The rhythmic heart repeatedly pumps, relaxes to “top-up” and pumps. In a cardiac cycle, there are two main phases, the contraction (systole) and the relaxation of the ventricles (diastole). Although the atria also have their own cycle of similar contractile activity, the use of the words systole and diastole refer to the ventricles that eject blood out with each stroke volume. There are cyclical intraventricular pressure and volume changes. The pressure/volume changes can be matched to the electrical activity that starts at the sinoatrial pacemaker cells and its sequential transmission and spread across the whole myocardium (electrocardiogram, ECG). In addition, the profile of pressure changes in the atria, ventricles, and aorta/pulmonary artery which is associated with opening and closing of valves, the latter generating the major first and second heart sounds. The changes in aortic blood pressure during a cardiac cycle represent the peak systolic blood pressure and the minimum diastolic blood pressure. Understanding the cyclical changes in these parameters takes time, to ponder the step by step cardiac events (Fig. 2.1).

1. Why is the P wave of a normal ECG always smaller than the QRS complex?

**Answer** The amplitude of the deflections of a normal ECG is determined by the mass of the tissue that has been depolarized/repolarized.

**Concept** The ECG is a measurement of the electrical activity on the surface of the body. The ECG tracing is not the same as action potential electrical changes of the membrane potentials. The ECG recorded does result from the spread of action potentials through the heart.

The heart is in a conducting medium and electrical currents generated around the surface of the heart as it is being progressively depolarized are transmitted to the body’s surface.

If we look at the scale of an action potential, the amplitude is ~100 mV. The amplitude of the major ECG wave, the QRS complex is less than 2 mV.

The mass of cardiac muscle that is “electrified” by the spreading action potentials will determine the size of the electrical currents generated. Therefore, the atrial electrical activity during a cardiac cycle will produce a smaller deflection than the larger ventricles.
Note that the smaller amplitude of the ECG “P” wave is not that the atria contract less strongly than the ventricles. It is also not explained by the smaller volume size of the atria.

When there is an increase in the mass of a cardiac chamber, this is then reflected in the ECG deflection. In ventricular hypertrophy, the amplitude of the QRS wave will be bigger.

2. How does the parasympathetic nerve affect the P–R interval and the R–R interval?

**Answer**  Parasympathetic nerve acts to increase the duration of both the R–R and the P–R intervals of the ECG.

**Concept**  The heart rate is spontaneously generated by the pacemaker activity of the sinoatrial (SA) nodal cells. These action potential self-generating cells have dual autonomic control from the parasympathetic and the sympathetic nerves.

The normal resting heart rate is due to a dominant vagal parasympathetic input. If this vagal chronotropic tone is reduced, tachycardia occurs.

The R–R interval is one cardiac cycle, from one ventricular depolarization to the next. A tachycardic effect will decrease the R–R interval.

From the SA node, cardiac impulses are transmitted synchronously through the atrial functional syncytium. The cardiac impulse is slightly “delayed” at the atrioventricular (AV) node to allow for sequential atrial and ventricular contractions.

The AV node is the sole electrical conduction pathway from the atria to the ventricles. In the normal ECG, the P–R interval represents the time taken for the cardiac impulse to be transmitted from the beginning of atria depolarization to the initiation of ventricular depolarization.

Most of the P–R interval is the time transit at the AV node.

The AV node is also innervated by parasympathetic fibers. Parasympathetic impulses to the AV node slow the impulse transmission. The P–R interval is lengthened.

3. Which portion of the normal ECG accounts for the long electrical refractory period of ventricular muscle?
**Answer** The prolonged depolarization of the ventricle, as thus the longer refractory period, coincides with the ST segment of the ECG.

**Concept** The cardiac ventricles have a unique electrical profile of their action potential. There is a prolonged depolarization phase (or delayed repolarization). The ventricular action potential has thus a plateau phase when the ventricle cardiomyocytes remain depolarized.

This extended action potential also means that the electrical refractory period of the ventricles is also prolonged. This property protects the cardiac muscle pump from a tetanic contraction. A heart that goes into tetanic contraction will not be filled and the essential perfusion to the brain and the heart will be cut off during the abnormal, sustained contraction.

The QRS wave represents the depolarization event of the ventricles and the T-deflection, the ventricular repolarization. Thus, the time period between the de- and the beginning of the T repolarization wave is the prolonged depolarization seen as the plateau phase of the ventricular action potential. This is the ST segment.

By convention a “segment” of an ECG does not include a wave, while an ECG wave is part of an “interval” period.

This ST segment is thus. When the calcium ions from the extracellular fluid influx into the ventricular cardiomyocytes. The additional calcium cation influx is the reason for the delayed repolarization of the ventricles. The entry of extracellular fluid (ECF) calcium into the cytoplasm of the ventricular muscle fibers triggers more calcium release from the sarcoplasmic reticulum (SR). This ECF calcium-SR calcium trigger is described as “calcium induced calcium release.”

4. How would you expect the increased circulating adrenaline to affect the QRS amplitude?

**Answer** Adrenaline should not alter the amplitude of the QRS complex.

**Concept** The amplitude of the ECF waves is dependent on the mass of the cardiac tissue where the electrical action potential event has occurred. The strength of cardiac muscle contraction is not reflected in the ECG electrical profile.

Adrenaline increases both the heart rate and the myocardial contractility. The R–R interval and the P–R interval will be shortened as the catecholamine binds to the same beta receptors that are bound by noradrenaline released from the cardiac sympathetic nerves.

However, the increased stroke volume due to the positive inotropic effect of a greater cardiac ejection fraction cannot be derived from looking at the ECG. A greater strength of contraction produced by adrenaline action does not increase the amplitude of QRS deflection.

Only in case of ventricle hypertrophy and a more cardiac muscle mass does the ECG inform us by a bigger amplitude of the QRS.

Adrenaline also does contribute to the coronary vasodilation when the heart is more active. Increased coronary perfusion during exercise to supply the greater metabolic demands of the cardiac muscle is not registered either by exercise ECG.
However, the converse condition of coronary ischemia can produce some characteristic ECG changes.

5. When does iso-volumetric relaxation occur along the ECG?

**Answer** Isovolumetric relaxation is the initial brief phase of ventricular diastole and begins just after the T repolarization wave along the ECG.

**Concept** The electrical event precedes the mechanical event in the heart. The first short stage of diastole occurs when the aortic/pulmonary valves shut. The intraventricular pressure drops markedly during this phase when all the valves including the tricuspid/mitral valves are closed.

Diastolic ventricular filling starts when the tricuspid/mitral atrioventricular valves open.

Ventricular diastolic relaxation occurs after the ventricles are repolarized. Thus, diastole begins just after the T wave. Diastole will proceed until the beginning of systole when the ventricles begin to contract and shut the tricuspid/mitral valves. This point is just after the QRS wave. The period of diastole during a cardiac cycle is then from the end of T wave to the end of the QRS complex.

Thus, the systolic isovolumetric contraction begins just after the QRS deflection and ends when the aortic/pulmonary valves are pressurized open during ejection phase of systole (Fig. 2.2).

6. How does tachycardia affect the myocardial contractility? (Note the opposite effects to no 9.)

**Answer** Tachycardia has an indirect effect in increasing myocardial contractility via the elevation of intracellular calcium in the ventricular myocytes.

**Concept** When the heart is more active, it pumps more frequently (tachycardia) and more strongly (increased ejection fraction). Both these chronotropic and inotropic actions are effected by the cardiac sympathetic nerves and adrenaline, respectively.
There is some additional increased cardiac contractility that results from a higher frequency of heart beat. Each cardiac cycle of contraction is followed by relaxation which is initiated when calcium ions are pumped by Ca-ATPase back into the sarcoplasmic reticulum (SR) or extruded by the cell membrane Na/Ca exchanger into the ECF.

This lowering of the cytosolic calcium precedes cardiac muscle relaxation. With tachycardia, there is relatively less time to reduce the intracellular calcium to resting, precontraction level.

During the next muscle depolarization event, there will be a higher intracellular calcium when calcium from ECF influx is released from SR. The myocardial contractility is increased proportionately to the rise in cytosolic calcium.

Note that in skeletal muscles, graded increase in contraction strength is not mediated by increasing intracellular calcium. Skeletal muscle tension is increased by activation of motor unit recruitment and a higher frequency of impulses in the alpha motor neurons that innervate the muscles.

7. How does right heart failure lead to development of peripheral edema?

**Answer** In right heart failure, the venous congestion leads to increased capillary hydrostatic pressure and higher net capillary filtration that results in fluid accumulation in the interstitium.

**Concept** In a normal heart, the stroke volume (SV) is proportionately related to end-diastolic volume (EDV, preload) over a physiologic range. In the right side of the heart, this EDV/SV pairing ensures that the central venous pressure/right atrial pressure is consistently at a low value to maintain optimal ventricular filling.

When the right ventricular function is compromised, the ejection volume of the preload is not effectively pumped out. With time, venous congestion develops with elevated central venous pressure. The increased venous pressure will “radiate” and be transmitted into the microcirculation. This backlog of vascular pressure easily occurs because unlike the presence of high resistance precapillary arteriole, the postcapillary venular resistance is low.

At the capillary, the raised capillary hydrostatic pressure will disturb the balance of Starling’s forces. The net filtration along the capillary will soon exceed the capacity of the lymphatic drainage to maintain a low interstitial hydrostatic pressure. Fluid accumulates in the tissue spaces (edema) (Fig. 2.3).

8. How does the ventricular volume/pressure diagram illustrate the dynamic changes during a cardiac cycle?

**Answer** The ventricular x-axis volume/y-axis pressure diagram demonstrates the beginning and ending of each of the four phases within the systole and diastole of a cardiac cycle (Fig. 2.4).

**Concept** The ventricular volume along the x-axis will be the same for the right and left ventricle. However, the y-axis intraventricular pressure will be on a different scale (maximum for left ventricle is 120 mmHg and for right ventricle is ~30 mmHg).
Fig. 2.3 Cardiac sympathetic action increases the stroke volume directly by increasing the ejection fraction. Indirectly, the reduced venous capacitance with sympathetic vasoconstriction will also increase venous filling that will produce a bigger stroke volume. $SV$ stroke volume. $EjF$ ejection fraction. $VR$ venous return

Sharp changes in pressures are clearly evident in the two vertical sides of the volume/pressure (V/P) diagram. The diagram must also be followed anticlockwise. This means that the right vertical line shows a steep increase in pressure and the left vertical, a precipitous drop in ventricular pressure. These two pressure lines at constant ventricular volumes would represent the isovolumetric systolic contraction and isovolumetric diastolic relaxation phase.

The maximum volume in the V/P diagram is the end-diastolic volume, $EDV$ (~120 ml) and the minimum ventricular volume is the end-systolic volume (ESV, around 40 ml). The lower horizontal line that links the two verticals is thus the stroke volume $SV$ (EDV–ESV). This bottom horizontal line with little change in ventricular pressure, moving anticlockwise from ESV to EDV is the event of ventricular filling.

The south east (SE) corner of the V/P diagram, the start of the vertical rise in pressure is the beginning of systole. The isovolumetric contraction phase begins when the atrioventricular valve shuts and pressure builds up rapidly before the aortic/pulmonary valve is pressurized open. Thus, the SE is where the mitral/tricuspid valves closes.

The upper line that extends from the upper right (NE) to the upper left (NW) corner of the V/P diagram represents a decrease of ventricular volume from EDV to ESV. This is the ejection phase when the ventricles pump out each of their stroke volumes. The NE point is when the pulmonary/aortic valves are opened.

Beginning at the NW corner of the V/P diagram, the intraventricular pressure drops rapidly. The NW corner spot is the beginning of diastole when the aortic/pulmonary valves shut. There is no change in volume, this initial brief phase of diastole until the intraventricular pressure falls to below the atrial pressure. When this is reached, tricuspid/mitral valves open (bottom, left SW corner) and diastolic ventricular filling proceeds.

9. How is the increased myocardial contractility and Starling’s mechanism of the heart represented by the ventricular/pressure loop diagram?

**Answer** Sympathetic nerve action on the heart increases the ejection fraction and the end-systolic volume (SW corner) is shifted to the left. Starling’s intrinsic car-
Cardiac muscle contraction mechanism is effected when the ventricular filling or end-diastolic volume (SE corner) is increased or shifted to the right.

**Concept** For both cardiac sympathetic and Starling’s effects, the stroke volume is increased. The higher SV for sympathetically—increased contractility results in less volume (ESV) remaining in the ventricle, although the precontraction EDV is not changed.

For the Starling’s effect, the greater stroke volume is due to a bigger volume that fills the ventricle before contraction (higher EDV), stretching the ventricle to a greater systolic muscle tension. The ESV is not altered by Starling’s. The increased preload or EDV produce the larger stroke volume.

In the situation when the aortic pressure is elevated (afterload), how would the ventricular volume/pressure loop look like? In chronic hypertension, the left ventricle has to generate additional cardiac work force to pump the same stroke volume against the raised afterload. For a given EDV, if the ventricle begins to weaken, the SV will decrease and the remaining ESV will be more, shifted to the right.

The vertical rise in pressure during the isovolumetric contraction phase of systole (right vertical of V/P loop) will also be greater (contraction against a higher afterload) before the aortic valve opens for the ejection of stroke volume.

10. Why does the venous return curve have the same x-axis as the cardiac output curve, drawn on the same graph?

**Answer** The venous return (y-axis) is quite obviously related to the x-axis right atrial pressure (rap). Venous return as a primary cause proportionately affects the rap, and thus the expected x-axis venous return for the cardiac output (y-axis) curve can be harmonized by using the rap as the x-axis also.

**Concept** The circulatory system is a closed circuit. Conceptually, the cause and effect in a particular cardiovascular event can quite often by puzzling and confusing to the students. The cardiac output or cardiac function curve relates the venous
return (x-axis) to the cardiac output. This is basically describing the intrinsic Starling’s mechanism of the heart, where the ventricular stroke volume proportionately changes with the EDV.

In the presence of cardiac sympathetic activity, the cardiac function curve is shifted to the left; an indication that for the same EDV a positive inotropic effect of sympathetic stimulation gives a bigger stroke volume.

What is the rationale for substituting the x-axis venous return with right atrial pressure?

The students would have heard that changes in the right atrial pressure (central venous pressure), as a cause, would be expected to cause an inverse effect on venous return since the driving pressure for blood entry into the heart would have been reduced (the inverse relationship is seen in the venous return curve).

Because the circulatory system is a closed flow system, it is also true that if we consider venous return as the cause, then the right atrial pressure would change proportionately with the magnitude of the venous return. The Bainbridge effect of increased venous return producing a reflex tachycardia is due to the increased right atrial pressure.

The combined cardiac function and venous return (or vascular function) curves intersect at a certain right atrial pressure. In the closed circulatory system, this equilibrium rap is thus a net value from the dynamics of inflow venous return and outflow cardiac output.

When we consider the cardiac output, functionally, a normal ventricular pumping maintains an optimal rap (we have just discussed above the reverse interactions that the rap affects cardiac output). In right/left ventricular failure, the right/left atrial pressure begins soon to be elevated.
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