

(9/09) 6: Blood Cells & Hematopoiesis

Monday, September 15, 2014
2:03 PM

Topics:

- Blood smears
- Cells in blood
 - Red blood cells
 - White blood cells (leukocytes)
- Hematopoiesis (Epo, G-CSF)
 - Erythropoiesis
 - Granulocytopoiesis
 - (lymphocytes are covered in Immunology)

Learning Objectives:

- List the types of cells that are found in the blood stream, and explain the major roles these cells normally play.
- Identify all cell types in a blood smear stained with hematoxylin and eosin (H&E).
- Describe the production of new red blood cells, the regulation of this production, and the commonly measured laboratory values that provide insight into a patient's red blood cell production.
- List biologicals that are available commercially and that can be used to stimulate select portions of hematopoiesis. Describe the common effects of these hormones.

RBC - ERYTH
WBC - LEUK

Composition of Blood after Centrifugation:

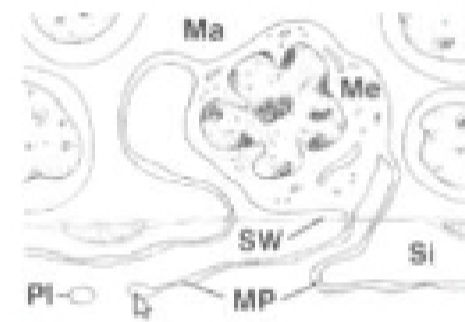
- Plasma
- Buffy Coat (WBC & Platelets)
- RBC



BLOOD SMEAR - 1. Smear, 2. Dry, 3. Stain, 4. Coverslip

H & E Stain:

- HEMATOXYLIN (nuclei of WBC) & EOSIN (binds to hemoglobin on RBC)
- HEMOGLOBIN - transports O₂
- PLATELETS (PI) - play role in coagulation; formed in bone marrow



Formation of Platelets in Bone Marrow:

- MEGAKARYOCYTE (Me) - bone marrow cell inside blood vessel; large nucleus
- CYTOPLASMIC EXTENSION (MP) - extensions of Me outside blood vessel that pinch off to form platelets

- LEUKOCYTES (WBC) - have nuclei; use blood to move from bone marrow to tissues; attack foreign material

- LYMPHOCYTES: (nucleus fills up most of cell)

- B CELLS
- T CELLS



- MONOCYTES - migrate from blood to tissues; phagocytosis of debris, digest in lysosomes, & present Ag to T-Cells; (dented nucleus (2 lobes))

... become MACROPHAGES (long-lived, adaptive immune response)

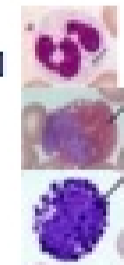
- SPLENIC MACROPHAGES - in spleen
- ALVEOLAR MACROPHAGES - in alveoli
- KUPFFER CELLS - in liver
- OSTEOCLASTS - in bone



... become DENDRITIC CELLS

- Granulocytes: (segmented nucleus)

- NEUTROPHILS - secrete enzymes degrading bacterial cell walls/proteins; phagocytosis of opsonized bacteria; kill in variety of ways (ROS); [infection/pus] (polymorphonuclear (PMN), 3-4 lobes, barely show granules bc neutral to eosin)
- EOSINOPHILS - secrete vesicles containing MBP (2 lobes, shows granules bc picks up eosin); [allergic reactions]
 - MAJOR BASIC PROTEIN (MBP) - kill parasites, activates neutrophils, basophils, & macrophages;
- BASOPHILS - vesicles pick up hematoxylin; granules contain histamine & heparin (2 lobes)



LEUKEMIA - overproduction of WBC

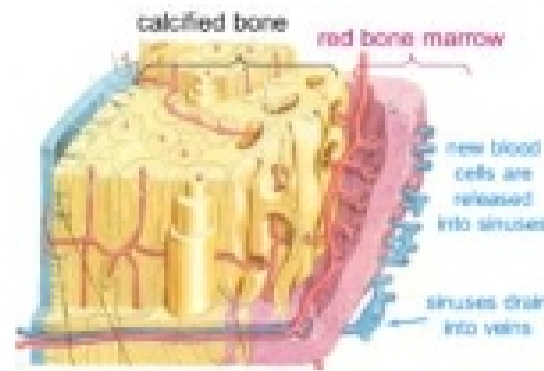
Summary of Photos:

| | | | |
|-------------|-------------|------------|--|
| Erythrocyte | | | |
| Leukocytes | Lymphocyte | | |
| | Monocyte | | |
| | Granulocyte | Neutrophil | |
| | | Eosinophil | |
| | | Basophil | |

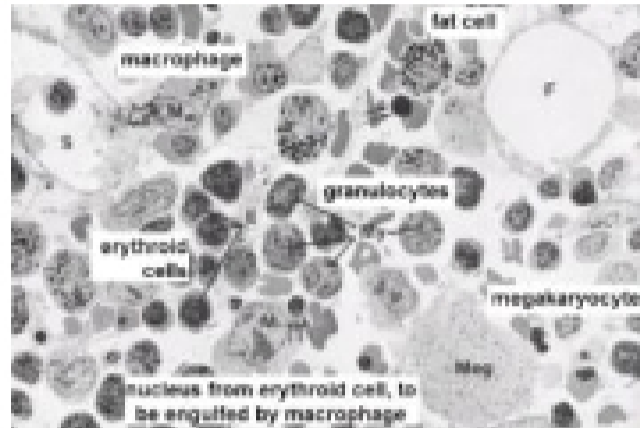
HEMATOPOIESIS - formed in RED bone marrow (trunk, proximal limbs)

- RBC = 200 billion/day
- WBC = 100 billion/day
- Pl = 100 billion/day

Production can increase 10x in peak demand



** all the cells are made next to each other **



HEMATOPOIETIC STEM CELLS (HSC) - look like lymphocytes, move around body; (1/10,000 cells in RED bone marrow); divide SLOWLY

- LYMPHOID:

- Lymphocytes (B-Cells/T-Cells)

- MYELOID:

- Megakaryocyte & Erythroid:

- Pl
- RBC

- Granulocytes & Macrophage:

- Neutrophils/Eosinophils/Basophils
- Monocytes

- CD34 - surface protein on outer membrane of HSC; allows for labeling with Abs to sort HSCs (for transplantation/research)

HSC > Me & Erythroid Progenitor > Proerythroblasts > Polychromatophilic Erythroblasts > RBC

THROMBOPOETIN (Tpo) - protein that stimulates production of platelets (no current Tpo without too many side effects)

ERYTHROPOETIN (Epo) - protein that stimulates production of RBCs in earlier stages

G-CSF (FIGRASTIM) - protein that stimulates Neutrophil production (infection) & HSCs release into blood

GM-CSF - protein that stimulates myeloid progeny (no longer used)

ERYTHROPOIESIS:

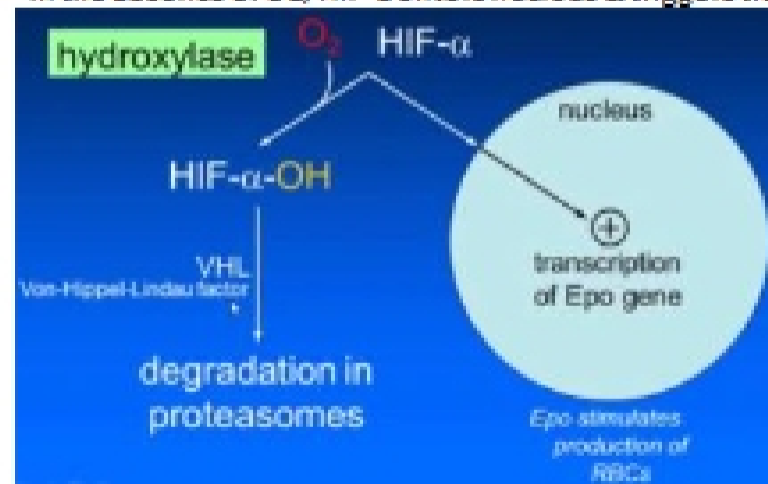
| | | |
|------------------------------------|----------|-----|
| - Proerythroblast | } 7 days | Epo |
| - Polychromatophilic Erythroblasts | | Epo |
| - Reticulocyte (Marrow) | | Fe |
| - Reticulocyte (Blood) | 1 day | Fe |
| - RBC | 120 days | Fe |

RBCs start out with nucleus, but it is later rejected

Production of Epo:

*in the presence of O₂, HIF- α is hydroxylated and degraded

*in the absence of O₂, HIF- α enters nucleus & triggers transcription of Epo




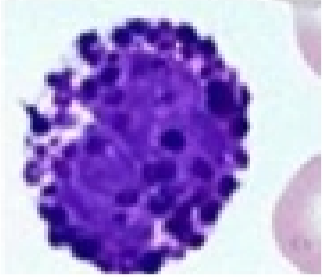

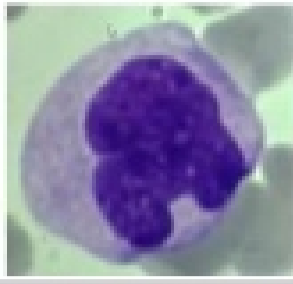
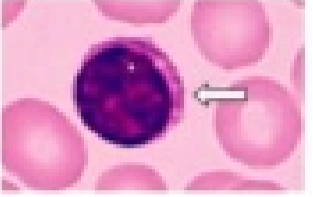

Production of Neutrophils:

- BAND CELL - immature neutrophils

Main Points:

- Blood Smears: mostly RBC, some platelets, some WBC
- WBC: lymphocytes (B/T), monocytes, granulocytes (neutrophils, eosinophils, basophils)
- G-CSF: stimulates Neutrophil production & HSC release into blood
- BAND CELLS: immature neutrophils
- Epo: secreted by kidneys depending on O₂; stimulates RBC
- RETICULOCYTES - released by bone marrow into blood; early stage of RBCs; no nucleus, still synthesizes Hb

Sample Questions:

| | | | |
|--|--|---|--|
| <p>1. The photograph shows which of the following?</p>  <ol style="list-style-type: none"> 1. B-cell 2. Basophil 3. Eosinophil ✓ 4. Erythrocyte 5. Monocyte 6. Neutrophil 7. Platelet 8. T-cell | <p>2. In an H&E-stained blood smear, a cell shows many blue granules. The nucleus is hard to see. This cell is most likely a(n) ...</p>  <ol style="list-style-type: none"> 1. B-cell ● 2. Basophil 3. Eosinophil 4. Erythrocyte 5. Monocyte 6. Neutrophil 7. Platelet 8. T-cell | <p>3. The cartoon depicts which of the following?</p>  <ol style="list-style-type: none"> 1. B-cell 2. Basophil 3. Eosinophil 4. Erythrocyte 5. Monocyte ★ 6. Neutrophil 7. Platelet 8. T-cell | <p>4. A cell in an H&E-stained blood smear has a nucleus of an irregular shape, much like a terribly misshapen cookie. (These cells are unusually abundant in young adults who have a long-lasting infectious illness.) The cell is a(n) ...</p>  <ol style="list-style-type: none"> 1. B-cell 2. Basophil 3. Eosinophil 4. Erythrocyte ★ 5. Monocyte 6. Neutrophil 7. Platelet 8. T-cell |
| <p>5. The arrow in the photograph points to which of the following?</p>  <ol style="list-style-type: none"> 1. Basophil 2. Eosinophil 3. Erythrocyte ● 4. Lymphocyte 5. Monocyte 6. Neutrophil 7. Platelet | <p>6. The cartoon depicts which of the following?</p>  <ol style="list-style-type: none"> 1. B-cell 2. Basophil ★ 3. Eosinophil 4. Erythrocyte 5. Monocyte 6. Neutrophil 7. Platelet 8. T-cell | <p>7. Which one of the following hormones physiologically stimulates the production of platelets?</p> <ol style="list-style-type: none"> 1. Erythropoietin 2. G-CSF 3. GM-CSF ✓ 4. Thrombopoietin | <p>8. A recombinant form of which one of the following can be injected into a patient to increase the number of neutrophils in the blood?</p> <ol style="list-style-type: none"> 1. Erythropoietin ★ 2. G-CSF 3. Thrombopoietin 4. VHL (von-Hippel-Lindau factor) |
| <p>9. Which one of the following hormones is often injected into patients who have too few red blood cells due to chronic kidney dialysis?</p> <ol style="list-style-type: none"> ● 1. Erythropoietin 2. G-CSF 3. GM-CSF 4. Thrombopoietin | <p>10. Which one of the following cells in the bone marrow can give rise to erythrocytes, megakaryocytes, monocytes, neutrophils, basophils, and eosinophils?</p> <ol style="list-style-type: none"> 1. Granulocyte and macrophage progenitor cell 2. Megakaryocyte and erythroid progenitor cell ✓ 3. Myeloid progenitor cell | | |