Hematology

The significance of CBC

- Find the cause of symptoms such as fatigue, weakness, fever, bruising, or weight loss
- Diagnosis of anemia
- Estimation of blood loss
- Diagnosis of polycythemia
- Find an infection
- Diagnosis of blood diseases as leukemia
- Response to drug or radiation treatment
- Screening before surgery
- Abnormal count of certain types of cells

Complete Blood Count (CBC)

- Panel of tests that examine different components of the blood.

❖ ***CBC values***

- RBC count
- Hemoglobin
- Hematocrit
- RBC indices
- WBC count and differential
- Platelet count

- White Blood Count (WBC): actual number of white blood cells per volume of blood.
- WBC differential: types of WBC present.

- Red Blood Cells (RBC): actual number of red blood cells per volume of blood

- Hemoglobin (Hb): amount of the oxygen carrying protein in the blood

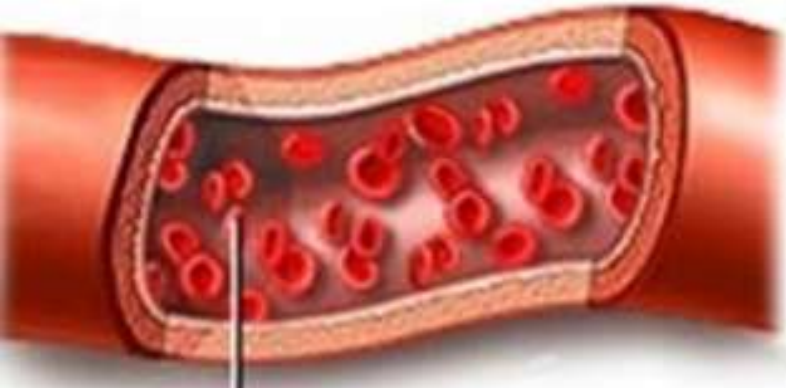
- Platelets (PLT): actual number of platelets per volume of blood

- Mean Corpuscular Volume (MCV):
  a measurement of the average size of RBCs

- Mean Corpuscular Hemoglobin (MCH): the average amount of oxygen-carrying hemoglobin inside a RBC

- Mean Corpuscular Hemoglobin Concentration (MCHC): the average concentration of hemoglobin inside a RBC

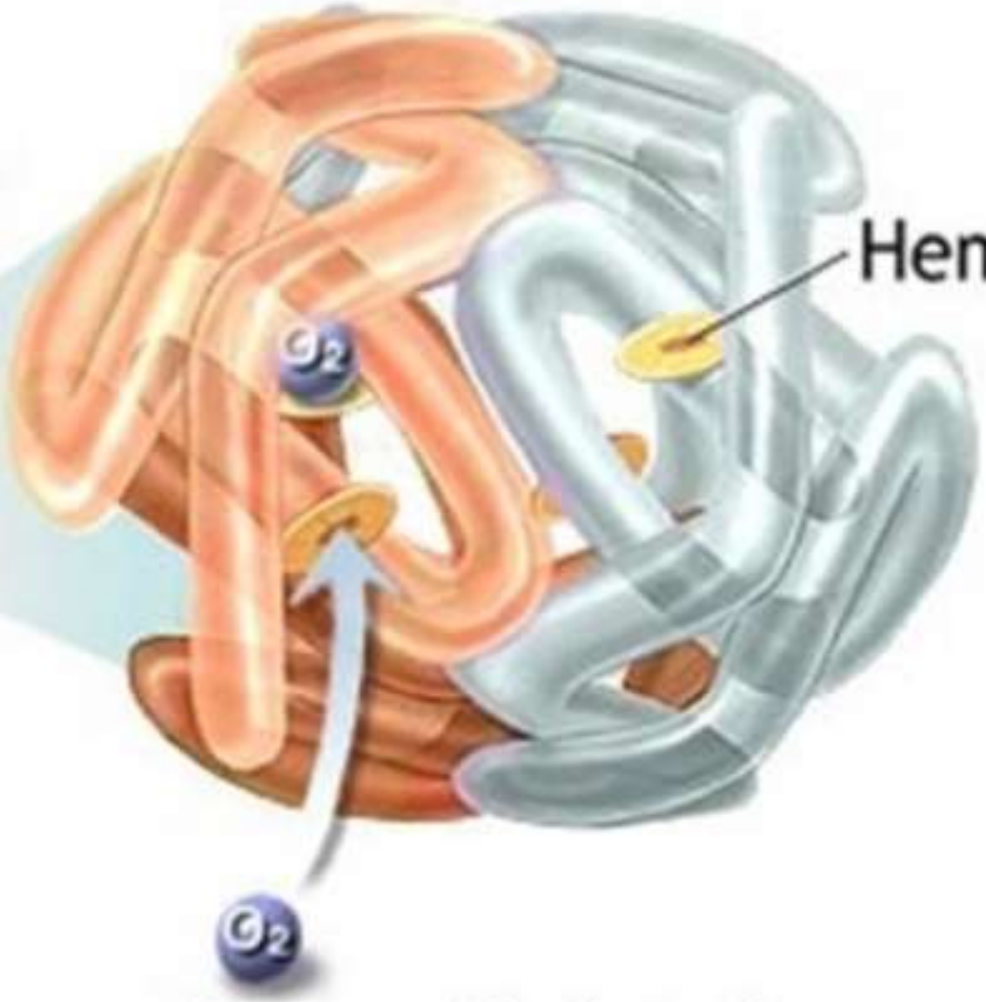
- Red Cell Distribution Width (RDW): a variation in the size of RBCs



Red blood cell

Red blood cells contain several hundred thousand hemoglobin molecules, which transport oxygen

Hemoglobin molecule



Oxygen binds to heme on the hemoglobin molecule

Red Blood Cell Count (RBC)

- Normal value = 4.6 to 6.2 x 10^6 cells/μL
- Decreased with anemia
- Increased with erythrocytotic states such as polycythemia vera, erythrocytosis of chronic hypoxia, dehydration, stress polycythemia, and thalassemia minor.

Hematocrit

- Hematocrit is the volume of the red cells as compared to the volume of the whole blood sample.
- Hematocrits on the automated systems are calculated.
  - Calculated: (MCV)×(RBC) = Hct
- Usually expressed in percentage (42%)
  - Males 42-52 %
  - Females 37-47% (pregnant>33%)

- Provides information on the amount of red blood cells (RBC) present in the blood.

- Decreased levels means anemia from hemorrhage, parasites, nutritional deficiencies or chronic disease process, such as liver disease, cancer, etc.

- Increased levels are often seen in dehydration or polycythemia

MCV

- Mean cell volume
- MCV is average size of RBC
- $$MCV = \frac{Hct \times 10}{RBC \text{ (millions)}}$$
- If 80-100 fL, normal range, RBCs considered ***Normocytic***
- If < 80 fL are ***Microcytic***
- If > 100 fL are ***Macrocytic***

- Not reliable when have marked anisocytosis

MCH

- MCH is average weight of hemoglobin per RBC.

- $$\text{MCH} = \frac{\text{Hgb} \times 10}{\text{RBC (millions)}}$$

MCHC

- MCHC is average hemoglobin concentration per RBC
- $\text{MCHC} = \frac{\text{Hgb} \times 100}{\text{Hct (\%)}}$
- If MCHC is normal, cell described as ***Normochromic***
- If MCHC is less than normal, cell described as ***Hypochromic***
- There are no ***Hyperchromic*** RBCs

RDW

- An index of RBC size variation
- May be used to quantitate the amount of anisocytosis on peripheral blood smear
- Normal range is 11.5% to 14.5% for both men and women.

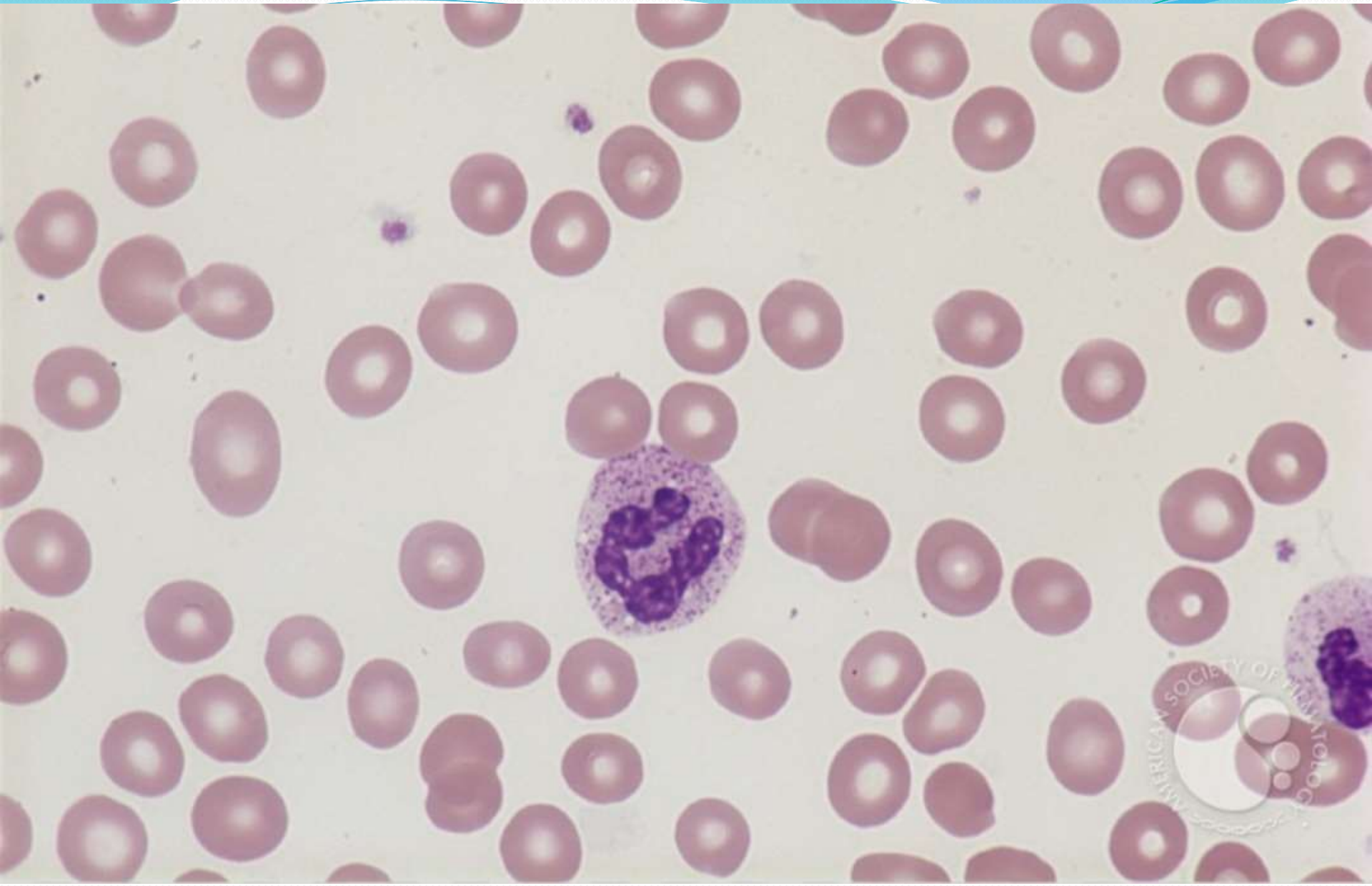
***MPV*:** The MPV is a measure of the average volume of platelets in a sample and is analogous to the erythrocytic MCV.

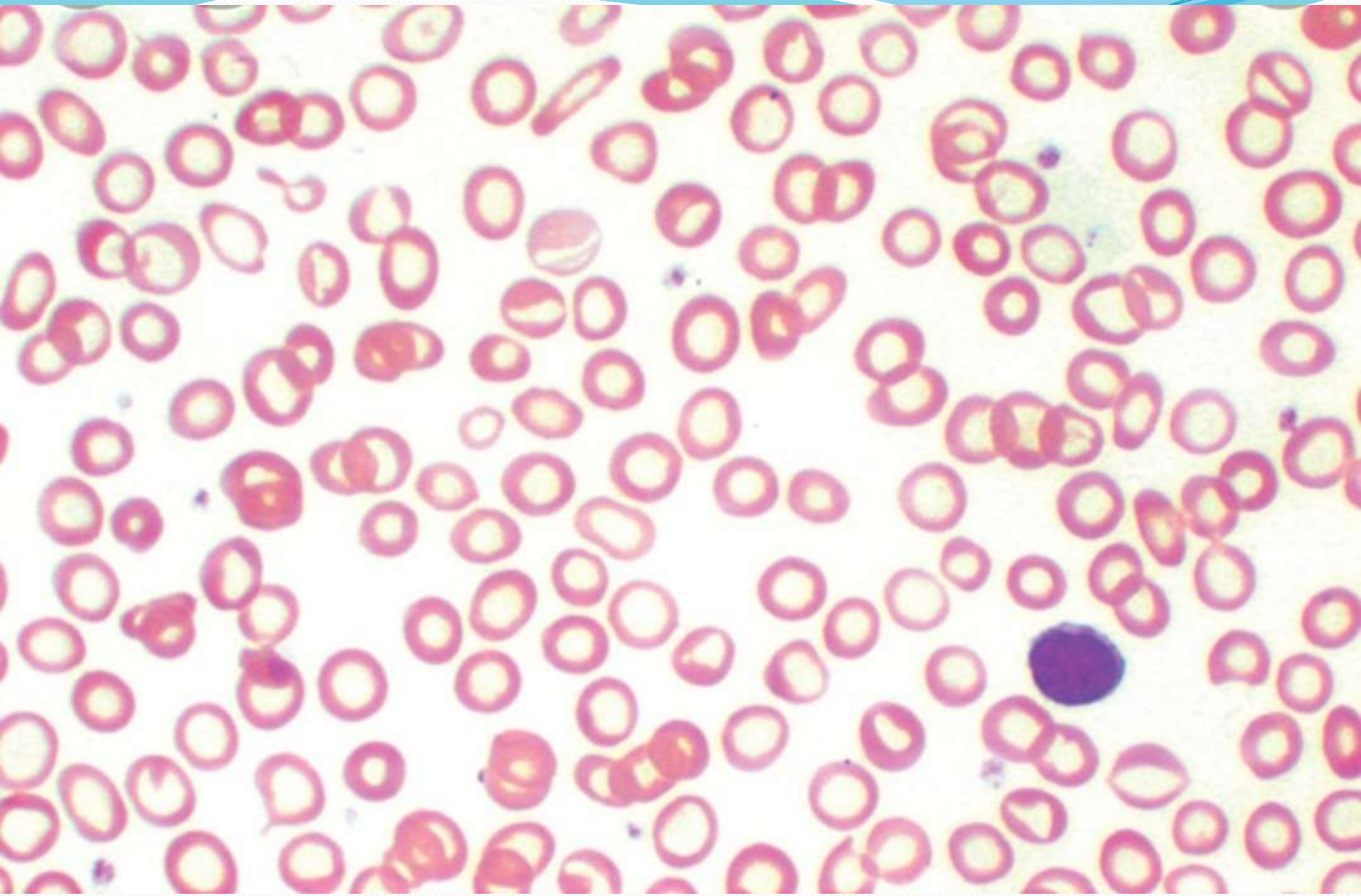
***Pct* :** analogues to HCT for RBCs

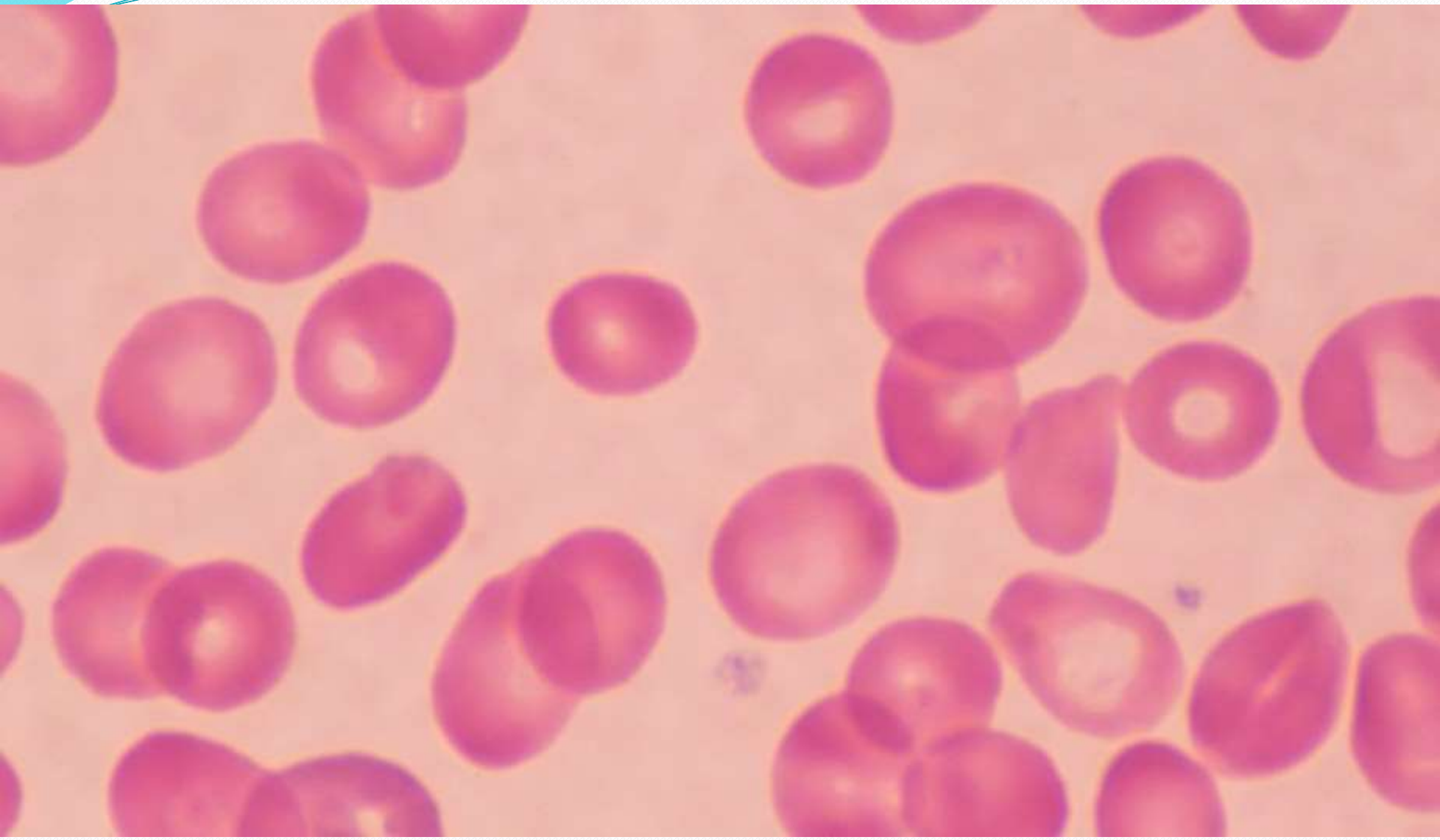
Platelet Count

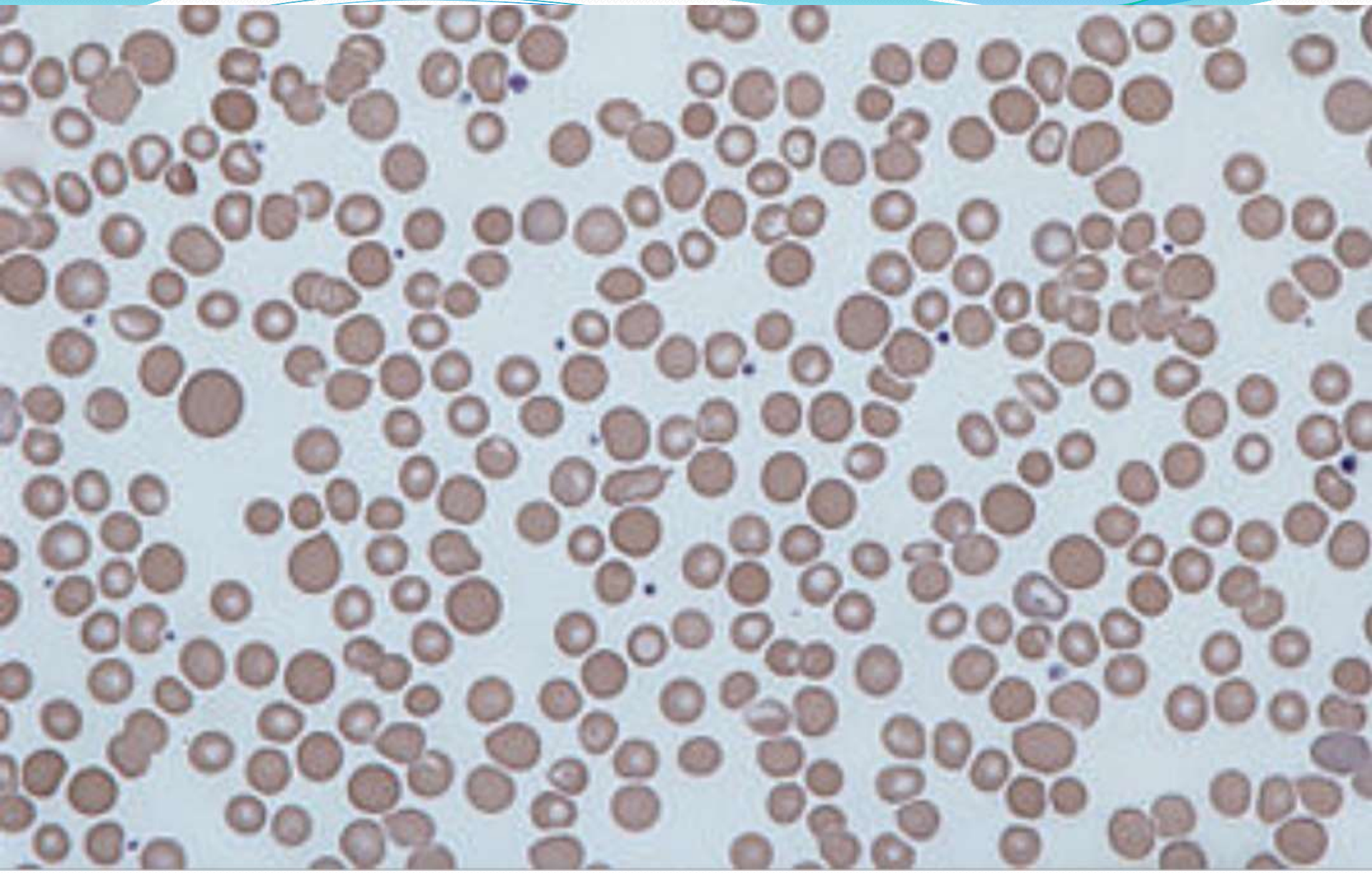
- Normal Range = 150 to 450 x 10^3 cells/μL
- ***Thrombocytosis***
  - inflammatory disorders
  - myeloproliferative states
  - acute blood loss
  - hemolytic anemias
  - carcinomatosis
  - status post-splenectomy
  - exercise etc.

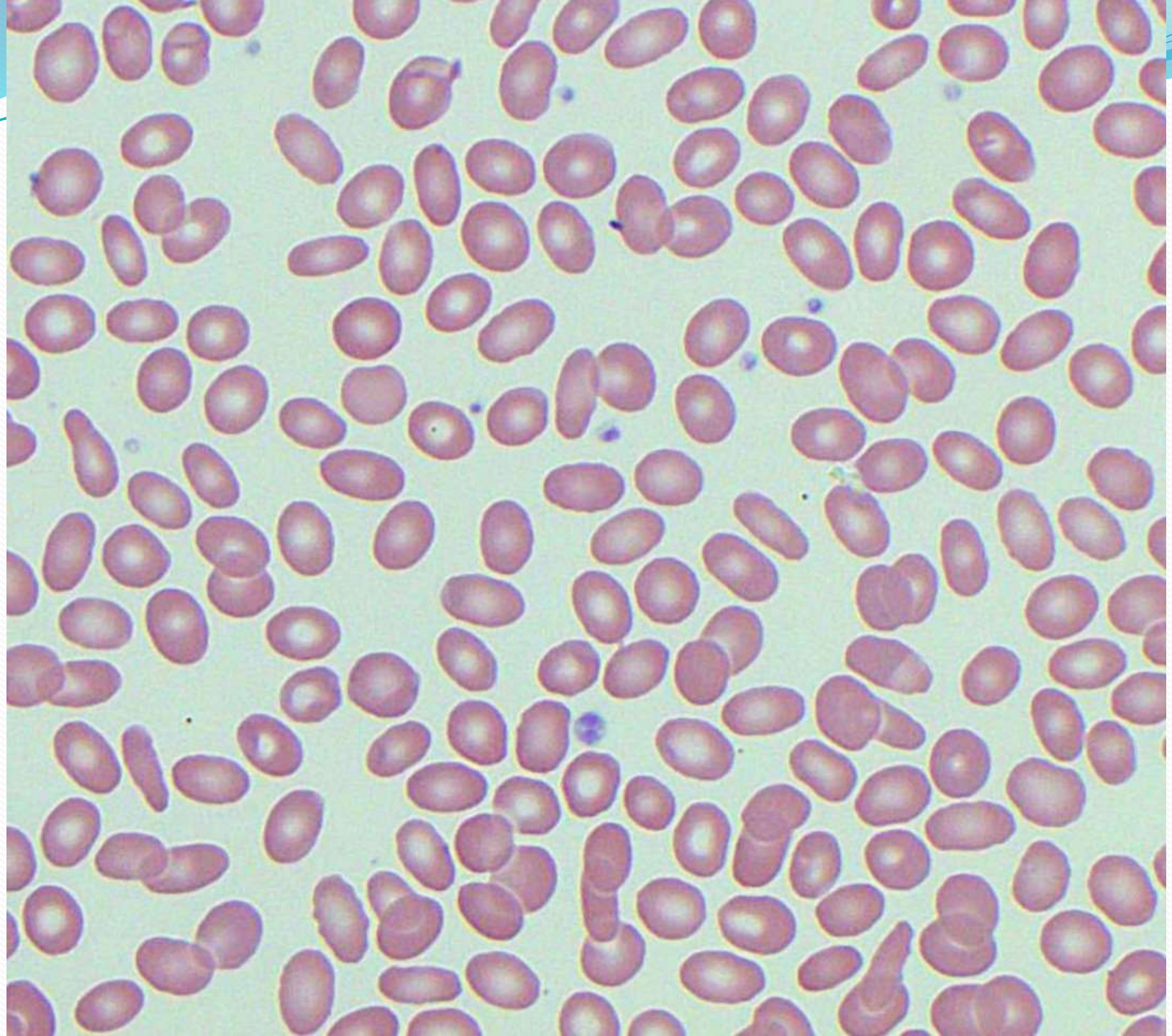
- ***Thrombocytopenia***
  - Production defects such as aplastic anemia, marrow replacement, megaloblastic and severe iron deficiency anemias, uremia etc.
  - Consumption defects with autoimmune thrombocytopenias, DIC, hypersplenism, massive hemorrhage and many severe infections.

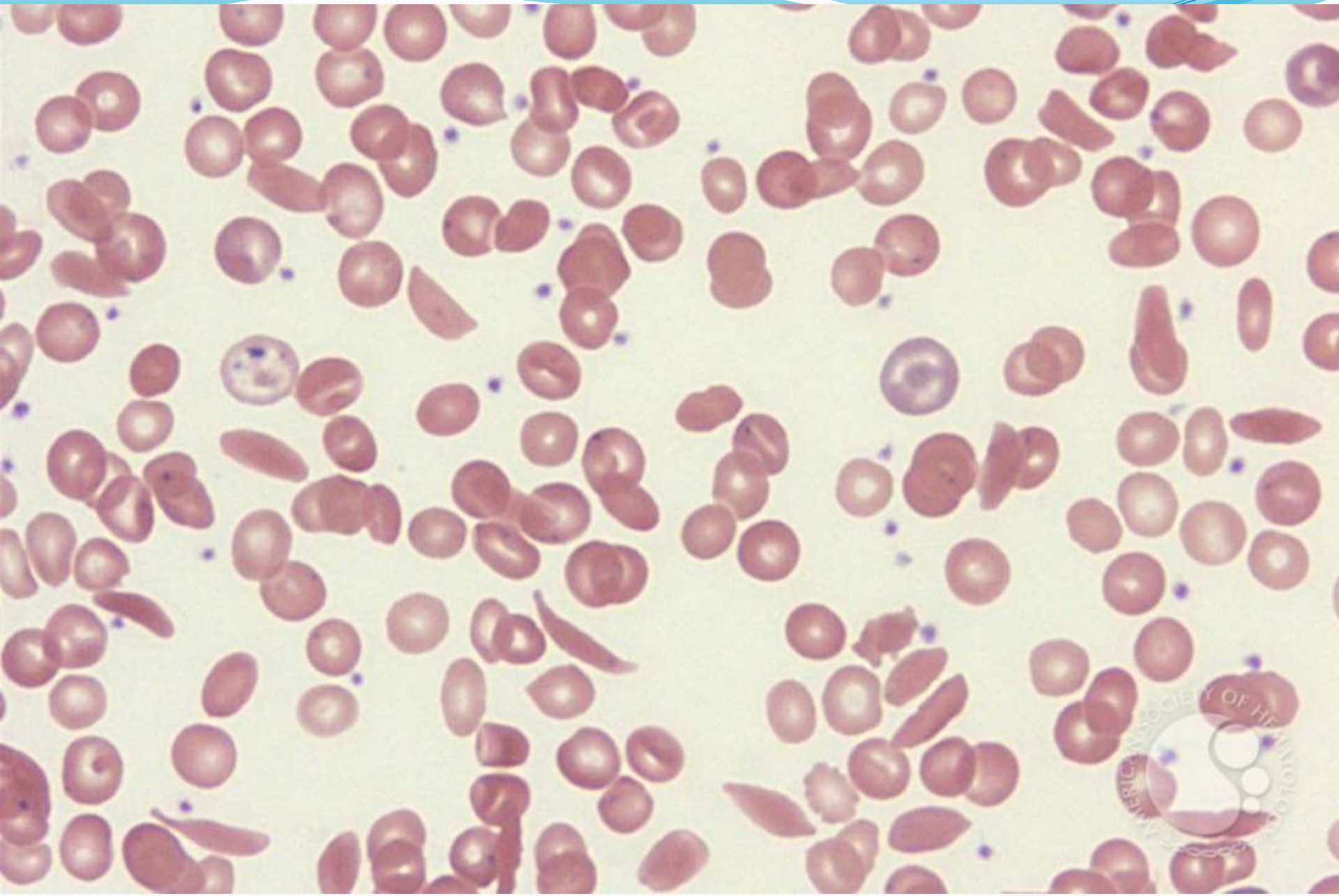












RED BLOOD CELL MORPHOLOGY

Size variation

- Normal
- Microcyte
- Macrocyte
- Oval macrocyte
- Hypochromic macrocyte

Hemoglobin distribution

- Hypochromia
  - 1+
  - 2+
  - 3+
  - 4+
- Polychromasia
  - (Reticulocyte)

Shape variation

- Target cell
- Acanthocyte
- Spherocyte
- Helmet cell (fragmented cell)
- Ovalocyte
- Schistocyte (fragmented cell)
- Stomatocyte
- Tear drop
- Sickle cell
- Burr cell

Inclusions

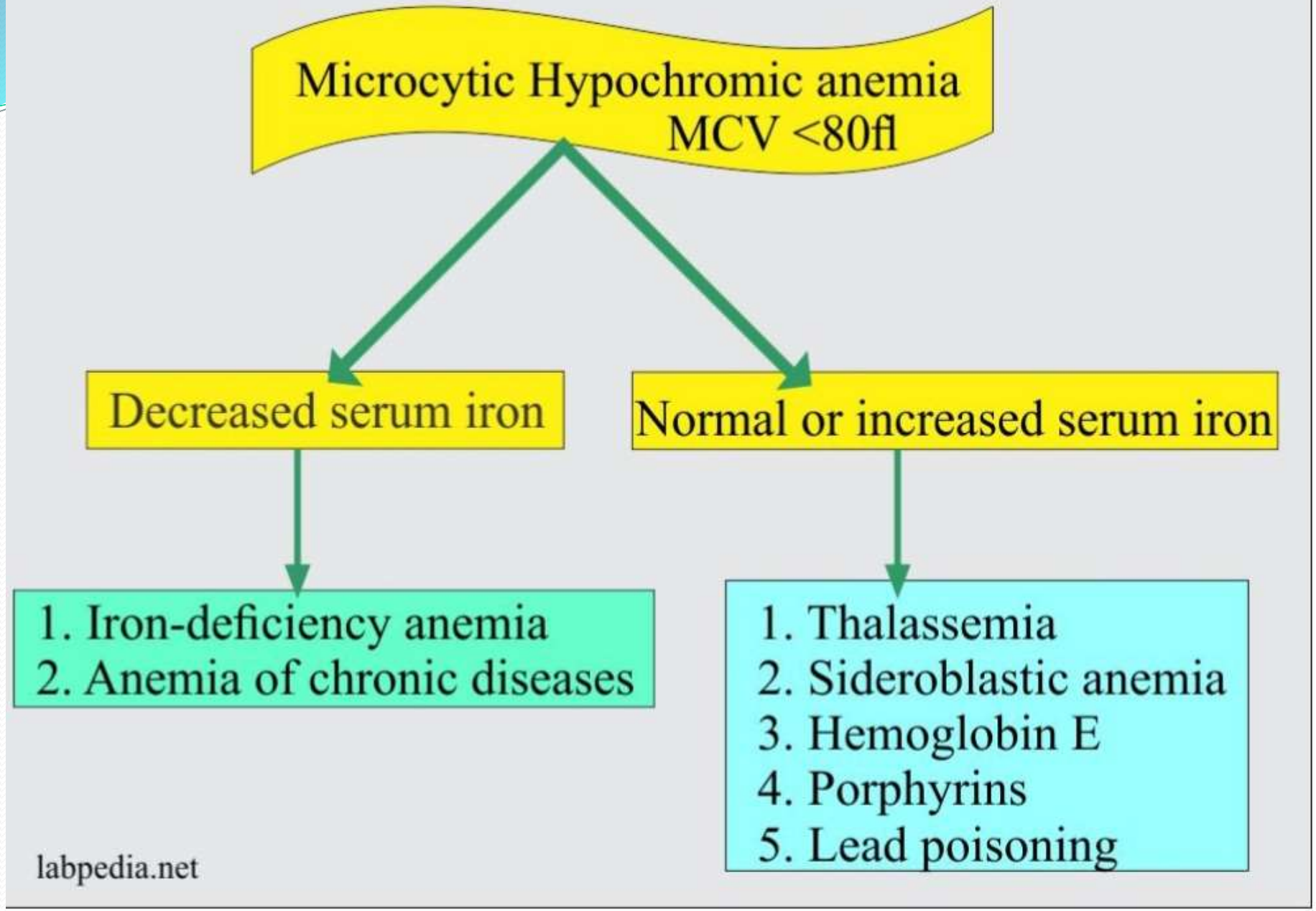
- Pappenheimer bodies (siderotic granules)
- Cabot's ring
- Basophilic stippling (coarse)
- Howell-Jolly

Red cell distribution

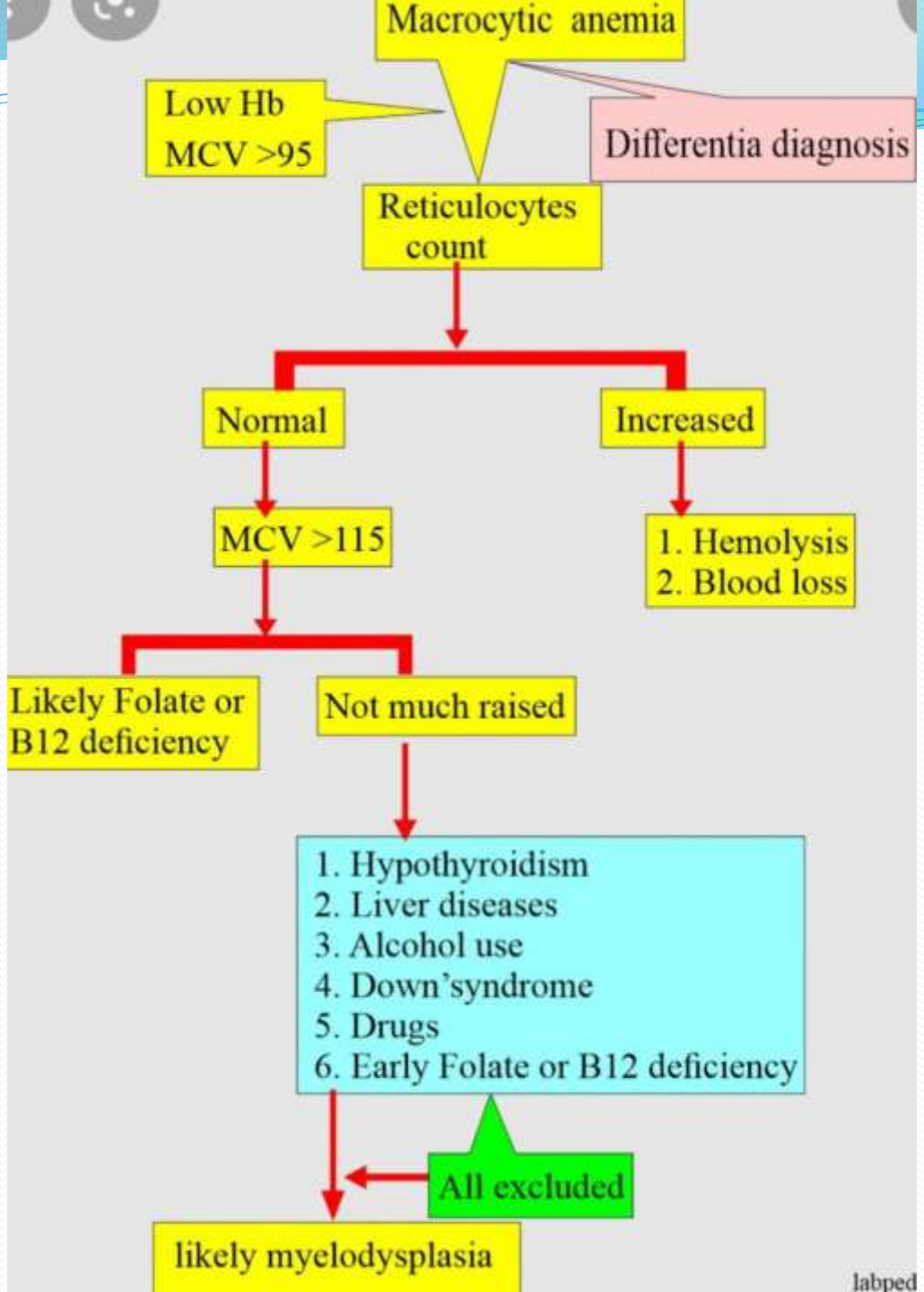
- Agglutination
- Rouleaux

Crystal formation

- HbSC
- HbC



Causes of Iron Deficiency Anemia


Macrocytic anemia
Low Hb
MCV >95
Differentia diagnosis
Reticulocytes count
Normal
Increased
MCV >115
1. Hemolysis
2. Blood loss
Likely Folate or B12 deficiency
Not much raised
1. Hypothyroidism
2. Liver diseases
3. Alcohol use
4. Down'syndrome
5. Drugs
6. Early Folate or B12 deficiency
All excluded
likely myelodysplasia
labped

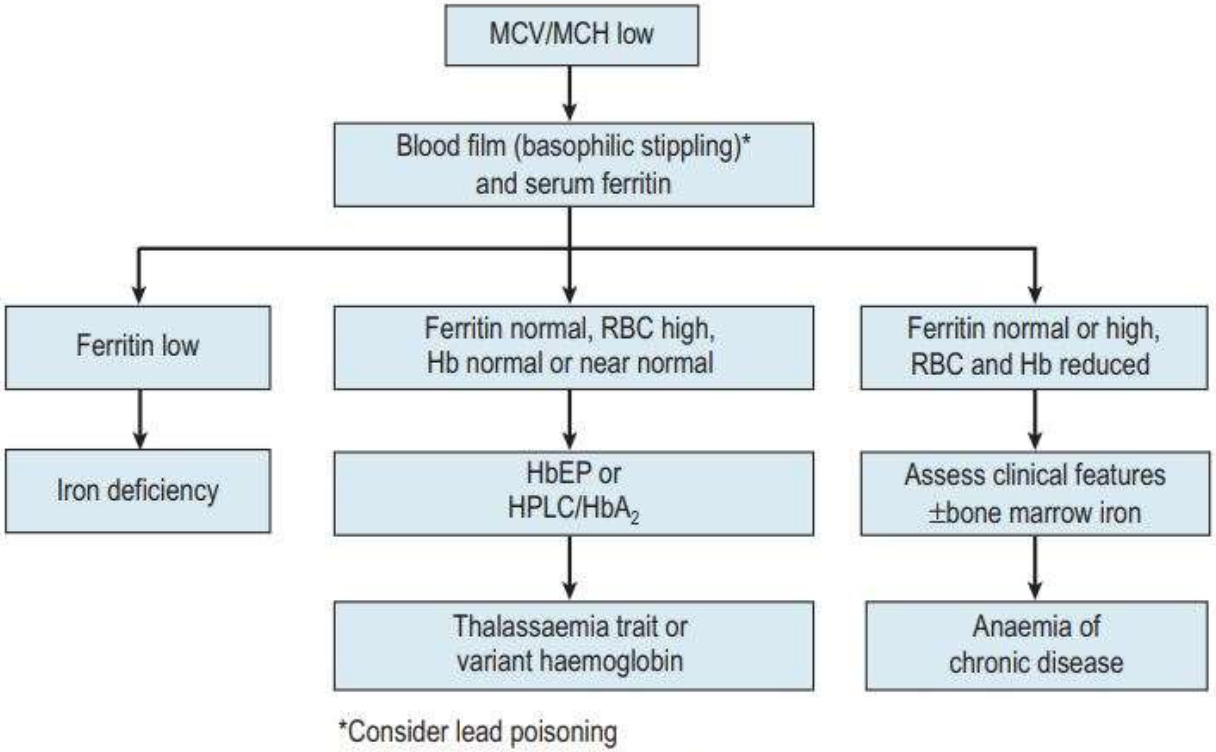


FIGURE 23-1 Investigation of a microcytic hypochromic anaemia. HbEP, haemoglobin electrophoresis; HPLC, high performance liquid chromatography.

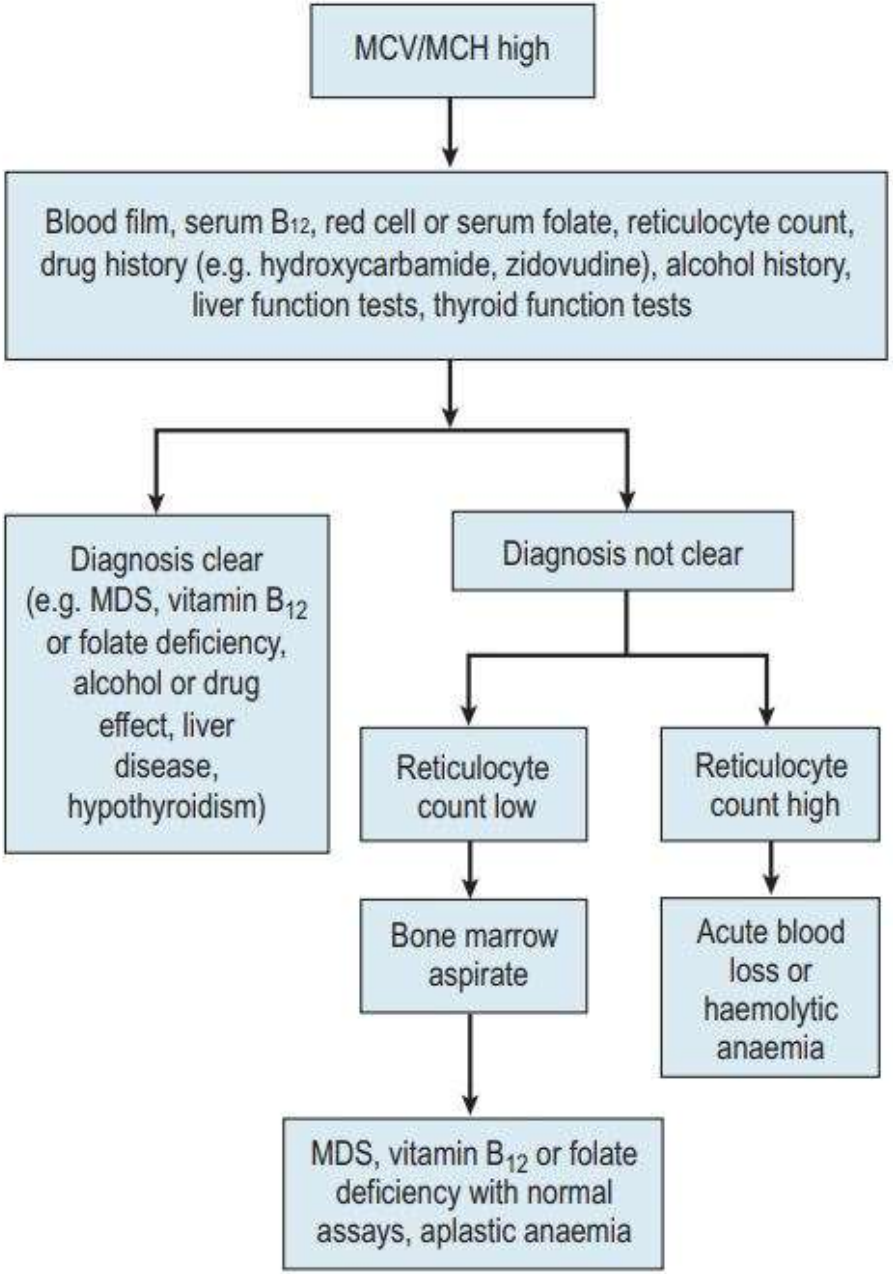


FIGURE 23-2 Investigation of a macrocytic anaemia. MDS, myelodysplastic syndrome.

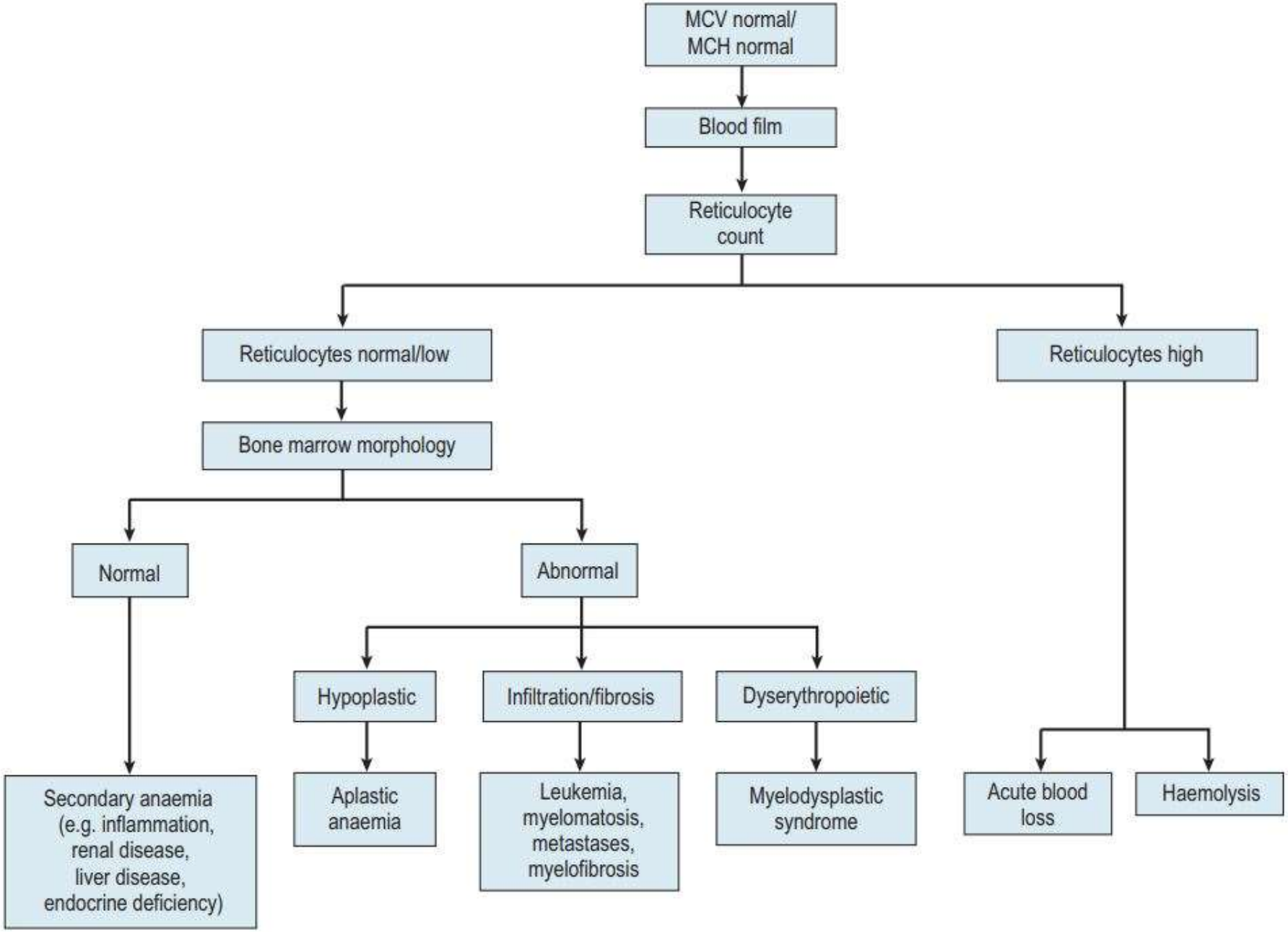


FIGURE 23-3 Investigation of a normocytic, normochromic anaemia.

LEUKOCYTIC DISORDERS

NONNEOPLASTIC DISORDERS

Ref : Henry's Clinical Diagnosis and Management by Laboratory Methods 22nd Edition

WBC

Leukocytes, or white blood cells, are found within the **bone marrow** (BM), the **peripheral blood**, and the **tissues**. Leukocytes are among the essential elements of the **hematopoietic-lymphoreticular-immune system**, which functions to protect the human body from nonself cells (**infection**) and altered-self cells (**cancer**).

Neutrophilia

absolute concentration of neutrophils in the blood above normal for age.

Adults

1800-7000/µL

Children

1000-8500/µL

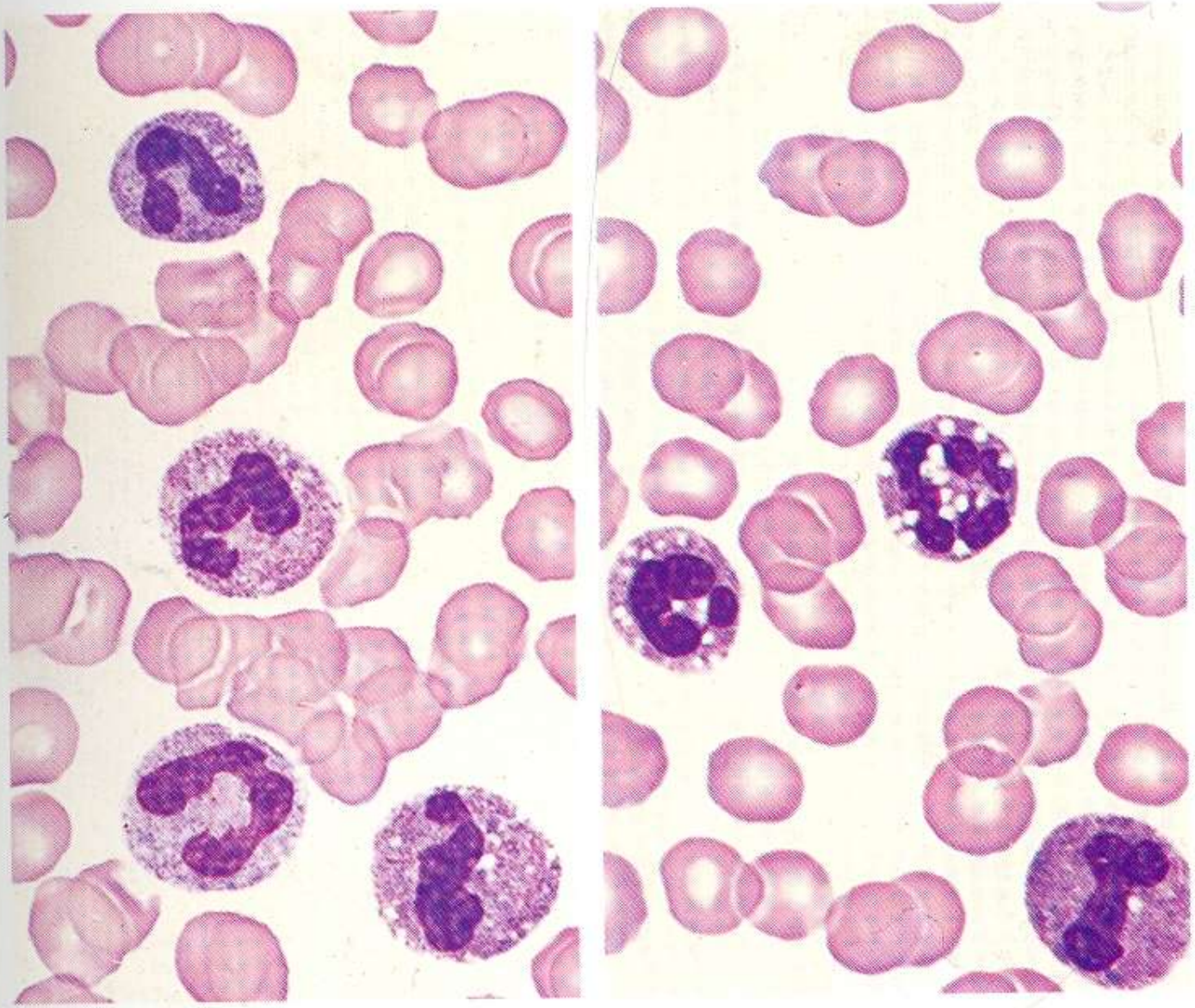


Fig. 7.9 Neutrophil leucocytosis: toxic changes in neutrophils include the presence of red-purple granules in the band-form neutrophils (left) and cytoplasmic vacuolation (right).

Mechanisms

(1) the **rate of inflow** of cells from the BM (mitosis/proliferation, maturation/storage, and release)

(2) the **proportion** of neutrophils in the **marginal (cells adhering to vessel walls) granulocyte pool (MGP) and the circulating (nonadhering cells) granulocyte pool (CGP)** of the blood

-MGP and CGP are approximately **equal in size** and in equilibrium in health

(3) the **rate of outflow** of neutrophils from the blood

(i.e., migration from and through vessels into tissue, both randomly and at sites of inflammation, infection, etc.).

Causes of Neutrophilia

- **Acute inflammatory**— collagen vascular, vasculitis
- **Acute infectious**— bacterial, some viral, fungal, parasitic
  - Children respond more intensely than adults
  - The more localized the process, the more pronounced is the neutrophilia
  - Pyogenic bacteria, especially, induce neutrophilia
- **Drugs, toxins, metabolic**—corticosteroids, growth factors, uremia, ketoacidosis, endotoxin , Interleukin-6
- **Tissue necrosis**—burns, trauma, MI, RBC hemolysis

gastrointestinal and hepatic tumors, HL, renal cell carcinoma, and metastatic BM disease

- **Physiologic**—hypoxia,stress, exercise, smoking, pregnancy ,injection of epinephrine,
- **Neoplastic**—carcinomas, sarcomas, myeloproliferative disorders

Neutropenia

reduction in the absolute neutrophil count (ANC)

below 1500-2000/μL for white adults

below 1200-1300/μL for black adults

agranulocytosis

has been used for severe neutropenia,

usually <500/µL

If the neutrophil count is less than 1000/µL, the risk of infection is considerably increased over normal

mechanisms

(1) Decreased flow of neutrophils from marrow into blood as a result of lack of production or ineffective production (i.e., a proliferation or maturation defect);

(2) increased removal of neutrophils from the blood (survival defect)

(3) altered distribution between CGP and MGP

(4) combinations of these mechanisms

Causes of Neutropenia

- **Drugs --**

cancer chemotherapy ,
chloramphenicol,
sulfas/other antibiotics ,
phenothiazines,
benzodiazepine ,
antithyroids,
anticonvulsants ,
quinine,
quinidine,
indomethacin,
procainamide,
thiazides

Causes of Neutropenia

- **Radiation**

Lymphocytes are most sensitive and are directly killed by exposure. The lymphocyte count correlates with, and has been used to assess, dose and severity of exposure .In addition, hematopoietic precursors undergoing mitosis are very sensitive to injury and death

- **Toxins—** alcohol, benzene compounds

Causes of Neutropenia

- **Intrinsic defects**

----myeloid hypoplasia or a proliferation defet :

- **Fanconi's anemia (FA)** aplastic anemia and congenital physical malformations,
- **Kostmann's syndrome,** infantile genetic agranulocytosis
- **Schwachman-Diamond syndrome,**
- **Cyclic neutropenia ;** recurrent episodes of symptomatic infection (fatigue, mouth ulcers, cervical lymphadenopathy, fever) due to cyclic episodes of severe neutropenia
- **Males with X-linked agammaglobulinemia (XLA)**
- **Two most common causes of congenital neutropenia** ; neutropenia of pregnancy-induced hypertension (PIH—most common) and overwhelming bacterial infection

----maturation defects :

- **Myelokathexis**
- **Chediak-Higashi syndrome**

Causes of Neutropenia

- **Immune-mediated—collagen vascular disorders, RA, AIDS**
- **Hematologic—megaloblastic anemia, myelodysplasia, marrow failure, marrow replacement**
- **Infectious—any overwhelming infection(**Salmonella infections, measles and rubella , hepatitis, infectious mononucleosis, and influenza)
- **Others—starvation(**a morphologic marrow change termed serous fat atrophy or gelatinous transformation of the BM)**,**

  hypersplenism(congestive splenomegaly, Felty's syndrome, Gaucher's disease, and lymphoma.)

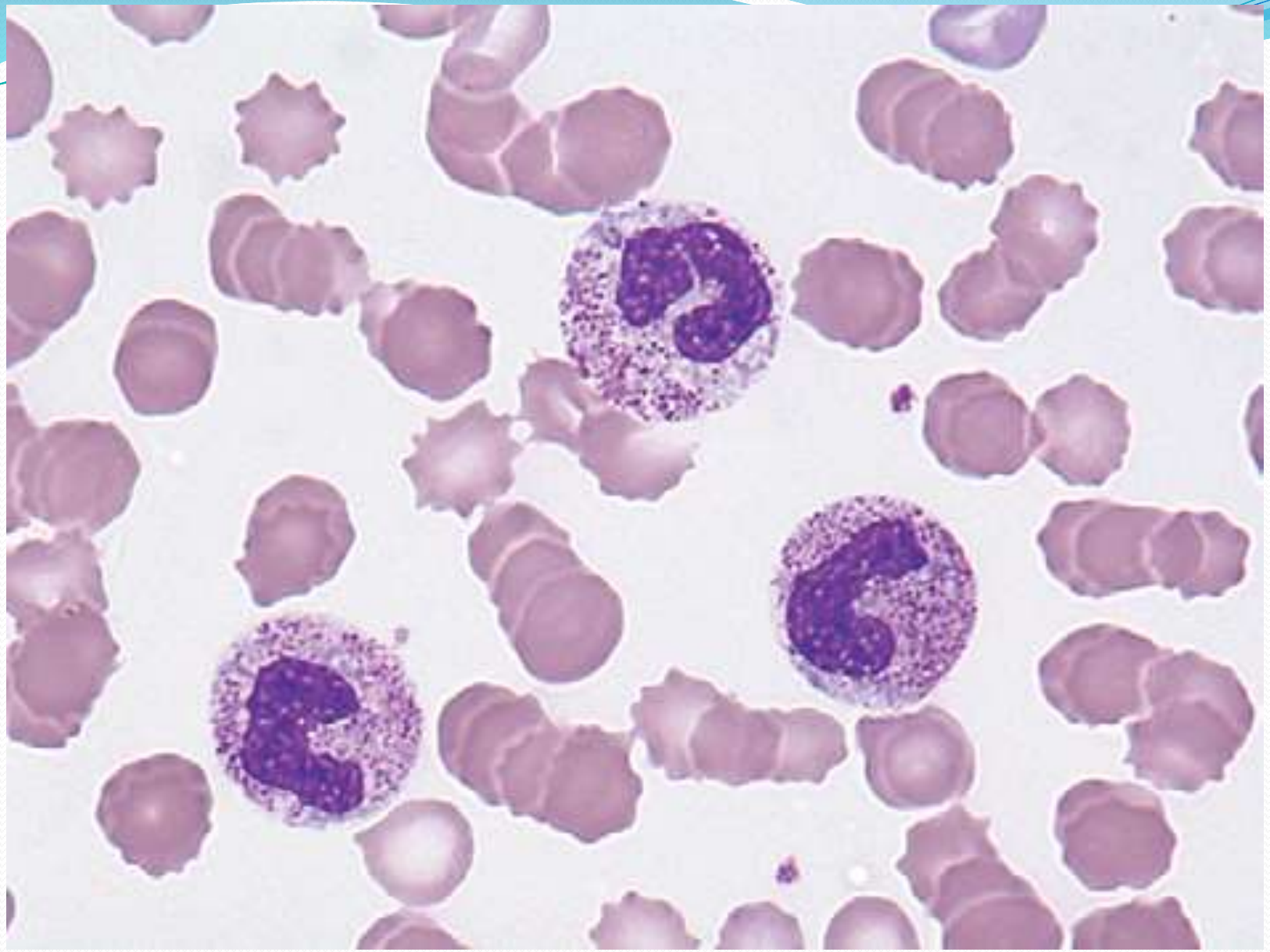
Morphologic Alterations in Neutrophils

Toxic granulation—

azurophilic cytoplasmic granules seen in severe infections, other toxic conditions, and reactive conditions

Döhle bodies—

pale blue, oval cytoplasmic remnants of ribosomes seen in infection and other toxic conditions

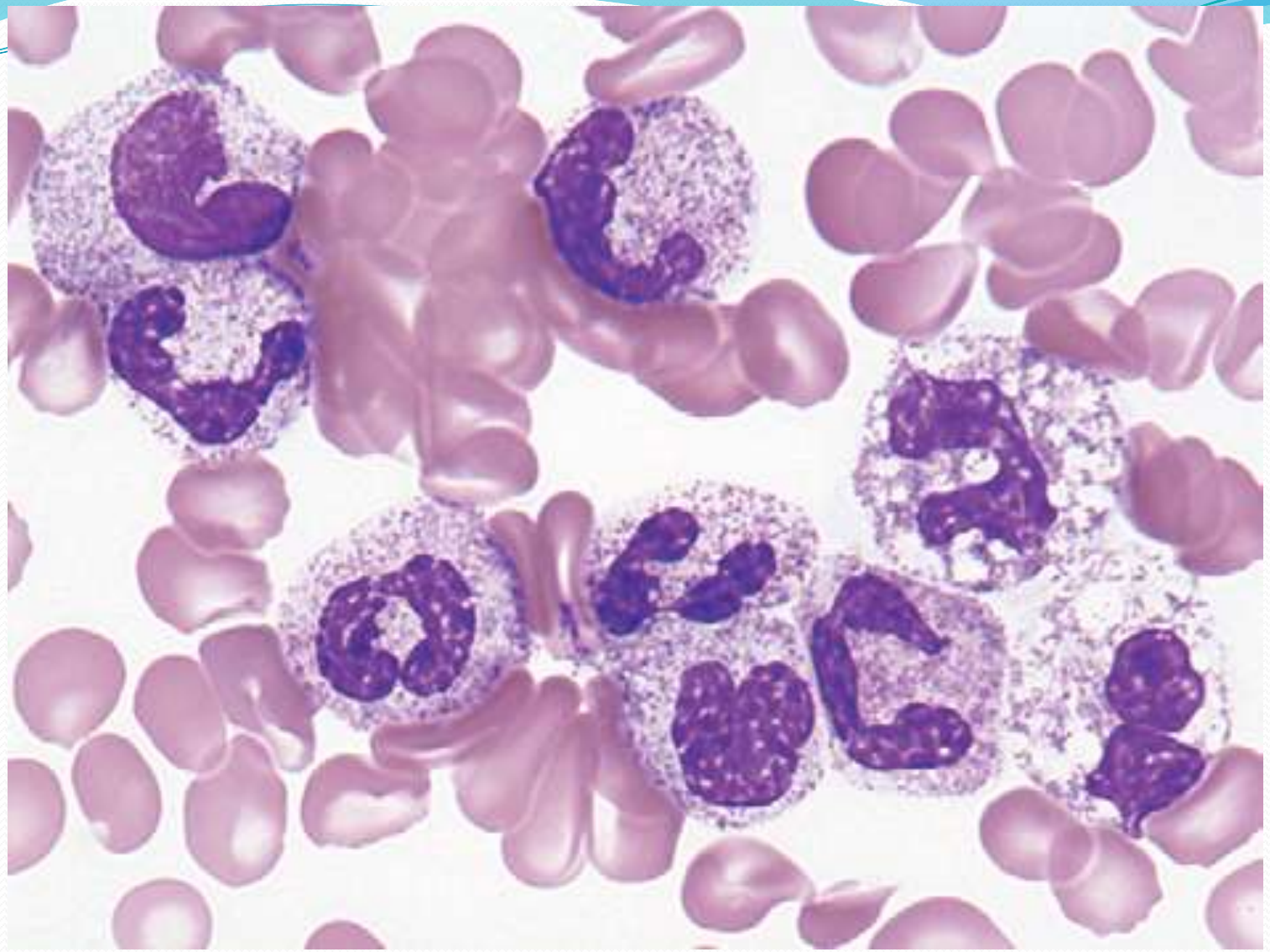


Toxic granulation & Basophilic inclusions (Döhle bodies)

Morphologic Alterations in Neutrophils

Cytoplasmic vacuoles—

Seen in infection, indicating phagocytosis



Leukemoid toxic neutrophilia with left shift and toxic vacuolization

Morphologic Alterations in Neutrophils

May-Hegglin anomaly—

Rare autosomal dominant condition with

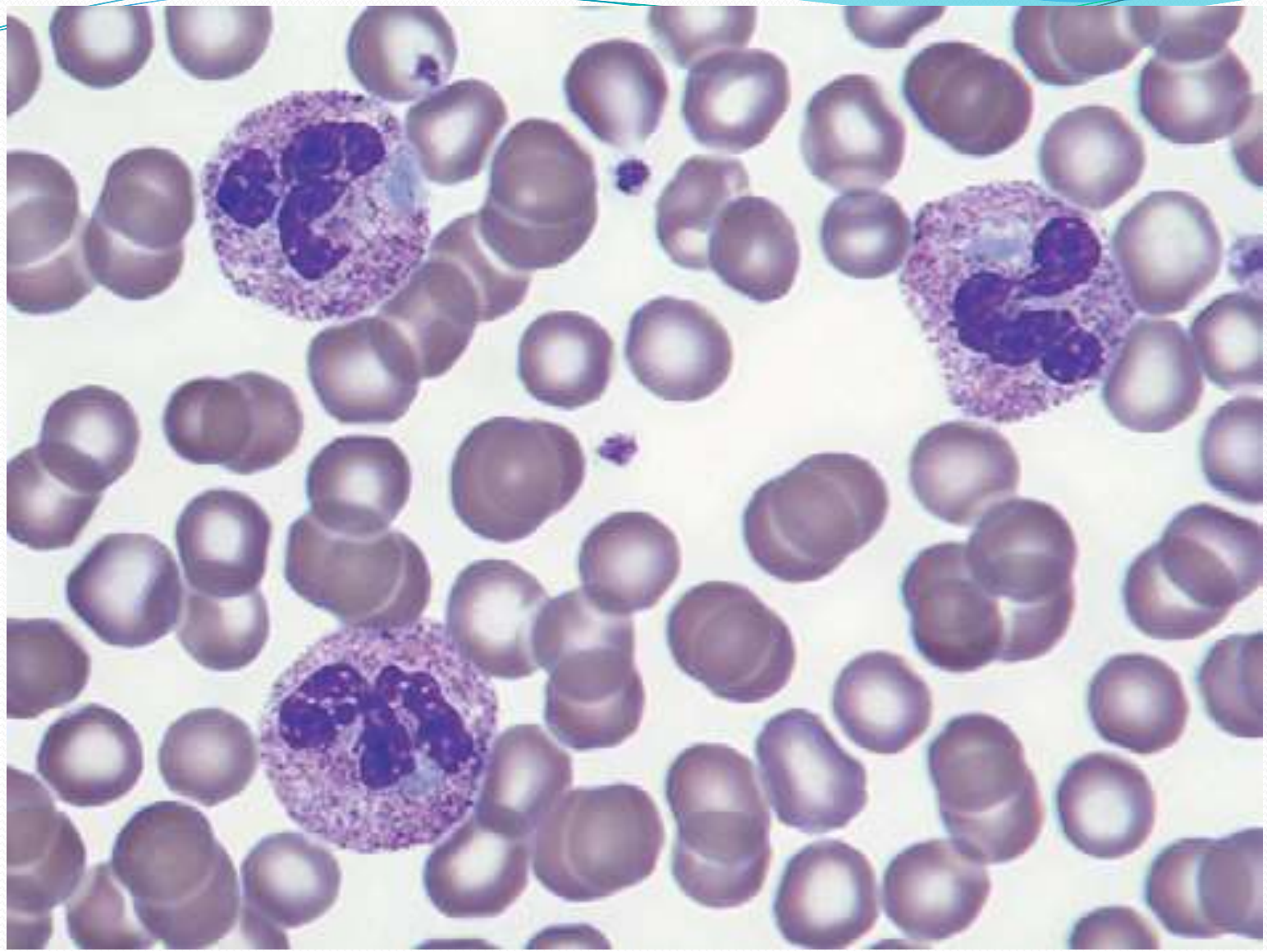
pale blue cytoplasmic ribosomal inclusions

resembling Döhle bodies

giant platelets, and, in some persons, by thrombocytopenia

suggesting structural alterations in RNA and ribosomes

Granulocyte function is normal



May-Hegglin anomaly, showing Döhle-like inclusions

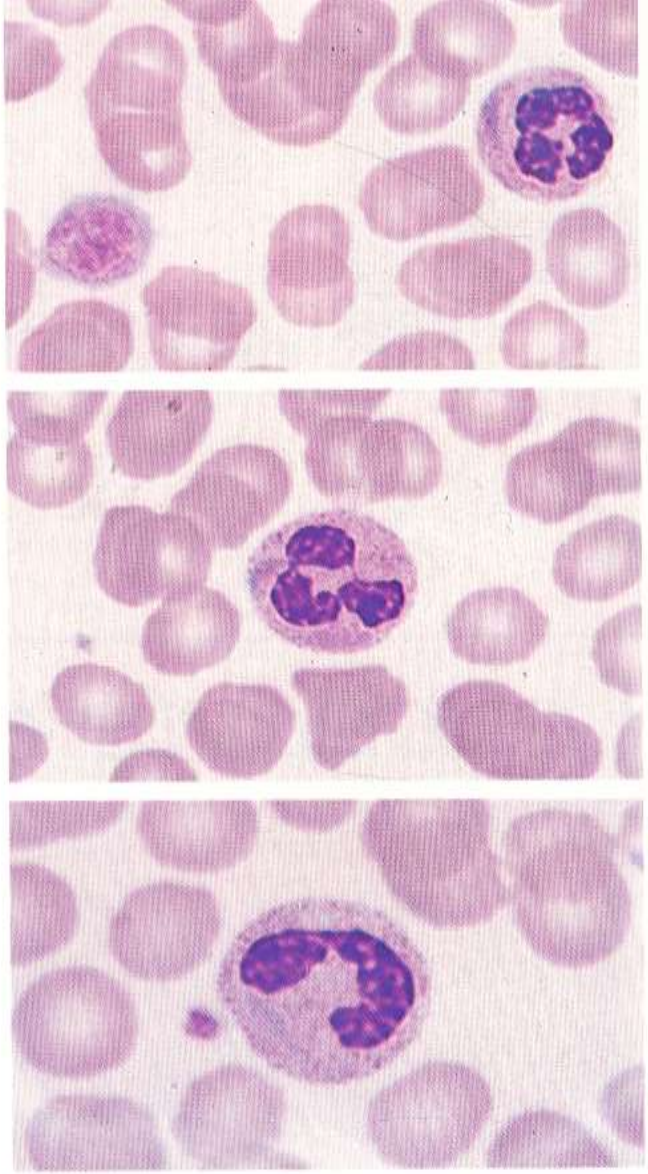


Fig. 7.2 May–Hegglin anomaly: the neutrophils contain basophilic inclusions 2–5μm in diameter. These inclusions are similar to Döhle bodies (see Fig. 7.10*) but are not related to infection. There is an associated mild thrombocytopenia with giant platelets (upper).*

Morphologic Alterations in Neutrophils

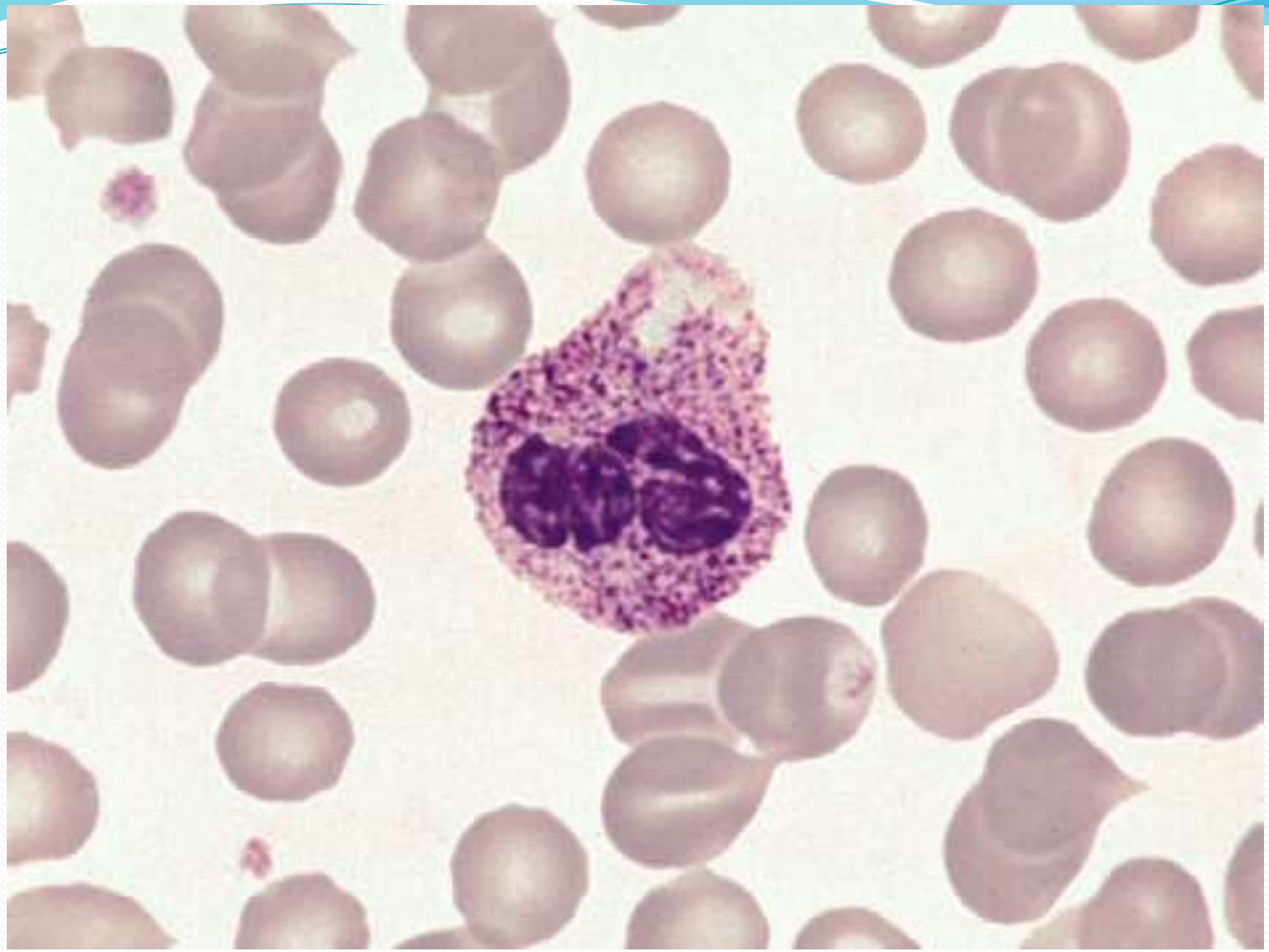
Alder-Reilly anomaly—

resemble toxic granulation

prominent azurophilic granulation not related to Infection

is not transient

patients with gargoylism, Hurler's syndrome, or, more generally, the genetic mucopolysaccharidoses



The Alder-Reilly anomaly may be found in healthy individuals or in those with mucopolysaccharidoses, in which granules are metachromatic