

The heart is responsible for generating the pressure that propels blood thru blood vessels. It helps keep oxygenated and deoxygenated blood separate and also is involved in the regulation of the body's blood supply.

The heart is located within the **mediastinum**, the medial cavity of the thorax. It rests on the superior surface of the diaphragm, medial to the lungs, anterior to the esophagus and vertebral column, and posterior to the sternum. Its **base** is directed toward the right shoulder. Its **apex** points to the left hip.

The heart is enclosed by the **pericardium** – a double-walled sac. The superficial layer is the **fibrous pericardium** – a collagenous structure that anchors the heart and prevents its over distention. Deeper is the **serous pericardium**, a 2 layered serous membrane. The **parietal pericardium** is the outer of the 2 and lines the inner surface of fibrous pericardium. The **visceral pericardium** is the inner of the 2 and is also the external covering of the heart. It is a.k.a. the **epicardium**. The parietal and visceral layers are continuous with one another where the great vessels leave the heart. The **pericardial cavity** is the potential space btwn the parietal and visceral layers. It contains serous fluid, which reduces friction.

The wall of the heart is divided into 3 layers. The **epicardium** is the most superficial and is a.k.a. visceral pericardium. It is composed of simple squamous epithelium overlaying a thin bit of loose CT. The **myocardium** is the middle layer. It's primarily cardiac muscle, but also contains blood vessels, nerves, and connective tissue. The inner layer is the **endocardium**. It consists of **endothelium** (simple squamous epithelium) resting on a layer of thin connective tissue. It lines the heart chambers and its folds create the heart valves.

The heart is a 4-chambered organ with 2 superior **atria** and 2 inferior **ventricles**. The thin **interatrial septum** divides the 2 atria, while the thick **interventricular septum** divides the 2 ventricles. The heart consists of 2 pumps connected in series. Each pump sends blood to a different circuit. The **pulmonary circuit** runs btwn the heart and the lungs. The **systemic circuit** runs btwn the heart and the rest of the body tissues. The right side of the heart receives deoxygenated blood from the systemic circuit and pumps it thru the pulmonary circuit. The left side of the heart receives oxygenated blood from the pulmonary circuit and pumps it thru the systemic circuit.

The atria are the heart's receiving chambers. They are small and thinly muscled. Large muscle mass is not necessary, b/c atrial muscle contraction is only used to propel a small amount of blood to the ventricle below.

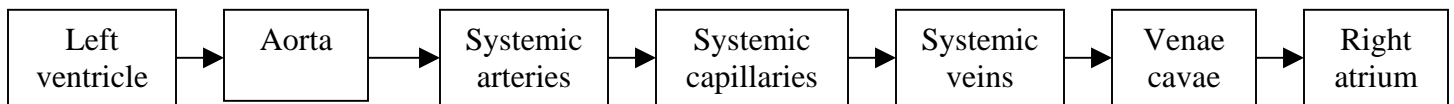
The right atrium receives blood from 3 sources: (1) **Superior vena cava** carries low O₂/high CO₂ blood from arms, head, and upper torso; (2) **Inferior vena cava** carries low O₂/high CO₂ blood from the legs, abdomen, and pelvis; (3) **Coronary sinus** carries low O₂/high CO₂ blood from the **coronary circulation** – which nourishes the heart wall. The right atrium passes blood to the right ventricle thru the **tricuspid orifice**, which is associated with the **tricuspid valve**.

Left atrium receives O₂ blood from the **4 pulmonary veins**. It passes blood to the left ventricle via the **mitral orifice**, which is associated with the **mitral** (or **bicuspid**) **valve**.

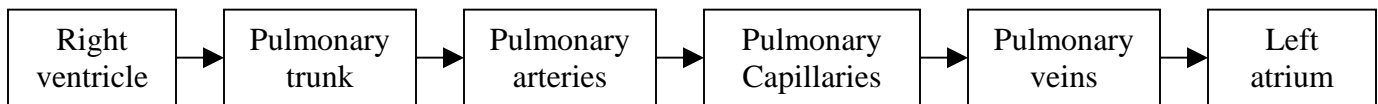
There is a shallow depression in both sides of the adult atrial septum known as the **fossa ovalis**. It's a remnant of the **foramen ovale**, a hole in the fetal atrial septum. Fetal blood flowed through the hole from RA to LA thus bypassing the pulmonary circuit (since the fetal lungs are neither developed nor oxygenated).

The ventricles are large, muscular chambers. Thick musculature is necessary because they are the actual pumps. The right ventricle discharges blood into the **pulmonary trunk**, the first vessel of the pulmonary circuit. The **pulmonary semilunar valve** separates the right ventricle and the pulmonary trunk. The left ventricle discharges blood into the **aorta**, the first vessel of the systemic circuit. The **aortic semilunar valve** separates the LV and aortic trunk. The left ventricle is larger (more muscular) than the right. More muscle is necessary because the left ventricle pumps blood a farther distance and against greater pressure (note – the right and left ventricle pump the same volume of blood per beat).

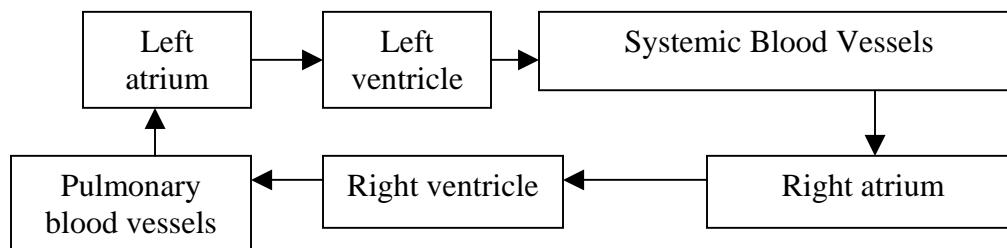
Systemic circuit:



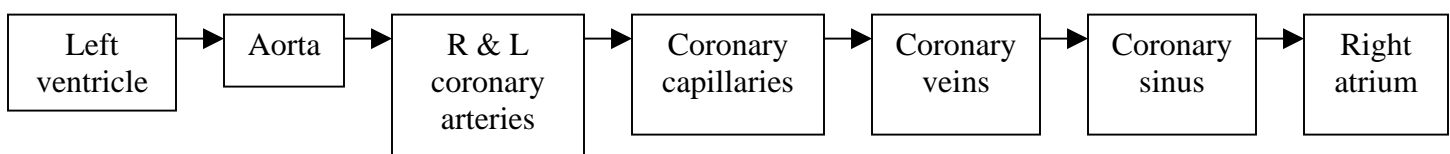
Pulmonary circuit:



If we combine the 2 circuits, note that we have 2 pumps in series:



The heart has its own network of blood vessels (known as the coronary circuit). It's necessary b/c the heart requires a prodigious amount of oxygen and nutrients, and little oxygen and/or nutrients from blood within the chambers can diffuse thru the thick myocardium. The basic pathway of blood is:



Realize that only a small % of the aortic blood will enter the coronary circulation. And likewise, only a small % of the deoxygenated blood returning to the right atrium is from the coronary circulation. There exist multiple **anastomoses** along the coronary arterial branches. These are fusing networks that provide **collateral routes** for blood to reach the cardiac tissue.

Heart valves ensure 1-way flow within the heart. There are 4 valves: 2 **atrioventricular valves** separating the atria from the ventricles; and 2 **semilunar valves** separating the ventricles from their great vessels.

The atrioventricular valves consist of a flap of endothelium with a core of connective tissue. The tricuspid valve prevents backflow of blood from the RV to the RA. It's called the tricuspid because it has 3 flaps. The mitral valve prevents backflow from the LV to the LA. It contains 2 valve flaps and is also known as the bicuspid valve. Attached to the valve flaps are strings of collagen called **chordae tendineae**. These chordae tendineae attach to bulges in the ventricle floor known as **papillary muscles**. When blood is entering the ventricle, the valve is open, the chordae tendineae are slack, and papillary muscles are relaxed. When the ventricle contracts, blood pushes the valve flaps towards the ventricles. This closes the valves. The chordae tendineae tighten and the papillary muscles contract to prevent the valve flaps from flipping up into the atrium. Note that the chordae tendineae and papillary muscles do NOT close the AV valves themselves. Blood's attempt to flow upward is what pushes the valves shut.

The aortic semilunar valve prevents backflow from the aorta into the left ventricle. The pulmonary semilunar valve prevents backflow from the pulmonary trunk into the right ventricle. The semilunar valves have no associated chordae tendineae or papillary muscles.

The bulk of the heart wall is composed of cardiac muscle. There are 2 types of cardiac muscle cells. The **contractile cells** (99%) generate the force involved in pumping. The **autorhythmic cells** (1%) spontaneously depolarize to set the rate of contraction. Contractile cells are striated, short, and often branching. They are involuntary and are linked to one another and to the autorhythmic cells by **intercalated discs**. Intercalated discs consist of 2 separate structures: **gap junctions** and **desmosomes**. Gap junctions are protein channels that allow ions to flow btwn adjacent cells. They amount to an electrical connection btwn cardiac muscle cells. They allow the depolarization wave initiated by autorhythmic cells to spread through the cardiac musculature. This allows the heart to function as a single coordinated unit (a **functional syncytium**), which helps maximize its efficiency. Desmosomes physically connect adjacent cardiac muscle cells. This prevents cells from separating during contraction. Electrical excitation of cardiac muscle cells causes an increase in intracellular Ca^{2+} levels. Calcium binds w/ troponin to produce contraction via the familiar sliding filament mechanism.

Atrial cardiac muscle is separated from ventricular cardiac muscle by the **fibrous skeleton**, which consists of 4 rings of dense connective tissue joined together. Each ring

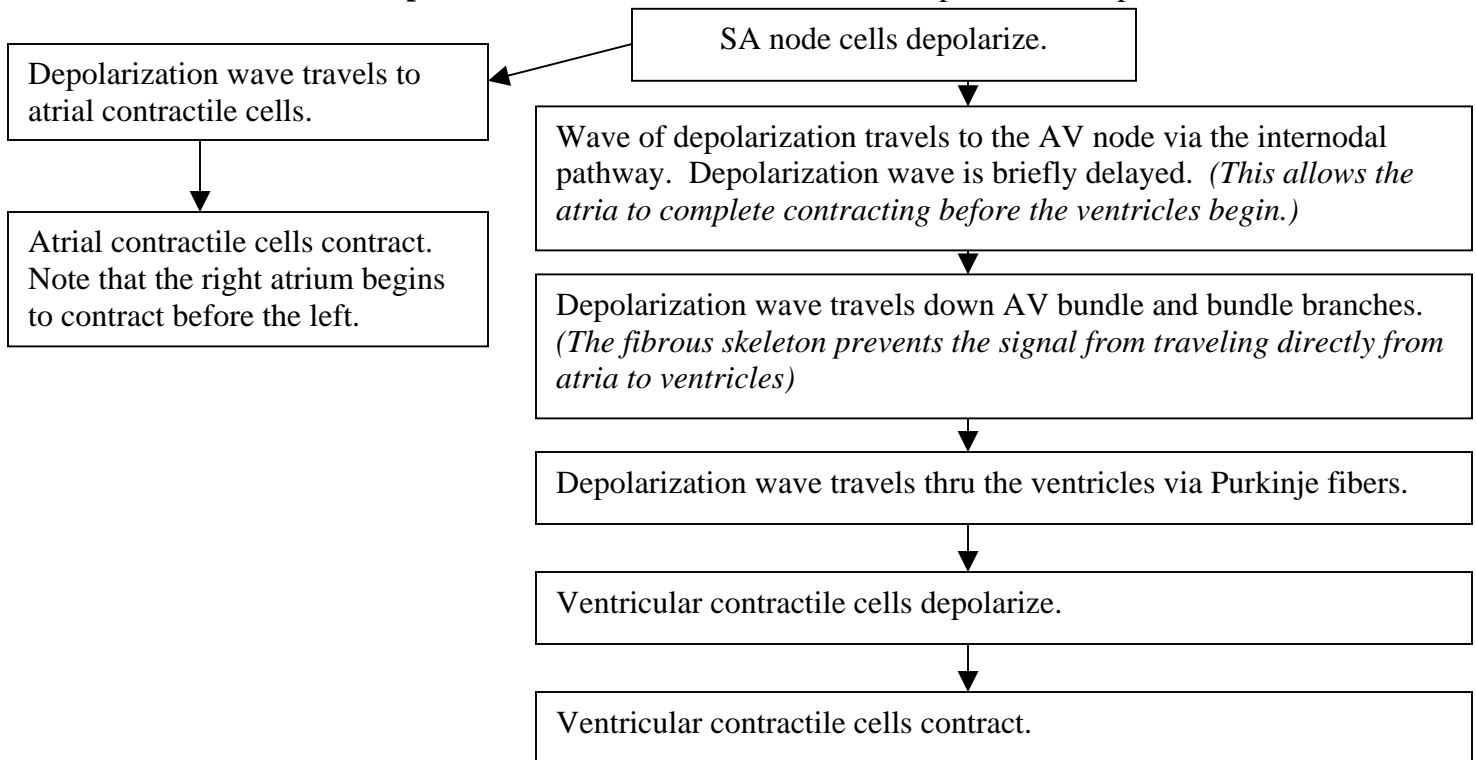
has a heart valve attached to it. The skeleton helps separate the atria from the ventricles both physically and electrically and provides an attachment site for cardiac muscle cells.

Both **heart rate** (measured in beats/minute) and the **force of contraction** are controlled **intrinsically** (by heart tissue itself) and **extrinsically** (via nerve signals, hormones, and other blood-borne substances).

Intrinsic control of the heart rate is the province of the autorhythmic cells (which have the ability to spontaneously and rhythmically depolarize). Groups of autorhythmic cells are found at the:

1. **Sinoatrial node** – located near the opening of the SVC.
2. **Atrioventricular node** – located in the inferior interatrial septum near the tricuspid orifice.
3. **Atrioventricular bundle** – found in the superior interventricular septum.
4. **Right and left bundle branches** – travel thru the interventricular septum to the apex of the heart.
5. **Purkinje fibers** – autorhythmic cells that wind their way through the ventricles.

The above list also gives the path of the electrical conduction system within the heart. All autorhythmic cells have the ability to rhythmically and spontaneously depolarize. However, SA node cells have the fastest rate of depolarization and therefore set the pace for other autorhythmic cells as well as the rest of the heart. For this reason, the SA node is known as the **pacemaker** of the heart. Here's how the process takes place:



Without any input (neural or hormonal), the rate of SA node depolarization determines the heart rate. The fibrous skeleton of the heart electrically isolates the atria and the

ventricles. The AV bundle is the only electrical connection btwn them. Note that ventricular depolarization and thus contraction begin at the apex of the heart and proceed upward. Recall that the great vessels leave the heart at its superior edge (the base). So, since blood exits the top of the heart, we must begin squeezing at the inferior end (apex) of the heart.

The extrinsic control of the heart rate refers to factors originating outside of cardiac tissue that affect heart rate. The **medulla oblongata** contains **cardiac centers** that can alter the heart's activity. The **cardioacceleratory center** projects via the **cardiac sympathetic nerves** to the SA node, AV node, and the ventricular myocardium. These neurons release **norepinephrine**, which causes an increase in contraction rate and force. The **cardioinhibitory center** contains **parasympathetic** neurons that project (via the **vagus nerve**, CN X) to the SA node and AV nodes. These neurons release **acetylcholine**, which causes a decrease in heart rate but no change in the heart's contractile strength. At rest, both parasympathetic and sympathetic neurons are releasing neurotransmitters onto the heart, but the parasympathetic branch is dominant. During stress, exercise, and excessive heat the sympathetic influence is dominant. Hormones such as **epinephrine** (released by the **adrenal medulla**), **thyroxine** (released by the **thyroid gland**), and others affect heart rate as well. More on them later.

The **cardiac cycle** refers to all the events associated with blood flow thru the heart during one complete heartbeat. It includes the contraction (**systole**) and relaxation (**diastole**) of all 4 chambers. *Remember that in order for blood to move from point A to point B, the pressure at point A must be greater than the pressure at point B.* We'll discuss the cardiac cycle in terms of the left side of the heart, but analogous events are occurring on the right side. The cardiac cycle is divided into 4 parts: **ventricular filling**, **isovolumetric contraction**, **ventricular ejection**, and **isovolumetric relaxation**.

During **ventricular filling** left atrial blood pressure is lower than pressure in the pulmonary vasculature, so blood enters the left atrium. LA pressure is greater than LV pressure, so blood enters the LV. B/c LA pressure is greater than LV pressure, the AV valves are pushed open. Note that LV pressure is less than aortic pressure. As a result, blood tries to back flow from the aorta into the LV and this forces the semilunar valves closed. Neither the atrial or ventricular muscle is contracting during this phase. At this point both the left atrium and the left ventricle are in diastole. About 80% of the ultimate ventricular volume will enter in a passive manner. However, at the end of ventricular filling, while the ventricle is still relaxing, the atrium depolarizes and contracts. This pushes roughly the final 20% of blood into the left ventricle. The left ventricle now has the maximum volume it will contain during this particular cycle. This is known as the **end diastolic volume (EDV)**. A typical value for EDV is 130mL. Note that for the rest of the cycle, the atrium will be in diastole.

During **isovolumetric contraction** the ventricle depolarizes and begins to contract. As the ventricle contracts, its pressure rises quickly. LV pressure quickly exceeds LA pressure and blood is pushed upward forcing the mitral valve shut – this creates the **1st heart sound** (the LUB). However, the opening of the aortic semilunar valve requires

much more pressure than was necessary to close the mitral valve. So after the mitral valve is shut, the ventricle continues to contract and the pressure within it rises, but until ventricular pressure exceeds aortic pressure, the aortic semilunar valve remains shut. Thus, during this period, the AV and semilunar valves are shut and the volume within the ventricle is not changing. Hence this phase is known as “iso” “volumetric” contraction.

During **ventricular ejection** the pressure in the left ventricle exceeds aortic pressure (typically about 80mmHg), the semilunar valve is forced open, and blood is ejected from the left ventricle. Not all of the blood is ejected. The amount remaining after ventricular contraction is known as the **end systolic volume (ESV)**. A typical value is 70mL. This gives a reserve amount of blood that could also be ejected if necessary (e.g., during exercise). The amount of blood ejected during this phase is known as the **stroke volume**. Mathematically the stroke volume can be expressed as the difference btwn the end diastolic and end systolic volumes: $SV=EDV-ESV$. A more vigorous contraction will result in a decreased ESV and an increased SV.

The final phase is **isovolumetric relaxation**. Once the ventricle has completed contracting, the pressure within it begins to fall. It quickly becomes less than aortic pressure, blood tries to back flow and the semilunar valve snaps shut – this creates the **2nd heart sound** (the DUP). However, it takes a bit longer for the pressure in the ventricle to drop below the pressure in the left atrium – which will cause the mitral valve to open. During this time, as ventricular pressure is falling, the AV and semilunar valves are shut and ventricular volume is not changing. Once left ventricle pressure falls below left atrium pressure (which is rising as blood returns to the heart), the mitral valve will open and the cycle will begin anew with another round of ventricular filling.

Note that the events on the left side of the heart during a normal cardiac cycle are mirrored by the events on the right side of the heart. Both the right and the left side of the heart contract at the same rate. They have identical stroke volumes. The only difference is the pressure involved. The left ventricle must contract harder to open its semilunar valve. This is because the systemic circuit is under a much higher pressure than the pulmonary circuit. The left and right ventricle must have identical stroke volumes. If left ventricle SV > right ventricle SV, then blood would back up in the systemic circuit. If left ventricle SV < right ventricle SV, then blood would back up in the pulmonary circuit.

Cardiac output is the amount of blood pumped by each ventricle in one minute. Cardiac output can be expressed mathematically as the product of heart rate and stroke volume: $CO(mL/min) = HR(beats/min) \times SV(mL/beat)$. Changes in either stroke volume or heart rate can alter cardiac output. During exercise, cardiac output can increase dramatically.

The nervous system plays a large role in the regulation of heart rate. Recall that the cardiac centers in the medulla oblongata exert influence on the rate of SA node depolarization, i.e., heart rate. Increases in heart rate are achieved by:

1. Increase in cardioacceleratory center activity. This results in an increase in sympathetic nerve activity and an increase in norepinephrine release on the heart.
2. Decrease in cardioinhibitory center activity. This results in a decrease in parasympathetic nerve activity and a decrease in acetylcholine release on the heart.

Decreases in heart rate are achieved by a decrease in cardioacceleratory center activity or an increase in cardioinhibitory center activity. It should be noted that the main parasympathetic pathway to the heart is via the **vagus nerve** (CN X). So, an increase in parasympathetic nervous activity will result in increased vagus nerve activity. This is known as increased **vagal tone**.

Changes in blood pressure can also influence HR. A rise in BP will initiate an increase in parasympathetic outflow to the heart. This'll decrease HR and by extension decrease BP. A drop in BP will initiate an increase in sympathetic outflow to the heart. This'll increase HR and by extension increase BP.

Heart rate is also sensitive to changes in plasma levels of O₂, CO₂, and pH. Low levels of O₂ are usually accompanied by high levels of CO₂ and a drop in pH. These changes will activate the cardioacceleratory center causing an increase in heart rate. This will increase the output of blood to the lungs so that O₂ can be picked up and CO₂ removed.

Note that if heart rate changes without a change in contractility (the strength of the contraction), stroke volume will change also. This is because changing the heart rate alters the **filling time** (i.e., the time btwn beats during which the heart fills up with blood).

There are also hormonal influences on heart rate. Epinephrine, released by the adrenal medulla (an endocrine organ found atop the kidney), causes an increase in heart rate. Thyroxine, released by the thyroid gland (located in the anterior neck), also causes an increase in heart rate.

There are other factors that can affect heart rate. Changes in body electrolyte levels (K⁺, Ca²⁺) can exert effects on heart rate. Drugs can alter heart rate. Some drugs that increase heart rate are: **caffeine**, **nicotine**, and **sympathetic mimics** (e.g., ephedrine). **Beta-blockers** are a type of drug that decreases heart rate. Psychic and emotional factors can also influence the heart's action.

Stroke volume depends on 3 main variables: **preload**, **contractility**, and **afterload**.

Preload refers to the degree of ventricular stretch during filling. The more heart muscle is stretched (up to a point), the more forceful its contraction. The increase in stretch causes more optimum cross-bridge formation btwn actin and myosin and a stronger contraction, thus ejecting a larger volume. The Frank-Starling law nicely sums it up nicely: "*What returns to the heart will get pumped out of the heart.*" In other words, as **venous return** (the volume of blood returning to the heart per minute) increases, EDV increases, and stroke volume increases. Changes in heart rate change the filling time and thus the EDV

(preload). During exercise skeletal muscles massage the veins and increase the venous return, thus increasing EDV (preload). The stroke volume is greatly influenced by changes in preload.

Contractility is the strength of the heart's contraction independent of its degree of stretch. Think of it as how hard the heart contracts no matter how much blood is within it. An increase in contractility will result in an increase in stroke volume and a decrease in end systolic volume. Factors that increase contractility include: increased cardioacceleratory activity; hormones such as epinephrine and thyroxine; drugs such as **digitalis**. Drug types that decrease contractility include beta-blockers and **calcium channel blockers**.

Afterload refers to the pressure that must be overcome to open the semilunar valve and eject blood. Afterload is equivalent to arterial blood pressure. An increase in arterial BP will increase afterload. This makes the heart expend more time/energy on opening the semilunar valve and less on ejecting blood. Thus, an increase in afterload will cause stroke volume to decrease and end systolic volume to increase. However, it takes a significant increase in afterload before the pumping output of the heart is hampered.