

Leukocytosis and Leukemia

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KEYWORDS

• Leukocytosis • White blood cell count • Inflammation • Leukemia

KEY POINTS

- Leukocytosis may be caused by a variety of benign and malignant conditions. Careful history and laboratory evaluation can assist in differentiating these causes.
- Use of white blood cell differential as well as peripheral blood smear and morphologic characteristics may improve the ability to diagnose the underlying causative process.
- Nonmalignant causes of leukocytosis include infection, inflammation, medication, surgery, and physical/physiologic stress.
- The presence of blasts or other early progenitors of cells is highly suggestive of a primary bone marrow disorder that should prompt an immediate evaluation by a hematology specialist.
- Patients with leukemia often require chemotherapy or bone marrow transplant. Following treatment, they need to be monitored closely for late complications.

INTRODUCTION

The accepted normal range of white blood cell (WBC) counts in nonpregnant adults is approximately 4000 to 11,000 cells/mm³; thus, leukocytosis is defined as any WBC count greater than 11,000 cells/mm³ (Table 1 for normal WBC differential). An abnormally increased leukocyte count can be caused by a wide range of benign and malignant conditions. Cell differentiation type, chronicity of abnormal values, degree of WBC increase, patient gender and ethnicity, and associated symptoms are important characteristics used to differentiate between these causes.

WHITE BLOOD CELL LINEAGES

Leukocytes are derived from 2 distinct pathways: the myeloid pathway, which produces all granulocytes and monocytes, and the lymphoid pathway, which produces

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White Blood Cell Lines	Total Leukocyte Count (%)
Lymphocytes	20–40
Neutrophils	40–60
Monocytes	2–8
Eosinophils	1–4
Basophils	0.5–1

B and T lymphocytes. Granulocytes, including neutrophils, basophils, and eosinophils, are the major cellular components in inflammatory and antimicrobial responses. These cells are produced in the bone marrow, which stores roughly 90% of all granulocytes in the body. A small percentage of neutrophils are also present along the endothelium of blood vessels. The localization of these two granulocyte populations allows rapid upregulation of granulocyte production as well as prompt mobilization in response to external stress.¹

Monocytes comprise another subset of the myeloid pathway, and these cells function by consuming foreign material. Monocytes are produced within the bone marrow. On traveling to damaged tissues, monocytes differentiate into tissue-fixed macrophages that are responsible for consumption of local pathogens.

In contrast with cells of the myeloid lineage, which mount a nonspecific innate immune response, the cells in the lymphoid lineage directly respond to specific antigens. B cells respond to antigens encountered in the blood, whereas T cells are activated by the presentation of antigens by other cells. The presentation of an antigen to either of these types of lymphocytes activates clonal proliferation aimed at that particular target. Proliferation of any of these cell types (neutrophils, basophils, eosinophils, monocytes, or lymphocytes) can result in a peripheral leukocytosis (Fig. 1); however, the predominance of a particular cell subtype may assist in development of a differential diagnosis.¹

NONMALIGNANT CONDITIONS

Reactive Neutrophilia

Reactive leukocytosis, an increased WBC count in response to a stress, usually provokes WBC counts between 12,000 and 30,000 cells/mm³ with a neutrophilic predominance. Catecholamine-induced demargination of neutrophils may result from exercise, surgery, trauma, and even emotional stress. Reid and colleagues² evaluated 155 runners postmarathon and found that 100% of them developed a leukocytosis with neutrophilic predominance, likely secondary to demargination of mature neutrophils from the endothelium. Another study, by Nieman and colleagues,³ reported that leukocyte counts reverted to normal by 24 hours postrace. The same phenomenon can be found in patients who are postictal and postoperative. Reactive leukocytosis is a normal physiologic response but, if leukocytosis persists for greater than 48 hours following a given stressor, further evaluation is recommended.

Acute Infection

Acute infection remains the most common nonmalignant cause of leukocytosis. The acute inflammatory response leads to dilation of small blood vessels, increased vascular permeability, and emigration of leukocytes from circulation to the site of injury.⁴ Although circulating neutrophils are the initial responders to acute infection, Furze and Rankin⁵ discovered that the bone marrow release of mature granulocytes

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