intestinal pathology:

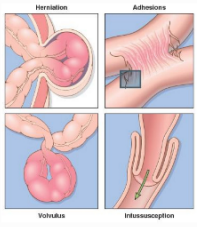
• Small and large intestines are formed histologically from the same tissue layers, which are: mucosa, submucosa, muscularis propria and serosa.
• Large intestine wall is thicker, small intestine lumen is narrower.

- **Intestinal diseases:**

1-Intestinal **obstruction**
2- **Vascular** disorders.
3- **Malabsorptive** diseases and infections.
4- **Inflammatory** bowel disease.
5- **Polyps and neoplastic** diseases.

1) Intestinal obstruction:

- **Clinically:** Abdominal pain • Distention (gases distention) • Vomiting • Constipation.
- **Acute:** intussusception, volvulus, or infarction
- **Chronic:** Hirschsprung disease or tumors.



A) mechanical:

- Intussusception | Hernias | Adhesions | Volvulus. (80% of cases)
- Tumors, diverticulitisانبعاجات and infarction. (20%)

*Hernia: protrusion of bowel segment and its mesentery through a defect in abdominal wall.
*Adhesions: a complication of previous inflammatory condition or surgical procedures, result in scarring and adhesion between two bowel lobes.
*Volvulusالتواء: torsion of intestine & impaired venous drainage, edema, congestion with possible infarction and ischemic bowel damage.
*Intussusception:

- constriction of proximal segment of intestine by a peristaltic wave, thus it telescopes into distal segment, once trapped, invaginated segment is propelled by peristalsis, and pulls mesentery with it.
- In children <2 years (most common).
- If untreated it progresses to infarction.
- **Causes**:
- <2 years: Idiopathic.
- Children: Peyer patches hyperplasia (**lymphoid hyperplasia**) due to **rotavirus**, which is responsible for most cases of viral gastroenteritis in childhood.
- adults: Intraluminal tumors.
- Meckel's diverticulum (congenital disorder in the ileum).
- **Clinical features:**

abdominal swelling (distention), vomiting, & **currant jelly stool** (stool mixed with blood and mucus).

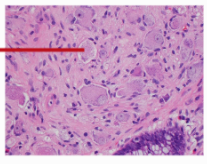
- **Management**:

- Contrast enemas حقنة شرجية in early stages.
- Surgery if complicated/masses.

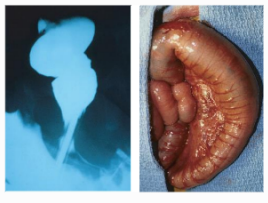
B) non-mechanical: Hirschsprung disease | Neurological disorders | Drugs | Paralytic ileus (due to intestinal muscle paralysis caused by surgical procedures).

Hirschsprung Disease (Congenital aganglionic megacolon):

- Congenital (after birth), aganglionic (no ganglion cells), & Megacolon (dilated colon)
- It is a congenital defect in colonic innervations.
- Affects **rectum (rectosigmoid)** (mostly), severe cases may involve the entire colon.
- More common in males, **but** more severe in females.
- Risk increases in siblings
- **Clinical features**:
- Neonates fail to pass **meconium** (first stool after delivery).
- Later, it is followed by **chronic obstructive constipation**.
- **Pathogenesis**
- during embryogenesis: failure of **neural crest cells** migration from **cecum** to **rectum,** thus Lack of development of Meissner submucosal plexus and Auerbach myenteric plexus, that cause failure of coordinated peristaltic contractions & result in constipation.
- **Causes**: Mutations in **RET** gene (in familial cases, and in 15% of sporadic cases)
- Other genes and environmental factors.
- **Macroscopically:**



- Aganglionic rectosigmoid, normal or contracted region on **barium enema**.
- Proximal normal segment is progressively dilated, rectum is contracted.



- **Diagnosis**: BIOPSY, microscope.
- The typical ganglion cells have an abundant eosinophilic cytoplasm and eccentrically (peripherally) located nucleus with prominent nucleolus.
- **Complications**:
- Enterocolitis, fluid & electrolyte disturbances (dehydration), perforation & peritonitis.
- **Treatment**:
- Surgical resection of Aganglionic segment then anastomosis of normal segments.

2) Vascular disorders:

- Subdivided into:

A) Ischemic bowel disease: result from ischemia (acute or chronic), in elderly.

B) Hemorrhoids: common in outpatient clinics.

Hemorrhoids: البواسير

- Thin walled, dilated **veins** in anal or rectal submucosa (beneath mucosa).
- **Predisposing factors**:
• Constipation إمساك & straining إجهاد.
• Venous stasis رقود الدم of pregnancy
• Portal hypertension.
- **Maybe internal/external:**

Internal: above the anal rectal line (ano-rectal junction) (in rectal mucosa).

- External: below the anal rectal line (ano-rectal junction).

- **Symptoms**: Bleeding (**fresh colored blood**), pain, thrombosis, & inflammation.

3) Malabsorptive diseases:

Diarrheal Diseases:

- **Diarrhea:** increase in mass, frequency or fluidity of stool .
- **Dysentery:** a painful, bloody, small volume diarrhea.
- **Causes**:

1) Infectious Enterocolitis.
2) Inflammatory bowel diseases.
3) Malabsorptive diarrhea.
4) Ischemic colitis.
5) Nutritional deficiency.

Malabsorptive Diarrhea:

- Chronic defect in absorption of fats, fat-/water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water.
- **Steatorrhea** is the hallmark; which is a greasy, fatty, bulky, yellow to clay colored stool.
- **Causes**:

1) Pancreatic insufficiency: due to lack of pancreatic enzymes.
2) Celiac disease.
3) Crohn's disease.
4) Cystic fibrosis.
5) Lactase (Disaccharide) deficiency.
6) Abetalipoproteinemia.

* First 3 are the most common causes of chronic malabsorption in west.

- **Mechanism:** usually defect in one or more of:

A) Intraluminal digestion: malabsorption of **macromolecules** (fat, carbs & proteins) due to main enzymes deficiency (e.g. Pancreatic enzymes).
B) Terminal digestion: malabsorption of **end products** due to deficiency in disaccharidases/ peptidases at the intestinal brush border (e.g. Lactase enzyme).
C) Transepithelial transport: defect in the **transport** across epithelial cells (nutrients can't reach vascular side).
D) Lymphatic transport: absorbed lipids arn't transported by lymphatics to reach circulation.

- **General symptoms**:
- Weight loss | Anorexia | Flatus | Borborygmi | Muscle wasting.

*flatus: انتفاخ gaseous abdominal distention (unabsorbed disaccharides get fermented by intestinal flora producing gas).
*Borborygmi: قرقعة-صوت الهواء في الأمعاء rumbling noise due to intestinal gas movement.
*muscle wasting: atrophied main intestinal muscles.

- **Specific symptoms**:

1) Anemia and mucositis (mucous membranes inflammation at mouth angle):
(iron, pyridoxine (Vitamin B6), folate (vitamin B9), or vitamin B12 deficiency)
2) Bleeding (no thrombotic activity):
(vitamin K deficiency)

3) Osteopenia and tetany (may develop to osteoporosis):

(calcium, magnesium, or vitamin D deficiency)

4) Neuropathy (peripheral numbness, burning sensation in hands & feet, muscle weakness):

(vitamin A or B12 deficiency)

5) Skin and endocrine disorders:

(Iodine results in thyroid hormone deficiency)

Cystic Fibrosis:

- a **multiorgan** systemic disease with genetic basis.
- mutations in (CFTR) cystic fibrosis transmembrane conductance regulator gene.
- **Defects in ion transport** across intestinal & pancreatic epithelium, which causes the pancreatic secretions to be thick and viscous.

less ions ➡️ less water ➡️ more viscous secretions

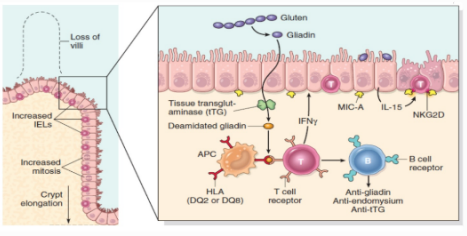
- Mucus secretions plugs pancreatic ducts ➡️ pancreatic insufficiency (80% of cases), leading to defect in intraluminal digestion.

Celiac Disease:

- **Immune mediated** reaction to **gluten** (found in Wheat, rye or barley القمح، الذرة، الشعير)
- affecting the small intestine (enteropathy).
- Due to genetic predisposition; patients carry **HLA-DQ2** or **HLA-DQ8** alleles on the surface of their APCs (antigen presenting cells)
- Associated with other immune diseases like **type 1 diabetes**, **thyroiditis** and **Sjogren syndrome**
- **Treatment:** gluten-free diet.
- if the patient develops resistance to gluten-free diet and shows refractory symptoms, we suspect **enteropathy associated T cell lymphoma or Small intestinal adenocarcinoma**.
- **Pathogenesis:**
- **gluten** gets digested by small intestine enzymes to **Gliadin** (**shorter peptide).**
- **Gliadin** enters lamina propria & gets **deamidated** by tissue transglutaminase, then it reacts with **HLA-DQ2 or HLA-DQ8** on APCs surface, this **activates CD4+ T helper** cells in lamina propria, causing loss of villus architecture and loss of epithelial cells lining the mucosa, thus decrease the surface area of absorption leading to malabsorption, by:

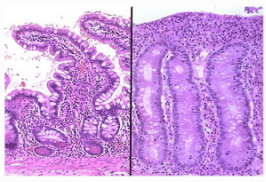
1) **releasing cytokines**.
2) **attracting CD8+ Cytotoxic T Cells** (intraepithelial lymphocytes).
3) **activating B cells** to produce:

Anti-tissue transglutaminase antibodies
Anti-gliadin antibodies
Anti-endomysial antibodies

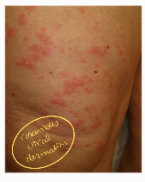


- **Serologically: Abs are useful in diagnosis & monitoring response of gluten-free diet**.
- Loss of villi could be total (flattening), subtotal or just shortening of villi.
- **Morphology**:
- Multiple biopsies (to increase diagnostic yield) from second portion of **duodenum** or **proximal jejunum** (avoiding proximal duodenum because gastric juice effects it)

- **Microscopically**, looking for a **triad**:



1) **IEL; Intraepithelial lymphocytosis (CD8+ T cells)** (the earliest manifestation).
2) **Crypt hyperplasia** (elongated grooves result from increased damage & intestinal epithelium turnover).
3) **Villous atrophy.**
- IEL & villous atrophy are not pathognomonic as they're seen in viral enteritis.
- In lamina propria their is lymphocytes, plasma cells, & eosinophils.
- **Clinical features in children:**
Symptoms start **6-24 months after birth;** due to introduction of gluten to diet (cereals)
- **Symptoms,** divided to classical and non-classical:



- Classical: Irritability, abdominal distention, anorexia, diarrhea, failure to thrive (due to decreased anabolic reaction), weight loss, or muscle wasting
- **Non-classical**: abdominal pain, nausea, vomiting, bloating, or constipation
- 10% of patients develop highly itchy, blistering skin lesions (**look like herpetic vesicles in dermatitis herpetiformis**)
- **Clinical features in adults:**
- Usually aged (30–60 years).
- iron deficiency anemia (**common** because iron is mainly absorbed in the duodenum and jejunum which get affected by celiac disease)
- B12 and folate deficiency (less common because they're mainly absorbed in ileum)
- **Classical**: diarrhea, bloating (gaseous abdominal distention), fatigue (due to iron deficiency), weight loss & muscle wasting.
- **Silent celiac: Positive Serology + Positive histological diagnosis but no clinical symptoms.**
- **Latent celiac: Positive Serology but normal histological appearance and asymptomatic**
- if the patient develops resistance to gluten-free diet and shows refractory symptoms, we suspect **enteropathy associated T cell lymphoma or Small intestinal adenocarcinoma**.
- **Diagnosis**:
- Correlation between clinical, histologic and serologic (clinical history, physical examination, laboratory investigation, imaging and histopathology).
Tests are divided to non-invasive and invasive; **we start with the non-invasive test**.
- **Non-invasive**:
- Most sensitive but less specific.
Anti-tissue transglutaminase antibody, IgA.
Anti-deamidated gliadin antibodies, IgA & IgG.
- Most specific but less sensitive: Anti-endomysial antibody
- Invasive:
Small bowel biopsy, microscopically look for the triad.

Lactase (Disaccharidase) Deficiency:

- Lactase is found on apical brush border membrane.
- It hydrolyses lactose to glucose and galactose.
- If deficient, **lactose accumulates in gut lumen** absorbing water & causing osmotic diarrhea.
- **Biopsies are normal** because the problem is on a biochemical level (enzymes).
- When patient stops ingestion of milk & diary products symptoms abate.
- Has two types:

1) **Congenital**: Due to autosomal recessive (**AR**) genetic mutation (rare).
Presents as **explosive diarrhea, watery & frothy stools, abdominal distention**. (after milk ingestion (lactose))
2) **Acquired**: Following viral or bacterial enteritis (which damage the apical brush border, thue loss of lactase). Or due to **downregulation of the lactase gene after childhood** as the need for milk decreases.

Abetalipoproteinemia:

- **NO β-lipoproteins in blood** (inability to secrete **triglyceride-rich lipoproteins** due to a **transepithelial transport defect of triglycerides**, **monoglycerides and fatty acids** in which they enter the epithelial cells but don't reach the blood (accumulate), so there is a lack of absorption of fat and fat-soluble vitamins, & decreased synthesis of lipoproteins)
*lipoproteins are important in plasma membranes.
- Autosomal recessive (rare).
- Infants present with **failure to thrive, diarrhea and steatorrhea**.
- **Microscopically**: **clear cytoplasm** due to fat globules and lipid accumulation in enterocytes *enterocytes=epithelial cells of small intestines*