Ch 16: Blood

- Plasma and Cellular Elements of Blood
- Hematopoiesis
- RBC Physiology
- Coagulation
Blood = connective tissue

extracellular matrix:
Plasma

specialized cels:
(Formed elements)
RBCs
WBCs
Platelets
Fig 16-1

BLOOD is composed of

- Water
- Ions
- Organic molecules such as
  - Amino acids
  - Proteins
  - Globulins
  - Glucose
  - Lipids
  - Fibrinogen
- Trace elements and vitamins
- Nitrogenous wastes
- Gases such as
  - CO₂
  - O₂

BLOOD is composed of cellular elements

- Red blood cells
- White blood cells include
  - Lymphocytes
  - Monocytes
  - Neutrophils
  - Eosinophils
  - Basophils

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Plasma

- **Water**
- **Plasma proteins**
  - Albumin (60%)
    - Osmotic Gradient
  - Globulins (Ab)
  - Fibrinogen
- **Molecules**
  - Electrolytes
  - Nutrients
  - Trace Elements
  - Dissolved gases

Serum = Plasma – Clotting factors
Hem(at)opoiesis = Blood Cell Formation

- Few uncommitted, pluripotent **stem cells** in red bone marrow throughout life time *(Fig 16-2)*

- Controlled by cytokines, e.g.
  - Erythropoietin *(hormone or cytokine?)*
  - CSFs (Colony-stimulating factor) and ILs (interleukins): e.g. M-CSF, IL-3 (= multi CSF)
    - Neulasta (pegfilgrastim) is a CSF
    - Thrombopoietin (TPO)

- Some Terminology:
  - Anemia vs. Leukemia vs. leukocytosis vs. leukopenia
EPO Regulates RBC Production

- "Hormone" synthesized by **kidneys** in response to hypoxemia
- EPO gene cloned in 1985 ⇒ Recombinant EPO **now available** (Epogen®, Procrit®)
- Use in therapy, abuse in sport
  - Bone marrow damage from chemotherapy
  - Chronic renal failure
- Your book calls it a cytokine because it is made on demand, not stored. (p540).
- Trivia Dept.: Neulasta® (pegfilgrastim) stimulates production of WBC

Running Problem: Blood Doping
The Erythrocyte (RBC)

- Biconcave Disk, 7 μm diameter, Carry O₂
- 120 day lifespan
- No mitochondria, no nucleus
  - ATP from glycolysis
- Bag of Hb
- HCT = hematocrit = PCV
- MCV-Mean Cell Volume
  - ↓ in Fe-deficiency anemia
Hemoglobin (Hb)

- [Hb] often reported in CBC
  - Four globulin proteins *(Fig 18-8)*
    - Two α-
    - Two β-
    - Each has the heme group
    - Heme is a porphyrin that binds Fe

- Fe is considered a trace mineral
  - Meat, beans, spinach
  - Stored in liver, “recycled”
  - Fe deficiency
Hemoglobin (Hb) Synthesis and Breakdown

- Requires iron (Fe) + Vit. B₁₂ (cobalamin)
- Reversible binding between Fe & O₂
- Hb Breakdown:
  - Hb → Bilirubin → bile.
    - Hyperbilirubinemia
      - Too fast causes icterus (jaundice)
  - HbA vs. HbF
    - Fetal Hb has two γ chains instead of two β chains
RBC Disorders

- Too high PCV:
  - Polycythemia vera (PCV ~ 60-70%)
  - Dehydration

- Anemias (O₂ carrying capacity of blood too low)
  - Hemorrhagic anemia \(\Rightarrow\) Fe deficiency anemia
  - Hemolytic anemia, due to genetic diseases (e.g. Hereditary spherocytosis) or infections
  - Pernicious anemia
    - Vit. B₁₂ Deficiency
  - Aplastic anemia
  - Renal anemia
    - ↓ EPO
  - Sickle Cell Anemia
Platelets = Thrombocytes

- Megakaryocyte (MK) is polypoid. *Mechanism?*

- MK produces ~ 4,000 platelets
  - Lifespan 10 days.

- Platelets contain granules filled with clotting proteins & cytokines

- Activated when blood vessel wall damaged
Hemostasis

= Opposite of hemorrhage ⇒ stops bleeding

Too little hemostasis ⇒ too much bleeding

Too much hemostasis ⇒ thrombi / emboli

Three major steps:

1. **Vasoconstriction**
2. **Platelet plug** Temporarily blocks the hole
   1. Platelet-derived cytokines further the process
3. **Coagulation cascade** (= clot formation seals hole until tissues repaired)
   1. Two pathways: Extrinsic and Intrinsic
4. After vessel repair, plasmin dissolves the clot
Steps of Hemostasis

Vessel damage exposes collagen fibers

Platelets adhere to collagen & release factors

- local vasoconstriction
- platelet aggregation

+ feedback loop

decreased blood flow

platelet plug formation

Fig 16-10, 11
Steps of Hemostasis cont.

1. Two coagulation pathways converge onto common pathway
   1. **Intrinsic Pathway.** Collagen exposure. All factors needed are present in blood. Slower.
   2. **Extrinsic Pathway.** Uses Tissue Factors released by injured cells and a shortcut.

2. Usually both pathways are triggered by same tissue damaging events.

3. The different factors can be subject to a variety of problems
   1. Hemophilia
   2. Hypercoagulable states
Vit K needed for synthesis of several clotting factors

Fig 16-12
Structure of Blood Clot

Plasmin, trapped in clot, will dissolve clot by fibrinolysis

Clot formation limited to area of injury: Intact endothelial cells release anticoagulants (heparin, antithrombin III, protein C).
**Clot Busters** & **Anticoagulants**

**Clot Busters**
- Dissolve obsolete or unwanted clots
- Enhance fibrinolysis

*Examples: Urokinase, Streptokinase & t-PA*

**Anticoagulants**
- Prevent coagulation by blocking 1 or more steps in fibrin forming cascade
- Inhibit platelet adhesion ⇒ plug prevention

*Examples:*
- *Coumadin (warfarin) blocks Vit K*
- *EDTA chelates Ca^{2+}*
- *Aspirin prevents platelet plug*