Malabsorption
• **Malabsorption**, is characterized by defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes and minerals, and water.

presents most commonly as **chronic diarrhea**.

A hallmark of malabsorption is **steatorrhea**, characterized by excessive fecal fat and bulky, frothy, greasy, yellow or clay-colored stools.
• General symptoms include: diarrhea (from nutrient malabsorption and excessive intestinal secretion).
flatus, abdominal pain, and weight loss, anorexia, abdominal distention, borborygmi, and muscle wasting.
Inadequate absorption of vitamins and minerals can result in:
- anemia and mucositis due to pyridoxine (B6), folate, or vitamin B12 deficiency;
- bleeding, due to vitamin K deficiency;
- osteopenia and tetany due to calcium, magnesium, or vitamin D deficiencies;
- peripheral neuropathy due to vitamin A or B12 deficiencies.
• Malabsorption results from disturbance in at least one of the four phases of nutrient absorption:

**Intraluminal digestion**: in which proteins, carbohydrates, and fats are broken down into forms suitable for absorption.

**Terminal digestion**: which involves the hydrolysis of carbohydrates and peptides by disaccharidases and peptidases in the brush border of the small intestinal mucosa.

**Transepithelial transport**: in which nutrients, fluid, and electrolytes are transported across and processed within the small intestinal epithelium.

**Lymphatic transport** of absorbed lipids.
• **Diarrhea** is defined as an increase in stool mass, frequency, or fluidity, typically greater than 200 gm per day.

• **Dysentery**: Painful, bloody, small-volume diarrhea.
Diarrhea can be classified into four major categories:

**Secretory diarrhea** is characterized by isotonic stool and persists during fasting.

**Osmotic diarrhea** is due to the excessive osmotic forces exerted by unabsorbed luminal solutes. The diarrhea fluid is more than 50 mOsm more concentrated than plasma and abates with fasting. such as that which occurs with **lactase deficiency**.

**Malabsorptive diarrhea** follows generalized failure of nutrient absorption, is associated with steatorrhea, and is relieved by fasting.

**Exudative diarrhea** due to inflammatory disease is characterized by purulent, bloody stools that continue during fasting.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Intraluminal Digestion</th>
<th>Terminal Digestion</th>
<th>Transepithelial Transport</th>
<th>Lymphatic Transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac disease</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Environmental enteropathy</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td></td>
<td>+</td>
<td></td>
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<tr>
<td>Cystic fibrosis</td>
<td></td>
<td>+</td>
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<tr>
<td>Primary bile acid malabsorption</td>
<td></td>
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<tr>
<td>Carcinoid syndrome</td>
<td></td>
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<tr>
<td>Autoimmune enteropathy</td>
<td></td>
<td>+</td>
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<tr>
<td>Disaccharidase deficiency</td>
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<tr>
<td>Whipple disease</td>
<td></td>
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<td>+</td>
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<tr>
<td>Abetalipoproteinemia</td>
<td></td>
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<td>+</td>
<td></td>
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<tr>
<td>Viral gastroenteritis</td>
<td></td>
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<td>+</td>
</tr>
<tr>
<td>Bacterial gastroenteritis</td>
<td></td>
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<tr>
<td>Parasitic gastroenteritis</td>
<td></td>
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<td>+</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

+ indicates that the process is abnormal in the disease indicated. Other processes are not affected.
Cystic Fibrosis

• exocrine pancreatic insufficiency in more than 80% of patients. The result is failure of the intraluminal phase of nutrient absorption.

• Due to the absence of the epithelial cystic fibrosis transmembrane conductance regulator (CFTR).
Celiac Disease

• Also known as celiac sprue or glutensensitive enteropathy.

• It is an immune-mediated enteropathy triggered by the ingestion of gluten-containing foods, such as wheat, rye, or barley, in genetically predisposed individuals.

• Celiac disease has an overall worldwide incidence of 0.6% to 1%,
• Pathogenesis:
Celiac disease is triggered by ingestion of gluten, which is the major storage protein of wheat and similar grains. The alcohol-soluble fraction of gluten, *gliadin*, contains most of the disease-producing components.
• **Gluten** is digested by luminal and brush-border enzymes into amino acids and peptides, including a 33-amino acid α-gliadin peptide that is resistant to degradation by gastric, pancreatic, and small intestinal proteases.

• Some gliadin peptides may induce epithelial cells to express **IL-15**, which in turn triggers activation and proliferation of **CD8**+ intraepithelial lymphocytes.

• These lymphocytes express NKG2D, a natural killer cell marker and receptor for MIC-A.

• Enterocytes that have been induced to express surface MIC-A, in response to stress, are then attacked by NKG2D-expressing intraepithelial lymphocytes.

• The resulting epithelial damage may enhance passage of other gliadin peptides into the lamina propria where they are deamidated by tissue transglutaminase.

• These gliadin peptides interact with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells and, in turn, can stimulate **CD4**+ T cells to produce cytokines that contribute to tissue damage.
Figure 17-25 The left panel illustrates the morphologic alterations that may be present celiac disease, including villous atrophy, increased numbers of intraepithelial lymphocytes (IELs), and epithelial proliferation with crypt elongation (compare to Fig. 17-26). The right panel depicts a model for the pathogenesis of celiac disease. Note that both innate (CD8+ intraepithelial T cells, activated by IL-15) and adaptive (CD4+ T cells, and B cells sensitization to gliadin) immune mechanisms are involved in the tissue responses to gliadin.
• While nearly all people eat grain and are exposed to gluten and gliadin, most do not develop celiac disease. Thus, **host factors determine whether disease develops.** Among these, HLA proteins seem to be critical, since almost all people with celiac disease carry the class II HLA-DQ2 or HLA-DQ8 allele.

• However, the HLA locus accounts for less than half of the genetic component of celiac disease. Remaining genetic factors may include polymorphisms of genes involved in immune regulation and epithelial function.
• These genetic variables may also contribute to associations between celiac disease and other immune diseases, including type 1 diabetes, thyroiditis, and Sjögren syndrome, IgA nephropathy, as well as neurologic disorders, such as ataxia, autism, depression, epilepsy, Down syndrome, and Turner syndrome.
• This loss of mucosal and brush-border surface area probably accounts for the malabsorption. In addition, increased rates of epithelial turnover, reflected in increased crypt mitotic activity, may limit the ability of absorptive enterocytes to fully differentiate and express proteins necessary for terminal digestion and transepithelial transport.
Figure 17-26 Celiac disease. A, Advanced cases of celiac disease show complete loss of villi, or total villous atrophy. Note the dense plasma cell infiltrates in the lamina propria. B, Infiltration of the surface epithelium by T lymphocytes, which can be recognized by their densely stained nuclei (labelled T). Compare to elongated, pale-staining epithelial nuclei (labeled E).
• The combination of histology and serology, therefore, is most specific for diagnosis of celiac disease.

• Adherence to a gluten-free diet typically results in resolution of symptoms, decreasing titers of anti-tissue transglutaminase or other celiac disease-associated antibodies, and restoration of normal or near normal mucosal histology within 6 to 24 months.
Clinical Features:

**In adults:**
Celiac disease presents most commonly between the ages of 30 and 60.

**Silent celiac disease:** defined as positive serology and villous atrophy without symptoms.

**Latent celiac disease:** in which positive serology is not accompanied by villous atrophy.

Celiac disease may be associated with chronic diarrhea, bloating, or chronic fatigue, but is often asymptomatic. These cases may present with anemia due to chronic iron and vitamin malabsorption.

In adults, celiac disease is detected twice as frequently in women, perhaps because monthly menstrual bleeding accentuates the effects of impaired absorption.
Pediatric celiac disease: affects males and females equally. may present with malabsorption or atypical symptoms affecting almost any organ. In those with classic symptoms, disease typically begins after introduction of gluten to the diet, between ages of 6 and 24 months, and manifests as irritability, abdominal distention, anorexia, chronic diarrhea, failure to thrive, weight loss, or muscle wasting. Children with nonclassic symptoms tend to present at older ages with complaints of abdominal pain, nausea, vomiting, bloating, or constipation. Common extraintestinal complaints include arthritis or joint pain, aphthous stomatitis, iron deficiency anemia, delayed puberty, and short stature.
• A characteristic itchy, blistering skin lesion, dermatitis herpetiformis, can be present in as many as 10% of patients.
• the only treatment currently available for celiac disease is a gluten-free diet. While adhering to this diet can be challenging, it does result in symptomatic improvement for most patients.

• A gluten-free diet may also reduce the risk of long-term complications including anemia, female infertility, osteoporosis, and cancer.
Noninvasive serologic tests are generally performed prior to biopsy:
The most sensitive tests are the measurement of IgA antibodies against tissue transglutaminase. IgA anti-endomysial antibodies can also be present. IgG anti-tissue transglutaminase antibodies may be detected in patients with IgA deficiency.

The absence of HLA-DQ2 and HLA-DQ8 is useful for its high negative predictive value, but the presence of these alleles is not helpful in confirming the diagnosis.
• Individuals with celiac disease have a higher than normal rate of malignancy: enteropathy-associated T-cell lymphoma Small intestinal adenocarcinoma

when symptoms such as abdominal pain, diarrhea, and weight loss develop despite a strict gluten-free diet, cancer or refractory sprue, in which the response to a gluten-free diet is lost, must be considered.
Environmental Enteropathy

- referred to as tropical enteropathy or **tropical sprue**.
- It is a disorder prevalent in areas and populations with poor sanitation and hygiene, such as those in developing countries.
- is estimated to affect more than 150 million children worldwide and may contribute to a very large number of childhood deaths.
- Affected individuals often suffer from malabsorption and malnutrition and stunted growth.
- The underlying causes of environmental enteropathy are unknown, but defective intestinal barrier function, chronic exposure to fecal pathogens and other microbial contaminants, and repeated bouts of diarrhea within the first 2 or 3 years of life are likely involved.
- Many pathogens are endemic in these communities, but no single infectious agent has been linked to environmental enteropathy.
- The relatively high oral vaccine failure rates in regions where environmental enteropathy is endemic has been proposed to be due to **defective mucosal immune function**.
Autoimmune Enteropathy

- X-linked disorder
- Characterized by severe persistent diarrhea and autoimmune disease that occurs most often in young children.

- **IPEX**: A particularly severe familial form due to a germline mutation in the FOXP3 gene, which is located on the X chromosome. FOXP3 is a transcription factor expressed in CD4+ regulatory T cells. Net result: defects in regulatory T cell function.

I: immune dysregulation
P: polyendocrinopathy
E: enteropathy
X: X-linkage
Lactase (Disaccharidase) Deficiency

• The disaccharidases, including lactase, are located in the apical brush-border membrane of the villus absorptive epithelial cells. Because the defect is biochemical, biopsy histology is generally unremarkable.
Lactase deficiency is of two types:

**Congenital lactase deficiency:**
- autosomal recessive disorder.
- caused by a mutation in the gene encoding lactase.
- The disease is rare and presents as explosive diarrhea with watery, frothy stools and abdominal distention upon milk ingestion.
- Symptoms abate when exposure to milk and milk products is terminated, thus removing the osmotically active but unabsorbable lactose from the lumen —— osmotic diarrhea.
- congenital lactase deficiency was often fatal prior to the availability of soy based infant formula.
• Acquired lactase deficiency:
  - caused by down-regulation of lactase gene expression.
  - Can develop following enteric viral or bacterial infections and may resolve over time.
  - Symptoms of acquired lactase deficiency, including abdominal fullness, diarrhea, and flatulence, due to fermentation of the unabsorbed sugars by colonic bacteria, are triggered by ingestion of lactose-containing dairy products.
Abetalipoproteinemia

• rare autosomal recessive disease
• characterized by an inability of enterocytes to secrete triglyceride-rich lipoproteins. caused by a mutation in the microsomal triglyceride transfer protein (MTP). This results in intracellular lipid accumulation.
• Patients also have a complete absence of all plasma lipoproteins containing apolipoprotein B.
• The malabsorption of abetalipoproteinemia is therefore a failure of intraepithelial processing and transport.
• presents in infancy and the clinical picture is dominated by failure to thrive, diarrhea, and steatorrhea.
Inflammatory Bowel Disease
Ischemic bowel disease
Inflammatory Bowel Disease

- The two disorders that comprise IBD are: ulcerative colitis, Crohn disease
The distinction between ulcerative colitis and Crohn disease is based, in large part, on the distribution of affected sites and the morphologic expression of disease at those sites.

**Ulcerative colitis** is limited to the colon and rectum and extends only into the mucosa and submucosa. **Crohn disease**, which has also been referred to as regional enteritis (because of frequent ileal involvement) may involve any area of the GI tract and is typically transmural.
Figure 17-32 Distribution of lesions in inflammatory bowel disease. The distinction between Crohn disease and ulcerative colitis is primarily based on morphology.
• Epidemiology:
Ulcerative colitis and Crohn disease frequently present in the teens and early 20s, with the former being slightly more common in females. IBD is most common among Caucasians and, in the United States, occurs 3 to 5 times more often among eastern European (Ashkenazi) Jews than the general population.
IBD incidence worldwide is on the rise, and it is becoming more common in regions such as Africa, South America, and Asia where its prevalence was historically low. The hygiene hypothesis suggests that this increasing incidence is related to improved food storage conditions, decreased food contamination, and changes in gut microbiome composition. Apparently this results in inadequate development of regulatory processes that limit mucosal immune responses. This in turn allows some mucosa-associated microbial organisms to trigger persistent and chronic inflammation in susceptible hosts.
• Pathogenesis:
Although precise causes are not yet defined, most investigators believe that IBD results from the combined effects of alterations in host interactions with intestinal microbiota, intestinal epithelial dysfunction, aberrant mucosal immune responses, and altered composition of the gut microbiome.
• Genetics. There is compelling evidence that genetic factors contribute to IBD. Risk of disease is increased when there is an affected family member. Genetic factors are more dominant in Crohn disease.

3 genes strongly associated with Crohn disease: **NOD2**, ATG16L1, and IRGM. These genes involved in recognition and response to intracellular pathogens.
• **Mucosal immune responses:** it is clear that deranged mucosal immune activation and defective immunoregulation contribute to the development of ulcerative colitis and Crohn disease. Immunosuppressive agents remain the mainstay of treatment for these conditions.

• **Epithelial defects:** Defects in intestinal epithelial tight junction barrier function
Figure 17-33 One model of IBD pathogenesis. Aspects of both Crohn disease and ulcerative colitis are shown. See text for details.
Crohn Disease

• Crohn disease may occur in any area of the GI tract, but the most common sites involved at presentation are the terminal ileum, ileocecal valve, and cecum.

• Disease is limited to the small intestine alone in about 40% of cases; the small intestine and colon are both involved in 30% of patients; the remainder have only colonic involvement.
The presence of multiple, separate, sharply delineated areas of disease, resulting in skip lesions, is characteristic of Crohn disease and may help in the differentiation from ulcerative colitis. Sparing of interspersed mucosa, a result of the patchy distribution of Crohn disease, results in a coarsely textured, cobblestone appearance in which diseased tissue is depressed below the level of normal mucosa.

The earliest lesion called aphthous ulcer
• **Fissures** frequently develop between mucosal folds and may extend deeply to become **fistula tracts** or sites of **perforation**.

• The **intestinal wall is thickened** and rubbery as a consequence of transmural edema, inflammation, submucosal fibrosis, and hypertrophy of the muscularis propria, all of which contribute to **stricture formation**.

• In cases with extensive transmural disease, mesenteric fat frequently extends around the serosal surface (**creeping fat**)
Figure 17-35 Microscopic pathology of Crohn disease. A, Haphazard crypt organization results from repeated injury and regeneration. B, Noncaseating granuloma. C, Transmural Crohn disease with submucosal and serosal granulomas (arrows).
Figure 17-34 Gross pathology of Crohn disease. A, Small-intestinal stricture. B, Linear mucosal ulcers, which impart a cobblestone appearance to the mucosa, and thickened intestinal wall. C, Perforation and associated serositis. D, Creeping fat.
• Noncaseating granulomas, a hallmark of Crohn disease, are found in approximately 35% of cases.
Clinical Features:
diarrhea, fever, and abdominal pain.
Periods of active disease are typically interrupted by asymptomatic periods that last for weeks to many months.
Disease re-activation can be associated with a variety of external triggers, including physical or emotional stress, specific dietary items, and cigarette smoking.
nutrient malabsorption (small bowel disease)
Iron-deficiency anemia (colonic disease)
Fistulae develop between loops of bowel and may also involve the urinary bladder, vagina, and abdominal or perianal skin.

Extraintestinal manifestations of Crohn disease include uveitis, migratory polyarthritis, sacroiliitis, ankylosing spondylitis, erythema nodosum, and clubbing of the fingertips, any of which may develop before intestinal disease is recognized. Pericholangitis and primary sclerosing cholangitis occur in Crohn disease, but are more common in those who have ulcerative colitis
• risk of colonic adenocarcinoma is increased in patients with long-standing IBD affecting the colon.

• Anti-TNF antibodies have revolutionized treatment of Crohn disease, and other biologic therapies are becoming available.
Ulcerative Colitis

• the disease in ulcerative colitis is limited to the colon and rectum.

• Common extraintestinal manifestations of ulcerative colitis overlap with those of Crohn disease (but Pericholangitis and primary sclerosing cholangitis are more in UC)
ulcerative colitis always involves the rectum (ulcerative proctitis) and extends proximally in a continuous fashion to involve part or all of the colon.

Disease of the entire colon is termed pancolitis.

The small intestine is normal, although mild mucosal inflammation of the distal ileum, termed backwash ileitis, may be present in severe cases of pancolitis.

broad-based ulcers

Isolated islands of regenerating mucosa often bulge into the lumen to create pseudopolyps, and the tips of these polyps may fuse to create mucosal bridges
• inflammation and inflammatory mediators can damage the muscularis propria and disturb neuromuscular function leading to colonic dilation and **toxic megacolon**, which carries a significant risk of perforation.
Figure 17-36 Gross pathology of ulcerative colitis. A, Total colectomy with pancolitis showing active disease, with red, granular mucosa in the cecum (left) and smooth, atrophic mucosa distally (right). B, Sharp demarcation between active ulcerative colitis (right) and normal mucosa (left). C, Inflammatory polyp. D, Mucosal bridges.
Figure 17-37 Microscopic pathology of ulcerative colitis. A, Crypt abscess. B, Pseudopyloric metaplasia (bottom). C, Disease is limited to the mucosa. Compare to Figure 17-35C.
Clinical Features:

Ulcerative colitis is a relapsing disorder characterized by attacks of bloody diarrhea with stringy, mucoid material, lower abdominal pain, and cramps that are temporarily relieved by defecation. These symptoms may persist for days, weeks, or months before they subside. The initial attack may, in some cases, be severe enough to constitute a medical or surgical emergency. More than half of patients have clinically mild disease, although almost all experience at least one relapse during a 10-year period, and up to 30% require colectomy within the first 3 years after presentation because of uncontrollable symptoms.

Colectomy effectively cures intestinal disease in ulcerative colitis, but extraintestinal manifestations may persist.
The factors that trigger ulcerative colitis are not known, but infectious enteritis precedes disease onset in some cases.

In other cases the first attack is preceded by psychologic stress, which may also be linked to relapse during remission.

The initial onset of symptoms has also been reported to occur shortly after smoking cessation in some patients, and smoking may partially relieve symptoms.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Crohn Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macroscopic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bowel region</td>
<td>Ileum ± colon</td>
<td>Colon only</td>
</tr>
<tr>
<td>Distribution</td>
<td>Skip lesions</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Stricture</td>
<td>Yes</td>
<td>Rare</td>
</tr>
<tr>
<td>Wall appearance</td>
<td>Thick</td>
<td>Thin</td>
</tr>
<tr>
<td><strong>Microscopic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation</td>
<td>Transmural</td>
<td>Limited to mucosa</td>
</tr>
<tr>
<td>Pseudopolyps</td>
<td>Moderate</td>
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</tr>
<tr>
<td>Ulcers</td>
<td>Deep, knife-like</td>
<td>Superficial, broad-based</td>
</tr>
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<td>Lymphoid reaction</td>
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<td>Granulomas</td>
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<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
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<tr>
<td>Perianal fistula</td>
<td>Yes (in colonic disease)</td>
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<tr>
<td>Fat/vitamin malabsorption</td>
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</tr>
<tr>
<td>Malignant potential</td>
<td>With colonic involvement</td>
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<tr>
<td>Recurrence after surgery</td>
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<td>No</td>
</tr>
<tr>
<td>Toxic megacolon</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*All features may not be present in a single case.*
Irritable Bowel Syndrome

• Irritable bowel syndrome (IBS) is characterized by chronic, relapsing abdominal pain, bloating, and changes in bowel habits.
• IBS is currently divided into several subtypes, as defined by successive revisions of the Rome criteria:
  IBS with diarrhea (IBS-D),
  IBS with constipation (IBS-C),
  mixed IBS (IBS-M)
• Pathogenesis:
The pathogenesis of IBS remains poorly defined, although there is clearly interplay between psychologic stressors, diet, perturbation of the gut microbiome, increased enteric sensory responses to gastrointestinal stimuli, and abnormal GI motility. Other data link disturbances in enteric nervous system function to IBS, suggesting a role for defective brain-gut axis signaling.
Several candidate genes to IBS, including: serotonin reuptake transporters, cannabinoid receptors, TNF-related inflammatory mediators.

5-HT3 receptor antagonists are effective in many cases of diarrhea-predominant IBS. Opioids and psychoactive drugs with anti-cholinergic effects are also commonly used to treat diarrhea predominant IBS.
• A separate group of IBS patients, relate onset to a bout of infectious gastroenteritis, suggesting that immune activation or, alternatively, a shift in the gut microbiome.
Clinical Features.
The peak prevalence of IBS is between 20 and 40 years of age, and there is a significant female predominance.

IBS is presently diagnosed using clinical criteria that require the occurrence of abdominal pain or discomfort at least 3 days per month over 3 months with improvement following defecation and a change in stool frequency or form. Other causes, such as enteric infection or inflammatory bowel disease, must be excluded.

IBS is not associated with serious long-term sequelae.
Ischemic Bowel Disease

- the colon is the most common site of gastrointestinal ischemia.
- The severity of vascular compromise, the time frame during which it develops, and the vessels affected are the major variables in ischemic bowel disease.
Two aspects of intestinal vascular anatomy also contribute to the distribution of ischemic damage and are worthy of note:

- Intestinal segments at the end of their respective arterial supplies are particularly susceptible to ischemia. These watershed zones include the splenic flexure, where the superior and inferior mesenteric arterial circulations terminate, and, to a lesser extent, the sigmoid colon and rectum where inferior mesenteric, pudendal, and iliac arterial circulations end.

- Intestinal capillaries run alongside the glands, from crypt to surface, before making a hairpin turn to empty into the post-capillary venules. This arrangement makes the surface epithelium particularly vulnerable to ischemic injury, relative to the crypts. Organization of the blood supply in this patterns has advantages, as it protects the epithelial stem cells, which are located within the crypts and are necessary for recovery from epithelial injury.
• **mucosal and mural infarctions** can follow acute or chronic hypoperfusion *(non-occlusive)*, causes: cardiac failure, shock, dehydration, or use of vasoconstrictive drugs.

• **transmural infarction** is typically caused by acute vascular obstruction *(occlusive)*, causes: severe atherosclerosis, aortic aneurysm, hypercoagulable states, oral contraceptive use, and embolization of cardiac vegetations or aortic atheromas.
• **Mesenteric venous thrombosis**, which can also lead to ischemic disease, is uncommon but can result from inherited or acquired hypercoagulable states, invasive neoplasms, cirrhosis, trauma, or abdominal masses that compress the portal drainage.
• Intestinal responses to ischemia occur in two phases.
  - The initial **hypoxic injury** occurs at the onset of vascular compromise. While some damage occurs during this phase, the epithelial cells lining the intestine are relatively resistant to transient hypoxia.
  - The second phase, **reperfusion injury**, is initiated by restoration of the blood supply and it is at this time that the greatest damage occurs. In severe cases this may trigger multiorgan failure. Leakage of gut lumen bacterial products into the systemic circulation, free radical production, neutrophil infiltration, and release of additional inflammatory mediators.
• Clinical Features:
Ischemic disease of the colon is most common in patients older than 70 years of age, and occurs slightly more often in women.

**Acute colonic ischemia** typically presents with sudden onset of cramping, left lower abdominal pain, a desire to defecate, and passage of blood or bloody diarrhea.----- resemble acute abdomin.

**Chronic ischemia**: episodes of bloody diarrhea interspersed with periods of healing------ resemble IBD

Necrotizing enterocolitis (NEC): transmural necrosis--neonates
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