Blood & Hematology

the human body is made up mostly of water (~65%)
most (almost 2/3’s) is in our body cells
about 30% in between cells (tissue spaces)
only ~8% of that water is in the circulatory system

the 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’

the total blood volume varies due to:
dehydration
hemorrhage
amount of body fat
etc.

Average person (150lb) has ~5 L (1 gallon) of blood

loss of 15-30% of blood → pallor and weakness
loss of >30% → severe shock, death

Composition:

plasma 55% of volume
formed elements 45%

Plasma

the liquid portion of blood
clear straw colored fluid
plasma consists of:

liquid solvent (water) 93%
solutes (7%)

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

the new science of epigenetics allows us to extract even more information from a drop of blood:

plasma proteins (most solutes are proteins)

1. albumins (over half of plasma proteins)

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

2. globulins (over a third of plasma proteins)

→ some are antibodies, part of immune system
→ some help transport solutes
→ some involved in clotting

3. fibrinogen (~4% of plasma proteins)

→ soluble precursor to fibrin = framework for clotting

serum = plasma with clotting factors removed

most blood proteins (except ‘gamma’ globulins) are synthesized by liver
‘gamma’ globulins produced by WBC’s

are you a smoker
did you have loving parents
abused as a child
do you live near a busy roadway
what is your socioeconomic status
have you been exposed to pesticides or toxins

Formed Elements

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

leukocytes (WBC’s)

thrombocytes (Platelets)

of the formed elements only leukocytes are true (complete) cells

→RBC’s missing nucleus and some organelles
→platelets are small pieces of cells

all three are produced by blood stem cell
**Erythrocytes (Red Blood Cells)**

most abundant of the three types of formed elements

99% of formed elements (2.5 trillion RBC’s in whole body)

main job is to carry oxygen to cells

also deliver some carbon dioxide to lungs

RBC’s are packed full of **hemoglobin** molecules

in each RBC are 200-300 Million hemoglobin molecules (transport proteins)

hemoglobin contains 4 Iron (Fe) atoms; 2/3’s of body’s iron is contained in our blood’s hemoglobin

each iron atom can combine with 1 O₂ molecule

each hemoglobin molecule can combine with 4 O₂’s = oxyhemoglobin

therefore, each RBC can carry ~1 Billion O₂ molecules

RBC’s are not true “cells” since they lack a nucleus

RBC’s have unique shape = **biconcave disc**

thin center, thick edges

→ high surface/volume ratio

greater efficiency of gas exchange

→ flexible

**Erythropoiesis**

=formation of RBC’s (vs hemopoiesis)

RBC’s are formed from stem cells in bone marrow

critical nutrients required for hemopoiesis:

iron, copper, B₁₂(riboflavin), B₉, pyridoxine, & folic acid

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

blood doping = injection of erythropoietin

increases O₂ carrying capacity of blood but can cause blood to become too thick → heart attack

average RBC lives 100-120 days (4 months)
as they age they become less flexible

8 million blood cells die each second

each day ~230 billion RBC’s are replaced

they are destroyed by fragmentation as they squeeze through capillaries
dead cells removed from blood and destroyed by macrophages in spleen, liver and marrow

**spleen** = “erythrocyte graveyard”

→ since RBC’s have an especially hard time squeezing through its small channels

hemoglobin components are recycled after death and transported to the liver

→ biliverdin (green) & bilirubin (yellow/orange) → bile

→ iron stored in liver

**Some Erythrocyte Disorders**

1. **Anemias**

   inability of blood to carry enough O₂

   → due to not enough RBC’s or not enough hemoglobin in RBC’s

   symptoms: pale

   lack energy, physical weakness

   shortness of breath

   difficulty concentration

due to low hematocrit:

![Hematocrit Values](image)

<table>
<thead>
<tr>
<th></th>
<th>normal:</th>
</tr>
</thead>
<tbody>
<tr>
<td>men</td>
<td>42 – 52%</td>
</tr>
<tr>
<td>women</td>
<td>37 – 48%</td>
</tr>
</tbody>
</table>

anemia: hematocrit is <37%
or low hemoglobin

some causes of anemia:

hemorrhagic (bleeding)

hemolytic (disease, parasites, drug reactions, genetic)

aplastic (cancer)

Iron deficiency

Pernicious (no B₁₂)

2. **Abnormal Hemoglobin**

anemia like symptoms

eg. thalassemias

thin and delicate blood cells

eg. 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 (White Blood Cells)

slightly larger than RBC’s
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:
- least abundant formed element in blood: 1% of blood volume
- 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:

the two most common WBC’s in a normal blood sample are neutrophils & lymphocytes
the others account for only a few % of all WBC’s
the numbers of each type per unit of blood are clinically important:

= differential WBC count
eg. neutrophils (normally ~65% of WBC’s in blood)
   especially attack bacteria and some fungi
   increase may indicate acute bacterial infections & appendicitis
eg. eosinophils (normally ~3% of WBC’s in blood)
   secrete chemicals that weaken or destroy parasitic worms and dispose of inflammatory chemicals and allergens
   increase may indicate allergies, parasitic worm infections
eg. monocytes (normally ~ 30% of WBC’s in blood)
   destroy dead or dying host and foreign cells and some chemicals
   increase during chronic inflammation (eg. TB) and viral infections (eg mononucleosis)

Leucopoiesis

some WBCs are formed from stem cells in bone marrow
other WBC’s are formed in lymphatic tissue
their production is also controlled by a hormone
WBC’s can live for hours or a lifetime, though most have short lifespan
most WBC’s live < 1 week
dead neutrophils however are responsible for the creamy color of pus

Some Leukocyte Disorders

1. Leukocytosis (high WBC count)
   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

2. **Leukopenia** (low WBC count)
   
   total WBC count <5,000/mm³
   
   may be due to excessive destruction of WBC’s from bone marrow defects or irradiation
   
   or may indicate viral infections
   
   eg. influenza, measles, mumps, chickenpox

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**Thrombocytes (Platelets)**

not whole cells

→ small, irregular shaped cell fragments

second most abundant formed elements

diverse functions in stopping the flow of blood

= Hemostasis (NOT Homeostasis)

Hemostasis is a group of chemical cascades that include:

1. vascular spasm
2. platelet plug
3. clotting cascade

1. **vascular spasm**
   
   occurs instantly at site of injury
   
   platelets release vasoconstrictors at injury site to reduce blood loss

2. **platelet plug**
   
   1-5 seconds after injury platelets become sticky

   adhere to damaged area and to each other forming a plug
   
   if leak is sealed the process ends
   
   if not hemostasis triggers clumping

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: damage to blood vessel
   2. clumps of platelets adhere to site (1-2sec)
   3. platelets and damaged tissues release clotting factors that trigger a series of enzymatic reactions
   4. at last step, thrombin converts circulating fibrinogen to fibrin
   
   (fibrinogen – soluble protein)
   
   (fibrin – insoluble protein)

5. once leak is sealed, platelets release growth factors to stimulate repair of damaged area

6. when tissue repair is complete platelets release chemicals to dissolve and remove the old clot

**Thrombopoiesis**

platelets are formed in red marrow, lungs and spleen

formed by fragmentation of large cells

their production is also controlled by hormone

platelets have a short life span: ~1-2 weeks

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

**Some Thrombocyte Disorders**

1. **Spontaneous Clotting (Thrombus)**

   typically clotting is triggered by some kind of damage to blood vessels
Body has mechanism that help prevent spontaneous clotting without vessel damage:
- Endothelium is normally very smooth
  - Platelets do not adhere
- Blood also contains antithrombins
  - Inactivate thrombin
  - E.g. heparin (a natural blood constituent)
Some times clots are triggered by internal factors
- Rough spots on blood vessels
  - Atherosclerosis may trigger clotting
- Abnormally slow flow of blood
  - Bedridden or immobilized patients

**Thrombus** – a fixed persistent clot

**Embolism** – a traveling clot

2. **Thrombocytopenia** (low platelet count)

  Abnormally low number of platelets (<50,000 platelets/µL)
  - Increased risk of internal hemorrhage from trauma or surgery
  - May produce hemorrhagic spots (petechiae) in skin and sometimes spontaneous bleeding from mucous membranes

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 (generally large organic molecules)

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

There are many potential antigens on surface of blood cells creating many different "blood types"

Only a few of these antigens are usually important in transfusions:

**ABO System & Rh System**

If these antigens are attacked by our antibodies it causes agglutination (clumping) of blood cells
**Rh System**

involves a 3rd blood antigen:

<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>Rh+</td>
<td>Rh</td>
<td>none</td>
<td>Rh+, Rh-</td>
<td>Rh+, Rh-</td>
</tr>
<tr>
<td>Rh-</td>
<td>none</td>
<td>anti-Rh</td>
<td>Rh, Rh-</td>
<td>Rh+, Rh-</td>
</tr>
</tbody>
</table>

these 3 antigens produce 8 possible blood types

however there are dozens of other potential antigens on blood cells

they usually don’t cause a problem but sometimes they do

**cross-matching** confirms compatibility

since many other antigens are present and some may occasionally 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

RhGAM blocks the mother’s immune system’s response and prevents her sensitization to Rh+ blood of child.

RhGAM is a serum containing anti-Rh agglutinins that agglutinate the

**Organ Transplants**

blood transfusions = tissue transplants

organ transplants are similar in that you don’t want to make antibodies against foreign antigens.

the problem is more complex since not only the 3 blood antigens must be matched

of the 100 or so additional antigens the most important, after the blood antigens, are 6 ‘tissue antigens’ also called ‘HLA antigens’

greater success in transplants with closely matched donors

eg. Self to self → autotransplants (autograph) → completely compatible

- tissue or organ is moved from one place to another in the same person
- eg. hair, bone, skin, bypass surgery
- eg. toe to thumb
- eg. endocrine glands

if overactive: remove, cut up, freeze some replace in arm, can more easily adjust

eg. Self, Identical Twins → complete compatibility

eg. Brother and sister → 25% chance of match

eg. general public

The chance of a perfect, or six-antigen match, between two unrelated people is about one in 100,000.

**Immunosuppressive Drugs**

cyclosporin a drug that selectively knocks out cells of the immune system most likely to cause organ rejection

does cause some impairment in body’s ability to fight infections and cancers

must take it for life