Malabsorptive Disorders

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The Digestive System

“Bad digestion is the root of all evil.”
Hippocrates 400 BC

Digestive system processes 60 tons of food during a lifetime

Objectives

- Understand basic principles of digestion/absorption
- Understand the mechanisms of injury causing malabsorption
- Recognize signs/symptoms of malabsorption
- Describe common malabsorption disorders
- Evaluate a patient for suspected malabsorption
Slide and Test Hints

- Concepts that are highlighted in board review books such as First Aid for the USMLE STEP 1 will have the symbol on the slide.
- Concepts that are key to recognizing and understanding malabsorption will have the symbol on the slide.
- Test questions will come from slides with.

Mal- Absorption vs Mal-Digestion

- Malabsorption: Latin malus “bad/evil” + absorptionem, “to swallow up”
  - Poor transport of micronutrients from the gut into the body.
- Maldigestion: Latin digerēre, digestum, “to carry asunder or dissolve”—di (= dis), “asunder, separate” and gerēre “to bear or carry”
  - Incomplete breakdown of food particles.

Building Blocks-Macronutrients

- Building blocks include proteins, carbohydrates, fats, and vitamins.
Building Blocks - Micronutrients

What systems are required for digestion and absorption?

- Mechanical (Chewing, Trituration, Peristalsis)
- Enzymatic/Chemical (amylase, HCL, pepsin, lactase)
- Hormonal (CCK, peptide YY)
- Structural (Villi, intestinal length, IC valve)
- Transport proteins/barrier function (GLUT, desmosomes)
- Microbiome (Vit K, fermentation)
- Lymphatic (chyle transport)
- Vascular (nutrient transport, tissue oxygenation)
- Metabolic (mitochondria, glycogen storage/glycolysis)
- Neurologic (control center)
- Electric (gastric pacemaker waves)
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A defect in any one of these systems can cause malabsorption

- Normal Length of GI Tract
  - Measurement varies
    - Autopsy - Pylorus to IC valve
    - Surgery – Treitz lig to IC valve
  - Normal length (achieved by age 9)
    - Small bowel 600cm (14-23 ft; Men 630cm, women 592cm)
    - Duodenum 26 cm (9.8 in)
    - Jejunum 360cm (3/5 length)
    - Ileum 240cm (2/5 of length)
    - Total Surface Area ~250 m²
  - Colon 150cm (5 feet)

- Small Intestine Brush Border
  - Intestinal Lumen
  - Unstirred Layer
  - Glycocalyx
  - Cell Membrane
  - Enterocyte Cytoplasma
  - Basal or Lateral Membrane
  - Intercellular Space
  - Basement Membrane
  - Capillary/lymph vessel membrane
Passive & Facilitated Diffusion

- Carbohydrates broken down by brush border enzymes into simple sugars
  - Glucose & Galactose (SGLT1), Fructose (GLUT5)
- Electrolytes
- Some proteins
- Fats
  - First stage of absorption by passive diffusion
  - SCT, MCT diffuse without packaging
  - LCT packed into micelles

Absence of brush border enzymes causes one of the most common malabsorption disorders—lactose intolerance; generalized loss also seen after infection.

Active Transport

- Fats – broken down into mono/triglycerides, free fatty acids, glycerol, sterols, phospholipids
  - Lymphatic absorption, combine with cholesterol, phospholipids -> circulatory system
- Proteins - broken down into single peptides, dipeptides and tripeptides.
  - Pass into portal blood system and travel to liver for metabolism

Absence of transporters, mucosal infiltration (amyloid), inflammation (celiac), obstruction of venous or lymphatic outflow will cause malabsorption.

Value and Limitations of MCT Oil

- Medium chain triglycerides
  - Water-soluble and pass through unstirred water layer more easily
  - No bile salts, lipase, colipase, ileum required
  - Direct absorption across mucosa to portal vein
  - Useful in short gut syndrome & fat malabsorptive disorders

Limitations
- Doesn’t contain essential fatty acids – EFA deficiency
- Excess metabolized to ketones – Metabolic acidosis
Diagram of Absorption

Duodenum

Jejunum

Ileum

Liver and Gallbladder

Bile
250 ml - 1 L secreted daily
Bile Acids (cholic, chenodeoxycholic, deoxycholic, lithocholic)
Phospholipids (lecithin)
Cholesterol
Pigments (bilirubin)
Inorganic ions

Fat and Fat Soluble Vitamin Absorption

PBC, PSC, infections, loss of IC valve, SIBO affect bile & result in fat malabsorption

Pancreas

Pancreatic Secretions
1 L secreted daily
Aqueous Component (HC03-) neutralizes acid; activates enzymes
Enzymatic Component
Amylase, lipase, protease

Fat, protein, and carbohydrate absorption

CF, chronic pancreatitis, end-stage DM, surgical resection, Gastric hypersecretion (Zollinger-Ellison) affect pancreatic secretion and can result in malabsorption, primarily of fat
Duodenal Absorption

Site of bile/pancreatic secretion & mixing with chyme
Limited direct nutrient absorption
save some key minerals/vitamins
Important site of medication absorption
Usually preserved in disease states

Surgical alteration (RYBG, Whipple) can cause fat malabsorption due to mismatch of food to bile/pancreatic secretions. Inflammatory diseases (celiac), infections (H. Pylori) can cause malabsorption of iron (anemia), B vitamins

Surgical Resection & Malabsorption

- Whipple Procedure, Gastrectomy, RYGB
- Mismatch between food and bilopancreatic secretions
- SIBO & “Blind Loop” syndrome contribute to malabsorption

Jejunal Absorption

90% absorption occurs in first 100cm jejunum
Jejunal losses are well tolerated b/c ileum adapts to provide absorption
Limited capability for adaptation; cannot make up for loss of ileum/IC valve

Surgery, ischemia, infiltrative diseases (amyloid), inflammation (Crohn’s, celiac), infections, motility d/o (pseudo-obstruction) affecting jejunum can result in diarrhea and malabsorption of nutrients listed above
Ileum & IC Valve

- Very important to absorption
- Can adapt to loss of significant intestinal length
- Ileal brake stops gastric emptying
- Site of absorption of bile salts, B12, & some meds (imodium)
- Prevents SB bacterial overgrowth

Crohn’s, surgery, ischemia, infiltrative diseases, motility d/o, infections (Campylobacter, Yersinia, TB) affecting ileum & IC valve can cause fat malabsorption, SIBO, motility disturbances, water/electrolyte loss, poor medication response, choleretic diarrhea from unabsorbed bile salts in colon

Value of Retained Colon

- Colonic adaptation (dilation, lengthening, proliferation)
- Provides huge fluid/electrolyte absorption advantage (90% of secreted fluid is reabsorbed)
- Capability of “colonic salvage”
  - Bacteria act on carb/fiber to produce short chain fatty acids
  - Colon can absorb up to 500 kcal/d as SCFAs and lactate
- Particularly useful in short gut syndrome

- Colonic loss from surgical resection or mucosal diseases (microscopic colitis, UC/Crohn’s, radiation enteritis)
- Primarily causes electrolyte/water malabsorption

Clinical Signs of Malabsorption

- Diarrhea (watery diarrhea → carb malabsorption)
- Steatorrhea (large volume, greasy fatty, diarrhea)
- Bloating
- Weight loss
- Dehydration
- Growth retardation, failure to thrive
- Edema (loss of oncotic pressure 2/2 hypoalbuminemia)
- Anemia/bleeding tendencies (B12, iron, folate, vit K)
- Muscle cramping (Ca, Mg, phosphorous, Vitamin D)
- Bone deterioration (Vitamin D, calcium)
Classic Malabsorptive Disorders
- Celiac Disease - inflammation (villi loss), SIBO
- Cystic Fibrosis - multifactorial
- Chronic Pancreatitis - pancreatic insufficiency
- Lactose Intolerance - disaccharidase loss
- Bacterial Overgrowth - ineffective bile salts, B12 consumption/malabsorption
- Whipple’s Disease - villi loss due to *Tropheryma Whippelii* infection
- Tropical Sprue - villi loss due to unknown infectious agent

Less Commonly Tested Malabsorptive Disorders
- PBC/PSC - cholestasis (bile loss)
- Short Bowel Syndrome - loss of surface area; loss of key absorptive segments (TI, colon)
- Amyloidosis - infiltrative (villi loss), motility, bacterial overgrowth
- Scleroderma - motility, bacterial overgrowth

Celiac Disease
Multifactorial, autoimmune disorder in genetically susceptible individuals
Triggered by the protein gluten (wheat) & proteins in rye & barley
Infiltration of the small intestine by lymphocytes attacking TTG causes an inflammatory reaction leading to flattening of the small intestinal mucosa
Celiac patients have loss of villus surface area & leaky epithelium, sometimes bacterial overgrowth & decreased pancreatic enzyme secretion. Iron, folate, calcium, & Vit D malabsorption (osteopenia) is common* B12 IS RARE. Associated with HLA DQ2/8. Screen with serum TTG antibody test; confirm with small bowel biopsy.
Cystic Fibrosis
- Decreased Pancreatic Enzyme Secretion
- Decreased HCO3 secretion
  - Acidic duodenal fluid
  - Inactivates pancreatic enzymes/BA
- Multiple effects on Bile Acid
  - Inadequate Secretion
  - Secretion of less effective BA
  - Inadequate re-absorption
  - Binding to un-hydrolyzed lipids
  - De-conjugation of BA by bacteria
  - Inactivation by low pH
- Impact on Motility
- Physical barrier (mucus)

Diagnostic tests for suspected malabsorption
- General
  - Basic Chemistries and Blood Count
    - Albumin levels, anemia, liver function abnormalities, particularly bilirubin and alkaline phosphatase (cholestasis)
  - Micronutrient Absorption Studies
    - Vitamins, Minerals, INR (functional vitamin K level), DEXA scan
- Structural
  - Upper and Lower GI endoscopy with Small Bowel Biopsy
  - Anatomical Imaging (CT, MRI, capsule endoscopy, barium)
  - D-Xylose test (small bowel absorption, rarely done)
  - Diarrhea Studies
    - Stool Cultures particularly for giardia & parasites
    - Stool Fat
    - Stool Alpha-1 Antitrypsin (protein losing enteropathy)

Diagnostic tests for suspected malabsorption
- Mechanical (motility):
  - Gastric Emptying, Small Bowel Follow Through, Smart Pill
- Enzymatic/Chemical:
  - Hydrogen Breath Tests for lactose/fructose malabsorption
  - Stool pH (<6), presence of reducing substances (carbohydrates)
  - Fecal Elastase or Chymotrypsin (marker of pancreatic exocrine function, decreased in pancreatic insufficiency)
- Microbiome (Bacterial Overgrowth/SIBO):
  - Hydrogen Breath Test
  - Small bowel aspirate
- Metabolic:
  - Specific serum/urine byproducts of cycle disorders
Diagnostic tests for suspected malabsorption

- **Hormonal:**
  - Pancreatic secretion testing using secretin/CCK
  - Gastrin, somatostatin, VIP, (secretory neuroendocrine tumors)

- **Transport proteins/barrier function (desmosomes):**
  - Individual transporter testing (Hartnup disease, Cystinuria)
  - Confocal microscopy in SB may be useful in near future

- **Neurologic:**
  - Autonomic function testing

- **Electric:**
  - Electrogastrogram (EGG); Rarely done in clinical practice

Lymphatic (chyle leaks, lymphangiectasia):

- Lymphangiogram
- Lymphoscintigraphy

Vascular:

- Angiograms, Endoscopy with biopsies

Targeted Disease States

- Sweat testing (CF)
- Tissue Transglutaminase (Celiac Disease)
- Rheum markers (Scleroderma)

Diagnostic tests for suspected malabsorption-Board Exam Pearls

- **Serum Tests**
  - Hypoalbuminemia, anemia (macroscopic due to folate or B12 deficiency or microscopic due to iron deficiency)
  - Low vitamin levels, particularly fat soluble vitamins (A, E, D, K), iron, folate, vitamin B12, elevated INR (low vitamin K)
  - Anti-Tissue Transglutaminase Antibody, HLA DQ2/8 genetic testing (celiac disease)
Diagnostic test for suspected malabsorption-Board Exam Pearls

**Special Studies**

- **#1 MOST IMPORTANT TEST IS FECAL FAT (SUDAN STAIN)**
- Lactose Hydrogen Breath test (elevated hydrogen >20 ppm in response to lactose ingestion)
- Fecal elastase (low in pancreatic insufficiency; not affected by oral pancreatic enzyme use)
- Stool pH (low pH indicates carbohydrate malabsorption)
- D-Xylose test (differentiates malabsorption secondary to mucosal damage from malabsorption due to pancreatic insufficiency/other)
- Biopsies with PAS stain + “foamy macrophages” (Whipple’s)

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**Case 1**

- A 56-year-old **Caucasian man** with a history of **nonspecific arthritis** complains of chronic GI upset. He has had **diarrhea** almost daily for several months now. He has **lost 10 lbs unintentionally**. His family has also noticed some **loss of memory**, such as forgetting where his keys are or forgetting someone’s birthday.
- He undergoes upper endoscopy with biopsies of the small intestine.
  - What has most likely developed?
  - What will be seen on microscopic examination?
  - What is the treatment?

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**Conclusion**

- Digestion is a complicated process involving multiple systems
- Malabsorption etiologies are many; a breakdown in any one system can cause malabsorption
- Symptoms are often similar and initial w/u is similar for all etiologies
- Use knowledge of individual diseases to anticipate defects and sequelae
- Treatment often requires knowing the cause and treating the underlying disease
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