Primary Cast Episode 13 - Cardiac & Circulation Physiology

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1. **ECGs**

What does each section of the ECG trace represent?

- P wave = atrial depolarisation
- PR = atrial depolarisation and AV nodal delay
- QRS complex = ventricular depolarisation
- T wave = ventricular repolarisation

What are the typical ECG features of hyperkalaemia?

- Peaked T waves
- P wave flattening and loss of P waves
- Wide or bizarre QRS
- Sinusoidal ECG pattern
- Ventricular arrhythmias
- Asystole

Explain the electrophysiological changes that cause the ST segment changes seen in a myocardial infarction.

- Abnormally rapid repolarisation from infarcted muscle (accelerated opening of K channels)
- Decreased resting membrane potential (due to loss of intracellular K)
- Slowed depolarization of affected cells compared to normal cells.

2. **Cardiac Conduction**

Describe the normal cardiac conduction pathway

SA node (pacemaker)

- Spreads through the atria via 3 internodal pathways
- AV Node
- Bundle of His
- Right and left bundle branches (anterior and posterior fascicles on the left)
- Purkinje fibres
- Ventricular muscle (left side of septum first, to apex, from endo to epicardial surfaces)

What are the common mechanisms that cause abnormalities of cardiac conduction and what are their clinical consequences?

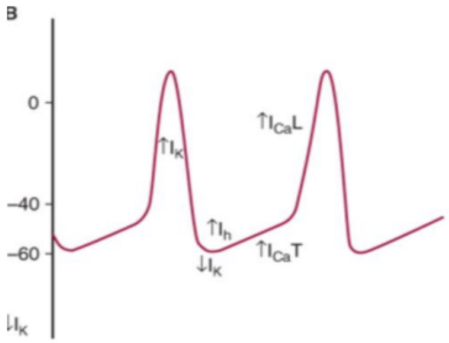
- Abnormal pacemakers
    - Ectopic beats
    - Sinus arrest
    - Atrial or ventricular fibrillation
- Re-entry circuits
    - tachyarrhythmias

- Conduction deficits/blocks
    - Heart blocks
    - Bundle branch blocks
- Prolonged repolarisation
    - Long QTc
- Accessory pathways
    - WPW
- Electrolyte disturbance

What conditions may predispose to increased automaticity?

- IHD
- Scarring, i.e. from a previous repair of a congenital heart defect
- Structural heart disease
- Channelopathies
- Electrolyte imbalances
- Sympathomimetic agents
- Infiltrative cardiac diseases

3. **Cardiac Action Potentials**
Describe the action potential of a cardiac pacemaker cell



- Prepotential (begins at -60) initially due to K efflux, then completed by Ca influx through calcium T channels
- Action potential (begins at -40) is due to influx of Ca with L-type calcium channels
- Repolarisation due to K efflux, no plateau phase

How does sympathetic and parasympathetic stimulation change the prepotential?
Sympathetic

- Noradrenaline binds beta 1 receptor and raises cAMP
- This causes increased opening of L type C2+ channels and Ca2+ influx
- This increases the slope of the prepotential and increases the firing rate of the pacemaker

Parasympathetic

- Ach binds the M2 receptor and decreases cAMP
- resulting in both slowing of Ca channel opening and opening of special potassium channels (which counter the K efflux decay)
- This leads to a greater fall in prepotential
- Which decreases the slope of the prepotential and the firing rate

Describe the action potential of a ventricular muscle cell

- Resting membrane potential -90mV
- Phase 0 rapid depolarisation due to opening of voltage gated Na channels
- Phase 1 rapid repolarisation from closure of Na channels
- Phase 2 plateau phase - opening of voltage gated Ca2+ channels
- Phase 3 repolarisation after closure of Ca2+ channels
- Phase 4 resting membrane potential set up by Na/K ATPase

Describe the major differences between a ventricular muscle action potential and a pacemaker cell potential

Ventricular muscle has

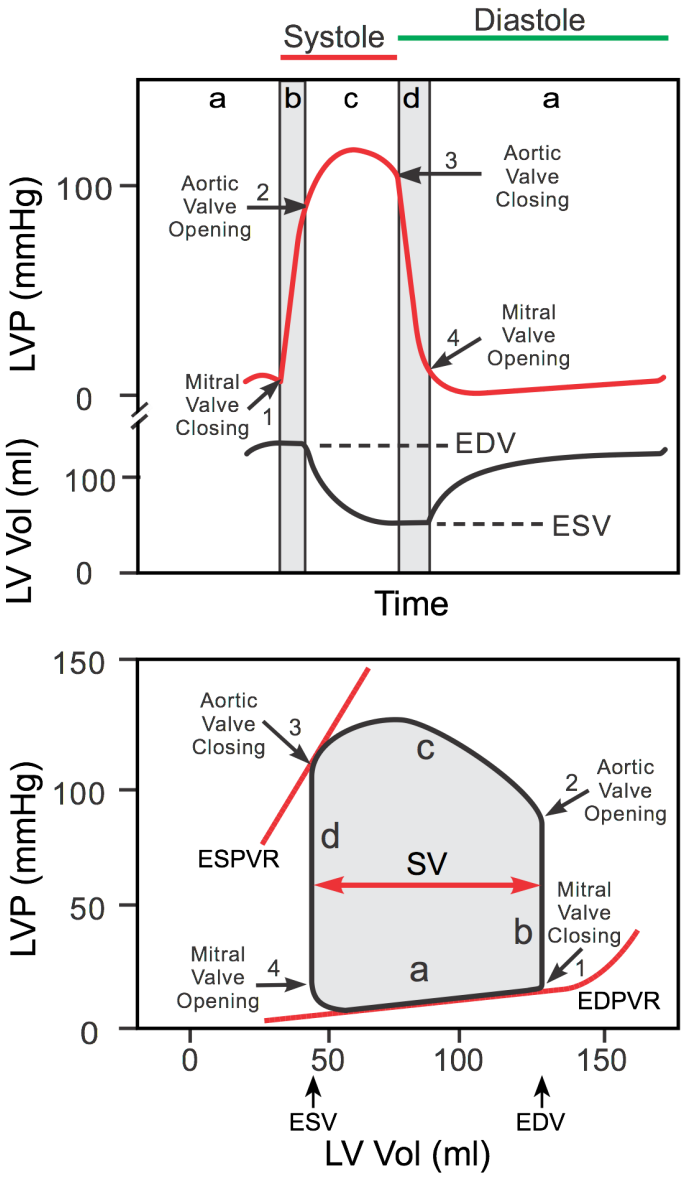
- a greater negative resting membrane potential (-90mV)
- Fast depolarisation via Na, versus slower calcium dependent depolarisation in pacemaker cells
- No prepotential or automaticity in ventricular muscle
- Plateau phase in ventricular but not in pacemaker

4. **Cardiac Cycle**

Starting with systole, please describe the pressure and volume changes in the left ventricle. You might also be asked to draw the pressure/volume loop.

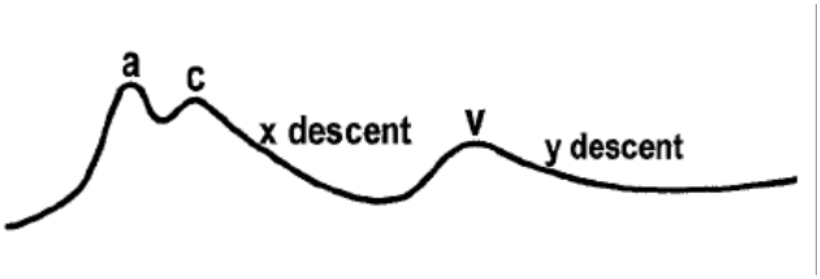
- Start of systole = isovolumetric contraction
    - Mitral valve closes
    - Ventricle contracts and pressure rises sharply without a change in volume
    - When LV pressure > aortic pressure the aortic valve opens
- Ventricular ejection
    - Pressure rises to a plateau and the volume falls during ejection
    - Normal stroke volume is 70-90 mls
- Start of diastole = Isovolumetric relaxation
    - Momentum of ejected blood overcome by arterial pressure and the aortic valve closes
    - Pressure falls but volume stays the same
    - When ventricular pressure is less than atrial pressure, the mitral valve opens
- Filling
    - Mitral valve is open and filling occurs
    - End diastolic volume is 130ml

- Atrial systole
    - Final part of ventricular filling prior to systole, small increase in volume and pressure



Describe how the waveforms of an ECG relate to the cardiac cycle
Atrial systole starts just after the p wave
Ventricular systole starts near the end of the R wave and ends just after the T wave

Please describe (or draw) the jugular venous pressure wave and outline the origins of the fluctuations in this wave
Up, up, down, up, down.



a = atrial systole. Form regurgitation from blood when atria contract.
C = triCuspid bulge back into the atria during isovolumetric contraction
Bit that dips between the a and c occurs when the atria relaxes and blood flows into the ventricle
X descent = ventricular contraction, downward movement of tricuspid
V = atrial filling and relaxation prior to tricuspid opening
Y = ventricular filling

5. **Cardiac Output**

What factors determine cardiac output?

- Cardiac output = stroke volume x HR
- Stroke volume is related to preload (the degree of stretch prior to contraction) and afterload (resistance to flow) of the heart and the intrinsic contractility of the myocardial cells
- HR responds to sympathetic or parasympathetic stimulation

What methods can be used to measure cardiac output?

The direct Fick method or the thermal dilution method

- *Fick method* relies on the Fick principle which states that the amount of substance taken up by an organ per unit time is equal to the (AV concentration difference) x blood flow. For the heart, we use oxygen.
- *Thermal or indicator dilution method* involves injecting the substance into a vein and doing serial sampling of arterial blood. This is then plotted and extrapolated to find the circulation time.
- These days we mostly just use ultrasound doppler

Can you draw (or describe) the Frank-Starling curve as it relates to the cardiac muscle.

Important points:

- X axis = ventricular end diastolic volume
- Y axis = stroke volume
- Curves arch up and to the right with dashed lines at the ends of the lower lines where there is high end diastolic volume. These dashed lines indicate portions of the ventricular function curves where maximum contractility has been exceeded

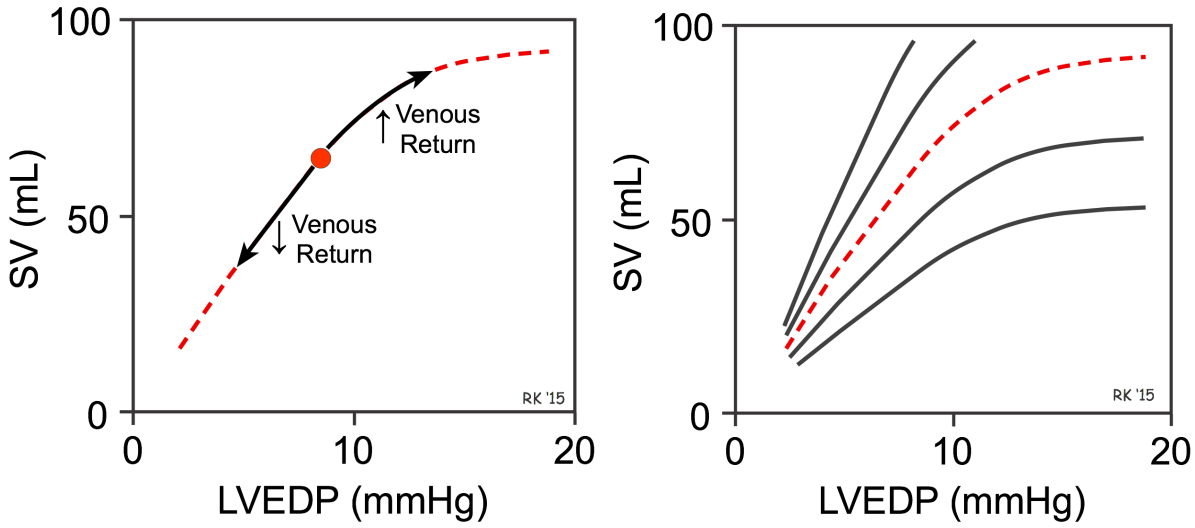
What factors shift the Frank Starling curve?

Things that shift the curve up and to the left.

- Circulating catecholamines
- Inotropic agents - digitalis, caffeine, adrenergic agents
- Sympathetic stimulation
- Increased myocardial mass

Things that shift the curve down and to the right

- Metabolic changes = acidosis, hypercarbia, hypoxia
- Vagal or parasympathetic stimulation
- Pharmacological depressants such as barbiturates
- Intrinsic depression as in myocardial failure
- Hypothermia



What clinical scenarios can cause a decrease in cardiac output?

- Arrhythmias or heart blocks causing abnormal heart rate
- Reduced preload i.e. from reduced venous return, cardiac tamponade
- Increased afterload
- Reduced contractility from ischaemia, venoms or drugs

6. **Myocardial Oxygen Demand**

What factors influence myocardial oxygen consumption?

- Intramyocardial tension which is dependent on pressure (afterload + contractility), radius (preload) and wall thickness
- The contractile state of the heart
- Heart rate
- Note: pressure load increases oxygen consumption more than volume load

How does decreasing a patient's heart rate improve symptoms of angina?
Decreasing the HR decreases the O2 demand
At a slower heart rate there is more time for coronary circulation which occurs in diastole

7. **Autoregulation**

What is autoregulation of tissue blood flow?
Refers to the capacity of tissues to regulate their own blood flow, which remains relatively constant despite moderate changes in perfusion pressure. This is achieved by altering vascular resistance.

What are the proposed mechanisms involved in autoregulation?

- Myogenic - intrinsic contractile response of smooth muscle to stretch. As pressure rises, vascular smooth muscles surrounding the vessels contract to maintain wall tension
- Metabolic - production of vasodilator metabolites by active tissues → vessel vasodilation → increased flow
- Endothelial products - vasoconstrictors (endothelin, thromboxane A2) and vasodilators (nitric oxide prostacyclin)
- Circulating neurohumoral substances - vasoconstrictors (adrenaline, noradrenaline, vasopressin, angiotensin II) and vasodilators (kinins, ANP)
- Neural - sympathetic (alpha -adrenergic receptors, vasoconstriction, beta adrenergic receptors - vasodilation) and parasympathetic (muscarinic receptors - vasodilation)

What are some local factors that lead to vasodilation?

- Hypoxia
- Hypercarbia
- Increased local temperature
- Hyperkalaemia
- Adenosine
- Lactate
- Prostaglandins
- Histamine

8. **Baroreceptors**

What are baroreceptors?
Stretch receptors in the adventitia layer of vessels

Where are they located?
Aortic arch and carotid sinus
Walls of the right and left atria (at the SVC and IVC entrances) and pulmonary circulation

What is their mechanism of action in hypotension?

- Baroreceptors are very sensitive to changes in pulse pressure
- They increase firing in response to raised blood pressure, which travels via glossopharyngeal and vagus nerves to the medulla and inhibits tonic sympathetic discharge. It also excites vagal innervation of the heart.
- When hypotension occurs, the arterial baroreceptors are less stimulated because they are less stretched
- Reduced baroreceptor discharge results in reduced signalling to the medulla and an overall increase in sympathetic discharge.
- This increases the heart rate and stimulates vasoconstriction, raising the blood pressure. It also reduces vagal drive.

9. **Cerebral blood flow**

What factors affect cerebral blood flow?

- Intracranial pressure
- Mean arterial pressure
- Mean venous pressure
- Local factors: pH, pCO_2 - influence constriction and dilation of cerebral arterioles
- Blood viscosity

What is meant by the term autoregulation of blood flow?

The process by which cerebral blood flow is maintained at a constant level despite variation of arterial pressure. Can maintain a constant flow over the mean arterial pressure range 65-140mmHg.

What is the Monro-Kellie doctrine?

- Volume of blood, CSF and brain tissue must be relatively constant.
- When the ICP rises, cerebral vessels are compressed resulting in reduced cerebral blood flow
- A rise in venous pressure also causes decreased cerebral blood flow by decreasing effective perfusion pressure and compressing cerebral vessels

How is brain perfusion maintained in brain injury?

- Aim is to maintain the cerebral perfusion pressure
- With a high ICP the body increases MAP to maintain the cerebral perfusion pressure
- Raised MAP results in hypertension and reflex bradycardia

What proportion of total body oxygen does the brain consume?

20%

What energy substrates can be used by the brain?

Glucose, glutamate and amino acids in starvation

What is the cushing reflex?

- Occurs when there is an increase in ICP which compromises blood flow to the medulla
- This leads to increased sympathetic outflow from the vasomotor centre
- Blood pressure increases in attempt to restore medullary flow
- Causes stretch of baroreceptors, leading to vagal stimulation and resultant bradycardia

10. Coronary blood flow

Describe the factors that control blood flow to the myocardium

- Pressure differences - flow depends on the gradient between arteries and veins, or the external compression from muscle. During systole, ventricular muscle pressure limits flow especially to the subendocardium of the left ventricle
- Local factors - these control the radius of the blood vessels. Hypoxia causes vasodilation in the heart, nitrous oxide also causes vasodilation.
- Neurogenic factors - parasympathetic and sympathetic (alpha = vasoconstriction, beta = vasodilation) and circulating catecholamines
- Blood viscosity

11. Renal blood flow

What percentage of cardiac output goes to the kidneys?

25%

How is renal blood flow regulated?

Substance/chemicals

- Noradrenaline - constricts renal vessels and stimulates renin release
- Dopamine - dilates the renal vein
- Angiotensin II - arteriolar constrictor
- PG - increased cortical flow, decreased medullary flow
- ACh - vasodilation
- High protein - increases blood flow

Renal Nerves

- Stimulation of the nerves = increased renal secretion, increase the juxtaglomerular sensitivity, increased sodium reabsorption and renal vasoconstriction
- Fall in BP causes vasoconstriction

Autoregulation

- Renal vascular resistance varies with pressure to keep the renal blood flow constant
- Independent of innervation

12. Shock

How is blood pressure maintained in the setting of acute blood loss?

Seconds to minutes

- Baroreceptors - sense the drop in BP and decrease firing which leads to increased sympathetic outflow
- Chemoreceptors - stimulation leads to peripheral vasoconstriction and rise ion BP
- CNS ischaemic receptors also activated

Minutes to hours

- Renin- angiotensin system activated
- Blood volume changes
- Fluid shift through capillaries

Longer term

- Renal compensation via aldosterone
- Blood volume changes
- Salt intake

Describe the non-cardiovascular compensatory responses to shock

- Renal response - efferent arterioles constrict more than afferent. Renal plasma flow decreased more than the GFR
- Sodium retention - retained nitrogenous products of metabolism (uraemia)
- Angiotensin II - plasma renin causing AG II release which causes a raise in BP and stimulation of thirst centre in the brain
- ADH - causes retention of sodium and water
- Aldosterone - stimulated by circulating AG II and ACTH
- Adrenal stimulation - adrenal medulla secretion catecholamines
- Increased circulation of NA - from increased discharge of sympathetic NA nerves

What other factors influence the vasomotor centre

- Direct stimulation - CO_2 and hypoxia
- Excitatory input - from the cortex via hypothalamus, from pain pathways and muscles, chemoreceptors (carotid and aortic)
- Inhibitory inputs - from the cortex via hypothalamus, from the lung, from baroreceptors