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:

plasma	55% of volume
formed elements	45%

=RBC's, WBC's, Platelets

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

<u>Formed Elements</u>

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; ~5.5 mil/µl (µl=$mm^{3)}$

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 ~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/mm^3

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/mm^3 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/mm^3

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

or may indicate:
influenza

measles
mumps
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

<u>Hemostasis</u>

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 imobilized patients

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

thrombus – a fixed persistant 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
→ associated with multiple small bruises
(purpura), hemorrhagic spots (petechiae) in skin and sometimes spontaneous bleeding from mucous membranes

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

2. <u>Bleeding Disorders</u> (=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
→ 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

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)

cross-matching confirms compatability
since many other antigens are present and some may 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

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