Physiology week 15 – Renal (GFR/Na/K) VIVAs

TOPIC: Functional anatomy of the nephron _____ NUMBER: _____

OPENING QUESTION	Describe the cell types in the glomerulus and their functions ?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Capillary endothelial cells – Afferent arteriole becomes a tuft of capillaries invaginated into Bowman's capsule. Endothelium fenestrated with 70-90 nm pores. Separated from capsule epithelium by basal lamina.	What types of cells lie between blood and the capillary and filtrate in Bowman's capsule? What are their functions?	Need fenestrated capillary membrane.
	2 Epithelial cells of Bowman's capsule: (a) Podocytes possess pseudopodia that interdigitate to form 25 nm wide filtration slits over capillary endothelium. Each slit is closed by a thin membrane. (b) Mesangial cells are stellate and lie between capillary endothelium and basal lamina. Involved in regulation of filtration, secretion of various substances and absorption of immune complexes.		Need podocytes with pseudopodia forming filtration slits.
SECOND QUESTION	What properties of substances in the blood prevent free passage across the glomerular membrane?		Need both
POINTS REQUIRED	1 Larger diameter > 8 nm		
	2 Lack of neutrality (charged)		

TOPIC: Functional anatomy of the nephron_____ **NUMBER:** _____

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POINTS REQUIRED	1 Capillary **endothelial** cells – Afferent arteriole becomes a tuft of capillaries invaginated into Bowman's capsule. Endothelium fenestrated with 70-90 nm pores ie 'leaky' to facilitate filtration. Separated from capsule epithelium by basal lamina.	What types of cells lie between blood and the capillary and filtrate in Bowman's capsule? What are their functions?	Need fenestrated capillary membrane.
	2 **Epithelial** cells of Bowman's capsule: (a) **Podocytes** possess pseudopodia that interdigitate to form 25 nm wide filtration slits over capillary endothelium. Each slit is closed by a thin membrane. (b) **Mesangial cells** are stellate and lie between capillary endothelium and basal lamina. Involved in: • regulation of filtration • secretion of various substances • absorption of immune complexes		Need podocytes with pseudopodia forming filtration slits.
SECOND QUESTION	What properties of substances in the blood **prevent** free passage across the glomerular membrane?		Need both
POINTS REQUIRED	1 Larger diameter > 8 nm		
	2 Lack of neutrality (charged)		

TOPIC: Glomerular filtration rate _____

OPENING QUESTION	What is a normal Glomerular Filtration Rate in humans?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. 125 ml/min	1	
SECOND QUESTION (if needed)	What factors would cause a decrease in GFR?		3/5 to pass
POINTS REQUIRED	1. Hydrostatic pressure	1	
	2. Renal blood flow	2	
	3. Capillary permeability	3	
	4. Plasma protein osmotic pressure	4	
	5. Size of capillary beds	5	

SUBJECT: PHYSIOLOGY Session 3 Question 5

TOPIC: Potassium handling by the kidney _____ NUMBER: ___

OPENING QUESTION	What happens to potassium as it passes through a nephron?	**PROMPTS**	C
POINTS REQUIRED	1 Freely filtered	1 Reabs/secret^{n}?	
	2 67% reabsorbed prox tub (with Na + H^2O)	2	
	3 20% reabsorbed asc limb (with Na and Cl)	3	
	4 Dist tub reabs or secretes (H/K/ATPase)	4	
	5 Reabs in alpha intercalated cells	5	
	6 Secretion by principal cells	6	
	7 Diet,aldosterone,A/B,lumen ions,diuretics	7	
	8		
SECOND QUESTION (if needed)	How does potassium handling by the kidney change in response to changes in pH?		
POINTS REQUIRED	1 H and K are exchanged	1	
	2 Acidosis dec K excretion	2	
	3 H makes K move into circ, less for excret^{n}	3	
	4 Alkalosis increases K excretion	4	
	5	5	
	6	6	
	7		
THIRD QUESTION (if needed)	How does aldosterone increase K secretion?		
POINTS REQUIRED	1 Increased Na entry into cells	1 Effect on Na?	
	2 Inc pumping out of Na by Na-K pump	2	
	3 Inc K uptake into principal cells	3	
	4 Inc K conc inc secretion driving force	4	
	5 Also inc luminal membrane K channels	5	
	6	6	

Renal regulation of sodium balance.	How is the secretion of renin regulated?	**Stimulatory:** Increased sympathetic nervous activity ; Increased circulating catecholamines; Prostaglandins **Inhibitory:** Increased Na^+ and Cl^- reabsorption across the macula densa; Increased afferent arteriolar pressure; Angiotensin II; Vasopressin. Three of the above with one from each.
	Describe the juxtaglomerular apparatus	Afferent and efferent arterioles and tubule touch at one point.. Macula densa and juxtaglomerular cells.
	resistance?	One of low pH, autonomic or passive factors
Factors affecting GFR	What factors affect filtration across the glomerular capillary bed?	• Permeability and area of the glomerular capillary bed. • Hydrostatic pressures in the capillary and the tubule. • Oncotic pressure in the plasma and the filtrate.
	How can GFR be measured?	$U_X\dot{V}/P_X$ or concepts.
1.4 Loop of Henle – structure and function	Describe the structure of the Loop of Henle	**Thin descending, thin ascending, thick ascending** limbs. Cortical nephrons with short loops (85%) & juxtamedullary nephrons with long loops into medullary pyramids (15%).
	Describe the function of the Loop of Henle	**Counter current multiplier**: maintains gradient of osmolality; requires **vasa recta as countercurrent exchangers** **Thin descending: high permeability to water**; it moves out of tubule into interstitium **Thin ascending: high permeability to NaCl**; it moves out of tubule into interstitium **Thick ascending: active transport Na, K, Cl**, from tubule to interstitium; impermeable to H2O

TOPIC: Renal sodium & potassium excretion **NUMBER: 3**

OPENING QUESTION	What are the major physiological factors affecting sodium excretion from the kidney?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Amount filtered versus amount reabsorbed, therefore 2. ECF, 3. GFR, 4. Na intake, 5. hormonal e.g. aldosterone angiotensin and K and H excretion	How does the kidney regulate sodium excretion?	4 to pass
SECOND QUESTION (if needed)	What are the major physiological factors affecting potassium excretion from the kidney?		2 to pass
POINTS REQUIRED	1. K is reabsorbed in PTs and secreted in distal tubule, 2. Amount secreted relates to tubular flow, 3. Na excretion or reabsorption, 4. K intake	How does the kidney regulate potassium excretion?	

TOPIC: Water excretion by the kidney NUMBER: 3

OPENING QUESTION	Describe how water is reabsorbed in the different parts of the nephron.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. 60-70% in the Proximal tubule		Need to understand that water is reabsorbed in different parts & the role of vasopressin in the collecting duct.
	2. 15% in the loop of Henle		
	3. 5% in the distal tubule		
	4. Up to 10% in the collecting duct depending on the presence of antidiuretic hormone.		
SECOND QUESTION (if needed)	What hormonal factor influences water excretion?	What does vasopressin do?	
POINTS REQUIRED	1. Vasopressin increases the permeability of the collecting duct to water & allow water to be reabsorbed.		

TOPIC: Glomerular filtration **NUMBER: 3**

OPENING QUESTION	What factors control glomerular filtration?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	Mention average 125ml/min or 0.16-0.2 of RPF and its derivation Ui x V/ Pi= Ci= GFR for inulin; Creatinine Clearance is approximation Control of GFR depends on 1. size of capillary bed*, 2. permeability of capills*, 3. hydrostatic pressure*, 4. oncotic pressure*. These influenced by changes in RBF, MAP,[plasma proteins}, effective surface area, changes in pressure across Bowman's capsule eg ureteric obstruction, renal oedema. Glomerular capills are 50x permeable as skeletal.		Need ¾ to pass.

2.2 Renal blood flow, normal values and regulation	Describe the control renal blood flow	- **Chemical: Noradrenaline** constricts interlobular and afferent arterioles. **Angiotensin 11** constricts efferent arterioles > afferent arterioles. Dopamine (made in kidney) vasodilates. Acetylcholine vasodilates. Prostaglandins inc. bl flow in cortex, dec. bl flow in medulla. - **Neural: SNS** -> dec bl flow. Fall of BP, vasoconstrictor response includes renal bl flow. - **Autoregulation**: contractile response of smooth muscle of afferent arteriole to stretch (BP). NO may be involved. Angiotensin 11 plays a role in constricting efferent arterioles, maintaining GFR.

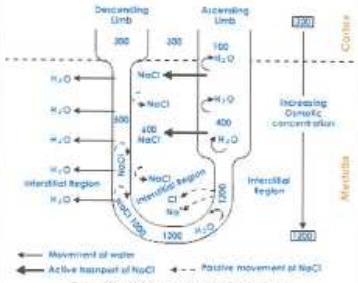
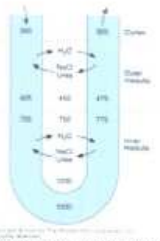
Describe water handling in the collecting ducts of the kidneys Prompt ; How does vasopressin affect water handling in the collecting ducts ?	1) The collecting ducts (CD) have two portions: a cortical portion and a medullary portion **2) Changes in osmolality and volume in the CDs depend on amount of **vasopressin** acting on cucts **3) This antidiuretic hormone from the post pituitary gland **increases the permeability of CDs to H2O** 4) Key to action of vasopressin on the CDs is aquaporin-2. Unlike other aquaporins, this is stored in vesicles in cytoplasm of principal cells. 5) Vasopressin causes rapid insertion of these vesicles into apical membrane of cells. Effect is mediated via the vasopressin V_2 receptor, cyclic AMP, protein kinase A, and a molecular motor, one of the dyneins **6) In presence of enough vasopressin to produce maximal antidiuresis, **H2O moves out of hypotonic fluid entering cortical CDs into interstitium** of cortex, and the tubular fluid becomes isotonic 7) As much as 10% of the filtered H2O is removed 8) When vasopressin is absent, the collecting duct epithelium is relatively impermeable to water and the fluid therefore remains hypotonic, and large amounts flow into renal pelvis.	2 3 6

TOPIC: Renal Blood Flow _____ **NUMBER:** _____

OPENING QUESTION	**What is normal renal blood flow and how can it be measured?**	**COMMENT**
POINTS REQUIRED	1. **Fick principle** (amount of a substance taken up per unit time divided by arterio-venous concentration difference)	
	2. PAH (excreted, not metabolised or stored, doesn't affect flow) is used to measure effective renal plasma flow (90% cleared) ERPF = Clearance of PAH = UV/P = 630 mL/min	2 of 3
	3. Actual renal plasma flow = ERPF/0.9 = 700 mL/min	
	4. Renal blood flow = RPF x 1/1-Hct (Hct = 0.45)	
	5. Renal blood flow = approx 1250 mL/min	
PROMPTS	What substance can be used to measure renal plasma flow?	
SECOND QUESTION (if needed)	**How do blood flow and oxygen extraction vary in different parts of the kidney?**	
POINTS REQUIRED	1. **Cortical flow is high** (5 mL/gm of tissue) and oxygen extraction is low	
	2. **Medullary blood flow is low** (2.5 mL/gm in outer cortex, 0.6 mL/gm in inner cortex) and oxygen extraction is higher (more metabolic work done)	2 of 3
	3. **Medulla is vulnerable to hypoxic damage** if flow is reduced (low flow, high oxygen usage)	
PROMPTS	How much blood flows to the renal medulla?	

What is an osmotic diuresis ? *Prompt:* *Describe how it occurs.* *Prompt:* *Can you give me an example*	** 1) Presence of large quantities of unreabsorbed solutes in renal tubules causes an ↑ in urine volume called **osmotic diuresis** ** 2) Solutes that are not reabsorbed in the proximal tubules exert an appreciable osmotic effect as volume of tubular fluid ↓ and their concentration ↑ ** 3) Therefore, they "hold water in the tubules 4) Concentration gradient against which Na^+ can be pumped out of proximal tubules is limited. Normally, movement of H2O out of proximal tubule prevents any appreciable gradient from developing, but Na^+ concentration in fluid ↓ when H2O reabsorption is ↓ because of presence in tubular fluid of ↑ amounts of unreabsorbable solutes. Limiting concentration gradient is reached, and further proximal reabsorption of Na^+ is prevented; more Na^+ remains in tubule, and H2O stays with it 5) The result is that loop of Henle is presented with a greatly ↑ volume of isotonic fluid. 6) This fluid has a ↓ Na^+ concentration, but total amount of Na^+ reaching the loop per unit time is ↑ 7) In loop, reabsorption of water and Na^+ is ↓ because the medullary hypertonicity is ↓. The ↓ is due primarily to ↓ reabsorption of Na^+, K^+, and Cl^- in the ascending limb of loop because limiting concentration gradient for Na^+ reabsorption is reached. More fluid passes through the distal tubule, and because of the ↓ in osmotic gradient along the medullary pyramids, less water is reabsorbed in collecting ducts. Result is a marked ↑ in urine volume and excretion of Na^+ and other electrolytes. 8) Osmotic diuresis is produced by administration of compounds such as mannitol and related polysaccharides that are filtered but not reabsorbed. It is also produced by naturally occurring substances when present in amounts exceeding the capacity of the tubules to reabsorb them. E.g. diabetes mellitus, glucose that remains in tubules when filtered load exceeds TmG causes polyuria. Osmotic diuresis can also be produced by infusion of large amounts of sodium chloride or urea.	1 2 3

	[Key items marked with*]	
Describe a method for measuring the glomerular filtration rate Prompt Describe the properties of a suitable substance and give an example	Measure excretion of a substance which is ***freely filtered*** through the ***glomeruli neither secreted nor reabsorbed*** by the ***tubules*** Non toxic, not metablised Eg Inulin, NB Endogenous Creatinine has limitations $GFR = \frac{UX \times V}{PX}$ where Ux is the conc of X in the urine, P is the urine flow per unit time Px is the arterial plasma level of X. If X is not metabolized in the tissues then the peripheral venous plasma level can be substituted for the arterial plasma level.	Three of five One example Definition or description and basic formula
What is normal GFR and what are the factors which affect it	125ml/min in normal 70 kg male, 10% less for women, and correlates with surface area. Factors RBF, Systemic BP, Ureteric obstruction, compression by oedema within renal capsule, Plasma proteins, Permeability changes, Filtration surface area	Value (100 – 150) and three factors

Question 3: Counter-Current mechanism Ganong pp 716-8	i) Describe the counter-current mechanism in the kidney. Prompt: What is the role of the vasta recta?  **Countercurrent multipliers**	a) **Countercurrent multipliers** in the **LOH** through active transport of Na (& Cl⁻) out of its thick ascending limb. Water moves out of the thin descending limb, with inflow of tubular fluid from the PCT. This increases the interstitial osmolarity. This results in hypotonic fluid flows into DCT, isotonic fluid flows into the asc thick LOH. The final result is a gradient conc from the top to the bottom of the LOH & **a gradient hyperosmolarity in the medulla interstitium.** b) **Vasta recta as countercurrent exchangers** in the kidney in which NaCl & urea diffuse out of the asc limb of the vessel & into the desc limb, while water diffuses out of the desc into the ascending limb of the vascular loop. As a result the solute remains in the medulla pyramid & maintain the interstitial conc.	 Countercurrent exchangers

Question 3: Renal regulation of sodium Ganong pp 709-10, 723-4	i) Where does sodium reabsorption occur in the nephron? ii) What are the mechanisms of sodium re-absorption in the nephron?	a) All parts of the nephron except thin part of the LoH (+Specify at least two of:) b) 60% **PCT primarily** by Na^+-H^+ exchange but also a range of cotransport (glc, Pi, AA, lactate) c) 30% thick ascending limb of LoH (Na^+-$2Cl^-$-K^+ cotransporter) d) 7% DCT LoH (Na^+-Cl^- cotransporter) e) 3% collecting ducts through Na+ channels (ENaC) • **Na/K ATPase active transport.** Moves (by gradient thus generated) across apical membranes from tubular lumen into cell via cotransport & exchanger proteins. Driven by active transport by Na-K ATPase (3Na/2K) from tubular cell into interstitium (mainly into lateral interstitial spaced)	Must get **bold** to pass.
	iii) What mechanisms in the kidney reduce sodium excretion? Prompt (if they get it ar**-about-t**) *What mechanisms in the kidney cause the body to retain sodium by reducing sodium excretion?*	Multiple regulatory mechanisms (reflects importance of Na as the prime determinant of ECF volume) • **Reduced GFR** • Increased tubular reabsorption ○ ↑**adrenocortical hormones esp. aldosterone** - act primarily on collecting ducts (activation of ENaC) ○ ↓ANP (inhibit ENaC) ○ AT-II (PCT) ○ [↓secretion of K^+ and H^+]	Must get **bold** to pass.

TOPIC: Renal regulation of K+ excretion _____ NUMBER:

OPENING QUESTION	**Describe how the nephron handles potassium.**	**COMMENTS**
POINTS REQUIRED	**1. K+ is freely filtered at the glomerulus (~600 mEq/day).** **2. Most is reabsorbed by active transport in the proximal tubule (~560 mEq/day).** 3. K+ is then secreted by passive diffusion into the tubular fluid in the distal tubule. 4. K+ is also generally passively secreted into the tubular fluid in the collecting ducts. 5. The total K+ excretion is approximately equal to K+ intake (~90 mEq/day) and K+ balance is maintained. 6. There is no direct exchange of K+ for Na+ in the tubular fluid of the distal nephron. However reabsorption of Na+ into the tubular cell tends to promote secretion of K+ (or H+) to maintain the potential difference across the apical membrane.	Bolded + at least one other
PROMPTS		
SECOND QUESTION (if needed)	**What factors influence this?**	
POINTS REQUIRED	**1. The rate of secretion of K+ is proportional to the rate of flow of tubular fluid through the distal nephron. With rapid flow the concentration of K+ in the fluid remains lower and secretion continues.** 2. Increased delivery of Na+ to the collecting ducts promotes increased secretion of K+ (e.g. thiazide diuretics). 3. Conversely decreased delivery of Na+ to the collecting ducts promotes decreased secretion of K+. 4. Inhibition of K+ absorption in the proximal nephron (e.g. osmotic or loop diuretics) promotes excretion of K+. **5. In the distal nephron K+ and H+ compete for secretion in association with reabsorption of Na+. Therefore in acidosis when H+ excretion is increased, K+ secretion is decreased.** **6. Aldosterone increases reabsorption of Na+ in the collecting ducts and thereby promotes K+ secretion.**	At least two of the three bolded

TOPIC: Tubular function _____ **NUMBER:** _____

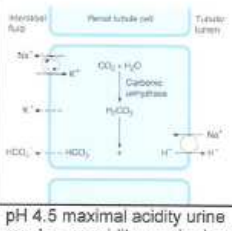
OPENING QUESTION	What factors influence clearance of substances by the kidney?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Amount of substance excreted = amount filtered + net amount transferred		Need 3.
	2 Changes in RBF and systemic BP		
	3 Active transport (primary and secondary)		
	4 Hormonal (aldosterone, angiotensin, endothelin)		
SECOND QUESTION	Explain the mechanism of tubuloglomerular feedback.		Explain feedback mechanism
POINTS REQUIRED	1 Increased rate of flow in LoH and DCT increases GFR and local Na^+		
	2 Macula densa adenosine A1 receptors activated by increased Na^+/K^+ activity, causing increased Ca^{2+}, vasoconstriction and decreased GFR		
	3 % solute reabsorbed remains constant (glomerulotubular balance)		

1.2 Renal regulation K^+ (Ganong pp 724)	How does the kidney handle potassium?	• K+ filtered ~600meq/24hrs • Active K+ reabsorption in prox tubules ~560meq/24hrs • K+ secretion ~502meq/24hrs at distal tubule – amount proportionate to flow rate through distal tubules • Secretion - Electrical coupling to Na+ reab, thus H+ also
	How do other ions affect potassium transport across the membranes in the nephron? Prompt: ***How is potassium transported into and out of the tubules?***	• Collecting tubules Na reab'd, K excreted, electrical coupling and passive K movement • Na reab'd in association with H secretion, K excretion decreased if Na low in distal tubule • Na/K 2Cl apical transporter/transport protein • 3Na/2K ATPase
3.2 Loop of Henle, structure & function Ganong pp 700, 714-718	Please outline the structure of the Lof H	• Thin/descending, Thick/ascending. Situated mostly in the renal medulla • **Origin from PCT** • Short (cortical) and long (juxta med.)loops • **Macula densa at distal end, where joins DCT**
	What happens to electrolytes in the loop	• **(Thin) Descending limb water permeable** • **Fluid becomes hypertonic as descends loop** • **(Thick) Asc limb impermeable to water, NaK Cl transported out, hypotonic at end, so K+ diffuses back** • **Active trans. ATPase**
	Explain the counter-current concentrating mechanism	• Gradient • Exchange (vasa recta)

3 a). What general mechanisms are involved in renal tubular reabsorption and secretion?	Mechanisms involved in re-absorption and secretion include **endocytosis, passive diffusion** and **facilitated diffusion** and **active transport.**	2 of **Bold** to Pass
3 b). How is Sodium reabsorped in the various parts of the nephron?	No sodium transport in Thin descending Loop of Henle. In rest of system, sodium moves by **co-transport, exchange** or down **concentration gradient.** **Sodium pumped out of cell by Active Sodium-Cl-Potassium pump in basolateral membrane.** **60% in PCT by Sodium-Hydrogen exchange.** 30% in thick ascending Limb via Sodium –Potassium co-transport. 7% in DCT via Sodium-Chloride exchange	**Bold** to pass, demonstrating reasonable understanding of different processes

Site	Apical Transporter	Function
Proximal tubule	Na/. . . . . CT	Na^+ uptake, . . . uptake
	Na^+/P_i CT	Na^+ uptake, P_i uptak
	Na^+ . . . . . CT	Na^+ uptake, ... uptake
	Na/lactate CT	Na^+ uptake, lactate uptake
	Na/H exchanger	Na^+ uptake, H^+ extrusi
	Cl/base exchanger	Cl^- uptake
Thick ascending limb	Na–K–2Cl CT	Na^+ uptake, Cl^- uptake, K^+ uptake
	Na/H exchanger	Na^+ uptake, H^+ extrusio
	K^+ channels	K^+ extrusion (recycling)
Distal convoluted tubule	. . . CT	Na^+ uptake, Cl^- uptake
Collecting duct	Na^+ channel (ENaC)	Na^+ uptake

Question 3: a) b)	**Describe how sodium is handled in the glomerulus and the PCT** **List the mechanisms that effect Na reabsorption**	**Most Filtered** out with solutes/ AAs (90%) **Most (60%)** Na-H counter-transport, **Bicarbonate** is main anion reabsorbed with Na Absolutely depends on Na K ATP ase (Basement M)/ C Anhydrase-tub cell to generate H+/ Bic Small co-transport with nutrients /anions/ Cl latter part Approx 60% 1)Tubulo-glom - Macula Densa,↑Na↑adenos/ Ca, aff vasocon 2)Glomer/tub balance- > filtered = > resorbed (good capacity)- mainly oncotic p in eff capillaries 3) Humeral Aldosterone- distal CT / ENaC, K+/H+ PGE2 – pron Na K ATP ase block/ Ca ++ > Ouabain endog- ATP ase block effect Endothelin and IL-1 cause natriuresis (prob > PGE2) ANP-↑ cGMP – less ENaC Angio 2- renal ACE ↑circ Ang 1 + renal -↑ PCT > reabs	NB – good candidates will volunteer Na resorbtion through out except TALH, 60/30/7/3 % - all Na excretion last 3% **Reqd :1 humeral / 1other**

Question 3a: Score:	**Discuss how and where H+ is secreted in the kidney?** **Prompt: how is Bicarbonate involved.**	Prox Na Bic co tranport Distal H+ ATPase H+/K+ (I cells) with large C Anh conc + Cl/ HCO3 BM exchanger 	Active secretion H+ (H+/Na+ co transport- 2ary active secretion), allows reuptake of HCO3- fromC anhydrase brush border_- H20/ CO2- Bic then into interstitium with Na via Na/K ATPase) Bic in cell transferred to Interstitium along gdt_ In DCT/ Coll ducts- Principle cells/ Aldo- have H+ ATPAse channels + H/K ATPAse linked to Bic/ Cl- exchanger in BM **PASS-FAIL must know 2 diff mechanisms, and mention bicarb**
3b:	**What is the limiting pH of urine and how is this limitation dealt with?**	pH 4.5 maximal acidity urine much > er acidity required excreted 3 major BUFFER systems H2CO3 (proximal), NH4+(throughout) and HPo4 (distal)	H+ load would be 100-100 x greater than max pH, Buffers all inc (partic H2CO3 and NH4 when acidotic)- NH4 via glutamate in interstitium, H2CO3 inc with H+ extra = >substrate + > C anh. HPO4 v concentrated in DCT

TOPIC: Renal sodium handling_____ **NUMBER:** _____

OPENING QUESTION	How does the kidney reabsorb filtered sodium?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Overview: a **2-step process**: [a] Co-transport or exchange from lumen into tubular epithelial cell down its concentration gradient [b] then actively pumped from cell to interstitium and lateral intercellular spaces by ***sodium/potassium ATPase at the basolateral part of the cell.***		Need the 1st 2 points and at least 3 examples. [JB]
	2. Sites involved: PCT, thick ascending loop, distal tubules and collecting ducts. Specific co-transporters or exchangers are as follows:		
	3. **PCT (60%): [5]** • Sodium/glucose co-transporter • Sodium/phosphate co-transporter • Sodium/amino acid co-transporter • Sodium/lactate co-transporter • ***Sodium/hydrogen exchanger***		
	4. **Thick ascending limb (30%): [2]** • Sodium/potassium/2 chloride cotransporter *(note that due to the action of the sodium/potassium/chloride cotransporter and sodium potassium ATPase, there is accumulation of **potassium** in the cell. Potassium diffuses out of the cell down its concentration gradient in exchange for magnesium or calcium)* • ***Sodium/hydrogen exchanger***		
	5. **DCT**: Sodium/chloride co-transporter		
	6 . **CD**: Sodium channel (sodium exchanged for potassium or hydrogen)		
SECOND QUESTION	How much filtered sodium is reabsorbed?		
POINTS REQUIRED	At least 99.4% [under normal conditions]		

TOPIC: *Regulation* of renal sodium handling_____ **NUMBER:** _____

OPENING QUESTION	Why is it important to regulate renal sodium handling?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Sodium is the most abundant cation in the ECF and accounts for over 90% of the osmotically active solute in the plasma and interstitial fluid	Why is sodium so important to the body?	At least 2 points are essential.
	2. It also underpins most of the activity of cells and their communication with interstitium, by its role [with K+] in maintaining electrical/concentration gradients.		
	3. In excess, it can harm the body esp via dehydration [short term] & HT [longterm]		
SECOND QUESTION	How does the kidney REGULATE sodium handling?		
POINTS REQUIRED	Multiple mechanisms, mainly via local and systemic hormonal mechanisms. There is a balance between hormones which increase & decrease Na uptake. **Here is summary:** 1. TG feedback 2. Balance between competing factors: • ↑ Na reabsorption by: aldosterone, ang II (ie the rennin-angiotensin-aldosterone system) • ↓ Na uptake from lumen [natriuresis] by: ANP, PGE2		
	1. Tubuloglomerular feedback: Macula densa cells in the ascending limb and DCT control GFR – as flow in the DCT rises, GFR falls.	Describe tubuloglomerular feedback.	
	Let's follow the steps if ↑ Na intake: ↑ Na intake → ↑ECF vol → ↑blood vol → ↑BP → vasa recta act as sensors and release adenosine → ↓stimulus on JG apparatus to secrete renin (via macula densa) → ↓renin-angioT-aldosterone → ↓renal **retention** of Na /H2O → BP & ECF volume return to normal		
	Aldosterone: causes **increased CD reabsorption** of sodium in association with secretion of potassium and hydrogen. • Acts on P cells in CD that contain epithelial sodium channels. • Also increases the **number** of sodium/potassium ATPase molecules in the basal membrane. • Small action in bladder.		
	Angiotensin II: increases reabsorption of sodium and bicarbonate by an action on the PCT.		

Question 3: Acid secretion & absorption in kidney Ganong pp 720-1	i) How is H+ ion secreted in the proximal tubule of the kidney?	a) **Secondary active transport** (The renal tubular cells secrete H^+ into the tubular fluid in **exchange for** Na^+; and for each H^+ secreted, one Na^+ and one HCO_3^- are added to the blood) b) Linked to **Na+/K+ ATPase**	
	ii) Outline the buffer systems that act to bind H+ ion in the tubular fluid	i) 3 systems – **HCO3, HPO4, NH3** ii) Major role of carbonic anhydrase/HCO3 system	To pass: 2/3, must have bicarbonate
	iii) What is the importance of H+ buffering systems in the urine ?	**Limiting pH (~4.5) would rapidly be reached unless free H+ is buffered**	

TOPIC: Micturition **NUMBER:**

OPENING QUESTION	**Describe the physiologic process of Micturition**	**COMMENTS**
POINTS REQUIRED	1 **A spinal reflex inhibited and facilitated by higher centres** Intravesical pressure rises only after 400mls urine in bladder **Anatomy: Detrusor m, int and ext urethral sphincters** **During micturition Detrusor contracts, and perineal muscles and EUS relax.**	
	2.Nerve Supply **Parasympathetic (S 2,3,4,) via pelvic nn (afferent and efferents) to/from detrusor (efferent contraction) and pudendal nn to EUS (relaxation)** **Sympathetic** (L1,2,3) – Hypogastric nn via Inf Mesenteric Ganglion play no role in active micturition per se but role in prevention. (cause contraction of bladder muscle to prevent reflux of semen into bladder during ejaculation)	
	4. Initiation – remains unsettled, pelvic floor muscle relaxation initiates. Perineal muscles and EUS can be contracted voluntarily for prolonged periods. Bladder SM has intrinsic contractile activity Post urination, female urethra empties by gravity. Male expels by contraction of bulbocavernosus m	(optional/extra detail)
PROMPTS	What muscles and nerves are involved?	
SECOND QUESTION (if needed)	**List other factors that stimulate and inhibit micturition**	
POINTS REQUIRED	**1. Stimulants –** **a) Stretch/pressure** (intravesical volume > 400mls) **b) Higher centre input** **c) Parasympathetics** (eg organophosphates) **d) Sympathetic inhibiting drug**(eg a-blockers) **e)**Voluntary abdominal muscle contraction augments stream but does not initiate micturition per se	**(3 of 5 to pass)**
	2. Inhibitors **a) Parasympathetic inhibitors (atropine)** **b) Higher centres** **c) Sympathomimetics**	**(b) + one other**
PROMPTS	a) What is the effect of autonomic agents on micturition ? b) What non autonomic precipitants and inhibitors do you know?	(optional)

2.2 Renal blood flow Ganong pp 702-705	What is a typical value for renal blood flow in an adult at rest?	**~25% of cardiac output or 1250 ml/min**
	What factors regulate renal blood flow?	**Chemical**: (**3 of 5**) Noradrenaline constricts interlobular and afferent arterioles. Dopamine causes renal vasodilation. Angiotensin II constricts efferent arterioles to a greater extent than the afferent arterioles. Prostaglandins increase blood flow in the cortex and decrease blood flow in the medulla. Acetylcholine produces renal vasodilation. **Neural**: Strong stimulation of the sympathetic nervous system produces renal vasoconstriction. **Autoregulation**: Direct contractile response of smooth muscle of afferent arteriole to stretch. NO may be involved. **At low perfusion pressures angiotensin II plays a role in constricting efferent arterioles.**

TOPIC: The factors in the control of renal blood flow ____ **NUMBER:** _

OPENING QUESTION	What determines renal blood flow?	**PROMPTS**
POINTS REQUIRED	Systemic blood pressure	
	Renal vascular resistance, which is in turn influenced by:	
	Catecholamines (nerves & systemic)	
	Angiotensin II (JG cells -> renin)	
	Prostaglandins	
	Control systems:	
	Renal autoregulation (myogenic-stretch response, vasodilator metabolites, ?NO, ?prostaglandins)	What control systems influence renal blood flow?
	JG apparatus	
	Renal sympathetic nerves	
SECOND QUESTION (if needed)	What are the consequences of a sustained reduction of renal blood flow?	
POINTS REQUIRED	(Renal blood flow maintained MBP >70)	
	Medulla is vulnerable to hypoxia (high MR)	
	ATN	
	Uraemia	

Please describe how the urinary bladder empties Prompt ; Could you describe the relationship between pressure and volume in the bladder as it relates to bladder emptying	1)Smooth muscle of the bladder is arranged in spiral, longitudinal, and circular bundles 2)Contraction of the circular muscle, **(detrusor muscle),** is mainly responsible for emptying the bladder during urination ** 3)Micturition is fundamentally a **spinal reflex** facilitated and inhibited by higher brain centers and, like defecation, subject to voluntary facilitation and inhibition ** 4)Urine enters the bladder without producing much increase in intravesical pressure until the viscus is well filled 5) The bladder muscle has the property of plasticity; when it is stretched, the tension initially produced is not maintained 6) The curve shows an initial slight rise in pressure when the first increments in volume are produced; a long, nearly flat segment as further increments are produced; and a sudden, sharp rise in pressure as the micturition reflex is triggered 7) The first urge to void is felt at a bladder volume of about 150 mL, and a marked sense of fullness at about 400 mL. 9) The flatness of segment Ib is a manifestation of the law of Laplace which states that the pressure in a spherical viscus is equal to twice the wall tension divided by the radius. In the case of the bladder, the tension increases as the organ fills, but so does the radius. Therefore, the pressure increase is slight until the organ is relatively full	2 3 11 Basic understanding the process in an organised fashion

	. 11) **During micturition, the perineal muscles and external urethral sphincter are relaxed; the detrusor muscle contracts; and urine passes out through the urethra. **** 12)The mechanism by which voluntary urination is initiated remains unsettled. One of the initial events is relaxation of the muscles of the pelvic floor, and this may cause a sufficient downward tug on the detrusor muscle to initiate its contraction. 14)The perineal muscles and external sphincter can be contracted voluntarily, preventing urine from passing down the urethra or interrupting the flow once urination has begun.	
Describe the reflex control associated with voiding	1)The bladder smooth muscle has some inherent contractile activity; however, when its nerve supply is intact, stretch receptors in the bladder wall initiate a reflex contraction that has a lower threshold than the inherent contractile response of the muscle. **2)Fibers in the pelvic nerves are the afferent limb of the voiding reflex, and the parasympathetic fibers to the bladder that constitute the efferent limb also travel in these nerves. **3)The reflex is integrated in the sacral portion of the spinal cord. **4) In the adult, the volume of urine in the bladder that normally initiates a reflex contraction is about 300–400 mL. **5) The sympathetic nerves to the bladder play no part in micturition, 6) They do mediate the contraction of the bladder muscle that prevents semen from entering the bladder during ejaculation	Parasympathethetic reflex Sacral portion of cord Vol to trigger 300 – 400mls