

- ***S. typhi*** can cause systemic disease (typhoid fever).
- **Pseudomembranous colitis** is often triggered by antibiotic therapy that allows colonization by ***Clostridium difficile***. The organism releases toxins that disrupt epithelial function. The associated inflammatory response includes characteristic volcano-like eruptions of neutrophils from colonic crypts that spread to form mucopurulent pseudomembranes.
- **Norovirus** is a very common cause of self limited diarrhea both in adults and children. It spreads from person to person in sporadic cases and by water in epidemic cases.
- **Rotavirus** is the most common cause of severe childhood diarrhea and diarrheal mortality worldwide. The diarrhea is caused by loss of mature enterocytes, resulting in malabsorption as well as secretion.
- **Parasitic and protozoal infections** affect more than one half of the world's population on a chronic or recurrent basis. Each parasite has a distinctive life cycle and tissue reaction. Most are associated with tissue and systemic eosinophilia.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is characterized by chronic, relapsing abdominal pain, bloating, and changes in bowel habits. Despite very real symptoms, the gross and microscopic evaluation is normal in most IBS patients. Thus, the diagnosis depends on clinical symptoms and functional testing. It should be recognized that IBS is a syndrome, and that multiple illnesses are represented under this global descriptor. IBS is currently divided into several subtypes, as defined by successive revisions of the Rome criteria.

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. For example, patients with *constipation-predominant* or *diarrhea-predominant* IBS tend to have decreased or increased colonic contractions and transit rates, respectively. Excess bile acid synthesis or bile acid malabsorption has been identified as one cause of diarrhea-predominant IBS, likely due to the effects of bile acids on intestinal motility.

Other data link disturbances in enteric nervous system function to IBS, suggesting a role for defective brain-gut axis signaling. Consistent with this, deep sequencing and genome wide association studies have linked several candidate genes to IBS, including serotonin reuptake transporters, cannabinoid receptors, and TNF-related inflammatory mediators. Further, 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 may

trigger some cases. While unproven, this could explain the efficacy of fecal transplantation in some IBS cases.

There may be some overlap in mechanisms underlying constipation-predominant and diarrhea-predominant IBS. For example, single nucleotide polymorphisms in immune mediators have been detected in both.

Clinical Features. The peak prevalence of IBS is between 20 and 40 years of age, and there is a significant female predominance. Variability in diagnostic criteria makes it difficult to establish the incidence, but most authors report prevalence in developed countries of between 5% and 10%. 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, but affected patients may undergo unnecessary abdominal surgery due to chronic pain and their ability to function socially may be compromised. The prognosis of IBS is most closely related to symptom duration, with longer duration correlating with reduced likelihood of improvement.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic condition resulting from inappropriate mucosal immune activation. The two disorders that comprise IBD are *ulcerative colitis* and *Crohn disease*. Descriptions of ulcerative colitis and Crohn disease date back to antiquity and at least the sixteenth century, respectively, but it took modern microbiologic techniques to exclude conventional infectious etiologies for these diseases. As will be discussed later, however, the luminal microbiota likely play a role in the pathogenesis of IBD.

The distinction between ulcerative colitis and Crohn disease is based, in large part, on the distribution of affected sites (Fig. 17-32) and the morphologic expression of disease (Table 17-9) at those sites. **Ulcerative colitis is limited to the colon and rectum and extends only into the mucosa and submucosa. In contrast, 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.**

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. This is at least partly due to genetic factors, as discussed later. The geographic distribution of IBD is highly variable, but it is most common in North America, northern Europe, and Australia. However, 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