

HOSPITAL PHYSICIAN®

HEMATOLOGY BOARD REVIEW MANUAL

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

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Acute and Chronic Graft-Versus-Host Disease

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Acute and Chronic Graft-Versus-Host Disease

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INTRODUCTION

Graft-versus-host disease (GVHD) is a common complication of allogeneic hematopoietic stem cell transplantation (HSCT) that occurs when donor T cells attack the tissues of an immunocompromised host. There are 2 distinct syndromes of GVHD: acute GVHD and chronic GVHD. Acute GVHD remains one of the most significant barriers to successful allogeneic HSCT, accounting for a substantial portion of early transplant-related morbidity and mortality. Clinically relevant acute GVHD occurs in 35% to 40% of patients transplanted from a matched sibling donor¹ and in 40% to more than 50% of recipients of unrelated donor grafts.^{2,3} Severe acute GVHD occurs in up to 20% of recipients of related donors¹ and up to 35% of unrelated donors.^{2,3} Likewise, chronic GVHD has become increasingly more common as the proportion of patients who become long-term survivors of HSCT increases. It is estimated that up to 50% to 70% of long-term survivors of allogeneic HSCT will have some manifestations of chronic GVHD. Chronic GVHD and its complications are the most frequent cause of late (> 2 yr) death after transplantation, underscoring its importance.^{4,5} Although there is an association between chronic GVHD and a protective graft-versus-tumor effect, the morbidity and mortality associated with chronic GVHD remains substantial. Chronic GVHD is also associated with important limitations on patient quality of life. Using an illustrative case, this review discusses the pathophysiology, risk factors, clinical features, and management of both acute and chronic GVHD.

ACUTE GVHD

CASE PRESENTATION

A 43-year-old man is referred for allogeneic HSCT. He was previously diagnosed with acute myelogenous leukemia with normal cytogenetics. He received induction chemotherapy followed by consolidation and attained a complete remission. Fifteen months after the initial diagnosis, the patient suffers a relapse. He re-

ceives reinduction chemotherapy and attains a second remission. The patient has a healthy, human leukocyte antigen (HLA)-matched sibling who will donate stem cells, but he is concerned about the risk of developing acute GVHD.

• What is the pathophysiology of acute GVHD?

Acute GVHD results from the complex interaction of donor T cells and host tissues that involves recognition of major and minor histocompatibility antigens in an inflammatory milieu. Critical factors that modulate the alloreactivity seen in acute GVHD include donor–host tolerance mechanisms and the judicious use of immune suppression. The pathophysiology of acute GVHD involves both the innate and adaptive immune systems and is thought to follow a reproducible pattern of (1) tissue damage from conditioning regimen, (2) donor T-cell activation, and (3) an inflammatory effector phase.⁶

• What are the risks for developing acute GVHD?

Several risk factors can predict the occurrence of acute GVHD (**Table 1**). These factors can be separated into distinct categories, of which only some may be selectively modulated by clinical decision making. For example, many of the donor-recipient factors often cannot be altered, particularly when only a single donor is available for stem cell donation (eg, sex matching). However, risk factors related to the graft composition and the choice of the conditioning regimen often can be selected by the transplant team at the time of transplantation.

• How is acute GVHD prevented?

ACUTE GVHD PROPHYLAXIS

Without prophylaxis, acute GVHD would be nearly universal; therefore, some form of prophylaxis is always employed in the peritransplant period. Two main strategies are used in preventing GVHD: graft manipulation and pharmacologic prophylaxis.

Graft Manipulation

Consistent with the notion that GVHD is induced by donor T cells coinfecting with the stem cell graft, graft manipulation to remove T cells (T-cell depletion [TCD]) is