Endocrine Physiology

Thyroid

1. Describe thyroid hormone synthesis

The thyroid is made of follicles – a single layer of cells surrounds proteinaceous material called colloid.

Thyroid secretes T4 and T3. T4 is also deiodinated to T3 by peripheral tissues

Thyroglobulin is synthesized in thyroid cells and secreted into colloid.

Thyroid hormone is secreted by ingestion of colloid, hydrolysis of peptide bonds and free T4 and T3 are discharged into capillaries.

Na and I- are co transported into the thyroid cell and the Na is pumped out by Na K ATPase. I- then diffuses down it's electrical gradient (-50mV) into the colloid.

Iodide is oxidized and bound to tyrosine molecules attached to thyroglobulin by thyroid peroxidase, forming monoiodotyrosine (MIT). Another iodine can attach forming diiodotyrosine (DIT). Two DIT's can condense to form T4 or a MIT and a DIT can condense to form T3 or RT3 if it goes round the wrong way.

Colloid is ingested by the cells. These combine with lysosymes and are broken up into T4, T3, DIT and MIT which float in the cytoplasm. Iodine is taken off MIT and DIT by iodotyrosine deiodinase and can be reutilised, but T4 and T3 are left alone to pass into the circulation

2. Describe the effects of thyroid hormones

T3 binds less tightly to plasma proteins and more tightly to thyroid hormone receptors than T4 and so is more potent. RT3 is inert.

Calorigenic action

- Metabolic rate is increased.
- Rise in temperature
- Increased HR, widened pulse pressure (peripheral vasodilation and increase CO)
- Vitamin requirements increased (or deficiencies unmasked)
- Increased mentation
- Increase the number and affinity of B adrenergic receptors in the heart, etc
- Increased protein catabolism may cause weakness in hyperthyroidism

Growth and development
Essential for normal growth and development

Regulate lipid metabolism
Lower circulating cholesterol levels as it increases LDL receptors in the liver

Increase intestinal carbohydrate absorption

Increase red cell 2,3 DPG

3. **How is thyroid function regulated?**

Anterior pituitary secretes Thyroid Stimulating Hormone (TSH) which increases iodide binding, synthesis of T3/4, secretion of thyroglobulin into the colloid, endocytosis of colloid, hypertrophy of the thyroid gland. Thyroid gland also contains receptors for growth factor.

Free T4 and T3 exert negative feedback onto anterior pituitary, to reduce TSH secretion but also on hypothalamus to reduce Thyroid Releasing Hormone (TRH).

Endocrine Pancreas

1. **What are the effects of insulin?**

The net effect of insulin is the storage of carbohydrate, protein and fat

Rapid
- increase transport of glucose, amino acids and K+ into insulin sensitive cells

Intermediate
- Stimulation of protein synthesis
- Inhibition of protein degradation
- Activation of glycolytic enzymes and glycogen synthase
- Inhibition of phosphorylase and gluconeogenic enzymes

Delayed
- increase in mRNAs for lipogenic and other enzymes

2. **What are the actions of glucagon?**

Produced by the A pancreatic islet cells
Glycogenolytic, gluconeogenic, lipolytic and ketogenic
In large doses has ionotropic effect on heart.

Stimulates insulin, growth hormone and somatostatin secretion

3. What is somatostatin?

Also secreted by pancreatic islet cells.
Inhibit the secretion of insulin, glucagon,
Increases plasma glucose
Decreases gastric acid secretion
Slows gastric emptying
Inhibits CCK secretion so decreases gallbladder contraction and leads to gallstone

The Adrenal Medulla and Cortex

Describe the adrenal cortex.

The adrenal cortex is essential for life. It secretes glucocorticoids which affect carbohydrate and protein metabolism, it secretes mineralocorticoid which is essential to the maintenance of Na and ECF volume. It also secretes sex hormone that have minor effects on reproductive function.
ACTH from the anterior pituitary regulates adrenal cortex activity, but the mineralocorticoid function is also affected independently by other factors, mostly angiotensin II.
There are 3 zones in the cortex. The outer zona glomerulosa (mineralocorticoid), middle zona fasciculata (mostly glucocorticoids) and inner zona reticularis (mostly sex hormones).

The main mineralocorticoid is aldosterone.
Aldosterone increases the reabsorption of Na from the urine, sweat, saliva and colon. In the kidneys, aldosterone acts on the principal cells of the collecting ducts where it increase the amount of Na exchanged for K and H in the tubules, causing a K and acid diuresis. Aldosterone is increased by angiotensin II and ACTH.

The main glucocorticoid is cortisol and corticosterone.
Glucocorticoids act on intermediary metabolism of carbohydrate, protein and fat. This includes increased protein catabolism, increased hepatic glycogenesis and gluconeogenesis, resulting in hyperglycaemia if insulin is insufficient. Glucocorticoids must be present for a number of reactions to occur – such as the calorigenic actions of glucagon and catecholamines. Glucocorticoids inhibit ACTH secretion, make vascular smooth muscle responsive to catecholamines, increases GFR. Glucocorticoids inhibit the inflammatory response to tissue injury and suppress manifestations of allergic disease that are due to the release of histamine.
Glucocorticoids accelerate the maturation of surfactant in the foetal lungs

The main sex hormones are DHEA and androstenedione. Androgens such as DHEA exert masculinising effects and promote protein anabolism and growth. Adrenal andorgens

have less than 20% the activity of testosterone from the testes. Androstenedione is converted to oestrogen and is an important source of oestrogen for males an postmenopausal women.

What is Cushing's syndrome?

The clinical picture produced by prolonged increases in plasma glucocorticoids. Patients are protein deplete from excessive catabolism, leaving the skin and subcutaneous tissues thin. Wounds heal poorly. Minor injuries cause bruising. Hair is thin and scraggly. There may be increases in adrenal androgens that causes increases in facial hair and acne.
Body fat is redistributed with thin extremities and fat abdomen, face and buffalo hump.
Dark purple striae develop where skin is stretched.
Catabolised proteins are converted to glucose in the liver and insulin resistant diabetes may result.
The glucocorticoids can exert a mineralocorticoid action with salt and water retention, K depletion and weakness and hypertension.
Glucocorticoid excess causes bone dissolution by decreased formation and increased resorption leading to osteoporosis.
Excess glucocorticoids accelerate the basic EEG rhythms and produce mental abberations that range from increased apetite, insomnia, euphoria, psychosis.

What is an Addisonian Crisis?

An Addisonian crisis is the severe hypotension of adrenal insufficiency due to a lack of mineralocorticoids and glucocorticoids. Primary adrenal insufficiency used to be caused by TB, but now the most common cause is autoimmune (in developed countries). Patients lose weight, are tired and chronically hypotensive. Fasting can cause fatal hypoglycaemia, and any stress causes collapse. Water is retained and there is always the danger of water intoxication. ACTH is elevated in primary hypoaldosteronism and causes tanning and spotty pigmentation from MSH activity. Sex hormone changes are not relevant in the presence of normal ovaries or testes.

Bone physiology

1. **What hormones regulate calcium metabolism?**

1,25 dihydroxycholecalciferol is formed from Vit Dl It increases calcium absorption from the intestine
Parathryoid hormone is secreted by the parathyroid glands and it mobilizes calcium from bone and increases urinary phosphate excretion
Calcitonin is secreted by cells in thyroid gland inhibits bone resorption

2. **What are the actions of parathyroid hormone?**

Acts directly on bone to increase resorption and mobilize Ca.

Increases phosphate excretion in the urine.
Increases Ca reabsorption of Ca in tubules
Increases 1.25 dihydroxycholecalciferol formation with increases Ca absorption from GIT
Stimulates osteoclasts

The pituitary gland

What hormones are secreted by the pituitary gland?

The anterior pituitary secretes 6 main hormones. Thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin and growth hormone. The anterior pituitary also secretes B-lipotropin but the function of this is unknown. The intermediate lobe is rudimentary in humans.
The posterior pituitary secretes oxytocin and vasopressin.

Endocrine Functions of Kidney, Heart and Pineal Gland

What is the Renin-angiotensin system?

Renin is produced by the juxtaglomerular cells cells in the kidneys and secreted into the blood stream. Renin converts angiotensinogen to angiotensin I. Angiotensin I is physiologically inactive. Angiotensinogen is synthesized in the liver.

Angiotensin-converting enzyme (ACE) is found in endothelial cells and converts angiotensin I into angiotensin II as its name suggests. Most of this conversion occurs in the lungs. ACE also inactivates bradykinin.

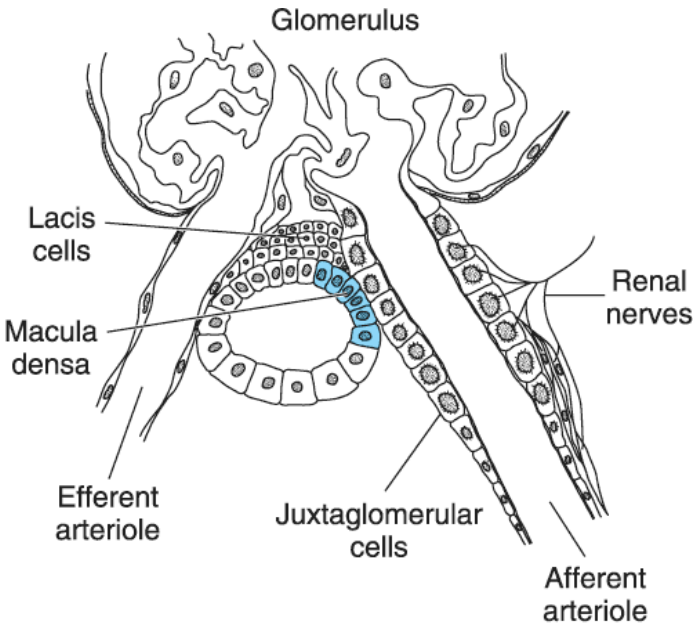
Angiotensin II has the following effects:

1. Arteriolar constriction and a rise in systolic and diastolic blood pressure.
2. Acts directly on the adrenal cortex to increase the secretion of aldosterone.
3. Facilitates the release of noradrenaline by acting on post ganglionic sympathetic neurons
4. Contracts mesangial cells and so decreases GFR
5. Directly increases Na reabsorption from the renal tubules.
6. It acts on the brain to decrease the sensitivity of the baroreflex and increase water intake
7. Increases secretion of vasopressin
8. Increases ACTH secretion

Angiotensin II is metabolized rapidly – half life 1-2 mins – metabolized by various peptidases in RBCs and other tissues. Angiotensin III can be formed which is also

physiologically active, having 40% of the pressor activity of angiotensin II but 100% of the aldosterone stimulating activity.

The juxtaglomerular apparatus is the point where the afferent arteriole enters the glomerulus, the efferent arteriole leaves it and the tubule at the start of distal convolution touches these arterioles. The tubule here has different epithelium called the macula densa and is in close proximity to the juxtaglomerular cells. This constitutes the JG apparatus.



Renin secretion is determined by a number of factors. One of these is an intrarenal baroreceptor mechanism where changes in arteriolar pressure cause an inverse change I renin secretion. Another mechanism is the macula densa detecting the Na and Cl concentrations in the tubular fluid and inversely affecting renin secretion.
Angiotensin feedsback to inhibit renin secretion by acting on the JG cells. Vasopressin also feeds back to inhibit renin secretion. Increased sympathetic stimulation increases renin secretion by catecholamines acting directly on B1 adrenergic receptors on the JG cells causing an increase in cAMP which increases renin secretion. Renal artery constriction and constriction of the aorta proximal to the renal arteries produces as decrease in renal arteriolar pressure which increases renin secretion.
Conditions that increase renin secretion include Na depletion,diuretics, hypotension, haemorrhage, upright posture, dehydration, heart failure, cirrhosis, constriction of the renal artery or aorta and psychologic stimuli.

What is erythropoietin?

Erythropoietin is a hormone that stimulates erythropoiesis. Haemorrhage or hypoxia stimulate its release and overtransfusion decreases it.

Erythropoietin increases the number of erythropoietin sensitive committed stem cells in the bone marrow that are converted to red blood cell precursors and subsequently to mature erythrocytes
85% comes from the kidneys and 15 % from the liver but the liver source is inadequate in the absence of kidneys. Recombinant erythropoietin is used to treat anaemia of EDRF.
Erythropoietin is inactivated by the liver and has a 5 hour half life, but the red cell changes takes 2-3 days to appear

What is the function of the pineal gland?

The pineal gland secretes melatonin and may function as a timing device to keep internal events synchronized with the light-dark cycle in the environment
The gland arises from the roof of the third ventricle. In infants it is large, in adults in can contain small concretions of calcium phosphate and calcium carbonate.
Serotonin is converted to melatonin in the cells of the pineal gland and melatonin is secreted into the blood and CSF. Synthesis and secretion are increased during dark hours and decreased during daylight hours. The diurnal variation is produced sympathetic nerves that innervate the pineal gland and secrete noradrenaline which acts on B adrenergic receptors to increase cAMP which increase the enzyme activity to convert serotonin to melatonin. The sympathetic nerves get their signal from retinohypothalamic nerve fibres. It is thought that melatonin functions as a timing signal to coordinate endrocrine and other internal events with the light-dark cycle of the environment.