Malabsorption

Michelle Pietzak, M.D.
Assistant Professor of Clinical Pediatrics
USC Keck School of Medicine
Division of Gastroenterology and Nutrition
LAC+USC Medical Center
Childrens Hospital Los Angeles

Objectives

1. Recognize that congenital mucosal malabsorptive defects almost always present in early infancy with massive diarrhea and dehydration because of defective carbohydrate malabsorption
2. Know that infants and young children most often have dietary carbohydrate intolerance (such as lactose intolerance) secondary to acquired secondary intestinal damage as opposed to the rare occurrence of congenital intestinal mucosal brush border enzyme or transport defects
3. Understand that some patients with generalized malabsorption do not have diarrhea

Objectives

4. Be able to distinguish between pancreatic and other intraluminal causes of malabsorption from intestinal mucosal absorptive defects with specific tests
5. Learn the screening tests for malabsorption, and when they are useful
6. Know the specific signs of fat soluble vitamin deficiencies which are frequently associated with generalized malabsorption

Signs of malabsorption

- Malodorous stools
- Chronic diarrhea
- Failure to thrive
- Weight loss
- Subnormal growth

Signs of severe malnutrition

- Edema
- Rickets
- “Potbelly”
- Decreased muscle mass
- Decreased fat stores
- Excessive bruising or bleeding

Failure to thrive

- GI dysfunction is often a cause of failure to thrive
- Questions that need to be asked:
  - Deficient diet?
  - Malabsorption?
  - Abnormal energy utilization?
Initial workup of FTT

- **History**
  - Detailed dietary intake
  - Assessment of family environment
  - Developmental milestones

- **Physical exam**
  - Serial height, weight, head circumference, weight for length or BMI
  - Phenotypic findings of a congenital disorder or syndrome
  - Fat stores, muscle mass, organomegaly, goiter, anemia, joint swelling, rash, edema

Basic Questions

- Does this patient need special nutritional support?
- Does this patient need an elemental formula?
- Does this patient need parenteral nutrition?
- Does this patient need medications?
- Do I need to refer to a gastroenterologist?

Causes of Malabsorption

- Pancreatic disorders
- Chronic cholestasis
- Gastrointestinal surface injury
  - Celiac disease
  - Crohn's disease
  - Short bowel syndrome
  - Infectious and post-infectious diarrhea
  - Congenital intestinal enterocyte brush border enzyme deficiencies
  - Bacterial overgrowth
- Abnormal lymphatic drainage

Cystic Fibrosis

- Defective chloride channel secretion
- Dysregulation of salt and water flux across epithelial glandular cells
- Multiorgan involvement: lung, pancreas, GI tract, hepatobiliary system, reproductive
- Inspissated plugging by proteinaceous secretions in affected organs (pancreas, photo)

Pancreatic disorders

- Cystic fibrosis (CF) is one of the most common malabsorptive disorders
- Defect in intraluminal fat digestion
- Mutation in CFTR gene, chromosome 7q31
- Most common mutation $\Delta F508$
- U.S. incidence 1:2000-4000
- 1:25 Caucasians carriers of at least one mutation

Presentations of Cystic Fibrosis

- Chronic lung disease, FTT, bulky loose stools, cholestasis, pancreatitis, edema, rectal prolapse, sinusitis, nasal polyps, digital clubbing, edema
- Meconium ileus: accumulates in terminal ileum and colon, 20%, atresias, present with obstruction
- Long term complications: cirrhosis, obstipation, diabetes
Pancreatic insufficiency in CF

CF: Diagnosis

- Sweat chloride test
  - False + many conditions
  - False - malnutrition, edema
- CF DNA mutations
- Tests of pancreatic sufficiency
  - Stool trypsin (presence of trypsin in the stool is good)
  - Pancreatic enzyme levels endoscopically

Rare causes pancreatic insufficiency: Shwachman-Diamond syndrome

- Lipomatosis of pancreas with congenital pancreatic insufficiency
- Bone marrow dysfunction with recurrent infections
  - 1:10,000
  - Autosomal recessive on 7q11
  - Incidence 1:10,000
  - Short stature, skeletal abnormalities

Rare causes pancreatic insufficiency: Johanson-Blizzard syndrome

- Fatty replacement of pancreas (diabetes)
- GI anomalies (imperforate anus)
- Nasal alae hypoplasia (bird beak nose)
- Deafness
- Hypothyroidism
- Malformed teeth
- Sparse, dry, coarse hair

CT shows the loss of pancreatic parenchyma from atrophy and infiltration of the pancreas by fat (arrows) in a young boy with Shwachman-Diamond syndrome.
Chronic cholestasis

- Any liver disease that results in cholestasis can lead to fat malabsorption
- Deficiencies of fat-soluble vitamins
  - Vitamin E: ataxia, hyporeflexia, ocular palsy, hemolytic anemia
  - Vitamin K: reduced synthesis of coagulation factors
  - Vitamin D: osteopenia
  - Vitamin A: night blindness

Chronic cholestasis: Presentation

- Jaundice since infancy
  - Biliary atresia- acholic stools
  - Bile acid transport defects
- Alagille syndrome
  - Cholestasis
  - Congenital heart disease, rib, vertebrae
  - Short stature,
  - Characteristic facies

Malabsorption Case Studies

Celiac Disease

Immune-mediated disease induced by the ingestion of gluten proteins in subjects who are genetically predisposed.

- Malabsorption due to villous damage
- Iron, fat soluble vitamin deficiencies
- Screen with antibodies; need biopsy
- Treatment: Gluten free diet

Monozygotic twins at 12 years of age. The patient on the left was 3 inches shorter and 15 pounds lighter at presentation than his brother.

Inflammatory Bowel Disease

Genetic Predisposition
Mucosal Immune System (Immunoregulatory defect)
Environmental Triggers (Lumenal bacteria, infection)
**Crohn's disease**
- Clinical presentation varied
- Malabsorption from
  - Lactose intolerance
  - Full thickness bowel injury
  - Strictures with bacterial overgrowth
  - Rapid intestinal transit
- Can result in
  - Growth Failure
  - Anemia: iron, B12, folate

**Short Bowel Syndrome**
- A complex disorder characterized by multiple disruptions of normal intestinal anatomy and physiology, complicated by a variety of nutritional, infectious, and metabolic alterations
- Exists when the patient has malabsorption of fluids, electrolytes, and nutrients, in the presence of shortened small intestine

**Bowel Loss:**
- NEC (necrotizing enterocolitis)
- Congenital Atresia
- Malrotation with volvulus
- Hypercoagulable state
- Trauma
- Inflammatory bowel disease

**Functional:**
- Hirschsprung's Disease (total intestinal aganglionosis)
- Pseudo obstruction (megacystis microcolon intestinal hypoperistalsis syndrome)
- Congenital Malabsorption (GGM, microvillus inclusion disease)

**Case Study: Diarrhea**
- A previously healthy 4 year old girl presents to the office with 6 weeks of nonbloody diarrhea and weight loss
- The family had been camping up at Big Bear Lake about 2 months ago
- Everyone went swimming in the lake
- The 4 year old is the only one with diarrhea

**Infectious diarrhea leading to malabsorption: Giardia**
- Can infect healthy children as well as IgA deficient, immunodeficient
- Poor growth, diarrhea, bulky stool
- Diagnosed by stool DAA test, biopsy
- Child care, well water, lakes, streams, under developed nations
Infectious diarrhea leading to malabsorption: Cryptosporidium
- Usually acute and limited
- Immune deficient
- Malabsorption of fluid, electrolytes, vitamins, minerals
- Diarrhea watery and nonbloody
- Diagnosis: find organism in stool, effluent or biopsies

Post-infectious diarrhea
- Can be chronic, requiring IV nutrition
- Most children and adults do not need long-term dietary restrictions after diarrhea
- Secondary lactose malabsorption
  - previous GI disease, 3rd World, repetitive diarrhea
- Diagnosis: stool for pH (normal >6), presence of reducing substances

Intractable diarrhea of infancy
- In young infants with diarrhea greater than 2-3 weeks
- Malnutrition and malabsorption can be lethal
- Secondary milk and soy formula allergies
- Realimentation with elemental formula, drip feeds

Rotavirus
- Frequent cause of acute diarrheal disease in young children
- Injury of brush border of proximal small bowel by toxin
- Vomiting, fever, watery diarrhea which can be both osmotic and secretory
- Treatment is supportive
- Avoid lactose
- Breast feeding OK
Congenital intestinal enterocyte brush border enzyme deficiencies

- Present with watery diarrhea, bloating, abdominal distension, acidosis and dehydration after birth
- Stools + for acid and reducing substances
- Cannot be maintained on standard infant formulas or human milk
- Are RARE, have not survived due to natural selection

Histologically normal appearing mucosa
Often have abnormal brush border on EM
Hydrogen breath test
Genetic tests
- Glucose galactose transporter deficiency
- Congenital lactase deficiency
- Sucrase-isomaltase deficiency
- Microvillus inclusion disease

Lactose Intolerance: A Deficiency in Lactase

- Lactase is the enzyme that digests a complex sugar (lactose) into glucose and galactose
- Inability to digest lactose leads to these symptoms
  - Increased water in the colon: diarrhea
  - Fermentation of lactose in colon: gas
  - Shortened transit time: urgency
- Prolonged avoidance of dairy products may result in calcium depletion and osteoporosis
Causes of Lactose Intolerance

• Lactase nonpersistence/hypolactasia
  – Normal
  – Lactase nonpersistence is primary mechanism
  – Genetically determined; after weaning, lactase decreases throughout life in most normal individuals
• Secondary lactose intolerance (lactase deficiency):
  – Common
  – Loss of lactase due to other intestinal diseases/disorders
• Congenital lactase deficiency
  – Genetic, but extremely rare
  – Presents in infancy as failure to thrive

Secondary Lactase Deficiency Has Many Causes

Small bowel
• Celiac Disease
• Crohn's disease
• HIV enteropathy
• Whipple's disease
• Severe gastroenteritis (viral or bacterial)

Multisystem
• Carcinoid syndrome
• Cystic fibrosis
• Diabetic gastropathy
• Kwashiorkor
• Zollinger-Ellison syndrome

Congenital lactase deficiency – Genetic, but extremely rare – Presents in infancy as failure to thrive

Secondary Lactase Deficiency

Small bowel
• Celiac Disease
• Crohn's disease
• HIV enteropathy
• Whipple's disease
• Severe gastroenteritis (viral or bacterial)

Multisystem
• Carcinoid syndrome
• Cystic fibrosis
• Diabetic gastropathy
• Kwashiorkor
• Zollinger-Ellison syndrome

Diagnostic Testing for Lactose Intolerance

• Functional testing for lactose intolerance
  – Empiric response to lactose-free diet
  – Lactose challenge
  – Lactose intolerance blood glucose test
  – Hydrogen breath test
  – Stool acidity test (infants)
• Mucosal biopsy with assay
• Genetic testing for etiology of lactose intolerance
  – Lactase nonpersistence (hypolactasia variant) testing

Functional Testing: Stool Acidity Test

• Stool lactose increases acidity
• Lactose challenge—stool sample—measure stool pH
• Not very accurate

Functional Testing: Hydrogen Breath Test

• Undigested lactose in colon is metabolized into H₂ gas by bacteria
• Overnight fast, lactose challenge
• Baseline H₂ level, serial measurements
• 90% sensitive
• Nonspecific: many false positives
**Bacterial overgrowth**

- Disorders of intestinal peristalsis result in stasis leading to bacterial overgrowth
- Can deplete vitamins (B12), minerals and other nutrients
- Results in steatorrhea
- Sx: macrocytic anemia, bloating, diarrhea
- “Good bacteria” make Vitamin K and folate

**Bacterial Overgrowth**

- Frequent in patients who lack ICV (ileocecal valve), or dilated small intestine secondary to poor motility, tight anastomosis, ischemic strictures, adhesions
- Mucosa is friable and hemorrhagic
- Treatment: Similar to treatment for IBD: antibiotics (Flagyl), other anti-inflammatory agents (sulfasalazine, corticosteroids)

**Diarrhea Case Study**

- A 1 year old male has chronic steatorrhea
- The mother brings him into your clinic because he has now developed asymmetric edema
- Labs show lymphopenia, elevated stool alpha one antitrypsin and low fat-soluble vitamins

**Abnormal lymphatic drainage**

- Primary intestinal lymphangiectasia
- Results in malabsorption of fat-soluble vitamins and LCFA (long chain fatty acids)
- Defect can be generalized or segmental
- Lymphatic scans useful
- Tx: medium chain dietary fat, vitamins, low Na, diuretics, supplemental protein
- Prognosis: generally improves over time; may require resection
Abnormal lymphatic drainage

• Secondary intestinal lymphangiectasia
• Mycobacterial intestinal infections
• Radiation enteritis
• Tumors
• Heart disease
  – s/p Fontan for hypoplastic LV with elevated RV pressure
  – Tx: diet, steroids, heparin, heart transplant

Screening blood tests for malabsorption

• CBC with differential
• Chemistry panel for albumin, total protein
• Celiac panel with IgA level
• Cystic fibrosis DNA
• Fat soluble vitamin levels (A, E, 25OHD, PT)
• B12, folate iron studies (serum iron, TIBC, ferritin)

Stool analyses for malabsorption

• Stain for dietary fat (not a great screen)
• 3 day quantitative fecal fat (with 3 day diet history to measure fat intake)
• Fecal alpha-one antitrypsin for protein-losing enteropathy
• Stool trypsin
• Stool pH
• Clinitest for sugars

Summary

• The pathophysiology of malabsorption varies according to the nutrient
• There are many different types of malabsorption, including in the intraluminal, mucosal, venous and lymphatic transport phases
• There are excellent serologic and stool tests which can be used to screen for the different malabsorptive conditions
• Refer to a GI specialist if you suspect that your patient has one of these underlying conditions which requires biopsy or special nutritional or medical support

THE END