Diseases of the Small Intestine

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Malabsorption

- Defined as defective intra-luminal hydrolysis of nutrients and defective mucosal absorption.
**Structure**

- From Jejunum to ileocecal valve
- About 6 m in length
- Surface area is enormously increased by folds, in addition it has numerous villi.
- Each villous is formed from core (contain vessels, lymphatics and cells), and covered by columnar epithelium; epithelial cell has a brush border.
- Blood supply mostly from the superior mesenteric artery; terminal branches.
- Enteric nervous system; autonomic: three types: adrenergic, cholinergic, and NANC
Function

• Digestion:
  Secretion of digestive enzymes as proteases and disaccharidases

• Absorption:
  Throughout the small intestine except vit. B\textsubscript{12} & bile salts which have specific receptors in the terminal ileum.

• Defense:
  - Innate immune response
  - Adaptive immune response
**Principles of Intestinal Absorption**

- **Simple Diffusion:**
  According to concentration gradient. No energy is required.

- **Facilitated diffusion:**
  Energy-independent, carrier-mediated, allow faster transport.

- **Active transport:**
  Requires energy can occur against concentration gradient. A carrier protein is required.
Digestion and Absorption

Carbohydrates

- Mainly starch, some sucrose and lactose
- Hydrolysis by salivary and pancreatic amylases
- Breakdown products hydrolysed on the brush border by their appropriate oligo and disaccharidases to monosaccharides
- Monosaccharides are transported into the cells.
- Glucose and galactose absorbed by active transport, Fructose absorbed by simple diffusion.
Proteins

- Digested by pepsin to polypeptides
- Polypeptides and A.A. → CCK release from jejunum > pancreatic trypsinogen > trypsin > Other pancreatic proenzymes.
- Peptidases on the brush border digest polypeptides to dipeptides and amino acids.
- Absorbed by active transport.
Fats

• Comprises: long chain triglycerides, cholesterol esters and fat soluble vitamins.

• Emulsification of fat in the stomach followed by hydrolysis in the duodenum by pancreatic lipase into fatty acids and monoglycerides.

• CCK release from jejunum in response to luminal fat stimulates gall bladder contraction.

• Bile act as a detergent; bind with products of fat digestion to form micelles.

• At the cell membrane, lipid contents of micelles are absorbed.

• Inside enterocytes they are re-estrified into triglycerides, coated with apoproteins, phospholipids and cholesterol to form chylomicrons to be absorbed into lymphatics.
Digestion and Absorption

Water and electrolytes

- Large amount absorbed coupled with monosaccharides, amino acids and bicarbonates in the upper jejunum.
- Some are absorbed in the ileum and right side of the colon by active transport a (not coupled by solute).
- Water soluble vitamins, essential metals are all absorbed in the small intestine.
- Special elements: vit. $B_{12}$, iorn and calcium
Defense Mechanisms

1. Innate immune response; Mucosal barrier:
   - mucous secreted from goblet cells (physical barrier, enzymes have antibacterial effect).
   - Anti-microbial peptides (e.g. defensin family) secreted by epithelium.
   - The membrane of the enterocytes & tight junction between them.

2. Adaptive immune response: By the immune cells:
   Intestinal T-cells: - GALT (as Peyer’s patches).
   - Mucosal lamina propria.
   - Surface epithelium (intraepithelial lymphocytes)
Causes/Mechanism of Malabsorption

- Impaired mixing
  - Partial gastrectomy
  - Gastric bypass surgery
- Impaired lipolysis
  - Chronic pancreatitis
  - Pancreatic cancer
  - Gastrinoma
  - Congenital pancreatic insufficiency
Causes/Mechanism of Malabsorption

- **Impaired micelle formation**
  - Severe chronic liver disease
  - Cholestatic liver disease
  - Bacterial overgrowth
  - Crohn's disease, Ileal resection

- **Impaired nutrient delivery**
  - Intestinal lymphangiectasia
  - Lymphoma, Tuberculosis
  - Constrictive pericarditis
  - Severe congestive heart failure
Causes/Mechanism of Malabsorption

- Impaired mucosal absorption
  - lactase deficiency
  - Giardiasis, AIDS-related
  - Celiac disease
  - Whipple's disease
  - Graft-versus-host disease
  - Tropical sprue, Collagenous sprue
  - Radiation enteritis
  - Lymphoma, Amyloidosis
  - Bacterial overgrowth
  - Short-bowel syndrome
**Clinical features of Malabsorption**

<table>
<thead>
<tr>
<th>Malabsorption</th>
<th>Clinical feature</th>
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</thead>
<tbody>
<tr>
<td>Calories</td>
<td>Wt loss with normal appetite</td>
</tr>
<tr>
<td>Fat</td>
<td>Steatorrhea</td>
</tr>
<tr>
<td>Protein</td>
<td>Edema, muscle atrophy, azotorrhea</td>
</tr>
<tr>
<td>carbohydrate</td>
<td>Watery diarrhea, flatulence, milk intolerance</td>
</tr>
<tr>
<td>Vit B12</td>
<td>Anemia, SCDSC (paraesthesia, ataxia, loss of position/vibration sense)</td>
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<tr>
<td>Folic acid</td>
<td>Anemia</td>
</tr>
<tr>
<td>Iron</td>
<td>Anemia, glossitis, Pica (pagophagia)</td>
</tr>
<tr>
<td>Ca and Vit D</td>
<td>Tetany, pathological fractures, paraesthesia</td>
</tr>
<tr>
<td>Vit A</td>
<td>Follicular hyperkeratosis, night blindness</td>
</tr>
<tr>
<td>Vit K</td>
<td>Easy bruising, bleeding disorders</td>
</tr>
<tr>
<td>Vit B</td>
<td>Cheilosis, painless glossitis, angular stomatitis, acrodermatitis</td>
</tr>
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Investigations of Small Bowel Diseases

• Blood tests:
  1. Full blood count
  2. Serum albumin.
  3. Serum calcium, Alkaline phosphatase
  4. Autoantibodies: for the diagnosis of celiac disease

• Small bowel anatomy and histology:
  1. Barium follow-through, CT, MRI.
  2. VCE, Enteroscopy.
  3. Small intestinal Biopsy
Investigations of Small Bowel Diseases

- Tests of Absorption:
  1. Fat malabsorption: 3-days collection of stools on a diet containing 100g fat daily (Normally <6g)
  2. $B_{12}$ absorption studies (Schilling test)
  3. Lactose tolerance test

- Other tests
  1. Hydrogen breath test (detect bacterial overgrowth)
  2. Direct intubation
  3. IV $^{51}$CrCl$_3$ used to label circulating albumin to detect protein loosing enteropathy.
  4. Pancreatic tests
1. **Coeliac disease (gluten-sensitive enteropathy):**

- Chronic Inflammation of the small intestinal mucosa, immune mediated, that is precipitated by dietary gluten in genetically predisposed individuals.

- **Incidence:**
  - common in Northern Europe.
  - Increased incidence within families (10-15% of first degree relatives).
  - A strong association with HLA-B8, DR17 and DQ.
**Etiology:**

- Gluten is the water insoluble component of wheat and barley protein, can be fractionated into α, β and γ gliadin. γ gliadin is the main damaging peptide.

- The precise mechanism is unclear but T cells play a central role.

- T cells react with the enzyme tissue transglutaminase, it modifies gliadin and enhance gliadin specific T cell response in genetically predisposed individuals.

- The jejunal mucosa contains an excess of IgA-secreting cells. Circulating antibodies to gliadin and endomysium are found.
Pathology:

- Pathological changes variable according to severity.
- In mild to moderate cases, heris partial villous atrophy
- In severe cases, the jejunal mucosa is flattened with loss of surface villi
- There increased number of intraepithelial lymphocytes and accumulation of lymphocytes and plasma cells in the lamina propria.
Clinical Features:

• Any age, most common in young adults.
• Presentation depends on severity; ranges from tiredness, weight loss and anemia to florid malabsorption.
• On Examination; features of malnutrition & mild abdominal distension may be present.
• The disease may be associated with other autoimmune disorders.
Other extraintestinal manifestations of celiac disease;

- Rash (dermatitis herpetiformis),
- Psychiatric disorders (depression, paranoia),
- Neurologic disorders (peripheral neuropathy, ataxia, epilepsy),
- Short stature, dental enamel hypoplasia,
- Chronic hepatitis, or cardiomyopathy,
- Reproductive disorders (infertility, spontaneous abortion).
**Investigations:**

1. Endomysial (EMA) and Tissue transglutaminase (tTG) antibodies (IgA): high sensitivity and specificity.
2. Antigliadin antibodies (AGA), IgA and IgG sensitive but not specific.
3. Duodenal and jejunal biopsy; the gold standard for diagnosis.
4. Haematological examination; anemia.
5. Small bowel follow-through may show dilatation with change in fold pattern.
Treatment
1. Gluten-free diet usually produces rapid response. A gluten challenge confirm the diagnosis. Rice and corn grains are tolerated. Oats are tolerated by most.
2. Replacement heamatenics; iron, folic acid, calcium.

Complications
1. Unresponsive coeliac disease; often no cause could be found but ulcerative jejunitis, intestinal lymphoma or carcinoma may be responsible. Steroids or immunosuppressive agents are used.
2. Increased incidence of enteropathy-associated T-cell lymphoma, carcinoma of the small bowel and esophagus as well as extra-GIT cancers.
3. Metabolic bone diseases is common in long standing cases.
2. *Dermatitis Herpetiformis*:

- Uncommon blistering subepidermal eruptions of the skin associated with a gluten-sensitive enteropathy. Usually malabsorption and jejunal morphological abnormalities are less severe than coeliac disease.

- Both skin manifestations and malabsorption respond to gluten-free diet

- Skin manifestations sometimes require additional treatment with dapsone (100-150 mg daily)
3. *Tropical sprue*

- Malabsorption that occurs in residents or visitors to a tropical area where the disease is endemic (India, Malaysia and Indonesia and parts of south America).

**Etiology:**

Unknown, but it is likely to be infective because of its epidemiological pattern, occasional epidemics and improvement on antibiotics although no single bacterium have been isolated.
Clinical Features:

- Variable in intensity.
- Usually there is diarrhea, abdominal distension, fatigue, anorexia and weight loss.
- The onset may be acute and associated with fever or insidious with chronic diarrhea and nutritional deficiencies.

Diagnosis:

- Acute infective causes of diarrhea must be excluded particularly Giardiasis.
- Jejunal mucosa: partial villous atrophy.

Treatment:

- Antibiotics as tetracyclin 1gm daily.
- Folic acid replacement (5 mg daily)
4. **Bacterial overgrowth (SIBO)**

- Upper small intestine is usually sterile (Less than $10^4$/ml), ileum contains fecal-type organisms particularly E. coli and anaerobes.

- *Causes of Bacterial overgrowth:*
  1. Hypo or achlorhydria.
  2. Impaired intestinal motility (e.g. scleoderma, diabetic autonomic neuropathy)
  3. Structural abnormality of the intestine; e.g. Chron’s disease, enterocolic fistula, stricture, multiple diverticula, or grossly dilated bowel.
  4. Impaired immune function (hypogammaglobulinemia)
**Pathogenesis**

- Organisms are capable of deconjugating bile salts preventing absorption of fat and resulting in steatorrhea.
- It also metabolize vit. B12, interfere with its binding to intrinsic factor and cause B12 deficiency.

**Clinical features:**
Diarrhea, steatorrhea and B12 deficiency.
N.B. symptoms may be due to underlying intestinal pathology.
**Diagnosis:**
1. Hydrogen Breath test
2. Jejunal aspiration (not routinely performed).

**Treatment:**
1. Correction of the underlying lesion if possible.
2. Rotating courses of antibiotics
5. Whipple’s Disease

• A rare condition characterized by chronic systemic infection caused by a gram positive actinomycete, Tropheryma whippeli.

• EM revealed small gram positive bacilli ) Tropheryma whippelli) within the macrophages.

• Densely packed macrophages occur in the lamina propria and may obstruct lymphatics causing fat malabsorption.
Clinical Features

• Middle aged men are commonly affected.
• The disease sometimes a multisystem one with:
  1. GI manifestations: diarrhea, steatorrhea, weight loss, bloating, Protein-loosing enteropathy and hepatosplenomegally.
  2. Seronegative arthropathy
  3. Neurological manifestations: apathy, fits, dementia, Cranial nerve lesions.
  5. Others: fever, pigmentations, myocarditis.
**Management**

- Diagnosis: EGD with mucosal biopsy.
- The disease may be so severe to be fatal if untreated but it respond well to treatment.
- Antibiotics: parental induction phase for 2 weeks (penicillin G, cephalosporin), followed by oral maintenance phase for 1 year.
- Symptoms resolves within a week but relapse may occur in up to 1/3 of the patients.
6. Intestinal Resection

- The effect depend on the site and amount of intestine resected.

- **Ileal resection:** Can lead to
  - B12 deficiency
  - Unabsorbed bile salts pass to the colon and stimulate water and electrolyte secretion resulting in diarrhea. If hepatic synthesis can’t compensate it will cause malabsorption.
  - Gall stones.
  - Urinary oxalate calculi
• **Massive resection (short bowel syndrome):**
  • Loss of surface area for digestion and absorption is the key problem.
  • Enteral feeding is usually possible if the proximal 100 cm of the jejunum are preserved.
  • Presence of some or all the colon, intact ileocecal valve ameliorate the symptoms.
  • Adaption can occur over months.
  • The main effect is fluid loss, hypovolemia and dehydration.
  • Management: nutritional and fluid replacement, antidiarrheal agents.
7. **Radiation enteritis**

- In patients undergoing radiotherapy, occur in 10-155 of patients.
- It causes acute inflammation and shortening of villi, edema, crypt abscess formation and progressive ischemic fibrosis.

**Clinical features:**

- Acute phase: nausea, vomiting, cramping abdominal pain and diarrhea. Affection of the rectum can cause bleeding and tenesmus.
- Chronic phase: after 5-10 years: proctocolitis, strictures, fistulae, adhesions, malabsorption.
THANK YOU