Regulation of Erythrocyte Production

- **Erythropoietin**
  - Secreted by kidney, liver
  - Acts on bone marrow to stimulate production of erythrocytes
  - Increased secretion when less $O_2$ delivered to kidneys
  - Testosterone also stimulates release of erythropoietin
Leukocytes

- Produced by bone marrow
- Monocytes and many lymphocytes undergo further development outside the bone marrow

<table>
<thead>
<tr>
<th>Erythrocytes</th>
<th>Leukocytes</th>
<th>Platelets</th>
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<td>Polymorphonuclear granulocytes</td>
<td>Monocytes</td>
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<tr>
<td></td>
<td>Neutrophils</td>
<td>Eosinophils</td>
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</table>
Platelets

- Fragments of large cells called megakaryocytes
- Involved in blood clotting
- *Clot formation can not occur without platelets*
Hemostasis

• Prevention of blood loss (stoppage of bleeding)
• Injuries to small vessels (arterioles, capillaries, venules)
• Immediate response to injury is vasoconstriction
  – Reduces flow to the area
  – Presses together the sides of the endothelium
    • Induces stickiness
    • “glues” the endothelium together
• Requires 2 processes
  1. Platelet plug formation
  2. Blood coagulation (clotting)
Formation of a Platelet Plug

1. **Platelet adhesion**
   - Exposed collagen in connective tissue
   - von Willebrand factor
     - Secreted by endothelial cells and platelets

2. **Triggers platelet activation**
   - Release contents of secretory vesicles that act locally

3. **Triggers platelet aggregation**
   - Formation of platelet plug
Platelet Plug Localization

• Adjacent, undamaged endothelial cells release *prostacyclin (PGI₂)*
  – Strong inhibitor of platelet aggregation

• Adjacent, undamaged endothelial cells also release *NO*
  – Vasodilator
  – Inhibits platelet adhesion, activation and aggregation
Blood Coagulation
Clot Formation

• The transformation of blood into a solid gel called a **clot** or **thrombus**
  – Consists mainly of **fibrin**
• Clotting occurs locally around the platelet plug
• Function is to support and reinforce the platelet plug and to solidify blood that remains in the wound channel
Clotting Pathway
Role of Thrombin

• Cascade of events leads to the conversion of prothrombin (plasma protein) to thrombin

• Thrombin catalyzes the split of fibrinogen to loose fibrin
  – Fibrin network then becomes stabilized

• Thrombin also stimulates platelet activation
Clotting Pathway

Vessel damage

Exposure of blood to subendothelial tissue

Inactive plasma protein → Enzyme → Inactive plasma protein

Prothrombin → Enzyme → Thrombin

Thrombin → XIII → XIlla

Fibrinogen → Loose fibrin → Stabilized fibrin

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Clotting Pathway
Role of Platelets

• Clotting can not occur in the absence of platelets
• Activated platelets are essential because several of the cascade reactions take place on the surface of activated platelets
• Activated platelets display specific membrane receptors that bind several of the clotting factors which permits the reactions to occur
Clotting Pathway

- **Intrinsic pathway**
  - Everything necessary for this pathway is in the blood

- **Extrinsic pathway**
  - A cellular element outside the blood is needed
    - **Tissue factor**
      - Not a plasma protein
      - Located on the outer plasma membrane of fibroblasts
Dissolving the Clot
Fibrinolytic System

• A fibrin clot is a temporary fix until the blood vessel is repaired
  • *Plasminogen* is activated to plasmin
  • *Plasmin* digests fibrin which dissolves the clot