Section Three: Chapter 14: Cardiovascular Physiology - The Heart

The Cardiovascular System

The cardiovascular system is complex, dynamic and elegant in the way that it achieves its basic function, which is to transport blood throughout the body. The blood stream is the fundamental way that substances are delivered to and removed from all the tissues of the body. The heart is multifaceted, it is not only central to the pumping aspect for the transport system, but the heart is also a secondary endocrine gland since it releases hormones.

In simplest terms, the **cardiovascular** system consists of the **heart**, which contains the base of both circuits (systemic and pulmonary) and oversees two pumps in one, and the **vascular** system, which is a series of blood vessels that interconnect to the heart and all other parts of the body, helping to control the flow of blood through these vessels. The cardiovascular system is a closed system in that the blood never leaves the vessels, but elements of it are filtered out into the tissues and reabsorbed back into the blood vessels.

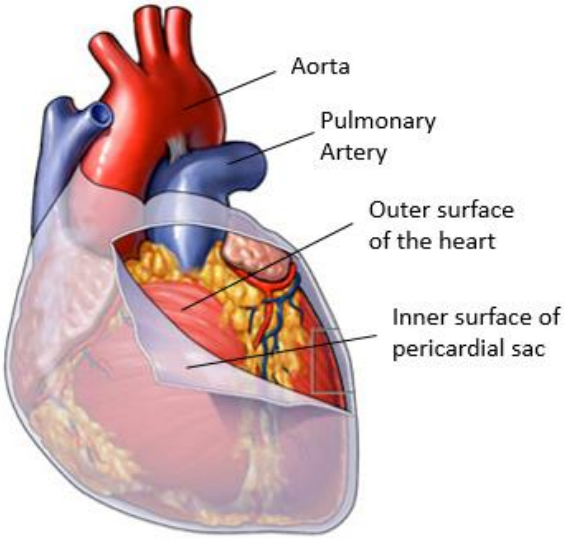
The Cardiovascular System primary function is **transportation** around the body of:

- O_2 from the lungs to body tissues.
- CO_2 from body tissues to lungs.
- Delivery of Nutrients to all cells and tissues of the body.
- Removal of Waste (+ toxins) from cells and tissues of the body.
- Circulation of Hormones.
- Circulation of defense, healing, immune cells for the repair and protection of body tissues.

The circulation of blood is also a key factor in the **thermoregulation** of the body. Blood is the warmest element of the body and its continuous kinetic energy offers heat to any area it heavily perfuses.

The Heart in in a Protective Sac

The heart is a muscular organ that lies in the center-left of the thoracic cavity. It is protected by the ribcage, nestled in between the two lungs and enclosed in the **pericardial sac**. In **Figure 14.1** (left) we see the very thin serous ('watery') membrane that is pericardial sac. This bag-like structure creates the fluid filled **pericardial cavity** that is in between the inner surface of the bag (**parietal pericardium**) and the outer surface of the heart (**visceral pericardium**), see **Figure 14.2** below for a zoomed in look at the arrangement of the tissues and the sac.



The main purpose of the pericardial sac is to **reduce friction** between the heart and the other nearby structures. Since the heart is constantly beating (about 100,000 beats/day), and the nearby lungs are also constantly expanding and deflating, it is vital to have a wet slippery surface that reduces the friction between two surfaces that must constantly move across one another.

Figure 14.1 Shows the heart covered by the pericardial sac which offers protection to the constantly moving heart.

The Tissue Layers of the Heart

The heart has 3 tissue layers (see **Fig. 14.2**). The **outermost** layer is called the **epicardium** (epi means on top of). This is also called the visceral pericardium as it is one of the two surfaces of the serous membrane (between the inner surface of the pericardial sac and the outermost surface of the heart). The **middle** layer is called the **myocardium**, this is cardiac muscle and composes most (**90%**) of the heart. This muscle tissue contracts and generates force to pump blood. The **innermost** layer is the **endocardium** across which blood flows. It is lined with endothelium which contains a single layer of vey flat epithelial cells. This also lines all blood vessels.

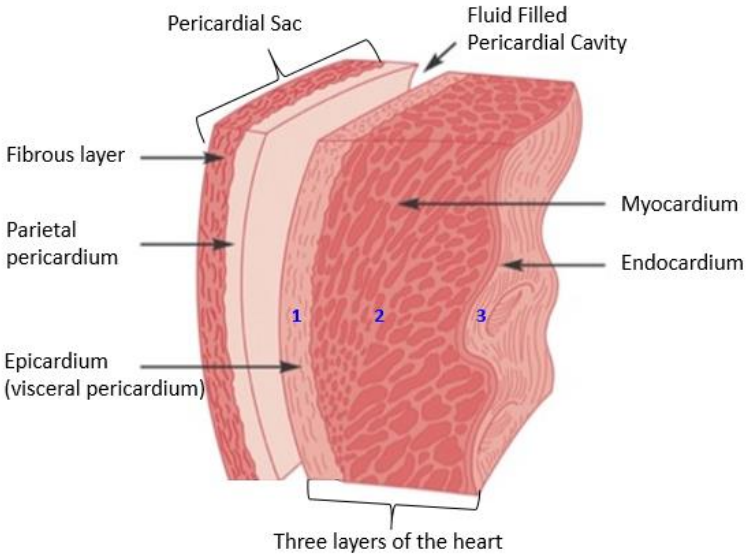
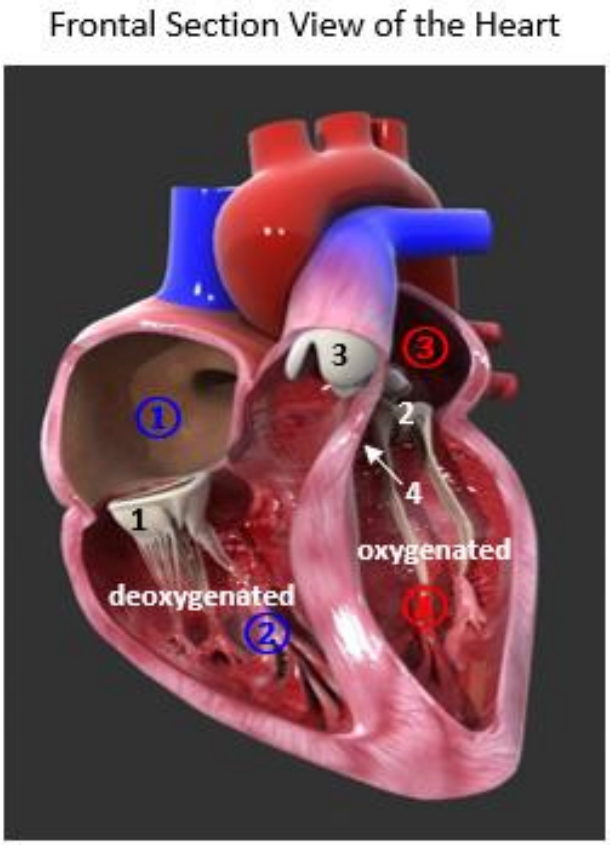


Figure 14.2 The 3 tissue layers of the heart, their arrangement and thickness are numbered and shown as follows: **1** epicardium, **2** myocardium and **3** endocardium. The pericardial sac which surrounds the heart is also shown on the left side.

The Heart's Structures and Dual Pump

The heart has four chambers that are divided into two halves; the **Right** half and the **Left** half. These two sides represent the foundations of two circuits of the cardiovascular system.



The four chambers of the heart operate in parallel, with the two halves having the same basic structures which work in a synchronized fashion. The top two chambers of the heart are called **atria** (plural), the term atrium (singular) means 'receiving room' and these two chambers both receive blood from veins that carry blood back toward the heart. The lower two chambers of the heart are called **ventricles** (meaning belly) and these are the muscular pumps that eject blood into arteries that take blood away from the heart. In this way, the heart has two separate **dual pumps** that have different but integrated functions.

Figure 14.3 The heart (to the left) is shown in a frontal section that displays the chambers and valves. The four heart valves are shown numbered (1, 2, 3 and 4), along with the chambers; ① R atrium, ② R ventricle, ③ L atrium, and ④ L ventricle. Also shown are the pumping chambers of the right ventricle with deoxygenated blood and the left ventricle with oxygenated blood which are always kept separate.

Coordinated Contraction of the Heart

Each side of the heart contracts together in a coordinated fashion. First both of the atria contract in synch pushing blood into the ventricles below them. There is a slight delay period, this is then followed by both of the ventricles contracting simultaneously to push blood out of the heart via arteries. The full details of the **cardiac cycle** will be described later in this section.

The Arteries and Veins of the Heart

We first need to have accurate definitions for arteries and veins. Some may be surprised to find out that arteries and veins are not determined by the levels of oxygen in their blood, but very simply by the direction the vessels carry blood; either to the heart or away from the heart.

- **Arteries** - are vessels that carry blood away from the heart.
- **Veins** - are vessels that carry blood toward the heart.

Without going into too much anatomy, here are the main blood vessels involved in the circuitries of the heart. The **superior vena cava** and the **inferior vena cava** (together called the venae cavae), are large veins carrying **deoxygenated blood** to the right atrium, from above and below the heart respectively (see **Figure 14.4**). The **left and right pulmonary veins** return **oxygenated blood** to left atrium from the left and right lungs respectively (see **Figure 14.5** below for circuits). The **pulmonary trunk** leaves the right ventricle and becomes the **left and right pulmonary arteries** taking blood to the lungs. Finally, the **aorta** (the largest artery in the human body) leaves the left ventricle to deliver **oxygenated blood** to the entire body.

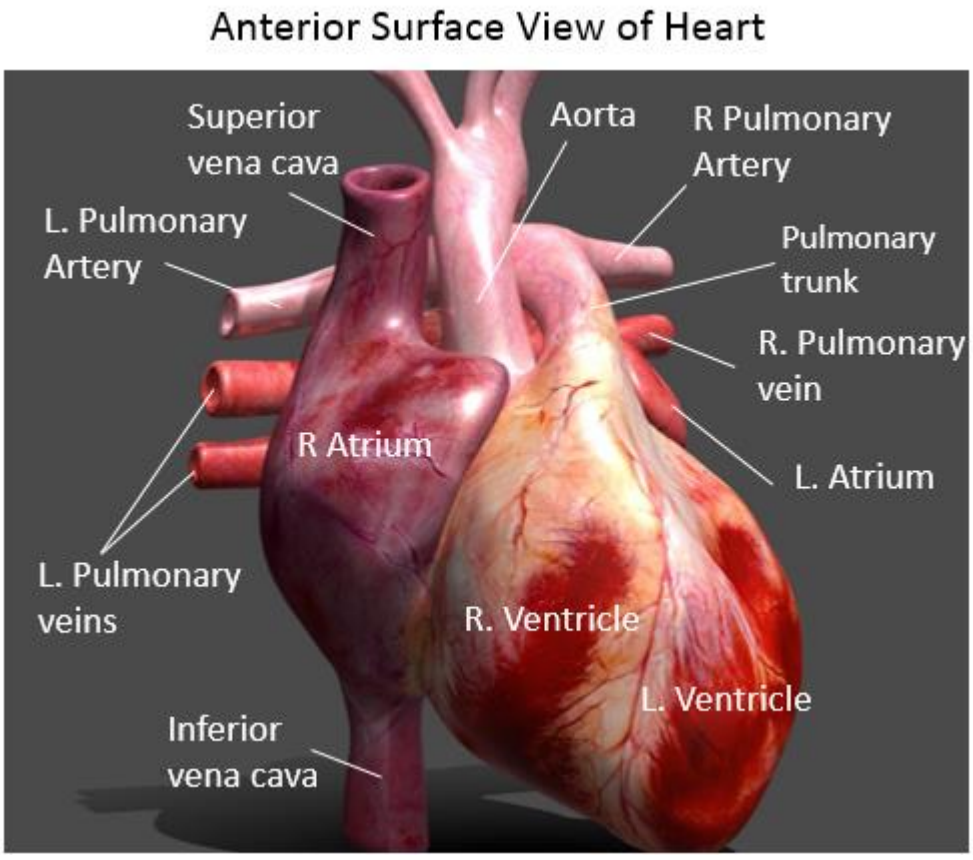


Figure 14.4 Shown here is a model of the heart from the anterior (front) view, where the outer surfaces of the four chambers can be seen. Also labeled are all of the main blood vessels that bring blood to, and take blood away from the heart.

The Circuits of the Heart

Within the cardiovascular system there are two circuits or circulations - the ***pulmonary circuit*** takes blood to and from the lungs, while the ***systemic circuit*** takes blood to and from the rest of the body. The way the two circuits are elegantly intertwined is nicely represented in **Figure 14.5** below.

The Pulmonary Circulation - Pumps blood from the heart, to the Lungs and back to the Heart. Often it is termed the "right side" of the heart. This circuit more specifically can be described as starting at the Right Ventricle (which is the Pump for the Pulmonary Circuit) and ending at the Left Atrium, which is the receiving room for the newly oxygenated blood arriving from the lungs.

The Systemic Circulation – Pumps blood from the heart, to the Body and back to the Heart. Often it is termed the "left side" of the heart. This circuit more specifically can be described as starting at the Left Ventricle (which is the Pump for the Systemic Circuit) and ending at the Right Atrium, which is the receiving room for the now depleted (deoxygenated) blood returning from the body.

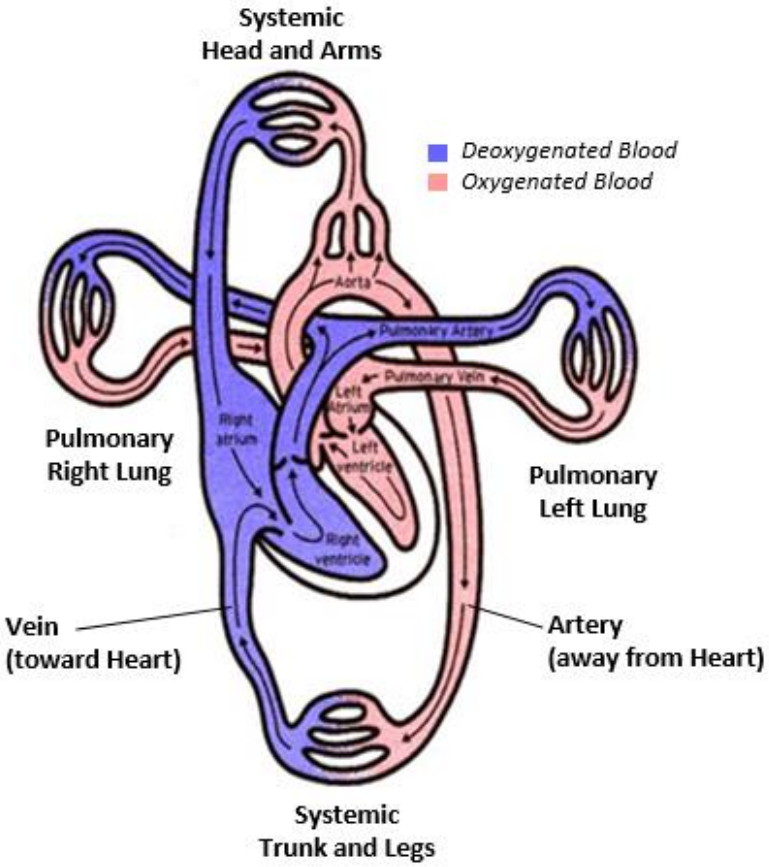


Figure 14.5 The 2 circuits of the heart constantly intertwine, somewhat like an infinity sign (∞), with the systemic circuit delivering oxygenated blood to the body and the pulmonary circuit delivering deoxygenated blood to the lungs. As we will see, one circuit becomes the other. Regardless of the circuit, arteries carry blood away from the heart and veins return blood to the heart.

The One-way Valves of the Heart

The role of one-way valves in the heart is to **prevent retrograde blood flow**, that is, it prevents the blood from moving backwards such that the flow is always in one direction only. There are four one-way valves in the heart, two atrioventricular (AV) Valves

They are: aortic valve, mitral valve, tricuspid valve, and pulmonary valve. The valves are designed to control the direction of blood flow through the heart. The opening and closing of the heart valves produce the heart-beat sounds.

One-way flow in the heart is ensured by the 4 heart valves (see **Figure 14.8** further below):

1) The Right (Tricuspid) Atrioventricular (AV) Valve.
2) The Left (Bicuspid/Mitral) Atrioventricular (AV) Valve.
3) The Pulmonary Semilunar Valve (between Right Ventricle and Pulmonary Trunk).
4) The Aortic Semilunar Valve (between Left Ventricle and Aorta).

The specific roles locations and disorders of the heart valves will be covered below in this section.

Review of Chambers, Vessels and Valves of the Heart

Combining what we have just learned about the chambers, vessels and valves of the heart, it is now a useful time to put all of these elements together and see how the circuits (pulmonary and systemic) are seamlessly and elegantly integrated. Use **Figure 14.6** below to trace the path of a single erythrocyte, also known as red blood cell (RBC), from the Inferior Vena Cava (IVC), the largest vessel in the human body, through all the structures and the two circuits of the heart.

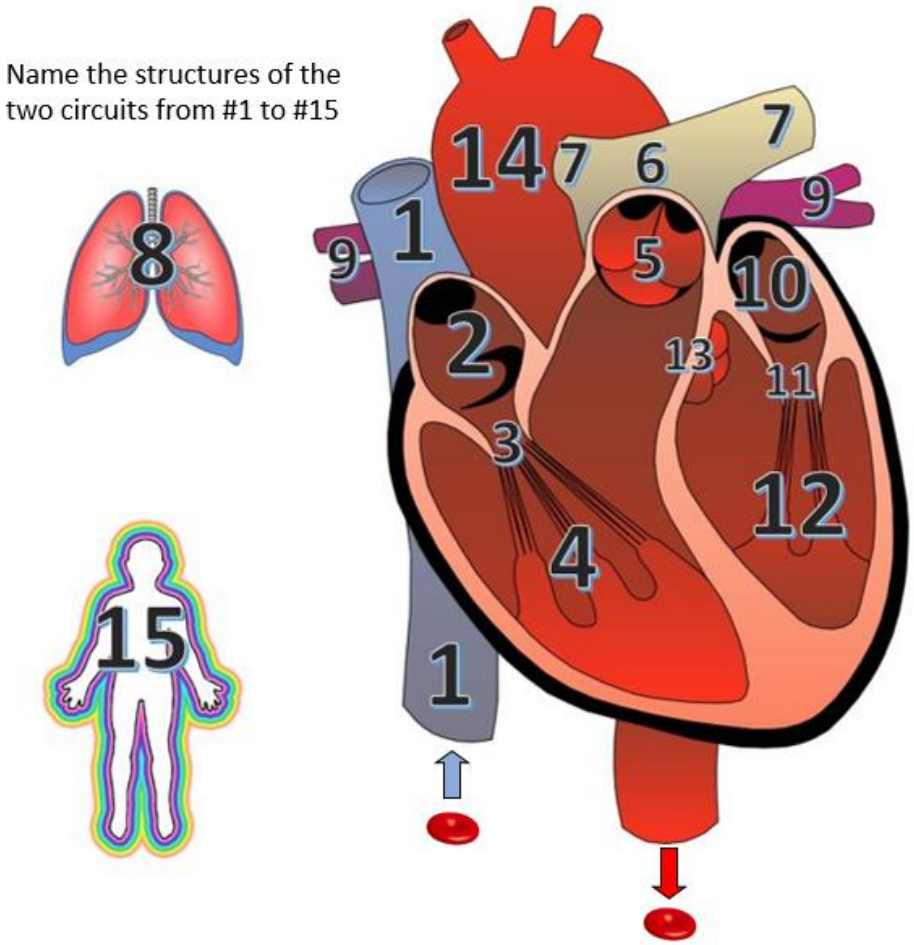


Figure 14.6 As an exercise, examine the figure above and go through the two circuits of the heart, starting at number 1 (which together are the venae cave), all the way to number 15 (which is the rest of the body). Name all of the structures in between in sequential order.

It is worth noting that in the systemic circuit (which is the one we will be studying in more depth), all of the arteries do indeed contain oxygenated blood and the veins carry deoxygenated blood. However, in the pulmonary and fetal circuits this is not the case.

The Fibroskeleton Connective Tissue of the Heart

The heart contains a ring of fibrous connective tissue called the **fibroskeleton** which is found in between the top and bottom chambers, and surrounding the openings of all the valves between the two sets of chambers (see **Figure 14.8**). This connective tissue of the heart has several important roles.

Here are three critical functions of the fibroskeleton:

1. Provides a site of **attachment** and **anchors** the valves of the heart to the myocardium above and below the valves. This keep openings patent during contraction.
2. Maintains **integrity of heart's shape** when ventricles contract, as apex and base are pulled together.
3. It **electrically separates** (insulates) the atria from the ventricles, thus guarding against the spread of electrical signals that are not through the **intrinsic electrical conduction system** (discussed later).

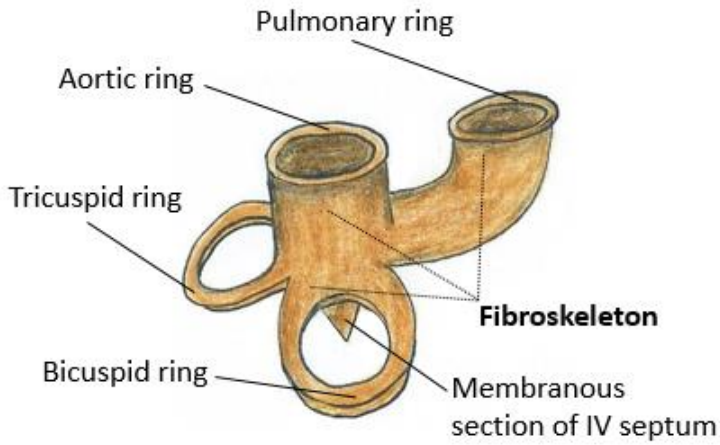


Figure 14.7. If the fibrous skeleton of the heart were shown by itself, it would look similar to the image above. This fibro-connective tissue provides a site for attachment of the valves and part of the interventricular (IV) septum.

Volumes and Pressures of the Dual Pump

The cardiovascular system is a ***closed circulatory system***, and for that to exist, the volume of blood in both sides of the pump ***must be equal***. Total blood volume is about 5.0 liters and in a very short time the volume pumped by one circuit will be in the other, thus the two circuits must pump the same volumes.

However, **the pressures of the fluid on either side of the heart are very different**. The proximity of the lungs to the heart is about 4 inches. And this means that the right pump (R ventricle) does not have to work very hard to move the blood over to the lung tissue. The distance is not that great. The minimum pressure required from the pulmonary circuit is normally about **25 mmHg**. It turns out that this is the minimum pressure required for the pulmonary semilunar valve to open.

The systemic circuit is much more involved and the left pump (L ventricle) needs to work very hard to move the blood to every part of the body. The distance covered is vastly greater. Therefore, the minimum pressure required from the systemic circuit is normally about **80 mmHg**. This is the minimum pressure required for the aortic semilunar valve to open. Thus, the pressure generated by the left side of the heart

is **over three times greater** than that generated by the right side. As a consequence, the muscular wall of the left ventricle is about three times thicker than the right ventricle.

Heart Valves and the Normal Heart Sounds

When the heart beats, it makes sounds. There are two heart characteristic sounds in one heartbeat, the "Lub" and the "Dup" which are created by the snapping shut of the heart valves. During auscultation of the heart (which means listening to the internal sounds of the body, usually with a stethoscope), these unique and distinct auditory sounds can provide important information regarding the condition of the heart.

In the convention of the events of the cardiac cycle*: The 1st heart sound (S1) the "Lub" is caused by closure of the 2 AV valves at the same time. The 2nd heart sound (S2) the "Dup" is caused by closure of the 2 Semilunar valves at the same time.

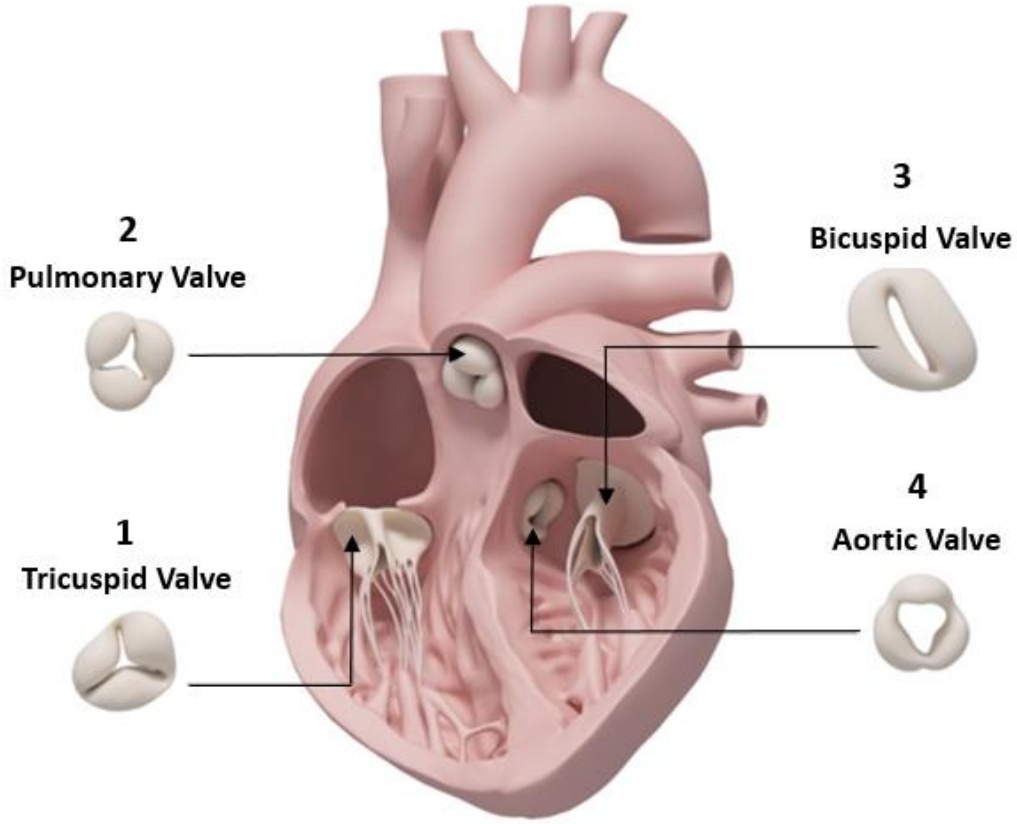


Figure 14.8 Here all four heart valves can be seen. Following the flow through the heart, **1** the right tricuspid atrioventricular (AV) valve; **2** the pulmonary semilunar valve (between right ventricle and pulmonary trunk); **3** the left bicuspid AV (mitral) valve; and 4 the aortic semilunar valve (between left ventricle and aorta).

Disorders of the Heart Valve – these make 'abnormal' sounds or Heart Murmurs

Heart valve disorders are not that uncommon and can affect people of any age. People may be born with disorders (congenital) or they can be acquired through infections of the heart, such as rheumatic fever or endocarditis, or from having a heart attack (myocardial infarction). The two main types of disorders of heart valves are **Stenosis** and **Insufficiency**. They can both cause abnormal heart sounds called **murmurs***. An important thing to remember the spectrum to these disorders, like most other conditions. Heart valve disorders can go from very mild (some have no idea they have a valvular disorder) to very serious.

**See discussion of cardiac cycle further into chapter for references to normal heart sounds.*

Heart Valves - Problems Opening:

Valvular Stenosis refers to a narrowing of the opening of the valves, often associated with an inflammation or a stiffness of the valve. It is a condition in which a valve outlet becomes too narrow because it is not able to open up wide enough, and this restricts normal flow through the valve. As seen in **Figure 14.9** to the left, a normal aortic valve has quite a wide opening, which allows for tremendous blood flow through it. The bedraggled stenotic aortic valve has a much smaller opening, which significantly restricts blood flow. In order to have the same blood flow through a smaller opening, there must be greater pressure on the blood. The heart has to work harder to maintain normal flow, this causes turbulent blood flow, which makes noise and is detected as a **heart murmur**.

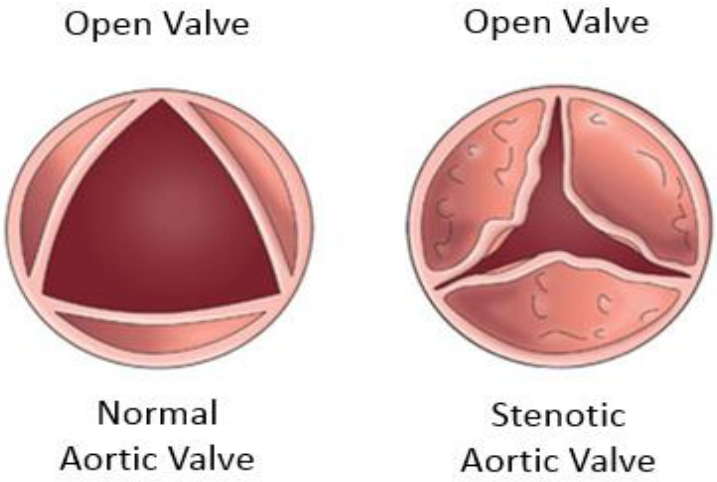
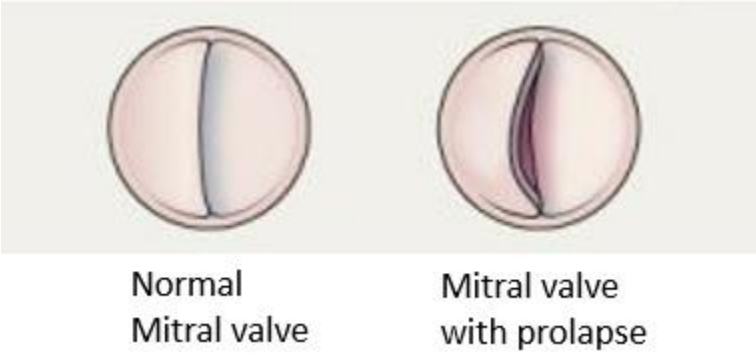


Figure 14.9 Shows the widely open aortic valve in its normal state (left), in contrast to the comparatively much reduced opening of the aortic valve when it has become stenotic (right).

Heart Valves - Problems Closing:

Valvular Insufficiency means retrograde blood flow or back flow occurs. **Valvular Prolapse** is an example of valvular insufficiency caused when the cusps overlap and don't close tightly so the valve fails to close properly and tightly. Prolapsed heart valves are often called **incompetent** or **insufficient** valves as they allow regurgitation of blood in the wrong direction, which is another way of saying **retrograde flow**. A common example of how this occurs is from an inherited weakness of the chordae tendineae (the 'cords' that attach to the 'flaps' of the AV valve). During ventricular systole (contraction), if the cords are too long, they cannot keep the valves tightly closed against the fluid pressure created by the powerful force of contraction of the ventricles. This results in some back flow into the atria. Somewhat like the force of a strong wind on an umbrella, when it cannot maintain its integrity. Typically this condition makes a *click* sound followed by a *swish* sound when blood leaks back into atria. Again the abnormal heart sound is a type of heart murmur.



As indicated, these heart murmurs can range from unnoticeable and harmless to severe and life threatening. Most valvular disorders commonly occur on the **left** side of the heart because these valves are subjected to greater degrees of pressure and other forces during contraction of the powerful left ventricle. For instance, **mitral valve prolapse** is the most common valvular disorder (see **Figure 14.10**).

Figure 14.10. The left bicuspid AV valve, or mitral valve normally created a tight seal when closed (left). However, when this valves cannot close properly and allows retrograde blood flow, it makes the heart have to work harder and can be detected by as a heart murmur by auscultation, the act of listening to sounds from the heart, lungs, or other organs, typically with a stethoscope.

Clinical Significance of Heart Valve Disorders

- **AV valve stenosis** reduces the heart's efficiency and thus increases its work load. This can result in atrial hypertrophy, an enlarging of the myocardium of the atria due to overwork! This can be seen as an enlarged P wave on an ECG due to the increase in mass of the atria.

- **Semilunar valve stenosis** can result in ventricular hypertrophy, an enlarging of the myocardium of the ventricles due to overwork. This can be seen as an enlarged QRS complex on an ECG due to the increase in mass of the ventricles, yielding a greater electrical signal.

Here are some other specific examples (the sounds they makes can be heard at the link listed below):

- **Aortic Sclerosis** - is a loud murmur early in systole characterized by regular vibrations which give the murmur a musical "cooing" quality and is called a Musical Murmur. It is caused by turbulent blood flow into the aorta.

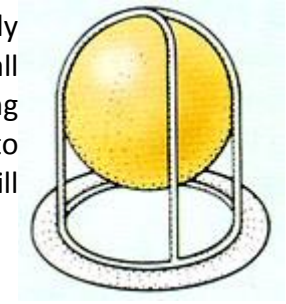
- **Mitral Valve Prolapse** - is a medium pitched murmur which begins right after a mid-systolic click and runs to the end of systole.

- **Severe Aortic Stenosis** - is a loud and higher pitched murmur which lasts throughout systole. It is caused by calcification of the aortic valve leaflets.

These and other heart murmurs can be heard at: https://www.easyauscultation.com/systolic-murmur

Replacement Valves

Replacement heart valves used to be from animals, like the pig. They are now mostly made from many other materials, like metal and plastic. Some may employ a ball and cage model (seen to the right) or tilting disk mechanism. Both are long-lasting but may cause blood clots, thus patients with heart valve replacements may need to take anticoagulant substances. Valves made from animal or human tissues are still used and though they are less durable they do not cause blood clots.



Cardiac Muscle and the Heart

In the heart, there are two major types of cardiac muscle cells or myocardiocytes. There are **1)** auto**rhythmic myocardiocytes**, these are myocardial conducting cells that coordinate the sequence of the heart beat; and **2) contractile myocardiocytes**, these are the myocardial contractile cells that make up most of the cells in the atria and ventricles and contract to generate force.

Two Types of Myocardiocytes

There are autorhythmic cells and contractile cells. What is the difference between the two types of cardiomyocytes? Autorhythmic cells are specialized cells that generate their own action potential. Contractile cells are cells that cannot generate their own action potential but cause mechanical contraction.

1) Autorhythmic Myocardiocytes

This cell population represents only about **1%** of the total myocardiocytes. Structurally similar to contractile myocardiocytes but are smaller and have no significant myofibrils (the actin and myosin arranged in sarcomeres) and so do not really contribute to generating force. Instead, these cells are strategically located throughout the heart to facilitate and the electrical signals that orchestrate the heartbeat.

About 1% of myocardial cells are **autorhythmic** and they spontaneously and rhythmically generate their own action potentials (APs) without nervous stimulation. In this way, control of heart activity is considered to be within the heart itself, and it is called ***intrinsic myogenic control*** - that is, it is derived from within the myocardiocytes. In contrast, skeletal muscle is ***neurogenic*** - that is, it requires stimulation by the somatic nervous system to initiate contraction. Autorhythmic cells are anatomically distinct from contractile myocardiocytes. They are smaller, have few contractile fibers or organelles and contain no organized sarcomeres - so they don't contribute to force generation.

In cardiac muscle, input from the autonomic nervous system (**ANS**) and **hormones** from endocrine glands can ***modify*** the contraction rate set by the pacemaker cells and can ***modify*** the force of contraction. However, the heart will contract in the absence of all neural input. In fact, if a healthy heart is removed from a body and supplied with O_2 and nutrients, it will continue contact, and at a **higher rate** since the resting parasympathetic modulation which keeps the heart rate lower at rest is removed.

2) Contractile Myocardiocytes (~99%) Contract to generate force.

This cell population represents only about **99%** of myocardiocytes. Recall from the chapter 13 that introduced the three muscle tissues that these cells are branched, with striations, centrally located nuclei, many blood vessels and they are all connected together with intercalated discs (see **Fig. 14.11** below). These cells are loaded with myofibrils and mitochondria because these are the cells that contract and generate the force that keeps the blood moving day and night.

About 99% of cardiac muscle cells are **contractile myocardiocytes**. These cells are striated, have organized sarcomeres and have high energy demands, with about **1/3** of their cell volume being mitochondria. A characteristic of cardiac muscle are that they contain **intercalated disks**, which are interdigitated membranes joined by ***desmosomes*** and ***gap junctions***. The desmosomes are a type of cell attachment, so that adjacent cells are physically attached to each other to cope with the stressful mechanical activity of the heart. Gap junctions are simply protein channels connecting adjacent myocardiocytes, they allow ions (predominantly Na^+) to pass though and thus waves of depolarization to spread throughout the muscle tissue - creating nearly simultaneous contraction.

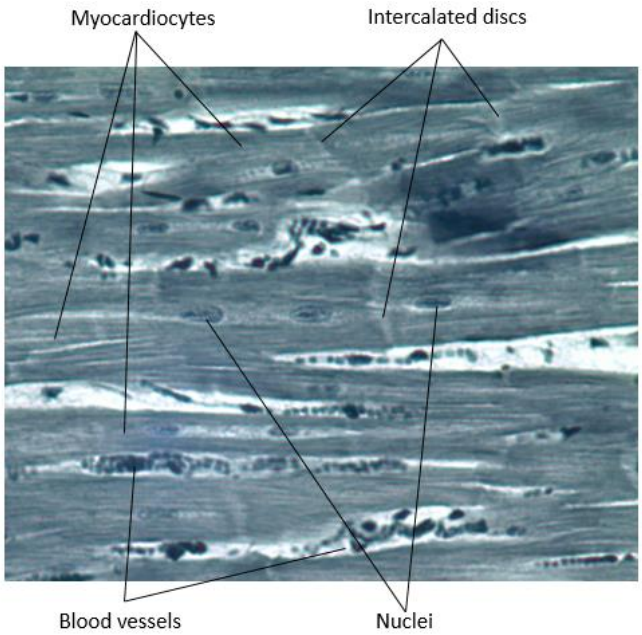


Figure 14.11 A histological preparation of heart tissue showing contractile myocardiocytes. Not the banding pattern (striations), the branching cells, the nuclei and the intercalated discs. Also seen is an

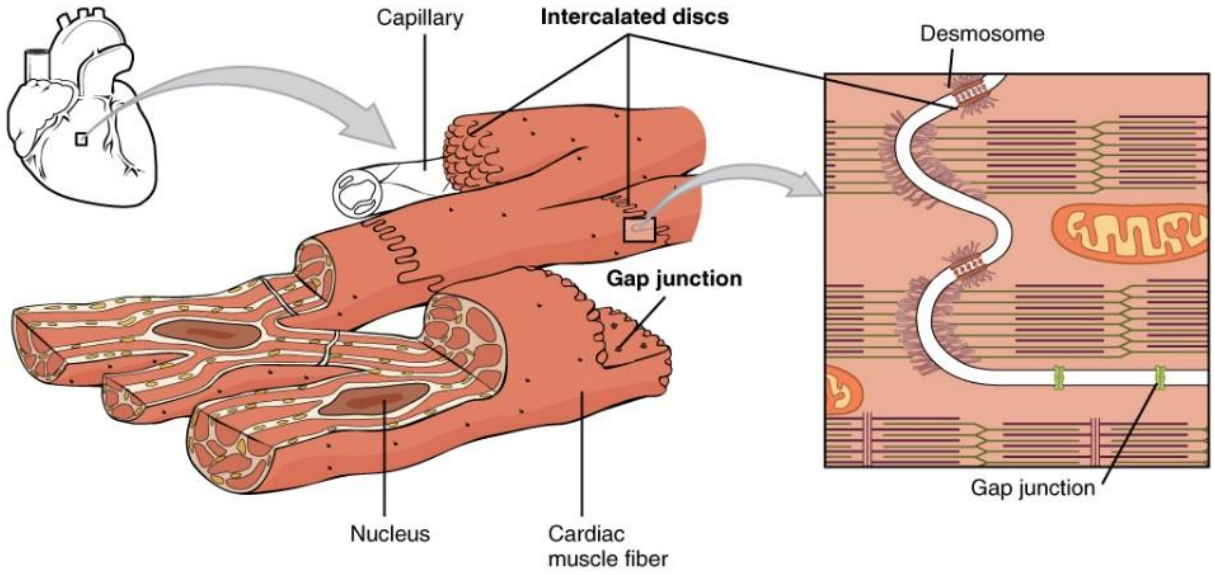


Figure 14.12 This image shows the progressive increase in magnification of the contractile myocardiocytes of the heart. A key aspect to their function is the way they are interconnected with intercalated discs, which contain desmosomes and gap junctions that are essential to their function. There is also a large mitochondria supply to provide plenty of ATP for these highly active cell.

Excitation-Contraction Coupling in Cardiac Muscle is Similar to Skeletal Muscle

Contraction occurs by the same sliding filament activity as in skeletal muscle. However, an important difference is that in **cardiac** contractile muscle cells, the AP opens membrane voltage-gated Ca^{2+} channels that are residing in the t-tubules. This allows Ca^{2+} from the extracellular Fluid (ECF) to enter the cardiac muscle cell. This entry of Ca^{2+} from the ECF is required for cardiac muscle to release its internal Ca^{2+} stores in the sarcoplasmic reticulum (SR) so that the cardiac muscle can contract. Without the influx of Ca^{2+} from the ECF, cardiac muscle cannot release its internal Ca^{2+} stores and will not contract!

There are 2 Sources id Ca^{2+} in Myocardiocytes

As already mentioned, there are **2 Sources of Ca^{2+}** in cardiac muscle contraction:

1) Ca^{2+} from the EFC is about **10%**. This must enter the myocardiocytes first to release the 2nd source.
2) Ca^{2+} release from the SR. This accounts for about **90%** of the total Ca^{2+}.

Where the Ca^{2+} for Contraction in Cardiac Muscle come from

The vast majority of the Ca^{2+} used to generate force in the contractile myocardiocytes is stored in the SR, about 90%. Only about 10% of the Ca^{2+} comes from the ECF. It turns out that the stores of Ca^{2+} in the SR are triggered to be released by the Ca^{2+} that comes into the cell from the ECF during an action potential. This is called "Ca^{2+}- induced Ca^{2+} release" (see **Figure 14.13** below). If **no** Ca^{2+} comes into the myocardiocyte from the ECF, there would be **no** Ca^{2+} released from the SR.

Calcium-Induced Calcium Release

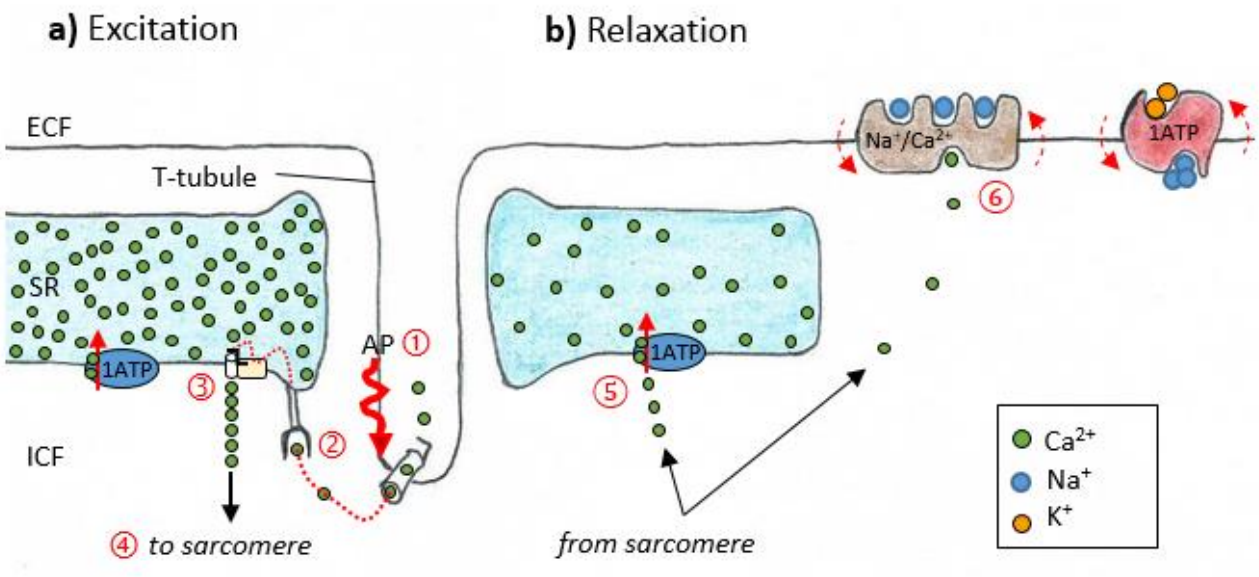


Figure 14.13 This drawing shows contractile myocardiocytes **a)** during excitation from ① an action potential which triggers opening of voltage gated Ca^{2+} channels in the T-tubules allowing the influx of Ca^{2+} from the ECF. The incoming Ca^{2+} ② binds to ryanodine receptors on the SR, ③ which open channels on the SR allowing release of Ca^{2+} from the SR. The Ca^{2+} diffuses through sarcoplasm ④ to the sarcomere and binds to troponin, moving tropomyosin and allowing cross-bridge cycling and contraction to occur. When the action potential stops, **b)** muscle relaxation occurs and the Ca^{2+} returns from the sarcomere back to the two places it came from. It is ⑤ re-sequestered into the SR at the cost of 1 ATP per 2 Ca^{2+} being imported into the SR by the Ca^{2+}-ATPase pump. It is also returned to the ECF ⑥ by the Na^+/Ca^{2+} exchanger whereby one Ca^{2+} is expelled for the importation of 3 Na^+.

Step by Step of Ca^{2+}-Induced Ca^{2+} Release Process

Cardiac muscle, like skeletal muscle, has action potentials and it is the electrical excitation (action potential) of these cells that triggers Ca^{2+} release into the sarcoplasm.

As the action potential comes down the T-tubules ①, it triggers the opening of the voltage gated Ca^{2+} channels. Because the concentration of Ca^{2+} is higher in the ECF that the ICF, there is an influx of Ca^{2+}. The Ca^{2+} that enters the myocardiocytes from the ECF binds to **ryanodine receptors** on the SR ②, which are linked mechanically to the gates on the SR, triggering them to open. Since the concentration of Ca^{2+} in the SR is very high, Ca^{2+} rushes out of the SR into the ICF (sarcoplasm) ③of the contractile cardiac muscle cell. This causes a 'spike' in the intracellular of Ca^{2+} concentration ($[Ca^{2+}]_i$). The Ca^{2+} diffuse and move to the sarcomere ④ where they bind with the regulatory protein **troponin**. The sarcomere and contraction of cardiac muscle is much the same as in skeletal muscle (covered in chapter 13). Therefore, the troponin that sits on top of the other regulatory protein **tropomyosin**, causes it to move which allows the actin myosin cross-bridge cycling to occur promoting contraction and generating force.

Once the signal for contraction in cardiac muscle stops, the Ca^{2+} needs to go back from whence it came. The removal of free Ca^{2+} from the cytosol requires the constant activity of the **Ca^{2+}-ATPase** pump on the SR ⑤, which is re-sequestering the Ca^{2+} back into the SR at the cost of 1 ATP per 2 Ca^{2+} being imported back into the SR. Since a small portion of the Ca^{2+} came from the ECF, it also must be put back there. This removal of Ca^{2+} is achieved by Na^+/Ca^{2+} indirect active transporter ⑥, which is sometimes called the **Na^+/Ca^{2+} exchanger**. This is an antiport membrane transporter that moves a single Ca^{2+} out of the cell and

at the same time imports 3 Na^+ for each cycle. In this transporter the Ca^{2+} is being moved up or 'against' its gradient, this makes this an active transport mechanism and therefore, somewhere, ATP is indirectly required. It turns out, the ATP is being used directly by the **Na^+/K^+ pump** which creates and maintains the electrochemical gradient (thus energy is constantly being stored across the membrane). By harnessing the Na^+ gradient generated by the Na+/K+ pump, this Na^+/Ca^{2+} exchanger is a **secondary** (indirect) active transport mechanism, as this transport requires ATP (to move something against its gradient), but does not directly use it.

In Cardiac Muscle, Contraction can be Graded (varied in Force)

A single cardiac muscle fiber can execute graded contractions, *so that the fiber varies the amount of force it generates*. Recall that graded contractions in ***skeletal muscle*** can occur in 3 ways: Through motor unit recruitment (spatial summation); through increased firing frequency of the somatic motor neuron (temporal summation); and by the length of the resting sarcomere (optimal length).

However, the first two methods cannot be used in cardiac muscle to vary the force of contraction. Firstly, there are **no motor units in cardiac muscle**, thus there cannot be motor unit recruitment; secondly, tetanus is continuous complete contraction and **tetanus is prevented in cardiac muscle** by the extremely long absolute refractory period in the myocardiocytes action potential. The heart is a pump, and we understand that complete continuous contraction (tetanus) is contrary to the actions required by a pump. Tetanus is verboten! The one mechanism both skeletal and cardiac muscle have in common for varying the force of contraction is based on the optimal length of the resting sarcomere. In cardiac muscle, this is related to the stretch response and Starling's Law of the Heart (more on that later!).

The answer to how cardiac muscle varies its force of contraction is that the force generated in cardiac muscle **depends on the number of cross-bridges formed**. When cytosolic [Ca^{2+}] is **low**, fewer cross-bridges are activated or engaged, giving a **weaker** force of contraction. If cytosolic [Ca^{2+}] is **increased**, more cross-bridges are formed giving additional force generated for a **stronger** contraction. **Thus, the strength of myocardial contraction is directly related to the amount of Ca^{2+} present in the cytosol**. The greater the amount of free Ca^{2+} inside the cell ([Ca^{2+}]*i*,), the stronger the force of contraction.

How are Ca^{2+} levels changed (increased) in the heart?

This *directly proportional relationship* between the amount of Ca^{2+} in the sarcoplasm and the force of contraction in the heart is a critical point to understand. Now we must identify the ways that this important variable (Ca^{2+}) can be increased or decreased in myocardiocytes. For the most part (as we will see in the cardiac output section) the heart at 'rest' operates with a great potential to increase its pumping ability. As such, the critical issue is how can the Ca^{2+} in the sarcoplasm be increased in order to meet the needs of the body as quickly as possible?

The sarcoplasmic concentration of free Ca^{2+} in myocardiocytes can be increased two ways:

1) By increasing the amount of Ca^{2+} that enters the cell through voltage-gated calcium channels.

2) By storing more Ca^{2+} in the sarcoplasmic reticulum (SR).

1) The Ca^{2+} entering voltage-gated Ca^{2+} channels

Recall from the earlier section, the Ca^{2+} influx from the ECF when the action potential travels along the T-tubule is what releases the enormous stores of Ca^{2+} in the SR ("Ca^{2+}- induced Ca^{2+} release"). It turns out that if more Ca^{2+} comes in from the ECF, it stimulates greater Ca^{2+} release from the SR.

The catecholamines norepinephrine (NE) and epinephrine (E) can increase [Ca^{2+}] and alter the electrical activity of the myocardiocytes by achieving both objectives 1) and 2) above. From our previous sections, we know that NE and (E) are be released by both the nervous system (sympathetic division of the ANS) and the endocrine system (from the adrenal medulla). Thus their release is linked to states of excitement or perceived danger, when the 'fight or flight' of the sympathetic kicks in, and when the 'adrenals are pumping'. Physiologically it makes sense that elevated NE and E signaling would increase the activity of the heart and it does. The vital function of these catecholamines is that they augment (increase) the amount of Ca^{2+} available for cardiac muscle contraction. Both NE and E bind beta-1 (β_1) receptors on cardiac muscle membrane and **increase the force of contraction.** How do they do this?

The Ol' Second Messenger System!

The way that NE and E act is by increasing the 'open' probability of the voltage gated Ca^{2+} channels in myocardial contractile cells. They both do this by activating ***second messenger systems*** in myocardiocytes. Recall from earlier sections on cell transmission, that the second messenger system is part of the **metabotropic effect**. These responses take a bit longer to commence but their effects are very powerful and longer lasting than ionotropic effects. As we have also seen before, it is cyclic AMP (**cAMP**) that activates protein kinases (e.g., PKA) inside the cell. This triggers the **phosphorylation** of the voltage gated Ca^{2+} channels. Phosphorylated voltage-gated Ca^{2+} channels increase the probability of them opening, this allows more Ca^{2+} to enter cell.

At the same time, NE and E also increase the K^+ permeability, enhancing outward K^+ flow and **terminating the plateau phase sooner**. Therefore, NE and E increase Ca^{2+} influx into the sarcoplasm, and as we will see below, they enhance intracellular SR stores of Ca^{2+} without increasing the duration of the contraction. Functionally, this makes sense. Since NE and E also increase heart rate, it would be counterproductive to lengthen the time of cardiac contraction if the objective is to increase cardiac output (CO).

2) Storing more Ca^{2+} in the Sarcoplasmic Reticulum

The regulatory protein **phospholamban** sits within the membrane of the SR and operates to adjust (increase) the calcium pump in cardiac muscle cells in order to help concentrate more Ca^{2+} in the SR. Stimulation of β_1 receptors by NE triggers the *phosphorylation of phospholamban*, which activates it and then allows it to facilitate the enhancement of the Ca^{2+}-ATPase activity on the SR. **This means that more Ca^{2+} can be stored in the SR and more quickly**. The net result of this 'activation' of phospholamban is a stronger contraction and a shorter duration of cardiac contraction, that is, a faster, stronger heartbeat.

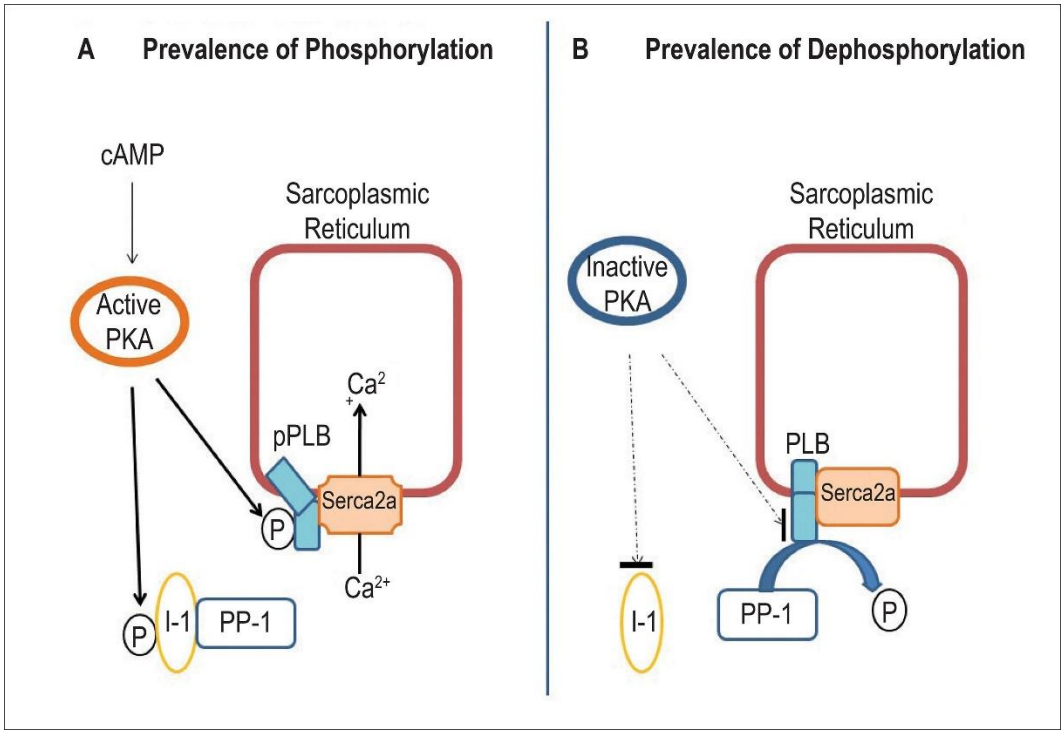


Figure 14.14 A. The prevalence of phosphorylation occurs when PKA is activated preventing PLB de-phosphorylation. **B.** The prevalence of de-phosphorylation occurs when PKA is not activated. The activation of the beta-adrenergic system promotes G protein stimulation via cyclic adenosine monophosphate (cAMP) alters the structure of protein kinase A (PKA) and leads to phospholamban (PLB) phosphorylation. This protein participates in the system that controls intracellular calcium in muscle cells, and it is the primary regulator of sarcoplasmic reticulum calcium pump activity. In this study examining obesity, the beta-adrenergic system was activated by the influence of increased leptin, resulting in higher myocardial phospholamban phosphorylation via cAMP-PKA. It was concluded that obesity did not promote an imbalance between myocardial PLB phosphorylation and de-phosphorylation via beta-adrenergic system.

The inclusion of the fairly complex issues outlined regarding the regulation of calcium handling in heart cells in **Fig. 14.14** above provides some insight into the nature of how the heart can modify its own behavior.

The Effects of the Autonomic Nervous System (ANS) on the Heart

In summing up the effects of the ANS on the ability to vary the force of contraction of myocardiocytes (as well as modifying the rate of beating), we see that there is a balance of forces from both divisions of the ANS. The sympathetic increases heart rate and the force of contraction, and the para sympathetic decreases heart rate and reduces the force of contraction (see **Figure 14.15** below).

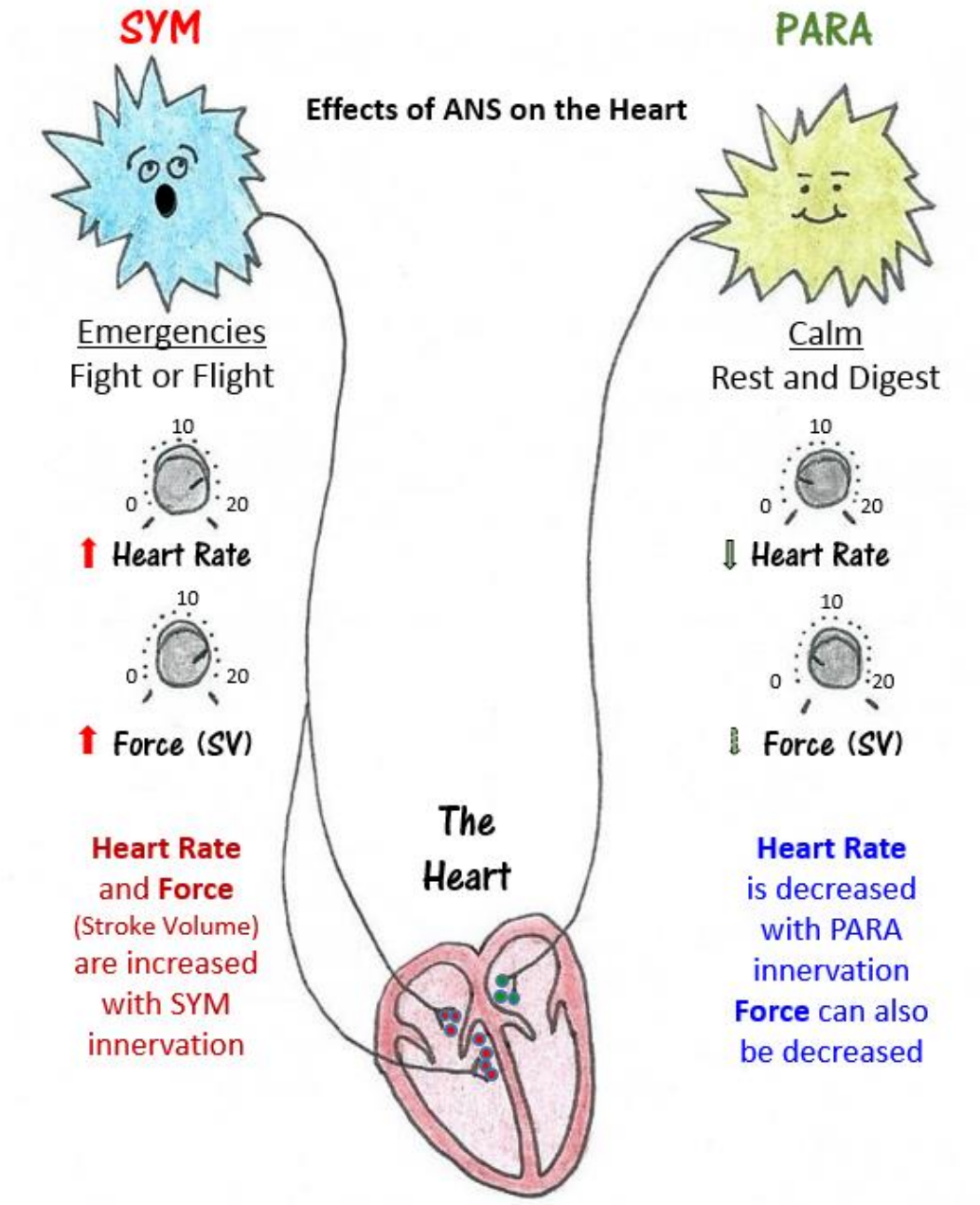


Figure 14.15 The drawing above illustrates the opposing effects the two divisions of the autonomic nervous system (ANS) have on the actions of the heart. The sympathetic division (SYM) acts on the SA Node, the AV node and the contractile myocardiocytes to increase both heart rate (beats/min) force (stroke volume) of the heart in times of emergencies. In contrast, the parasympathetic division (PARA) acts predominantly on the SA Node to decrease the heart rate (beats/min). It may also decrease the force (stroke volume) of contraction of the heart at rest.

The Stretch and Length-Tension Relationship

Another property of cardiac muscle is that **when it is stretched, it contracts more forcefully**. This is due to the length-tension relationship that we have already seen in skeletal muscle. The degree of overlap between thick and thin filaments of the sarcomere will affect the tension generated by that muscle cell. The muscle cells of the heart are a little different to skeletal muscle in that at rest the cardiac sarcomeres are not at their optimal length; it is when they are stretched (for example by an increase in venous return to the heart) that they are lengthened to the optimal sarcomere length and can exert a greater force (see **Figure 14.16** below).

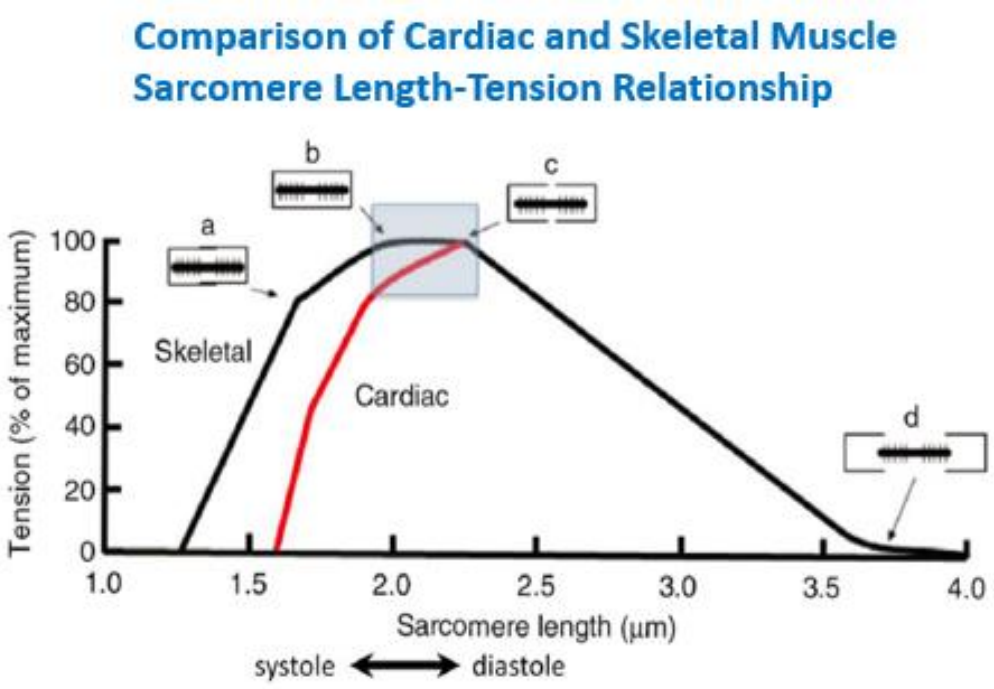


Figure 14.16 The Length-Tension relationship for both skeletal and cardiac muscle is shown in graph to the left. We do not need to know the specific values, just the pattern. That is, there is an optimal length (related to myofilament overlap) which gives the greatest tension for both types of muscle.

The degree of overlap is important, however, there is an additional element that relates to stretching of cardiac muscle and increasing the force of contraction. The physical stretching of myocardial cells also **opens mechanically gated (stretch-sensitive) Ca^{2+} channels**. Therefore the stretching allows more Ca^{2+} entry into the myocardiocyte, which also leads to a stronger contraction (more Ca^{2+}= more force). The degree of stretch of myocardiocytes at any one time depends on blood volume in the chambers when filling is occurring.

Starling's Law of the Heart

In the segments covering cardiac output to follow, the relationship to the filling of the heart and how it impacts stroke volume will be explored in detail. Stroke volume is the volume of blood that is ejected from a ventricle (left or right) in one beat. As the force of contraction of a ventricle increases, so too does stroke volume. This is why when the force of the heart beat is discussed, the term stroke volume is equivalent to it. Starling's law of the heart expresses the relationship between **stroke volume** (force) **and end diastolic volume** (EDV). Put simply, this law declares that stroke volume increases in response to an increase in the volume of blood in the ventricles prior to contraction (if all other factors are constant). This relationship will be explored in more detail in the cardiac cycle and cardiac output sections.

Action Potentials in Myocardial Cells

These cells experience action potentials (APs) similar to those of skeletal muscles and neurons. However, autorhythmic and contractile myocardiocytes show distinctive action potentials (APs) to those we have been familiar with so far. It turns out that the role of Ca^{2+} in the function and pattern of the myocardiocyte APs are important and different to that seen in skeletal muscle and in neurons.

Action Potentials in Autorhythmic Myocardiocytes

The pacemaker ability of these **autorhythmic** cells results from an unstable membrane potential. Rather than having a stable resting membrane potential (RMP), these autorhythmic cells have a 'drifting' membrane potential. It starts at -60 mV and drifts upward to -40 mV, which is the threshold for these cells. This drifting membrane potential can be called a ***pacemaker potential***. When it reaches the threshold value of -40 mV, the cell fires an AP. The membrane potential instability or 'drift' is caused by "funny" (I_f) cation channels that are permeable to Na^+ and K^+, and at -60 mV this channel allows more Na^+ in than K^+ out and this induces a current flow and allows the drifting membrane.

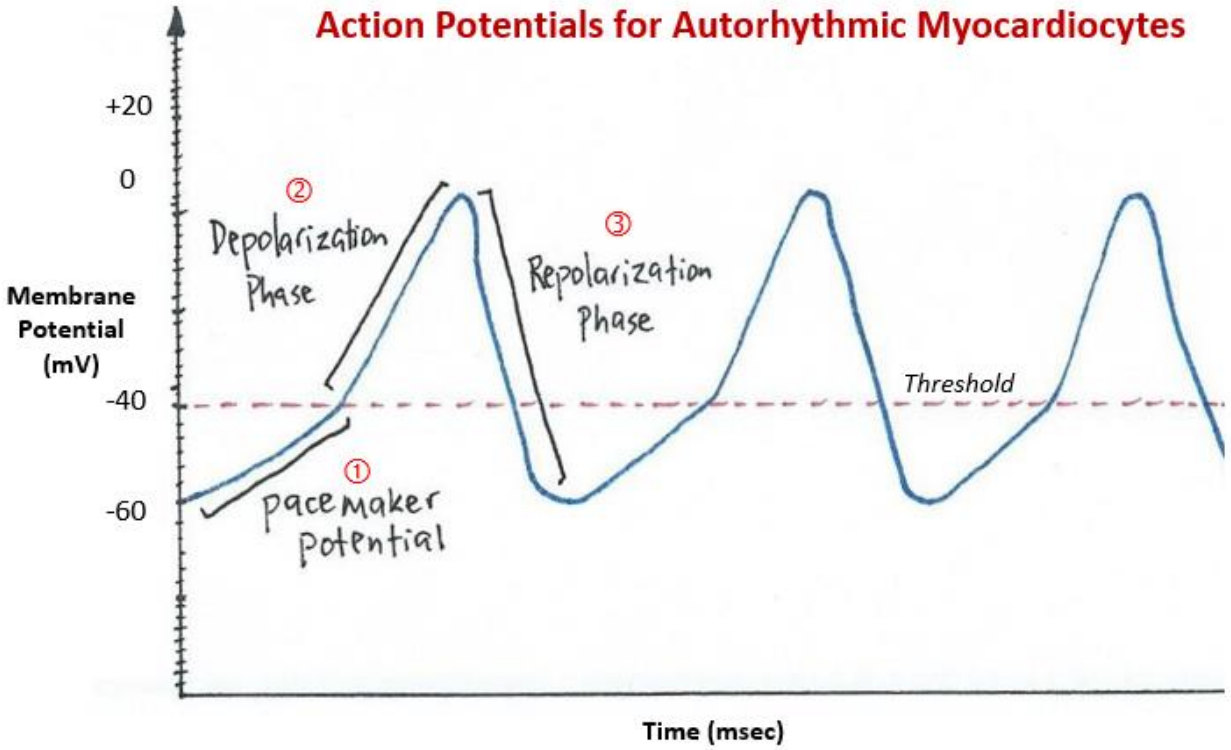


Figure 14.17 This is a graph of an autorhythmic myocardiocyte action potential showing the changing voltages of the membrane during the ① the pacemaker potential, ② the depolarization and ③ repolarization phases.

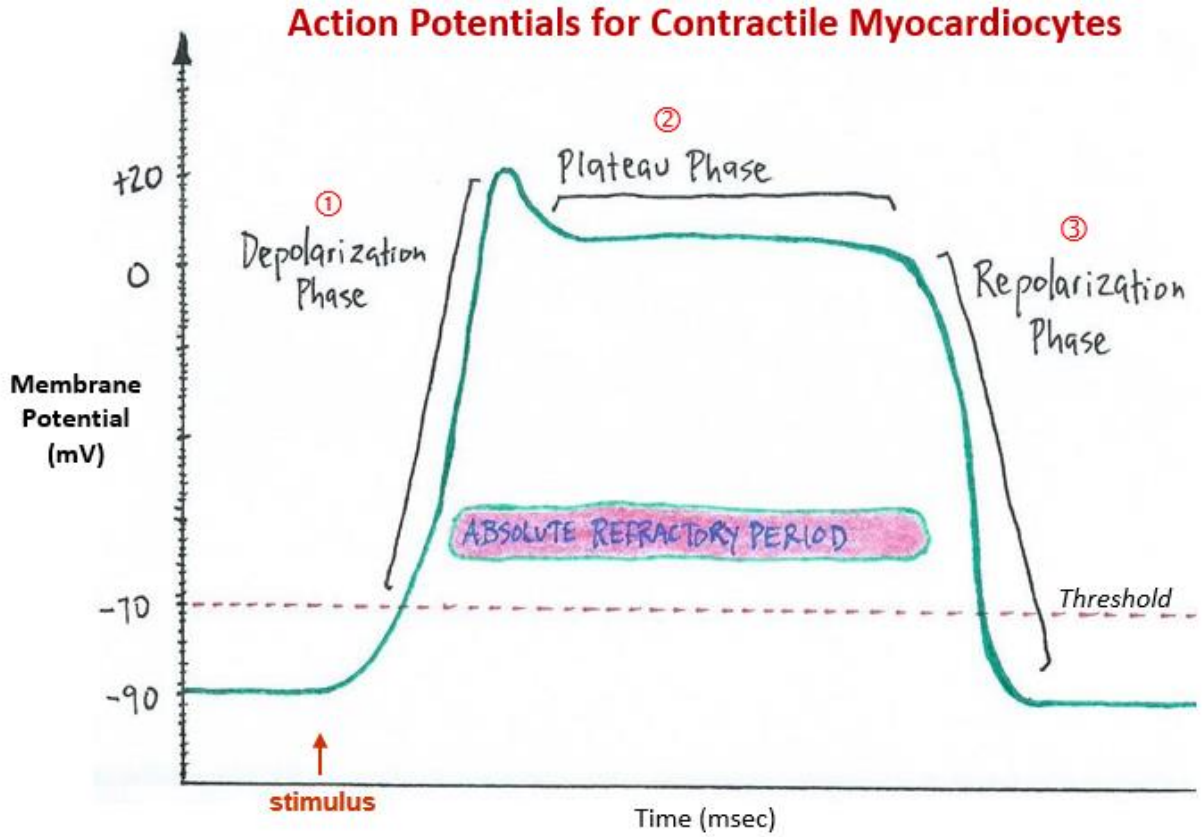
The opening of the funny Na^+/K^+ channels creates a net influx of positive charge and this is what steadily depolarizes autorhythmic cells. When it incrementally depolarizes the membrane to **threshold**, this then closes these I_f channels, and opens Ca^{2+} channels, thus at threshold, many Ca^{2+} channels are opened creating rapid Ca^{2+} influx and the **depolarization phase**. At the peak of the action potential, the Ca^{2+} channels close and K^+ channels the open. The efflux of K^+ causes the **repolarization phase**. Thus there are really just 2 phases of this action potential (AP) after threshold is reached.

There is typically no hyperpolarization phase in these AP's, though elevated **parasympathetic innervation** by the vagus nerve can create hyperpolarization by pulling the membrane voltage down below -60 mV and making the cell take longer to reach threshold. This slowing of the AP rate (and thus slowing of the heart rate) is achieved by increasing the K^+ efflux and decreasing the Ca^{2+} influx. In the opposite manner, **sympathetic innervation** of these pacemaker cells reduces the repolarization phase and thus speeds up the depolarization phase. This increases the rate of APs the (and thus increases the heart rate) by increasing the Ca^{2+} influx which creates the depolarization phase.

The timing of APs in these cells can be influenced by norepinephrine (NE) and epinephrine (E). Both NE and E stimulate β_1 receptors and increase ion flow in I_f and Ca^{2+} channels. This then increases the rate of depolarization, which increases heart rate. The ACh released by the parasympathetic division of ANS acts on muscarinic receptors to slow heart rate by altering K^+ and Ca^{2+} permeability, as stated above.

Action Potentials in Myocardial Contractile Cells

The action potential for myocardial contractile cells is shown in detail in **Figure 14.18** below. In **contractile** myocardiocytes, there is a stable resting membrane potential of -90 mV. These cells require a stimulus to reach **threshold** (which is -70 mV). Reaching threshold triggers the rapid **depolarization phase** which is due to the entry of Na^+ through the very fast opening voltage gated Na^+ channels. At the peak of the AP (about +20 mV) these fast Na^+ channels close and voltage gated K^+ channels actually open here, the efflux of K^+ brings the membrane down to about +5 mV, but then the voltage gated Ca^{2+} channels open and this positive charge coming into the cytosol keeps the membrane elevated at about +5 mV for a very long **plateau phase**. Only when theses Ca^{2+} channels close does the membrane begins to fall, this is now coupled with the outward rectifier K^+ channel which is responsible for the rapid and steep **repolarization**



phase that takes the membrane all the way back down to -90 mV, where RMP is restored.

Figure 14.18 This is a graph of a contractile myocardiocyte action potential, showing the stimulation (stimulus) and the changing voltages of the membrane during the ① the depolarization phase, ② the plateau phase, and ③ repolarization phase. Also shown is the absolute refractory period.

Note in **Figure 14.18** above, a unique feature of action potentials in myocardial contractile cells is the absence of a hyperpolarization phase at the end. The myocardial cell returns directly to its stable resting membrane potential of -90 mV (the equilibrium potential for potassium). Because efflux and influx are exactly, balanced at -90 mV, there is no driving force to cause K^+ to continue to leave the cell and

hyperpolarize it. Also note that the myocardiocyte action potential (AP) is lengthened compared to skeletal muscle AP, due to Ca^{2+} entry that creates the *elongated plateau phase* before repolarization. This creates a very long AP for these myocardiocytes.

The typical skeletal muscle AP duration is **1-5** msec, but the time taken for a contractile myocardial AP is about **250** msec. Most of the duration of this AP is also the ***absolute refractory period***. As we have seen before, no other AP can occur during an absolute refractory period, so this helps to prevent any kind of temporal summation, and consequent tetanus contraction, which would be incompatible with the heart as a pump, as it prevents the effective filling of the heart's chambers.

Electrical Conduction System of the Heart

Location of the Myocardiocytes

The two types of myocardiocytes, autorhythmic and contractile, not only have distinctive action potentials and different structural components, they also have different locations in the heart. As we have seen, the vast majority of the heart cells are contractile myocardiocytes which assist the heart in pumping. It is the remaining cells, the **autorhythmic myocardiocytes** that are located in definitive regions to create the electrical conduction system of the heart.

The electrical conduction system in the heart coordinates contraction. The APs originate in one part of the strategically located autorhythmic cells and then spreads this signal between cells via gap junctions in intercalated disks. The depolarization of the contractile muscle cells is followed by a wave of muscle contraction that passes across the atria then moves into the ventricles. The electrical conduction system consists of five major sites:

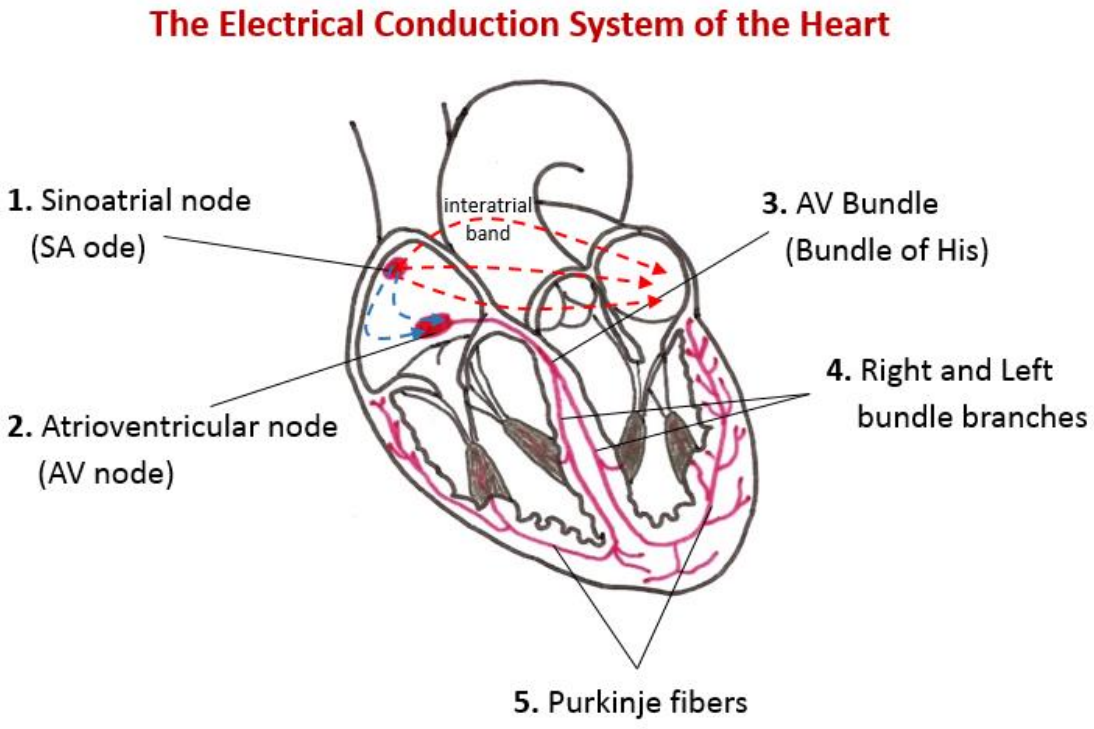


Figure 14.19 This diagram show the electrical conduction system of the heart and the five (5) major components. The SA node is the first site and has the fasted intrinsic firing, making it the 'pacemaker' of the heartbeat. The interatrial band (Bachmann's bundle) connects the 2 atria (shown by the red dashed lines). The internodal pathway connects the SA node to atrioventricular (AV) node (shown by light blue dashed lines).

Specific Location of the Autorhythmic cells

1. Sinoatrial (SA) node
(superior posterior right atrium)

2. Atrioventricular (AV) node
(inferior medial right atrium)

3. AV Bundle (of His)
(superior I.V. septum)

4. Right and Left bundle branches
(down along the I.V. septum)

5. Purkinje fibers
(from apex to base of heart)

Table 14.1. The intrinsic rate of Action Potential for electrical conduction system regions.

Electrical Conduction Region	Spontaneous Rate of Action Potentials/min
SA Node (sets the pace)	70-80
AV Node	no intrinsic rate
AV Bundle	40-60
R and L Bundle Branches	no intrinsic rate
Purkinje Fibers	20-40

The sinoatrial (SA) node, in the superior, posterior portion of the right atrium, initiates contraction of the heart because it fires APs at the highest rate (see table below). For this reason, it is called the ***pacemaker*** of heart.

The **Interatrial band** (Bachmann's bundle) connects the 2 atria. It is a group of specialized conducting cells that transmit the impulse directly from the SA node in the right atrium to the left atrium. The **internodal pathway** connects the SA node to atrioventricular (AV) node, located in the floor of right atrium. This connects to the AV Bundle (of His) located in the IV septum. This then splits into right and left bundle branches running down the IV septum and finally into Purkinje fibers at the apex of the heart. Due to the electrical insulation of the fibroskeleton, the direction of the electrical signal (AP) is controlled and results in the **apex-to-base** (bottom to the top) contraction of ventricles. Thus, the ventricles are squeezed from the bottom to the top of the chambers and blood is ejected out. This is also aided by the spiral arrangement of myocardiocyte in the walls of the heart, which impart great force.

The slow conduction of the electrical signal through AV node cells lengthens their refractory period, this helps to create the *AV nodal delay* and allows the atria to complete their contraction and fill the ventricles before ventricular contraction begins. If the SA pacemaker malfunctions and fires at a very rapid rate, the AV nodal delay prevents every action potential from passing into the ventricles, in this way permitting the ventricles to function at a slower pace so that they have time to fill with blood. The SA node sets the heart rate because it fires APs at the fastest rate and the other regions follow the lead of the SA node. If the SA node is damaged, then another pacemaker sets the heart rate. An **ectopic focus** is when the pacemaker is somewhere other than the SA node. Ec 'out', topic 'of place' = out of place. Think of ectopic pregnancy.

The Electrocardiogram (ECG)

The electrocardiogram reflects the electrical activity of the heart, it is **a recording of the electrical activity of the heart**, detected by recording electrodes placed on the skin. Because the ventricles have more muscle than the atria, they create a larger electrical signal so the waves associated with the ventricles are usually larger than the waves associated with the atria. An ECG is not a single action potential, but shows the sum of all the electrical potentials generated by all heart cells at any moment.

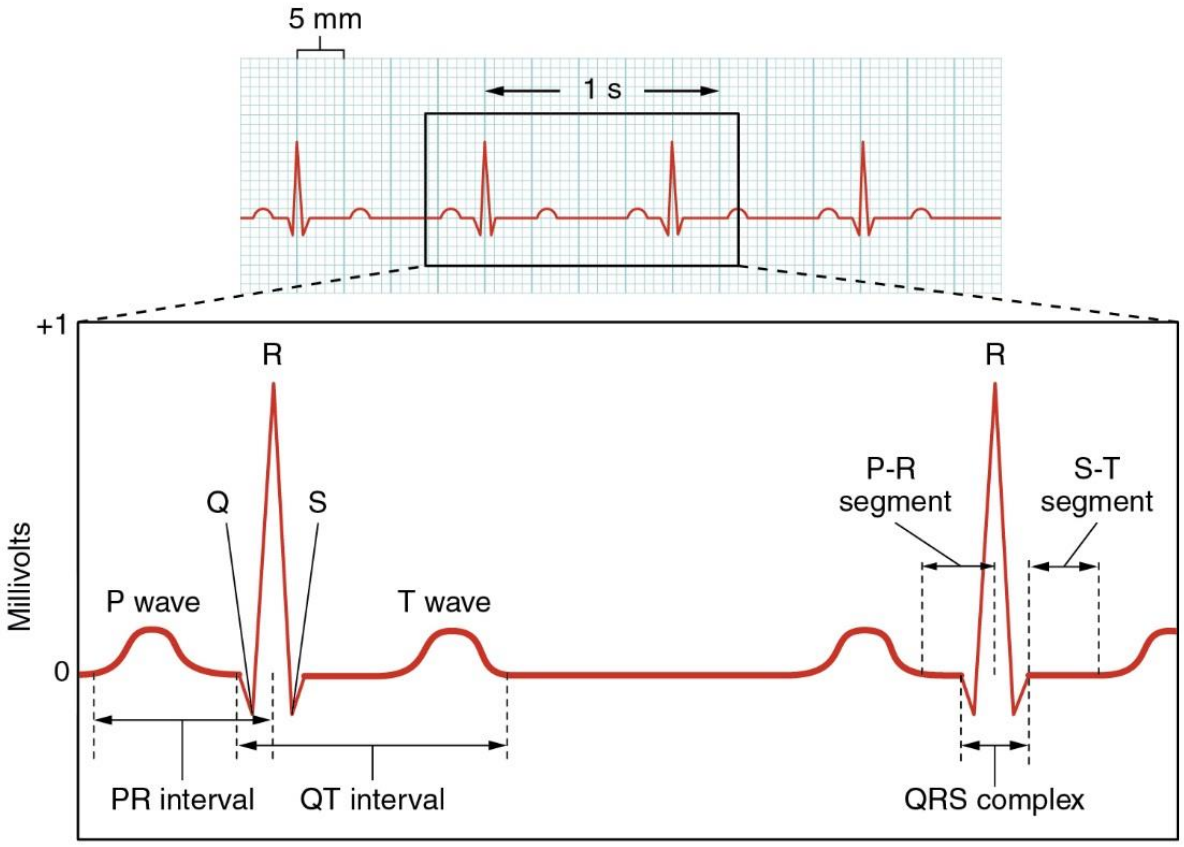


Figure 14.20 Shown above is a typical 'textbook' electrocardiogram (ECG) trace of a normal heart at rest. The electrical recordings are measured in millivolts (mV) over time (sec). An ECG is a recording of all the electrical events of the heart and is not an action potential. The electrical activity during the various segments, intervals, waves and complexes indicate the activity that the heart is about to engage in, since electrical signals precede (come before) mechanical events in all muscle tissue.

Basic Definitions for an ECG Trace

In order to get the best understanding of an ECG, it is helpful to know the basic components of an ECG, as the terms used have specific definitions.

- **Segment** – a straight line between waveforms.
- **Wave** – deflection from the baseline (straight line) in either a positive or negative direction (0 millivolts).
- **Interval** – a segment and a waveform.
- **Complex** – Consists a series of waveforms.

The Main Components of an ECG

Knowing the main components of an ECG can provide information about heart rate and rhythm of the heart, and can also show if there are disorders or myopathies of the heart present. In some sample ECG's it is possible to recognize if there is an enlargement of specific chambers of the heart, or if there are signs of myocardial ischemia (reduced blood flow) or myocardial infarction (a heart attack).

The term EKG is from the German version electrocardiogram, where it was initially developed. The naming of the waves portions of the EKG or ECG start with the letter P and move chronologically in alphabetical order: P, Q, R, S, T and there is even a U wave.

Each portion of the ECG can be described in terms of the electrical events occurring. Below are brief descriptions what is occurring during each portion.

- **P wave:** The depolarization of the atria (both right and left at the same time).
- **QRS Complex:** These are 3 waves together in sequence Q, R and S forming a complex. It is the depolarization of ventricles (both right and left at the same time). Note that atrial repolarization occurs at the same time and is typically masked by this large signal on the ECG).
- **T wave:** The repolarization of the ventricles.
- **P-R Interval:** Is the time from the onset of the P wave to the start of the QRS complex. It reflects conduction through the AV node, and the time delay between atrial and ventricular activation ('AV nodal delay').
- **S-T Segment:** The portion between the QRS complex and the T wave. It represents the early part of repolarization of the ventricles.
- **T-P Segment:** This is a flat line with no net electrical events, is a time of ventricular diastole (filling).

ECG's Vocabulary Terms and use as a Tool

Common terms applied to heart activity (and ECG's) include: **tachycardia** – abnormally fast resting heart rate (above 100bpm); **bradycardia** - abnormally slow resting heart rate (below 60bpm). At very rapid heart rates, there may be less blood pumped per beat because the muscle has not had time to relax completely, but remember, the longer refractory period of myocardial cells prevents tetanus! Tetanus would not allow the heart to relax at all. In that state, no blood would be pumped to the brain or rest of the body. **Arrhythmias** can result from benign extra beats or more serious conditions discussed in lab.

In a laboratory exercise or in a clinical setting, no two EKGs will look identical, nor will they look exactly like a "normal" textbook example, but there are fundamental properties that are shared amongst all normal EKG traces. We can however learn a lot of foundational information from the normal trace, including what the normal orientation (up or down) should be, the amplitude (height) and what the duration (time interval) of the segments, interval, wave and complexes should usually be.

Practical Examinations: Sample ECG's and what they may indicate

In a laboratory exercise or in a clinical setting, no two EKGs will look identical, nor will they look exactly like a "normal" textbook example, but there are fundamental properties that are shared amongst all normal EKG traces. We can however learn a lot of foundational information from the normal trace, including what the normal orientation (up or down) should be, the amplitude (height) and what the duration (time interval) of the segments, interval, wave and complexes should usually be.

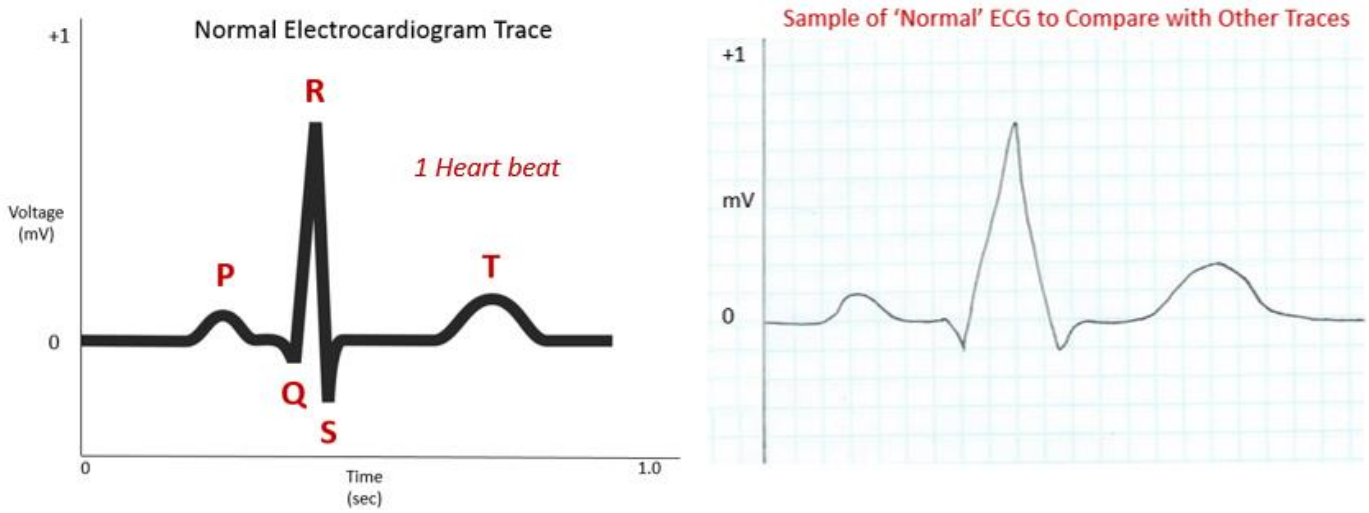


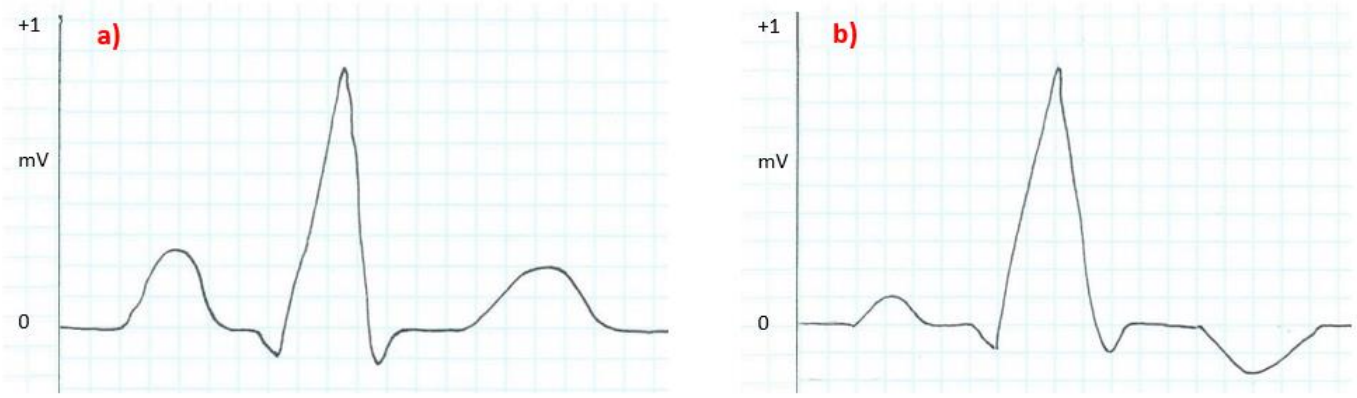
Figure 14.21 On the left shows a simplified normal ECG trace of a heart at rest. The waves P, Q, R, S and T are shown. On the right is a trace without any labels but it also represents a normal ECG trace of a heart at rest. Use this one (on the right) as the model to compare to when looking for any abnormalities on the example ECG traces below.

ECG Trace Exercises

Below on the following pages are some examples (**a to j**) of ECG traces with anomalies. Compare these samples to the ECG trace in Fig. X above (on the right) which shows a normal rate and rhythm, along with the typical healthy pattern at rest. The answers are in appendix B.

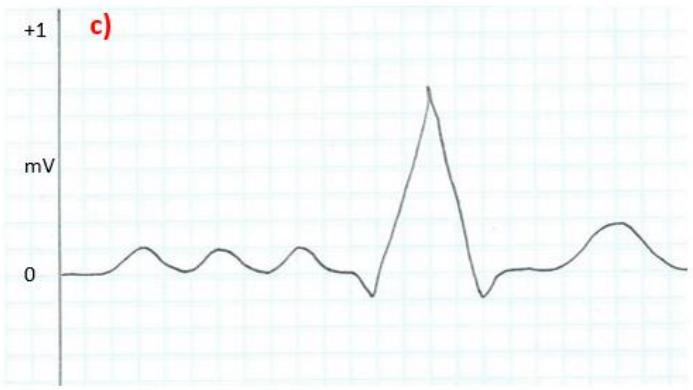
The examples below show various arrhythmias and myopathies (disease states). Take a look, and for each one find what the specific abnormal component is (e.g., an enlarger P-wave), and secondly, what that anomaly on an ECG trace may indicate (e.g., enlarged atria; perhaps from a stenotic AV valve).

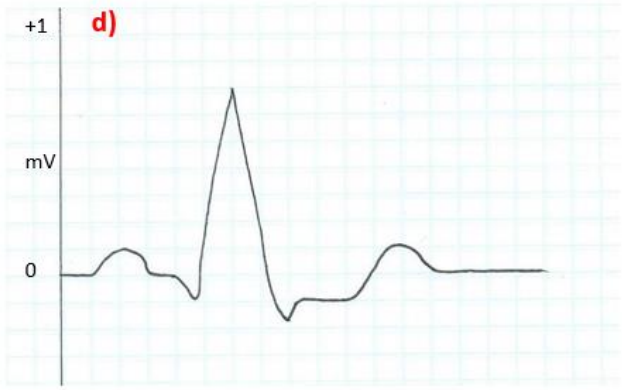
Samples ECG traces



a) The abnormal component is _____. It may indicate _____.

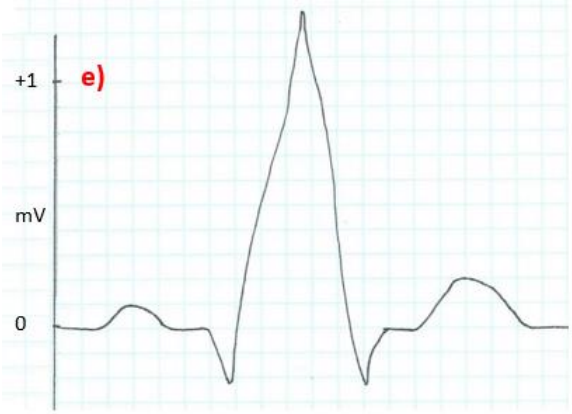
b) The abnormal component is _____. It may indicate _____.

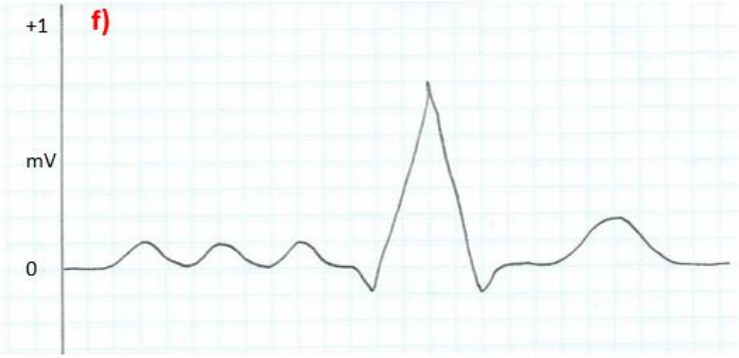




c) The abnormal component is _____. It may indicate _____.

d) The abnormal component is _____. It may indicate _____.





e) The abnormal component is _____. It may indicate _____.

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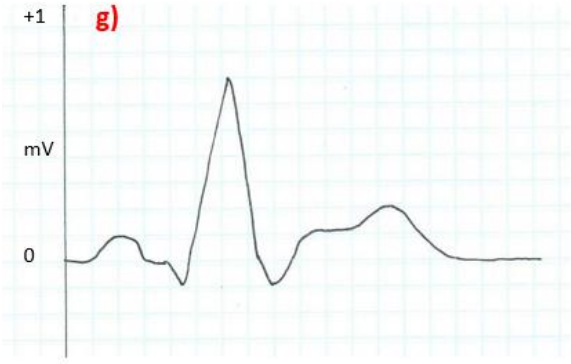
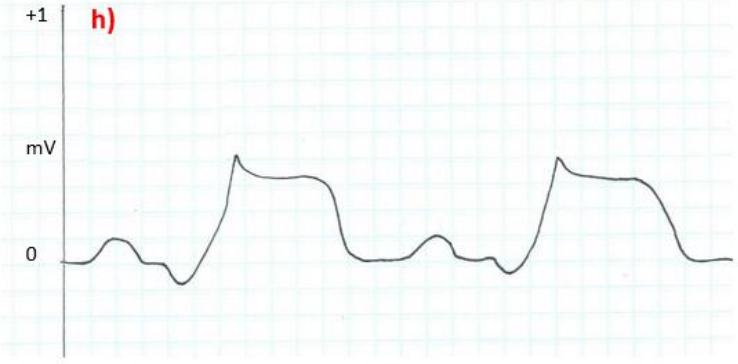
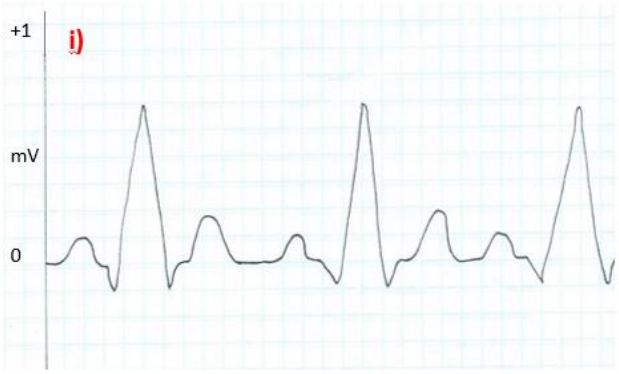
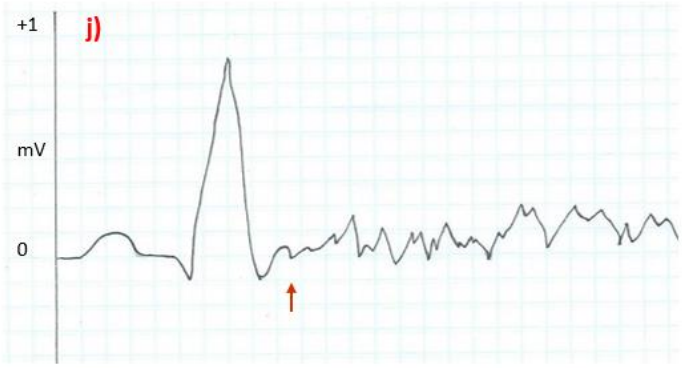




g) The abnormal component is _____. It may indicate _____.

h) The abnormal component is _____. It may indicate _____.





i) The abnormal component is _____. It may indicate _____.

j) The abnormal component is _____. It may indicate _____.

Important Note: The main purpose of the electrical conduction system of the heart is to orchestrate (like a conductor of a symphony) the perfect Heart Beat. Therefore, all electrical events precede (come before) any mechanical events in the heart. See summary of electrical and mechanical events **Table 14.2** below. This is because the electrical events are instructing the heart's activity so that it is elegantly coordinated in order to be the perfect purveyor of flow, creating the efficient and graceful two circuits in one!

The Cardiac Cycle

The cardiac cycle is the period of time from the beginning of one heartbeat to the beginning of the next. It focuses on the **mechanical activity** of the heart that is coordinated by the electrical activity of the conduction system of the heart. A close examination of the 5 phases (or stages) of the cardiac cycle will give an indication of how precise its function is.

Before we examine the cardiac cycle in detail it is important to know some key terms and understand exactly what they mean, as some terms can be quite critical, and the better we understand them, the more straightforward the discussions that follow will be.

There are two main stages or conditions of the heart and they are **Diastole** and **Systole.**

- **Diastole** (like the term 'dilate') means dilated or relaxed. Therefore diastole is the time during which **cardiac muscle is relaxing**. If the chambers are relaxing, then the **pressure is low.** If a chamber is relaxed with low pressure, then they are **filling**.

- **Systole** (to bring together or draw in) means contraction. Therefore, systole is the time during which **cardiac muscle is contracting**. If the chambers are contracting, then the **pressure is high**. If a chamber is contracting with high pressure, they are **ejecting blood**.

In the body (and elsewhere), substances move and flow according to gradients. When we examine fluid or gas movement in the body, they appear to **move down their pressure gradients**, that is, they go from regions of higher pressure to regions of lower pressure. This is how blood flows in the heart. Pressure and electrical changes in the chambers of the heart assist in the flow of blood. The atria of each side of the heart contract at the same time, followed by a slight delay, then both of the ventricles of each side of the heart contract at same time as each other. In terms of analysis, the cardiac cycle can be divided into 5

phases as described below and illustrated in **Fig. 14.22**. The cycle can start anywhere, since, wherever it starts, it will go through all stages and end up back where it started. Typically, by convention, the cardiac cycle discussions begin when the heart is at rest, or in Late Diastole.

The 5 Phases of the Cardiac Cycle

① Atrial and Ventricular Diastole: The Heart at Rest

The heart is at 'rest' and the atria and ventricles are relaxing. The atria are filling with venous blood. The AV valves are open as ventricles relax and blood flows by gravity from atria to ventricles. During this phase, the ventricles are about **80%** filled with blood, this is termed *passive filling*. *(T-P Segment of ECG)*

② Atrial Systole: Completion of Ventricular Filling

When the atria contract (systole), the remaining **20%** of blood fills the ventricles, this is like a "topping off" of the ventricles. Atrial systole begins following depolarization of the SA node, as a wave of depolarization (electrical signal) across the atria is followed by a wave of contraction that pushes blood into the ventricles to complete ventricular filling. Some blood is forced back into veins, creating a small retrograde blood movement, measured as a pulse in the jugular vein. *(Atrial systole follows P wave on ECG)*

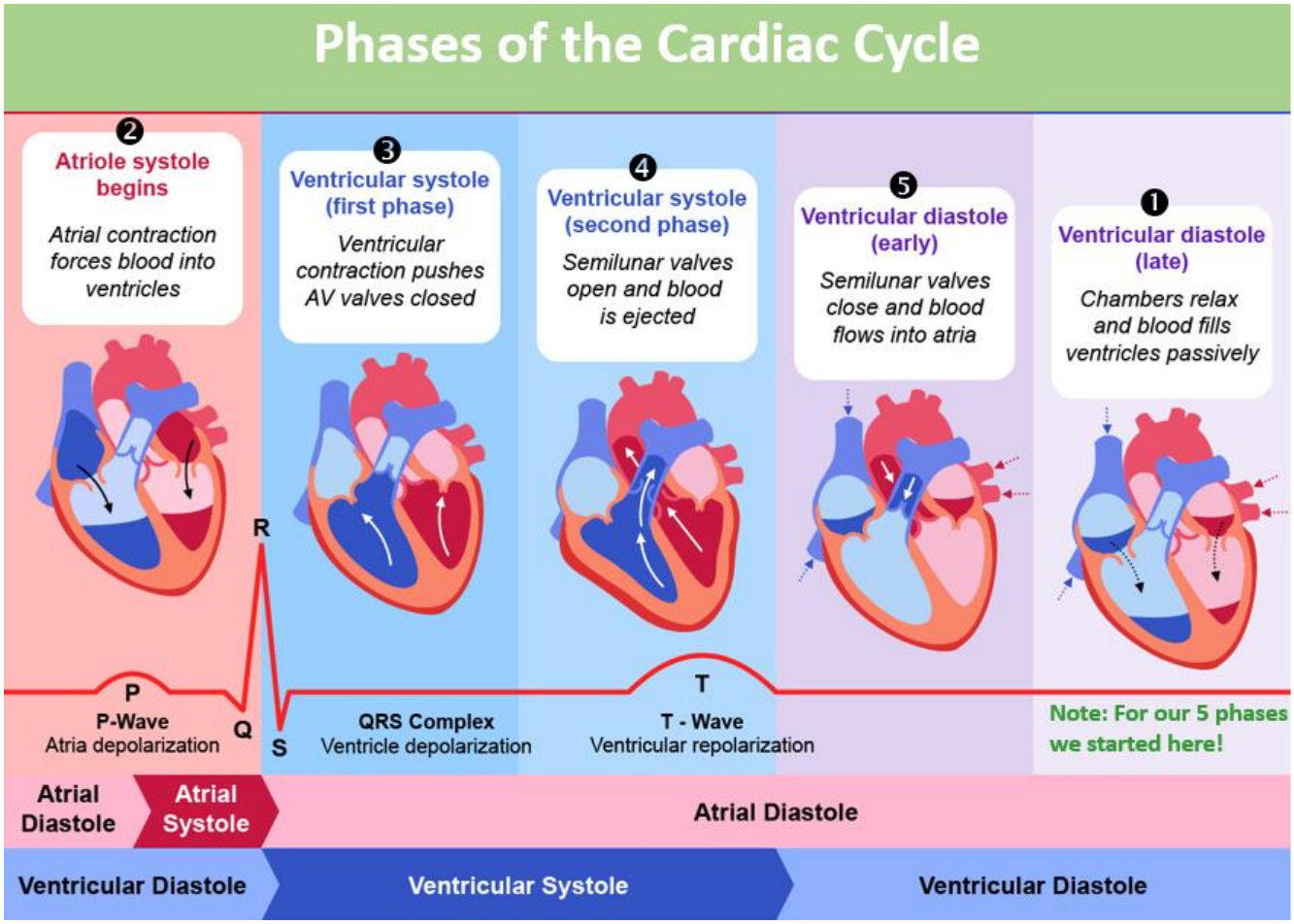


Figure 14.22 This shows how the chamber blood volumes and major ECG activity changes during the different phases of the cardiac cycle. Where we start on this image in terms of the phases does not matter since the phases always proceed in the same sequence because it is a 'cycle' (circle), thus we can start anywhere in the cycle. The convention is usually to start the description of the cycle with late ventricular and atrial diastole, that brief moment when the entire heart is 'at rest'. In this image, that is the very last panel to the right, and is labeled #1. From there, just move to #2 (at the left) and then proceed in the right direction through the entire cycle, ending at #5.

② Atrial Systole: Completion of Ventricular Filling

When the atria contract (systole), the remaining **20%** of blood fills the ventricles, this is like a "topping off" of the ventricles. Atrial systole begins following depolarization of the SA node, as a wave of depolarization (electrical signal) across the atria is followed by a wave of contraction that pushes blood into the ventricles to complete ventricular filling. Some blood is forced back into veins, creating a small retrograde blood movement, measured as a pulse in the jugular vein. *(Atrial systole follows P wave on ECG)*

At this time, just prior to ventricular systole (the next phase), the ventricles are full of blood, this is termed End Diastolic Volume (**EDV**) and represents the **maximum ventricular volume**. At rest in a 70 Kg male, this value is typically **135 ml** in each ventricle.

Clinical Note: Because most of ventricular filling occurs passively, pathologies in which atrial contraction is disturbed may have very little effect on overall cardiovascular function. It is not uncommon for people with atrial fibrillation to have few symptoms.

③ Early Ventricular Systole (part one) and the First Heart Sound

Ventricular systole begins at the apex (bottom) of the heart as spiral bands of muscle squeeze blood upward toward the base. The increasing pressure of the blood in the ventricles forces the AV valves closed - creating the **1st heart sound** (S_1) the "lub" of "lub dup". *(QRS complex on ECG)*

Both ventricles are now 'sealed' compartments because now both the AV and Semilunar valves are closed. The ventricles are continuing to contract, but because all valves are closed, the blood has nowhere to go except to generate more pressure. The heart is in **Isovolumic Ventricular Contraction**. This occurs when the blood volume inside the ventricles remains the same (prefix iso- means 'same'), but **pressure is increasing**. During this phase, the atria repolarize and relax as the ventricles continue to contract.

④ Ventricular Systole (part two): Ventricular Ejection

When ventricular contraction generates enough pressure, it opens the semilunar valves, and blood enters arteries (RV > pulmonary trunk/artery, LV > aorta). The high-pressure blood is forced into the **arteries** (ejection of blood from ventricles), which displaces lower-pressure blood, creating blood movement. Remember that each ventricle has equivalent blood volumes but different pressures. The RV requires a min of **25 mmHg** and the LV requires a min of **80 mmHg** to open the semilunar valves. Reaching these respective pressures creates the pressure gradients which drive blood flow out of the heart into arteries.

At this time, just after ventricular systole, the ventricles have just ejected blood but the ventricles do not empty. In fact, at rest they only eject about half of the blood volume in the ventricle. The blood volume remaining in the ventricles after ejection is termed End Systolic Volume (**ESV**). A typical value for a 70 Kg male at rest is about **65 ml** per ventricle that remains in the heart after ejection. We can calculate how much blood was ejected from the heart (called **Stroke Volume**) if we know the maximum volume, EDV, and subtract the volume remaining after contraction, ESV. This means that about **70 ml** of blood is ejected per beat. See calculation below from this formula: **Stroke Volume (SV) = EDV - ESV**

⑤ Ventricular Diastole and the Second Heart Sound

In ventricular diastole, the ventricles **relax** and the **pressure of the blood inside decreases**. The blood in the large arteries leaving the ventricles falls back toward the heart as the driving force subsides. This reversal of blood toward the heart fills the cusps of the semilunar valves, slamming the semilunar valves closed - creating the **2nd heart sound**, (S_2) "dup" of "lub dup". *(T wave on ECG)*

The AV valves still remain closed because ventricular pressure is still greater than the atrial pressure above it. Since the ventricles began to relax and the pressure decreased allowing the semilunar valves to close (to prevent backflow), now all heart valves are closed. Once again the ventricles are 'sealed' compartments. Now the ventricles are undergoing **Isovolumetric Ventricular Relaxation**. This is a state where pressure is decreasing but volume remains constant (as no blood can come into ventricles yet).

When ventricular pressure finally becomes less than atrial pressure, the weight of the blood in the atria opens the AV valves (like a trap door) and blood moves into ventricles from the atria above. The cardiac cycle is now complete because it is at the filling stage again, where we started.

As will be discussed in the blood vessel section to follow, **mean arterial pressure** (MAP) is a measure of the 'average' pressure in a person's systemic arterial system. When we make calculations of MAP in the future, you will see that it is not a strict mean or average, but is weighted toward diastolic pressure. This is because in a normal cardiac cycle at rest, the heart spends more time in diastole than in systole.

Mechanical (Cardiac Cycle) and Electrical (ECG) Events

The mechanical events of the contraction and relaxation during the cardiac cycle lag slightly behind the electrical signals orchestrated by the electrical condition system and seen in the ECG recordings. Atrial contraction begins really as the P wave ends and continues during P-R segment. Ventricular contraction begins just after Q wave and continues through S-T segment. **Table 14.2** below is also in the lab manual. It is filled in here to shows the relationship between the electrical and mechanical events of a single heartbeat.

Table 14.2 The Electrical and Mechanical events for the various portions of a normal ECG.

Segment, Wave or Interval	Electrical Event	Mechanical Event
P-Wave	Depolarization of the atria.	Late ventricular diastole (relaxation). Passive filling of the ventricles (AV valves open).
PR Interval	Reflects delayed conduction through AV node, or the 'AV nodal delay'.	Atrial systole (contraction), top off of ventricular volume (AV valves still open).
QRS Complex	Depolarization of ventricles	Early ventricular systole (contraction). Closure of AV Valves (1st heart sound). Increased ventricular pressure
ST Segment	No net electrical events.	Late ventricular systole. Opening of semilunar valves. Ejection of blood from ventricles into arteries.
T-Wave	Repolarization of the ventricles.	Early ventricular diastole (relaxation). Decreasing pressure, closure of semilunar valves (2nd heart sound).
TP Segment	No net electrical events.	Ventricles continue to relax as pressure falls even lower, AV valves open.

Cardiac Output is a Measure of Cardiac Performance

Cardiac Output (**CO**) specifically is the volume of blood pumped by each ventricle per unit time.

In general, CO is an indicator of total blood flow throughout the circulation. It doesn't describe blood distribution among tissues, but is a measure of the amount of blood pumped by each ventricle in one minute. Remember that the Left and Right ventricular volumes should be equivalent.

Cardiac Output is typically reported or measured in **L/min** for each ventricle. It is calculated using the formula:

CO = Heart Rate (HR) x Stroke Volume (SV)

The heart rate (**HR**) is contractions per minute described in the unit of beats per minute (bpm). Stroke Volume **(SV)** is the amount (volume) of blood pumped by one ventricle during a single contraction, in the unit of ml per beat (ml/beat).

The SV must be calculated from two volumes in the cardiac cycle (discussed above). It is calculated by the difference between End Diastolic Volume (**EDV:** maximum volume at the end of the resting for 'filling' phase of the ventricles) and End Systolic Volume (**ESV:** volume remaining in ventricles after contraction or 'ejection' phase of the ventricles), therefore, **SV = EDV - ESV**

Sample Calculation of Cardiac Output!

To calculate CO we will use typical values for a 70 Kg (150-lb) adult male at rest, with HR of **72** beats/min; If we use the values given in the cardiac cycle describe above, we can calculate SV. If EDV = 135 ml and ESV = 65 ml, then SV = EDV - ESV; => 135 ml – 65 ml = **70** ml/beat.

C.O. = $\frac{72 \text{ beats}}{\text{min}} \times \frac{70 \text{ ml}}{\text{beat}}$ (cancel the terms that show up in both the nominator and the denominator!)

C.O. = 5,040 ml/min, or **5.0 L/min**

Thus, at rest in a 70 Kg (150-lb) man, CO is about 5 L/min (average). Normally, both sides have equal CO, they must have equivalent circulations because the pulmonary circuit soon becomes the systemic. :)

If for some reason the CO's become unequal, for instance in **Congestive Heart Failure**, blood will pool behind the weaker side of the heart. This is not good as the increased vascular pooling creates an increase in venous pressure which causes edema and makes it even more difficult for the weaker side to catch up.

Note: Stroke volume is normally measured using an *echocardiogram* to record EDV and ESV, and calculating the difference: SV = EDV – ESV. Stroke volume (SV) can also be measured using a specialized catheter, but this is an invasive procedure and far more dangerous to the patient.

The Heart Rate is Modified by Autonomic Neurons and Catecholamines

The rhythm and rate of the heart is initiated by **SA node**, which represents the **intrinsic** control center of the heart and sets the pace for the electrical conduction system. The heart's activity can also be modulated by neural and hormonal input.

In a normal adult heart, the resting rate of the SA node is about 70 action potentials (APs) per minute, this translates to a heart rate of about 70 bpm. An average resting HR is approximately 75 bpm but may range from 60–100 in some individuals. The parasympathetic and sympathetic branches of the ANS exert antagonistic (opposing) control over heart rate.

Parasympathetic activity **slows** heart rate and **Sympathetic** activity **increases** heart rate and force of contraction. If the heart were separated from ANS innervation, the intrinsic rate of the SA node would actually be about 90-100 APs per minute, but inside the body it is brought down to about 70 by parasympathetic modulation via the vagus nerve. The parasympathetic division releases ACh from the vagus nerve on to muscarinic receptors at autorhythmic cells of the SA and AV nodes to decrease heart rate, by increasing K^+ efflux. The sympathetic division releases NE and E on β_1 receptors to increases heart rate (via AV node conduction). This can elevate heart rate up to 120 bpm and greater. In general, if suddenly someone is frightened, first Para innervation stops and heart rate goes up from 70 to about 90 bpm. Then the Sympathetic division kicks in and boosts HR up to 120 bpm or greater.

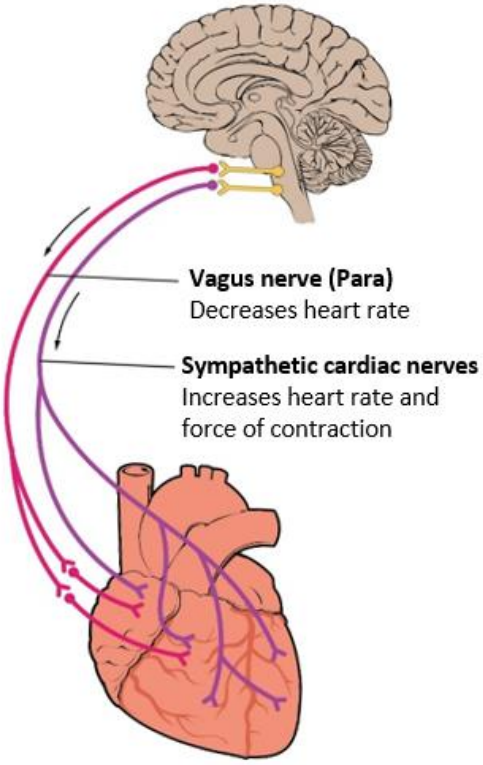


Figure 14.23 There are two vital nerves innervating the heart. They are the vagus nerve, which is part of the parasympathetic division and slows the heart down. And the sympathetic cardiac (accelerator) nerves, which increase both the force and speed of contraction, having and significant effect on heart activity.

Table 14.3 Factors Effecting Heart Rate and Stroke Volume.

Factors Affecting Cardiac Output (CO)	Heart Rate (HR)	Stroke Volume (SV)
ANS	□	□
Hormones	□	□
Gender	□	□
Physical Fitness	□	□
Age	□	□
Heart size		□
Contractility (force)		□
Preload (EDV)		□
Afterload (resistance)		□

Multiple Factors Influence Stroke Volume

Stroke volume isn't constant, it is homeostatically regulated as it needs to change and adjust to the different needs of the body moment by moment. It can decrease when you are at rest and increase greatly during exercise. A mean SV for a resting 70kg (150lb) individual would be approximately 70 ml (for one ventricle). That means that a volume of 70 ml of blood would be ejected from each ventricle per heartbeat. In general terms it is often said there are three main factors that influence stroke volume, and they are **contractility** (the forcefulness of contraction), **preload** (the incoming volume of blood to the heart), and **afterload** (the peripheral resistance from blood out in circulation). These are all examine in more detail below.

There are several important variables, including size of the heart, physical and mental condition of the individual, sex, contractility, duration of contraction, preload (EDV), and afterload (peripheral resistance), all listed in **Table 14.3** above. The normal range for SV is from 55–100 ml.

Stroke volume is directly related to the **force generated by cardiac muscle during contraction**. Greater force means greater stroke volume. The force is affected by 2 parameters: **1)** the length of muscle fiber at beginning of contraction, and **2)** the amount of Ca^{2+} in the myocardiocytes, the more Ca^{2+} the stronger the force!

Length-Tension (Stretch-Force) Relationships - Starling's Law of the Heart

As cardiac muscle sarcomere length increases, the tension generated by the contracting muscle increases (see graph on bottom of page 8). This leads to increases in stroke volume, as the more forceful the contraction, the greater amount of blood ejected. As additional blood flows into the ventricles, this causes muscle fibers to stretch, lengthening the fibers more, increasing the force of contraction. Stretch and force are related by the **Frank-Starling law of the heart**: "The stretch of the myocardium (sarcomere length) is proportional to EDV", which just means the more stretched the cardiac muscle cells are by more blood volume in the ventricles, the greater the force of contraction and the greater the stroke volume.

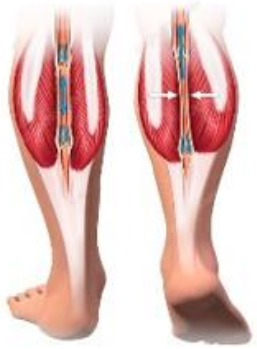
Venous Return or Cardiovascular Preload

As we know, veins bring blood back to the heart. The blood that returns to the heart from the venous circulation is termed '**venous return**' and the greater the venous return, the more forcefully the heart will contract. This is because when the additional blood enters the heart, it stretches the myocardiocytes and this in turn causes the myocardiocytes to contract more forcefully. Venous return determines **EDV** and this determines stroke volume.

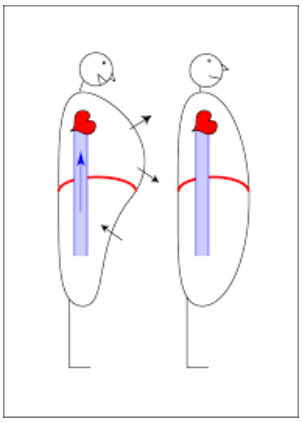
Several Factors Affecting Venous Return

Skeletal Muscle Pump

The skeletal muscle pump is created by skeletal muscle contractions all over the body. It becomes critically important when standing for long periods of time, as venous return from the lower limbs struggles to move up towards the heart. The actions of the skeletal muscle pump can easily be seen using the calf muscles in the leg as an example (see right). Since large veins have **venous valves**, when they are compressed, the blood flows in only one direction - toward the heart. The large veins of the leg are embedded in skeletal muscle and when these skeletal muscles contract, its squeezes and compresses the low pressure veins nearby, this pushes venous blood with increases (albeit temporary) force, in the only direction it can flow – toward the heart.



Respiratory Pump The respiratory pump is another factor that augments venous return. It is created by the movement of the thorax (thoracic cavity) during respiration. Breathing in and out causes oscillatory changes in thoracic and abdominal pressures. Imagine you are standing and breathing in and out. During inspiration there is a **decrease in pressure** in the thoracic cavity and therefore a decrease in pressure in thoracic veins. At that moment, the abdominal veins below them have higher pressure than the blood in the thoracic veins. This promotes greater blood flow ('down' its pressure gradient) towards the heart (see left). During the expiration (breathing out) there is an **increase in pressure** of the thoracic cavity (and in thoracic veins), taking away this temporary favorable pressured gradient. However, the venous valves prevent blood from dropping too far back. The result is that the lower thoracic pressure draws more blood in from the abdominal veins intermittently.



Sympathetic Activity

The sympathetic division of the ANS causes constriction of veins in the systemic circuit, this will immediately move more blood into heart, thus it increases venous return. Sympathetic innervation of veins also allows for the redistribution of venous blood from the venous reservoir, into the arterial side of the cardiovascular circulation, where it can be pumped with greater pressure.

Preload and Afterload effect Stroke Volume

Cardiovascular Preload

Preload is the degree of stretching of cardiac myocytes prior to contraction, the greater the stretching the greater the preload. It is another way of expressing **end diastolic volume** (**EDV)**. The greater the EDV, the greater the preload. **Venous return** is the volume of blood returning to the heart from the venous system, and when we are discussing the systemic circuit it means returning blood from the body.

When venous return increases this increases preload. See **Figure 14.24** below, and think of increased preload as a valve that can open up and spring the heart into greater action. Preload can be increased by increased blood volume (hypervolemia), physical activity (exercise), sympathetic stimulation (fight or flight) and an increase in the skeletal pump activity.

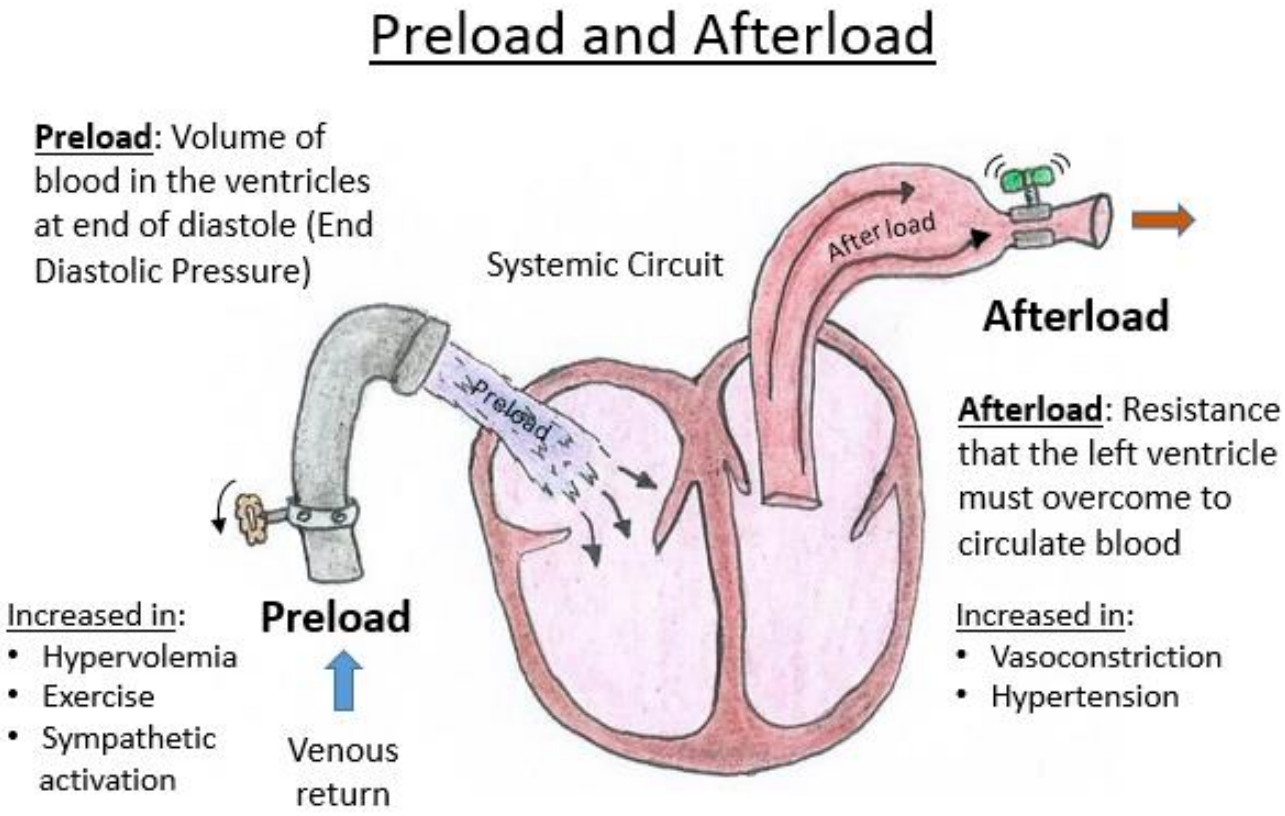


Figure 14.24 Preload is the stretching of myocytes of the ventricles prior to contraction. It is particularly related to ventricular filling and the maximum volume, or end diastolic volume (EDV) of the ventricles before contraction. Preload is increased by increased blood volume (hypervolemia), physical activity, and sympathetic stimulation (fight or flight). Afterload in the systemic system is the force or load against which the left ventricle has to contract to eject blood. It is the 'load' to which the heart must pump against or overcome, in order to circulate the blood throughout the body systemically. Afterload can increase if aortic pressure increases, if systemic vascular resistance increase, or if aortic valves are stenotic.

Cardiovascular Afterload

Afterload refers to the force the ventricles must develop in order to pump blood effectively **against the peripheral resistance in the vascular system**. *Any condition that increases resistance requires a greater afterload* to force open the semilunar valves and pump the blood into the arteries. See **Figure 14.24** above, and think of increased afterload as a clamp on the aorta, the more tightly it is screwed, the harder it will be to pump blood out of the heart to the body. If afterload increases, then the heart must generate more force in order to overcome the increases resistance that more afterload brings.

Damage to the semilunar valves, such as **stenosis** (making them harder to open) will **increase afterload** – this makes it more difficult to pump blood out of ventricles. Afterload may also be raised due to **increased vascular resistance** (e.g., high blood pressure). Both of these factors increase **end systolic volume** (**ESV**), this is the volume of blood remaining in ventricles after contraction, and this therefore decreases **stroke volume** (SV), as less blood has been ejected during ventricular contraction.

In contrast, any **decrease in vascular resistance** will **decrease afterload** – and this makes it easier to pump blood out of the ventricles. For example, a decrease in peripheral resistance (lower blood pressure) decreases afterload. This factor decreases ESV, and therefore increases SV.

At rest, Cardiac Sarcomeres are not at Optimal Length

At rest, there is little stretch of the ventricular muscle and the sarcomeres remain short, but with increased ventricular filling it stretches muscle to a longer sarcomere length, moving toward their optimal lengths. As the sarcomeres reach their optimal lengths, they will contract more forcefully (more myosin heads bind to actin, more cross bridges from) and therefore this increases the strength of contraction and generates a larger SV. If this process were to continue and the sarcomeres stretched beyond their optimal lengths, the force of contraction would decrease.

A factor to consider is ventricular filling time (duration of ventricular diastole). The more rapidly the heart contracts, the ***shorter the filling time becomes***, and the lower the EDV and preload will be. This aspect can be partially overcome by increasing contractility (strength of contraction) which produces a larger SV, but over time, the heart is unable to compensate for decreased filling time, and preload also decreases.

Starling's Law of the Heart

Starling's Law of the Heart states that, within physiological limits, the force of heart contraction is directly proportional to the initial length of the muscle fiber. This means that the greater the stretch of the ventricular muscle (within limits), the more powerful the contraction is, which in turn increases SV. Therefore, by increasing **preload**, you increase the second variable, **contractility**.

Heart Contractility

Contractility refers to the **force** of contraction of the heart muscle - it is the primary factor impacting ESV (the amount of blood remaining in ventricle after contraction. The more forceful the contraction, the more blood is ejected (pumped) from the heart, thus the greater the SV, and less blood remains in ventricle (lower ESV). When the ventricles have less forceful contractions, they have smaller SV, and more blood remains in the ventricles (larger ESVs). The term **inotropic** describes heart contractility. Positive inotropic factors increase contractility, and negative inotropic factors decrease contractility.

Table 14.4. Outline the several important factors that impact heart rate and the force of contraction.

Major Factors Affecting Heart Rate and Force of Contraction		
Specific Factor	**Effect Increases Heart Rate and Force of Contraction**	**Effect Decreases Heart Rate and Force of Contraction**
Sym Accelerator nerves **Para** Vagus nerve	Release of norepinephrine -----	----- Release of acetylcholine
Proprioceptors	Increased rates of firing during exercise	Decreased rates of firing following exercise
Chemoreceptors	Decreased levels of O_2; Increased H^+, CO_2, lactic acid	Increased levels of O_2; Decreased levels H^+ and CO_2
Baroreceptors	Decreased rates of firing, indicating falling blood volume/pressure	Increased rates of firing, indicating higher blood volume/pressure
Limbic System	Anticipation of physical Exercise or strong Emotions	Anticipation of relaxation, calm Emotions
Catecholamines	Increased NE and E	Decreased NE and E
Thyroid Hormones	Increased T_3 and T_4	Decreased T_3 and T_4
Calcium	Increased Ca^{2+}	Decreased Ca^{2+}
Potassium	Decreased K^+	Increased K^+
Body Temperature	Increase in Body Temperature	Decrease in Body Temperature
Nicotine and **Caffeine** **Saturated Fats** and **nuts**	Stimulants, increased heart rate -----	----- Calming, decreased heart rate

General Summary of Factors Affecting Heart Rate and Force of Contraction

It may sound repetitive, as all that follows about the **Parasympathetic** (**Para**) and **Sympathetic** (**Sym**) divisions of the ANS have been stated before, but it helps to be redundant at times.

Parasympathetic stimulation decreases contractility (is a negative inotrope) and releases ACh at the NMJ for cardiac muscle at the vagus nerve. It hyperpolarizes the membrane and inhibits contraction to decrease the strength of contraction and SV, and to raise ESV. Since parasympathetic fibers are more widespread in the atria than in the ventricles, the primary site of action is in the upper chambers. Parasympathetic stimulation in the atria decreases the atrial kick and reduces EDV, which decreases ventricular stretch and preload, thereby further limiting the force of ventricular contraction. Stronger parasympathetic stimulation also directly decreases the force of contraction of the ventricles.

Sympathetic stimulation, in contrast, increases contractility (is a positive inotrope). Sympathetic stimulation triggers NE release at NMJ for cardiac nerves and also stimulates the adrenal cortex to secrete NE and E. In addition to increasing HR, they also bind to both alpha and beta receptors on the cardiac muscle cell membrane to increase metabolic rate and the force of contraction. This combination of actions has the net effect of a smaller residual ESV in the ventricles, and an increased stroke volume (SV).

Higher concentrations of intracellular calcium ions ($[Ca^{2+}]_i$) increases the strength of contraction. Excess Ca^{2+} above normal (***hypercalcemia**) also acts as a positive inotropic agent. The drug **digitalis** is given to

patients with congestive heart failure because it lowers HR but *increases the force of contraction*. It slows the Na^+/K^+ pump and slows the sequestration of Ca^{2+} into the SR. This leads to higher free intracellular Ca^{2+} ($[Ca^{2+}]_i$) levels, greater force of contraction, and therefore greater stroke volume. This helps the side of the heart that is lagging behind to catch up. In addition to NE and E from the adrenal medulla, other hormones also demonstrate positive inotropic effects, including thyroid hormones and glucagon from the pancreas.

**Note on the meaning of terms: Hyper = above normal; hypo = below normal; emia = blood; cal = calcium, natr = sodium, kal = potassium.*

So if you see the word hyponatremia, you could use the 'key' above to figure it out. That term means there is lower than normal sodium in the blood.

The Heart is a Secondary Endocrine Gland

The heart is known to release at least 2 hormones; **atrial natriuretic peptide** (**ANP**); and **brain natriuretic peptide** (**BNP**). The hormone ANP is secreted by myocardiocytes in the walls of the **atria** in response to elevated blood pressure. See the Endocrine section for a fuller description of these hormones.

The atria make the ANP (atrial for atria; natri- for Na^+; and uretic for urine) and this hormone makes the renal system get rid of more sodium in the urine. The atrial myocardiocytes have mechanoreceptors which stretch when there is an increase in atrial blood volume. This triggers release of ANP. The ANP travels to the kidneys and acts to increase the excretion of Na^+ and water in the renal system. By doing this, there is a reduction in the extracellular fluid (ECF) volume in the body, and this lowers systemic blood pressure.

The brain natriuretic peptide (BNP) is not made in the brain but by the myocardiocytes of the **ventricles** of the heart. It has similar effects to ANP, though it is less intense and has a shorted half-life. These two cardiac hormones, ANP and BNP, **lower blood pressure**. They do so by inhibiting the release of the renal hormone **renin** and the adrenal hormone **aldosterone** (which normally act to conserve water and Na^+ in the body). In addition, ANP and BNP both promote vasodilation in arterioles, which lowers blood pressure.

The Heart's Electromagnetic Field

It is worthwhile mentioning another very important physiological aspect of the heart regarding its energetic components. From within the heart emanates an extremely powerful **electromagnetic energetic field**. In fact, the human heart is the most powerful generator of electromagnetic energy in the entire body. From what we have covered regarding the electrical activity of the myocardiocytes, it is clear that the heart is a very active and interconnected organ.

The heart's electrical field typically radiates out at least 6 feet in radius from the body and can go much further. The heart's electrical component is about **60** times greater than that of the brain, with an electromagnetic energy field that is **5,000** times greater than the brain's.

The Heart's Electromagnetic Frequency Field in the form of a Torus

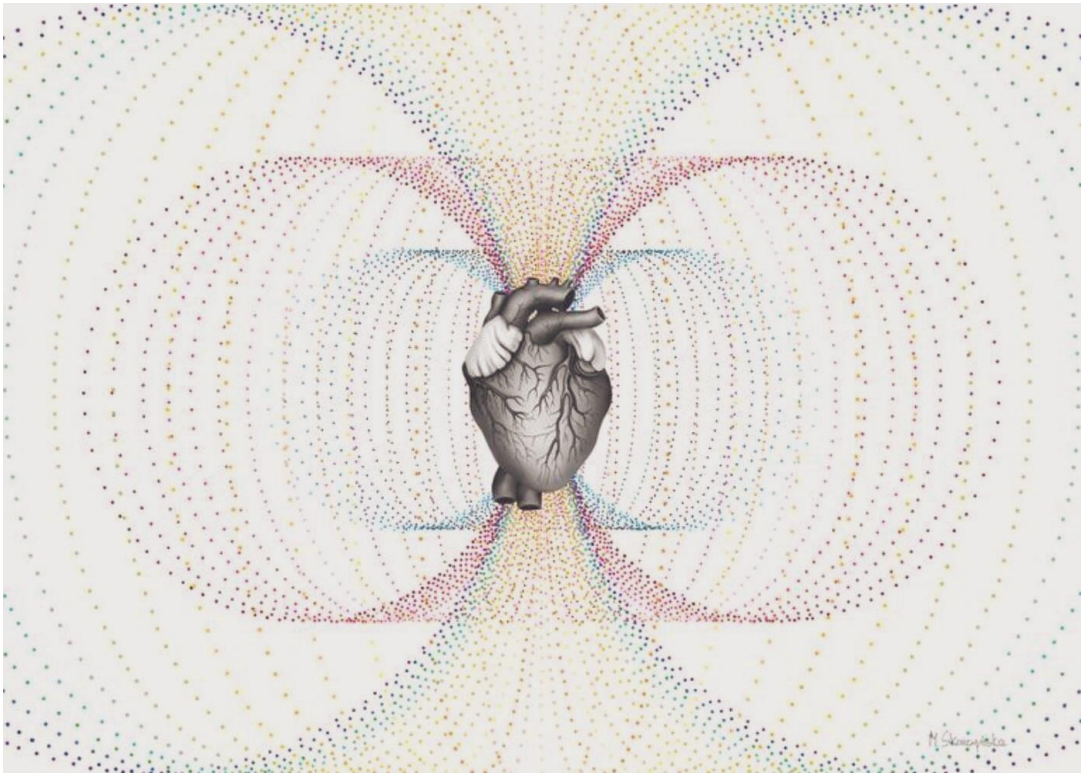


Figure 14.25 This shows a depiction of the heart's electromagnetic field (EMF) that arches out from the heart and back to itself creating a toroidal field all around it. On average the heart's EMF radiates out at least 6 feet in all directions from an individual.

This electromagnetic frequency radiating from the heart arcs out from and back to the heart in the form of a **torus** or **toroidal field** (see **Fig. 14.25** above). This is a shape generated by a closed curve rotating about (but not intersecting or containing) an axis in its own plane. Some have noticed that the torus field has the shape that somewhat looks like a donut, but perhaps a better and maybe more noble comparison would be the resemblance to the shape of an **apple**!

Interestingly, for a long time apples have been revered not only for their medicinal properties but also for the complex sacred geometry contained within them, almost anyway they are examined (see images above). The seeds at the center of the apple would be right where the heart is in the human torus field, with flows folding upon and circulating within itself, having a top and bottom portal that allows the torus energy to constantly refresh and influence itself.

Most reports are that this electromagnetic field of the heart can be measured with sensitive **magnetometers** at least 6 feet out from the center of the human body. Research conducted at the heart math institute (HMI) suggests the heart's field is an important carrier of information and impacts the body and other individuals nearby. Indeed, **its strength can be seen as a measure of good health**. In other reports, this field from the heart has actually been scientifically measured to go out as far as 5 miles from your heart. This kind of scientific information should help to begin to inform us about the extraordinary

complexity, sensitivity and capabilities of the human heart. The influence of the heart on the entire body and of course other individuals goes far beyond any 'pumping' it might do!

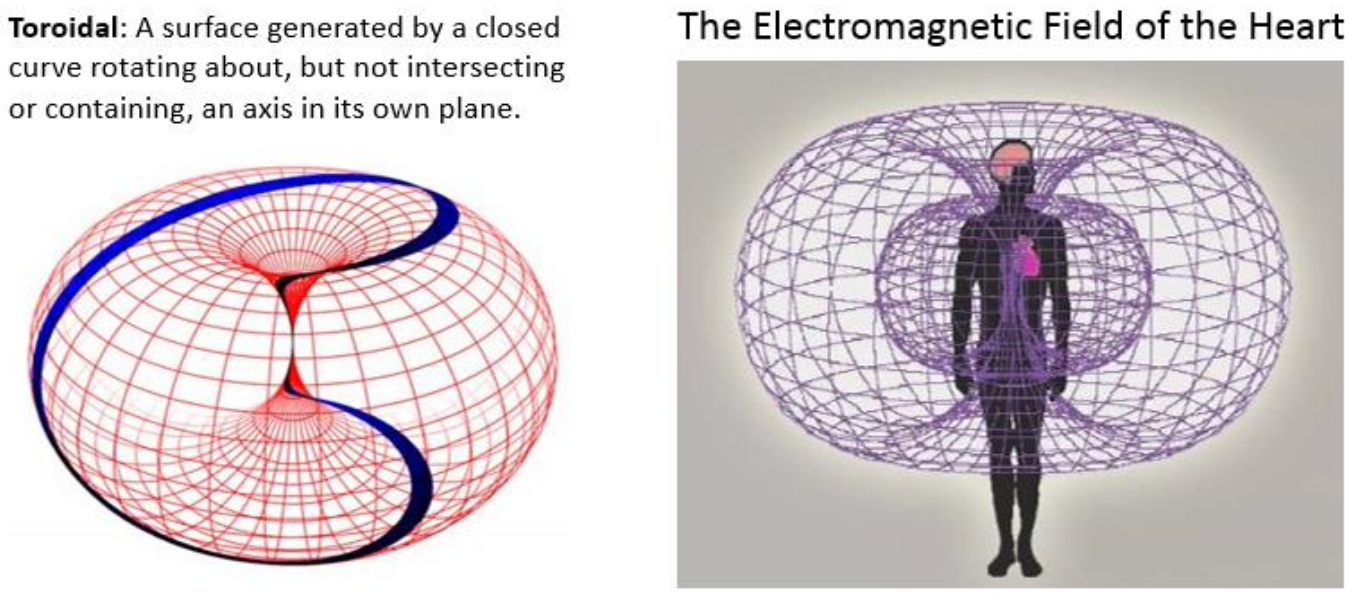


Figure 14.26 Shown above to the left is a toroidal field as defined, and to the right is the toroidal field generated by the human heart that emanates from and surrounds the human body.

Since the heart generates the strongest electromagnetic field in the body, the effect on this field and the exchange of electromagnetic energy created by the heart can be detected and it can fluctuate. Important factors that alter this field appear to be when people physically touch or are in close proximity to each other. In addition, when people focus on and display genuine positive feelings, such as **appreciation** and **compassion**, it has an effect of increases the heart's coherence with others.

Heart Field Coherence

For centuries philosophers and scientists have understood that awareness, responsiveness to the mind, and emotions are brought into coherent alignment within the heart. Hopefully it is a no secret that the heart has intelligence and in many ways is the center of the body. This energetic field generated by the heart can be picked up by the nervous systems of *other* people and animals around us. Importantly, the nature of this field is affected by the main pillars of health: physical, emotional, mental, and spiritual well-being.

Emotions and the Heart's Electromagnetic Field

When people experience chronic stress, anxiety, frustration, fear and other negative emotions, it can induce a state of heart or cardiac **incoherence**. This has a direct impact on cardiac function, often leading to irregular heart rhythms and a diminishment of the electromagnetic field radiating from the heart.

In contrast, being able to express thoughts and feelings of gratitude and joy work to create heart or cardiac **coherence**, which has a powerful positive effect on the entire body. This coherence state generates the torus-shaped electromagnetic field described (see in **Figure 14.26** above), which signals more ordered and rhythmic heart patterns.

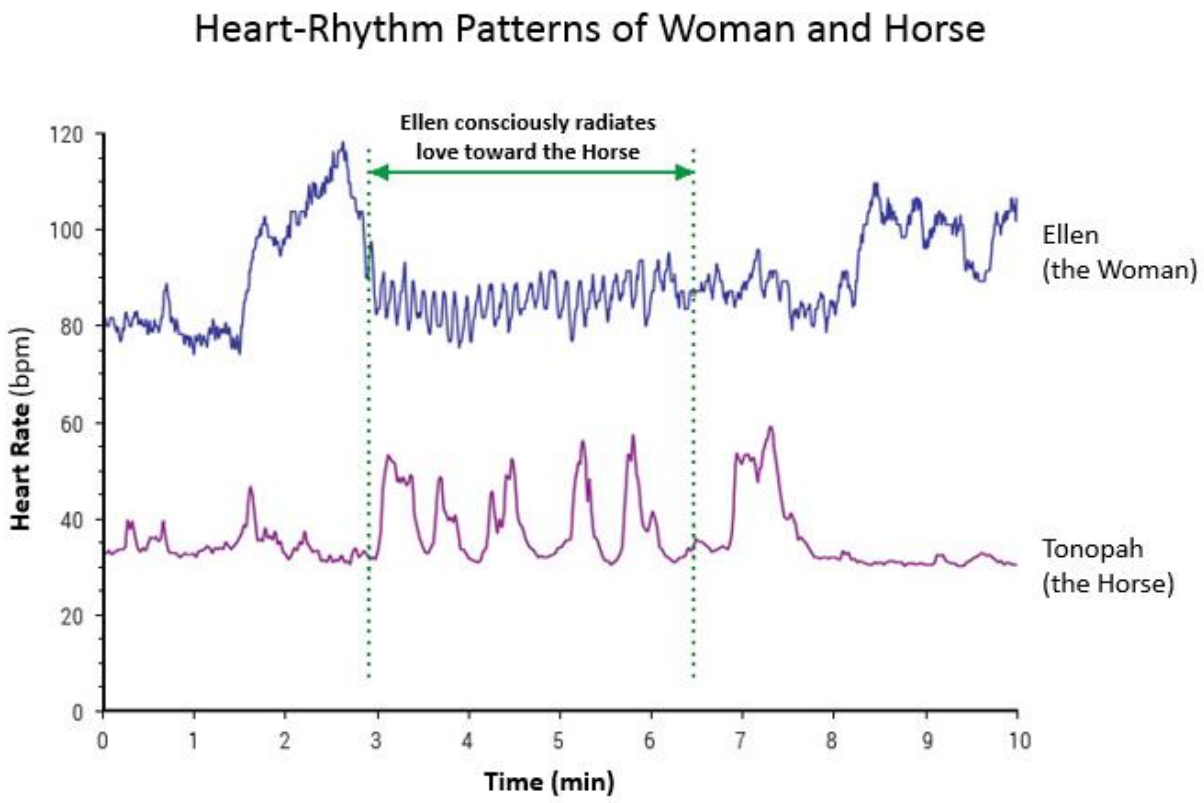


Figure 14.27 The graph above shows heart rate in beats per minute (bpm) for both a woman Ellen and a horse Tonopah. Their heart rates are continuously monitored as they are in close proximity to each other, and when Ellen consciously sends feelings of love and appreciation to the horse (during length of green arrow) the heart rate and patterns of both individuals appear to synchronize, becoming coherent.

The Heart's Complex Communication with the Body

There are specialized cardiac neurons intrinsic to the heart, often called **the brain of the heart**, but they are heart cells made up of approximately **40,000 neurons** that send signals to the brain, many more than the number of neurons from the brain to the heart! As more is explored and discovered about the complexities of the heart, its integration with the rest of the body is fascinating.

Neuronal: Several studies reveal the hearts communication with the nervous system, in that the heart has its own logic center and is able to send signals independently to the brain and autonomic nervous system (ANS). It's been shown that when there is a high coherence of the heart's myocardial rhythms, there is a congruent increase in **parasympathetic** activities in the body, such as being in a state of relaxation, enhanced digestion and elevated metabolism. This state promotes improved synchronization between various systems within the body. In turn, these signals from the heart also impact motor skills and the frontal cortex, influencing the regulation of memory, attention, motivation levels, intuition, and emotional balance.

Hormonal: As covered in various sections of this text, the heart produces hormones, such as atrial natriuretic peptide (ANP), the 'balance hormone' that regulating the health and stability of a number of organs, glands, and centers of our brain. Release of ANP also reduces the release of stress hormones, such as cortisol and epinephrine, it interacts with our immune system, and even impacts our behavior and motivation levels.

Experiments conducted over the years show that the heart also produces **oxytocin**, known as the 'bonding' and 'love' hormone because it is involved in promoting trust, friendship, and social bonding between individuals who are close. The heart also produces classic neurotransmitters, such as epinephrine, which were never previously associated with the heart.

Biological Encoding of Information

From research conducted at the Heart Math Institute (HMI), a primary way that information is encoded and transmitted in physiology is in patterns of signals. For instance as we have seen, information in the nervous system is encoded in the time intervals between action potentials. Within endocrine structures, humoral signals are encoded in the time interval between hormonal pulses. As the heart secretes hormones with each contraction, there is a hormonal pulse pattern correlating with the heart's rhythms. It's appears that information can also be encoded in the inter-beat intervals of the pressure and electromagnetic waves produced by the heart. In other words, the heart is sending a lot of signals.

From research by Karl Pribram in the 1990's, low-frequency oscillations that are generated by the heart (and rest of the body) in the form of afferent neural, hormonal and electrical patterns, appear to be the carriers of emotional information. The higher the frequency oscillations in the electroencephalogram (EEG) tend to reflect the greater conscious perception of feelings and emotions in test subjects. It has been suggested that these same rhythmic patterns can transmit emotional information via the electromagnetic field into the environment, which can then be detected by other individuals and processed in the same manner as internally generated signals.

The Helical Heart

For over at least 500 years the heart was thought to be a helical structure and apparently only recently has this been demonstrated to be accurate. The ventricular myocardium can be viewed as singular muscular band that has been coiled and folded in two helical loops (see **Fig. 14.28** below), such that it is really all one structure. This concept originated from the ontogenetic (morphological) similarities between heart and blood vessels, which exhibit a continuum of form that allows for efficient function.

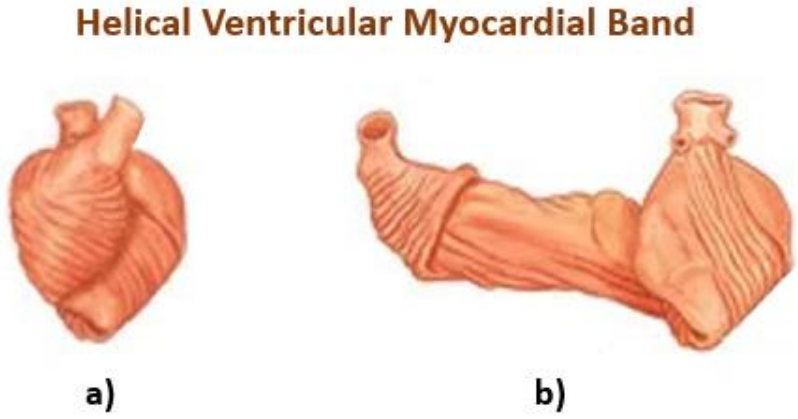


Figure 14.28 The structure of the myocardial band is shown in **a)** the intact heart and in **b)** the unfolded helical ventricular myocardial band (HVMB) model of the heart. The entire muscular arranagement of the heart is organized as a spiral ventricular folding.

Note that the heart's pacemaker cells also respond to hormones that modulate heart function. The heart displays **functional syncytium**, when a groups of cells (myocardiocytes) function as a single coordinated unit. The wave of contraction that establishes functional syncytium begins with the pacemaker cells.

Review Questions for Chapter 14: The Heart

1. The pacemaker of the heart is normally the
- **a)** sinoatrial node.
- **b)** atrioventricular node.
- **c)** mitral valve.
- **d)** bundle of His.
- **e)** left ventricle.

2. In an electrocardiogram, the QRS complex represents the _____.
- **a)** depolarization of the atria.
- **b)** repolarization of the atria.
- **c)** depolarization of the ventricles.
- **d)** repolarization of the ventricles.
- **e)** the delay at the AV node.

3. An ECG would be useful for determining a patient's _____.
- **a)** heart murmur.
- **b)** stroke volume.
- **c)** cardiac output.
- **d)** blockage of conduction of electrical signals between the atria and the ventricles.
- **e)** none of the above.

4. During the cardiac cycle,
- **a)** the volume of blood leaving the left side of the heart is greater than that leaving the right side.
- **b)** the pressure of blood leaving the right side of the heart is greater than that leaving the left side.
- **c)** the duration of systole is greater than that of diastole.
- **d)** the duration of diastole is greater than that of systole.
- **e)** a and d.

5. The aortic semilunar valve
- **a)** Prevents the backflow of blood into the aorta during ventricular diastole.
- **b)** Prevents the backflow of blood into the left ventricle during ventricular diastole.
- **c)** Prevents the backflow of blood into the left ventricle during ventricular ejection.
- **d)** Prevents the backflow of blood into the aorta during ventricular ejection.
- **e)** Closes when the first heart sound is heard.

6. Cardiac output is the _____.
- **a)** volume of blood pumped per minute by both ventricles.
- **b)** volume of blood flowing through the systemic circulation only each minute.
- **c)** summation of the number of heart beats per minute and the volume pumped per beat.
- **d)** a and c.
- **e)** b and c.

7. According to the Frank-Starling mechanism of the heart,

a) the left ventricle ejects a larger volume of blood with each systole than the right ventricle.
b) the intrinsic rate of the heart's pacemaker is 100 beats/min.
c) cardiac output increases with increased heart rate.
d) stroke volume increases with increased venous return.
e) both ventricles contract simultaneously.

8. Which of the following does <u>not</u> contribute to increased stroke volume during exercise?

a) Increased contractility of cardiac muscle.
b) Increased venous return.
c) Increased length of filling time during diastole.
d) Increased sympathetic stimulation of ventricular muscle.
e) Increased end-diastolic volume.

9. Which of these are **true** about the **plateau phase** of action potentials in **contractile** myocardiocytes?

a) It is caused by the slow influx Na^+ ions across the cell membrane
b) It is caused by the influx of Ca^{2+} ions
c) It creates the absolute refractory period
d) Ensures that tetanus contraction cannot occur
e) b, c and d are true

10. What happens to **preload** when there is a <u>decrease</u> in venous return?

a) It increases.
b) It decreases.
c) It remains constant.
d) There is no way to predict what would occur.
e) It increases then immediately decreases.

Answers in Appendix B