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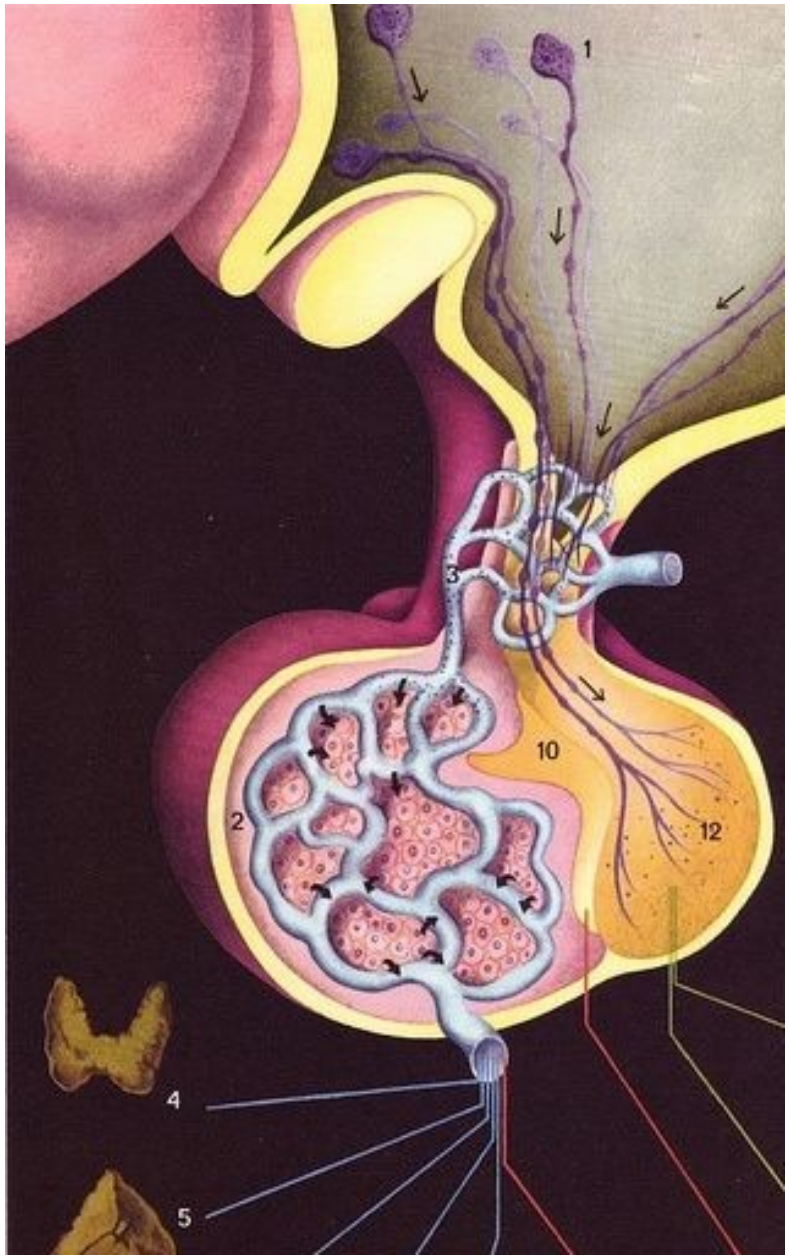


Adrenal Medullary Hormones 2014-1-A

Stem: We are moving to Physiology. She is shocked			
Question 3 Circulatory Catecholamines **Subject:** Phys LOA: 1	1. Name the endogenous catecholamines? Where are they produced? (prompt to match catechol with source) 2. What are the physiological effects of adrenaline and noradrenaline?	**Adrenal Medulla: Adrenaline, Noradrenaline**, Dopamine. Intrinsic Cardiac Adrenergic Cells: Adrenaline. Sympathetic Nervous System Cells: Dopamine **Metabolic**- Glycogenolysis, increased metabolic rate, mobilisation of free fatty acids, increased lactic acid Cardiovascular- **vasoconstriction and dilation, increase heart rate and strength** α1:Constriction of blood vessels, smooth muscles (esp norad) α2:Mixed smooth muscle effects (esp adren) β1:Cardiac ionotropy and chronotropy, irritability (both) β2:Dilation blood vessels liver & muscle, other smooth muscle relaxation (adrenaline) β3: Lipolysis, detrusor relaxation (esp adren)	Bold One metabolic and bold cardiovascular Extra info only

Adrenal Medullary Hormones 2006-1

TOPIC: Adrenal medullary hormones **NUMBER: 4**

OPENING QUESTION	What hormones are secreted by the adrenal medulla?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	Adrenalin, noradrenalin and dopamine. *Must have all 3*		
SECOND QUESTION (if needed)	What are the major effects of these hormones?		
POINTS REQUIRED	1. α and β effects 2. increase HR and force contraction, vasoconstriction, hypertension, alertness, metabolic rate, glycogenolysis **Must describe at least 5 effects**		

Adrenal Medullary Hormones 2004-2

TOPIC: Adrenomedullary hormones_____ **NUMBER:** _____

OPENING QUESTION	How do the effects of noradrenaline and adrenaline differ on the cardiovascular system?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 BP: norad; ad	1	
	2 HR: norad; ad	2	
	3 CO: norad; ad	3	
	4 TPR: norad; ad	4	
	5	5	
	6	6	
	7	7	
	8		
SECOND QUESTION (if needed)	How do the effects of adrenaline differ with serum concentration?		
POINTS REQUIRED	1Low concentrations – some beta effects, high concentrations alpha predominates	1	
THIRD QUESTION (if needed)			
POINTS REQUIRED	1	1	
	2	2	
	7		

Aldosterone 2010-2

Question 3 Mineralocorticoids	(a) What is the physiological role of aldosterone (b) What conditions increase aldosterone secretion?	(a) **Aldosterone causes Na+ and water retention, expanded ECF volume and shutting off the stimulus to increased renin secretion**. (b) Primary: – stress hormone, low pressure/volume states secondary hyperaldosteronism: (eg. CCF, cirrhosis & nephrosis). Drugs:	Bold to pass To Pass: Primary and secondary

Aldosterone 2009-2

Question 5:a	**Describe the typical serum / urine effects in hyperaldosteronism**	Na/ Cl mild ↑, fluid retention (follows Na), ↓K, alkalosis (alkalaemia only if K+ depletes) Urine K+/ H↑	**Na +/ Cl- mild rise in serum + fluid retention** **K+ <, mild alkalosis/ alkalaemia** **Why: Na + retained/ but drags fluid into ECFV01 (dilutes) + Na+ excretion >– escape phenomena** **C1 –retention with Na+.** **K+ depletion – K+ diuresis* (due to effect of aldosterone)** **H+ lost in urine - ↑ urinary acidity*, H+ loss in serum- only seen if K+ depletes and rely on H+ excretion**
5b	**How does aldosterone exert its effects in the kidney?**	Mineralocorticoid- Via Principal cells- collecting ducts, 2 effects 1) Genomic- Intracellular to nuc signalling > mRNA – a) Inc ENAC insertion/ activity (quick) b) > production (slow) 2) membrane bind IP3 mediated Na/K exchange > All = > Na reabsorb K/H loss to urine	**Is a medullary mineralo corticoid.** **Acts on P(rinciple cells ?) cells in collecting duct* (** **↑ reabsorption of Na+ and ct from urine in exchange for K+ and H+ causing ↑ pH and K+ diuresis.** **Action takes 10-30 minutes to develop and peaks later*** **Aldosterone – cytoplasmic receptor complex moves to nucleus where it alters transcription of mRNA.** **This now has 2 effects:** **1 Rapid - ↑ activity (+insertion*) of preformed/ active EpithNaChannels s, via activation of genes for SGK** **2 slower* - ↑ synthesis of ENaCs. There is a non genomic action. ↑ activitiy of the Na+ K+ exchangers via IP3 - ↑ intracellular Na+**

Aldosterone 2008-2

TOPIC: Aldosterone synthesis/effects/feedback loop____ NUMBER: _____

OPENING QUESTION	**Describe the actions of Aldosterone.**	**COMMENTS**
POINTS REQUIRED	1. **increase reabsorption of Na^+ from urine** **Acts on principal cells (P cells) of collecting ducts, leading to increased amounts of Na^+ exchanged for K^+ and H^+ in renal tubules, producing a K^+ diuresis and fall in urine pH.**	Aldosterone cause retention of Na^+ in ECF leading to ECF volume expansion
	2. increase reabsorption of Na^+ from sweat, saliva and colon	
PROMPTS		
SECOND QUESTION (if needed)	**List the stimuli that increase aldosterone secretion**	
POINTS REQUIRED	**1. ACTH from pituitary**	1, 2 and two others at least
	2. renin from kidney via angiotensin II	
	3. direct stimulatory effect of rise in plasma K^+ concentration on adrenal cortex	
	4. Clinical causes: Surgery Anxiety Physical trauma Haemorrhage High K intake Low Na intake Standing Constriction of IVC in thorax 2^0hyperaldosteronism (eg CCF, cirrhosis, nephrosis)	
PROMPTS		
THIRD QUESTION (if needed)	**Describe the feedback regulation of aldosterone secretion.**	via **renin-angiotensin** system feedback loop.
POINTS REQUIRED	1. Fall in ECF / blood volume → reflex increase in **renal nerve discharge & decrease in renal artery pressure**	Bolded
	2. → increase in **renin** secretion → increase in **angiotensin II** → increase in aldosterone secretion	
	3. → Na^+ & water retention → expanded ECF volume → decrease in stimulus that initiated renin secretion	
PROMPTS		

COMMENTS

Aldosterone 2007-1

OPENING QUESTION	Describe the effects of increased aldosterone	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Increased reabsorption of Na^+ from urine, sweat, saliva and colonic contents		3/5 to pass
	2 Na^+ retention in ECF		
	3 K^+ diuresis and depletion		
	4 Hypertension		
	5 ECF volume expansion		
SECOND QUESTION	List factors that increase aldosterone secretion?		
POINTS REQUIRED	1 Haemorrhage / physical trauma / ECV contraction / surgery		3 to pass
	2 Anxiety		
	3 Low Na^+ intake		
	4 High K^+ intake		
	5 Constriction of IVC in thorax		
	6 Secondary hyperaldosteronism (CCF, cirrhosis, nephrosis)		
THIRD QUESTION	How is aldosterone secretion regulated?	Biochemical factors	
POINTS REQUIRED	1 ACTH from the pituitary		
	2 Renin from kidney, via angiotensin II		
	3 Direct stimulatory effect of K^+ on adrenal cortex		

Aldosterone 2003-2

TOPIC: Aldosterone secretion _____ **NUMBER:** _____ 3c

OPENING QUESTION	**What are the main regulatory factors for aldosterone secretion?**		
POINTS REQUIRED	1 **Renin-angiotensin system**	1	**Must have to pass**
	2 **ACTH**	2	**Must have to pass**
	3 **Rise in plasma K concentration** (via the adrenal cortex)	3	**Must have to pass**
SECOND QUESTION	Describe the actions of aldosterone		
	4	4	
	6	6	
	7		

Glucocorticoids 2015-1-A

Stem: Moving onto Physiology. The child appears very unwell.			
Question 4 Effects of Glucocorticoids **Subject:** Physiol LOA: 1	What are the physiological effects of glucocorticoids?	Permissive action – **catecholamine effects – pressor / vascular reactivity**; bronchodilation **Metabolic** - Increase protein catabolism; increase hepatic glycogenolysis and gluconeogenesis -> increase in plasma glucose; anti-insulin effects on peripheral tissues; increase lipolysis. Free water excretion (decreased vasopressin) Immunological – decreased inflammation/ allergic response/ lymphocyte activity Haematological – increase neutrophils/ platelets/ red blood cells CNS – EEG slowing, personality changes	Bold + 2 metabolic + 1 other
	How is glucocorticoid secretion regulated?	**Glucocorticoids** (cortisol) - **secreted from the adrenal cortex**; secretion **dependant on ACTH secretion** from the **anterior pituitary** ACTH secretion is regulated by CRH released from the hypothalamus (in response to low cortisol levels or stress) **Glucocorticoids** provide a **negative feedback loop on the hypothalamus and the anterior pituitary** to **reduce ACTH secretion**	Bold

Glucocorticoids 2013-2-B

Question 2 PHYSIOLOGY LOA: 1	Question 2 - Physiology 1. List the physiological effects of glucocorticoids	a) **Inc protein catabolism.** b) Inc hepatic glycogenolysis and gluconeogenesis, inc Glu-6-phosphatase → **inc plasma glucose** c) Antiinsulin effects on peripheral tissues d) Inhibit ACTH secretion e) **Controls vascular reactivity to NAd and Ad** f) Control ability to excrete water load g) Increased neutrophils/ plts/ RBC and dec eosinophils/ lymphocytes/ basophils	2 bold and 2 others
	2. What are the vascular effects of abruptly stopping long term glucocorticoids?	Vascular smooth muscle becomes **unresponsive to NAd and Ad** Capillaries dilate and inc permeability Failure to respond to NAd **impairs vascular compensation** for hypovolaemia and promotes **vascular collapse**	Must have general concept
	Bonus: What is the benefit of elevated glucocorticoid levels in stress?	Effect on **vascular activity to catecholamines** plus necessary for catacholamines to mobilise **FFA** for emergency energy source	

Glucocorticoids 2013-1

Question 4 Glucocorticoids LOA: 1	a. What are the physiological effects of glucocorticoids? Prompt: "Can you expand on non-vascular effects"	1. Essential for survival stress response 2. 'Permissive action' for **catecholamine effects: pressor/ vascular reactivity,** bronchodilation, calorigenesis, lipolysis **3. Metabolic**: protein catabolism, hepatic glycogenesis & gluconeogenesis. Rise in plasma glucose + peripheral anti-insulin effect. Increase plasma lipids. 4. Permit 'free water' excretion: plasma tonicity 5. Immunological: Decrease inflamm + allergic responses. Reduced lymphocytic activity, lymph tissue, cytokines 6. Haematological: increased neutrophils, RBC, platelets. Decreased basophils, eosinophils 7. Mental: EEG slowing, personality changes	**Must get bold, at least 2 metabolic + 1 other**
	b. How is glucocorticoid secretion regulated?	**Released adrenal cortex in response to ACTH from ant pituitary.** ACTH release driven by CRH from hypothalamus (response to low corticoid level or stress) **Glucocorticoid –ve feedback on hypothal/ pit to reduce ACTH secretion**	Must get **bold.**

Glucocorticoids 2010-1

4. What are the physiologic effects of the glucocorticoids?	1. Intermediary metabolism of carbohydrate, protein, fat* 2. Inhibit ACTH secretion* 3. Maintain reactivity of vascular (and bronchial) smooth muscle to catecholamines* 4. Allow excretion of a water load (mechanism unclear) 5. Blood - ↑ RCC, ↑ WCC (mainly PMNs), but ↓ Lymphocites and Lymph node size 6. CNS – irritability, apprehension, inability to concentrate (eg in exams) 7. "stress response" (Up to 3 specific prompts, eg "what are the vascular effects of glucocorticoids?")	3 asterisked

Glucocorticoids 2008-1

2.4 Glucocorticoids Ganong pp 372-380	What are the physiological effects of glucocorticoids?	• **Metabolic;** increased protein catabolism, increased hepatic glycogenesis and gluconeogenesis (raised plasma glucose). Raise peripheral tissue insulin resistance • Permissive effects on other reactions • Are required for catecholamines to produce **calorigenic and lipolytic** effects, **pressor responses** (vascular reactivity) and vasodilatation • Inhibit ACTH secretion (feedback) • Impair water excretion (mechanism unclear) • Reduce circulating basophils and eosinophils and increase other elements • Required for stress response • Affect EEG waveforms (mild personality changes in insufficiency)	
	How is glucocorticoid secretion regulated?	• Basal secretion and stress response both dependent on **ACTH** • (Other substances may stimulate adrenal directly but no evidence of role in physiologic regulation) • Free glucocorticoids produce negative feedback on ACTH secretion at both hypothalamic and pituitary levels. Effect mediated by action on DNA • Stress response ACTH secretion mediated almost exclusively via hypothalamic release of corticotrophin releasing hormone • **Circadian rhythm.** ACTH released in irregular bursts throughout day but much more common in early morning. 75% of cortisol secreted at this time	/2

Glucocorticoids 2005-2

3.5 Physiology of glucocorticoids	What are the effects of glucocorticoids. How are they metabolised? How are they controlled?	Action on intermediary metabolism of carbo, proteins, fats. Permissive action for glucagon, catecholamines – calorigenic, lipolytic, pressor, bronchodilator, vascular reactivity. CNS vs irritability, apprehension, inability to concentrate. Renal – excretion of water by increased GFR. Anti-inflammatory vs cytokines. Resistance to 'stress' – noxious stimuli increasing ACTH. Cortisol liver, conjugated to glucuronic acid; inactivation depressed by liver disease	5/

Calcium Regulation 2014-2-B

Stem: We will now move on to Physiology. She has a raised corrected calcium level.			
Question 2 Calcium metabolism (pp 377-378) **Subject**: Phys LOA: 1	1. Where in the body is Ca2+ stored?	**Bone**: 99%, **Plasma – bound to protein**, **Plasma – unbound (free/ionised)** - important second messenger and is required for coagulation, nerve function and muscle contraction.	Bold to pass
	2. How is the plasma Ca2+ level regulated? Prompt: What hormones increase or decrease plasma Calcium?	**Parathyroid Hormone**: Increases plasma Ca2+ by mobilising Ca2+ from bone. Increases Ca2+ reabsorption in kidney. Increases formation of 1,25 DHCC in the kidney. **1, 25 DHCC** (from Vit D) increases Ca2+ absorption from intestine and kidneys. **Calcitonin** (from thyroid) lowers circulating Ca2+ levels. Effect by inhibition of bone reabsorption. It also increases Ca2+ excretion in urine Glucocorticoids – decrease plasma Ca2+ by inhibition osteoclast formation and activity. Oestrogens – inhibit stimulatory effects of cytokines on osteoclasts Growth Hormone – increases Ca2+ excretion in urine & absorption in intestine. Net balance may be positive. Hypercalcaemia is a complication of cancer. Raised Ca2+ from either: - bone erosion (local osteolytic hyperCa2+ - elevated Parathyroid hormone related protein (PTHrP)	Bold and their effects on plasma Ca2+ (increase / decrease)
	3. How does bone resorption occur	**Osteoclasts** are monocytes that develop from stromal cells under influence of RANKL. • Attach to bone via integrins in sealing zone of the membrane. • Hydrogen dependent proton pumps move into cell and acidify the area. • Acid dissolves hydroxyapatite and acid proteases break down collagen. • Products move across osteoclast into interstitial fluid.	Osteoclasts + 1 other RANKL – receptor activator of nuclear factor kappa B ligand

Calcium Regulation 2010-2

Question 4 Regulation of serum calcium level	a. What hormones are involved in serum calcium regulation Outline the effects of PTH (Parathyroid Hormone)	**PTH, Calcitonin, 1,25 DHCC** ↑ Parathyroid hormone secretion **A** Kidneys - ↑Calcium reabsorption ↑ 1,25- (OH)2D formation ↓ Urinary excretion of Calcium ↑ Plasma 1,25- leads to (OH)2D levels cause – **B** Intestine - ↑ Calcium absorption **C** Bone – ↑ Resorption ↑ Release of Ca 2+ into plasma	To Pass 2 of 3 **<u>Additional</u>** To Pass: 1 of each

Calcium Regulation 2009-2

Question 5:	**What are the actions of the parathyroid hormone on Calcium?** **What are the other effects of PTH?**	PTH- 1. ↑ plasma Ca^{++} by: ↑ Ca^{++} mobilization ↑ bone reabsorption, ↑ Ca^{++} reabsorption in distal tubule and (3) Ca reabsorption 2. ↓ plasma phosphate: ↓ PO_4 reabsorption in proximal tubules 3. ↑ 1,25 dihydrocholecalciferol: renal (> Ca absorption) 4. Over a longer time: ↑ osteoblastic *and* osteoclastic stimulation- prob anabolic	Pass: Ca ++ ↑ PO4 ↓ + some idea of how these achieved OR additional other mechs Parathyroid related hormone- (prob fetal/ cartilage growth + teeth/ breast- skin) ? **PO4 < +1 other in either section**

Calcium Regulation 2009-1

Question 4: Regulation of plasma calcium levels. Ganong pp 382-95	i) How plasma calcium levels are regulated? Prompt: What increases or decreases plasma calcium?	a) **1,25-Dihydroxycholecalciferol (from Vit D)** incr Ca absorption from gut and kidneys. b) **Parathyroid hormone** mobilizes Ca from bone. c) **Calcitonin** (from thyroid) inhibits bone resorption. Glucocorticoids, GH, oestrogens and others also effect Ca. 95% in bone (some readily available). In plasma, some bound and some free (depends on plasma protein levels and pH). Incr phosphate decr Ca.	Need to list all 3 and discuss its effect on Ca (inc or dec).
	ii) Describe the regulation of parathyroid hormone levels. Prompt: What stimulates production of parathyroid hormone?	i) **Negative feedback** by Ca via a membrane Ca receptor and G protein. 1,25-Dihydroxycholecalciferol acts to decrease preproPTH mRNA. Incr phosphate incr PTH by decr Ca and 1,25 DHCC. Mg required for PTH secretion.	

Calcium Regulation 2008-
1

3.5
Regulation of calcium
Ganong pp 383-395
	What factors influence the level of free calcium in plasma?	• Protein binding - depends on plasma protein level and pH.
		• Total body calcium
		  ○ bound in bone; bone calcium readily exchangeable or slowly exchangeable (resorption / deposition)
		  ○ Intake
		  ○ GI absorption under influence of vitamin D
		  ○ Renal excretion under vitamin D influence
		  ○ Parathyroid hormone
		  ○ Calcitonin	

	How does bone resorption occur?	• Osteoclasts are monocytes that develop from stromal cells under influence of RANKL. • Attach to bone via integrins in sealing zone of the membrane. • Hydrogen dependent proton pumps move into cell and acidify the area. • Acid dissolves hydroxyapatite and collagen. • Products move across osteoclast into interstitial fluid.	/2

Calcium Regulation 2006-1

TOPIC: Calcium metabolism **NUMBER: 5**

OPENING QUESTION	Name the principal hormones associated with regulation of Ca metabolism	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. 1,25 dihydroxy cholecalciferol 2. Parathyroid hormone 3. Calcitonin		Need 2 to pass
SECOND QUESTION (if needed)	Describe the action of parathyroid hormone.		
POINTS REQUIRED	PTH- reabsorption of Ca from Bone; increase urine Phosphate excretion. Increase formation of 1,25 dihyrdroxycholecalciferol --> incre Ca absorption in GIT. Increased PO4 stimulate PTH prod'n by lowering serum Ca and inhibit form of 1,25 DIHYDRO		Need 2/3
THIRD QUESTION (if needed)	Describe the action of 1, 25 dihydroxycholecalciferol & calcitonin.		
POINTS REQUIRED	1,25 dihydrox –increase Ca and Phosphate absorption from intestine via calbindin proteins, Also Increase Ca reabsorption in Kidneys, increase synthetic activity of osteoblasts, necessary for normal Ca of bony matrix.		Need 1 point to pass
	Calcitonin- inhibits bone resorption (inhibits osteoclastic activity) → lowers serum Ca AND PO4 levels. Increases Ca excretion in urine. Parafiollicular cells.	Only if doing well.	

Calcium Regulation 2004-2

TOPIC: Calcium metabolism_____ **NUMBER:** _____

OPENING QUESTION	Discuss the hormonal control of calcium metabolism.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 1, 25 DHC, inc uptake (gut and renal)	1 What are the three hormones involved?	
	2 PTH, inc reabsorption from bone	2	
	3 Calcitonin, dec reabsorption from bone	3	
	4	4	
	5	5	
	6	6	
SECOND QUESTION (if needed)	What are the secondary hormones involved?		
POINTS REQUIRED	1 GH, inc gut reabsorption	1	
	2 Glucocorticoids, inc bone reabsorption	2	
	3 Oestrogens, inhibit osteoclasts	3	
	4	4	
	5	5	
	6	6	
	7		
THIRD QUESTION (if needed)	How does a high calcium affect the mechanism you just discussed?		
POINTS REQUIRED	1 Decreased 1,25 DHC	1	
	2 Decreased PTH	2	
	3	3	
	4	4	
	5	5	
	6	6	
	7		

Parathyroid Hormone 2011-2

Question 5 LOA: 2	1)Describe the role of parathyroid hormone in calcium metabolism.	• Directly increases bone resorption and mobilises Ca^{2+} causing increased serum calcium. • Directly increases Ca^{2+} reabsorption by the distal renal tubules although increased filtered Ca^{2+} may cause increased excretion. • Indirectly increases gut absorption of Ca^{2+} by increasing formation of 1,25-dihydrocholecalciferol.	2/3 bullet points to pass
	2)How is parathyroid hormone secretion regulated?	• Serum Ca^{2+} exerts negative feedback on PTH secretion via a membrane Ca^{2+} receptor. • Serum PO_4^{2-} exerts negative feedback on PTH secretion by decreasing Ca^{2+} and via a membrane Ca^{2+} receptor. • 1,25-dihydrocholecalciferol acts to decrease preproPTH mRNA. • Increased phosphate increases PTH by decreasing Ca2+ and 1,25-dihydrocholecalciferol. • Mg^{2+} is required for PTH secretion.	Three of five bulleted points to pass

Vitamin D 2008-1

1.5 Vitamin D Ganong pp 387-388	What are the actions of vitamin D?	**(3 of 4)** • Increased absorption of calcium from the intestine by induction of calbindin-D proteins. • Increased resorption of calcium in the kidneys. • Increased osteoblast activity. • Aids calcification of bone matrix.	
	How is the synthesis of vitamin D regulated?	**(3 of 5)** • Not closely regulated. • Low calcium leads to increased PTH secretion and increased vitamin D is produced. • High calcium inhibits PTH and the kidneys produce inactive metabolites. • Low phosphate increases vitamin D production (and high phosphate inhibits it). • Vitamin D inhibits the enzyme involved in its synthesis.	/2

Blood Glucose Level 2011-2

Question 4 LOA: 2	1) What factors determine the plasma glucose level? 2) Explain how the blood glucose is maintained during fasting.	Dietary intake Rate of entry into cells (Muscle, adipose tissue, other organs) Glucostatic activity in liver **fasting** Liver glycogen broken down-glucose released into bloodstream. **Prolonged fasting** Glycogen depleted – increase gluconeogenesis from glycerol and amino acids in liver	2/3 to pass 2/2 to pass

Glucagon 2012-1

Question 4 LOA: 1	4.1 What factors stimulate glucagon release?	**Hypoglycaemia**; increased sympathetic drive to pancreas; vagal stimulation; protein load; amino acids oral or IV infusion; exercise; stress; starvation; CCK; gastrin; cortisol; theophylline.	Must give hypoglycaemia + 2 others
	4.2 What are the physiological effects of glucagon?	**Gluconeogenesis**; glycogenolysis (not in muscle); lipolysis; ketogenesis; calorigenic – through hepatic deamination of amino acids; +ve inotropic effect in large doses; stimulates secretion of GH, insulin and pancreatic somatostatin.	Gluconeogenesis + 1 others

Glucagon 2010-2

Question 4 Glycogen	1) What are the physiologic actions of glucagon?	• Glycogenolysis in liver – not muscle • Gluconeogenesis from aa's only at very high levels • Lipolysis – • Ketogenesis • +ve inotropic effect on heart • Inc blood flow to kidneys • • Stimulates secretion of GH, insulin and somatostatin	3 bulleted – essential to pass. Rest additional –3 to pass from each Rest additional
	2)What factors affect glucagon secretion?	**2)Stimulators** beta adrenergic stimulants Cortisol, protein meal,vagal stimulation, starvation,stress, exercise CCK gastrin theophylline **Inhibitors** Glucose ----most important,nsulin Somatostatin FFA Ketones α Adrenergic stimulators. GABA Phenytoin	

Glucose Homeostasis 2014-1-C

Stem: An 80 year old woman presents with a diabetic foot ulcer. We start with physiology.

TOPIC	QUESTIONS	KNOWLEDGE (essential in bold)	NOTES
Question 1 Glucose homeostasis (Ganong 24th ed pp 431-432, 433-434, 441-442, 444-445) **Subject:** Phys LOA: 1	1.1 What factors determine glucose homeostasis?	**1.1** Glucose absorption from **intestine** Glucose **uptake** in the **periphery** - muscle, brain, fat, red cells and **liver** Reabsorption in **kidney** **Gluconeogenesis** in liver (Insulin and Glucagon)	1.1 Name at least 3 mechanisms
	1.2 What happens to glucose homeostasis in the absence of insulin?	1.2 Hyperglycaemia due to a) **decreased peripheral uptake** of glucose into muscle and fat (direct effect) b) **reduced glucose uptake by liver** (indirect effect) c) **increased glucose output** by the liver and lack of glycogen synthesis (GIT, renal, brain and red cells glucose uptake unaffected)	1.2 2 out of 3 mechanisms
	1.3 What effect does glucagon have on blood glucose?	1.3 Increase BSL due to increased glycogenolysis and increased gluconeogenesis in liver	1.3 know that glucagon increases liver glucose output

Glucose Homeostasis 2012-2

Question 4 LOA: 1 Blood glucose control (Ganong 23) 22-23, 326-332	4.1 What factors determine blood glucose level? (Prompt: what are the broad principles [rather than specifics?]) 4.2 How does exercise affect glucose levels? **PROMPT**: By what mechanism?	4.1 Balance between glucose entering & leaving bloodstream • dietary intake • entry into muscle, adipose tissue, other organs • glucostatic activity of the liver (GNG, glycogenesis, glycogenolysis) 4.2 Increased entry of glucose into skeletal muscle • **insulin-independent incr in GLUT 4 transporters in muscle cell membranes** • persists for several hours • regular exercise can -> prolonged incr in insulin sens Exercise in T1DM can ppt hypo also cos abs of injected insulin more rapid during exercise	4.1 All three (**intake, uptake, hepatic**) Hepatic GNG acceptable if only mention 1 other mech ?  4.2 Bold

Glucose Homeostasis 2005-1

Endocrine regulation of glucose homeostasis	Physiologically what are the acute consequences of insulin deficiency? Describe the biosynthesis of insulin Describe the structure of the insulin receptor	Intracellular glucose deficiency; extracellular excess; protein and fat catabolism B cells as a precursor hormone; insulin released from the cell with C peptide. 2 alpha and 2 beta glycoprotein subunits.	

Insulin 2011-1

Insulin Deficiency	4.1 What are the effects of insulin deficiency? PROMPTS: What are the effects on the liver? What are the effects on other tissues?	**Decreased Peripheral Utilisation** (uptake) of glucose **Hyperglycaemia** but low intracellular glucose Derangement of the glucostatic function of the liver Hyperglycaemia with no decrease in gluconeogenesis Secondary osmotic diuresis with dehydration Electrolyte and calorie loss Catabolism of protein & fat due to low intracellular glucose **Contributes to ketosis – acidosis** Breakdown of amino acids for energy Increased Free fatty acids from breakdown of triglycerides Secondary Acidosis, Coma, raised cholesterol	3 bold essential

Insulin 2010-2

Question 2: Insulin	(a) What metabolic effects does insulin have on the liver? B, What are the effects of insulin deficiency on the body over	(a) ↓ketogenesis; ↑protein synthesis; ↑lipid synthesis; ↓glucose output due to ↓gluconeogenesis, ↑glycogen synthesis, ↑glycolysis (b) 1. Decreased cellular glucose uptake – ; **total body dehydration and acidosis.**	2 to pass

Insulin 2010-1

2 a). What are the principal actions of insulin?	Storage of carbohydrate, prot and fat, varies with tissues Rapid- seconds. Glc, amino acids and K+ into insulin sens cells Intermediate- minutes. Stimulates prot synthesis, inhibits prot degradation, activates glycolytic enzymes & glycogen synthase, inhibits phosphorylase and gluconeogenic enzymes. Delayed- Hrs. increase in mRNA for lipogenic & other enzymes	Glc and K from rapid. 2 others Answer must reflect understanding of effects on carbohydrate, protein and fat
2 b) What happens when insulin binds to its receptor?	• Binds to a cell membrane-based stereospecific insulin receptor on insulin-sensitive cells • Insulin binding triggers tyrosine kinase activity of β subunits → autophosphorylation of β subunits on tyrosine residues • The above reaction → phosphorylation and de-phosphorylation of proteins that are effectors and secondary mediators.	Binding results in activation of secondary protein effectors (tyrosine kinase activity) and mediators (phosphorylation)
3 What are the factors which	a)Starling's Law (Theoretical Concept, exact values of pressures unknown)	

Insulin 2008-2

OPENING QUESTION	**What happens when insulin binds to an insulin receptor?**	**COMMENTS**
POINTS REQUIRED	1. Insulin receptor: tetramer - 2 α and 2 β glycosolated subunits α subunits extracellular + bind insulin; β subunits span membrane, intracellular parts have tyrosine kinase activity	
	2. Insulin binding triggers **tyrosine kinase** activity of β subunits → **autophosphorylation** of β subunits on tyrosine residues	2 of points 2 - 5
	3. → phosphorylation and de-phosphorylation of proteins	
	4. → **Effectors and secondary mediators** – Insulin receptor substrate (IRS-1);phosphoinositol 3-kinase (PI3K)	
	5. Once bound, insulin receptors aggregate in patches and are endocytosed → enter lysosomes → broken down or recycled;	
PROMPTS	What is the structure of an insulin receptor?	
SECOND QUESTION	**What are the principal actions of insulin?**	
POINTS REQUIRED	**Net effect: storage of CHO, protein and fat**	
	1. **Rapid (seconds):** ↑ transport of glucose, amino acids and K into insulin-sensitive cells	All 3
	2. **Intermediate (minutes):** stimulation of **protein synthesis** and inhibition of protein degradation; activation of **glycolytic** enzymes and glycogen synthase; **inhibition** of phosphorylase and **gluconeogenic** enzymes	
	3. **Delayed (hours):** ↑ mRNAs for **lipogenic**\other enzymes	
PROMPTS	What happens seconds, minutes and hours after insulin binds?	

COMMENTS

Insulin 2008-
1

3.4 Insulin & Glucose Ganong pp 336-340	Describe the effects of insulin on various tissues What is the time frame for these effects	• **Adipose:** glucose in, fatty acid + glycerol synthesis, TG deposition, K in • **Muscle:** glucose in, glycogen synthesis, Aas in, protein synthesis, ketones in, K in • **Liver:** glycogen, protein + lipid synthesis, • General: cell growth • **Rapid:** glucose, AAs, K into sensitive cells • **Intermediate:** protein synthesis, glycolysis and synthesis, inhibition gluconeogenesis • **Delayed:** lipogenesis	/2

Insulin 2006-1

TOPIC Insulin mechanism NUMBER: 4

OPENING QUESTION	What are the main effects of insulin?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. Increased glucose into cells (adipose, liver, muscle) 2. Protein synthesis 3. Glyogenolysis 4. K into cells	1	Need to know ¾ to pass
SECOND QUESTION (if needed)	What is the mechanism of action of insulin?		
POINTS REQUIRED	Insulin binds to insulin receptors on insulin sensitive cells, triggers autophosphorylation of the insulin receptor which is necessary for the insulin effects. There is receptor mediated endocytosis into the cell and the insulin-receptor complexes trigger cytoplasmic proteins to produce various other proteins. There are at least 4 insulin related substrate (IRS) proteins in cells.	1	*Must describe that insulin binds to receptor and is taken into cell where secondary mediators are formed*

Insulin 2003-1

TOPIC: Insulin secretion **NUMBER:**

OPENING QUESTION	What happens to the insulin secretion when a person is injected with 50ml of 50% Dx?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. It would go up	1	
SECOND QUESTION (if needed)	Describe the mechanism of insulin secretion.		
POINTS REQUIRED	1. The insulin is dumped from the beta cells of the Islets of Langerhans within 3-5 minutes followed by a plateau at 2-3 hrs by activation of the enzyme system	1	
	2. Glucose is metabolised by the glucokinase and this involve ATP, decrease potassium efflux and increase calcium entry into cells that cause release of insulin by exocytosis.	2	

ACTH 2012-1

Question 5	5.1 What is the main hormonal factor that stimulates the release of cortisol from the adrenal cortex?	Adrenocorticotropic hormone (**ACTH**)	
	5.2 What factors determine the rate of ACTH secretion?	**Increased by stress** (pain, emotional), drive for circadian rhythm through the hypothalamus via release of CRH (corticotropin releasing hormone) **Inhibited by circulating glucocorticoids** and afferent from baroreceptors	
	5.3 What happens to ACTH levels after prolonged treatment with high doses of glucocorticoids is stopped abruptly?	**Slowly increases over weeks** (the pituitary may not be able to secrete normal amounts of ACTH for as long as a month. Presumed to be secondary to diminished ACTH synthesis)	
	5.4 How can this be avoided?	This can usually be avoided by **slowly decreasing the dose over a long period of time.**	

ACTH 2006-2

TOPIC: ACTH – response to stress and feedback loops NUMBER: 5

OPENING QUESTION	Describe the changes in ACTH secretion that occur in response to stress?	**PROMPTS C**	**OMMENTS**
POINTS REQUIRED	**1 Increased ACTH secretion**	1	Pass = 2 bold plus 1
	2 mediated through hypothalamus by CRH	2	
	3 CRH produced in paraventricular nuclei, secreted in medial eminence and transported in portal hyperphysical vessels to anterior pituitary	3	
	4 Multiple nerve endings converge on paraventricular nucleii	4	
	5 Destruction of median eminence means stress response is blocked	5	
SECOND QUESTION (if needed)	What are the physiological consequences of sudden cessation of steroid therapy after prolonged treatment?		Pass = 3 bold plus 1
POINTS REQUIRED	**1 Low glucorticoid levels with inability to increase**	1	
	2 Prolonged exogenous glucocorticoid inhibits ACTH secretion **Normally a drop in resting corticoid levels stimulate ACTH secretion (feedback loop)** - inhibitory effect pituitary and hypothalamus due action on DNA - degree of pituitary inhibition proportional to level glucocorticoid - ACTH inhibiting activity of steroids parallels glucocorticoid potency		
	3 Adrenal atrophic and unresponsive	2	
	4 Pituitary unable to secrete normal amounts of ACTH for one month, probably secondary to decreased ACTH synthesis	3	
	5 After one month a slow rise in ACTH levels to supranormal levels, stimulates adrenal with increased glucocorticoid output. Feedback inhibition causes a gradual decrease in ACTH levels to normal	4	
	6 Avoid by tapering dose over long period	5	

Anterior Pituitary Hormones 2013-1

Question 4 Anterior Pituitary Hormones including insufficiency LOA: 1	a. What hormones are secreted by the anterior pituitary? b. What are the clinical effects of anterior pituitary insufficiency?	**TSH; ACTH;** Growth hormone; LH; FSH; Prolactin 1. Adrenal cortical atrophy: glucocorticoid + sex hormone levels fall. Mineralocort secretion maintained: salt loss/ hypovolaemic shock does not occur. But unable to mount stress response. 2.Hypothyroidism; 3.Growth inhibition 4.Gonadal atrophy, sexual cycles cease, loss of some secondary sex characteristics 5.Tendency to hypoglycaemia (increased insulin sensitivity)	Bold + 2 other Pass: Adrenocortical effects + 2 other

Pituitary Hormones 2005-1

Pituitary hormones	What hormones are produced by the pituitary? What are the physiologic effects of vasopressin?	Knowledge of anterior and posterior pituitary with 4 of 6 of the anterior pituitary (TSH, ACTH, GH, FSH, LH, prolactin) and one of vasopressin or oxytocin. Renal retention of water in excess of solute reducing body fluid osmolality **or** concept.	

Thyroid Hormones 2016-1-C

Moving onto Physiology			
Question 2 Regulation of thyroid hormones **Suplject** Phys LOA: 2	1. How are thyroid hormones regulated? (Prompt Describe the feedback mechanism) 2. Other than cardiovascular, what are the physiological effects of thyroid hormones?	TRH from hypothalamus=> TSH from ant pituitary=> T4 (& small amount T3)=> T3 in periphery. **Negative feedback on TSH by free T3 & T4** (in hypothalamus and pituitary. Effect of **T3>T4**). Both secretion & synthesis of TSH affected by ↓ py cold, ↓py warmth (esp in infants. Effect in adults not clear) ↓py stress (TRH) and glucocorticoids (TSH). ↓ py dopamine & somatostatin (TSH) **Calorigenic** (↑ metabolic rate, ↑ stimulation O2 consumption) Adipose tissue: catabolic (stimulated lipolysis): Muscle: catabolic (↓protein breakdown): Bone: development (promote normal growth(Cretin) and skeletal development): Nervous system: promote normal development & maturation Gut: metabolic (↑ carbohydrate absorption): Cholesterol: formation of LDL receptors and removal of circulating cholesterol	Bold & concept Bold plus one other system One factor

Thyroid Hormones 2011-2

Question 4 LOA: 2	Q1. What factors are involved in regulating thyroid hormone secretion?	Predominant factor controlling thyroid secretion is the **circulating level of TSH** released from the anterior pituitary. TRH from hypothalamus serves to increase TSH secretion. Important point – **negative feedback loop – whereby circulating T4 and T3 block the increase in TSH secretion produced by TRH.** Thyroid hormones inhibit TSH secretion before they inhibit synthesis. T3 – principal feedback regulator of TSH secretion. Other inhibitors of TSH secretion Stress Warmth (in exp animals) Dopamine, somatostatin and glucocorticoids (but physiological role in regulation of TSH secretion is not known)	Pass criteria – LOA 2 Bold to pass 2 to pass
	Q2. What else affects TSH secretion?	Cold – stimulates TSH secretion (exp animals and human infants)	

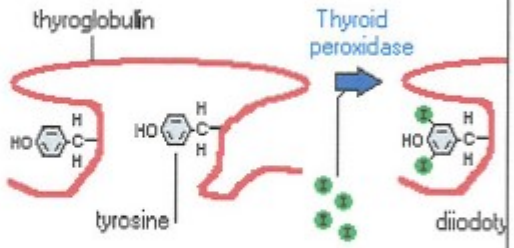
Thyroid Hormones 2010-2

Question 2: Thyroid hormones	1) Outline the physiological effects of thyroid hormones 2) Describe the mechanism regulating thyroid hormone	(a) **Heart**: chronotropic; inotropic (↑ number of B-adrenergic receptors; ↑response to catecholamines; ↑ proportion of a-myosin heavy chain); **Adipose tissue**: catabolic (stimulated lipolysis); **Muscle**: catabolic (↑protein breakdown); **Bone**: developmental (promote normal growth(Cretin) and skeletal development); **Nervous system**: promote normal brain development; **Gut**: metabolic (↑ CHO absorption); **Lipoprotein**: metabolic (formation of LDL receptors); **other** – calorigenic (↑ metabolic rate, ↑ stimulation O_2 consumption) (b) Negative feedback effect of T4 and T3 on hypothalamus and pituitary to inhibit TRH and TSH secretion respectively. Cold stimulates thyroid hormone secretion, stress and glucocorticoids inhibit.	3 to pass incl cardiac

Thyroid Hormones 2009-2

Question5:	**What are the effects of thyroid hormones on nervous and vascular systems**	CNS- 1)**Development CNS** -cerebral cortex, basal ganglia cochlea 2)↑ **activity, mentation speed/ agitation** (catechol / dop+ direct brain effects) 3) ↑ **refexes** CVS- 1)**vasodil** (2ary heat)- 2) > **circ vol/ HR/ CO** - **3)Ht- > myosin heavy chain (+ isoforms)**/ faster twitch genes (+ Ca ++, Na K ATPase etc↑) + down reg others, **> contraction/ HR**/ speed of contraction - **4) > sens to Catechols** (synergistic effects + up regulated ß receptors and effector systems) HR, contract more	Impt issues highlighted 3/6 for a pass. **Pass: 3-4 overall at least 1 in each** **Prompt- what features of thyrotoxicosis**
	What other physiological effects does thyroid hormone have on the body?	Lipolysis - adipose tissue Formation of LDL receptors on lipoprotein Protein breakdown in muscle Skeletal development promoted Increased carbohydrate absorption from the gut Stimulates O_2 consumption by metabolically active tissues Increased BSL/ insulin resistance	**2 required**

Thyroid Hormones 2009-1

Question 4: Thyroid hormone synthesis and effects. Ganong pp 319, 323-6	i) Describe the steps in synthesis of thyroid hormones. Prompt: What are thyroid hormones made from?  ii) What are the physiological effects of T4? Prompt: How do thyroid hormones alter metabolism?	i) Thyroid epithelial cells secrete **thyroglobulin** (comprising 134 tyrosines) and **iodine** into colloid. Iodide transport is via a symport with sodium (NIS). Thyroid peroxidise makes iodotyrosines (MIT and DIT) then combines them to **make T3 and T4**. Some reverse T3 (inactive) also made. Endocytosis and lysis of colloid releases free hormone. All steps TSH controlled. T3 also made peripherally by deiodination of T4. ii) Binds to intracellular thyroid receptors in the nuclei. Complex binds to DNA and alters gene expression. T3 more rapid and potent. **Incr metabolism and catabolism** of most cells (brain and others excluded). Lipid and carb mobilisation and usage. **Inc CVS** and CNS **activity**. Normal reproductive cycle and growth. Effects incr by catecholamines.	Core knowledge in bold. Subunits combine together

Thyroid Hormones 2008-1

1.4 Thyroid hormones Ganong pp 319-328	What are the effects of thyroid hormones?	**(4 out of 7)** • Widespread actions • Metabolically active tissues • Heart - increased rate • Brain - development reticular Act. Sys. • Gut - increased carbohydrate absorbtion. • Muskuloskeletal growth • Adipose – lipolysis	
	What is the mechanism of action?	**(4 out of 8)** Intracellular--- • At the nuclear level • O2 consumption regulator. • T3 binds better than T4 to receptor • Hormone/receptor binds to DNA • Affects gene expression • Two genesites • Alpha Chromosome 17 • Beta Chromosome 3	/2

Thyroid Hormones 2007-1

TOPIC: Effects of thyroid hormones_____ **NUMBER:** _____

OPENING QUESTION	What are the effects of thyroid hormones on different body tissues?	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Heart: chronotropic, inotropic (increased beta receptors, enhanced response to catecholamines)	What are the effects of thyroid hormone on the heart?	Need 2 of first 4 to pass plus 2 others.
	2 Adipose tissue: catabolic (lipolysis)		
	3 Musculoskeletal: catabolic (increased protein breakdown), developmental (promote growth and development)		
	4 Most (except adult brain, uterus, testes, spleen): calorigenic (increased O2 consumption of metabolically active tissues)		
	5 CNS: developmental (promotes brain development)		
	6 GIT: metabolic (increased carbohydrate absorption)		
	7 Lipoprotein: metabolic (increased LDL receptors)		

Thyroid Hormones 2005-1

Thyroid hormones	What are the effects of thyroid hormones?	At least two organ systems and one effect on each	
	How are thyroid hormones synthesised?	Active iodide transport; binding to thyroglobulin; MIT and DIT join to form T3 and T4.	
	What is the mechanism of action of thyroid hormones?	Enter cells; binds to specific receptors; hormone–receptor complex binds DNA & effects gene expression.	