Bowel obstruction and tumors
Intestinal Obstruction

• Obstruction of the GI tract may occur at any level, but the **small intestine** is most often involved because of its relatively narrow lumen.
• Causes:
  Hernias
  intestinal adhesions
  Intussusception
  volvulus
  Tumors
  Infarction----- strictures
  Crohn disease----- strictures
Figure 17-22 Intestinal obstruction. The four major causes of intestinal obstruction are (1) herniation of a segment in the umbilical or inguinal regions, (2) adhesion between loops of intestine, (3) volvulus, and (4) intussusception.
• The clinical manifestations of intestinal obstruction include:
  - abdominal pain and distention
  - Vomiting
  - constipation
- **Hernias:**
  - Hernias are the most frequent cause of intestinal obstruction worldwide.
  - Any weakness or defect in the abdominal wall may permit protrusion of a hernia sac (serosa-lined pouch of peritoneum)
  - Inguinal and femoral canals, umbilicus, or at sites of surgical scars.
  - Small bowel loops are typically involved, but omentum or large bowel may also protrude, and any of these may become entrapped.
  - Incarceration (permanent entrapment)
  - Strangulation (arterial and venous compromise)
  - Infarction
• Adhesions:
  - causes: Surgical procedures, peritoneal inflammation (such as infection, endometriosis)
  - resulting in internal herniation
  - Fibrous adhesions are most often acquired, but can be congenital in rare cases. Therefore, internal herniation must be considered even in the absence of a history of peritonitis or surgery.
• **Volvulus:**
  - Twisting of a loop of bowel about its mesenteric point of attachment is termed volvulus; it results in both luminal and vascular compromise.
  - It occurs most often in large redundant loops of **sigmoid colon**, followed in frequency by the cecum, small bowel, stomach, or, rarely, transverse colon.
• **Intussusception:**
  - Intussusception occurs when a segment of the intestine, constricted by a wave of peristalsis, telescopes into the immediately distal segment. Once trapped, the invaginated segment is propelled by peristalsis and pulls the mesentery along.
  - Intussusception is the most common cause of intestinal obstruction in **children younger than 2 years of age.**
  - Some cases are idiopathic, but many cases have been associated with viral infection and rotavirus vaccines, perhaps due to reactive hyperplasia of Peyer patches and other mucosa-associated lymphoid tissue which can act as the leading edge of the intussusception.
  - Intussusception is rare in older children and adults, and is generally caused by an intraluminal mass or tumor that serves as the initiating point of traction.
Sigmoid Diverticular Disease

- Pseudodiverticula: outpouchings of the mucosa and submucosa
- True diverticula: such as Meckel diverticulum, invested by all three layers of the colonic wall.
- Diverticula are generally multiple and the condition is referred to as diverticulosis.

Where nerves, arterial vasa recta, and their connective tissue sheaths penetrate the inner circular muscle coat, focal discontinuities in the muscle wall are created. In other parts of the intestine these gaps are reinforced by the external longitudinal layer of the muscularis propria, but, in the colon, this muscle layer is gathered into the three bands termed taeniae coli. Increased intraluminal pressure is probably due to exaggerated peristaltic contractions, with spasmodic sequestration of bowel segments, and may be enhanced by diets low in fiber, which reduce stool bulk, particularly in the sigmoid colon.
Clinical Features:
More in Western adult populations older than age 60.
Most individuals with diverticular disease remain asymptomatic throughout their lives.
However, about 20% of individuals with diverticuli develop manifestations of diverticular disease, such as intermittent cramping, continuous lower abdominal discomfort, constipation, distention, or a sensation of never being able to completely empty the rectum. Patients sometimes experience alternating constipation and diarrhea that can mimic IBS.
Occasionally there may be minimal chronic or intermittent blood loss, and, rarely, massive hemorrhage.
Meckel diverticulum

• Meckel diverticulum occurs as a result of failed involution of the vitelline duct, which connects the lumen of the developing gut to the yolk sac.

• rule of 2s:
  • - Occur in approximately 2% of the population
  • - Are generally present within 2 feet (60 cm) of the ileocecal valve
  • - Are approximately 2 inches (5 cm) long
  • - Are twice as common in males
  • Are most often symptomatic by age 2

• Symptoms: bleeding, obstruction
Polyps

- Polyps are most common in the **colo-rectal region** but may occur in the esophagus, stomach, or small intestine.
- Intestinal polyps can be classified as non-neoplastic or neoplastic in nature.
- The most common neoplastic polyp is the adenoma, which has the potential to progress to cancer.
- The non-neoplastic polyps can be further classified as inflammatory, hamartomatous, or hyperplastic.
• Pedunculated polyp: with stalks
• sessile polyp: without stalks
• **hyperplastic Polyps:**
  - The pathogenesis of hyperplastic polyps is incompletely understood, but they are thought to result from decreased epithelial cell turnover and delayed shedding of surface epithelial cells.
  - It is now appreciated that these lesions are **without malignant potential**.
  - Most commonly found in the left colon
Figure 17-41 Hyperplastic polyp. A, Polyp surface with irregular tufting of epithelial cells. B, Tufting results from epithelial overcrowding. C, Epithelial crowding produces a serrated architecture when crypts are cut in cross-section.
• **Hamartomatous Polyps:**
- Hamartomatous polyps occur sporadically or as components of various genetically determined or acquired syndromes.

- **Juvenile Polyps:**
  may be sporadic (solitary lesions) or syndromic (3 to as many as 100 polyps, AD disorder, 30% to 50% of patients with juvenile polyposis develop colonic adenocarcinoma by age 45).

  occur in children younger than 5 years of age, Most juvenile polyps are located in the rectum, typically present with rectal bleeding.

  **Peutz-Jeghers Syndrome:**
  This rare autosomal dominant syndrome presents at a median age of 11 years with multiple GI hamartomatous polyps and mucocutaneous hyperpigmentation.

  The polyps of Peutz-Jeghers syndrome are most common in the small intestine.

  associated with a markedly increased risk of several malignancies.
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Mean Age at Presentation (yr)</th>
<th>Mutated Gene(s); Pathway</th>
<th>Gastrointestinal Lesions</th>
<th>Selected Extra-Gastrointestinal Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvenile polyposis</td>
<td>&lt;5</td>
<td>$Smad4, Bmp1A$; TGF-$\beta$ signaling pathway</td>
<td>Juvenile polyps; risk of gastric, small intestinal, colonic, and pancreatic adenocarcinoma</td>
<td>Congenital malformations, digital clubbing</td>
</tr>
<tr>
<td>Peutz-Jeghers syndrome</td>
<td>10-15</td>
<td>$Stk11$; AMP kinase-related pathways</td>
<td>Arborizing polyps; Small intestine $&gt; colon &gt; stomach$; colonic adenocarcinoma</td>
<td>Pigmented macules; risk of colon, breast, lung, pancreatic, and thyroid cancer</td>
</tr>
<tr>
<td>Cowden syndrome, Bannayan-Ruvalcaba-Riley syndrome*</td>
<td>&lt;15</td>
<td>$Pten$; PI3K/AKT pathway</td>
<td>Hamartomatous/ inflammatory intestinal polyps, lipomas, ganglioneuromas</td>
<td>Benign skin tumors, benign and malignant thyroid and breast lesions; no increase in GI cancers</td>
</tr>
<tr>
<td>Cronkhite-Canada syndrome</td>
<td>&gt;50</td>
<td>Nonhereditary, unknown cause</td>
<td>Hamartomatous polyps of stomach, small intestine colon; abnormalities in nonpolypoid mucosa</td>
<td>Nail atrophy, hair loss, abnormal skin pigmentation, cachexia, and anemia. Fatal in up to 50%.</td>
</tr>
</tbody>
</table>
Adenomas:
colic adenomas are precursors to the majority of colorectal adenocarcinomas. But majority of adenomas do not progress to become adenocarcinomas.
characterized by the presence of epithelial dysplasia.
Adenomas can be classified as tubular, tubulovillous, or villous based on their architecture. These categories, however, have little clinical significance in isolation. Size is the most important characteristic that correlates with risk of malignancy.
Most adenomas are clinically silent, with the exception of large polyps that produce occult bleeding and anemia and rare villous adenomas that cause hypoproteinemic hypokalemia by secreting large amounts of protein and potassium.
Familial adenomatous polyposis (FAP):
is an autosomal dominant disorder in which patients develop numerous colorectal adenomas as teenagers. At least 100 polyps are necessary for a diagnosis of classic FAP, but as many as several thousand may be present. caused by mutations of the adenomatous polyposis coli (APC) gene. 75% of cases are inherited, while the remaining appear to be caused by de novo mutations.

Colorectal adenocarcinoma develops in 100% of untreated FAP patients, often before age 30 and nearly always by age 50. As a result, prophylactic colectomy is the standard therapy for individuals carrying APC mutations.
• Hereditary non-polyposis colorectal cancer (HNPCC): Lynch syndrome

HNPCC is caused by inherited mutations in genes that encode proteins responsible for the detection, excision, and repair of errors that occur during DNA replication.
<table>
<thead>
<tr>
<th>Etiology</th>
<th>Molecular Defect</th>
<th>Target Gene(s)</th>
<th>Transmission</th>
<th>Predominant Site(s)</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial adenomatous polyposis</td>
<td>APC/WNT pathway</td>
<td>APC</td>
<td>Autosomal dominant</td>
<td>None</td>
<td>Tubular, villous; typical adenocarcinoma</td>
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<tr>
<td>Hereditary nonpolyposis colorectal cancer</td>
<td>DNA mismatch repair</td>
<td>MSH2, MLH1</td>
<td>Autosomal dominant</td>
<td>Right side</td>
<td>Sessile serrated adenoma; mucinous adenocarcinoma</td>
</tr>
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Adenocarcinoma

- Adenocarcinoma of the colon is the most common malignancy of the GI tract and is a major cause of morbidity and mortality worldwide.
- In contrast, the small intestine, which accounts for 75% of the overall length of the GI tract, is an uncommon site for benign and malignant tumors.
Colorectal cancer incidence peaks at 60 to 70 years of age,
The dietary factors most closely associated with increased rates of colorectal cancer are low intake of unabsorbable vegetable fiber and high intake of refined carbohydrates and fat. It is theorized that reduced fiber content leads to decreased stool bulk and altered composition of the intestinal microbiota. This change may increase synthesis of potentially toxic oxidative by-products of bacterial metabolism, which would be expected to remain in contact with the colonic mucosa for longer periods of time as a result of reduced stool bulk. High fat intake also enhances hepatic synthesis of cholesterol and bile acids, which can be converted into carcinogens by intestinal bacteria.

aspirin or other NSAIDs have a protective effect.
• Pathogenesis:
At least two genetic pathways have been described:
- **APC/β-catenin pathway**, which is activated in the classic adenoma-carcinoma sequence. accounts for up to 80% of sporadic colon tumors.
- **microsatellite instability pathway**, which is associated with defects in DNA mismatch repair and accumulation of mutations in microsatellite repeat regions of the genome.
Figure 17-49  Morphologic and molecular changes in the adenoma-carcinoma sequence. Loss of one normal copy of the tumor suppressor gene APC occurs early. Individuals born with one mutant allele are therefore at increased risk of developing colon cancer. Alternatively, inactivation of APC in colonic epithelium may occur later in life. This is the “first hit” according to the Knudson hypothesis (Chapter 7). The loss of the intact second copy of APC follows (“second hit”). Other changes, including mutation of K-RAS, losses at 18q21 involving SMAD2 and SMAD4, and inactivation of the tumor suppressor gene TP53, lead to the emergence of carcinoma, in which further mutations occur. Although there seems to be a temporal sequence of changes, the accumulation of mutations, rather than their occurrence in a specific order, is most critical.
Figure 17-50. Morphologic and molecular changes in the mismatch repair pathway of colon carcinogenesis. Defects in mismatch repair genes result in microsatellite instability and permit accumulation of mutations in numerous genes. If these mutations affect genes involved in cell survival and proliferation, cancer may develop.
<table>
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<tr>
<th>Sporadic colon cancer (70%-80%)</th>
<th>APC/WNT pathway</th>
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<th>None</th>
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<th>Tubular, villous; typical adenocarcinoma</th>
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<td>None</td>
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• Clinical Features:
Cecal and other right-sided colon cancers are most often called to clinical attention by the appearance of fatigue and weakness due to iron deficiency anemia. Iron deficiency anemia in an older man or postmenopausal woman is GI cancer until proven otherwise.

Left-sided colorectal adenocarcinomas may produce occult bleeding, changes in bowel habits, or cramping and left lower quadrant discomfort.
• the two most important prognostic factors are depth of invasion and the presence of lymph node metastases----- stage

• the liver is the most common site of metastatic lesions. The rectum does not drain via the portal circulation, hence carcinomas of the anal region that metastasize often circumvent the liver.
• Tumors of the Anal Canal:
Carcinomas of the anal canal may have typical glandular or squamous patterns of differentiation, recapitulating the normal epithelium of the upper and lower thirds, respectively.
• **Acute appendicitis**: is most common in children and adolescents. It is thought to be initiated by increased intraluminal pressure and compromised venous outflow, usually caused by a small stone-like mass of stool, or fecalith, or, less commonly, a gallstone, tumor, or mass of worms (oxyuriasis vermicularis).

Typically, early acute appendicitis produces periumbilical pain that ultimately localizes to the right lower quadrant, followed by nausea, vomiting, low-grade fever, and a mildly elevated peripheral white cell count.

A classic physical finding is the **McBurney sign**, deep tenderness located two thirds of the distance from the umbilicus to the right anterior superior iliac spine (McBurney point).
• **Tumors of the Appendix:**
The most common tumor of the appendix is the well-differentiated neuroendocrine (carcinoid) tumor. It is usually discovered incidentally at the time of surgery or examination of a resected appendix.

- Other tumors:
  Conventional adenomas
  non–mucin-producing adenocarcinomas
  Mucinous cystadenoma
  mucinous cystadenocarcinoma---- pseudomyxoma peritonei