Physiology week 16 – Renal (volumes/buffers)
VIVAs

Question 3:	**Describe how anti-diuretic hormone/ Vasopressin acts on the kidney.**	ADH binds to G-receptor, V2 activates adenylate cyclase. ↑ IC c-AMP ►migration of IC endosomes. **H20 channels (aquaporin2) inserted into luminal membrane** **↑water permeability, with ↑water reabsorption**	
	What factors influence ADH secretion	**Table 39-1.** Summary of stimuli affecting vasopressin secretion. **Vasopressin Secretion** **Increased** / **Decreased** osmotic P of plasma↑ 285mmol / osmotic P of plasma ↓ Decreased ECF / Increased ECF volume Pain, emotion, "stress," exercise / Alcohol Nausea and vomiting Standing Clofibrate, carbamazepine Angiotensin II	Osmolality mediated via osmoreceptors OVLT **ECF via Baroeceptors** **NB low P baro rec (pulm/atria > arterial) via NTS/ CVLM).** **If bled/ hypotens reinforces via Angio 2 > ADH and allows lower osmolality to trigger ADH** **Pass /Fail** **must know ECF/ Osmolality + 1 other or some sensor/ effector pathway**

TOPIC: Vasopressin _____ **NUMBER:**

OPENING QUESTION	**Describe the effects of Vasopressin**	**COMMENTS**
POINTS REQUIRED	**1 Retention of water (antidiuretic hormone) (V2 receptors)**	1 and 2 plus one other
	2 Vasoconstrictor effect (V1A receptors)	
	3 Central effect brain (area postrema) to decrease CO	
	4 Glycogenolysis in liver (V1A receptors)	
	5 Mediate increased ACTH secretion (V1B receptors)	
	6. Neurotransmitter in brain and spinal cord	
PROMPTS		
SECOND QUESTION	**How does vasopressin cause retention of water ?**	
POINTS REQUIRED	**Increases permeability of CD, acting on** V2 receptors **Insertion of protein water channels (aquaporin 2)** in luminal membranes. Water enters hypertonic interstitium Urine becomes concentrated and volume decreases Retention of water in excess of solute	Bolded
THIRD QUESTION	**What stimuli affect vasopressin secretion ?**	
POINTS REQUIRED	**1. Factors increasing vasopressin secretion** - **↑ effective osmotic pressure of plasma** - **↓ ECF volume** - Pain, emotion, "stress", exercise, standing - Nausea and vomiting - Clofibrate, carbamezepine, angiotensin 2	At least 2
	2. Factors decreasing vasopressin secretion - **↓ effective osmotic pressure of plasma** - **↑ ECF volume** - Alcohol	At least 2
PROMPTS		

TOPIC: ADH release _____ **NUMBER:** _____ 3a

OPENING QUESTION	**What factors affect Antidiuretic Hormone (ADH) secretion**	**PROMPTS** **ADH is also known as vasopressin. What stimulates vasopressin secretion? Prompt to get the list**	**COMMENTS** Must be able to distinguish the most important, esp. osmotic pressure
POINTS REQUIRED	1 **Plasma osmotic pressure** – increase POP leads to increase ADH secretion. Sensitive to changes around 285mosm/kn\g	1 how does that affect it?	**Must have to pass**
	2 **Extracellular fluid volume** – inverse relationship between ADH secretion and ECF volume. Primary mediators are the low pressure receptors in great veins, atria and pulmonary vessels	2	**Must have to pass**
	3 **Pain, emotion**, stress, **nausea vomiting**– all increase ADH	3	**Must be able to name and explain 2 of the 4 last group to pass**
	4 **Standing**	4	
	5 **Drugs** – eg, carbamazepine, clofibrate increase, alcohol decreases	5	
	6 **Angiotensin II** - increases	6	
	7	7	
	8		

4 a). What is the normal range of osmolality of ECF 4b). How is this maintained? 4 c). What other stimuli affect Vp secretion? Prompt- Anti-diuretic Hormone	285-295mosm/L Maintained by **Vasopressin-secreting** and **thirst** mechanisms If osm ↓, thirst is ↓, Vp secretion is ↓, resulting in **urinary loss of free water** If osm ↑, thirst is ↑, Vp secretion is ↑, leading to **renal reabsorption of free water** in renal collecting ducts/pyramids VP secretion ↑ by: (↑ effective plasma osm pressure) ↓ **ECF volume** (via low pressure receptors) **Pain, emotion, exercise, stress** (eg surgery) **Nausea & vomiting** **Angiotensin II** Standing Clofibrate, carbamazepine VP secretion ↓ by: (↓ effective plasma osm pressure) ↑ **ECF volume** Alcohol	Accept 280-300 3/4Bold 2/4 Bold 1 of 2 Bold

1.2 Respiratory compensation for acid base changes Davenport	Describe how respiration compensates for acid-base changes What clinical conditions might cause metabolic acidosis? / metabolic alkalosis?	**$CO_2 + H_2O = H_2CO_3 = H + HCO_3$. Rapid responder.** Respiratory Centre responds to H, mainly at peripheral chemoreceptors, also transferred to CSF by CO_2. **Metabolic acidosis –> inc ventilation, dec CO_2 -> dec H, dec HCO_3** ('base deficit'). **Metabolic alkalosis –> dec ventilation, inc CO_2 -> inc H, inc HCO_3** ('base excess'). In reality often no compensation. Davenport Diagram. - DKA; hypoxia -> lactic acid - Vomiting ->loss of acid.

TOPIC: Renal regulation of acid excretion _____

OPENING QUESTION	What is the renal response to acidaemia?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Hydrogen ions actively secreted into the proximal tubule, thick ascending loop of Henle and distal tubules, facilitated the re-absorption of bicarbonate ions by forming the carbonic acid, which dissociates to form CO_2 and water.	1	
	2.	2	
SECOND QUESTION (if needed)	Describe the buffer systems involved.		2/3
POINTS REQUIRED	1. Bicarbonate	1	
	2. Phosphate	2	
	3. Ammonia	3	

Renal regulation of H^+	What is the renal response to respiratory acidosis? What buffering systems are there for H^+ in renal tubular fluid?	Increased H^+ secretion and HCO_3^- absorption. At least HCO_3^- and one of HPO_4^{2-} or NH_3 with explanation of buffering mechanism.

3.4 Buffers in body fluids	What are the major buffers of blood? How do they work? What are the major buffers in cells. Describe the Henderson-Hasselbalch equation	**Proteins**, albumin; **Haemoglobin**; histidine residues = x6 proteins; Deoxygenated Hb better than HbO_2; **Carbonic Acid**-Bicarb system, fast with carbonic anhydrase; Hb deoxygenated; Hb histidine residues; proteins anions Hproteins = H+ and Protein- ; $H_2PO_4 = 2H^+$ and HPO_4 -- .pH = .pK + log [A-] / [HA]. Most effective when [A-] / [HA] = 1, so pH = pK.

TOPIC: Acidification of Urine_____

OPENING QUESTION	**How does the kidney acidify the urine?**	**COMMENTS**
POINTS	Secretion of hydrogen ions.	2/3
	Binding of the hydrogen ions with buffers.	
	Secretion/absorption of bicarbonate ions.	
PROMPTS		
SECOND QUESTION	**Is there a difference between the proximal and distal tubules?**	Needs to understand
POINTS	PCT/DCT/CD secrete H+.	
	PCT via Na+/H+ exchange. Na+/K+ATPase – Na+ from cell to interstitium.	
	DCT/CD H+ secretion ATP driven proton pump.	
PROMPTS	**Prompt if necessary**	
THIRD QUESTION	**What factors increase acid secretion?**	4/7
POINTS	Factors which increase acid secretion ↑ PCO2 ↑ PaCO2 ↑ aldosterone ↓ K+, ↑ CA concentration ↑ K+ ↓ H+ secretion.	
PROMPTS		

5. Describe the renal response to metabolic acidosis.	• Renal mechanisms operate to compensate for metabolic acidosis and return the serum pH towards normal • Anions that replace $HCO3^-$ are filtered at the glomerulus along with corresponding cations (mainly Na^+) • Renal tubule cells secrete H^+ into tubular fluid in exchange for Na^+ and HCO_3^- • Buffering in the urine gives greater capacity to this system (otherwise limiting pH of 4.5 would stop futher H^+ secretion) • Buffering systems include: Bicarbonate, Phosphate, Ammonia Prompts: (i) What prevents H^+ secretion stopping when urine pH falls to 4.5? (ii) Can you name any of the buffers that operate?	Compensatory mechanisms identified Must know H^+ secreted into tubular fluid in exchange for Na^+ Must know about buffering and give two buffers

OPENING QUESTION	What are the buffer systems in **blood?**	PROMPTS	COMMENTS
POINTS REQUIRED	1 Especially **carbonic acid / bicarbonate** system [responsible for **80%** of ECF buffering]: Carbonic anhydrase required. Present in Red blood cells; also gastric parietal cells & renal tubule cells. Not a very powerful buffer [dissoc constant 6.1, which means that at pH 7.4 it's v much skewed towards HCO3- [ie not at maximal buffering capacity]. Inhibited by Cyanide Azide Sulphide Sulphonamides	What binds to H^+ in blood?	This + one other
	2 Plasma proteins – esp albumin (free carboxyl and amino groups)		
	3 Hb (imidazole groups of histidine residues): **Six times** the buffering capacity of plasma proteins. Deoxygenated haemoglobin is a better buffer, which is useful bc venous blood is more acidic.		
	Background: *an acid-base buffer is a solution of 2 or more compounds which together prevent marked changes in [H+] when either an acid or base is added.*		
SECOND QUESTION (if needed)	Explain how carbonic acid / bicarbonate system works.		
POINTS REQUIRED	1 Write equation: Henderson-Hasselbach pH = pKa + log [A-]/[HA] **For bicarb:** **pH = 6.1 + log [HCO3]/[CO2].** The pKa is derived from the Ka value of the following reaction: **$CO_2 + H_2O$ <=> H_2CO_3 <=> $H^+ + HCO_3$-** (where CO_2 refers to dissolved CO_2) The concentration of carbonic acid is very low compared to the other components so the above equation is usually simplified to: $CO_2 + H_2O$ <=> $H^+ + HCO_3$-		Essential
	2 Carbonic anhydrase is the catalyst (it increases speed of reaction). There are different subtypes of carbonic anhydrase, but most of the significant ones are intracellular [present in Red blood cells; also gastric parietal cells & renal tubule cells]. Carbonic anhydrase is a metalloenzyme *[all known forms of carbonic anhydrase in living creatures use Zinc ... except marine diatoms, which use cadmium! This is the only known example of a cadmium based reaction*	Where is carbonic anhydrase found?	Essential bits: Mention the enzyme Know it's intracellular esp RBC

	used by organisms.]	
	3 The power of the system lies in the fact that CO2 can be altered by respiration, and HCO3 by the kidneys. **This is why it's so effective** despite having such a low pKa. The excretion of CO_2 via the lungs is particularly important because of the rapidity of the response. Because of this, the resp system has been called 'the 4th buffer' [the 4th musketeer?].	
THIRD QUESTION (if needed)	What are the non-blood buffers?	
POINTS REQUIRED	1. Interstitial fluid buffers (*Bicarbonate)*	
	2. Intracellular **fluid** buffers (*Phosphate)*	
	3. Intracellular **protein** buffers- in fact, these are responsible for 75% of the **body**'s total buffering capacity.	

TOPIC: Buffers _____ **NUMBER:** _____

OPENING QUESTION	What are the buffer systems in blood?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Especially carbonic acid / bicarbonate system	What binds to H^+ in blood?	This + one other
	2 Plasma proteins (free carboxyl and amino groups)		
	3 Hb (imidazole groups of histidine residues)		
SECOND QUESTION (if needed)	Explain how carbonic acid / bicarbonate system works.		
POINTS REQUIRED	1 Draw equations		Essential
	2 Highlight importance of carbonic anhydrase (increases speed of reaction) and where carbonic anhydrase is (intracellular)		Essential
	3 Outline control by respiratory and renal systems.		