

# 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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## Hematopoietic Growth Factor Usage in Patients with Solid Tissue Malignancies

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# Hematopoietic Growth Factor Usage in Patients with Solid Tissue Malignancies

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## INTRODUCTION

*Hematopoiesis* refers to the process in which circulating blood cells are formed in the bone marrow (Figure). Glycoprotein molecules known as hematopoietic growth factors control the process of hematopoiesis, which includes the differentiation, proliferation, and survival of precursor cells. Hematopoietic growth factors also govern the function of mature blood cells. In patients with cancer, hematopoiesis may be interrupted due to infiltration of the bone marrow with cancer cells or suppression of hematopoiesis due to chemotherapy. As a result, insufficient production of blood cells or production of abnormal cells occurs, which is manifested as neutropenia, anemia, and thrombocytopenia. Different chemotherapeutic agents also suppress hematopoiesis to varying degrees by mechanisms identical to those by which they affect cell kill in rapidly dividing tumors. Hematopoietic growth factors, including granulocyte colony-stimulating factors (G-CSFs), granulocyte-macrophage colony-stimulating factors (GM-CSFs), and erythropoietin, are used in such circumstances to treat or, in some cases, prevent the resulting neutropenia and anemia.

The purpose of this review is to discuss the physiology of hematopoiesis and the role of hematopoietic growth factors in the process. Furthermore, the use of growth factors in patients with solid tissue malignancies will be reviewed, with cases provided to illustrate important facets of supportive care. In addition, this review will include a discussion of the evidence behind recent revision of guidelines for the use of erythropoiesis-stimulating agents (ESAs) as they apply to patients with cancer and the potential uses of thrombopoietin mimetic molecules currently in development.

## NEUTROPENIA

Transient neutropenia can result from numerous viral, bacterial, and rickettsial infections as well as from the administration of nonchemotherapeutic drugs.

Several primary neutropenic disorders also exist that can cause neutropenia in the absence of infection or the use of drugs. This review focuses on neutropenia associated with solid malignancies, which is caused by tumors infiltrating the bone marrow or by interruption of hematopoiesis in cancer patients, most likely the result of either cancer pathophysiology or due to chemotherapy administered for the treatment of the cancer.

### NEUTROPENIA PROPHYLAXIS

*Neutropenia* is defined as an absolute neutrophil count (ANC) below 1500 cells/ $\mu$ L. The ANC is defined as the percentage of neutrophils and band forms multiplied with the leukocyte count (expressed as cells/ $\mu$ L). Normal ranges vary by laboratory but are generally between 1500 and 8000 neutrophils/ $\mu$ L and band forms/ $\mu$ L of blood. An ANC between 1500 and 1000 cells/ $\mu$ L is defined as mild neutropenia. Values between 500 and 1000 cells/ $\mu$ L is considered moderate neutropenia, whereas an ANC below 500 cells/ $\mu$ L is considered severe neutropenia.<sup>1</sup>

Patients undergoing chemotherapy may receive either primary or secondary prophylaxis for neutropenia. Primary prophylaxis is defined as the administration of synthetic G-CSFs or GM-CSFs after the first cycle of chemotherapy, whereas secondary prophylaxis is the administration of G-CSFs or GM-CSFs after the second and subsequent cycles of chemotherapy. Secondary prophylaxis is instituted only if the patient has developed febrile neutropenia after the first cycle. The following will discuss how these factors affect hematopoiesis and how synthetic G-CSF and GM-CSF are used to address neutropenia in patients with solid malignancies.

### Granulocyte Colony-Stimulating Factor

**Physiology.** G-CSF is a myeloid growth factor produced by monocytes, macrophages, endothelial cells, and fibroblasts in response to the presence of interleukin (IL)-1, tumor necrosis factor (TNF), endotoxin, and neutropenia. This factor functions through the G-CSF receptor, expressed on immature and mature granulocytes, and, to a lesser extent, on monocytes and macrophages. G-CSF acts on late myeloid progenitors or