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Aggressive Non-Hodgkin's Lymphoma

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Aggressive Non-Hodgkin's Lymphoma

I. INTRODUCTION

A. Definition

1. The term *non-Hodgkin's lymphoma* (NHL) applies to a broad range of lymphoid neoplasms with distinct clinical and biologic features. The category of NHL includes many distinct disease entities, most of which can be grouped according to their natural history. In particular, one group of NHLs tends to have an aggressive clinical course if left untreated, with survival of untreated patients measured in weeks to months. This group is referred to as the aggressive NHLs.
2. Within the new Revised European–American Lymphoma (REAL) classification of NHL, several subtypes are considered aggressive or highly aggressive. Many of these entities had other names under previous classification schemes, and these are summarized in **Table 1**. The working formulation classification system from the National Cancer Institute traditionally categorized lymphomas as low grade or indolent (survival for many years [groups A–C]), intermediate grade or aggressive (survival for only a few years [groups D–G]), and high grade or very (highly) aggressive (survival for only a few weeks to months in untreated patients [groups H–J]). The corresponding B-cell lymphomas are also listed in Table 1.
3. About 10% of lymphomas have T-cell phenotypes, with clinical behavior varying from low to high grade. For example, most lymphoblastic lymphomas (group I) arise from early T-cells, although rare cases have precursor B-cell markers. Mantle cell lymphoma can be low grade, intermediate grade, or high grade. This review will describe lymphomas in general but will focus specifically on aggressive and very or highly aggressive lymphomas, which for brevity will be called *aggressive lymphomas*.

B. **Pathogenesis.** The aggressive NHLs are clonal disorders of B and (less commonly) T lymphocytes. The following information applies to both indolent and aggressive NHL.

1. B-cell NHLs may arise from pre-germinal

center origin, germinal center origin, or post-germinal center origin as they pass from antigen-independent to antigen-dependent development. The origin site determines the clinically distinct form of NHL with specific cell surface antigens.

2. T-cell NHLs may arise from thymic cells at various stages of antigen-independent or antigen-dependent development, again giving rise to distinct clinical pathologic entities with distinct phenotypes.

C. Epidemiology

1. Approximately 45,000 cases of NHL are diagnosed in the United States each year. NHL is responsible for 21,000 deaths annually, making NHL the sixth most common cause of cancer-related deaths.^{1,2} Almost 50% of these deaths are attributed to aggressive NHL subtypes.
2. The average age of NHL patients is 42 years. Males are somewhat more likely to develop NHL than females.
3. The incidence of NHL is increasing,^{2–4} which is only partly explained by HIV and AIDS. Potential etiologic factors are listed in **Table 2**, but most patients do not have these risk factors.

D. Diagnosis

1. In general, most patients present with asymptomatic adenopathy (commonly in the neck, axilla, or inguinal regions); multiple nodal sites may become enlarged. Rapid increases in size over several weeks suggest the presence of an aggressive lymphoma category. Patients with this category more often have associated B-symptoms when compared with low- or intermediate-grade categories.
 - a. Extranodal presentation is less common but suggests an aggressive lymphoma. Typical sites include head and neck, breast, lung, gastrointestinal tract, and bone marrow. The latter site can be involved by all types of lymphoma and may result in pancytopenia with related symptoms.
 - b. Development of a leukemic phase is most common in patients with small lymphocytic lymphomas, follicular center lymphomas, and especially lymphoblastic and Burkitt's categories.