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 disaccaridases

- Absorption:

  Throughout the small intestine except vit. B_{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.

Digestion and Absorption

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.

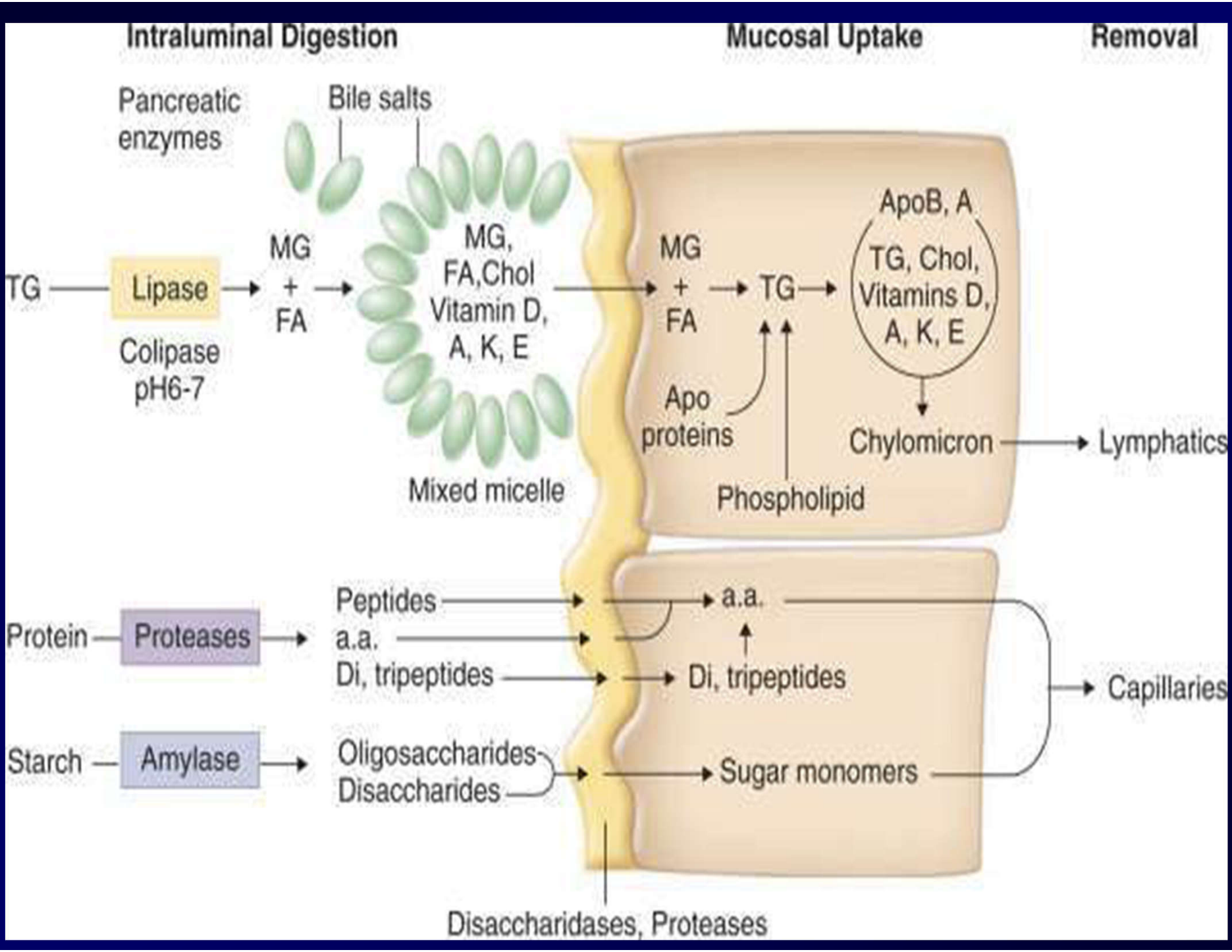
Fats

- 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 trasport 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


Intraluminal Digestion
Mucosal Uptake
Removal
Pancreatic enzymes
Bile salts
TG
Lipase
Colipase pH6-7
MG + FA
MG, FA,Chol Vitamin D, A, K, E
Mixed micelle
MG + FA
Apo proteins
TG
Phospholipid
ApoB, A
TG, Chol, Vitamins D, A, K, E
Chylomicron
Lymphatics
Protein
Proteases
Peptides
a.a.
Di, tripeptides
a.a.
Di, tripeptides
Capillaries
Starch
Amylase
Oligosaccharides
Disaccharides
Sugar monomers
Disaccharidases, Proteases

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

Malabsorption	Clinical feature
Calories	Wt loss with normal appetite
Fat	Staetorrhea
Protein	Edema, muscle atrophy, aztorrhea
carbohydrate	Watery diarrhea, flatulence, milk intolerance
Vit B12	Anemia, SCDSC (paraesthesia,ataxia,loss of position/vibration sense)
Folic acid	Anemia
Iron	Anemia, glossitis, Pica (pagophagia)
Ca and Vit D	Tetany, pathological fractures, paraesthesia
Vit A	Follicular hyperkeratosis, night blindness
Vit K	Easy bruising, bleeding disorders
Vit B	Cheilosis, painless glossitis, angular stomatitis, acrodermatitis

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

Malabsorption

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 γgliadin. 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.
- Presentaion depend 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. Doudenal and jejunal biopsy; the gold standard for diagnosis.
4. Heamatological examination; anemia.
5. Small bowel follow-through may show dilatation with change in fold pattern.
6. Others: serum albumin, calcium and phosphate.

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 immunosupprressive 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. Usaully malabsorption and jejunal morphological abnormalities are less severe than coeliac disease.
- Both skin manifestations and malabsorption respond to gluten-free diet
- Skin manifestations some times require additional treatment with dapson (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 whipplei.
- EM revealed small gram positive bacilli) Tropheryma whippelli) within the macrophages.
- Densely packed macrophages occur in the 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.
4. Heamatological: anemia, lymphadenopathy.
5. Others: fever, pigmentations, myocarditid.

Management

- Diagnosis: EGD with mucosal biopsy.
- The disease may be so severe to be fatal if untreated but it respond well to treatment.
- Antibiotics: parentral 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 I 10-155 of patients
- It cause acute inflammation and shortening of villi, edema, crypt abscess formation and progressive ischemic fibrosis.
- ***Clinical features:***
- Acute phase: nausea, vomitting, 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