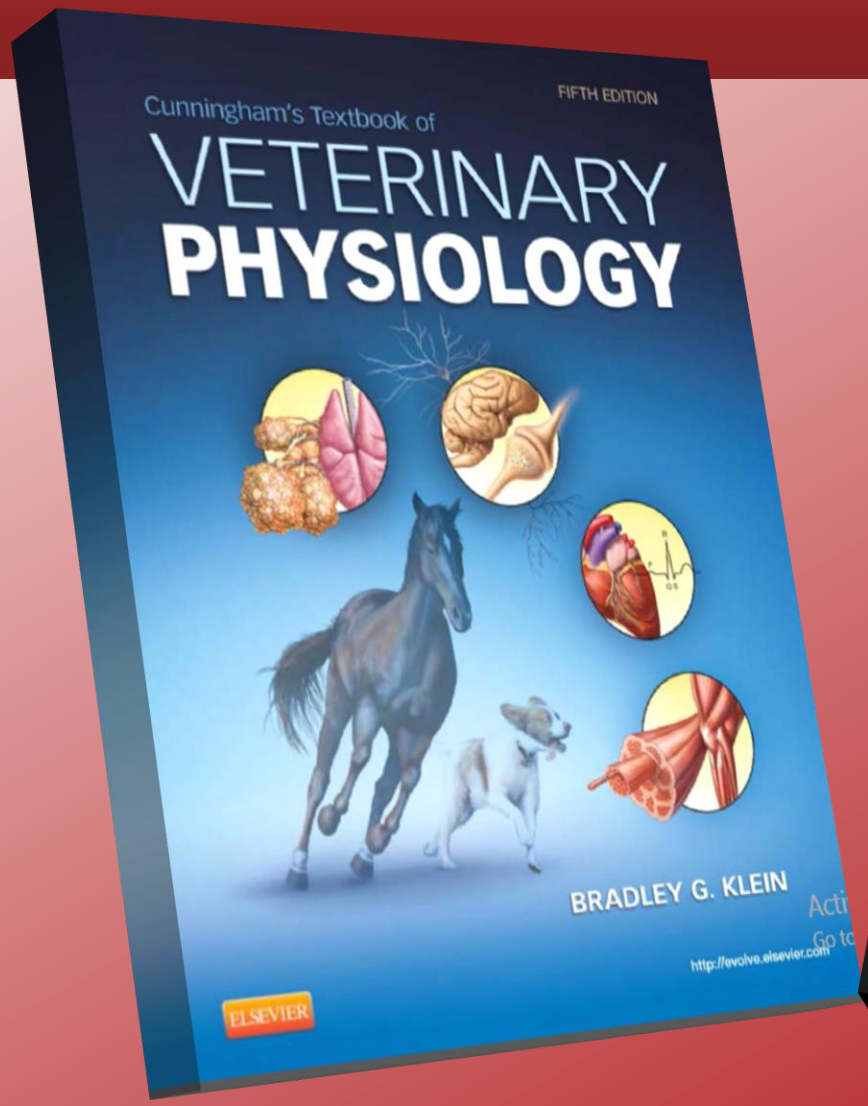
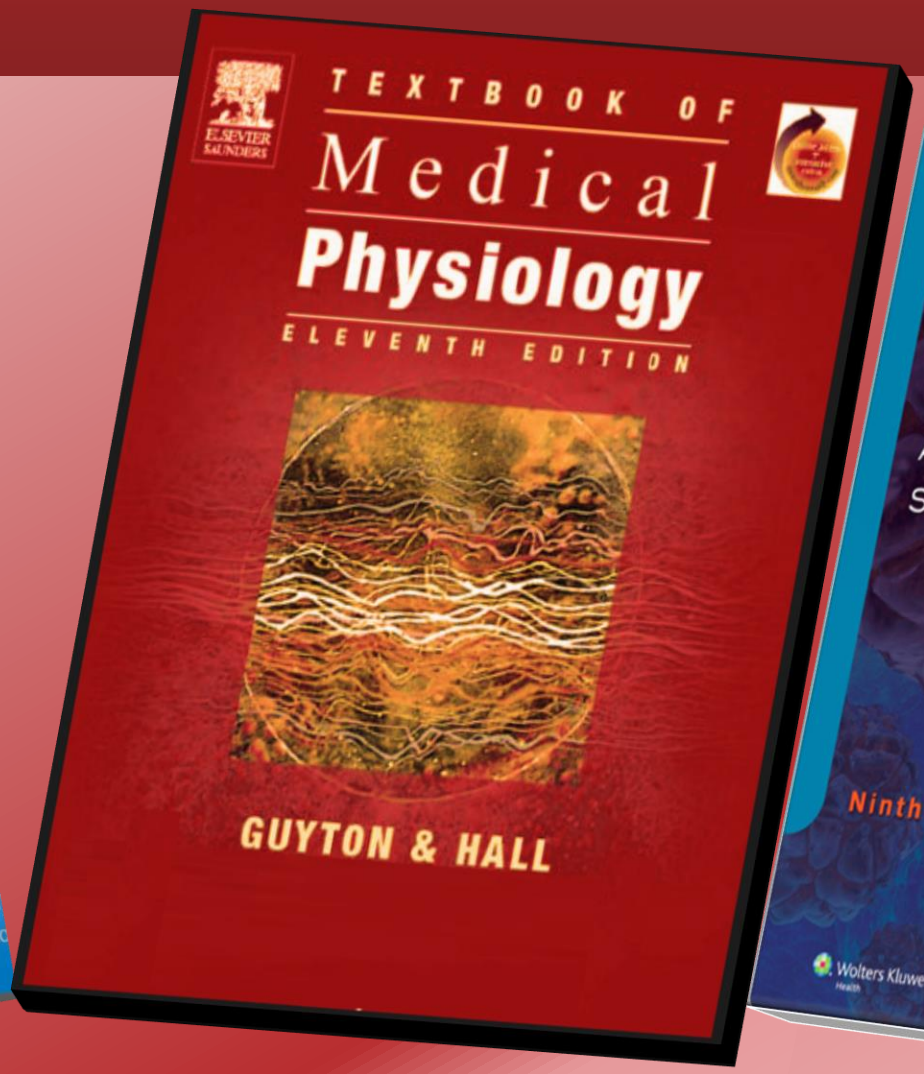
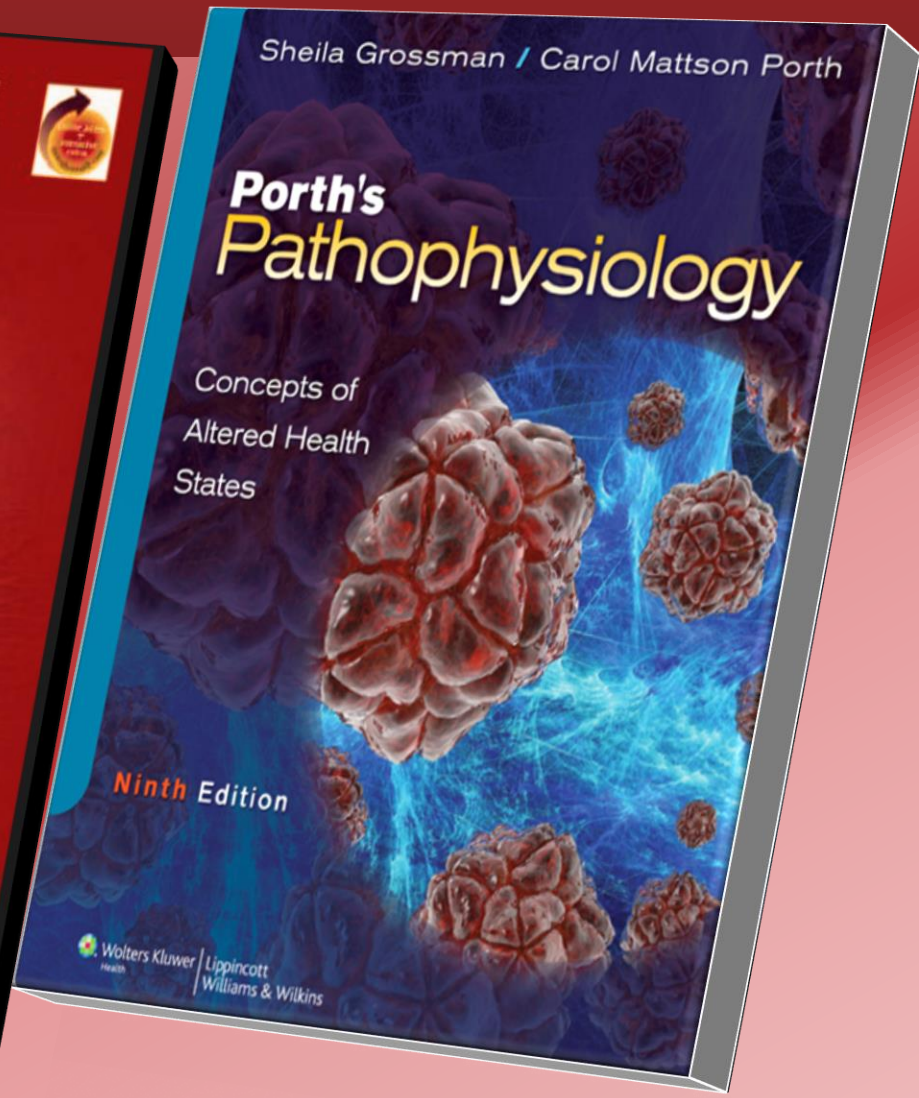
Cardiovascular System Physiology

Dr. A. K.Goudarzi, D.V.M, Ph.D
Department of Basic Sciences
School of Veterinary Medicine
I.A. University

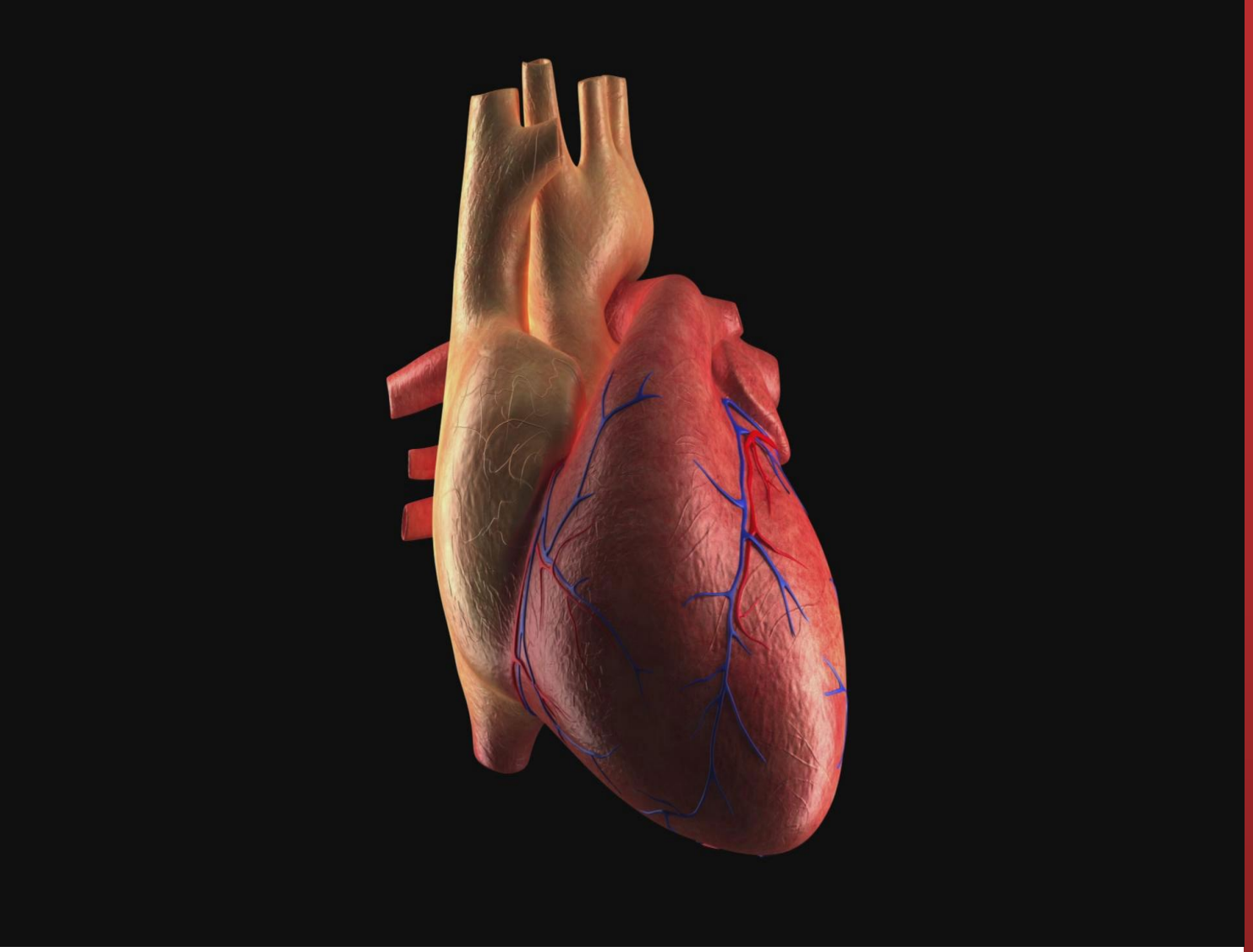
References







For PDF file visit: www.kajalpetclinic.com



Because Normal Cardiovascular Function Is Essential for Life and Health, a Practical Understanding of Cardiovascular Function and Dysfunction Is Vital to the Veterinary Clinician

1

Overview of Cardiovascular Function

Overview of Cardiovascular Function

- Functional components of the cardiovascular system:
  - Heart
  - Blood Vessels
  - Blood
- **General functions:**
  - Transportation
    - Oxygen and nutrients to the cells
    - Carbon dioxide and other metabolic waste products to the lungs, kidneys, or liver
    - Circulates electrolytes and hormones needed to regulate body function
  - Temperature regulation
    - By transporting core heat to the periphery, where it is dissipated into the external environment

Overview of Cardiovascular Function

- **Cardiovascular Dysfunctions:**

- **Primary**: the fundamental disturbance or disease process affects the cardiovascular system directly (e.g. hemorrhage, myocarditis, . . .)
  - **Congenital:** present at birth
    - frequently involve defective heart valves, which either cannot open fully or cannot close completely
    - are common in certain breeds of dogs and horses
    - heart can pump an adequate amount of blood when the animal is at rest, but not during exercise (heart failure)
    - The animal exhibits exercise intolerance
  - **Acquired:** developing after birth
    - Parasites: e.g. adult heartworms (Dirofilaria immitis) in dogs disturbs animal's ability to control blood pressure and blood flow, and In horses, bloodworms (Strongylus vulgaris) which decrease the blood flow to the intestine that leads to equine colic

Overview of Cardiovascular Function

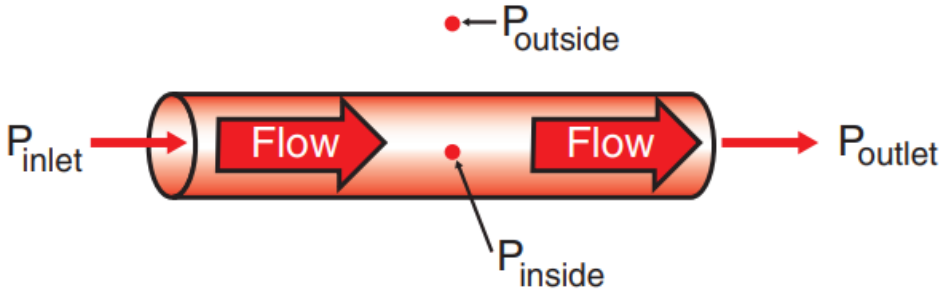
- **Secondary:** often become the most serious and life-threatening aspects of the disease
  - Severe burns or persistent vomiting or diarrhea leads to water and electrolyte disturbances and cause abnormal heart rhythms (cardiac arrhythmias) and ineffective pumping of blood by the heart (heart failure)
    - The electrolyte abnormalities in such a patient can be made even worse if incorrect fluid therapy is given.
    - Incorrect fluid therapy can also lead to an accumulation of excess fluid in the tissues of the body; called edema.
    - If the excess fluid gathers in the lung tissue, the condition is called pulmonary edema. Pulmonary edema is life threatening because it slows the flow of oxygen from the pulmonary air sacs (alveoli) into the bloodstream.
  - Different types of shocks (hemorrhagic, cardiogenic, septic, and endotoxic) depress the pumping ability of the heart which leads to low blood flow and ischemia in all the vital body organs. Kidney (or renal) failure, respiratory failure, central nervous system (CNS) depression, and death follow

Overview of Cardiovascular Function

- Most anesthetics depress the CNS, and the resulting abnormal neural signals to the heart and the blood vessels can depress cardiac output and lower blood pressure.
  - Some anesthetics, particularly the barbiturates, also depress the pumping ability of the heart directly
  - Anesthetic overdose is the most serious and life-threatening symptoms as secondary cardiovascular complications

Modes of Blood Transportation

1. **Bulk flow:**
   - is rapid over long distances (within 10 seconds it reaches distant parts of the body, including the head and limbs)
   - the source of energy for bulk flow is a hydrostatic pressure difference
   - The difference in pressure between two points in a blood vessel is called the perfusion pressure
     - the perfusion pressure is the pressure difference that causes blood to flow through blood vessels
   - transmural pressure is the difference between the blood pressure inside a blood vessel and the fluid pressure in the tissue immediately outside the vessel



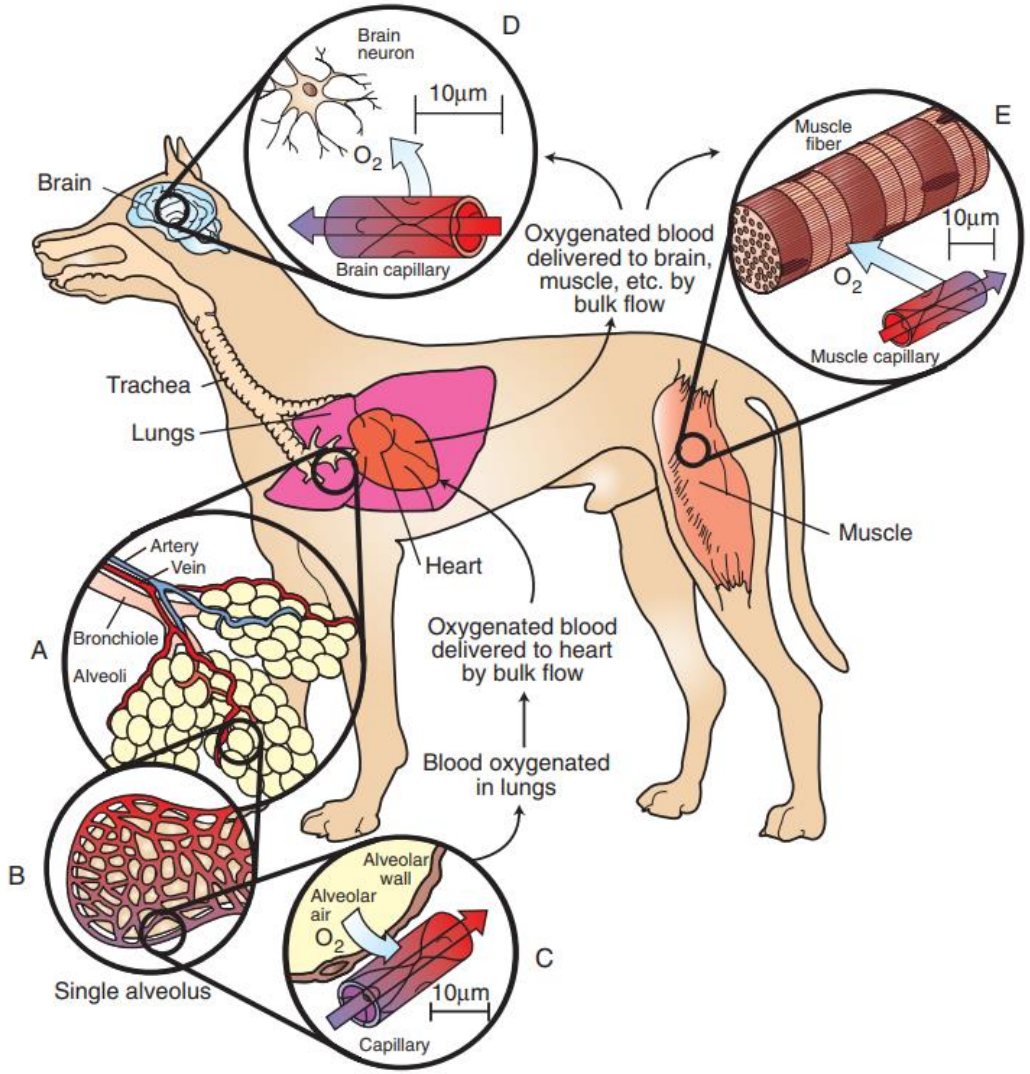
Perfusion pressure = $(P_{inlet} - P_{outlet})$

Transmural pressure = $(P_{inside} - P_{outside})$

Modes of Blood Transportation

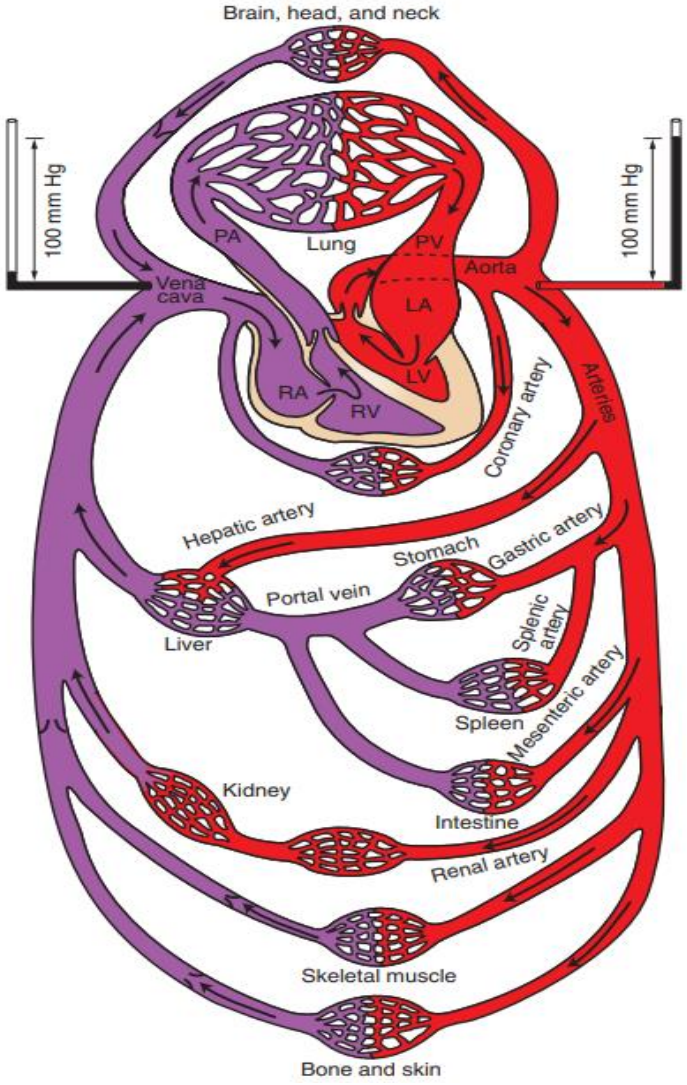
2. Diffusion:

- The primary mechanism by which dissolved substances move across the walls of blood vessels, from the bloodstream (usually through capillaries) into the interstitial fluid, or vice versa is diffusion
- The source of energy for diffusion is a concentration difference (and if the capillary wall is permeable to the substance)
- Because Diffusion Is Very Slow, Every Metabolically Active Cell in the Body Must Be Close to a Capillary Carrying Blood by Bulk Flow



The Pulmonary and Systemic Circulations

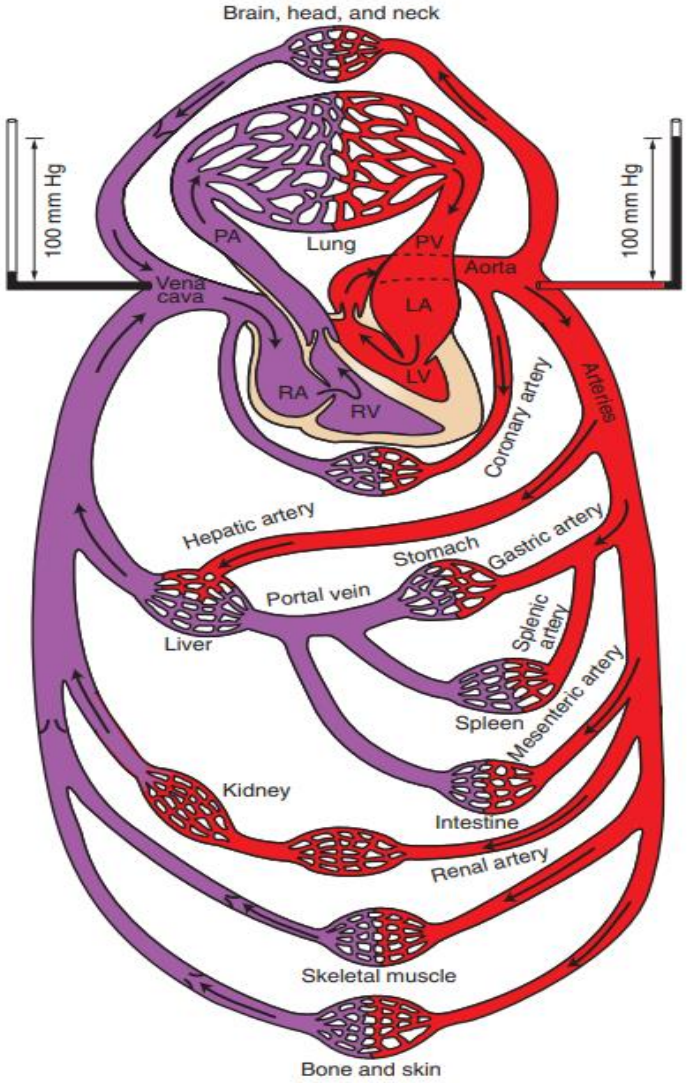
- General layout of the cardiovascular system, showing that the systemic and pulmonary circulations are arranged in series and that the organs within the systemic circulation are arranged in parallel
  - The pulmonary circulation, which moves blood through the lungs and creates a link with the gas exchange function of the respiratory system
  - The systemic circulation, which supplies all the other tissues of the body
    - except for a few specialized portal systems (hepatic, renal and hypothalamus-hypophysial), blood encounters only one capillary bed in a single pass through the systemic circulation



Cardiac Output

- **Cardiac Output** Is the Volume of Blood Pumped Each Minute by One Ventricle
  - CO = HR x SV (Heart Rate x Stroke Volume)
  - **Heart Rate**: number of heart beats (one contraction or systole + one relaxation or diastole)
  - **Stroke Volume**: the amount of blood that ejects from one ventricle on each contraction

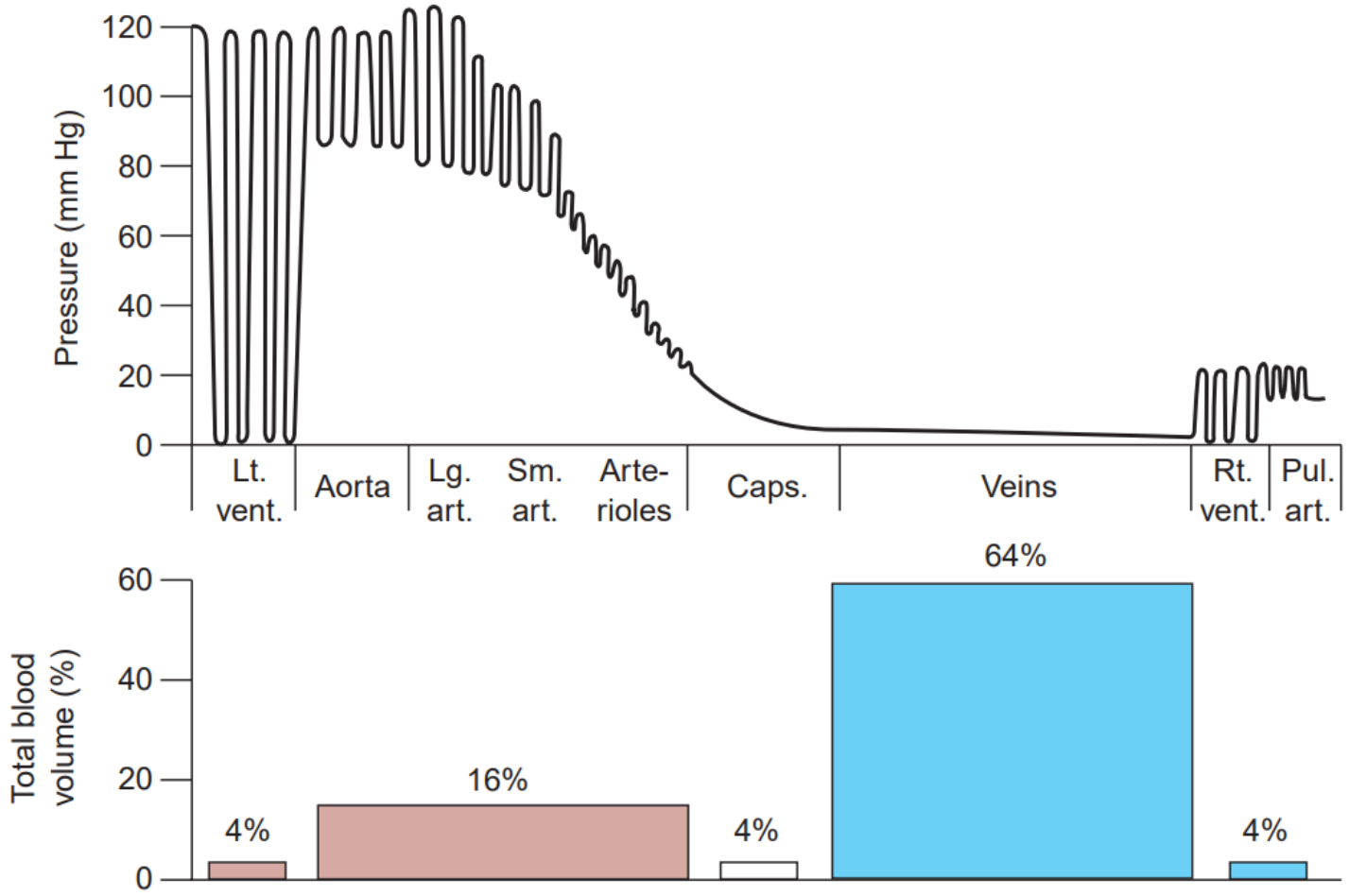
- In a resting dog, it takes about 1 minute for blood to traverse the entire circulation. Because the pulmonary and systemic circulations are in series, the volume of blood pumped by the right side of the heart each minute must equal the volume of blood pumped by the left side of the heart each minute



Systolic, Diastolic and Mean Arterial Pressure

- When the left ventricle contracts and ejects blood into the aorta, the aortic blood pressure rises to a peak value called **systolic pressure**.
- Between ejections, blood continues to flow out of the aorta into the downstream arteries. This outflow of blood from the aorta causes aortic pressure to decrease. The minimal value of aortic blood pressure, just before the next cardiac ejection, is called **diastolic pressure**.
- The **mean arterial pressure (MAP)** represents a potential energy for driving blood through the systemic circulation. As blood flows through the systemic blood vessels, this pressure energy is dissipated through friction.
- The perfusion pressure is the difference between MAPs from start to end
  - Systemic circulation: 98mmHg – 3mmHg = 95mmHg
  - Pulmonary circulation: 13mmHg – 5mmHg = 8mmHg

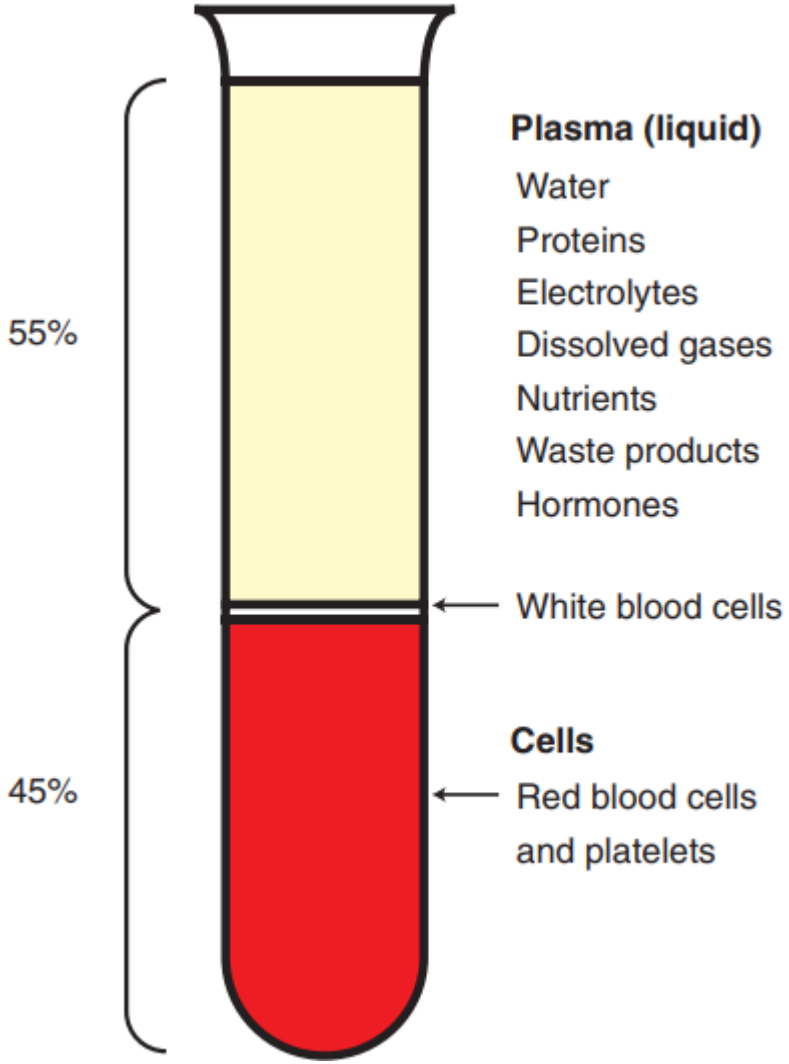
Blood Pressure and Volume Distribution



The graphs show the inverse relation between internal pressure and volume in different portions of the circulatory system.

The pressure on the arterial side of the circulation, which contains only approximately one sixth of the blood volume, is much greater than the pressure on the venous side of the circulation, which contains approximately two thirds of the blood.

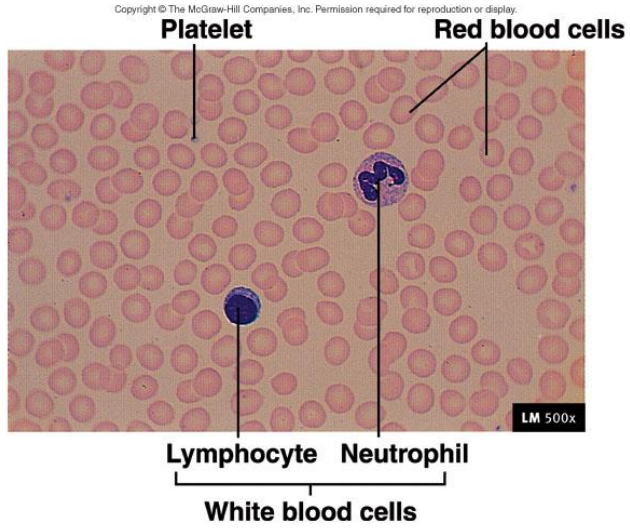
Blood Components



Component	Normal Range	Units
Plasma Proteins (Carried in Colloidal Suspension)		
Globulin (total)	2.7-4.4	g/dL
Albumin	2.3-3.1	g/dL
Fibrinogen	0.15-0.30	g/dL
Electrolytes (Dissolved)		
Na^+	140-150	mmol/L
K^+	3.9-5.1	mmol/L
Ca^{2+} (ionized)	1.2-1.5	mmol/L
Mg^{2+} (ionized)	0.5-0.9	mmol/L
Cl^-	110-124	mmol/L
HCO_3^-	17-24	mmol/L
HPO_4^{2-} and $H_2PO_4^-$	1-1.4	mmol/L
H^+	38-49	nmol/L*
(H^+ expressed as pH)†	(7.31-7.42)	
Dissolved Gases (Values for Arterial Plasma)		
O_2	0.26-0.30	mL/dL
CO_2	2-2.5	mL/dL
Examples of Nutrients, Waste Products, Hormones		
Cholesterol	140-280	mg/dL
Glucose	76-120	mg/dL
Triglycerides	40-170	mg/dL
Urea nitrogen	8-28	mg/dL
Creatinine	0.5-1.7	mg/dL
Bile acids (fasting)	0-8	µmol/L
Thyroxine (T_4)	1.5-4	nmol/L*

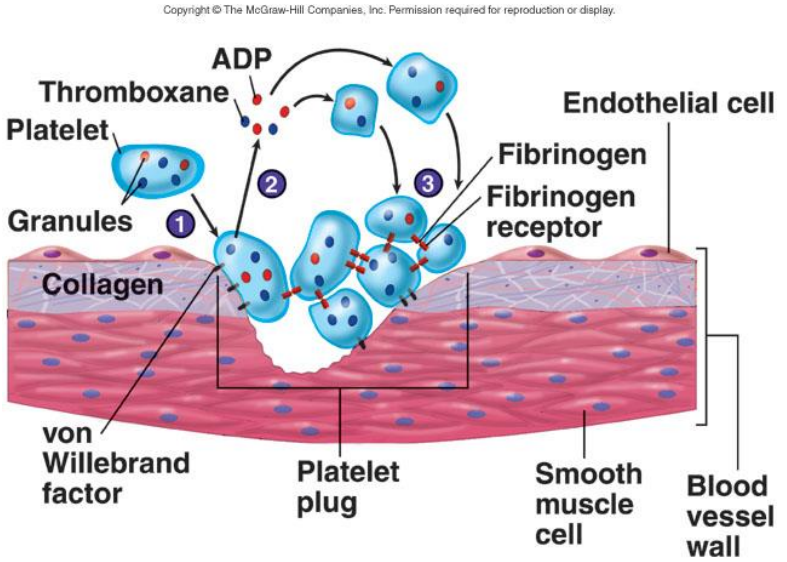
The Cellular Component of Blood

- The fraction of cells in blood is called the **hematocrit**.
  - Because centrifugation results in a packing of the blood cells in the bottom of the tube, the hematocrit is sometimes called the **packed cell volume (PCV).**
  - Most of the cell component looks red because most of the blood cells are **erythrocytes** (red blood cells, RBCs).
- The **leukocytes** (white blood cells, WBCs) are slightly lighter in weight than the RBCs; in a centrifuge tube the WBCs gather in a white buffy coat on top of the RBCs.
  - Leukocytes are critical in immune and allergic responses of the body. The subtypes of leukocytes include **neutrophils, lymphocytes, monocytes, eosinophils, and basophils**. A laboratory analysis of the total number and relative distribution of the various WBC subtypes (**differential WBC count**) provides important clues in the diagnosis of disease



The Cellular Component of Blood

- **Platelets**, or **thrombocytes**, which are cellular fragments from their precursor cells, the megakaryocytes.
  - The megakaryocytes reside in the bone marrow, and they shed bits of their cytoplasm, bounded by cell membrane, into the bloodstream.
  - Platelets participate in hemostasis (the control of blood loss from injured or severed blood vessels). In this process a clumping together of platelets (**platelet aggregation**) begins to create a physical barrier across openings in blood vessels.
  - The platelets also release the substance serotonin, which causes these blood vessels to constrict.
  - Several laboratory tests are used to assess the status of an animal's coagulation system. Two common tests involve determination of the **prothrombin time (PT)** and the **partial thromboplastin time (PTT)**.



The Cellular Component of Blood

- If blood is allowed to coagulate and then is centrifuged, the fibrin and other plasma clotting factors settle to the bottom along with the RBCs, WBCs, and platelets.
- The liquid portion remaining above (essentially plasma without fibrinogen and other clotting factors) is called serum. Most of the common clinical blood chemistry analyses are performed on serum.
- If blood is treated with an anticoagulant and then allowed simply to sit in a tube (without centrifugation), the erythrocytes slowly begin to settle.
  - For reasons that are not completely understood, the rate of their settling tends to be increased to above normal in certain disease states and decreased to below normal in others. Therefore the erythrocyte sedimentation rate (ESR) is a clinically useful diagnostic measurement.

The Cellular Component of Blood

- The ability of blood to carry oxygen is determined by the amount of **hemoglobin** in the blood and by the chemical characteristics of that Hb
  - Several disease states (**hemoglobinopathies**) result in the synthesis of chemically abnormal Hb, with a diminished capacity to bind O_2.
  - Also, several common toxins, including carbon monoxide (CO) and nitrates, cause life-threatening alterations in the ability of Hb to bind O_2.

Test	Normal Range	Units
Hematocrit	35-57	%
Blood Cell Counts		
Red blood cells	5000-7900	$\times 10^3/\mu L$
White blood cells	5-14	$\times 10^3/\mu L$
Platelets	210-620	$\times 10^3/\mu L$
Hemoglobin Measures		
Blood hemoglobin	12-19	g/dL
MCH (mean corpuscular hemoglobin)	21-26	pg
MCHC (mean corpuscular hemoglobin concentration)	32-36	g/dL

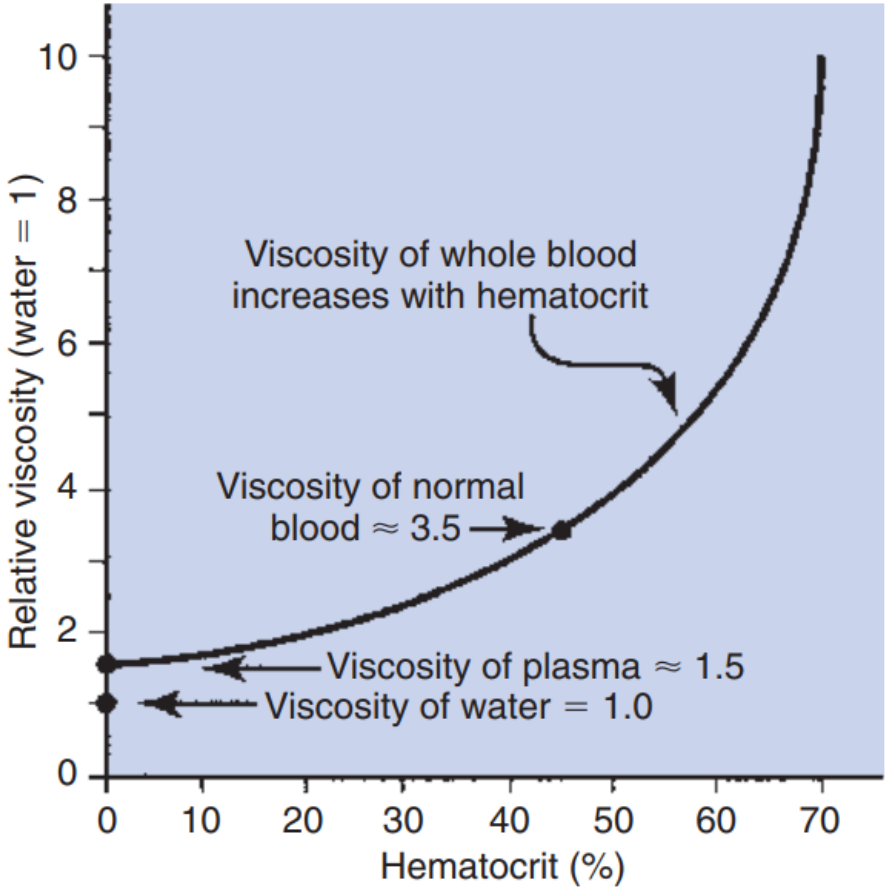
The Cellular Component of Blood

- Because hemoglobin is localized inside RBCs, it is possible to derive several clinically useful relationships among the blood Hb content, RBC count, Hb content of each RBC, and hematocrit.
- mean corpuscular hemoglobin (MCH): average amount of Hb in 1 µL of RBC
  - MCH = Hb/RBC (pg)
- mean corpuscular hemoglobin concentration (MCHC): determine how much hemoglobin is contained in each deciliter of packed RBCs.
  - MCHC = [hemoglobin]/hematocrit (g/dL)
- Low value of MCH or MCHC points to a deficit in hemoglobin synthesis, RBC synthesis, addition of excess plasma fluid and loss of RBCs.

Test	Normal Range	Units
Hematocrit	35-57	%
Blood Cell Counts		
Red blood cells	5000-7900	$\times 10^3/\mu L$
White blood cells	5-14	$\times 10^3/\mu L$
Platelets	210-620	$\times 10^3/\mu L$
Hemoglobin Measures		
Blood hemoglobin	12-19	g/dL
MCH (mean corpuscular hemoglobin)	21-26	pg
MCHC (mean corpuscular hemoglobin concentration)	32-36	g/dL

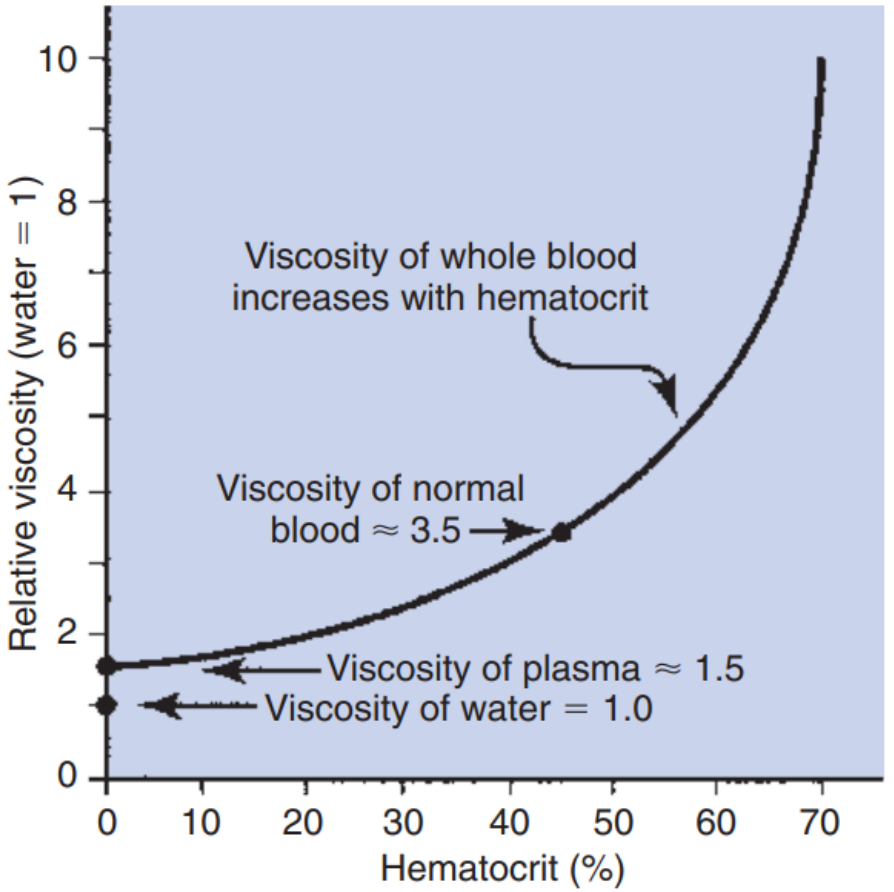
The Cellular Component of Blood

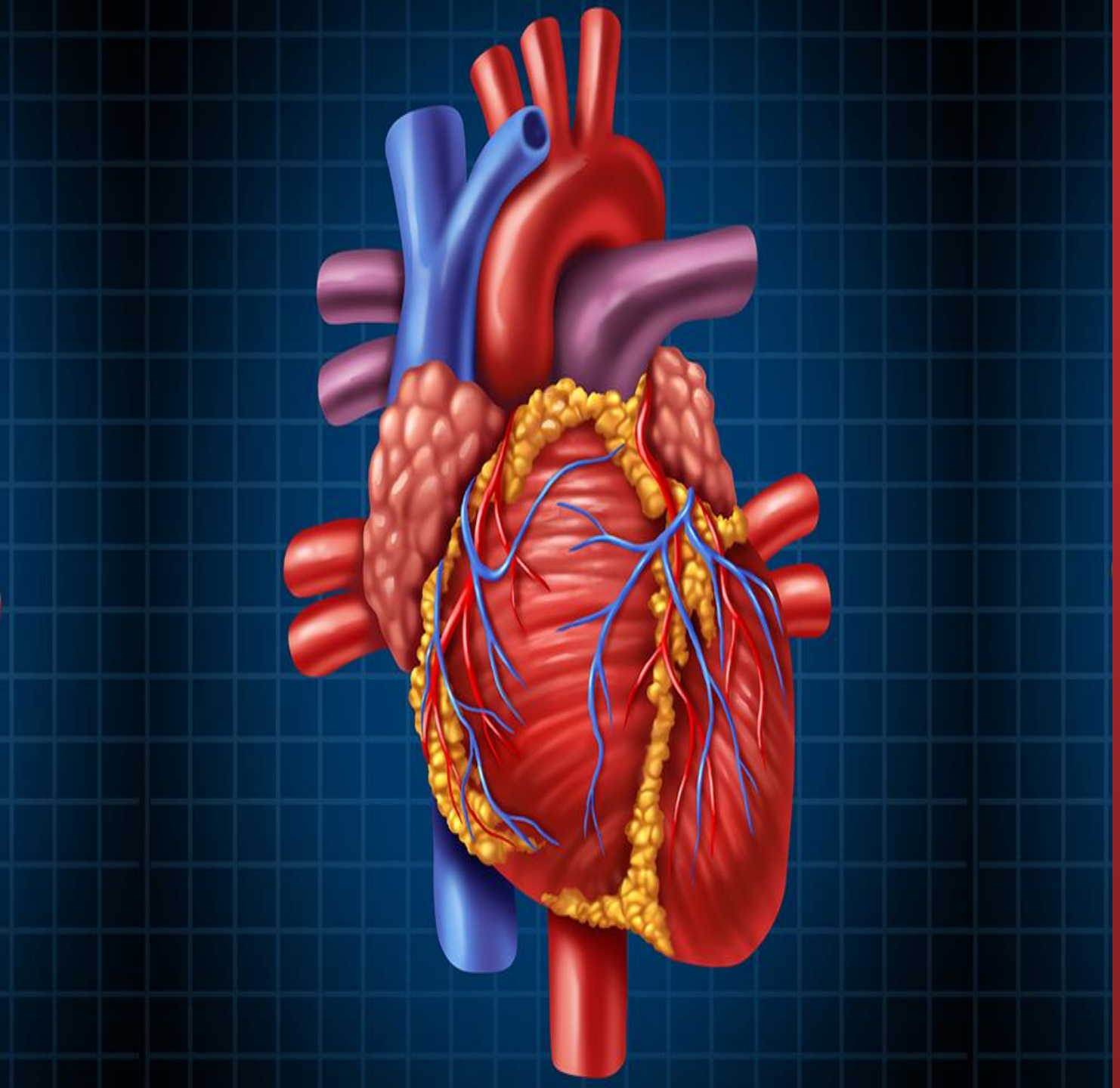
- Deviations from a normal hematocrit (Hct) can have important consequences in terms of the ability of blood to carry oxygen.
  - Hematocrit also affects the viscosity of blood, **Viscosity** is a measure of resistance to flow
  - Plasma, by itself, is about 1.5 times more viscous than water because of the presence of plasma protein molecules (albumin, globulin, fibrinogen).
  - Blood with an Hct of 40% has twice the viscosity of plasma.
  - For Hct exceeding 50%, viscosity increases rapidly
- An abnormally high hematocrit is called **polycythemia**
  - the increased viscosity makes it difficult for the heart to pump the blood.



The Cellular Component of Blood

- When the hematocrit is too low, is called **anemia**. It refers to a condition which there are abnormally few RBCs in each dL or a condition in which there is an abnormally low hemoglobin concentration in each RBC (i.e., MCH and/or MCHC is low)
  - Each deciliter of blood of an anemic patient carries less than the normal 20 mL of O_2. Therefore, **cardiac output** must be **increased** above normal to deliver the normal amount of O_2 to the tissues each minute.
  - The necessity to increase cardiac output also imposes an increased workload on the heart and can lead to the **failure** of a diseased heart



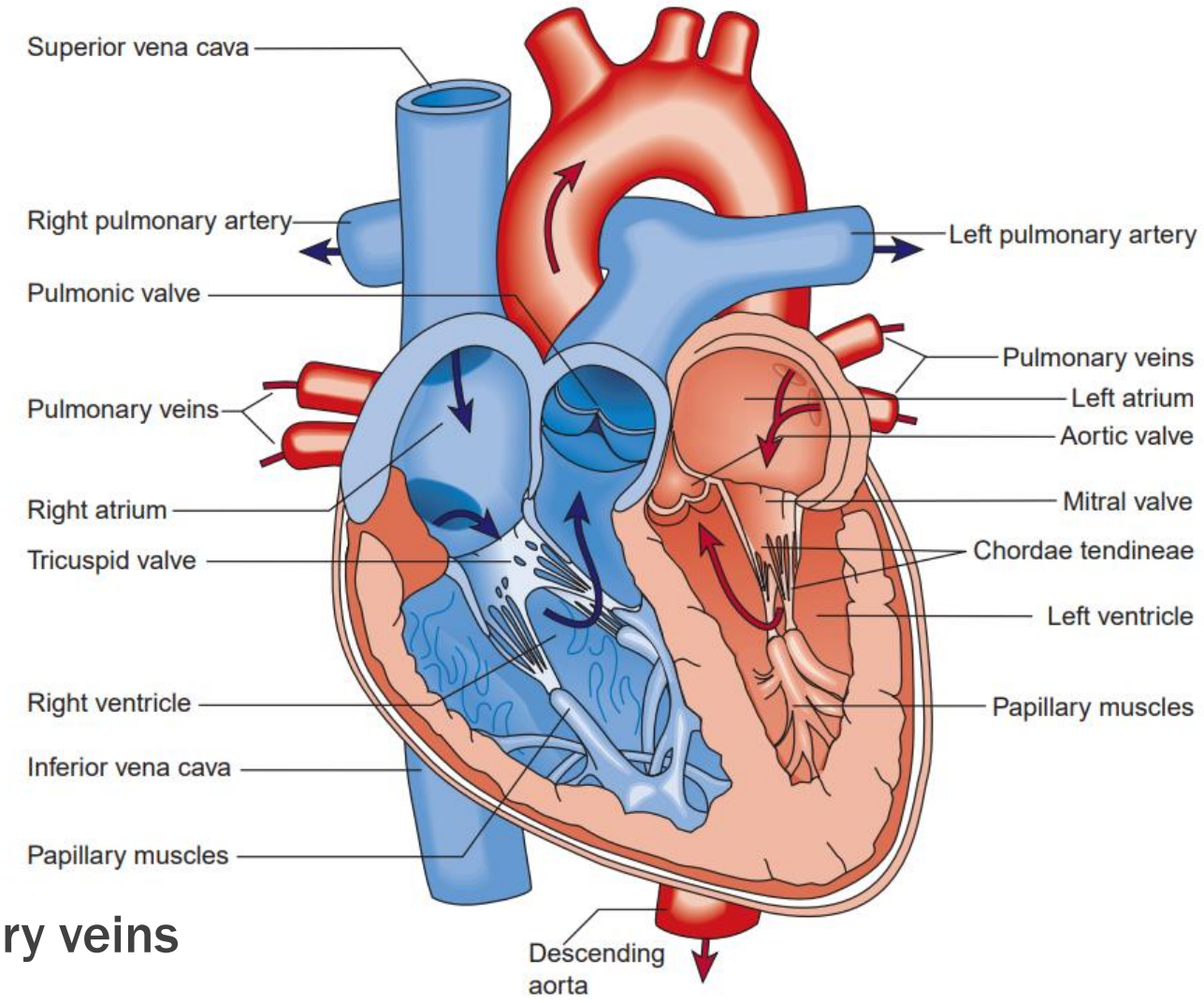


2

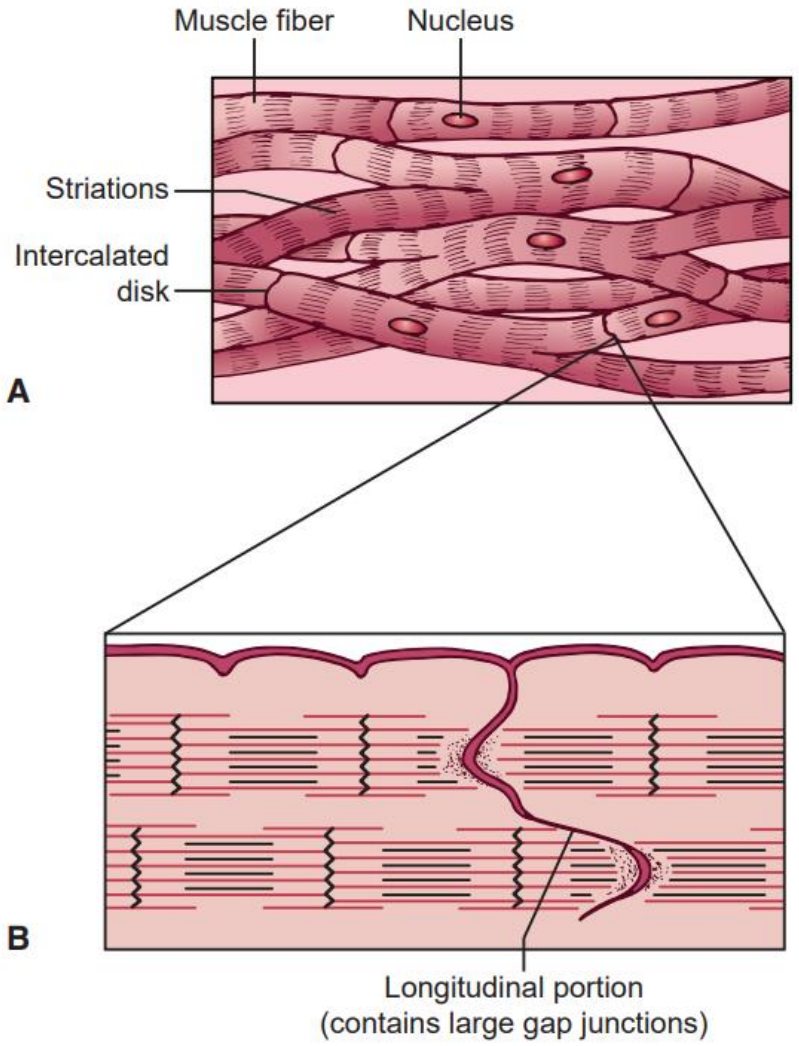
The Heart as a Pump

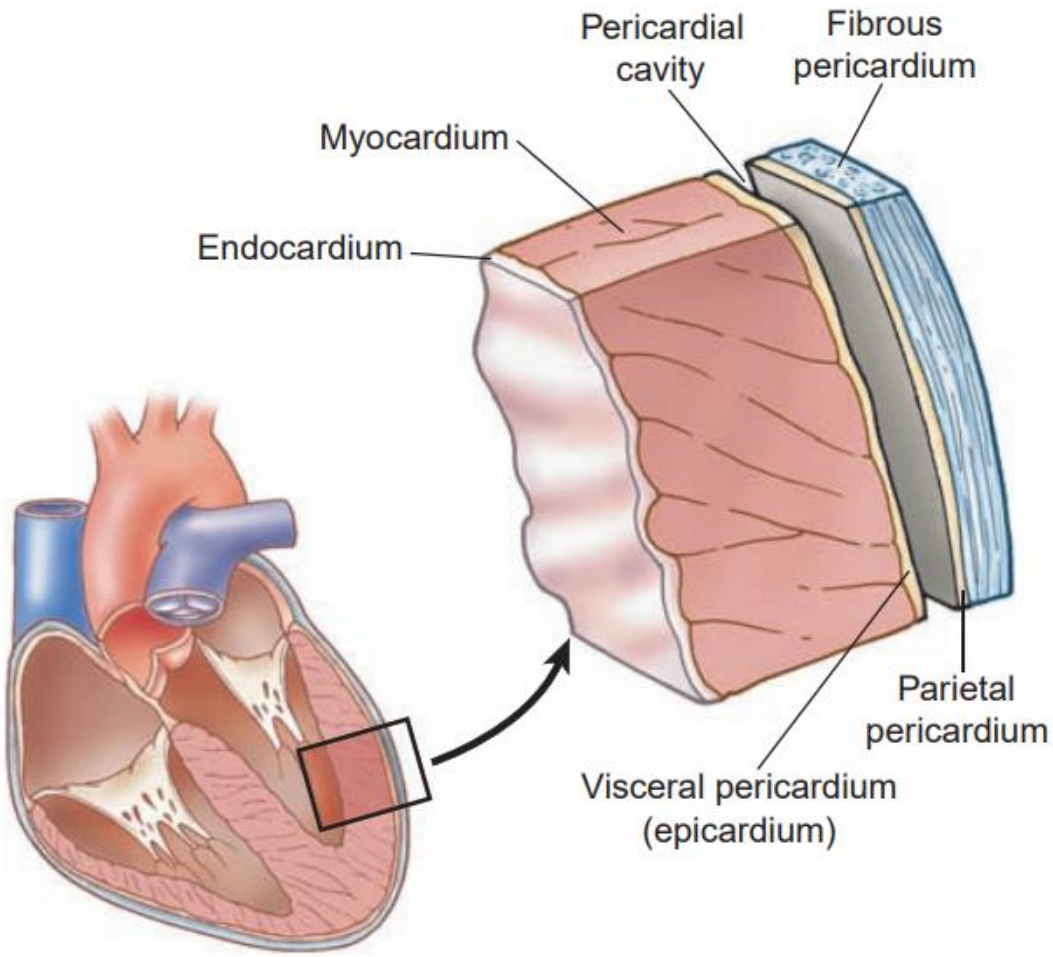
Functional Anatomy of the Heart

- **Four chambers**
  - Two atria
  - Two ventricles
- **Four valves**
  - Two atrio-ventricular (AV)
  - Two semilunar
- **Two systems**
  - Pulmonary circulation
  - Systemic circulation
- **Main vessels**
  - Aorta, Pulmonary artery
  - Cranial and Caudal vena cava, Pulmonary veins

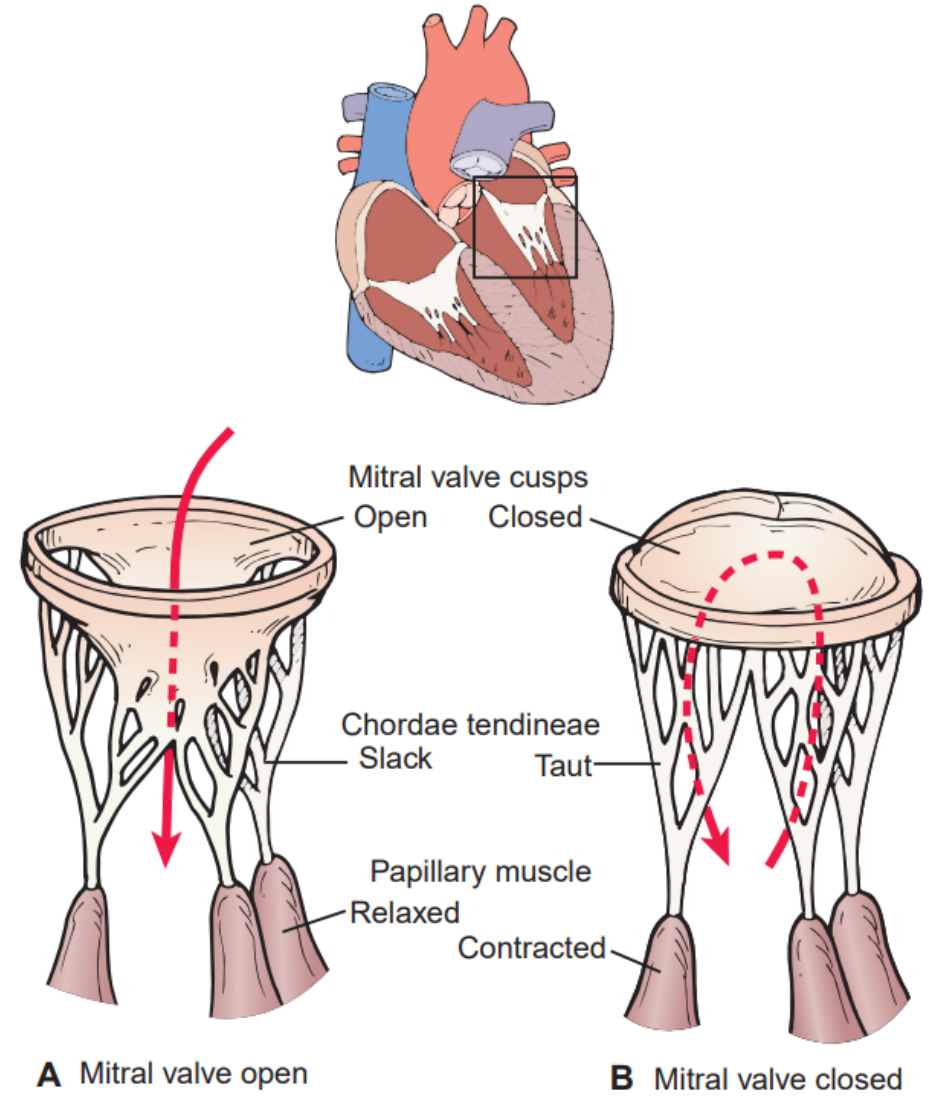


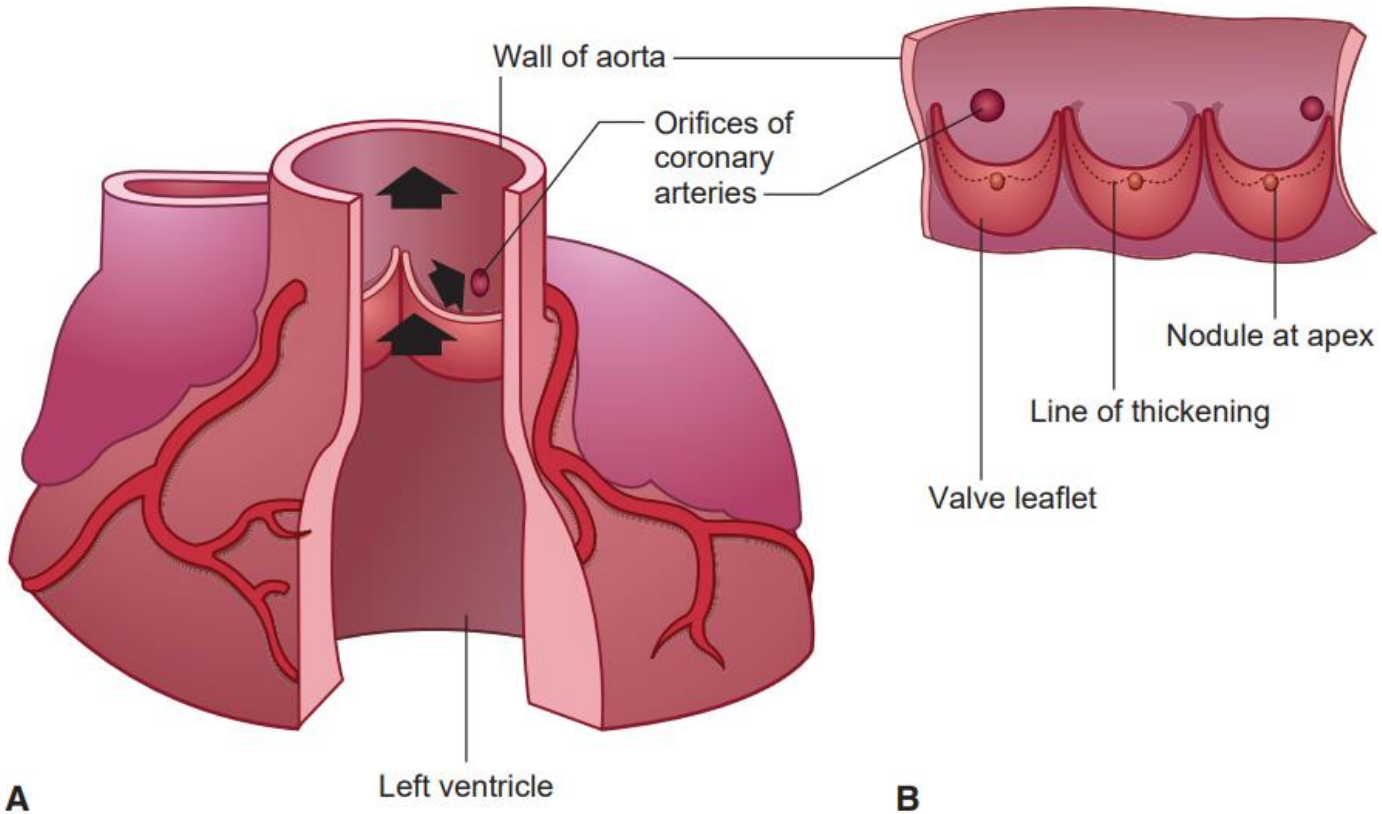
Functional Anatomy of the Heart





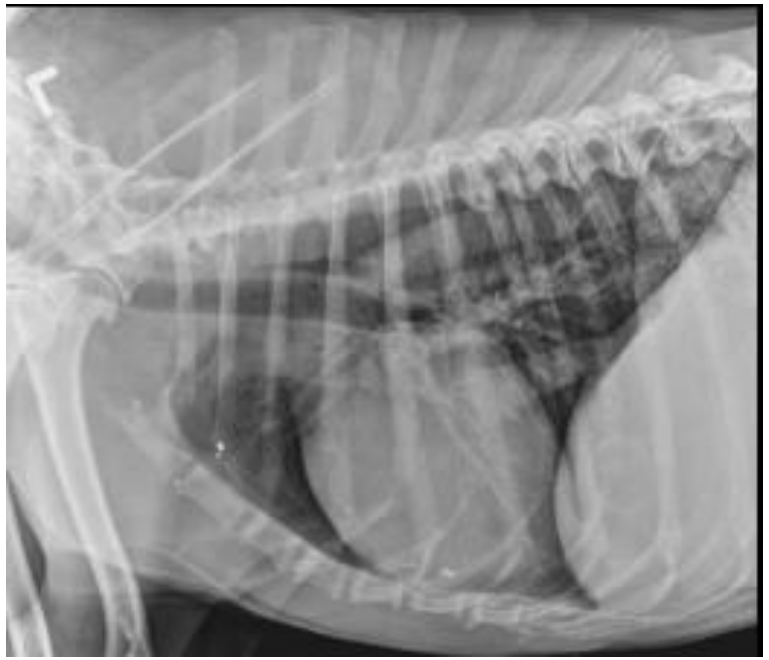
Functional Anatomy of the Heart

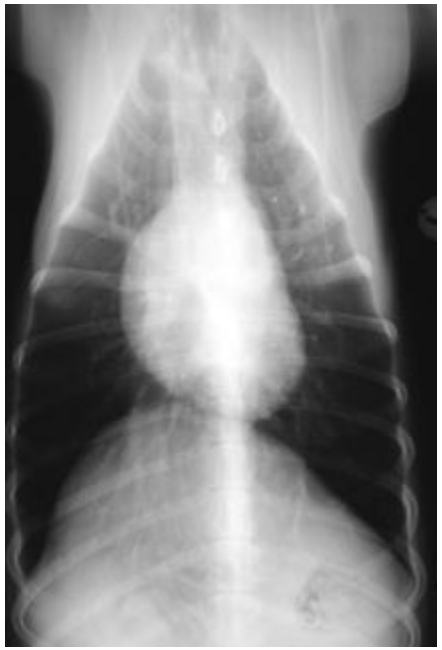


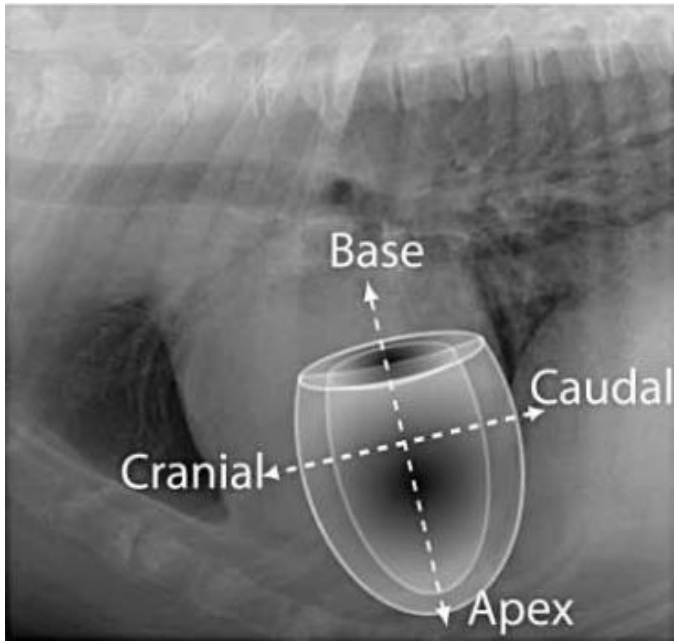


Functional Anatomy of the Heart

- Heart image in radiology

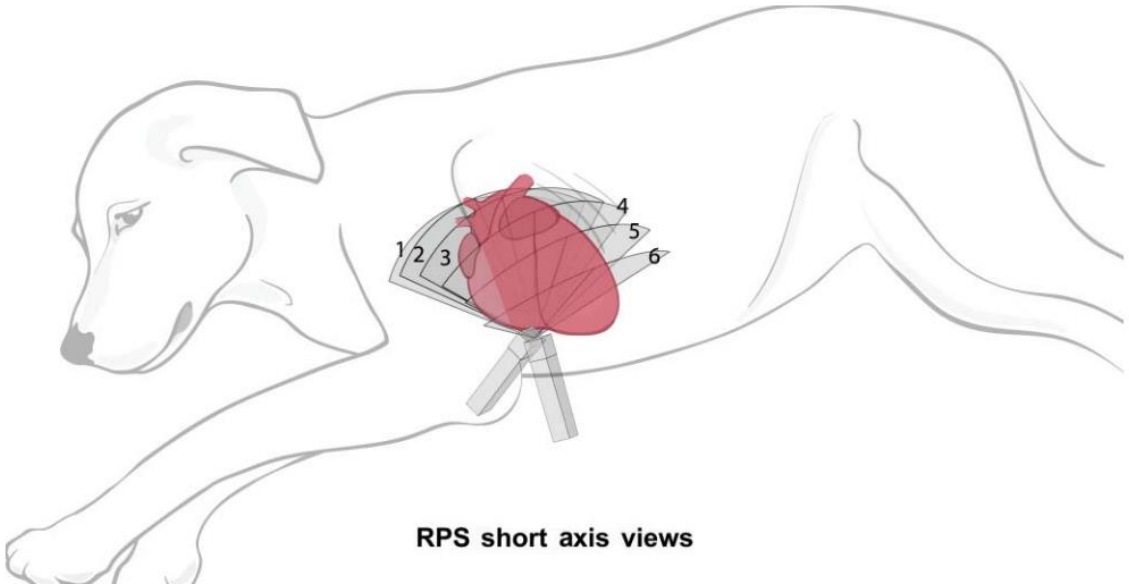




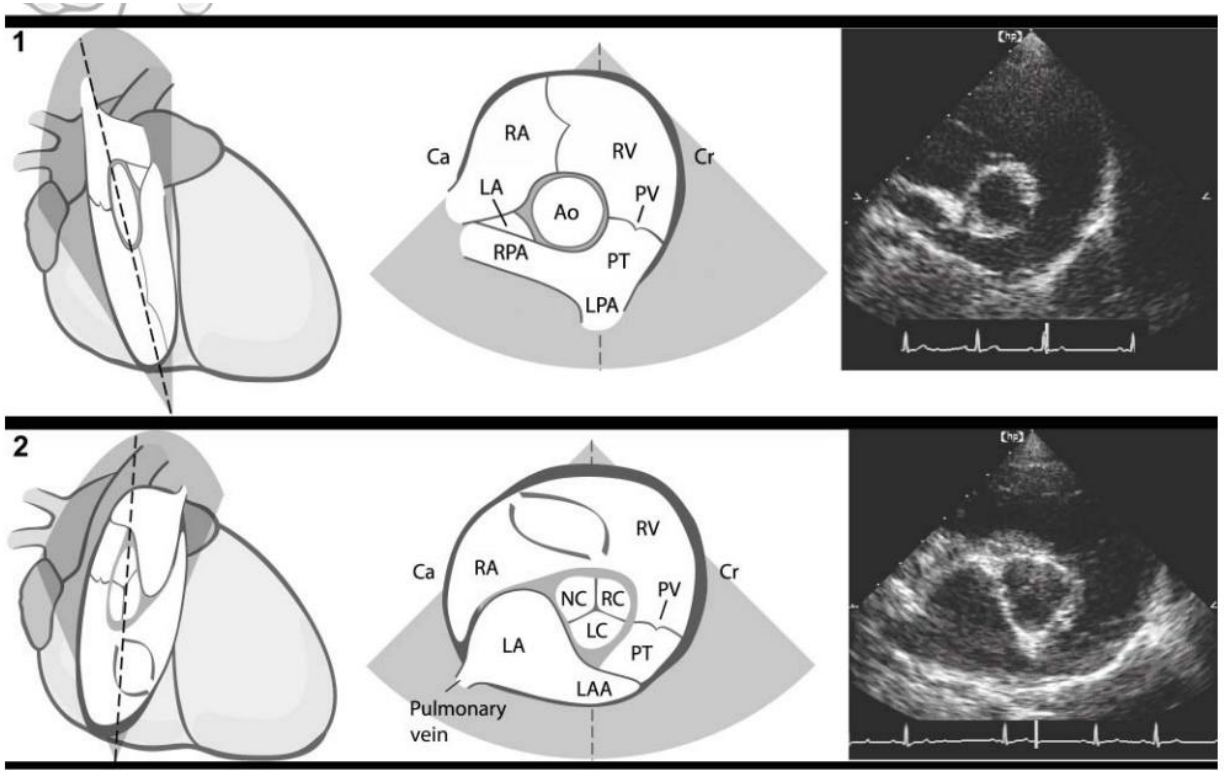


Functional Anatomy of the Heart

- Heart image in echocardiography

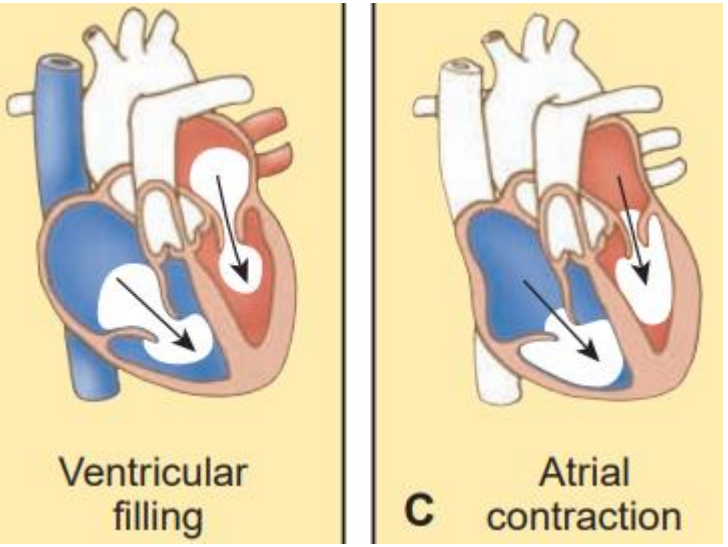


RPS short axis views



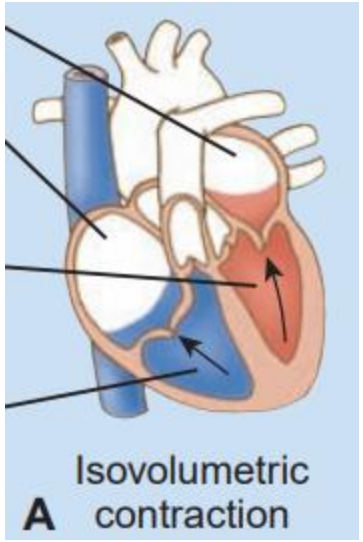
Cardiac Cycle

- **Systole** (period of contraction) + **Diastole** (period of relaxation) = cardiac cycle
- Phases of the cardiac cycle



1. Ventricular filling

- Both atria and ventricles in diastole
- Blood is filling both atria and ventricles due to low pressure conditions
- Atrial Systole: at the end of this phase, atria contract and empty the remaining blood to the ventricles



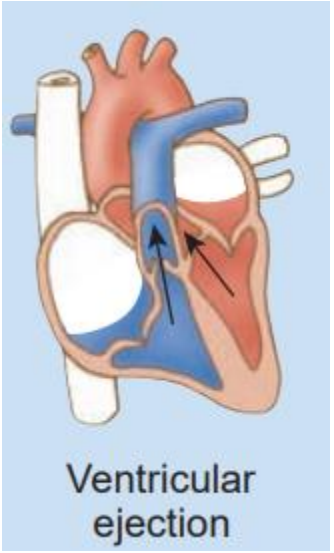
2. Isovolumetric Ventricular Contraction

- Increased pressure in the ventricles causes the AV valves to close
- Creates the first heart sound (lub)
- Atria go back to diastole
- No blood flow as semilunar valves are closed as well

Cardiac Cycle

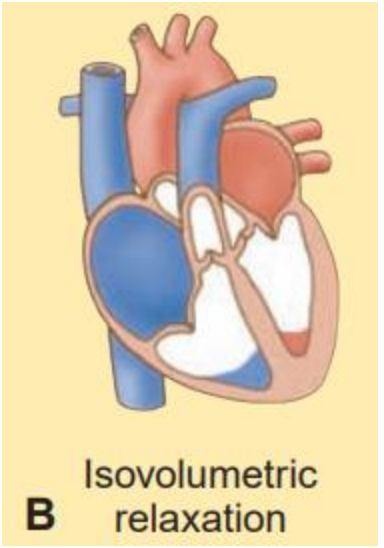
3. Ventricular Ejection

- Intraventricular pressure overcomes aortic pressure
- Semilunar valves open
- Blood is ejected

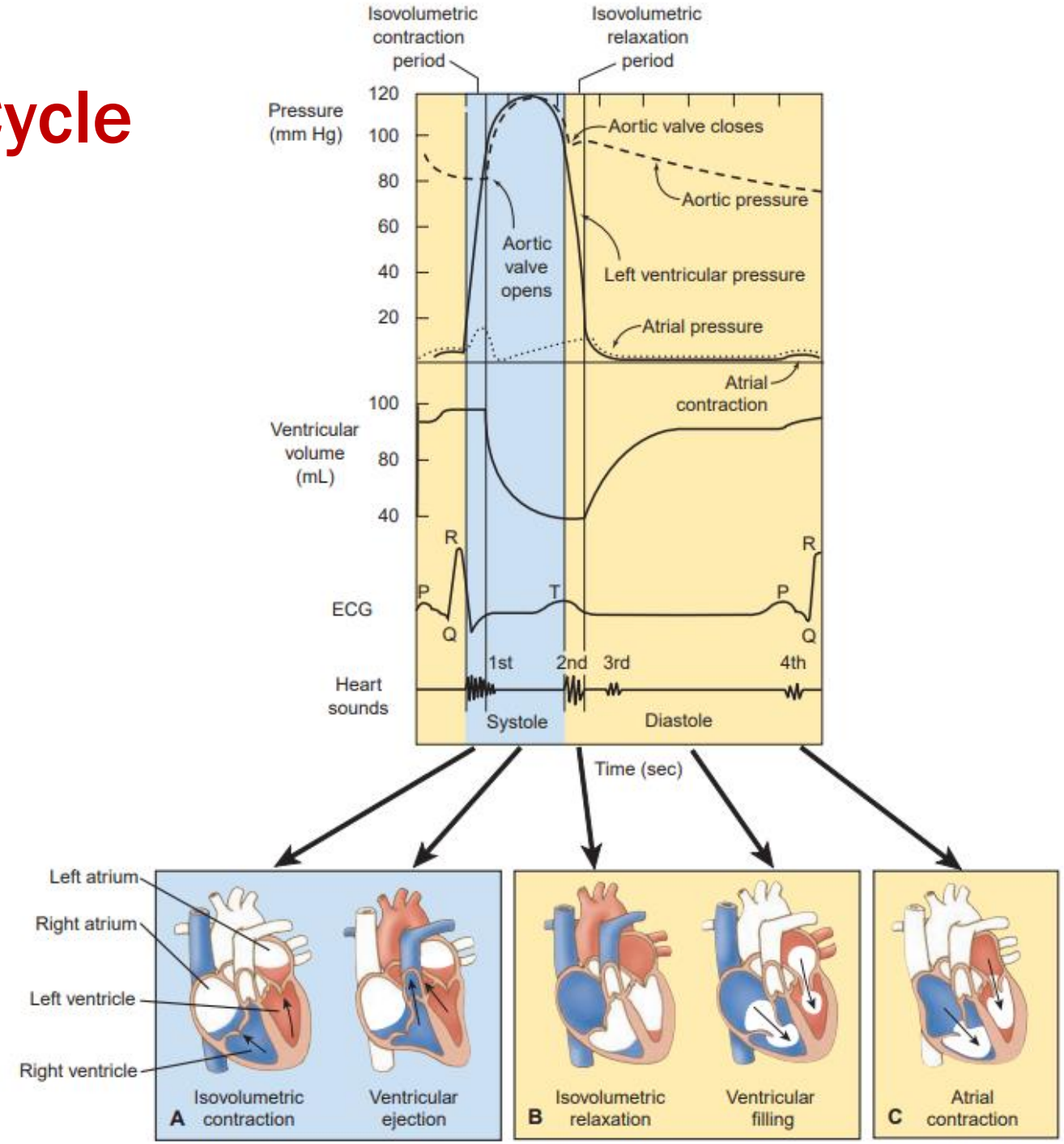


4. Isovolumetric Ventricular Relaxation

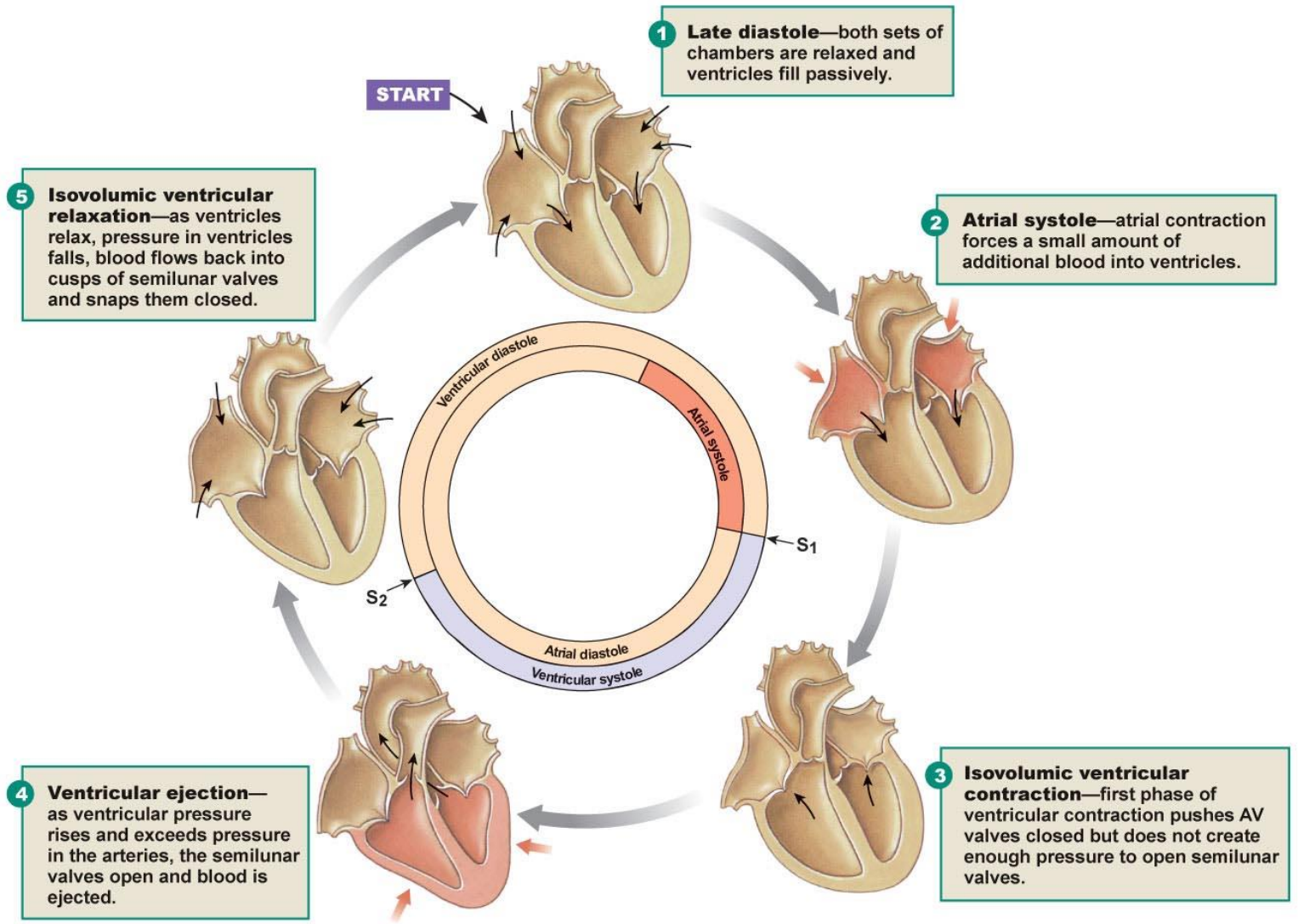
- Intraventricular pressure drops below aortic pressure
- Semilunar valves close = second heart sound (dup)
- Pressure still hasn't dropped enough to open AV valves so volume remains same (isovolumetric)



Cardiac Cycle

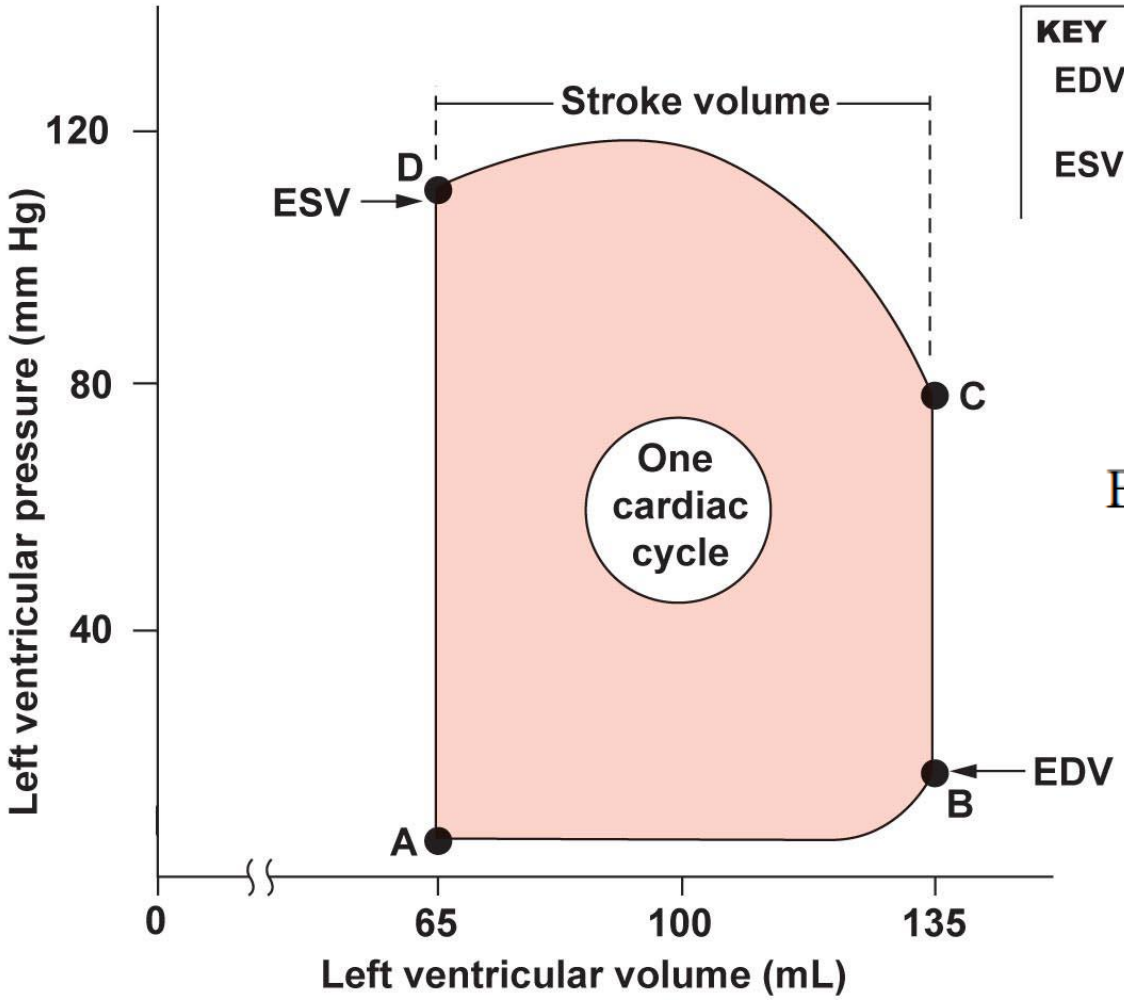


Cardiac Cycle



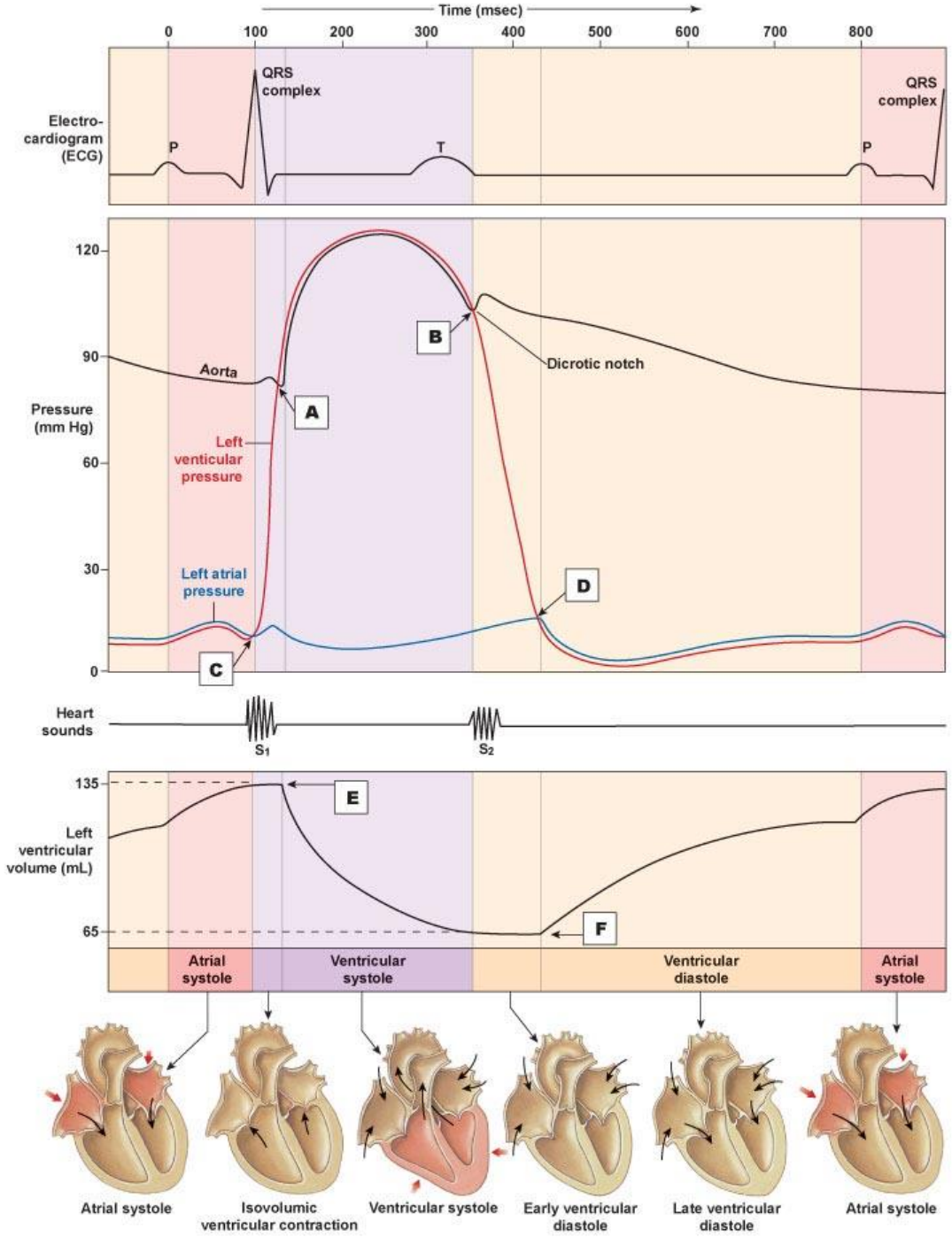
Cardiac Cycle

- Blood volume and pressure



$$\text{Ejection fraction} = \frac{\text{Stroke volume}}{\text{End-diastolic volume}}$$

Cardiac Cycle



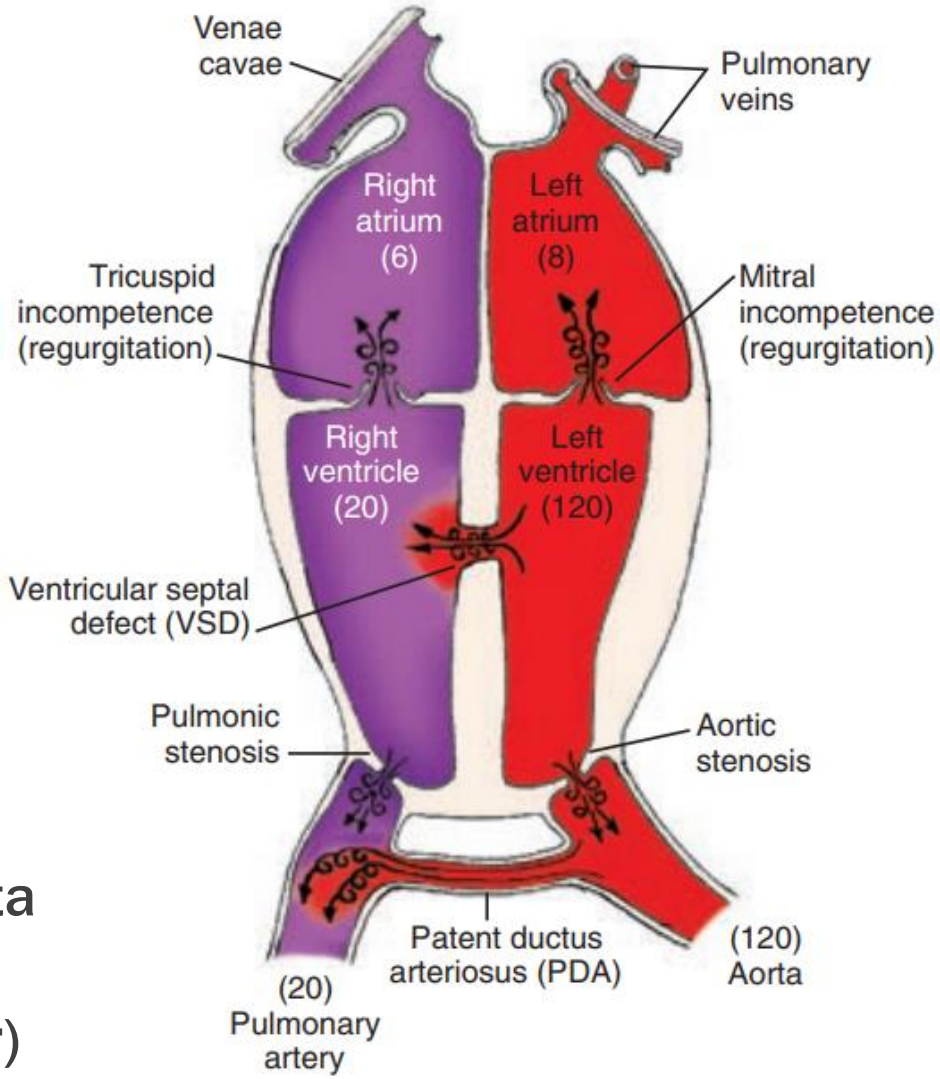
Abnormal Heart Sounds

- **Cardiac murmurs** are abnormal heart sounds, and they often indicate the presence of cardiac abnormalities.
  - Some murmurs are exaggerations of normal heart sounds; others are additional ("extra") heart sounds.
- Murmurs are caused by **turbulent flow** through cardiac defects which make audible sound.
  - **Systolic murmurs** occur during ventricular systole
  - **Diastolic murmurs** occur during ventricular diastole
  - **Continuous murmurs** occur throughout both systole and diastole

Site of Defect	Nature of Defect	
	Incompetence or Insufficiency (Allows Regurgitation)	Stenosis (Narrow Valve Opening, Creates Restriction)
Atrioventricular valves	Systolic murmur	Diastolic murmur
Aortic or pulmonic valves	Diastolic murmur	Systolic murmur

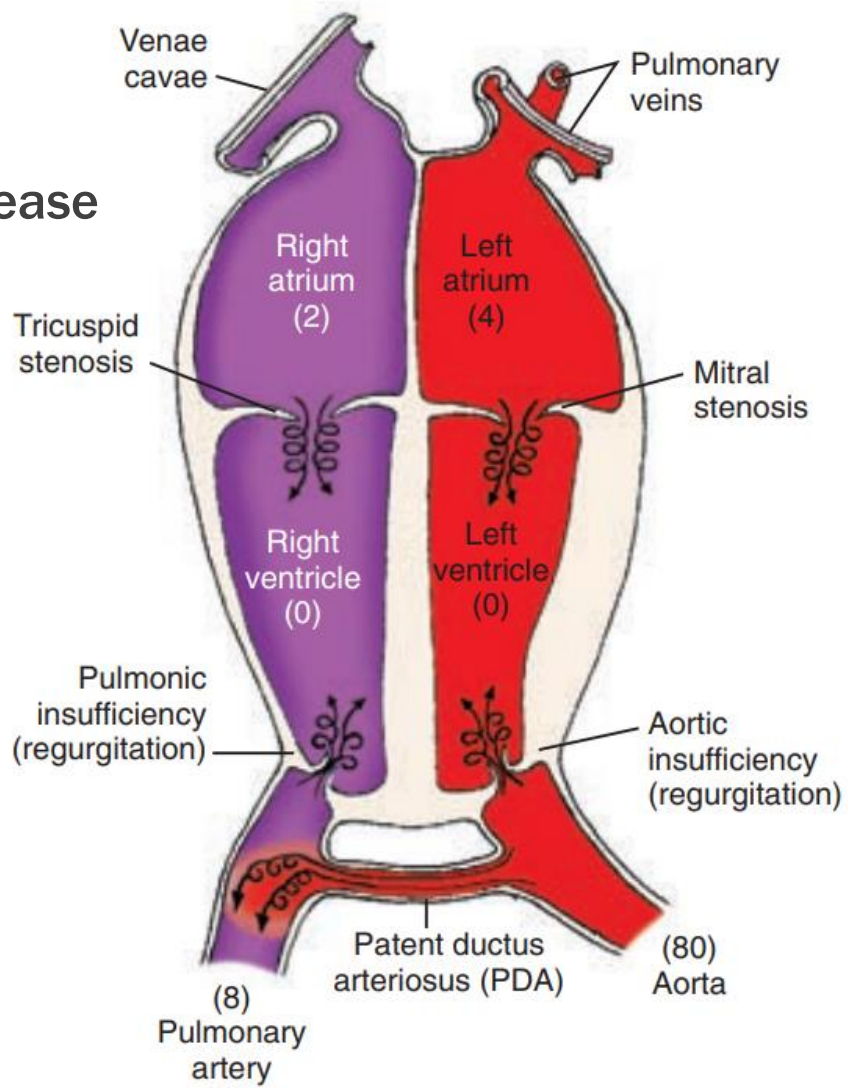
Systolic murmurs

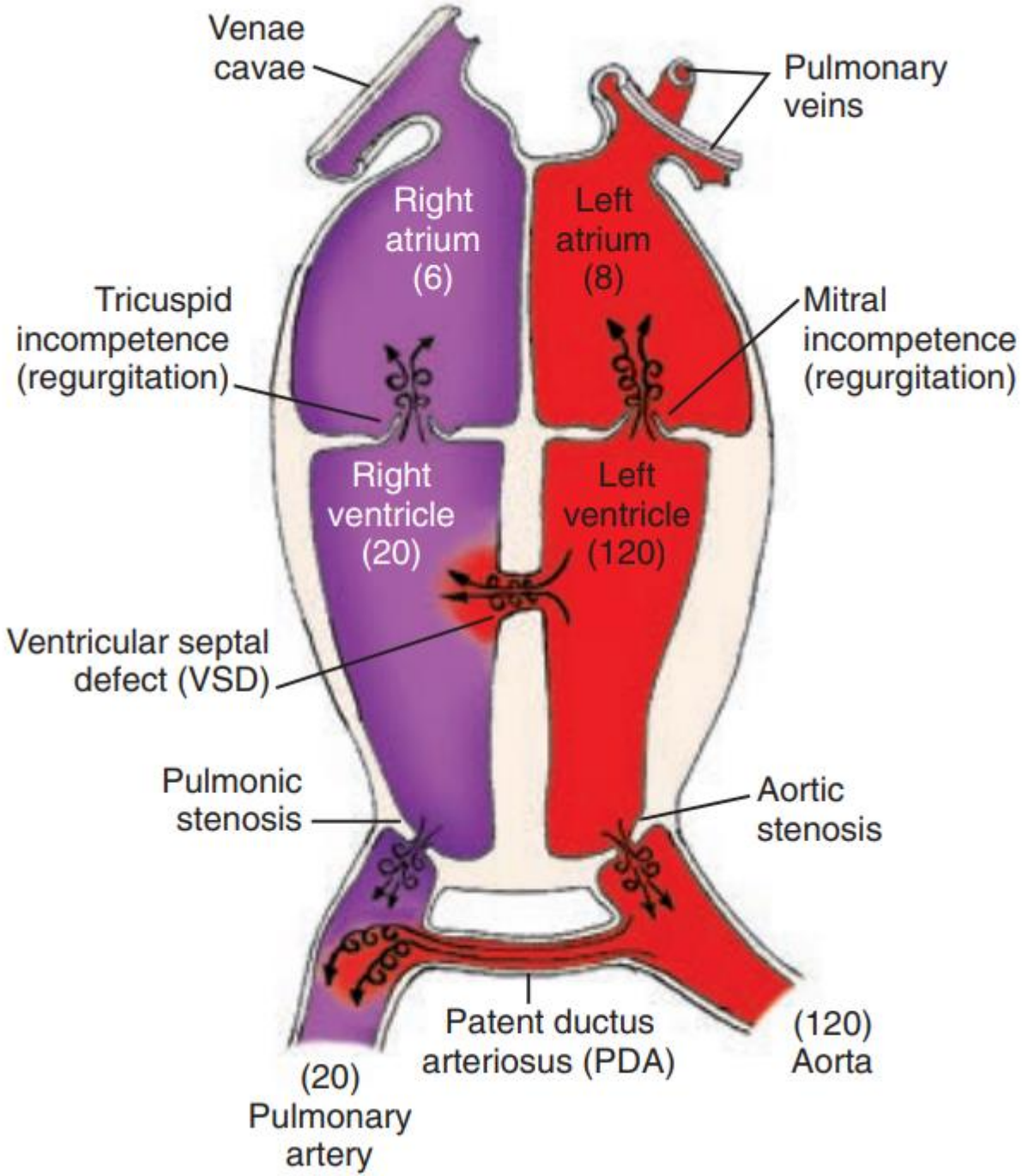
- **Mitral and Tricuspid incompetence (regurgitation)**
  - valves fail to close completely
  - MR is present in about 8% of dogs over 5 years of age
- **Ventricular septal defect (VSD)**
  - Blood flows through a VSD from the left ventricle to the right ventricle during ventricular systole
- **Aortic and Pulmonic stenosis**
  - valves fail to open widely enough
  - are common congenital defects in dogs
- **Patent ductus arteriosus (PDA)**
  - is persistence after birth of the opening between the aorta and the pulmonary artery
  - is heard in both systole and diastole (continuous murmur)

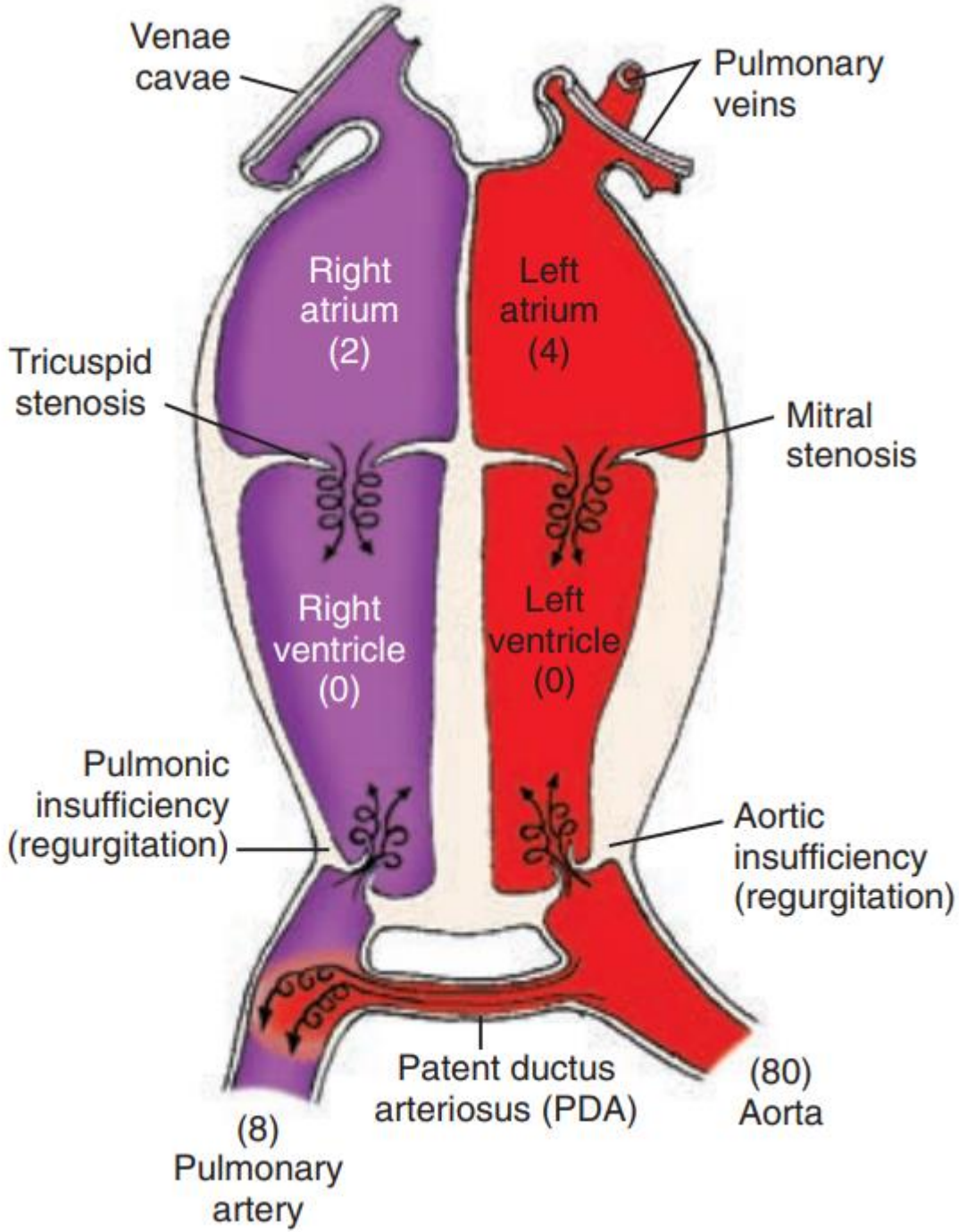


Diastolic murmurs

- **Mitral stenosis**
  - the mitral valve fails to open widely
  - is a common murmur among humans who have developed calcification of the mitral valve as a result of rheumatic heart disease
- **Tricuspid stenosis**
  - the valve fails to open widely
  - is uncommon, at least as a congenital defect
  - heavy infestation of heartworms in the right side of the heart can create a stenosis at the tricuspid valve
- **Aortic insufficiency (regurgitation)**
  - valve does not close tightly
  - is common in horses but not in dogs
- **Pulmonic insufficiency (regurgitation)**
  - the pulmonic valve fails to open widely
  - it is relatively rare

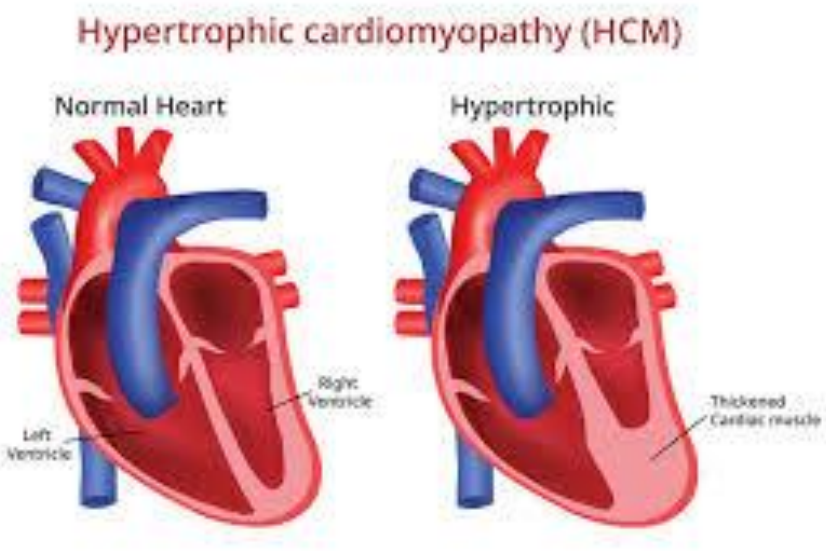



Venae cavae
Pulmonary veins
Right atrium (6)
Left atrium (8)
Tricuspid incompetence (regurgitation)
Mitral incompetence (regurgitation)
Right ventricle (20)
Left ventricle (120)
Ventricular septal defect (VSD)
Pulmonic stenosis
Aortic stenosis
Patent ductus arteriosus (PDA)
(120) Aorta
(20) Pulmonary artery


Venae cavae
Pulmonary veins
Right atrium (2)
Left atrium (4)
Tricuspid stenosis
Mitral stenosis
Right ventricle (0)
Left ventricle (0)
Pulmonic insufficiency (regurgitation)
Aortic insufficiency (regurgitation)
Patent ductus arteriosus (PDA)
(80) Aorta
(8) Pulmonary artery

Cardiac murmurs

- Cardiac murmurs themselves are not harmful but they typically can lead to one or more of these consequences:
  - (1) abnormally high or low blood flow to a region of the body,
  - (2) abnormally high or low blood pressure in a region of the body, and
  - (3) cardiac hypertrophy (enlargement of cardiac muscle)
- Cardiac defects often compromise the heart's ability to supply the systemic organs with the blood flow they need to support their metabolism. Compensating for such a pump failure frequently requires one or both ventricles to pump more blood than normal or to pump blood at a higher pressure than normal. These adaptations increase the workload of the heart.
- A persistent increase in cardiac workload leads, over several weeks, to cardiac hypertrophy.



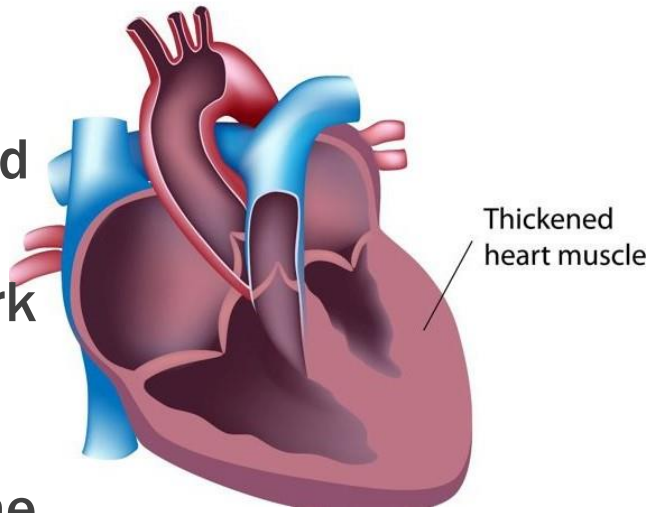
Cardiac Hypertrophy

- A ventricle that must pump more blood volume than normal will develop some hypertrophy, whereas a ventricle that must pump blood at a higher pressure than normal develops a huge hypertrophy.
  - This observation is the basis for the clinical aphorism, "Pressure work is harder for the heart [i.e., causes more hypertrophy] than volume work."
  - Both "weight work" (weight lifting) and "distance work" (running) lead to skeletal muscle hypertrophy. However, weight work causes substantially more hypertrophy than does distance work.
- The heart does work by pumping blood. The useful mechanical work (external work) done by any pump is equal to the pressure generated by the pump, multiplied by the volume of fluid that is pumped in one pump stroke, multiplied by the number of pump strokes.
  - . It is the total work of the cardiac muscle, not just the external work, that is the primary stimulus for hypertrophy.

Cardiac Hypertrophy

- Under normal resting conditions, about 85% of the metabolic energy consumed by the heart appears as heat, and only **15%** appears as **external work**.
- So "**thermodynamic efficiency**" of the heart is about 15%. However, the "**cardiac efficiency**" depends on the type of work being done by the ventricles.
  - The heart becomes **less efficient** when the external work is increased by **increasing the pressure**.
  - Conversely, the heart becomes **more efficient** when the external work is increased by an **increase in the volume** of blood pumped.
  - That's why the left ventricle develops much heavier and thicker muscle walls than the right ventricle (because the external work done by the left ventricle is approximately five times greater than the external work done by the right ventricle).

Hypertrophic cardiomyopathy



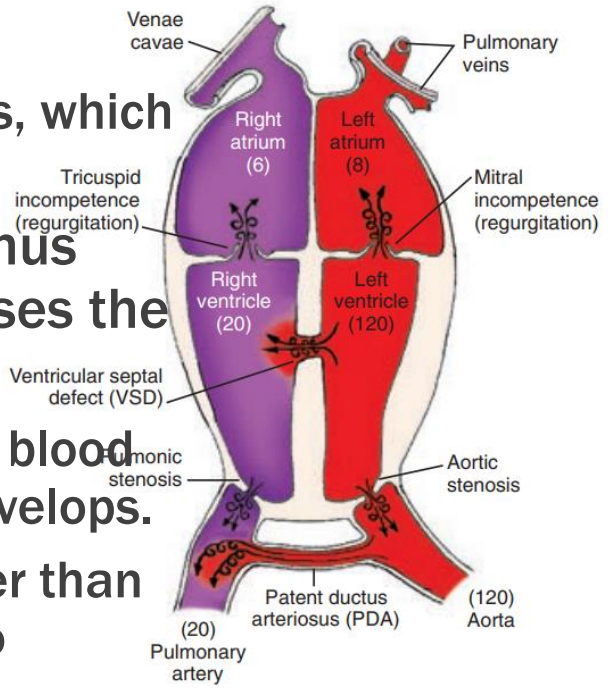
The Pathophysiological Consequences of Cardiac Defects

- **Mitral regurgitation:**
  - a normal volume of blood is ejected into the aorta, and an additional volume of blood is ejected backward (through the regurgitant valve) into the left atrium.
    - As a result, there is an increase in the volume work performed by the left ventricle. Therefore, mild to moderate **left ventricular hypertrophy** develops.
  - the left atrium becomes distended, and left atrial pressure increases, as does pulmonary venous pressure.
    - Elevated pressure in the pulmonary blood vessels forces water and electrolytes out of the bloodstream and into the pulmonary interstitial spaces, causing **pulmonary edema** which eventually leads to respiratory distress.

- **Aortic stenosis:**
  - To eject a normal volume of blood with each beat through a stenotic aortic valve, the left ventricle must develop an abnormally high systolic pressure. This increases the pressure work of the left ventricle, which leads to a marked **left ventricular hypertrophy**

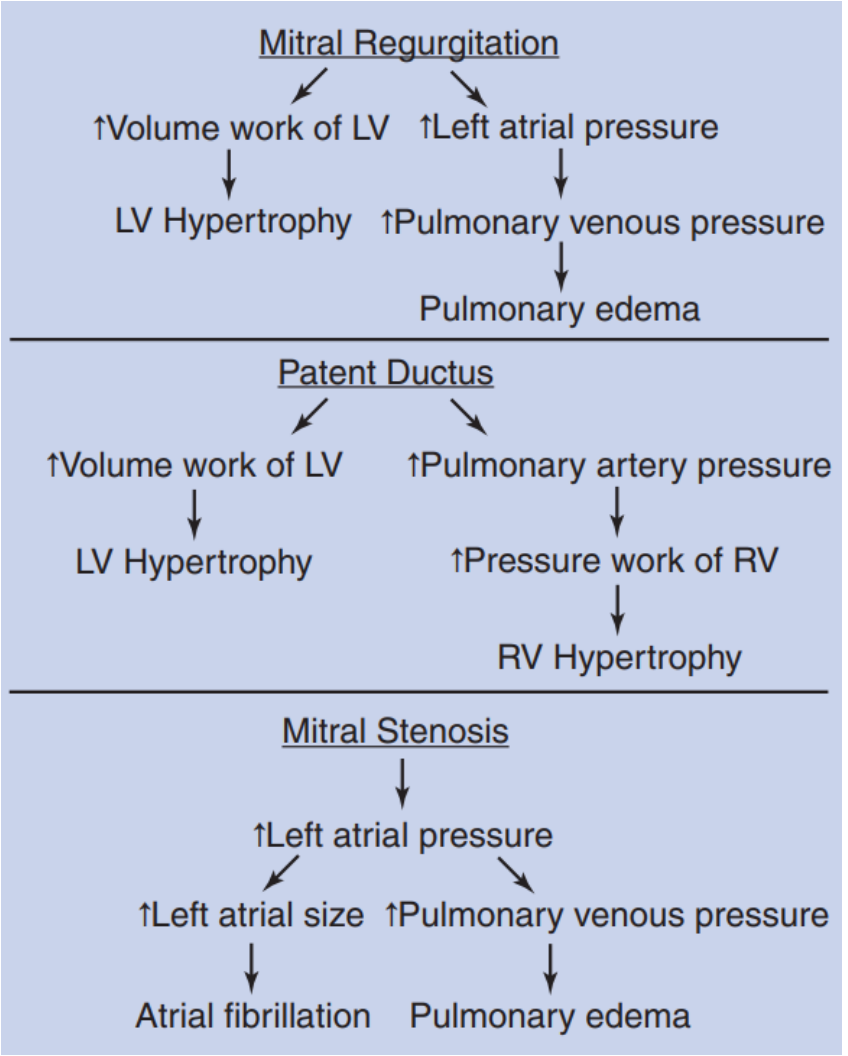
The Pathophysiological Consequences of Cardiac Defects

- **Patent ductus arteriosus (PDA):**
  - is a defect that typically results in **both left and right ventricular hypertrophy**
  - In a typical patient with a PDA, the left ventricle pumps **a near-normal volume** of blood per minute to the **systemic circulation** and pumps **two to three times** that volume of blood per minute through the **PDA**.
    - the volume work done by the left ventricle greatly exceeds normal amounts, which leads to left ventricular hypertrophy.
  - The blood flowing through the PDA enters the pulmonary artery, and thus **pulmonary arterial pressure exceeds normal levels**. This in turn increases the pressure work that must be done by the right ventricle.
    - the right ventricle must generate an elevated systolic pressure to eject this blood into the high-pressure pulmonary artery so **right ventricular hypertrophy** develops.
    - In a severe case, pulmonary blood flow can be more than four times greater than normal. The resulting increases in pulmonary vascular pressure can lead to **pulmonary edema**.



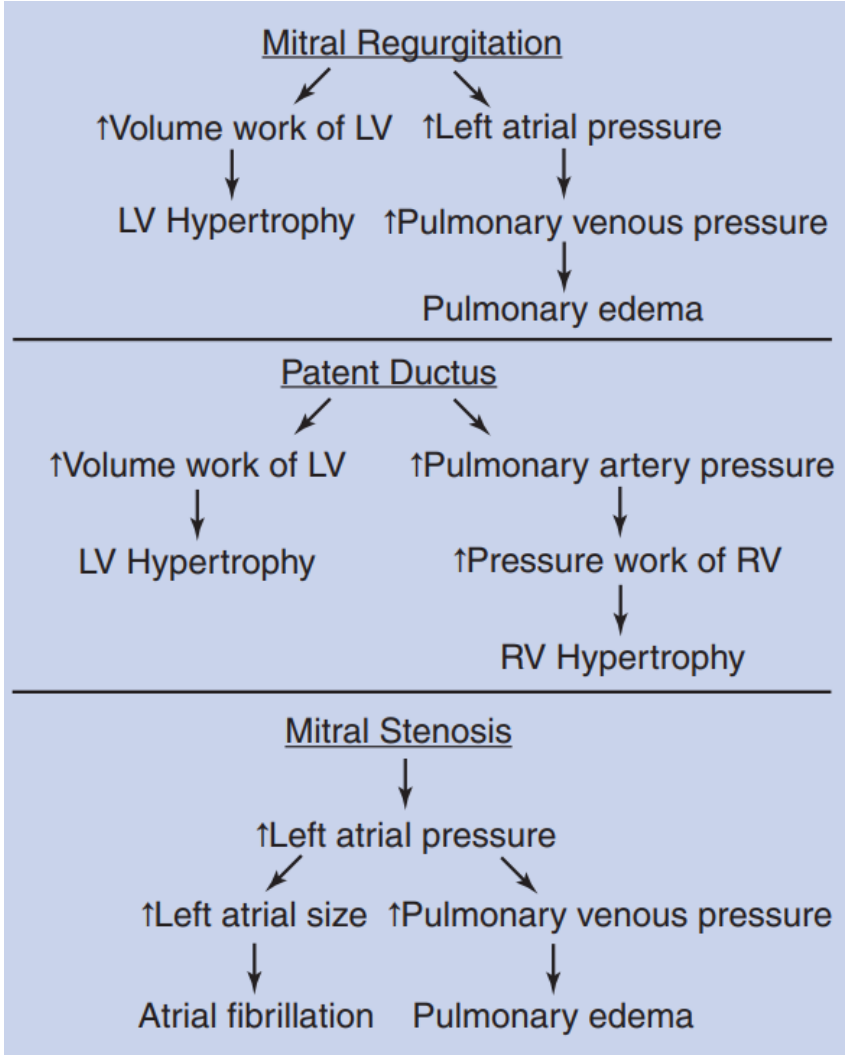
The Pathophysiological Consequences of Cardiac Defects

- **Ventricular Septal Defect:**
  - increased volume work of the left ventricle
    - moderate **left ventricular hypertrophy**
  - increased volume and pressure work of the right ventricle
    - pronounced **right ventricular hypertrophy**
  - increased blood flow through the lungs
    - possible **pulmonary edema**
  - probable exercise intolerance
- **Pulmonic stenosis:**
  - increased pressure work for the right ventricle
    - pronounced **right ventricular hypertrophy**



The Pathophysiological Consequences of Cardiac Defects

- **Mitral stenosis:**
  - The left atrial pressure must exceed normal levels to force a normal volume of blood through the stenotic mitral valve and into the left ventricle during each ventricular diastole.
    - The elevated left atrial pressure **distends the left atrium**
    - atrial action potentials tend to become discoordinated in a distended atrium, and **atrial fibrillation** is a common consequence
  - The increase in the left atrial pressure causes blood to back up and accumulate in the pulmonary blood vessels, so **pulmonary edema** is likely
- **Aortic regurgitation**
  - With each systole, the left ventricle must eject an abnormally large volume of blood into the aorta.
    - the volume work of the left ventricle is increased to above-normal levels, and left ventricular pressures may rise as well. Both these factors stimulate **left ventricular hypertrophy**.

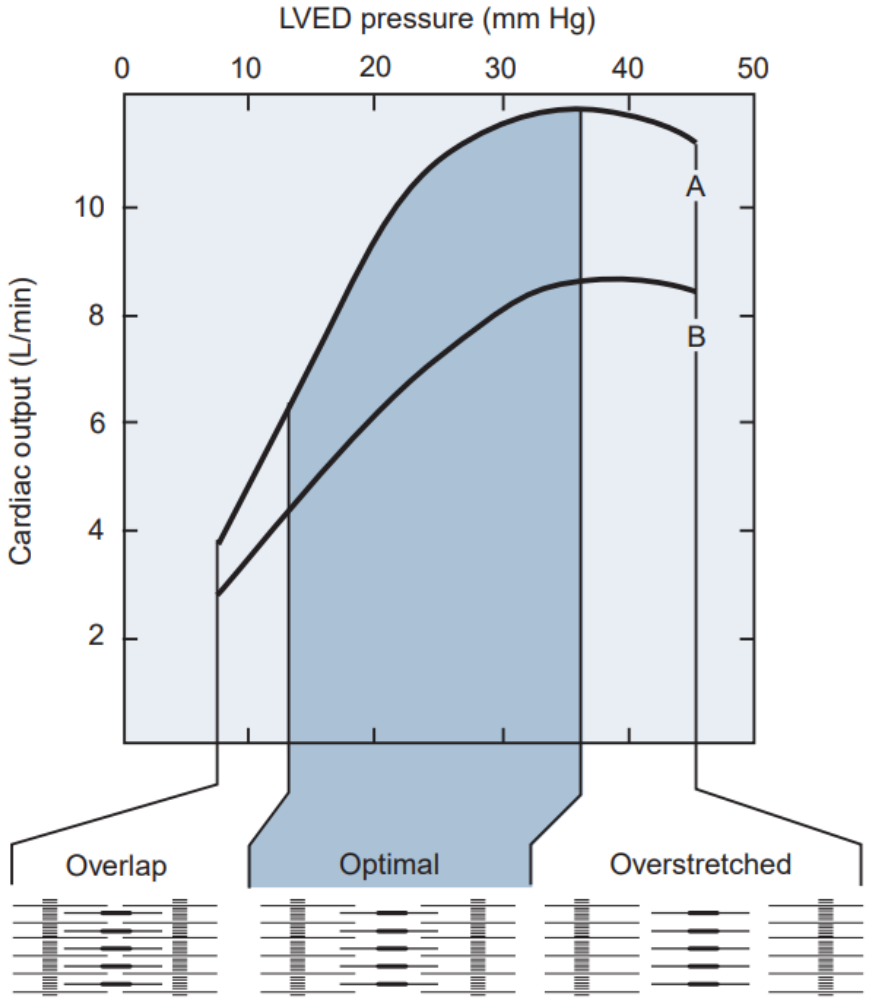


Regulation of Cardiac Performance

- The efficiency of the heart as a pump often is measured in terms of **cardiac output**
  - Definition: the amount of blood the heart pumps from each ventricle in each minute.
  - $CO = SV \times HR$
  - It increases with **physical activity** and decreases during **rest and sleep**
- The heart's ability to increase its output according to body needs mainly depends on four factors:
  - **Preload**, or ventricular filling
  - **Afterload**, or resistance to ejection of blood from the heart
  - **Cardiac contractility**
  - **Heart rate**

Regulation of Cardiac Performance

- **Preload:**
  - Preload represents the amount of blood that the heart must pump with each beat
  - It is usually considered the **end-diastolic pressure** when the ventricle has been filled
  - Preload is largely determined by the **venous return** to the heart and the **accompanying stretch** of the cardiac muscle fibers
  - The increased force of contraction that accompanies an increase in ventricular end-diastolic volume is referred to as the **Frank-Starling mechanism** or **Starling law** of the heart



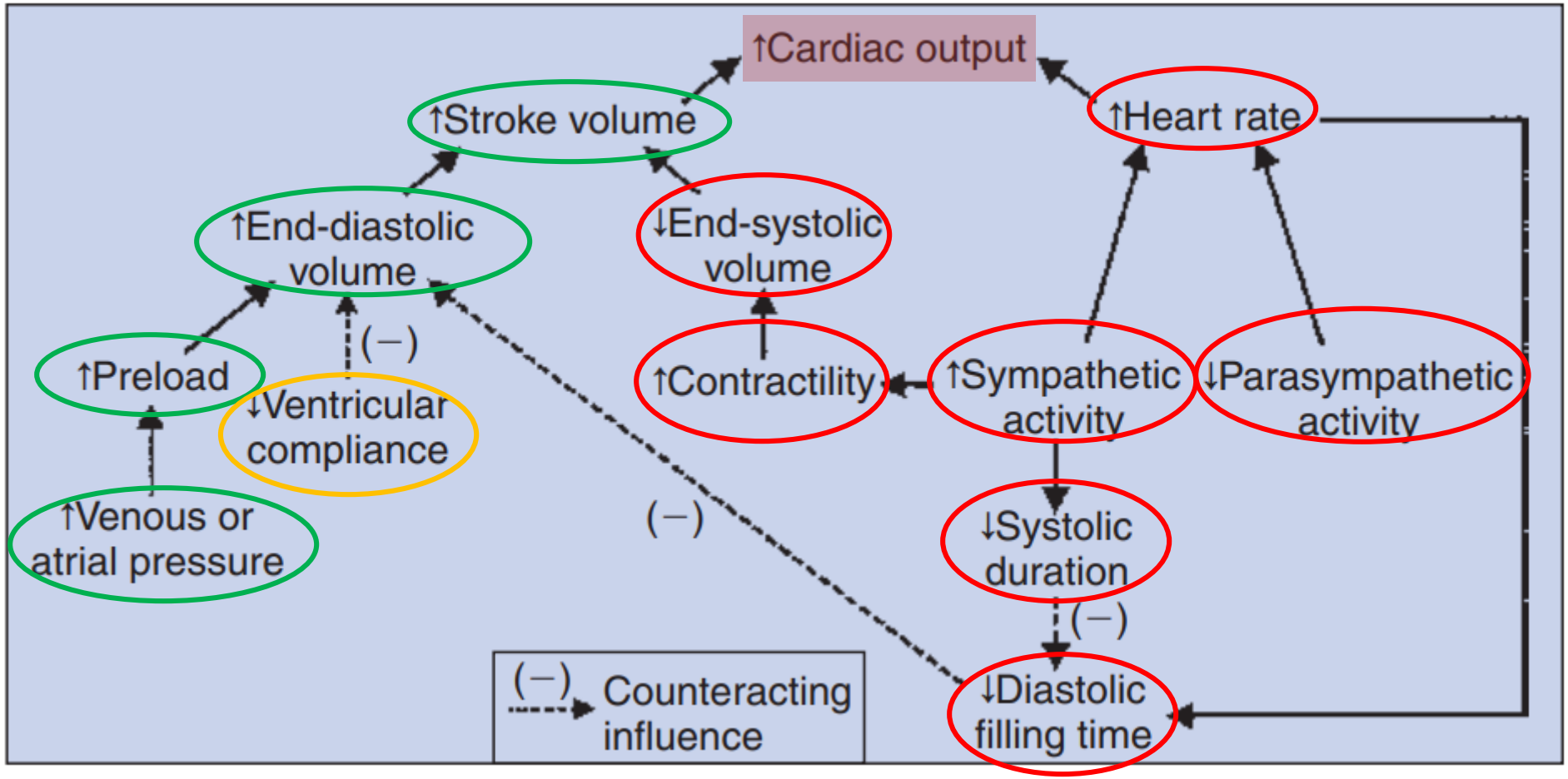
Regulation of Cardiac Performance

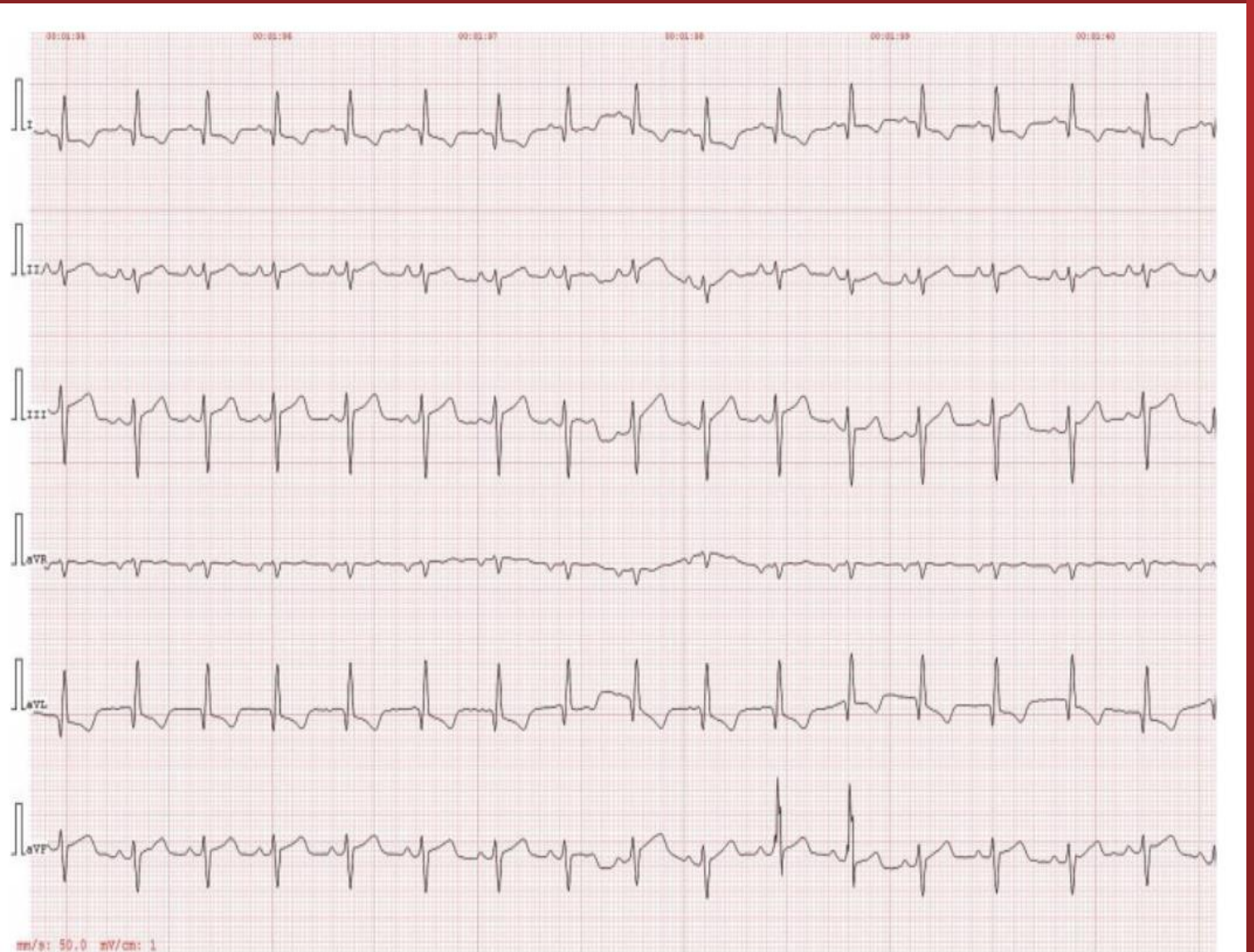
- **Afterload:**
  - The afterload is the pressure in which the muscle exerts its contractile force in order to move blood into the aorta.
  - It is called the afterload because it is the work presented to the heart after the contraction.
  - The systemic arterial blood pressure is the main source of afterload work on the left heart
  - the pulmonary arterial pressure is the main source of afterload work on the right heart.
- **Cardiac Contractility:**
  - Cardiac contractility refers to the ability of the heart to change its force of contraction without changing its resting (i.e., diastolic) length.
  - It is strongly influenced by the number of calcium ions that are available to participate in the contractile process.
  - An inotropic influence is one that modifies the contractile state of the myocardium independent of the Frank-Starling mechanism
    - Sympathetic stimulation produces a positive inotropic effect by increasing the calcium that is available for interaction between the actin and myosin filaments.
    - Hypoxia exerts a negative inotropic effect by interfering with the generation of adenosine triphosphate (ATP), which is needed for muscle contraction.

Regulation of Cardiac Performance

- **Heart Rate:**
  - The heart rate determines the frequency with which blood is ejected from the heart. Therefore, as the heart rate increases, cardiac output tends to increase.
  - As the heart rate increases, the time spent in diastole is reduced, and there is less time for the ventricles to fill.
  - As the heart rate increases, the time spent in systole remains approximately the same, whereas that spent in diastole decreases. This leads to a decrease in stroke volume and, at high heart rates, a decrease in cardiac output.
  - One of the dangers of ventricular tachycardia is a reduction in cardiac output because the heart does not have time to fill adequately.

Control of Cardiac Output





3

Electrocardiography

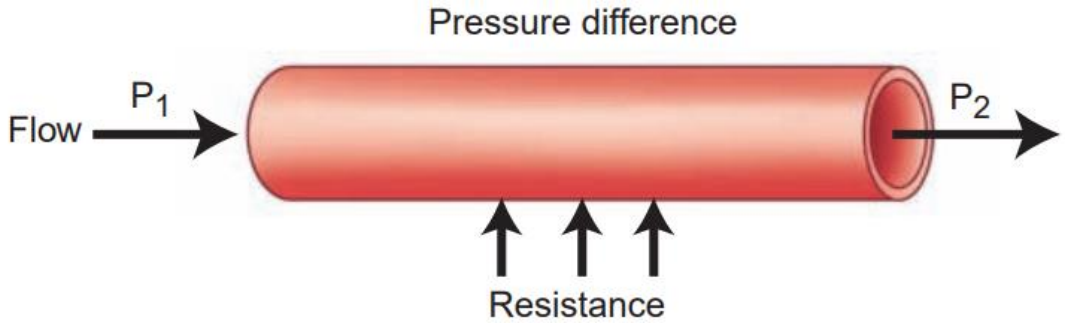
. . . presented in another file

4

Principles of Blood Flow

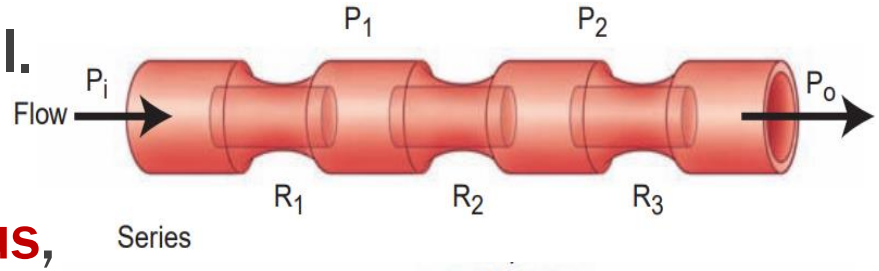
Hemodynamics

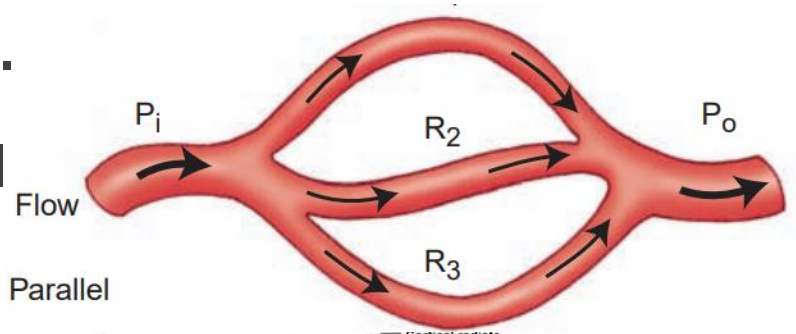
- The term **hemodynamics** refers to the principles that govern blood flow in the circulatory system.
- The most important factors governing the flow of blood in the cardiovascular system are **pressure**, **resistance**, and **flow**.
- **The flow** (**F**) of fluid through a tube, such as blood through a blood vessel, is directly related to a pressure difference (P1 – P2) between the two ends of the tube and inversely proportional to the resistance (R) that the fluid encounters as it moves through the tube ($F = \Delta P/R$).
- In the cardiovascular system, blood flow is represented by the **cardiac output**.

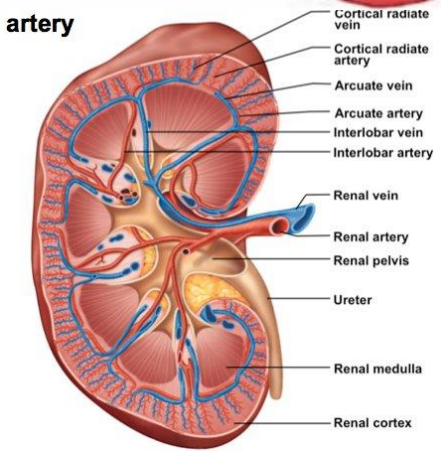


Hemodynamics

- **Resistance** is the opposition to flow caused by friction between the moving blood and the stationary vessel wall.
- **The resistance** to flow, in peripheral resistance units (PRUs), is determined by the **blood viscosity**, **vessel radius**, and whether the vessels are **aligned** in series or in parallel.
- In the peripheral circulation, the collective resistance of all the vessels in that part of the circulation is referred to as the **peripheral vascular resistance** (**PVR**).
- The **flow**, **pressure**, and **resistance** relationships determine the blood flow to a single organ
  - For example, Renal artery pressure, renal vein pressure, and renal vascular resistance determine blood flow to the kidney.







Hemodynamics

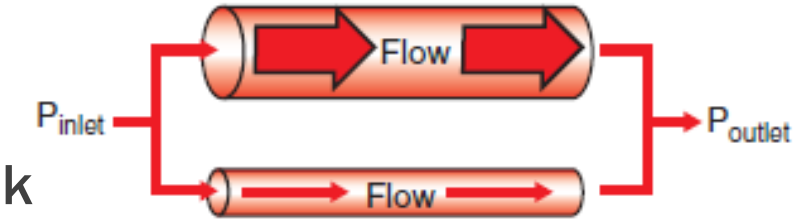
- **Resistance to Flow:**
  - Everyday experience tells us that it is easier to force fluid through a large tube than through a small tube (drinking milk shake through a large-diameter straw vs. a small-diameter straw)
  - The precise definition of resistance is:

$$\text{Resistance} = \frac{\Delta\text{Pressure}}{\text{Flow}}$$

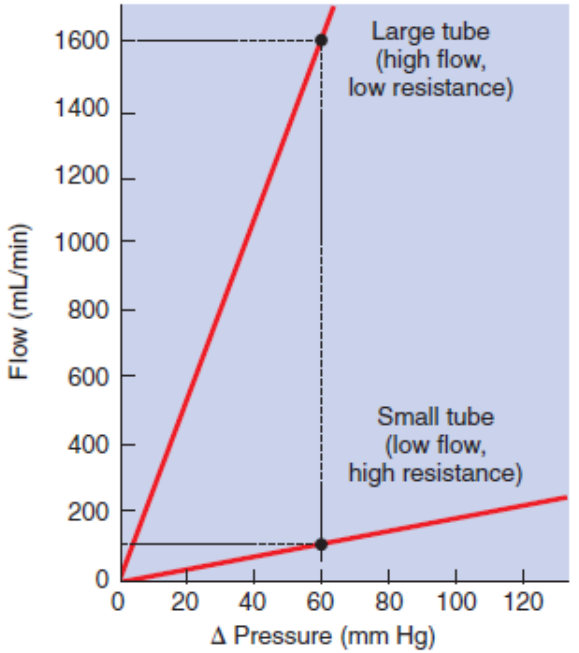
  - In the late 1800s the French physician J.L.M. Poiseuille demonstrated the dominant effect of radius on the resistance of a tube:

$$\text{Resistance of a tube} \cong \frac{8\eta l}{\pi r^4}$$

    - l is the length of the tube, r is the radius, η is the viscosity of the fluid flowing through the tube, and π has its usual meaning.

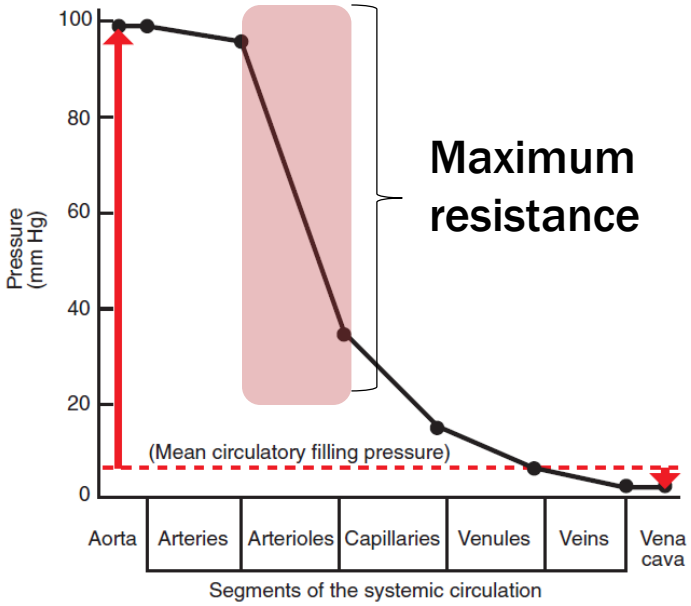


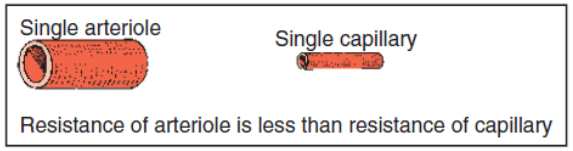
Δ Pressure = ($P_{inlet} - P_{outlet}$)

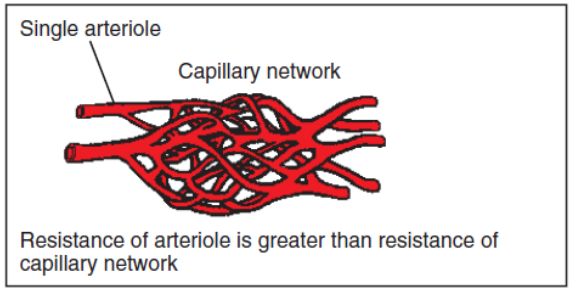


Hemodynamics

- **Resistance to Flow:**
  - The arterioles are the segment of the systemic circulation with the highest resistance to blood flow
  - It may seem paradoxical that the arterioles are the site of highest resistance when the capillaries are smaller vessels.
    - Each arteriole in the body distributes blood to many capillaries, and the net resistance of all those capillaries is less than the resistance of the single arteriole that delivers blood to them
  - Arterioles are the site of adjustable resistance.
    - Arterioles change their resistance, moment to moment, by changing their radius.
    - Vasoconstriction of arterioles increases and vasodilation reduces the resistance to blood flow

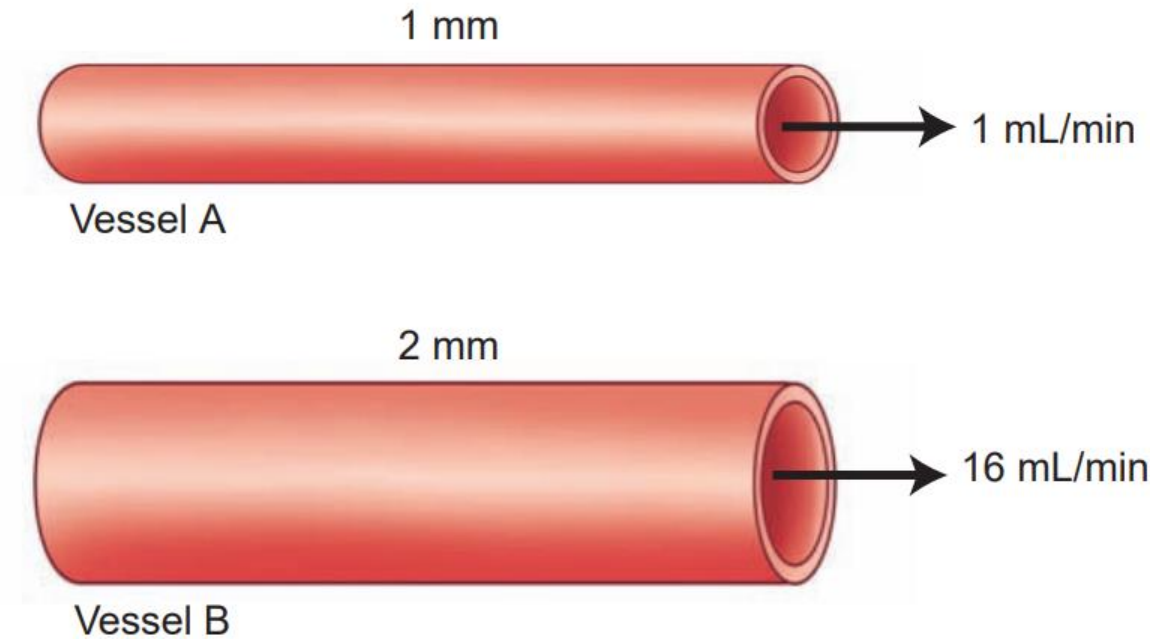






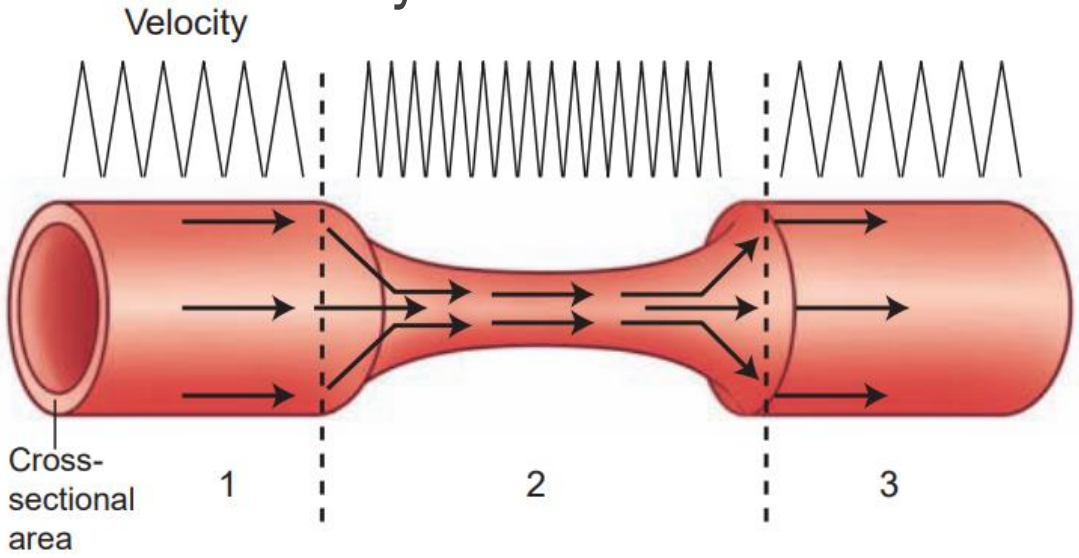
Hemodynamics

- **The rate** of blood flow through a vessel is affected by the fourth power of its **radius** (the radius multiplied by itself four times).
  - Thus, blood flow in vessel B with a radius of 2 mm will be 16 times greater than in vessel A with a radius of 1 mm.



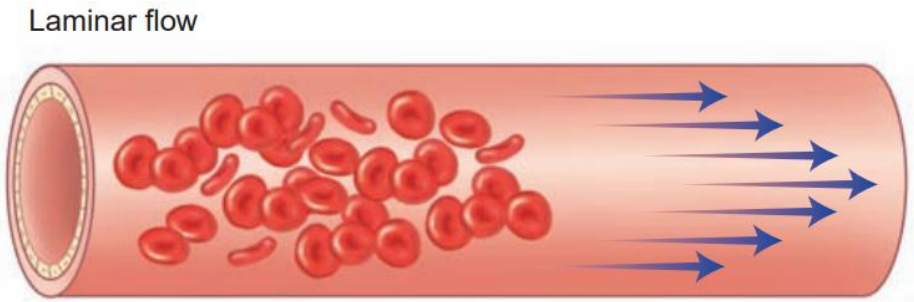
Hemodynamics

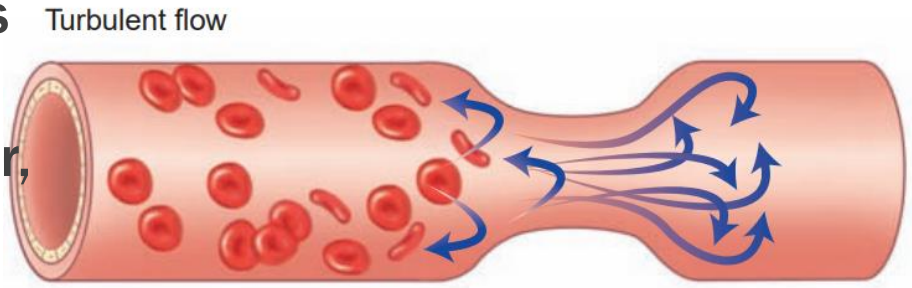
- The **velocity** or **rate** of forward movement of the blood is affected by **the cross-sectional area** of a blood vessel.
  - As the cross-sectional area of a vessel increases (sections 1 and 3), blood must flow laterally as well as forward to fill the increased area. As a result, the mean forward velocity decreases.
  - In contrast, when the cross-sectional area is decreased (section 2), the lateral flow decreases and the mean forward velocity is increased



Hemodynamics

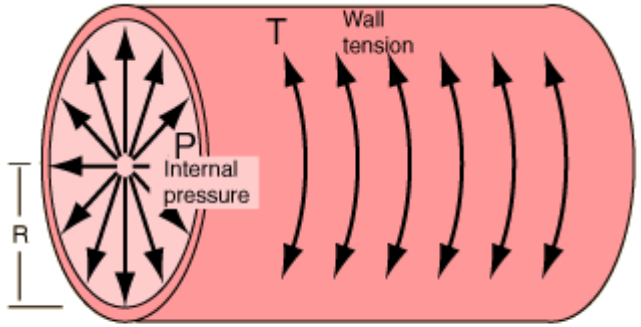
- **Laminar** and **Turbulent** Flow:
- Blood flow is normally laminar, with platelets and blood cells remaining in the center or axis of the bloodstream.
  - The greatest velocity occurring in the central part of the bloodstream
  - Turbulent blood flow is flow in which the blood elements do not remain confined to a definite lamina or layer, but develop vortices (i.e., a whirlpool effect).
  - More pressure is required to force a given flow of blood through the same vessel (or heart valve) when the flow is turbulent rather than laminar
  - Increase in velocity of flow, a decrease in vessel diameter, and low blood viscosity can cause a turbulent flow which may create audible sound.



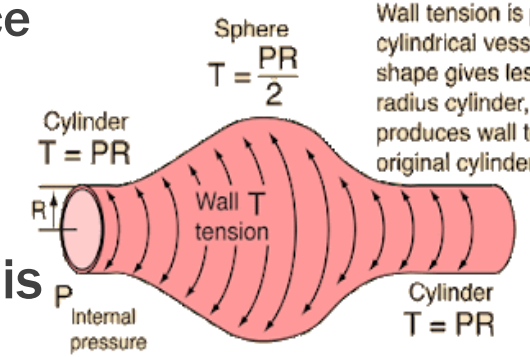


Hemodynamics

- **Wall Tension, Radius and Pressure:**
  - In a blood vessel, wall tension is the force in the vessel wall that opposes the distending pressure inside the vessel.
  - The law of Laplace, expresses this relationship with the equation P = T/r, in which T is wall tension, P is the intraluminal pressure, and r is vessel radius.
  - Accordingly, the internal pressure expands the vessel until it is exactly balanced by the tension in the vessel wall.
    - The smaller the radius, the greater the pressure needed to balance the wall tension.
  - This correlation can be compared with a partially inflated balloon. Because the pressure in the balloon is equal throughout, the tension in the section with the smaller radius is less than the tension in the section with the larger radius.
    - The same principle holds true for an arterial aneurysm, in which the tension and risk of rupture increase as the aneurysm grows.



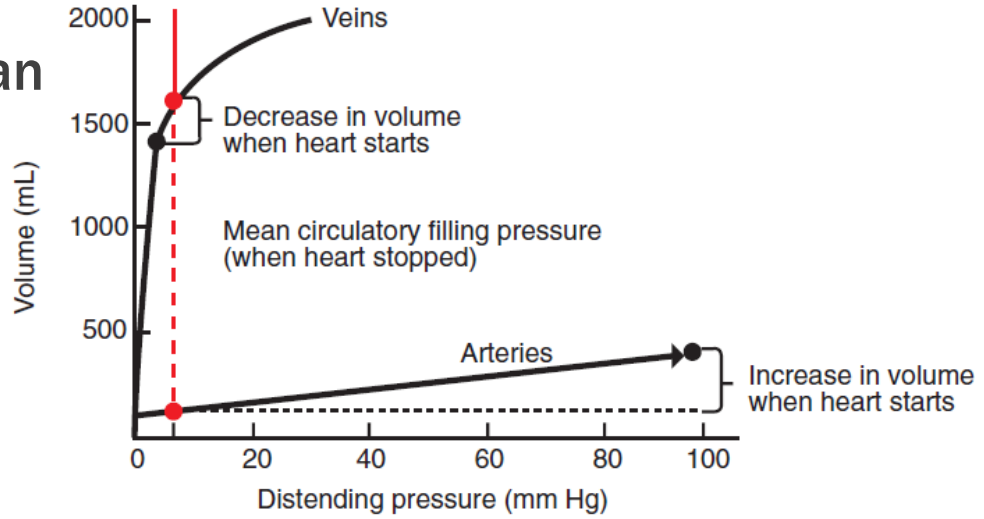
Cylindrical Vessel
T = PR



Wall tension is proportional to vessel radius for cylindrical vessels. Approaching a spherical shape gives less tension than the same radius cylinder, but continued expansion produces wall tension exceeding that of the original cylinder.

Hemodynamics

- **Distension and Compliance:**
  - Compliance refers to the total quantity of blood that can be stored in a given portion of the circulation for each millimeter of mercury (mm Hg) rise in pressure.
  - In other words, the ability of a vessel to distend and increase volume with increasing pressure is quantified as compliance.
  - The most distensible of all vessels are the veins, which can increase their volume with only slight changes in pressure.
  - This allows the veins to function as a reservoir for storing large quantities of blood that can be returned to the circulation when it is needed.



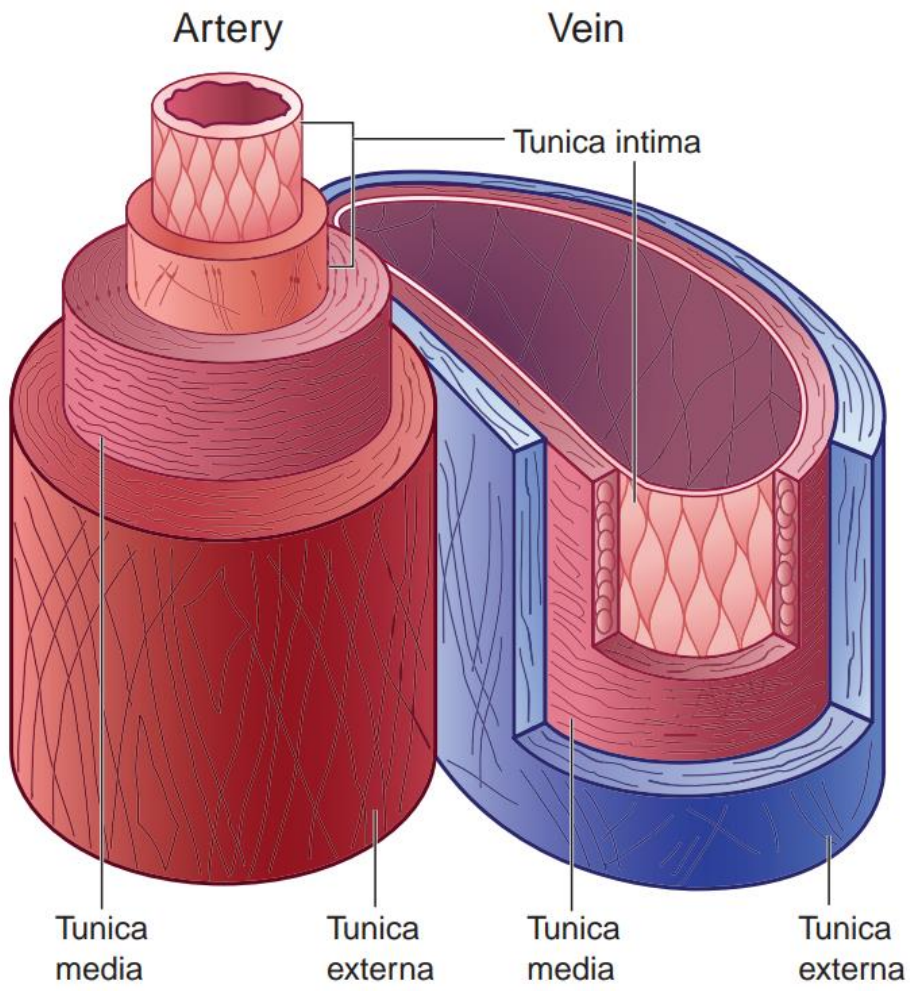
$$\text{Compliance} = \frac{\Delta \text{Volume}}{\Delta \text{Transmural pressure}}$$

5

Neural and Hormonal Control of Blood Pressure and Volume

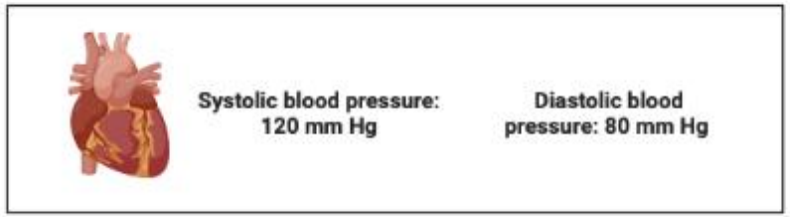
The Blood Vessels

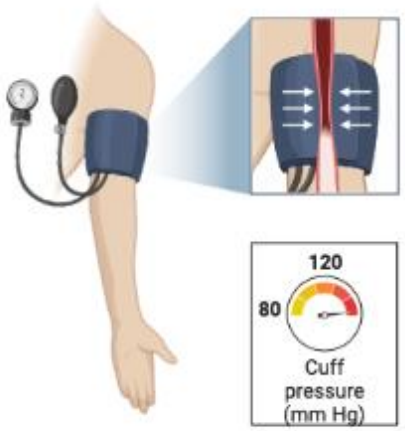
- The vascular system functions in the delivery of oxygen and nutrients and removal of waste products from the tissues. It consists of the arteries and arterioles, the capillaries, and the venules and veins.
- Blood vessels are dynamic structures that constrict and relax to adjust blood pressure and flow to meet the varying needs of the many different tissue types and organ systems
- All blood vessels, except the capillaries, have walls composed of three layers, or coats, called tunicae



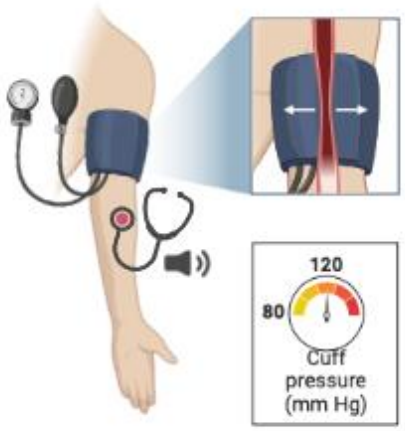
Blood Pressure Measurement

Measurement of Blood Pressure
The Auscultatory Method

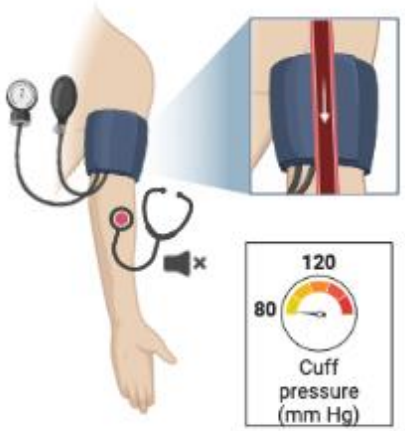




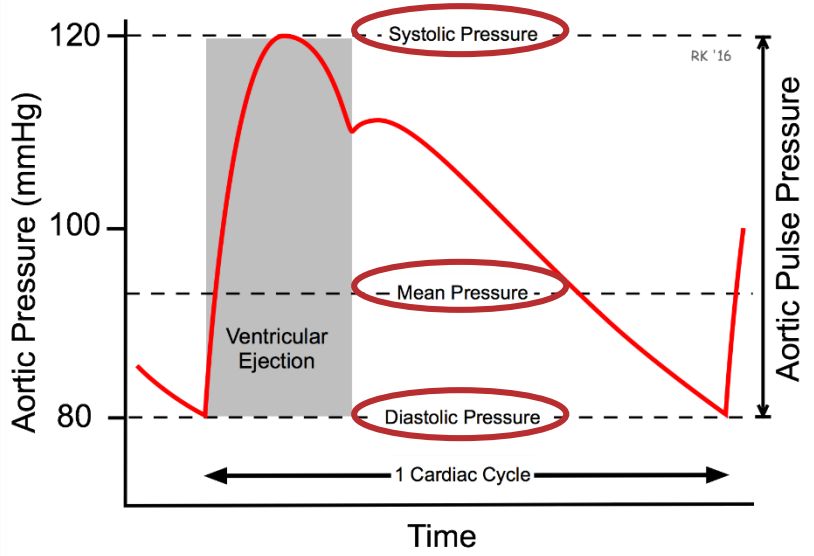
1. The blood pressure cuff is wrapped around the arm and inflated until blood flow is stopped.



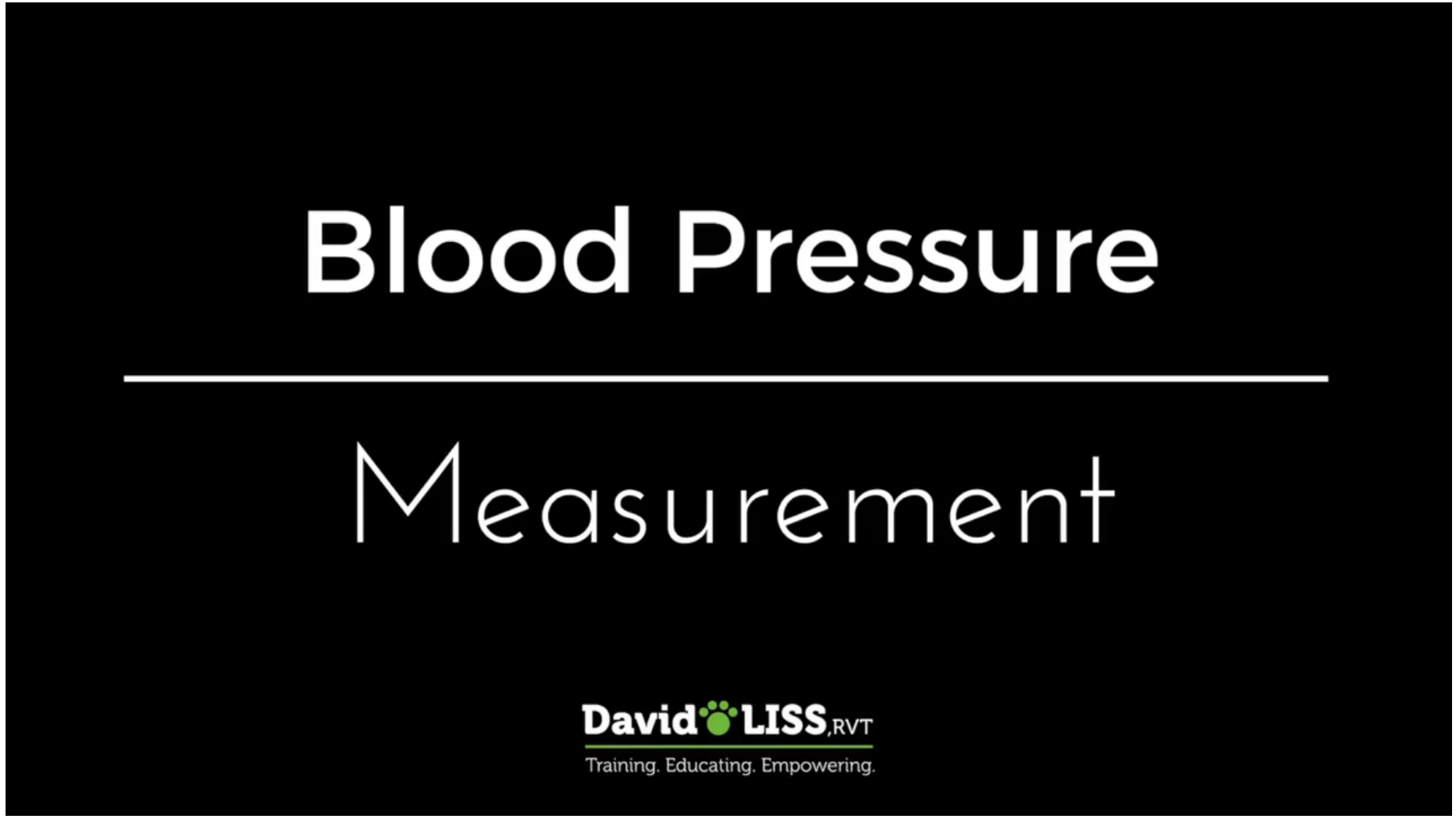
2. The examiner listens for arterial sounds as the cuff is deflated. Pressure at which sounds are first heard is recorded as the systolic pressure.



3. The pressure at which sounds are no longer heard is recorded as the diastolic pressure.



Blood Pressure Measurement



Blood Pressure Regulation

- The neural control of the circulatory system occurs primarily through the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS).
- The ANS contributes to the control of cardiovascular function through modulation of cardiac (i.e., heart rate and cardiac contractility) and vascular (i.e., PVR) functions.
- **Cardiovascular Reflexes:**
  - The arterial baroreceptor reflex works to regulate arterial pressure through the continual adjustment of cardiac output and vascular resistance (in the noncritical organs)
  - The atrial volume receptor reflex works in conjunction with the arterial baroreceptor reflex to regulate arterial pressure and to adjust cardiac preload
- **Psychogenic mechanisms:**
  - The defense-alarm reaction (the “fight or flight response”)
  - The vasovagal syncope (the “playing dead” reaction).

Cardiovascular Reflexes

- Sympathetic and parasympathetic neurons influence the cardiovascular system through the release of the neurotransmitters norepinephrine and acetylcholine.
- In addition, sympathetic nerves affect the cardiovascular system by stimulating the release of epinephrine and norepinephrine from the adrenal medulla.
- The receptors activated by **epinephrine** and **norepinephrine** are called adrenergic receptors (named after the adrenal gland).
  - α-adrenergic receptors
    - α1 and α2
  - β-adrenergic receptors.
    - β1, β2, and β3
- Acetylcholine activates cholinergic receptors
  - muscarinic and nicotinic cholinergic receptors
    - M2 and M3

ANS Receptors in Blood Pressure Regulation

Receptor Type	Location	Usual Activator	Effect of Activation	Function
		α Adrenergic		
α_1 and α_2	Arterioles (all organs)	Norepinephrine from sympathetic neurons, or circulating epinephrine and norepinephrine	Vasoconstriction	Decreases blood flow to organs; increases total peripheral resistance **(major effect)**
	Veins (abdominal organs)	Norepinephrine from sympathetic neurons, or circulating epinephrine and norepinephrine	Venoconstriction	Displaces venous blood toward heart
		β Adrenergic		
β_1	Heart (all cardiac muscle cells)	Norepinephrine from sympathetic neurons, or circulating epinephrine and norepinephrine	Increased pacemaker rate; faster speed of conduction; decreased refractory period; quicker, stronger contractions	Increases heart rate, stroke volume, and cardiac output **(major effects)**
β_2	Arterioles (coronary and skeletal muscle)	Circulating epinephrine and norepinephrine [β_2 receptors not innervated]	Vasodilation	Increases coronary blood flow; increases skeletal muscle blood flow
		Muscarinic Cholinergic		
M_2	Heart (all cardiac muscle cells, but sparse direct innervation of ventricular muscle cells)	Acetylcholine from parasympathetic neurons	Opposite of β_1	Decreases heart rate and cardiac output **(major effect)**
	Sympathetic nerve endings at ventricular muscle cells	Acetylcholine from parasympathetic neurons	Inhibition of norepinephrine release from sympathetic neurons	Decreases magnitude of sympathetic effects on ventricular muscle cells
M_3	Arterioles (coronary)	Acetylcholine from parasympathetic neurons	Vasodilation (mediated via nitric oxide)	Increases coronary blood flow (minor effect)
	Arterioles (genitals)	Acetylcholine from parasympathetic neurons	Vasodilation (mediated via nitric oxide)	Causes engorgement and erection
	Arterioles (skeletal muscle)	Acetylcholine from specialized sympathetic neurons	Vasodilation (mediated via nitric oxide)	Increases muscle blood flow (in anticipation of exercise)
	Arterioles (most other organs)	[Receptors not innervated; normal activator unknown]	Vasodilation (mediated via nitric oxide)	Function unknown

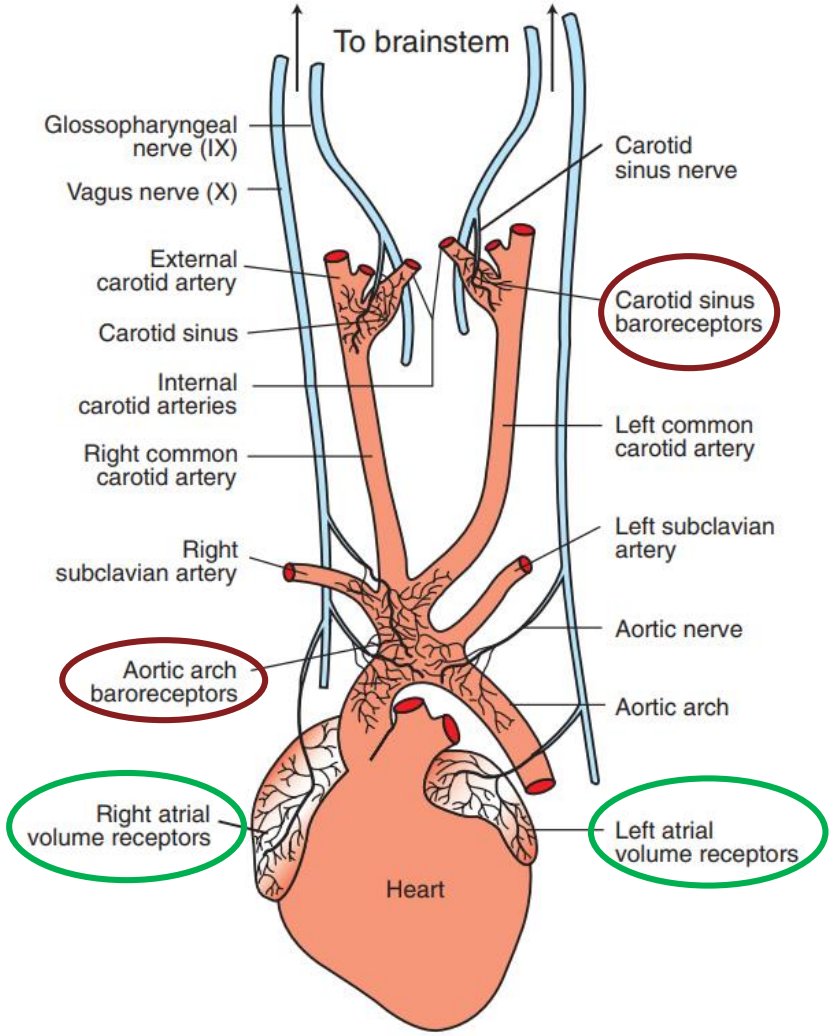
ANS Receptors in Blood Pressure Regulation

- Of all the autonomic influences on the cardiovascular system just mentioned, three stand out as most important.

1. α1- and α2-adrenergic vasoconstriction in the arterioles of all body organs, which is brought about by the sympathetic nervous system.
2. β1-adrenergic excitation of cardiac muscle, which is brought about by the sympathetic nervous system and results in an increased heart rate and stroke volume.
3. The decrease in heart rate brought about by parasympathetic activation of cardiac M2-cholinergic receptors

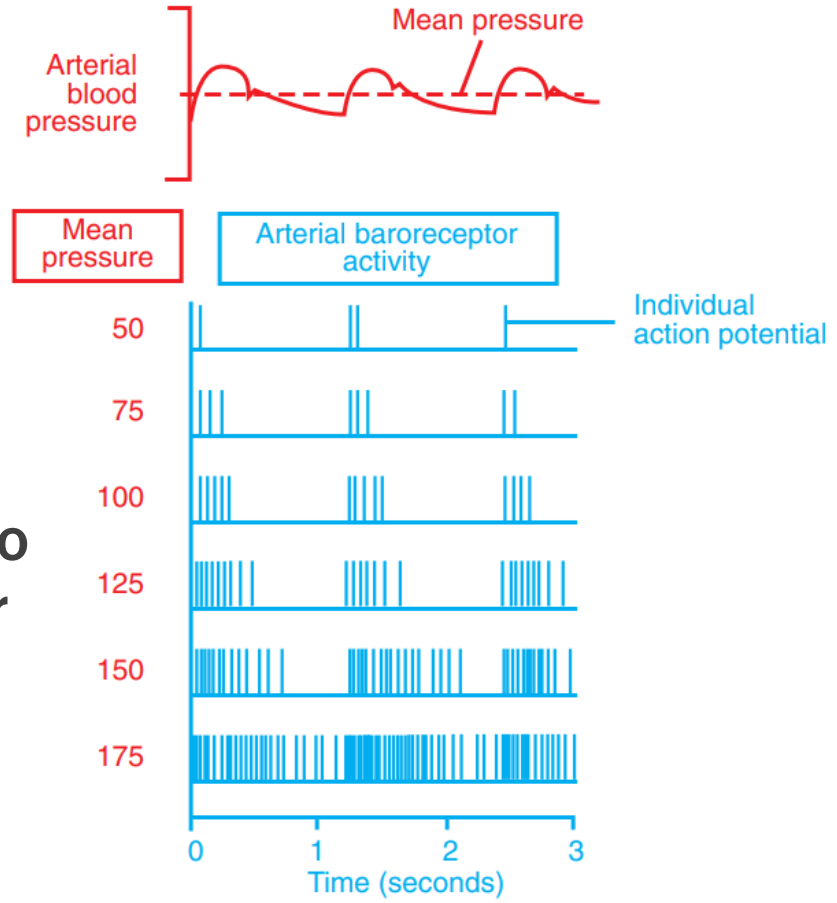
1. The Arterial Baroreceptor Reflex

- Arterial blood pressure is monitored by pressure-sensitive nerve endings known as baroreceptors.
- The baroreceptors send afferent impulses to the central nervous system (CNS), which reflexively alters cardiac output and vascular resistance (in noncritical organs: the kidneys, the splanchnic organs, and resting skeletal muscle) to keep blood pressure at a set point.
- The arterial baroreceptors are specialized nerve endings that are embedded in the walls of the carotid arteries and aortic arch.
- These nerve endings are sensitive to stretch (distention) of the arterial wall

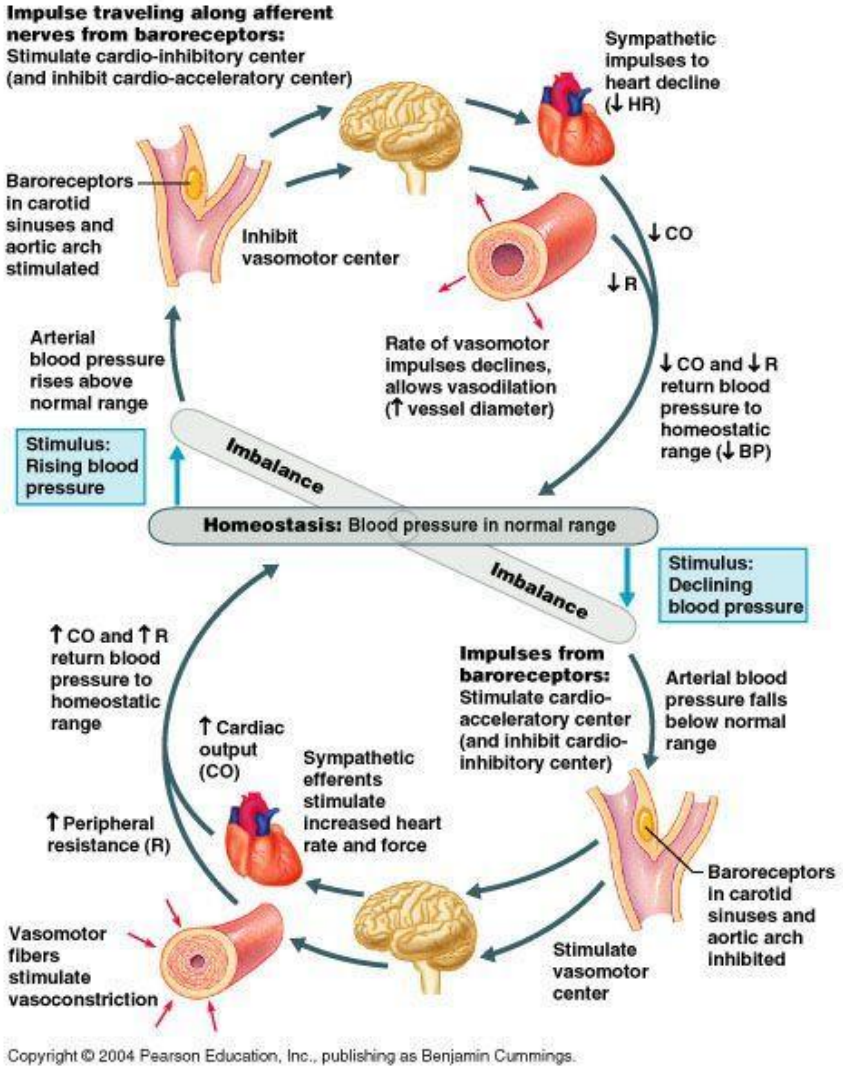


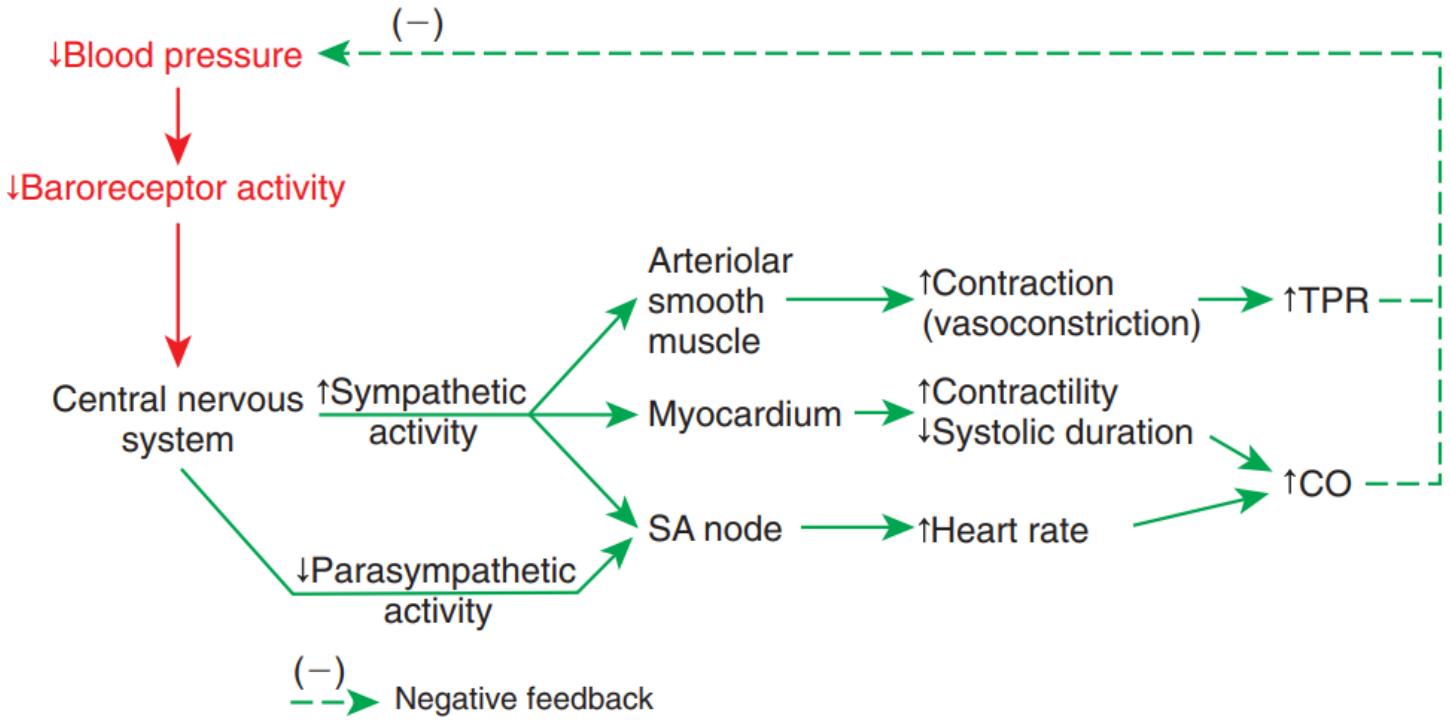
The Arterial Baroreceptor Reflex

- With every systolic ejection from the heart, blood distends the aorta and arteries, including the carotid sinuses, which causes the baroreceptors to initiate neural impulses (action potentials).
- The higher the MAP, the more action potentials are formed in each heartbeat.
- Because the baroreceptors are active when arterial pressure is normal (MAP near 100 mm Hg), they can also signal a decrease in arterial pressure by decreasing their action potential frequency.



The Arterial Baroreceptor Reflex

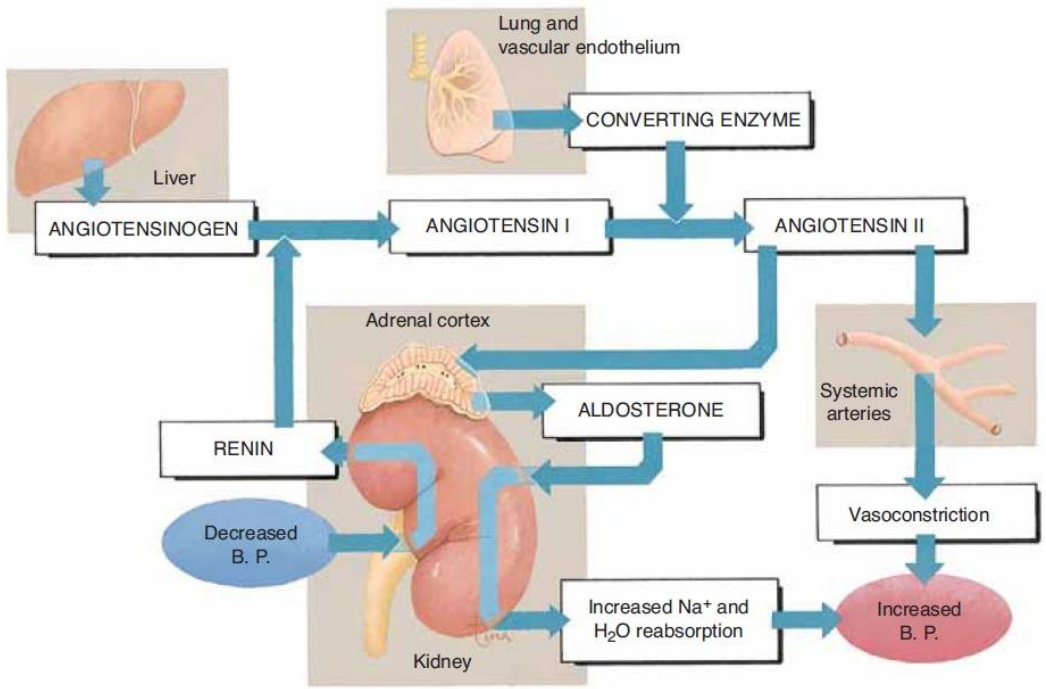


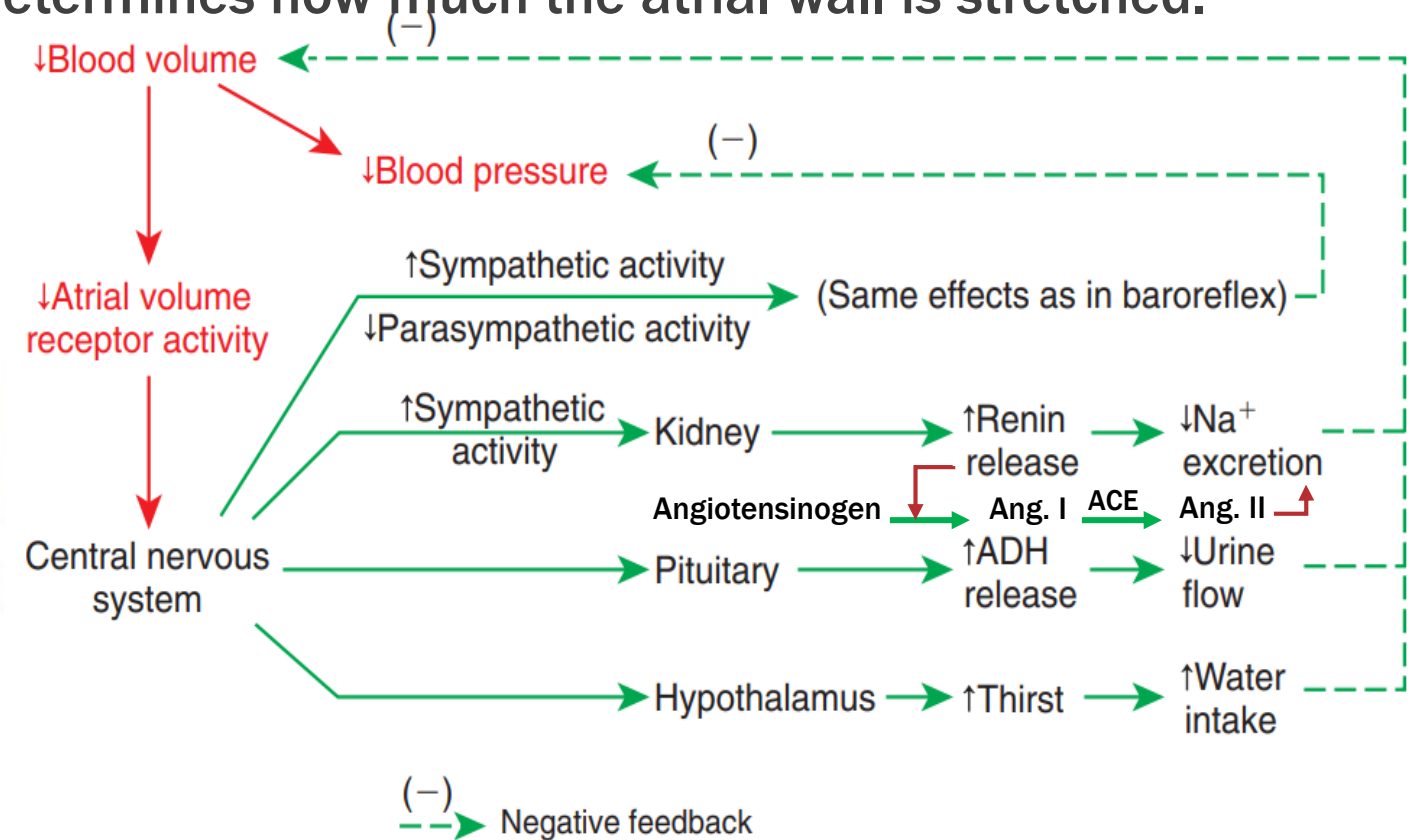


In summary, the baroreflex responds quickly and powerfully to counteract sudden changes in blood pressure, but it has little influence on the long-term level of blood pressure over days or weeks.

2. The Atrial Volume Receptor Reflex

- The atrial volume receptor reflex is initiated by specialized sensory nerve endings that are located primarily in the walls of the left and right atria.
  - These nerve endings are activated by stretch, but they are called volume receptors because the volume of blood in each atrium determines how much the atrial wall is stretched.



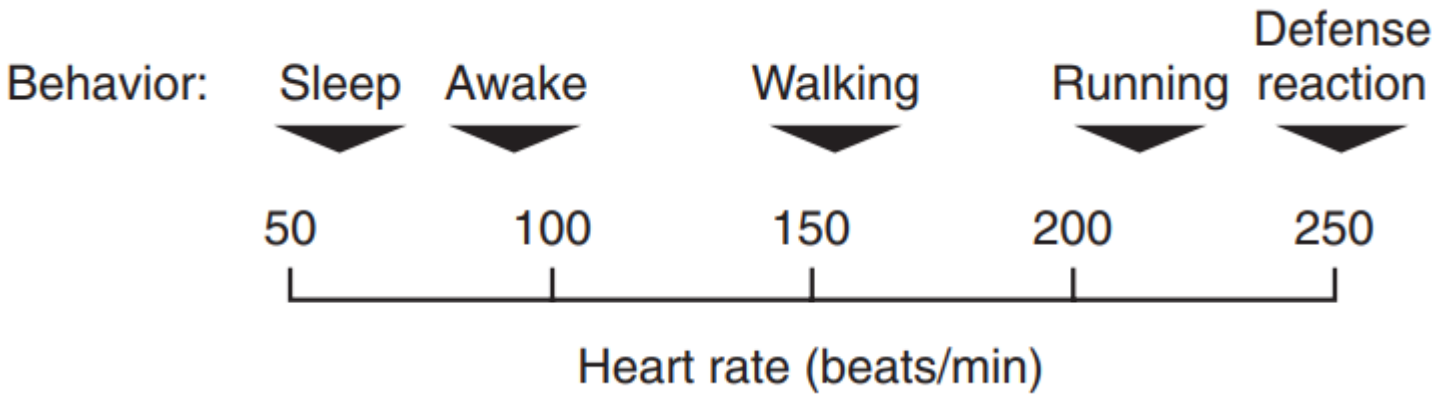


Psychogenic mechanisms

- The baroreceptor reflex and the atrial volume receptor reflex are primarily responsible for the regulation of blood pressure and blood volume, and they originate from changes detected by peripheral sensory receptors.
- They occur at a subconscious level, through neural pathways that primarily involve cardiovascular centers in the brainstem and midbrain.
- Cardiovascular reflexes persist in unconscious and anesthetized subjects, although the strength and character of the reflexes are altered by anesthesia.
- Psychogenic responses originate from conscious perceptions or emotional reactions. They are eliminated by unconsciousness or general anesthesia.
  - They involve neural pathways of the midbrain and forebrain, including the limbic system and cerebral cortex.

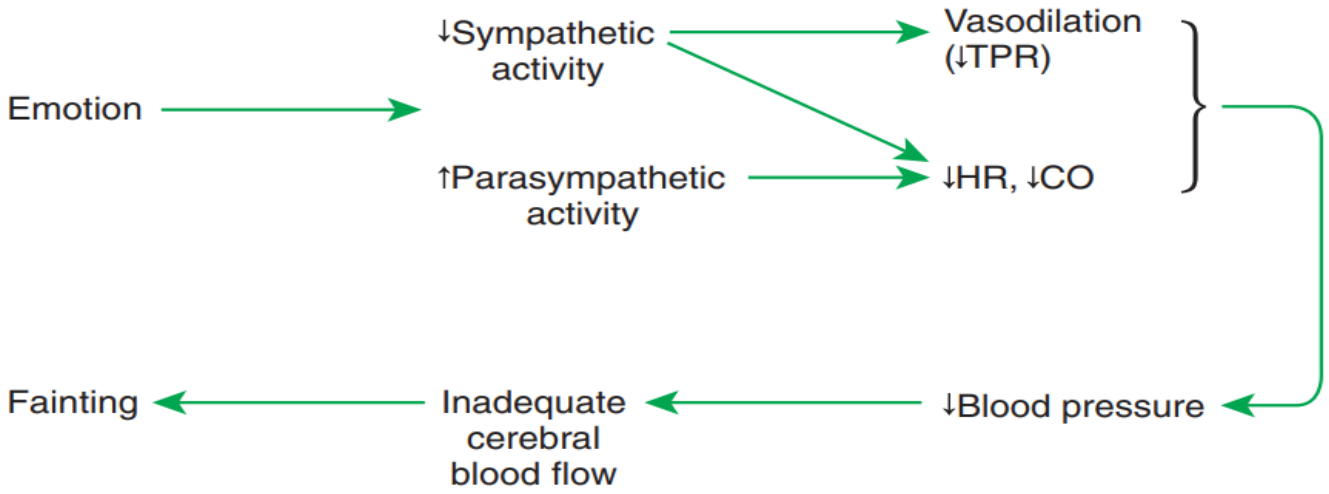
1. The Defense-Alarm Reaction

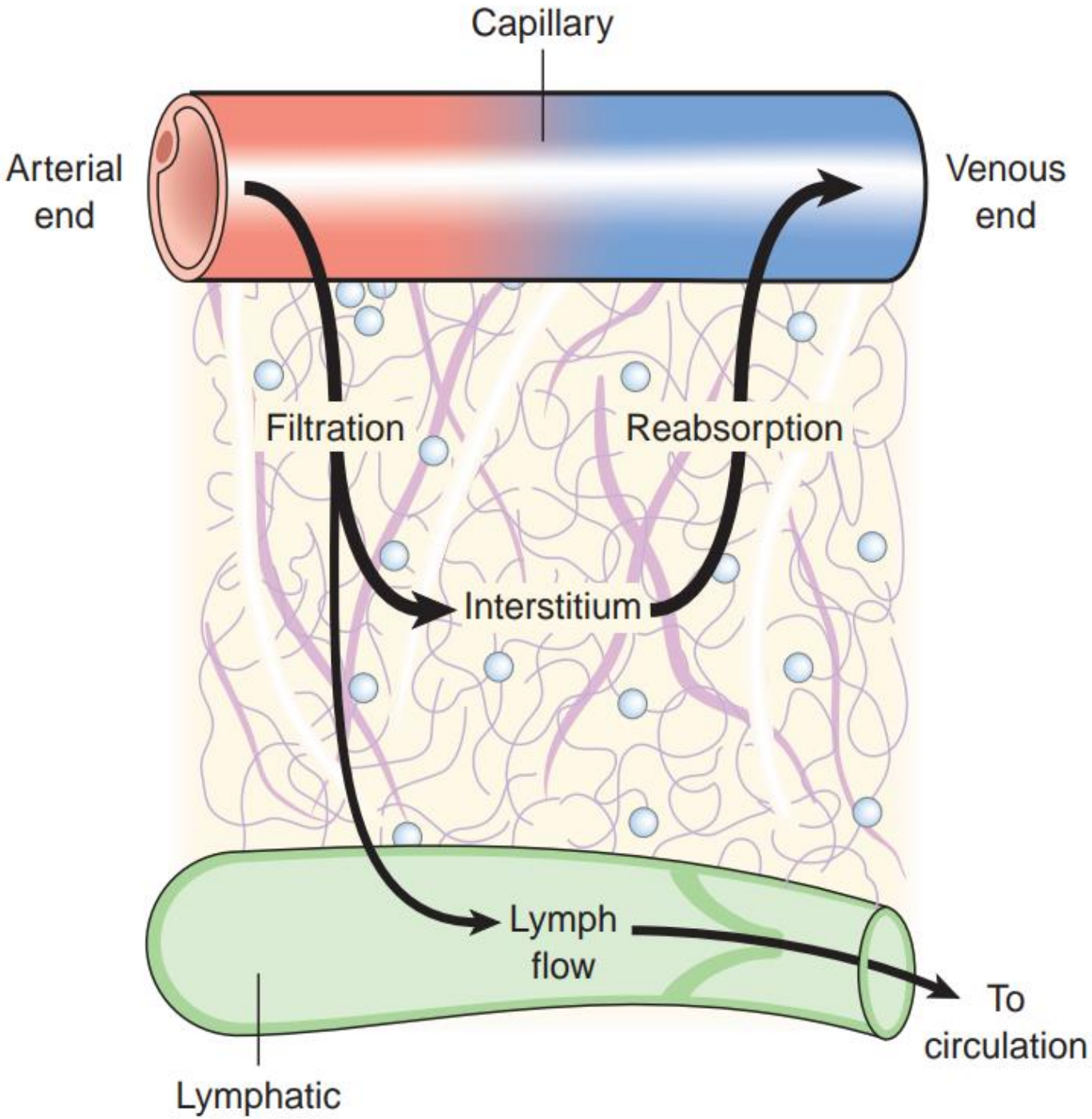
- **The defense-alarm reaction** ("fear, fight, or flight" response) is an emotional and behavioral response to a threatening situation, physical injury, or trauma.
- The defense-alarm reaction is simply the extreme on a continuum of emotional and physical arousal.
  - Cardiovascular variables (e.g., heart rate, stroke volume, vasoconstriction in non-critical organs and skin, vasodilation in coronary vessels and in working skeletal muscles) respond sensitively to every change along this arousal scale:



2. Vasovagal Syncope

- In response to certain threatening or emotional situations, some humans and animals experience a psychogenic decrease in blood pressure and may faint which is called vasovagal syncope.
  - This response is also called "playing dead"
  - In many ways, this response is the opposite of the defense-alarm reaction.
- It is not clear why some animals respond to a threatening situation with a defense-alarm reaction, whereas others exhibit vasovagal syncope.

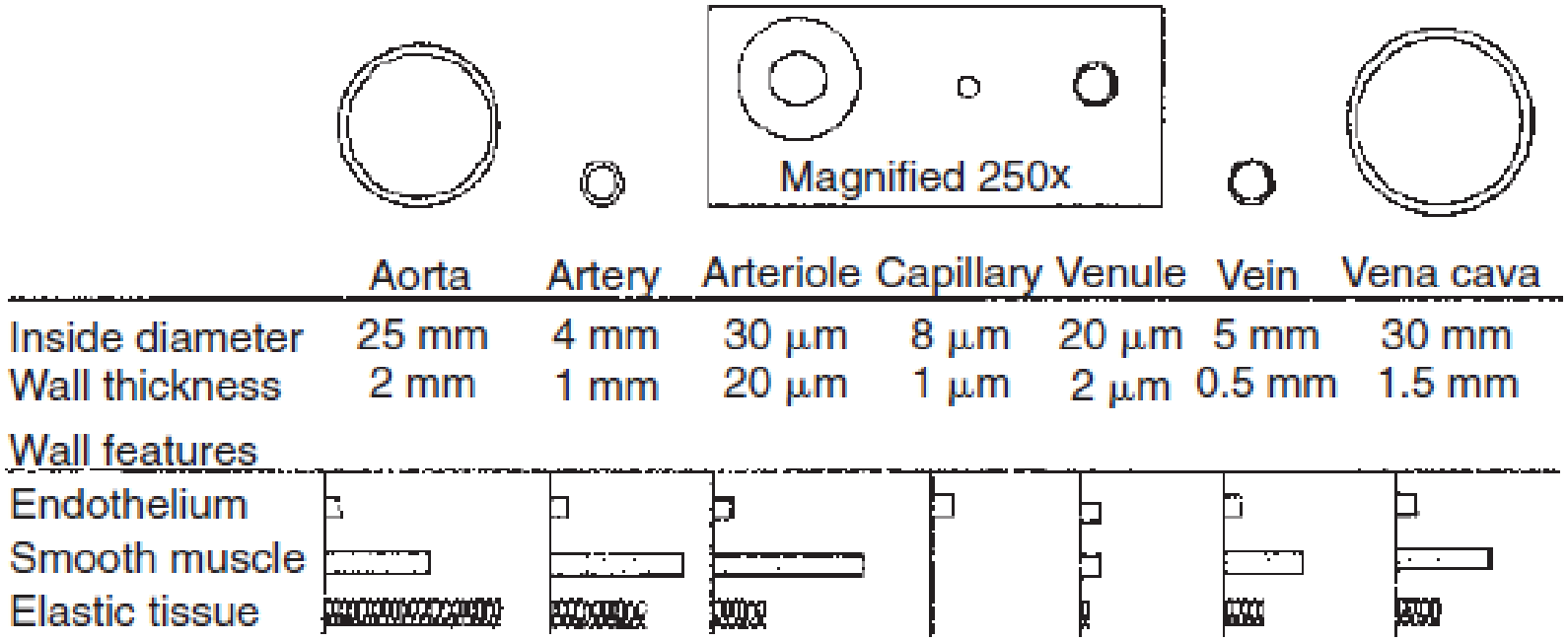




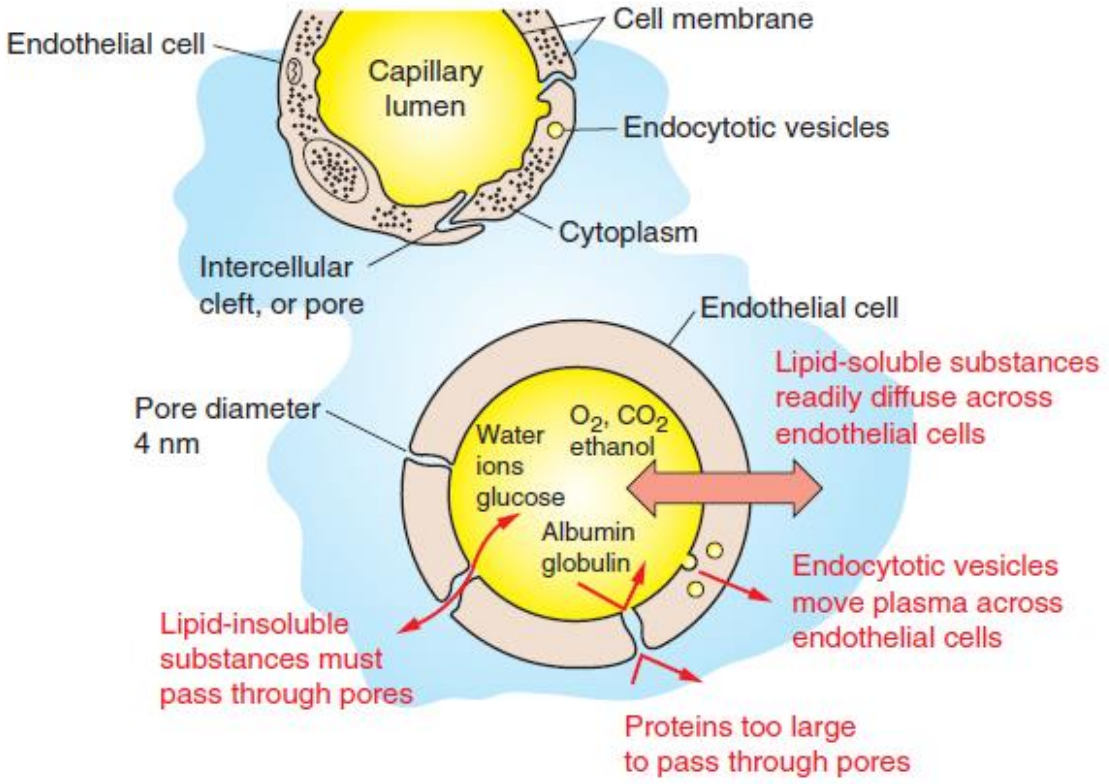
6

Capillaries and fluid exchange

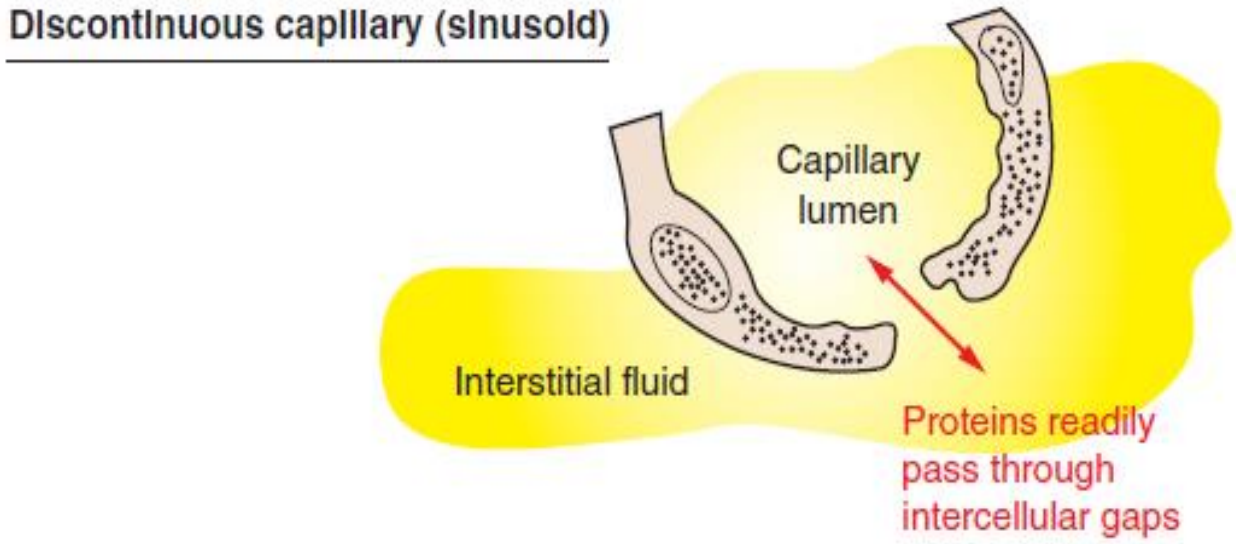
Types of blood vessels



Types of Capillaries



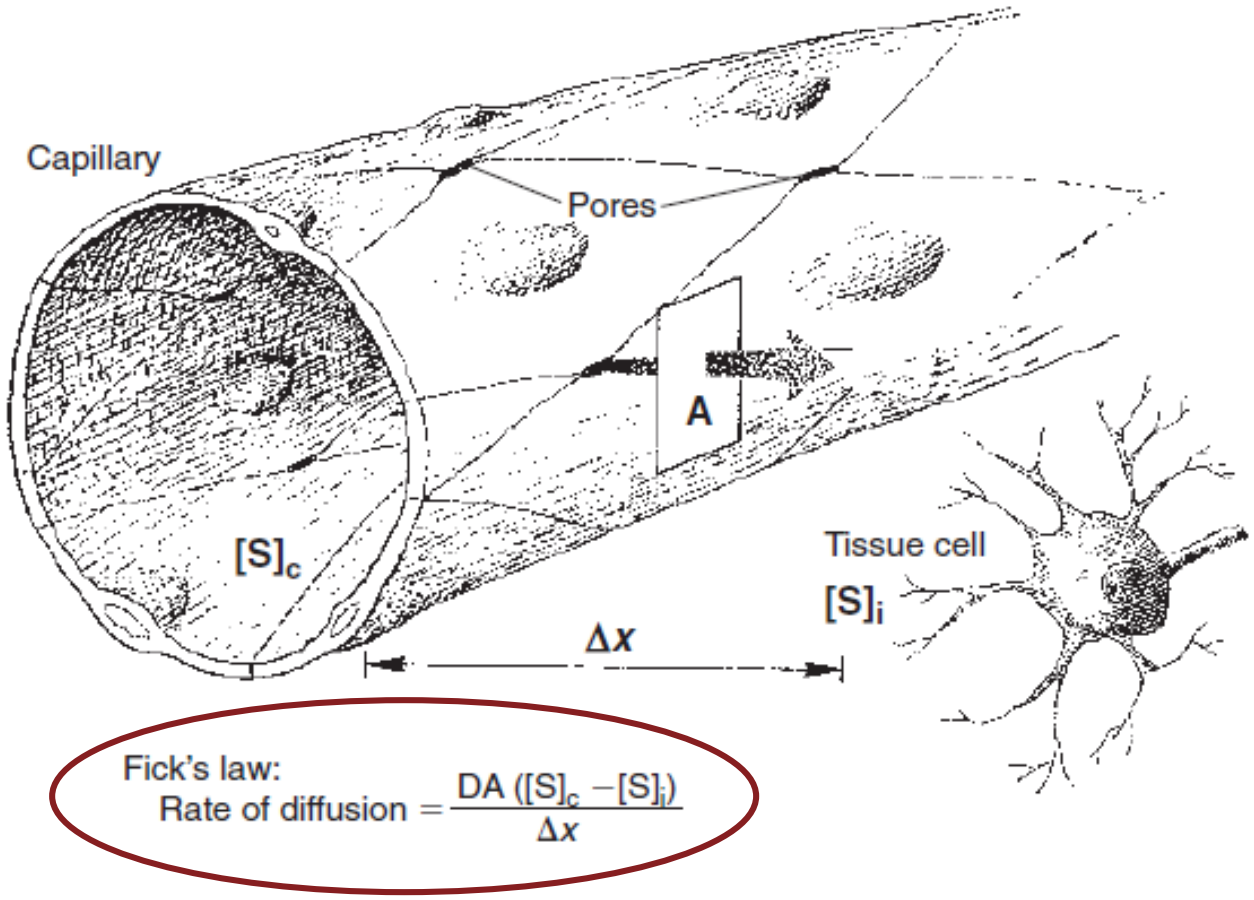
Typical continuous capillary



Fick's Law of Diffusion

Diffusion coefficient:

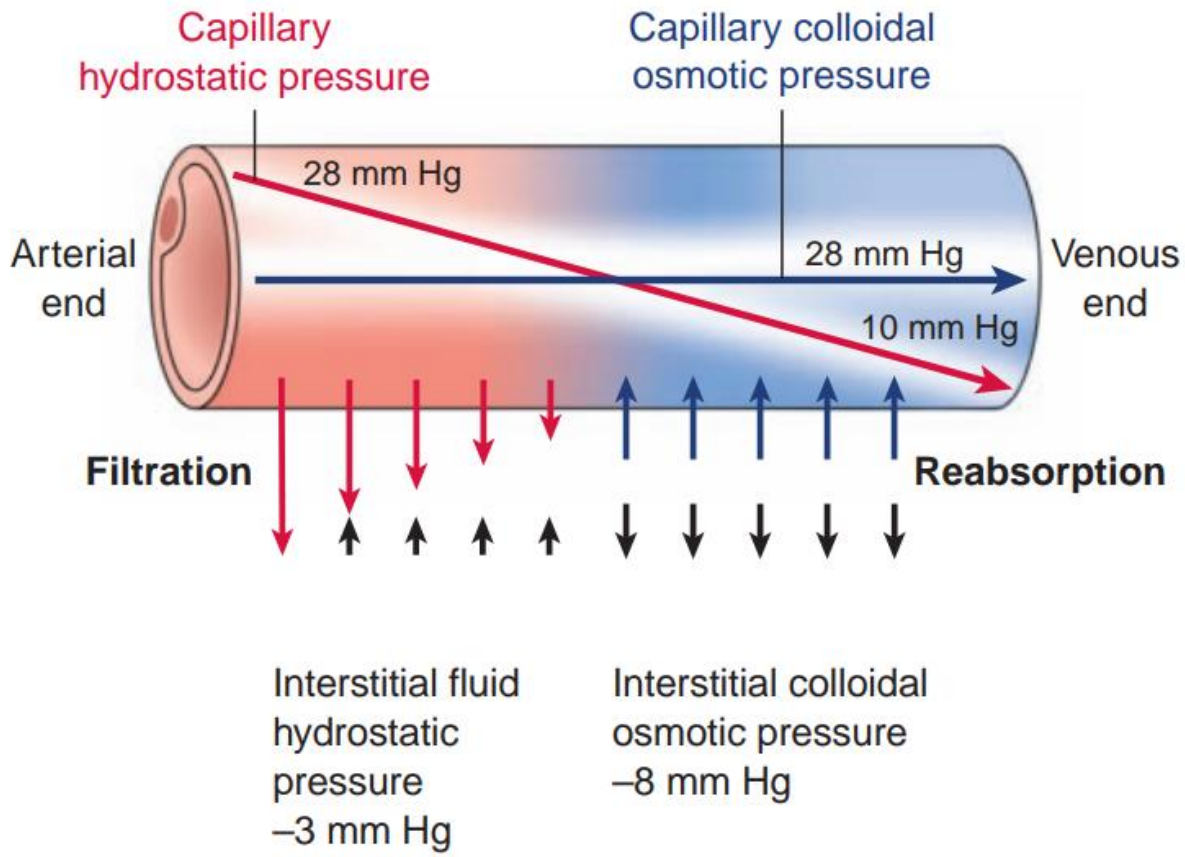
- Temperature
  - Increase random (Brownian) motion
  - Increase velocity
- Molecular weight
- Solubility



Autoregulation and capillary dynamics

- The Starling Equation Quantifies the Interaction of Oncotic and Hydrostatic Forces Acting on Water

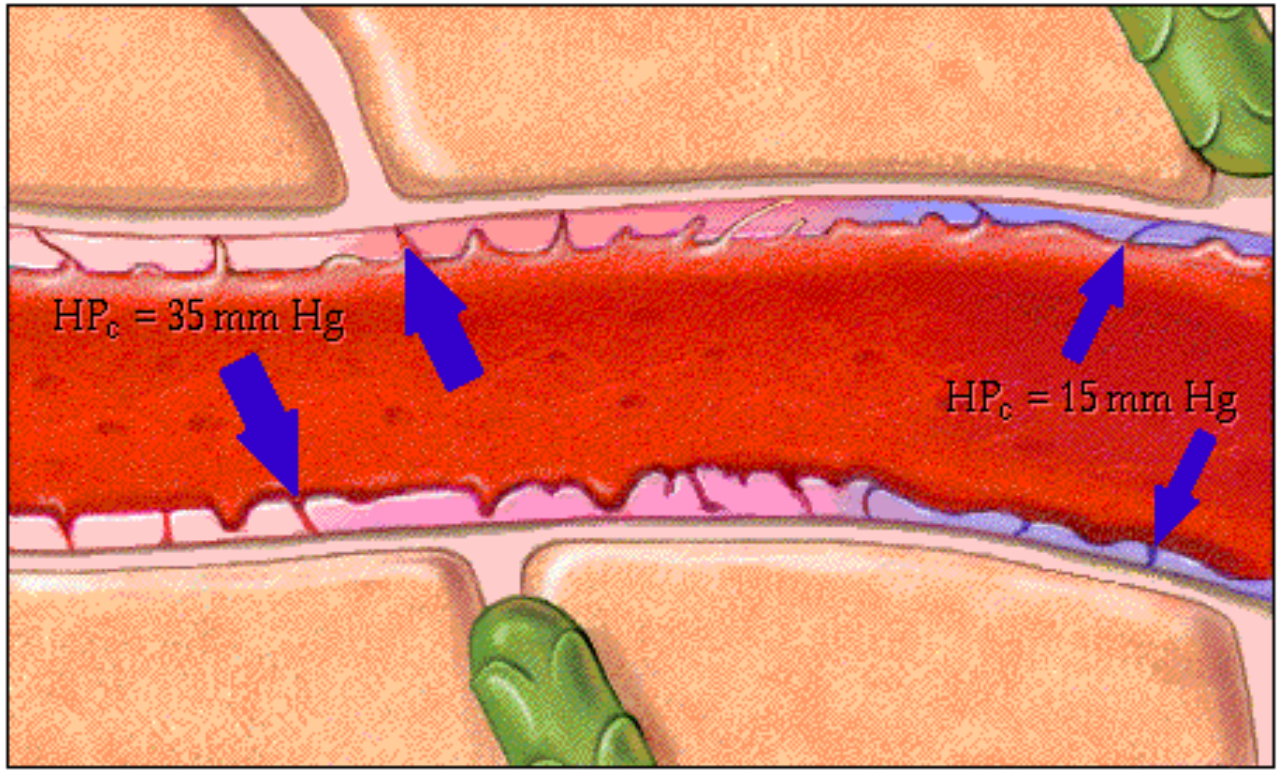
- Net pressure = (Pc – Pi) – (πc – πi)
  - Pc : capillary hydrostatic pressure
  - Pi : interstitial fluid hydrostatic pressure
  - πc : capillary plasma oncotic pressure
  - πi : interstitial fluid oncotic pressure



Autoregulation and capillary dynamics

In capillaries, **hydrostatic pressure** is exerted by blood. Thus, capillary hydrostatic pressure(HP_c) is equivalent to the blood pressure in the capillaries.

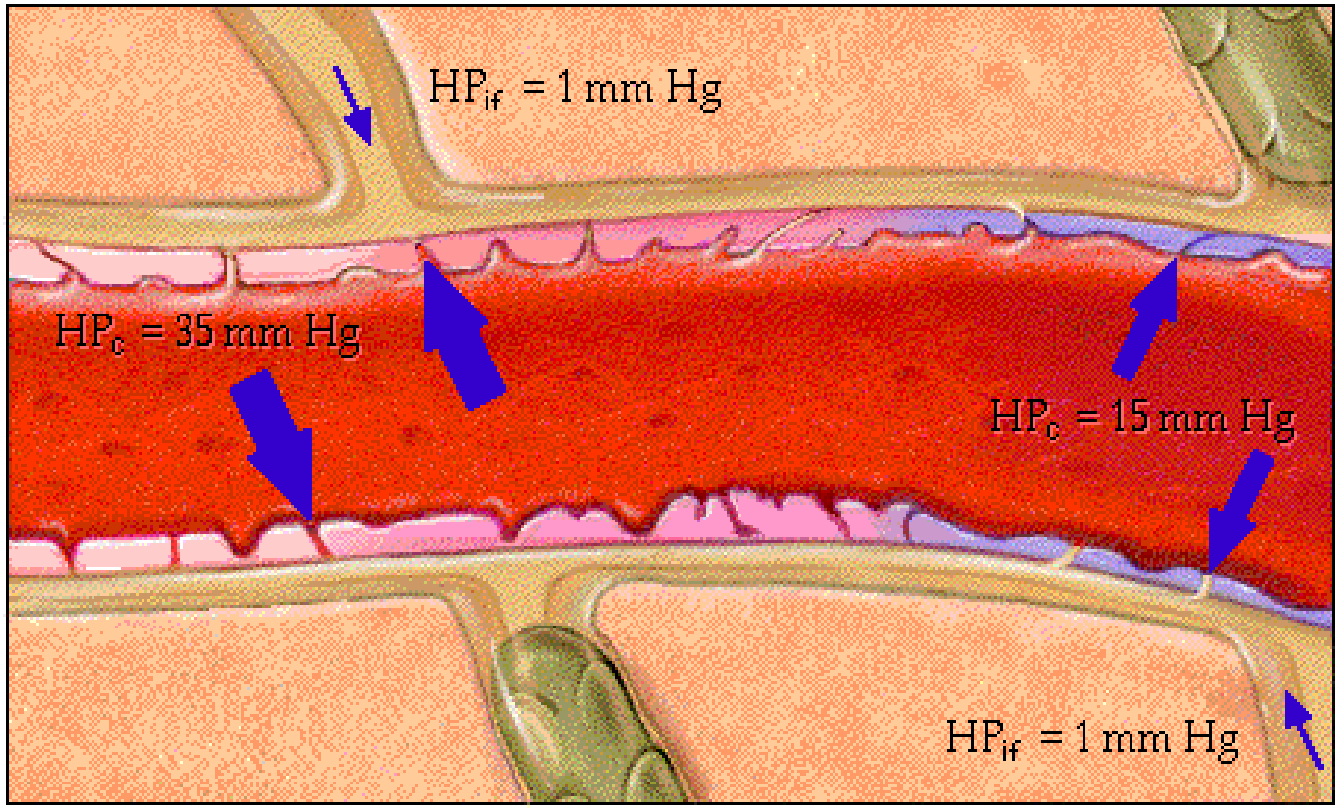
Arteriole end



Venule end

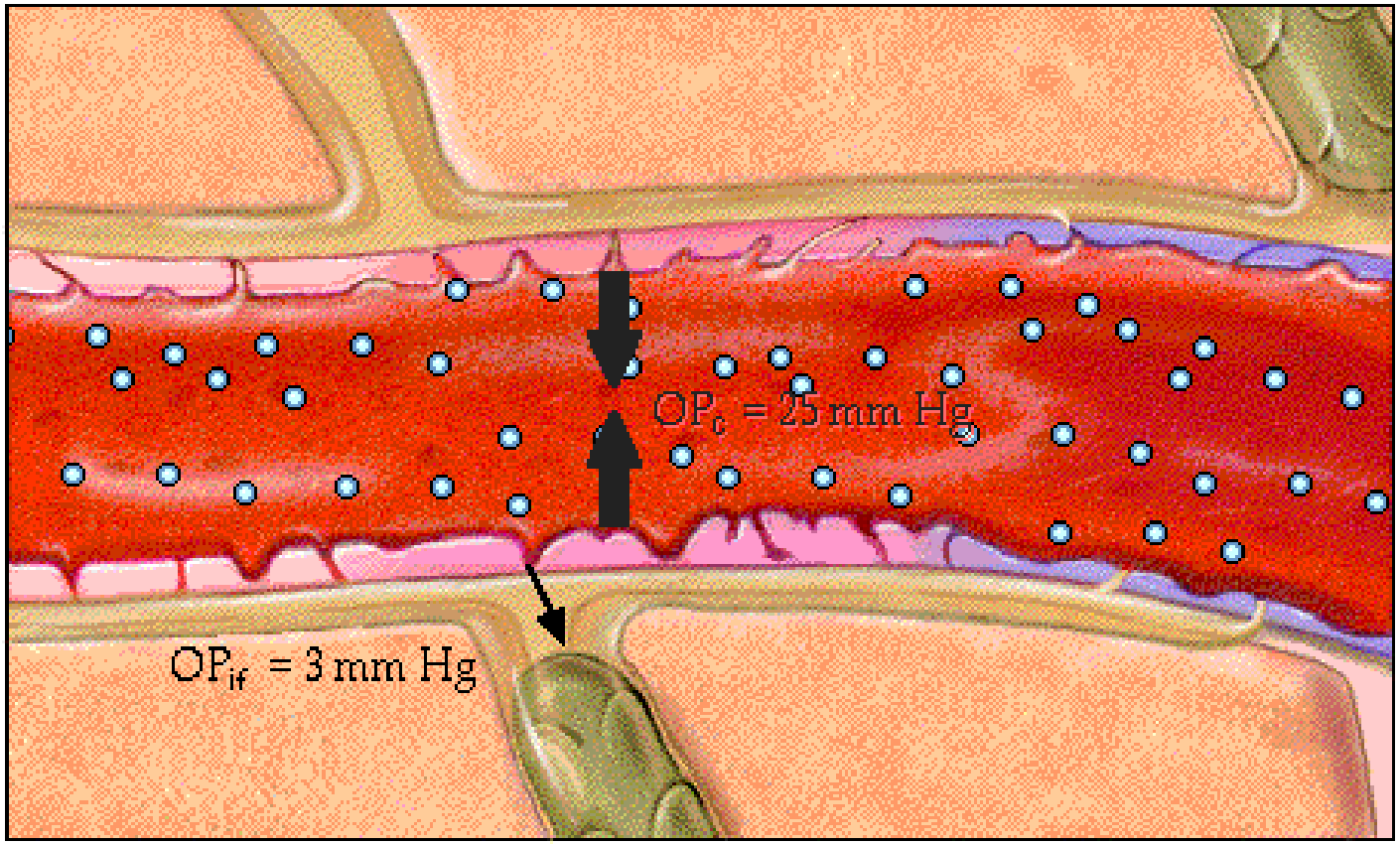
Autoregulation and capillary dynamics

Arteriole end



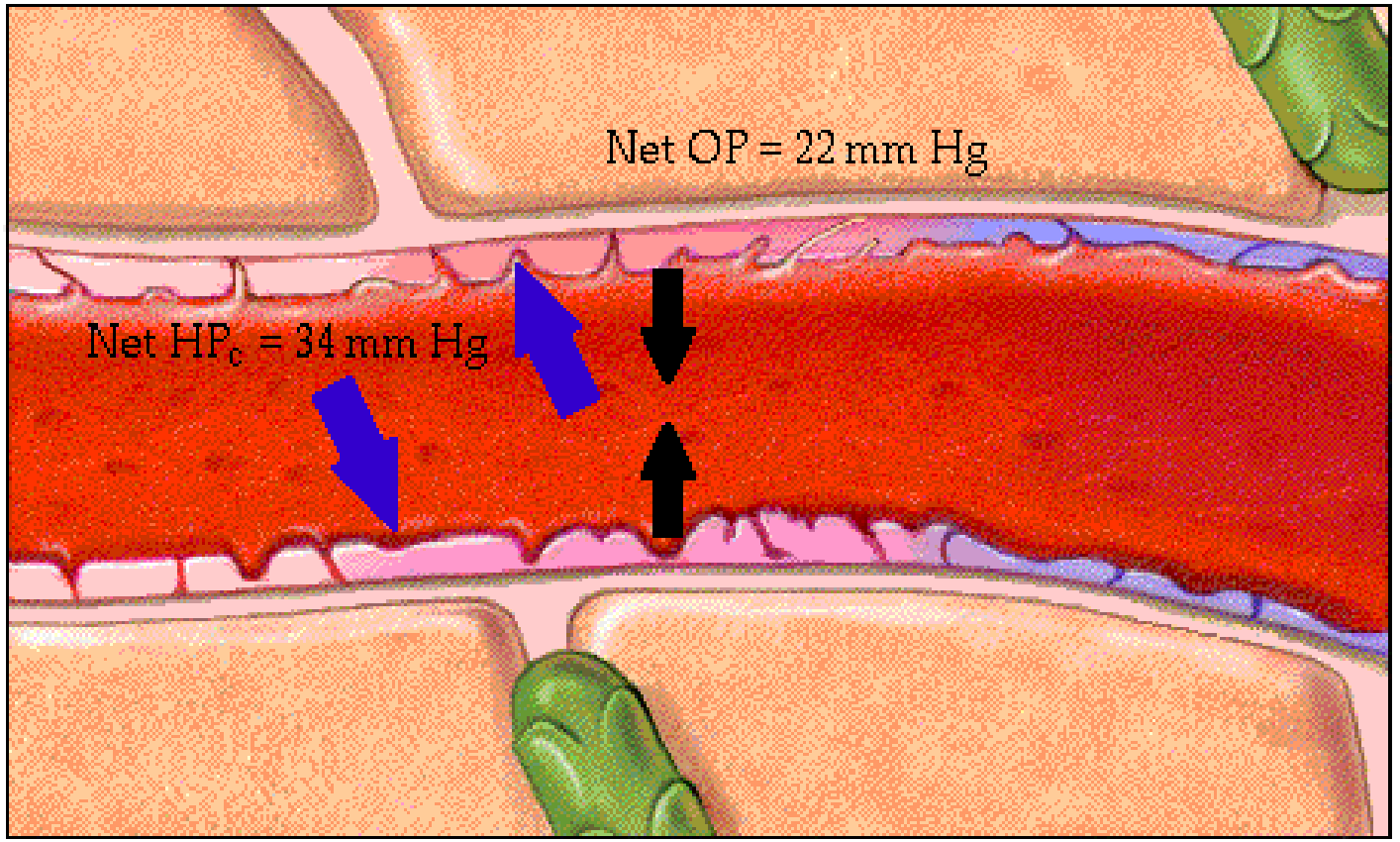
Venule end

Autoregulation and capillary dynamics



Autoregulation and capillary dynamics

Arteriole end

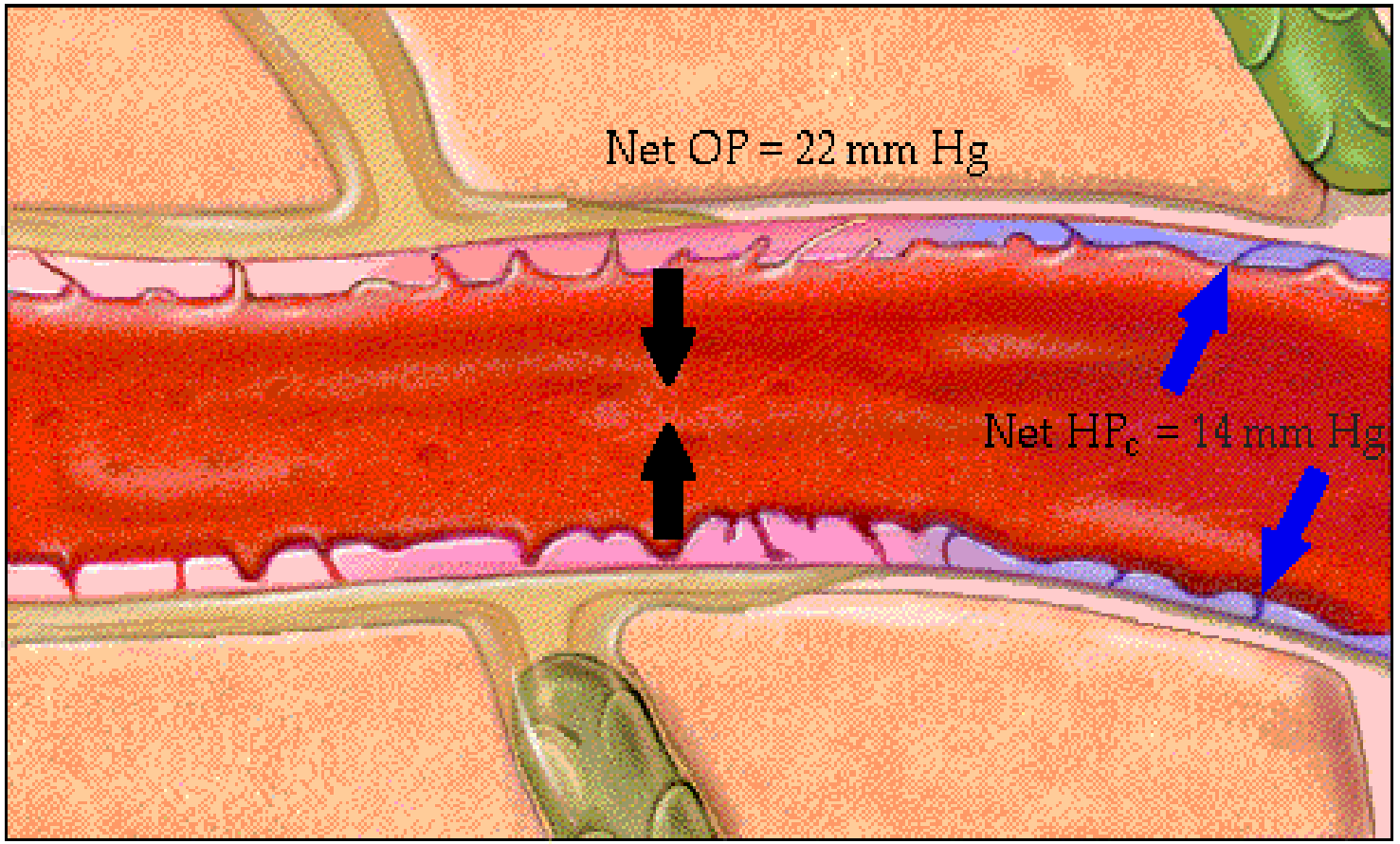


Venule end

Net force (determines direction of flow) = Net HP - Net OP

Autoregulation and capillary dynamics

Arteriole end

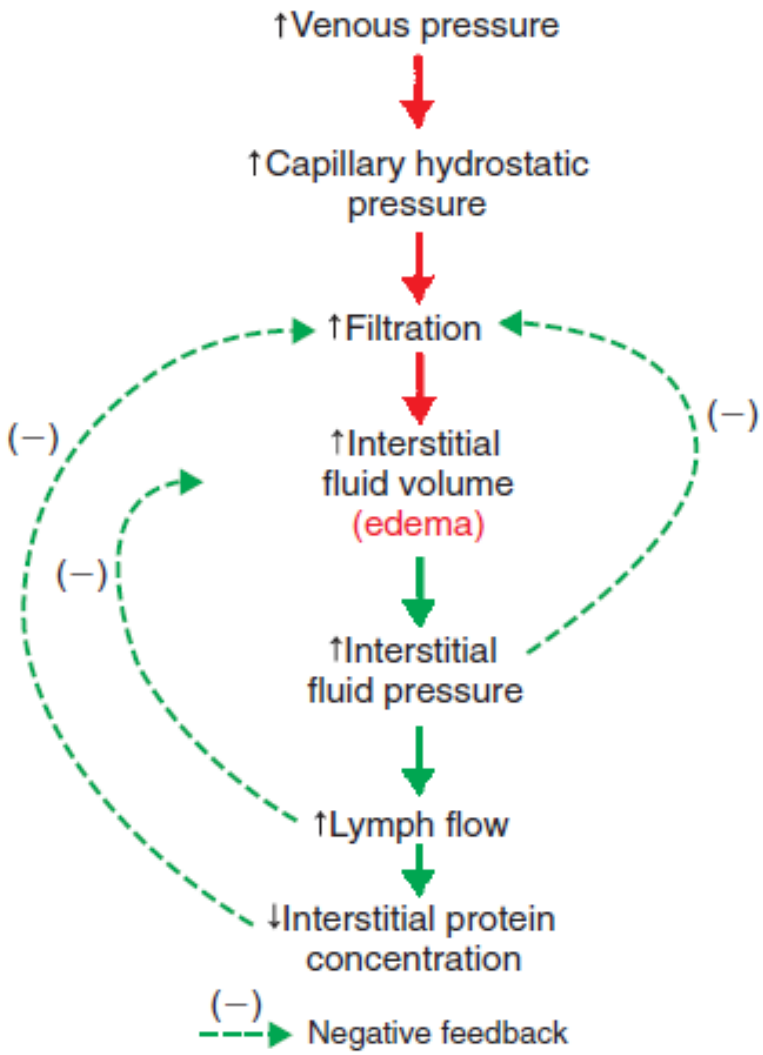


Venule end

Net force (determines direction of flow) = Net HP - Net OP

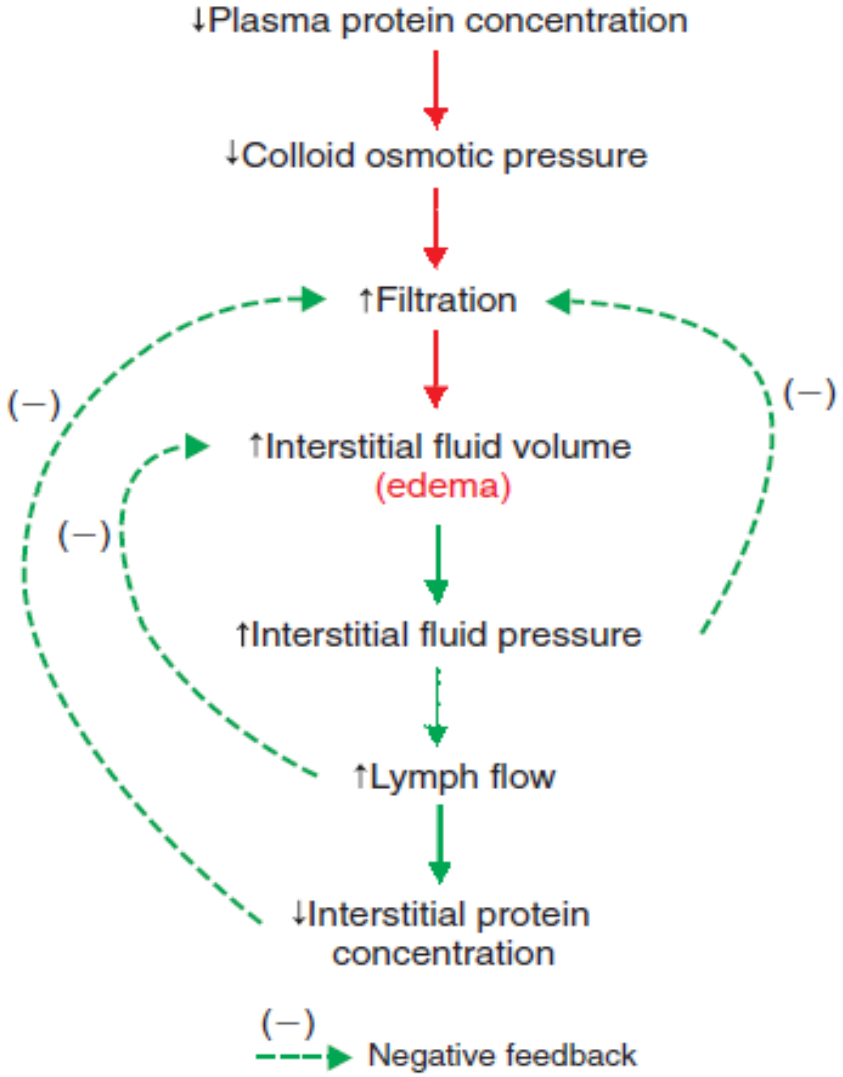
Edema

- Increase in venous pressure leads to increase in interstitial fluid volume (edema).
- The dashed lines (negative feedback) indicate the counteracting effects of the three safety factors against edema.
  - First, an increase in interstitial fluid hydrostatic pressure reduces the rate of filtration back toward normal.
  - Second, an increase in lymph flow reduces interstitial fluid volume back toward normal.
  - Third, a decrease in interstitial fluid protein concentration reduces the rate of filtration back toward normal.



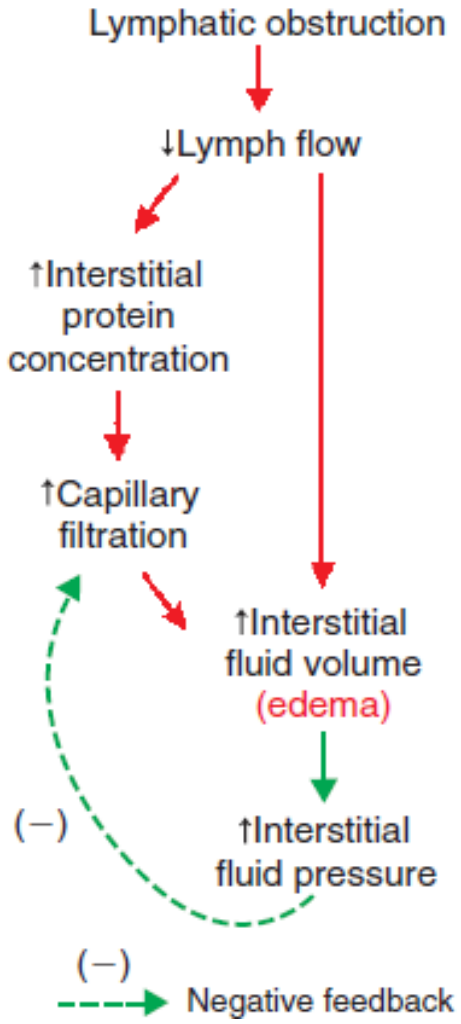
Edema

- Decrease in plasma protein concentration leads to edema, but the degree of edema is limited by the same three safety factors as shown in previous diagram



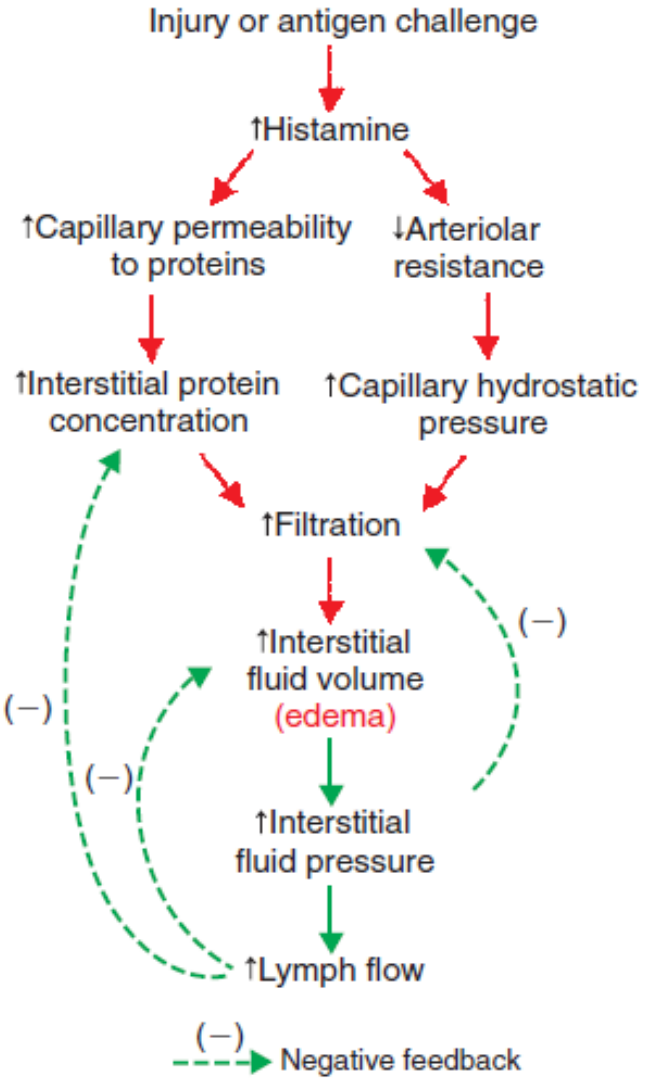
Edema

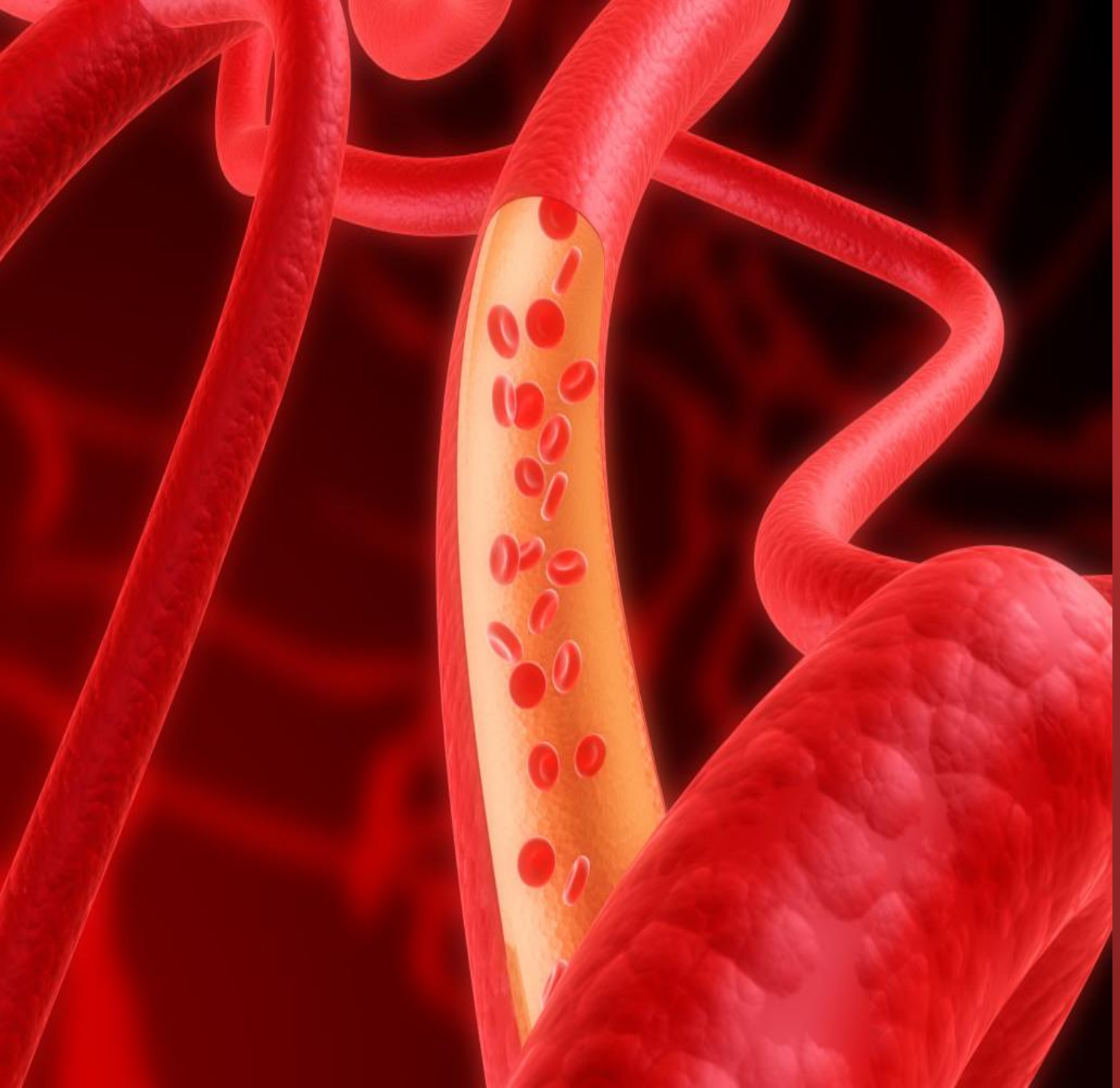
- **Lymphatic obstruction** leads to edema.
  - **Lymphedema** is clinically troublesome because only one of the normal three safety factors is operative to limit the degree of edema.



Edema

- Histamine mediates the changes that lead to edema in response to a physical injury or an antigen challenge.
- The normal three safety factors against edema are intact and help to limit the degree of edema.
- Treatment with an antihistamine (a drug that blocks histamine receptors on arterioles and capillaries) also helps to reduce edema in these cases.
-



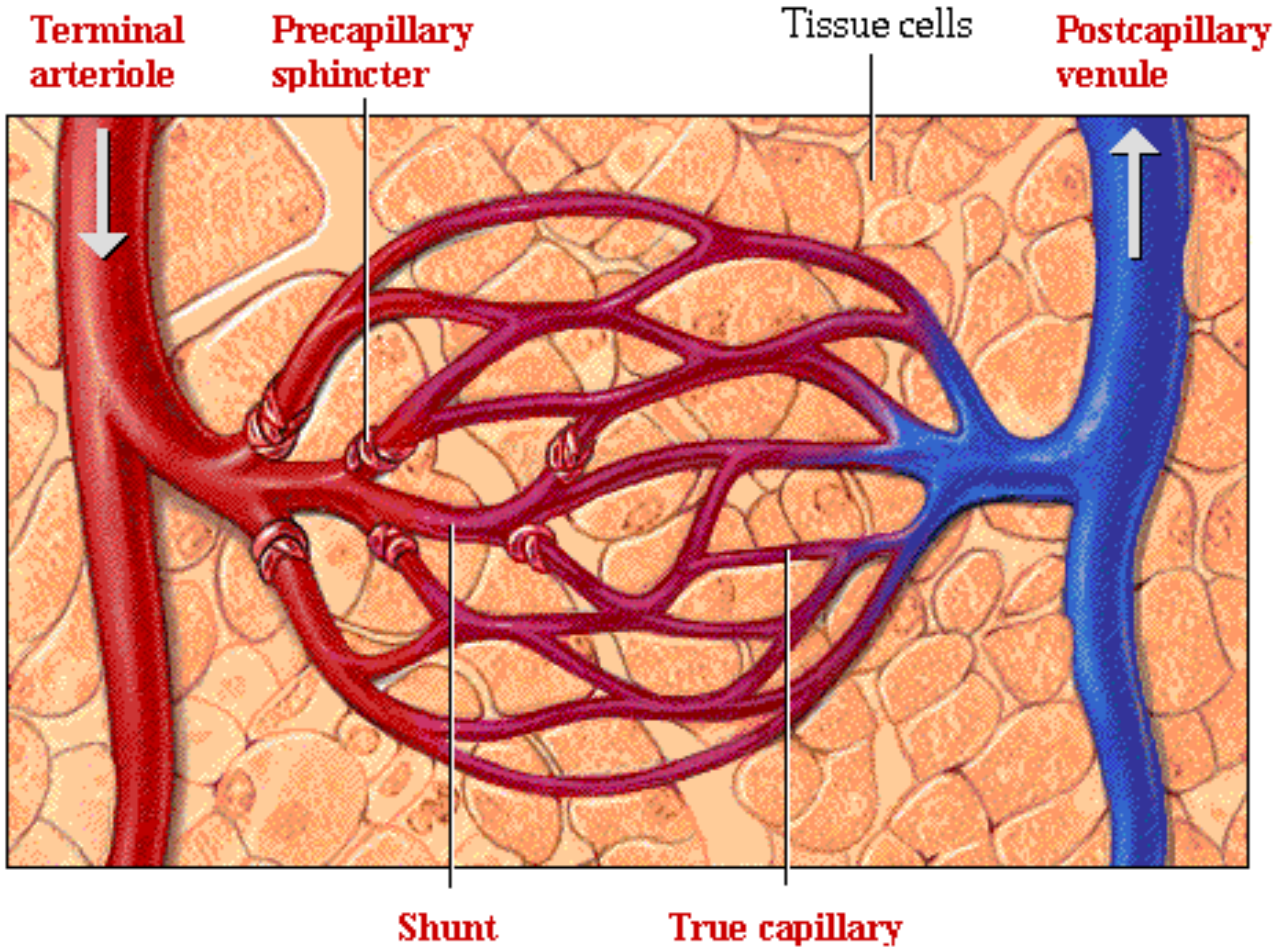


7

Local Control of Blood Flow

Local Control of Blood Flow

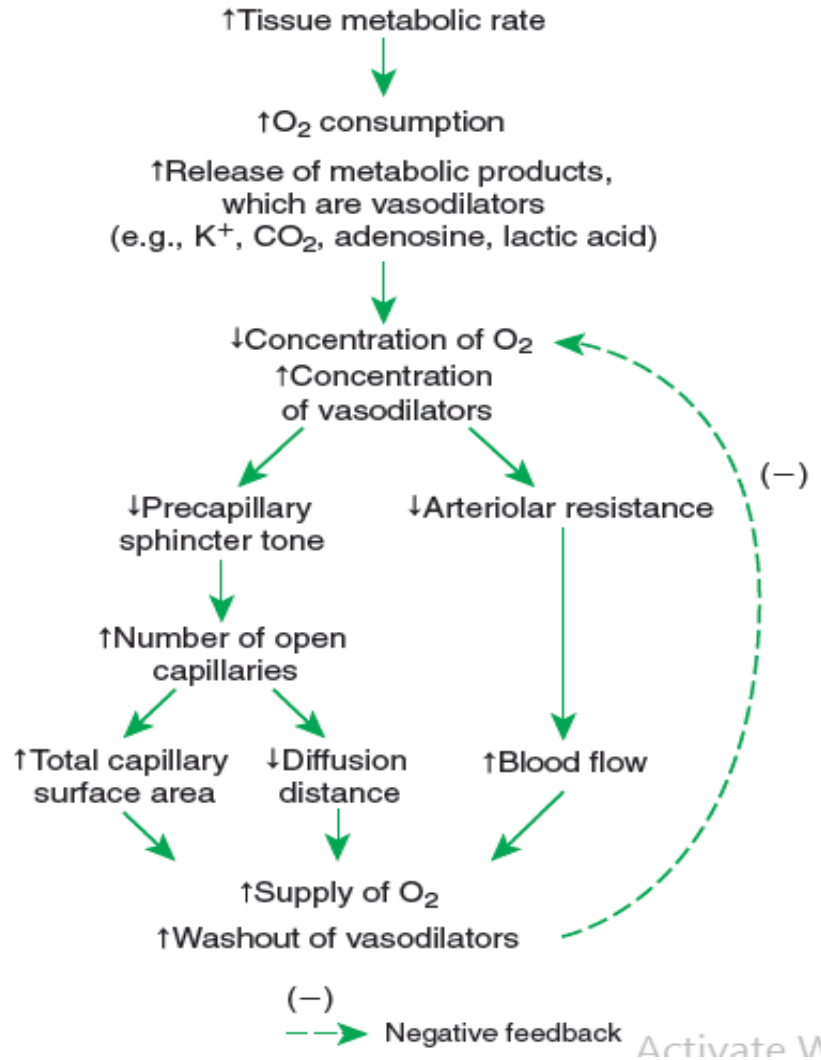
Blood flow regulation occurs at arterioles and within capillary beds.



Metabolic Control of Blood Flow

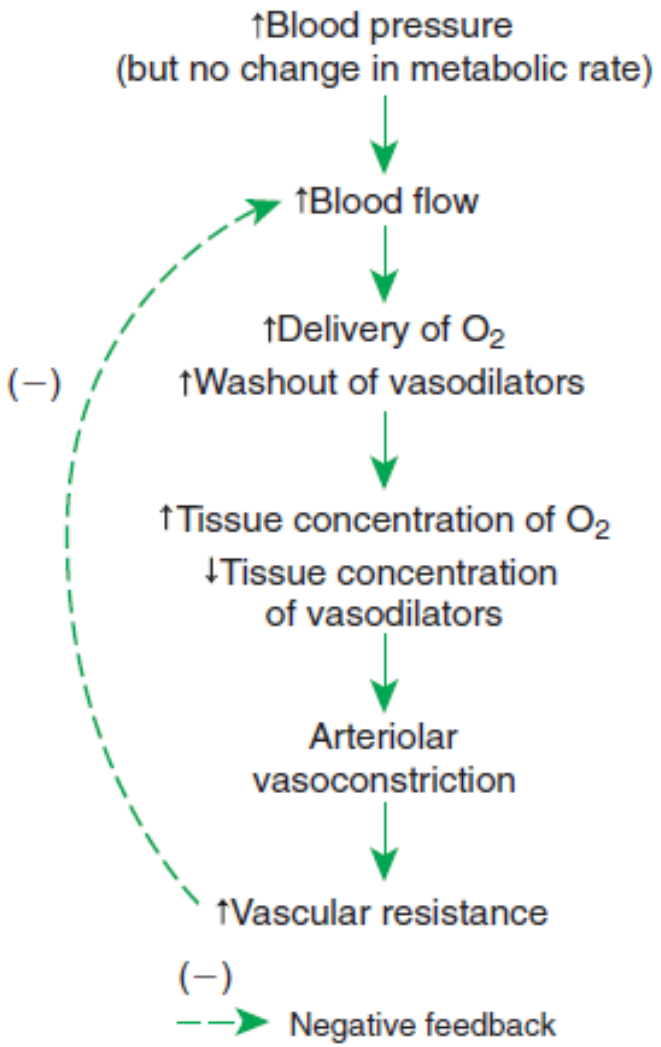
- Metabolic control of blood flow is a local (intrinsic) mechanism that acts within a tissue to match the blood flow to the tissue with the metabolic activity of the tissue.

- As a tissue becomes more active metabolically, the metabolic control mechanism increases blood flow and thereby regulates the concentration of oxygen and metabolic products in the tissue.



Autoregulation of Blood Flow

- The same metabolic mechanism that is responsible for active hyperemia and reactive hyperemia can also account for autoregulation, in which blood flow to an organ stays relatively constant despite changes in perfusion pressure.



Good Luck