

Why is My Patient Neutropenic?

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KEYWORDS

- Neutrophil • Neutropenia • Differential diagnosis
- Consultative hematology

NEUTROPHIL OVERVIEW

Neutrophils (also called granulocytes) are produced exclusively in the bone marrow during normal conditions. Approximately 10^{12} neutrophils are produced per day in the bone marrow and then stored in the marrow until prompted for release by chemokines, cytokines, microbial products, or other mediators of inflammation. Once released into the bloodstream the average half-life of neutrophils is 6 to 8 hours. Circulating neutrophils, the ones reported in a standard complete blood count (CBC), account for only 2% to 3% of all neutrophils. Clearance occurs in the liver, spleen, or bone marrow and occurs through macrophage phagocytosis of aged or apoptotic neutrophils. The local production of inflammatory cytokines and chemokines leads to neutrophil attachment to the vascular endothelium and the subsequent transmigration of neutrophils into tissue. The migration of neutrophils into tissue is a key component of the innate immune system, as evident by the increased risk of infections seen in the setting of neutropenia.

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Neutropenia is defined as an absolute neutrophil count (ANC) less than 1500 cells/ μ L; it may be mild (ANC 1000–1500 cells/ μ L), moderate (500–1000 cells/ μ L), or severe (<500 cells/ μ L) (**Table 1**). In general, infection risk increases with ANC less than 1000 cells/ μ L; however, the risk for infections varies depending on the cause of neutropenia. For example, patients with neutropenia and acute leukemia seem to have a high risk for overwhelming infection in the setting of neutropenia, particularly in cases with ANC less than 500 cells/ μ L.¹ Therefore, the context in which neutropenia occurs must be considered because some causes of neutropenia, namely ethnic neutropenia and chronic idiopathic neutropenia (CIN), have few overall infection risks.

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Table 1 Severity of neutropenia		
	ANC	Risk of Infection
Mild neutropenia	ANC <1500 but >1000	Mild
Moderate neutropenia	ANC <1000 but >500	Moderate
Severe neutropenia	ANC <500 but >200	Severe
Agranulocytosis	ANC <200	Severe

DIAGNOSTIC WORKUP

Initial workup consists of a CBC, with a differential count to evaluate the severity of the neutropenia. A full history is also essential to determine race, ethnicity, new medications (including over-the-counter and complementary medications), and potential infectious exposures. Review of systems should focus on fevers, chills, night sweats, weight loss, excess bleeding or bruising, or recurrent infections. A comprehensive physical examination should be performed, with a focus on an examination for signs of infection, hepatosplenomegaly, and lymphadenopathy. After this examination, a detailed review of the peripheral smear should follow, to look for neutrophil abnormalities such as Döhle bodies (infection), immature neutrophil precursors (infection, myelodysplasia, myelophthisis), hypoplastic changes in the neutrophils (myelodysplasia), hyperlobulation (nutritional deficiencies), and white cell inclusions (eg, anaplasmosis (**Fig. 1**), bartonellosis). Review of red cell morphology on peripheral smear may also offer clues to the cause of neutropenia because dacryocytes (teardrop cells) and nucleated red cells (myelodysplasia, fibrosis, myelophthisis) in addition to red cell inclusions (eg, babesiosis, malaria) may all be seen in disease states associated with neutropenia.

Additional routine blood work should include:

- Reticulocyte count
- Lactate dehydrogenase
- Erythrocyte sedimentation rate
- Rheumatoid factor/anticyclic citrullinated protein antibody
- Antinuclear antibodies
- Thyroid-stimulating hormone

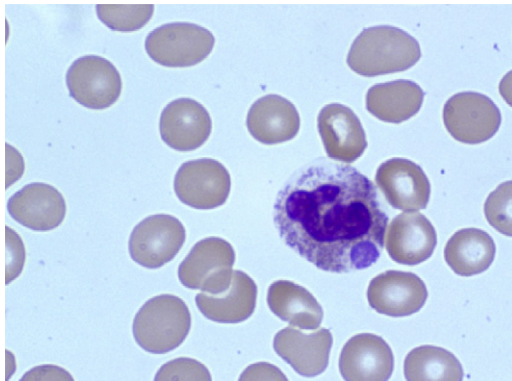


Fig. 1. Neutrophil with an intracellular morula in a patient with anaplasmosis.

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