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Classification and interpretation of GIT-related tests

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1. Introduction
   - The major organs of the gastrointestinal (GI) tract include the stomach, small and large intestines, pancreas, and gallbladder, all of which are involved in the digestive processes that commence with the ingestion of food and water and culminate with the excretion of waste products as feces.

2. Stomach: Diseases and Laboratory Investigations

(1) Helicobacter pylori
   - *H. pylori* is now accepted to be the predominant cause of gastric and duodenal ulcers, the remainder being associated with the long-term use of nonsteroidal antiinflammatory drugs (NSAIDS) and, rarely, gastrinomas.

(2) Diagnostic tests for *Helicobacter pylori*
   - Invasive tests: Using gastric mucosal biopsy samples
   - Histology: Microscopy after Giemsa or silver staining
   - Histology: Microscopy after immunohistochemical staining
   - Direct urease test: Biopsy included in urea/indicator solution—visual end point
   - Culture: Incubation in suitable media for 4 to 10 days
   - Polymerase chain reaction: Amplification of specific DNA sequences
   - Noninvasive tests: Using breath, blood, saliva, or feces
   - Breath tests: Rise in $^{14}CO_2$ or $^{13}CO_2$ after ingestion of ^{14}C- or ^{13}C-labeled urea
   - Serum, saliva, or feces tests: Detection of IgG antibody

(3) Gastric Acid Secretion and Gastrinomas
   - Zollinger-Ellison syndrome
     - a syndrome consisting of multiple peptic ulcers, gastric hypersecretion, and non–β islet cell tumors of the pancreas secreting gastrin
   - Gastrinomas
     - commonly located in the pancreas, but can arise from the stomach, duodenum, or other tissues.
     - more often (60%) malignant than benign, with metastases frequently present at the time of diagnosis.
     - Measurement of plasma gastrin in a fasting sample is the initial step in aiding the differential diagnosis.
   - Measurement of Plasma Gastrin
     - In plasma from healthy subjects, the predominant forms of gastrin are amidated G-34 and G-17.
     - For the detection of gastrinomas, the assay should be able to detect all secreted forms of gastrin to prevent false-negative findings.

- Blood samples should be collected into tubes containing an anticoagulant (eg, heparin) and a protease inhibitor (eg, aprotinin) to prevent degradation.

3. Intestinal Disorders

(1) Celiac Disease

- Comparison of Serologic Tests for Celiac Disease

Antibody	Method	Sensitivity (%)	Specificity (%)
IgA-endomysial antibody	Immunofluorescence on monkey esophagus or human umbilical cord	80-100	>99
IgA-antigliadin antibody	Quantitative ELISA	75-95%	95
IgA-antitissue transglutaminase antibody	Quantitative ELISA	>90	>99
IgA-deamidated gliadin peptide antibody	Quantitative ELISA	90	90

(2) Disaccharidase Deficiencies

- Carbohydrate malabsorption can result in osmotic diarrhea with abdominal pain and distention and flatulence resembling the symptoms of IBS. Inherited
  - Lactase Deficiency
    - Lactase activity has its highest prevalence in the earliest months of life and declines after weaning
    - Congenital lactase deficiency is a very rare disorder that becomes apparent once the infant has been exposed to milk feeds.
    - Secondary lactase deficiency is common in celiac disease owing to villous atrophy but also may occur in other conditions.

(3) Bacterial Overgrowth

- Abnormalities of the Small Intestine Associated With Bacterial Overgrowth
  - Jejunal diverticuli
  - Crohn disease
  - Autonomic neuropathy
  - Scleroderma (systemic sclerosis)
  - Pseudo-obstruction
  - Postgastrectomy
- Diagnostic procedure for bacterial overgrowth
  - Microbiologic examination of small bowel contents; gold standard, but not practical
  - Noninvasive procedures based on oral administration of substances metabolized by bacteria to yield products that can be detected in breath
    - ^{14}C-glycocholate breath test

(4) Bile Acid Malabsorption

- Bile acids
  - Bile acids are synthesized in the liver and pass into the lumen of the small bowel via the gallbladder.

- Major function is to act as surface-active agents, forming micelles and facilitating the digestion of triglycerides and the absorption of cholesterol and fat-soluble vitamins
- Bile acid malabsorption
  - leading to chronic diarrhea occurs when ileal disease is present, or after resection of the terminal ileum
  - It should be suspected in patients with unexplained chronic diarrhea
- Tests for bile acid malabsorption
  - Oral administration of the synthetic radiolabeled bile acid[75] selenohomocholyltaurine (SeHCAT).
  - Blood test: Fibroblast growth factor-19 (FGF-19) and 7α-hydroxy-4-cholesten-3-one (C4).

(5) Inflammatory Bowel Disease and Irritable Bowel Syndrome

- Intestinal symptoms: abdominal pain or discomfort with diarrhea or constipation
- IBD: ulcerative colitis (UC), Crohn disease (CD) and many microscopic inflammatory bowel conditions
- IBS: a functional bowel disorder for which there is no identifiable pathologic process or known cause
- Prevalence
  - UC (100-200/100,000 people), CD (50-100/100,000 people), IBS (10-20% of the adult)
- The cause of IBD
  - Not fully understood, but both genetic and environmental factors have been implicated
  - The enteric GI microbiota are accepted as a central etiologic factor in the pathogenesis
- Calprotectin
  - A member of the S100 family of zinc- and calcium-binding proteins and a heterodimer of S100A8/9.
  - The fecal concentration of calprotectin has been shown to correlate well with the gold standard indium-111–labeled granulocyte test
  - It is directly related to the extent of inflammation
  - It has been found to differentiate between active and inactive IBD
  - However fecal calprotectin is not specific to IBD
    - Increased in patients with colorectal carcinoma, the chronic use of NSAIDs, bacterial infections, and diverticular disease
- Other Fecal Markers
  - M2-PK
  - Lactoferrin
  - S100A12
- Therapeutic Drug Monitoring in Patients with Inflammatory Bowel Disease
  - Thiopurine analogs (azathioprine [AZA] and mercaptopurine [MP])
  - Anti-TNF drugs infliximab (IFX) and adalimumab (ADA) have
- Assessment of Functional Small Bowel Length
  - Citrulline is predominantly synthesized in the enterocytes of the small intestine.
  - Plasma citrulline levels have been shown to correlate well with small bowel length and absorption of xylose.

- Protein-Losing Enteropathy
  - Plasma protein excretion in feces is associated with a range of GI disorders.
  - GI disorders: IBD, lymphoma, Whipple disease, disorders of immune status

- Gold standard: methods using the administration of radioactive albumin or dextran
- Fecal excretion of 1-antiprotease inhibitor (AAT) is a marker of GI protein loss
- Increased AAT excretion can be found in b oth small and large bowel disease