Diseases of the intestines

Intestinal obstruction

- Clinical pictures
  - Abdominal pain
  - Distention
  - Vomiting
  - Constipation
  - Acute or chronic
- Divided into
  - Mechanical obstruction (MO) 80%
    - Intussusception (Most common cause of MO in <2 yr)
      - Mechanism — Segment of the intestine constricted by a wave of peristalsis — Telescopes (Slides) into the immediately distal segment — Once trapped, invaginated segment is propelled by peristalsis — And pulls mesentery with it
      - Causes
        - < 2years
          - Idiopathic in most cases — Peyer patches hyperplasia
          - Ileum folds into the cecum
        - Old children & adults
          - Intraluminal mass or tumors — Leading edge are polyps and tumors
          - Ileum folds into the cecum
        - Meckles diverticulum (ileum)
      - Clinical features
        - Abdominal swelling
        - Vomiting
        - Passing stools mixed with blood and mucus (currant jelly stool)
        - Pain.
      - Management
        - If complicated or if masses are the leading point. — Surgery
        - Uncomplicated idiopathic cases. — Contrast enemas
      - Untreated progresses to infarction
    - Hernias — Hernial sac
      - Due to weakness of the pertonium
      - Loop pf intestine enters this sac — If this sac neck is narrow will result in — Strangulated hernia — Ischemia
    - Adhesions
      - Increased fibrous tissue in serosa
      - Causes
        - Idiopathic
        - Previous surgery infection
    - Volvulus — loop twisting — Ischemia
    - Tumors
    - Diverticulitis
    - Infarction
  - Non-mechanical obstruction 20%
    - Hurschsprung disease "Congenital Aganglionic megacolon"
      - General characteristics
        - Congenital — Defect in colonic innervations
        - More common in males, but more sever in females
        - Risk increase in siblings
      - Typical presentation
        - Neonatal failure to pass meconium
        - Obstructive constipation
      - Morphology
        - **Rectum** always involved.
        - Extent is variable.
        - Most cases in rectosigmoid
      - Macroscopic
        - Aganglionic region normal or contracted
        - Proximal normal segment progressively dilated.
      - Complications
        - Enterocolitis
        - Fluid and electrolyte disturbances
        - Perforation
        - Peritonitis
      - Tx — Surgical resection of aganglionic segment and anastomosis of normal segments
      - Diagnosis
        - Biopsy
        - Microscopic
      - Pathogenesis
        - During embryogenesis — Disrupted migration of neural crest cells from cecum to rectum.
        - Lack of Meissner submucosal plexus and the Auerbach
        - myenteric plexus.
        - Failure of coordinated peristaltic contractions.
        - Mutations in RET: in familial cases and 15% of sporadic
        - Other genes and environmental factors play role.
    - Neurological disorders.
    - Drugs

Vascular disorders

- Ischemic Bowel Disease
- Hemorrhoids
  - Defintion — Dilated anal and perianal collateral vessels that connect the portal and caval venous systems
  - Predisposing factors
    - Constipation and straining
    - Venous stasis of pregnancy
    - Portal hypertension
  - External and internal hemorrhoids
  - Microscopic findings
    - **Dilated, thick walled**, congested submucosal vessels and **sinusoidal** spaces, often with **thrombosis**; variable hemorrhage into connective tissue
    - Dilated spaces may show exuberant vascular proliferation confined to vessel known as **papillary endothelial hyperplasia**
    - Internal hemorrhoids are lined by rectal or transitional mucosa, external hemorrhoids have a squamous lining
    - Surface may show ulceration
  - Clinical features
    - Patients usually have **painless bleeding**, noticing blood in the toilet or on lavatory paper
    - Patients may experience pain or discomfort, especially with thrombosis, strangulation or ulceration
    - Anemia from hemorrhoids is unusual - patients should undergo hematologic evaluation
  - Clinically four grades
    - First degree, anal cushions that slide down past dentate line with straining at stool, that bleed with defecation
    - Second, anal cushions that prolapse with straining, but **reduce spontaneously**
    - Third, hemorrhoids that remain outside of the anal canal unless **manually replaced**
    - Fourth, hemorrhoids that **cannot be reduced**

Malabsorptive diseases and infections

- DIARRHEAL DISEASE
  - It can be classified into four major categories
    - Secretory diarrhea — Is characterized by isotonic stool and persists during fasting.
    - Osmotic diarrhea
      - Such as that occurring with lactase deficiency — Is due to osmotic forces exerted by unabsorbed luminal solutes more concentrated than plasma, and the condition **abates with fasting.**
      - Lactose remains in the gut lumen.
      - Lactase found at apical brush border membrane
      - Normal biopsy findings
      - Two types
        - Congenital : AR, genetic mutation, rare, explosive diarrhea, watery, frothy stools & abdominal distention, after milk ingestion
        - Acquired : follow viral or bacterial enteritis, downregulation of gene, after childhood
      - Lymphatic transport defect
    - Exudative diarrhea — Is due to inflammatory disease and characterized by purulent, bloody stools that **continue during fasting.**
    - Malabsorbative diarhhea
  - Characteristics
    - Increase in stool mass, frequency or fluidity (more than 200 grams per day
    - In severe cases, stool volume can exceed 14 L per day and, without fluid resuscitation, result in death.
    - Worldwide, diarrheal diseases account for greater than 700,000 deaths of children under 5 years of age, making them the second leading cause of death in this age group
    - Painful, bloody, small-volume diarrhea is known as **dysentery**
    - Diarrhea is a common symptom of many intestinal diseases, including those due to infection, inflammation, ischemia, malabsorption, and nutritional deficiency

Malabsorptive diarrhea

- **Caused by inadequate nutrient absorption is associated with steatorrhea and is relieved by fasting.**
- **Characteristics**
  - Manifests most commonly as chronic diarrhea
  - Defective absorption of
    - Fats
    - Fat- and water-soluble vitamins
    - Proteins
    - Carbohydrates
    - Electrolytes
- **Manifestations**
  - Weight loss, anorexia,
  - Flatus, abdominal distention,
  - Borborygmi, Muscle wasting
  - Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency)
  - Bleeding (vitamin K deficiency)
  - Osteopenia and tetany (calcium, magnesium, or vitamin D deficiency)
  - Neuropathy (vitamin A or B12 deficiency)
  - Skin and endocrine disorders.
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- A hallmark of malabsorption is ***steatorrhea***
  - Characterized by excessive fecal fat and bulky, frothy, greasy, yellow, or clay-colored stools
- **Causes**
  - Pancreatic insufficiency.
  - Crohn disease
  - Lactase (Disaccharides) Deficiency
  - Inflammatory bowel diseases
  - Infectious Enterocolitis
  - Celiac disease "celiac sprue or glutensensitive enteropathy"
    - Immune-mediated enteropathy triggered by the ingestion of gluten-containing cereals
      - In genetically predisposed individuals
        - ***HLA-DQ2***
        - ***HLA-DQ8***
      - Such as
        - Wheat
        - Rye
        - Barley
    - Treatment
      - Gluten free diet
    - Associated with
      - Type 1 diabetes
      - Thyroiditis
      - Sjogren syndrome
    - Pathogenesis
      - Celiac disease is an intestinal immune reaction to gluten, the major storage protein of wheat and similar grains
      - Gluten is digested by luminal and brush border enzymes into
        - Amino acids and peptides, including a 33–amino acid **gliadin peptide** that is
          - **Resistant** to degradation by gastric, pancreatic, and small-intestinal proteases
            - Gliadin is delaminated by tissue transglutaminase and is then able to interact with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells
              - Presented to CD4+ T cells.
                - These T cells in lamina propria produce cytokines that likely contribute to the tissue damage and characteristic mucosal histopathology
    - Serology
      - Anti- tissue transglutaminase antibodies
      - Anti-gliadin antibodies.
      - Anti -endomysial antibodies
    - Mophology
      - Second portion of the duodenum or proximal jejunum.
      - **Triad: intraepithelial lymphocytosis (CD8+ T cells), crypt hyperplasia, and villous atrophy.**
      - Lamina propria: lymphocytes, plasma cells, eosinophils…….
      - IEL & villous atrophy are not pathognomonic, seen in viral enteritis.
    - Diagnosis
      - Non invasive serologic tests
        - Most sensitive
          - Anti tissue transglutaminase antibody, IgA
          - Anti deamidated gliadin antibodies, IgA & IgG
        - Most specific, but less sensitive
          - Antiendomysial antibody
      - Invasive tests
        - small bowel biopsy
    - Clinical features
      - Children 6-24 months : classical or non classical symptoms
        - Classical
          - Irritability
          - Abdominal distention
          - Anorexia
          - Diarrhea
          - Failure to thrive
          - Weight loss
          - Muscle wasting
        - Non-classical
          - Abdominal pain
          - Nausea
          - Vomiting
          - Bloating
          - Constipation.
        - Blistering skin lesion, dermatitis herpetiformis, in 10% of Pnts.
      - Adults (30-60 years)
        - Anemia: iron deficiency
        - B12 and folate deficiency: less common.
        - Diarrhea , bloating, and fatigue.
        - Missed diagnosis: Silent celiac or latent celiac.
        - Increased risk of enteropathy associated T cell lymphoma & Small intestinal adenocarcinoma
    - Terminal digestion & Transepithelial transport **defect**
  - Cystic Fibrosis
    - Mutation in **CFTR**
    - Defects in intestinal and pancreatic ductal ion transport
      - **In the pancreas the ducts are plugged by thick mucus**
        - **This leads to obstruction, low-grade chronic autodigestion of the pancreas**
          - **Eventually, exocrine pancreatic insufficiency in more than 80% of patients**
    - Interferes with bicarbonate, sodium, and water secretion, ultimately resulting in inadequate luminal hydration
    - The viscous luminal contents may result in meconium ileus
      - Which is present in up to 10% of newborns with cystic fibrosis
    - The result is failure of the intraluminal phase of nutrient absorption, which can be effectively treated in most patients with oral enzyme supplementation
    - **Interluminal digestion defect**
  - Abetalipoproteinemia
    - Characteristics
      - Beta apolipoproteins are very large apolipoproteins. They are critically important for the secretion and formation of chylomicrons (CMs) and VLDL.
        - Abnormalities that impede this process result in abetalipoproteinemia and hypobetalipoproteinemia
      - Autosomal recessive, rare.
      - The underlying defect is a mutation in the microsomal triglyceride transfer protein **(MTP)** responsible for lipoprotein and fatty acid export from mucosal cells.
    - Manifetations
      - Infants w/ failure to thrive, diarrhea, and steatorrhea
      - Lack of absorption of fat and fat soluble vitamins
      - Inability to secrete triglyceride-rich lipoproteins.
      - Transepithelial transport defect of TG and FAs.
      - Monoglycerides and triglycerides accumulate in epithelial cells
    - Acanthocytosis is a hallmark
      - Acanthocytes are abnormally spiked RBCs due to the defective phospholipid cell membrane.
        They are also seen in liver dysfunction
    - **Transepithelial transport defect**
- **Malabsorptive diarrhea Defect in**
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  - Intraluminal digestion
    - In which proteins, carbohydrates, and fats are broken down into absorbable forms
  - Terminal digestion
    - Which involves the hydrolysis of carbohydrates and peptides by disaccharidases and peptidases, respectively, in the brush border of the small-intestinal mucosa
  - Transepithelial transport
    - In which nutrients, fluid, and electrolytes are transported across and processed within the small-intestinal epithelium
  - Lymphatic transport
    - Of absorbed lipid