Physiology week 18-20 - Endocrine VIVAs

What factors control blood glucose levels?

1. Absorption: dietary intake, renal tubule reabsorption
2. rate of entry into cells (including factors which affect this such as insulin, glucagon)
3. glucostatic activity of the liver (storage of glycogen, breakdown of glycogen, gluconeogenesis)

What are the potential pathways for glucose metabolism in the body?

1. aerobic
2. anaerobic
3. glycogen
4. pentoses

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		

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+**

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 2^0 hyperaldosteronism (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		

Insulin

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	

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.

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*

COMMENTS

TOPIC: Physiology of Insulin **NUMBER:**

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?	

3.4 Insulin & Glucose Ganong pp 336-340	Describe the effects of insulin on various tissues	• **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
	What is the time frame for these effects	• **Rapid**: glucose, AAs, K into sensitive cells • **Intermediate**: protein synthesis, glycolysis and synthesis, inhibition gluconeogenesis • **Delayed**: lipogenesis

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)

Question 4a: *Score:*	**What are the major factors determining the plasma glucose level?** PROMPTS If discussing hormones XS- how does glucose enter and leave the plasma	1) Concept: Balance between glucose entering the bloodstream and glucose leaving the bloodstream. 2. Dietary intake 3. Cellular uptake (partic muscle/fat/ hepatic) 4. Hepatic glucostat / glycogenisis, glycogenolysis, gluconeogenisis 5. Renal freely filtered but PT reabsorbed to Tmax 6) Hormonal effects on these (partic 1, 3,4)	COMMENTS 3 for a pass + concept Complex hormonal effects not required 

4b :	**List the hormones which effect plasma glucose levels?** **Prompt- which way does gluc move**	↓BSL - Insulin (),Ins like GF 1and 2- (NSILA) ↑ BSL Catecholamines (Nor / Epi partic) (>),Glucagon (>), GH>, Cortisol>, Thyroid Pass requires 3 hormones + correct < or >	Insulin via glucose uptake (al tissues), glycogenogenesis, Liver - gluc to fat, - IGF- similar but much < Catechol –b receptor > cAMP- glycogenolysis/ gluconeogenesis Glucagon- cAMP direct- as catech TFTs- > absorption + ↑glycogenolysiss (liver partic) + ins bkdown↑ Cortisol- permissive to Glucagon/Catechols + some glucgenesis, prot to gluc liver- < uptake GH- > gluc liver, insulin block, <tissue upotake

Overview: Ultimate fate of ingested glucose:

- 5% converted to glycogen in the liver
- 30-40% converted into fat
- 55-65% metabolized into energy

1. First, glucose phosphorylated to glucose-6-PO4 [G6P] inside cells (hexokinase, glucokinase)- this is the essential 1st step which makes it 'usable'
2. Then, G6P can go one of two ways:
   a. polymerized to ***glycogen [5% ends up this way]. NB I think needs to be reconverted to glucose-1-PO4***
   b. catabolized to *pyruvate* [via the Embden Meyerhof pathway or hexose monophosphate shunt]
3. Pyruvate then can go one of two ways:
   a. *Aerobic* conditions: converted to acetyl CoA, which is the essential fuel for the citric acid [Krebs] cycle. This generates net **38 ATP** per glucose. [Some say 30.]
   b. *Anaerobic* conditions: converted to lactate which is converted back when oxygen becomes available. This generates only **2 ATP.**

	Insulin has a hypoglycaemic action but it has many other effects on amino acid and electrolyte transport, enzymes and growth. The net effect is storage of carbohydrate, protein and fat.		
THIRD QUESTION	• ***Rapid (seconds)*** Increased transport of glucose, amino acids and potassium into insulin sensitive cells. • ***Intermediate (minutes)*** Stimulation of protein synthesis Inhibition of protein degradation Activation of glycolytic enzymes and glycogen synthase Inhibition of phosphorylase and gluconeogenic enzymes • ***Delayed (hours)*** Increase in mRNAs for lipogenic and other enzymes. How is insulin secretion **regulated?**		
POINTS REQUIRED	Overview: 1. insulin is secreted by Beta cells, which form the majority of islet cells in the Islets of Langerhans (endocrine pancreas). 80% is degraded in liver and kidney.		
	Stimulators • **Glucose**, mannose, fructose Glucose enters B cells via GLUT 2 transporters. Glucose is then metabolized by glucokinase generating ATP that closes ATP sensitive potassium channels. Depolarisation results in opening of voltage sensitive calcium channels and intracellular calcium triggers insulin release. • **Intestinal hormones** Gastrin Secretin CCK Glucagon GIP **Protein and fat derivatives** Amino acids (leucine, arginine) Beta keto acids • **Autonomic nervous system** Acetylcholine via M4 receptors and right vagus nerve Causes activation of phospholipase C, release of IPs and subsequent calcium release from endoplasmic reticulum. Beta adrenergic agonists alpha agonists cause inhibition and this tends to be the dominant effect unless there an alpha antagonist is present. • **Increased cAMP** due to: Glucagon Theophylline **Sulphonylureas** (Cause membrane depolarization of B cells and calcium influx.)		

OPENING QUESTION	Describe the effects of insulin	PROMP	COMMENTS
	General: Increased cell growth		
POINTS REQUIRED	**Liver** • Decreased glucose output due to decreased gluconeogenesis and increased glycogen synthesis. • Increased protein synthesis • Increased lipid synthesis • Decreased ketogenesis		
	Fat • Increased glucose entry • Increased fatty acid synthesis • Increased triglyceride deposition • Activation of lipoprotein lipase • Increased potassium uptake		
	Muscle • Increased glucose entry • Increased glycogen synthesis • Increased amino acid uptake • Increased protein synthesis • Decreased protein catabolism • Decreased release of gluconeogenic amino acids • Increased ketone uptake • Increased potassium uptake		
	Heart: positive inotropy, chronotropy		
SECOND QUESTION	How does insulin cause these effects?	What is its cellular mechanism of action?	
POINTS REQUIRED	Insulin binds with an insulin transmembrane receptor that binds and stimulates a protein **tyrosine kinase.** Exposure to increased insulin down regulates receptor concentration and affinity.		

	Inhibitors • **Somatostatin** • **Glucose metabolism preventors** 2-deoxyglucose Mannoheptulose • **Autonomic nervous system** Alpha adrenergic agonists Beta antagonists • Galanin Polypeptide found in some of the autonomic nerve innervating the islets Causes opening of potassium channels • **Hypokalaemia and potassium depleters** Thiazide diuretics **Phenytoin Alloxan Microtubule inhibitors Insulin**		
OURTH UESTION	DESCRIBE THE PRODUCTION & METABOLISM OF INSULIN		
OINTS EQUIRED	*Production* Polypeptide containing 2 chains (A and B) of amino acids linked by disulfide bridges. Synthesised as part of preproinsulin. Removal of a peptide leader sequence forms proinsulin. Connecting peptide is removed in the granules prior to release.		
	Metabolism Half life 5 minutes. Binds to insulin receptors and is internalized. Destroyed by insulin protease.		

Calcium

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	

What are the actions of the parathyroid hormone on Calcium?	PTH- 1. ↑ plasma Ca^{++} by: ↑ Ca^{++} mobilization ↑ bone reabsorption, ↑ Ca^{++} reabsorption in distal tubule and (3) Ca reabsorption	Pass: Ca ++ ↑ PO4 ↓ + some idea of how these achieved OR additional other mechs
What are the other effects of PTH?	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	Parathyroid related hormone- (prob fetal/ cartilage growth + teeth/ breast- skin) ? **PO4 < +1 other in either section**

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 dihydroxycholecalciferol --> 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.	

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.	
		• **Reflex arc** consisting of **sensory** organ(s) | **afferent** limb(s) | central integrator(s) | **efferent** limbs | **effectors.** • Sensory organs are nociceptors in the skin or subcutaneous tissues, responding to noxious (usually painful) stimuli. • Afferent limb is/are sensory (pain) fibre(s) to the	

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
		  o bound in bone; bone calcium readily exchangeable or slowly exchangeable (resorption / deposition)
		  o Intake
		  o GI absorption under influence of vitamin D
		  o Renal excretion under vitamin D influence
		  o Parathyroid hormone
		  o 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.

1.5 Vitamin D Gonzong 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.

Adrenal

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	

3.5 Physiology of glucocorticoids	What are the effects of glucocorticoids.	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.
	How are they metabolised? How are they controlled?	Cortisol liver, conjugated to glucuronic acid; inactivation depressed by liver disease

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

OPENING QUESTION	What hormones are secreted by the adrenal medulla?	**PROMPTS**	**CO**
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**		

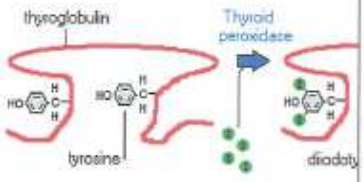
2.4 Glucocorticoids Gonzong pp 372-380	What are the physiological effects of glucocorticoids?	• **Metabolic**; increased protein catabolism, increased hepatic glycogenesis and gluconeogenesis (raised plasma glucose). Raise peripheral tissue insulin resistance • Permissive effects on other reactions • 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

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?")

Pituitary

Pituitary hormones	What hormones are produced by the pituitary?	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.
	What are the physiologic effects of vasopressin?	Renal retention of water in excess of solute reducing body fluid osmolality or concept.

Thyroid

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.
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.

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)		

COMMENTS

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

		Impt issues highlighted 3/6 for a pass. **Pass: 3-4 overall at least 1 in each** **Prompt- what features of thyrotoxicosis**
What are the effects of thyroid hormones on nervous and vascular systems	CNS- 1)**Development CNS** -cerebral cortex, basa 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	
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**