

This is due to secondary *KIT* or *PDGFRA* mutations. Tumors with secondary mutations may respond to other tyrosine kinase inhibitors as well as experimental therapies that target other pathways.

KEY CONCEPTS

Neoplastic and Non neoplastic proliferations of the stomach

- **Ménétrier disease** is a rare disorder caused by excessive secretion of transforming growth factor α (TGF- α) and characterized by diffuse foveolar hyperplasia and protein-losing enteropathy.
- **Zollinger-Ellison syndrome** is caused by gastrin-secreting tumors that cause parietal cell hyperplasia and acid hypersecretion; 60% to 90% of gastrinomas are malignant.
- The majority of gastric polyps are **inflammatory or hyperplastic polyps**, reactive lesions that are associated with chronic gastritis.
- **Fundic gland polyps** occur sporadically, most often as a consequence of proton pump inhibitor therapy, and in familial adenomatous polyposis (FAP) patients.
- **Gastric adenomas** develop in a background of chronic gastritis and are particularly associated with intestinal metaplasia and mucosal (glandular) atrophy. Adenocarcinoma is frequent in gastric adenomas, which

therefore require more aggressive therapy than adenomas of the colon.

- **Gastric adenocarcinoma** incidence varies markedly with geography. Individual tumors are classified according to location, gross, and histologic morphology. Gastric tumors with an **intestinal histology tend to form bulky tumors** and may be ulcerated, while those composed of **signet-ring cells typically display a diffuse infiltrative growth pattern** that may thicken the gastric wall without forming a discrete mass. Gastric adenocarcinomas are linked to *H. pylori* induced chronic gastritis.
- **Primary gastric lymphomas** are most often derived from mucosa-associated lymphoid tissue (MALT), whose development is induced by chronic gastritis that is most often induced by *H. pylori*.
- **Carcinoid tumors** (well-differentiated neuroendocrine tumors) arise from diffuse components of the endocrine system and are most common in the GI tract, particularly the small intestine. Prognosis is based on location; tumors of the small intestine tend to be most aggressive, while those of the appendix are typically benign.
- **Gastrointestinal stromal tumor (GIST)** is the most common mesenchymal tumor of the abdomen, occurs most often in the stomach, and is related to benign pacemaker cells, or interstitial cells of Cajal. Tumors generally have activating mutations in either *KIT* or *PDGFRA* tyrosine kinases and respond to specific kinase inhibitors.

SMALL INTESTINE AND COLON

The small intestine and colon make up the majority of the GI tract and are the sites of a broad array of diseases. Some of these relate to nutrient and water transport. Perturbation of these processes can cause malabsorption and diarrhea. The intestines are also the principal site where the immune system interfaces with a diverse array of antigens present in food and gut microbes. Indeed, intestinal bacteria outnumber eukaryotic cells in our bodies by tenfold. Thus, it is not surprising that the small intestine and colon are frequently affected by infectious and inflammatory disorders. Finally, the colon is the most common site of GI neoplasia in Western populations.

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. Collectively, *hernias*, *intestinal adhesions*, *intussusception*, and *volvulus* account for 80% of mechanical obstructions (Fig. 17-22), while tumors, infarction, and other causes of strictures, for example, Crohn disease, account for an additional 10% to 15%. **The clinical manifestations of intestinal obstruction include abdominal pain and distention, vomiting, and constipation.** Surgical intervention is usually required in cases where the obstruction has a mechanical basis or is associated with bowel infarction.

Hernias

Any weakness or defect in the abdominal wall may permit protrusion of a serosa-lined pouch of peritoneum called a hernia sac. Acquired hernias typically occur anteriorly, via the inguinal and femoral canals, umbilicus, or at sites of surgical scars, and are common, occurring in up to 5% of the population. *Hernias are the most frequent cause of intestinal obstruction worldwide* and the third most common cause of obstruction in the U.S. Obstruction usually occurs because of visceral protrusion (external herniation) and is most frequently-associated with inguinal hernias, which tend to have narrow orifices and large sacs. Small bowel loops are typically involved, but omentum or large bowel may also protrude, and any of these may become entrapped. Pressure at the neck of the pouch may impair venous drainage of the entrapped viscus. The resultant stasis and edema increase the bulk of the herniated loop, leading to permanent entrapment (incarceration) and, over time, arterial and venous compromise (strangulation), and infarction (Fig. 17-23A).

Adhesions

Surgical procedures, infection, or other causes of peritoneal inflammation, such as endometriosis, may result in development of adhesions between bowel segments, the abdominal wall, or operative sites. These fibrous bridges can