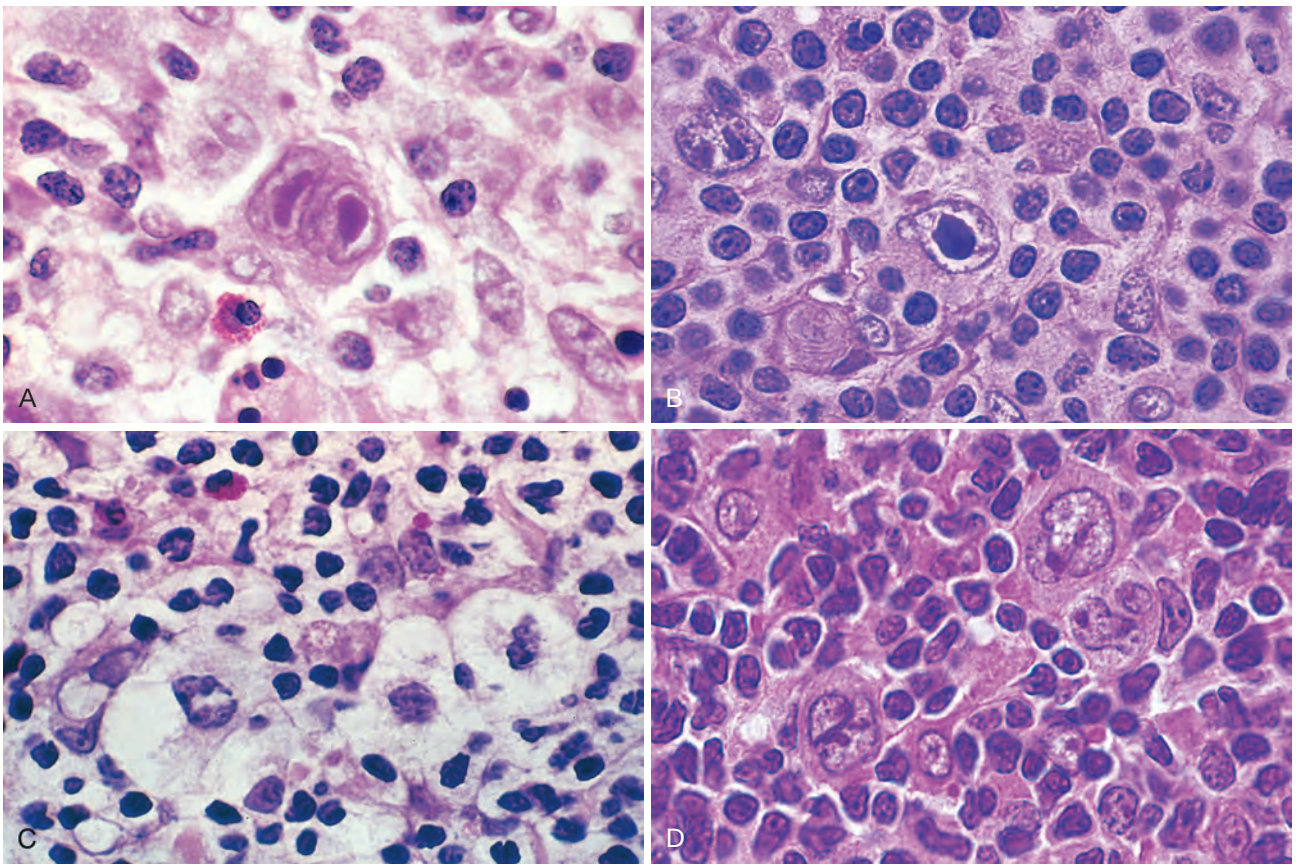

Figure 13-24 Reed-Sternberg cells and variants. **A,** Diagnostic Reed-Sternberg cell, with two nuclear lobes, large inclusion-like nucleoli, and abundant cytoplasm, surrounded by lymphocytes, macrophages, and an eosinophil. **B,** Reed-Sternberg cell, mononuclear variant. **C,** Reed-Sternberg cell, lacunar variant. This variant has a folded or multilobated nucleus and lies within a open space, which is an artifact created by disruption of the cytoplasm during tissue sectioning. **D,** Reed-Sternberg cell, lymphohistiocytic variant. Several such variants with multiply infolded nuclear membranes, small nucleoli, fine chromatin, and abundant pale cytoplasm are present. (**A,** Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex.)

13-24*C*). In classical forms of HL, Reed-Sternberg cells undergo a peculiar form of cell death in which the cells shrink and become pyknotic, a process described as "mummification." **Lymphohistiocytic variants** (L&H cells) with polypoid nuclei, inconspicuous nucleoli, and moderately abundant cytoplasm are characteristic of the lymphocyte predominance subtype (Fig. 13-24*D*).

HL must be distinguished from other conditions in which cells resembling Reed-Sternberg cells can be seen, such as infectious mononucleosis, solid tissue cancers, and large-cell NHLs. The diagnosis of HL depends on the identification of Reed-Sternberg cells in a background of non-neoplastic inflammatory cells. The Reed-Sternberg cells of HL also have a characteristic immunohistochemical profile.

With this as background, we turn to the subclasses of HL, pointing out some of the salient morphologic and immunophenotypic features of each (Table 13-8). The clinical manifestations common to all are presented later.

Nodular Sclerosis Type. This is the most common form of HL, constituting 65% to 70% of cases. It is characterized by the presence of lacunar variant Reed-Sternberg cells and the **deposition of collagen in bands that divide involved lymph nodes into circumscribed nodules** (Fig. 13-25). The fibrosis may be scant or abundant. The Reed-Sternberg cells are found in a polymorphous background of T cells, eosinophils, plasma cells, and macrophages. Diagnostic Reed-Sternberg cells are often uncommon. The Reed-Sternberg cells in this and other "classical" HL subtypes have a characteristic immunophenotype; they are positive for PAX5 (a B-cell transcription factor), CD15, and CD30, and negative for other B-cell markers, T-cell markers, and CD45 (leukocyte common antigen). As in other forms of HL, involvement of the spleen, liver, bone marrow, and other organs and tissues can appear in due course in the form of irregular tumor nodules resembling those seen in lymph nodes. This subtype is uncommonly associated with EBV.

The nodular sclerosis type occurs with equal frequency in males and females. It has a propensity to involve the lower cervical, supraclavicular, and mediastinal lymph nodes of adolescents or young adults. The prognosis is excellent.

Mixed-Cellularity Type. This form of HL constitutes about 20% to 25% of cases. Involved lymph nodes are diffusely effaced by a heterogeneous cellular infiltrate, which includes T cells, eosinophils, plasma cells, and benign macrophages admixed with Reed-Sternberg cells (Fig. 13-26). **Diagnostic Reed-Sternberg cells and mononuclear variants are usually plentiful. The Reed-Sternberg cells are infected with EBV in about 70% of cases.** The immunophenotype is identical to that observed in the nodular sclerosis type.

Mixed-cellularity HL is more common in males. Compared with the lymphocyte predominance and nodular sclerosis subtypes, it is more likely to be associated with older age, systemic symptoms such as night sweats and weight loss, and