Chronic Lymphocytic Leukemia: 
An Historical Perspective

John G. Gribben

Despite the major advances that have been made on the molecular pathogenesis, diagnosis and treatment of chronic lymphocytic leukemia (CLL) it is remarkable how much of the current approach to management of this disease was appreciated by the physicians caring for patients with CLL 50 years ago. 

CLL was known to be a disease of later age and twice as common in men. Not all patients diagnosed with CLL in the 1950s would have this disease when assessed with modern diagnostic techniques, but would instead have had leukemic involvement with other lymphomas, but the presenting features of lymphocytosis, lymphadenopathy and splenomegaly were well recognized. The concept of cell surface markers for B- and T-cell lineage would require more than another decade of work. Hematologic examination was becoming more routine and it was felt likely that this contributed in part to the apparent increase in incidence of leukemia. There was general recognition that this diagnosis could be an incidental finding requiring no therapy and that the disease course could be lengthy. In these circumstances, “the leukemia may be said to co-exist peacefully with its host” (Bethell FH, et al. Blood. 1955). Immune deficiency in CLL and the role of hypogammaglobulinemia was recognized. The association between CLL and acquired hemolytic anemia was the focus of much interest, and was known to be Coombs’ test positive, and responsive to corticosteroids.

In a “Panels in Therapy” article in Blood in 1955 (Bethell FH et al), the great names of the day discussed the management of two cases of CLL, one presenting with generalized lymphadenopathy and a white blood count of 150,000 and another asymptomatic patient with little adenopathy and a white count of 50,000. Options for treatment at the time consisted of watchful waiting, radiation to enlarged nodes (“in the order of two or three times 200r in air”), oral doses of 32P and triethylene melanine (TEM) at doses of 2.5 to 5 mg daily. William Dameshek, commenting on the management of CLL, noted that there was “by no means a standard method in the therapy of chronic lymphocytic leukemia; whether it is benign or aggressive in its course.” (Noli me tangere was still the motto of the day. Although everyone agreed that treatment should be instituted for the symptomatic patient, doubts were expressed as to whether this treatment actually prolonged life. Three years later, by the time of the first ASH meeting, the usefulness of chlorambucil was recognized and studies were underway to examine the utility of corticosteroids.

Today, we recognize the same tenets. The clinical utility of the vast array of biomarkers that can now be applied to this disease is unknown. When and how to initiate therapy and how this impacts upon survival remain clinical trial questions. Corticosteroids remain the mainstay of the management of hemolytic anemia, and chlorambucil still has a role to play in the management of this disease. These are exciting times in CLL and now, as 50 years ago, we have to learn to apply our full understanding of this disease and its treatment to enhance the quality and duration of life of our patients.

See the related ASH 50th Anniversary Review articles under the ACUTE AND CHRONIC LEUKEMIAS section of the publication ASH 50th Anniversary Reviews: A Salute to the American Society of Hematology.