THE CARDIOVASCULAR SYSTEM

The functional anatomy of the heart

The heart acts as two separate pumps operating side by side; the right heart generates the circulation to the lungs and the left heart feeds the rest of the body.

The right atrium (RA) drains deoxygenated blood from the superior and inferior venae cavae and discharges blood to the right ventricle (RV), which in turn pumps it into the pulmonary artery.

The left atrium (LA) drains oxygenated blood from the lungs through four pulmonary veins and discharges blood into the left ventricle (LV), which in turn pumps it into the aorta.

During ventricular contraction (systole), the tricuspid valve in the right heart and the mitral valve in the left heart close, and the pulmonary and aortic valves open. In diastole, the pulmonary and aortic valves close, and the two atrioventricular valves open.

The systolic pressure in the LV is normally at least four times greater than that in the right, and the wall of the LV is usually at least 1 cm thick compared with 2-3 mm for the RV.

The atria lie within the mediastinum, anterior to the oesophagus and the descending aorta. The ventricles lie anterior to the atria and taper towards the apex of the heart, which lies to the left of the midline. The RV lies immediately behind the sternum and is not only to the right of but also anterior to the LV.

The left main and right coronary arteries arise from the left and right coronary sinuses, just distal to the aortic valve.

Within 2.5 cm of its origin the left main coronary artery divides into the left anterior descending artery (LAD), which runs in the anterior interventricular groove, and the left circumflex artery (CX), which runs posteriorly in the atrioventricular groove. The LAD gives branches to supply the anterior part of the septum (septal perforators) and the anterior wall and apex of the LV. The CX gives marginal branches that supply the lateral, posterior and inferior segments of the LV.

The right coronary artery (RCA) runs in the right atrioventricular groove, giving branches that supply the RA, RV and infero-posterior aspects of the LV. The posterior descending artery runs in the posterior interventricular groove and supplies the inferior part of the interventricular
septum. This vessel is a branch of the RCA in approximately 90% of people (dominant right system) and is supplied by the CX in the remainder (dominant left system). The exact coronary anatomy varies greatly from person to person and there are many 'normal variants'.

The right coronary artery supplies the sinoatrial (SA) node in about 60% of individuals, and the atrioventricular (AV) node in about 90%.

The venous system mainly follows the coronary arteries but drains to the coronary sinus in the atrioventricular groove, and then to the right atrium. An extensive lymphatic system drains into vessels that travel with the coronary vessels and then into the thoracic duct.

**Nerve supply of the heart**

The heart is innervated by both sympathetic and parasympathetic fibres. 

Nerves (adrenergic) from the cervical sympathetic chain supply muscle fibres in the atria and ventricles and the electrical conducting system. Positive inotropic (power) and chronotropic (rate) effects are mediated by β<sub>1</sub>-adrenoceptors, whereas β<sub>2</sub>-adrenoceptors predominate in vascular smooth muscle and mediate vasodilatation.

Parasympathetic pre-ganglionic fibres and sensory fibres reach the heart through the vagus nerves. Cholinergic nerves supply the AV and SA nodes via muscarinic (M2) receptors.

Under resting conditions, vagal inhibitory activity predominates and the heart rate is slow. Adrenergic stimulation associated with exercise, emotional stress, fever and so on causes the heart rate to increase.

The heart beat is normally initiated by an electrical discharge from the sinoatrial (sinus) node. The atria ,the AV node and ventricles then depolarise sequentially as electrical depolarisation passes through specialised conducting tissues.

**PHYSIOLOGY of Myocardial contraction**

Myocardial cells (myocytes) are about 50-100 μm long; each cell branches and interdigitates with adjacent cells. An intercalated disc permits electrical (via gap junctions) and mechanical conduction (via the fascia adherens) to adjacent cells.

The basic unit of contraction is the sarcomere , which is aligned to those of adjacent myofibrils, giving a striated appearance due to the Z-lines. Actin filaments are attached at right angles to the Z-lines and interdigitate with thicker parallel myosin filaments . The cross-links between actin and myosin molecules contain myofibrillar ATPase, which breaks down adenosine triphosphate (ATP) to
provide the energy for contraction. Two chains of actin molecules form a helical structure, with a second molecule, tropomyosin, in the grooves of the actin helix, and a further molecule complex, troponin, attached to every seventh actin molecule.

During contraction, shortening of the sarcomere results from the interdigitation of the actin and myosin molecules, without altering the length of either molecule. Contraction is initiated when calcium is made available during the plateau phase of the action potential by calcium ions entering the cell. As its concentration rises, calcium binds to troponin, precipitating contraction. The force of cardiac muscle contraction, or inotropic state, is regulated by the influx of calcium ions through 'slow calcium channels'.

The extent to which the sarcomere can shorten determines stroke volume of the ventricle. It is maximally shortened in response to powerful inotropic drugs or severe exercise. However, the enlargement of the heart seen in heart failure is due to slippage of the myofibrils and adjacent cells rather than lengthening of the sarcomere.
Origin of the Heartbeat & the Electrical Activity of the Heart

INTRODUCTION
The parts of the heart normally beat in orderly sequence: Contraction of the atria (atrial systole) is followed by contraction of the ventricles (ventricular systole), and during mid diastole all four chambers are relaxed.

The heartbeat originates in a specialized cardiac conduction system and spreads via this system to all parts of the myocardium. The various parts of the conduction system are capable of spontaneous discharge. The structures that make up the conduction system are the node (SA node), the internodal atrial pathways, the node (AV node), the bundle of His and its branches, and the Purkinje system.

The sinoatrial (SA) node normally discharges most rapidly, depolarization spreading from it to the other regions before they discharge spontaneously. The SA node is therefore the normal cardiac pacemaker, its rate of discharge determining the rate at which the heart beats. Impulses generated in the SA node pass through the atrial pathways to the atrioventricular (AV) node, through this node to the bundle of His, and through the branches of the bundle of His via the Purkinje system to the ventricular muscle.

ORIGIN & SPREAD OF CARDIAC EXCITATION
Anatomic Considerations
In the human heart, the SA node is located at the junction of the superior vena cava with the right atrium. The AV node is located in the right posterior portion of the interatrial septum. There are three bundles of atrial fibers that contain Purkinje type fibers and connect the SA node to the AV node. Conduction also occurs through atrial myocytes.
The AV node is normally the only conducting pathway between the atria and ventricles. It is continuous with the bundle of His, which gives off a left bundle branch at the top of the interventricular septum and continues as the right bundle branch. The left bundle branch divides into an anterior fascicle and a posterior fascicle. The branches and fascicles run subendocardially down either side of the septum and come into contact with the Purkinje system, whose fibers spread to all parts of the ventricular myocardium.

Myocardial fibers have a resting membrane potential of approximately -90 mV. The individual fibers are separated by membranes, but depolarization spreads radially through them as if they were a syncytium, because of the presence of gap junctions.

The transmembrane action potential of single cardiac muscle cells is characterized by rapid depolarization, a plateau, and a slow repolarization process. The initial depolarization is due to Na\(^+\) influx through rapidly opening Na\(^+\) channels (the Na\(^+\) current, I\(_{Na}\)). Ca\(^{2+}\) influx through more slowly opening Ca\(^{2+}\) channels (the Ca\(^{2+}\) current, I\(_{Ca}\)) produces the plateau phase, and repolarization is due to net K\(^+\) efflux through three types of K\(^+\) channels. Recorded extracellularly, the summed electrical activity of all the cardiac muscle fibers is the ECG.

When the cholinergic vagal fibers to nodal tissue are stimulated, the membrane becomes hyperpolarized and the slope of the prepotentials is decreased, decreases cAMP in the cells, and this slows the opening of the Ca\(^{2+}\) channels. The result is a decrease in firing rate. Strong vagal stimulation may abolish spontaneous discharge for some time.

Conversely, stimulation of the sympathetic cardiac nerves makes the membrane potential fall more rapidly, and the rate of spontaneous discharge increases. Norepinephrine secreted by the sympathetic endings binds to β\(_1\) receptors, and the resulting increase in intracellular cAMP facilitates the opening of L channels, increasing I\(_{Ca}\) and the rapidity of the depolarization phase of the impulse.
Because of the "sidedness" of the cardiac innervation (see above), stimulation of the right vagus slows the heart by inhibiting the SA node, whereas stimulation of the left vagus mainly slows AV conduction. Similarly, stimulation of the right stellate ganglion accelerates the heart, whereas stimulation of the left stellate ganglion shortens the AV nodal conduction time and refractoriness.

The rate of discharge of the SA node and other nodal tissue is influenced by temperature and by drugs.
Atrial activation

Septal activation from left to right

Activation of anteroseptal region of the ventricular myocardium

Activation of major portion of ventricular myocardium from endocardial surfaces

Late activation of posterobasal portion of the left ventricle and the pulmonary conus
**INTRODUCTION**

In single muscle fibers, contraction starts just after depolarization and lasts until about 50 ms after repolarization is completed. Atrial systole starts after the P wave of the ECG; ventricular systole starts near the end of the R wave and ends just after the T wave. It should be noted that the term **systolic pressure** in the vascular system refers to the peak pressure reached during systole, not the mean pressure; similarly, the **diastolic pressure** refers to the lowest pressure during diastole.

**MECHANICAL EVENTS OF THE CARDIAC CYCLE**

**Events in Late Diastole**

Late in diastole, the mitral and tricuspid valves between the atria and ventricles are open and the aortic and pulmonary valves are closed. Blood flows into the heart throughout diastole, filling the atria and ventricles. The rate of filling declines as the ventricles become distended, and—especially when the heart rate is low—the cusps of the atrioventricular (AV) valves drift toward the closed position pressure in the ventricles remains low.
Atrial Systole
Contraction of the atria propels some additional blood into the ventricles, but about 70% of the ventricular filling occurs passively during diastole. Contraction of the atrial muscle that surrounds the orifices of the superior and inferior vena cava and pulmonary veins narrows their orifices, and the inertia of the blood moving toward the heart tends to keep blood in it; however, there is some regurgitation of blood into the veins during atrial systole.

Ventricular Systole
At the start of ventricular systole, the mitral and tricuspid (AV) valves close. Ventricular muscle initially shortens relatively little, but intraventricular pressure rises sharply as the myocardium presses on the blood in the ventricle. This period of isovolumetric (isovolumic, isometric) ventricular contraction lasts about 0.05 s, until the pressures in the left and right ventricles exceed the pressures in the aorta (80 mm Hg; 10.6 kPa) and pulmonary artery (10 mm Hg) and the aortic and pulmonary valves open. During isovolumetric contraction, the AV valves bulge into the atria, causing a small but sharp rise in atrial pressure.

When the aortic and pulmonary valves open, the phase of ventricular ejection begins. Ejection is rapid at first, slowing down as systole progresses. The intraventricular pressure rises to a maximum and then declines somewhat before ventricular systole ends. Peak left ventricular pressure is about 120 mm Hg, and peak right ventricular pressure is 25 mm Hg or less. Late in systole, the aortic pressure actually exceeds the ventricular, but for a short period momentum keeps the blood moving forward. The AV valves are pulled down by the contractions of the ventricular muscle, and atrial pressure drops. The amount of blood ejected by each ventricle per stroke at rest is 70-90 mL. The end-diastolic ventricular volume is about 130 mL. Thus, about 50 mL of blood remains in each ventricle at the end of systole (end-systolic ventricular volume), and the ejection fraction, the percent of the end-diastolic ventricular volume that is ejected with each stroke, is about 65%. The ejection fraction is a valuable index of ventricular function. It can be measured by injecting radionuclide-labeled red blood cells, imaging the cardiac blood pool at the end of diastole and the end of systole (equilibrium radionuclide angiocardiography), and then calculating the ejection fraction.
**Early Diastole**

Once the ventricular muscle is fully contracted, the already falling ventricular pressures drop more rapidly. This is the period of **protodiastole**. It lasts about 0.04 s. It ends when the momentum of the ejected blood is overcome and the aortic and pulmonary valves close, setting up transient vibrations in the blood and blood vessel walls. After the valves are closed, pressure continues to drop rapidly during the period of **isovolumetric ventricular relaxation**. Isovolumetric relaxation ends when the ventricular pressure falls below the atrial pressure and the AV valves open, permitting the ventricles to fill. Filling is rapid at first, then slows as the next cardiac contraction approaches. Atrial pressure continues to rise after the end of ventricular systole until the AV valves open, then drops and slowly rises again until the next atrial systole.

**Pericardium**

The heart is separated from the rest of the thoracic viscera by the pericardium. The myocardium itself is covered by the fibrous epicardium. The pericardial sac normally contains 5-30 mL of clear fluid, which lubricates the heart and permits it to contract with minimal friction.

**Timing**

Although events on the two sides of the heart are similar, they are somewhat asynchronous. Right atrial systole precedes left atrial systole, and contraction of the right ventricle starts after that of the left. However, since pulmonary arterial pressure is lower than aortic pressure, right ventricular ejection begins before left ventricular ejection. During expiration, the pulmonary and aortic valves close at the same time; but during inspiration, the aortic valve closes slightly before the pulmonary. The slower closure of the pulmonary valve is due to lower impedance of the pulmonary vascular tree. When measured over a period of minutes, the outputs of the two ventricles are, of course, equal, but transient differences in output during the respiratory cycle occur in normal individuals.
**Arterial Pulse**

The blood forced into the aorta during systole not only moves the blood in the vessels forward but also sets up a pressure wave that travels along the arteries. The pressure wave expands the arterial walls as it travels, and the expansion is palpable as the pulse. The rate at which the wave travels, which is independent of and much higher than the velocity of blood flow, is about 4 m/s in the aorta, 8 m/s in the large arteries, and 16 m/s in the small arteries of young adults. Consequently, the pulse is felt in the radial artery at the wrist about 0.1 s after the peak of systolic ejection into the aorta. With advancing age, the arteries become more rigid, and the pulse wave moves faster.

The strength of the pulse is determined by the pulse pressure and bears little relation to the mean pressure. The pulse is weak ("thready") in shock. It is strong when stroke volume is large, eg, during exercise. When the pulse pressure is high, the pulse waves may be large enough to be felt or even heard by the individual (palpitation, "pounding heart").

**Atrial Pressure Changes & the Jugular Pulse**

Atrial pressure rises during atrial systole and continues to rise during isovolumetric ventricular contraction when the AV valves bulge into the atria. When the AV valves are pulled down by the contracting ventricular muscle, pressure falls rapidly and then rises as blood flows into the atria until the AV valves open early in diastole. The return of the AV valves to their relaxed position also contributes to this pressure rise by reducing atrial capacity. The atrial pressure changes are transmitted to the great veins, producing three characteristic waves in the record of jugular pressure. The a wave is due to atrial systole. As noted above, some blood regurgitates into the great veins when the atria contract, even though the orifices of the great veins are constricted. In addition, venous inflow stops, and the resultant rise in venous pressure contributes to the a wave. The c wave is the transmitted manifestation of the rise in atrial pressure produced by the bulging of the tricuspid valve into the atria during isovolumetric ventricular contraction. The v wave mirrors the rise in atrial pressure before the tricuspid valve opens during diastole. The jugular pulse waves are superimposed on the respiratory fluctuations.
in venous pressure. Venous pressure falls during inspiration as a result of the increased negative intrathoracic pressure and rises again during expiration.
Heart Sounds

Two sounds are normally heard through a stethoscope during each cardiac cycle. The first is a low, slightly prolonged "lub" (first sound), caused by vibrations set up by the sudden closure of the mitral and tricuspid valves at the start of ventricular systole. The second is a shorter, high-pitched "dup" (second sound), caused by vibrations associated with closure of the aortic and pulmonary valves just after the end of ventricular systole.

The first sound has a duration of about 0.15 s and a frequency of 25-45 Hz. It is soft when the heart rate is low, because the ventricles are well filled with blood and the leaflets of the AV valves float together before systole. The second sound lasts about 0.12 s, with a frequency of 50 Hz. It is loud and sharp when the diastolic pressure in the aorta or pulmonary artery is elevated, causing the respective valves to shut briskly at the end of systole. The interval between aortic and pulmonary valve closure during inspiration is frequently long enough for the second sound to be reduplicated (physiologic splitting of the second sound). Splitting also occurs in various diseases.

Murmurs

Murmurs, or bruits, are abnormal sounds heard in various parts of the vascular system. The two terms are used interchangeably, though "murmur" is more commonly used to denote noise heard over the heart than over blood vessels. The major, but certainly not the only, cause of cardiac murmurs is disease of the heart valves. When the orifice of a valve is narrowed (stenosis), blood flow through it in the normal direction is accelerated and turbulent. When a valve is incompetent, blood flows backward through it (regurgitation or insufficiency), again through a narrow orifice that accelerates flow.
**Cardiac Output in Various Conditions**

The amount of blood pumped out of each ventricle per beat, the **stroke volume**, is about 70 mL in a resting man of average size in the supine position (70 mL from the left ventricle and 70 mL from the right, with the two ventricular pumps in series). The output of the heart per unit time is the **cardiac output**. In a resting, supine man, it averages about 5.0 L/min (70 mL × 72 beats/min). There is a correlation between resting cardiac output and body surface area. The output per minute per square meter of body surface (the **cardiac index**) averages 3.2 L.

**Echocardiography**

Wall movement and other aspects of cardiac function can be evaluated by **echocardiography**, a noninvasive technique that does not involve injections or insertion of a catheter. In echocardiography, pulses of ultrasonic waves, commonly at a frequency of 2.25 MHz, are emitted from a transducer that also functions as a receiver to detect waves reflected back from various parts of the heart to provide a record of the movements of the ventricular wall, septum, and valves during the cardiac cycle.

When combined with Doppler techniques, echocardiography can be used to measure velocity and volume of flow through valves.

It has considerable clinical usefulness, particularly in evaluating and planning therapy in patients with valvular lesions, ischemic heart disease and heart failure.

**Factors Controlling Cardiac Output**

Variations in cardiac output can be produced by changes in cardiac rate or stroke volume. The cardiac rate is controlled primarily by the cardiac innervation, sympathetic stimulation increasing the rate and parasympathetic stimulation decreasing it. The stroke volume is also determined in part by neural input, sympathetic stimuli making the myocardial muscle fibers contract with greater strength at any given length and parasympathetic stimuli having the opposite effect. When the strength of contraction increases without an increase in fiber length, more of the blood that normally remains in the ventricles is expelled; ie, the ejection fraction.
increases and the end-systolic ventricular blood volume falls. The cardiac accelerator action of the catecholamines liberated by sympathetic stimulation is referred to as their **chronotropic action**, whereas their effect on the strength of cardiac contraction is called their **inotropic action**. Factors that increase the strength of cardiac contraction are said to be positively inotropic; those that decrease it are said to be negatively inotropic.

The force of contraction of cardiac muscle is dependent upon its preloading and its afterloading. The initial phase of the contraction is isometric; the elastic component in series with the contractile element is stretched, and tension increases until it is sufficient to lift the load. The tension at which the load is lifted is the **afterload**. The muscle then contracts isotonically without developing further tension. In vivo, the preload is the degree to which the myocardium is stretched before it contracts and the afterload is the resistance against which blood is expelled.

**Relation of Tension to Length in Cardiac Muscle**

The length-tension relationship in cardiac muscle is similar to that in skeletal muscle (see; as the muscle is stretched, the developed tension increases to a maximum and then declines as stretch becomes more extreme. Starling pointed this out when he stated that the "energy of contraction is proportional to the initial length of the cardiac muscle fiber." This pronouncement has come to be known as **Starling's law of the heart** or the **Frank-Starling law**. For the heart, the length of the muscle fibers (ie, the extent of the preload) is proportionate to the end-diastolic volume. The relation between ventricular stroke volume and end-diastolic volume is called the Frank-Starling curve.
THE ELECTROCARDIOGRAM (ECG)

Because the body fluids are good conductors, fluctuations in potential that represent the algebraic sum of the action potentials of myocardial fibers can be recorded extracellularly. The record of these potential fluctuations during the cardiac cycle is the ECG. Most machines record these fluctuations on a moving strip of paper.

The ECG may be recorded by using an active or exploring electrode connected to an indifferent electrode at zero potential (unipolar recording) or by using two active electrodes (bipolar recording). In a volume conductor, the sum of the potentials at the points of an equilateral triangle with a current source in the center is zero at all times. A triangle with the heart at its center (Einthoven's triangle) can be approximated by placing electrodes on both arms and on the left leg. These are the three standard limb leads used in electrocardiography. If these electrodes are connected to a common terminal, an indifferent electrode that stays near zero potential is obtained. Depolarization moving toward an active electrode produces a positive deflection,
whereas depolarization moving in the opposite direction is negative.

An upward deflection is written when the active electrode becomes positive relative to the indifferent electrode, and a downward deflection is written when the active electrode becomes negative.

The P wave is produced by atrial depolarization, the QRS complex by ventricular depolarization, and the ST segment and T wave by ventricular repolarization. The atrial repolarization is not normally seen because they are obscured by the QRS complex. The U wave is an inconstant finding, believed to be due to slow repolarization of the papillary muscles.

**Bipolar Leads**

Bipolar leads were used before unipolar leads were developed. The standard limb leads, leads I, II, and III, each record the differences in potential between two limbs. Since current flows only in the body fluids, the records obtained are those that would be obtained if the electrodes were at the points of attachment of the limbs, no matter where on the limbs the electrodes are placed. In lead I, the electrodes are connected so that an upward deflection is inscribed when the left arm becomes positive relative to the right (left arm positive). In lead II, the electrodes are on the right arm and left leg, with the leg positive; and in lead III, the electrodes are on the left arm and left leg, with the leg positive.

**Unipolar (V) Leads**

An additional nine unipolar leads, ie, leads that record the potential difference between an
exploring electrode and an indifferent electrode, are commonly used in clinical electrocardiography. There are six unipolar chest leads (precardial leads) designated V₁-V₆ and three unipolar limb leads: VR (right arm), VL (left arm), and VF (left foot). Augmented limb leads, designated by the letter a (aVR, aVL, aVF), are generally used. The augmented limb leads are recordings between one limb and the other two limbs. Unipolar leads can also be placed at the tips of catheters and inserted into the esophagus or heart.

**The Normal ECG**

The sequence in which the parts of the heart are depolarized position of the heart relative to the electrodes are the important considerations in interpreting the configurations of the waves in each lead.

The atria are located posteriorly in the chest. The ventricles form the base and anterior surface of the heart, and the right ventricle is anterolateral to the left.

Thus, aVR "looks at" the cavities of the ventricles. Atrial depolarization, ventricular depolarization, and ventricular repolarization move away from the exploring electrode, and the P wave, QRS complex, and T wave are therefore all negative (downward) deflections;

aVL and aVF look at the ventricles, and the deflections are therefore predominantly positive. There is no Q wave in V₁ and V₂, and the initial portion of the QRS complex is a small upward deflection because ventricular depolarization first moves across the midportion of the septum from left to right toward the exploring electrode. The wave of excitation then moves down the septum and into the left ventricle away from the electrode, producing a large S wave. Finally, it moves back along the ventricular wall toward the electrode, producing the return to the isoelectric line. Conversely, in the left ventricular leads (V₄-V₆) there may be an initial small Q wave (left to right septal depolarization), and there is a large R wave (septal and left ventricular depolarization) followed in V₄ and V₅ by a moderate S wave (late depolarization of the ventricular walls moving back toward the AV junction). There is considerable variation in the
position of the normal heart, that affects the configuration of the ECG.

**Bipolar Limb Leads & the Cardiac Vector**

Because the standard limb leads are records of the potential differences between two points, the deflection in each lead at any instant indicates the magnitude and direction in the axis of the lead of the electromotive force generated in the heart (cardiac vector or axis).

The vector at any given moment in the two dimensions of the frontal plane can be calculated from any two standard limb leads if it is assumed that the three electrode locations form the points of an equilateral triangle (Einthoven's triangle) and that the heart lies in the center of the triangle. These assumptions are not completely warranted, but calculated vectors are useful approximations.
The normal direction of the mean QRS vector is generally said to be -30 to +110 degrees on the coordinate system.

Left or right axis deviation is said to be present if the calculated axis falls to the left of -30 degrees or to the right of +110 degrees, respectively. Right axis deviation suggests right ventricular hypertrophy, and left axis deviation may be due to left ventricular hypertrophy, but there are better and more reliable electrocardiographic criteria for ventricular hypertrophy.