be ready to begin therapy. In ALL, prognosis is dependent on the genetic characteristics of the tumor, the patient's age, the white cell count, and the patient's overall clinical status and major organ function.

In CLL, the patient evaluation should include a complete blood count, chemistry tests to measure major organ function, serum protein electrophoresis, and a bone marrow biopsy. However, some physicians believe that the diagnosis would not always require a bone marrow biopsy. Patients often have imaging studies of the chest and abdomen looking for pathologic lymphadenopathy. Patients with typical B-cell CLL can be subdivided into three major prognostic groups. Those patients with only blood and bone marrow involvement by leukemia but no lymphadenopathy, organomegaly, or signs of bone marrow failure have the best prognosis. Those with lymphadenopathy and organomegaly have an intermediate prognosis, and patients with bone marrow failure, defined as hemoglobin <100 g/L (10 g/dL) or platelet count <100,000/μL, have the worst prognosis. The pathogenesis of the anemia or thrombocytopenia is important to discern. The prognosis is adversely affected when either or both of these abnormalities are due to progressive marrow infiltration and loss of productive marrow. However, either or both may be due to autoimmune phenomena or to hypersplenism that can develop during the course of the disease. These destructive mechanisms are usually completely reversible (glucocorticoids for autoimmune disease; splenectomy for hypersplenism) and do not influence disease prognosis.

Two popular staging systems have been developed to reflect these prognostic groupings (Table 134-7). Patients with typical B-cell CLL can have their course complicated by immunologic abnormalities, including autoimmune hemolytic anemia, autoimmune thrombocytopenia, and hypogammaglobulinemia. Patients with hypogammaglobulinemia benefit from regular (monthly) γ globulin administration. Because of expense, γ globulin is often withheld until the patient experiences a significant infection. These abnormalities do not have a clear prognostic significance and should not be used to assign a higher stage.

Two other features may be used to assess prognosis in B-cell CLL, but neither has yet been incorporated into a staging classification. At least two subsets of CLL have been identified based on the cytoplasmic expression of ZAP-70; expression of this protein, which is usually expressed in T cells, identifies a subgroup with poorer prognosis. A less powerful subsetting tool is CD38 expression. CD38+ tumors tend to have a poorer prognosis than CD38– tumors. A less easily measured feature, the presence of immunoglobulin variable region gene mutations, is also able to separate prognostic groups; patients with mutated immunoglobulin variable region genes respond better to treatment and have better survival than those with unmutated immunoglobulin variable region genes.

TABLE 134-7 STAGING OF TYPICAL B-CELL LYMPHOID LEUKEMIA

Stage	Clinical Features	Median Survival, Years
Rai System		
0: Low risk	Lymphocytosis only in blood and marrow	>10
I: Intermediate risk	Lymphocytosis + lymphadenopathy	7
II: Intermediate risk	Lymphocytosis + lymphadenopathy + splenomegaly ± hepatomegaly	
III: High risk	Lymphocytosis + anemia	1.5
IV: High risk	Lymphocytosis + thrombocytopenia	
Binet System		
A	Fewer than three areas of clinical lymphadenopathy; no anemia or thrombocytopenia	>10
B	Three or more involved node areas; no anemia or thrombocytopenia	7
C	Hemoglobin ≤10 g/dL and/or platelets <100,000/μL	2

TABLE 134-8 THE ANN ARBOR STAGING SYSTEM FOR HODGKIN'S LYMPHOMA

Stage	Definition
I	Involvement of a single lymph node region or lymphoid structure (e.g., spleen, thymus, Waldeyer's ring)
II	Involvement of two or more lymph node regions on the same side of the diaphragm (the mediastinum is a single site; hilar lymph nodes should be considered "lateralized" and, when involved on both sides, constitute stage II disease)
III	Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm
III_1	Subdiaphragmatic involvement limited to spleen, splenic hilar nodes, celiac nodes, or portal nodes
III_2	Subdiaphragmatic involvement includes paraaortic, iliac, or mesenteric nodes plus structures in III_1
IV	Involvement of extranodal site(s) beyond that designated as "E"
	More than one extranodal deposit at any location
	Any involvement of liver or bone marrow
A	No symptoms
B	Unexplained weight loss of >10% of the body weight during the 6 months before staging investigation
	Unexplained, persistent, or recurrent fever with temperatures >38°C during the previous month
	Recurrent drenching night sweats during the previous month
E	Localized, solitary involvement of extralymphatic tissue, excluding liver and bone marrow

The initial evaluation of a patient with Hodgkin's lymphoma or non-Hodgkin's lymphoma is similar. In both situations, the determination of an accurate anatomic stage is an important part of the evaluation. Staging is done using the Ann Arbor staging system originally developed for Hodgkin's lymphoma (Table 134-8).

Evaluation of patients with Hodgkin's lymphoma will typically include a complete blood count; erythrocyte sedimentation rate; chemistry studies reflecting major organ function; computed tomography (CT) scans of the chest, abdomen, and pelvis; and a bone marrow biopsy. Neither a positron emission tomography (PET) scan nor a gallium scan is absolutely necessary for primary staging, but one performed at the completion of therapy allows evaluation of persisting radiographic abnormalities, particularly the mediastinum. Knowing that the PET scan or gallium scan is abnormal before treatment can help in this assessment. In most cases, these studies will allow assignment of anatomic stage and the development of a therapeutic plan.

In patients with non-Hodgkin's lymphoma, the same evaluation described for patients with Hodgkin's lymphoma is usually carried out. In addition, serum levels of lactate dehydrogenase (LDH) and β_2-microglobulin and serum protein electrophoresis are often included in the evaluation. Anatomic stage is assigned in the same manner as used for Hodgkin's lymphoma. However, the prognosis of patients with non-Hodgkin's lymphoma is best assigned using the International Prognostic Index (IPI) (Table 134-9). This is a powerful predictor of outcome in all subtypes of non-Hodgkin's lymphoma. Patients are assigned an IPI score based on the presence or absence of five adverse prognostic factors and may have none or all five of these adverse prognostic factors. Figure 134-4 shows the prognostic significance of this score in 1300 patients with all types of non-Hodgkin's lymphoma. With the addition of rituximab to CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), treatment outcomes have improved and the original IPI has lost some of its discrimination power. A revised IPI has been proposed that better predicts outcome of rituximab plus chemotherapy-based programs (Table 134-9). CT scans are routinely used in the evaluation of patients with all subtypes of non-Hodgkin's lymphoma, but PET and