Blood & Hematology

the human body is made up mostly of water (~65%)

most (almost 2/3rd'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:

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

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:
eg. 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

Formed Elements

about 45% of whole blood

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; 2/3rd's of body's iron is contained in our blood's hemoglobin

each iron atom can combine with 1 O_2 molecule

each hemoglobin molecule can combine with 4 O_2's = **oxyhemoglobin**

therefore, each RBC can carry ~1 Billion O_2 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

easily deforms to fit through narrow capillaries

Erythropoiesis

=formation of RBC's (vs hemopoiesis)

RBC's are formed from stem cells in bone marrow

critical nutrients required for hemopoiesis:

iron, copper, B_2(riboflavin) , B_{12}, pyridoxine, & folic acid

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

blood doping = injection of erythropoietin
increases O_2 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 O_2
→ 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:

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

some causes of anemia:

hemorrhagic (bleeding)
hemolytic (disease, parasites, drug reactions, genetic)
aplastic (cancer)
Iron deficiency
Pernicious (no B_{12})

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/mm^3; 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 puss

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/mm^3

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

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 **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: 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)

fibrin is a protein forming fine threads that tangle together forming a clot

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

<u>Thrombopoiesis</u>

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

<u>Some Thrombocyte Disorders</u>

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

eg. heparin (a natural blood constituent)

sometimes clots are triggered by internal factors

→rough spots on blood vessels

atherosclerosis may trigger clotting

→abnormally slow flow of blood

bedridden or imobilized patients

thrombus – a fixed persistant 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

→ when extremely low can cause 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

eg. decreased # of platelets

abnormal thrombopoiesis

eg. liver disease

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

→ liver cant produce prothrombin at normal rate

eg. inability to form various clotting factors

typically a genetic cause:

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 (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

leads to (eg.): heart attack
stroke
kidney failure

***most important consideration in transfusions:**

don't want **recipient** to be able to make **antibodies** that would react with **donor's antigens**

while there are 100's of potential antigens on blood cells

blood transfusions only involve 3 different antigens in two "systems":

ABO System

involves two different blood antigens:

Blood Type	Antigens	antibodies produced	can receive blood from	can donate blood to
A	A	anti-B	A, O	A, AB
B	B	anti-A	B, O	B, AB
AB	A & B	neither	A, B, AB, O (universal recipient)	AB
O	none	both	O	A, B, AB, O (universal donor)

Rh System

involves a 3rd blood antigen:

Blood Type	Antigens	antibodies produced	can receive blood from		can donate blood to
Rh+	Rh	none	Rh+, Rh-		Rh+
Rh-	none	anti-Rh	Rh-		Rh+, Rh-

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 compatability
since many other antigens are present and some may occasionally cause reactions

even type O donors must be **cross matched**

Rh incompatability:

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

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 compatable

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 compatability

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