of lesions, although the percentage of each component is variable (Fig. 10-29*A*). Sheets of small blue cells with few distinctive features characterize the blastemal component. Epithelial differentiation is usually in the form of abortive tubules or glomeruli. Stromal cells are usually fibrocytic or myxoid in nature, although skeletal muscle differentiation is not uncommon. Rarely, other heterologous elements are identified, including squamous or mucinous epithelium, smooth muscle, adipose tissue, cartilage, and osteoid and neurogenic tissue. Approximately 5% of tumors reveal **anaplasia**, defined as the presence of cells with large, hyperchromatic, pleomorphic nuclei and abnormal mitoses (Fig. 10-29*B*). The presence of anaplasia correlates with the presence of *TP53* mutations and the emergence of resistance to chemotherapy. Recall that p53 elicits pro-apoptotic signals in response to DNA damage (Chapter 7). The loss of p53 function might explain the relative unresponsiveness of anaplastic cells to cytotoxic chemotherapy.

Clinical Features. Most children with Wilms tumors present with a large abdominal mass that may be unilateral or, when very large, may extend across the midline and down into the pelvis. Hematuria, pain in the abdomen after some traumatic incident, intestinal obstruction, and appearance of hypertension are other patterns of presentation. In a considerable number of these patients, pulmonary metastases are present at the time of primary diagnosis.

As stated, most patients with Wilms tumor can expect to be cured of their malignancy. Anaplastic histology remains a critical determinant of adverse prognosis. Even anaplasia restricted to the kidney (i.e., without extra-renal spread) confers an increased risk of recurrence and death, emphasizing the need for accurate identification of this histologic feature. Molecular parameters that correlate with adverse prognosis include loss of genetic material on chromosomes 11q and 16q, and gain of chromosome 1q in the tumor cells. Along with the increased survival of individuals with Wilms tumor have come reports of an increased risk of developing second primary tumors, including bone and soft-tissue sarcomas, leukemia and lymphomas, and breast cancers. While some of these neoplasms result from the presence of a germline mutation in a cancer predisposition gene, others are a consequence of therapy, most commonly radiation administered to the cancer field. This tragic, albeit uncommon, outcome has mandated that radiation therapy be used judiciously in the treatment of this and other childhood cancers.

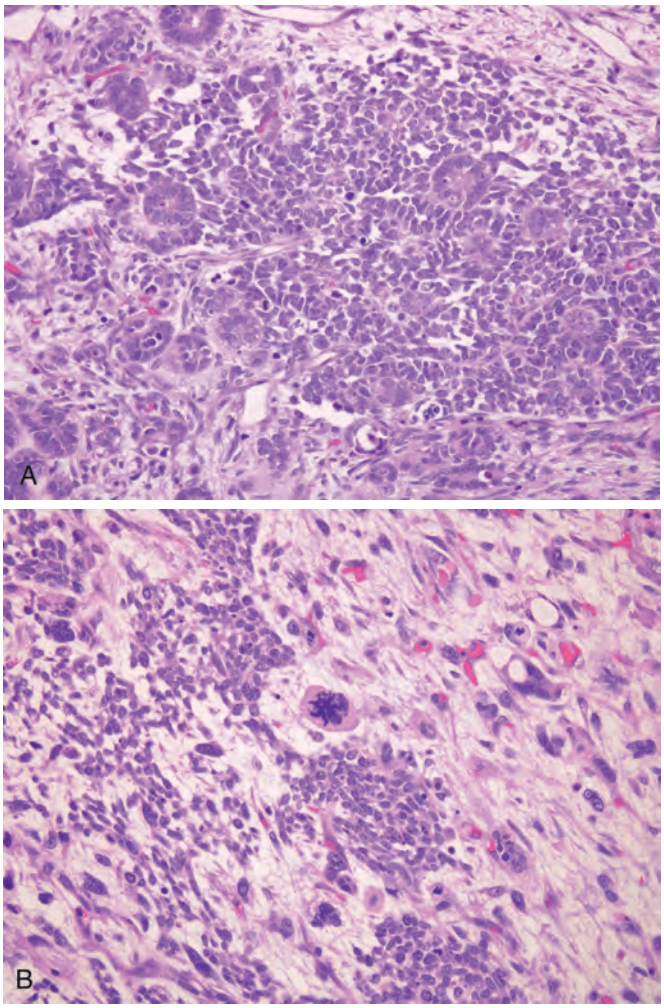

Figure 10-29 **A,** Wilms tumor with tightly packed blue cells consistent with the blastemal component and interspersed primitive tubules, representing the epithelial component. Although multiple mitotic figures are seen, none are atypical in this field. **B,** Focal anaplasia was present in this Wilms tumor in other areas, characterized by cells with hyperchromatic, pleomorphic nuclei, and abnormal mitoses.

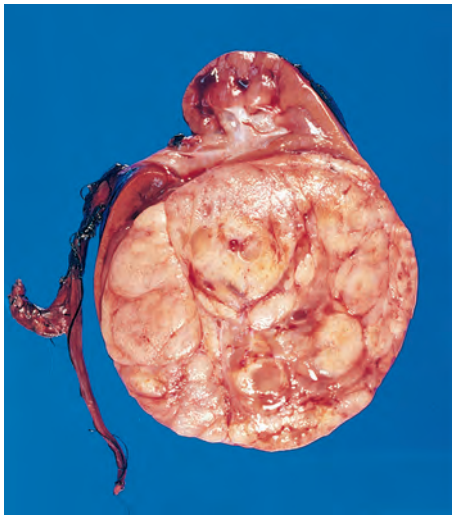

Figure 10-28 Wilms tumor in the lower pole of the kidney with the characteristic tan-to-gray color and well-circumscribed margins.

SUGGESTED READINGS

Congenital Anomalies

Bellini C, Hennekam RC: Non-immune hydrops fetalis: a short review of etiology and pathophysiology. *Am J Med Genet A* 158A:597-605, 2012. [*A well written review on non-immune hydrops, which accounts for the overhwelming majority of fetal hydrops in the Western world.*]

de Jong EP, Walther FJ, Kroes AC, et al: Parvovirus B19 infection in pregnancy: new insights and management. *Prenat Diagn* 31:419-25, 2011. [*A comprehesive review that discusses the epidemiology, natural history, and complications of intrauterine Parvovirus B19 infection, along with diagnostic and treatment guidelines.*]

Kochanek KD, Kirmeyer SE, Martin JA, et al: Annual summary of vital statistics: 2009. *Pediatrics* 129:338-48, 2012. [*A periodically updated*

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