

Neutropenic Fever



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KEYWORDS

• Neutropenic fever • Bacterial infection • Risk stratification

KEY POINTS

- Neutropenic fever is an oncologic/hematologic emergency that may be encountered in the emergency department setting.
- Engaging patients' hematologist/oncologist in disposition decision making is of critical importance to managing patients with febrile neutropenia.
- Factors such as chemotherapeutic regimen, history of stem cell transplant, and cancer type place patients at varying levels of risk for serious infection.
- Neutropenic fever should trigger the initiation of rapid work-up and the administration of empiric systemic antibiotic therapy.

INTRODUCTION

Fever is a common presenting complaint among adult or pediatric patients in the emergency department (ED) setting. Although fever in healthy individuals does not necessarily indicate severe illness, fever in patients with neutropenia may herald life-threatening infection. Therefore, prompt recognition of patients with neutropenic fever is imperative. Serious bacterial illness is a significant cause of morbidity and mortality for neutropenic patients.¹ Neutropenic fever should trigger the initiation of a rapid work-up and administration of empiric systemic antibiotic therapy to attenuate or avoid the progression along the spectrum of sepsis, severe sepsis, septic shock syndrome, and death.¹

Patients at risk for the development of neutropenic fever include patients using chemotherapeutic agents or other medications that alter immune function; patients with infections, such as human immunodeficiency virus (HIV); or individuals with other underlying immune deficiency states (congenital or acquired).

Fever may be the only presenting sign of infection. In the absence of fever, other potential signs of infection include vital sign alterations or evidence of new organ dysfunction. Emergency physicians should be aware of the infection risks, diagnostic

This article originally appeared in *Emergency Medicine Clinics of North America*, Volume 32, Issue 3, August 2014.

Disclosure: None.

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Hematol Oncol Clin N Am 31 (2017) 981–993

<http://dx.doi.org/10.1016/j.hoc.2017.08.004>

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methods, and antimicrobial agents required for appropriate management of febrile neutropenia. The initial clinical evaluation focuses on assessing the risk of serious complications. This risk assessment determines the approach to therapy, including the need for inpatient admission and intravenous (IV) antibiotics. Therefore, algorithms for evaluation, diagnosis, and prophylactic treatment have been developed.

DEFINITIONS

The Infectious Disease Society of America (IDSA) defines fever in neutropenic patients as a single oral temperature of greater than 38.0°C, or 100.4°F, for greater than 1 hour.² Although rectal measurement most accurately reflects the core body temperature, oral or axillary temperature measurements are recommended because of the theoretical risk of bacterial translocation during the procedure of inserting the thermometer probe into the anus.

Although the definition of neutropenia varies from institution to institution, neutropenia is typically defined as an absolute neutrophil count (ANC) of less than 1500 cells per microliter.² Severe neutropenia is defined as an ANC less than 500 cells per microliter or an ANC that is expected to decrease to less than 500 cells per microliter over the next 48 hours.² Neutropenia can be further categorized as mild, moderate, or severe. Mild neutropenia is defined as an ANC between 1000 and 1500 cells per microliter. Moderate neutropenia is defined by an ANC between 500 and 1000 cells per microliter, and severe neutropenia is defined as an ANC less than 500 cells per microliter. This classification is depicted in **Table 1**.

Because the risk of clinically significant infection increases as the neutrophil count decreases to less than 500 cells per microliter,³ for the purposes of the discussion that follows, the authors *define neutropenia as an ANC less than 500 cells per microliter*. Furthermore, the risk of clinically significant infection is higher in those with a prolonged duration of neutropenia (more than 7 days).² There is an inverse relationship between mortality associated with febrile neutropenia and the absolute neutrophil count.⁴

Although some laboratories report a calculated ANC, it is important for the emergency physician to know how to calculate the ANC. The ANC can be calculated by multiplying the total white blood cell (WBC) count by the percentage of polymorphonuclear cells and bands (**Table 2**).

For example, in a patient with the following complete blood count (CBC), the ANC is equal to 2000 cells per microliter \times (10% neutrophils + 15% bands) = 2000 \times 25% = 500 cells per microliter.

When the ANC count decreases to less than 500 cells per microliter, there is impairment in control of normal microflora of the mouth and gut.⁵ In addition, acute development of neutropenia is associated with a higher risk of infection than chronic neutropenia that results over months to years. The mortality from uncontrolled

Degree of Neutropenia	ANC (cells per microliter)
Mild	1000–1500
Moderate	500–999
Severe	<500

Data from Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2011;52(4):e56–93.

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