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ASPECTS OF MYOCARDIAL PHYSIOLOGY

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Introduction

This is the first of two articles covering aspects of myocardial physiology which are important to candidates for Primary FRCA.

Cardiac action potentials

Action potentials (APs) are sequential changes in transmembrane potential that occur as a result of activity of ion channels, this results in the propagation of electrical impulses in excitable cells. The heart has a multicellular structure but behaves like a syncytium because the individual muscle cells communicate with their neighbours through gap junctions which provide low resistance pathways for easy movement of action potentials between cells. The cardiac action potential is much longer than those of nerve or skeletal muscle (~250ms compared with ~ 1-3ms) This is due to a prolonged plateau phase caused by calcium ions in cardiac muscles. Two types of action potential occur in the heart:

The fast response - found in heart muscle and Purkinje fibres (figure 1). The resting heart muscle potential of cardiac muscle and Purkinje fibres is ~ -90mmV (interior negative to exterior). An AP is initiated when the membrane is depolarised to a threshold potential (~-65mV). The initial depolarisation originates from transmission from an adjacent cell via gap junctions.

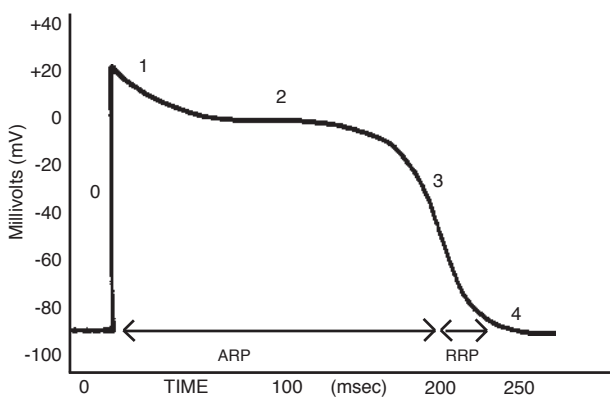

Figure 1. The Purkinje fibre action potential

Phase 0 - Rapid depolarisation - the inward current caused by opening of fast Na^+ channels becomes large enough to overcome the outward current through K^+ channels resulting in a very rapid upstroke. T-type (transient) Ca^{2+} channels open at negative membrane potentials of -70mmV to -40mV causing Ca^{2+} influx.

Phase 1 - Early incomplete repolarisation - due to inactivation of fast Na^+ channels and efflux of K^+ ions.

Phase 2 - Plateau phase - a period of slow decay mainly due to Ca^{2+} entering the cell via L-type (L=long lasting) Ca^{2+} channels which are activated slowly when the membrane potential is more positive then ~ -35mV. There is also slow closure/inactivation of some of the Na^+ channels. Reduced K^+ outward current continues. Calcium entry during the plateau is essential for contraction; blockers of L-type Ca^{2+} channels (e.g. verapamil) reduce force of contraction.

Phase 3 - rapid repolarisation - Ca^{2+} influx declines and the K+ outward current becomes dominant, with an increased rate of repolarisation.

Phase 4 - Electrical diastole - resting membrane potential is restored.

The slow response (figure 2) - found in pacemaker tissues; for example Sinoatrial and Atrioventricular nodes. These cells sponaneously depolarise and are said to have automaticity.

Phases 1 and 2 are absent. There is no depolarisation plateau.

Phase 4 - Pacemaker potential - The cells have an unstable resting membrane potential during phase 4; they gradually depolarise from ~-60mV to a threshold of ~-40mV due to a slow continuous influx of Na^+ ions and a decreased efflux of K^+ ions. A Ca^{2+} current due to the opening of T-type (transient_ Ca^{2+} channels completes the pacemaker potential.

Phase 0 - Depolarisation - when the membrane potential reaches threshold potential fast (L-type_ calcium channels open, causing Ca^{2+} influx and an AP is generated.

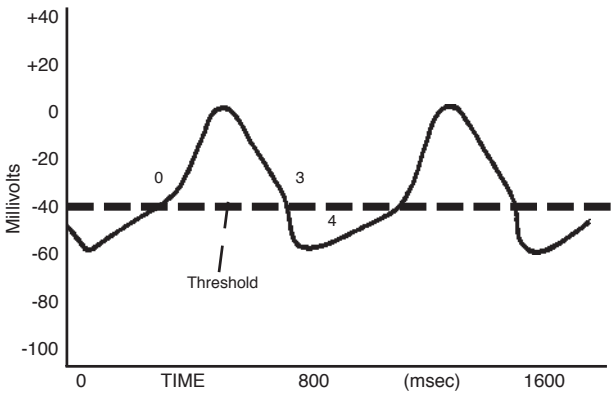

Figure 2. The Sinoatrial node action potentials

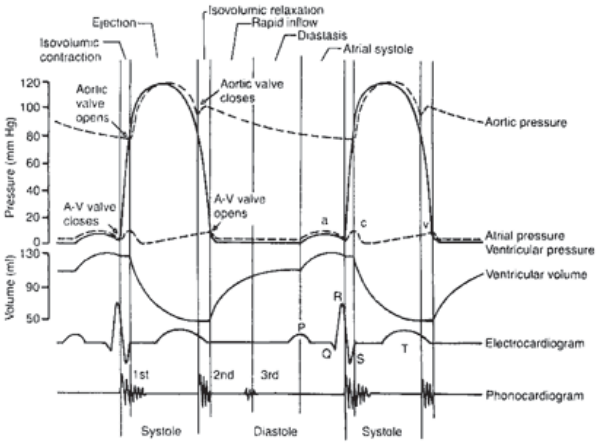

Figure 3. Events of the cardiac cycle.
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Phase 3 - Repolarisation - due to efflux of K^+.

Noradrenaline and adrenaline (mediated via β1 - receptors) increase the slope of phase 4 by increasing Ca^{2+} influx, therefore increasing the heart rate. Ca^{2+} influx also increases the force of contraction. Acetylcholine (mediated via M2 receptors) decreases the slope of phase 4 by increasing K^+ efflux and causing hyperpolarisation (increased negativity within the cells). This makes the conduction tissue much less excitable so it takes longer to spontaneously reach the threshold level. This results in a decrease in heart rate. The intrinsic rate of the SA node is 100 beats/minute however, vagal tone decreases this to ~70 beats/min.

Refractory periods

During the absolute refractory period (ARP) (figure 1) the cardiac cell is totally inexcitable. During the following relative refractory period (RRP) there is a gradual recovery of excitability. A supramaximal stimulus can elicit an AP in the RRP. This AP, however, has a slower rate of depolarisation, a lower amplitude and shorter duration than normal and, therefore, the contraction produced is weaker. Peak muscle tension occurs just before the end of the ARP and the muscle is halfway through its relaxation phase by the end of the RRP. The long refractory period protects the ventricles from too rapid a re-exitation which would impair their ability to relax long enough to refill sufficiently with blood. Unlike skeletal muscle, two contractions cannot summate and a fused tetanic contraction cannot occur.

The Cardiac Cycle

The cardiac cycle refers to the relationship between electrical, mechanical (pressure and volume) and valvular events occuring during one complete heartbeat.

Passive filling (early diastole)

The atria and ventricles are relaxed, ventricular pressure is zero. The atrioventricular (AV) valves are open and the semilunar valves are closed. Blood flows from the great veins into the atria and ventricles (from higher pressure to a lower pressure.) About 80% of ventricular filling occurs during this phase.

Atrial contraction (late diastole)

A wave of depolarisation beginning at the sinoatrial (SA) node, spreads across both atria, and reaches the AV node - the P wave of the ECG. The atria contract and atrial pressures increases producing the wave of the central venous pressure trace. Blood continues to flow into the ventricles and ventricular pressure increases slightly. The atrial contribution to ventricular fillinf increases as heart rate increases, as diastole shortens and there is less time for diastolic filling. Ventricular volume (EDV) = volume of blood in the ventricle at the end of diastole. Arterial pressure is at its lowest at this stage of the cycle.

Isovolumetric ventricular contraction (early diastole)

The action potential is conducted through the AV node, down the bundle of His, across both ventricles and ventricular depolarisation occurs - the QRS complex of the ECG. Ventricular contraction causes a sharp rise in ventricular pressure, and the AV vavles close (first heart sound) once this exceeds atrial pressure, preventing backflow into the atria. Ventricular pressure increases dramatically with no change in ventricular volume. During this initial phase of ventricular contraction pressure is less than in the pulmonary artery and aorta, so the outflow valves remain closed - the ventricular volume does not change. The increasing pressure causes the AV valves to bulge into the atria, resulting in a small atrial pressure wave - the c wave of the central venous pressure trace.

Ejection (systole)

The semilunar valves open as evntricular pressure exceeds aortic blood pressure. Approximately two thirds of the blood in the ventricles is ejected into the arteries. Flow into the arteries is initially very rapid (**rapid ejection phase**), but subsequently decreases (**reduced ejection phase**).

Stroke volume (SV) = volume of blood ejected from each ventricle in a single beat.

Ejection fraction = SV/EDV. Arterial blood pressure rises to its highest point - systolic blood pressure. During the last two thirds of systole before the AV valves open again, atrial pressure rises as a result of filling from the veins - the v wave of the central venous pressure trace. Active contraction ceases during the second half of ejection, and the ventricular muscler repolarises - the T wave of the ECG. Ventricular pressure during the reduced ejection phase is slightly less than in the artery, but blood vontinues to flow out of the ventricle because of momentum. Eventually the flow briefly reverses, causing closure of the outflow valve and a small increase in aortic pressure, the **dicrotic notch**.

Isovolumetric relation (early diastole)

The ventricles relax and the ventricular pressure falls below arterial blood pressure. this causes the semilunar valves to close - the second heart sound. The ventricular pressure falls with no change in ventricular volume. When ventricular pressure falls below atrial pressure, the AV valves open and the cycle begins again.

Figure 4a. Re-printed from: Smith JJ, Kampine JP, Circulatory Physiology - The Essentials 3rd edition, with permission from Lippincott, Williams and Wilkins. Figure 4b re-printed from Aaronson PI, Ward PT, The Cardiovascular System at a Glance, 1st edition with permission from Blackwell Publishing Ltd.

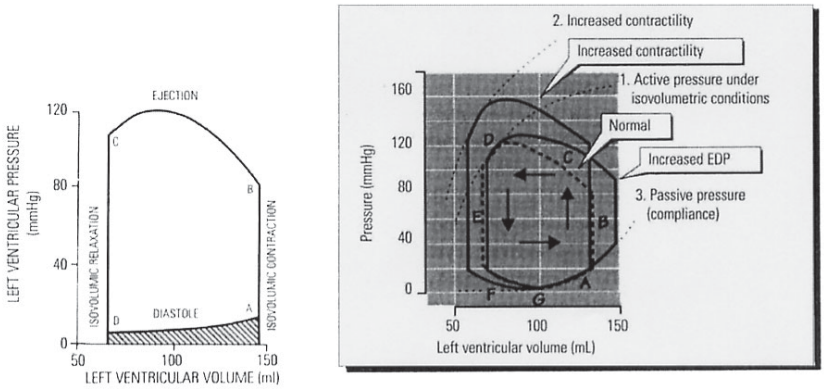

Figure 4a. Left ventricular pressure-volume loop showing left ventricular volume and pressure changes during a single heart cycle in a normal adult at rest. Figure 4b. The pressure-volume loop is affected by the contractility and compliance of the ventricle, and factors that alter refilling or ejection (e.g. CVP, afterload).

X descent of CVP trace - results from atrial relaxation and downward displacement of the tricuspid valve during ventricular systole.

Y descent of CVP trace - due to atrial emptying as the tricuspid valve opens and blood enters the ventricle.

The pressure volume loop

This represents the events of the cardiac cycle. the cardiac cycle proceeds in an anticlockwise direction. (A) End diastole, (B) aortic valve opening, (C) aortic vavle closure, (D) mitral valve opening. EDV and end systolic volume (ESV) are represented by points A and C respectively. The area close by the loop represents the stroke work (since work = pressure x volume).; The pressure - volume curve in diastole is initially quite flat, indicating that large increases in volume can be accommodated by only small increases in pressure. However, the ventricle becomes less distensible with greater filling, as evidenced by the sharp rise of the diastole curve at large intraventricular volumes.

Coronary circulation

The heart is supplied by the right and left coronary arteries. They arise separately from the aortic sinus at the origin of the ascending aorta, behind the right and left cusps of the aortic valve. The right coronary artery (RCA) runs forward between the pulmonary trunk and right atrium, to the AV sulcus. As it descends to the lower margin of the heart, it divides into posterior descending (interventricular) and right marginal branches. The left coronary artery (LCA) runs behind the pulmonary trunk and forward between it and the left atrium. It divides into the circumflex, left marginal and anterior anastomoses between the left and right posterior descending branches, but these are not enough to maintain perfusion if one side of the coronary circulation is acutely occluded. The LCA supplies mainly the left ventricle and septum and left atrium. The RCA supplies mainly the right ventricle and right atrium, SA node (in 60%) and AV node (in 80%). The 'dominant' supply to the heart is usually determined by the artery that forms the posterior descending and supplies the major arterial supply to the posterior inferior wall of the LV and to the AV node. The RCA is dominant in 70% of individuals, the LCA is dominant in another 20% and the flow delivered by each main artery is approximately equal in the remaining 10%

Venous drainage

Venous drainage is mainly via the coronary sinus and anterior cardiac vein which both empty into the right atrium. Some venous blood empties directly via the Thebesian veins and small venules into all heart chambers. Venous blood entering the left side of the heart will cause a small reduction in the O_2 content of systemic arterial blood.

Control of the coronary circulation

The heart at rest receives about 5% of the cardiac output. Coronary blood flow is ~250ml/min. O_2 extraction by the myocardium at rest is very high (65%) compared to other tissues (35%). Therefore, the myocardium cannot compensate for reductions in blood flow by extracting more oxygen from heamoglobin. Any increases in myocardial O_2 demand must be met by an increase in coronary blood flow. The three main factors influencing coronary flow are:

1. Mechanical, mainly external compression and perfusion pressure
2. Metabolic
3. Neural

Coronary artery compression and blood flow

Coronary blood flow is unique in that there is interruption of flow during systole (mechnical compression of vessels by myocardial contraction. Coronary blood flow occurs predominatly during diastole when cardiac muscle relaxes and no longer obstructs blood flow through ventricular vessels. Conversely, right coronary arterial flow rate is highest during systole, because th aortic pressure driving flow increases more during systole (from 80 to 120mmHg) that the right ventricular pressure which opposes flow (from 0 to 25mmHg). As about 80% of the total coronary arterial flow occurs during diastole, a pressure around the aortic diastole

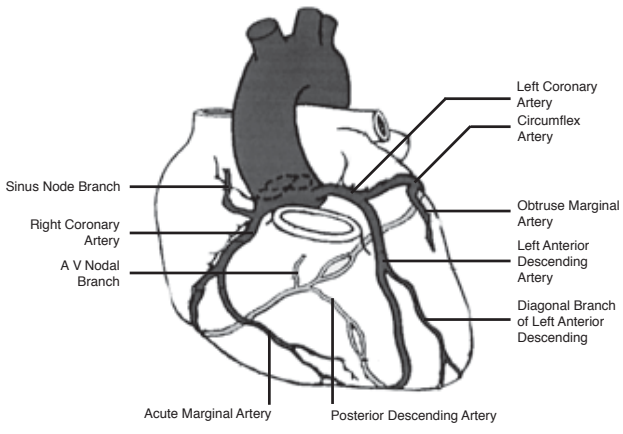

Figure 5. Coronary arteries

pressure becomes the primary determinant of the pressure gradient for coronary flow. CPP = arterial diastole pressure - LVEDP. Increases in heart rate that shorten diastole time for coronary blood flow are likely to increase oxygen consumption more than elevations in blood pressure, which are likely to offset increased oxygen demands by enhanced pressure-dependent coronary blood flow. The myocardium regulates its own blood flow (autoregulation) closely between perfusion pressures of 50 and 150mmHg. Beyond this range, blood flow becomes increasingly pressure dependent. This autoregulation is due to a combination of myogenic and metabolic mechanisms.

Metabolic factors

The close relationship between coronary blood flow and myocardial O_2 consumption indicates that one or more of the products of metabolism cause coronary vasodilation. Hypoxia and adenosine are potent coronary vasodilators. Others factors suspected of playing this role include PCO_2, H^+, K^+, lactate and prostaglandins. Under normal conditions, changes in blood flow are entirely due to variations in coronary artery tone (resistance) in response to metabolic demand.

Neural Factors

The coronary arterioles contain α1-adrenergic receptors which mediate vasoconstriction, and β2-adrenergic receptors which mediate vasodilation. Sympathetic stimulation generally increases myocardial blood flow becuase of an increase to metabolic demand and a predominance of B2-activation.

Further reading

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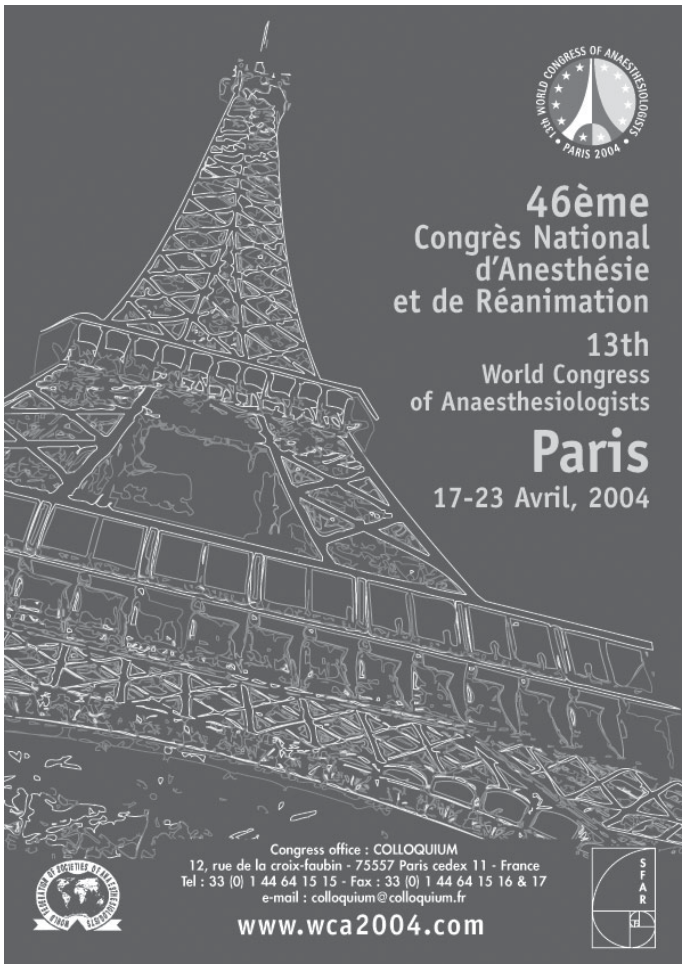

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