Causes of Leukocytosis, Leokopenia, Lymphocytosis and Leukemoid Reactions.

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Normal WBC counts

TLC	
Adults	4,000–11,000/µl
Infants (Full term, at birth)	10,000–25,000/µl
Infants (1 year)	6,000–16,000/µl
Children (4–7 years)	5,000–15,000/µl
Children (8–12 years)	4,500–13,500/µl
DLC IN ADULTS	
Polymorphs (neutrophils) 40–75%	2,000–7,500/µl
Lymphocytes 20–50%	1,500–4,000/µl
Monocytes 2–10%	200–800/µl
Eosinophils 1–6%	40–400/µl

Introduction

- Disorders of white blood cells can be classified into two broad categories:
  - ❑ Proliferative disorders
  - ❑ Leukopenias

- Proliferations of white cells can be reactive or neoplastic.
- Reactive proliferations in the setting of infections or inflammatory processes, when large numbers of leukocytes are needed for an effective host response, are fairly common.
- Neoplastic disorders, though less frequent, are much more important clinically.

Leukopenia

- Leukopenia usually results from reduced numbers of neutrophils (neutropenia, granulocytopenia). Lymphopenia is less common, in addition to congenital immunodeficiency diseases, it is most commonly observed in advanced human immunodeficiency virus (HIV) infection, following therapy with glucocorticoids or cytotoxic drugs, autoimmune disorders, malnutrition, and certain acute viral infections.
- Neutropenia, a reduction in the number of neutrophils in the blood.
- Agranulocytosis is referred to a marked reduction in neutrophils, has the serious consequence of making individuals susceptible to bacterial and fungal infections.

Neutropenia

- Neutropenia can be caused by

(1) Inadequate or ineffective granulopoiesis

- Suppression of HSCs, as occurs in aplastic anemia and a variety of infiltrative marrow disorders (e.g.,tumors, granulomatous disease)
- Suppression of committed granulocytic precursors by exposure to certain drugs.
- Disease states associated with ineffective hematopoiesis, such as megaloblastic anemia and myelo-dysplastic syndrome, in which defective precursors die in the marrow.
- Rare congenital conditions (e.g., Kostmann syndrome), in which inherited defects in specific genes impair granulocytic differentiation.

(2) Increased destruction or sequestration of neutrophils in the periphery.

- Immunologically mediated injury to neutrophils, which can be idiopathic, associated with an immunologic disorder (e.g., SLE), or caused by exposure to drugs.
- Splenomegaly.
- Increased peripheral utilization.

Agranulocytosis

- The most common cause of agranulocytosis is drug toxicity. Certain drugs, such as alkylating agents and antimetabolites used in cancer treatment, produce agranulocytosis in a predictable, dose-related fashion.
- Production of red cells and platelets is also affected.
- Idiosyncratic reaction to a large variety of agents including certain antibiotics, anticonvulsants, antiinflammatory drugs, antipsychotic drugs, and diuretics.
- Severe neutropenia may also occur in association with monoclonal proliferations of large granular lymphocytes (so-called LGL leukemia).

Clinical features of neutropenia

- Malaise, chills, and fever, often followed by marked weakness and fatigability.
- With agranulocytosis, infections are often overwhelming and may cause death within hours to days.
- Serious infections are most likely when the neutrophil count falls below 500/mm3.
- Because infections are often fulminant, broad-spectrum antibiotics must be given expeditiously whenever signs or symptoms appear.

Leukocytosis

- Peripheral blood leukocyte count is influenced by several factors
  - Size of the myeloid and lymphoid precursor and storage cell pools in the bone marrow, thymus, circulation, and peripheral tissues
  - Rate of release of cells from the storage pools into the circulation
  - Proportion of cells that are adherent to blood vessel walls at any time (the marginal pool)
  - Rate of extravasation of cells from the blood into tissues

Leukocytosis

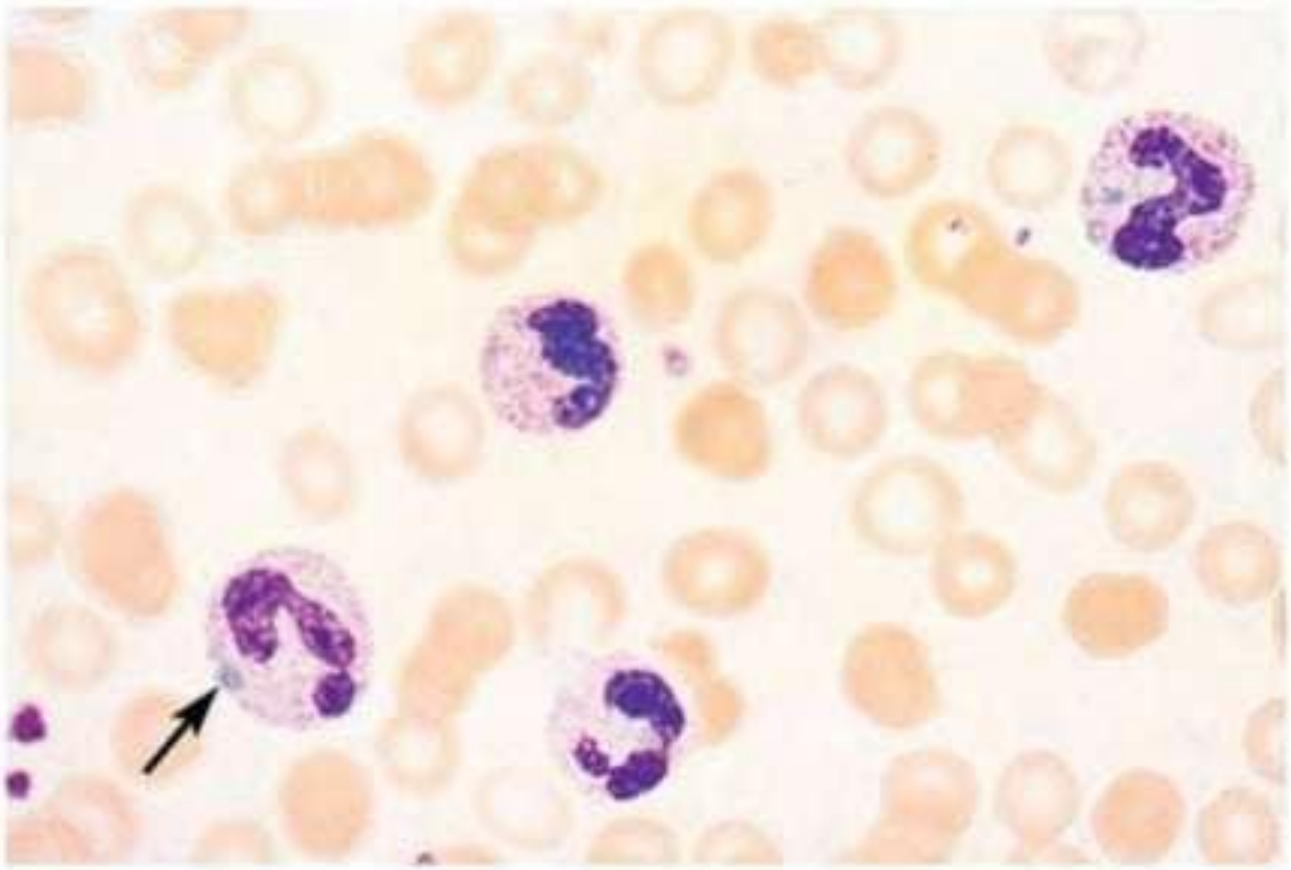
- Mechanisms of leukocytosis

Increased Marrow Production
Chronic infection or inflammation (growth factor–dependent) Paraneoplastic (e.g., Hodgkin lymphoma; growth factor–dependent) Myeloproliferative neoplasms (e.g., chronic myeloid leukemia; growth factor–independent)
Increased Release From Marrow Stores
Acute inflammation (e.g., with infection) Chronic inflammation (many causes)
Decreased Margination
Exercise Catecholamines
Decreased Extravasation Into Tissues
Glucocorticoids

- Causes of leukocytosis

Type of Leukocytosis	Causes
Neutrophilic leukocytosis	Acute bacterial infections, especially those caused by pyogenic organisms; sterile inflammation caused by, for example, tissue necrosis (myocardial infarction, burns)
Eosinophilic leukocytosis (eosinophilia)	Allergic disorders such as asthma, hay fever, parasitic infestations; drug reactions; certain malignancies (e.g., Hodgkin and some non-Hodgkin lymphomas); autoimmune disorders (e.g., pemphigus, dermatitis herpetiformis) and some vasculitides; atheroembolic disease (transient)
Basophilic leukocytosis (basophilia)	Rare, often indicative of a myeloproliferative neoplasm (e.g., chronic myeloid leukemia)
Monocytosis	Chronic infections (e.g., tuberculosis), bacterial endocarditis, rickettsiosis, and malaria; autoimmune disorders (e.g., systemic lupus erythematosus); inflammatory bowel diseases (e.g., ulcerative colitis)
Lymphocytosis	Accompanies monocytosis in many disorders associated with chronic immunologic stimulation (e.g., tuberculosis, brucellosis); viral infections (e.g., hepatitis A, cytomegalovirus, Epstein-Barr virus); *Bordetella pertussis* infection

- In sepsis or severe inflammatory disorders (e.g., Kawasaki disease), leukocytosis is often accompanied by morphologic changes in neutrophils, such as toxic granulations, Döhle bodies, and cytoplasmic vacuoles.
- Toxic granules, which are coarser and darker than normal neutrophilic granules, represent abnormal azurophilic (primary) granules.
- Döhle bodies are patches of dilated endoplasmic reticulum that appear as sky-blue cytoplasmic "puddles."



Reactive changes in neutrophils. Neutrophils containing coarse purple cytoplasmic granules (toxic granulations) and blue cytoplasmic patches of dilated endoplasmic reticulum (Döhle bodies) (arrow) are observed in this peripheral blood smear prepared from a patient with bacterial sepsis.

Leukemoid Reactions

- This refers to the presence of markedly increased total leukocyte count (>50,000/cmm) with immature cells in peripheral blood resembling leukaemia but occurring in non-leukemic disorders. Its causes are

- ❑ Severe bacterial infections, e.g. septicemia, pneumonia
- ❑ Severe hemorrhage
- ❑ Severe acute hemolysis
- ❑ Poisoning
- ❑ Burns
- ❑ Carcinoma metastatic to bone marrow

Leukemoid Reaction vs Leukemia

Parameter	*Leukemoid reaction*	*Leukemia*
1. Clinical presentation	Features of underlying disease; fever common	Splenomegaly
2. Examination of blood		
a. Total leukocyte count	< 50000/µl	Variable, usually > 1 lac/µl
b. Course of neutrophilia	Disappears with resolution of underlying disease	Progressive increase
c. Evidence of infection	Toxic granules, Döhle inclusion bodies	Absent
d. Basophilia	Absent	Present
e. Immature cells	Few; cells up to myelocyte stage	Many; cells up to blasts
3. Examination of marrow	Myeloid hyperplasia	Increased blasts and immature cells of neutrophil series; Suppression of other cell lines
4. Clonality	Polyclonal	Monoclonal
5. Karyotype	Normal	Abnormal

Thank You