Pocket Guide to Digestive Disorders

Jane Mijovic Kondejewski

Anejo Health Communications
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<th>Full Form</th>
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<tr>
<td>AFP</td>
<td>α-Fetoprotein</td>
</tr>
<tr>
<td>AFP-L3</td>
<td>Lens Culinaris Agglutinin-reactive Fraction</td>
</tr>
<tr>
<td>ALT</td>
<td>Alanine Aminotransferase</td>
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<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
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<tr>
<td>CD</td>
<td>Celiac Disease</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CF</td>
<td>Cystic Fibrosis</td>
</tr>
<tr>
<td>CFTR</td>
<td>Cystic Fibrosis Transmembrane Conductance Regulator</td>
</tr>
<tr>
<td>CRC</td>
<td>Colorectal Cancer</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>DCP</td>
<td>Des-gamma-carboxy Prothrombin</td>
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<tr>
<td>EA</td>
<td>Esophageal Atresia</td>
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<tr>
<td>EAEC</td>
<td>Enteraggregative E. coli</td>
</tr>
<tr>
<td>EHEC</td>
<td>Enterohemorrhagic E. coli</td>
</tr>
<tr>
<td>EIA</td>
<td>Enzyme Immunoassay</td>
</tr>
<tr>
<td>EIEC</td>
<td>Enteroinvasive E. coli</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme Linked Immunosorbent Assay</td>
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<tr>
<td>EPEC</td>
<td>Enteropathogenic E. coli</td>
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<td>EPS</td>
<td>Encapsulating Sclerosing Peritonitis</td>
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<tr>
<td>ETEC</td>
<td>Enterotoxigenic E. coli</td>
</tr>
<tr>
<td>ERCP</td>
<td>Endoscopic Retrograde Cholangiopancreatography</td>
</tr>
<tr>
<td>EUS</td>
<td>Endoscopic Ultrasound</td>
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<tr>
<td>GERD</td>
<td>Gastroesophageal Reflux Disease</td>
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<tr>
<td>HAV</td>
<td>Hepatitis A Virus</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis B e Antigen</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>HC</td>
<td>Hemorrhagic Colitis</td>
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<tr>
<td>HCC</td>
<td>Hepatocellular Carcinoma</td>
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</table>
HCV  Hepatitis C Virus
HDV  Hepatitis D Virus
HEV  Hepatitis E Virus
HIV  Human Immunodeficiency Virus
HUS  Hemolytic Uremic Syndrome
IBD  Inflammatory Bowel Disease
IBS  Irritable Bowel Syndrome
LES  Lower Esophageal Sphincter
LGIB  Lower Gastrointestinal Bleeding
MALT  Mucosa Associated Lymphoid Tissue
MRCP  Magnetic Resonance Cholangiopancreatography
MRI  Magnetic Resonance Imaging
MVT  Mesenteric Venous Thrombosis
NIDDK  National Institute of Diabetes and Digestive and Kidney Diseases
NOMI  Non-Occlusive Mesenteric Ischemia
NSAIDS  Non-Steroidal Anti-Inflammatory Drugs
OTC  Over The Counter
PET  Positron Emission Tomography
PD  Peritoneal dialysis
PMN  Polymorphonuclear
PPC  Primary Peritoneal Carcinoma
PPIs  Proton Pump Inhibitors
PSC  Primary Sclerosing Cholangitis
PTCA  Percutaneous Transhepatic Cholangiogram
PUD  Peptic Ulcer Disease
SBP  Spontaneous Bacterial Peritonitis
S-S agar  Salmonella - Shigella Agar
SNP  Single Nucleotide Polymorphism
TCBS  Thiosulfate-Citrate-Bile Salt-Sucrose
TEF  Tracheoesophageal Fistula
UC  Ulcerative Colitis
UES  Upper Esophageal Sphincter
UGIB  Upper Gastrointestinal Bleeding
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>USPTF</td>
<td>U.S. Preventive Services Task Force</td>
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<tr>
<td>WBC</td>
<td>White Blood Cell</td>
</tr>
<tr>
<td>WGO</td>
<td>World gastroenterology Organization</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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Chapter 1: The Digestive System

The overall function of the digestive system is to transfer the nutrients in food from the external environment to the internal environment, where they can be distributed to the cells of the body via the circulation. The cells of the body require adequate amounts of nutrients for their energy requiring processes and synthetic processes.

The digestive system (digestive tract) includes the mouth (oral cavity), the esophagus, the stomach, the gallbladder, the small intestine, the large intestine, and the anus. In addition, associated organs situated outside the digestive tract are essential for the digestive process. These are exocrine glands that secrete important digestive juices; they include salivary glands that produce saliva, the exocrine pancreas that secretes pancreatic juice, and the exocrine liver that produces bile (Figure 1.1).

Figure 1.1: The Digestive System
The Oral Cavity
Food enters the digestive tract via the oral cavity. Little digestion of food takes place in the oral cavity. However, through mastication (chewing), food is prepared for transport through the upper digestive tract into the stomach and small intestine, where the principal digestive processes take place.

The Salivary Glands
The salivary glands secrete saliva that is mixed with food during mastication. There are three major pairs of salivary glands: the parotid, the submandibular, and the sublingual glands. Normally secretion of saliva is constant, regardless of the presence of food in the mouth. When something touches the gums, the tongue, or some region of the mouth lining, or when chewing occurs, the amount of saliva secreted increases.

Saliva
Saliva dissolves some of the chewed food and acts as a lubricant, facilitating passage of food through the subsequent portions of the digestive tract. Saliva also contains an enzyme called amylase (ptyalin), which initiates the process of enzymatic hydrolysis to break down starch.

Pharynx
The pharynx, or throat, is the passageway leading from the mouth and nose to the esophagus and larynx. The pharynx permits the passage of swallowed solids and liquids into the esophagus, and conducts air to and from the trachea, or windpipe, during respiration.

Esophagus
The esophagus passes food from the pharynx to the stomach. It is about 25 cm (10 inches) in length; the width varies from 1.5 to 2 cm (about 1 inch). The esophagus lies behind the trachea and heart and in front of the spinal column; it traverses the diaphragm before entering the stomach.

Stomach
The stomach receives ingested food and liquids from the esophagus and retains them for grinding and mixing with gastric juice so that food particles are smaller and more soluble. The main functions of the stomach
are to commence the digestion of carbohydrates and proteins, to convert food into chyme, and to discharge the chyme into the small intestine periodically, as the physical and chemical condition of the mixture is rendered suitable for the next phase of digestion. The stomach absorbs few of the products of digestion.

The Small Intestine
The small intestine is about 6 meters long and consists of the duodenum, jejunum, and ileum. The common bile duct from the liver and the pancreatic duct from the pancreas join each other and empty into the duodenum (Figure 1.2). The small intestine is the major site of digestion and absorption of food. This is accomplished by the presence of a large surface area of villus structure.

Figure 1.2: Structures of the Small Intestine

Liver
The liver is located in the right upper quadrant of the abdomen. Liver cells process nutrients and detoxify harmful substances from the blood. The liver secretes bile which plays an important role in digestion by diluting and neutralizing stomach acid and by dramatically increasing the efficiency of fat digestion and absorption.
Chapter 2: Diseases of the Esophagus and Stomach

Disorders of the Esophagus

Gastroesophageal Reflux Disease (GERD)/Heartburn

Gastroesophageal reflux disease (GERD) is defined as symptoms or mucosal damage caused by abnormal reflux of stomach contents into the esophagus. GERD occurs due to defects in esophagogastric motility as a result of lower esophageal sphincter (LES) incompetence, poor esophageal clearance, and delayed gastric emptying (DeVault and Castell, 2005). Intermittent reflux symptoms are experienced by 55% of the population.

Symptoms

Common symptoms of GERD are shown in Box 2.1.

Box 2.1: Common Symptoms of GERD

1. Heartburn (pyrosis)
2. Regurgitation
3. Sour taste in the mouth
Alarm signals (Box 2.2) indicate complicated disease and require further attention (DeVault and Castell, 2005).

**Box 2.2: Alarm Signals in Gerd Evaluation**

1. Chronic cough
2. Choking sensation
3. Trouble breathing while asleep
4. Swallowing problems
5. Sore throat
6. Bleeding
7. Weight loss
8. Anemia
9. Recurrent pneumonia
10. Chronic sinusitis

**Diagnosis**

GERD may be diagnosed from a history of signs and symptoms. Ambulatory pH monitoring of the esophagus may help to confirm gastroesophageal reflux in patients with persistent symptoms. Endoscopy is recommended for patients who do not respond to therapy and have symptoms suggesting complicated disease or those who have a sufficient duration of symptoms to put them at risk for Barrett’s esophagus. Biopsy is added to confirm the presence of Barrett’s epithelium (Hirano and Richter, 2007; DeVault and Castell, 2005).

**Treatment**

Treatment strategies include lifestyle management, dietary modifications and physical techniques, acid suppression, and promobility agents (Box 2.3) (DeVault and Castell, 2005).
Box 2.3: Treatment Strategies for Gerd

1. Lifestyle management
   a) Weight loss
   b) Smoking cessation
   c) Relaxation techniques
2. Dietary modifications
   a) Limit aggravating foods (e.g. acidic food, spices, alcohol, carbonated beverages)
3. Physical measures
   a) Elevating head when lying down, avoiding bending forwards at the waist, avoiding tight fitting clothing
4. Acid suppression
   a) Antacids
   b) Over the counter acid suppressants
   c) Proton pump inhibitors (PPIs) (omerprazole, lansoprazole, rabeprazole, esomeprazole)
5. Promotility agents
   a) Cisapride, domaperidone
6. Anti-reflux surgery
7. Endoscopy therapy

Prognosis

The vast majority of patients with GERD will not develop serious complications, particularly when reflux is adequately treated. However, ulcers can form in the esophagus as a result of burning from stomach acid; damage from acid can cause the esophagus to scar and narrow, causing a stricture that can cause an obstruction; reflux acid into the throat can cause inflammation of the vocal cords, a sore throat, or a hoarse voice. The acid can be inhaled into the lungs and cause aspiration pneumonia or asthma symptoms. Chronic acid reflux into the lungs may eventually cause permanent lung damage (pulmonary fibrosis or bronchiectasis). Repeated damage to the esophageal lining can cause Barrett’s esophagus, when the squamous cells that line the lower esophagus are replaced by intestinal cells. The intestinal cells have a small risk of transforming into cancer cells (DeVault and Castell, 2005; Hirano and Richter, 2007).
Chapter 3: Diseases of the Liver, Pancreas, and Gallbladder

Disorders of the Liver

Hepatitis
Hepatitis refers to inflammation of the liver and can be acute (inflammation of the liver that lasts less than six months) or chronic (inflammation of the liver that lasts greater than six months), and can be due to infection or toxic substances. Infectious agents include viruses, bacteria, richettsia, spirochete, and parasites; toxic agents include drugs, anesthetics, industrial chemicals, insecticides, aflatoxin, yeasts, metallic compounds, and alcohol.

Acute Viral Hepatitis
Acute viral hepatitis is diffuse liver inflammation caused by specific hepatotropic viruses that have diverse modes of transmission and epidemiologies. Most cases resolve spontaneously, but some progress to chronic hepatitis. Occasionally, acute viral hepatitis progresses to acute hepatic failure (fulminant hepatitis).

Viral hepatitis has different causes; each type shares clinical, biochemical, and morphologic features (see Table 3.1). Acute viral hepatitis is a common, worldwide disease and is ranked 4th among the 30 leading communicable diseases (Cohen, 2007a).
Table 3.1: Characteristics of Viral Hepatitis (Cohen, 2007a)

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<th>Characteristics of Hepatitis Viruses</th>
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<tr>
<td><strong>Nucleic acid</strong></td>
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<td>RNA</td>
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<tr>
<td><strong>Serologic diagnosis</strong></td>
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<td><strong>Major transmission</strong></td>
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<tr>
<td><strong>Incubation period (days)</strong></td>
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<tr>
<td><strong>Epidemics</strong></td>
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<td><strong>Chronicity</strong></td>
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<td><strong>Liver cancer</strong></td>
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</table>

*Incomplete RNA; requires presence of hepatitis B virus for replication.

IgM anti-HAV = IgM antibody to hepatitis A virus; HBsAg = hepatitis B surface antigen; anti-HCV = antibody to hepatitis C virus; anti-HDV = antibody to hepatitis D virus; anti-HEV = antibody to hepatitis E virus.

**Symptoms**

Acute infection tends to develop in predictable phases. Infection begins with an incubation period during which the virus multiplies and spreads without symptoms. The prodromal, or pre-icteric phase follows, causing nonspecific symptoms, such as profound anorexia, malaise, nausea and vomiting, and often fever or right upper quadrant abdominal pain (Table 3.2). The icteric phase develops after 3 to 10 days, during which the urine darkens, jaundice develops, and the liver is enlarged and tender. Jaundice peaks within 1–2 weeks and then fades during a 2- to 4-week recovery phase. Appetite returns after the first week. Acute viral hepatitis usually resolves spontaneously 4–8 weeks after symptom onset (Cohen, 2007a).
### Table 3.2: Characteristics of Acute Viral Hepatitis Infection
(Adapted from Centers for Disease Control, 2010a)

<table>
<thead>
<tr>
<th>U.S. Statistics</th>
<th>HEPATITIS A is caused by the Hepatitis A virus (HAV)</th>
<th>HEPATITIS B is caused by the Hepatitis B virus (HBV)</th>
<th>HEPATITIS C is caused by the Hepatitis C virus (HCV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Estimated 25,000 new infections in 2007</td>
<td>• Estimated 43,000 new infections in 2007</td>
<td>• Estimated 17,000 new infections in 2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Estimated 1.2 million people with chronic HBV infection</td>
<td>• Estimated 3.2 million people with chronic HCV infection</td>
</tr>
<tr>
<td>Symptoms of Acute Infection</td>
<td>Symptoms of all types of viral hepatitis are similar and can include one or more of the following: • Fever • Fatigue • Loss of appetite • Nausea • Vomiting • Abdominal pain • Clay-colored bowel movements • Joint pain • Jaundice</td>
<td>• &lt; 10% of children &lt; 6 years have jaundice • 40%–50% of children age 6–14 years have jaundice • 70%–80% of persons &gt; 14 years have jaundice</td>
<td>• &lt; 1% of infants &lt; 1 year develop symptoms • 5%–15% of children age 1-5 years develop symptoms • 30%–50% of persons &gt; 5 years develop symptoms Note: Symptoms appear in 5%–15% of newly infected adults who are immunosuppressed</td>
</tr>
<tr>
<td>Likelihood of Symptomatic Acute Infection</td>
<td>• Among unimmunized persons, chronic infection occurs in &gt; 90% of infants, 25%–50% of children aged 1-5 years, and 6%–10% of older children and adults</td>
<td>• Most persons with acute disease recover with no lasting liver damage; acute illness is rarely fatal • 15%–25% of chronically infected persons develop chronic liver disease, including cirrhosis, liver failure, or liver cancer • Estimated 3,000 persons in the United States die from HBV-related illness per year</td>
<td>• 75%–85% of newly infected persons develop chronic infection • 15%–20% of newly infected persons clear the virus</td>
</tr>
<tr>
<td>Potential for Chronic Infection</td>
<td>None</td>
<td>• Most persons with acute disease recover with no lasting liver damage; acute illness is rarely fatal</td>
<td>• Acute illness is uncommon. Those who do develop acute illness recover with no lasting liver damage. • 60%–70% of chronically infected persons develop chronic liver disease • 5%–20% develop cirrhosis over a period of 20–30 years • 1%–5% will die from cirrhosis or liver cancer • Estimated 12,000 persons in the United States die from HCV-related illness per year</td>
</tr>
<tr>
<td>Severity</td>
<td>Most persons with acute disease recover with no lasting liver damage; rarely fatal</td>
<td>• HBsAg in acute and chronic infection • IgM anti-HBc is positive in acute infection only</td>
<td>• No serologic marker for acute infection</td>
</tr>
<tr>
<td>Serologic Tests for Acute Infection</td>
<td>• IgM anti-HAV</td>
<td></td>
<td></td>
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</tbody>
</table>
common type of pancreatic cancer, accounting for 95% of these tumors, is adenocarcinoma (tumors exhibiting glandular architecture on light microscopy) arising within the exocrine component of the pancreas. A minority arise from islet cells, and are classified as neuroendocrine tumors.

Prominent risk factors for pancreatic cancer include smoking, a history of chronic pancreatitis, obesity, alcohol consumption, exposure to certain chemicals, and possibly long-standing diabetes mellitus (primarily in women). Heredity plays some role. (Livstone, 2012a; National Comprehensive Cancer Network, 2012).

Pancreatic cancer is eighth most common cause of cancer-related deaths worldwide.

**Symptoms**
Symptoms of pancreatic cancer occur late (Box 3.10). By diagnosis, 90% of patients have locally advanced tumors that involve retroperitoneal structures, have spread to regional lymph nodes, or metastasized to the liver or lung.

<table>
<thead>
<tr>
<th>Box 3.10: Common Symptoms of Pancreatic Cancer</th>
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<tbody>
<tr>
<td>1. Severe abdominal pain radiating to the back</td>
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<tr>
<td>2. Weight loss</td>
</tr>
<tr>
<td>3. Jaundice</td>
</tr>
<tr>
<td>4. GI hemorrhage (if cancer is in body or head of pancreas)</td>
</tr>
<tr>
<td>5. Diabetes (in 25 to 50% of patients)</td>
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<tr>
<td>6. Floating stools</td>
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<tr>
<td>7. Nausea</td>
</tr>
<tr>
<td>8. Dyspepsia</td>
</tr>
</tbody>
</table>

**Diagnosis**
CT or MRI is typically performed first based on clinical suspicion of pancreatic cancer or evidence of dilated pancreatic and/or bile duct (stricture). The diagnostic algorithm recommended by the National Comprehensive Cancer Network Clinical Practice Guidelines is shown in Figure 3.4
Chapter 4: Diseases of the Small and Large Intestines

Disorders of the Small Intestine

Ileitis

Ileitis is chronic inflammation of the ileum. Ileitis may be caused by a variety of other diseases (Box 4.1) (DiLauro and Crum-Cianflone, 2010). Ileitis can affect persons of both sexes and of all ages; however, the disease most commonly strikes those between age 20 and 50.

Box 4.1: Selected Causes of Ileitis

1. Infectious: Yersinia spp., Salmonella spp., Clostridium difficile, Typhilitis, Mycobacterium tuberculosis, Mycobacterium avium, Actinomycosis, Anisakiasis, Cytomegalovirus, Histoplasma capsulatum
2. Spondyloarthropathies: Ankylosing spondylitis, Reactive arthritis, Arthritis associated with inflammatory bowel disease, Psoriasis with arthritis, Undifferentiated spondylarthropathy
3. Vascular: Vasculitides (Systemic lupus erythematosus, Polyarteritis nodosa, Henoch-Schönlein purpura, Behçet's disease), Other vasculitides (Churg-Strauss syndrome, rheumatoid arthritis vasculitis, Wegener granulomatosis, lymphomatoid granulomatosis, giant-cell, arteritis, Takayasu arteritis, thromboangiitis obliterans), Ischemia
4. Small-bowel neoplasms: Cecal or small-bowel (ileal) adenocarcinoma, Lymphoma, Carcinoid tumor, Lymphosarcoma, Metastatic cancer
5. Drug-related: NSAID enteropathy, Other drugs (KCL tablets, parenteral gold therapy, oral contraceptives, ergotamine, digoxin, diuretics, antihypertensives)
6. Infiltrative: Eosinophilic enteritis, Sarcoidosis, Amyloidosis

KCL: Potassium Chloride; NSAID: Nonsteroidal Anti-Inflammatory Drugs
**Symptoms**
The clinical presentation of ileitis varies from an acute and self-limited form of right lower quadrant pain and/or diarrhea, as in the majority of cases of bacterial ileitis, to a chronic and debilitating course complicated by obstructive symptoms, hemorrhage, and/or extraintestinal manifestation, as in vasculitis or Mycobacterium tuberculosis. Ileitis associated with spondylarthropathy or NSAIDs is typically subclinical and often escapes detection. In a minority of patients with long-standing Crohn’s ileitis, the recrudescence of symptoms may represent a neoplasm involving the ileum.

**Diagnosis**
Diagnosis involves a detailed history and physical examination, laboratory testing, and ileocolonoscopy and/or radiologic data. The diagnosis of the cause of ileitis is of paramount importance, as misdiagnosis may result in critical delays or errors in management (DiLauro and Crum-Cianflone, 2010).

**Treatment**
In some instances ileitis is self-limiting, and a full recovery can be expected. However, most cases of ileitis are chronic and require treatment to relieve symptoms. Rest and eating a healthy, balanced diet is advised. Medications include appropriate antibiotics such as penicillin, erythromycin, deoxycline, amoxicillin and ampicillin and immunosuppressive drugs including infliximab, azathioprine, mesalamine methotrexate, and metronidazole. Surgery can be used to go around or remove the damaged area of the ileum, although surgery usually does not eliminate the condition.

**Appendicitis**
Appendicitis is a condition characterized by inflammation of the appendix. It is classified as a medical emergency and many cases require removal of the inflamed appendix.

Appendicitis is the result of a primary obstruction of the appendix lumen. The appendix becomes filled with mucus and swells, increasing pressures within the lumen and the walls of the appendix. This causes thrombosis and occlusion of the small vessels, and stasis of lymphatic flow. Subsequently, the appendix becomes ischemic and necrotic. As bacteria begin to leak out through the dying walls, pus forms within and around
Chapter 5: Disorders of the Peritoneum

Introduction
The peritoneum is the largest and most complex serous membrane in the body. It forms a closed sac (i.e., coelom) by lining the interior surfaces of the abdominal wall (anterior and lateral), by forming the boundary to the retroperitoneum (posterior), by covering the extraperitoneal structures in the pelvis (inferior), and by covering the undersurface of the diaphragm (superior). The parietal layer of the peritoneum reflects onto the abdominal visceral organs to form the visceral peritoneum creating the peritoneal cavity (Figure 5.1).

Any pathologic process involving the peritoneal cavity can easily disseminate by means of unrestricted movement of fluid and cells. Disorders of the peritoneum include peritonitis, peritoneal cancer, and complications from peritoneal dialysis.

Figure 5.1: The Peritoneal Cavity
Peritonitis
Peritonitis is defined as inflammation of the peritoneum. Peritonitis is most often caused by introduction of an infection into the sterile peritoneal environment through organ perforation, but it may also result from other irritants, such as foreign bodies, bile from a perforated gall bladder or a lacerated liver, or gastric acid from a perforated ulcer. Women also experience localized peritonitis from an infected fallopian tube or a ruptured ovarian cyst.

Peritonitis is categorized as primary, secondary, or tertiary. In primary peritonitis, there is no known intra-abdominal or distant source. Secondary peritonitis is caused by an intra-abdominal process, such as a ruptured appendix or a perforated peptic ulcer. Tertiary peritonitis is defined as late-stage disease, whereby the infection persists or recurs after treatment of secondary peritonitis.

Primary Peritonitis/Spontaneous Bacterial Peritonitis
Most cases of spontaneous bacterial peritonitis (SBP) are caused by translocation of bacteria from the gastrointestinal tract. E. coli is the most frequently recovered pathogen, followed by Klebsiella pneumoniae, Streptococcus pneumoniae, other streptococcal species, and enterococci. SBP is the most frequent and life-threatening infection in patients with cirrhosis.

Symptoms
Typically, patients with acute peritonitis present with symptoms shown in Box 5.1.

Box 5.1: Symptoms of Acute Peritonitis (Singh and Khadori, 2012)

1. Abdominal pain
2. Nausea
3. Vomiting
4. Diarrhea
5. Diffuse and rebound abdominal tenderness
6. Bowel sounds are hypoactive or absent
Chapter 6: Gastrointestinal Hemorrhage

Introduction

Gastrointestinal hemorrhage or bleeding describes every form of hemorrhage (loss of blood) in the gastrointestinal tract, from the pharynx to the rectum. The causes of gastrointestinal bleeding are classified into upper or lower, depending on their location in the gastrointestinal tract.

Upper gastrointestinal bleeding (UGIB) refers to hemorrhage in the upper gastrointestinal tract. The anatomic cut-off for UGIB is the ligament of Treitz, which connects the fourth portion of the duodenum to the diaphragm near the splenic flexure of the colon. Lower gastrointestinal bleeding (LGIB) refers to any form of bleeding distal to the ligament of Treitz.

UGIB accounts for 100–200 per 100,000 cases of gastrointestinal bleeding versus 20–27 per 100,000 cases for LGIB.

Upper Gastrointestinal Bleeding

About 75% of patients presenting to the emergency room with GI bleeding have an upper source. Causes are anatomically divided into their location in the upper gastrointestinal tract (Box 6.1). Patients are stratified into having either variceal or non-variceal sources of UGIB, as the two have different treatment algorithms and prognosis. Variceal sources account for 10–25% of UGIB (Cappell, 2008).
### Box 6.1: Major Causes of Upper Gastrointestinal Bleeding (Cappell, 2008)

1. Peptic ulcer disease
2. Esophageal and gastric varices
3. Hemorrhagic gastritis
4. Esophagitis
5. Duodenitis
6. Mallory-Weiss tear
7. Angiodysplasia
8. Upper gastrointestinal malignancy
9. Anastomotic ulcers (after PUD surgery or bariatric surgery)
10. Medications including NSAIDs, SSRIs, corticosteroids, and anticoagulants

NSAID: Non-steroidal Anti-inflammatory Drugs; PUD: Peptic Ulcer Diseases; SSRIs: Selective Serotonin Re-uptake Inhibitors

### Lower Gastrointestinal Bleeding

Most cases of LGIB involve the colon (85%) and 3–5% cases are secondary to bleeding from the small intestine. Common causes of LGIB are shown in Box 6.2.

### Box 6.2: Common Causes of Lower Gastrointestinal Bleeding

1. Anal fissures
2. Angiodysplasia (vascular ectasia)
3. Colitis: Radiation, ischemic, infectious
4. Colonic carcinoma
5. Colonic polyps
6. Diverticular disease
7. Inflammatory bowel disease: Ulcerative proctitis/colitis, Crohn disease
8. Internal hemorrhoids
Symptoms - Upper gastrointestinal bleeding
Patients with UGIB often present with hematemesis, coffee ground vomiting, melena (black tarry stools), or hematochezia (maroon colored stool) if the hemorrhage is severe. The presentation of bleeding depends on the amount and location of hemorrhage. Patients may also present with complications of anemia, including chest pain, syncope, fatigue, and shortness of breath.

Symptoms - Lower gastrointestinal bleeding
Patients with LGIB typically present with hematochezia, which is a sign of a fast moving active gastrointestinal bleed. Melena may occur, but is four times more likely to come from a UGIB than LGIB.

Occasionally, a person with a LGIB will not present with any signs of internal bleeding. In these cases, a diagnostic assessment or pre-assessment should watch for signs and symptoms such as hypotension, tachycardia, angina, syncope, weakness, confusion, stroke, myocardial infarction/heart attack, and shock.

Diagnosis
Stabilization with airway management, intravenous fluids, or transfusions is essential before and during diagnostic evaluation of gastrointestinal bleeding. The evaluation should encompass items in Box 6.3.

Box 6.3: Initial Assessment of Gastrointestinal Bleeding

1. History of the present illness to ascertain quantity and frequency of blood passage.
2. Review of symptoms including presence of abdominal discomfort, weight loss, easy bleeding or bruising, previous colonoscopy results, and symptoms of anemia (e.g., weakness, easy fatigability, dizziness).
3. Past medical history inquiring about previous gastrointestinal bleeding (diagnosed or undiagnosed); known IBS, bleeding diatheses, and liver disease; and use of any drugs that increase the likelihood of bleeding or chronic liver disease (e.g., alcohol).
4. Physical examination focusing on vital signs and other indicators of shock or hypovolemia (e.g., tachycardia, tachypnea, pallor, diaphoresis, oliguria, confusion) and anemia (e.g., pallor, diaphoresis).

IBS: inflammatory bowel disease
The history and physical examination suggest a diagnosis in about 50% of patients, but confirmatory testing is required (Box 6.4).

**Box 6.4: Diagnosis of Gastrointestinal Bleeding**

1. CBC, coagulation profile, liver function tests
2. Abdominal CT scan
3. Abdominal MRI scan
4. Abdominal x-ray
5. Angiography
6. Bleeding scan (tagged red blood cell scan)
7. Blood clotting tests
8. Capsule endoscopy (camera pill that is swallowed to look at the small intestine)
9. Colonoscopy
10. Enteroscopy
11. Sigmoidoscopy

CRC: Complete Blood Count; CT: Computed Tomography; MRI: Magnetic Resonance Imaging

**Treatment**

Hematemesis, hematochezia, or melena should be considered an emergency. Admission to an ICU, with consultation by both a gastroenterologist and a surgeon, is recommended for all patients with severe gastrointestinal bleeding. General treatment is directed at maintenance of the airway and restoration of circulating volume.

Hemostasis and other treatment depend on the pathophysiology of the bleed (see corresponding sections) (Ansari, 2012b).

**Prognosis**

Gastrointestinal bleeding stops spontaneously in about 80% of patients. In patients with UGIB, re-bleeding occurs in about 7–16%, despite treatment.
Chapter 7: Infections of the Digestive Tract

Introduction
Infections of the digestive tract are caused by a variety of microbes, including bacteria (E. coli, Campylobacter), viruses (norwalk agent, rotavirus), and parasites (Giardia, Entamoeba, Ascaris). If the infection is in the small intestine, symptoms include watery diarrhea and/or vomiting. Infections in the large intestine usually result in dysentery (small fecal volume, with mucus and blood).

Gastroenteritis
Gastroenteritis is the inflammation of the lining of the stomach and small and large intestines. Most cases are infectious, caused by viruses, bacteria, or parasites. Viral gastroenteritis is more common than bacterial gastroenteritis. Acquisition may be foodborne, waterborne, or via person-to-person spread. Worldwide, an estimated 1.5 million children die each year from infectious gastroenteritis; although high, this number represents one half to one quarter of previous mortality. Improvements in water sanitation in many parts of the world and the appropriate use of oral rehydration therapy for infants with diarrhea are likely responsible for this decrease (Boyce, 2012).

Viral Gastroenteritis
Several different viruses cause gastroenteritis, including rotavirus, adenovirus, astrovirus, calicivirus, noroviruses, and norwalk virus (Center for Disease Control and Prevention, 2011; National Institute of Diabetes and Digestive and Kidney Diseases, 2011).

Symptoms
Symptoms (Box 7.1) usually appear within 12 to 48 hours after exposure to a gastroenteritis-causing virus and last for 1 to 3 days. Dehydration is the most common complication of viral gastroenteritis.
**Box 7.1: Symptoms of Viral Gastroenteritis** (National Institute of Diabetes and Digestive and Kidney Diseases, 2011)

<table>
<thead>
<tr>
<th>1. Main symptoms</th>
<th>2. Other symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Watery diarrhea</td>
<td>a. Headache</td>
</tr>
<tr>
<td>b. Vomiting</td>
<td>b. Fever</td>
</tr>
</tbody>
</table>

**Diagnosis**

Diagnosis is based on physical examination and symptoms. No diagnostic tests are usually performed, although a rapid antigen test of the stool, either by enzyme immune assay (EIA; >98% sensitivity and specificity) or latex agglutination tests (less sensitive and specific as compared to EIA) may be used to aid in the diagnosis of rotavirus infection.

**Treatment**

Viral gastroenteritis is a self-limiting disease but it is often necessary to administer fluids and electrolytes. The following parameters are used to assess the degree of dehydration: blood pressure, pulse, heart rate, skin turgor, fontanelle, mucous membranes, eyes, extremities, mental status, urine output, and thirst.

Oral rehydration therapy is required for preventing and treating early dehydration, and continued replacement therapy is recommended for ongoing loses. Shock, severe dehydration, and decreased consciousness require intravenous therapy.

Research has consistently shown that probiotics, such as Lactobacillus casei GG and Saccharomyces boulardii, reduce the frequency and/or duration of diarrhea in acute infantile gastroenteritis by 30–70%. However, their role in the treatment and prevention of acute infantile gastroenteritis is still undefined (Centers for Disease Control and Prevention, 2011; National Institute of Diabetes and Digestive and Kidney Diseases, 2011).
Chapter 8: Genetics and Epigenetics of Digestive System Disorders

Introduction
Genetics refers to how genes are inherited amongst individuals. A genetic disorder may or may not be a heritable disorder. Some genetic disorders are passed down from parents' genes, but others are caused by new mutations or changes to DNA. Many diseases, including numerous disorders of the digestive system, have a genetic basis.

Epigenetics refers to changes in gene expression involving molecular and structural changes of DNA that do not alter the DNA sequence. DNA methylation, post translational modification of chromatin, and microRNA (miRNA) expression are all known to effect changes in gene expression in many diseases.

Genetics and Epigenetics of Disorders of the Esophagus

Gastroesophageal Reflux Disease (GERD)/Heartburn
The pathophysiology of GERD is thought to be influenced by host genetic factors and genetic polymorphisms (Table 8.1) (Ghoshal, 2011).

Table 8.1: Genes Associated with Gastroesophageal Reflux Disease

<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>GNB3</td>
<td>G-protein beta3 subunit gene</td>
<td>Cell signaling</td>
</tr>
<tr>
<td>CCND1</td>
<td>Cyclin D1</td>
<td>Cell cycle regulation</td>
</tr>
<tr>
<td>GSTPI</td>
<td>Glutathione-S-transferase</td>
<td>Detoxification</td>
</tr>
</tbody>
</table>
Esophageal Perforation
Esophageal perforation may be associated with mutations in COL7A1, which encodes the protein Type VII A-7 collagen. COL7A1 is a structural protein found in the basement membrane zone beneath stratified squamous epithelia. It has an important role as an anchoring fibril between the external epithelia and the underlying stroma (Martin, 2002).

Structural Abnormalities of the Esophagus
EA may be the result of a failure in the expression of genes encoding transcription factors and signaling molecules (Table 8.2). Epigenetic control through abnormal histone acetylation of BAXP1 is implicated in oculo-auriculo-vertebral syndrome, a rare cause of EA (Genevieve, 2011). Environmental factors may increase the risk for the development of tracheoesophageal anomalies (Fernando, 2012).

Table 8.2: Genes Associated with Esophageal Atresia and Tracheoesophageal Fistula

<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sox2</td>
<td>Transcription factor SOX-2</td>
<td>Transcription factor</td>
</tr>
<tr>
<td>Shh</td>
<td>Sonic hedgehog homolog</td>
<td>Signaling modulator</td>
</tr>
<tr>
<td>Gli-2</td>
<td>Glioma-associated oncogene family zinc finger 2</td>
<td>Transcription factor</td>
</tr>
<tr>
<td>Gli-3</td>
<td>Glioma-associated oncogene family zinc finger 2</td>
<td>Transcription factor</td>
</tr>
<tr>
<td>Pcsk5</td>
<td>Proprotein convertase subtilisin/kexin type 5</td>
<td>Proprotein convertase</td>
</tr>
<tr>
<td>FOX</td>
<td>Forkhead box proteins</td>
<td>Transcription factor</td>
</tr>
<tr>
<td>Nkx2.1</td>
<td>NK2 homeobox 1</td>
<td>Transcription factor</td>
</tr>
<tr>
<td>Tbx4</td>
<td>T-box transcription factor TBX4</td>
<td>Transcription factor</td>
</tr>
</tbody>
</table>
Motility Abnormalities
Achalasia may have a familial occurrence and is associated with well-defined genetic syndromes. Genetic factors involved in achalasia have been revealed by the candidate gene approach (Table 8.3) (Gockel, 2010).

Table 8.3: Genes Associated with Achalasia

<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-DQ</td>
<td>Major histocompatibility complex, class II</td>
<td>Autoimmunity and immunity response</td>
</tr>
<tr>
<td>PTPN22</td>
<td>Protein tyrosine phosphatase N22</td>
<td>Autoimmunity and immunity response</td>
</tr>
<tr>
<td>VIPR1</td>
<td>Vasoactive intestinal peptide receptor 1</td>
<td>Inflammatory response</td>
</tr>
<tr>
<td>GDNF</td>
<td>Glial cell line derived neurotrophic factor</td>
<td>Development, structure, and function of the enteric nervous system</td>
</tr>
<tr>
<td>RET</td>
<td>RET transforming sequence</td>
<td>Development, structure, and function of the enteric nervous system</td>
</tr>
<tr>
<td>SPRY2</td>
<td>Protein sprouty homolog 2</td>
<td>Development, structure, and function of the enteric nervous system</td>
</tr>
</tbody>
</table>

Inflammatory Disorders (Esophagitis)
Erosive esophagitis may be associated with the increased expression of a number of genes from the Aurora kinase family AURKA, AURKC, HDAC9 (Histone deacetylase 9) and NEK6 (never in mitosis A-related kinase 6); these proteins are involved in mitosis (Kasap, 2012).

Genomic research has led to the identification of single nucleotide polymorphisms (SNPs) in the gene encoding thymic stromal lymphopoietin (TSLP), and subsequently in the gene encoding its receptor (TSLPR), as disease susceptibility markers for eosinophilic esophagitis (Spergel, 2010).

Esophageal Cancer
Esophageal squamous-cell carcinoma may result from upregulation of
Chapter 9: Digestive System Links

American Association for the Study of Liver Diseases www.aasld.org
American College of Gastroenterology http://gi.org/
American Gastroenterological Association http://www.gastro.org
Centers for Disease Control and Prevention www.cdc.gov/
Genetic and Rare Diseases Information Center (GARD) http://rarediseases.info.nih.gov
Mayo Clinic www.mayoclinic.com
National Organization for Rare Disorders (NORD) http://www.rarediseases.org
The National Pancreas Foundation www.pancreasfoundation.org
World Gastroenterology Organization www.worldgastroenterology.org/
World Health Organization www.who.int
Chapter 10: Selected References


http://www.merckmanuals.com/professional/infectious_diseases/a naerobic_bacteria/clostridium_difficile%E2%80%93induced_diarrhea.html Website accessed 280213.


Livstone EM (2012b) Polyps of the Colon and Rectum.

Livstone EM (2012c) Colorectal Cancer.


