Physiology week 2 – Excitable Tissues VIVAs

ACEM PRIMARY 20010.1 Physiology VIVA Thursday 25 March pm Candidate Number:..... Mark.....

3a). What is the basis of the resting membrane potential?	a). Potassium – more open Potassium channels at rest therefore intracellular/extracellular Potassium concentrations are prime determinants of resting membrane potential b).Sodium c). Separated by the cellular membrane 1.Na actively transported out of cells 2.K actively transported into cells 3.Activity of Na-K ATPase pump	Na, K, ATPase and correct directions.
3b). Describe the ionic fluxes during the action potential	Voltage gated Na channels open (short lived), Na channels overwhelm K once threshold reached. Memb potential approaches Na (+60mV) . Na stops as short open phase, then they close/become inactivated, then resting state again. Also electrical gradient reversed. Then opening of volt gated K channels-slower and more prolonged than Na. Slow return to closed state causes after hyperpolarization	Na and K and sequence.

Question 4:	**What are the sequence of events in contraction and relaxation of a skeletal muscle?** **Prompt: what about relaxation**	1)Motor neurone d/c + Ach presyn release 2)AcH to post syn- Nicotinic receptors ↑ Na/K in end plate generates AP along muscle fibre 3) T tubules spread depolarisation releases Ca++ from sarcoplasmic reticulum (terminal cisterns) 4) ↑ Ca around myosin/actin filaments, to TropC uncovers myosin binding sites on Actin 5) 5) X-links form thin/ thick – shorten as slide **Relaxation** Ca pumped out, trop C reactivated and blocks actin/myosin bind.	Pass /FailShould have 3 /5 steps mentioned with some detail and know active Ca ++ reverses for relation

Describe the sequence of events in the contraction of skeletal muscle after discharge of the motor neurone.	*1 Discharge of motor neuron* *2 Release of ACh at motor endplate *** *3 ACh binds nicotinic ACh receptors* *4 Increase in Na and K conductance in end plate membrane* *5 end plate potential* *6 Muscle action potential* *7 Depolarization along T tubules* *8 Ca release at SR* *9 Ca binds Trop C and uncovers myosin binding sites on actin *** *10 actin myosin cross links and thin filaments slide on thick ***	Release Ach Ca release and Trop C bind actin myosin link and slide
How does tetanic contraction occur? *How does this differ from Treppe ?* *(Differentiation)*	*Contractile mechanism has **no refractory period**.*** *Repeated stimulation before relaxation has occurred - **summation** of contractions* *Fast repeated stimulation causes a fused continuous tetanic contraction. Can be complete or incomplete.* *Series of maximal stimuli at a frequency just below tetanizing causes increasing tension between each twitch. Due to increased calcium availability.*	*Describe tetanic contraction.*

What are the major differences in types of skeletal muscle?	*Type 1* *slow oxidative red,* *Moderate Ca2+ pumping,diameter and glycolytic capacity* *Slow myosin ATPase rate. High oxidative capacity.* *Type 11* *fast glycolytic white.* *High Ca2+ pumping,diameter and glycolytic capacity* *Fast myosin ATPase rate. Low oxidative capacity*	*Know two types and three differences*

		Macula densa and juxtaglomerular cells.
Neuromuscular excitation contraction coupling	Describe the sequence of events in transmission of a motor nerve impulse to a muscle How does the muscle them become depolarised?	Motor neurone action potential; end-plate potential; Acetylcholine release; Ach binding to nicotinic receptors; muscle end-plate potential. T tubules and release of Ca^{2+} from sarcoplasmic reticulum.

TOPIC: Skeletal muscle excitation /contraction / relaxation NUMBER:

FIRST QUESTION	**Describe the sequence of events in contraction and relaxation of skeletal muscle.**	
POINTS REQUIRED	Steps in contraction **(1) Discharge of motor neuron.** **(2) Release of transmitter (acetylcholine) at motor end-plate.** **(3) Binding of acetylcholine to nicotinic acetylcholine receptors.** (4) Increased Na+ and K+ conductance in end-plate membrane. **(5) Generation of end-plate potential.** **(6) Generation of action potential in muscle fibers.** (7) Inward spread of depolarization along T tubules. **(8) Release of Ca2+ from terminal cisterns of sarcoplasmic reticulum and diffusion to thick and thin filaments.** **(9) Binding of Ca2+ to troponin C, uncovering myosin-binding sites on actin.** **(10) Formation of cross-linkages between actin and myosin and sliding of thin on thick filaments, producing movement.**	Bolded at least?
	Steps in relaxation **(1) Ca2+ pumped back into sarcoplasmic reticulum.** (2) Release of Ca2+ from troponin. **(3) Cessation of interaction between actin and myosin.**	Bolded at least
PROMPTS		

SECOND QUESTION	**What is summation of contractions?**	COMMENTS
POINTS REQUIRED	1. The electrical response of a muscle fibre to repeated stimulation.	
	2. Contractile mechanism does not have a refractory period, so repeated stimulation before relaxation has occurred produces additional activation and a response added to the contraction already present.	
	3. With rapidly repeated stimulation, individual responses fuse into one continuous contraction (tetanus; tetanic contraction).	
	4. Complete tetanus: no relaxation between stimuli; tension developed ~ 4 times that of an individual twitch contraction	
	5. Incomplete tetanus: periods of incomplete relaxation between summated stimuli	
PROMPTS	Describe the response of a muscle fibre to repeated stimulation. What is a tetanic contraction?	

TOPIC: Smooth muscle contraction _____ **NUMBER:** _____

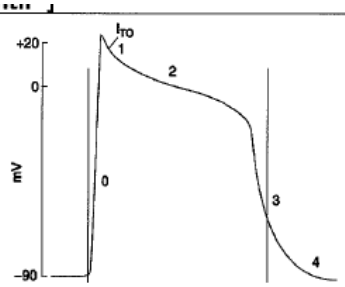
OPENING QUESTION	Describe the sequence of events in contraction and relaxation of visceral smooth muscle.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Binding of ACh to muscarinic receptors	Is there a difference between smooth muscle and other muscle?	
	2 Increased influx of Ca^{2+} into the cell		Essential
	3 Activation of calmodulin-dependent myosin light chain kinase		Essential
	4 Phosphorylation of myosin		
	5 Increased myosin ATPase activity and binding of myosin to actin		
	6 Contraction		
	7 Dephosphorylation of myosin light chain phosphatase		
	8 Relaxation or sustained contraction due to latch bridge and other mechanisms		
SECOND QUESTION	What factors influence intestinal smooth muscle contraction?		
POINTS REQUIRED	1 Stretch of visceral smooth muscle causes contraction in the absence of innervation		Essential
	2 Cold increases activity		
	3 ACh decreases smooth muscle potential and increases spike frequency so resulting in more active muscle		
	4 Adrenaline and noradrenaline increase smooth muscle potential and decrease spike frequency causing decreased muscle activity		
	5 Neural		

TOPIC: Conduction along a nerve cell _____

OPENING QUESTION	Draw & label the action potential in a nerve cell	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Resting membrane potential	1	
	2. Movement of sodium potassium ions.	2	
	3.	3	
SECOND QUESTION (if needed)	Discuss the factors that affect conduction.		2/4
POINTS REQUIRED	1. Myelinated vs demyelinated	1	
	2. Saltatory vs non-saltatory	2	
	3. Size	3	
	4. Direction of the conduction	4	

2.3 Action potential in cardiac cells	Describe the action potential in cardiac muscle fibre Why does tetany not occur in cardiac muscle?	Diagram. **–90 mv. Voltage gated Na channels -> rapid depolarisation (phase 0); closure of channels -> initial rapid repolarisation (phase 1); slower but prolonged opening of Ca channels -> plateau (phase 2); closure of Ca channels and opening of K channels -> final repolarisation (phase 3) to resting potential (phase 4).** Muscle still contracting in relative refractory period and beyond the duration of AP so cannot develop tetany.	4/5

	[Key items marked with*]	
Draw and label an action potential of a neuron. Prompt: What are the phases of a nerve action potential?	1 Latent period at –70 mV then upslope until firing level is reached at –55mV. 2 Spike potential with overshoot to +35 mV. 3 Rapid repolarization then slow after-depolarization. 4 After-hyperpolarization beyond –70 mV. 5 Return to latent period.	Shape From negative to positive
What ionic fluxes occur during the action potential? Prompt: What ions are involved in nerve conduction?	1 At firing level, rapid influx of Na towards equilibrium (+ 60 mV). 2 Na channels rapidly close (inactivated state) and Na inhibits further Na influx. 3 Voltage-gated K channels open. 4 Slow K efflux completes repolarization. 5 Decrease (increase) in extracellular Ca decreases (increases) the Na and K conductance required for an action potential.	Na influx (depol) K efflux (repol)
Where are ion channels distributed in myelinated neurons?	1 Voltage-gated Na channels concentrated in **node of Ranvier** and initial segment. 2 Na channels flanked by K channels	Nodes of Ranvier

	[Key items marked with*]	
Please describe or draw an action potential in ventricular muscle.	• RMP -90 mV (+/- 20) • No prepotential • Phase 0 rapid upstroke to +20 mV (+/- 20) • Phase 1 short-lived rapid depolarisation to around 0 mV. • Phase 2 prolonged plateau. • Phase 3 moderately fast repolarisation to RMP. • Phase 4 is the RMP. 	Shape including plateau General voltages (negative to positive)
What are the ion fluxes that produce this action potential?	• Phase 0 - opening of voltage-gated Na^+ channels allows Na^+ influx. • Phase 1 - due to closure of Na^+ channels and transient K^+ efflux. • Phase 2 - due to slower but prolonged opening of voltage-gated Ca^{2+} channels with Ca^{2+} influx. • Phase 3 - due to closure of Ca^{2+} channels and opening of various types of K^+ channels allowing K^+ efflux • Phase 4 - RMP is due to membrane permeability at rest being much higher for K^+ than for Na^+.	Na influx (depol) Ca influx (plateau) K efflux (repol)

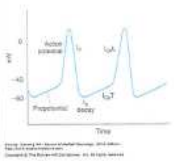
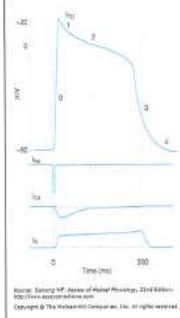
TOPIC: AP in Cardiac pacemaker cell + effect SNS/PNS NUMBER: _____

OPENING QUESTION	**Draw the action potential in a cardiac pacemaker cell, and explain the ionic fluxes.**	**COMMENTS**
POINTS REQUIRED	**1 Prepotential initially due to decrease in efflux K^+ , then completed by influx Ca^{2+} through T channels**	Suggested Pass/Fail Criteria in Bolded Type
	2 AP due to influx Ca^{2+} via L channels	
	3 Repolarisation due to efflux K, no plateau	All essential
PROMPTS	What electrolytes are responsible for each phase of the AP?	Stress cardiac pacemaker cell
SECOND QUESTION	**How do sympathetic and parasympathetic stimulation change the prepotential?**	
POINTS REQUIRED	1 Noradrenaline binds to Beta 1 receptor and raises cAMP, resulting in increased opening of L channels and Ca^{2+} influx. **Thus increased slope of prepotential and firing rate**	
	2 ACh binds to M2 receptor and decreases cAMP, resulting in both slowing of Ca channel opening and opening of special K channels (counters decay of K efflux) leading to greater fall in prepotential **Thus decreased slope of prepotential and firing rate**	
PROMPTS	What does noradrenaline do? What does vagal stimulation do?	

TOPIC: Pacemaker potential _____ **NUMBER:** _____

OPENING QUESTION	Describe the features of the action potential in cardiac pacemaker tissue.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Prepotential initially due to decrease in inward K^+ movement then inward Ca^{2+} through T channels	Compare it to vent muscle	All essential
	2 Action potential due to inward Ca^{2+} through L channels		
	3 Repolarization due to inward K^+ movement		
	4 No plateau		
SECOND QUESTION	How do autonomic factors alter the slope of the prepotential?	What does noradrenaline do?	
POINTS REQUIRED	1 Noradrenaline from sympathetic endings raises intracellular cAMP		
	2 Facilitates opening of L channels		
	3 Increased Ca^{2+} influx		
	4 Increased heart rate		
	5 ACh acts via muscarinic receptors and G protein to open K^+ channels and decrease rate		

COMMENTS

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1a:	**Draw and explain the action potential in a cardiac pacemaker cell.**	 PROMPTS: What electrolytes are responsible for each phase of the AP?	**Pass-fail** **Must have shape to pass and know ion fluxes (↓effK + infCa T)- InfCa L – Eff K)** **1 Pre-potential initially due to decrease in efflux K^+, then completed by influx Ca^{2+} through T channels** **2 AP due to influx Ca^{2+} via L channels** **3 Repolarisation due to efflux K, no plateau**
Question 1b:	**Describe the major differences between a cardiac myocyte AP and the pacemaker**		1. Resting membrane potential, , –90mV rapid depolarisation voltage gated Na (overshoots) 2. Phase 1 rapid repolarisation = closure of Na channels.(inner v outer gates) 3. Plateau phase 2 voltage gated Ca2+ channels open (slower L type) 4. Phase 3 repolarisation Ca2+ ch close 5. Phase 4 due to various K+ efflux Differences- 1) Na fast v Ca dependent, 2) automaticity due to rising prepotential (K+/ Ca+), 3) plateau phase, 4) > resting potentials **Pass-Fail: Need correct shape + some knowledge of different channels (partic Na v Ca), no automaticity (no-prepotential, as no leaking K/ Ca) and plateau due to Ca ++ (>er inactive phase)**

TOPIC: Pacemaker potential_____ **NUMBER**: _____

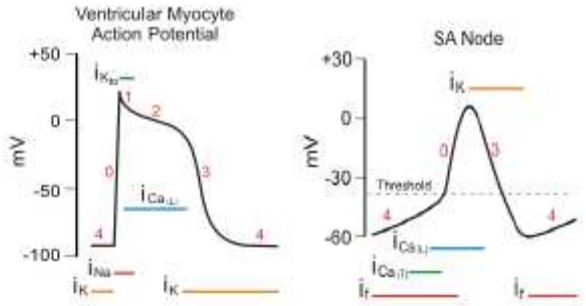
OPENING QUESTION	Describe the features of the action potential in cardiac pacemaker tissue.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Prepotential initially due to ***decrease*** in K^+ efflux, then ***increase in inward*** Ca^{2+} through **T channels**.	Compare it to vent muscle	All essential
	2 Action potential due to inward Ca^{2+} through **L channels**. Na+ is fairly unimportant, unlike ventric myocytes.	Can you draw it? [see graph below]	
	3 Repolarization due to inward K^+ movement		
	4 No plateau		
SECOND QUESTION	How do autonomic factors alter the slope of the prepotential?	What does noradrenaline do?	
POINTS REQUIRED	1 Noradrenaline from sympathetic endings raises intracellular cAMP		
	2 Facilitates opening of L channels		
	3 Increased Ca^{2+} influx		
	4 Increased heart rate		
	5 ACh acts via muscarinic receptors and G protein to open K^+ channels and decrease rate		

DETAILS

Describe the features of the action potential in cardiac pacemaker tissue… esp how it differs to ventricular muscle AP

NB draw two graphs:

- *Ventricular muscle AP: fig 3-16, p80*
- *Pacemaker AP: my graph back of p9.2-1 = fig 28-2, p549*



Remember the stages of ventricular AP:

0 depolarisation
1 initial rapid repolarisation
2 plateau
3 late rapid repolarisation
4 baseline

Overview:

- SAN has greatest capacity for self-excitation [duh!]
- The key is that the cell membrane is **inherently leaky** to Na+, & the **fast Na channels don't work**, unlike the ventricular muscle cells. Who cares? Well…
    - The constant Na inflow is always tending to depolarize the cell- that's why phase 4 is up-sloping
    - The phases of the AP are due to slow Na+ and Ca++ channels only [& K+ too of course], rather than fast Na+ channels [which don't work at -55mV]
    - This smooths out the curve because overall Na+ has little effect on the AP

With that in mind, the key features are:

- resting potential is -55 to -60 mV [cf -90] [note the different y-axes]
- ironically, phase 0 [depolarization] is slower, because fast Na channels don't work [blocked bc the cell membrane is partly repolarised at -55]
- phases 1 & 2 don't happen

- repolarisation [phase 3 here] is not due to Na channels closuring but voltage-gated K channels **opening** & K+ floods out.
- When these K channels close, depolarization starts again.
- Phase 4 is up-sloping as noted.

The gory details:

1. there are 2 types of Ca++ channel:
    a. When T-channels [transient] open, they cause phase 4 to be an up-sloping 'prepotential'
    b. When L-channels [long-lasting] open, true depolarization begins.
2. Depolarisation [Phase 0] due to inward Ca^{2+} through L channels, and the ongoing inward Na+ drift
3. Repolarization due to inward K^+ movement
    a. Phase 1 [initial rapid repolarisation] **doesn't happen** [bc no fast Na+ channels to close]
    b. Phase 2 [plateau phase due to Ca++ channels] practically doesn't occur
    c. Phase 3 [late rapid repolarisation] still occurs.
4. Phase 4 [baseline] is upward sloping because it's so excitable that it starts gradually depolarizing again almost immediately. As noted above, best to call phase 4 the *prepotential*. Its upward slope is doe to 2 things:
    a. The repolarising K-channels close, so decrease in outward K^+ movement
    b. then inward Ca^{2+} flow through T channels

How do autonomic factors alter the slope of the prepotential? [fig 28-3, p549]

- Noradrenaline from sympathetic endings raises the slope
    - raises intracellular cAMP_
    - this facilitates opening of L channels, and Ca++ enters more rapidly
    - end result: ↑HR
- ACh decreases the slope
    - acts via muscarinic receptors and G protein
    - this opens K^+ channels & more K floods out, prolonging the baseline
    - ↓HR

Nerve action potential	Draw a nerve action potential. What are the ion fluxes that occur during an action potential?	Resting membrane potential (-70mV); firing potential (-55mV); depolarises to positive level (+35mV) (Concept, not exact figures) Fast sodium influx; slow potassium efflux	