- **Familial adenomatous polyposis** (FAP) and **hereditary non-polyposis colorectal cancer** (HNPCC) are the most common forms of familial colon cancer.
- **FAP** is caused by *APC* mutations. Patients typically have more than 100 adenomas and develop colon cancer before 30 years of age.
- **HNPCC** is caused by mutations in DNA mismatch repair enzymes. HNPCC patients have far fewer polyps and develop cancer at older ages than FAP patients but younger ages than those with sporadic colon cancer.
- FAP and HNPCC typify **distinct pathways of neoplastic transformation and progression** that also contribute to the majority of **sporadic colon cancers**.
- Nearly all colonic cancers are **adenocarcinomas**. The two most important prognostic factors are **depth of invasion** and the presence or absence of **lymph node metastases**.

Tumors of the Anal Canal

The anal canal can be divided into thirds. The upper zone is lined by columnar rectal epithelium; the middle third by transitional epithelium; and the lower third by stratified squamous epithelium. 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 (Fig. 17-54*A*). An additional differentiation pattern, termed basaloid, is present in tumors populated by immature cells derived from the basal layer of transitional epithelium (Fig. 17-54*B*). When the entire tumor displays a basaloid pattern, the archaic term cloacogenic carcinoma is still often applied. Alternatively, basaloid differentiation may be mixed with squamous or mucinous differentiation. All are considered variants of anal canal carcinoma. Pure squamous cell carcinoma of the anal canal is frequently associated with HPV infection, which also causes precursor lesions such as condyloma acuminatum (Fig. 17-54*C*).

Hemorrhoids

Hemorrhoids affect about 5% of the general population and develop secondary to persistently elevated venous pressure within the hemorrhoidal plexus. The most frequent predisposing influences are straining at defecation, because of constipation, and the venous stasis of pregnancy. Hemorrhoids may also develop in association with portal hypertension. The pathogenesis of hemorrhoids (anal varices) in portal hypertension is similar to that of esophageal varices, although anal varices are both more common and much less serious. Variceal dilations of the anal and perianal venous plexuses form collaterals that connect the portal and caval venous systems, thereby relieving the venous hypertension.

MORPHOLOGY

Collateral vessels within the inferior hemorrhoidal plexus are located below the anorectal line and are termed **external hemorrhoids**, while those that result from dilation of the superior hemorrhoidal plexus within the distal rectum are referred to as **internal hemorrhoids.** Histologically, hemorrhoids consist of thin-walled, dilated, submucosal vessels that protrude beneath the anal or rectal mucosa. In their exposed position, they are subject to trauma and tend to become inflamed, thrombosed, and, in the course of time, recanalized. Superficial ulceration may occur.

Hemorrhoids often present with pain and rectal bleeding, particularly bright red blood seen on toilet tissue. Except for pregnant women, hemorrhoids are rarely encountered in persons younger than age 30. Hemorrhoidal bleeding is not generally a medical emergency and can be treated by sclerotherapy, rubber band ligation, or infrared coagulation. Extensive or severe internal or external hemorrhoids may be removed surgically by hemorrhoidectomy.

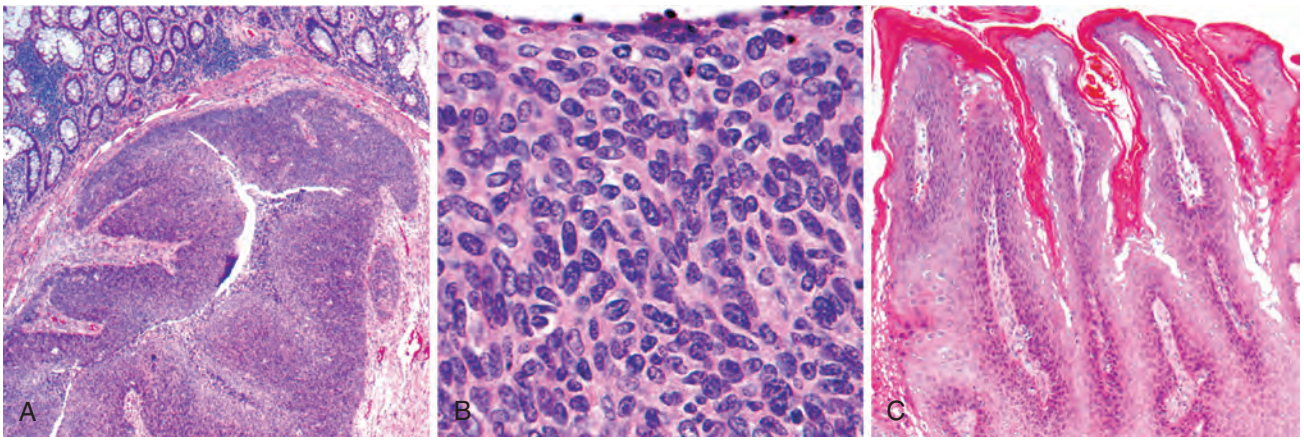

Figure 17-54 Anal tumors. **A,** This anal transition zone carcinoma demonstrates a multilayered organization reminiscent of benign squamous mucosa. The adjacent rectal mucosa is intact. **B,** This basaloid anal transition zone tumor is composed of hyperchromatic cells that resemble the basal layer of normal squamous mucosa. **C,** Condyloma acuminatum with verrucous architecture.