Peripheral Blood
Objectives

Gross description and general properties of blood

The structure and function of red blood cells, white blood cells, and platelets
Blood

Diagnostic value = most examined

Types of information:

1) **Identify nature** of disease
   - Viral – T lymphocytes
   - Bacterial – neutrophils
   - Parasitic – eosinophils

2) **Follows the course** of disease

3) Allows method to **evaluate** the effectiveness of **treatment**
Blood - connective tissue

Like CT

Has abundant extracellular matrix (fluid).
Maintains logistic support and communication between tissues and organs.

Unlike CT

Blood has no rigid physical connection among cells.
Blood Composition

Blood plasma
(liquid component of blood)

Buffy coat
(White blood cells)

Packed red blood cells
(Hematocrit)
Blood Plasma

Liquid part of blood - 55% of whole blood

Composition –

- Water
- Albumin: Osmotic pressure and neutralizes proteases
- Globulin: antibodies (IgG, IgE, ETC.)
- Transferrin: iron, copper, zinc
- Chylomicrons: lipids from intestine
- Low-density lipoprotein: cholesterol removal
Blood plasma

Composition con’t:

• Plasma clotting factors
  o Fibrinogen
  o Prothrombin
  o Thromboplastin
  o Thrombin

• Hormones - direct activity of cells

• Chemotaxis factors – attract immune cells
Blood serum

Serum – yellow liquid from clotted blood (e.g., plasma minus clotting factors)
Blood (definition and function)

Blood - fluid tissue composed of erythrocytes (RBC), leukocytes (WBC), and platelets suspended in blood plasma.

Function of blood is the **transportation** of cells and fluid.

RBC carry O$_2$ to and CO$_2$ from tissues.
Function of blood is **transportation** of cells and fluid.

**WBC**
- Immune defense for body.

**Plasma**
- Nutrients to tissues.
- Waste from tissues.
- Proteins to hold water in plasma.
- Hormones and other informational mediators.

**Platelets**
- Prevent loss of transportation.
Blood
Volume 5-6 L = 12-13 pints/person

Travel/day 172,000 miles (960 trips/day at 179 miles of blood vessels/trip and trip/60-90 sec.)
http://www.youtube.com/watch?v=q0s-1MC1hcE&feature=related
## Size of human blood cells

<table>
<thead>
<tr>
<th>Cell/platelet</th>
<th>size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Erythrocytes</td>
<td>6.5-8 µm</td>
</tr>
<tr>
<td>2. Leukocytes (WBC)</td>
<td></td>
</tr>
<tr>
<td>% of WBC</td>
<td></td>
</tr>
<tr>
<td>a) Neutrophil</td>
<td>12-15 µm</td>
</tr>
<tr>
<td>60-70%</td>
<td></td>
</tr>
<tr>
<td>b) Eosinophil</td>
<td>12-15 µm</td>
</tr>
<tr>
<td>2-4%</td>
<td></td>
</tr>
<tr>
<td>c) Basophil</td>
<td>12-15 µm</td>
</tr>
<tr>
<td>0-1%</td>
<td></td>
</tr>
<tr>
<td>d) Lymphocyte</td>
<td>6-18 µm</td>
</tr>
<tr>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>e) Monocyte</td>
<td>12-20 µm</td>
</tr>
<tr>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>3. Platelets</td>
<td>2-4 µm</td>
</tr>
</tbody>
</table>
### Formed elements (non-fluid, cellular) and functions in blood

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Main functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes</td>
<td>CO(_2) and O(_2) transport</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>phagocytosis of bacteria</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>parasitic infections, inflammatory processes</td>
</tr>
<tr>
<td>Basophils</td>
<td>release of histamine and other inflammation mediators</td>
</tr>
<tr>
<td>Monocytes</td>
<td>Mononuclear-phagocyte system become macrophages</td>
</tr>
</tbody>
</table>
**Formed elements** (non-fluid, cellular) and functions in blood con’t

<table>
<thead>
<tr>
<th>Cell type</th>
<th>main functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>B lymphocytes</td>
<td>generation of antibody-producing plasma cells</td>
</tr>
<tr>
<td>T lymphocytes</td>
<td>killing of virus-infected cells</td>
</tr>
<tr>
<td>Natural killer (cytotoxic T cell)</td>
<td>killing of some tumor and virus-infected cells</td>
</tr>
<tr>
<td>Platelets</td>
<td>clotting of blood</td>
</tr>
</tbody>
</table>
Erythrocytes

Minute corpuscles - red color of blood (iron)
Bone marrow derived
Anucleate cells (mammals)
  - Nonfunctional nuclei in birds, reptiles, amphibian, and fish
4.8 to 5.4 x 10^6/MM^3 = 1µl of blood, 45% of blood
25-30 x 10^{12}/person (larger at high elevation)
Erythrocytes

Total surface area 3,800 m² = 2,000 times total body surface area

Rouleaux - aggregate like stacked coins

Crenation – spines due to hypertonicity
Descriptive terms for erythrocytes (RBC)

<table>
<thead>
<tr>
<th>Term</th>
<th>variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anisocytosis</td>
<td>size</td>
</tr>
<tr>
<td>- Microcyte</td>
<td>&lt; 6 µm</td>
</tr>
<tr>
<td>- Macrocyte</td>
<td>&gt;9 µm</td>
</tr>
<tr>
<td>Poikilocytosis</td>
<td>shape</td>
</tr>
<tr>
<td>Chromasia</td>
<td>shade/color</td>
</tr>
<tr>
<td>- hypochromic</td>
<td>(due to amount of hemoglobin)</td>
</tr>
</tbody>
</table>
Biconcave shape of erythrocytes
Erythrocytes

Biconcave shape is important:

Surface area increased
  by 20-30% for greater diffusion of $O_2$ and $CO_2$

It facilitates passage through the smallest (<6 $\mu$m) of capillaries

Hemoglobin - 65,000 MW
  protein with 4 polypeptide globin chains, each has an iron-containing heme group to attach $O_2$ or $CO_2$. 
Case study: Globins

- **Myoglobin**
  - heart and skeletal muscle
  - functions as O$_2$ reservoir & transport *within* muscle cells
  - single polypeptide chain
  - 1 heme in hydrophobic pocket
  - 8 $\alpha$-helices, 153 AA

- **Hemoglobin**
  - red blood cells
  - O$_2$ reservoir & transport from lungs to capillaries
  - 4 polypeptide chains
  - 4 hemes
  - each chain is similar in sequence and structure to myoglobin
  - 2 $\alpha$-chains (141 AA), 2 $\beta$-chains (146 AA)
  - chains held together by non-covalent forces
Erythrocytes

**Sickle cell anemia** - valine substituted for glutamic acid (one out of 514 AA) on the beta chain of the tetramer

- Reduces solubility of O$_2$,
- causing crystals to form
- In the shape of long tactoids or sickles
- Prone to hemolysis and to block capillaries
- Homozygous carriers of the HbS gene
Consequences of mutation

- **Severity of disease**
  - Depends on nature of substitution
  - Radical or conservative physicochemically

- **Hb missense mutations**
  - Sickle cell anemia Glu6Val substitution (charged to non-polar) arises from GAA codon mutated to GUA
  - Sickle cell Hb polymerizes in low oxygen conditions
  - Cell ‘sickles’
Erythrocytes

Reticulocytes –
released from bone marrow, matures (looses ribonucleoprotein) in 24 hours to become a mature RBC or

Erythrocyte – lifespan of 120 days then removed in spleen
5th month of pregnancy
<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes</td>
<td>No nucleus and red cytoplasm</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>No nucleus and blue - grey cytoplasm</td>
</tr>
<tr>
<td>Orthochromatophilic</td>
<td>Dark, small, spherical nucleus blue – grey cytoplasm</td>
</tr>
<tr>
<td>erythroblasts</td>
<td></td>
</tr>
<tr>
<td>Polychromatophilic</td>
<td>Darkening, fractured ,spherical nucleus and mixed pools of grey and blue cytoplasm</td>
</tr>
<tr>
<td>erythroblasts</td>
<td></td>
</tr>
<tr>
<td>Basophilic erythroblasts</td>
<td>Fractured, spherical nucleus and thin rim of dark blue cytoplasm</td>
</tr>
<tr>
<td>Proerythroblasts</td>
<td>Uniformly light, spherical nucleus with thin rim of medium to dark blue cytoplasm</td>
</tr>
</tbody>
</table>
Nucleus is removed creating the reticulocyte

Orthochromatophilic erythroblasts

reticulocyte
Erythropoiesis

Erythrocytes

Proerythroblasts

Reticulocytes

Orthochromatophilic erythroblasts

Basophilic erythroblasts

Polychromatophilic erythroblasts

Erythropoiesis
Granular leukocytes

Nongranular leukocytes

Leukocytes

Granular leukocytes (Granulocytes)

- Neutrophils (*"")
- Eosinophils (*)
- Basophils (*)
- Lymphocytes (*)

Nongranular leukocytes (Mononuclear leukocytes)

- Monocytes (*)
<table>
<thead>
<tr>
<th>Cells</th>
<th>Specific Granules</th>
<th>Azurophilic Granules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>Alkaline phosphatase</td>
<td>Acid phosphatase</td>
</tr>
<tr>
<td></td>
<td>Collagenase</td>
<td>α-Mannosidase</td>
</tr>
<tr>
<td></td>
<td>Lactoferrin</td>
<td>Arylsulfatase</td>
</tr>
<tr>
<td></td>
<td>Lysozyme (2/3)</td>
<td>β-Galactosidase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>β-Glucuronidase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cathepsin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5′Nucleotidase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elastase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collagenase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myeloperoxidase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lysozyme</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acidic mucosubstances</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cationic antibacterial proteins</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Acid phosphatase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arylsulfatase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>β-Glucuronidase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cathepsin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phospholipase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RNAase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eosinophilic peroxidase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Major basic protein</td>
<td></td>
</tr>
<tr>
<td>Basophils</td>
<td>Eosinophilic chemotactic factor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heparin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Histamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peroxidase</td>
<td></td>
</tr>
</tbody>
</table>

![Cell diagram](image1)

![Cell diagram](image2)
Marrow
(development, 14 days)

- Myeloblast
- Promyelocyte
- Myelocyte
- Metamyelocyte
- Band cell
- Mature PMN

MITOTIC (7.5 days)
POST-MITOTIC (6.5 days)

Blood (transit, \( T_{1/2} \) 6 hrs)

Tissues (function, \( \sim 1-2 \) days)
**Granulopoiesis**

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Lobulated, dark nucleus, mature grey cytoplasm with small granules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophilic band or stab cells</td>
<td>Horse-shoe shaped, darkening nucleus, grey mature cytoplasm</td>
</tr>
<tr>
<td>Neutrophilic metamyelocytes</td>
<td>Oval to kidney bean-shaped, indented nucleus, grey mature cytoplasm with a weak blue tent</td>
</tr>
<tr>
<td>Neutrophilic myelocytes</td>
<td>Large, oval, non-indented nucleus, large amount of cytoplasm with specific and non-specific granules</td>
</tr>
<tr>
<td>Promyelocytes</td>
<td>Large, oval, non-indented nucleus, large amount of sky blue cytoplasm with non-specific granules</td>
</tr>
</tbody>
</table>
Bone marrow

Developing granulocytes
Granulopoiesis

Neutrophils

Promyelocytes

Neutrophilic band cells

Neutrophilic myelocytes

Neutrophilic metamyelocytes
Types of Leukocytes

Granular leukocytes
• Neutrophils (polymorphs, PMNs)
• Eosinophils
• Basophils

Nongranular leukocytes
• Lymphocytes
• Monocytes
Neutrophils (PMN)

20 to 30 billion in circulation at any time 55-65% of WBC
5,000 to 9,000 /µl whole blood
40,000 /µl (e.g., 5 times higher) with acute infection

Segmented lobes of condensed nucleus – drumstick
(Barr body in women)
Neutrophils (granules)

Azurophilic granules
  Acid phosphatase
    (Hydrolytic enzymes)
  Primary lysosomes

Specific granules
  Basic protein
    (Phagocytins, anti-bacterial action)
Neutrophils (PMN)

Band cells – immature release of cells indicative of infection

Phagocytosis
  - Opsin enhanced
  - Nonspecific

Basic cellular functions – random motility, chemotaxis, phagocytosis, and killing bacteria
Eosinophils

8-12 day life span
Transient component of blood - 3 to 4 hrs
Specific granules - red/orange, large crystalloids
  • Major basic protein (kills parasitic worms)
Common in lamina propria (CT under lining epithelium)
  • Alimentary tract
  • Respiratory tract
Attracted by chemotactic factors
given off by mast cells and basophils.
Role
  • Parasitic diseases
  • Allergy
Basophils

Least numerous WBC

Specific granules (blue, large, histamine)
- Metachromasia (Heparin in several varied colors)

May be induced to degranulation (like mast cells)

Specific receptors for IgE immunoglobulin
- IgE usually dilutes in blood
  - 20 fold in persons with hay fever, asthma, or allergic dermatitis
Basophils

Histamine - itching and increased vascular permeability – edema

Cutaneous basophil hypersensitivity - rebuck window
  – (Basophils migrate to dermis - cell mediated Immunity)

Note granules above nucleus
## Lymphocyte Types and Functions

<table>
<thead>
<tr>
<th>Type</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Plasma cells</td>
</tr>
<tr>
<td></td>
<td>Antibodies (Memory B cells)</td>
</tr>
<tr>
<td>T lymphocyte</td>
<td>T cell receptors specialized to recognize surface antigens of cells</td>
</tr>
<tr>
<td>1) Memory</td>
<td>Sensitive to previous antigens</td>
</tr>
<tr>
<td>2) Cytotoxic cells</td>
<td>Destroys transplants</td>
</tr>
<tr>
<td>3) Helper cells</td>
<td>Secretes substances - help T &amp; B respond</td>
</tr>
<tr>
<td>4) Suppressor cells</td>
<td>Dampens response to foreign antigens, self antigens</td>
</tr>
</tbody>
</table>
Plasma cells
Lymphocytes, Summary

Humoral immune response

B cells → plasma cells
→ Immunoglobins (antibodies)
Lymphocytes, Summary

Cell mediated immune response

T cells

- Memory - specific receptors for predisposed antigens/mount quick second response
- Helper - stimulates immune response
- Suppressor - inhibits immune response

Interact with macrophages - cytotoxic and phagocytic mechanism

Interferon - produced by T cells

- Capable of inhibiting replication of certain viruses
- Capable of reducing multiplication of some intracellular parasites
Platelets
megakaryocyte
Platelet function - blood clotting

1. Primary aggregation of platelet plug - attachment to damaged tissue

2. Secondary aggregation
   - Alpha and delta granules – induce further aggregation

3. Blood coagulation - cascade of plasma proteins to form blood clot or thrombus

4. Clot retraction - platelet actin, myosin and ATP

5. Clot removal - plasmin (proteolytic enzyme) and platelet enzyme containing granules
Platelet’s role in stopping bleeding

Production of Serotonin – vasoconstriction to stop blood flow
Produce thromboplastin

THROMBOPLASTIN

PROTHROMBIN → THROMBIN

FIBRINOGEN → FIBRIN

Fibrin polymerizes and produces the hemostatic plug
Figure 4-7. (A) Schematic representation of the events in formation of a blood clot in an injured vessel. Platelets adhere to the site of injury and release ADP and adhesive glycoproteins that accelerate platelet aggregation. Tissue thromboplastin released from injured cells induces conversion of plasma prothrombin to thrombin. This catalyzes conversion of fibrinogen to fibrin which polymerizes to form fibers enmeshing the platelets and impounding erythrocytes in a gelatinous clot. (B) A later stage in the process of clot formation.
Summary of Platelets - Thromboplastins

Have many metabolic function of whole cells
When exposed to damaged cells, sticky - aggregation - Stick to each other
Release ADP (from ATP inside platelets) which attaches to other platelets
Produce thromboplastic which catalyzes prothrombin to thrombin which catalyzes fibrinogen to fibrin,
forms net to catch RBC and other platelets (basis of the blood clot).
Summary of Platelets - Thromboplastins

Hemophilia - bleeding disease
- Inherited single deficiencies of any and/or many of the 12 plasma clotting factors
Summary of Platelets

Thromboplastins

Anucleate (mammals)

Zones

• Hyalomere – microtubules and small vesicles
• Granulomere - azurophilic granules

Granules - some contain serotonin for vasoconstriction

Platelets produced by megakaryocytes (bone marrow)

Last 8 to 11 days
Next time

EPITHELIUM

(One of four basic types of TISSUE)

EPITHELIUM
CONNECTIVE TISSUE
MUSCULAR TISSUE
NERVOUS TISSUE
Many illustrations in these VIBS Histology YouTube videos were modified from the following books and sources: Many thanks to original sources!

- Internet images and videos on biological presentations