The Heart: Anatomy, Physiology and Exercise Physiology

1

Syed Shah, Gopinath Gnanasegaran, Jeanette Sundberg-Cohon, and John R Buscombe

Contents

1.1	Introduction	3
1.2	Anatomy of the Heart	3
1.2.1	Chamber and Valves	4
1.2.2	Cardiac Cell and Cardiac Muscle	4
1.2.3	Coronary Arteries and Cardiac Veins	6
1.2.4	Venous Circulation	6
1.2.5	Nerve Supply of the Heart	9
1.2.6	Conduction System of the Heart	10
1.3	Physiology of the Heart	11
1.3.1	Circulatory System: Systemic and Pulmonary Circulation	11
1.3.2	Conduction System of the Heart (Excitation Sequence)	11
1.3.3	Action Potential (AP)	11
1.3.4	Mechanism of Excitation and Contraction Coupling of Cardiac Myocytes	13
1.3.5	Autonomic Nervous System and Heart	16
1.3.6	Cardiac Cycle	16
1.3.7	Physiology of Coronary Circulation	17
1.3.8	Coronary Collaterals	17
1.4	Exercise Physiology	18
1.4.1	Gender and Exercise Performance	19
1.4.2	Age and Exercise Performance	19
1.5	Conclusion	20
	References	20

1.1 Introduction

The impact of anatomy on medicine was first recognised by Andreas Vesalius during the 16th century [1] and from birth to death, the heart is the most talked about organ of the human body. It is the centre of attraction for people from many lifestyles, such as philosophers, artists, poets and physicians/surgeons. The heart is one of the most efficient organs in the human body and heart disease is one of the commonest causes of morbidity and mortality in both developing and developed countries. Understanding the anatomy and pathophysiology is very important and challenging. With innovative changes in the imaging world, the perception of these has changed radically and applied anatomy and physiology plays an important role in understanding structure and function.

1.2 Anatomy of the Heart

The heart is located in the chest, directly above the diaphragm in the region of the thorax called mediastinum, specifically the middle mediastinum. The normal human heart varies with height and weight (Table 1.1). The tip (apex) of the heart is pointed forward, downward, and toward the left. The (inferior) diaphragmatic surface lies directly on the diaphragm. The heart lies in a double walled fibroserous sac called the pericardial sac, which is divided into (a) fibrous pericardium, and (b) serous pericardium. The fibrous pericardium envelops the heart and attaches onto the great vessels [2]. The serous pericardium is a closed sac consisting of two layers – a visceral layer or epicardium forming the outer lining of the great vessels and the heart, and a parietal layer forming an inner lining of the fibrous pericardium [2–4]. The two layers of the serous pericardium contain the pericardial fluid, which prevents friction between the heart and the pericardium [2–4].

Table 1.1 Anatomical facts about the human heart

Normal human heart varies with height and weight
Weighs approximately 300–350 grams in males
Weighs approximately 250–300 grams in females
Right ventricle thickness is 0.3–0.5 cm
Left ventricle thickness is 1.3–1.5 cm
Divided into four distinct chambers
Composed of three layers (epicardium, myocardium and endocardium)
Contains two atria (left and right)
Contains two ventricles (left and right)
Contains four valves (aortic, mitral, tricuspid, pulmonary)

The wall of the heart is composed of three layers: (a) epicardium; (b) myocardium; and (c) endocardium (Fig. 1.1) [5, 6]. The epicardium is the outer lining of the cardiac chambers and is formed by the visceral layer of the serous pericardium. The myocardium is the intermediate layer of the heart and is composed of three discernable layers of muscle [5, 6] that are seen predominantly in the left ventricle and inter-ventricular septum alone and includes a subepicardial layer, a middle concentric layer and a subendocardial layer. The rest of the heart is composed mainly of the subepicardial and subendocardial layers [7, 8]. The myocardium also contains important structures such as excitable nodal tissue and the conducting system. The endocardium the innermost layer of the heart is formed of the endothelium and subendothelial connective tissue [5, 6].

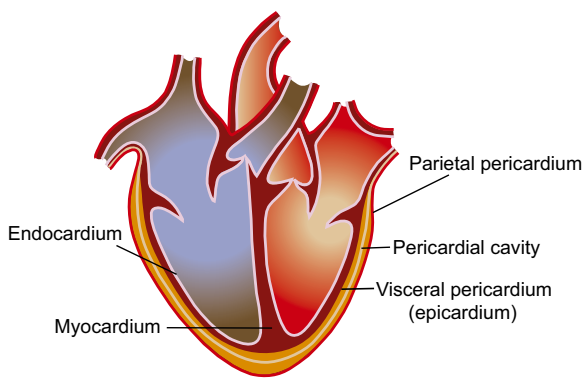

Fig 1.1 Layers of the heart

1.2.1 Chamber and Valves

The heart is divided into four distinct chambers with muscular walls of different thickness [2, 4, 9]. The left atrium (LA) and right atrium (RA) are small, thin-walled chambers located just above the left ventricle (LV) and right ventricle (RV), respectively. The ventricles are larger thick-walled chambers that perform most of the work [2, 4, 9] (Table 1.2). The atria receive blood from the venous system and lungs and then contract and eject the blood into the ventricles. The ventricles then pump the blood throughout the body or into the lungs. The heart contains four valves and the fibrous skeleton of the heart contains the annuli of the four valves, membranous septum, aortic intervalvular, right, and left fibrous trigones [3, 4, 6, 10, 11] (Fig. 1.2, Table 1.3). The right trigone and the membranous septum together form the central fibrous body, which is penetrated by the bundle of His [3, 4, 6, 10, 11]. The fibrous skeleton functions not only to provide an electrophysiological dissociation of atria and the ventricles but also provides structural support to the heart [8, 12, 13]. Each of the four valves has a distinctive role in maintaining physiological stability [3].

1.2.2 Cardiac Cell and Cardiac Muscle

The cardiac cell contains bundles of protein strands called myofibrils. These myofibrils are surrounded by sarcoplasmic reticulum, which contains cysternae (dilated terminals) [6, 10, 11, 14–16]. The sarcomeres are the contractile unit of myofibrils and the T tubules are continuations of the cell membrane located near the Z-lines, which conduct the action potential (AP) to the interior of the cell [6, 14]. The T tubules connect the sarcolemma to the sarcoplasmic reticulum in the skeletal muscle and the cardiac muscle [14, 15].

Cardiac muscle is an involuntary striated muscle, which is mononucleated and has cross-striations formed by alternate segments of thick and thin protein filaments, which are anchored by segments called Z-lines. Cardiac muscle is relatively shorter than skeletal muscle [6, 10, 11, 14–16] and actin and myosin are the primary structural proteins. When the cardiac muscle is observed by a light microscope, the thinner actin filaments appear as lighter bands, while thicker myosin filaments appear as darker bands [8, 12, 13, 15]. The dark bands are actually the region of overlap between the actin and myosin filaments and the light bands are the region of actin filaments [8, 12, 13, 15]. The thinner actin flaments contain two others proteins called troponin and tropomyosin, which play an important role in contraction [6, 14, 15]. Cardiac muscle also contains dense bands (specialised

Table 1.2 Cardiac atrial and ventricular chambers [2, 4–6, 9]

Left ventricle (LV)
1. Made of an inlet portion comprised of mitral valve apparatus, subaortic outflow portion and a trabeculated apical zone
2. Three times thicker than the RV and most muscular
3. Thickest towards the base and thinnest towards the apex
4. LV free wall and septal thickness is three times the thickness of the RV free wall
5. Mitral and aortic valves share fibrous continuity
6. LV apex is relatively less trabeculated than the RV apex
Right ventricle (RV)
1. Comprised of inlet and outflow segments
2. Inlet extends from tricuspid annulus to the insertions of the papillary muscles
3. Apical trabecular zone extends inferiorly beyond the papillary muscle attachment toward the ventricular apex and halfway along the anterior wall.
4. Outflow portion (conus) is a muscular subpulmonary channel
5. Arch shaped muscular ridge separates the tricuspid and pulmonary valves
Right atrium (RA)
1. Thinnest walls of the four chambers
2. Forms the right border of the heart
3. Gives off the right auricular appendage
4. Receives the superior vena cava, inferior vena cava and coronary sinus
5. Discharges into right ventricle through the tricuspid valve
Left atrium (LA)
1. Forms base of the heart (posterior surface)
2. Gives off the left auricular appendage.
3. Receives two right pulmonary veins (sometimes three) and two left pulmonary veins (sometimes one)
4. Discharges into the left ventricle through the mitral valve
Ventricular septum
1. Intracardiac partition having four parts (inlet, membranous, trabecular and infundibular)
2. Divided into muscular and membranous septum
3. Membranous septum lies beneath the right and posterior aortic cusps and contact mitral and tricuspid annuli
Atrial septum
1. Composed of interatrial and atrioventricular regions when viewed from right
2. Composed of entirely interatrial regions when viewed from the left
3. Interatrial region is characterised by fossa ovalis
4. Atrioventricular portion separates the right atrium from the left ventricle

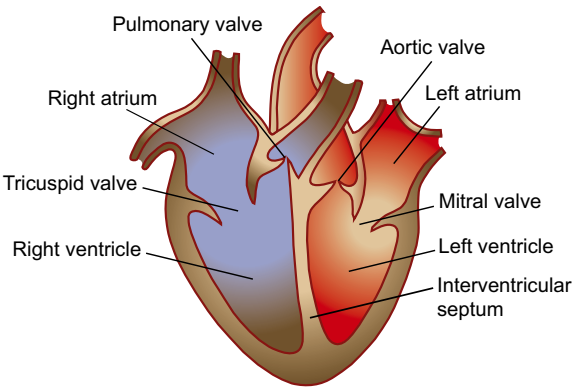

Fig 1.2 Cardiac chambers and valves

cell junctions) called intercalated discs that separate individual cells from one another at their ends [6, 14, 15] and these discs consist of a transverse and a lateral portion. The transverse portion of the disc acts as a zone of firm adhesion and a route of transmission of contractile force and the lateral portion of the disc acts as a gap junction across which propagation of electrical impulses between the adjacent cardiac cells occurs [6, 14, 15]. This in effect allows the individual cells of the heart to act as a syncytium [8, 12–15].

1.2.3 Coronary Arteries and Cardiac Veins

The heart receives blood from left coronary arteries (LCA) and right coronary arteries (RCA) [17] (Fig. 1.3, Table 1.4). The left coronary artery arises from the left aortic sinus (at an acute angle from the aorta) [2, 3, 6, 8] as a single short main artery (left mainstem). The LCA bifurcates to form the left anterior descending artery (LAD) and left circumflex (LCx) [2, 3, 6]. The LAD anastomoses with the posterior descending artery (PDA) a branch of the right coronary artery (RCA) [2, 3, 6]. The LAD supplies the interventricular septum (anterior two-thirds), the apex, and the anterior aspects of the right and left ventricle. The LCx has a major branch, the left marginal artery, and in around 10–15% of the population, the LCx anastomoses with the RCA to give rise to the PDA [2, 3, 6–8]. In general, the LCx supplies the posterior aspect of the left atrium and superior portion of the left ventricle [2, 3, 6–8].

The RCA arises from the right aortic sinus and has major branches such as the PDA (supplying the posterior third of the interventricular septum and AV node [6, 7], the nodal artery (supplying the right atrium and the SA node), and the right marginal artery (supplying a portion of the right ventricle, the inferior left ventricular wall, and the PDA). In the majority (80–90%) of cases, the RCA supplies the atrioventricular node (AV node). Finally, the coronary arteries branch into small arteries and arterioles. These vessels terminate in end arteries that supply the myocardial tissue with blood [2, 3, 6–8].

In general, the RCA is dominant in 60–65% of cases because it gives off a PDA branch (balanced coronary circulation) [2, 3, 6–8]. In about 10–15% of cases, the LCx gives rise to the PDA (left predominant circulation). In 20-25% of cases, the RCA, in addition to supplying the PDA, crosses the posterior interventricular septum to reach as far as the left marginal artery and thereby supply the diaphragmatic surface of the left ventricle (right predominance) [2, 3, 8]. However, this term does not distinguish this condition from balanced coronary circulation (Table 1.5) [7].

1.2.4 Venous Circulation

The venous circulation of the heart is from the coronary sinus, anterior cardiac veins and the lesser cardiac (thebesian) veins [6]. The coronary sinus receives most of the venous return from the epicardium and myocardium [6] and it opens into the right atrium between the opening of the inferior vena cava and the right AV valve [2, 3, 5, 6]. The coronary sinus gives rise to tributaries such as the great cardiac vein, middle cardiac vein, smaller cardiac vein and oblique vein. The great cardiac vein drains the anterior portion of the interventricular septum and anterior aspects of both ventricles [2–6].

The middle cardiac vein drains the posterior portion of the interventricular septum and posterior aspect of

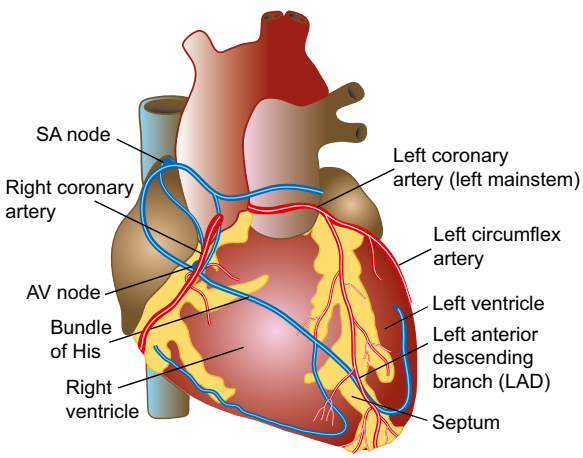

Fig 1.3 Coronary arteries

Table 1.3 Cardiac valves and cardiac skeleton [2, 4–6, 8, 9]

Tricuspid valve
1. Tricuspid valve (right atrioventricular valve) connects the right atrium and the right ventricle
2. Composed of five components (annulus, leaflets, commissures, chordae tendineae, papillary muscles)
3. Anterior tricuspid leaflet is the largest (most mobile) and the posterior leaflet is the smallest
4. Tricuspid valve has a triangular orifice
Mitral valve
1. Mitral valve (left atrioventricular valve) connects the left atrium to the left ventricle
2. Composed of five components (annulus, leaflets, commissures, chordae tendineae, papillary muscles)
3. Composed of two leaflets only
4. Anterior tricuspid leaflet is large, semicircular and twice the height of posterior leaflet
5. Posterior leaflet is rectangular and is divided into three scallops
6. Mitral valve has an elliptical orifice
Aortic valve
1. Aortic valve (semilunar valve) opens between the left ventricle and the aorta
2. Composed of three components (annulus, cusps, commissures)
3. Composed of three semilunar cusps
Pulmonary valves
1. Pulmonary valve (semilunar valve) regulates flow between the right ventricle and the pulmonary artery
2. Composed of three components (annulus, cusps, commissures)
Cardiac grooves
1. Atrioventricular (AV) groove separates the atria from the ventricle
2. Anterior and posterior interventricular (IV) grooves separate the ventricles
3. Right coronary arteries (RCA) travel in the right atrioventricular groove
4. Circumflex artery (Cx) travels in the left atrioventricular groove
5. The left anterior descending artery (LAD) travels along the anterior interventricular groove
6. Posterior descending artery (PDA) travels along posterior interventricular groove
Cardiac crux (external and internal)
1. External cardiac crux is the intersection between the AV, posterior IV and interatrial (IA) grooves
2. Internal cardiac crux is the posterior intersection between the mitral and tricuspid annuli and the atrial and ventricular septa
Cardiac margins
1. Acute margin – junction between anterior and inferior wall of the right ventricle
2. Obtuse margin – rounded lateral wall of left ventricle

Table 1.4 Coronary blood supply [2, 3, 6, 8]

Coronary arterial circulation

A. Left coronary artery (LCA)

1. Ostium of the left coronary artery originates from the left aortic sinus.
2. LCA arises at an acute angle from the aorta.
3. LCA courses to the left and anteriorly (Left anterior descending artery – LAD) and after variable length gives rise to left circumflex artery (LCx).
4. Diagonal artery may arise between LAD and LCx or from the LAD.
5. LAD continues towards the septum and gives rise to septal perforator branches.

B. Right coronary artery

1. Arises from the right aortic sinus.
2. Major branches are nodal, right marginal, PDA.
3. Supplies the RA, SA node, part of RV, posterior third of the interventricular septum, AV node and right branch of the AV bundle (of His).

C. Left circumflex artery (LCx)

1. Originates from the LAD and course is variable.
2. May terminate into one or more large obtuse marginal branches.
3. May continue as a large artery and give rise to posterior descending artery (PDA).
4. When the left circumflex artery supplies the major PDA, it is referred to as a dominant artery.

Coronary venous circulation

1. Composed of the coronary sinus, cardiac veins, and thebesian venous system.
2. Great cardiac vein and other cardiac veins (left posterior and middle) drain into the coronary sinus and finally empties into the right atrium.
3. Rarely, the coronary sinus drains directly into the left atrium.

Coronary collaterals

1. Provide communication between major coronary arteries and branches.
2. May dilate and provide blood supply beyond the obstructed/stenosed epicardial vessel.
3. May develop between the terminal extension of two arteries, between side branches of two arteries, between branches of same artery or within the same branch.
4. Most common in the ventricular septum, ventricular apex, anterior right ventricular free wall, anterolateral left ventricle free wall, cardiac crux and atrial surfaces.

Cardiac lymphatics

1. Lymphatics drain towards the epicardial surface and they merge to form the right and left channels.
2. Left and right channels travel in a retrograde fashion with their respective coronary arteries.
3. The left and right channels travel along the ascending aorta and merge before draining into the pretracheal lymph node.
4. The merged single lymphatic chain travels through a cardiac lymph node and finally empties into the right lymphatic duct.

Table 1.4 *(continued)* Coronary blood supply [2, 3, 6, 8]

Great vessels
1. Subclavian and internal jugular veins join together bilaterally to form right and left innominate (brachiocephalic) veins.
2. Right and left (longer) innominate veins join together to form superior vena cava (SVC).
3. SVC receives azygous vein before draining into the right atrium.
4. Thoracic aorta arises at the level of aortic valve and is made up of the ascending aorta (sinus and tubular portions), aortic arch and descending aorta.
5. Aortic arch gives rise to the innominate, left common carotid and subclavian arteries.
6. Descending aorta lies adjacent to the left atrium, oesophagus and vertebral column.

Table 1.5 Regions supplied by coronary arteries [7]

Right coronary artery	Left coronary artery (Left anterior descending)	Left coronary artery (Left circumflex artery)
Right ventricle	Anterior and lateral wall of LV	SA node (40–45%)
Right atrium	Most of the left ventricle	Left atrium
Diaphragmatic surface/inferior wall of left ventricle (LV)	Interventricular septum (anterior 2/3rd)	AV node and bundle of His (10%)
	Right and left bundle branches	Lateral wall of LV
Posterior wall of left ventricle (90%)		Posterior wall of left ventricle (10%)
Posterior third of interventricular septum (90%)		Posterior third of interventricular septum (10%)
SA node (55–60%)		
AV node and bundle of His (80–90%)		

both ventricles [4, 6] and the smaller cardiac vein drains the marginal aspect of the right ventricle [11]. The thebesian veins drain the endocardium and the innermost layers of the myocardium directly into the underlying chamber [11].

1.2.5 Nerve Supply of the Heart

The sympathetic and parasympathetic autonomic nervous supplies to the heart form the cardiac plexus, which is located close to the arch of the aorta. The fibres from the cardiac plexus accompany the coronary arteries and reach the heart, with most of them terminating at the SA node, AV node and a much less dense supply to the atrial and ventricular myocardium [11]. In general, the parasympathetic vagal fibres are inhibitory and reduce the heart rate and stroke volume. The sympathetic nerves act as accelatory nerves increasing both the heart rate and stroke volume [11]. The afferent nerves run along sympathetic pathways via both cardiac accelerator nerves and thoracic splanchnic nerves to reach the intermediolateral horn of T1–T4 of the spinal cord [11]. The noradrenergic or the sympathetic nervous system is mainly involved with increasing the heart rate (chronotropy), contractility (ionotropy) and the speed of conduction (dromotropy) in the cardiac muscle fibres and the conduction tissue; and the transmitter involved is mainly nor-epinephrine [6]. The SA node receives most of it nerve fibres from the right-sided thoracic sympathetic ganglia and the right vagus [8]. The AV nodes and ventricles receive their nerve supply form the left-sided thoracic sympathetic ganglia and the left vagus, which is mainly because SA node develops from the structures on the right side of the embryo and the AV node develops from the structures on the left side of the embryo [8].

The sympathetic effects are mediated mainly by the adrenergic receptors, which includes β-1 and β-2 adrenergic receptors [2, 11]. β-1 receptors are found mainly in the SA node and AV node, and the ventricular myocardium acts via activation of adenylate cyclase and an increase in cAMP (cyclic adenosine monophosphate) concentration in the cell to mediate the above mentioned sympathetic effects [2, 11]. β-2 receptors are mainly found in the vascular smooth muscles in addition to the bronchial smooth muscle and wall of the GI tract and the bladder. The mechanism of action is same as that of β-1 receptors, i.e., increase in cAMP levels but they cause relaxation of the vascular smooth muscle and are involved in regulation of blood flow and systemic blood pressure [2, 11].

The cholinergic or the parasympathetic nervous system effects in the heart are opposite to the ones mentioned above and the transmitter involved is mainly acetylcholine [8, 12, 13]. The vagi supply the parasympathetic fibres to the heart via the cardiac plexuses. The parasympathetic effects are mediated via the muscaranic receptors, which act by inhibition of adenylate cyclase and hence decrease the intracellular cAMP levels and result in a decrease in heart rate, contraction and conduction velocity [8, 12, 13].

The autonomic centres in the CNS, mainly the vasomotor centre of medulla and the hypothalamus regulate the balance between the level of sympathetic and the parasympathetic output to the cardiovascular system, depending on the afferent inputs from the periphery and the CNS [7, 8, 12, 13]. There is normally a tonic vagal discharge in humans, which overrides the moderate tonic discharge in the cardiac sympathetic nerves [7, 8, 12, 13]. Both the sympathetic and the parasympathetic fibres in the splanchnic thoracic nerves and the vagi carry afferent input mediated via baroreceptors and chemoreceptors to the autonomic centres in the CNS, in addition to the efferent output from the CNS. These afferents and efferents are involved in mediation of cardiovascular reflexes as baroreceptor and chemoreceptor reflexes [7, 8, 12, 13].

The receptors of the autonomic nervous system to the heart are the target of numerous drugs used in the treatment of various cardiovascular disorders in both acute and chronic settings [8, 12, 13].

1.2.6 Conduction System of the Heart

The cardiac conduction system consists of highly specialised cells, which are mainly involved in the conduction of impulses to the different regions of the myocardium [19, 20]. It has been seen to be composed of three types of morphologically and functionally distinct cells, which include P-cells (Pale/Pacemaker-cells), transitional cells and Purkinje cells [19, 20]. These are important in maintaining the heart's electrical activity in an orderly fashion. The conduction system consists of sinus node, in-

Table 1.6 Conduction system of the heart [2, 6, 9]

Sinoatrial (SA)/sinus node
1. Heart's normal pacemaker automatically initiates impulses/contraction cycle at a rate of approximately 72 depolarisations per minute
2. Located by the right atrium (cista terminalis) near the superior vena cava
3. Supplied by the nodal branch of RCA
4. Innervation is principally by the parasympathetic nervous system (slows the autorhythmicity)
5. Blood supply arises from RCA in 55–60% of people (close contact with right atrial appendage and SVC)
6. Blood supply arises from left circumflex in 40–45% of people (lies close to left atrial appendage)
Atrioventricular (AV) node/node of Tawara
1. Located in the right atrium along the lower part of the inter-atrial septum
2. Autorythmic with approximately 40 depolarisations per minute
3. In majority, supplied by RCA
4. It gives rise to the AV bundle
AV Bundle of His
1. Band of nerve fibres that originates from AV node and cross the A-V ring
2. AV bundle is closely related to the annuli of aortic, mitral and tricuspid valves
3. AV bundle receives dual blood supply (AV nodal artery and first septal perforator of LAD)
4. Divides into right and left bundle branches that are continuations of the bundle of His
5. These right and left bundles extend along the right and left sides of the inter-ventricular septum to the tips of the two ventricles
Purkinje fibres
1. Terminal branching of the right and left bundle (thousands of fibrils extending between myocardial fibres).

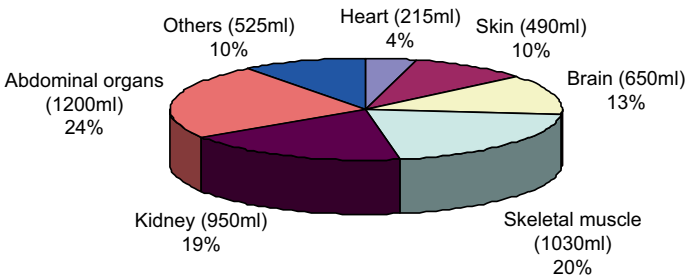

Fig 1.4 Distribution of systemic blood flow to various organs of the body during rest (adapted from Widmaier et al. [14])

ternodal tracts, AV node, AV (His) bundle, right and left bundle branches and Purkinje fibres [4, 18] (Table 1.6).

1.3 Physiology of the Heart

1.3.1 Circulatory System: Systemic and Pulmonary Circulation

The cardiovascular system delivers oxygen and nutrients to the tissues and carries away waste materials to be eliminated by organs such as lungs, liver and kidneys [1, 4] (Fig. 1.4). This system is required to function under various normalised and diseased conditions. The pulmonary and systemic circulations together help in fulfilling this role. Pulmonary circulation is a low resistance, high capacitance bed, and systemic circulation, in comparison, is a relatively high resistance vascular bed [4, 11, 14, 21] (Fig. 1.5).

The deoxygenated blood from the superior vena cava (from upper extremities, head, and chest wall), inferior vena cava (trunk, abdominal organs and lower extremities) and the coronary sinuses (from myocardium) reaches the RA [1, 4, 6, 11]. The RA is filled with deoxygenated blood, increasing pressure in the atrial chamber. When the atrial pressure exceeds the pressure in the RV, the tricuspid valve opens allowing this blood to enter the RV [1, 4, 6, 11]. As a result of this filling, and as the RV starts to contract the pressure in the RV builds up forcing the tricuspid valve to close and the pulmonic valve to open, thereby ejecting the blood into the pulmonary arteries and lungs [1, 4, 6, 11].

The oxygenated blood from the lungs reaches the LA via the pulmonary veins and as a result, pressure in LA builds up and when it exceeds that of the LV, the mitral valve opens, allowing the blood to enter the LV [1, 4, 6, 11]. When the blood fills the LV, and as the LV starts to contract, the LV chamber pressure increase forces the mitral valve to close and aortic valve to open, thus ejecting blood into the aorta, to be distributed throughout the body [1, 4, 6, 11].

1.3.2 Conduction System of the Heart (Excitation Sequence)

The cardiac myocytes have a unique ability of automatic impulse generation, which results in automatic rhythmicity. Normally the electrical impulse begins in the SA node, as it has the fastest impulse generation ability and hence drives the heart. The impulse then spreads to the rest of the right atrial walls directly, to the left atrium by the interatrial conducting fibres and then to the AV node (AV junctional tissue) [6] (Fig. 1.6). The AV node conducts the impulse with a delay and propagates through the ventricular myocardium via the AV bundle of His and Purkinje fibres [1, 3, 6, 8–13, 18]. From the Purkinje fibres, the excitation impulse then continues through myocardial cells outside the specialised conduction pathway to reach the subendocardial surface. This rapid, simultaneous and coordinated spread of excitation through the ventricles produces a coordinated contraction of both ventricles, thus ensuring efficient pumping of blood to the pulmonary and systemic circulations [1, 3, 6, 8–13, 18].

1.3.3 Action Potential (AP)

Ventricles, atria and the Purkinje system have a stable resting membrane potential of about −90 mV, determined mainly by K^+ conductance [12, 13]. The action potential is of long duration about 300 ms, which is prolonged in comparison with the action potential of the rest of the cells in the body. The action potential of the myocardial cells excluding the nodal tissue is initiated by a sudden transient inward increase in the membrane conductance of the Na^+ ion, referred to as the upstroke of the action potential or phase 0 (Figs. 1.7 and 1.8) [12, 13]. This is followed by a brief transient outward increase in K^+ ion membrane conductance resulting in a brief period of initial repolarisation. The decreasing Na^+ ion conductance also plays a part in this initial repolarisation phase and is referred to as phase 1 of action po-

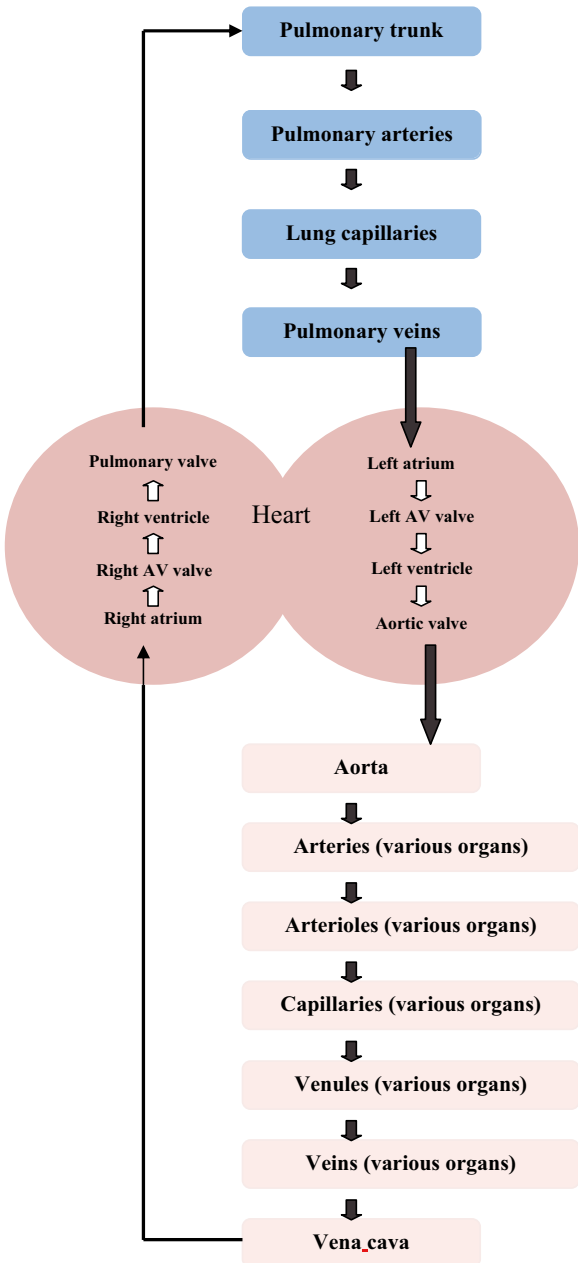

Fig 1.5 Circulatory pathway of the cardiovascular system [8]

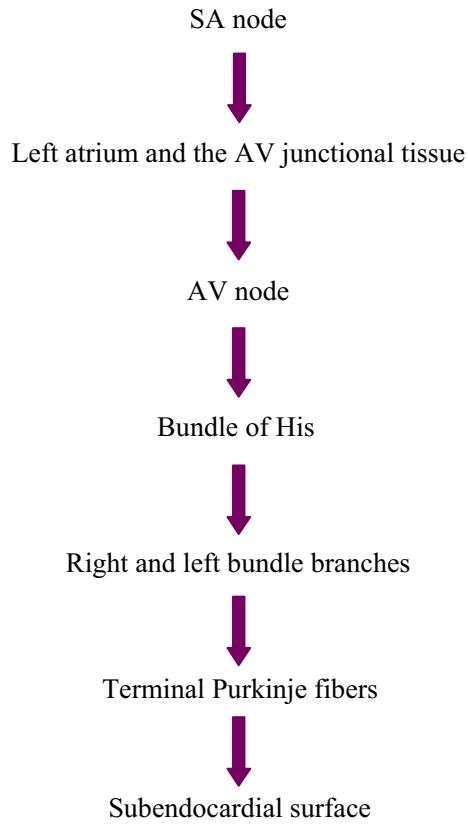

Fig 1.6 Conducting system of the heart

tential [12, 13]. After this phase comes the plateau phase or phase 2 of action potential, which is characterised by the transient increase in inward Ca^{++} ion conductance, accompanied by an increase in outward K^+ ion conductance [12, 13]. These outward and inward currents are such that they maintain the membrane potential in the plateau phase. The plateau phase is followed by the repolarisation phase of the action potential or phase 3, which results from the declining inward Ca^{++} ion conductance and an increase in the outward K^+ ion conductance [12, 13]. This outward K^+ ion conductance hyperpolarises the membrane towards K^+ ion equilibrium and brings about the repolarisation or phase 4 [12, 13].

The SA node action potential is different from the rest of the conducting system and the myocardium. It is characterised by an unstable resting membrane potential or phase 4. This results from an increased Na^+ ion conductance resulting in inward Na^+ current [12, 13]. The inward Na^+ current is triggered by the repolarisation of the preceding action potential. In addition, the phase 0 of the action potential in the SA node is the result of inward Ca^{++} ion conductance in contrast to Na^+ ion, as in the rest of the myocardium [12, 13]. In addition, the SA node action potential lacks the plateau or phase 2 of the myocardial cell action potential [12, 13]. The upstroke of the action potential in the AV node is also due to the Ca^{++} ion conductance as in the SA node. The conduction velocity is fastest in the Purkinje system and slowest in the AV node [12, 13].

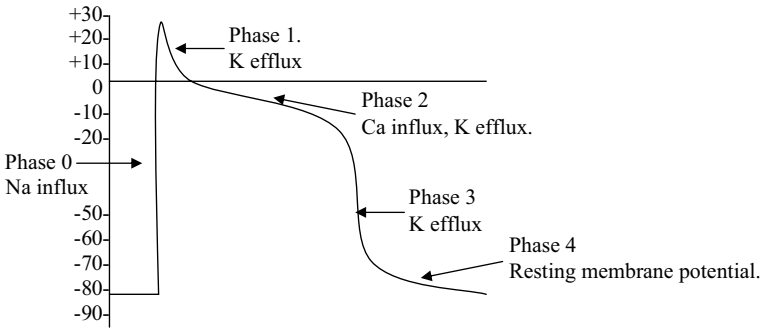

Fig 1.7 Cardiac action potential

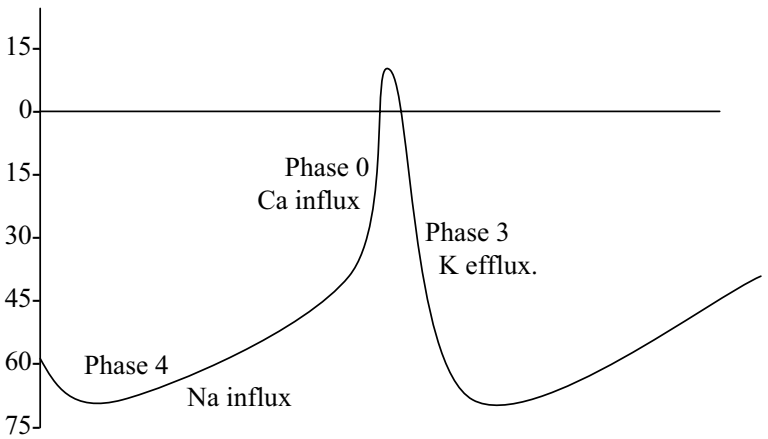

Fig 1.8 SA nodal action potential

1.3.4 Mechanism of Excitation and Contraction Coupling of Cardiac Myocytes

The regulation of cardiac muscle contraction has neural, hormonal and intrinsic components. The heart is composed of cylindrical cardiac cells and stimulation of one cardiac cell initiates stimulation of adjacent cells [7, 22]. In general, the cardiac cells are of two types (a) electrical cells and (b) myocardial cells [7]. The electrical cells are specialised myocardial cells that have essentially lost the ability to contract but have become specialised in the conduction of cardiac impulses.

The myocardial cells have two specific properties: contractility (ability of the cells to shorten and return to their original length) and extensibility (cell filaments' ability to stretch) [22]. The contraction mechanism contains numerous steps and "excitation–contraction coupling" is the term used to define the events that translate the depolarisation of the cardiac cell membrane to the contraction of the muscle fibres [5, 6, 11] (Fig. 1.9). The contractile filaments actin and myosin in the myocardium are responsible for the contraction. In the cardiac cell, the sarcoplasmic reticulum and the cisternae contains high concentrations of ionised Ca^{++} and depolarisation of the T tubules, which is an extension of the cell membrane, causes the release of Ca^{++} from these structures [5, 6, 11]. In general, an action potential precedes each contraction, and between contractions the Ca^{++} within the cell is very low. The cardiac action potential is unique in that it has a plateau phase, which is maintained by the inward Ca^{++} influx (current) [5, 6, 11]. It is this inward Ca^{++} current that triggers release of further Ca^{++} from the sarcoplasmic reticulum. The amount of Ca^{++} released depends on the strength of the inward Ca^{++} current. Compared with the resting or basal conditions, the concentration of Ca^{++} is ten times higher during an AP [5]. When the concentration of the Ca^{++} is high, the troponin-C is bound by four Ca^{++} ions per molecule and this changes the shape of troponin [6, 7, 11]. This change in shape allows the tropomyosin to uncover the cross-bridge sites, which allows the formation of cross bridges between actin and myosin filaments [6, 7, 11]. In the resting state, the troponin molecules shield the cross-bridges.

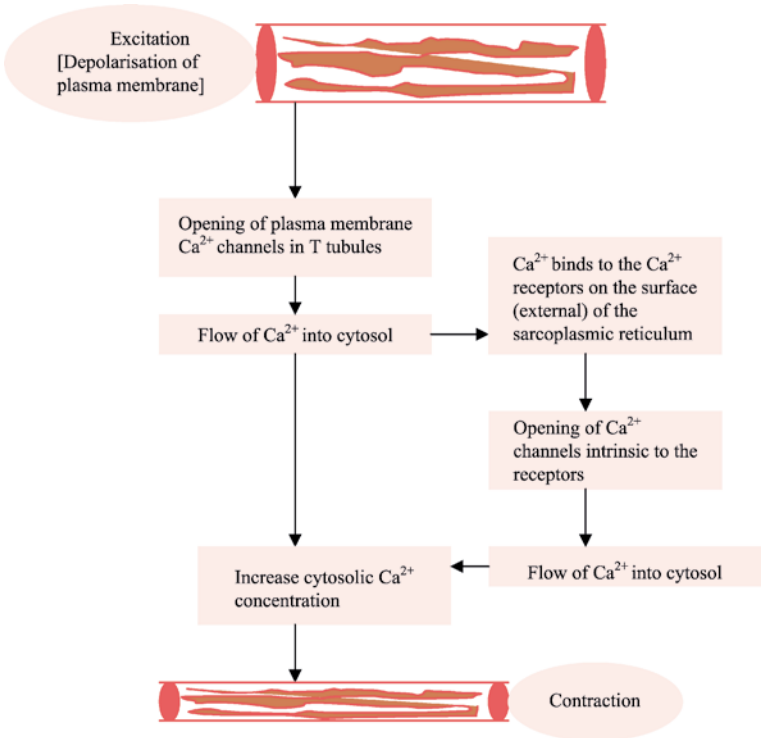

Fig 1.9 Excitation contraction coupling

The presence of adenosine triphosphate (ATP) is important in the contractile process. The actin–myosin cross-bridges are formed in the presence of ATP, which later hydrolyses. The energy derived from ATP hydrolysis leads to changes in the myosin head configuration so that actin can be detached from myosin (10 nm/cycle). Finally, ATP is required for relaxation of the muscle by dissociating the cross-bridges [6]. In general, an increase in the number of bridges causes an increase in the force of contraction, which is proportional to the intracellular Ca^{++} concentration [6]. Relaxation occurs when the intracellular Ca^{++} is re-sequestered back into the sarcoplasmic reticulum by the Ca^{++}-ATPase pump. Administration of drugs like epinephrine, norepinephrine, and digitalis and sympathetic nerve stimulation increases the intracellular Ca^{++} levels, which results in forceful contraction [6]. Norepinephrine not only causes forceful contraction but also shortens the AP and contraction by causing more rapid uptake of Ca^{++} by the sarcoplasmic reticulum [6]. The contractility can be quantified by calculating the ejection fraction (EF), which is defined as the ratio of stroke volume (SV) to end-diastolic volume (*EDV*) ($EF = SV/EDV$) [11, 23, 24].

The electrical cells are special cardiac cells of the conducting system [22]. These cells are primarily responsible for the formation and conduction of the impulses. They have some specific properties such as (a) conductivity (ability to transmit electrical impulse from one cell to another), (b) excitability (ability of the cell to respond to electrical impulses) and (c) automaticity (ability of the cell to spontaneously generate and discharge an electrical impulse) [7, 22]. The depolarisation (electrical activation), contraction and repolarisation (Fig. 1.10) of cardiac cells is due to the ability of the electrical cells to generate and conduct electrical impulses. The flow of positively charged ions across the cardiac cell membranes results in the formation of these electrical impulses [7, 22]. The extracellular fluid surrounding the cardiac cells contains positively and negatively charged ions. However, the composition of these ions in the extra- and intracellular spaces is different [7]. The intracellular space contains positively charged potassium ions in high concentration and positively charged sodium in lower concentration. The extracellular space contains the positively charged sodium and negatively charged chloride in high concentration and a lower concentration of potassium [7]. The movement of the primary intracellular ion (potassium) and primary extracellular ion (sodium) mediates the regulation of electrical charges. The cyclical shift of ions changes the electrical field inside the cell leading to depolarisation and repolarisation [7, 22]. In part, the ionic shift is dependent on the pores or channels present on the cell membrane, and partly on the opening and closing of channels which is

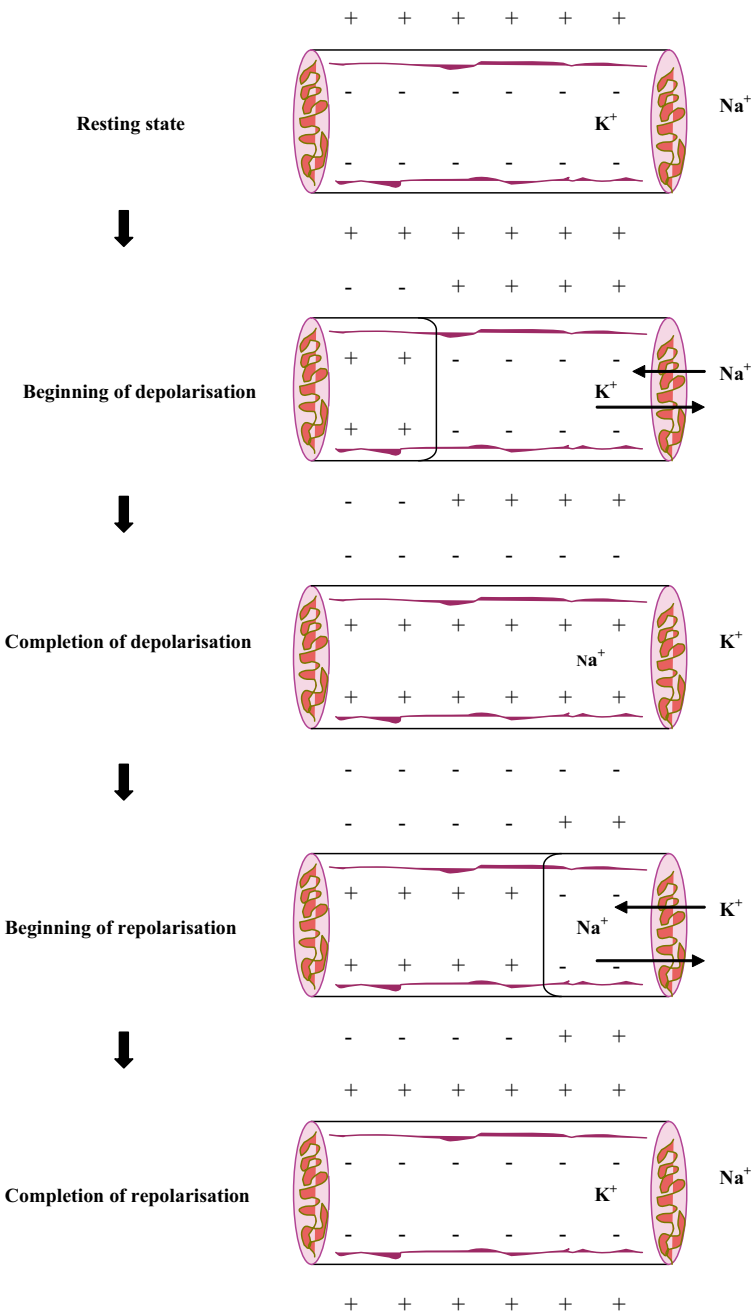

Fig 1.10 Cardiac cell depolarisation and repolarisation [7]

regulated by electrical, mechanical or chemical stimuli [7]. Furthermore, the concentration gradient affects the ion distribution across the cell membrane [7].

In the resting state of the cell, the electrical activity is more positive outside the cell and more negative inside the cell and no electrical activity occurs [7, 22]. When the cell is stimulated, the permeability of the membrane changes allowing sodium to enter the cell [7]. This results in the inside of the cell becoming more positive than the outside, resulting in a depolarised state [7]. Once depolarisation is complete, the membrane allows sodium to exit, once again making the cell more negative inside. This end result is called repolarisation (cell recovery) [7].

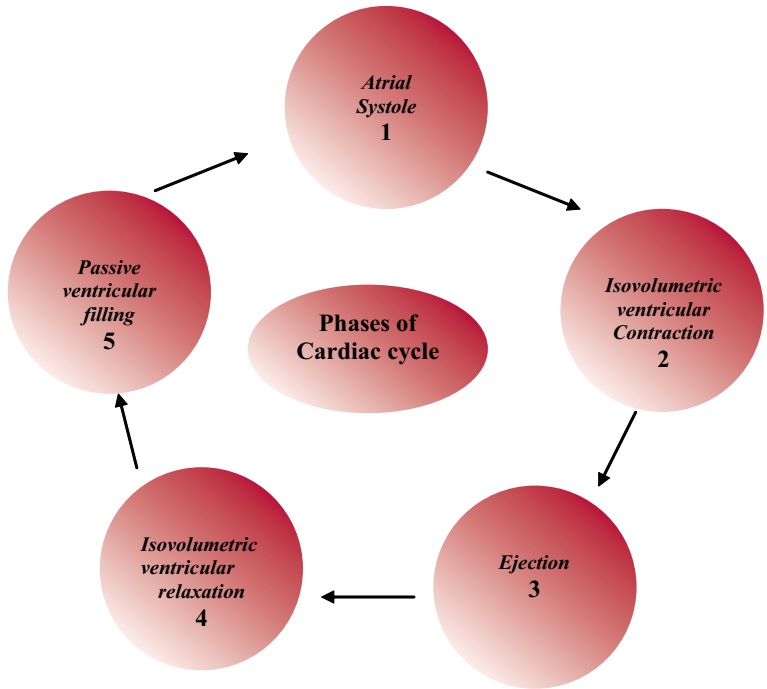

Fig 1.11 Phases of cardiac cycle

1.3.5 Autonomic Nervous System and Heart

The autonomic nervous system has both cardioacceleratory and cardioinhibitory effects on the heart, which are manifest both in the resting state and in times of stress [4–6, 8, 11–14]. The noradrenergic or the sympathetic nervous system is mainly involved with increasing the heart rate (chronotropy), contractility (ionotropy) and the speed of conduction (dromotropy) in the cardiac muscle fibres and the conduction tissue; and the transmitter involved is mainly nor-epinephrine [4–6, 8, 11–14]. The sympathetic effects are mediated mainly by the adrenergic receptors, which includes β-1 and β-2 adrenergic receptors. β-1 receptors are found mainly in the SA node, AV node and ventricular myocardium, and operate via activation of adenylate cyclase and increase in cAMP (cyclic adenosine monophosphate) concentration in the cell to mediate the above mentioned sympathetic effects [4–6, 8, 11–14]. β-2 receptors are mainly found in the vascular smooth muscles in addition to the bronchial smooth muscle and wall of the GI tract and the bladder [4–6, 8, 11–14]. The mechanism of action is same as that of β-1 receptors i.e, increase in cAMP levels but they cause relaxation of the vascular smooth muscle and are involved in regulation of blood flow and systemic blood pressure [4–6, 8, 11–14].

The cholinergic or the parasympathetic nervous system effects in the heart are opposite to the ones mentioned above and the transmitter involved is mainly acetylcholine [4–6, 8, 11–14]. The vagi supply the parasympathetic fibres to the heart via the cardiac plexuses. The parasympathetic effects are mediated via the muscaranic receptors, which act by inhibition of adenylate cyclase and hence decrease the intracellular cAMP levels and result in a decrease in heart rate, contraction and conduction velocity [4–6, 8, 11–14].

The autonomic centres in the CNS, mainly the vasomotor centre of medulla and the hypothalamus regulate the balance between the level of sympathetic and the parasympathetic output to the cardiovascular system depending on the afferent inputs from the periphery and the CNS [4–6, 8, 11–14]. There is normally a tonic vagal discharge in humans which overrides the moderate tonic discharge in the cardiac sympathetic nerves [12,13]. Both the sympathetic and the parasympathetic fibres in the splanchnic thoracic nerves and the vagi carry afferent input mediated via baroreceptors and chemoreceptors to the autonomic centres in the CNS, in addition to the efferent output from the CNS [12, 13]. These afferents and efferents are involved in mediation of cardiovascular reflexes such as baroreceptor and the chemoreceptor reflexes [4–6, 8, 11–14].

1.3.6 Cardiac Cycle

The cardiac cycle consists of contraction and relaxation of both atria and ventricles (Fig. 1.11). The heart

does not contract or relax as a single unit [11]. The cardiac cycle consists of cyclic structural and functional changes which the heart under goes every 0.8 s on average to maintain the blood flow through the body. The cycle starts with an atrial systole, which is preceded by an impulse generated in the SA node and is spread across the atria corresponding to a P-wave on the electrocardiogram [11]. The atrial systole contributes to, but is not essential for, ventricular filling, but it does become an important factor in a diseased heart [11, 14]. Filling of the ventricles by atrial contraction causes the fourth heart sound, this is not normally audible in adults. During this phase, the AV valves are open and the ventricles are relaxing. The semilunar valves (SL) are closed, which prevents re-entry of blood from the pulmonary artery or the aorta. The isovolumetric ventricular contraction (start of ventricular systole while the SL valves are closed) follows the atrial systole, during which the ventricular volume remains constant [6, 11, 14]. The isovolumetric ventricular contraction is preceded by the spread of the electric impulse from the AV node to the rest of the ventricular myocardium, and this is seen as the QRS complex on an electrocardiogram [6, 11, 14]. When the ventricular pressure becomes greater than the atrial pressure, the AV valves close, corresponding to the first heart sound, with the mitral valve closing fractionally before the tricuspid valve. The semilunar (SL) valves open as the pressure in the ventricles exceeds that of the pressure in the aorta and the pulmonary artery, resulting in rapid ventricular ejection. This results in a dramatic reduction in the ventricular volume as most of the ventricular blood (stroke volume) is ejected during this phase. The atria also begin to fill during this phase. The end of ventricular contraction corresponds to the onset of the T-wave on the electrocardiogram [6, 11, 14]. Towards the end of the ventricular contraction the ejection of blood from the ventricles is slower as the ventricular pressure starts to drop. This is followed by isovolumetric ventricular relaxation marked by closure of the aortic and pulmonic valves. The closure of the semilunar valves corresponds to the second heart sound. The AV valves are closed and the ventricular volume remains constant. The pressure in the ventricles is reduced rapidly [6, 11, 14]. When the ventricular pressure becomes less than the atrial pressure, the AV valves open marking the end of the isovolumetric phase of ventricular relaxation and the onset of rapid ventricular filling. During the beginning of this phase of ventricular relaxation, there is passive filling of the ventricles with the blood from the atria, which is rapid [6, 11, 14]. The rapid flow of blood from the atria into ventricles causes the third heart sound, which is normal in children but in adults is associated with disease. Reduced ventricular filling sometimes referred to as diastasis, which is the longest period of the cardiac cycle, follows the rapid filling. Most of the myocardium receives its blood supply during this phase of the cardiac cycle [6, 11, 14].

1.3.7 Physiology of Coronary Circulation

The primary function of the coronary circulation is to meet the metabolic demand of the heart. Coronary blood flow increases from the baseline or resting level to the maximum depending on myocardial oxygen requirements [25–27]. An adequate increase of coronary blood flow is required to meet myocardial oxygen consumption. During strenuous exercise or metabolic demand, the coronary blood flow increases up to 4–6 times [25–27]. In conditions such as left ventricular hypertrophy (LVH), myocardial ischaemia, and diabetes mellitus (DM) the normal increase in coronary flow can be blunted. The epicardial conduit resistance is produced by atherosclerotic stenosis and the distal vascular bed maintains satisfactory blood flow by dilating. The maximal increase in coronary flow above resting levels is defined as coronary flow reserve (CRF) [27,28]. The major determinants of myocardial oxygen consumption are heart rate (HR), myocardial wall tension/stress (after-load) and inotropic state (contractility) of the myocardium [27, 29]. Vascular resistance also plays an important role in coronary circulation and is mainly determined by myocardial oxygen consumption, and modulated mainly by local metabolic factors (vasoactive autacoids) with some contribution from neural stimuli, and circulating vasoactive substances [27].

1.3.8 Coronary Collaterals

The initial documentation of coronary collaterals in humans was not made until 1964, although their presence was considered as far back as the 16th century [21, 30]. There are few and small collateral vessels and they may develop into a major vascular network in patients with obstructive coronary artery disease [21]. It is generally believed that the collateral vessels, or network, develop only when the occlusive disease or stenosis is severe enough to produce a substantial transstenotic pressure drop [21]. When collaterals are present in patients with severe or significant occlusive CAD, the part of the myocardium supplied by the stenotic vessel seems to have better contractile function than in patients without collaterals [31]. Further, it is hypothesised that pre-existing collaterals may also play an important role by decreasing the extent and degree of myocardial damage at the time or during an acute coronary episode [21]. In general, the

Table 1.7 Physiological changes and cardiovascular response to moderate exercise [33, 35–38]

Physiological response and cardiovascular changes during moderate exercise	Contributing factors to fatigue during prolonged exercise	Contributing factors to muscle fatigue during exercise
Heart rate increases	Fatigue	Muscle fatigue
Increased sympathetic stimulation	Reduction in muscle glycogen	Acidosis
Decreased parasympathetic stimulation	Hyperthermia	Central nervous system (CNS) factors
CO increases	Dehydration	Increased NH_3
SV increases	Hypoglycaemia	Electrochemical changes
EDV increases	Muscle damage	Cell phosphorylation potential
Pulse pressure increases	Electrolyte imbalance	ATP Reduction
MAP (mean arterial pressure) increases	CNS/neuromuscular junction and muscle electrochemical abnormalities	Increased ADP
TPR decreases		Increased free inorganic phosphate
Oxygen extraction increases		
Blood flow to heart, muscle and skin increases		
Blood flow to brain increases (slightly)		
Blood flow to other viscera decreases		

coronary collaterals are capable of preserving the function and structure in a resting myocardium, however, the coronary flow per gram in a collateral-dependent myocardium is reduced when compared with the normally perfused myocardium. One reason for this could be the change in pressure gradient across the collateral vessels (arterial pressure is lower than aortic pressure in the collateralised segment) [21, 32].

1.4 Exercise Physiology

Exercise physiology is a branch of physiology, which studies how exercise alters the structure and function of the body. Exercise is now used as a therapy during rehabilitation from various injuries or illness and it is used as a preventive strategy to delay the onset and progression of atherosclerotic cardiovascular disease [33–35]. Exercise testing using a treadmill or bicycle ergometer is commonly used in the cardiology department to assess the exercise tolerance and diagnosis of ischaemic heart disease. However, exercise tolerance and capacity depends on multiple factors such as age, sex, physical/mental conditioning, medications, disease status, etc. [33–35].

During exercise, multiple physiological changes are encountered (Table 1.7). In general, cardiac output (CO) increase is due to a larger increase in heart rate (HR) and a smaller increase in stroke volume (SV). During exercise, the CO may increase to a maximum value of 35 L/min (baseline 5 L/min) [14]. Most of the increased cardiac output goes to the exercising muscle and part of it goes to the skin (to dissipate heat) and heart [14]. The increase in flow to these organs is due to vasodilatation and the flow to the gastrointestinal organs and kidneys decreases (secondary to increased sympathetic activity) [36–39].

The total peripheral resistance to blood flow is reduced due to the arteriolar vasodilatation in the skeletal muscle, skin, and cardiac muscle. The net result is a decrease in total peripheral resistance (TPR) [14]. In addition, there is increased venous return because of increased muscular activity, which in turn further increases the cardiac output. The cardiovascular and muscular changes in blood flow with exercise is also controlled by various factors including but not limited to (a) exercise centres in the brain, (b) local chemical changes in the

muscle, (c) mechanoreceptors and chemoreceptors in muscle, and (d) arterial baroreceptors [14] (Fig. 1.12).

1.4.1 Gender and Exercise Performance

Gender differences relating to the cardiovascular system in terms of body composition, metabolism, muscle morphology and endocrine responses are well reported and documented in the medical literature [40]. Women have smaller lung volume and pulmonary capillary volume than men, resulting in lower maximum pulmonary ventilation [40]. Women also have a smaller heart, with a lower filling volume, lower maximum stroke volume and lower cardiac output [40]. Women are reported to have a lower haemoglobin concentration, haematocrit and total blood volume; therefore, they are at a relative disadvantage for transport of oxygen to skeletal muscle during exercise. However, gender differences become less notable when cardiovascular parameters are expressed relative to body surface area and mass [40] (Table 1.8).

Research on men and women runners indicates that women tend to have smaller amounts of slow twitch fibres type in the gastrocnemius muscle. The greater lean body mass in men is a major determinant of greater muscle strength [40]. Maximum oxygen consumption is different for men and women and men seem to have higher maximal oxygen consumption [40]. However, when these are expressed in relation to lean body mass, there appears to be little significant difference between the sexes [40]. Finally, there are considerable endocrine or hormonal differences between men and women. In women who train very aggressively or too hard, the luteal phase of the menstrual cycle is shortened and eventually the cycle is lost (athletic amenorrhoea) [33, 40].

1.4.2 Age and Exercise Performance

Aging is a normal biological process, which is inevitable. Aging has been defined as a progressive loss of physiological capacities that culminates in death [40–42].

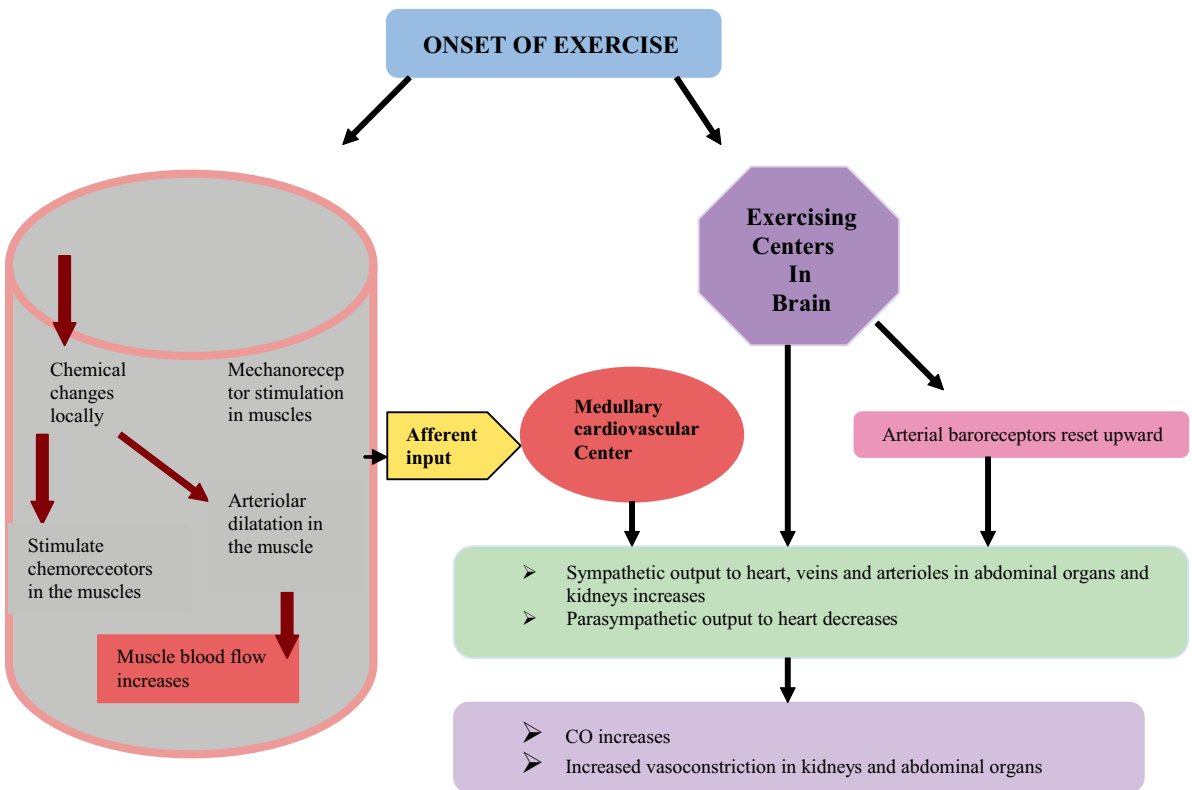

Fig 1.12 Changes in cardiovascular system during exercise [14]

Table 1.8 Gender, cardiovascular system and exercise physiology [40]

Females have higher percentage of body fat and is more often distributed around hips and thighs, as compared to males' body fat which tends to be distributed at the waist and stomach
Males have larger lean body mass and are generally taller than the average female
Males have a narrower pelvic region than females
Females have fewer sweat glands than males
Females have smaller hearts than males
Females have smaller lung volume and pulmonary capillary volume than males
Females have lower percentage of slow twitch motor unit than males
Females have a smaller blood volume than males
Females have lower haemoglobin concentration than males
Females have a lower haematocrit than males
Females have ovaries and they produce estrogen and progesterone
Men have testes and they produce testosterone

Various natural and pathophysiological changes occur during the course of life [41, 42] (Table 1.9). The commonest of these are loss of height, greying hair, changes in vision, reduction in lean body mass, wrinkling of skin, etc. [41, 42]. Many interesting theories have been implicated to explain the process of aging. However, how long an individual lives depends on multiple factors including heredity, environment, individual attitude towards health and life and finally access to health services [41, 42].

Table 1.9 Effect of aging on the cardiovascular system [40–42]

Maximum oxygen consumption	Reduced
Maximum heart rate	Reduced
Cardiac output	Reduced
Blood pressure	Increased
Vascular resistance	Increased
Total cholesterol	Increased
Triglycerides	Increased
LDL	Increased
HDL	Reduced
Maximum ventilation	Reduced
Respiratory muscle strength	Reduced
Vital capacity	Reduced
Expiratory flow rate	Reduced
Muscle strength, endurance, flexibility	Reduced
Pulmonary diffusion	Reduced
Alveolar surface area	Reduced
Chest wall structures	Altered
Alveolar elastic recoil	Altered
Pulmonary blood volume	Reduced
Lean body mass	Reduced
Adipose tissue	Increased
Basal metabolic rate	Reduced
Sleep	Reduced
Cognitive function	Reduced

1.5 Conclusion

Cardiac anatomy and physiology is extensive, fascinating and exciting. However, exploiting their role in clinical practice requires a thorough understanding of basic principles, mechanisms and functionality. Appreciating and understanding the anatomy and physiology and recognising their changes will help not only in anticipation of disease but also in appreciating the signs and symptoms produced by them.

References

1. Callahan JA, Kay JD (1991) Foundations of cardiology. In Giuliani ER et al. (eds), Cardiology Fundamentals and Practice, Vol. 1, 2nd edn. Mosby-Year Book, St Louis, pp. 3–25.
2. Edwards WD (1984) Anatomy of the Cardiovascular System; Clinical Medicine, Vol. 6. Harper & Row, Philadelphia, pp. 1–24.
3. Malouf JF, Edwards WD, Tajil AJ, Seward JB (2001) Functional anatomy of the heart. In Fuster F, Alexander RW,

O'Rourke RA (eds), Hurst's: The Heart, 10th edn. McGraw-Hill Inc., pp. 19–62.
4. Boulpaep EL (2005) Organisation of Cardiovascular System. Boron WF, Boulpaep EL, updated version. Elsevier Saunders, pp. 423–507.
5. Tortora GJ, Grabowski SR (1996) Principles of Anatomy and Physiology, 8th edn. HarperCollins College Publishers, New York, pp. 598–600.
6. Bullock J, Boyle J III, Wang MB (1991) Physiology, The National Medical Series for Independent Study, 2nd edn. Williams and Wilkins, pp. 93–148.
7. Huff J (2002) ECG Workout Exercise in Arrhythmia Interpretation, 4th edn. Lippincott.
8. Gray's PG (1995) In Gray's Anatomy, 38th edn. Churchill Livingston, New York, p.1498.
9. Edwards WD (1995) Cardiac anatomy and examination of cardiac specimens. In Emmanouilides G et al. (eds). Moss & Adams Heart Diseae in Infants, Children and Adolescents, 5th edn. Williams & Wilkins, Baltimore, pp. 70–105.
10. Edwards WD (1991) Applied anatomy of the heart. In Guiliani ER et al. Cardiology Fundamentals and Practice, Vol. 1, 2nd edn. Mosby-Year Book, St Louis, pp. 47–112.
11. Thibodeau GA, Patton KT (1996) Anatomy of the cardiovascular system. In Anthony's Textbook of Anatomy and Physiology, 15th edn, pp. 614–657.
12. Ganong WF (2003) Lange Review of Medical Physiology, 21st edn. McGraw-Hill.
13. Ganong WF (2005) Lange Review of Medical Physiology, 22nd edn. McGraw-Hill.
14. Widmaier EP, Raff H, Strang KT (2006) Cardiovascular physiology. In Vanders Human Physiology – The Mechanism of Body Function, 10th edn. McGraw-Hill, pp. 387–476.
15. Apkon M (2005) Cellular physiology of skeletal, cardiac and smooth muscle. In Boron WF, Boulpaep EL (eds), Medical Physiology. Elsevier Saunders, pp. 230–254.
16. Edwards WD (1984) Anatomic basis for tomographic analysis of the heart at autopsy. Cardiol Clin 2:485–506.
17. Katz AM (2006) Physiology of the Heart, 4th edn. Lippincott Williams & Wilkins, Philadelphia..
18. Lederer WJ (2005) Cardiac electrophysiology and electrocardiogram. In Boron WF, Boulpaep EL (eds), Medical Physiology. Elsevier Saunders, updated version, pp. 483–507.
19. Opie LH (2004) The Heart: Physiology, from Cell to Circulation, 4th edn. Lippincott Williams & Wilkins, Baltimore, MD.
20. Kurachi Y, Terzic A, Cohen M, Sperelakis N (2001) Heart Physiology and Pathophysiology, 4th edn. Academiv Press.
21. Klocke FJ, Ellis AK (1990) Physiology of the coronary circulation. In Parmley WW, Chatterjee K (eds), Cardiology. Philadelphia:, JB Lippincott Co., pp.1–16.
22. Seward W (1994) Transoesophageal echocardiograhic anatomy. In Feeman W, Seward J et al. (eds), Transeosophageal Echocardiography. Little, Boaston, pp. 55–101.
23. Boulpaep EL (2005) Heart as a pump. In Boron WF, Boulpaep EL (eds), Medical Physiology. Elsevier Saunders, updated version, pp. 509–533.
24. Boulpaep EL (2005) Regulation of arterial pressure and cardiac output. In Boron WF, Boulpaep EL (eds), Medical Physiology. Elsevier Saunders, updated version, pp. 534–557.
25. Porenta G, Cherry S, Czernin J, Brunken R, Kuhle W, Hashimoto T, Schelbert HR. (1999) Noninvasive determination of myocardial blood flow, oxygen consumption and efficiency in normal humans by carbon-11 acetate positron emission tomography imaging. Eur J Nucl Med 26:1465–74.
26. Pitkanen OP, Nuutila P, Raitakari OT et al. (1999) Coronary flow reserve in young men with familial combined hyperlipidemia. Circulation 99:1678–84.
27. Maseri A et al. (2001) Coronary blood flow and myocardial ischaemia. In Fuster F, Alexander RW, O'Rourke RA (eds), Hurst's: The Heart, 10th edn. McGraw-Hill, pp.1109–1131.
28. Vassalli G, Hess OM (1998) Measurement of coronary flow reserve and its role in patient care. Basic Res Cardiol 93:339–53.
29. Braunwald E. (1999) 50th anniversary historical article. Myocardial oxygen consumption: the quest for its determinants and some clinical fallout. J Am Coll Cardiol 34:1365–8.
30. Fulton WFW (1965) The Coronary Arteries. Charles C. Thomson, Springfield IL.
31. Schwarz F, Flameng W, Ensslen R et al. (1978) Effects of collaterals. Am Heart J 95:570.
32. Arani DT, Greene DG, Bunnell IL et al. (1984) Reductions in coronary flow under resting conditions in collateral-dependant myocardium of patients with complete occlusion left anterior descending coronary artery. J Am Coll Cardiol 3:668–2005.
33. McArdle WD, Katch FI, Katch V (2006) The cardiovascular system. In Exercise Physiology – Energy, Nutrition, Human Preference, 6th edn. Lippincott, William and Wilkins, pp. 313–332.
34. McArdle WD, Katch FI, Katch VL (2006) Physical activity health and aging. In Exercise Physiology – Energy, Nutrition, Human Preference, 6th edn. Lippincott, William and Wilkins, pp. 883–924.
35. Wilmore JH, Costill DL (2004) Cardiovascular control during exercise. In Physiology of Sport and Exercise, 3rd edn. Human Kinetics, pp. 206–241.
36. Roberts RA, Roberts SO (1997) Factors contributing to fatigue during exercise. In Exercise Physiology (Exercise, Performance & Clinical Application), Mosby, pp. 546–563.

37. Roberts RA, Roberts SO (1997) Cardiovascular function and adaptation to exercise. In Exercise Physiology (Exercise, Performance & Clinical Application), Mosby, 268–293.
38. Wilmore JH, Costill DL (2004) Cardiovascular and respiratory adaptations to training. In Physiology of Sport and Exercise, 3rd edn, Human Kinetics, pp. 270–305.
39. McArdle WD, Katch FI, Katch VL (2006) Cardiology regulation integration. In Exercise Physiology – Energy, Nutrition, Human Preference, 6th edn. Lippincott, William and Wilkins.
40. Roberts RA, Roberts SO (1997) Gender and exercise performance. In Exercise Physiology (Exercise, Performance & Clinical Application), Mosby, pp. 564-577.
41. Roberts RA, Roberts SO (1997) Exercise and aging. In Exercise Physiology (Exercise, Performance & Clinical Application). Mosby, pp. 578–599.
42. Wilmore JH, Costill DL (2004), Aging in sports and exercise. In Physiology of Sport and Exercise, 3rd edn, pp. 538–565.

Further Reading

1. Boron WF, Boulpaep E (2005) In Medical Physiology: a Cellular and Molecular Approach. Elsevier/Saunders, updated version, pp. 423–507.
2. Thibodeau GA, Patton KT (1996) Anthony's Textbook of Anatomy and Physiology, 15th edn. Mosby, pp. 614–657.
3. Ganong WF (2003) Lange Review of Medical Physiology, 21st edn. McGraw-Hill.
4. Gray's Anatomy 38th edn (1995) Churchill Livingston, New York.
5. Bullock J, Boyle J III, Wang MB (1991) Physiology, The National Medical Series for Independent Study, 2nd edn. Williams and Wilkins, pp. 93–148.

http://www.springer.com/978-3-540-78673-3

Integrating Cardiology for Nuclear Medicine Physicians
A Guide to Nuclear Medicine Physicians
Movahed, A.; Gnanasegaran, G.; Buscombe, J.; Hall, M. (Eds.)
2009, XIV, 544 p., Hardcover
ISBN: 978-3-540-78673-3