Blood
The Fluid Highway of Life

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Old Dialysis Guy

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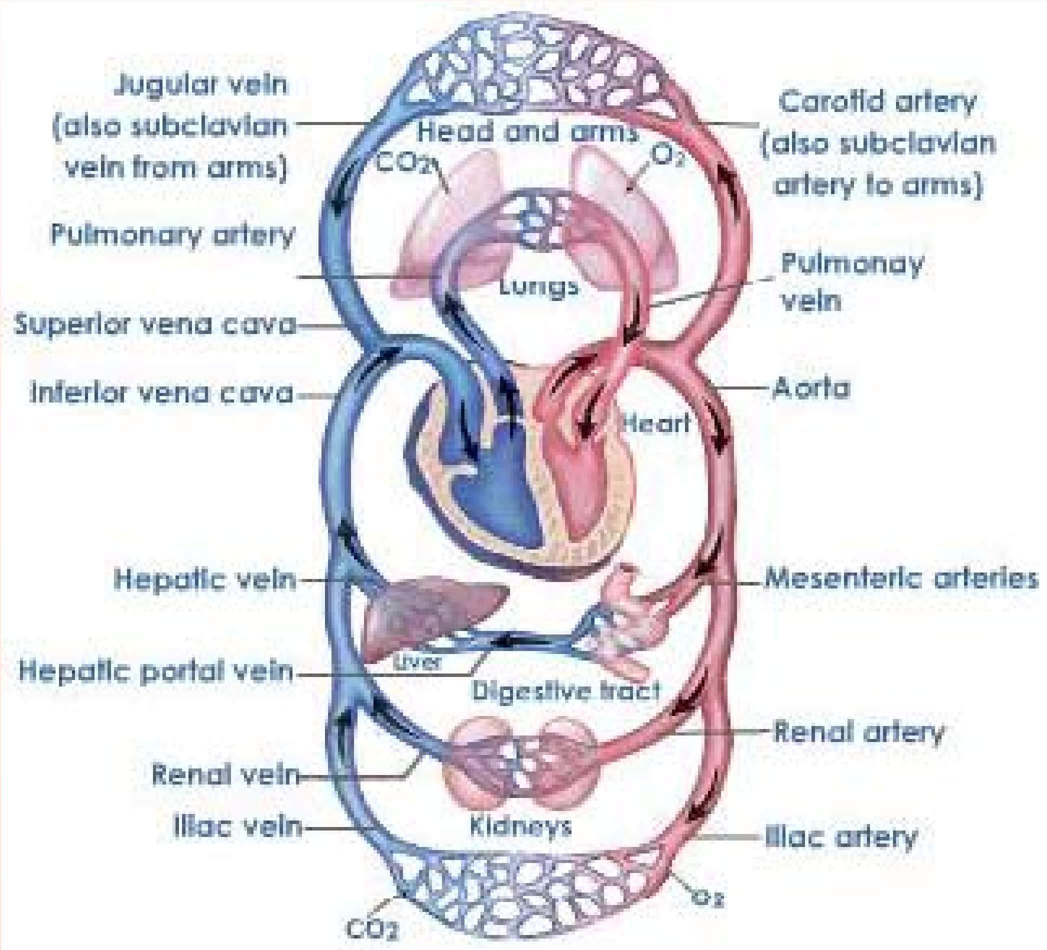
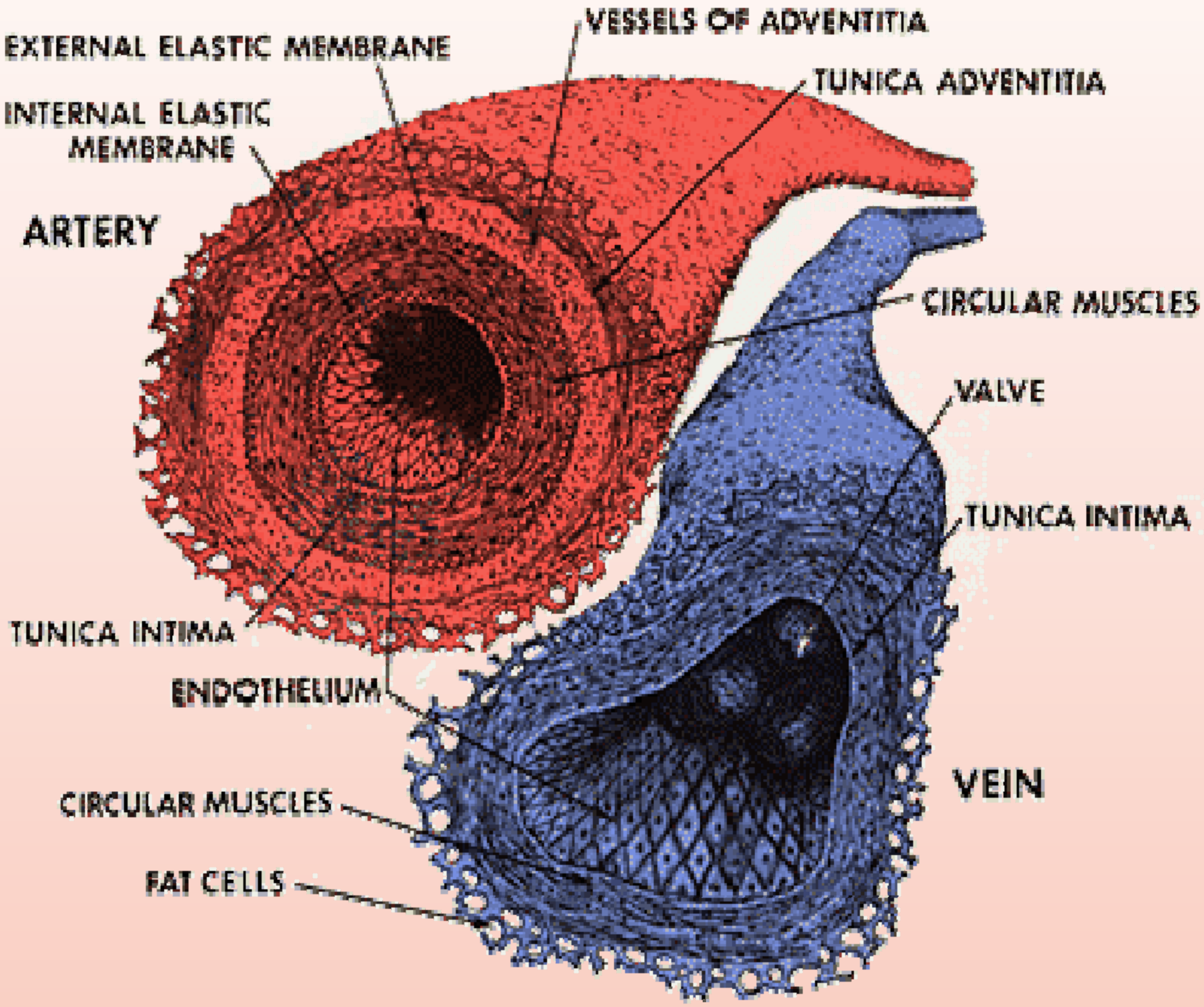
How much blood do you have?

- The average adult (70 kg) has about 10 pints (4.73 liters) of blood.
- About 7% of a person's weight is blood
- Volume calculator: BV = PV/(1 – HC)
  - BV = blood volume
  - PV = plasma volume
  - HC = hematocrit
- Too much volume = hypervolemia
- Too little volume = hypovolemia
- Key volume regulator = the kidneys

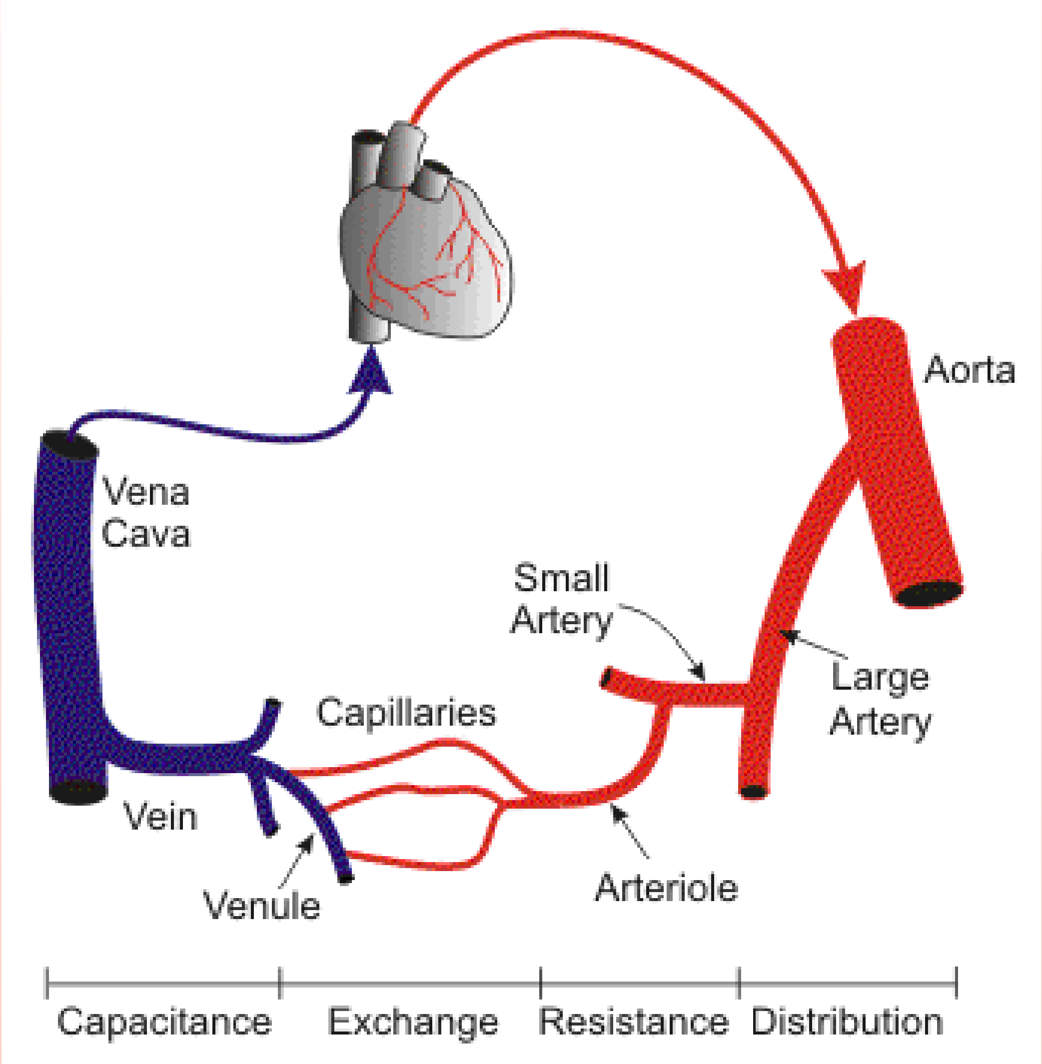
Blood Circulation



Our Blood Vessels



Circulation Vessels



Organ Blood Distribution

(Who gets how much)

Organ	Flow (mL/min)	Organ	Flow (mL/min)
Lungs	5,000	Bone	250
Liver	1,350	Heart	200
Kidney	1,100	Skin	200
Muscle	750	Spleen	77
Brain	700	Thyroid	50

Circulation Times

- The total circulation time for blood through the systemic and pulmonary circuits is one minute.
  - Typical blood volume = 5.0 liters
  - Typical cardiac output = 5.0 liters/minute
- Blood velocities are in inverse proportion to vessel cross sectional area
  - Aorta cross-sectional area = 4.5 cm^2
  - Total capillaries cross-sectional area = 4,500 cm^2
- Blood flowrate = 5L/min = 83.3 mL/sec = 83.3 cm^3/sec
  - Aorta velocity = 83.3 (cm^3/sec)/4.5 cm^2 = 18.5 cm/sec = 0.4 mph
  - Capillary velocity = 83.3 (cm^3/sec)/4,500 cm^2 = 0.0185 cm/sec
- Blood time in a capillary
  - Capillary length (0.05 cm)/velocity(0.0185 cm/sec = 2.7 seconds

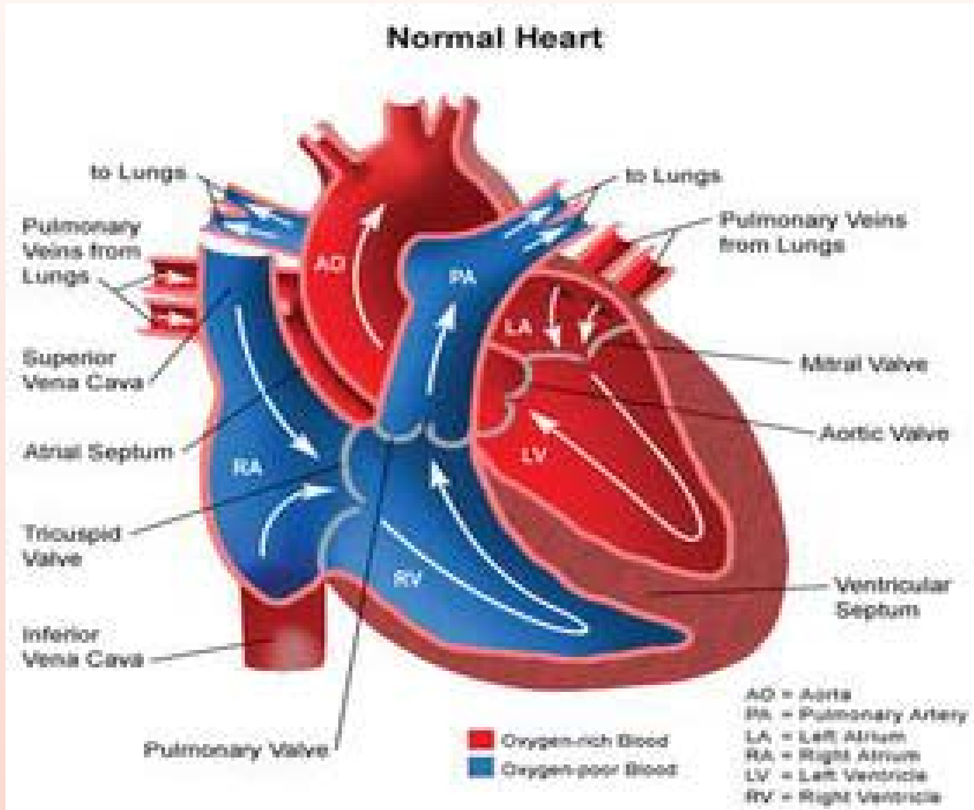
Burton, Richard B.; *Physiology by Numbers*; ©Cambridge University Press 1994; pp 30-33.

The Pump

Right Side
(Pulmonary Circuit)

Average Pressure
12 -15 mmHg

Output Energy
2 cal/min

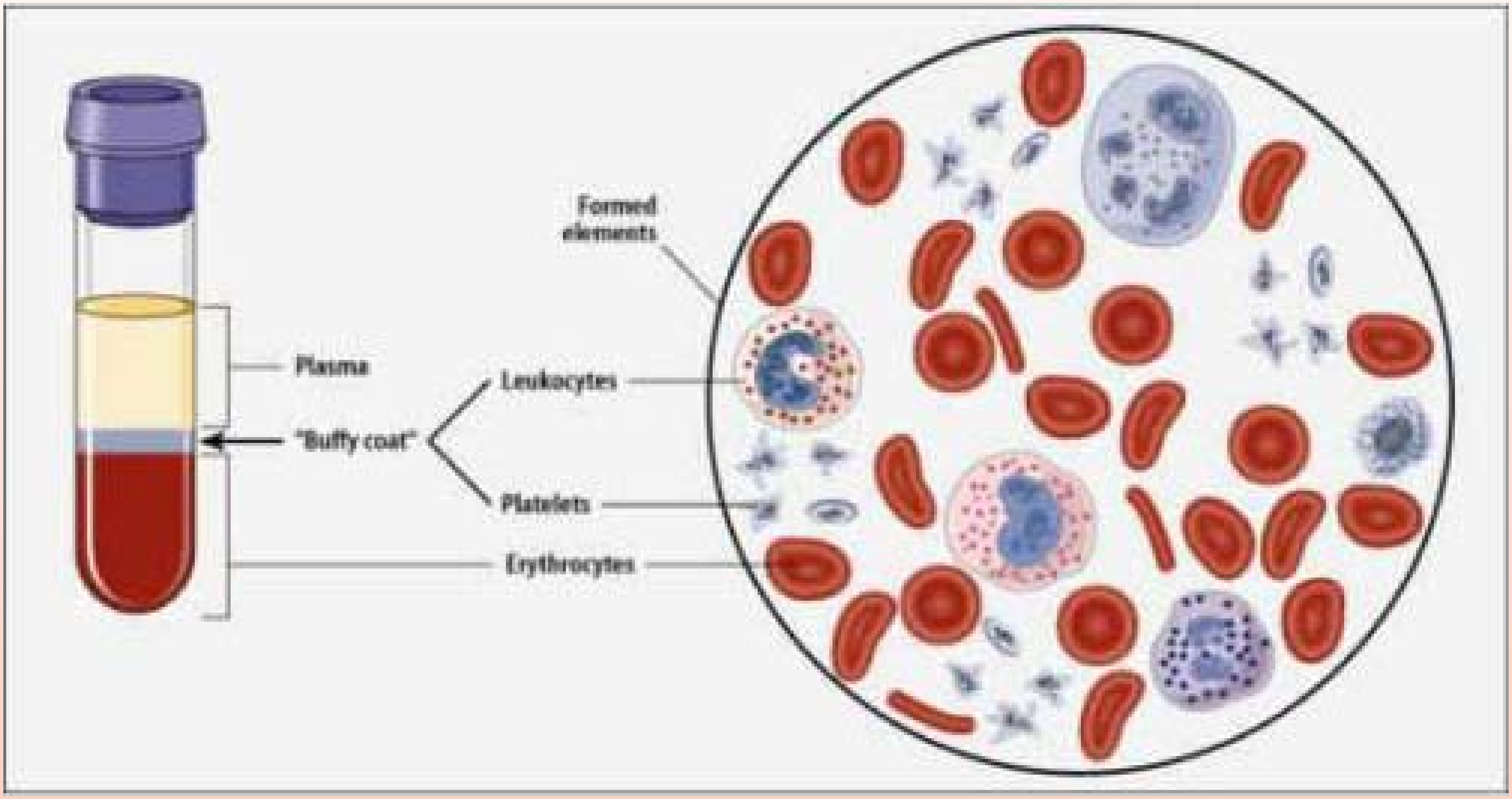


Left Side
(Systemic circuit)

Average Pressure
100 mmHg

Output Energy
16 cal/min

What's in Blood?



Blood Constituents

Item	Number	Blood Percentage	Average Age
RBC - Erythrocytes	4-5 x $10^6/mm^3$	45%	100-120 days
WBC - Leukocytes	6-8 x $10^3/mm^3$	<1.0%	3-4 days
Platelets - Thrombocytes	2-4 x $10^5/mm^3$	<0.1%	5-9 days
Plasma	55mL/dL	54%	

Dailey, John F.; *Dailey's Notes on Blood*; 4th Edition; ©Medical Consulting Group, 2002; pp 26, 48, 98.

Red Blood Cells

- Red cells are called erythrocytes
- Primary function:
  - Carry oxygen to the tissues
  - Carry Carbon dioxide to the lungs
- Red cells in circulation have no nucleus
- Why no nucleus?
  - Increases the space to carry O_2 and CO_2
  - Added cell mass = 20% additional load on the heart
  - Nucleus not needed for oxygen transport
- Their shape is biconcave which allows maximum surface area for oxygen transfer. Diameter = 7μ Thickness = 2μ
- Low amount = anemia High amount = erythrocytosis

Red Cell Production

- There are 4.5 million red cells per uL (mm^3) of blood
- The average amount of blood/person is 5 liters
  - 4.5 million x 5 L /μL = $4.5 \times 5 \times 10^6 \times 10^6 = 18 \times 10^{12}$ cells
- The average life of a red cell is 120 days. This means that one in 120 cells die each day and must be replaced
  - 18×10^{12} cells/120 = 15×10^{10} cells/day
  - That's 6,250,000,000 per hour (4.7 billion/NANT presentation)
  - Which is 104,170,000 per minute
  - Or an amazing 1,736,000 per second!

Hemoglobin – Oxygen Transport

- Hgb is a chemically complex protein made of two alpha (α) and two beta (β) chains with a heme molecule attached to each chain
- The heme molecule contains an iron atom and gives blood it's red color
- There are about 3×10^8 heme molecules per red cell
- Three factors determine the oxygen transport ability of the heme molecule
  - The pH (Hydrogen ion concentration) of blood
  - The partial pressure of carbon dioxide in the blood
  - The level of 2,3 – diphosphoglycerate (2,3-DPG) which controls the bonding of oxygen to the heme molecule

Blood pH Relationships

Blood pH is directly related to the concentrations of bicarbonate and carbon dioxide in the blood.

The relationship is defined by the Henderson-Hasselbalch Equation:

$$pH = pK + \log \frac{\left[HCO_3^-\right]}{0.03 \times pCO_2}$$

Where: pK = the blood pH from acids in the blood

HCO_3^- = bicarb concentration (mEq/L)

pCO_2 = carbon dioxide pressure (mmHg)

Burton, Richard B.; *Physiology by Numbers*; ©Cambridge University Press 1994; pp 127-130

Solving the equation

- Blood normal values for pK, HCO_3^- , and pCO_2 are:

  pK = 6.1, HCO_3^- = 24 mEq/L, and pCO_2 = 40 mmHg

- Placing these values in the equation yields:

$$\text{Blood pH} = 6.1 + \log\left(\frac{24\ \text{mEq/L}}{0.03 \times 40\ \text{mmHg}}\right)$$

$$\text{Blood pH} = 6.1 + \log\left(\frac{24}{1.2}\right)$$

$$\text{Blood pH} = 6.1 + \log(20) = 6.1 + 1.3 = 7.4$$

Burton, Richard B.; *Physiology by Numbers*; ©Cambridge University Press 1994; pp 127-130

The White Cells

Granulocytes			
Type	Life	Diameter	White cell %
Neutrophils	hours to days	10 – 15 µm	65 %
Eosinophils	12-24 hours	12 – 17 µm	2 – 5 %
Basophils	60 – 70 hours	5 – 7 µm	< 0.5 %
Monocytes/Macrophages			
	Years in tissue	12-20 µm	5 %
Lymphocytes			
T and B cells	Months/years	5 – 12 µm	25 %

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White Cell Function

- The white cells circulate throughout the entire body and protect our normal cells from foreign matter or non-self organisms
- ANTIGEN are molecules or parts of protein that attach to cell surfaces and act as labels for the immune system to identify them for destruction.
- White cells have a property called DIAPEDESIS which enables them to move through pores in the capillaries to attack invading antigen.
- Neutrophils and Macrophages possess an interesting property called PHAGOCYTOSIS which means they can encircle antigen and destroy it.
- Once a neutrophil consumes an antigen, it dies and is in turn consumed by a macrophage
- The remains of neutrophils creates a greenish-yellow fluid in the vicinity of the invading organism referred to as pus.

Dailey, John F.; *Dailey's Notes on Blood*; 4th Edition; ©Medical Consulting Group, 2002; pp 46-47.

White Cell Function

- The basophils' main function is to release heparin into the area of infection so the blood does not clot enabling white cells to reach the invaders.
- B cells produce a protein complex called antibody which attaches to antigen and activates the complement system which is part of the overall immune system.
- T cells destroy antigen. They also stimulate other white cells to attack antigen. They remember previous antigens to enable a quick response if past antigen should reappear.

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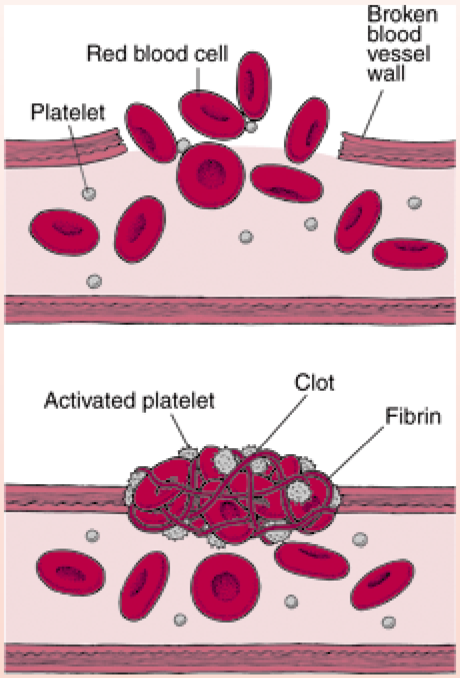
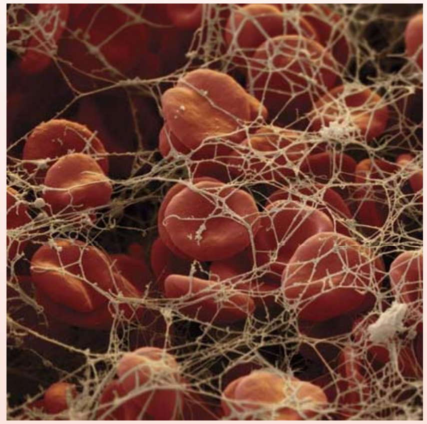
Platelets in Action



Platelets (also called thrombocytes) are the key players in maintaining hemostasis by forming a platelet plug when a blood vessel is ruptured. They also stimulate the formation of fibrin threads to anchor the plug in place. This anchoring is not necessary for capillary rupture.

For large artery and vein rupture, platelets can't help. Surgery is necessary.



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The Complement System

- The complement system consists of 25 proteins in the blood that are activated in the presence of antigen, antigen-antibody complexes, and inflamed tissue.
- The complement system works independently of the white cells and antibody.
- These proteins increase vascular permeability to help white cells move quickly into an antigen area
- They also can also rupture antigen membrane as well as coat antigen for easy identification by white cells
- They are the first line of defense, acting faster than the white cells.

Dailey, John F.; *Dailey's Notes on Blood*; 4th Edition; ©Medical Consulting Group, 2002; pp 60-62.

Blood Types

- In the early 20th century, an Austrian pathologist, Karl Landsteiner discovered the ABO blood groups.
- Blood groups are determined by two distinct antigens which appear on the surface of the red cell membrane.
- These antigens are inherited from your parents and are referred to as A and B.
- You inherit one of three types of gene from each parent, an A, B, or O gene.
- The 0 gene is called an amorph because no antigen is produced when this gene is inherited.

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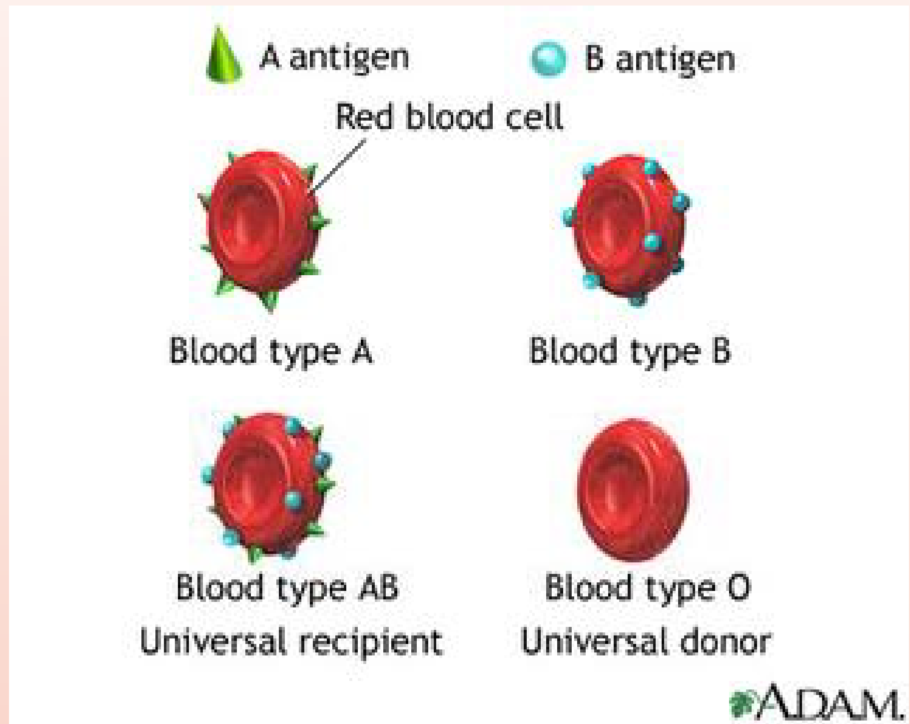
Inherited Blood Type

		Mother		
		A	B	O
Father	A	A	AB	A
	B	AB	B	B
	O	A	B	O



ABO Compatibility

- Landsteiner discovered that humans produce antibodies in the blood plasma to the antigen that is missing: anti-A antibody and/or anti-B antibody
  - Type A blood makes anti-B antibody
  - Type B blood makes anti-A antibody
  - Type O makes both anti-A and anti-B antibody
  - Type AB makes no antibody
- If the blood from a donor is incompatible with the blood from a recipient, the antigen on the red cells of the donor react with the antibodies in the plasma of the recipient causing an immune reaction which results in destruction of the donor red blood cells.
- This event is referred to as a hemolytic transfusion reaction which is serious, but usually nonfatal.

Dailey, John F.; *Dailey's Notes on Blood*; 4th Edition; ©Medical Consulting Group, 2002; pp 19-21.

The Rh antigen

- The Rh antigen was first discovered in the Rhesus monkey hence its "Rh" name.
- Humans may or may not have this antigen on their red cell membrane.
- If they have the Rh antigen, a plus sign is added to the blood type. If not, a negative sign is added.
- The first time a Rh- person receives Rh+ blood, there can be some reactions due to incompatibility, but generally nothing serious.
- The second exposure can be quite serious because the Rh- person has developed antibodies to the Rh+ blood
- These antibodies attack and destroy the red blood cells which can prove to be fatal especially in newborns.

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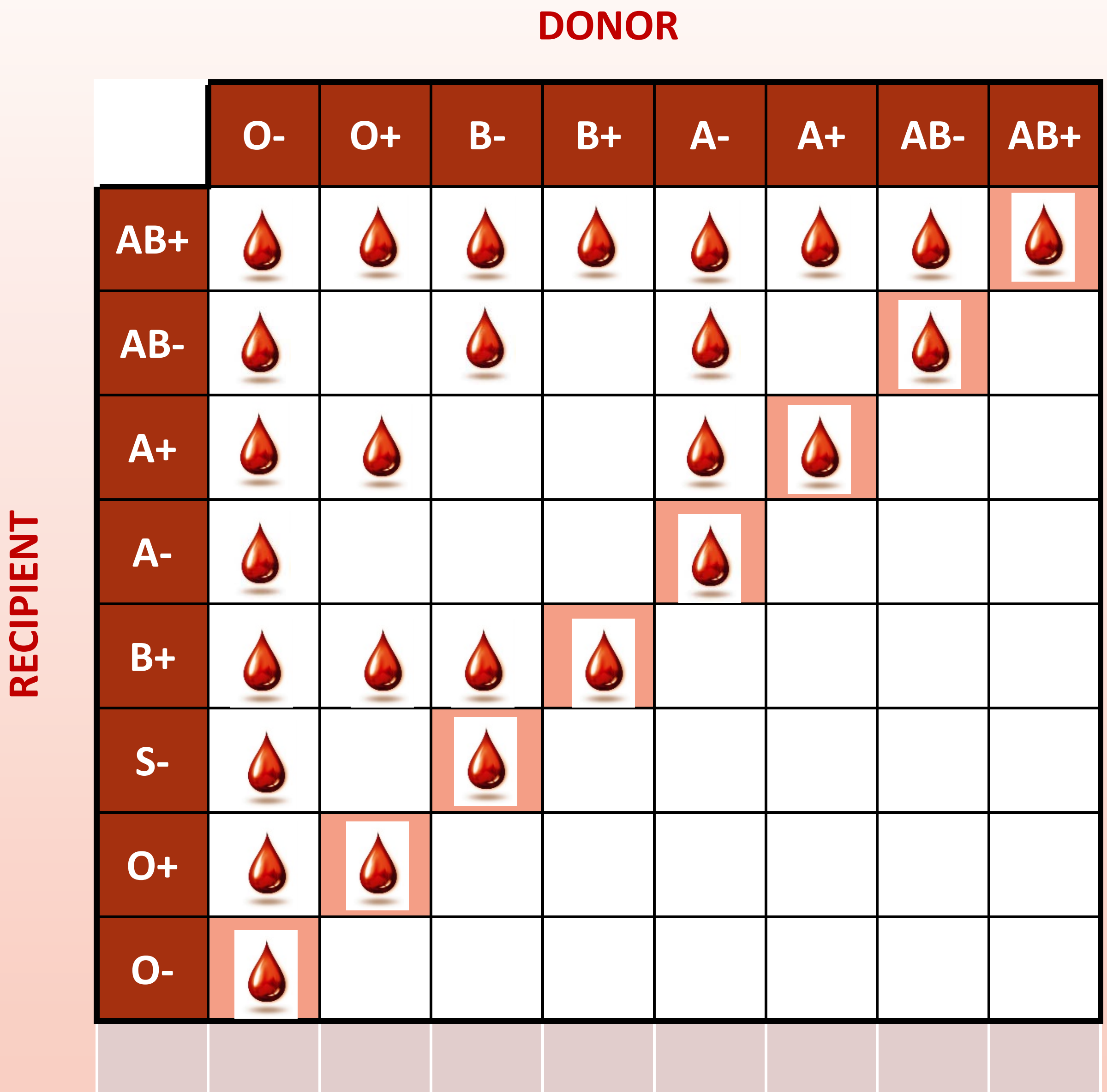
ABO Compatibility



Why do blood stem cells live so long?

- Most cells in the blood live only for a few days or months, but blood stem cells last for decades.
- The reason was believed to be that stem cells divide asymmetrically. This means that the cell divides unevenly with some internal components remaining with the original cell.
- The cellular mechanism that enables this kind of division was unknown.
- Researchers analyzed all of the genes expressed in stem cells as well as their “daughter” cells.
- Proteins that stayed to one side of the cell division were thought to be a key to the puzzle.
- Sure enough, they found a protein that fit the pattern they were looking for.

The Key to a Long Life

- Researchers* found the key was a motor protein called myosin II which comes in 2 forms, A and B
- This protein enables muscles to contract and in non-muscle cells it is used in cell division.
- Stem cells have both types whereas red and white cells have only one, myosin II A.
- By coloring the protein and using a microscope they were able to see the myosin II B stay with the stem cell during cell division.
- In *in vivo* testing they inhibited the myosin IIB protein and observed stem cells reproducing while blood cell counts dropped.
- Next step: Find a drug for chemo patients that can allow their bodies to produce more stem cells by inhibiting myosin II B.

* Discher D., Department of Chemical and Biomolecular Engineering, Univ. of Penna., and researches at Strasbourg University, Lawrence Berkeley National Laboratory, and the University of Cal., San Francisco.

Thanks for your Attention!

Please Note!!!

The rule: "What happens in Vegas stays in Vegas" does not apply to this presentation…

Please tell everyone you know!