



## Non-Infectious Causes of Leukocytosis

Leukocytosis is the presence of elevated white blood cells (WBC) often defined as  $> 11,000$  cells/ $\mu\text{L}$  on a complete blood count. Leukocytosis is a common cause for initiating empiric antibiotics or broadening the spectrum of activity. Is this appropriate?

### What causes leukocytosis?

A WBC count reflects the total number of neutrophils, lymphocytes, monocytes, eosinophils, basophils, and immature or atypical cells present in the blood.<sup>1</sup> Increases in these specific cell lineages (e.g., lymphocytosis, neutrophilia, eosinophilia) all contribute to leukocytosis.<sup>2</sup> As different cell lineages are altered by different pathways, multiple competing etiologies can induce leukocytosis. Specific etiologies of leukocytosis are described below.

**Table 1: Etiologies of Leukocytosis<sup>3</sup>**

Etiology	Comments
<b>Bacterial infection</b>	Often associated with a “left shift” with increased levels of immature neutrophils (band forms)
<b>Viral Infection</b>	Often associated with lymphocytosis. Seen with Epstein-Barr virus, hepatitis viruses
<b>Stress/tissue injury</b>	Surgery, myocardial injury, intensive exercise, mechanical injuries
<b>Medication-induced</b>	Corticosteroids, beta-agonists, lithium, granulocyte-colony stimulating factors
<b>Malignancy</b>	Both hematologic and non-hematologic cancers
<b>Drug hypersensitivity reactions</b>	Often associated with eosinophilia
<b>Chronic inflammation</b>	Rheumatic diseases, inflammatory bowel disease, chronic hepatitis, granulomatous disease
<b>Primary neutrophilia</b>	Congenital, hereditary, or chronic idiopathic neutrophilia

### Should antibiotics be started or broadened in patients with leukocytosis?

A comprehensive workup should be conducted before attributing leukocytosis to a specific cause such as infection. Duration of leukocytosis (e.g., new onset leukocytosis due to an infection or acute leukemia) as well as past medical history can help diagnose the etiology of leukocytosis.<sup>4</sup> Other clinical tools such as systemic inflammatory response syndrome (SIRS) criteria include leukocytosis as a marker for sepsis and severe infection, but guidelines advise clinicians to avoid solely relying on these tools to stratify critically ill patients.<sup>5</sup> One prospective study examined 173 patients with leukocytosis found that 43% were not diagnosed with systemic infection.<sup>6</sup>

Leukocytosis in hemodynamically stable patients on extracorporeal oxygenation (ECMO) with active influenza or COVID-19 infections has not been associated with acute bacterial infections.<sup>7</sup> In hemodynamically stable patients with leukocytosis and no additional signs and symptoms of infection, antibiotics may not always be indicated.

**Key Takeaway:** Leukocytosis has multiple etiologies. Non-infectious causes of leukocytosis should be considered when clinically evaluating the need for antimicrobials.

### References:

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