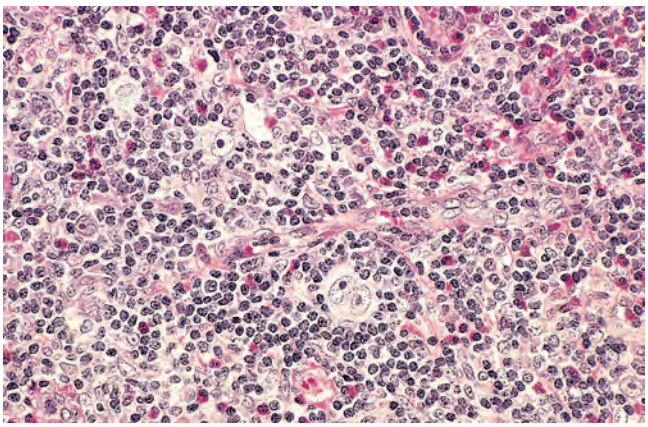

Figure 13-27 Hodgkin lymphoma, lymphocyte predominance type. Numerous mature-looking lymphocytes surround scattered, large, pale-staining lymphohistiocytic variants ("popcorn" cells). (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex.)

the L&H variants show evidence of ongoing somatic hypermutation, a modification that occurs only in germinal center B cells. In 3% to 5% of cases, this type transforms into a tumor resembling diffuse large B-cell lymphoma. EBV is not associated with this subtype.

A majority of patients are males, usually younger than 35 years of age, who typically present with cervical or axillary lymphadenopathy. Mediastinal and bone marrow involvement is rare. In some series, this form of HL is more likely to recur than the classical subtypes, but the prognosis is excellent.

Clinical Features. HL most commonly present as painless lymphadenopathy. Patients with the nodular sclerosis or lymphocyte predominance types tend to have stage I-II disease and are usually free of systemic manifestations. Patients with disseminated disease (stages III-IV) or the mixed-cellularity or lymphocyte depletion subtypes are more likely to have constitutional symptoms, such as fever, night sweats, and weight loss. Cutaneous immune unresponsiveness (also called anergy) resulting from depressed cell-mediated immunity is seen in most cases. The mix of factors released from Reed-Sternberg cells (Fig. 13-28) suppress T_H1 immune responses and may contribute to immune dysregulation.

The spread of HL is remarkably stereotyped: nodal disease first, then splenic disease, hepatic disease, and finally involvement of the marrow and other tissues. Staging involves physical examination, radiologic imaging of the abdomen, pelvis, and chest, and biopsy of the bone marrow (Table 13-9). With current treatment protocols, tumor stage rather than histologic type is the most important prognostic variable. The cure rate of patients with stages I and IIA is close to 90%. Even with advanced disease (stages IVA and IVB), disease-free survival at 5 years is 60% to 70%.

Low-stage localized HL can be cured with involved field radiotherapy, and indeed cure of such patients was one of the early success stories in oncology. However, it was subsequently recognized that long-term survivors treated with radiotherapy had a much higher incidence of certain malignancies, including lung cancer, melanoma, and breast cancer. Patients treated with early chemotherapy regimens containing alkylating agents also had a high

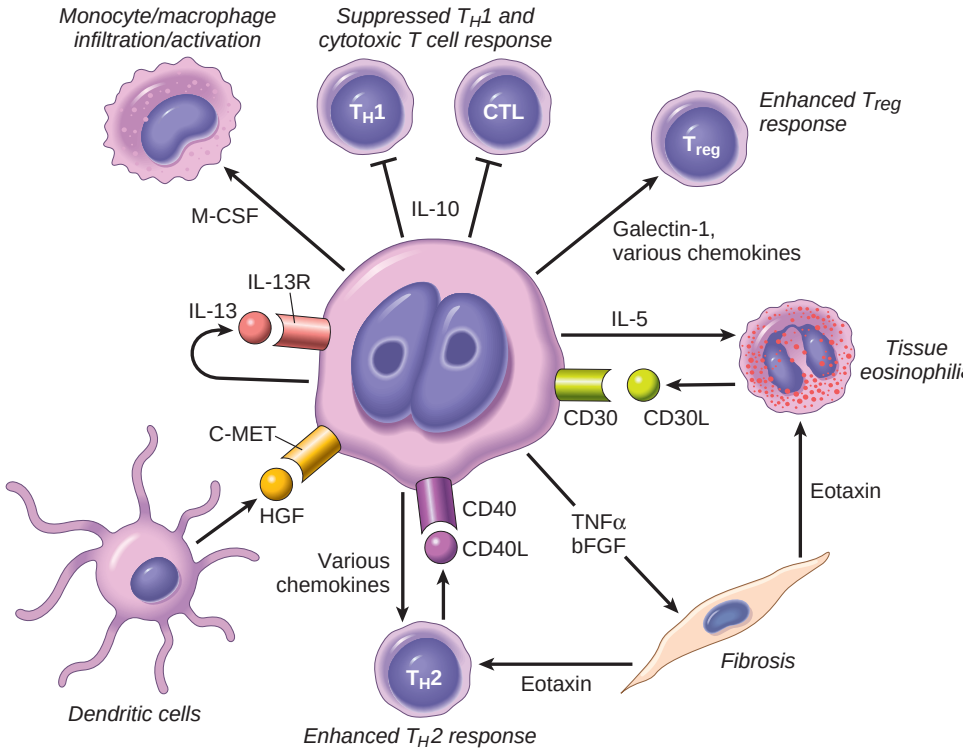

Figure 13-28 Proposed signals mediating "cross-talk" between Reed-Sternberg cells and surrounding normal cells in classical forms of Hodgkin lymphoma. *CD30L,* CD30 ligand; *bFGF,* basic fibroblast growth factor; *M-CSF,* monocyte colony-stimulating factor; *HGF,* hepatocyte growth factor (binds to the c-MET receptor); *TGFβ,* transforming growth factor β; *TNFα,* tumor necrosis factor α; *CTL,* CD8+ cytotoxic T cell; *T_H1* and *T_H2,* CD4+ T helper cell subsets; *Treg,* regulatory T cell.