

HOSPITAL PHYSICIAN®

ONCOLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Oncology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in oncology. Each quarterly manual reviews a topic essential to the current practice of oncology.

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Medical Education

Hodgkin's Disease

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Cover illustration by Christie Grams

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Hodgkin's Disease

Jonathan W. Friedberg, MD, and Andrea K. Ng, MD

I. INTRODUCTION

- A. Definition. Hodgkin's disease is a lymphoproliferative disorder that is defined histologically by characteristic Reed-Sternberg (RS) cells. A hallmark of this neoplasm is a paucity of malignant cells surrounded by abundant "bystander" cells, including eosinophils, lymphocytes, histiocytes, and neutrophils.
- B. Incidence. Age-specific incidence rates suggest a bimodal distribution, with one peak occurring between ages 15 to 34 years (increasing in part due to an association with HIV) and a second peak occurring after age 50 years. Approximately 7500 patients are diagnosed with Hodgkin's disease in the United States each year.¹
- C. There are several patterns of presentation, but the disease generally involves lymph nodes, is unicentric in origin, progresses in a predictable manner, and is fatal without therapy.
- D. Although the majority of patients with Hodgkin's disease are cured, significant limitations to therapy remain. Treatment-related morbidity, including a rising incidence of secondary malignancies, mandates improved staging and minimization of toxic therapy as important future goals for patients with a favorable prognosis.
- E. Patients with advanced-stage disease who relapse early after standard therapy, who achieve only a partial initial remission, or who relapse with clinically high-risk features represent a poor prognostic group. Even with aggressive approaches, the long-term overall survival of these patients is less than 50%.^{2,3}

II. BIOLOGY AND PATHOLOGY

- A. The etiology of Hodgkin's disease is unknown; however, epidemiologic studies, including case-clustering, familial associations, and relationship to infectious mononucleosis, support the role of viral infection in its pathogenesis.⁴

- B. Biology
 1. Molecular studies have determined that diagnostic RS cells are clonal populations of transformed germinal-center B-cells with immunoglobulin gene mutations.⁵
 2. Diagnostic RS cells contain Epstein-Barr virus (EBV) DNA in a subset of patients.⁶ These EBV genomes have been shown to be monoclonal in origin, suggesting that defective immune control of EBV-infected cells may contribute to Hodgkin's disease.
 - a. Patients with Hodgkin's disease that contains EBV or specifically expresses the EBV antigen LMP1 have a more favorable response to primary therapy and improved disease-free survival rates compared to patients with EBV-negative Hodgkin's disease.⁷
 - b. Moreover, RS cells have been shown to express viral antigens in vitro, and they can be lysed by EBV-specific cytotoxic T-lymphocytes that have been isolated from patients with Hodgkin's disease.⁸
 3. CD30, a member of the tumor necrosis factor receptor family, is present in the majority of RS cells.
- C. Pathology. In all cases, the malignant RS cells and variants are the minority of cells in the specimen, which consists of a rich inflammatory infiltrate of lymphocytes, eosinophils, neutrophils, histiocytes, and plasma cells. It is critical for specimens to be reviewed by an experienced hematopathologist to confirm the diagnosis.
 1. *Nodular sclerosis* (**Figure 1**) is the most common subtype of Hodgkin's disease in the United States. Diagnosis requires a nodular growth pattern, bands of fibrosis, and "lacunar" RS cells, with abundant cytoplasm. The disease usually presents in young adults, and anterior mediastinal involvement is very common.
 2. *Mixed cellularity* subtype is associated with diffuse architectural effacement and classic RS cells with prominent inclusion-like nucleoli.