GI pathologies 2

Lowe GI pathology done by
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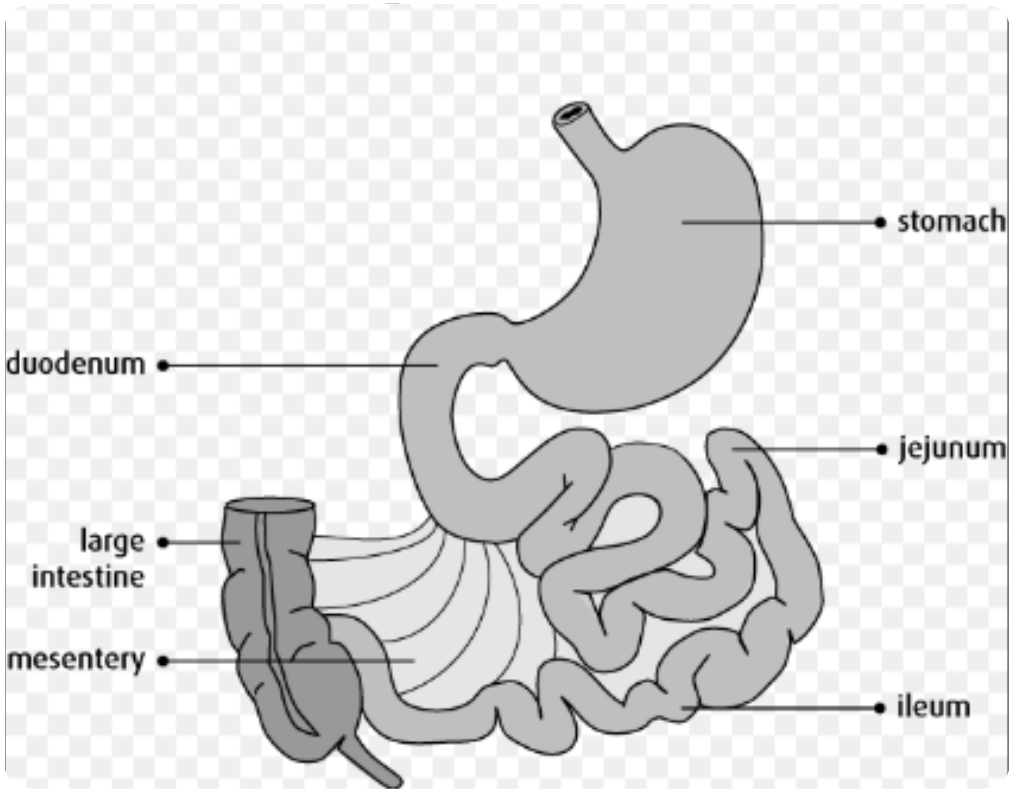
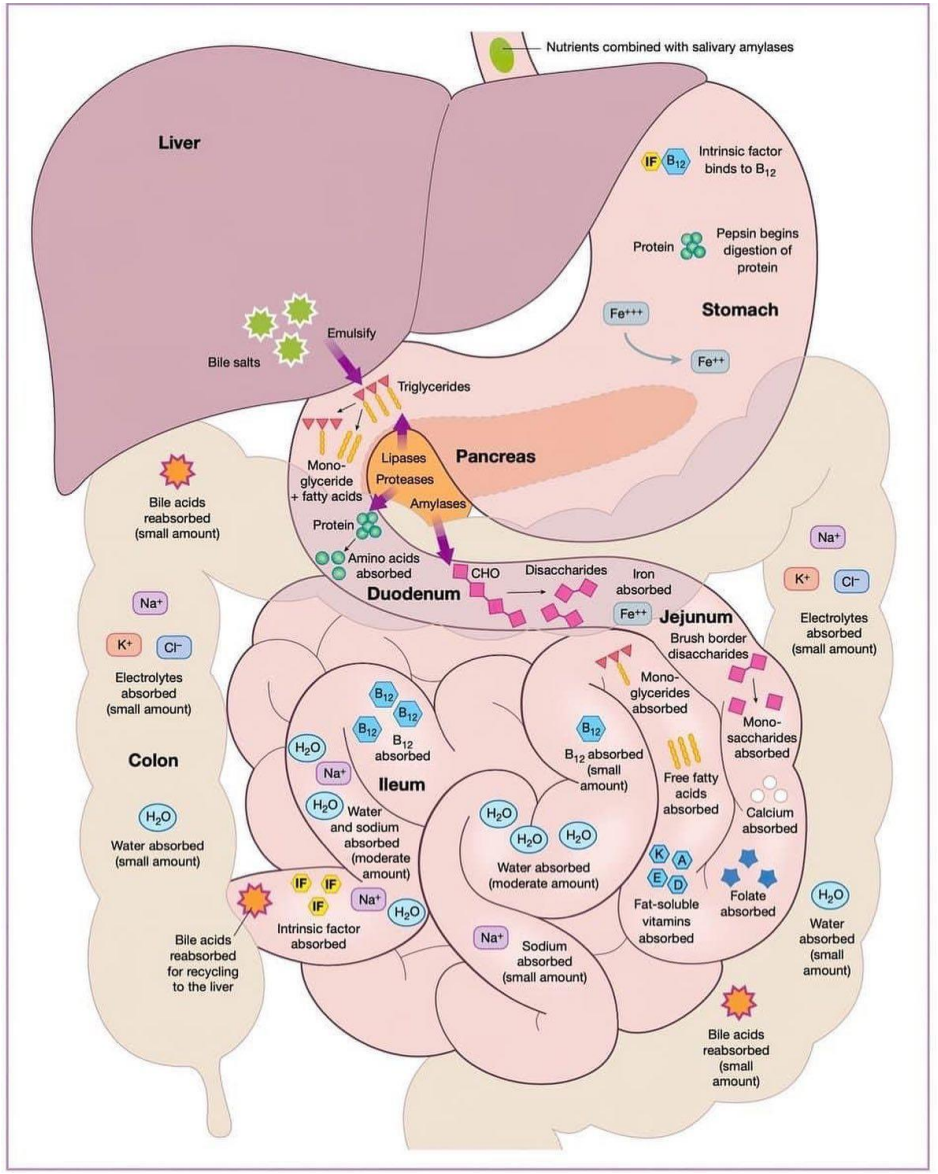
SMALL INTESTINE

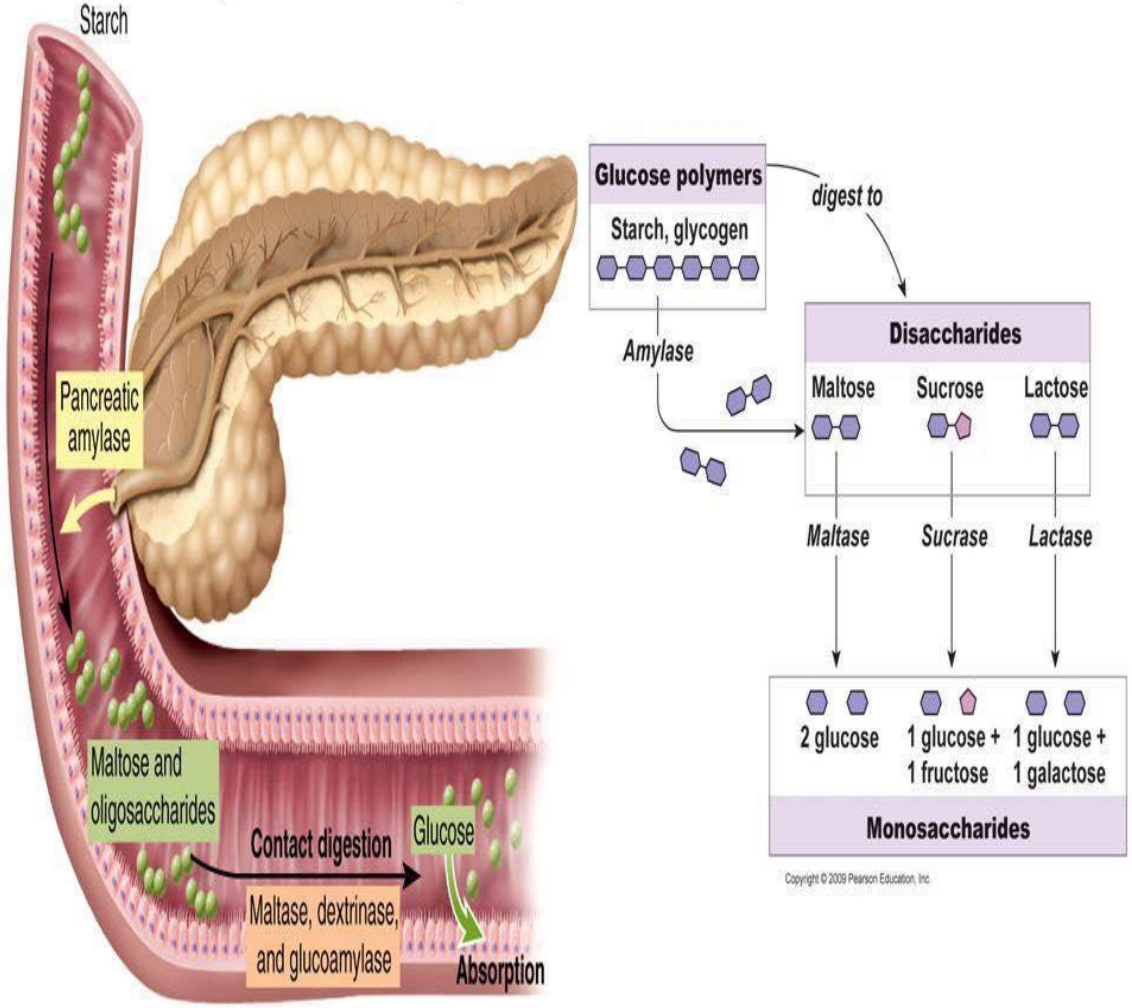


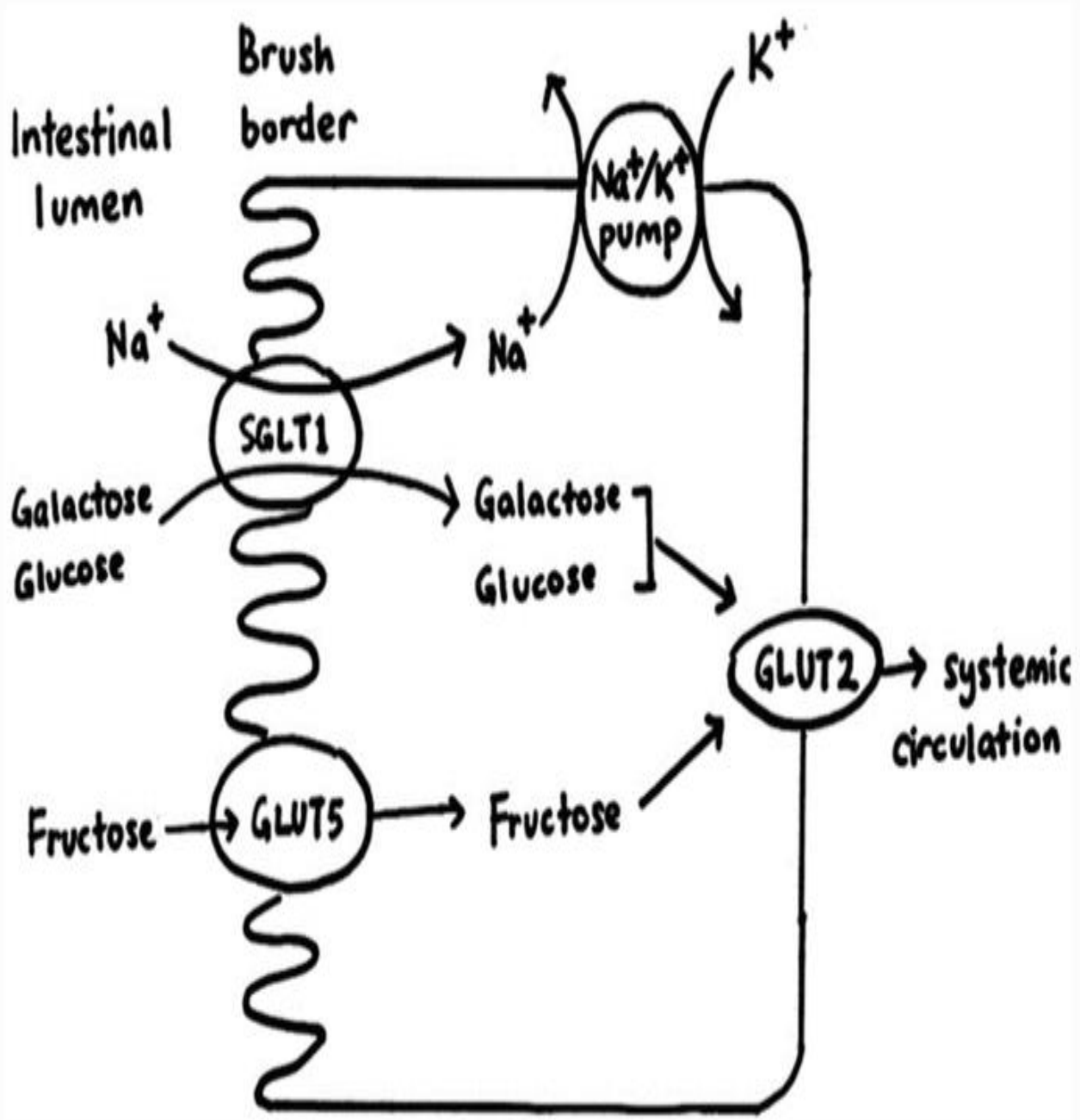
- Tubular organ that extends from the pyloric sphincter to the ileocecal junction(large intestine).
- Site of complete digestion and absorption of most of the products of digestion and water, electrolytes, and minerals.
- Consists of 3 parts:
  1- Duodenum
  2- Jejunum
  3- Ileum

The ultimate function of the GI tract is to digest and then absorb.

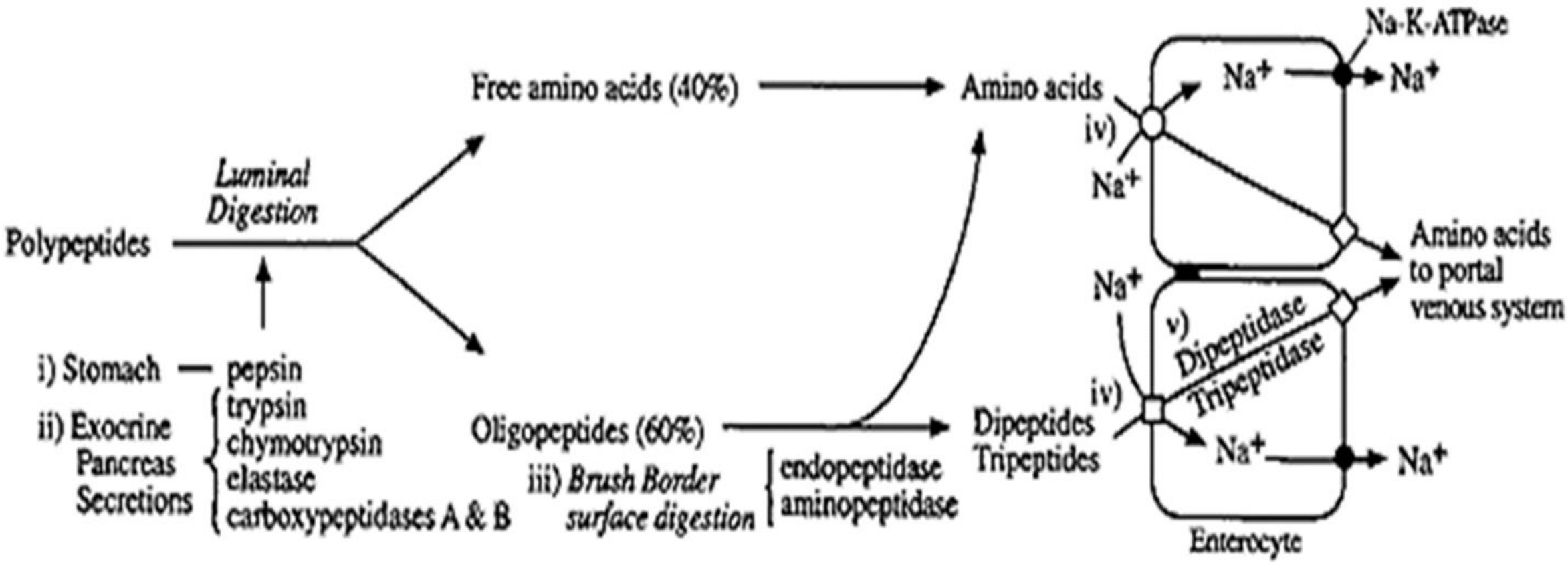


Carbohydrate Digestion - Small Intestine

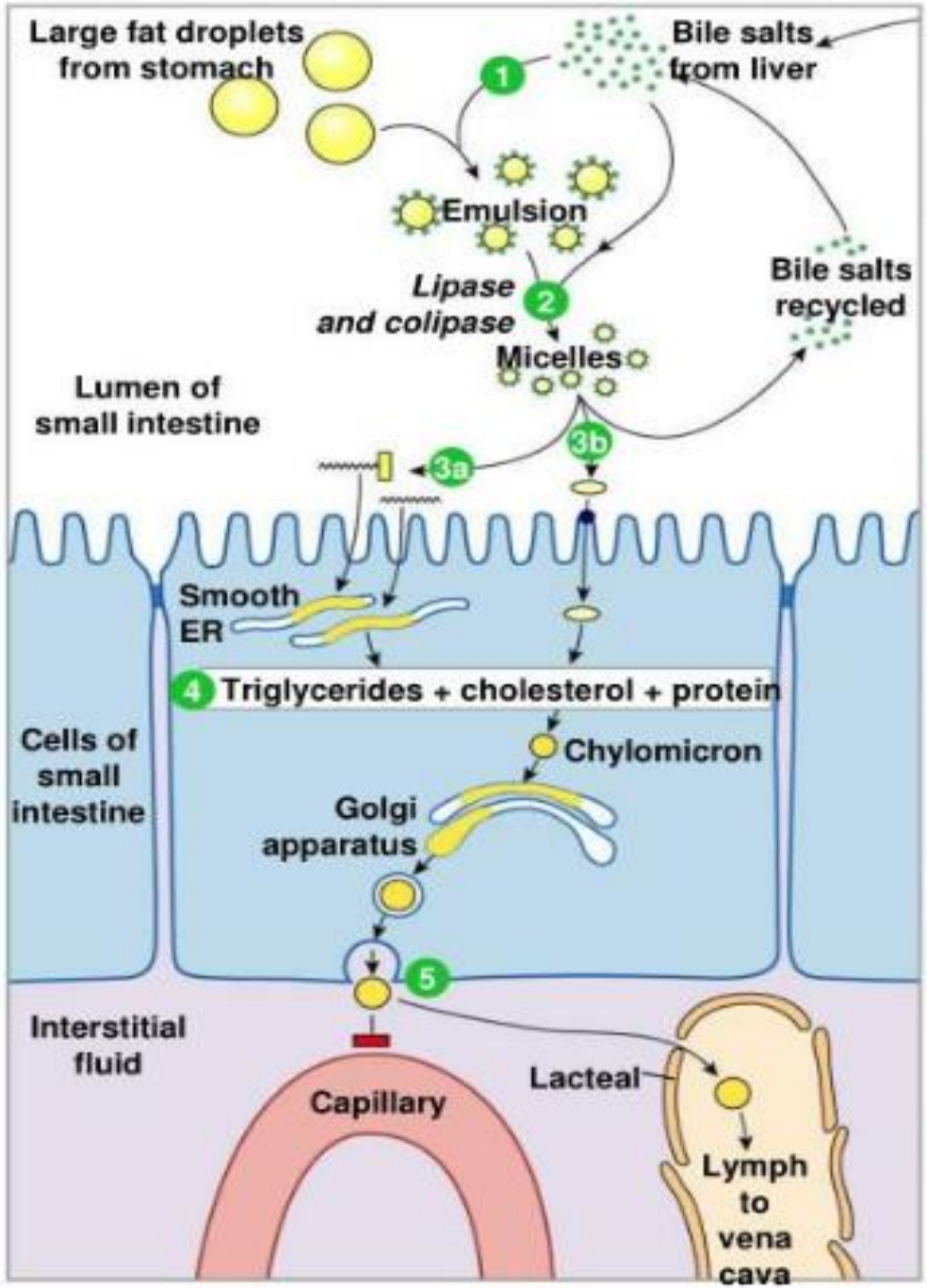




Protein digestion and absorption



Fat absorption and digestion



1. Bile salts from liver coat fat droplets.

2. Pancreatic lipase and colipase break down fats into monoglycerides and fatty acids stored in micelles.

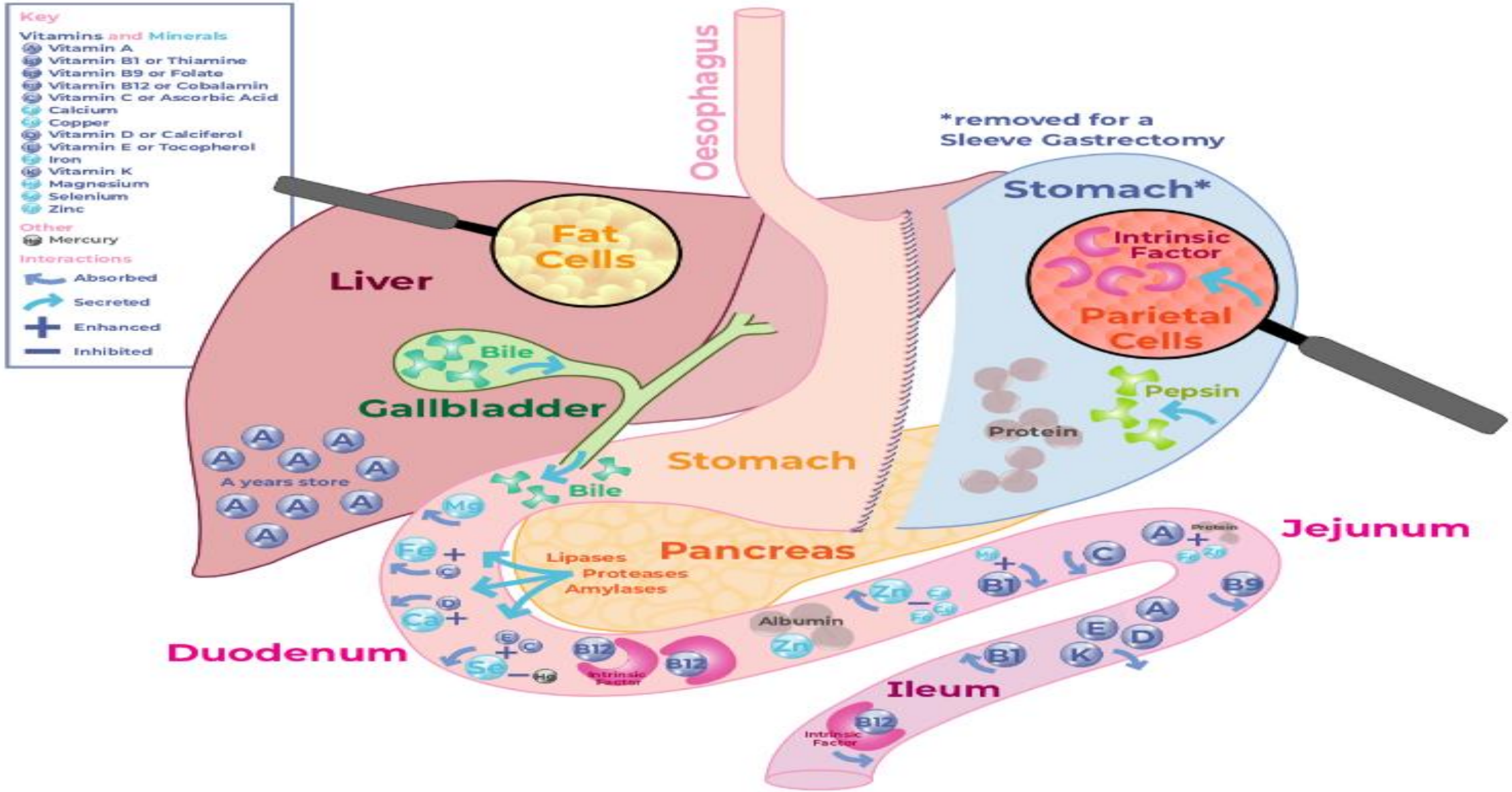
3a. Monoglycerides and fatty acids move out of micelles and enter cells by diffusion.

3b. Cholesterol is transported into cells by a membrane transporter.

4. Absorbed fats combine with cholesterol and proteins in the intestinal cells to form chylomicrons.

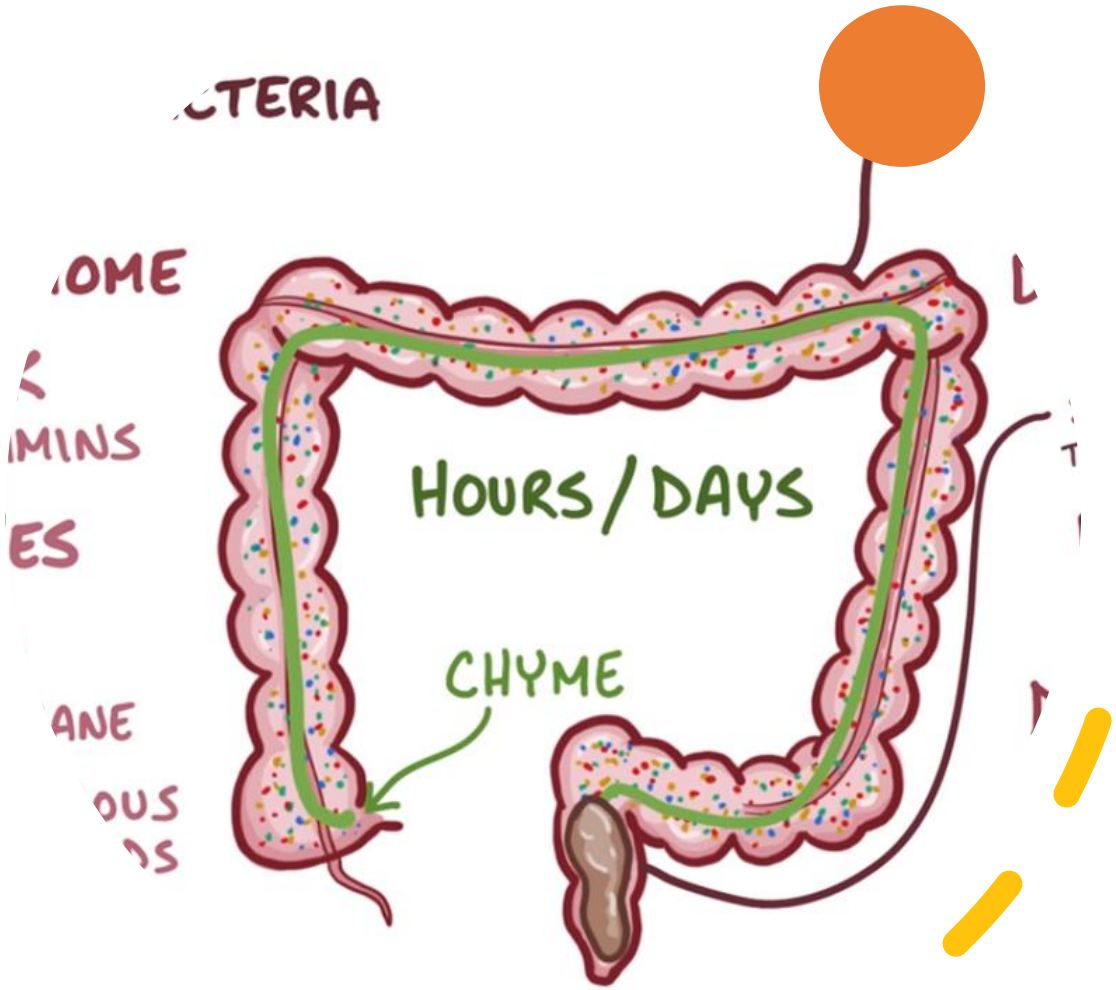
5. Chylomicrons are released into the lymphatic system.

Vitamins and Minerals



Large intestine

- Extends from the ileocecal junction to the anus
- Functions to convert the liquid contents of the ileum into semisolid feces by absorbing water, salts, and electrolytes.
- Consists of the cecum, appendix, colon, rectum, and anal canal.



Protracted diarrhea

* **Definition**

- Chronic diarrhea is defined as stool volume of more than 10 g/kg/day in toddlers/infants and greater than 200 g/day in older children that lasts for 14 days or more.
- The WHO defines diarrhea as the passage of loose or watery stool at least 3 times in a 24 hr.
- The terms chronic, persistent and protracted diarrhea are often used interchangeably

Risk factor

- Malnutrition
- Zinc deficiency
- lack of breast-feeding
- Male sex
- Enteric infection with Escherichia coli or Cryptosporidium
- systemic infections
- intrauterine growth retardation

Types

- Diarrhea may be secretory or osmotic, although both mechanisms may occur together in patients with severe enteropathy.

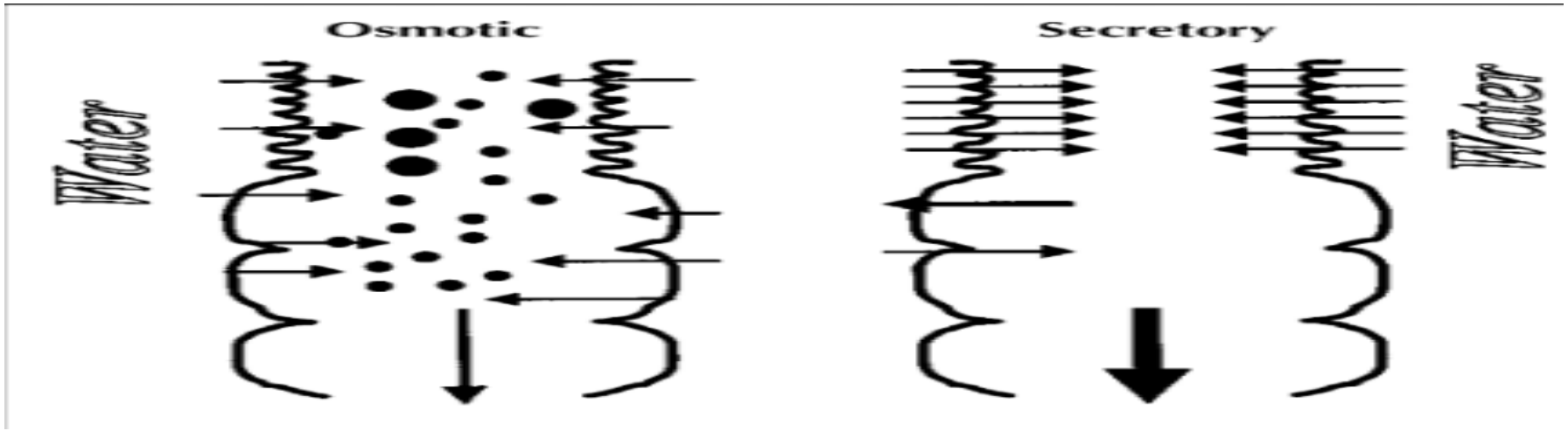
- To determine whether the diarrhea is osmotic or secretory, the **osmotic gap** is calculated:

Osmotic gap = 290 − 2([Na+] + [K+]) secretory---- 50 > osmotic------ 50 <

- Another way to differentiate between osmotic and secretory diarrhea is to stop all feedings (in hospitalized patients receiving IV fluids).

  stopped diarrhea ------ osmotic

  continuous ------ secretory



- due to unabsorbed nutrients in the stool
- Osmotic load causes fluid retention in the bowel
- Stool volume: < 200 mL / day
- Relived by fasting
- Stool Na: 30
- Stool k: 30
- Stool osmotic gap : <50

- Increase water and electrolyte secretion by toxin or VIP in the intestinal lumen
- Net inhibition of sodium and water absorption
- Stool volume: < 200mL / day
- Not relived by fasting
- Stool Na:100
- Stool K: 40
- Stool osmotic gap: >50 m.osmoles/ Kg

Secretory diarrhea

- occurs when there is significant excess secretion compared to absorption
- The two major mechanisms of intestinal electrolyte secretion:

  1- Chloride secretion by CFTR (plus reduced sodium absorption)

  2-Loss of tight junction integrity with increased paracellular permeability

- The result is more secretion from the crypts than absorption in the villous that persists during fasting.
- Examples include IBD and toxins such as cholera toxin, ***Escherichia coli*** toxin, ***Shigella*** toxins , and ***Salmonella***

Osmotic diarrhea

- occurs when ingested solutes are not digested and absorbed adequately within the small intestine. These then provide an osmotic gradient, drawing water into the intestinal lumen.
- Causes:

  1. Intestinal damage (e.g., enteric infection)
  2. Reduced absorptive surface area (e.g., active celiac disease)
  3. Defective digestive enzyme or nutrient carrier (e.g., lactase deficiency)
  4. Decreased intestinal transit time (e.g., functional diarrhea)
  5. Nutrient overload, exceeding the digestive capacity (e.g., overfeeding).

- A very common example of osmotic diarrhea is lactose intolerance.
- Lactose, if not absorbed in the small intestine, reaches the colon, where it is fermented to short-chain organic acids, releasing hydrogen that is detected in the lactose breath test, and generating an osmotic overload

Syndromes of intractable diarrhea of infancy

- The syndromes of intractable diarrhea in infancy represent some of the most difficult management problems, as they frequently lead to intestinal failure.
- Severe chronic diarrhea in an infant does not necessarily indicate an intractable diarrhea syndrome; common conditions should always be excluded.
- The recognized conditions are essentially of primarily epithelial or immunologic origin.
- The history of the time of first onset is critical. The epithelial defects are generally of early onset, within the first 1–2 weeks of life, whereas autoimmune enteropathies usually develop later, after 1 month of age.

- The syndrome had the following features:

  - Diarrhea of more than two weeks duration
  - Age, less than three months
  - Three or more stool cultures negative for bacterial pathogens
  - Despite hospital management, diarrhea was persistent and intractable
  - There was a high mortality.

- The main etiologies of intractable diarrhea include:

1. Structural enterocyte defects
2. Disorders of intestinal motility
3. Immune-based disorders
4. Short gut syndrome

1. **Structural enterocyte defects** are caused by specific molecular defects responsible for early onset, severe diarrhea.

- In microvillus inclusion disease, a rare autosomal disorder of enterocytes caused by MYO5B mutations, characterized by severe malabsorption and large watery stool up to 300ml/kg/day that can persist despite nil per oral status. This disorder thus causes profound intestinal failure.
- Intestinal epithelial dysplasia (or tufting enteropathy) is caused by focal crowding of enterocytes that produce epithelial abnormalities resembling tufts (tears).

2. Disorders of intestinal motility

include abnormal development and function of the enteric nervous system, such as in Hirschsprung disease.

- Other motility disorders may be secondary to extraintestinal disorders, such as hyperthyroidism and scleroderma

3. Autoimmune processes

may target the intestinal epithelium, alone or in association with extra-intestinal symptoms.
Autoimmune enteropathy is associated with the production of anti-enterocyte and anti-goblet cell antibodies, primarily immunoglobulin A, but also immunoglobulin G directed against components of the enterocyte brush-border or cytoplasm.

1. **X linked immune-dysregulation, polyendocrinopathy, and enteropathy (IPEX syndrome**) is associated with variable gene mutations and phenotypes of chronic diarrhea.
2. **Agammaglobulinemia**
3. **Isolated immunoglobulin A deficiency**

4. Short bowel syndrome

Is the single most frequent etiology of chronic diarrhea and intestinal failure.

- Many intestinal abnormalities such as stenosis, segmental atresia, and malrotation may require surgical resection, but the most frequent primary cause of short bowel is necrotizing enterocolitis.
- In these conditions, the residual intestine may be insufficient to carry on its digestive–absorptive functions. Rarely, a child may be born with a congenitally short small bowel resulting in delayed growth.

Syndromatic (phenotypic) diarrhea

- Is a rare disease presenting with facial abnormalities (hypertelorism, broad midface, and nose), abnormal hair development (woolly, under-pigmented), severe diarrhea, and malabsorption.
- Requiring long-term parenteral nutrition.
- Half of the patients have liver disease. (cirrhosis)

Management

- **General supportive measures**
  Replacement of fluid and electrolyte losses.

- **Nutritional rehabilitation**
  Micronutrient and vitamin supplementation (Zinc supplementation)

- **Elimination diet**
- A lactose-free diet should be started in all Children with chronic diarrhea and is recommended by the World Health Organization
- A sucrose-free formula is indicated in sucrose isomaltase deficiency

✓ **When oral nutrition is not feasible or fails, enteral or parenteral nutrition should be considered**

Celiac Disease

Definition

Gluten-sensitive enteropathy

immune mediated inflammatory disorder of small intestine triggered by an environmental agent (the gluten component of wheat and related cereals) in genetically predisposed individuals

Mucosal immune response — to gliadin fractions promote an inflammatory reaction, characterized by infiltration of the lamina propria and the epithelium with chronic inflammatory cells and villous atrophy.

. Incidence of celiac disease is estimated at 1%, but only a small

proportion has been diagnosed

Grains Containing Gluten

twitter.com/HealthNutCorner

Barley

Bulgur

Farina

(Cream of Wheat)

Durum Wheat

(Pasta, Semolina)

Kamut

(Khorasan wheat or Oriental wheat)

Farro

Rye

Semolina

(Couscous, Cream of Wheat, Pasta, Orzo)

Spelt

Triticale

Wheat

(All purpose flour, Enriched flour, Cake flour, Whole-wheat flour, Wheat berries)

NOTE: OATS are naturally gluten-free but may be contaminated with gluten during processing

Presentation

Gastrointestinal symptoms:

- **Persistent diarrhea**
- **Abdominal bloating/distension**
- **Poor weight gain/weight loss**
- **Abdominal pain**
- **Constipation**
- **Vomiting**

Extraintestinal manifestations :

- **Neurologic and behavioral symptoms such as headaches, difficulty concentrating, or irritability**
- **Arthritis or arthralgias (even if there is a presumed underlying rheumatic disease)**
- **Chronic fatigue**
- **Short stature or low height velocity**
- **Pubertal delay**
- **Iron deficiency anemia often poorly responsive to supplementation**
- **Dermatitis herpetiformis-like rash**

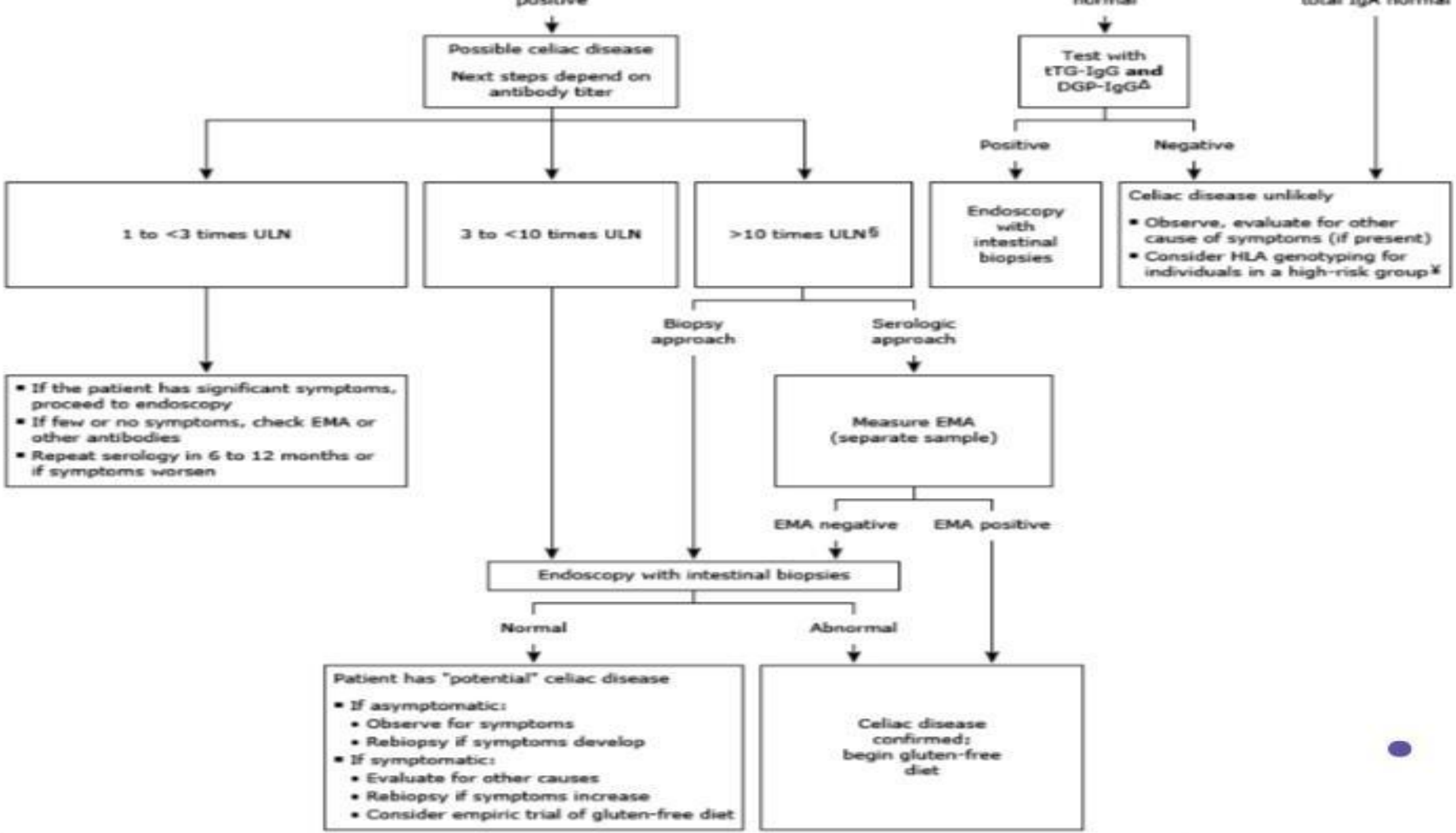
Erythema nodosum

- **Dental enamel hypoplasia of permanent teeth (symmetric distribution)**

OSTEOPNEA and elevated liver enzymes

High Risk people

- First-degree relatives of patients with celiac disease
- Autoimmune thyroiditis.
- Type 1 diabetes
- Autoimmune liver disease.
- Down syndrome
- Selective IgA deficiency
- Turner syndrome


Possible celiac disease
Next steps depend on antibody titer
Test with tTG-IgG and DGP-IgGΔ
Positive
Negative
1 to <3 times ULN
3 to <10 times ULN
>10 times ULN§
Endoscopy with intestinal biopsies
Celiac disease unlikely
• Observe, evaluate for other cause of symptoms (if present)
• Consider HLA genotyping for individuals in a high-risk group¥
• If the patient has significant symptoms, proceed to endoscopy
• If few or no symptoms, check EMA or other antibodies
• Repeat serology in 6 to 12 months or if symptoms worsen
Biopsy approach
Serologic approach
Measure EMA (separate sample)
EMA negative
EMA positive
Endoscopy with intestinal biopsies
Normal
Abnormal
Patient has "potential" celiac disease
• If asymptomatic:
• Observe for symptoms
• Rebiopsy if symptoms develop
• If symptomatic:
• Evaluate for other causes
• Rebiopsy if symptoms increase
• Consider empiric trial of gluten-free diet
Celiac disease confirmed: begin gluten-free diet

Management

complete elimination of gluten from the diet.

A consultation with a dietitian experienced in celiac disease is helpful, as is membership in a celiac disease support group.

Lists of starchy foods that are safe include:

rice, soy, tapioca, buckwheat, potatoes, and (pure) oats.

Most patients respond clinically within a few weeks with weight gain and improved appetite. Histological improvement requiresseveral months.

Protein losing enteropathy

Definition

- **Protein-losing gastroenteropathies are characterized by an excessive loss of serum proteins into the gastrointestinal tract, resulting in hypoproteinemia, edema, and, in some cases, pleural and pericardial effusions.**

- **In addition to proteins, other serum components that may also be lost in the gut include iron, lipids, fat soluble vitamins.**

- **It occurs when proteins loss exceed liver capacity of protein synthesis**

Diagnosis of protein-losing enteropathy should be suspected in patients with hypoproteinemia once the other common causes like severe malnutrition, nephrotic syndrome, or chronic liver diseases have been ruled out.

1-low albumin low glubulin

2-Alpha1 antitrypsin intestinal clearance

***normal clearance is 13 ml/24 h.. If more than 27 ml/24h, It indicates increased gastrointestinal protein loss**

3- 51Cr-labeled albumin clearance(considered gold standard),

Detailed history helps in narrowing down the list of conditions causing hypoproteinemia and PLE . In cases where symptoms suggest gastrointestinal causes of protein loss, tests for celiac disease, infectious work for chronic intestinal infections, appropriate imaging of abdomen and pelvis, upper and lower gastrointestinal endoscopies with biopsies, capsule endoscopies (if upper and lower endoscopies are unremarkable) should be performed. Autoimmune workup should be ordered if SLE or RA is suspected. Echocardiogram and workup on the lines of heart failure should be done if cardiac causes of PLE is suspected

Intestinal lymphangiectasia

- rare protein-losing gastroenteropathy characterized by dilatation of the intestinal lymphatics and loss of lymph fluid into the gastrointestinal tract, leading to the development of hypoproteinemia, edema, lymphocytopenia,and hypogammaglobinemia.
- Generally diagnosed before age of 3
- Edema is the Main symptom, others: fatigue, Vomiting, abd.pain,and may lymphedema
- low-fat diet associated with medium-chain triglyceride supplementation is the cornerstone of PIL medical managemenlt
- Surgical management may be used for segmental and localized intestinal lymphangiectasia.

Infectious causes

Viral ;Rota

Bacterial ; salmonella sheigella camplobacter C. dificilli

Parasite ; Giardia lamblia

- ***Flagillated protozoa**
- ***by feco-oral route / contaminated food with oocyte**
- ***dx.. 3 stool specimen looking for trophozite or cyst**
- ***treatment : metronidazole, tinidazole, nitazoxanide.**

Infectious Diarrhea

Definition

Acute gastroenteritis refers to a clinical syndrome of diarrhea (>3 stool episodes in 24 hours).

Transmitted by feco-oral route or ingestion of contaminated food or water.

- **Viral gastroenteritis is the most common cause of diarrhea in children.**
- **Rotavirus is most frequent cause of diarrhea in young**

children during the winter months

- **Norovirus is the most common cause of outbreaks of gastroenteritis**

Common Pathogenic Organisms Causing Diarrhea and Their Virulence Mechanisms

ORGANISMS	PATHOGENIC MECHANISM(S)
VIRUSES	
Rotaviruses	Damage to microvilli
Caliciviruses (noroviruses)	Mucosal lesion
Astroviruses	Mucosal lesion
Enteric adenoviruses (serotypes 40 and 41)	Mucosal lesion
BACTERIA	
Campylobacter jejuni	Invasion, enterotoxin
Clostridium difficile	Cytotoxin, enterotoxin
Escherichia coli	
Enteropathogenic (EPEC)	Adherence, effacement
Enterotoxigenic (ETEC) (traveler's diarrhea)	Enterotoxins (heat-stable or heat-labile)
Enteroinvasive (EIEC)	Invasion of mucosa
Enterohemorrhagic (EHEC) (includes O157: H7	Adherence, effacement, cytotoxin

causing HUS)	
Enteroaggregative (EAEC)	Adherence, mucosal damage
Salmonella	Invasion, enterotoxin
Shigella	Invasion, enterotoxin, cytotoxin
Vibrio cholerae	Enterotoxin
Vibrio parahaemolyticus	Invasion, cytotoxin
Yersinia enterocolitica	Invasion, enterotoxin
PARASITES	
Entamoeba histolytica	Invasion, enzyme and cytotoxin production; cyst resistant to physical destruction
Giardia lamblia	Adheres to mucosa; cyst resistant to physical destruction
Spore-forming intestinal protozoa *Cryptosporidium parvum* *Isospora belli* *Cyclospora cayetanensis*	Adherence, inflammation
Microsporidia (*Enterocytozoon bieneusi*, *Encephalitozoon intestinalis*)	

Presentation

- **Vomiting**
- **Diarrhea**

***Viral diarrhea watery stools with no blood or mucus.**

***Sheigella dysentery foul smelling stool with blood and mucus**

- **Edema**
- **Eosinophilia**
- **systemic findings (lethargy, myalgias, abdominal pain, fever)**

Most are self-limited

Supportive management:

- **dehydration (<10%) in absence of excessive vomiting or shock may be managed with ORS containing glucose and ELECTROLYTES.**
- **Continued breastfeeding**
- **Ondansetron for persistent emesis**

Antibiotics.? In sheigella, It reduces duration of symptoms and decrease transmission of infection

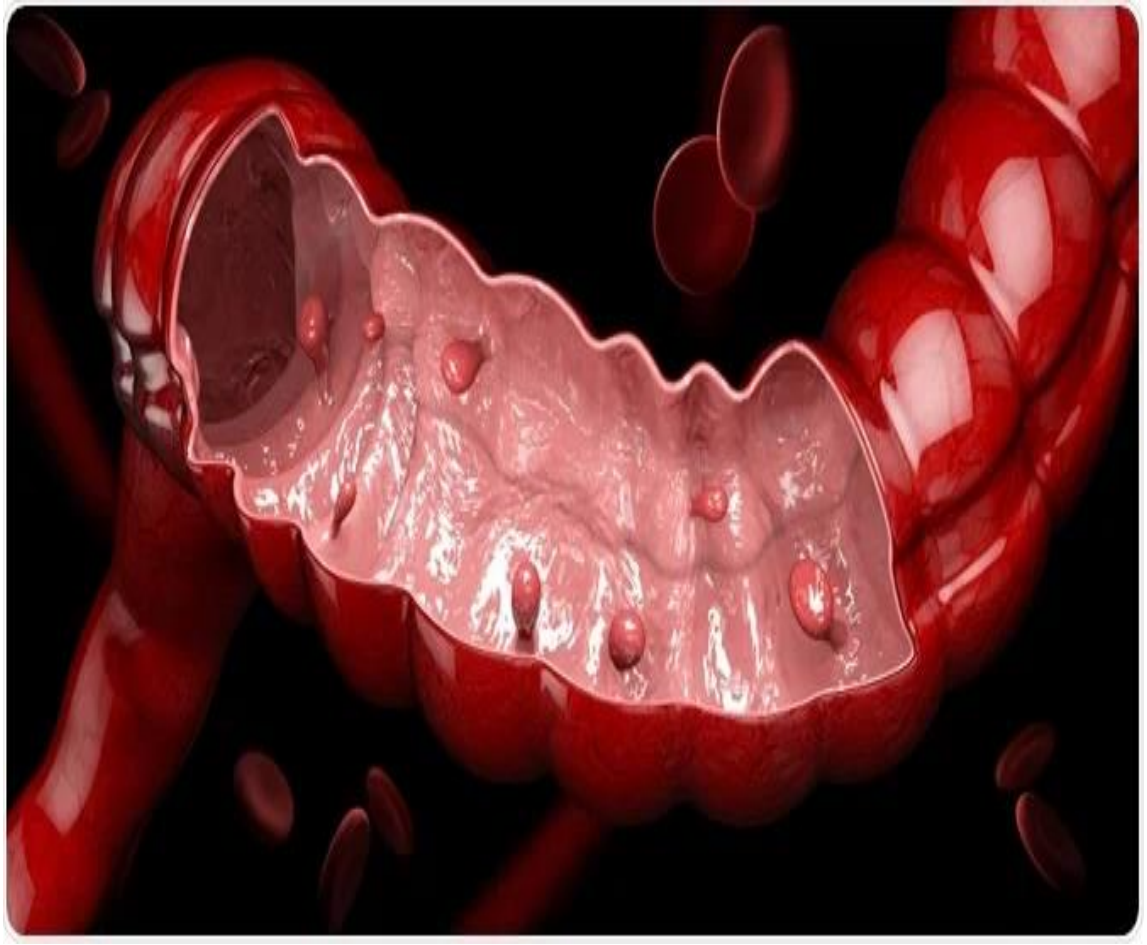
- **Antidiarrheal**
- **Antimotility or anti secretory**
- **Probiotics**

Juvenile polyposis syndrome

Juvenile polyposis syndrome (JPS):

is an **autosomal dominant** condition characterized by **multiple hamartomatous polyps** throughout the gastrointestinal tract.

Individuals with JPS are at increased risk for **colorectal** and **gastric cancer.**



Epidemiology

JPS is rare, with an estimated incidence of 1 in 100,000 individuals.

Genetics

JPS occurs as a result of germline mutations in the SMAD4 (MADH4) and BMPR1A genes.

Symptoms

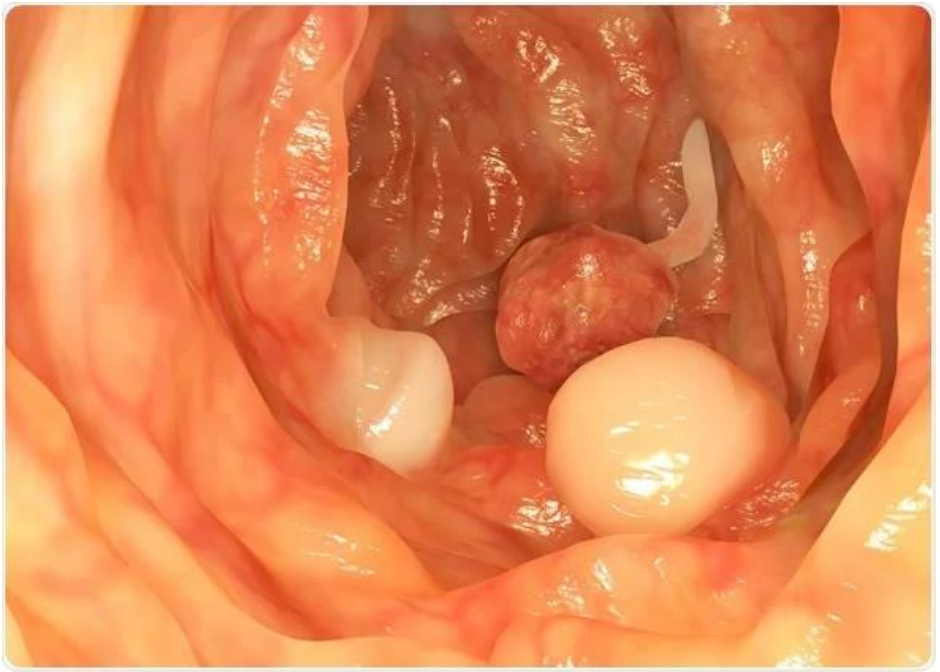
Juvenile polyposis of infancy ,occur in both the upper and lower gastrointestinal tract and polyps develop within the first few years of life.

Symptoms include diarrhea, bleeding, and intussusception. Macrocephalus and hypotonia may also occur, and patients often die at an early age.

JPS due to SMAD4 mutations may also be associated with hereditary hemorrhagic telangiectasia (HHT). The most common clinical manifestations of HHT are telangiectasias of the skin and buccal mucosa, epistaxis, and iron deficiency anemia from gastrointestinal telangiectasia; pulmonary, hepatic, cerebral, and rare arteriovenous malformations.

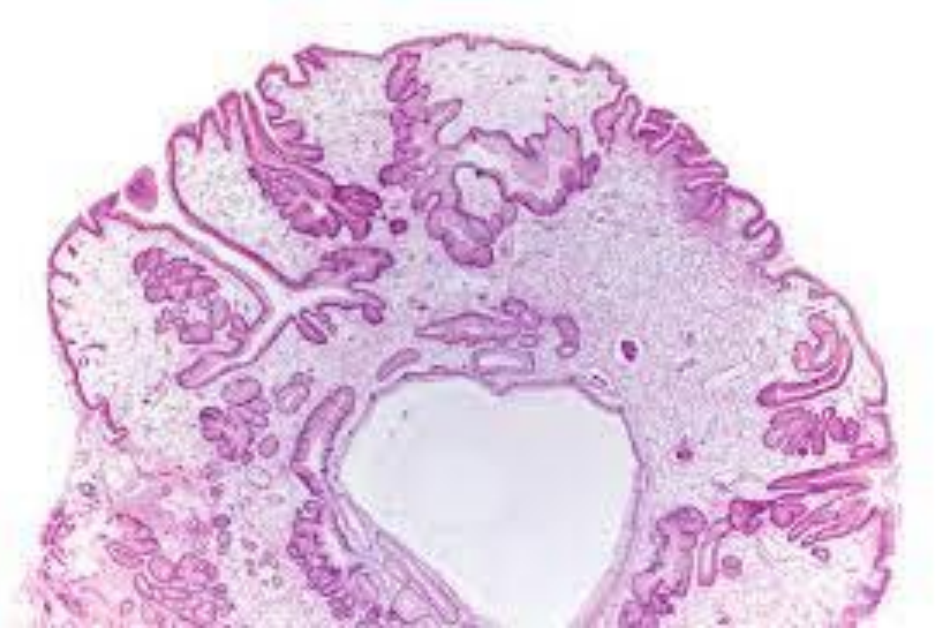
Endoscopic features – (Juvenile polyps are hamartomas)

Endoscopically, juvenile polyps vary in size from small sessile nodules to large pedunculated lesions measuring several centimeters.



Histologic features –

The histologic appearance of juvenile polyps is characterized by both abundant lamina propria, which may be edematous and contain inflammatory cells, and dilated glands forming mucin- filled cysts.



Diagnosis – A clinical diagnosis of JPS is based on the presence of at least one of the following and the absence of clinical manifestations of other hamartomatous polyposis syndromes:

- Five or more juvenile polyps in the colorectum
- Two or more juvenile polyps in other parts of the gastrointestinal tract
- Any number of juvenile polyps in a person with a known family history of juvenile polyps in a first-degree relative

Individuals who meet clinical criteria for JPS should undergo genetic testing for a germline mutation in the BMPR1A and SMAD4 genes.

Management – Our approach to the management of patients with JPS is as follows:

Annual physical examination including a cardiovascular examination with a complete blood count to evaluate for iron deficiency anemia. Screening for clinical manifestations and complications of HHT-associated vascular lesions in patients with pathogenic mutations in SMAD4.

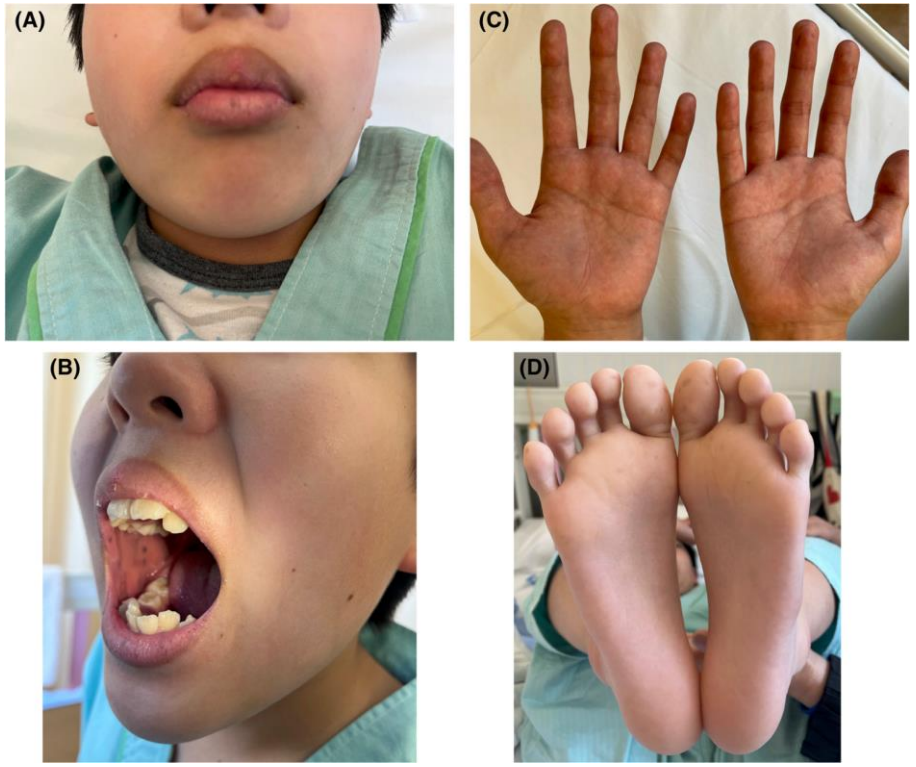
Colonoscopy and esophagogastroduodenoscopy beginning between the ages of 12 and 15, repeated annually if polyps are demonstrated or every two to three years in the Absence of polyps. Additional evaluation of small bowel based on the polyp burden and in patients with iron deficiency anemia or abdominal pain.

Gastrointestinal tract polyps in JPS can usually be resected endoscopically.

Peutz-Jeghers syndrome (PJS)

Peutz-Jeghers syndrome (PJS) is an autosomal dominant syndrome characterized by multiple hamartomatous polyps in the gastrointestinal tract, mucocutaneous pigmentation, and an **increased risk** of gastrointestinal and non gastrointestinal cancer.

Peutz-Jeghers syndrome (PJS) is rare with an estimated prevalence of 1:8000 to 1:200,000 births .Males and females are equally affected.



The two characteristic manifestations of Peutz-Jeghers syndrome (PJS) are :

- **pigmented mucocutaneous macules.**
- **multiple hamartomatous gastrointestinal polyps.**

Peutz-Jeghers syndrome (PJS)

Diagnosis :

- endoscopy
- biopsy
- genetic testing

Management :

- Routine management — Individuals with PJS should undergo an annual physical examination with a complete blood count to detect iron deficiency anemia.
- Cancer screening (ex ; colonoscopy).
- Surgical resection (polypectomy).
- Management of other cancers .

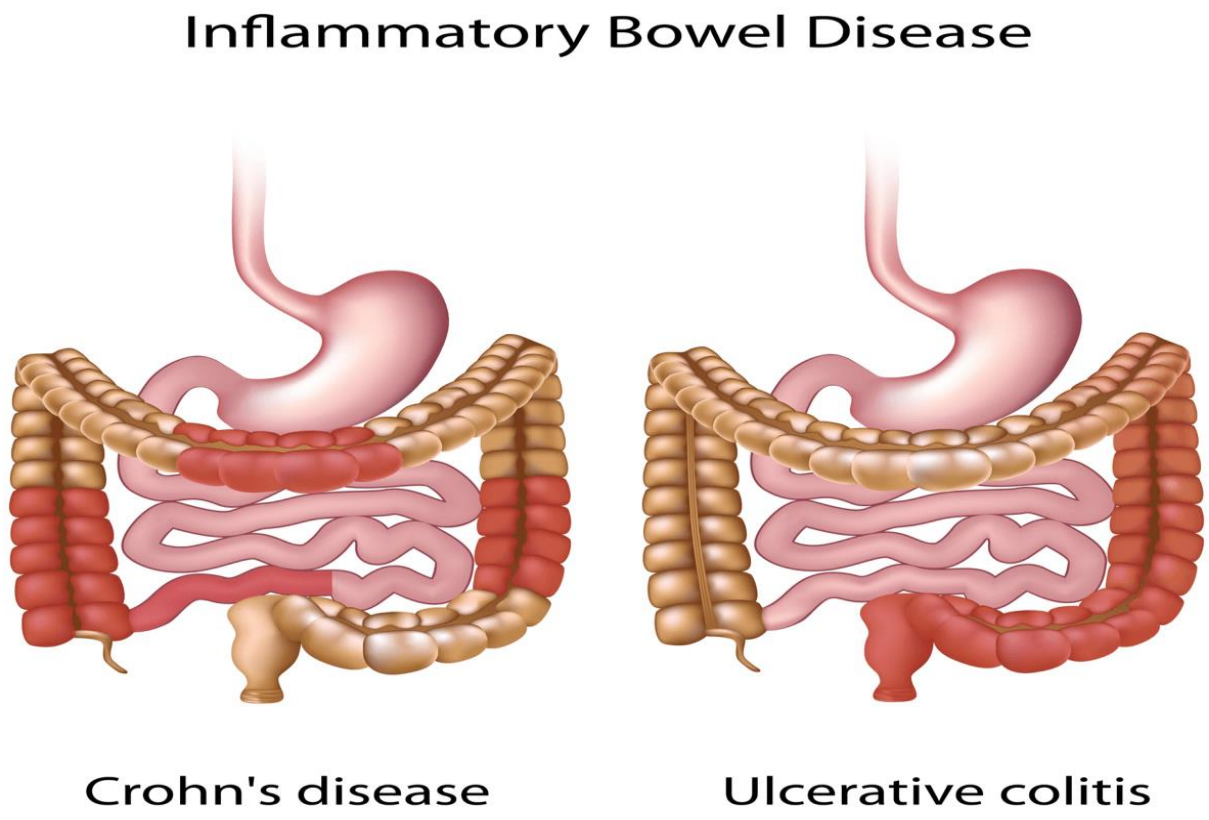
Inflammatory bowel disease

TYPES :

1. Crohn’s disease (CD).

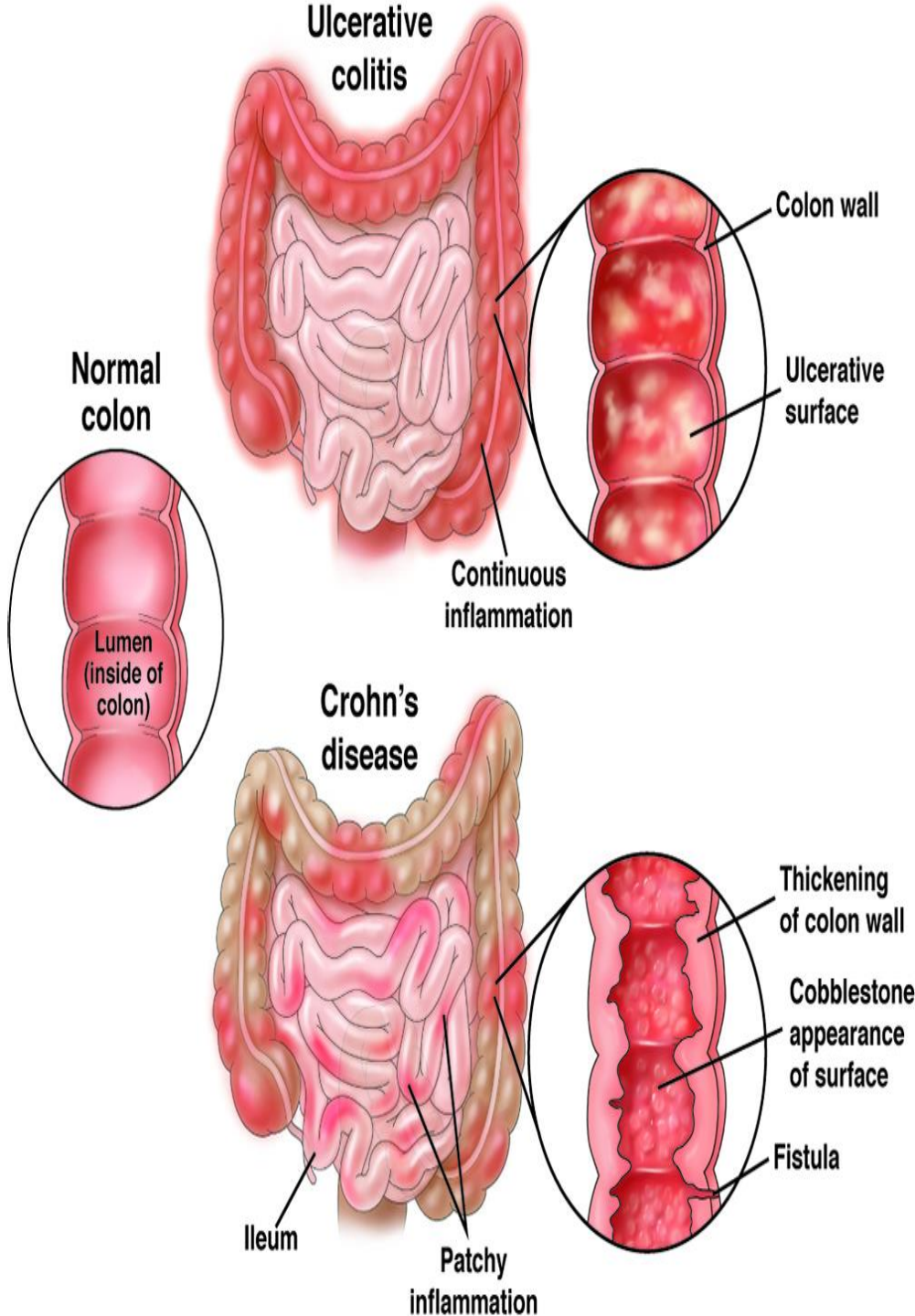
2. Ulcerative colitis (UC).

3. Indeterminate colitis(colitis unspecified)



pathology:

UC	CD
Mucosal disease	Transmural (full-thickness)
Starts in rectum and Proceeds proximally upto terminal ileum	involvement of discontinuous segments of the intestine (skip areas)
No skip lesions	Skip lesions +nt
Characteristically involves the large bowel	Can affect any part of GI tract



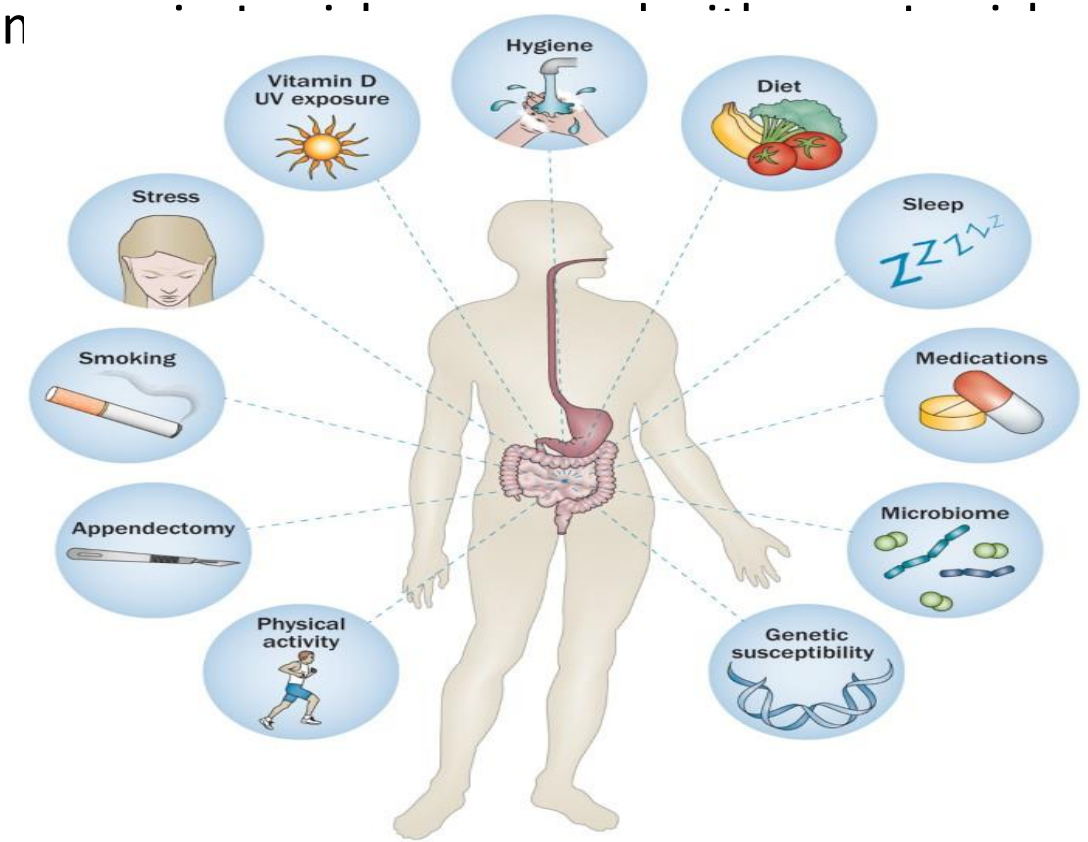
epidemiology ,the peak incidence of inflammatory bowel disease (IBD) in children is in the second decade of life.

Small differences in IBD incidence by sex have been reported. There is a slight female predominance in adult-onset Crohn disease In contrast, there may be a slight male predominance in ulcerative colitis.

Both ulcerative colitis and Crohn disease are more con
populations.

Risk factors :

- Lifestyle factors,Smoking
- Physical activity
- Dietary factors
- Sleep duration
- Infection and the immune response
- Medications(Antibiotics ,NSAIDs)
- Appendectomy
- Psychological factors
- Obesity



Clinical manifestations

Clinical manifestations depend on the region of involvement.

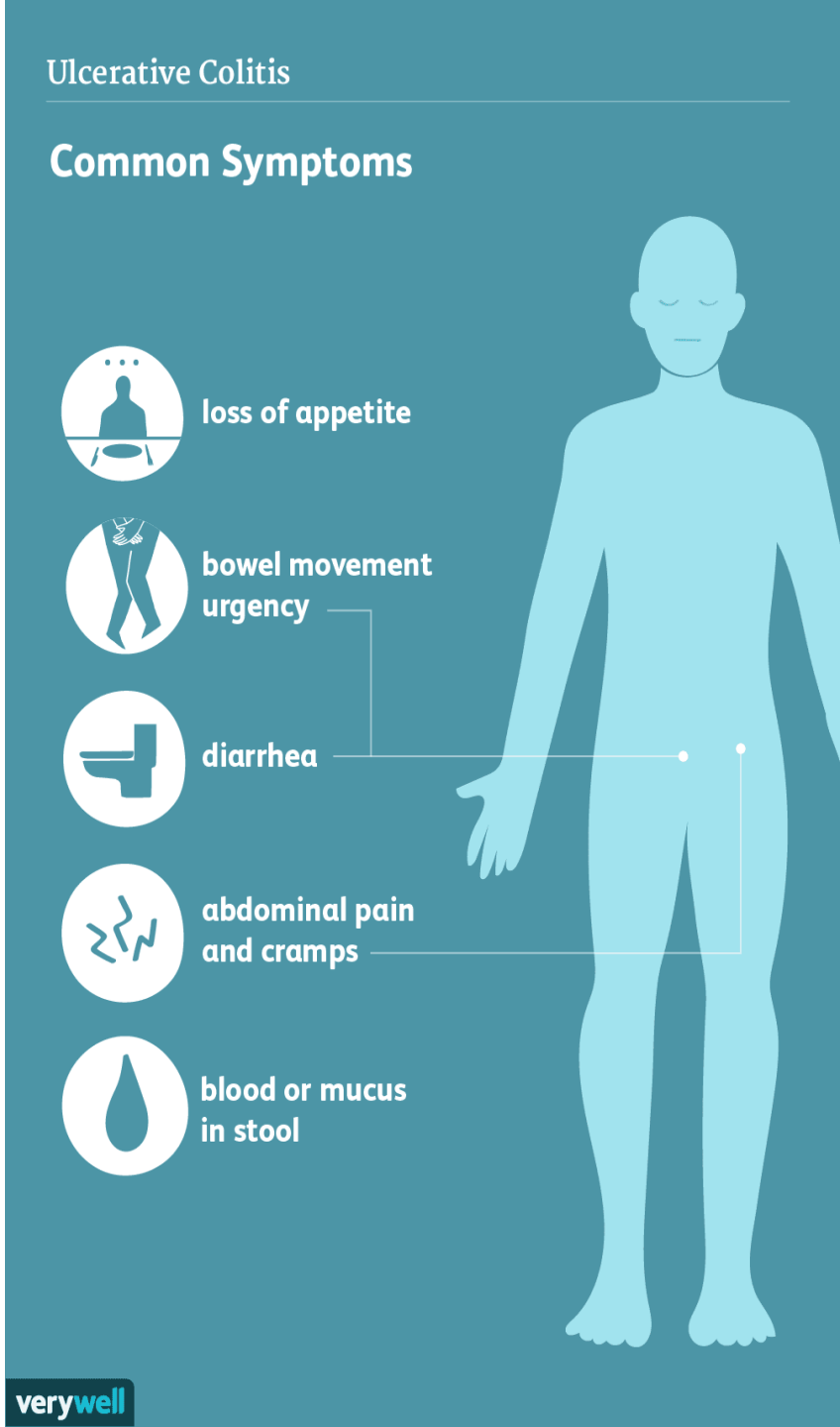
UC involves only the colon, whereas CD can include the entire gut

from mouth to anus.

Colitis from either condition results in

- diarrhea;
- blood and mucus in the stool;
- urgency;
- and tenesmus, a sensation of incomplete emptying after defecation.

- When colitis is severe, the child often awakens from sleep to pass stool.



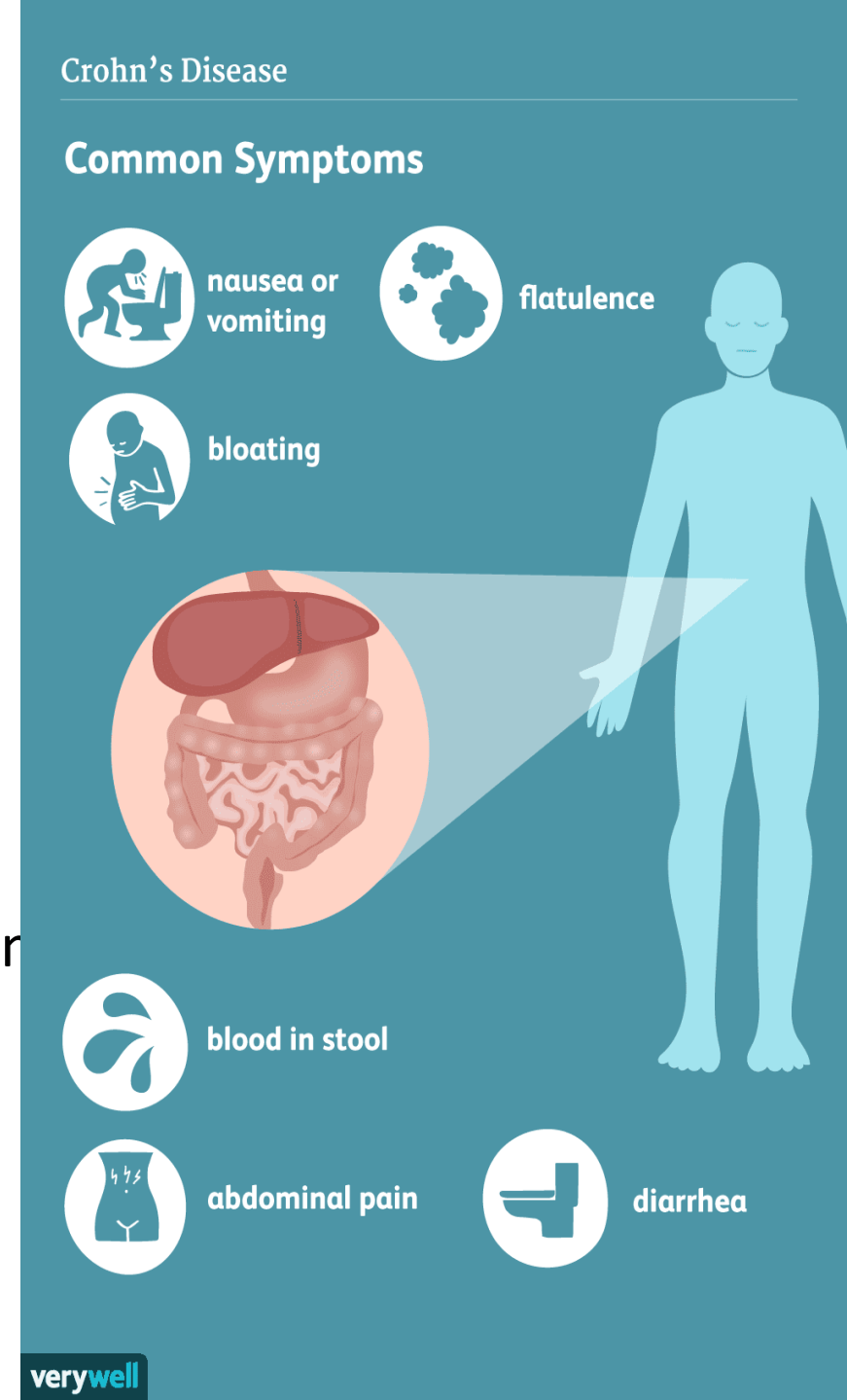
Clinical manifestations

Small bowel involvement in CD is associated with :

- ❑ loss of appetite,
- ❑ crampy postprandial pain,
- ❑ poor growth,
- ❑ delayed puberty,
- ❑ fever,
- ❑ anemia,
- ❑ and lethargy.

- Severe CD with fibrosis may cause partial or complete sr obstruction.

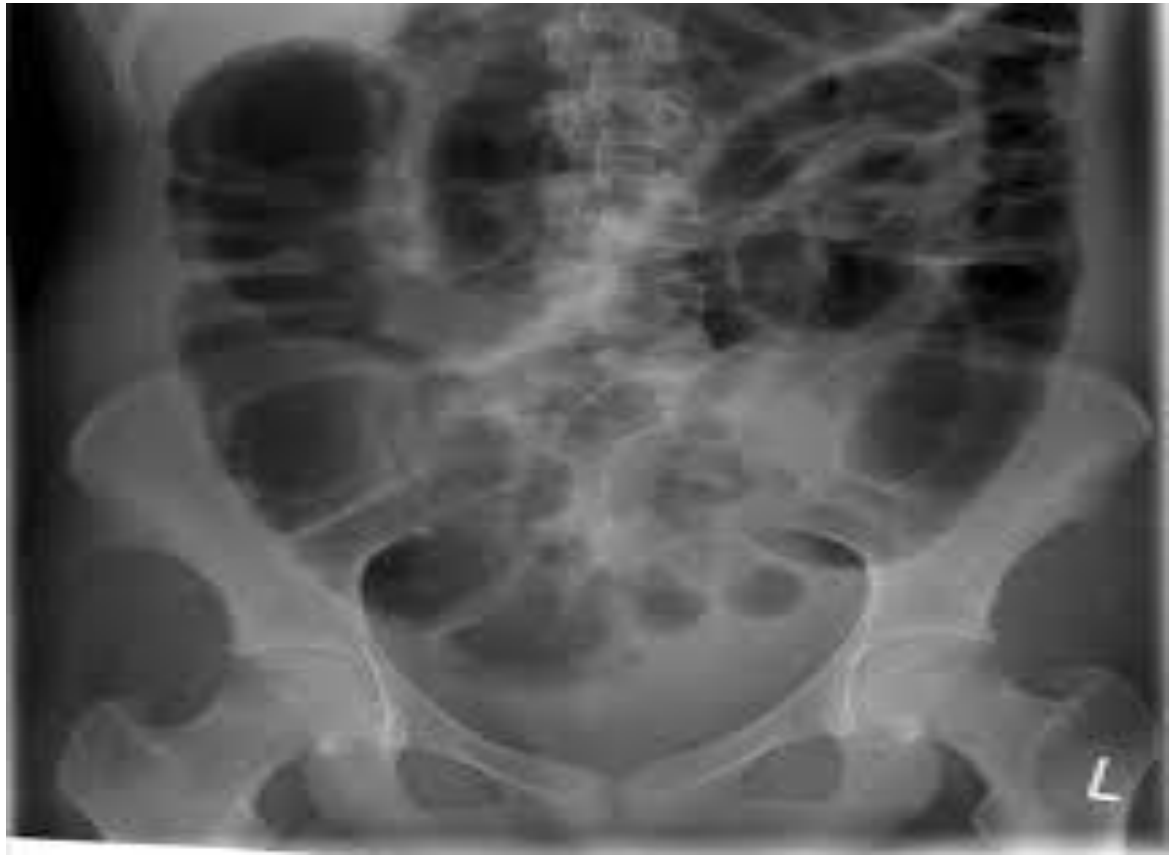
- Perineal abnormalities, including skin tags and fistulas, are another feature distinguishing CD from UC.



Clinical manifestations

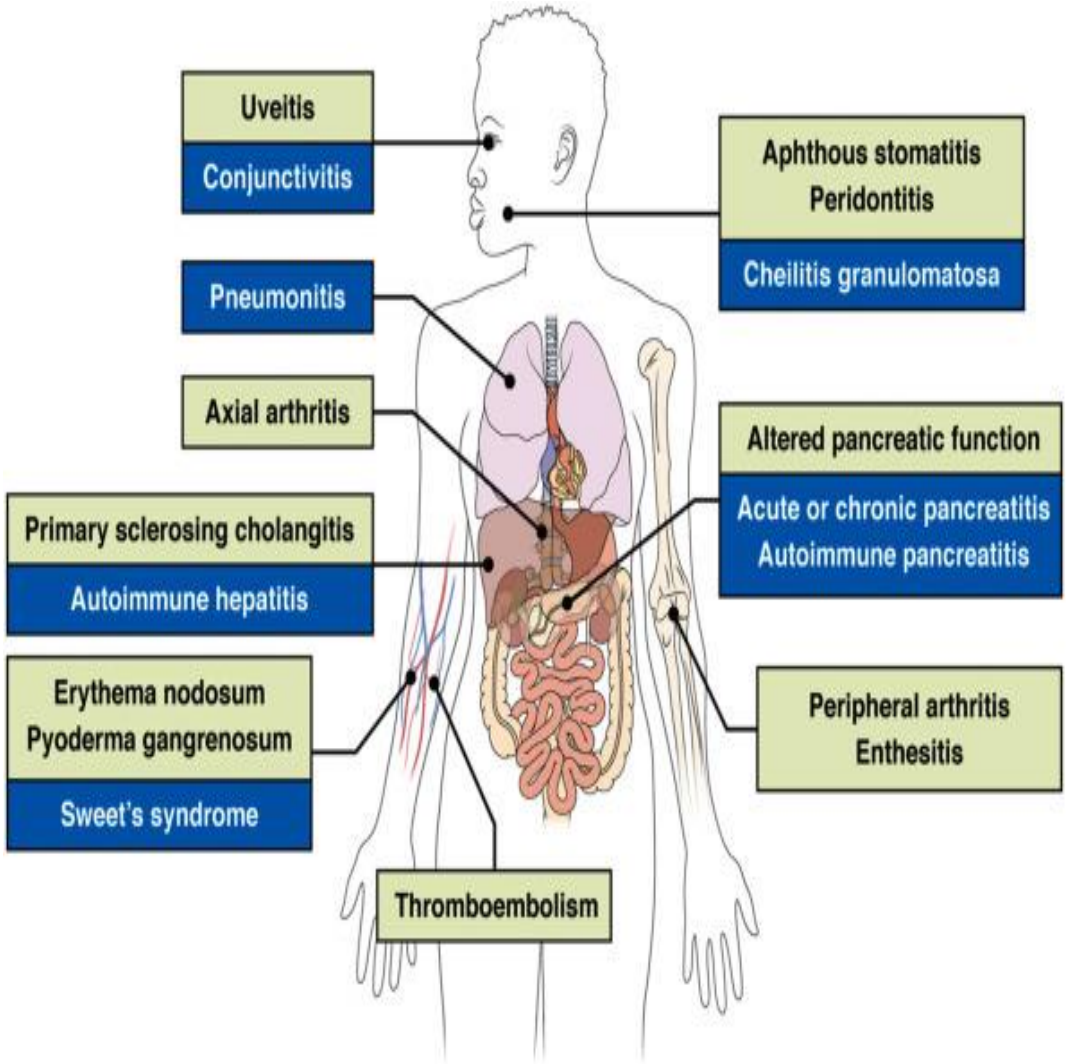
Toxic megacolon is a life-threatening complication characterized by

- fever,
- abdominal distention and pain,
- massively dilated colon,
- anemia,
- and low serum albumin owing to fecal protein losses.



extraintestinal manifestations of inflammatory bowel disease

UC	CD
primary sclerosing cholangitis,	erythema nodosum,
arthritis,	arthritis,
uveitis,	uveitis or iritis.
pyoderma gangrenosum.	



Investigation :

BLOOD TESTS

- CBC — Anemia, elevated platelets suggest IBD
- ESR — Elevated in many, but not all, IBD patients
- C-reactive protein — Elevated in many, but not all, IBD patients
- Albumin — May be low in IBD due to fecal loss
- serologic tests (ASCA, and pANCA).

STOOL STUDIES

Fecal calprotectin and lactoferrin Elevated in IBD and can differentiate from functional disorders

IMAGING STUDIES

- Upper GI series with SBFT Evaluate for ileal and jejunal CD.
- CT scan Used to detect abscess, small bowel involvement.
- Magnetic resonance enterography Used to detect bowel thickening, inflammation, and strictures as well as abscesses and fistulas.

ENDOSCOPY (Upper endoscopy , Colonoscopy , Video capsule endoscopy).

Treatment (UC)

1. medical

UC is treated with the **aminosalicylate drugs,**

When aminosalicylates alone cannot control the disease, **steroid** therapy may be required to induce remission.

An **immunosuppressive drug,** such as 6-mercaptopurine or azathioprine, is useful to spare excessive steroid use in difficult cases.

More potent immunosuppressives, such as cyclosporine or anti–tumor necrosis factor (TNF) agents such as infliximab, may be used as rescue therapy when other treatments fail.

2. surgical

Surgical colectomy with ileoanal anastomosis is an option for unresponsive severe disease or electively to end chronic symptoms and to reduce the risk of colon cancer, which is increased in patients with UC.

Treatment (CD)

1. medical

Inflammation in CD typically responds less well to **aminosalicylates** ,

oral or IV steroids are more important in inducing remission ,

To avoid the need for repetitive steroid therapy, **immunosuppressive drugs**, usually either azathioprine, 6-mercaptopurine, or methotrexate, are often started soon after diagnosis.

CD that is difficult to control may be treated with agents that block the action of TNFα such as infliximab or adalimumab. Other antibodies that inhibit white blood cell (WBC) migration or action, such as vedolizumab, also show promise.

2. Dietary

Exclusive enteral nutrition can be an effective therapy for CD.

Patients take formula as their sole source of nutrition for months as a steroid-sparing therapy.

Other diets such as the specific carbohydrate diet continue to be studied as a possible therapy.

3. surgical

Because surgery is not curative in CD, its use must be limited, and the length of bowel resection must be minimized

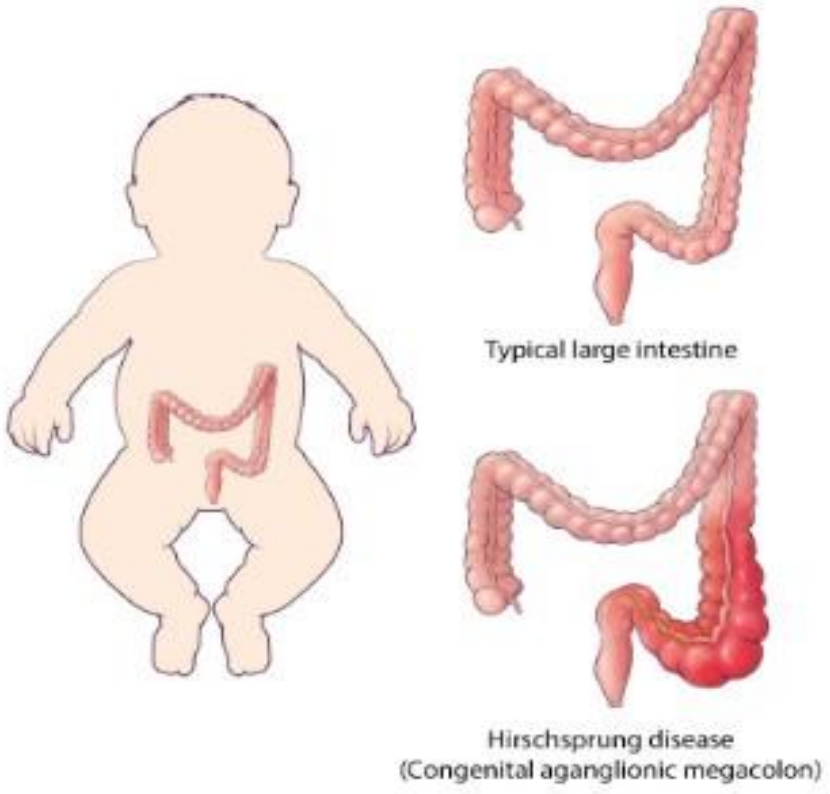
Hirschsprung disease

Hirschsprung disease is a **motility defect** caused by failure of ganglion cell precursors to migrate into the distal bowel during fetal life.

In **75%** of cases, the involved segment is **limited to** **rectosigmoid**; total colonic involvement is seen in 8

Rarely, long segments of small bowel also are agang

Ultrashort" segment involves only a few centimeter of distal rectum.



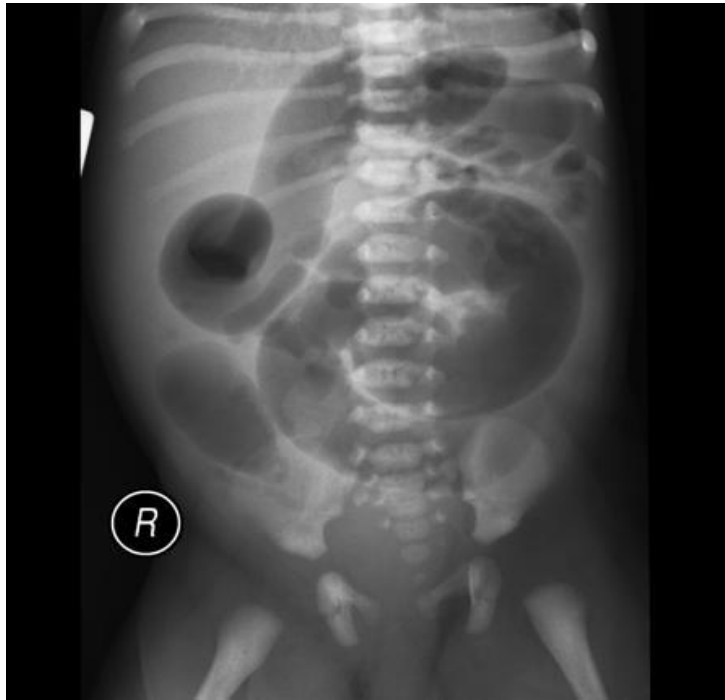
Hirschsprung disease

Symptoms :

- Symptoms of distal bowel obstruction occur with distention and bilious vomiting.
- About 95% of normal infants pass stool spontaneously by 24 hours of age; 95% of infants with Hirschsprung disease do not.

If the diagnosis is not made quickly, enterocolitis can result, associated with a high rate of mortality.

Diagnosis : is based on examination and one or more diagnostic studies.



1. A Full-thickness rectal biopsy .

-Gold standard

-Absence of ganglion cells

2. Barium enema .

3. Anorectal manometry.

Hirschsprung disease

Therapy is **surgical.**

(remove of aganglionic segment of bowels)

Pancreas

Function of pancreas

- The pancreas is a vital exocrine and endocrine organ responsible for the release of hormones and the secretion of fluid, electrolytes, and enzymes that are intricately necessary for the digestion of food and glucose homeostasis
  Exocrine function : It produces enzymes that help to break down food (digestion). Your pancreas releases the following enzymes:
  Lipase: Works with bile (a fluid produced by the liver) to break down fats.
  Amylase: Breaks down carbohydrates for energy.
  Protease: Breaks down proteins. Which is proenzymes, or zymogens, and the most abundant is trypsinogen
- The centroacinar and ductal cells are responsible for the secretion of the bicarbonate ($HCO3-$) rich fluid that transports the digestive enzymes into the small intestine

Pancreas function cont…

- Endocrine Function:
- The endocrine component of the pancreas consists of islet cells (islets of Langerhans) that create and release important hormones directly into the bloodstream. Two of the main pancreatic hormones are insulin, which acts to lower blood sugar, and glucagon, which acts to raise blood sugar. Maintaining proper blood sugar levels is crucial to the functioning of key organs including the brain, liver, and kidneys.

Acute pancreatitis

- Pancreatitis occurs when digestive enzymes are activated inside the pancreas, causing injury. (premature activation)
- **etiology**
  The most common etiology of AP is idiopathic
  Trauma : Blunt, Surgical
  Drugs : Acetaminophen, Valproate
  Infection : Viral , Malaria, Ascariasis.
  Obstructive : Choledochal cyst, biliary stone
  Systemic: IBD, HUS, DM.
- Genetic : CF, trypsin inhibitor gene .

- **CLINICAL PRESENTATION**

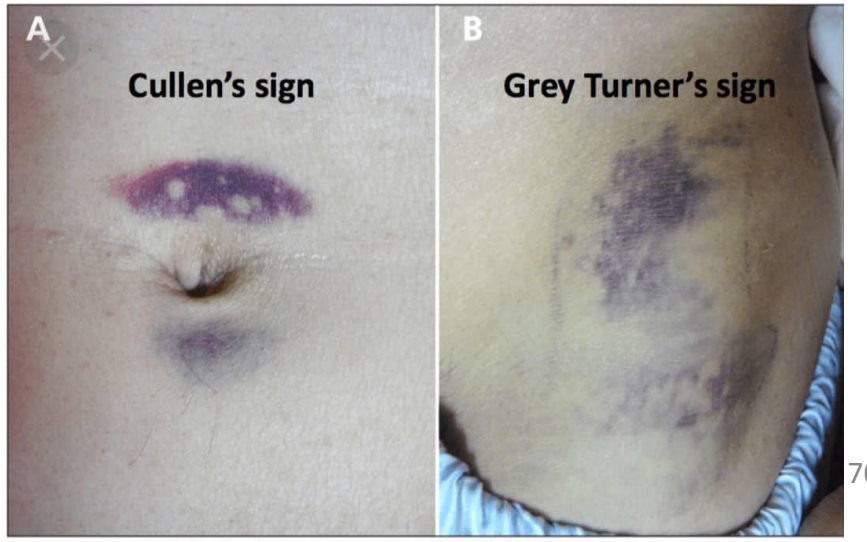
- The symptoms and signs of acute pancreatitis are nonspecific and vary with age .Upper abdominal pain and vomiting are the most common symptoms.

  Classical presentation : Acute pancreatitis presents with relatively rapid onset of pain, usually in the epigastric region. The pain may radiate to the back and is nearly always aggravated by eating. The patient moves frequently to find a position of comfort

  Symptoms: Abdominal pain Irritability (infants) ,Nausea ,Vomiting less common Back pain ,Jaundice ,Fever ,Feeding intolerance .

  Signs : Abdominal tenderness ,Abdominal distension ,

  in sever cases Grey Turner's sign, Cullen's sign



Diagnosis

- The diagnosis of acute pancreatitis is based on 2 of the following 3 criteria:
  1. abdominal pain consistent with the disease (severe epigastric pain typically),
  2.serum amylase and/or lipase greater than 3 time the upper limit of normal, 3. and/or characteristic findings on imaging

Laboratory :
1- Lipase and amylase activity. Serum lipase (longer half life , more specific).
2- cbc :leukocytosis
3- Hyperbilirubinemia
Imaging :
ultrasound : pancreatic hypertrophy, dilated pancreatic duct, and peripancreatic fluid. In addition, ultrasound can detect gallstones
CT : in case of obesity or air bowl gas cause limitation of US therefore CT performed Pancreatic enlargement, hypoechoic, edematous, necrosis , hemorrhage.
also can be used to monitor for the development of pseudocysts and for evidence of ductal dilation secondary to obstruction and role out gallstone

MANAGEMENT

- Treatment, as it always has, relies on supportive care to control pain, to provide adequate intravenous hydration, and to monitor for complications.
  Fluid Management intravenous fluids at a rate that exceeds basal requirements and to give additional fluids determined by the patients' hemodynamic status.
  Analgesia
  Antibiotics should be considered if the patient is febrile, has extensive pancreatic necrosis, or has laboratory evidence of infection as imipenem (bsa)

Chronic Pancreatitis

- recurrent or persistent attacks of pancreatitis, which have resulted in irreversible morphological changes in pancreatic structure
- Etiology :
  Genetic mutations Autosomal Dominant (PRSS1 mutations)
  Autosomal Recessive (CFTR mutations)
  Congenital anomalies of the pancreatic or biliary system.
  Toxic metabolic :Hyperlipidemia ,Hyperparathyroidism
  Drugs

- **Clinical presentation**
  recurrent episodes of acute pancreatitis may predominate. The signs and symptoms are the same as described for acute pancreatitis
  In some patients, mild to intense upper abdominal pain may be the only presenting symptom.
- **DIAGNOSIS** The diagnosis of chronic pancreatitis requires histologic or morphologic evidence or a combination of morphologic, functional, and clinical findings
  laboratory
  Serum lipid, calcium and phosphorus
  Stools : ascaris parasite
  Sweat test : CF
  Imaging
  ERCP has been considered the standard for evaluating the pancreatic ducts. ERCP shows main pancreatic duct dilation, ductal stones, and changes in main duct branches and in small ducts
  U/S : Enlarge/atrophied, stone, ductal stricture/dilation
  CT scan :Duct dilation, pseudocyst, pancreatic atrophy, calcifications, chain of lake
  The biliary tract is evaluated for the presence of stones.
  Genetic : to evaluation of PRSS1, SPINK1, CFTR, and CRTC

Management

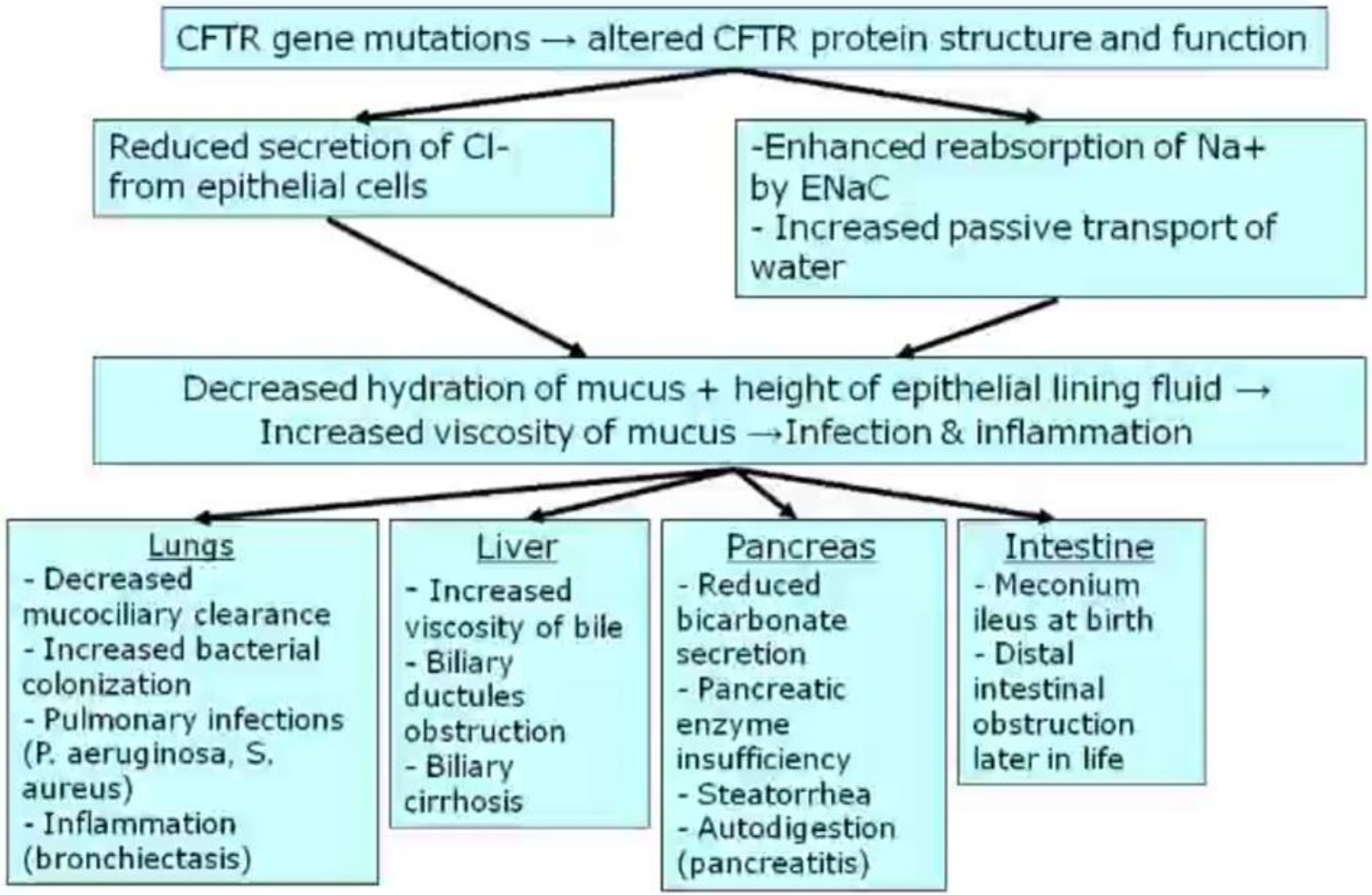
- the management is identical to that for acute pancreatitis. As the disease advances, therapy is directly mostly toward complications that arise such as chronic pain, pancreatic insufficiency, or diabetes mellitus.
- **Supportive** : As acute.
  Pancreatic enzyme and vitamins replacement , octreotide (somatostatin) to abort early attacks, low-fat diets, and daily antioxidant therapy.
- **Interventional: ERCP** to dilate large strictures and remove stones and **surgical pancreatic** drainage procedures to decompress dilated pancreatic ducts by creating a side-to-side pancreaticojejunostomy may have some value.

Cystic fibrosis

- is a life-shortening autosomal recessive disorder that affects over 70,000 individuals worldwide. The gene for CF, located on the long arm of chromosome 7, encodes for the cystic fibrosis transmembrane conductance regulator (CFTR), a chloride channel located on the apical surface of epithelial cells. CFTR is important for the proper movement of salt and water across cell membranes and maintaining the appropriate composition of various secretions, especially in the airways, liver, and pancreas.
  Ninety percent of patients with CF are born with exocrine pancreatic insufficiency.

- mucus and subsequent destruction of the pancreatic ducts result in the inability to excrete pancreatic enzymes into the intestine leads to
  1. exocrine pancreatic insufficiency 90% of pt within 1st year
  2. **malabsorption of fat : steatorrhea, deficiencies of fat-soluble vitamins** and **failure to thrive**
  3. **Protein malabsorption** can present early in infancy **as hypoproteinemia and peripheral edema**.
  Another feature (**meconium ileus**).

Pathophysiology of Cystic Fibrosis



- **Newborn screening for CF:**
  1- Elevated immunoreactive trypsinogen (IRT) levels – Heel-prick test.
  2- DNA test : CFTR mutation.
- **Diagnostic test :**
  1.Sweat test: two elevated test (positive if the value is ≥60 mEq/L, borderline if 30-59 mEq/L, and negative if <30 mEq/L, with adequate sweat collection)
  Or 2.DNA analysis .
  Or 3. Nasal potential difference test .

Management

- Multifactorial therapy
- Diet : higher caloric need
- Pancreatic enzyme replacement
- PPI : decrease acidic pH in duodenum.
- Vitamins (A, D, E, K) : daily
- Chest physiotherapy , albuterol, aerosolized dornase alfa (DNase), hypertonic saline facilitate mucus clearance.
- CFTR modulator therapy : Lumacaftor (corrects misfolded proteins and improves their transport to cell surface) and ivacaftor (open CL- channel)

References

- Nelson textbook
- Uptodate
- Pediatric gastrointestinal and liver disease by Robert Wyllie