PATHOLOGICAL MECHANISMS OF CHANGES IN THE AMOUNT OF LEUKOCYTES IN THE BLOOD

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Annotation: An elevated white blood cell count has many potential etiologies, including malignant and nonmalignant causes. It is important to use age- and pregnancy-specific normal ranges for the white blood cell count. A repeat complete blood count with peripheral smear may provide helpful information, such as types and maturity of white blood cells, uniformity of white blood cells, and toxic granulations. The leukocyte differential may show eosinophilia in parasitic or allergic conditions, or it may reveal lymphocytosis in childhood viral illnesses.

Key words: Leukocytosis , intravascular , trauma , blood, neutrophils .

Leukocytosis is a common sign of infection, particularly bacterial, and should prompt physicians to identify other signs and symptoms of infection. The peripheral white blood cell count can double within hours after certain stimuli because of the large bone marrow storage and intravascularly marginated pools of neutrophils. Stressors capable of causing an acute leukocytosis include surgery, exercise, trauma, and emotional stress. Other nonmalignant etiologies of leukocytosis include certain medications, asplenia, smoking, obesity, and chronic inflammatory conditions. Symptoms suggestive of a hematologic malignancy include fever, weight loss, bruising, or fatigue. If malignancy cannot be excluded or another more likely cause is not suspected, referral to a hematologist/oncologist is indicated.

Leukocytosis, often defined as an elevated white blood cell (WBC) count greater than 11,000 per mm^3 (11.0×10^9 per L) in nonpregnant adults, is a relatively common finding with a wide differential. It is important for clinicians to be able to distinguish malignant from non-malignant etiologies, and to differentiate between the most common nonmalignant causes of leukocytosis.

Leukocytosis in the range of approximately 50,000 to 100,000 per mm^3 (50.0 to 100.0 × 10^9 per L) is sometimes referred to as a leukemoid reaction. This level of elevation can occur in some severe infections, such as *Clostridium difficile* infection, sepsis, organ rejection, or in patients with solid tumors.[1] Leukocytosis greater than 100,000 per mm^3 is almost always caused by leukemias or myeloproliferative disorders.[2]

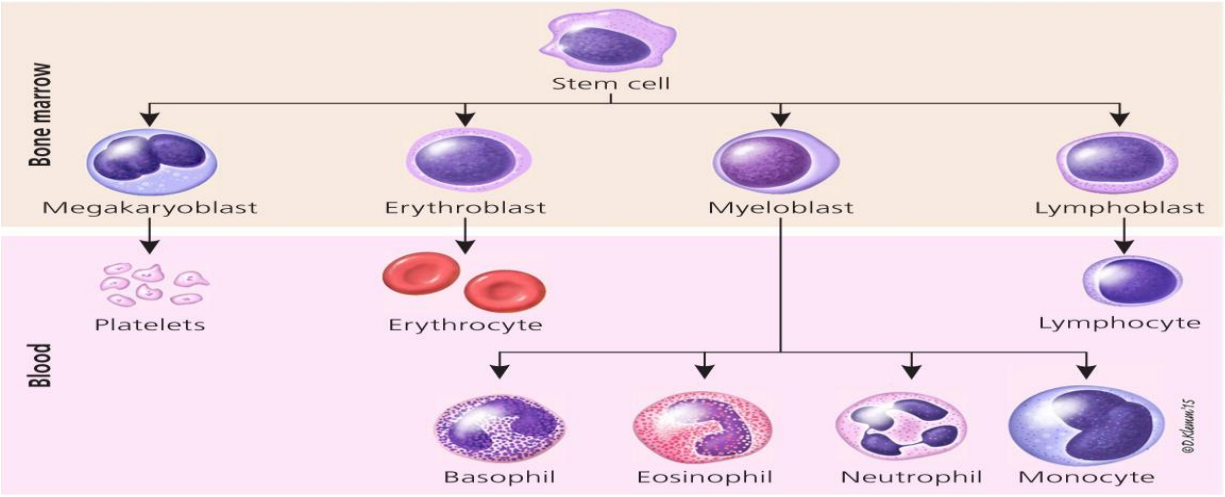
The normal range for WBC counts changes with age and pregnancy *(Table 1)*.[3] Healthy newborn infants may have a WBC count from 13,000 to 38,000 per mm^3 (13.0 to 38.0 × 10^9 per L) at 12 hours of life (95% confidence interval). By two weeks of age, this decreases to approximately 5,000 to 20,000 per mm^3 (5.0 to 20.0 × 10^9 per L), and gradually declines throughout childhood to reach adult levels of 4,500 to 11,000 per mm^3 (4.5 to 11.0 × 10^9 per L; 95% confidence interval) by about 21 years of age.[3] There is also a shift from relative lymphocyte to neutrophil predominance from early childhood to the teenage years and adulthood.[4] During pregnancy, there is a gradual increase in the normal WBC count (third trimester 95% upper limit = 13,200 per mm^3 [13.2 × 10^9 per L] and 99% upper limit = 15,900 per mm^3 [15.9 × 10^9 per L]), and a slight shift toward an increased percentage of neutrophils.[5] In one study of afebrile postpartum patients, the mean WBC count was 12,620 per mm^3 (12.62 × 10^9 per L) for women after vaginal deliveries and 12,710 per mm^3 (12.71 × 10^9 per L) after cesarean deliveries. Of note, positive bacterial cultures were not associated with leukocytosis or neutrophilia, making leukocytosis an unreliable discriminator in deciding which postpartum patients require antibiotic therapy.[6] Patients of black African descent tend to have a lower WBC count (by 1,000 per mm^3 [1.0 × 10^9 per L]) and lower absolute neutrophil counts.[7]

Table 1. White Blood Cell Count Variation with Age and Pregnancy

Patient characteristic	*Normal total leukocyte count*
Newborn infant	13,000 to 38,000 per mm^3 (13.0 to 38.0 × 10^9 per L)
Infant two weeks of age	5,000 to 20,000 per mm^3 (5.0 to 20.0 × 10^9 per L)
Adult	4,500 to 11,000 per mm^3 (4.5 to 11.0 × 10^9 per L)
Pregnant female (third trimester)	5,800 to 13,200 per mm^3 (5.8 to 13.2 × 10^9 per L)

Information from reference 3.

The life cycle of leukocytes includes development and differentiation, storage in the bone marrow, margination within the vascular spaces, and migration to tissues. Stem cells in the bone marrow produce cell lines of erythroblasts, which become red blood cells; megakaryoblasts, which become platelets; lymphoblasts; and myeloblasts. Lymphoblasts develop into various types of T and B cell lymphocytes. Myeloblasts further differentiate into monocytes and granulocytes, a designation that includes neutrophils, basophils, and eosinophils *(Figure 1)*. Once WBCs have matured within the bone marrow, 80% to 90% remain in storage in the bone marrow. This large reserve allows for a rapid increase in the circulating WBC count within hours. A relatively small pool (2% to 3%) of leukocytes circulate freely in the peripheral blood[1]; the rest stay deposited along the margins of blood vessel walls or in the spleen. Leukocytes spend most of their life span in storage. Once a leukocyte is released into circulation and peripheral tissues, its life span ranges from two to 16 days, depending on the type of cell.



Changes in the normal distribution of types of WBCs can indicate specific causes of leukocytosis *(Table 2)*.[8] Although the differential of the major types of WBCs is important for evaluating the cause of leukocytosis, it is sometimes helpful to think in terms of absolute, rather than relative, leukopenias and leukocytoses. To calculate the absolute cell count, the total leukocyte count is multiplied by the differential percentage. For example, with a normal WBC count of 10,000 per mm^3 (10.0×10^9 per L) and an elevated monocyte percentage of 12, the absolute monocyte count is 12% or 0.12 times the WBC count of 10,000 per mm^3, yielding 1,200 per mm^3 (1.2×10^9 per L), which is abnormally elevated.

Table 2. Normal White Blood Cell Distribution

White blood cell line	*Normal percentage of total leukocyte count*
Neutrophils	40 to 60
Lymphocytes	20 to 40
Monocytes	2 to 8
Eosinophils	1 to 4
Basophils	0.5 to 1

Information from reference 8.

The most common type of leukocytosis is neutrophilia (an increase in the absolute number of mature neutrophils to greater than 7,000 per mm^3 [7.0×10^9 per L]), which can arise from infections, stressful conditions, chronic inflammation, medication use, and other causes. Lymphocytosis (when lymphocytes make up more than 40% of the WBC count or the absolute count is greater than 4,500 per mm^3 [4.5

× 10^9 per L]) can occur in patients with pertussis, syphilis, viral infections, hypersensitivity reactions, and certain subtypes of leukemia or lymphoma. Lymphocytosis is more likely to be benign in children than in adults.[4]

Literatures:

1. Cerny J, Rosmarin AG. Why does my patient have leukocytosis?. *Hematol Oncol Clin North Am.* 2012;26(2):303-319.
2. Jain R, Bansal D, Marwaha RK. Hyperleukocytosis: emergency management. *Indian J Pediatr.* 2013;80(2):144-148.
3. Hoffman R, Benz EJ Jr, Silberstein LE, Heslop H, Weitz J, Anastasi J. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, Pa.: Elsevier/Saunders; 2013:table 164–20.
4. Chabot-Richards DS, George TI. Leukocytosis. *Int J Lab Hematol.* 2014;36(3):279-288.
5. Lurie S, Rahamim E, Piper I, Golan A, Sadan O. Total and differential leukocyte counts percentiles in normal pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2008;136(1):16-19.
6. Dior UP, Kogan L, Elchalal U, et al. Leukocyte blood count during early puerperium and its relation to puerperal infection. *J Matern Fetal Neonatal Med.* 2014;27(1):18-23.
7. Lim EM, Cembrowski G, Cembrowski M, Clarke G. Race-specific WBC and neutrophil count reference intervals. *Int J Lab Hematol.* 2010;32(6 pt 2):590-597.
8. Berliner N. Leukocytosis and leukopenia. In: Goldman L, Schafer AI, eds. *Goldman's Cecil Medicine*. 24th ed. Philadelphia, Pa.: Elsevier/Saunders; 2012.
9. Iskandar JW, Griffeth B, Sapra M, Singh K, Giugale JM. Panic-attack-induced transient leukocytosis in a healthy male: a case report. *Gen Hosp Psychiatry.* 2011;33(3):302.e11-302.e12.