Blood & Hematology

The human body is made up mostly of water; ~60 - 65% (40 L)

Body’s transport system plays key role in balancing fluids in the body’s compartments

“river of life” Marieb

strictly speaking, blood is not a “body fluid” like tears, mucous, or saliva or urine

→ it is a living tissue consisting of cells within a liquid ‘matrix’

Average person (150lb) has ~4.8 L of blood = 8% body weight

loss of 15-30% of blood → pallor and weakness

loss of >30% → severe shock, death

arterial blood: bright red = oxyhemoglobin
venous blood: darker red

Composition:

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>plasma</td>
<td>55% of volume</td>
</tr>
<tr>
<td>formed elements</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>=RBC’s, WBC’s, Platelets</td>
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</tbody>
</table>

Plasma

the liquid part of blood

clear straw colored fluid

plasma consists of liquid solvent → mostly water

and solutes without the formed elements

93% water
7% solutes

1000’s of different solutes

most solutes are proteins (=plasma proteins)

also: salts, ions, gasses, hormones, nutrients, wastes, enzymes

→ some of virtually every chemical found anywhere in the body
can be found in the blood

project now underway to identify every chemical in blood

**serum** = plasma with clotting factors removed

**plasma proteins** (8% of blood):

most proteins in blood do not readily pass through capillaries into interstitial spaces

1. **albumins**
   - (with other proteins) contribute to **viscosity, osmotic pressure**
     & **blood volume**
   - helps **buffer** the blood
   - **transports** many solutes by binding to them:
     - eg. drugs, penicillin, pigments, fatty acids, bile salts

2. **globulins**
   - some are **antibodies**, part of immune system
   - some help **transport** solutes
   - some involved in **clotting**

3. **fibrinogen**
   - soluble precursor to **fibrin** = framework for clotting

**Formed Elements**

about 45% of whole blood

**erythrocytes** (RBC’s) –most, 45%, of formed elements

**leukocytes** (WBC’s)

**thrombocytes** (Platelets)

all three are produced by stem cell

**Erythrocytes**

main job is to carry oxygen to cells

also deliver some carbon dioxide to lungs

most abundant of the three types of formed elements

99% of formed elements; \(\sim 5.5 \text{ mil/\mu l} \quad (\mu l=\text{mm}^3)\)

equivalent to 2.5 trillion blood cells in whole body
biconcave disc thin center, thick edges
7.5 µm diameter, 2.0 µm thick

→ high surface/volume ratio
  greater efficiency of gas exchange
  area of all RBC’s in body = >football field for gas exchange

→ flexible
  easily deforms to fit through narrow capillaries

RBC’s are packed full of hemoglobin molecules
→ in each RBC are 200-300 Million hemoglobin molecules
  each hemoglobin molecule can combine with 4 \( O_2 \) = oxyhemoglobin

  therefore, each RBC can carry \( \sim 1 \) Billion \( O_2 \) molecules

**Erythropoiesis**

= formation of RBC’s (vs hemopoiesis)

RBC’s are produced mainly in red bone marrow

kidneys produce hormone = **erythropoietin** that regulates erythropoiesis

average RBC lives 100-120 days

  as they age they become less flexible

**spleen** = “erythrocyte graveyard”

hemoglobin components are recycled after death:
  → biliverdin (green) & bilirubin (yellow/orange) → bile
  → iron stored in liver

**Erythrocyte Disorders**

1. **Anemias**

  inability of blood to carry enough \( O_2 \)
  → due to not enough RBC’s or
  → not enough hemoglobin in RBC’s

  due to low hematocrit:
    
    normal:
    men 42 – 52%
women 37 – 48%

anemia:
  hematocrit is <37%

or low hemoglobin

normal:
  males: 14-20 g/100ml
  women: 12-16 g/100ml

anemia:
  hemoglobin <12 g/dL or

symptoms: pale
  lack energy, physical weakness
  shortness of breath
  difficulty concentration

kinds: hemorrhagic (bleeding)
  hemolytic (disease, parasites, drug reactions, genetic)
  aplastic (cancer)
  Iron deficiency
  Pernicious (no B12)

2. Abnormal Hemoglobin

anemia like symptoms

kinds: thalassemias
  thin and delicate blood cells

sickle cell
  group of inherited diseases that afflicts several million worldwide
  include 80,000 african americans; 1 in 12 black babies in US carries at least 1 ss gene
  at worst: causes severe episodes of pain, stroke, damage to internal organs and death

3. Polycythemia

too many RBC’s
  8-11 million/mm³
  hematocrit = 80%

increased viscosity

causes:
overstimulation of stem cells
high altitude
prolonged physical activity
fluid loss
 genetic factors
Leucocytes

slightly larger than RBC’s = 8µm diameter

are the only “true cells” of the formed elements
they retain their organelles, including nucleus

large, irregular, lobed nucleus

relatively few are found circulating in blood: 4000-11,000/mm³ or 1% of blood

numbers are misleading since they do most of their work outside the blood vessels

mainly function in protection of body as part of immune system
→ attack and destroy bacteria and pathogens
→ remove dead cells and tissues

most WBC’s are motile by amoeboid motion (pseudopodia)
→ they squeeze out of capillaries into tissue spaces

5 different kinds of WBC’s

ID depends on presence and staining characteristics of granules and nucleus:

the numbers of each type per unit of blood are clinically important
= differential WBC count

eg. neutrophils
60-70% of circulating WBC’s
(also called band cells, stab cells or PMN’s)

attracted to sites of inflammation

carry out phagocytosis & release toxic chemicals
(eg hypochlorite and superoxide) to form
killing zone around each dying neutrophil

especially attack bacteria and some fungi

increase indicates: acute bacterial infections & appendicitis

eg. lymphocytes
25-33% of circulating WBC’s
increases in diverse infections and immune responses
some in nonspecific defenses eg. against viruses and
cancers

**Leucopoiesis**

WBC’s can live for hours to a lifetime, though most have short lifespan

most WBC’s live < 1 week

although some live for years

WBCs usually formed from stem cells in **bone marrow** or in **lymphatic tissue**

**Leukocyte Disorders**

1. **Leukocytosis**
   
   total WBC count >10,000/µL
   
   sometimes as high as 400,000/µL

   indicate:
   
   acute infections, eg appendicitis
   vigorous exercise
   excessive loss of body fluids

   eg. **Leukemia**
   
   cancer characterized by uncontrolled production of leucocytes

   but large numbers are usually nonfunctional

   crowd out functioning WBC’s

   may become anemic as normal marrow is crowded out

   **myeloid leukemia** > granulocytes
   **lymphoid leukemia** > lymphocytes

2. **Leukopenia**

   total WBC count <5,000/mm³

   may be due to bone marrow defects or irradiation, excessive destruction
   of WBC’s

   or may indicate:
   influenza
measles
mumps
cold
chickenpox
poliomyelitis
anemias
lead poisoning

**Thrombocytes (Platelets)**

not whole cells → small, irregular shape cell fragments

2-4 µm diameter

second most abundant formed elements → average 250,000/µL
range: 150,000 – 350,000/µL

number varies depending on site of collection

no gender differences

diverse functions:

1. **secrete vasoconstrictors**
   in small vessels, vasoconstriction can be maintained by chemicals released by platelets that begin to accumulate at the site of damage

2. **promote hemostasis**
   stopping the flow of blood by platelet plug &/or clotting

   [more below]

3. stimulate formation of **clot dissolving enzymes** to remove clots no longer needed

   clots are not permanent, after repair the clot is removed by chemicals activated by platelets

**Hemostasis**

stoppage of blood flow

include:

1. **vascular spasm**
2. **platelet plug**
3. **clotting cascade**
1. **vascular spasm**  
   occurs instantly  
   platelets release serotonin & thromboxane  
   → vasoconstriction at injury site  
   reduces blood loss

2. **platelet plug**  
   1-5 seconds after injury  
   platelets become sticky  
   adhere to exposed collagen fibers in damaged area and to each other  
   process may stop if leak is sealed  
   if not continues to clotting

3. **Blood Clotting**  
   if injury is extensive clotting cascade is initiated  
   mechanism must be rapid to stop bleeding  
   involve over 30 different chemicals  
   each is activated in a rapid sequence = cascade (positive feedback)  
   1. trigger: rough spot in lining of blood vessel slow blood flow  
      (also, bedridden)  
   2. clumps of platelets adhere to site (1-2sec)  
   3. platelets and damaged tissues release clotting factors that  
      trigger a series of enzymatic reactions  
      eg. thromboplastin, prothrombin activator  
   4. at last step, thrombin converts circulating fibrinogen to fibrin  
      (fibrinogen – soluble protein)  
      (fibrin – insoluble protein)  
      fibrin is a protein forming fine threads that tangle together  
      forming a clot

   **clot retraction**  
   30-60 minutes  
   draws edges of clot together  
   5. when tissue repair is complete and clot is no longer needed,  
   platelets secrete factor XII → stimulates formation of  
   enzymes that dissolve the old clot

   **fibrinolysis**  
   = clot dissolution  
   occurs continuously  
   plasmins & fibrolysin = clot busters

**Platelet Formation**

platelets have a short life span: ~1-2 weeks
formed in marrow, lungs and spleen by fragmentation of large cells; 1 gives rise to ~6000 platelets)

if not used they are destroyed by liver or spleen

spleen also stores large numbers of platelets
    → in time of stress (eg. hemorrhage or burns) can release large numbers into the blood

**Thrombocyte Disorders**

1. **Spontaneous Clotting**

   body has mechanism that prevent spontaneous clotting without vessel damage:
   - normal lining of vessels is smooth
     → platelets do not adhere
   - blood also contains antithrombins
     → inactivate thrombin
     eg. heparin (a natural blood constituent)

   sometimes clots are triggered by internal factors

   two conditions favor clots:
   rough spots on blood vessels
   atherosclerosis may trigger clotting

   abnormally slow flow of blood
   bedridden or immobilized patients

   these may be caused by:
   atherosclerosis
   severe burns
   inflammation
   slow flow

   **thrombus** – a fixed persistent clot
   **embolism** – a traveling clot

2. **Thrombocytopenia**

   abnormally low number of platelets
   (<50,000 platelets /µL)
   → increased risk of internal hemorrhage from trauma or surgery
if below 20,000 platelets/µL
   \rightarrow associated with multiple small bruises (purpura), hemorrhagic spots (petechiae) in skin and sometimes spontaneous bleeding from mucous membranes

if below 10,000
   \rightarrow potentially fatal hemorrhages in intestines or brain

2. **Bleeding Disorders (=Hemophilias)**
   inability of blood to clot in normal amount of time may be caused by
   decreased # of platelets
   liver disease
   inability to form various clotting factors

   prothrombin and fibrinogen are produced in liver require vitamin K (absorbed from intestine)

   absorption of vitamin K requires bile

   if bile ducts become obstructed results in vitamin K deficiency
      \rightarrow liver cant produce prothrombin at normal rate

   eg. factor VIII
      comprises 83% of cases

   eg. factor X
      a sex linked condition

**Blood Types**

blood type refers to the kinds of antigens found on the surface of blood cells (esp RBC’s)

related to immunity and how the body protects itself from pathogens:

   our immune system recognizes and distinguishes between “self” and “nonself”:

   **self** = all proteins and other chemicals that are part of our bodies; that belong there
**nonself** = any proteins or chemicals that don’t belong

**antigen** = any foreign substance that enters our body

**antibody** = special proteins made by our immune system to remove foreign substances

Many antigens are present on surface of blood cells creating many different “blood types”

Only a few are important in transfusions:
- ABO system
- Rh system

If these antigens are attacked by our antibodies, it causes agglutination (clumping) of cells

leads to:
- heart attack
- stroke
- kidney failure
- etc

Most important consideration in transfusions:

Don’t want recipient’s antibodies to react with donor’s antigens

**ABO System Only**

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>Antigens</th>
<th>Antibodies produced</th>
<th>can receive blood from</th>
<th>can donate blood to</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>anti B</td>
<td>A, O</td>
<td>A, AB</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>anti A</td>
<td>B, O</td>
<td>B, AB</td>
</tr>
<tr>
<td>AB</td>
<td>A &amp; B</td>
<td>neither</td>
<td>A, B, AB, O (universal recipient)</td>
<td>AB</td>
</tr>
<tr>
<td>O</td>
<td>none</td>
<td>both</td>
<td>O</td>
<td>A, B, AB, O (universal donor)</td>
</tr>
</tbody>
</table>

**Cross-matching** confirms compatibility
- Since many other antigens are present and some may cause reactions
- Even type O donors must be cross matched
**Rh incompatibility:**

mother is Rh - & fetus is Rh +

no reaction if normal pregnancy
  second such pregnancy antibodies cross placenta

RhoGAM blocks the mothers immune systems response and prevents her sensitization to Rh+ blood of child.

RhoGAM is a serum containing anti-Rh agglutinins that agglutinate the Rh factors that get into her blood

**Hematology in Old Age**

baseline rate of erythropoiesis doesn’t change much with aging

most effects of aging are due to changes in other systems

  eg. but if stomach is producing less intrinsic factor, B$_{12}$ will not be absorbed as well and may lead to anemia

  eg. atrophy of kidneys may reduce erythropoietin which could also affect erythropoiesis

  eg. thrombosis increases as plaques of atherosclerosis in blood vessels builds