Chapter 19 Blood Lecture Outline

Cardiovascular system
Circulatory system
Blood
Functions:
  1. distribution
  2. regulation
  3. protection
Characteristics:
  pH 7.4
  38°C
  4-6 L
Composition:
  Plasma
  Formed elements
    Erythrocytes
    Leukocytes
    Platelets / Thrombocytes

Plasma
  Water + solutes
  Proteins
    1. Albumins
    2. Globulins
      a. Gamma globulins / immunoglobulins / Antibodies
      b. Alpha & Beta globulins / Transport globulins
    3. Clotting proteins
      Fibrinogen
      Serum
    4. Other
      Metabolic enzymes
      Antibacterial proteins
      Hormones

Hematopoiesis
  Hemocytoblast
  Myeloid stem cell
  Progenitor cells
    Erythrocyte
    Megakaryocyte
    Platelet
  Granulocytes:
    Basophils,
    Eosinophils
    Neutrophils
  Monocytes → Macrophages

Lyphoid stem cell
  Lymphocytes
Erythrocytes
  Hematocrit
  Polycythemia
  Hemoglobin (Hb)
    2 α + 2 β chains
    heme
    oxyhemoglobin
deoxyhemoglobin
carboxyhemoglobin
Anemia
  Thalassemia
  Sickle-cell anemia
Erythropoiesis
  Hemocytoblast
  Myeloid stem cell
  Reticulocyte
  Vitamin B12
  Erythropoietin (EPO)
  blood doping
Erythrocyte recycling
  Transferrin
  Biliverdin
  Bilirubin
  Jaundice
  Urobilins
  Stercobilins
  Hemolysis
  Hemoglobinuria

Blood types
  Type A: A antigen, B antibody
  Type B: B antigen, A antibody
  Type AB: A&B antigens, no antibodies
  Type O: no antigen, A&B antibodies
  Rh+: D antigen
  Rh-: no antigen
  Agglutination
  Erythroblastosis fetalis

Leukocytes
Functions:
  defense
  detoxification
  removal of cells
Characteristics:
  1. amoeboid movement
  2. diapedesis
  3. migration
  4. emigration
  5. chemotaxis
  6. phagocytosis
Types:
  Granulocytes
  Neutrophils (PMNs)
    respiratory burst
degranulation: defensins
prostaglandins
leukotrienes
Eosinophils
  parasite defense
  Basophils / Mast cells
    histamine
    heparin
Agranulocytes
Monocytes / Macrophages
phagocytosis
chemoattractant
Lymphocytes
B cells: humoral immunity
T cells: cell mediated immunity
NK cells: immune surveillance

Leukopoiesis
Hemocytoblast
Myeloid stem cell
Basophil
Eosinophil
Neutrophil
Monocyte
CSF (colony stimulating factor)
Lymphoid stem cell
Lymphocyte
Leukopenia
Leukocytosis
Infection mononucleosis
Epstein Bar virus

Platelets / Thrombocytes
Functions:
Clotting chemicals
Platelet plug
Contraction
Thrombocytopoiesis
Hemocytoblast
Megakaryocyte
Thrombopoietin
Thrombocytopenia
Thrombocytosis

Hemostasis
1. Vascular spasms
   vasoconstriction
   endothelins
   von Willebrand factor
2. Platelet plug
   platelet adhesion
   platelet aggregation
   secretion
   ADP
   thromboxane & serotonin
   clotting factors
   PDGF
   calcium ions
   prostacyclin
3. Coagulation
   a. Prothrombinase formation
   b. Thrombin formation
   c. Fibrin formation
Clotting cascade (coagulation)
Extrinsic pathway
   Tissue factor (Factor III) + Factor VII + Ca^{2+}
Intrinsic pathway

Factor XII
Factor VIII + Factor IX
Common pathway
Factor X → Prothrombinase
Prothrombin → Thrombin
Fibrinogen → Fibrin

Fibrinolysis
Throbin
Tissue plasminogen activator
Plasminogen → Plasmin

Clotting prevention:
Antithrobin III
Heparin
Protein C
Prostacyclin

Disorders
Thrombosis
Embolus
Disseminated intravascular coagulation
Hemophilia
   Type A: Factor VIII
   Type B: Factor IX
   Type C: Factor XI
Calcium deficiency: clotting
Vitamin K deficiency: clotting
Iron deficiency: erythrocytes
Vitamin B12 deficiency: erythrocytes
Liver disorder: clotting factors
Kidney disorder: EPO, thrombopoietin

Amy Warenda Czura, Ph.D.

SCCC BIO132 Chapter 19 Handout
Hematopoiesis: Blood Cell Production

Basophils, Eosinophils, Neutrophils and platelets exit the bone marrow to blood as mature cells.

Monocytes must mature into Macrophages by migrating from the blood to the peripheral tissues.

Many lymphoid stem cells migrate from the bone marrow to lymphoid tissues to produce mature lymphocytes there.

Erythrocytes enter the blood as reticulocytes which mature in the blood stream.
<table>
<thead>
<tr>
<th>Granulocytes</th>
<th>Agranulocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neutrophil</strong> (a.k.a PMNs)</td>
<td><strong>Monocyte</strong></td>
</tr>
<tr>
<td>Non-specific defense</td>
<td>In tissues = Macrophage</td>
</tr>
<tr>
<td>Phagocytic</td>
<td></td>
</tr>
<tr>
<td>50-70%</td>
<td></td>
</tr>
<tr>
<td>3-5 lobed nucleus</td>
<td></td>
</tr>
<tr>
<td>12µm</td>
<td></td>
</tr>
<tr>
<td>Granules contain enzymes and defensins</td>
<td></td>
</tr>
<tr>
<td>Very mobile</td>
<td></td>
</tr>
<tr>
<td>Life span less than 10 h</td>
<td></td>
</tr>
<tr>
<td>Functions:</td>
<td></td>
</tr>
<tr>
<td>Respiratory burst</td>
<td></td>
</tr>
<tr>
<td>Degranulation</td>
<td></td>
</tr>
<tr>
<td>Prostaglandins</td>
<td></td>
</tr>
<tr>
<td>Leukotrienes</td>
<td></td>
</tr>
</tbody>
</table>

| **Eosinophil** | |
| Non-specific defense | |
| Phagocytic | |
| 2-4% | |
| Bilobed nucleus | |
| 12µm | |
| Granules contain toxins | |
| Life span 9 d | |
| Functions: | |
| Phagocytosis of Ab covered | |
| Defense against parasites | |
| Reduce inflammation | |

| **Basophil** | |
| Non-specific defense | |
| Less than 1% | |
| “U” shaped nucleus | |
| 8-10µm | |
| Granules contain | |
| Histamine | |
| Heparin | |
| Life span 9 d | |
| Functions: | |
| Inflammation | |
| Allergic response | |

| **Lymphocyte** | |
| Immune response | |
| 20-30% | |
| Large round nucleus | |
| 5-17µm | |
| Migratory | |
| Most in lymphatic | |
| Life span days-lifetime | |
| Function depends on type | |
| 3 types: | |
| B cells: humoral immunity | |
| T cells: cell-mediated immunity | |
| NK cells: immune surveillance | |
Hemostasis “stop bleeding”

Three phases:

1.) Vascular spasms - begins immediately after injury
   Vasoconstriction of the vessels involved in the injury
   Triggered by:
   - injury to the vessel
   - chemicals from damaged endothelial cells
   - reflex triggered by pain receptors
   Concurrently, endothelial cells release factors and hormones:
   - Endothelins: stimulate vascular spasms and cell division to begin repair
   - von Willebrand Factor: promotes platelet sticking to endothelium

2.) Platelet phase - begins 15 sec post injury
   Platelet adhesion – platelets stick to endothelium
   Platelet aggregation – platelets stick to each other forming a “platelet plug”
   Platelets activated by thrombin secrete:
   - ADP: stimulates platelet aggregation and secretion
   - thromboxane: stimulates vascular spasm and chemo-attract platelets
   - serotonin: stimulates vascular spasm
   - clotting factors (5 of the 11 proteins): act in clotting cascade
   - Platelet Derived Growth Factor (PDGF): promote vessel repair
   - calcium ions: required for aggregation and clotting
   *This sets up a positive feedback loop
   Platelet plug size is controlled by prostacyclin released by endothelial cells: it inhibits platelet aggregation.

3.) Coagulation - begins 30 sec post injury
   Multistep process, three important steps:
   1. Prothrombinase is formed from clotting factors
   2. Prothrombinase converts prothrombin to thrombin
   3. Thrombin converts fibrinogen into fibrin which forms a mesh to plug the hole
   (blood “clot” = big mesh of fibrin: cells will later get trapped in it making it appear red)
Clotting Cascade (events for coagulation)

Consists of calcium ions plus 11 proteins that each function as an enzyme to activate the next protein in a controlled series. 5 of the 11 clotting factors are released by activated platelets and/or endothelial cells, the remaining 6 are always present in the blood as plasma proteins produced by the liver.

Two methods to initiate clotting:

**Extrinsic Pathway**
- (fast, initiated by factors outside bloodstream)
- (only occurs in body)

**Intrinsic Pathway**
- (slow, initiated by factors present in blood)
- (can occur in a test tube)

### Factor III / Tissue Factor
released by damaged endothelial cells
(or other tissue, or activated platelets)

+ 

*Factor VII + Ca$^{2+}$*

↓

### Common Pathway

*Factor X is activated → prothrombinase*

↓

*prothrombin → thrombin*

↓

*fibrinogen → fibrin*

Fibrin forms a web that traps blood cells and platelets to seal off the wound. Thrombin has positive feedback activity on both extrinsic and intrinsic pathways and both work together to form a strong clot.

30-60 min post injury:

- clot retraction occurs to reduce wound size
- PDGF stimulates cell division to promote repair

After healing has occurred:

Fibrinolysis: clot is dissolved

- thrombin (common pathway) and tissue plasminogen activator (TPA from damaged tissue) activate plasminogen (in blood) to form plasmin which digests fibrin

Blood clotting normally prevented by:

1. anticoagulants in blood that inhibit clotting factors (e.g. Antithrombin III inactivates thrombin)
2. Heparin from basophils and endothelial cells activates Antithrombin III
3. Protein C from liver stimulates plasmin to digest fibrin
4. Prostacyclin from endothelial cells prevents platelet aggregation