

Cardiovascular Physiology - Lange

#11_Cardio

Chapter 1 - Overview of the Cardiovascular System

Total body water accounts for approximately 60% of body weight, distributed amongst 3 compartments:

1. intracellular (2/3 of TBW)
2. interstitial
3. plasma

As blood passes through capillaries, solutes exchange between plasma and interstitial fluid through the process of diffusion. This transport occurs over extremely small distances (no cell in the body is located farther than approximately 10 micrometers. Diffusion is a very rapid process. In order to move substances from organ to organ, the process of convection is used (substances move easily along with blood flow).

Regarding functional arrangement of the cardiovascular system ...

- the pulmonary and systemic circulations are arranged in **series** (the right and left hearts must pump an identical volume of blood per minute, i.e. the cardiac output)
- the systemic organs are arranged in **parallel** (nearly all systemic organs receive blood of identical composition, but the flow of blood through any one of the systemic organs can be independently controlled)

Many organs serve to recondition the composition of the blood (e.g. kidneys, skin) and thus can withstand temporary, severe reductions in blood flow. Alternatively, organs like brain, heart muscle and skeletal muscle, on receive blood flow needed to supply the metabolic needs of the tissue, so they do not tolerate reductions in blood flow well.

The basic physics of blood flow

Cardiac output in a resting individual is approximately 5 L/min.

Fluid flows through tube only when there is a pressure difference between the ends. Pressure differences supply the driving force for flow. Friction develops between the moving fluid and the stationary walls of the tube.

Vascular resistance = how much of a pressure difference it takes to make fluid flow through a tube

$$Q = \Delta P / R$$

Poiseuille's equation

$$Q = \Delta P \frac{\pi r^4}{8L\eta}$$

Q = flow rate (volume/ time)

ΔP = pressure difference (mmHg)

r = internal radius of the tube

L= tube length

η = fluid viscosity

There are two ways blood flow through an organ can be changed:

1. Changing the pressure difference across a vascular bed
2. Changing vascular resistance

Small changes in internal radius will have a large influence on resistance to flow. Thus individual organ blood flows are regulated primary through changes in the radius of the vessels within organs, thus resulting in significant changes in vascular resistance. Vessel length and blood viscosity also influence vascular resistance, but are not as easily manipulated for the purpose of moment-to-moment control of blood flow.

Individual resistance to flow exists within each organ, i.e. organs with relatively low resistance receive relatively high flow.

Blood flow through all organs is passive and occurs only because arterial pressure is kept higher than venous pressure by the pumping action of the heart

Requirements for effective operation of the heart

1. The contractions of individual cardiac muscle cells must occur at regular intervals and be synchronized (not arrhythmic)
2. The valves must open fully (not stenotic)
3. The valves must not leak (not insufficient or regurgitant)
4. The muscle contractions must be forceful (not failing)
5. The ventricles must fill adequately during diastole.

Control of the heart and cardiac output

Cardiac output = SV x HR

volume/ minute = volume/ beat x beats/ minute

Systole = phase of cardiac cycle during which ventricular muscle cells are contracting. As soon as the ventricular pressure exceeds the pressure in the pulmonary artery (right heart) or aorta (left heart), the pulmonic and aortic valve open and blood exits and the AV valves close.

Diastole = the ventricles relax and the pressure in the ventricles falls below that in the atrium, the AV valves open and the ventricle fills with blood. The pulmonic and aortic valves are closed because arterial pressure is greater than intraventricular pressure.

Frank Starling's Law of the heart:

As cardiac filling increases during diastole, the volume ejected during systole also increases. So, with other factors being equal, stroke volume increases as end-diastolic volume increase

- This is an intrinsic property of cardiac muscle and is one of the primary regulators of cardiac output
- Dependent on cardiac muscle cell's length-tension relationship

Autonomic Neural influences

All portions of the heart are richly innervated by **adrenergic sympathetic fibres**. When active, these nerves release **norepinephrine** and interact with **β1-adrenergic receptor** on cardiac muscle cells to increase the heart rate, increase the action potential conduction velocity and increase the force on contraction and rates of contraction and relaxation.

Cholinergic parasympathetic fibres travel to the heart via the **vagus nerve** and innervate the SA node, AV node and atrial muscle. When active, parasympathetic nerves release **acetylcholine**, which interacts with **muscarinic receptors** to decrease the heart rate (SA node), decrease the action potential conduction velocity (AV node) and decrease the force of contraction of atrial muscle (not ventricular muscle).






The vasculature

Major vessel classifications:

- ARTERIES:
 - thick-walled vessels that contain some smooth muscle, and a large component of

- elastin and collagen fibres
 - can expand and temporarily store some the blood ejected by the heart during systole, then by passive recoil, supply this blood to the organs downstream during diastole
 - Considered **conduit** vessels as they have relatively low and unchanging resistance to flow
- ARTERIOLES:
 - much smaller than arteries with relatively thicker walls.
 - have more smooth muscle and less elastic material
 - as they are so muscular, their dimensions can be actively changes to regulate blood flow
 - considered **resistance** vessels
- CAPILLARIES:
 - smallest vessels in the vasculature
 - consist of a single layer of endothelial cells
 - contain no smooth muscle thus lack ability to change their diameters actively
 - collective cross-section are is more than 1000x the aortic root
 - considered **exchange** vessels
- VENULES and VEINS:
 - collect and return blood to the heart
 - very thin walls making them very distensible
 - contain smooth muscle allowing for active change in diameter
 - have one valves that prevent reverse flow,
 - contain more than 50% of the total blood volume
 - Considered **capacitance** vessels
 - Changes in venous volume greatly influence cardiac filling and therefore cardiac pumping.

All vessels are lines with a contiguous layer of endothelial cells . The vascular bed is a continuum and the transition from one the of vascular segment to another does not occur abruptly.

	ARTERIES		ARTERIOLES	CAPILLARIES	VENULES	VEINS	
							
	Aorta						Venae cavae
Internal diameter	2.5 cm	0.4 cm	30 μm	5 μm	70 μm	0.5 cm	3 cm
Wall thickness	2 mm	1 mm	20 μm	1 μm	7 μm	0.5 mm	1.5 mm
Number	1	160	5×10^7	10^{10}	10^8	200	2
Total cross-sectional area	4.5 cm^2	20 cm^2	400 cm^2	4500 cm^2	4000 cm^2	40 cm^2	18 cm^2

Blood

Approximately 40% of whole blood volume is occupied by blood cells that are suspended in plasma. The fraction of blood volume occupied by cells is termed **hematocrit**. Red cells are the most abundant cell type. They carry oxygen via an iron-containing heme protein - hemoglobin. Because of hemoglobin, blood can transport 40-50x more oxygen than plasma alone could carry.

Plasma is the liquid component of blood. Serum is the fluid obtained after a blood sample is allowed to clot, i.e. is lacking clotting proteins.

Chapter 2 - Characteristics of Cardiac Muscle Cells

Special characteristics of cardiac muscle

Cardiac muscle cells action potential differs from that of skeletal muscle in 3 important ways:

1. They can be self-generating
2. They can be conducted directly from cell to cell
3. They have a long duration, which precludes fusion of individual twitch reactions

Electrical potentials

All cells have a electrical potential (voltage) across their membranes, i.e. **membrane potential**. The membrane potential changes as current flows across the cell membrane. (i.e. movement of ions). The 3 most important determinants of cardiac membrane potentials are **sodium, calcium** and **potassium**. These electrolytes cannot freely pass through lipid bilayer, and instead use various transmembrane protein structures: **ion channels, ion exchangers** and **ion pumps**.

Ion channels are responsible for the resting membrane potential and rapid change in potential in cardiac cells. Ion channels can be "open", "closed" or "inactivated", resulting in altered *permeability* to certain ions. i.e. high permeability to sodium implies that sodium ion channels are open in that moment.

Diffusion potential: potential difference generated across a membrane because of the concentration difference of an ion. A diffusion potential can only be generated if the membrane is permeable to that ion.

Equilibrium potential: the diffusion potential that exactly balanced (opposes) the tendency for diffusion caused by a concentration difference, i.e. when the membrane potential has this value, there is no net movement of the ion across the membrane. The **Nernst equation** is used to calculate equilibrium potentials.

- Potassium equilibrium potential = -90 mV
- Sodium equilibrium potential = + 70 mV
- Calcium equilibrium potential = + 100 mV

Real cell membranes are never permeable to just one electrolyte, and thus real membrane potentials will lie somewhere between the Na⁺ and K⁺ equilibrium potential. What membrane potential exists at any given moment depends on the relative permeability of membrane to both K⁺ and Na⁺. When the membrane is more permeable to K⁺, the membrane potential will be close to -90 mV, and when the membrane is more permeable to Na⁺, the membrane potential will be close to + 70 mV.

At resting states, the heart muscle cells have potentials close to the potassium equilibrium potential, thus the concentration gradients favour inward movement of Na⁺ and Ca⁺. However the resting cell membrane has low permeability to both Na⁺ and Ca⁺, and also has a Na⁺ pump that keeps Na⁺ out of the cell.

Resting membrane potential: potential difference across a cell membrane in mV, expressed as the intracellular potential relative to the extracellular potential. The RMP is

established by diffusion potentials; thus the ion with the highest permeability will make the greatest contribution to the RMP. The Na⁺/K⁺ pump contributes to the RMP indirectly by maintaining the concentration gradients that then produce diffusion potentials.

Cardiac Cell Action Potentials

Ventricular myocytes

Ordinary **cardiac myocytes** generally cannot spontaneously initiate an action potential and have a **“fast-response” action potential**. These action potentials are very **long duration**.

Fast-response action potential (cardiac muscle):

- **phase 0 = rapid depolarization** with substantial overshoot (positive inside voltage)
 - opening of voltage-gated fast Na⁺ channels
- **phase 1 = rapid reversal of the overshoot potential**
 - initial brief depolarization
 - less Na⁺ conductance due to closure of Na⁺ channels
 - transient outward K⁺ current (iTO)
- **phase 2 = long plateau**
 - slowly developed and prolonged opening of voltage-gated Ca⁺ channels, allowing inward Ca⁺ movement
 - action of Na⁺/Ca⁺ exchanger in which 3 Na⁺ ions move into the cell in exchange for a single Ca⁺ ion moving out
- **phase 3 = repolarization**
 - delayed increase in K⁺ permeability, resulting in high outward K⁺ current
 - closure of the Ca⁺⁺ and Na⁺ channels
- **phase 4 = stable, high (large negative) RMP**
 - resting membrane potential
 - period during which inward and outward current are equal

Pacemaker cells

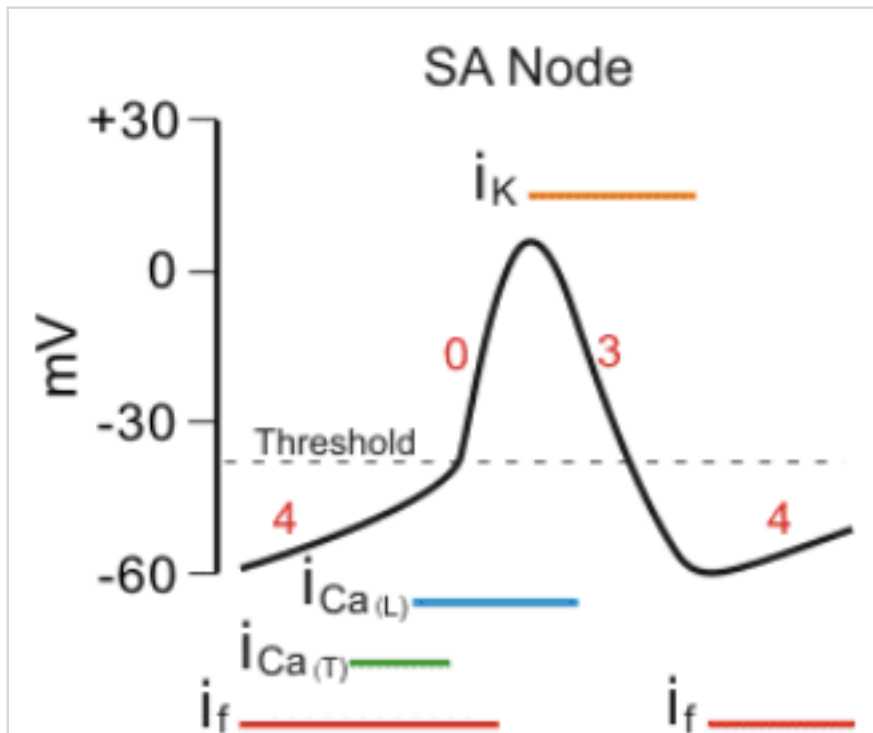
Pacemaker cells (found primarily in SA, AV node, Purkinje cells):

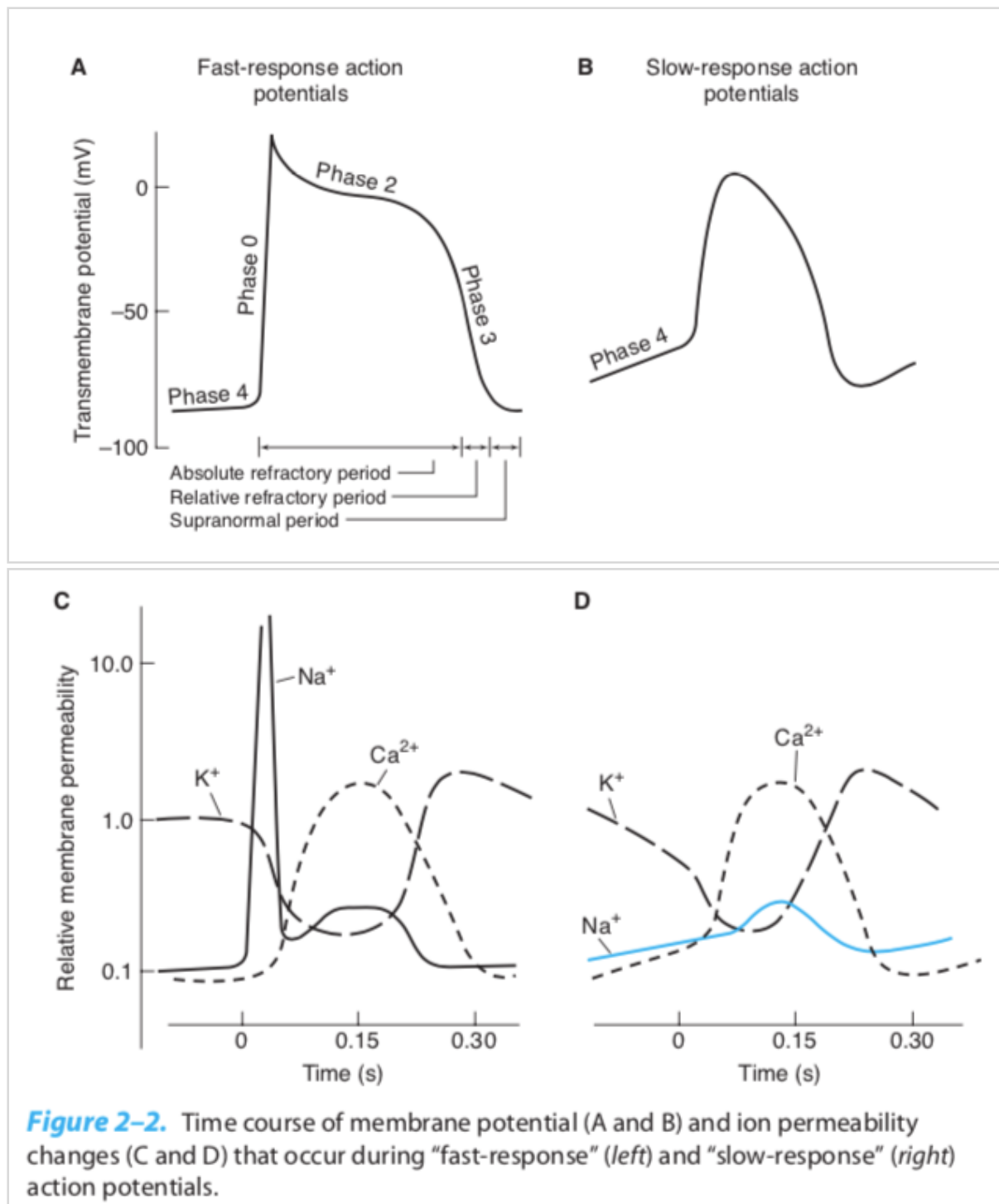
- cardiac muscle cells that can spontaneously initiate an action potential
- have **“slow-response” action potentials**

Slow-response action potential (pacemaker cells):

- **phase 4 = slow depolarization**
 - depolarization to an unstable, slowly depolarizing “resting” potential referred to as phase 4 depolarization, diastolic depolarization or pacemaker potential
 - occurs due to:

- conductance carried by “funny” channels (I_f)
 - funny current is turned on by repolarization of the membrane potential during the proceeding action potential
 - slight increase in permeability to Na^+ and Ca^{2+}
- progressive decrease in membrane’s permeability to K^+ during the resting phase
- **phase 0 = depolarization**
 - slower initial depolarization phase with lower amplitude overshoot
 - primarily a result of inward movement of Ca^{2+} ions
- **phase 3 = repolarization**
 - shorter and less stable plateau phase
 - increase in K^+ conductance, resulting in outward K^+ current
- phases 1 and 2 are not present





Cells are in an **absolute refractory period** for most of the action potential (i.e. they cannot be stimulated to fire another action potential). Near the end of the potential, the membrane is **relatively refractory** and can be re-excited only by a larger than normal stimulus. Immediately after the action potential, the membrane is transiently hyper excitable and is said to be in a "vulnerable" or "**supernormal**" period. Similar alteration in membrane excitability occur during slow action potentials.

The overall smoothly graded permeability changes that produce action potentials are the net result of alterations in each of the many individual ion channels within the plasma

membrane of a single cell. These ion channels may be voltage or ligand gated.

Cardiac conduction system

Certain cardiac muscle cells are adapted to control the frequency of cardiac excitation, the pathway of conduction, and the rate of impulse propagation through various regions of the heart...

1. Sinoatrial node

- Initiates the action potential and functions as the pacemaker
- Spontaneous electrical pacemaker activity (automaticity) of cells in the SA node results in normal rhythmic contractions
- Intrinsic rate of ~100 beats/minute in the absence of any outside influences

2. Atrioventricular node

- slowly conducting cells that function to create a slight delay between atrial contraction and ventricular contraction
- referred to as the latent pacemaker

3. Bundle of His

4. Right and left bundle branches

- made up of Purkinje fibres - specialized for rapid conduction ensuring that all ventricular cells contract at nearly the same instant

Control of Heart Rate

Autonomic nervous system can alter the course of spontaneous depolarization of the resting potential in the pacemaker cells

Sympathetic - increased heart rate

- neurotransmitter = norepinephrine
- increases inward currents carried by Na^+ (if) and Ca^{2+} during diastolic interval (increases rate of diastolic depolarization)

Parasympathetic - slows the heart rate

- via vagus nerve, neurotransmitter = acetylcholine
- increases permeability of the resting membrane to K^+ (hyperpolarize) and decreases the diastolic permeability to Na^+ (slows rate of spontaneous depolarization)
- tonic activity of the vagus nerve results in an average resting heart rate of approximately 70 beats/min

Number of other factors that can influence heart rate (positive or negative chronotropic effect): ions, circulating hormones, temperature, atrial wall stretch. All act through altering the time required for the resting membrane potential to depolarize the threshold potential

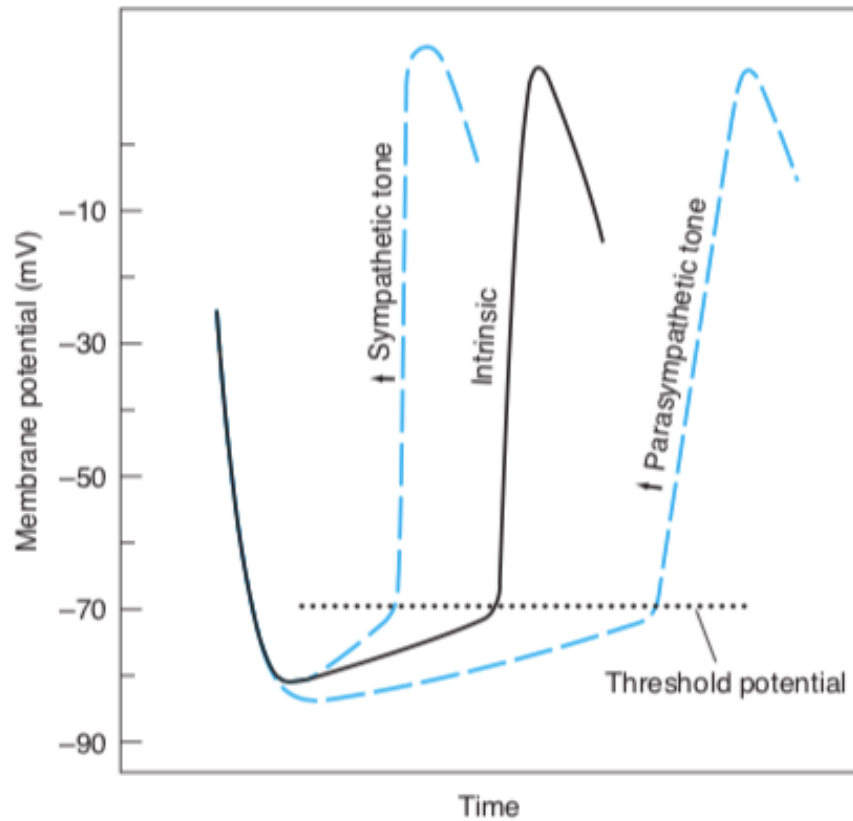


Figure 2-6. The effect of sympathetic and parasympathetic tone on pacemaker potential.

Autonomic fibres also influence the **conduction velocity** of action potential - sympathetic activity has a positive **dromotropic effect**, whereas parasympathetic activity has a negative dromotropic effect. These effects are most notable at the **AV node and can influence PR interval**. This is primarily achieved through alteration in the conductivity of gap junctions.

Mechanical activity of the heart

Cardiac muscle cells are histologically similar to skeletal muscle. They contain:

1. **sarcomeres:** parallel interdigitating thick and thin filaments arranged in serial units to make an extensive myofibrillar structure, allowing for shortening
2. **sarcoplasmic reticulum:** intracellular membrane forming a complex internal compartmentalization of the cytoplasm; sequesters calcium
3. **T-tubules:** regularly spaced, extensive invaginations of the sarcolemma (cell membrane) that carry action potential signal to the inner parts of the cells
4. Large number of **mitochondria** to provide oxidative phosphorylation needed to supply ATP and meet the high metabolic demands of cardiac muscle

Cardiac muscle is connected by end-to-end structures called **intercalated disks**. These disks contain:

1. **Desmosomes:** firm mechanical attachments between cell membranes
2. **Gap junctions:** Low-resistance electrical connections between adjacent cells formed by proteins called connexin. Allow for the heart to act as a **functional syncytium**

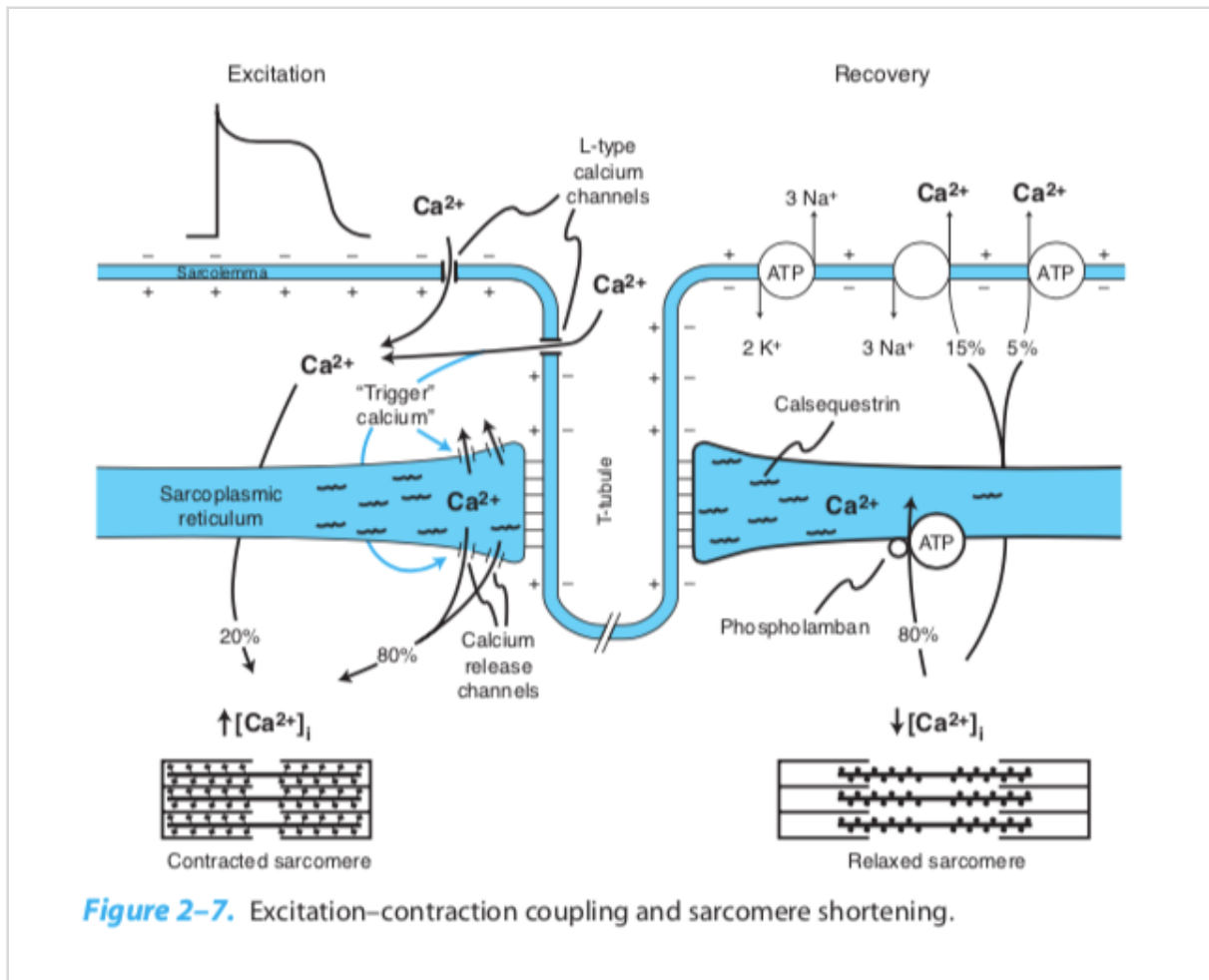
Excitation-Contraction Coupling

- When an action potential meets sarcolemma, a wave of depolarization passes down the T-tubule system
- calcium enters the cells via L-type calcium channels
- Increase in Ca^+ concentration just under the sarcolemma triggers a massive release of Ca^+ from the sarcoplasmic reticulum (**calcium-induced calcium release**)
- dramatic rise in intracellular free Ca^+
- Calcium binds with troponin C, releasing inhibition of actin
- cross-linking between myosin and actin (requires ATP)
- sliding of thick and thin filaments over one another
- termination of contraction: calcium is taken back up into the sarcoplasmic reticulum mostly through Ca^{++} ATPase pumps (SERCA); some is extruded into the extracellular fluid via Na^+ - Ca^+ exchanger or Ca^+ ATPase pumps in the sarcolemma

Excitation-contraction coupling is different from that in skeletal muscle:

1. it may be modulated (i.e. contractility!) - different intensities of actin-myosin interaction can result from a single action potential (largely dependent on variations in the amount of Ca^{++} reaching the myofilaments)
2. duration of cardiac muscle contraction is approximately the same as the action potential; therefore the refractory period is not over until the mechanical response is completed. This ensures that heart muscle cells cannot form fused contractions and enter state of tetanus.

Muscles, part 1 - Muscle Cells: Crash Course A&P #21 - YouTube



Isometric contraction: contraction without an appreciable decrease in the length of the whole muscle, i.e. fixed length

Isotonic contraction: contraction against a constant load with a decrease in muscle length, .e. fixed tension

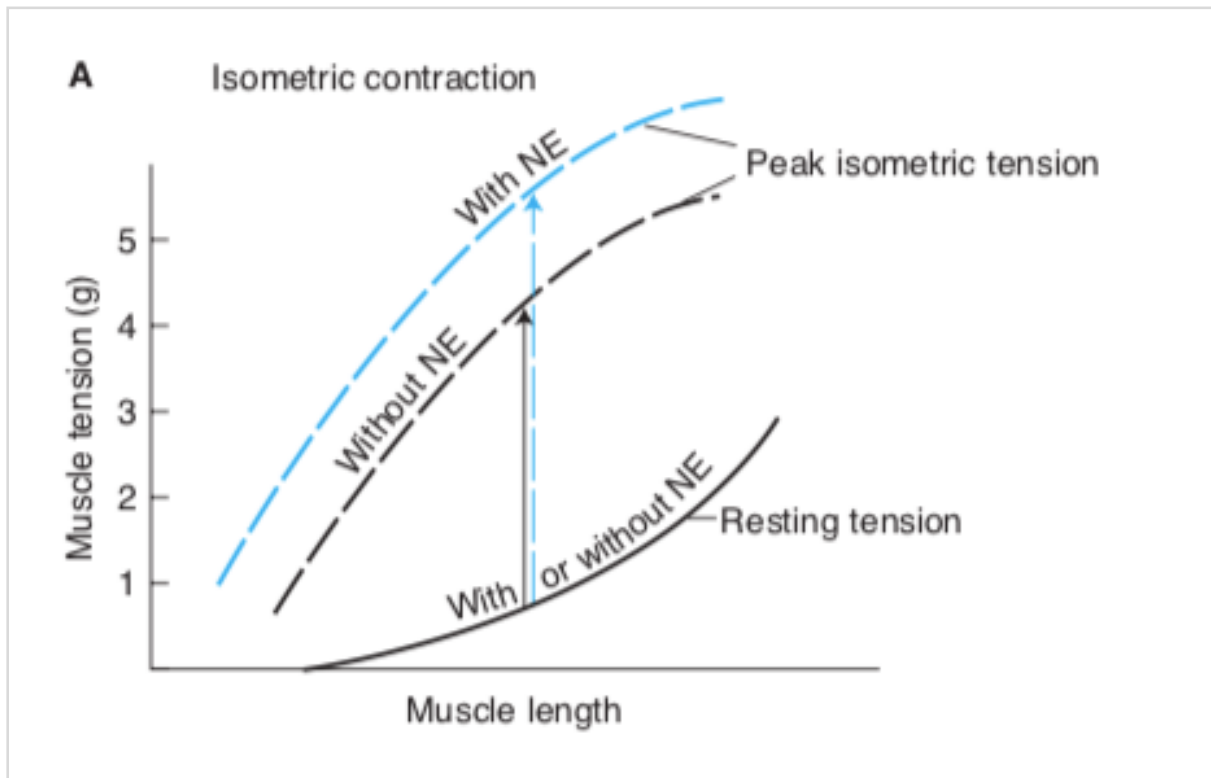
Positive inotropic effect: any intervention that increases the peak isometric tension that a muscle can develop at a fixed length

The most important regulator of cardiac muscle contractility (**inotropy**) is **norepinephrine**

- allows for development of more isometric tension at every length
- mediated through interaction with β 1-adrenergic receptor
 - activation of G protein-cAMP-protein kinase A, which phosphorylates Ca⁺⁺ channel, and increases inward calcium current during the plateau of the action potential → allows more cross-bridges to be formed and greater tension to develop

- also increases activity of sarcoplasmic reticular Ca^{++} -ATPase pump, increasing rate of calcium reuptake in the SR and thus enhanced rate of relaxation (**positive lusitropic effect**)
 - shortens action potential duration by increasing K^+ permeability, allowing for earlier termination of the plateau phase, preventing compromise of diastolic filling time at higher heart rates

Parasympathetic negative inotropic effect is small, mediated through decrease in the amount of Ca^{++} that enters the cells during the action potential



Staircase phenomenon/ homeometric auto regulation: increase heart rate will result in a progressive increase in contractility to a higher plateau. As heart rate increases, more calcium enters the cells per minute (during plateau phase), resulting in buildup of intracellular calcium and greater amount of Ca^{++} release into the sarcoplasm during each action potential.

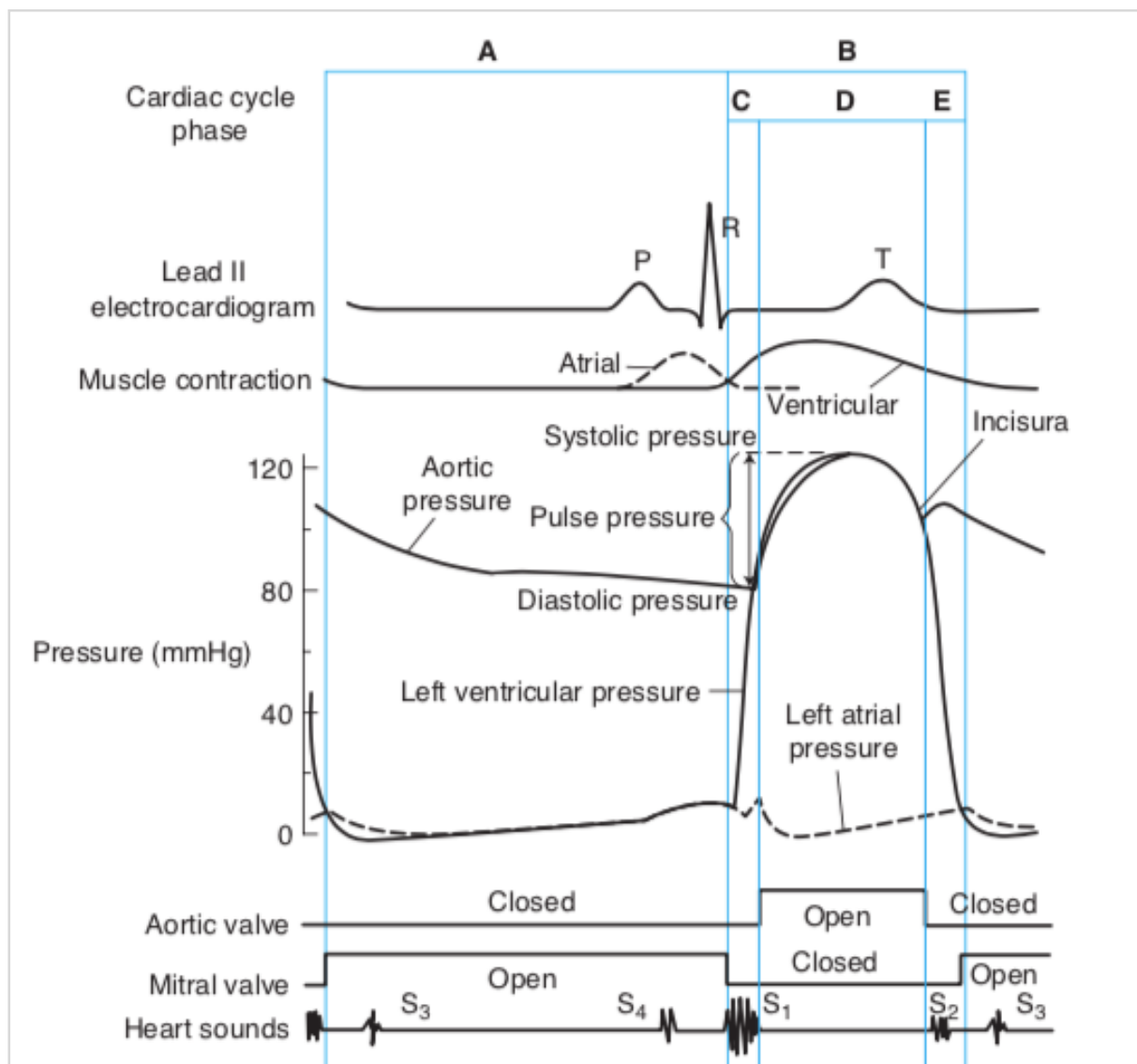
Summary of sympathetic neural influences on cardiac function

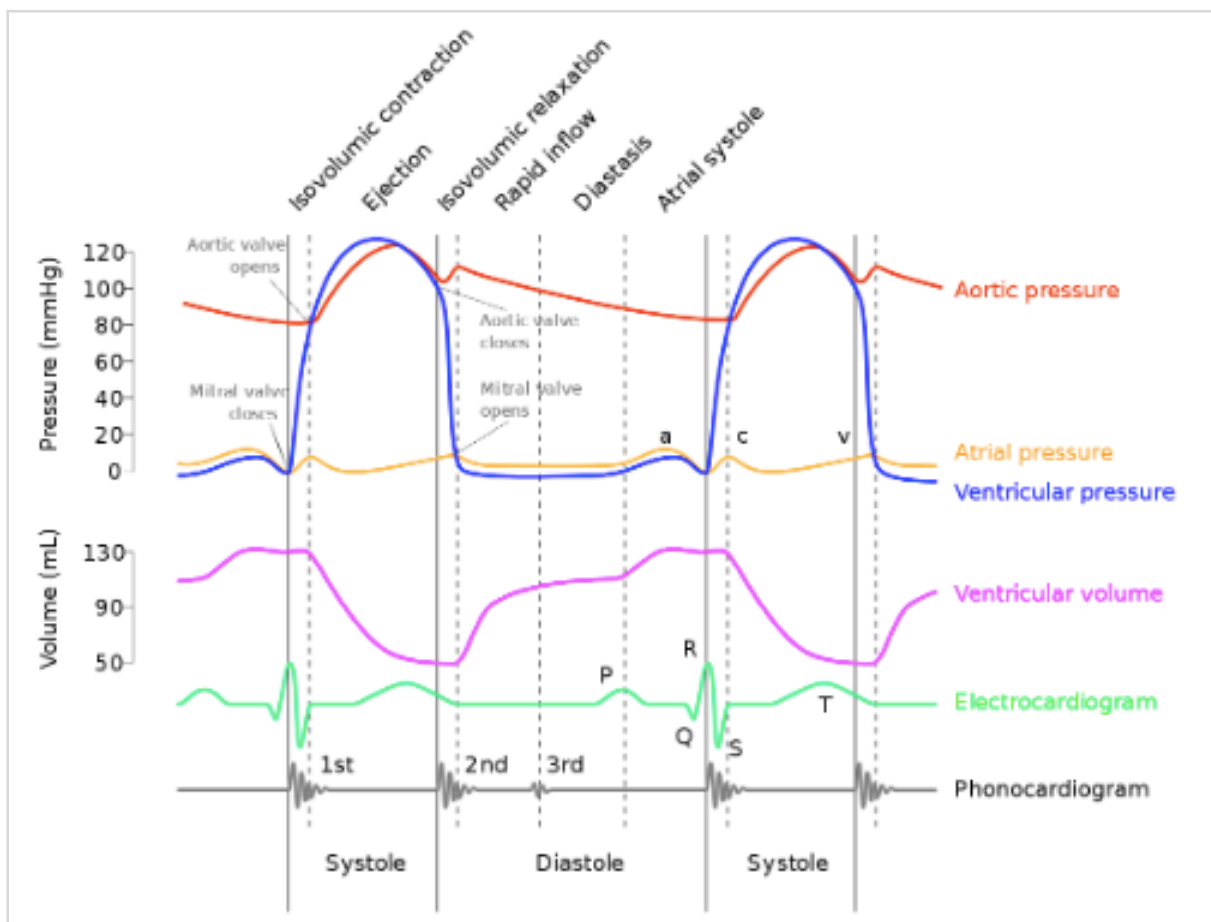
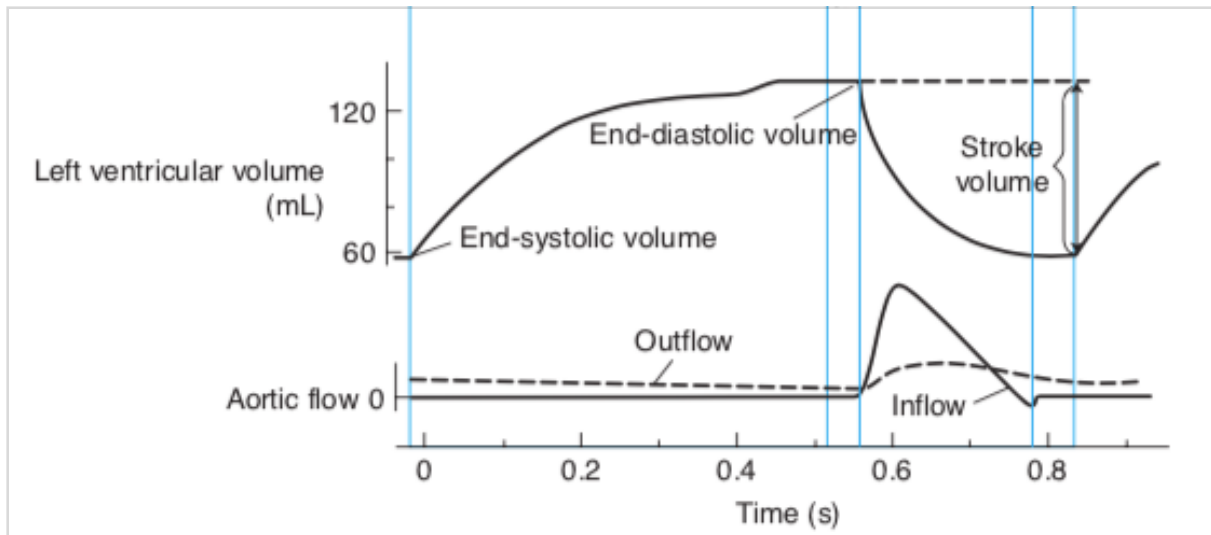
1. An increase in the heart rate (positive chronotropic effect) by activating the inward-going sodium if current in SA nodal cells
2. A decrease in cardiac action potential duration by early activation of the delayed iK current in cardiac myocytes, which minimizes the detrimental effect of high heart rates on diastolic filling time
3. An increase in the rate of action potential conduction, particularly evident in the AV node

(positive dromotropic effect) by altering conductivity of gap junctions

4. An increase in cardiac contractility (positive inotropic effect) by activating the iCa^{2+} current and increasing Ca^{2+} release from the sarcoplasmic reticulum, which increases the contractile ability of the cardiac muscle at any given preload
5. An increase in the rate of cardiac relaxation (positive lusitropic effect) by increasing Ca^{2+} uptake by the sarcoplasmic reticulum, which also helps minimize the detrimental effect of high heart rates on diastolic filling time

Chapter 3 - The Heart Pump





Diastole

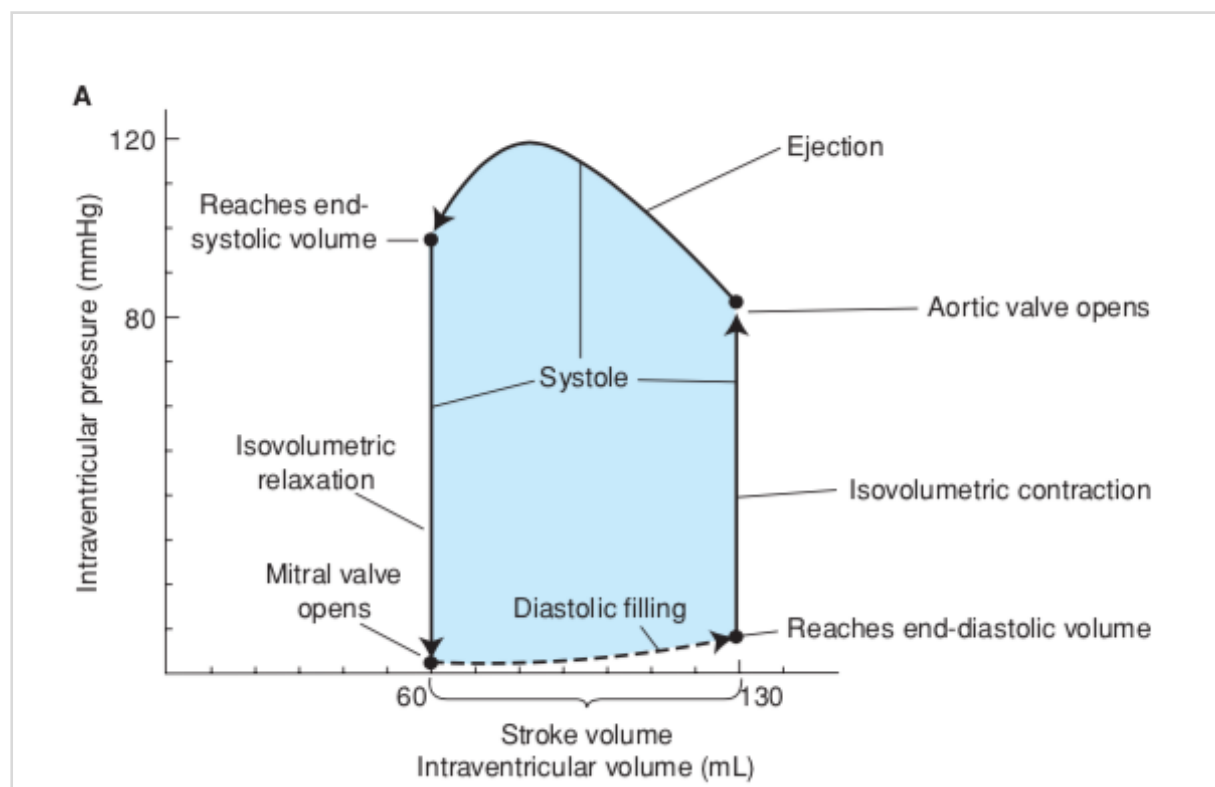
Diastole begins with opening of the AV valves when ventricular pressure falls below the atrial pressure. Previously accumulated blood in the atrium rapidly empties into the ventricles, causing initial drop in atrial pressure. Then the pressures in both chambers rise slowly together during passive filling.

Atrial contraction is initiated near the end of ventricular diastole, resulting in atrial kick. The ventricle has nearly reached its end diastolic volume even before atrial contraction at

normal heart rates. At **high heart rates**, the time interval for passive filling becomes progressively shorter and the atrial kick becomes more relevant.

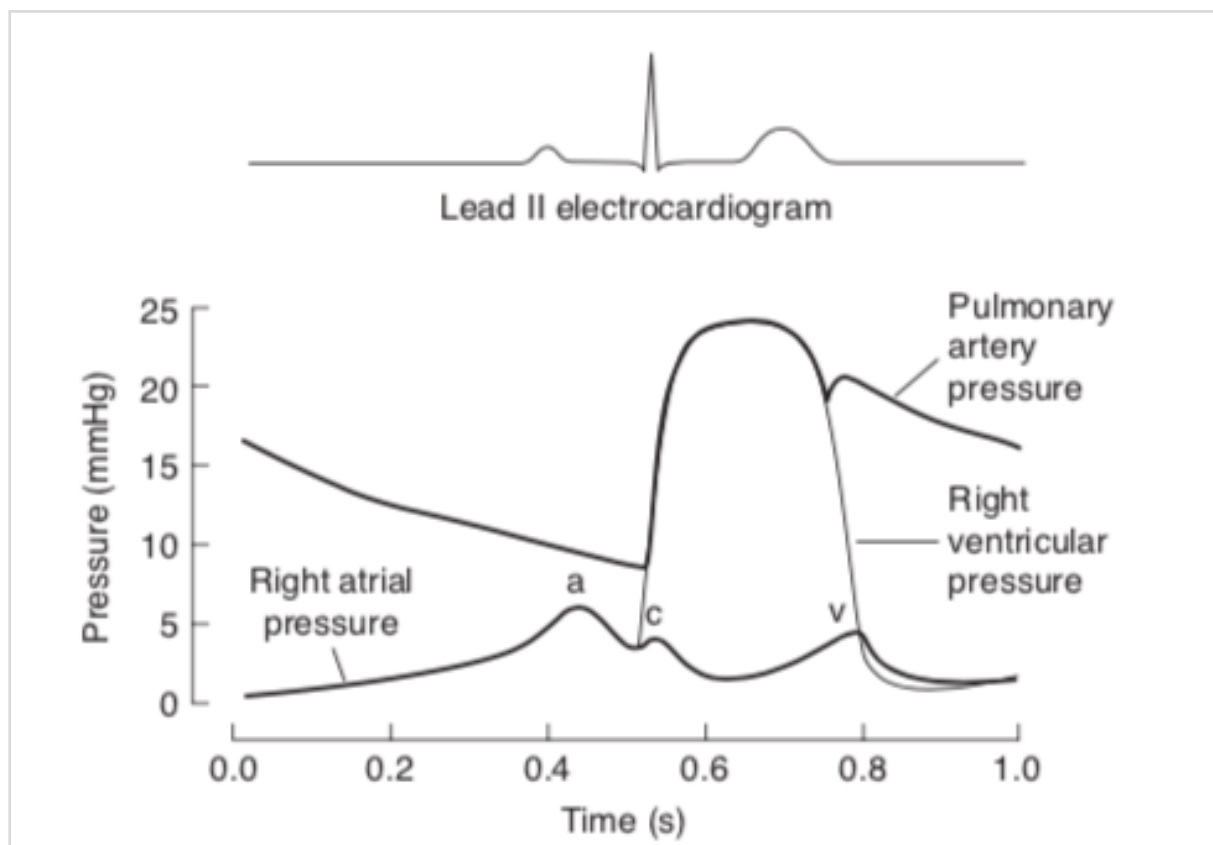
Systole

Once the action potential breaks through the AV node, the pressure in the left ventricle rises sharply. When pressure exceeds that in the aorta, the aortic valve opens. The period between mitral valve closure and aortic valve opening is **isovolumetric contraction**. When the aortic valve opens, blood rushes into the aorta rapidly and causes the pressure there to rise. Once peak systolic pressure is reached, ventricular muscle contraction slows and eventually the intraventricular pressure falls below the aortic pressure. The aortic valve closes abruptly and creates the **incisura/ dicrotic notch** (small volume of aortic blood flows backwards to fill the aortic valve leaflets as they close). After the aortic valve closes, the intraventricular pressure falls rapidly while the mitral valve is still closed, which is **isovolumetric relaxation**. Once the intraventricular pressure falls below atrial pressure, the AV valves open and a new cardiac cycle begins.

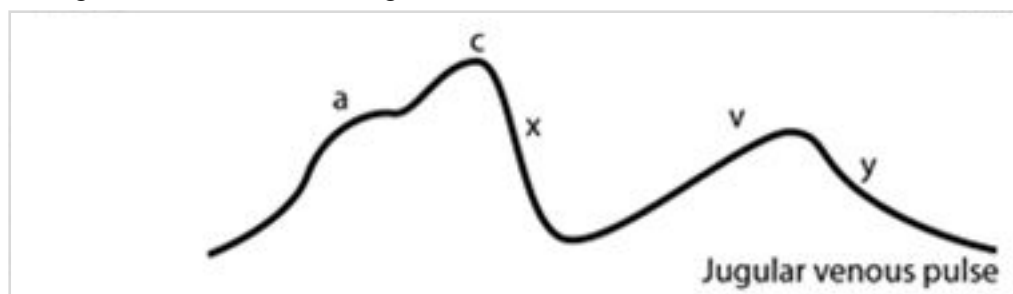


Right heart

The major difference between the right and left pumps is the magnitude of the peak systolic pressure. The pressures developed by the right side of the heart are considerably lower than for those on the left side of the heart. This is because the lungs provide considerably less resistance to blood flow than the systemic organs do. Typically pulmonary arterial systolic pressure is 24 mmHg and diastolic pressure is 8 mmHg.



Jugular Venous Pulse = pressure pulsations that occur in the right atrium are transmitted in retrograde fashion to the large veins near the heart



- a wave: atrial contraction
- c wave: ventricular contraction (causes an initial bulging of the tricuspid valve into the right atrium)
- x: atrial relaxation and downward displacement of the tricuspid valve during ventricular emptying
- v wave: late systole, right atrium begins to fill behind a closed tricuspid valve
- y: diastole, opening of the tricuspid valve and right ventricle fills

Length-Tension relationship

Each phase of the cardiac cycle has a corresponding phase of cardiac muscle length and tension change.

Heart Sounds

S1: abrupt closure of the AV valves at the beginning of systole

S2: closure of aortic and pulmonic valves at the beginning of isovolumetric relaxation

- inspiration (decreased intrathoracic pressures) can cause physiologic splitting of the second heart sound due to a slight delay of the pulmonic valve closing after the aortic valve

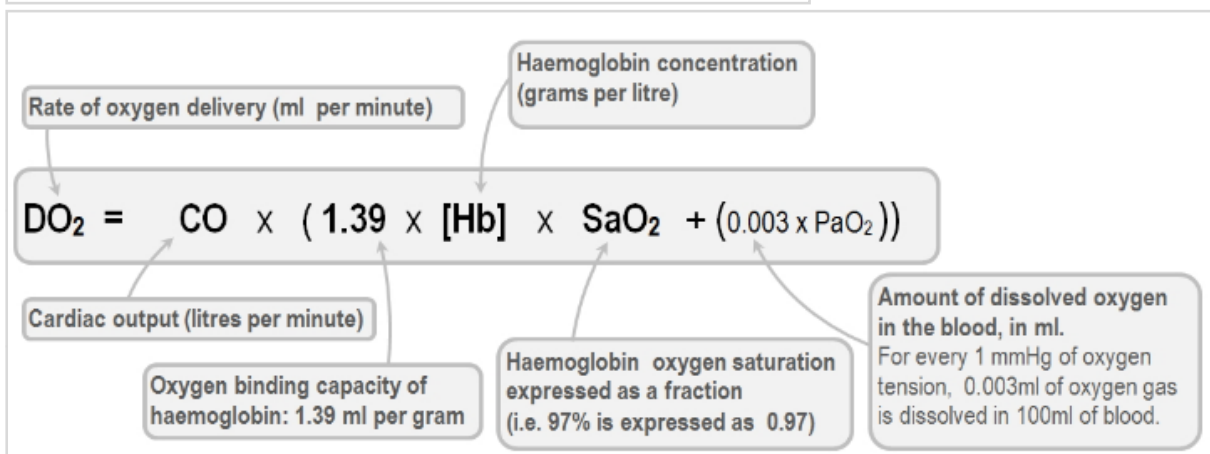
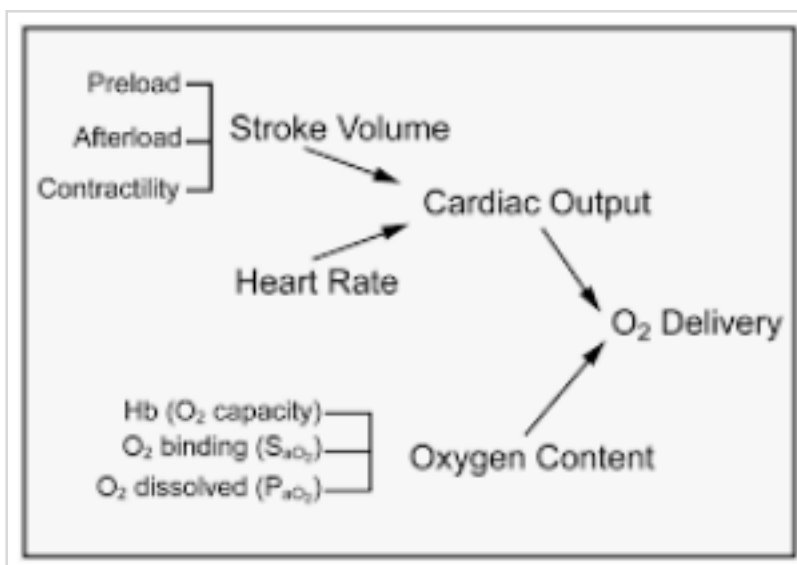
S3 and S4: not normally present, create gallop rhythm when present. S3 refers to a ventricular gallop (during period of rapid passive ventricular filling). S4 refers to an atrial gallop rhythm (during atrial contraction and rapid active filling of the ventricle).

Cardiac Output

Cardiac output refers to the litres of blood pumped by each of the ventricles per minute.

Cardiac output = heart rate x stroke volume

Stroke volume = contractility + preload + afterload



Preload

End-diastolic ventricular pressure is referred to as ventricular **preload** because it sets the end-diastolic ventricular volume and therefore the resting length of the cardiac muscle fibres at the end of diastole.

Increasing muscle preload will increase the extent of shortening during a subsequent contraction with a fixed total load, due to the length-tension relationship that exists in cardiac muscle.

♥ Frank Starling's Law of the Heart ♥

Stroke volume increases as cardiac filling increases.

i.e. increases in **preload (cardiac filling pressure)** will result in increased end-diastolic volume and stroke volume.

Afterload

Mean systemic arterial pressure is referred to as **afterload** because it determined the tension that muscle be developed by cardiac muscle fibres before they can shorten.

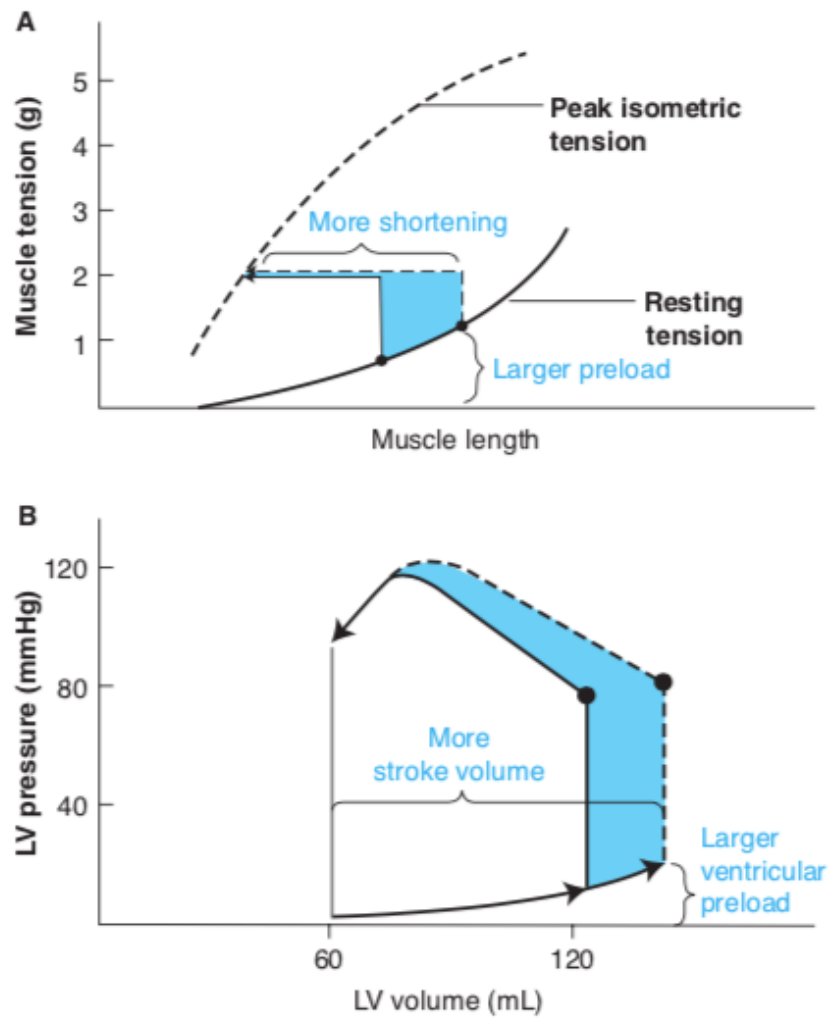


Figure 3-4. The effect of increased in preload on (A) cardiac muscle shortening during afterloaded contractions and (B) ventricular stroke volume.

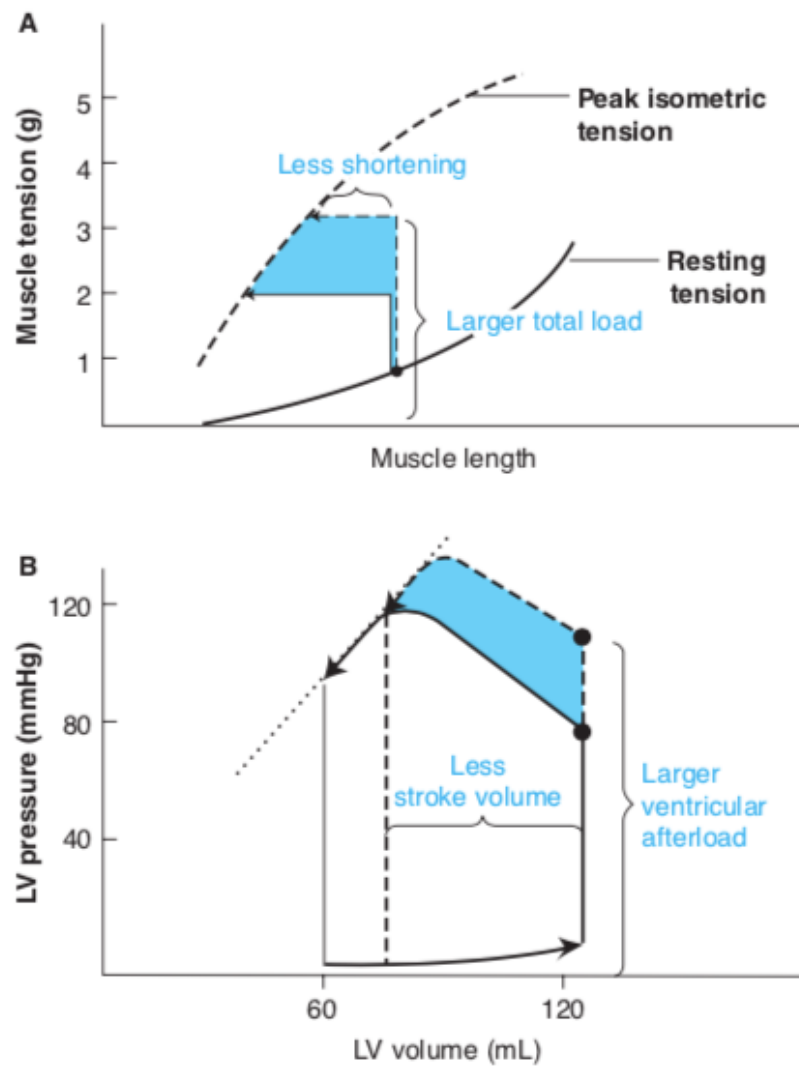


Figure 3-5. The effect of increased in afterload on (A) cardiac muscle shortening during afterloaded contractions and (B) ventricular stroke volume.

Cardiac Contractility

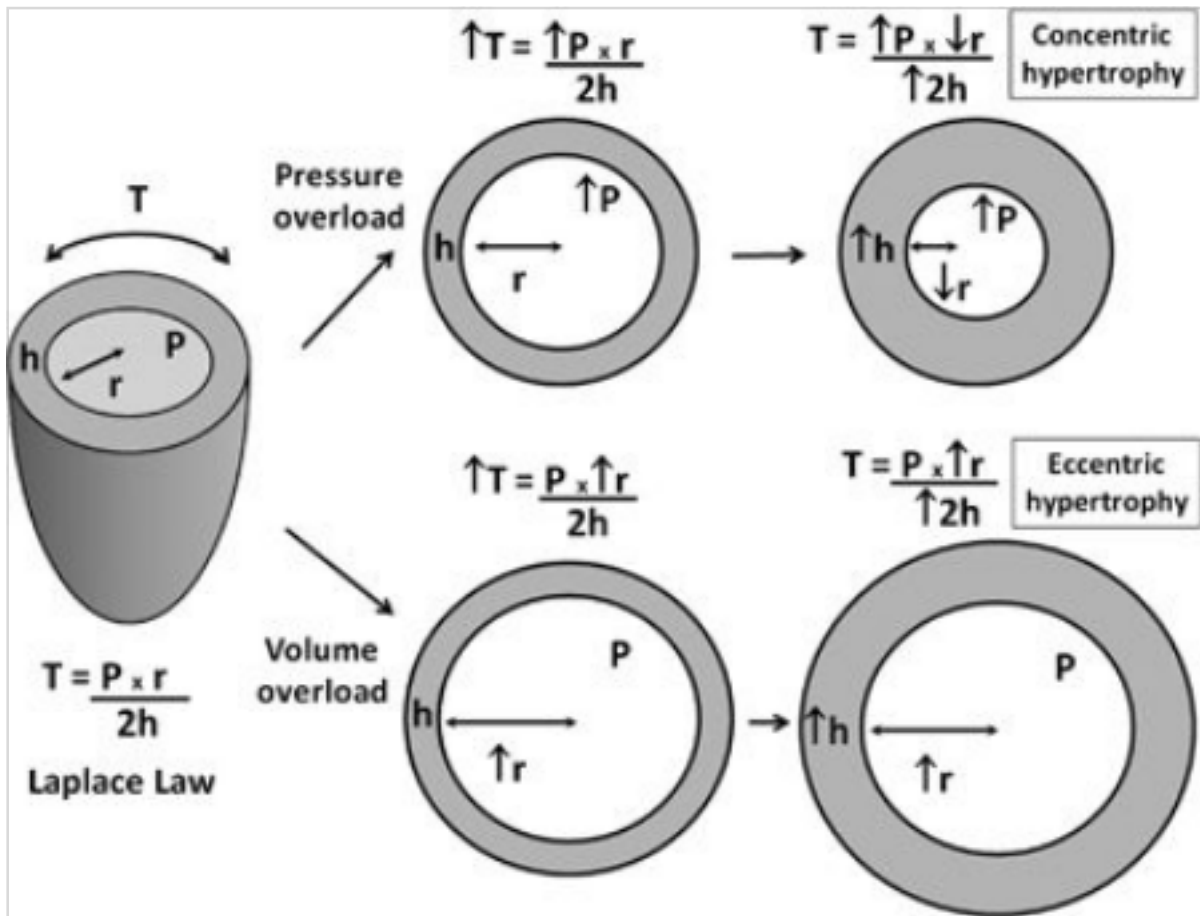
Increased SNS activation results in increased norepinephrine release and increase contractility of individual cardiac muscle cells.

Myocardial oxygen demand

The energy expended during the isovolumetric contraction phase of the cardiac cycle accounts for about 50% of total myocardial oxygen consumption. The energy needed for isovolumetric contraction depends heavily on the intraventricular pressure (more specifically the **isometric wall tension/ stress**) that must develop during this time. Thus, cardiac afterload is a major determinant of myocardial oxygen consumption, and reductions in after load are especially helpful in reducing myocardial oxygen requirements.

Law of Laplace

Wall stress = pressure x radius / 2(thickness of the walls)

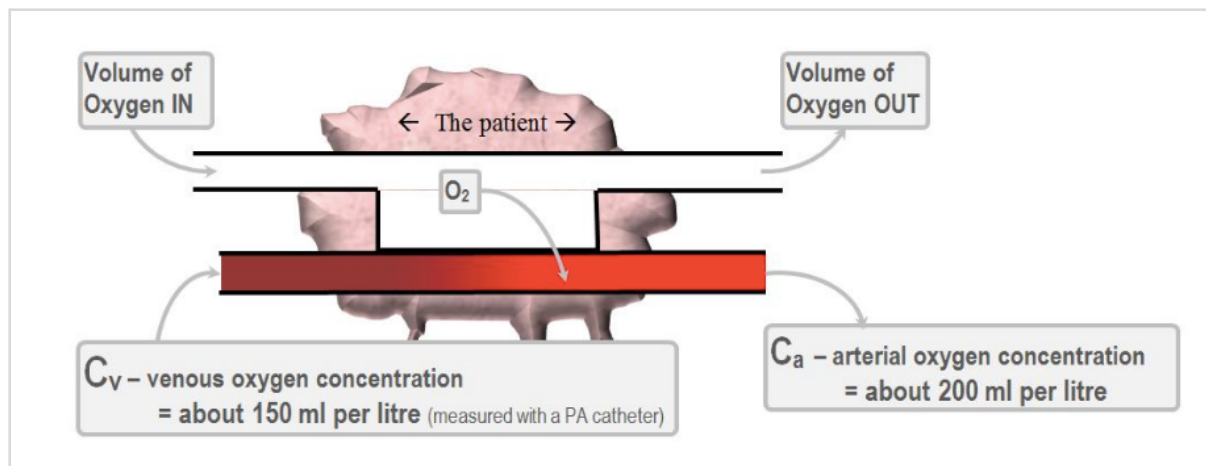


Heart rate is also an important determinant of myocardial oxygen consumption. In general, it is more efficient to achieve a given cardiac output with a low heart rate and high stroke volume than with a high heart rate and low stroke volume.

Chapter 4 - Measurements of Cardiac Function

Measurement of cardiac output

Fick principle is one of the most accurate methods of measuring cardiac output. This principle uses the whole body oxygen consumption rate, the oxygen concentration in arterial blood, and the oxygen concentration in mixed venous blood.



$$CO = \frac{VO_2}{C_a - C_v}$$

Fick's Principle of cardiac output measurement | Deranged Physiology

Other methods of determining cardiac output include **dye or thermal dilution**

- a known quantity of dye or heat is rapidly injected into the blood as it enters the right side of the heart, and detectors are used to measure the amount of indicator in the blood as it leaves the left side of the heart

Cardiac index: cardiac output correct for an individual's size

Cardiac output is usually expressed per body surface area rather than weight. In humans, cardiac index is approximately 3 L/min per m²

Ejection Fraction

Ejection fraction can be calculated from an echocardiogram and is a useful index of cardiac contractility (generally expressed as a percentage).

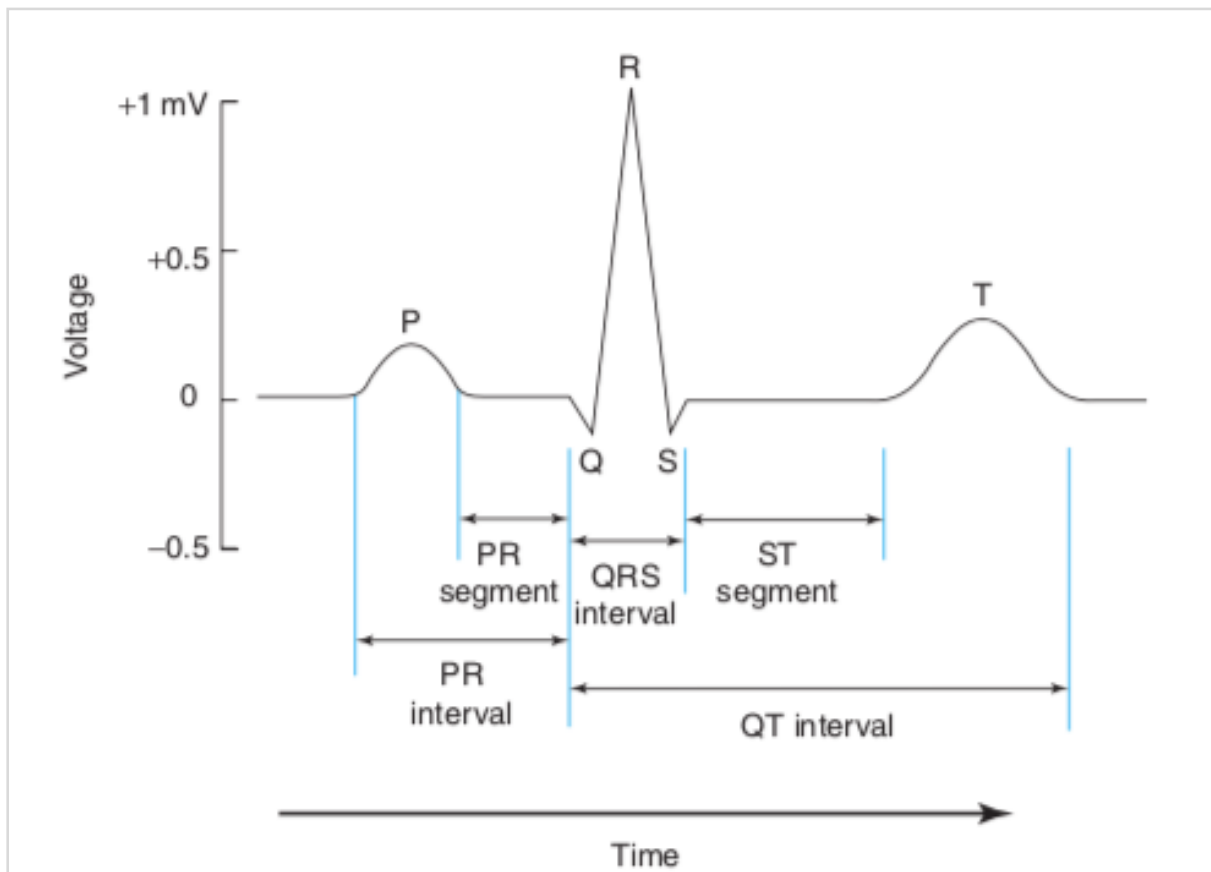
Ejection fraction = Stroke volume/ end diastolic volume

$$FS\% = \frac{LVID \text{ (diastole)} - LVID \text{ (systole)}}{LVID \text{ (diastole)}} \times 100$$

In general, normal FS% is 28%–45% in the dog and 30%–50% in the cat. A FS% below 20% suggests severe myocardial systolic failure, and a FS% above 55% is considered hyperdynamic LV function

Electrocardiogram

The ECG is a result of current propagated through the extracellular fluid that is generated by the spread of the wave of excitation through the heart. Electrodes placed on the surface of the body record the small potential differences between various recording sites that vary over the time course of the cardiac cycle.



P = atrial depolarization

QRS = ventricular depolarization

T = ventricular repolarization (less evident than depolarization because it is less synchronized)

PR interval = time it takes for an action potential to spread through the atria to the AV node

PR segment = atrial cells are depolarized (in plateau phase) and ventricular cells are resting, so no voltage is detected on the body surface

ST segment = atrial cells have returned to resting phase and ventricular cells are all depolarized (in plateau phase)

QT interval = roughly approximates ventricular myocyte depolarization, i.e. ventricular systole

*The depolarization of atrial cells occurs during the QRS complex but is overshadowed by ventricular depolarization

ECG recording equipment is often standardized so that a 1 cm deflection on the vertical axis always represents a potential difference of 1 mV and 25 mm on the horizontal axis represents 1 second

The net dipole that exists at any instant is oriented in the general direction of the wavefront movement at that instant. The magnitude of the dipole is determined by:

1. how many cells are simultaneously depolarizing
2. the consistency of orientation between individual dipoles at different points in the wavefront (i.e. dipoles in the same orientation reinforce each other and dipoles with the opposite orientation cancel each other)

Mean Electrical Axis (MEA)

The MEA is the orientation of the cardiac dipole during the most intense phase of ventricular depolarization (R wave). It is clinically used as an indicator of whether ventricular depolarization is proceeding over normal pathways.

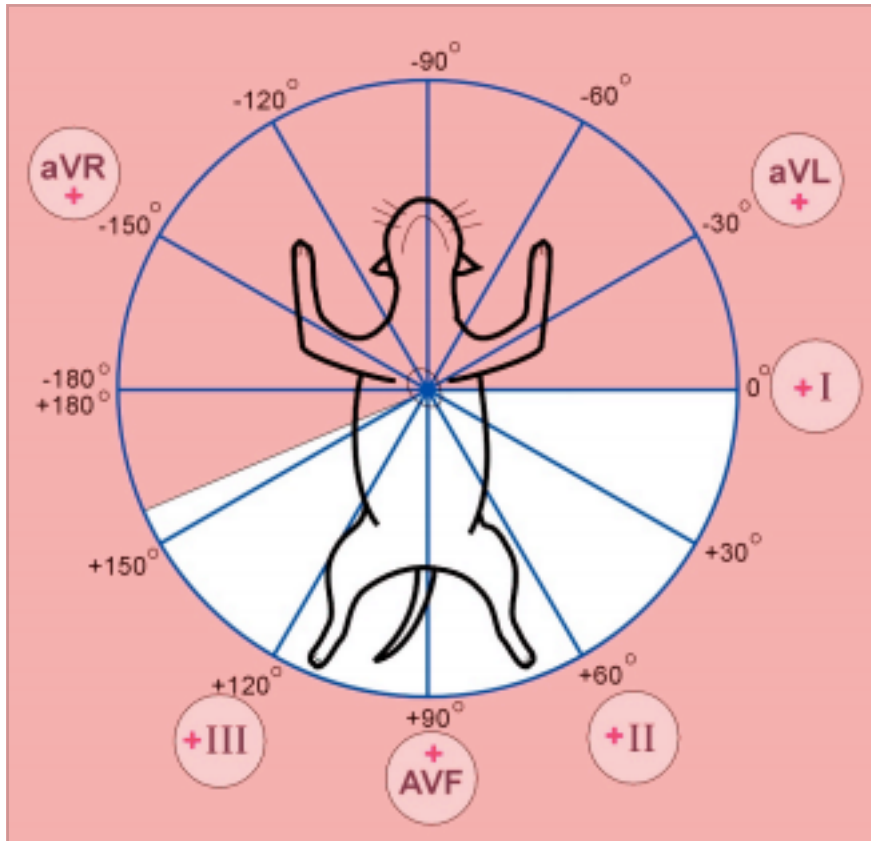
The normal mean electrical axis in a dog is about 0 to +150 degrees.

A left axis deviation may indicate a physical displacement of the heart to the left, left ventricular hypertrophy, or loss of electrical activity in the right ventricle. A right axis deviation may indicate physical displacement of the heart to the right, right ventricular hypertrophy, or loss of electrical activity in the left ventricle.

12-lead electrocardiogram:

- 3 leads are bipolar leads I, II and III
- 9 remaining leads are unipolar
 - 3 are generated by using the limb leads
 - 2 are electrically connected to form an indifferent electrode
 - third is made the positive pole of the pair
 - recordings from these are called augmented unipolar limb leads

- aVR is recorded from the right arm to indifferent electrode
- aVL is recorded from the electrode on the left arm
- aVF is recorded from the electrode on the left leg
- Other 6 leads are also unipolar that 'look' at the electrical vector projections in the transverse plane. These electrodes are placed at 6 positions along the chest wall (precordial/ chest leads; termed V1 through V6)



Chapter 5 - Cardiac Abnormalities

Electrical abnormalities and arrhythmias

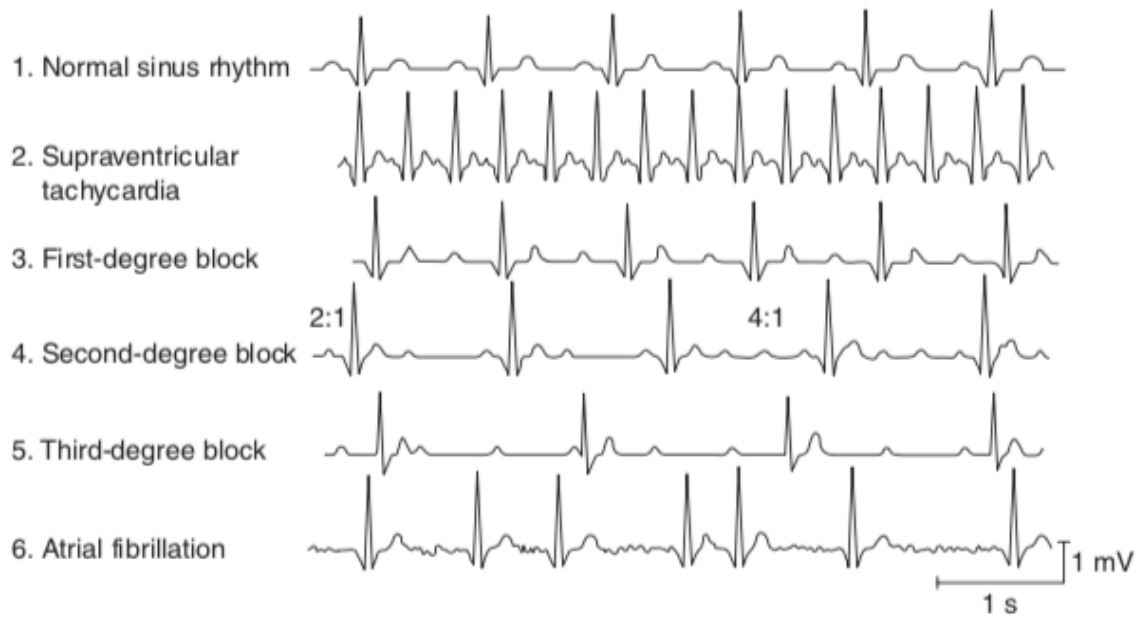


Figure 5-1. Supraventricular arrhythmias.

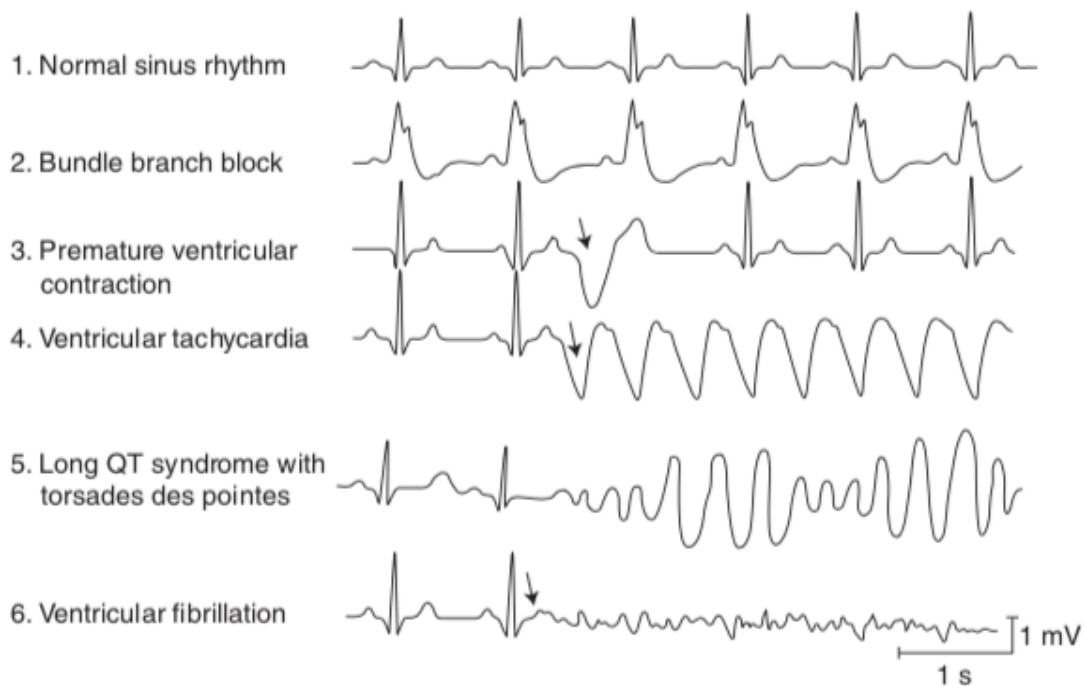


Figure 5-2. Ventricular arrhythmias.

Supraventricular tachycardia

SVT is also termed paroxysmal atrial tachycardia. It occurs when the atria are abnormally excited and drive the ventricles at a very rapid rate. The paroxysms start abruptly, may last minutes to hours, and then end abruptly. The QRS complexes appear normal because the ventricular conduction pathways are normal. The P and T waves may be superimposed because of the high heart rate.

There are two mechanisms that may account for supraventricular tachycardia.

- **ectopic focus** within an atrial region outside the SA node that fired rapidly and takes over pacemaker function
- atrial conduction may become altered so that a single wave of excitation does not die out but travels around some abnormal atrial conduction loop, creating a self-sustaining process called **reentry phenomenon**. This may occur due to abnormal depolarization and altered refractory periods in local areas of myocardium

Atrial Flutter

Special form of atrial tachycardia in which a large reentrant pathway drives the atria at very fast rates (250-300 beats/min). The normal refractory periods of the AV nodal tissue are overwhelmed and thus the ventricular rates are often at some fixed ratio of the atria rate (eg. 2:1 or 4:1). The ECG shows a sawtooth pattern of merged p waves with intermittent normal QRS complexes.

First-degree heart block

Results from unusually slow conductivity through the AV node, resulting in an abnormally long PR interval. At normal heart rates, the physiologic effects are inconsequential.

Second-degree heart block

Occur when some but not all atrial impulses are transmitted through the AV node to the ventricle. On the ECG, some but not all P waves will be accompanied by a corresponding QRS. The atrial rate is often 2-4x faster than the ventricular rate. This condition is typically not clinically relevant as long as the ventricular rate is adequate enough.

Third-degree heart block

Occurs when no impulses are transmitted through the AV node. In this event, some area in the ventricles (eg. common bundle or bundle branches near the AV node) assumes the pacemaker role. This results in the atrial and ventricular rates being completely independent, so the P waves and QRS complexes are totally dissociated. The ventricular rate is likely to be slower than normal and is often slow enough to impair cardiac output.

Atrial fibrillation

Characterized by complete loss of the normal synchrony of excitation and resting phases between individual cells. Consequently, no P waves appears, although there instead may be rapid, irregular, small waves apparent throughout diastole. The ventricular rate will be very irregular because impulses enter the AV node from the atria at unpredictable times. The mechanisms behind a-fib are thought to be due to impulses progressing repeatedly around irregular conduction pathways. A-fib is generally well tolerated by most patients as

long as ventricular rate is sufficient to maintain cardiac output.

Bundle branch blocks

Bundle branch blocks can occur in either of the branches of the Purkinje system of the intraventricular septum, often as a result of myocardial infarction. Ventricular depolarization is less synchronous than normal in the half of the heart with nonfunctional Purkinje system. This results in a widening of QRS complexes because a longer time is needed for ventricular depolarization to be completed. The direct physiologic effects of bundle branch blocks are usually inconsequential.

Premature Ventricular Contractions

PVCs are caused by action potentials initiated by an ectopic focus in the ventricle, causing the ventricle to depolarize and contract before it normally would. PVCs are often followed by a missed beat/ pause, because the ventricular cells are still refractory when the next impulse emerges from the SA node. The ECG shows a large-amplitude, long-duration deflection. The shape is highly variable and dependent on the ectopic site of origin and depolarization pathways involved. The volume of blood ejected from the abnormal beat is smaller than normal, whereas the volume ejected from the beat following the compensatory pause is large than normal (due to long filling time and a phenomenon of cardiac muscle called postextrasystolic potential). Single PVCs are not physiologically relevant, but if frequent may sign possible myocardial damage or perfusion problems.

Ventricular Tachycardia

Occurs when the ventricles are driven at high rates usually by impulses originating from ventricular ectopic focus. Diastolic filling time is compromised, and ventricular contraction is less synchronous and thus less effective than typical. Ventricular tachycardia often proceeds ventricular fibrillation.

Prolonged QT intervals

Occurs as a result of delayed ventricular myocyte depolarization, which may be due to inappropriate opening of the sodium channels or prolonged closure of the potassium channels during the action potential plateau phase. Long QT syndrome is identified when the QT interval is greater than 50% of the cardiac cycle duration. It may be genetic in origin, acquired from electrolyte disturbances, or induced by some antiarrhythmic agents. With long QT syndrome, patients are predisposed to torsades de pointes (a particularly dangerous type of ventricular tachycardia), during which ventricular electrical complexes cyclically vary in amplitude around the baseline and can rapidly deteriorate into ventricular fibrillation.

Ventricular fibrillation

Various areas of the ventricle are excited and contract asynchronously. The ventricle is especially susceptible to fibrillation whenever a premature excitation occurs at the end of the T wave of the previous excitation (i.e. when the ventricles are in the hyperexcitable/vulnerable period). No pumping action occurs in ventricular fibrillation, so the condition is fatal unless quickly corrected by cardiac conversion to depolarize all cells simultaneously.

Valvular Abnormalities

Stenosis of a valve requires that the upstream chamber has to develop more pressure during its systolic phase to achieve flow through the valve. This increase in 'pressure' work will induce hypertrophy.

When a valve has insufficiency, the regurgitant blood flow represents an additional volume that must be ejected in order to get sufficient forward flow. This increase in 'volume' work will lead to chamber dilation.

Aortic stenosis

A stenotic aortic valve requires a significant pressure difference between the left ventricle and aortic in order to eject blood. This results in high intraventricular pressure development and cardiac muscle cell hypertrophy, i.e. high ventricular afterload causes increased pressure workload on the left ventricle.

Mitral stenosis

A pressure difference of more than a few mmHg across the mitral valve is abnormal, and indicates stenosis. Consequently, the left atrial pressure is elevated and may induce hypertrophy.

Aortic insufficiency

When leaflets of the aortic valve do not provide an adequate seal, blood regurgitates from the aorta back into the left ventricle during diastole. Aortic pressure falls faster and further than normal during diastole, causing a low diastolic pressure and large pulse pressure. Additionally, ventricular end-diastolic volume and pressure are higher due to the regurgitant blood. This results in increased volume workload of the left ventricle.

Mitral regurgitation

When the mitral valve is insufficient, some blood regurgitates from the left ventricle into the left atrium during systole. Left atrial pressures are raised abnormally high. There is a resultant increase in volume workload of the left ventricle.

Chapter 6 - The Peripheral Vascular System

The Fick principle states that the amount of substance that goes into an organ over a given period, minus the amount that comes out, must equal the tissue utilization of the substance.

$$\dot{X}_{tc} = \dot{Q}([X]_a - [X]_v)$$

where \dot{X}_{tc} = transcapillary efflux rate of X (mass/time)
 \dot{Q} = blood flow rate (volume/time)
 $[X]_{a,v}$ = arterial and venous concentrations of X

Transcapillary fluid movement

Net movement out of capillaries is called filtration and fluid movement into capillaries is called reabsorption. Both hydrostatic and osmotic pressures influence transcapillary fluid movement. Oncotic pressure refers to a solution's total osmotic pressure that is due to particles that do not freely move across capillaries.

Starling's equation:

$$\text{Net filtration rate} = K[(P_c - P_i) - (\pi_c - \pi_i)]$$

where P_c = the hydrostatic pressure of intracapillary fluid

π_c = the oncotic pressure of intracapillary fluid

P_i and π_i = the same quantities for interstitial fluid

K = a constant expressing how readily fluid can move across capillaries (essentially the reciprocal of the resistance to fluid flow through the capillary wall)

Revised Starling' equation:

Net filtration rate = (capillary hydrostatic pressure - interstitial hydrostatic pressure) - (capillary oncotic pressure - subglycocalyx oncotic pressure)

Lymphatic System

Begins in the tissues with blind-end lymphatic capillaries that are roughly equivalent in size but less numerous than regular capillaries. Lymph moves through the converging lymphatic vessels, is filtered through lymph nodes where bacteria and particulate are

removed, and reenter the circulatory system near the point where the blood enters on the right side of the heart.

Lymph flow is stimulated by increases in tissue interstitial pressure or through contractions of the lymphatic vessels themselves. There are also valves within the lymphatics to prevent backward flow.

Resistance to flow

Ohm's Law = $I = V/R$

When vessels with individual resistances are connected in series, the overall resistance of the network is given by:

$$R_s = R_1 + R_2 + \dots + R_n$$

When vessels with individual resistances are connected in parallel, the overall resistance of the network is given by:

$$\frac{1}{R_p} = \frac{1}{R_1} + \frac{1}{R_2} + \dots + \frac{1}{R_n}$$

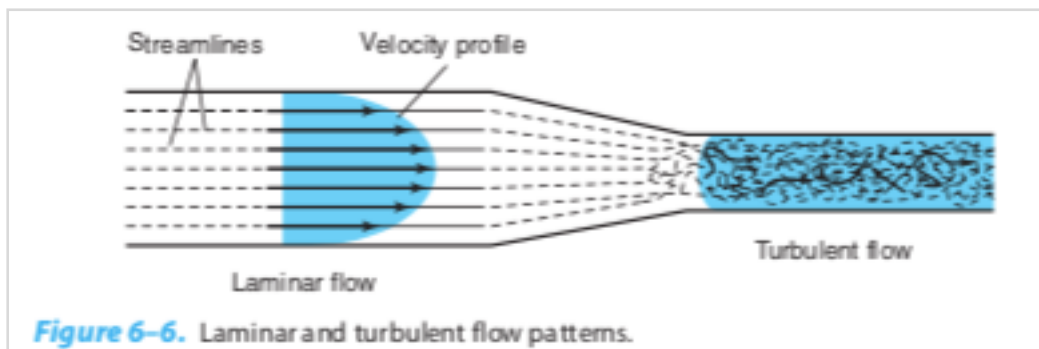
Peripheral blood flow velocities

Blood flows most rapidly in the region with the smallest total cross-sectional area (the aorta) and the most slowly in the region with the largest total cross-sectional area (the capillary beds). Flow rates (L/min) are the same, but flow velocity (distance/time) is much slower in the capillaries due to large cross-sectional area. This slow flow through capillaries is what allows for solute and fluid exchange between the vascular and interstitial compartment.

Bloodflow is normally laminar. Velocity is fastest along the central axis of the tube and falls to zero at the wall. Movement through the vessel exerts a shear stress on the walls of the vessel. This force wants to drag the inside surface (the endothelial cell layer) of the vessel along with the flow. With laminar flow, the shear stress on the wall of a vessel is proportional to the rate of flow through it. High shear stress can contribute to a variety of pathologic conditions.

When blood is forced to move with too high velocity through a narrow opening, turbulent flow may develop. With turbulent flow, there is internal mixing and friction. Turbulence

creates higher resistance to flow within the vessel (above what is predicted by Poiseuille's equation). Turbulent flow also generates sound (murmurs).



Peripheral blood volumes

Most of the circulating blood is contained within the veins of the systemic organs, often referred to as the **peripheral venous pool**. The **central venous pool** refers to blood contained in the great veins of the thorax and the right atrium. When peripheral veins constrict, blood is displaced from the peripheral venous pool and enters the central pool, which increases cardiac filling and by Starling's law, increases stroke volume

Peripheral blood pressures

Blood pressure decreases in consecutive segments. A large pressure drop occurs in the arterioles, and the capillary pressure is only about 25 mmHg. Pressure continues to decrease in the venules and veins as blood returns to the right heart. The central venous pressure is typically close to 0 mmHg.

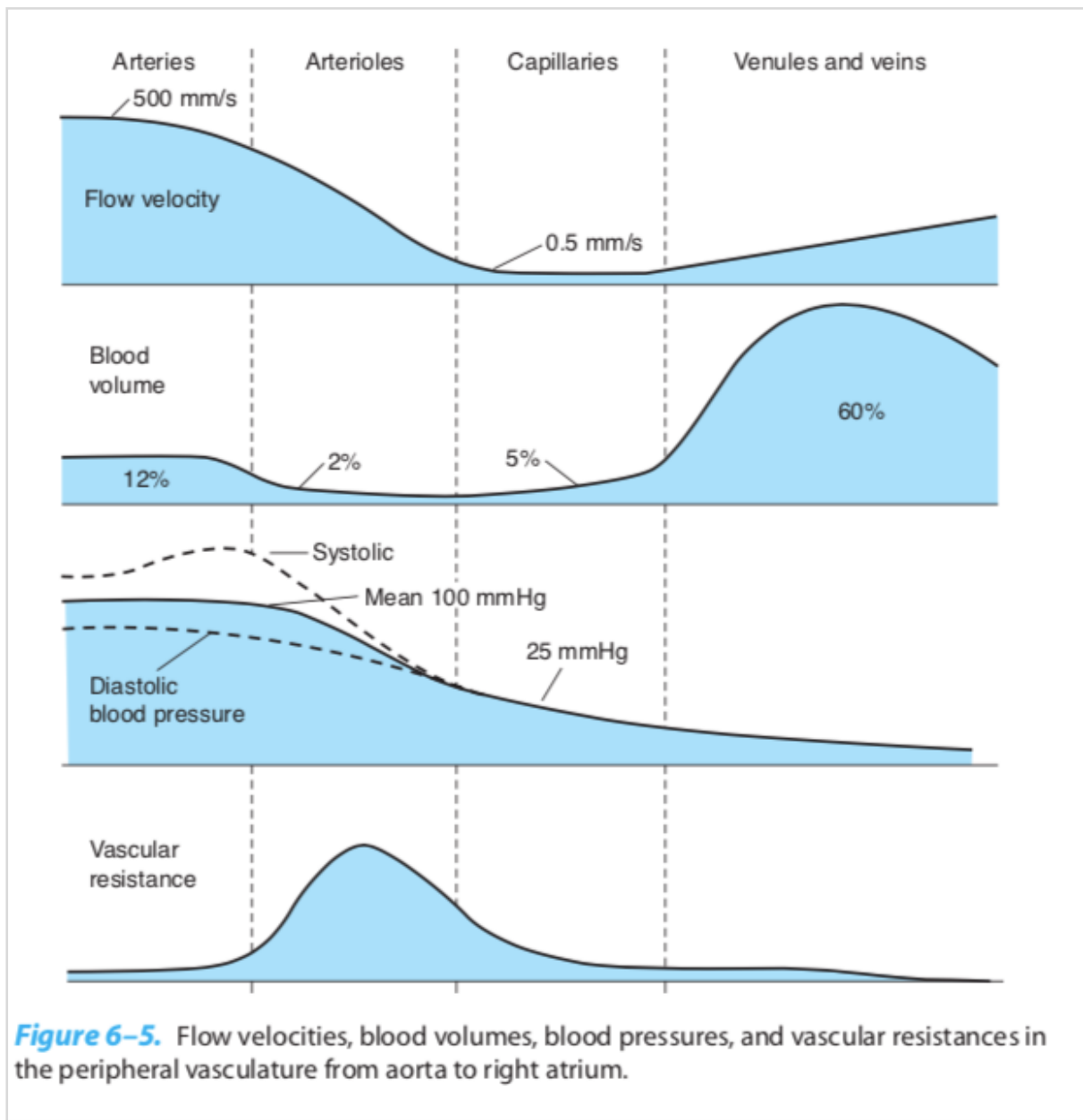
Peripheral vascular resistance

$$Q = P/R$$

The pressure drop that occurs across each segment corresponds to the resistance to flow within that region, i.e. the arterioles present a large resistance to flow. Arteriolar resistance is strongly influenced by arteriolar radius.

Veins are highly compliant, so even a small change in peripheral venous pressure can cause a significant amount of the circulating blood volume to shift into the peripheral venous pool.

The elasticity of arteries allows them to act as a reservoir on a beat-to-beat basis. They are able to convert the pulsatile flow output of the heart into a steady state flow through the vascular beds of systemic organs. If arteries were rigid tubes that could not store energy by expanding elastically, arterial pressure would fall immediately to zero with the termination of each cardiac ejection.



Blood pressure measurement

An inflatable cuff is placed over the arm and inflated to a pressure well above normal systolic values, causing all blood vessels to collapse. Air is then gradually let out of the cuff so that the pressure falls slowly and steadily. The moment the pressure cuff falls below the peak systolic arterial pressure, some blood is able to pass through the arteries beneath the cuff during systole, and produce sounds due to turbulent flow.

Mean arterial pressure

$$Q = \Delta P / R$$

$$\Delta P = Q \times R$$

$$\text{MAP} = \text{cardiac output} \times \text{total peripheral resistance}$$

*Assumes that central venous pressure is approximately zero

Arterial pulse pressure

Arterial pulse pressure is defined as systolic pressure minus diastolic pressure.

$$C = \Delta V / \Delta P$$

$$\Delta P = \Delta V / C$$

$$\text{Arterial pulse pressure} = \Delta V / C$$

$$\text{Arterial pulse pressure} = \text{stroke volume} / \text{arterial compliance}$$

Arterial compliance is relatively static, so changes in arterial pulse pressure is mostly a result of changes in stroke volume.

*The above equation assumes that not blood leaves the arteries during systolic ejection, which is obviously not true. As such, other factors can increase pulse pressure, such as increased myocardial contractility. Changes in TPR will not change pulse pressure as the same effects will occur on the diastolic side.