exact cause is unknown but it's most likely due to a bacterial infection, which leads to damage of the lining epithelium and villous atrophy throughout the intestine (the entire intestine)

   Whipple's disease

Whipple's disease is a rare systemic infection by a certain gram positive bacilli bacteria, this bacteria affects the CNS, lymph nodes, joints and the small intestine (SI). In the small intestine they accumulate in the mucosa within the macrophages, so the macrophages appear pink and PAS positive (periodic acid-Schiff stain) (when we use H&E stain they will appear as large cells) so accumulation of the cells will cause abnormality in the

   Giardiasis

Gradiasis; infection by protozoa. Usually it's not tissue invasive, (it's found on top) it grows on the surface of the SI, so it will cover all the enterocytes (intestinal absorption cells) which will cause chronic diarrhea and

   B. **Inadequate small intestine** e.g.
   Intestinal resection
   Crohn's disease

Crohn's disease is a chronic inflammatory disorder that affects any part of the GIT, but the most common affected site is the ileum (which is the most important area of absorption)

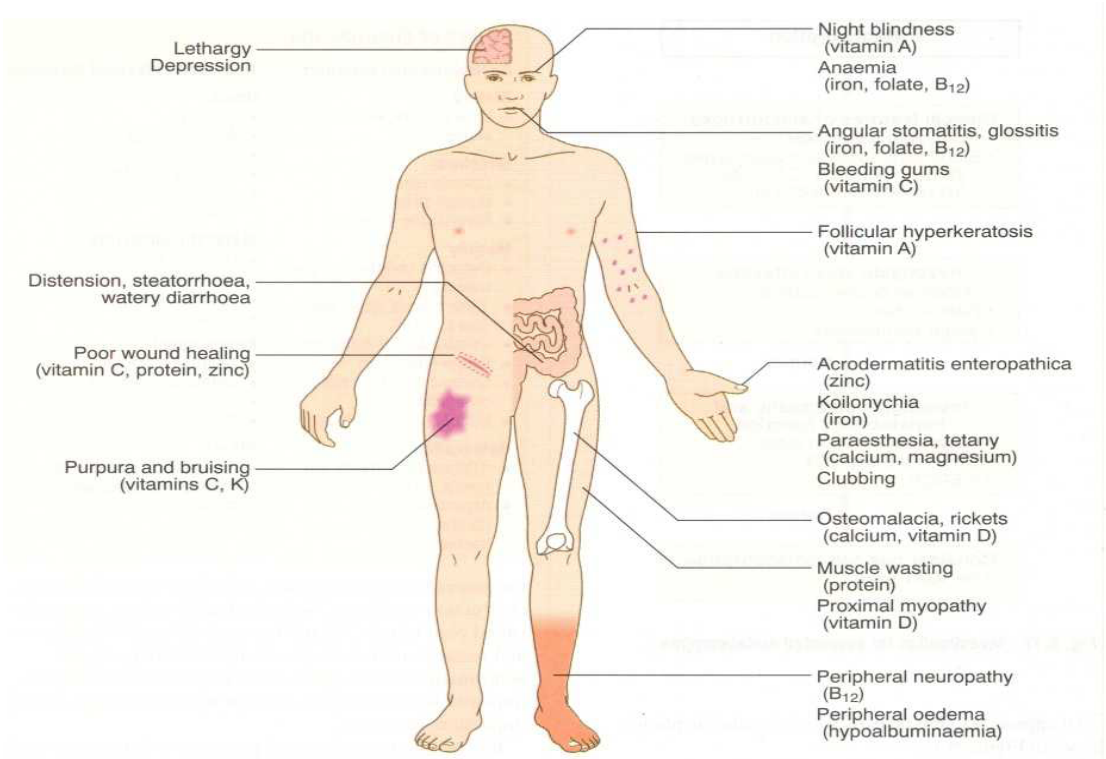
   C. **Lymphatic obstruction**:
   Intestinal lymphangiectasia (ectasia means dilation). It is a pathological dilation of lymph vessels, it rarely occurs in humans.
   Malignant lymphoma in this case the malignant lymphocytes are going to fill up the vessels and nodes causing obstruction of transport and absorption of nutrients.

Clinical features:

1. Chronic diarrhea characterized by is increased fecal excretion of fat (steatorrhea -is passage of soft, yellowish or pale, greasy stools containing an increased amount of fat) with offensive smell, and hard to flush stool.
2. The systemic effects of deficiency of vitamins, minerals, protein and carbohydrates.
   - Protein → Swelling or oedema
   - B_{12}, 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
   - Endocrine system: amenorrhea, infertility, hyperparathyroidism
   - Skin: purpura, dermatitis hyperkeratosis

- Nervous system: Neuropathy

3. Growth retardation, failure to thrive in children can't grow or gain weight.
4. Weight loss despite increased oral intake of nutrients (in adults)



Diagnosis:

There is no specific test for malabsorption.

Investigation is guided by symptoms and signs.

1. Fecal fat study to diagnose steatorrhoea (more than 6 grams of fat in 72 hours)
2. Blood tests for anemia and vitamins' deficiency
3. Stool studies; fat etc.
4. Endoscopy + Biopsy of small bowel (important in celiac disease)

Celiac disease:

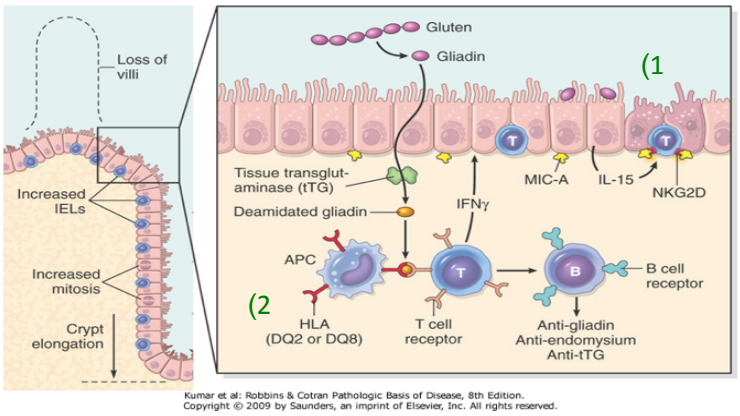
Characteristics:

It is an immune reaction to gliadin fraction (a water insoluble part) of the wheat protein gluten, in genetically predisposed individuals.

Note: This immune reaction causes damage to the small intestine mucosa, where the patient will have problems in absorption of all nutrients and not only gluten.

For you to understand- The immune reaction:

1-Gliaden may bind to the epithelial cells may



cause them to release cytokines that will cause damage to the mucosa.

2-Other parts of gliaden pass through the epithelium where they may be picked up by antigen presenting cells (this is where HLA DQ2 or HLA-DQ8 abnormalities play a role in the disease), and present them to T-cells which release cytokines which progress the damaging immune reaction

Usually diagnosed in childhood – mid adult.

Patients have raised antibodies to gluten autoantibodies

Members can be highly prone to develop celiac diseases if the family has class II HLA DQ2 (haplotypes DR-17 or DR5/7) and, to a lesser extent, DQ8 (haplotype DR-4).

Pathological findings:

1. Atrophy of villi (partial) or total (in advance cases)
2. Increases in the number of T lymphocytes not only in mucosa but also in the epithelium.

In the early stages you'll see increased T-cells. Later there will be partial loss of villi.

Clinical features:

Celiac disease can mimic the symptoms of more common problems and be misdiagnosed as Irritable Bowel Syndrome (IBS).

Typical presentation:

GI symptoms that characteristically appear at age 9-24 months. It begins in various times after introduction of gluten to the diet.

Typical presentation: [Diarrhea –abdominal pain –cramping-bloatedness]

Atypical presentation:
Extra-intestinal symptoms
[Weight loss –abnormal bleeding –anemia –osteoporosis & osteopenia]

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

Infants and toddler → GI symptoms and failure to thrive

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

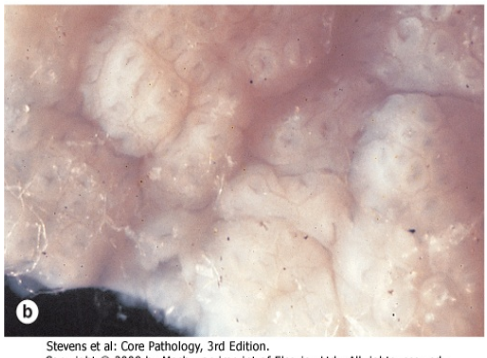
Young adults →anemia is the most common form of presentation.

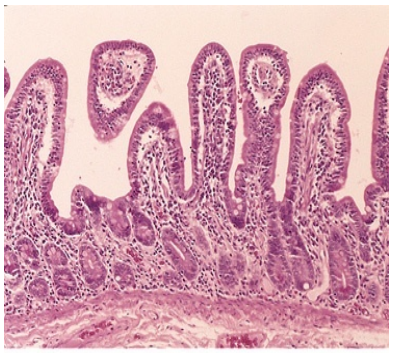
Adults and elderly → GI symptoms are more prevalent

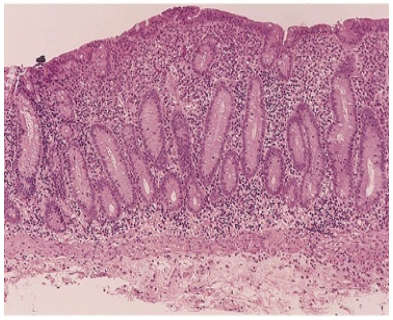
Note: Young adults with anemia may present with tiredness and shortness of breath when doing exercise or high activity, with pale skin.

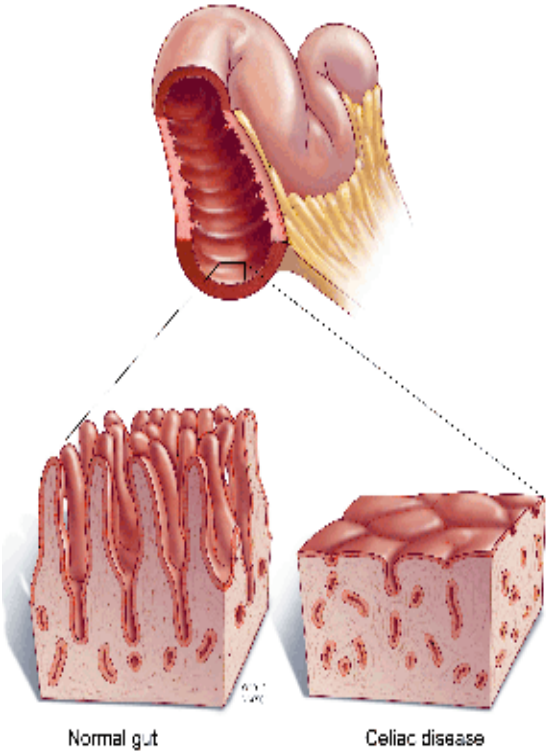
Endoscopy:

- Mucosa is flattened with marked villous atrophy.
- Increased intraepithelial lymphocytosis









Diagnosis:

1. Clinical documentations of malabsorption.
2. Fat greatly increased in stool
3. Small intestine biopsy demonstrates villous atrophy.
4. Improvement of symptom and mucosal histology on gluten withdrawal from diet that is replace wheat, barley, flour with other grains, such as rice and corn flour, do not have such an effect.

Complications:

- Osteopenia , osteoporosis
- Infertility in women
- Short stature, delayed puberty, anemia,
- Malignancies,[intestinal T-cell lymphoma] (common in patients with celiac disease)
- 10 to 15% risk of developing GI lymphoma.

Lactose Intolerance:

Normally:

Lactose $\xrightarrow[\text{At the brush border of enterocytes}]{\text{lactase}}$ glucose + galactose

Lactose intolerance happens due to lactase deficiency this will lead to accumulation of lactose in the intestine this will lead to chronic osmotic diarrhea.

Lactose will be fermented by the bacteria present in the intestine this will cause increased abdominal pain and distention.

Etiology of lactose intolerance:

Low or absent activity of the enzyme (lactase accumulation of lactose in the intestine this will lead to chronic osmotic diarrhea).

Lactose intolerance does not cause general malabsorption, but only malabsorption of lactose with no mucosal damage.

Because the defect is biochemical, biopsy histology is unremarkable.

Cause:

Inherited:

1. *Congenital lactase deficiency.* e.g: extremely rare
2. Childhood-onset and adult-onset lactase deficiency (common) e.g: Genetically programmed progressive loss of the activity of the small intestinal enzyme lactase.

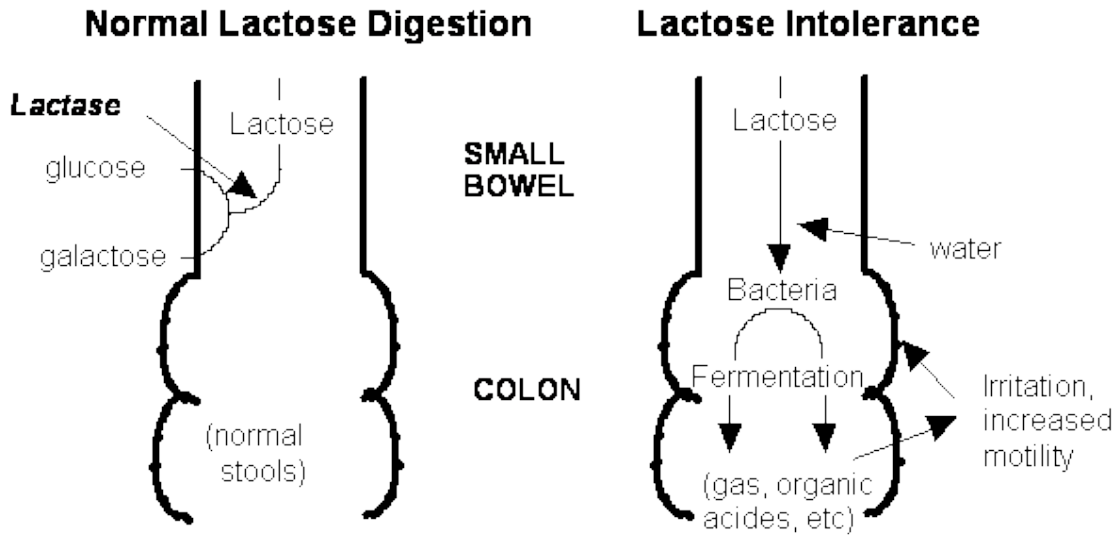
Acquired:

It is a transient. Secondary lactase deficiency due to intestinal mucosal injury by an infectious, allergic, or inflammatory process.

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

Clinical manifestations:

- Osmotic diarrhea, bloating, abdominal discomfort, and flatulence 1 hour to a few hours after ingestion of milk products



Note: Fermination products (especially organic salts) cause discomfort and irritation of the intestinal mucosa, which cause increased motility.

Diagnosis:

1. Hydrogen breath test :
    - An oral dose of lactose is administered
    - The sole source of H_2 is bacterial fermentation
    - Unabsorbed lactose makes its way to colonic bacteria, resulting in excess breath H_2.
    - Increased exhaled H_2 after lactose ingestion suggests lactose malabsorption.
2. A 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance

Treatment:

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

Summary of lactose intolerance:

- 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, CO2 and H2; acid is an irritant and exerts an osmotic effect
- Causes diarrhea, gaseousness, bloating and abdominal cramps