Lec 02: Hematology

Assist. Prof. Dr. Mudhir S. Shekha

3rd Medical Analysis

Tishk International University
Prenatal and neonatal hemopoiesis

- Progressive hemopoiesis in these organs results from in situ **differentiation** of **circulating stem cells**.
- The **liver and spleen** are inactive but retain potential to revert to hemopoiesis in **diseases** of bone marrow.
CENTRAL ILLUSTRATION: Clonal Hematopoiesis: A Potent Newly Recognized Risk Factor for Atherothrombosis and Adverse Heart Failure Outcomes

Bone Marrow

Mutagenic Event

Hematopoietic Stem Cell

Clonal Expansion

Blood

Somatically Mutated Cells in Peripheral Blood

Accelerated Atherosclerosis

Thrombosis

Heart Failure

Hematologic Malignancies

40% Increase in Risk of Cardiovascular Disease

Prenatal and neonatal hemopoiesis

• Hemopoietic cells in human embryo first appears in yolk sac wall.
• Later Thymus, liver and spleen are seeded.
• Towards term and postnatally bone marrow become major site of hemopoiesis.
• Figure 1: Sequence and contribution of hemopoietic organs to prenatal blood cell formation in cats
Sites of Hemopoiesis

- **Yolk sac**: Begins in mesoderm of yolk sac forming erythroid cells → site where blood cells and blood vessels are first formed. Production continues until 2.5 fetal months.

- **Liver and spleen**: Fetal liver assumes responsibility for hematopoiesis during second month.
Bone marrow

- The bone marrow is actually one of the largest organs in the body, approaching the size and weight of the liver. It is also one of the most active.
- Produces erythrocytes, granulocytes, monocytes, platelets and B-lymphocytes.
- Supplies stem cells for lymphocyte production in thymus and spleen.
- Stores iron

Q/ how many bones have bone marrow?

5% of total body mass around 3.65 kg
• Active Hemopoietic marrow is found, in children throughout the:

• **Axial skeleton:** (Cranium, Ribs, Sternum, Vertebrae and Pelvis)

• **Appendicular skeleton:** Bones of the Upper & Lower limbs

• In Adults active hemopoietic marrow is found only in:

• The axial skeleton and The proximal ends of the appendicular skeleton.

how many bones in human body at birth? at Adults?
Lymph nodes

- Produce **lymphocytes** and **plasma cells**
- Produce **antibodies**.
- **primary lymphoid organs** → Thymus
- Parenchyma consists of diffuse lymphoid tissues containing T-(thymus)
- **Secondary lymphoid organs** → (spleen, lymph nodes, hemal nodes, hemal lymph nodes, tonsils, Peyer’s patches and gut associated lymphoid tissues contain nodular and diffuse lymphoid tissues.)
Thymus

- Central lymphoid organ where bone marrow derived **precursor cells differentiate** into immunologically competent T-lymphocytes
Spleen

• Produces **lymphocytes** and **plasma** cells
• Synthesizes **antibodies**.
• **Reservoir** of **erythrocytes** and **thrombocytes**
• **Destroys** senescent and abnormal erythrocytes
• **Degraded** hemoglobin
• **Stores** iron

Why act as Graveyard for RBC?
Liver

• **Stores** vitamin B12, foliate and iron
• **Produces** coagulation factors, albumin, and some globulins.
• **Converts** free bilirubin to bilirubin glucuronide for excretion into bile
• **Participates** in entero-hepatic circulation of urobilinogen
• **Produces** α-globulin, a precursor of erythropoietin
Kidneys

• Produce **erythropoietin** and **thrombopoietin**
• Degrade excessive **hemoglobin** to **bilirubin** for urinary excretion

Stomach and intestines

• Produce HCl for **release of iron** from complex organic molecules.
• Produce **intrinsic factor** to facilitate absorption of vitamin B12.
• **Absorb vitamin B12 and folic acid** through intestinal epithelial cells.
• **Control** the rate of iron absorption in relation to body needs
## Lifespan and production of blood cells

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Approximate lifespan</th>
<th>Production rate cells/day</th>
<th>Production rate cells/sec</th>
<th>Production rate Kg/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Cells</td>
<td>100 days</td>
<td>$2 \times 10^{11}$</td>
<td>2.3 million</td>
<td>7.3</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>t½ 6 hours</td>
<td>$3 \times 10^{10}$</td>
<td>350,000</td>
<td>10.9</td>
</tr>
<tr>
<td>Platelets</td>
<td>7 days</td>
<td>$1 \times 10^{11}$</td>
<td>1.2 million</td>
<td>4.6</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>t½ 10 days</td>
<td>$1 \times 10^{10}$</td>
<td>116,000</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Annual total</strong></td>
</tr>
</tbody>
</table>
Next Lecture........

• SHAPE AND STRUCTURE OF ERYTHROCYTES
• erythrocytes production degradation
• HEMOGLOBIN
  • Heme and globin synthesis
  • Structure, Function and Variation
  • Oxygen and Hb Dissociation curve
ERYTHROCYTE
Structure, Function, Production & Destruction
Erythrocyte properties

- **Biconcave** discs $\rightarrow$ huge surface area relative to volume, **anucleate, no organelles**
- Filled with **hemoglobin**, a protein $\rightarrow$ gas transport
  - Contain the plasma membrane protein **spectrin** and other proteins $\rightarrow$ Give erythrocytes their **flexibility** $\rightarrow$ change **shape** as needed
Erythrocyte properties

- Erythrocytes account for slightly less than **half** the blood volume, and **99.9%** of the formed elements.

- **Hematocrit** measures the **percentage of whole blood** occupied by formed elements. Also → volume of packed red cells

\[
\text{Hematocrit} = \frac{\text{Height of RBC}}{\text{Height of all components of the blood}} \times 100
\]
Erythrocyte properties

- ATP is generated \textit{anaerobically}, so the erythrocytes do not \textbf{consume the oxygen} they transport

- Hb gives the \textbf{red color} of blood \textbf{Why}?

- Individual erythrocytes are \textbf{orange yellow}

- Erythrocytes are \textbf{non motile cells}, but \textbf{tolerate deformation}, pass though smallest capillaries and venules and are remarkably elastic
• RBC cytoplasmic contents
  • RBC has certain **proteins** and **lipids**
  • RBC has Hb; (1) **globin**, a protein and (2) **iron** containing heme pigment
  • **Old** RBCs are **sequestered** in the **spleen** and bone **marrow** by **phagocytes**
  • Heme iron is captured for re-use
  • Blood volume is 6–8 % of body weight
• PCV depends on number & size of cells and plasma volume RBC staining (affinity for Hb) may be
  • normal (normochromasia)
  • lower (hypochromasia)
  • higher Hb (hyperchromasia) than normal. Differences may be in sizes (anisocytosis), shapes (poikilocytosis) and number (hypererythrocytosis)
Lower than normal counts is oligoerythrocytosis or anemia
- RBC plasmalemma is **trilaminar**
  - Outermost layer: glycolipids, glycoproteins
  - Central layer: cholesterol, phospholipids
  - Inner layer: cytoskeleton

- spectrin
  - Composed of alpha & beta chains
  - Join to form a matrix which **strengthens** the membrane against sheer force and controls biconcave shape

- ankyrin
• membrane proteins

Function of plasmalemma

• Shape
  • Provides the optimum surface to volume ratio for respiratory exchange and is essential to deformability

• Provide **deformability, elasticity**
  • Allows for passage through *microvessels*

• Provides **permeability**
  • Allows water and electrolytes to exchange

• RBC **controls volume** and H₂O content primarily through control of *sodium* and *potassium* content
Erythrocyte membrane

- Cell membrane **selectively** permeable **Na** and **K**
- **Potassium** prevents escape of **Hb** and other cell material
- RBC contain → 60% **H₂O**, 40% conjugated proteins **globin** and **heme** pigment (4%) to form (hemoglobin)
- RBC membrane is **permeable** to **H₂O**, **electrolytes**, **polysaccharides** impermeable to Hb.
• **osmolarity** of RBC is estimated by Hb.

• Hb Osmolarity in RBC is = to that of plasma (isotonic), water absorption for plasma or RBC

• The osmotic fragility test (OFT) is used to measure *erythrocyte* resistance to hemolysis

• RBC is subjected to decreasing salt concentration until it hemolyses → **fragility value**

• RBC fragility is a diagnostic test for certain *anemias*. It means assess cells' ability (or lack thereof) to withstand sustained or repeated stress.
Erythrocyte Function

- Erythrocytes are adapted to respiratory gas transport
- Hemoglobin $\rightarrow$ oxygen in the blood is bound to hemoglobin
- Hemoglobin is composed of the protein globin, made up of two alpha and two beta chains, each bound to a heme group
- Each heme group bears an atom of iron, which can bind to one oxygen molecule
- Each hemoglobin molecule can transport four molecules of oxygen
Importance of Hb within RBC

• **Intra RBC** environment is a little more **acidic** than **plasma** for capable respiration

• Hb is removed from metabolic pool, preventing its rapid turn over.

• Half-Life for Hb in RBC is **months**,  
• Half-Life for Hb in plasma is **only 3 hrs**.

• Hb chemical **state** is required for **O2 transport absolutely**.

• Each Saturated gram of Hb can carries **1.3 ml** oxygen
Metabolism of erythrocytes

- Tricarboxylic acid (TCA) cycle or Krebs cycle
- Embden – Meyerhof (EM) pathway or glycolysis
- Pentose cycle (Hexose monophosphate shunt) or HMS

Mature erythrocyte lacks TCA cycle and capacity for oxidative phosphorylation because of lack of organelles such as mitochondria, ribosomes, and endoplasmic reticulum.
Abnormalities in RBC metabolism

- Deficiency of glucose – 6 – phosphate dehydrogenase
- Deficiency in pyruvate kinase
- Deficiency of NADH – methaemoglobin reductase
Destruction of erythrocytes

Cell decrease deformability in microcirculation is associated with:

* increase in red **cell rigidity**
* increase in **blood viscosity**,  
* **impeded blood flow**
* **cell fragmentation**

The changes in deformability depends on Maintenance of cell geometry or biconcave shape Normal internal or hemoglobin fluidity  Intrinsic membrane deformability or visco-elastic properties
Destruction of Red Blood Cells

- Macrophage in spleen or liver
- Hemoglobin
- Aged, abnormal, or damaged erythrocytes
- 120 days
- Erythrocytes
- Erythropoiesis
- Red bone marrow
- Liver
- Bilirubin excreted into intestine as part of bile
- Bilirubin converted into pigments that are part of feces
- Amino acids
- Iron
• When red blood cells are delivered from the bone marrow into the circulatory system, they normally circulate an average of 120 days before being destroyed.

• Even though mature red cells do not have a nucleus, mitochondria, or endoplasmic reticulum, they do have cytoplasmic enzymes that are capable of metabolizing glucose and forming small amounts of adenosine triphosphate.
• These enzymes also:
• (1) maintain pliability of the cell membrane.
• (2) maintain membrane transport of ions.
• (3) keep the iron of the cells’ hemoglobin in the ferrous form rather than ferric form (Which causes the formation of methemoglobin that will not carry oxygen)
• (4) prevent oxidation of the proteins in the red cells.