Chapter 8

Circulation & Immunity

Goals for This Chapter

1. Identify the major structures of the circulatory system
2. Describe the structure and function of blood vessels
3. Describe the action of the heart and the circulation of blood through the body
4. Investigate heart rate and blood pressure

5. Identify disorders of the circulatory system
6. Investigate the relationship between blood pressure, heart rate, and exercise
7. Describe the main components of blood
8. Explain the role of blood in regulating blood temperature

9. Explain the role of the circulatory system in the exchange of matter and energy
10. Identify blood disorders and the technologies used to treat them
11. Describe and explain the function of the lymphatic system
12. Identify and list the cellular and non-cellular components of the immune system
13. Describe the role of cellular and non-cellular components of the immune system

Section 8.1 – Structures of the Circulatory System

Main Functions of the Circulatory System

- Transport oxygen and nutrients to our cells, and transport waste to be removed by other organs (lungs, kidneys)
- Regulate internal temperature
- Protects us from blood loss due to injury and infections
- Transports hormones from endocrine system

Major Components of Circulatory System

3 major components include:

- **heart**
  - pumps blood through the body
- **blood vessels**
  - serve as tubes for blood to move through our bodies
- **blood**
  - carries nutrients, oxygen, carbon dioxide, water, wastes etc.

William Harvey

- Early theories suggested that blood ebbed and flowed like a tide
- William Harvey suggested that the heart pumped blood through the body
- He determined that the body’s blood volume is circulated over and over through the body

Circulation System – Closed System

- **Closed circulatory system**
  - Vertebrates, and a few invertebrates, have a closed circulatory system. Closed circulatory systems have the blood closed at all times within vessels of different size and wall thickness.
  - In this type of system, blood is pumped by a heart through vessels, and does not normally fill body cavities. Closed systems can exchange heat and work with their surrounding environment.
- **Open circulatory system**
  - The open circulatory system is common invertebrates. Open circulatory systems pump blood into a hemocoel where their organs just bath in the blood.

Circulatory Route

- The transport vessels your body uses to move blood to every cell in your body:

  - Arteries

  - Arterioles

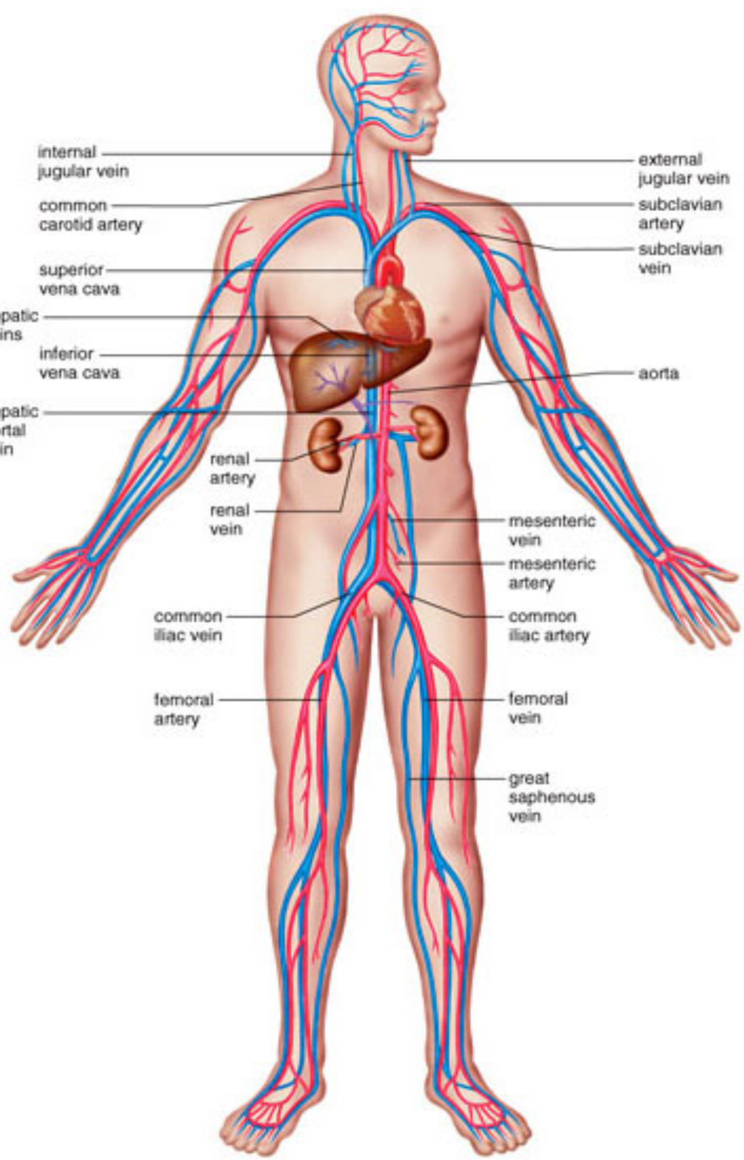
  - Capillaries

  - Venules

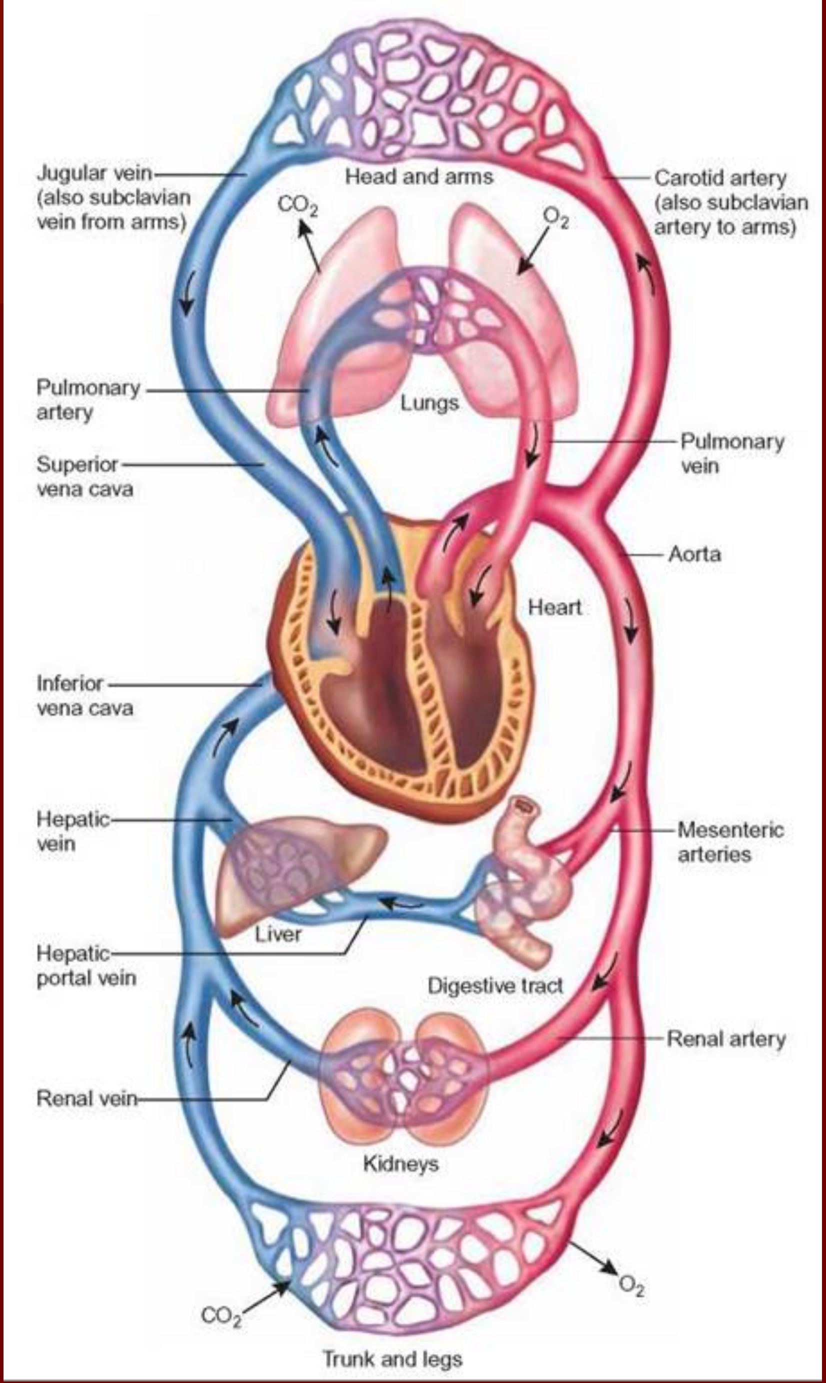
  - Veins

  - Heart - pumps blood through these vessels

Major Arteries & Veins



- Vessels that carry blood to and from the lungs form the pulmonary circulatory system
- Vessels that carry blood to and from the body's other tissues form the systemic circulatory system

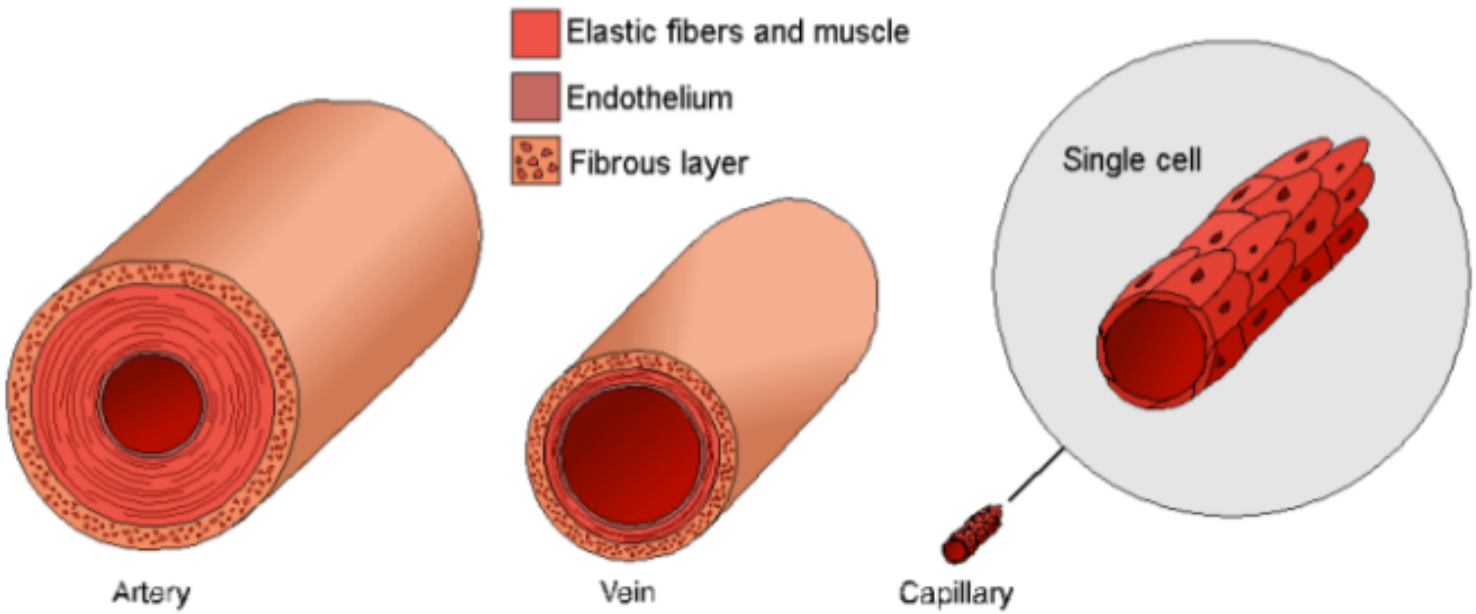


Major Arteries and Veins of the Body

- Arteries:
  - Aorta: biggest artery in the body; pumps blood to head, torso, and lower body.
  - Carotid artery: branches off from the aorta and goes to the brain.
  - Coronary artery: provides blood to the heart itself
  - Femoral artery: provides blood to the lower extremities
  - Hepatic artery: provides blood to the liver
  - Renal artery: provides blood to the kidneys

Major Blood Vessels Cont.

- Veins:
  - Vena Cava: biggest vein in the body; separated into 2 parts. Inferior VC comes from the body and Superior VC comes from the head
  - Jugular: vein coming down the neck from the brain
  - Coronary: vein taking blood from heart to VC
  - Femoral: carrying blood from lower body to heart (IVC)
  - Hepatic: carrying blood from liver
  - Renal: carrying blood from kidneys



Arteries take blood away from the heart (arteries=away)

Have thick muscular layer that expand and contract to push blood along.
Expansion of arteries is pulse

Veins take blood to the heart

Thinner
Have valves to stop blood from going backwards

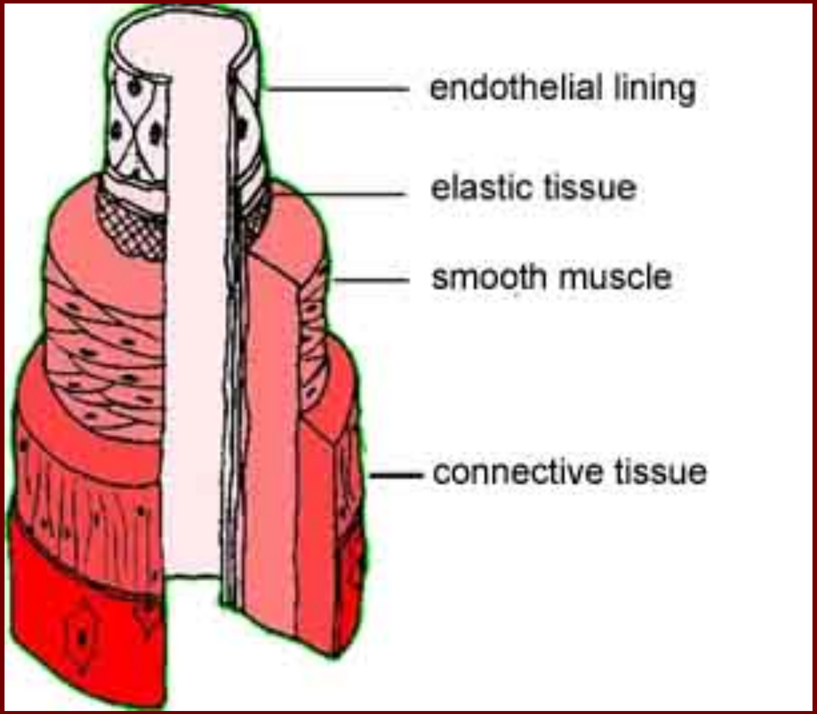
Capillaries are the smallest blood vessel. They are so small that only one blood cell can fit through at one time.They connect the veins and arteries.

Function: - where diffusion of nutrients and gases occurs

Blood Vessels - Arteries

- Arteries have thicker walls then veins (needed for higher pressures)
- The outer and inner layers are composed of rigid connective tissue to withstand greater pressures.
- The middle layers are made up of muscle and elastic fibers that stretch to allow the artery to be elastic as well.

- This allows the artery to expand as a wave of blood pumps through it and snap back into place during relaxation (pulse).
- Also important in the control of blood pressure.

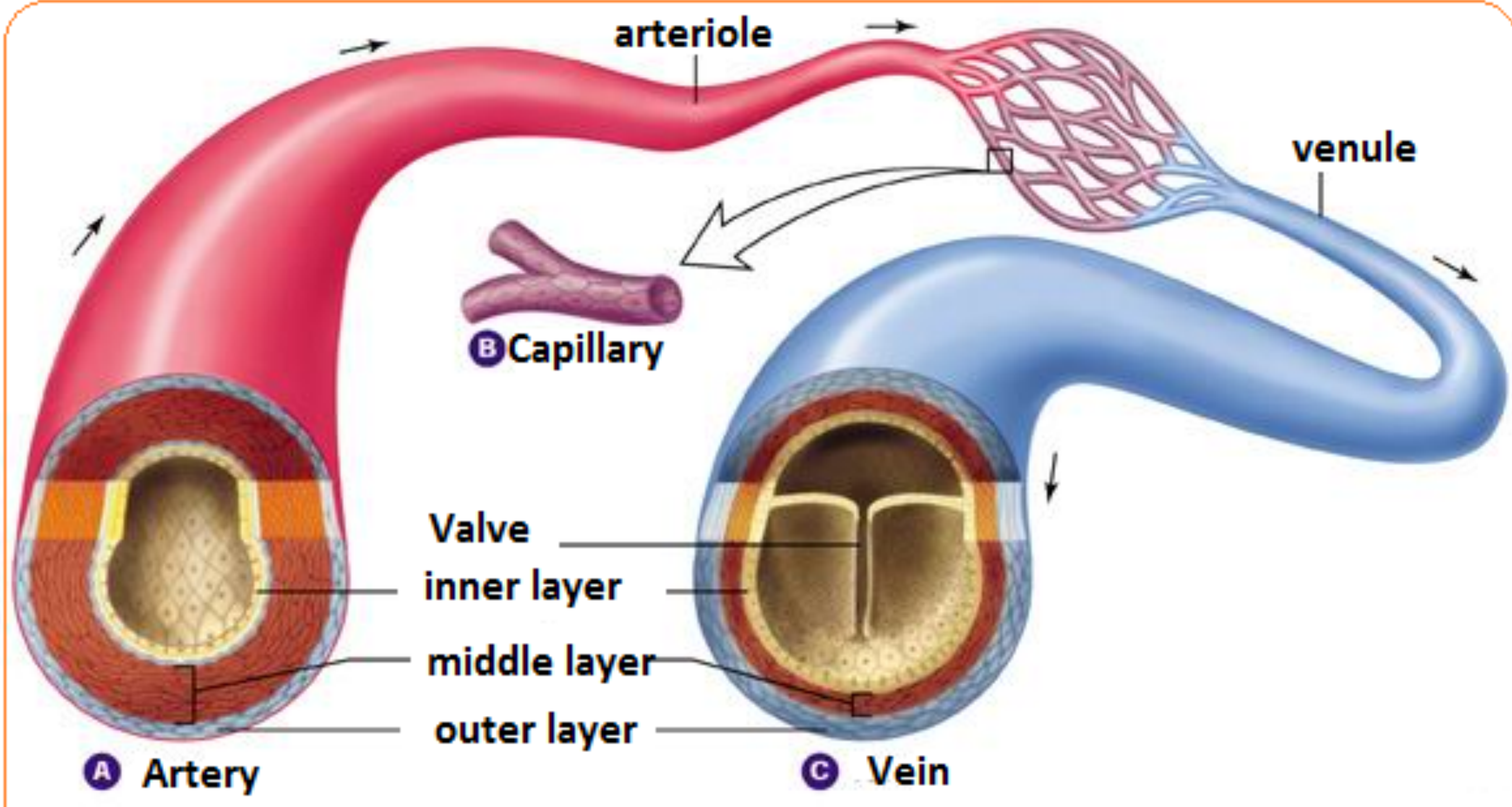


Arteries carry high pressure blood AWAY from the heart!

Blood Vessels - Arterioles

- From the arteries, the blood enters smaller vessels called arterioles
- The diameter of the arterioles is controlled by the sympathetic nervous system
- The arterioles can adjust their diameter to restrict blood flow (vasoconstriction) or to increase blood flow (vasodilation)

Blood Vessels



At any given moment, about 30% of the blood in your systemic circulation will be found in the arteries, 5% in the capillaries and 65% in the vein.

Blood Vessels - Capillaries

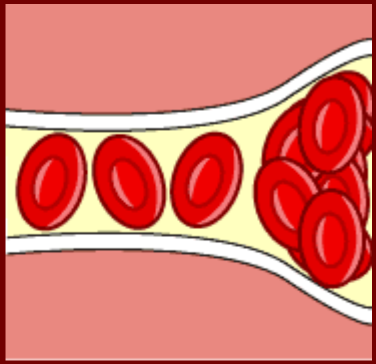
- From the arterioles, the blood flows into the capillaries (joins arterioles to venules)
- Smallest & thinnest blood vessels in your body that allow diffusion of O_2, CO_2, nutrients and wastes easily
- Have very thin walls because they are the exchange site of substances between tissues and blood
- Total surface area of capillary beds in body is $6000m^2$
- Blood pressure in the capillaries is less than arteries, but more than veins so that blood can flow through them

Blood Vessels - Capillaries

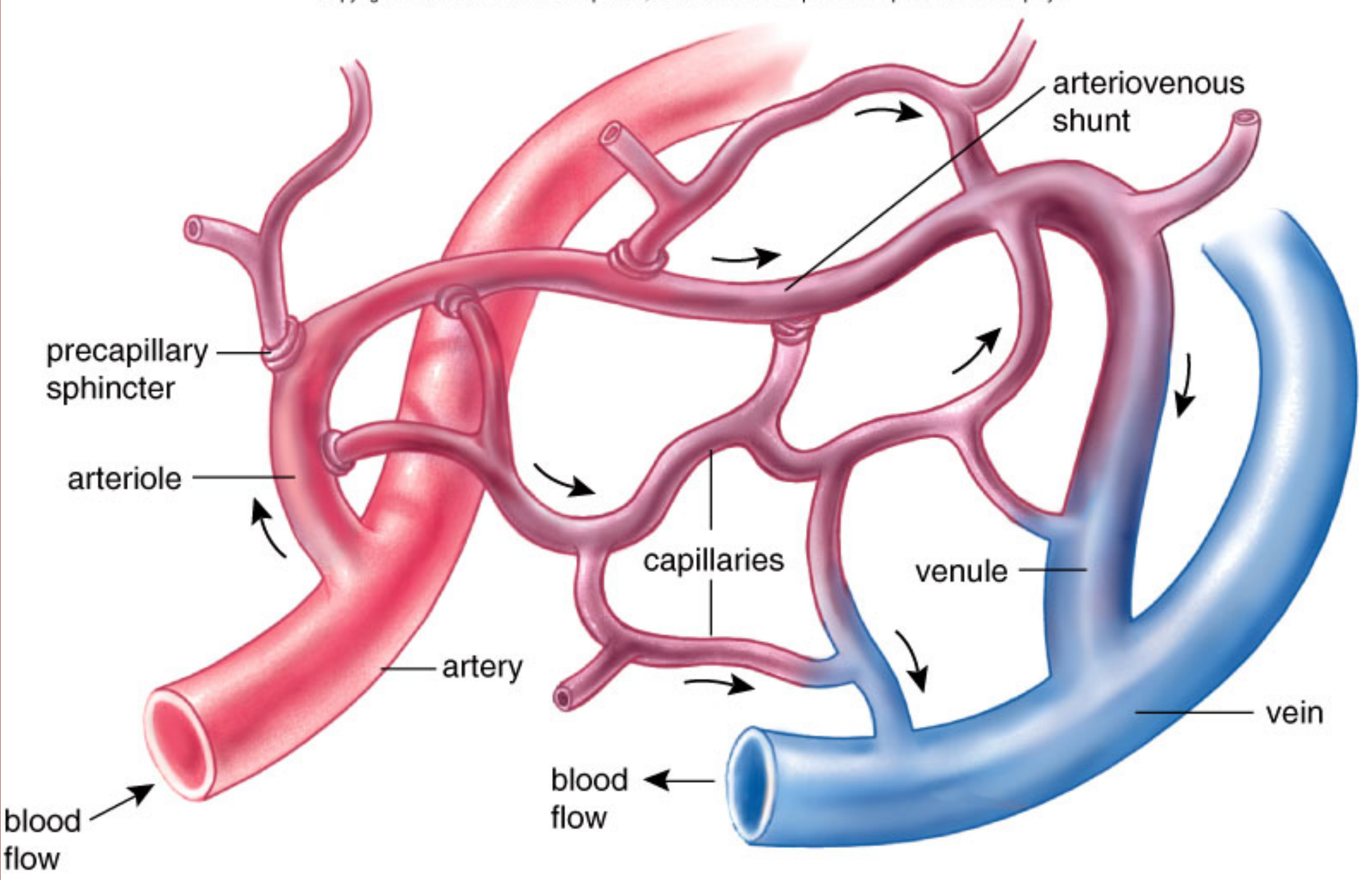
- Unlike other blood vessels, capillaries are only one cell thick
- Therefore, blood cells must move through these capillaries in single-file
- All cells in our body are constantly bathed in **extracellular (interstitial) fluid.**
  - keeps cells from drying out
  - provides way for O_2, CO_2, waste and nutrients to diffuse from capillaries to cells
  - Acts as a bridge between capillaries and cells

Blood Vessels - Capillaries

- However, capillaries are easily damaged
- When capillaries are broken, the blood leaves the capillary and enters the interstitial spaces between the cells and creates a bruise



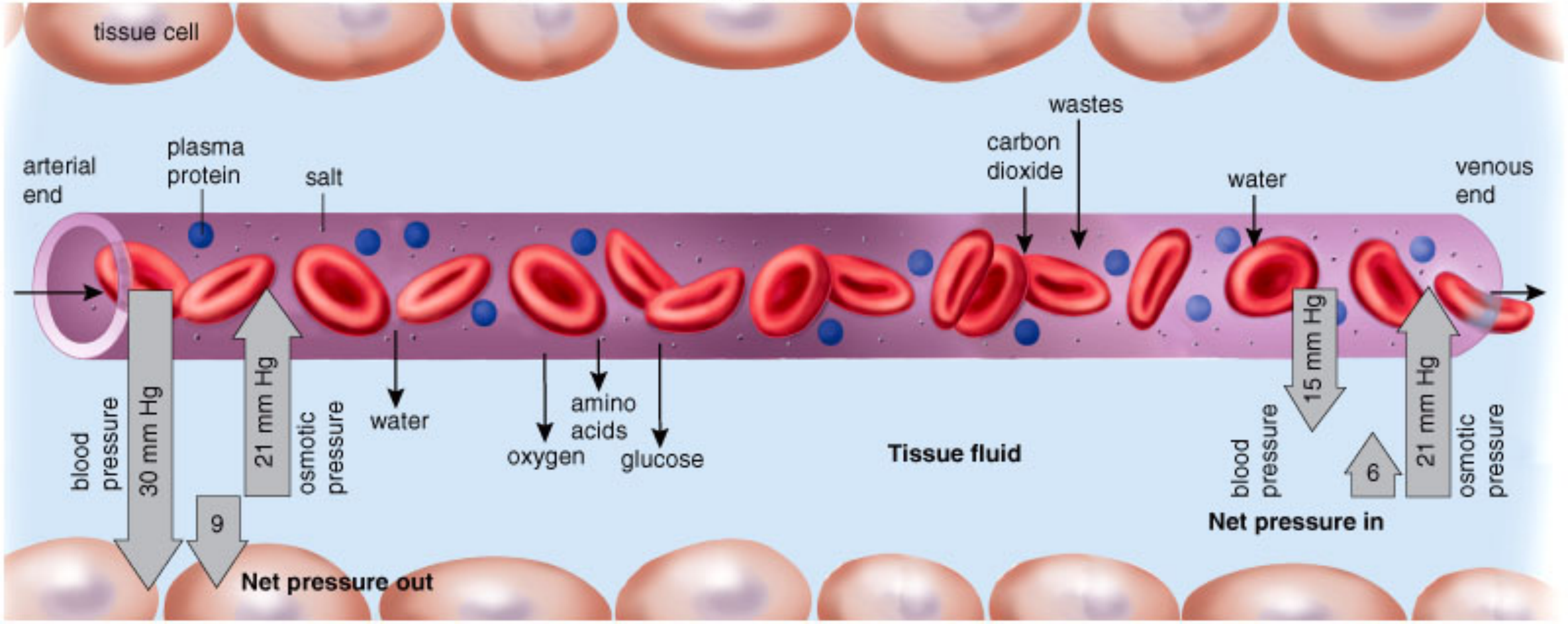
Anatomy of a capillary bed



Blood flow

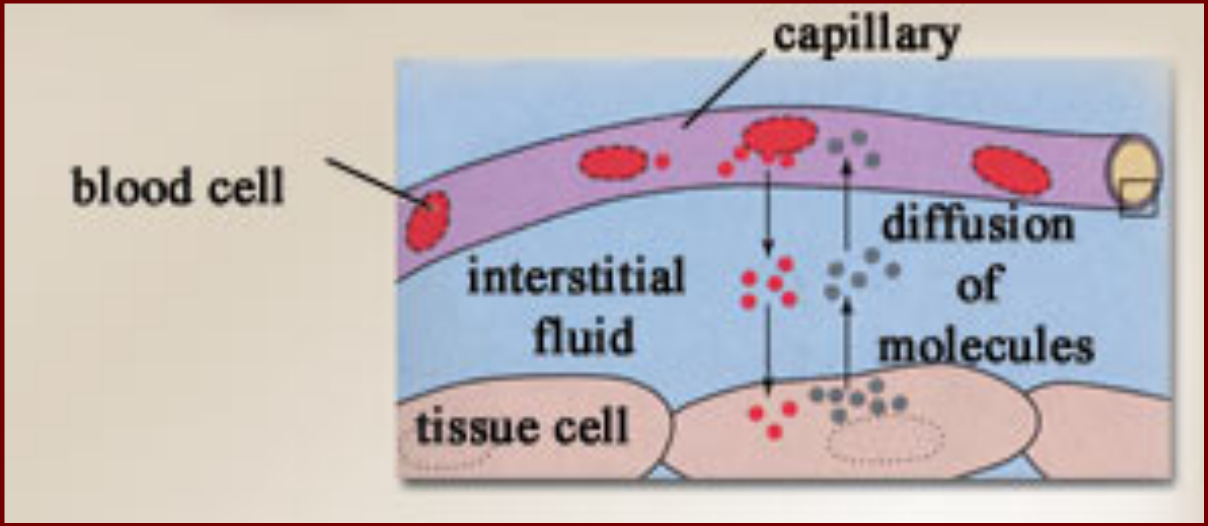
heart-> arteries -> arterioles -> (capillaries) -> venules -> veins -> heart

Capillary Exchange



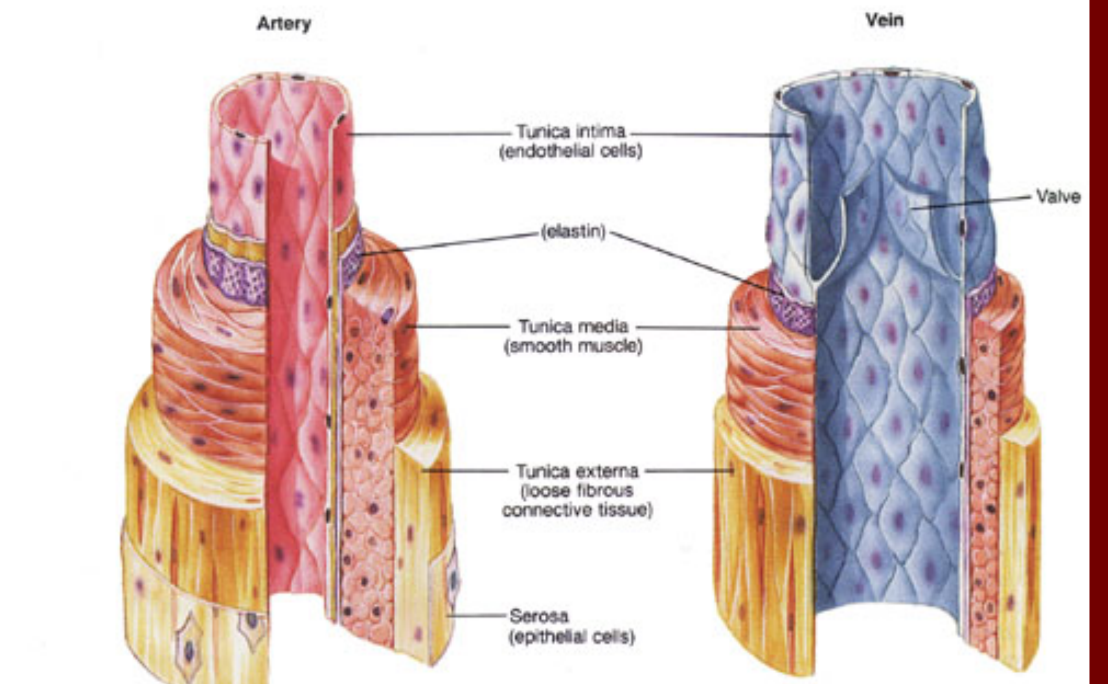
Blood Vessels - Capillaries

- Midway through the capillaries different molecules (including oxygen and metabolic wastes) diffuse through the capillaries and the extracellular fluid
- Diffusion depends on the concentration gradient
  - Oxygen has higher concentration in red blood cells therefore diffuses out of vessels into extracellular fluid and into cell.
  - Carbon dioxide has a higher concentration in the cell and therefore diffuses out into the extracellular fluid and into the vessel.



Blood Vessels - Veins and Venules

- The capillaries enlarge and turn into venules and veins
- Veins are under low pressure and are not elastic - cannot contract to help move the blood like arteries do
- So how does blood get back to the heart (especially against gravity)?



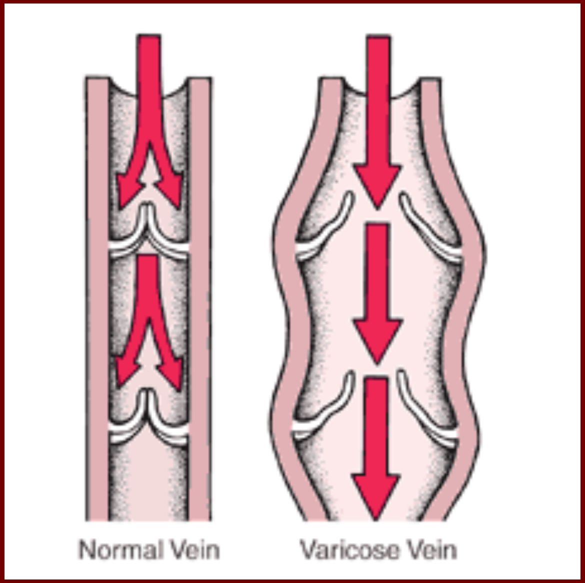
Fox, Stuart I.
Human Physiology 4th
Brown Publishers

Blood Vessels - Veins and Venules

- William Harvey discovered that veins have valves that prevent backflow
  - Important in your legs where blood needs to flow up against gravity. (Varicose veins formed when valves not longer work)
- As well, the skeletal muscles help to push the blood back to the heart as they contract and increase pressure in the veins
- **Venules** - small branches from capillaries connecting to the veins
- Largest veins are the vena cavae
- Carry oxygen poor blood to the heart (appear blue in pictures because the hemoglobin are lacking oxygen molecules)
- Up to 70% of blood is in the venous side of circulation at any one time

Blood Vessels - Disorders

- As people get older, the veins lose their elasticity
- Over time, the blood can pool in the vein and damage the valves
- This causes the blood to pool at the extremities, causing bulges in the hands and feet (known as varicose veins)



Blood Flow

Blood Vessels - Disorders

- Sometimes, an artery wall will become weak and bulge (known as an aneurysm)
- If this is not attended to, the artery will burst
- This can lead to a stroke if it occurs in the brain

Blood Vessels - Disorders

- If a person’s diet contains too much fat, it will build up in the arteries
- The fat encourages a fibrous growth of calcium and other minerals to deposit on its surface (known as plaque)
- The fat and plaque can partially (or in extreme cases almost completely) block the passage of blood – called atherosclerosis

Blood Vessels - Disorders

- Atherosclerosis leads to very high blood pressure
- Around the deposit, blood can clot
- This will reduce the amount of oxygen and nutrients from reaching the tissues
- If this occurs in the vessels of heart muscle - heart attack
- If this occurs in the vessels of the nervous tissue of the brain - stroke

Treatment of Atherosclerosis

- Angioplasty may be used to treat this condition

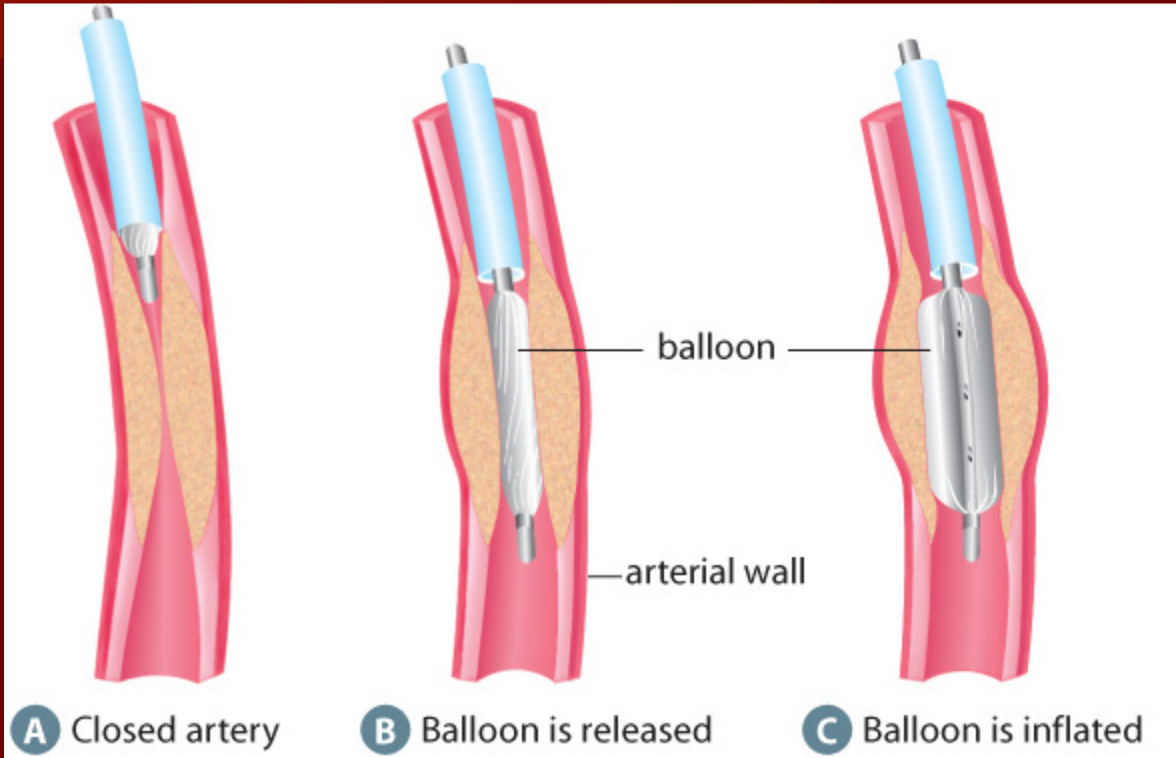
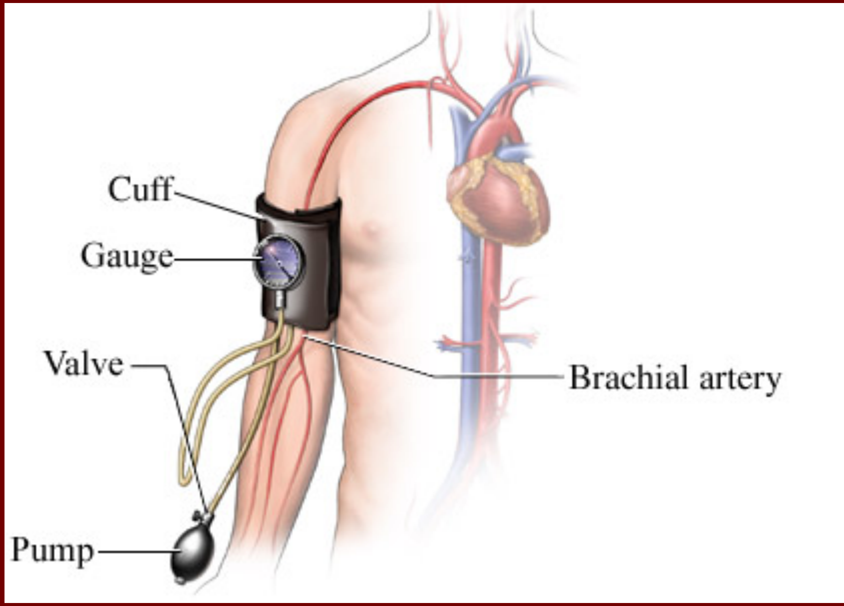


Figure 8.12 An angioplasty: The balloon is inflated to open up the blockage in the artery.

Blood Pressure

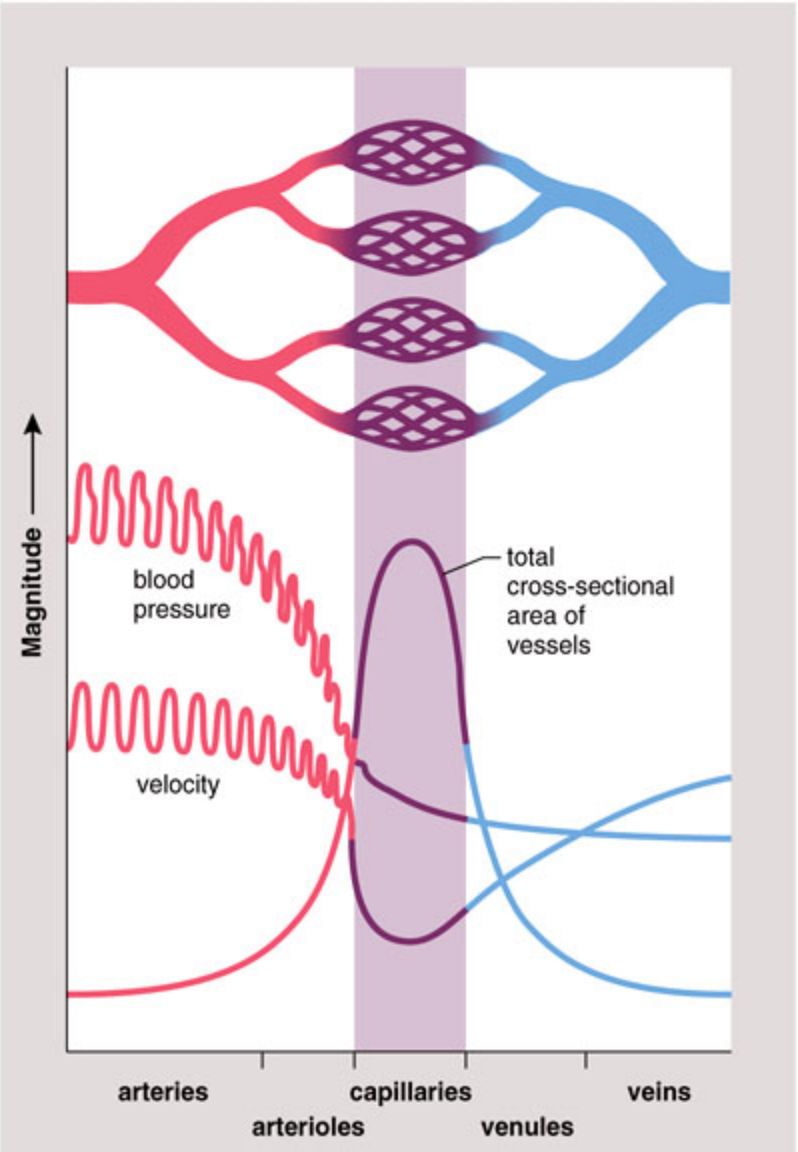
- Usually measured at an artery in the arm.
- It is recorded in millimeters of mercury or mmHg using a device called a sphygmomanometer.
- The systolic pressure is presented over the diastolic pressure in the form of a fraction.
- The blood pressure of a healthy adult is 120/80mmHg.



Blood Pressure

- Blood pressure is measured at two points:
- The highest pressure, the systolic blood pressure, is taken when the ventricles contract
- Highest pressure blood vessel is aorta
- The lowest pressure, the diastolic blood pressure, is taken when the ventricles are relaxed
- Lowest pressure blood vessel is the vena cavae

Cross-sectional Area, Blood Pressure, and Blood Velocity



Blood Pressure

- The highest blood pressures are found in the aorta because it is nearest to the heart
- Blood pressure drops rapidly as the blood enters the capillaries and slows
- Blood pressure is regulated by cardiac output and the diameter of the arteries and arterioles
- Dilation and constriction of the arterioles can depend on the presence of certain chemicals

Factors Affecting Arteriolar Resistance

Epinephrine	Arteriolar constriction, except to heart, muscles and skin
Sympathetic Nerves	Arteriolar constriction, except to skeletal and cardiac muscle
Acid Accumulation	Arteriolar dilation
CO_2 Accumulation	Arteriolar dilation
Lactic Acid Accumulation	Arteriolar dilation

Cardiac Output

- Cardiac output refers to the amount of blood that flows from each side of the heart per minute
- Two factors affect cardiac output:

1. Stroke Volume – the amount of blood pumped by each beat of the heart
2. Heart Rate – the number of times the heart beats per minute

Ex: Calculating Cardiac Output

Cardiac Output = Heart Rate (BPM) x Stroke Volume (mL or L)

- Tom's heart has a stroke volume of 50 mL and a heartrate of 100 beats per minute. Calculate his cardiac output.

Cardiac Output

- In general, the average person will have a cardiac output of about 5L per minute
- People with lower resting heart rates have a more muscular heart and can pump a greater volume with each beat

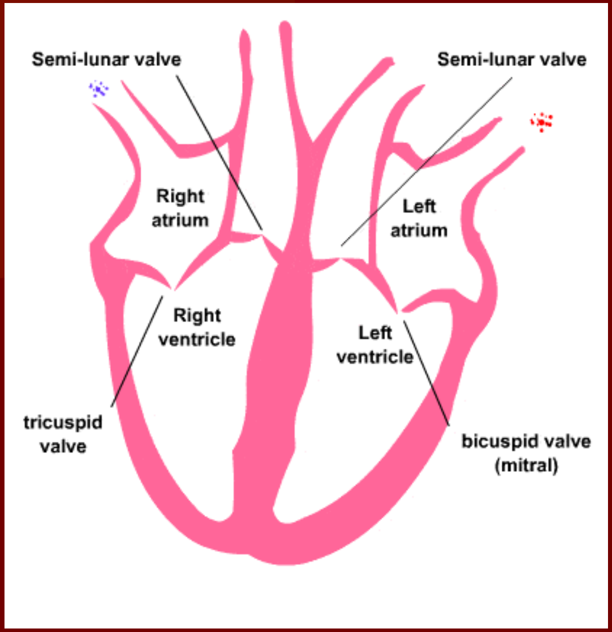
The Heart

- Make a fist with each hand and hold them together at the knuckles. This is the size of an average human heart.
- Important functions include:
  - pumping blood through body
  - keeping oxygen rich blood separate from oxygen poor blood
  - ensuring that blood flows in one direction.
- It is surrounded by a fluid-filled membrane called the pericardium

The Heart

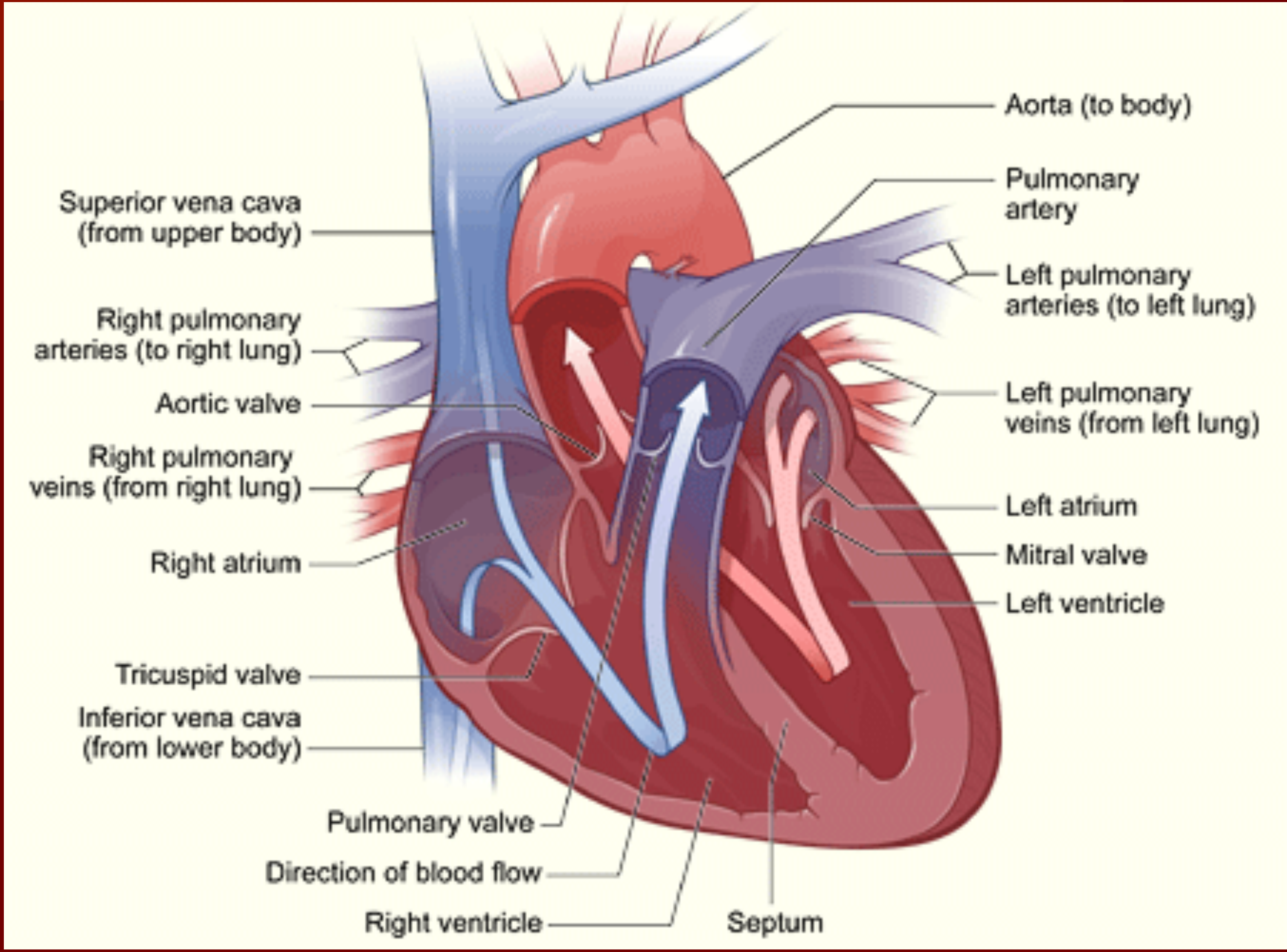
- The heart is made up of a special type of muscle called **cardiac** or **myogenic** muscle.
- It is found nowhere else in our bodies.
- Myogenic muscle contracts on its own without any stimulation from the brain.
  - the heart has its own ‘pacemaker’ – more on this later!

The Heart



- Structure of the heart
  - 4 chambers:
    - 2 upper atria
    - 2 lower ventricles
    - Left and right side separated by a septum
  - 4 valves:
    - 2 atrioventricular (AV) valves that lie between the atria and ventricles on each side of the heart
    - 2 semi lunar valves that lie between the ventricles and the arteries leaving the heart on each side of the heart

The Heart

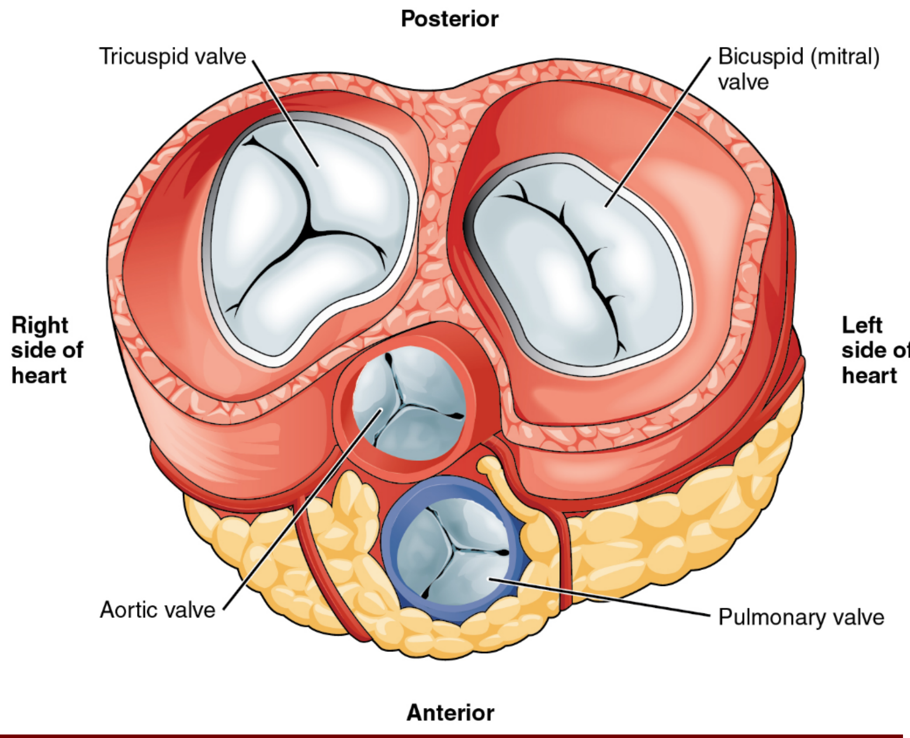


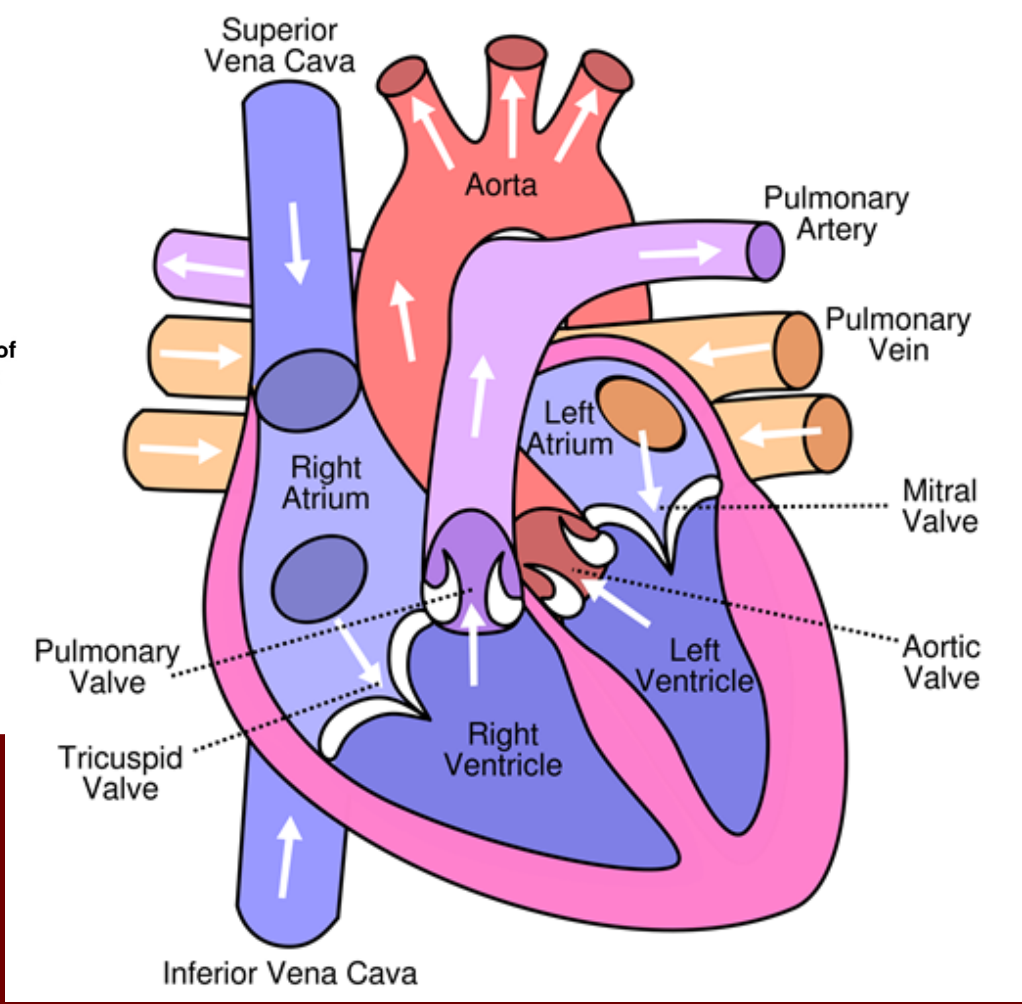
Aorta (to body)
Pulmonary artery
Left pulmonary arteries (to left lung)
Left pulmonary veins (from left lung)
Left atrium
Mitral valve
Left ventricle
Superior vena cava (from upper body)
Right pulmonary arteries (to right lung)
Aortic valve
Right pulmonary veins (from right lung)
Right atrium
Tricuspid valve
Inferior vena cava (from lower body)
Pulmonary valve
Direction of blood flow
Right ventricle
Septum

The Heart

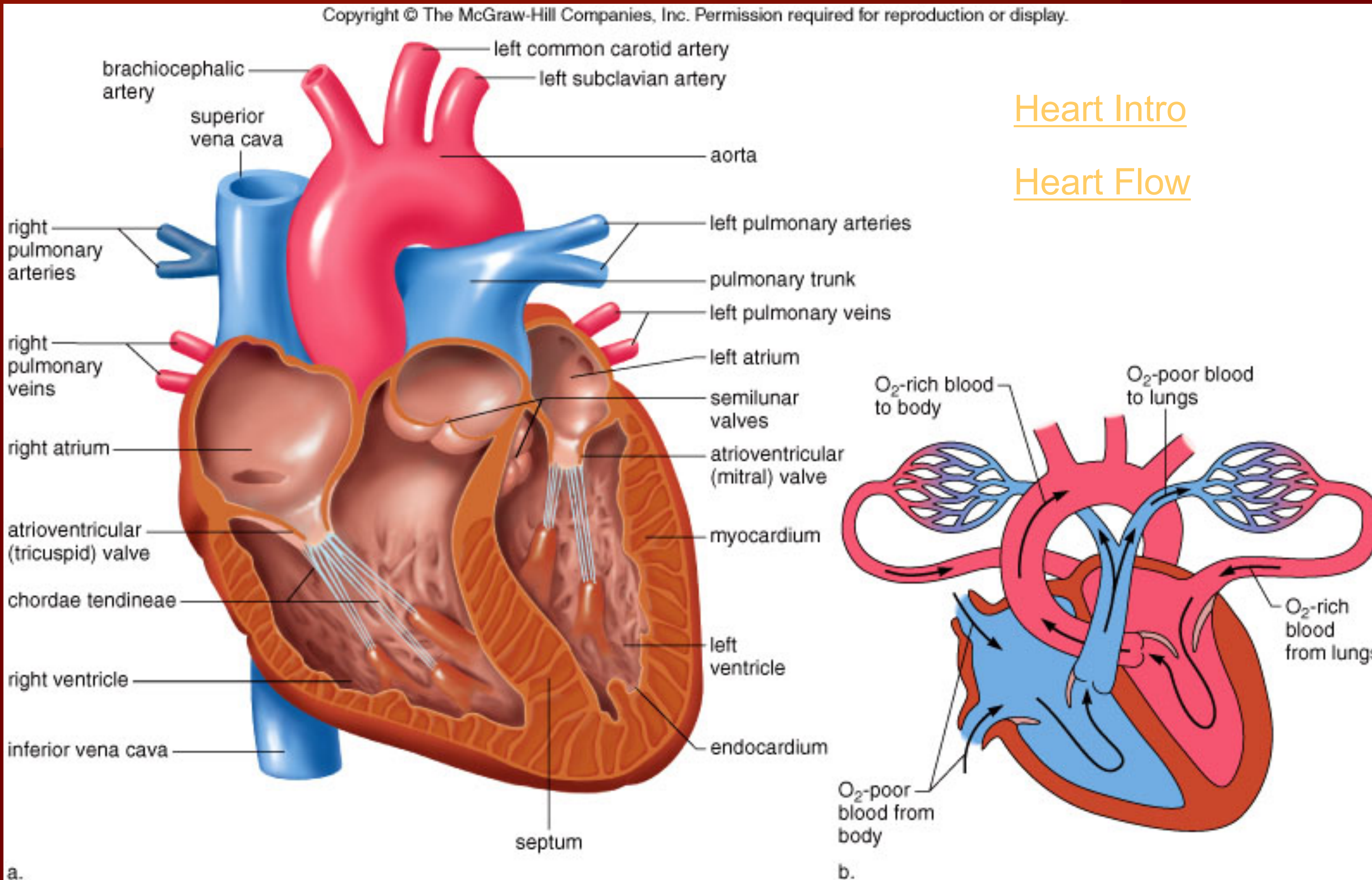
- Valves make sure that the blood is flowing in the right direction in the heart.
- **<u>Atrioventricular valves:</u>**
  - Lie between the atrium and ventricle on each side
  - **Tricuspid valve** (right AV valve) - between the right atrium and right ventricle
  - **Bicuspid valve** (left AV valve) - between the left atrium and left ventricle (aka mitral valve)
- **<u>Semilunar valves:</u>**
  - Between the ventricle and great vessel on each side
  - **Pulmonary semilunar valve** - between the right ventricle and the pulmonary artery
  - **Aortic semilunar valve** - between the left ventricle and aorta

Anatomy of the Heart





Internal View of the Heart



[Heart Intro]

[Heart Flow]

The Heart

The major veins and arteries entering and leaving the heart:

- **pulmonary artery -** brings the O_2 poor blood from the right ventricle to the lungs.
- **pulmonary vein -** brings O_2 rich blood from the lungs back to the left atrium.
- **aorta -** O_2 rich blood flows to the body from the heart
- **coronary artery -** delivers O_2 rich blood to the heart for it to use.
- **inferior (posterior) vena cava -**
- **superior (anterior) vena cava**

Bring O_2 poor blood to the right atrium.

The Heart

- The heart is 2 pumps
  - Right side is the pulmonary pump
    - Pumps deoxygenated blood to pulmonary circuit and lungs
  - Left side is the systemic pump
    - Pumps oxygenated blood out to systemic circulation
- Note:
  - deoxygenated and oxygenated blood never mix
  - Left ventricle pumps blood under higher pressure
  - Left ventricular wall is more muscular

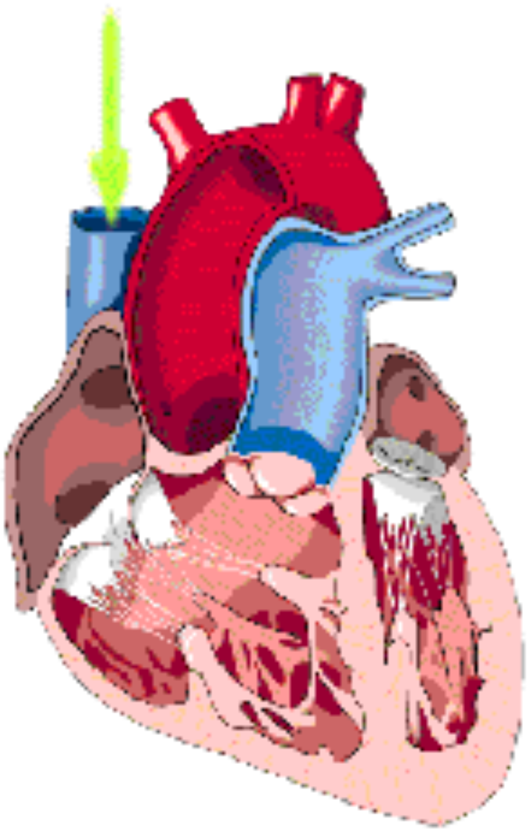
Anatomy of the Heart

- CO_2 rich / O_2 poor blood comes back to the heart through the Vena Cava (Inferior & Superior) and enters the Right Atrium.
- When the right atrium contracts, it pushes blood down through the Right AV (atrioventricular) valve, aka the tricuspid valve.
- The blood now enters the Right Ventricle. When the ventricle contracts, blood is pushed through the pulmonary semi-lunar valve and into the pulmonary artery (going to the lungs).

Anatomy Continued

- When deoxygenated blood is exchanged for oxygenated blood at the lungs, it returns to the heart via the pulmonary veins.
- Blood enters the Left Atrium now. When it contracts, blood is forced through the Left AV (atrioventricular) valve, aka the mitral valve into the Left Ventricle.
- When the ventricle contracts, blood is pumped through the aortic semi-lunar valve and out through the aorta to the rest of the body.
- NOTE: valves have **chordae tendinae** to prevent back-flow of blood through the heart.

Circulation Within The Heart

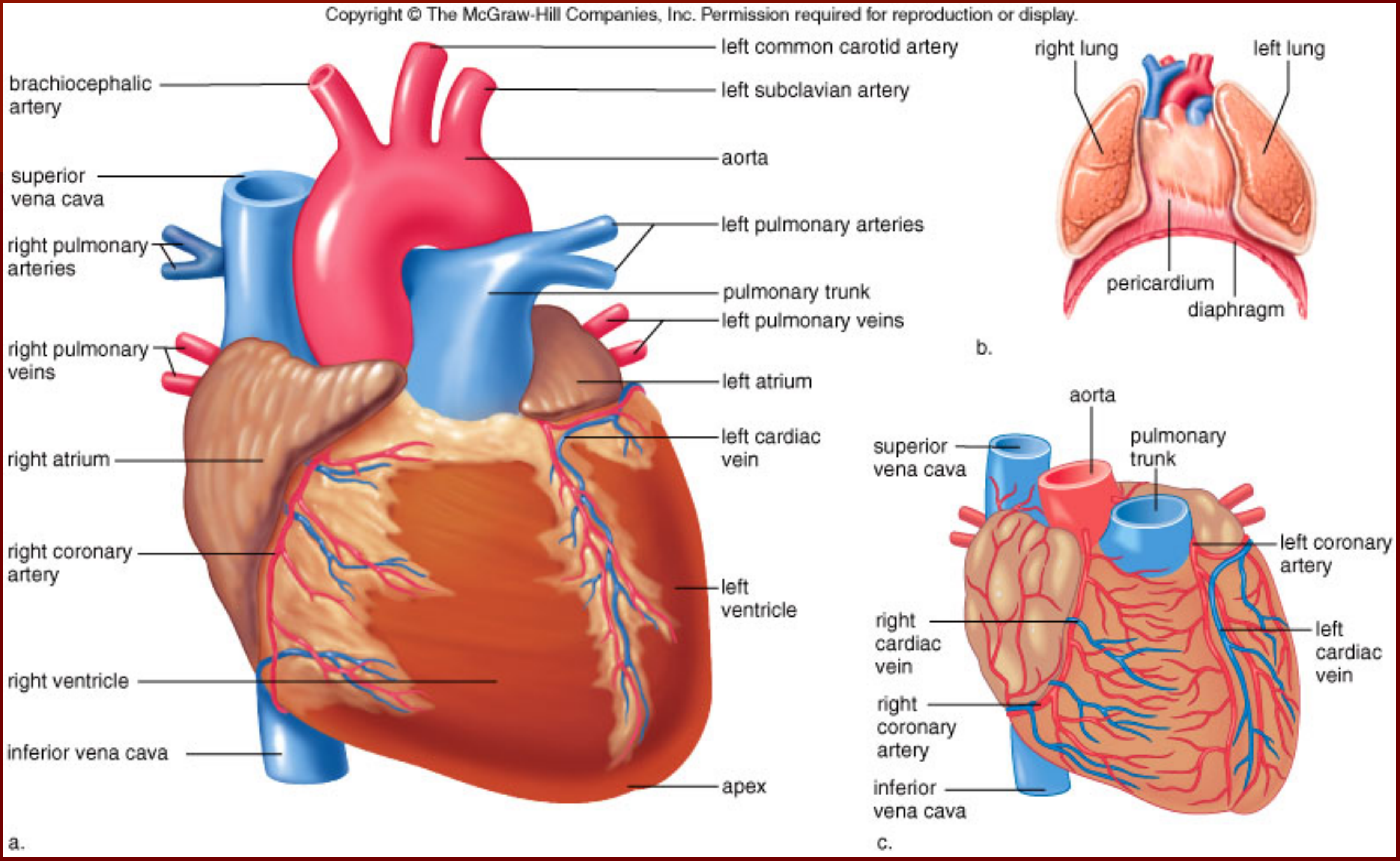


- Right Atrium
- Tricuspid Valve
- Right Ventricle
- Pulmonic Valve
- Pulmonary Arteries
- Pulmonic Veins
- Left Atrium
- Mitral Valve
- Left Ventricle
- Aortic Valve
- Aorta

Blood Flow through Heart – In a nutshell

Body > RA > RV > Lungs > LA > LV > Body

External Heart Anatomy



External Heart Anatomy

- Coronary arteries run along the muscle tissue on the surface of the heart, bringing oxygen and nutrients to the muscle
- If these arteries become blocked, then the muscle will slowly die
- The heart, unlike other organs, will not slow down if there are not enough nutrients or oxygen to support it

Coronary Bypass Surgery

- In this surgery, grafted veins are used to provide a route through which blood may travel around the blocked vessels

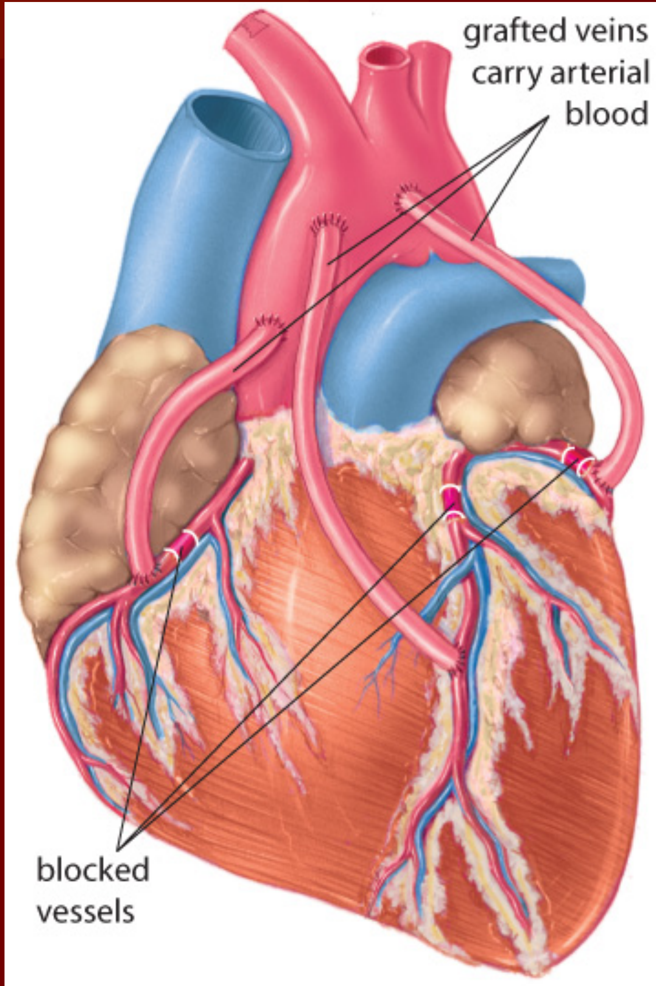
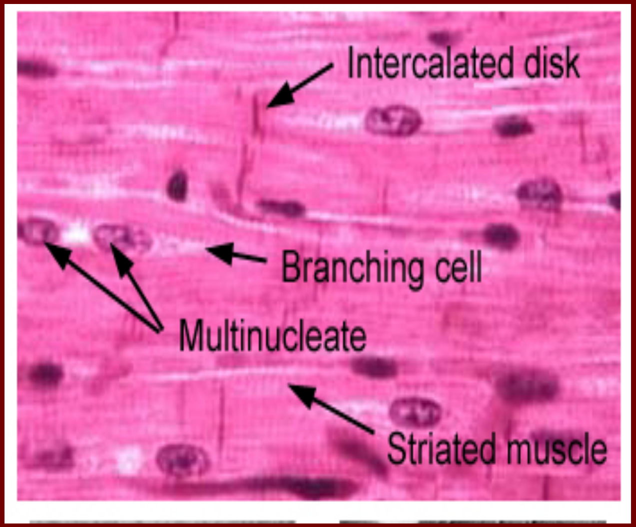


Figure 8.13 Coronary bypass operation: this heart shows a triple bypass, meaning that three new pathways were constructed to avoid blockages in three separate blood vessels.

The Heart - Muscle

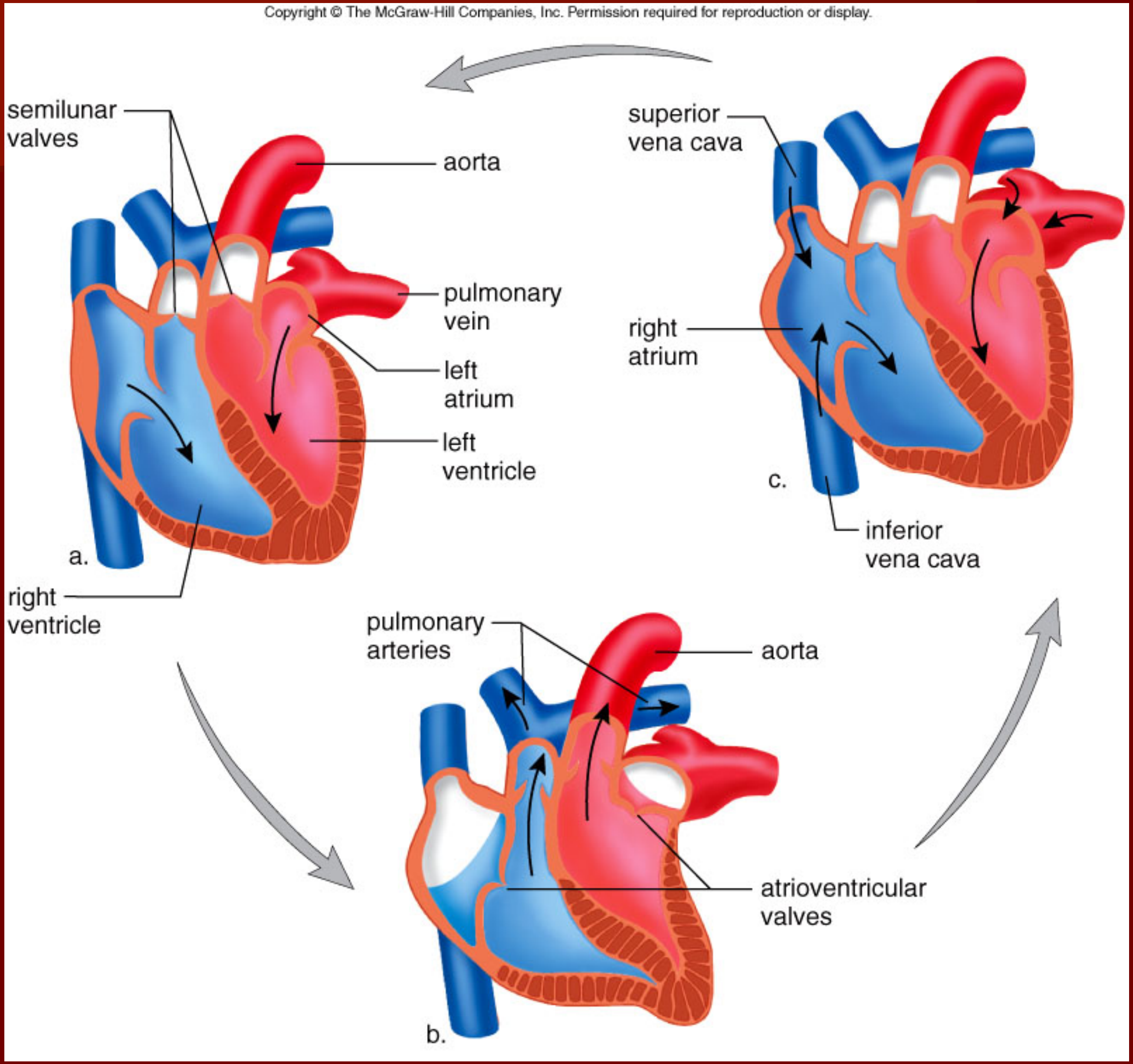
- Under a microscope, the heart muscle looks striated (regular strait pattern).
- Heart muscle contains lots of branching muscle cells → for better conduction of electrochemical signal
- Heart also has incredible stamina
- The heart has the ability to contract without external nerve stimulation. This unique kind of muscle is called **myogenic** muscle.
- Heart will continue to beat for a short time when removed from a body.



The Heartbeat

- The events of each heartbeat are called the cardiac cycle
  - Highly coordinated so that both atria contract together and then both ventricles contract together
  - Systole - contraction of heart muscle
  - Diastole - relaxation of heart muscle
- Normal heart rate at rest is about 60-80 beats per minute

Stages in the cardiac cycle



[Ted Talk Heart pumping]

The Heartbeat

- "Lub dub" heart sounds are produced by turbulence and tissue vibration as valves close
    - "lub" sound occurs as atrioventricular valves (AV) close
    - "dub" sound occurs as semilunar valves close
- Other abnormal sounds are referred to as heart murmurs

Heart murmurs

Setting the Heart's Rhythm

- The tempo of the heart is set by the sinoatrial (SA) node and the atrioventricular (AV) node

- These nodes act as a pacemaker, ensuring that all of the muscle beats at the same rhythm
- Surgeons that perform open-heart surgery must be very careful not to cut any of the nerves running from the SA node or the AV node

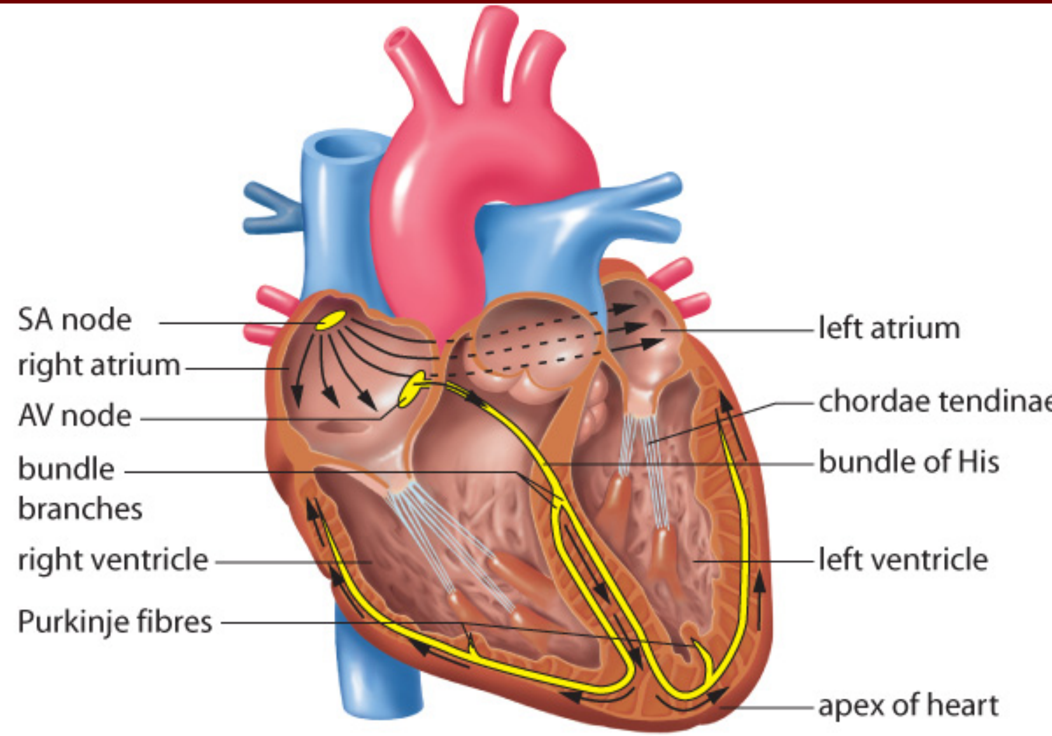


Figure 8.7 The SA node sends out an electrical stimulus that causes the atria to contract. When this stimulus reaches the AV node, it is passed through the bundle of His and the Purkinje fibres. The stimulus causes the ventricles to contract, starting from the apex and then upward, which forces blood toward the pulmonary artery and aorta. The chordae tendinae are strong, fibrous strings that prevent the valves in the heart from inverting when the heart contracts.

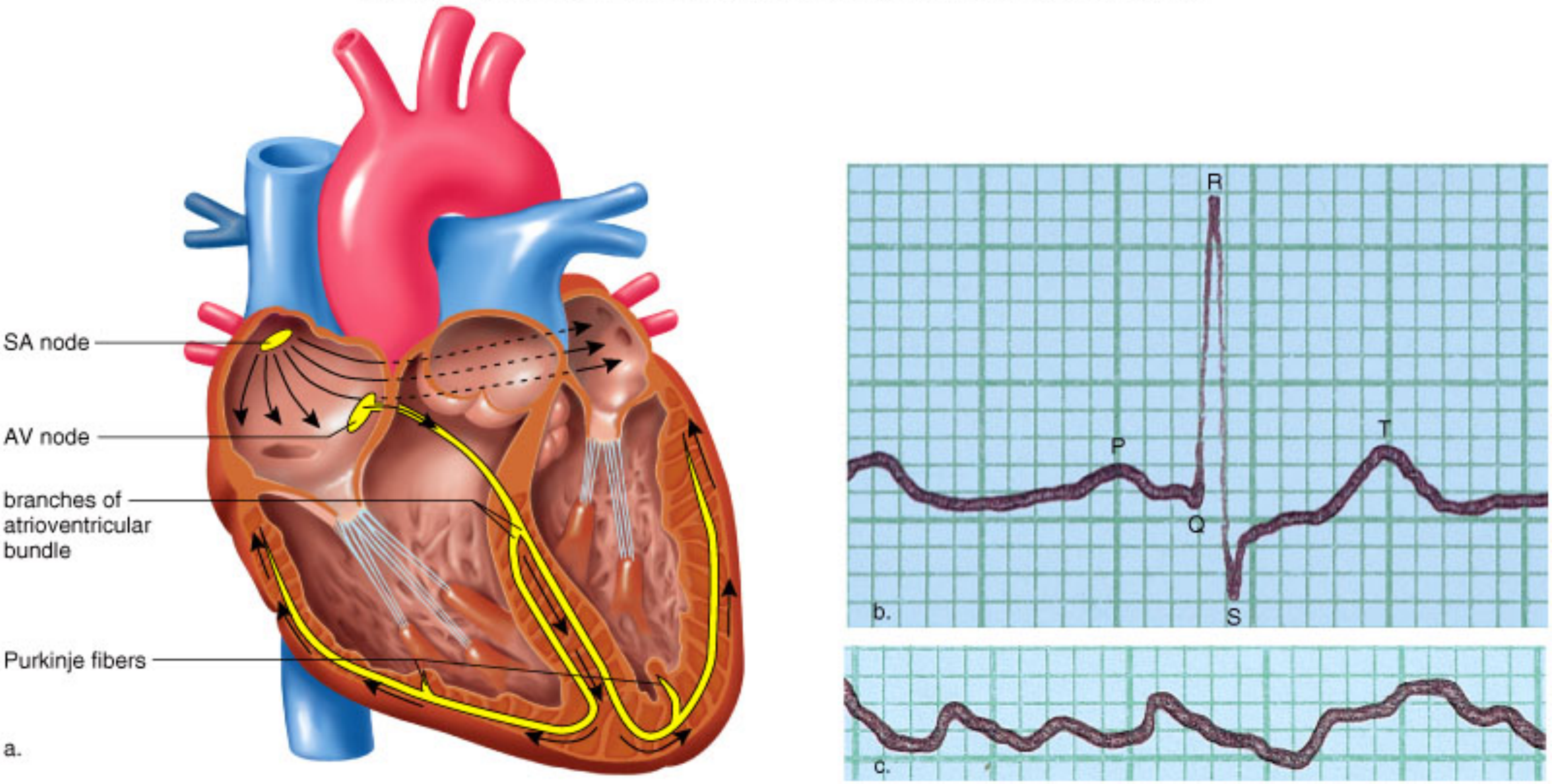
Setting the Heart's Rhythm

- Intrinsic control of heartbeat
  - Heart has its own intrinsic conduction system – cardiac muscle can contract without neural stimulation
  - The autonomic nervous system does have inputs to the heart and normally regulates rate
- Nodal tissue - 2 areas in the heart
  - Has both muscular and nervous characteristics
  - Can generate action potentials to cause contraction
  - SA node and AV node
- Stimulus is
  - CO_2 levels monitored by medulla oblongata
  - Blood pressure measured by baroreceptors in carotids and aorta

Setting the Heart's Rhythm

- Normal conduction pathway
  - **SA node** in right atrium initiates an **action potential** (AP) – electrochemical signal conducted by nerves
  - AP spreads throughout atrial muscles, causing contraction
  - AP is conducted to **AV node** lower in right atrium
  - AV node sends impulse to nerves in septum called the Bundle of His
  - **Bundle of His** conducts impulse down through the interventricular septum and then branches into many small **Purkinje fibers** that distribute impulse throughout ventricles, causing contraction
- Atria contract first, followed by the ventricles

Conduction System of the Heart

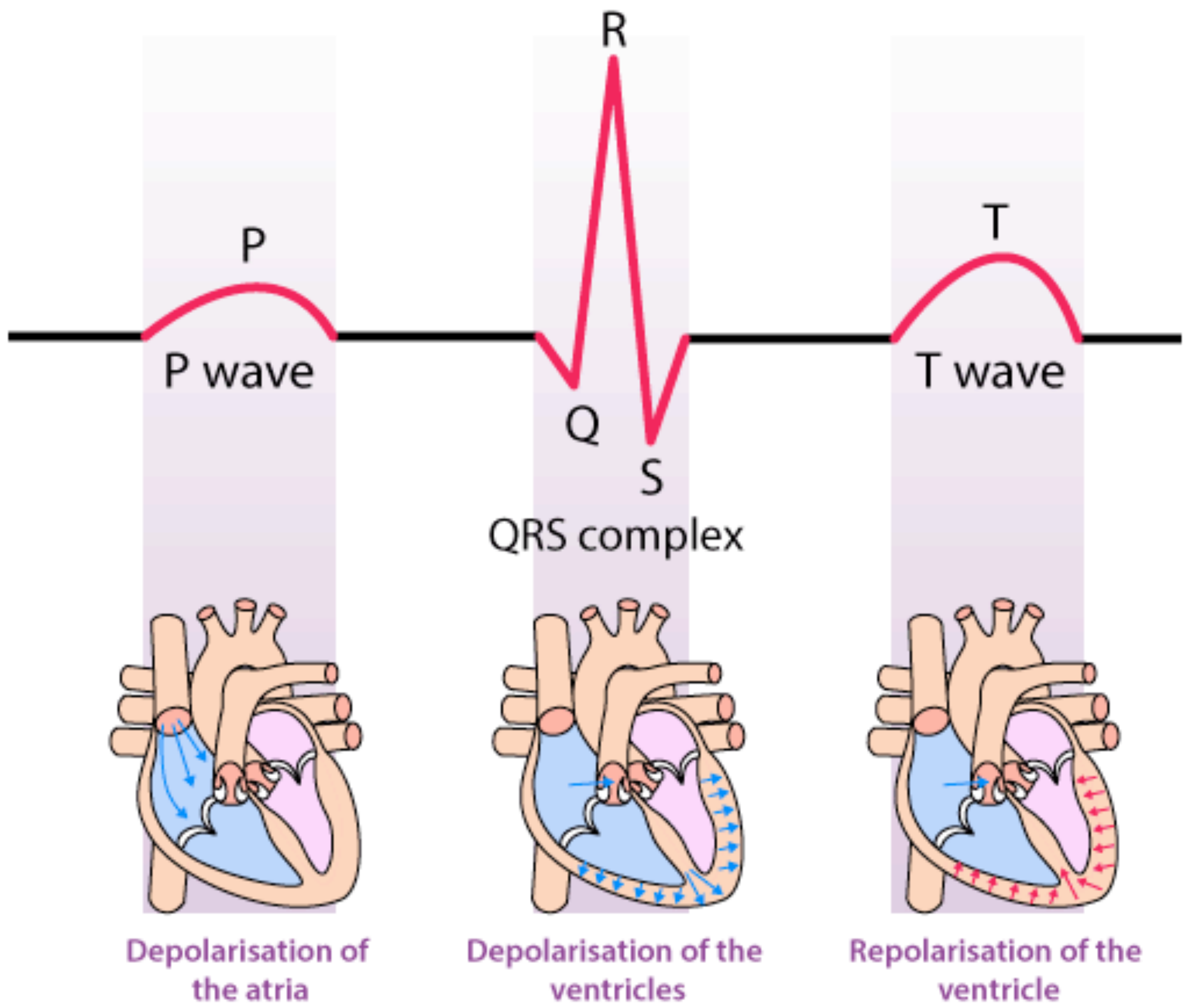


Heart beat   Better EKG   Laser Ablation   Crash Course

Electrocardiograms

- Records electrical activity of the heart
- Can give information about heart rate and rhythm
- Can indicate if conduction pathway is working normally
  - P wave - atrial depolarization (contraction)
  - QRS wave - ventricular depolarization
  - T wave - ventricular repolarization (recovery)

Electrocardiograms



Extrinsic Control of Heart

- Cardiac control center in the medulla has inputs to heart through the **autonomic nervous system** (ANS)
- **Parasympathetic** stimulation causes a decrease in heart rate
- **Sympathetic** stimulation causes an increase in heart rate and contractility
- Hormones also can control heartbeat
  - **Epinephrine** and **norepinephrine** cause increased heart rate
  - Occurs during exercise, "fight or flight" response

8.2 – Blood and Immunity

- Blood is considered a connective tissue because it links all cells and organs in the body
- Blood consists of a fluid portion and a solid portion

Vampires suck your blood for Vitamin D because they can't go out in the sun themselves.

You ever think about that?

No. You only think about yourself.

Composition of Blood

FORMED ELEMENTS	Function and Description	Source
Red Blood Cells (erythrocytes) 4 million–6 million per mm^3 blood	Transport O_2 and help transport CO_2; 7–8 µm in diameter; Bright-red to dark-purple biconcave disks without nuclei	Red bone marrow
White Blood Cells (leukocytes) 5,000–11,000 per mm^3 blood	Fight infection	Red bone marrow
Granular leukocytes		
• Neutrophils 40–70%	10–14 µm in diameter; Spherical cells with multilobed nuclei; fine, pink granules in cytoplasm; phagocytize pathogens	
• Eosinophils 1–4%	10–14 µm in diameter; Spherical cells with bilobed nuclei; coarse, deep-red, uniformly sized granules in cytoplasm; phagocytize antigen-antibody complexes and allergens	
• Basophils 0–1%	10–12 µm in diameter; Spherical cells with lobed nuclei; large, irregularly shaped, deep-blue granules in cytoplasm; release histamine, which promotes blood flow to injured tissues	

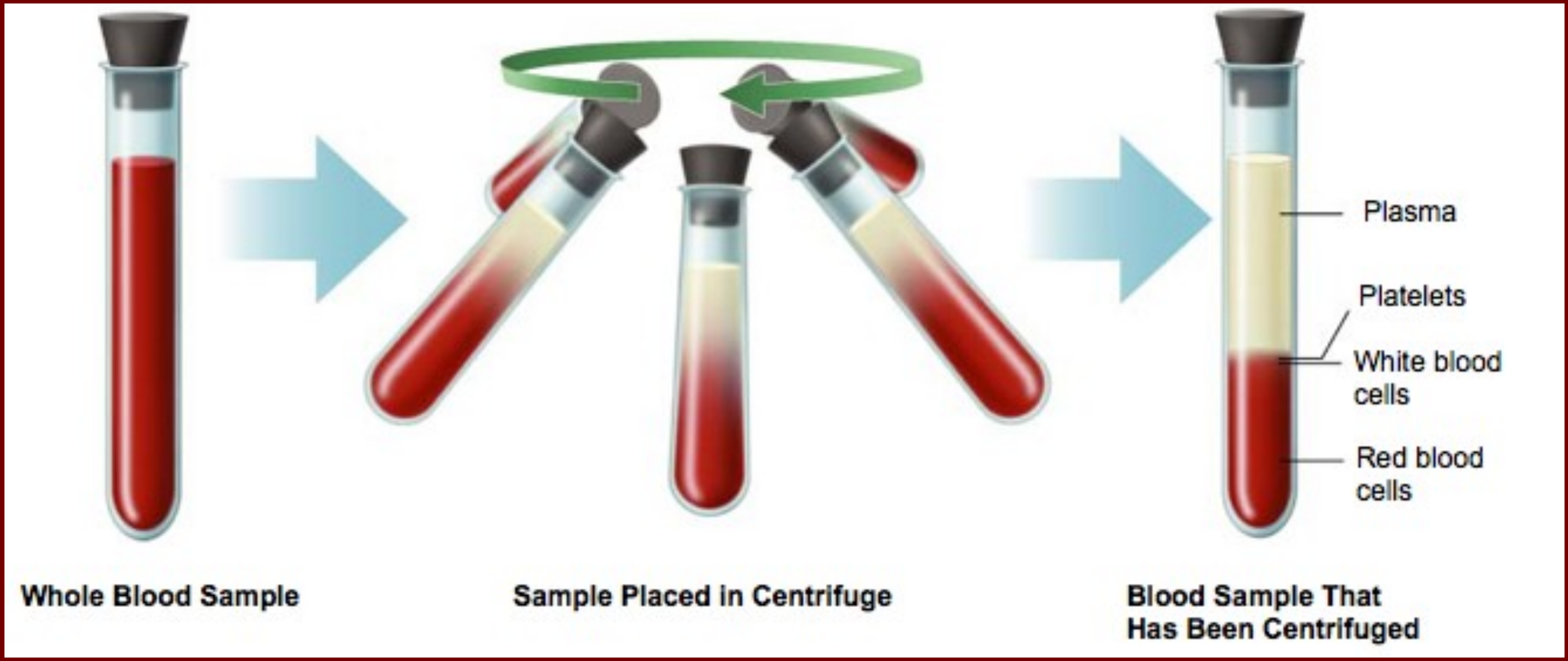
Agranular leukocytes		
• Lymphocytes 20–45%	5–17 µm in diameter (average 9–10 µm); Spherical cells with large round nuclei; responsible for specific immunity	
• Monocytes 4–8%	10–24 µm in diameter; Large spherical cells with kidney-shaped, round, or lobed nuclei; become macrophages that phagocytize pathogens and cellular debris	
Platelets (thrombocytes) 150,000–300,000 per mm^3 blood	Aid clotting; 2–4 µm in diameter; Disk-shaped cell fragments with no nuclei; purple granules in cytoplasm	Red bone marrow

PLASMA	Function	Source
Water (90–92% of plasma)	Maintains blood volume; transports molecules	Absorbed from intestine
Plasma proteins (7–8% of plasma)	Maintain blood osmotic pressure and pH	Liver
Albumins	Maintain blood volume and pressure	
Globulins	Transport; fight infection	
Fibrinogen	Clotting	
Salts (less than 1% of plasma)	Maintain blood osmotic pressure and pH; aid metabolism	Absorbed from intestine
Gases		
Oxygen	Cellular respiration	Lungs
Carbon dioxide	End product of metabolism	Tissues
Nutrients	Food for cells	Absorbed from intestine
Lipids, Glucose, Amino acids		
Nitrogenous wastes	Excretion by kidneys	Liver
Urea, Uric acid		
Other		
Hormones, vitamins, etc.	Aid metabolism	Varied

• Appearance with Wright's stain.

Composition of Blood

- Formed elements
  - Cells – white blood cells and red blood cells
  - Platelets – cell fragments
- Plasma
  - Liquid portion of blood
  - Dissolved nutrients, gases, hormones, etc



Plasma – The Fluid Component

- 55% of blood volume is plasma (fluids, proteins, glucose, gases, wastes and vitamins and minerals)
- Blood proteins come in 3 types:

1. Albumins – serve to maintain blood volume and pressure
2. Globulins – act as part of immune response (fight infection)
3. Fibrinogen – helps with blood clotting

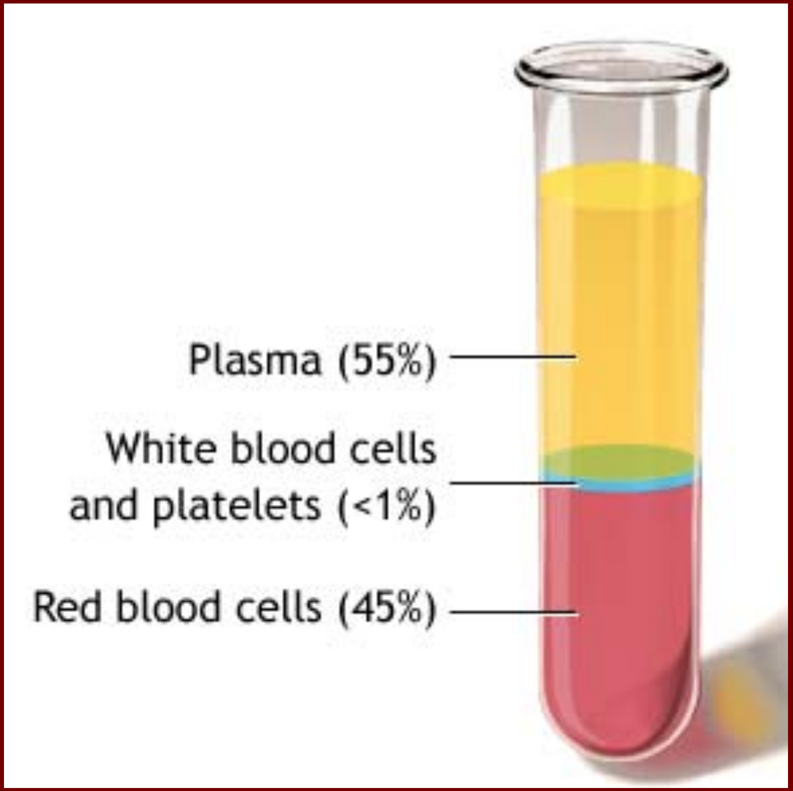
Plasma

- Fluid portion of the blood (blood cells are suspended in it).
- Plasma contains many other substances including:
  - **water (92%)** - maintains blood volume and transports molecules
  - **proteins (7%)**
  - **nutrients** - food for cells
  - **gases (oxygen/carbon dioxide)** - cellular respiration
    - End product of metabolism
  - **wastes** - excretion by kidneys

The Other 45%...

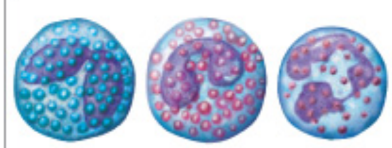
- There are several cell types that make up the remaining volume of blood:

1. Erythrocytes (RBC)
2. Leukocytes (WBC)
3. Platelets

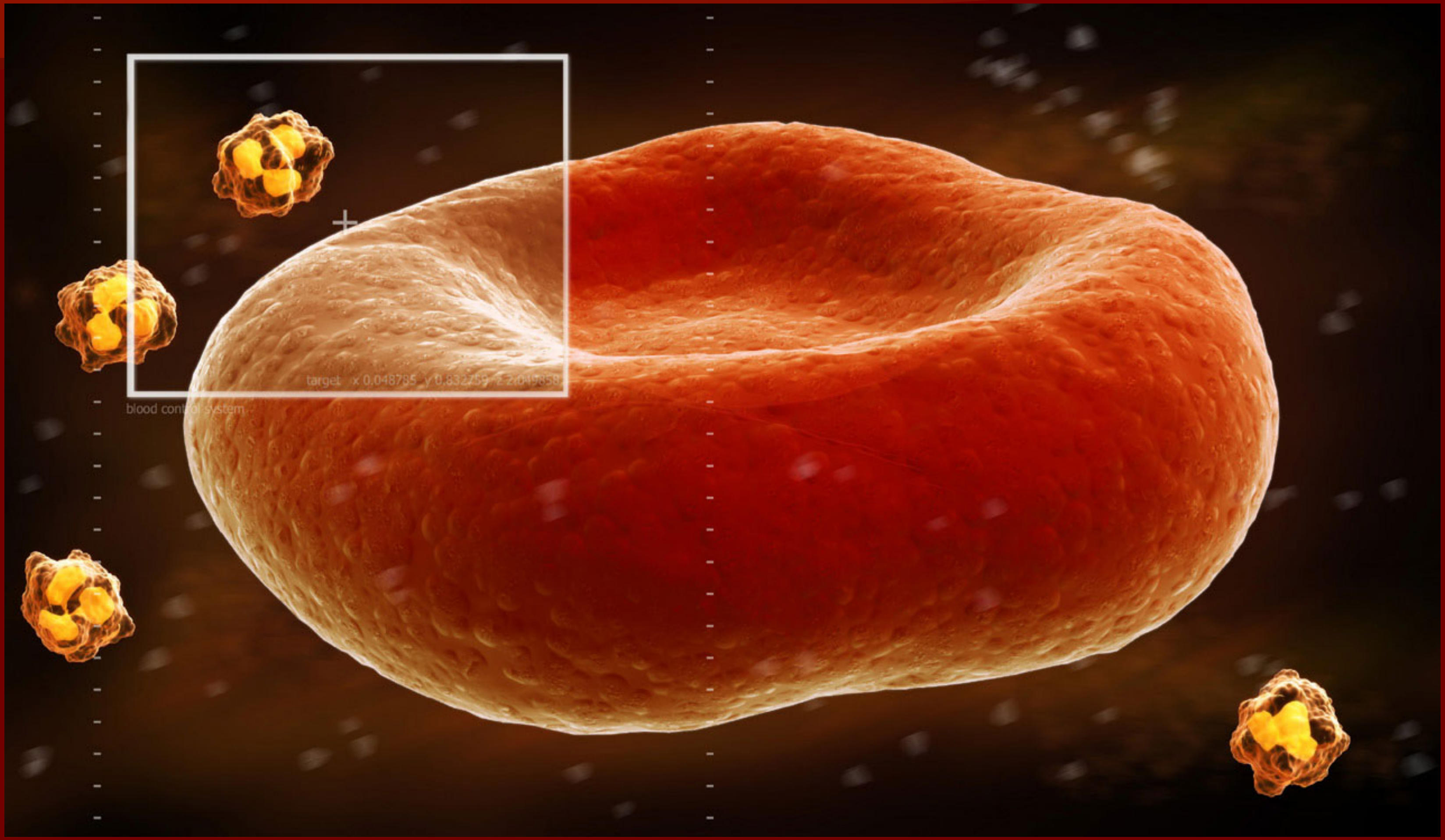


Cell Types

Table 8.2 The Cellular Components of Blood

Point of Comparison	Red blood cells	White blood cells		Platelets
		Granulocytes and monocytes	Lymphocytes	
Origin	red bone marrow	red bone marrow	thymus, red bone marrow	red bone marrow, lungs
Cells present per mm^3 of blood (approximate)	5 500 000 (male) 4 500 000 (female)	6000	2000	250 000
Relative size	small (8 μm diameter)	largest (up to 25 μm)	large (10 μm)	smallest (2 μm)
Function	to carry oxygen and carbon dioxide to and from cells	to engulf foreign particles	to play a role in the formation of antibodies (defence function)	to play a role in the clotting of blood (defence function)
Life span	120 days	a few hours to a few days	unknown	2–8 days
Appearance				

Formed Elements
Erythrocytes (Red Blood Cells)

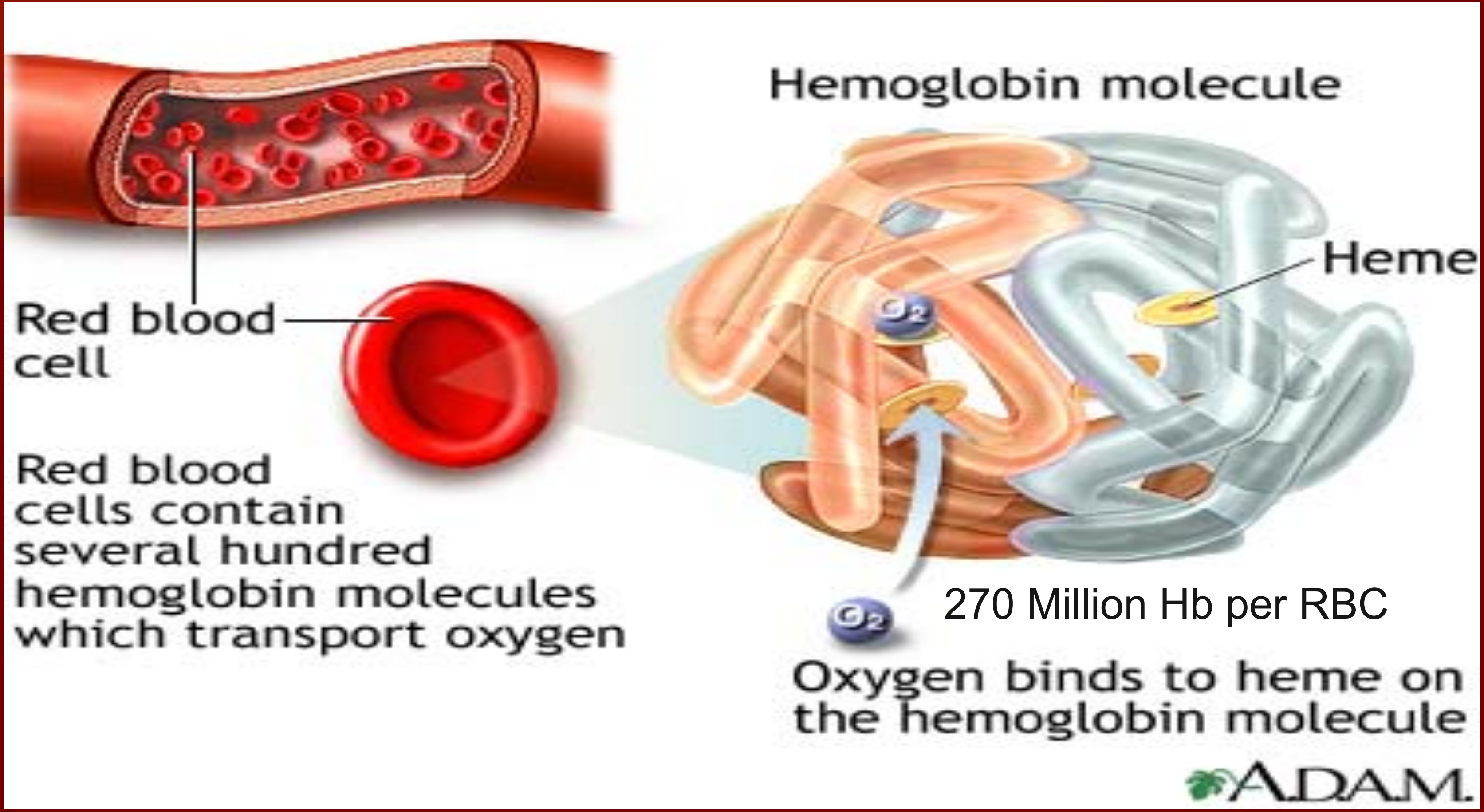


Function: Transports oxygen and helps transport carbon dioxide

Erythrocytes (Red Blood Cells)

- Biconcave disk shape for greater surface area to carry more oxygen molecules.
- Flattened shape is also vital for the cells' unimpeded passage through tiny capillaries.
- Contains no nucleus when mature, instead it is packed with a pigment called hemoglobin.
- Cannot divide without nucleus
- Hemoglobin is responsible for large quantities of oxygen (and carbon dioxide) to be transported in the blood

Physiology of Red Blood Cells

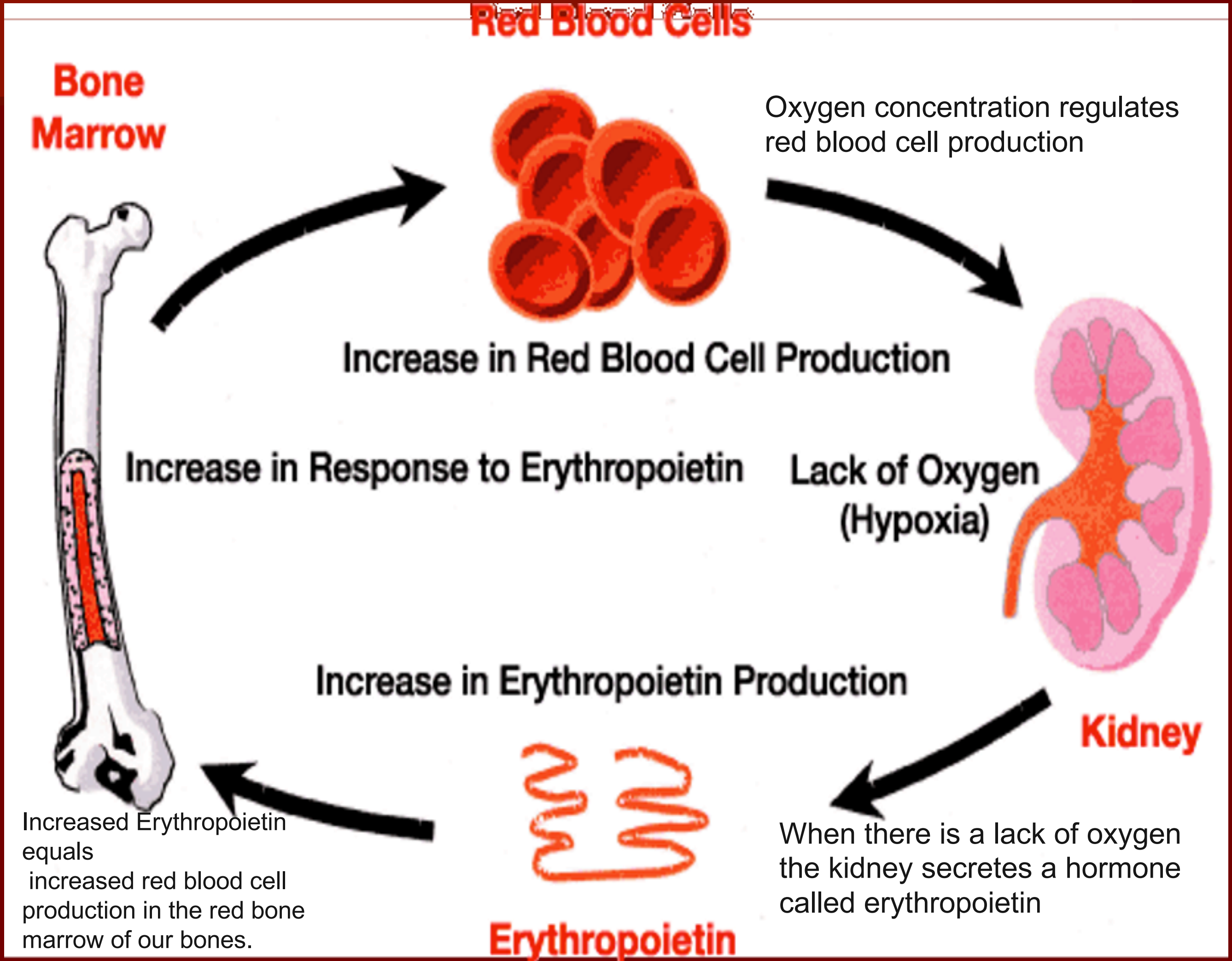


- Carries 20 ml oxygen per 100 ml of blood
- Carbon monoxide poisoning
    - carbon monoxide can also bind at heme sites more strongly than oxygen

Erythrocytes – RBC's

- Lifespan - 120 days
- Body makes about 2 million red blood cells per second
- Destroyed in liver by macrophages
- Hemoglobin is broken down
- Iron is recycled – taken to bone marrow
- Heme portion is degraded and excreted as bile pigments

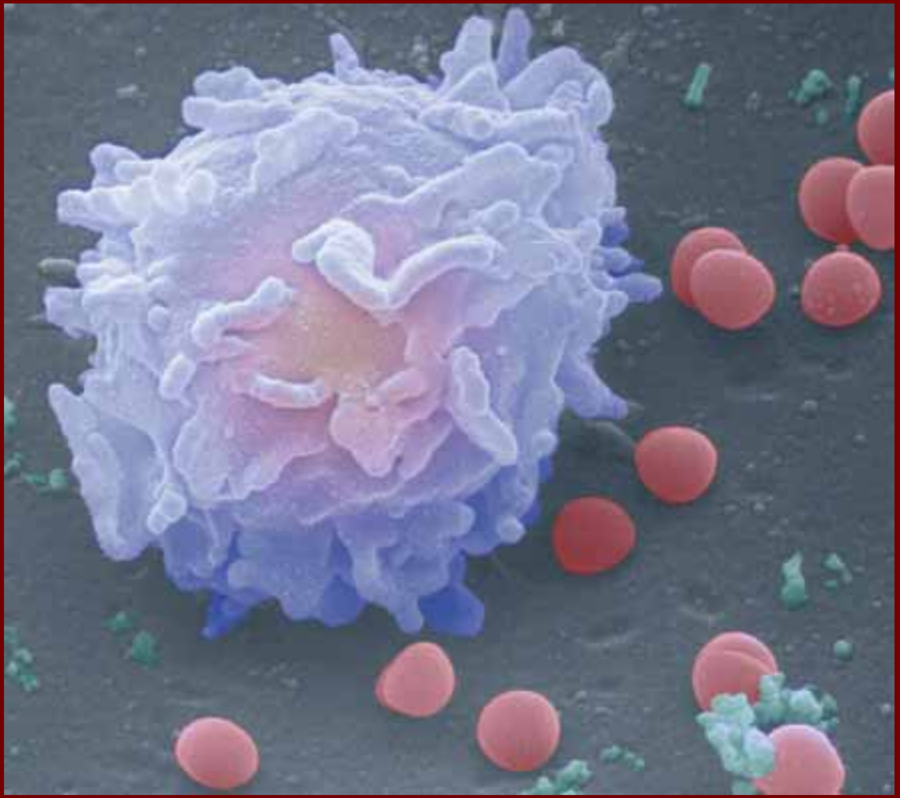
Erythropoiesis (Red Blood Cell Production)



Note: Erythropoietin can be used as a performance enhancing drug. (blood doping)

Formed Elements
Leucocytes (White-blood cells)

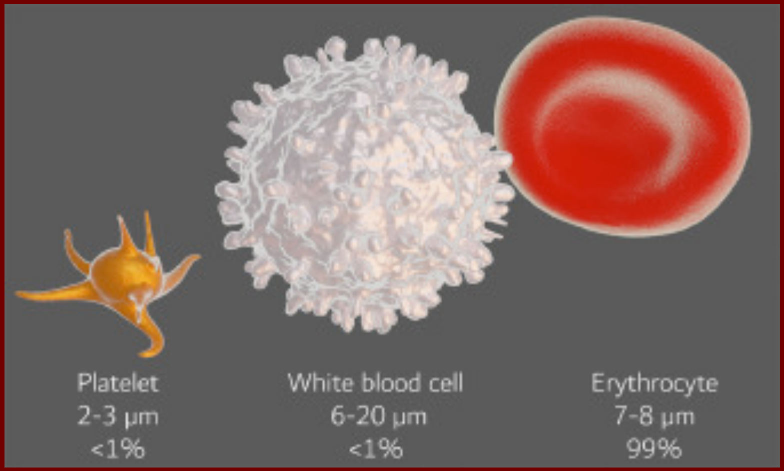
- For every 650 red blood cells there is only 1 white blood cell in a healthy individual.
- These levels will increase when fighting infection.
  - Ex. Leukemia (uncontrolled #'s WBC)
- Larger cells that are nucleated
- Fight infection and play a large role in immunity

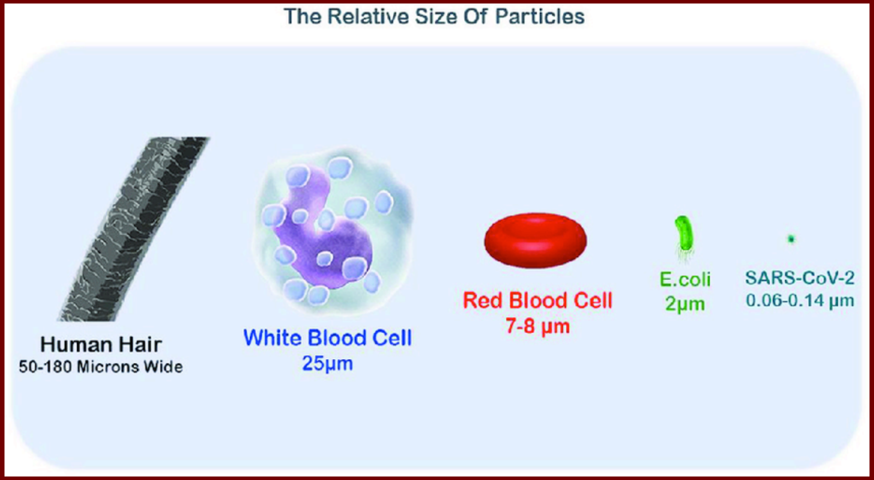


White blood cell attacking a toxic substance.

Leukocytes (White Blood Cells)

- These cells are responsible for immune system responses
- Lifespan
  - Different types live different lengths of time
  - Some live only a few days – die combating invading pathogens
  - Some live months or years





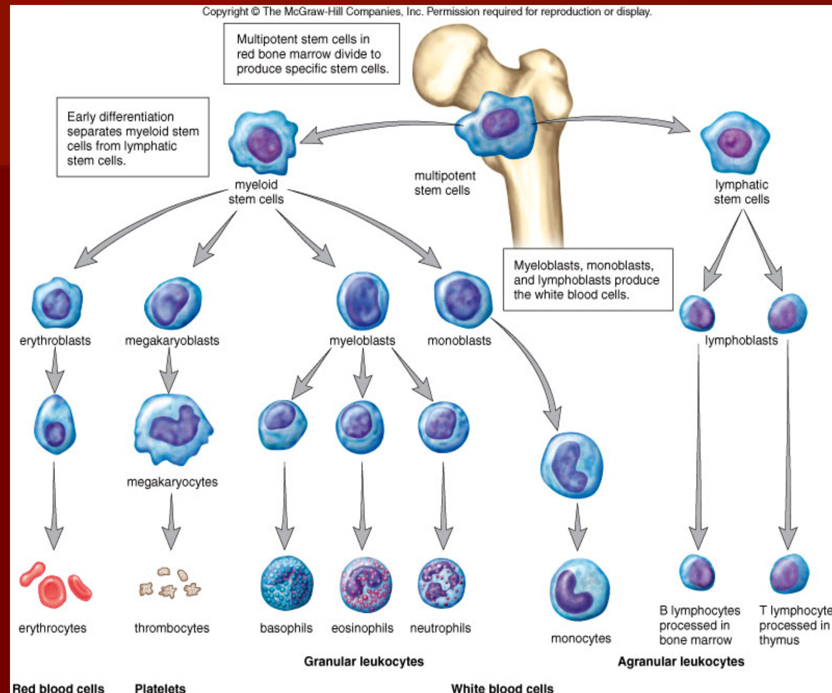
Leukocytes

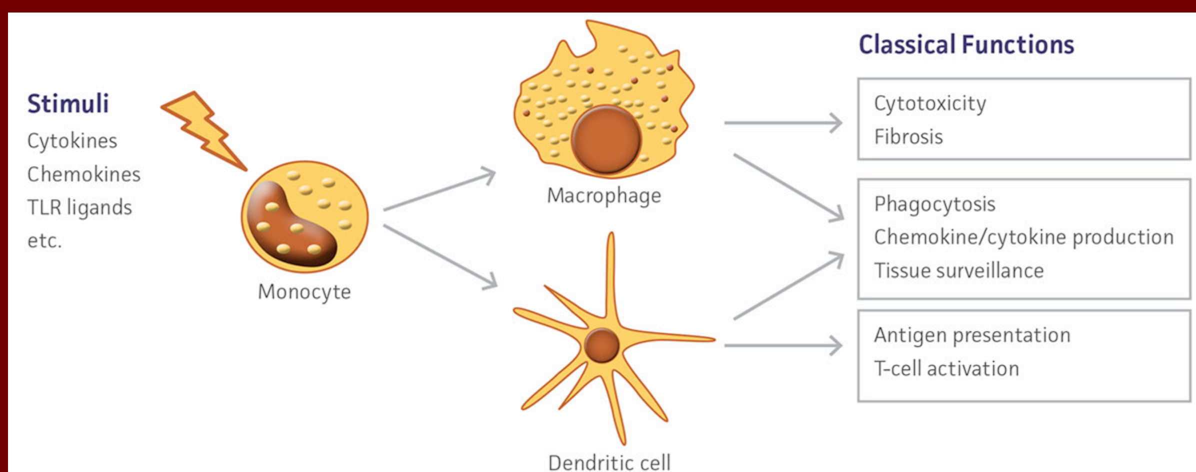
- There are a 2 different types:

1. Granulocytes – have visible granules in cytoplasm
   - Neutrophils – most abundant WBC; phagocytotic
   - Basophils – granules stained deep blue and release histamine (chemical that causes allergic response / swelling)
   - Eosinophils – granules stained red, phagocytose (engulf) allergens
2. Agranulocytes – lack visible granules
   - Lymphocytes – T and B cells; play roles in immune response
   - Monocytes – largest WBC's; phagocytotic
     - Can leave the bloodstream and differentiate into macrophages and dendritic cells

Macrophage Engulfing Bacteria

Blood Cell Formation in Red Bone Marrow





Red Bone Marrow Stem Cells

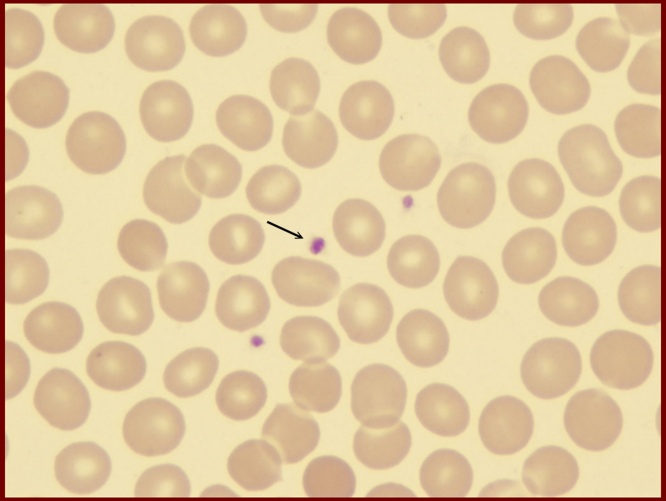
- Cell which is capable of dividing and differentiating into particular cell types
  - Red blood cells, white blood cells, and platelets
    - Erythropoiesis – RBC synthesis
    - Leukopoiesis – WBC synthesis
    - Thrombopoiesis – platelet synthesis
  - Some may even be able to give rise to liver, bone, fat, cartilage, heart, and some nerve cells
  - May provide solutions for diseases such as Alzheimer's and Parkinson's
- Many researchers prefer to work with embryonic stem cells
  - Totipotent – can become *any* cell type
  - Ethical issues…

Bone Marrow Transplant

Formed Elements Thrombocytes (Platelets)

- Are formed when larger cells in the bone marrow break apart
- Irregularly shaped, contain no nucleus and break down quickly in the blood.
- Involved in the process of clotting, which prevents excessive blood loss after an injury.

Platelets initiating clotting.



Microscope slide of platelets beside RBCs

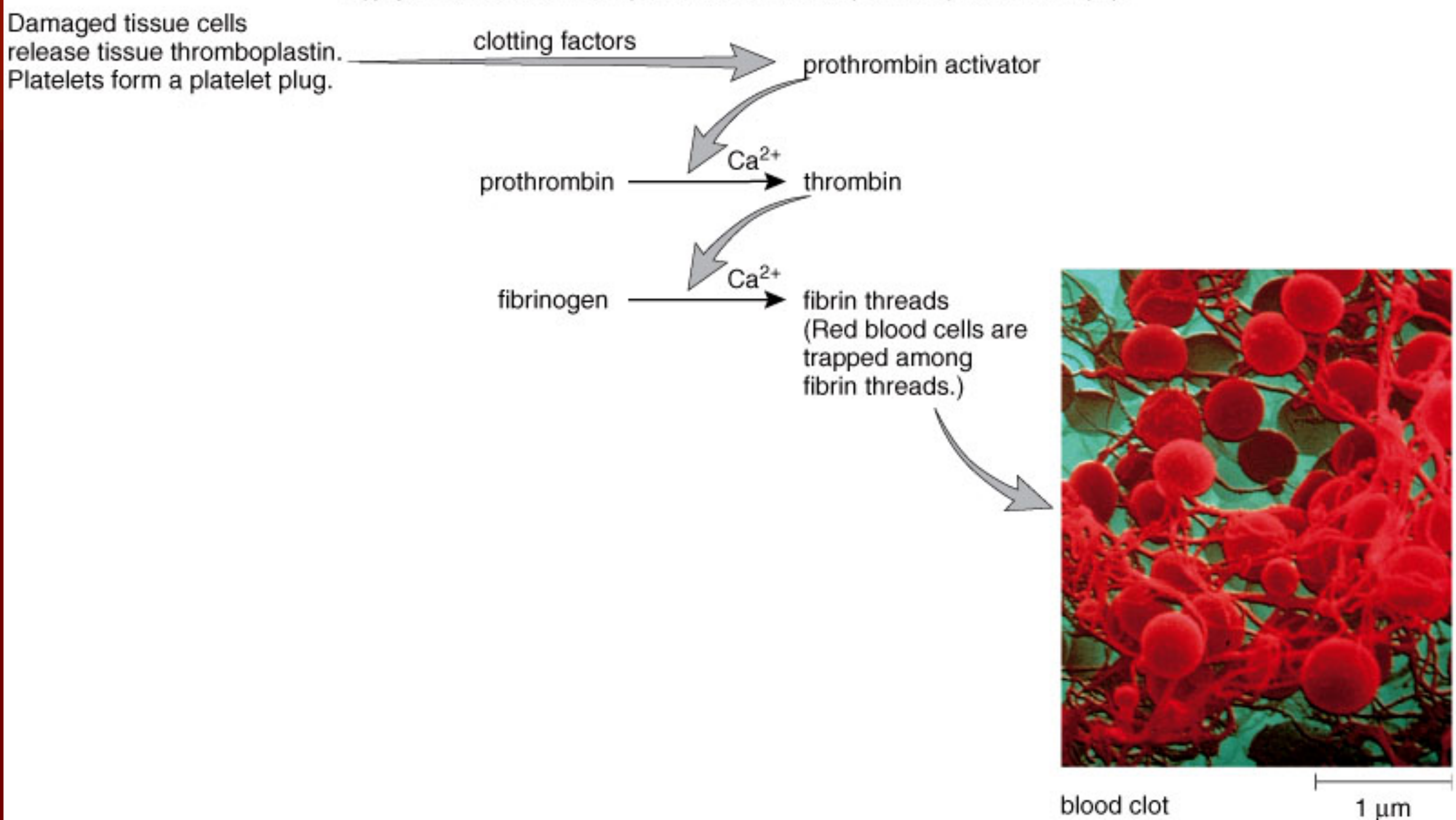
Blood Clotting

- Clotting maintains homeostasis by preventing massive blood loss
- This occurs in a series of steps

Clotting Process

1. When platelets burst on contact with a break in a vessel wall, they release compounds that combine with other blood components to form a protein known as *thromboplastin*
2. Platelets travel to cut and form a platelet plug
3. Thromboplastin and calcium ions activate a blood protein known as prothrombin
4. Prothrombin is converted to an enzyme known as thrombin, which splits up a fibrinogen molecule
5. Fibrinogen is converted into fibrin threads, which wrap around the damaged area, sealing it

Blood Clotting



The Functions of Blood

1. Transport:
   - Oxygen, carbon dioxide, nutrients, waste
   - Function of RBC's (erythrocytes)
2. Immune Response:
   - Engulf foreign pathogens, produce antibodies, puncture membranes of foreign cells, remember foreign pathogens for future encounters
   - Function of WBC's (leukocytes)
3. Blood Clotting:
   - Wrapping protein around injured areas to prevent blood loss
   - Function of platelets

4. Homeostatic Regulation

- Blood also helps regulate our body temperature. The water inside blood plasma carries a lot of energy (due to high specific heat capacity)
- Through vasodilation or vasoconstriction of blood vessels, more or less blood can be moved to or from an area of the body, thus heating it up or cooling it down

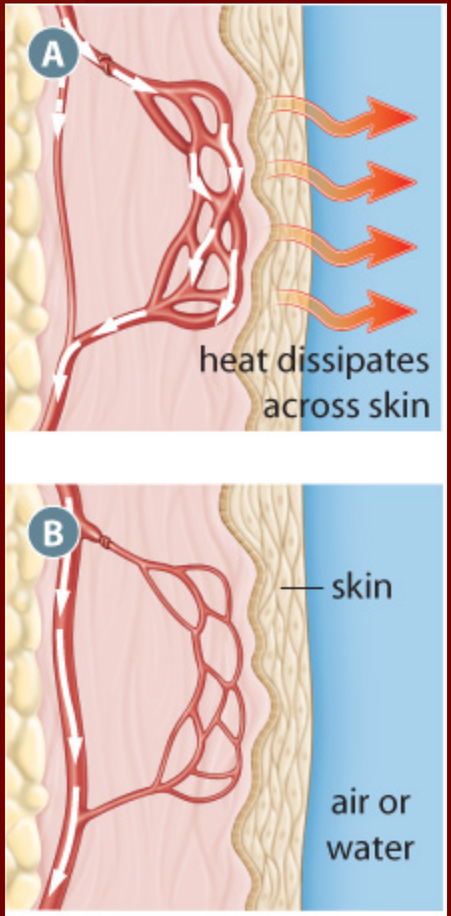


Figure 8.19 Vasodilation (A) and vasoconstriction (B)

Temperature Regulation

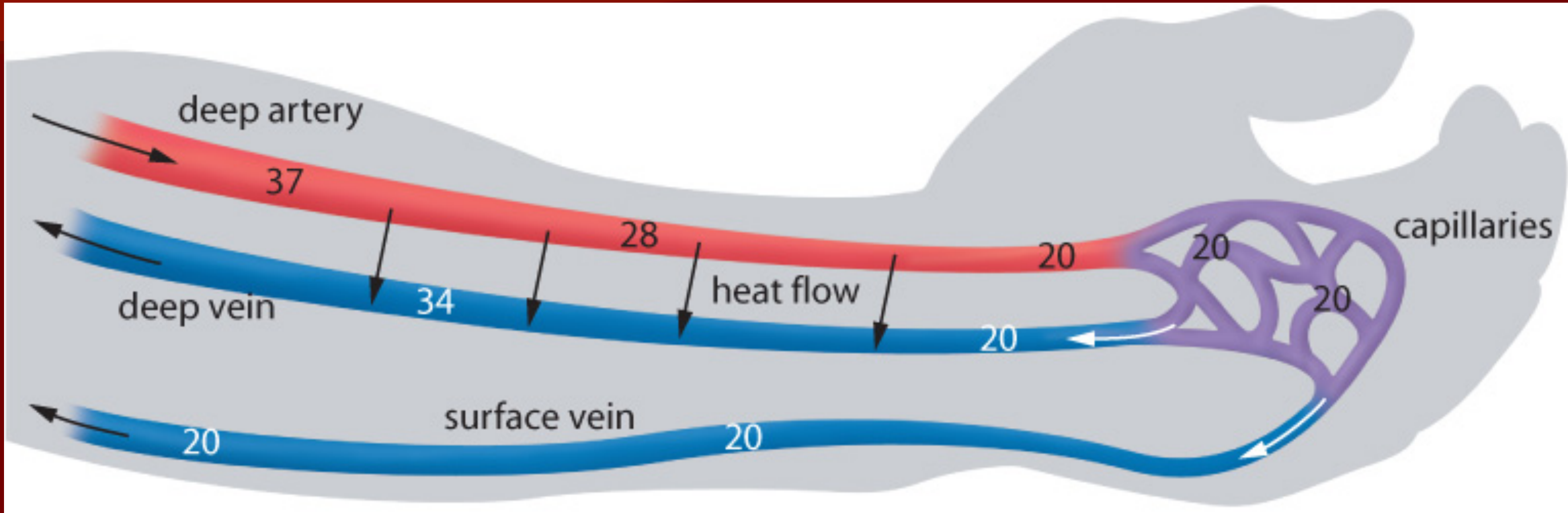


Figure 8.20 The countercurrent heat exchange mechanism between the blood vessels in the human arm: The deep vein and artery are adjacent to one another, so heat is exchanged from one to the other. As a result, arterial blood is cooled as it nears the hand, and venous blood is warmed as it leaves the hand and returns to the body core. When heat conservation is important, more blood returns to the heart through the deep vein. In higher-temperature conditions, when heat conservation is not a concern, more blood returns through the surface vein. Numerals indicate the temperature of the blood in degrees Celsius.

Blood Disorders

1. Hemophilia
   - Genetic disorder that can result in fewer numbers of platelets or clotting proteins. This can lead to massive blood loss if the person experiences a cut or internal hemorrhaging.
2. Leukemia
   - Cancer of the leukocytes (WBC's). This can result from tumor growth in lymph nodes or bone marrow.
3. Anemia
   - Deficiency in hemoglobin or iron - leads to low O_2 transport and thus lethargy (low energy)

8.3 – The Lymphatic System & Immunity

- The lymphatic system is a network of vessels, glands, and nodes spread throughout the body

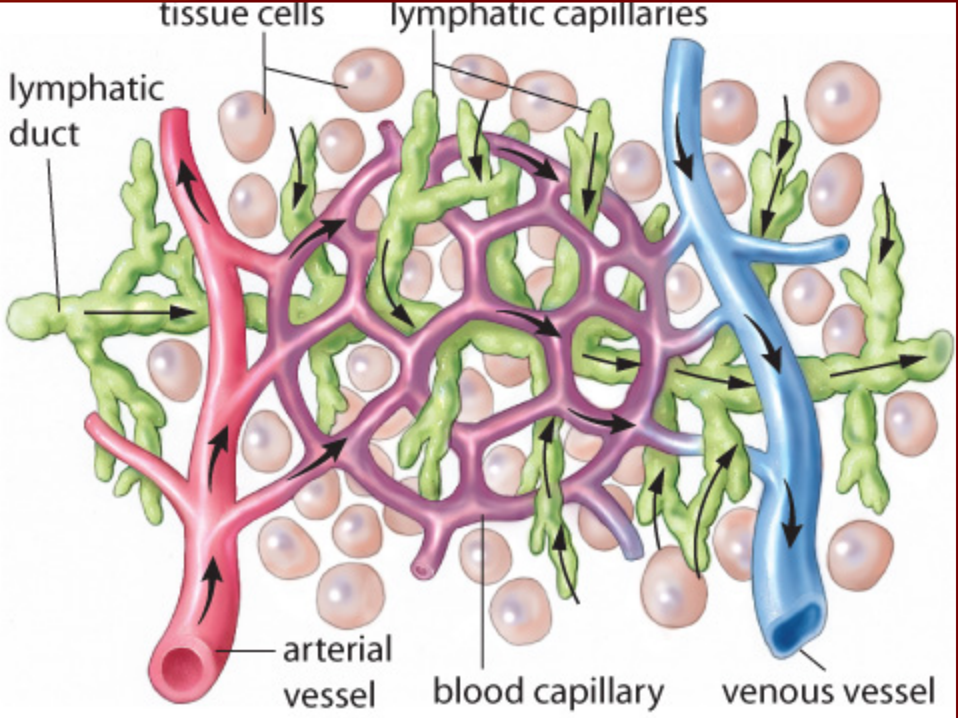


Figure 8.24 Lymph vessels are closely associated with the capillaries of the cardiovascular system. Fluid that escapes from the cardiovascular capillaries forms part of the interstitial fluid. Some of this fluid is collected in the lymphatic capillaries and eventually returned to the blood.

The Lymphatic System

- The lymphatic system connects to our circulatory system at the subclavian veins
- Lymph (the solution being transported) contains white blood cells to protect the body from infection (lymphocytes mature in the lymph nodes)
- The lymph nodes also contain macrophages which trap and destroy bacteria

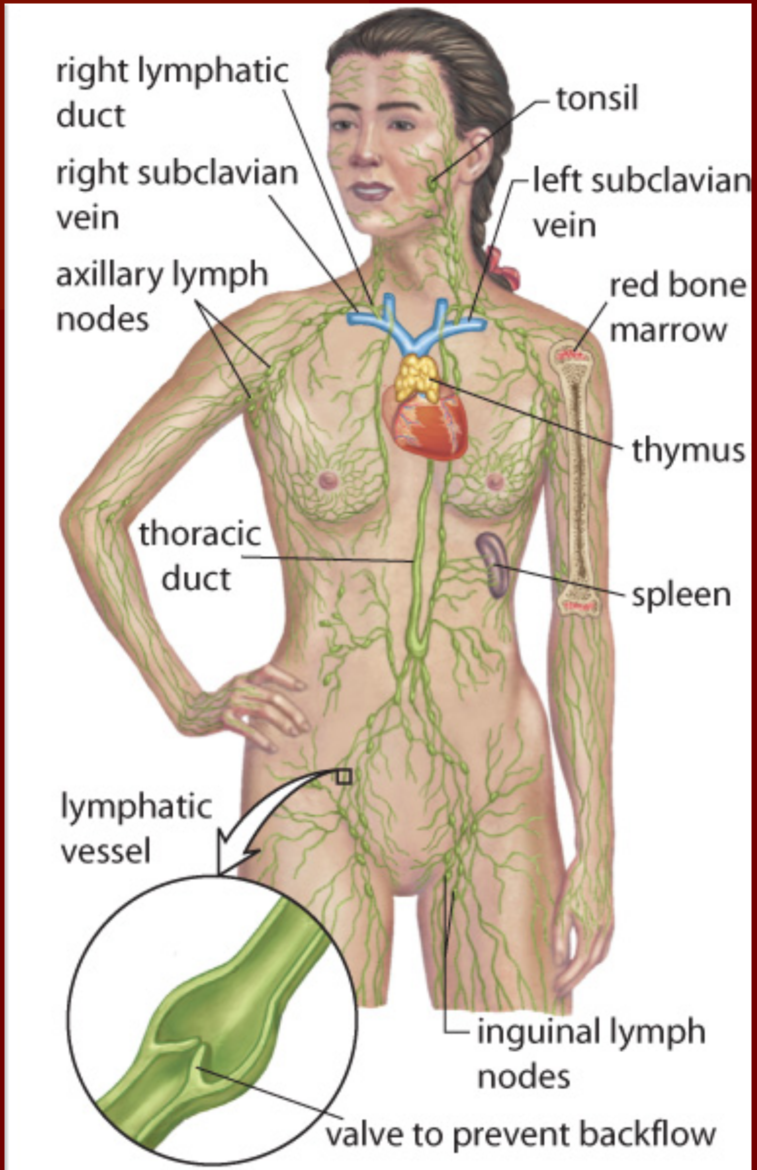


Figure 8.25 The human lymphatic system is spread throughout the body. Its largest vessels are in the region of the abdomen and thoracic cavity.

The Lymphatic System

- Functions:
  - Return excess tissue fluid to bloodstream
  - Lacteals absorb fats
  - Defense against disease
- Lymphatic vessels
  - One-way system
  - Begins with capillaries in tissues
  - Fluid inside is lymph
    - Water
    - Nutrients
    - Electrolytes
    - Cell products like hormones

The Lymphatic System

- Vessel structure
  - Small vessels and large vessels
    - Similar to veins
    - Valves to prevent backflow
    - Skeletal muscles “pump” lymph
- Edema
    - Accumulation of tissue fluid
    - Occurs if not enough drainage, or too much produced
    - Can cause tissue damage and death

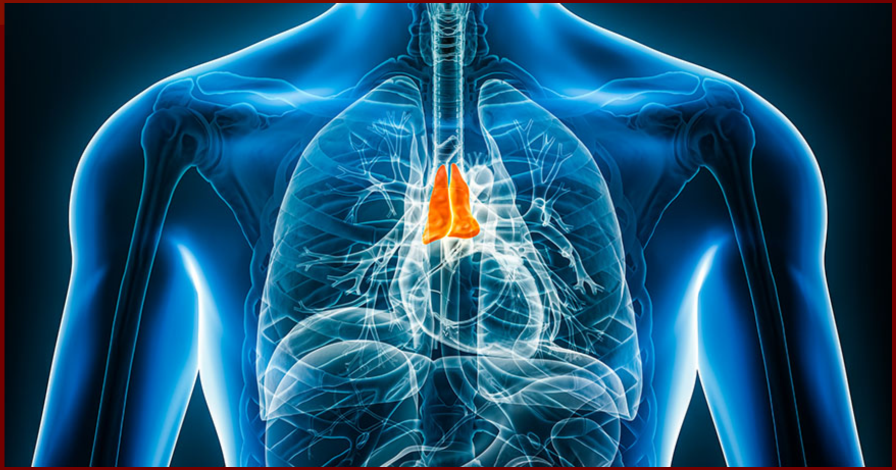
Figure 27.16
Elephantiasis. An infection with a filarial worm has caused this individual to experience extreme swelling in regions where the worms have blocked the lymph vessels.

The Lymphatic System

- Lymphatic organs:
  - Contain lymphocytes
    - Produced in thymus and bone marrow
    - B lymphocytes – antibodies
    - T lymphocytes – cellular immunity
  - Primary lymphatic organs:
    - Red bone marrow
      - Network of connective tissue fibers with sinuses
      - Stem cells produce blood cells
      - B lymphocytes mature in red marrow

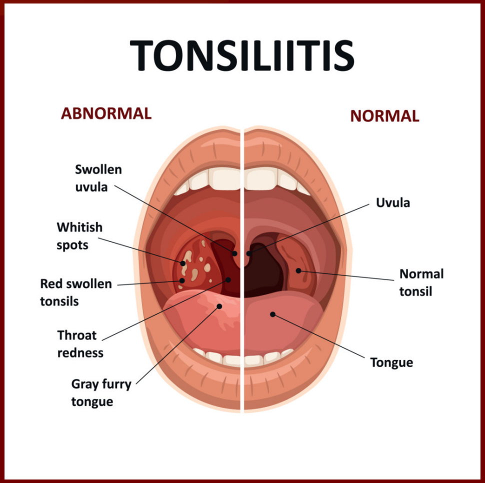
The Lymphatic System

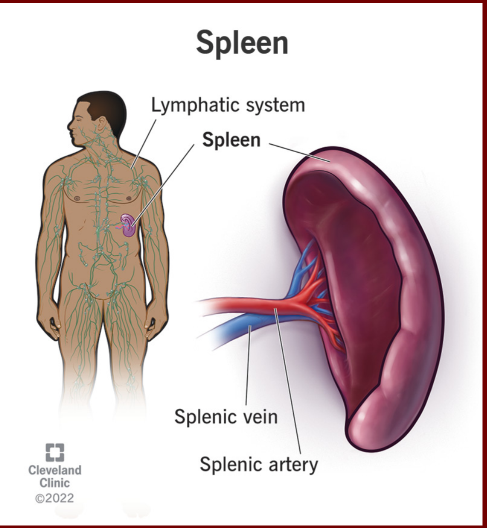
- Thymus
  - Between trachea and sternum above the heart
  - Shrinks with age
  - Divided into lobules by connective tissue
  - Lobules filled with T lymphocytes
    - Produced in bone marrow
    - Mature in the thymus
  - Produces hormones
    - Thymosin - aids maturation of T lymphocytes



The Lymphatic System

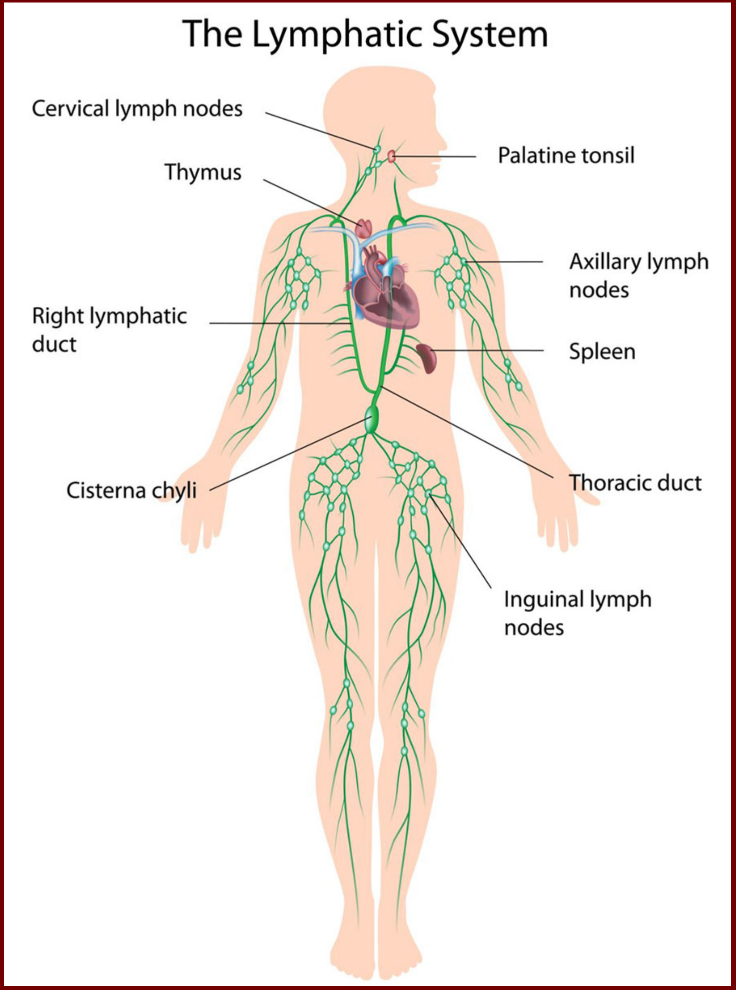
- Secondary lymphatic organs:
  - Tonsils
    - lymphatic tissue forms a protective ring around the entrance to the esophagus and respiratory tract
    - Filter out bacteria / pathogens entering mouth / nose
  - Spleen
    - Upper left side of abdomen
    - Filters blood
    - Macrophages destroy old RBC's





The Lymphatic System

- Lymph nodes
  - Located along lymphatic vessels
  - Divided into nodules by connective tissue
  - Nodules packed with B and T lymphocytes
  - Lymph filters through nodules



The Human Defense System

- There are two types of immune defense:
  1. Non-specific (general) defenses
  2. Specific defenses
- Non-specific defenses try to:
  - Prevent organisms from entering the body as the first line of defense
  - Initiate an inflammatory response to isolate infection and keep it from spreading

Immunity
Immune TED

Non-Specific Defenses

- These are defenses used on any pathogen
- Physical defenses:
  - Entry Prevention:
    - Hair (eyelashes, ear hair, nose hair) – traps particles and foreign pathogens
    - Eyelids – prevent entry into eye socket / eye ball
    - Skin – physical barrier and contains oil glands that secrete antibacterial substances
    - Tonsils / Adenoids – provide dedicated supply of WBC’s in oral cavity to catch / engulf foreign pathogens
    - Ear wax traps particles and foreign pathogens

Non-Specific Defenses

- Physical defenses:
  - Sweep or Flush pathogens:
    - Mucous membranes (nose / throat / sinuses) – trap particles and foreign pathogens to be flushed / wiped away
    - Cilia hairs in nose / trachea – sweep particles and pathogens towards mouth (can initiate coughing reflex)
    - Teardrops – tears trap particles and foreign pathogens and flush away from eye

Non-Specific Defenses

- If pathogens get past the physical barriers, the body sends WBC's to repel invaders and initiate an inflammatory response:
  - Initiated by chemical agents or pathogens
  - 4 signs
    - Redness
    - Heat
    - Swelling
    - Pain

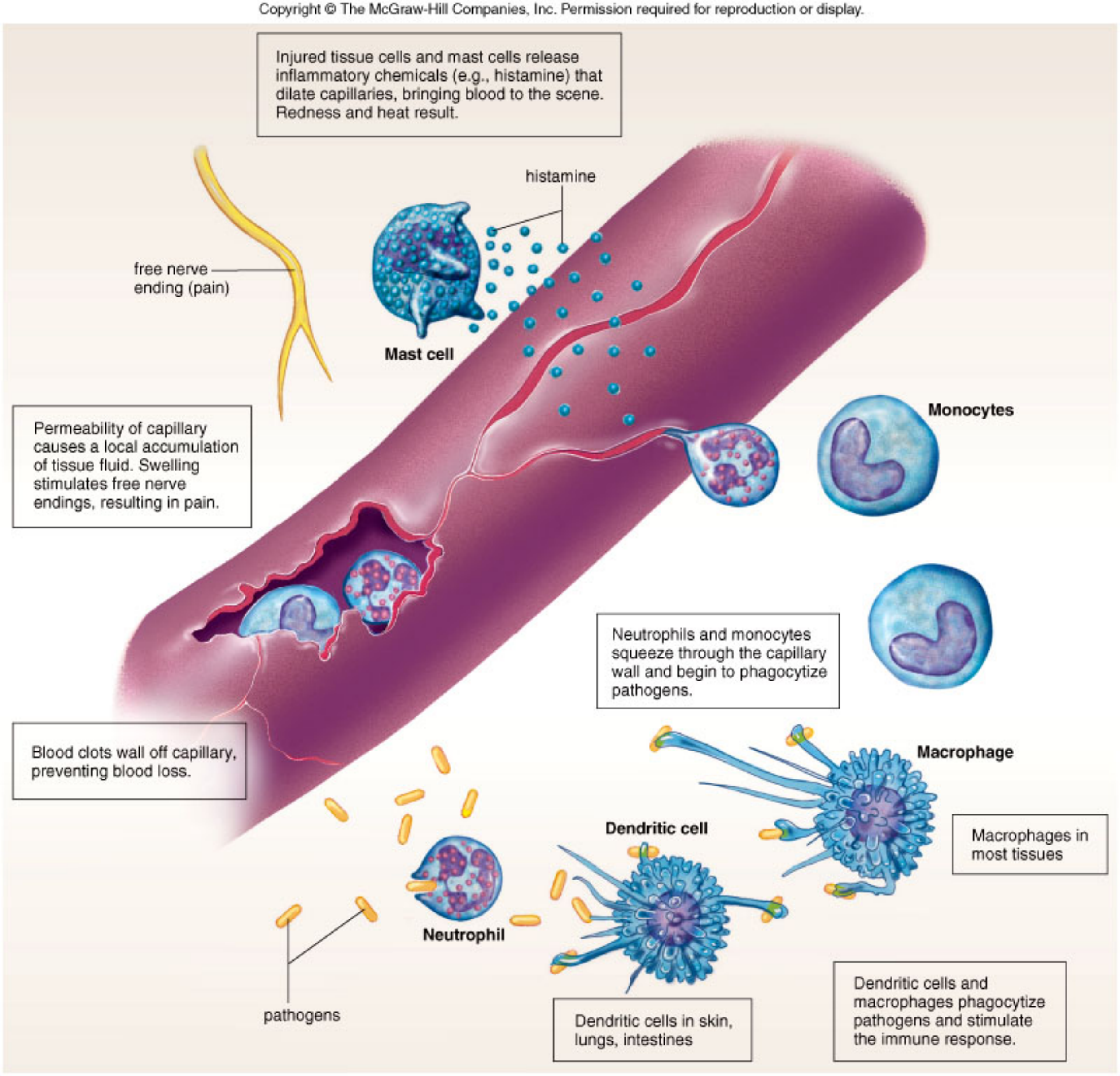
Non-Specific Defenses

- Inflammatory response:
  - Induced by chemical mediators
      - Histamine
        - Produced by basophil (mast) cells
        - Vasodilator – allows more blood to region
  - Migration of phagocytes to damaged area
    - Neutrophils – from bloodstream
    - Monocytes – from bloodstream
    - Dendritic cells – in skin
    - Macrophages – in tissues
  - Pus – dead phagocytes and pathogens

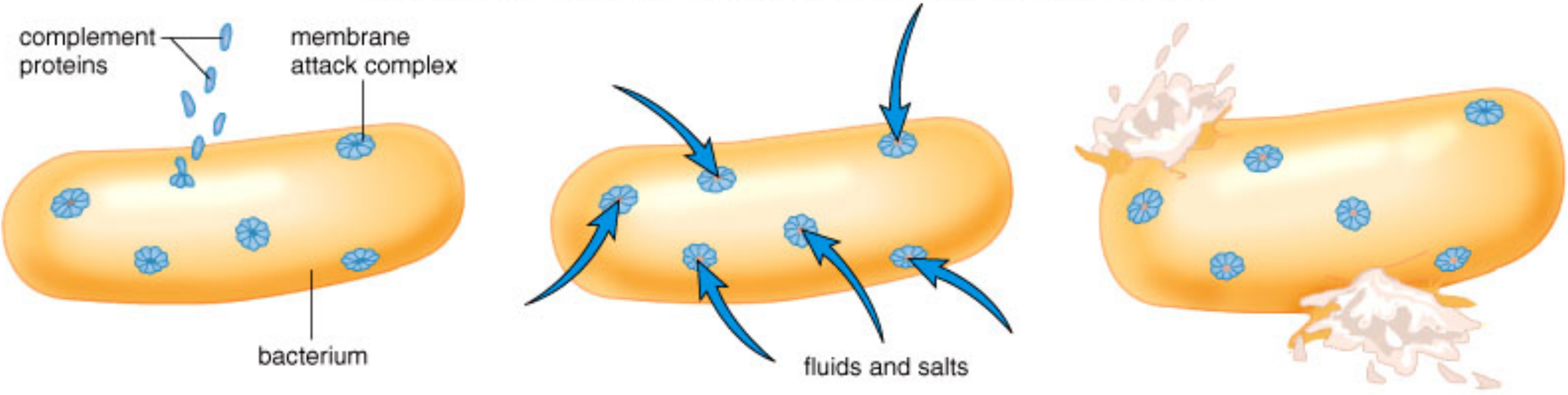
Non-Specific Defenses

- Inflammation can be accompanied by other responses
  - Clot formation
  - Specific defenses mediated by T & B cells
- Chronic inflammation
  - Persistent
  - Can use anti-inflammatory agents
    - Aspirin, NSAIDs, cortisone
    - Act against histamines released by WBC’s in damaged area (anti-histamine)

Inflammatory Response



Complementary System of Proteins Act Against a Bacterium



Complement proteins form a membrane attack complex in the bacterial cell wall and membrane.

Holes in the middle of the complexes allow fluids and salts to enter the bacterium.

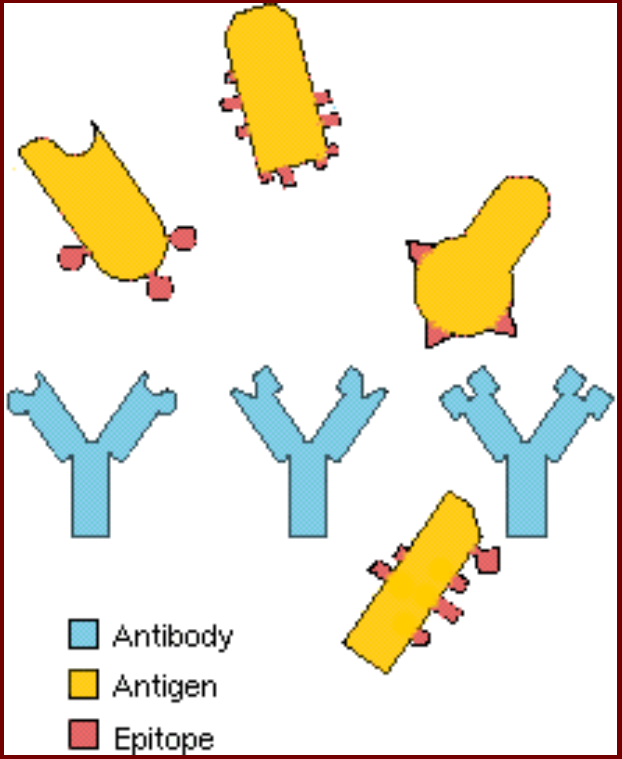
Bacterium expands until it bursts.

Specific Defenses (Antibody-Mediated Immunity)

- Engaged after non-specific immunity has failed
- Takes 5-7 days to activate; effects are long lasting
- Lymphocytes are primarily responsible for this immune response
- Antigens are protein markers present on almost all cells (including pathogens) and are unique to those cells
- Antibodies are proteins that recognize foreign substances (specifically their antigens) and either neutralize or destroy them

Antigens and Antibodies

- Antibodies are Y-shaped proteins
- An antibody attaches to specific antigens because they have similar shapes
- Often the antigen-antibody complex makes the invader more visible to wandering macrophages, which engulf the bacteria

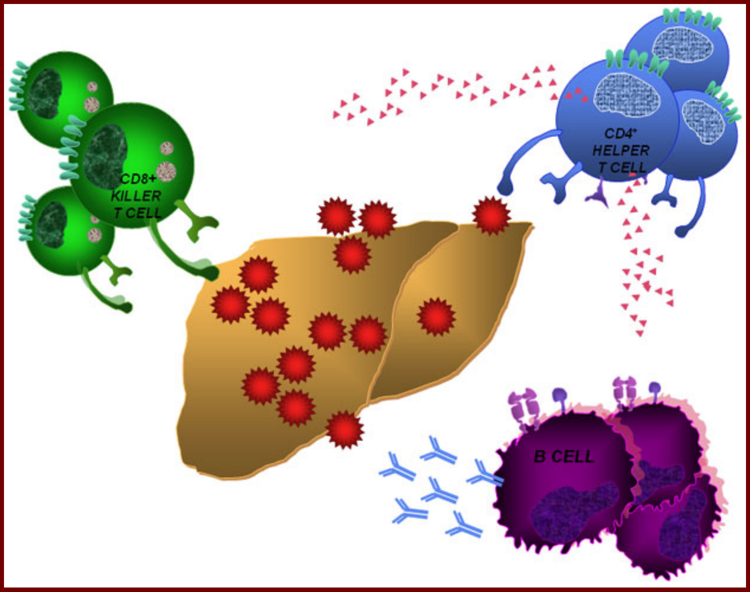


Antigens and Antibodies

- Antibodies can bind to toxins, changing their shape and preventing them from entering cells
- Antibodies also work in the same manner on viruses
- However, viruses quickly mutate and prevent the same antibodies from working for very long

T and B cells (Lymphocytes)

- T cells are produced in the bone marrow and mature in the thymus gland
- B cells are produced in the bone marrow the Y-shaped antibodies



T – Cells

- T- cell receptor - TCR on cells that wait in lymph nodes
  - Cannot recognize antigen without help
  - APC - antigen-presenting cell
    - Dendritic cells or macrophages engulf pathogen first
    - Break pathogens down
    - Display a piece of pathogen in major histocompatability complex (MHC) on surface of APC membrane
  - Travel to nodes
    - "Present" antigen to TCR lymphocytes

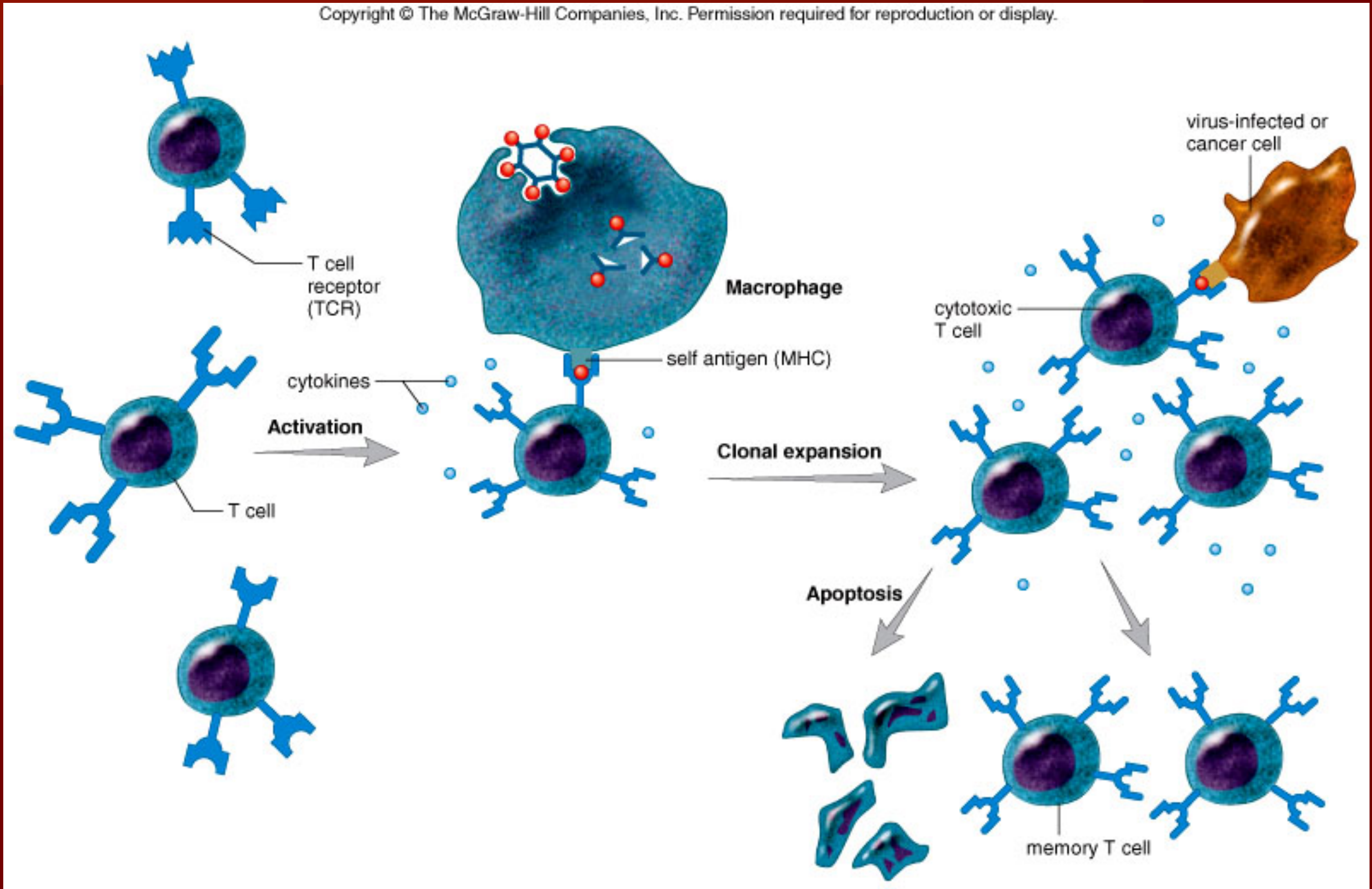
T – Cells

- T-cell with specific TCR bind to antigen (MHC) on macrophage (APC) surface
    - T-cell becomes activated
    - Undergoes clonal expansion (accelerated mitosis)
- Type of T-cell formed depends upon MHC type
    - MHC I -> cytotoxic (Killer) T-cells
    - MHC II -> Helper T-cells

T-Cells

- Helper T-cells
  - Bind to antigens on foreign pathogens
    - Secrete cytokines which activate all immune cells (calls for backup – Killer T-cells)
  - Helper T-cells needed for B-cell activation
  - Helper T-cells are infected by HIV virus
    - HIV can actually “hide” inside the T-cells (TCR) that are supposed to signal its presence
- Killer T-cells puncture pathogens or infected cells
- Small number of clonal cells become memory T-cells
  - When infection clears, T-cells undergo apoptosis (suicide)

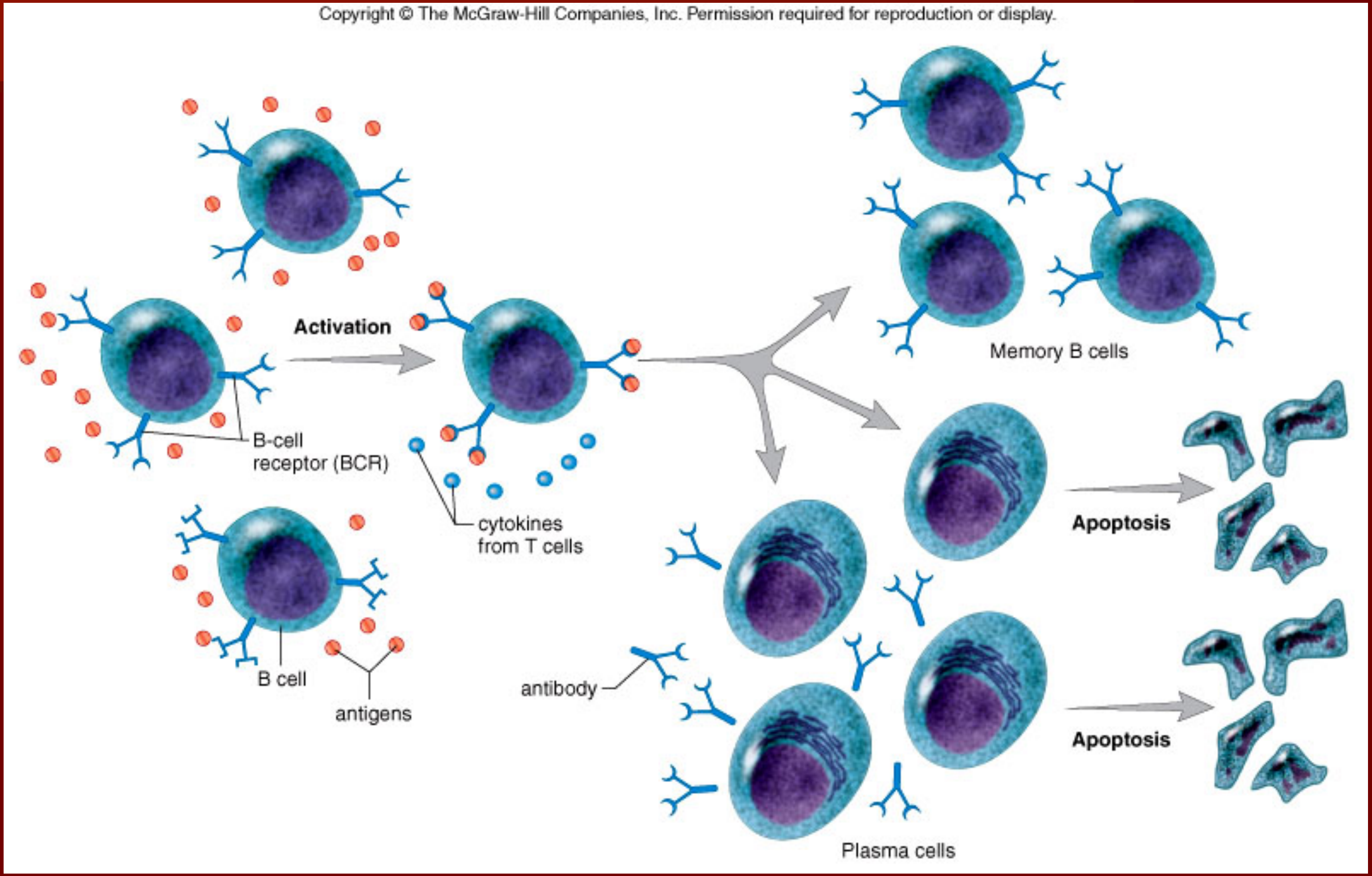
T-cells Differentiation



B-Cells

- B-cell receptor – BCR
- BCR binds to specific antigen on helper T-cells in lymph node or spleen
  - B-cell then activated and divides many times by mitosis (clones)
- Clones become:
  - Plasma B-cells – produce antibodies to specific antigens
  - Memory B-cells – remember antigen for later exposure (long term immunity)

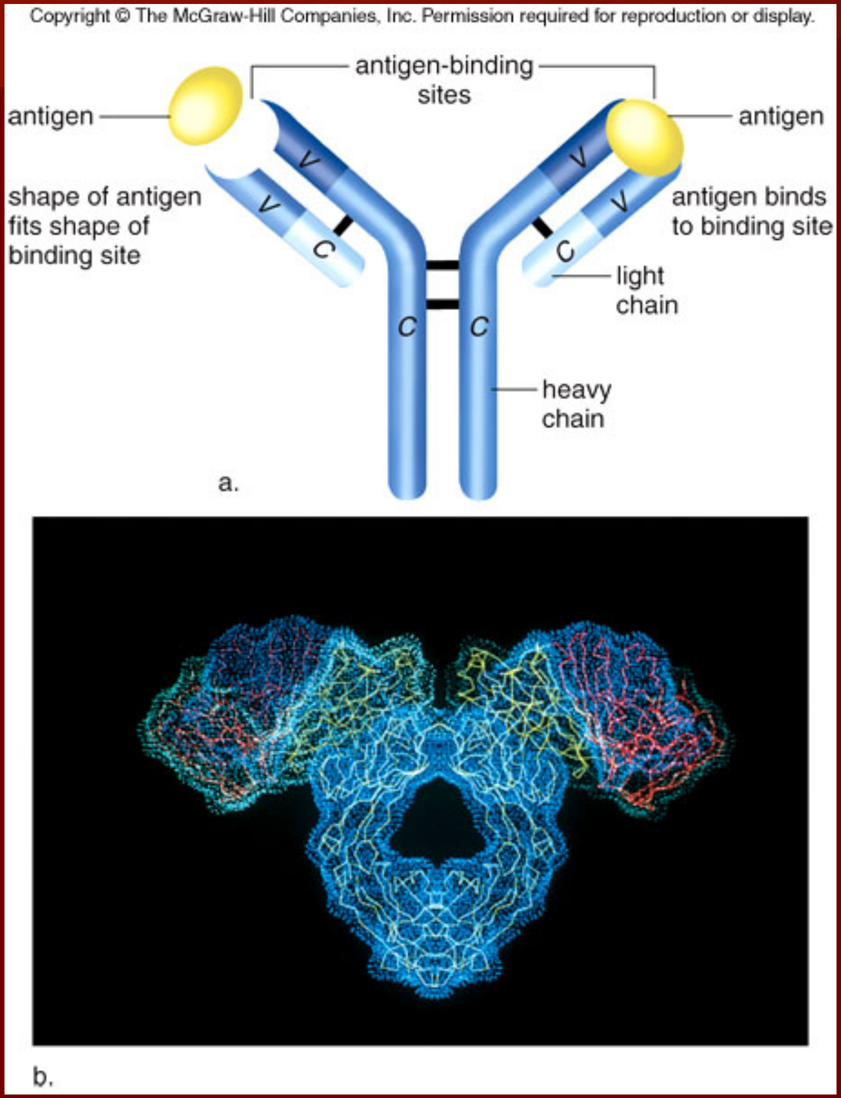
B-cell Differentiation



Plasma B-Cells: Antibody Factories

- Antibody structure
  - Y-shaped molecules with 2 “arms”
    - Each arm has a heavy and a light polypeptide chain
    - Antigen binding site at terminal end
      - Lock and key fit
- Antigen-antibody binding
  - Forms a complex
  - Marks antigen for destruction

Antibody structure



Immune Response Suppression

- Once an infection is fought off, suppressor T-cells signal the immune system to shut down (most cells undergo apoptosis)
- Phagocytes clean up any dead or injured B- and T-cells that remain
- Finally, memory T-cells produce copies of the invader antigens so that they can be more easily identified in the future

Blood Types

- Early blood transfusion experiments often led to the death of the patient
- It wasn't until the 20^{th} century that doctors realized that there were different blood groups
- The glycoproteins (antigens) on the surface of blood cells can differ from one person to another

Blood Groups – How They Work

- Individuals with A blood type have the "A" version of the antigen on the cell
- Individuals with B blood type have the "B" version of the antigen
- Individuals with AB blood types have both "A" and "B" antigens
- Individuals with O blood type do not have any antigens
- Based on codominance of A and B types over O type

ABO Antigens and Antibodies

Blood Type	Antigen Present	Antibodies in Plasma
A	A	b
B	B	a
AB	A and B	none
O	None	a and b

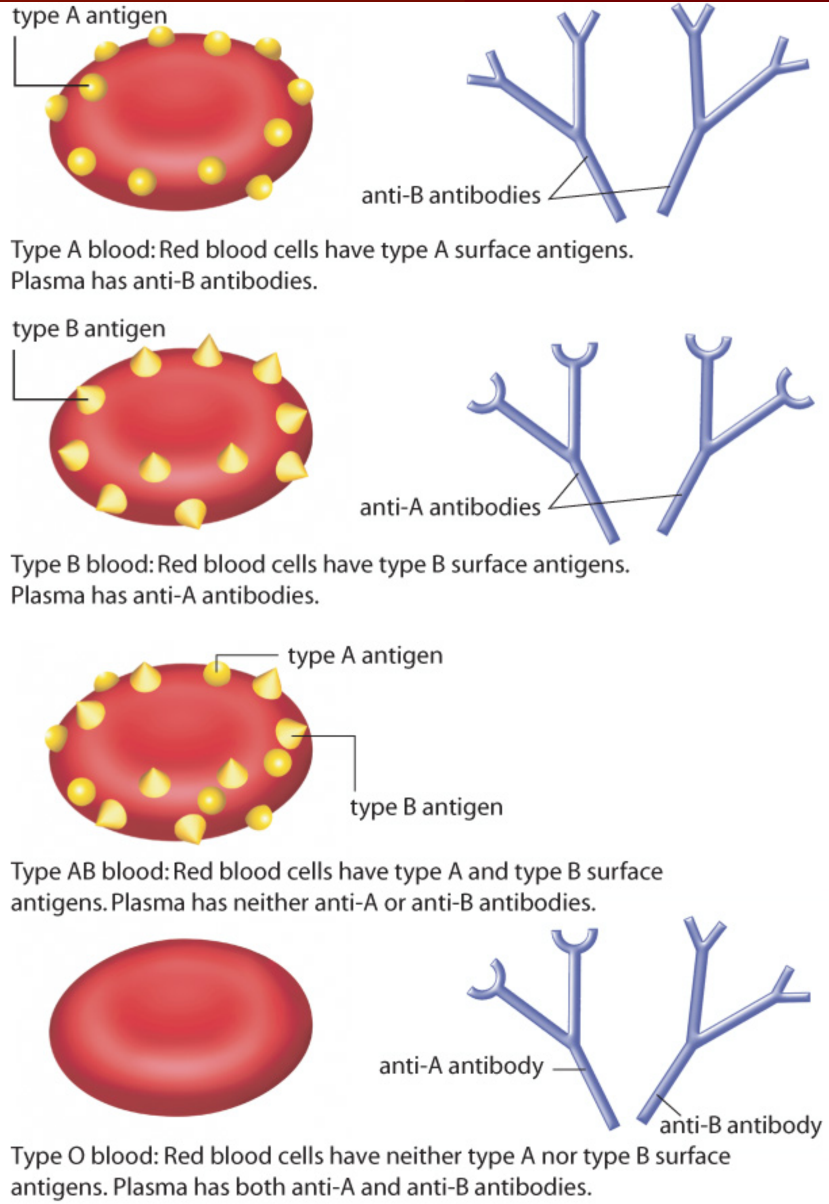
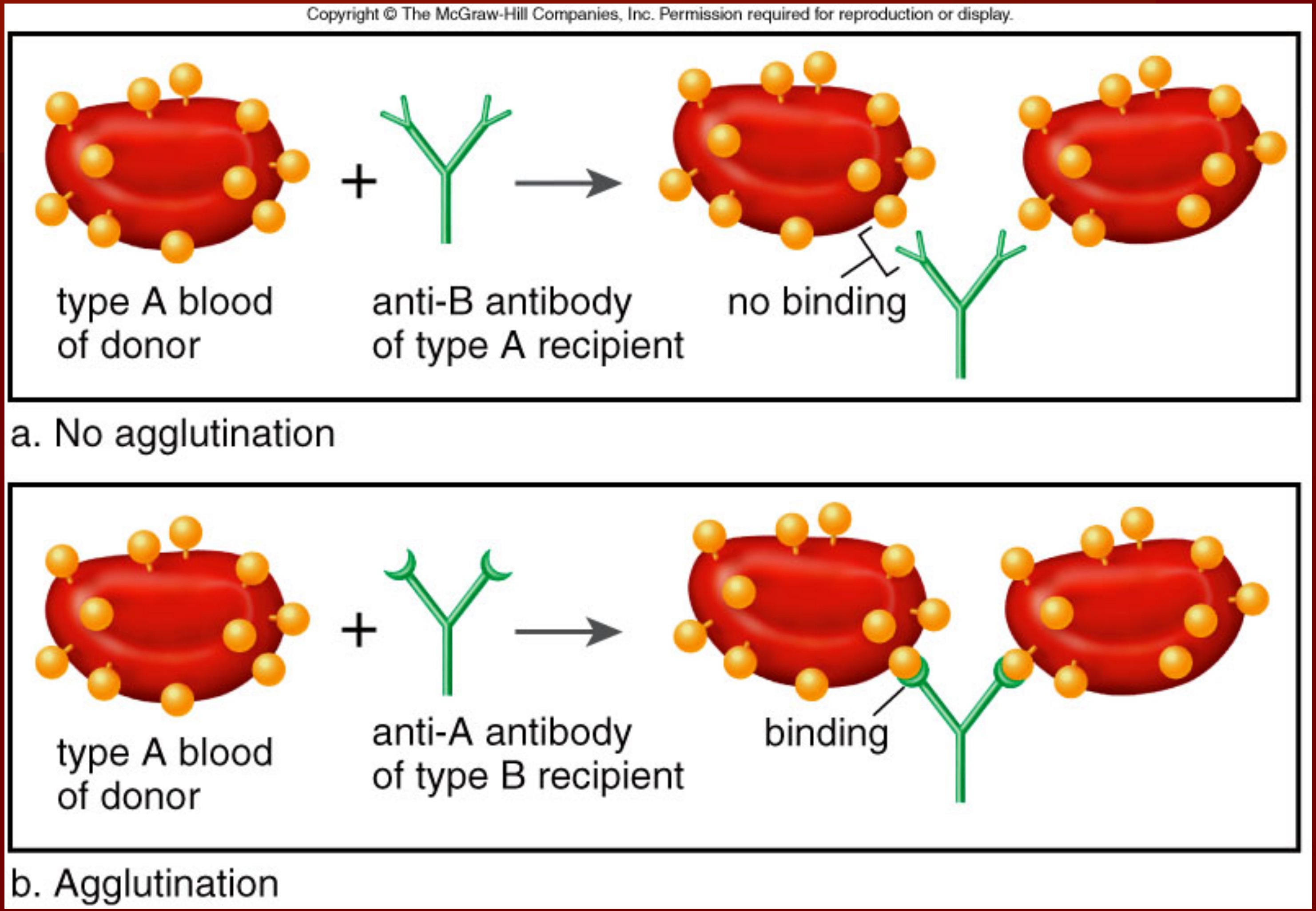


Figure 8.30 In the ABO system, blood type depends on the presence or absence of antigens A and B on the surface of red blood cells. In these diagrams, A and B antigens are represented by different shapes on the red blood cells. The possible anti-A and anti-B antibodies in the plasma are represented for each blood type.

Blood Transfusions

- Transfusions of RBC usually not whole blood
  - Must consider recipient's antibodies and donor's antigens to prevent agglutination and bad transfusion reaction
  - Type O is universal donor
    - Neither A nor B antigens
  - Type AB is universal recipient
    - Neither anti-A nor anti-B antibodies

Blood Transfusions



Rhesus Factor

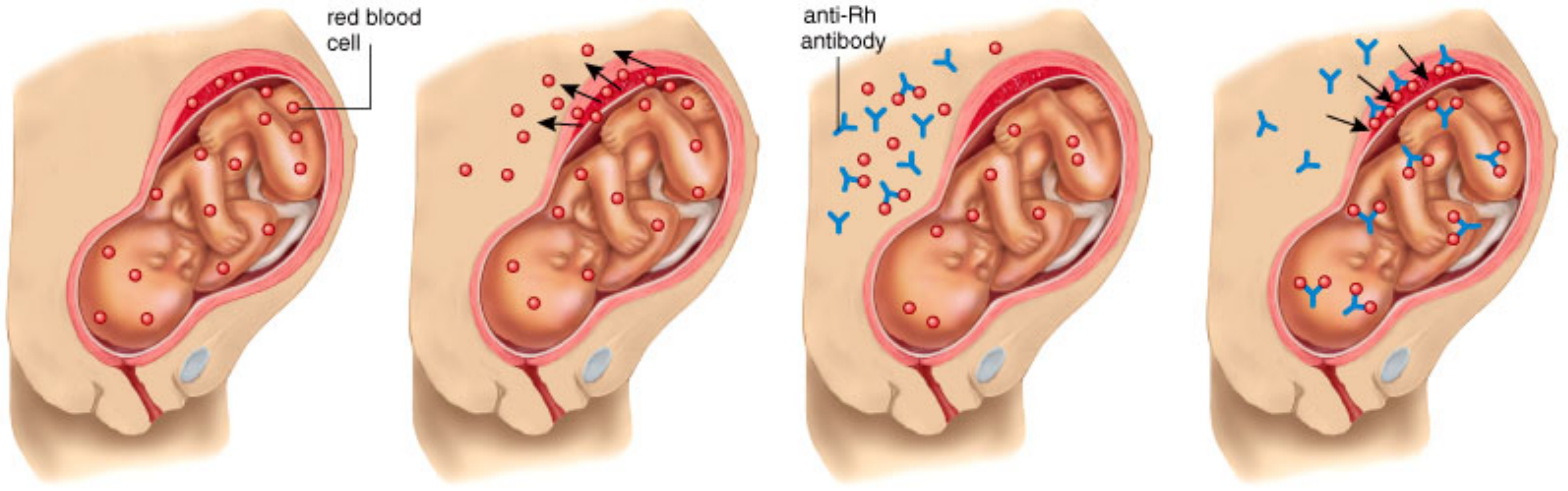
- A third antigen, Rhesus factor, is also found on red blood cells
- People can be Rh+ or Rh- (either the antigen is present or it is not)
- This can often affect the health of a fetus

Blood Typing Game

Rhesus Factor and Pregnancy

- The baby's blood will come into contact with the mother's immune system at birth (or possibly before)
- As a result, if the baby has received Rh+ antigen from the father, but the mother is Rh-, the mother starts to produce antibodies against the Rh+ blood
- Any fetuses that are Rh+ will experience clumping of blood in their veins due to the mother's antibodies
- Treatment for this condition usually involves a transfusion of Rh- blood into the baby at birth (it allows times for the mother's antibodies to break down)

Hemolytic Disease of the Newborn



Child is Rh positive; mother is Rh negative.

Red blood cells leak across placenta.

Mother makes anti-Rh antibodies.

Antibodies attack Rh-positive red blood cells in child.