predilection for adenocarcinoma to affect the distal esophagus in white males and squamous cell to affect the more proximal esophagus in black males with the added risk factors of smoking, alcohol consumption, caustic injury, and human papilloma virus infection (Chap. 109).

The typical presentation of esophageal cancer is of progressive solid food dysphagia and weight loss. Associated symptoms may include odynophagia, iron deficiency, and, with midesophageal tumors, hoarseness from left recurrent laryngeal nerve injury. Generally, these are indications of locally invasive or even metastatic disease manifest by tracheoesophageal fistulas and vocal cord paralysis. Even when detected as a small lesion, esophageal cancer has poor survival because of the abundant esophageal lymphatics leading to regional lymph node metastases.

Benign esophageal tumors are uncommon and usually discovered incidentally. In decreasing frequency of occurrence, cell types include leiomyoma, fibrovascular polyps, squamous papilloma, granular cell tumors, lipomas, neurofibromas, and inflammatory fibroid polyps. These generally become symptomatic only when they are associated with dysphagia and merit removal only under the same circumstances.

CONGENITAL ANOMALIES

The most common congenital esophageal anomaly is esophageal atresia, occurring in about 1 in 5000 live births. Atresia can occur in several permutations, the common denominator being developmental failure of fusion between the proximal and distal esophagus associated with a tracheoesophageal fistula, most commonly with the distal segment excluded. Alternatively, there can be an H-type configuration in which esophageal fusion has occurred, but with a tracheoesophageal fistula. Esophageal atresia is usually recognized and corrected surgically within the first few days of life. Later life complications include dysphagia from anastomotic strictures or absent peristalsis and reflux, which can be severe. Less common developmental anomalies include congenital esophageal stenosis, webs, and duplications.

Dysphagia can also result from congenital abnormalities that cause extrinsic compression of the esophagus. In dysphagia lusoria, the esophagus is compressed by an aberrant right subclavian artery arising from the descending aorta and passing behind the esophagus. Alternatively vascular rings may surround and constrict the esophagus.

Heterotopic gastric mucosa, also known as an esophageal inlet patch, is a focus of gastric type epithelium in the proximal cervical esophagus; the estimated prevalence is 4.5%. The inlet patch is thought to result from incomplete replacement of embryonic columnar epithelium with squamous epithelium. The majority of inlet patches are asymptomatic, but acid production can occur as most contain fundic type gastric epithelium with parietal cells.

ESOPHAGEAL MOTILITY DISORDERS

Esophageal motility disorders are diseases attributable to esophageal neuromuscular dysfunction commonly associated with dysphagia, chest pain, or heartburn. The major entities are achalasia, diffuse esophageal spasm (DES), and GERD. Motility disorders can also be secondary to broader disease processes as is the case with pseudoachalasia, Chagas' disease, and scleroderma. Not included in this discussion are diseases affecting the pharynx and proximal esophagus, the impairment of which is almost always part of a more global neuromuscular disease process.

ACHALASIA

Achalasia is a rare disease caused by loss of ganglion cells within the esophageal myenteric plexus with a population incidence of about 1:100,000 and usually presenting between age 25 and 60. With longstanding disease, aganglionosis is noted. The disease involves both excitatory (cholinergic) and inhibitory (nitric oxide) ganglionic neurons. Functionally, inhibitory neurons mediate deglutitive lower esophageal sphincter (LES) relaxation and the sequential propagation of peristalsis. Their absence leads to impaired deglutitive LES relaxation and absent peristalsis. Increasing evidence suggests that the ultimate cause of ganglion cell degeneration in achalasia is an autoimmune process attributable to a latent infection with human herpes simplex virus 1 combined with genetic susceptibility.

Long-standing achalasia is characterized by progressive dilatation and sigmoid deformity of the esophagus with hypertrophy of the LES. Clinical manifestations may include dysphagia, regurgitation, chest pain, and weight loss. Most patients report solid and liquid food dysphagia. Regurgitation occurs when food, fluid, and secretions are retained in the dilated esophagus. Patients with advanced achalasia are at risk for bronchitis, pneumonia, or lung abscess from chronic regurgitation and aspiration. Chest pain is frequent early in the course of achalasia, thought to result from esophageal spasm. Patients describe a squeezing, pressure-like retrosternal pain, sometimes radiating to the neck, arms, jaw, and back. Paradoxically, some patients complain of heartburn that may be a chest pain equivalent. Treatment of achalasia is less effective in relieving chest pain than it is in relieving dysphagia or regurgitation.

The differential diagnosis of achalasia includes DES, Chagas' disease, and pseudoachalasia. Chagas' disease is endemic in areas of central Brazil, Venezuela, and northern Argentina and spread by the bite of the reduviid (kissing) bug that transmits the protozoan, *Trypanosoma cruzi*. The chronic phase of the disease develops years after infection and results from destruction of autonomic ganglion cells throughout the body, including the heart, gut, urinary tract, and respiratory tract. Tumor infiltration, most commonly seen with carcinoma in the gastric fundus or distal esophagus, can mimic idiopathic achalasia. The resultant "pseudoachalasia" accounts for up to 5% of suspected cases and is more likely with advanced age, abrupt onset of symptoms (<1 year), and weight loss. Hence, endoscopy is a necessary part of the evaluation of achalasia. When the clinical suspicion for pseudoachalasia is high and endoscopy nondiagnostic, computed tomography (CT) scanning or EUS may be of value. Rarely, pseudoachalasia can result from a paraneoplastic syndrome with circulating antineuronal antibodies.

Achalasia is diagnosed by barium swallow x-ray and/or esophageal manometry; endoscopy has a relatively minor role other than to exclude pseudoachalasia. The barium swallow x-ray appearance is of a dilated esophagus with poor emptying, an air-fluid level, and tapering at the LES giving it a beak-like appearance (Fig. 347-5). Occasionally, an epiphrenic diverticulum is observed. In long-standing achalasia, the esophagus may assume a sigmoid configuration. The diagnostic criteria for achalasia with esophageal manometry are impaired LES relaxation and absent peristalsis. High-resolution manometry has somewhat advanced this diagnosis; three subtypes of achalasia are differentiated based on the pattern of pressurization in the nonperistaltic esophagus (Fig. 347-6). Because manometry identifies early disease before esophageal dilatation and food retention, it is the most sensitive diagnostic test.

There is no known way of preventing or reversing achalasia. Therapy is directed at reducing LES pressure so that gravity and esophageal pressurization promote esophageal emptying. Peristalsis rarely, if ever, recovers. However, in many instances, remnants of peristalsis masked by esophageal pressurization and dilatation prior to therapy are demonstrable following effective treatment. LES pressure can be reduced by pharmacologic therapy, pneumatic balloon dilatation, or surgical myotomy. No large, controlled trials of the therapeutic alternatives exist, and the optimal approach is debated. Pharmacologic therapies are relatively ineffective but are often used as temporizing therapies. Nitrates or calcium channel blockers are administered before eating, advising caution because of their effects on blood pressure. Botulinum toxin, injected into the LES under endoscopic guidance, inhibits acetylcholine release from nerve endings and improves dysphagia in about 66% of cases for at least 6 months. Sildenafil and alternative phosphodiesterase inhibitors effectively decrease LES pressure, but practicalities limit their clinical use in achalasia.