Aplastic Anemia

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Learning Objectives

- By the end of this lecture the students will be able to:
- Enumerate causes of Aplastic anemia
- Describe the pathophysiology of aplastic anemia
- Diagnose a case of aplastic anemia

- A syndrome of chronic primary hematopoietic failure
- Pancytopenia (anemia, neutropenia, and thrombocytopenia)

ETIOLOGY:

- Majority of the cases are idiopathic (65%)
- Exposure to chemicals and drugs
- Persistent marrow aplasia may occur following viral infection

- Whole-body irradiation destroy HSC
- Inherited defects such as Fanconi anemia is a rare autosomal recessive disorder
- Inherited defects in telomerase also seen adult-onset aplastic anemia

Acquired	
Idiopatic	
Secondary	Irradiation Drugs and chemical: cytotoxic agents, benzene, chloramphenicol, gold salts, nonsteroidal anti-inflammatory drugs Idiosyncratic reactions Viruses: Epstein-Barr virus, hepatitis virus unidentified, Parvovirus B19, HIV Immune diseases Pregnancy Paroxysmal nocturnal hemoglobinuria
Inherited aplastic anemia	Fanconi's anemia Dyskeratosis congenital Amegakaryocytic thrombocytopenia Shwachman-Diamond syndrome

Table 1. Classification of aplastic anemia

Pathogensis

- Not clear in majority cases

- Two major etiologies have been proposed

1. Extrinsic, immune-mediated suppression of marrow progenitors

2. Intrinsic abnormality of stem cells

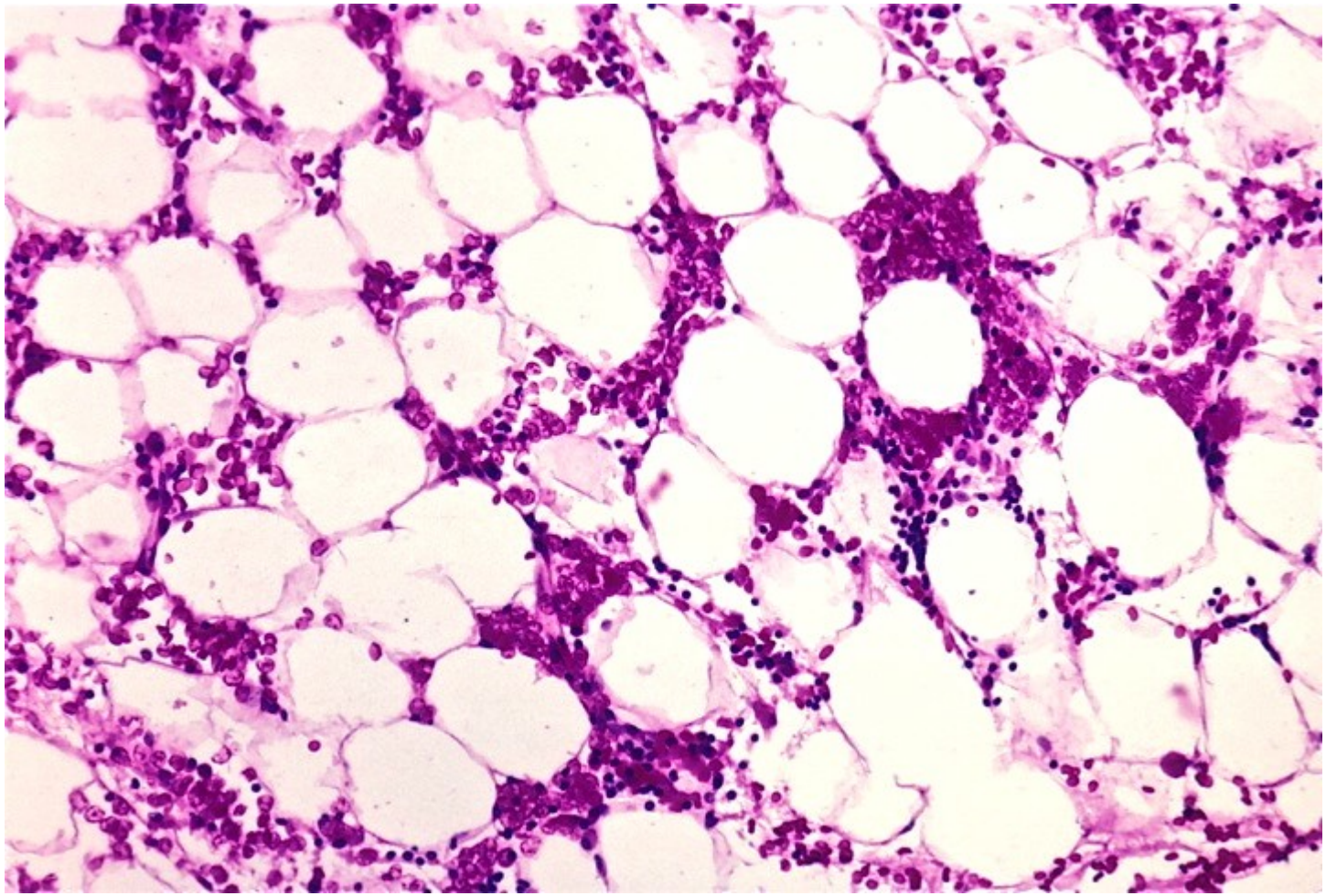
- Activated T cells suppress hematopoietic stem cells
- Initiating cellular immune response
- T_H1 cells are activated wich produce cytokines IFNγ and TNF
- Suppressing hematopoietic progenitors
- Genes involved in apoptosis are up-regulated

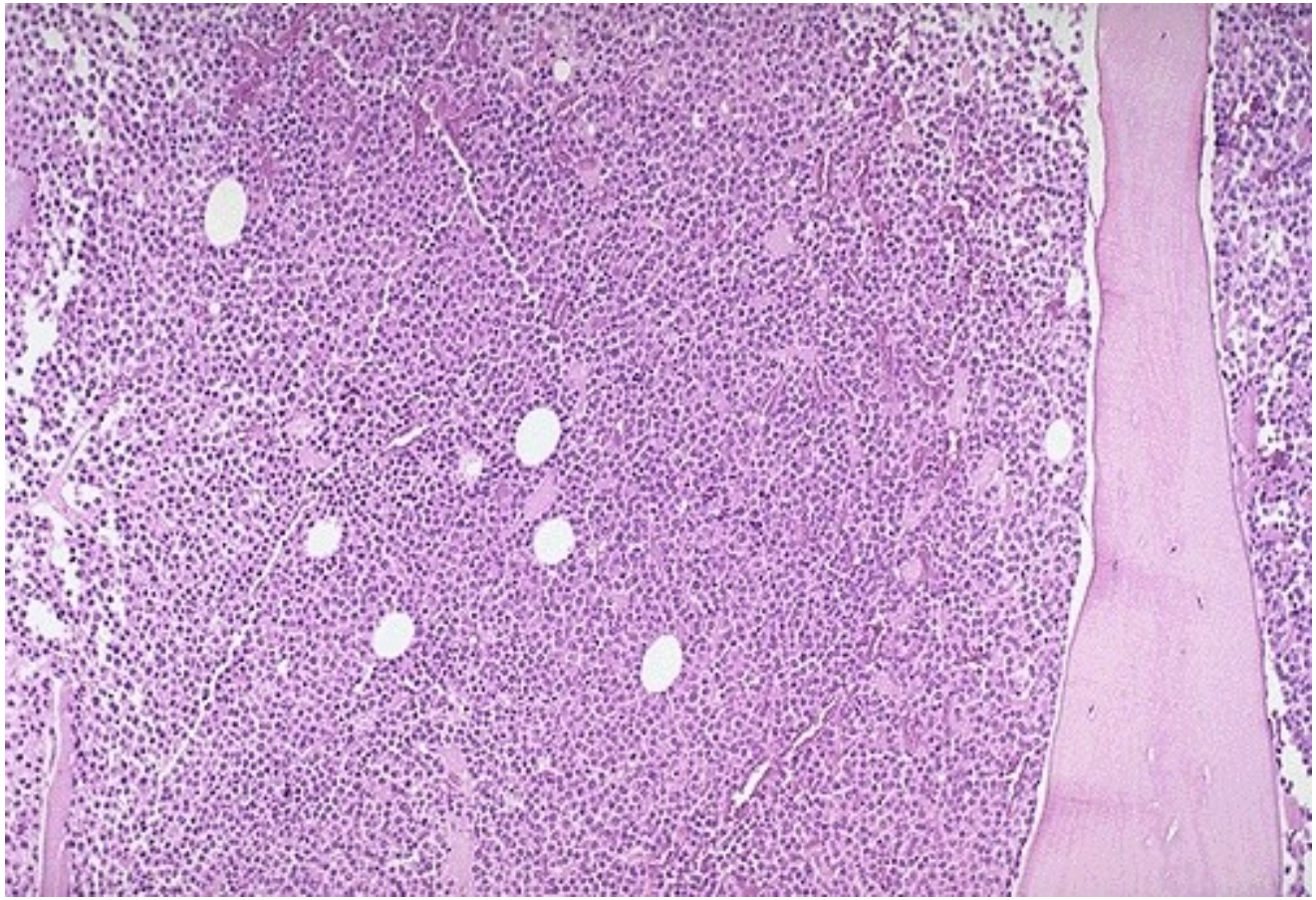
- The theory of intrinsic stem cell abnormality is supported by the presence of karyotypic aberrations

- Transformation of aplasias into myeloid neoplasms, typically myelodysplasia or acute myeloid leukemia and the association with short telomeres

Morphology

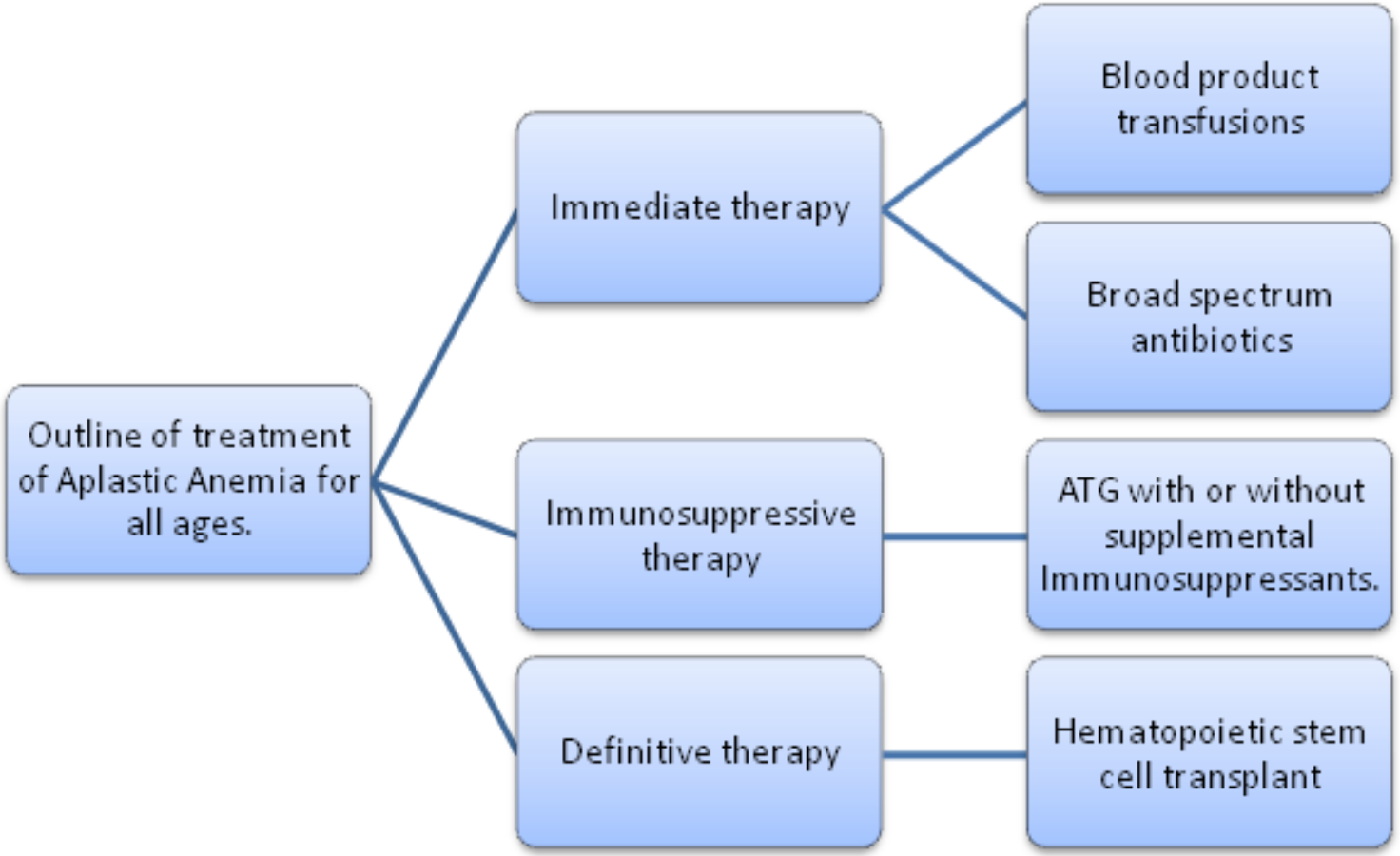
- Peripheral blood film show pancytopenia with marked neutropenia
- Retic count less than 0.5%
- Marrow is markedly hypocellular
- Increase in fatty spaces, fibrous stroma, and scattered lymphocytes and plasma cells remain
- Marrow aspirates often yield little or no material
- No Organomegaly
- No Lymphadenopathy





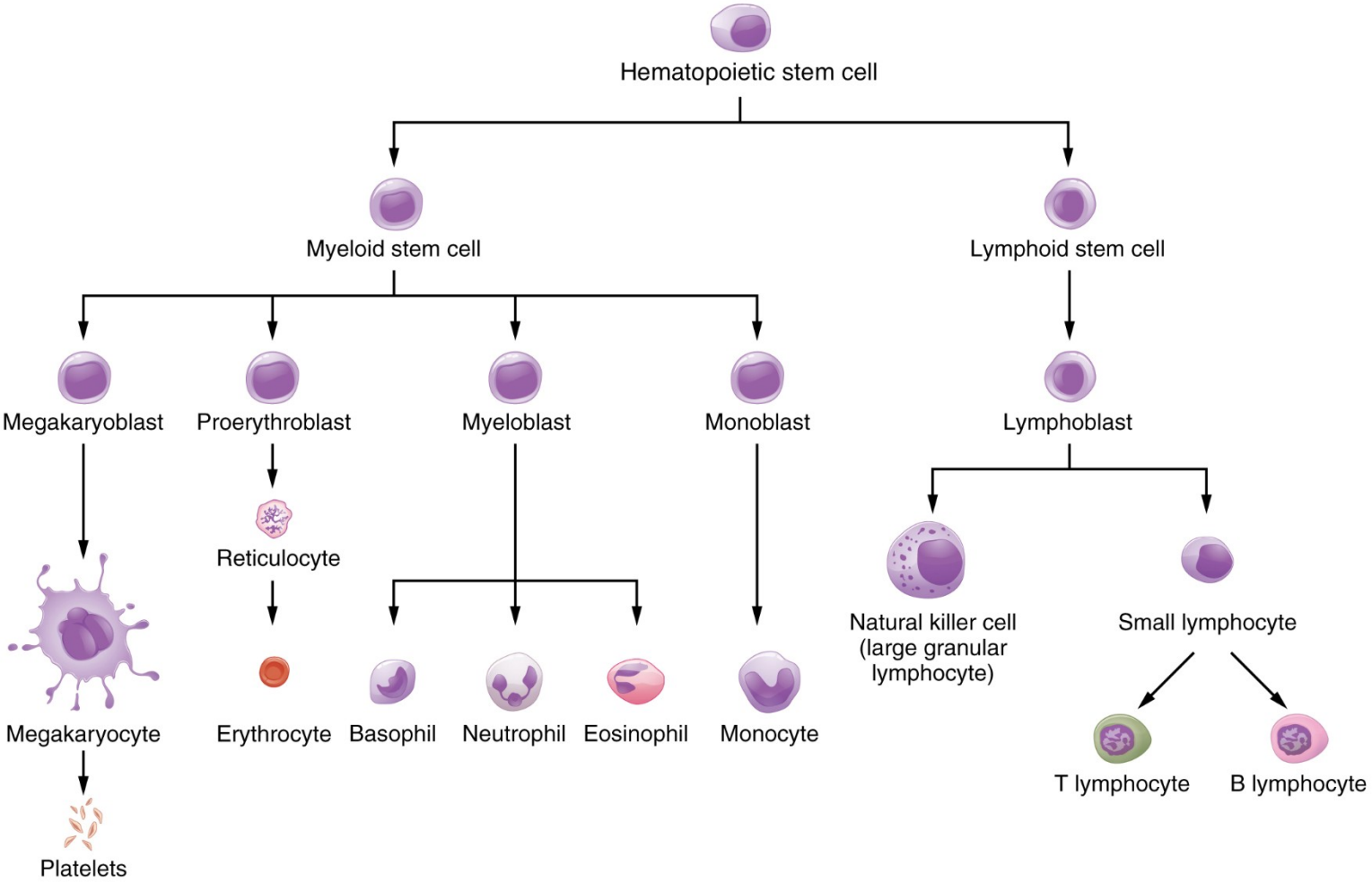
Clinical presentation

- Onset is usually insidious
- Anemia can cause progressive weakness, pallor, and dyspnea
- Thrombocytopenia presents as petechiae and ecchymoses
- Neutropenia manifests as frequent and persistent minor infections
- Splenomegaly is characteristically absent


Outline of treatment of Aplastic Anemia for all ages.
Immediate therapy
Blood product transfusions
Broad spectrum antibiotics
Immunosuppressive therapy
ATG with or without supplemental Immunosuppressants.
Definitive therapy
Hematopoietic stem cell transplant

- The prognosis is variable
- Bone marrow transplantation can give a cure with a suitable donor
- 5-year survival of over 75%
- Older patients or those without suitable donors often respond well to immunosuppressive therapy

Disorders of White blood cells


Hematopoietic stem cell
Myeloid stem cell
Lymphoid stem cell
Megakaryoblast
Proerythroblast
Myeloblast
Monoblast
Lymphoblast
Reticulocyte
Natural killer cell (large granular lymphocyte)
Small lymphocyte
Megakaryocyte
Erythrocyte
Basophil
Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Platelets

Adult Reference Ranges

Parameter	Adult Reference Range
WBC	4.5-11.0 X 10^3/µL
RBC	Male: 4.5-5.5 X 10^6 /µL Female: 4.0-5.0 X 10^6 /µL
HGB	Male: 14-17.4 g/dL Female: 12.0-16.0 g/dL
HCT	Male: 42-52% Female: 36-46%
MCV	80-100 fl
MCH	28-34 pg
MCHC	32-36 g/dL or %
RDW	12.0-14.6%
PLT	150-450 X 10^3 /µL
MPV	6.8-10.2 fl

Disorders of WBCs

- Disorders of white blood cells can be classified into two broad categories:

1. Proliferative disorders, in which there is an expansion of leukocytes
2. Leukopenias, which are defined as a deficiency of leukocytes.

Leukopenia

- Number of circulating white cells may be decreased in a variety of disorders
- Most Common is neutropenia or granulocytopenia
- Lymphopenia is less common Conditions associated with variety of conditions
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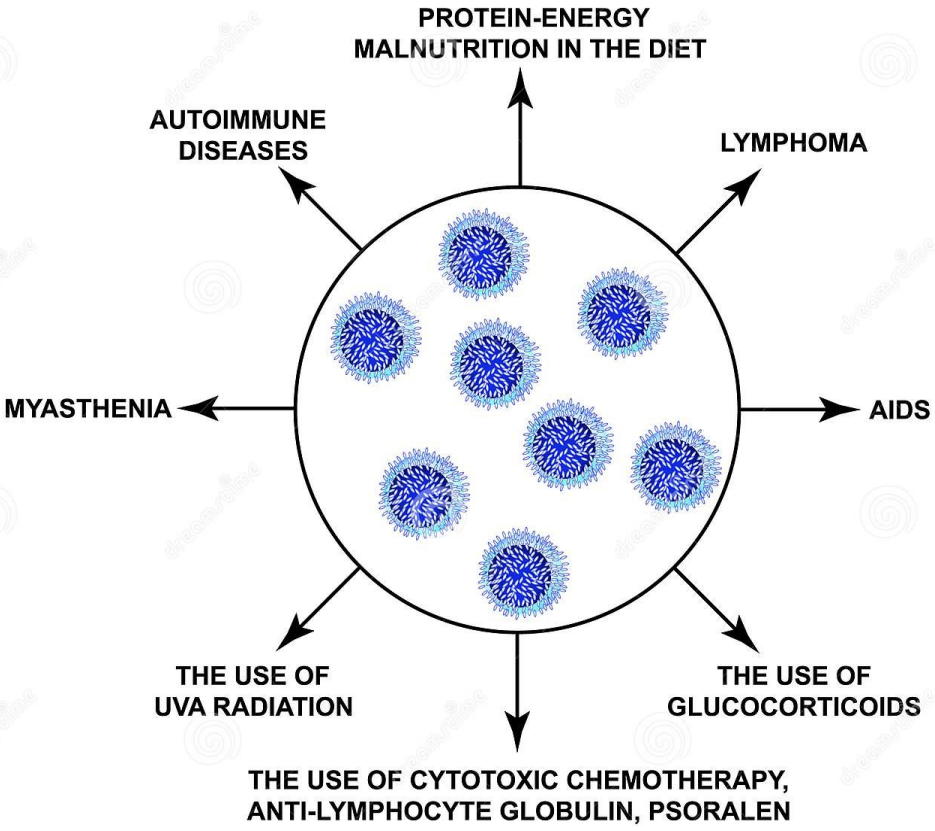
CAUSES OF LYMPHOCYTOPENIA



Neutropenia

- Neutropenia, a reduction in the number of neutrophils in the blood
- > 1500/cmm

- Agranulocytosis clinically significant reduction in neutrophils making individuals susceptible to bacterial and

Pathogenesis

- A reduction in circulating granulocytes will occur

1) Reduced or ineffective production of neutrophils

2) Accelerated removal of neutrophils from the circulating blood

1. Inadequate or ineffective granulopoiesis

A. Suppression of myeloid stem cells:

Aplastic anemia and a variety of infiltrative marrow disorders (tumors etc)

B. Suppression of granulocytic precursors :

Exposure to certain drugs like alkylating agents and antimetabolites used in cancer treatment

C. Diseases associated with ineffective granulopoiesis: Megaloblastic anemias, myelodysplastic syndromes

D. Rare inherited conditions: Kostmann syndrome genetic defects in specific genes result in impaired granulocytic differentiation.

2. Accelerated removal or destruction of

neutrophils

A . Immunologically mediated

- may be idiopathic
- Associated with an immunologic disorder (e.g. SLE)
- Exposure to drugs

B. Splenic sequestration.. Excessive destruction due to enlarge spleen

C. Increased peripheral utilization such as bacterial, fungal, or rickettsial infections.

- Eosnionpenia:

Normally 2 to 3 percent

Causes:

- Stress
- Acute shock
- Major pyogenic infection
- Truma and surgery
- Endocrine causes:ACTH, Epinephrine
- Drugs: Corticosteroid

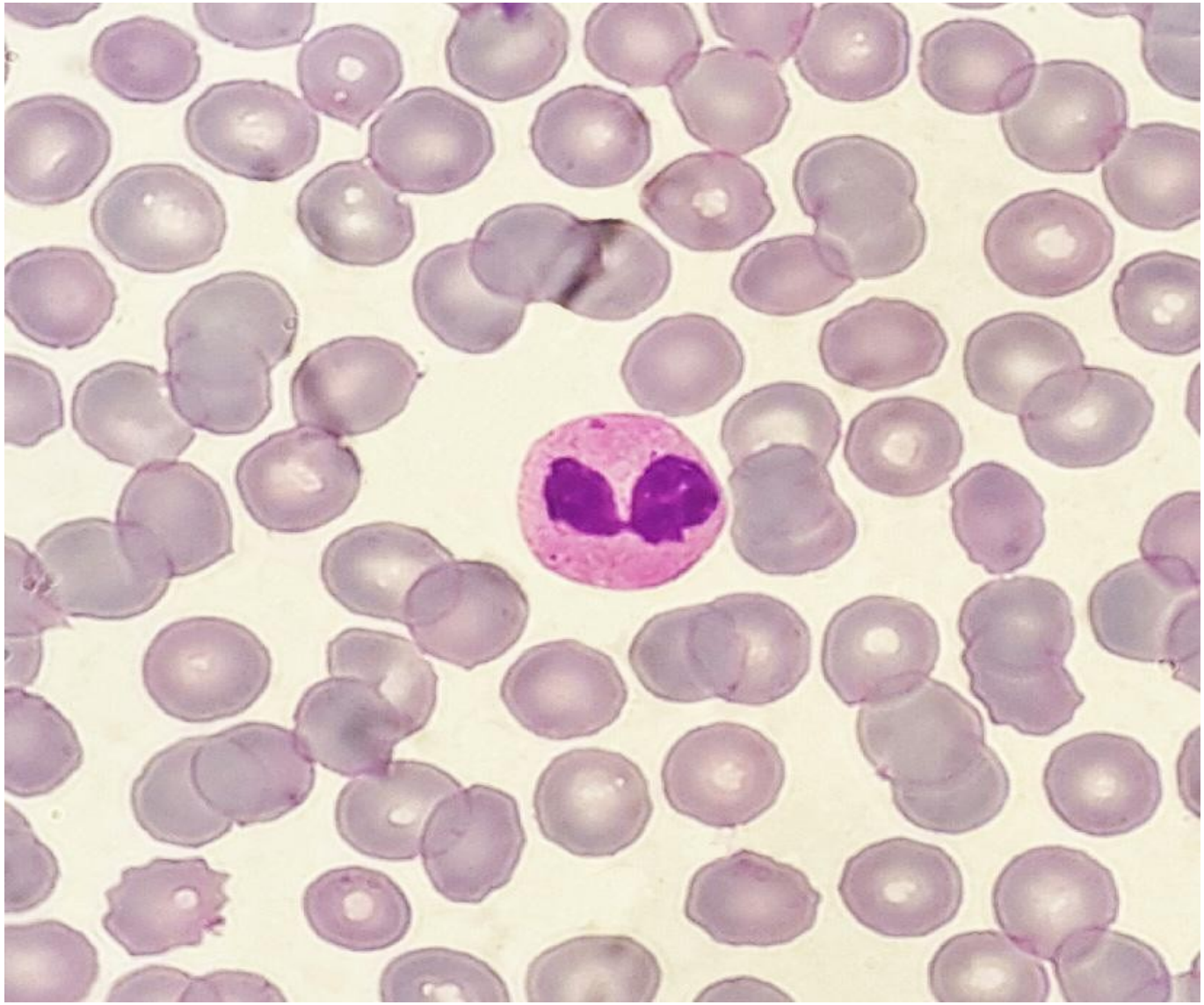
- Monocytopenia

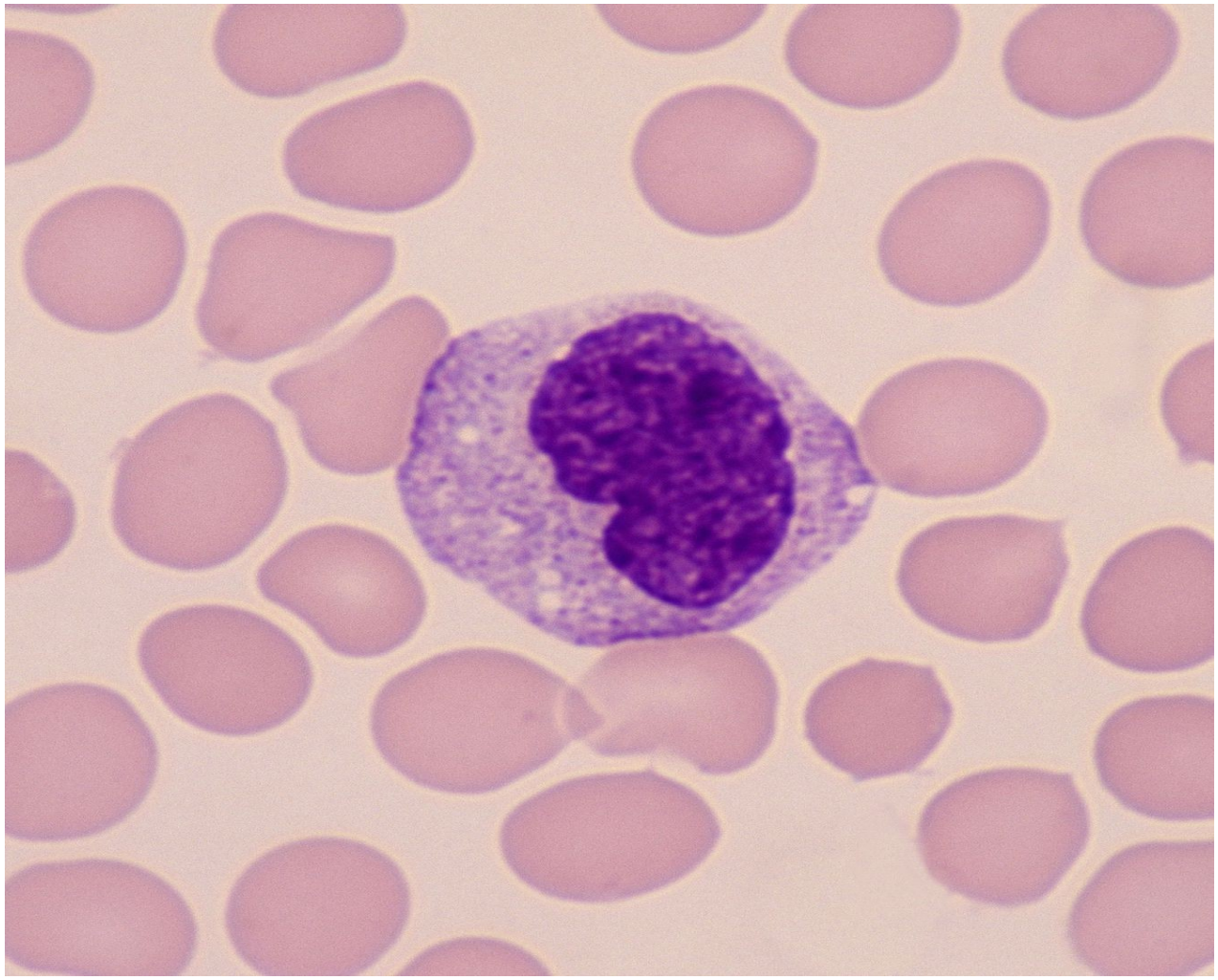
Causes of Monocytosis include

- Acute infections
- Stress
- Aplastic anemia
- Hairy cell leukemia
- Acute myeloid leukemia
- Use of myelotoxic drugs
- Treatment glucocorticoid

Basopenia

- Acute infection
- Hyperthyrodism
- Stress
- Radiation
- Steroid use





- Thanks for your attention