Ftplectures Endocrine system Lecture Notes

ENDOCRINE

Medicine made simple

Ftplectures Clinical Medicine
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Title: Adrenal gland physiology

Objectives for learning: parts of adrenal gland

Parts of adrenal gland
Adrenal gland has two parts-

1) outer layer ***cortex***- The cortex has 3 zones which are
- Zona glomerulosa- salt – aldosterone - sodium absorption to keep up blood pressure
- Zona fasciculata- sugar – glucocorticoids like cortisol
- Zona reticularis – sex – testosterone - related to sexual function

2) Inner layer ***medulla***
    - chromaffin cells

The acronym is GFR (similar to glomerular filtration rate). An easier way to remember is to think salt, sweet and sex for the three zones. The deeper it goes, the sweeter it gets.
Zona glomerulosa produces the hormone aldosterone that is related to sodium absorption (salty). Zona fasicculata produces glucocorticoids (sugary) like cortisol and zona reticularis produces sex hormones like testosterone. Medulla has chromaffin cells.

Steroid pathway
Cholesterol is a steroid and it gets converted to pregenenolone under the action of desmolase. The enzyme **desmolase** is activated by **ACTH** (adrenocorticotropic hormone). Pregenenolone breaks down to progesterone. Under the action of **21 alpha hydroxylase** progesterone gets converted to 11- deoxycorticosterone which again is converted to corticosterone under the action of **11 beta hydroxylase**. Under the effect of aldosterone synthase corticosterine gets converted to **aldosterone**. The whole pathway occurred in Zona Glomerulosa.
Pregenenolone gets converted to 17-OH pregenenolone under the action of **17 alpha hydroxylase**. 17-OH pregenenolone converts to DHEA (dehydroepialdosterone). 17-OH pregenenolone and progesterone (under the action of 17 alpha hydroxylase) get converted to 17-OH progesterone. 21 alpha hydroxylase mediates the conversion of 17-OH progesterone from 11-deoxycortisol. 11 beta hydroxylase converts 11-deoxycortisol to **cortisol**. This part of the pathway takes place in Zona Fasciculata.
17-OH progesterone gets converted to **androstenedione** which in turn gets converted to **testosterone**. Androstenedione gets aromatized to form **estrone**. Testosterone gets aromatized to form **estradiol** and under the action of **5 alpha reductase** it gets converted to **dihydrotestosterone (DHT).** This part of the pathway takes place in Zona Reticularis.
(Important terms in the cycle are marked in **bold** letters)

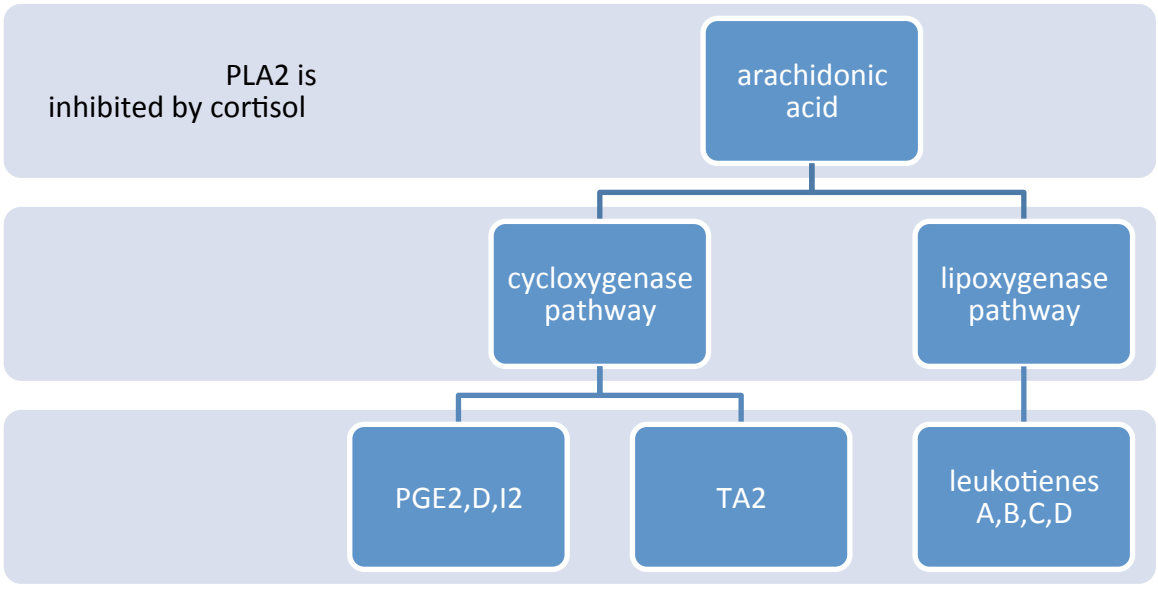
Adrenal medulla
The chromaffin cells of adrenal medulla are under the action of sympathetic nerve fibers. These presympathetic fibers contain acetylcholine that act on chromaffin cells so that they contract and produce epinephrine and norepinephrine. They are called as catecholamines. Adrenal medulla produces 80% of epinephrine and 20% norepinephrine. The venous

drainage from adrenal cortex has a high quantity of cortisol and increases the transcription of PNMT, an enzyme that catalyses the conversion of epinephrine to norepinephrine.
In a way cortisol is responsible for the conversion of epinephrine to norepinephrine.
Norepinehrine causes vasoconstriction, thereby increase the blood pressure.

How steroid hormones act?
Steroids are lipid soluble with a phospholipid bilayer. A steroid molecule penetrates the cellular cytoplasm and binds to the steroid binding protein (globulin). The complex of steroid-protein enters the nucleus and bind to the DNA. DNA gets transcribed into mRNA which in turn makes a protein (enzyme).

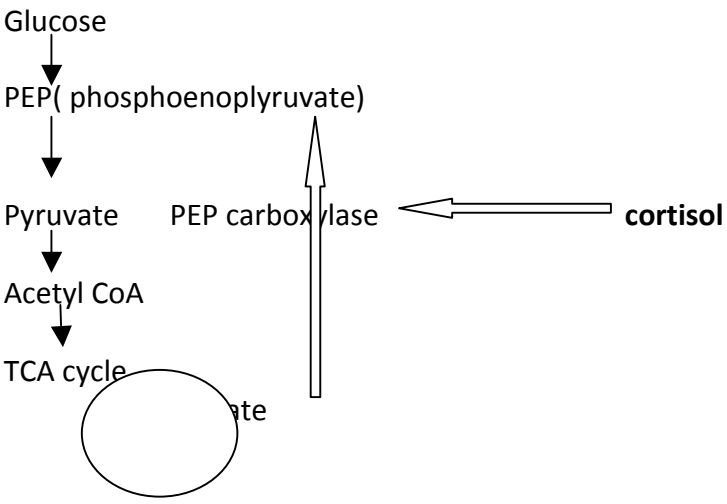
Functions of cortisol

1. **Anti-inflammatory agent**- It prevents the activation of arachidonic acid pathway. In arachidonic acid pathway,



Phospholipase A2 acts on arachidonic acid to start of the two pathways that eventually form mediators of inflammation. Cortisol inhibits PLA2, so causes anti-inflammation.

2. **Gluconeogenesis, lipolysis and proteolysis**



Cortisol acts on PEP carboxylase and reverses the glycolytic pathway by producing glucose. Cortisol breaks down fats and proteins also.

3. **Decreases your immunity-** it reduces the neutrophilic function. It reduces the capacity of adhesion of neutrophils to the endothelial cells of the capillaries. This way the neutrophils keep on floating in the blood and make the person immunosuppressive.
4. **Maintain your blood pressure-** Epinephrine gets converted to norepinephrine under the influence of cortisol. If there is a drop in B.P., cortisol causes the preload and afterload to increase, the cardiac output increases, heart rate increases and blood pressure increases. This way the B.P. is maintained.
5. **Decreases bone formation-** The patients are predisposed to osteoporosis.

Adrenal insufficiency

Definition

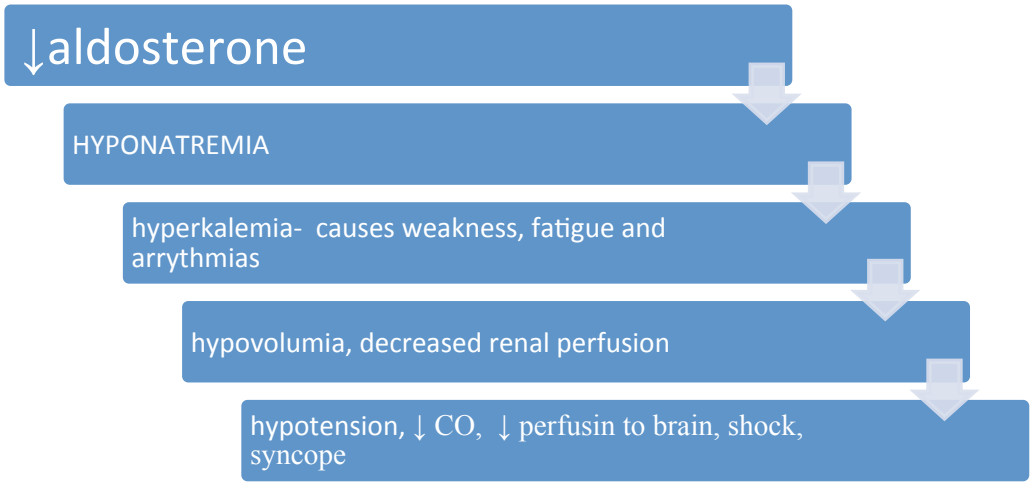
It is the decreased level of adrenal gland hormones like aldosterone and cortisol.

Types

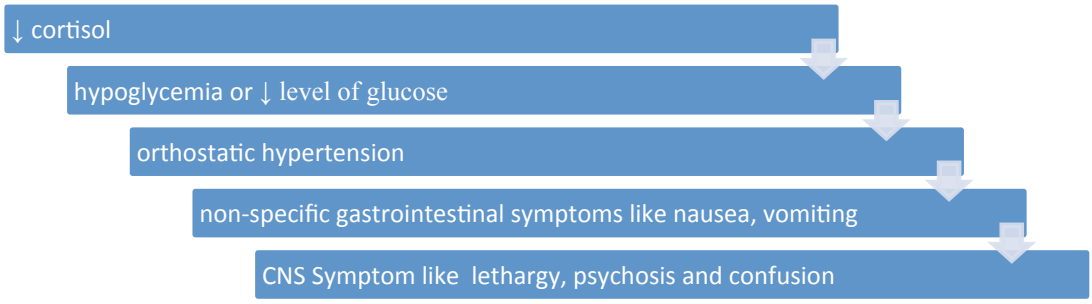
Primary	Secondary	Tertiary
Adrenal gland is affected	Pituitary gland is affected	Hypothalamus is affected
1. Addison disease - Cause of adrenal insufficiency in industrialized world. - autoimmune disorder - Antibodies generated against adrenal gland.	**Abrupt discontinuation of steroids** - The most common reason for adrenal insufficiency. - A person put on prolonged periods of steroid administration should never stop steroid use abruptly.	**Less production of CRH** - A rare cause - When corticotrophin releasing hormone is not released from hypothalamus, ACTH will not be produced by pituitary. Hence, cortisol will not be released from the adrenal gland.
2. Infection - Cause of adrenal insufficiency in third world countries - Tuberculosis like infections	- His adrenal glands are atrophied because of disuse for a long time.	Since aldosterone is not affected by ACTH, the level will remain in the same.
3. Iatrogenic - Cause of adrenal insufficiency is bilateral adrenal gland removal	- So tapering of steroids is recommended instead of abrupt discontinuation	
4. Metastasis - From lung or breast cancer, metastasis can take place to adrenal gland		

Clinical features

- These patients have ↑ ACTH levels.
- They have high levels of MSH (melanocyte stimulating hormone)
- So such patients are hyperpigmented.



Secondary adrenal insufficiency



Diagnosis

- Test the level of cortisol
- If the level is low, check for level of plasma ACTH.
- If the level is high, it is primary adrenal insufficiency
- If the level is low, it is secondary adrenal insufficiency
- On ordering standard ACTH stimulation test, there will be no change in the level of cortisol in both primary and secondary cases initially.
- The same test is repeated about 5 to 6 days later and if there is an increase in the level of cortisol, it is definitely, secondary adrenal insufficiency.
- Imaging methods like MRI of brain can be done to find out the cause of pituitary or hypothalamus malfunction

Treatment

For primary adrenal insufficiency-

- Prednisone (which is a glucocorticoid and acts as cortisol)
- Fludrocortisone (which is a mineralocorticoid and acts as aldosterone)

For secondary adrenal insufficiency

- Do not stop your steroid intake abruptly.
- Taper it down so that there is sufficient production of cortisol in the body.

Title: Diabetes Insipidus

Definition

Kidney does not respond to ADH. There are 2 types-

a. Central DI- The brain is affected. There is low or no ADH. The pituitary gland is affected.
b. Nephrogenic DI- Kidney does not respond to ADH.

Causes

For central DI-

- 50% cases are idiopathic
- Trauma – surgery
- Sarcoidosis, syphilis or TB in brain
- Eosinophilic granuloma
- Viral encephalitis

For nephrogenic DI

- Pyelonephritis
- Hypokalemia
- Hypercalcemia
- Lithium/ Demiclocycline – They block ADH effect on collecting tubules of kidney.

Signs and symptoms

1. Polyurea – They can urinate from 5 to 15 liters a day. Their urine is colorless because of low urine osmolality.
2. Polydipsea – They feel very thirsty as they have to replace the water that they have lost through urination.
   { polydipsea can be seen in –
   a. Diabetes mellitus I and II
   b. Diuretics
   c. Diabetes insipidus
   d. Primary polydipsea}
3. Mild hypernatremia

Diagnosis

- Check the specific gravity of urine, whether it is below 1.010 or not.
- Urine osmolality will also be low.
- Plasma osmolality is 250-290m osm/kg
- The formula for calculation is 2 (Na+) + glucose/18 + BUN/2.8 + ethanol/1.6
- Water deprivation test- Patient is deprived from drinking water. Urine osmolarity is checked every hour until it becomes stable.
- Desmopressin- a drug just like ADH (vasopressin)

Urine osmolarity	Central DI	Nephrogenic DI
Before vasopressin	Low	Low
After vasopressin	↑↑↑	↓↓

Treatment

For central DI

- Desmopressin (DDVAP)- Administartion of desmopressin is the primary therapy. It can be administered in the form of nasal or oral spray or even injectable form.
- Chlorpropamide- It increases the ADH production and enhances the effects on kidney

For nephrogenic DI

- Thiazide – It increases the re-absorption of sodium which in turn causes absorption of water making the urine concentrated.

Title: Diabetes mellitus

Diabetes is a growing epidemic and is becoming a leading cause for-

- Blindness
- Chronic renal failure
- Peripheral neuropathy
- Below the knee amputation.

Definition

It is a disorder in carbohydrate metabolism that causes elevated levels of glucose in circulation due to problems in maintenance of homeostasis in sugar level.

Types

	Diabetes Type I (juvenile)	**Diabetes Type II**
Prevalence	5%	90-95%
Age group	Less than 30 years	More than 40 years
Body habitat	Thin	Obese Obesity and family history are the risk factors
Pathogenesis	Autoimmune destruction of Beta cells of islets of Langerhans in pancreas. It is associated with HLA DR4 and DR3	Insulin resistance Down regulation of insulin receptors
Clinical presentation	**Polyurea** – glucose is being excreted and glucose causes osmotic dieresis and takes along with a lot of water. **Polydipsea** – The loss of water due to polyurea needs to be compensated so the patient feels thirsty and consumes a lot of water. **Polyphagea** – the food is not being used in the body as the glucose molecules are excreted in urine so there is always a hunger for food. **Weight loss**- this is due to the fact that the body shifts to starvation mode. **Fruity smell in breath**- body cannot use glucose so it starts utilizing fatty acids which break down to form ketone bodies like acetone and acetoacetate. **Hyperglycemia**	Hyperglycemia Polyurea Polydipsea Polyphagea Less number of ketone bodies produces (key difference from typeI) as they have some amount of insulin within them.
Treatment	Administration of insulin	Education- Diet and Exercise to

		manage obesity. Medications like 1. Sulphonylurea - Glyburide - Glipizide - Glimeperide They act on pancreas to produce insulin. Side effects- hypoglycemia and weight gain 2. Metformin- increases insulin sensitivity. It cannot be used in patients with renal insufficiency (patients with createnine level more than 1.5) as that may cause lactate acidosis. 3. TZDs- thiazolidinediones- reduce insulin resistance. Side effects- heparotoxic so need to check liver function test

Diagnosis

- Usually patients can have problems like blurry vision, which might bring them to a doctor. They may have cataract. This is due to the excess of glucose in circulation.

  Glucose → sorbitol (in the presence of aldose reductase)

  The lens gets swollen due to the excess water reabsorption caused by the sorbitol deposited within the lens.

- Patients may come up with a lot of fungal infections like vaginitis or oral fungal infection. They are seen as reddish white lesions with a lot of itching. The main causative agent is candida albicans.
- Patients may have peripheral neuropathy- numbness and tingling sensation of hands.
- Normal glucose level is 70-100mg/dl.
- **First test – FBG**- fasting blood glucose test- it needs a fasting of 8 hours midnight.
  - It should not be more than 126mg/dl
- **Second test – RBG**- random blood glucose test- from finger prick test- if it is more than 200mg/dl and there are symptoms (3Ps)
- If the blood glucose is 100-125mg/dl in RBG ask he patient to carry out FBG.
- **Third test- 75g oral glucose tolerance test**

5. Diabetes mellitus: complications

Title: DM complications

Two types of complications

(a) Micro-vascular complications
(b) Macro-vascular complications

Pathogenesis

(a) Poor glycemic control
- leads to Hyperglycemia (glucose)
- Key to diabetes is Non-enzymatic glycosylation of amino acids on proteins
- Sugar binding to aminoacids
- Stimulates process of Atherosclerosis
- Increase permeability of blood vessels to proteins
- Increase process of atherogenesis
- Inside the blood vessel, the glycosylated proteins get deposited into the tunica media of the blood vessel forming a plaque.
- Blood vessels get thickened.

Macro vascular complications

- Coronary artery disease (CAD)

Myocardial infarction is the most common cause of death in patients with diabetes. This happens due to their increased predisposition to atherosclerosis. A sclerotic plaque in the coronary artery may get dislodged and cause MI.

Stroke – due to the ischemia caused by sclerotic plaque, the brain undergoes damage and that is known as stroke.

Peripheral artery disease – 3rd most important macrovascular complication. Ischemia to lower extremities.

The glyosylation of heme group of hemoglobin can act as a marker for diagnosis. While checking the level of **HbA1c** it should not be more than 7.

Microvascular complications

1. **Diabetic Nephropathy**-

Physiology of glomerulus-
- Heparin sulphate on the basement membrane has a high negative charge on them. When albumin molecules enter the glomerulus the filteration does not take place due to repulsion between similar charges and the molecules move from afferent (A- comes first so afferent first) arteriole to efferent (E- can be remembered as Exit) arteriole.
- In case of diabetic nephropathy there is hyaline deposition causing thickening which are called as **Kiemosteil Wilson's nodules**. This is called nodular glomerular nephropathy/sclerosis.
- This can be found out in a pathology side

- **Microalbuminuria –** in normal cases, albumin molecules are not able to eak through the basement membrane of glomerulus due to the negative charges on both of them. With time, the basement membrane thickens due to the forceful deposition of glycosyated proteins on to the basement membrane. This reduces the negative charge and hence makes way for microalbumin to leak through. This way microalbumin is excreted in urine causing microalbuminuria.
- Hypoglycemia → ↑GFR→ microalbuminuria
- **Diagnosis**- normally the **microalbumin ratio** is 30-300mg/dl.
- Another sure test for microalbuminuria is **albumin/creatnine ratio** which if more than 0.20, confirms diabetic nephropathy.
- If microalbuminuria is left untreated there will be albumin excretion in urine which is even more dangerous as it leads to problems like oedema.
- After some time of increased GFR the GFR will become low because of arteriosclerosis of afferent arteriole. There will be hypertension as well.
- **Treatment**-
  ACE inhibitors- we try to decrease GFR by inhibiting the vasoconstrictive effect of vasopressor on efferent arteriole. This way loss of proteins can be controlled.

2. Diabetic Retinopathy

- Diabetes is the leading cause of blindness in the U.S.
- Two kinds of pathologies

1. Background (non-proliferative) retinopathy

- Ischemia caused due to deposition in blood vessels.
- Scar formation takes place. Ischemic blood vessels do not proliferate.
- There are other problems like a lot of exudates, haemorrhage, microaneurysms at the back of the eye.
- Generally asymptomatic till it affects the central macular oedema. This causes vision loss.

2. Proliferative retinopathy

- Due to ischemia, new blood vessels are produced-neovascularisation
- Scar due to ischemia
- Retinal detachment and vitreous haemorrhage can be there.

Advise your patient to go for an eye examination. The doctor may suggest **laser coagulation to** destroy the blood vessels.

3. Diabetic Neuropathy

Pathogenesis:

Hyperglycemia- narrowing of capillaries due to NEG proteins deposition- vasoconstriction- ischemia- death of nerve or tissue.

Symptoms:

1. Sensory and vibration- loss of sensory reflexes- since they don't have sensation in their lower extremities they may develop diabetic foot.
2. Paraesthesia
3. Loss ofVibration
4. Loss of propioception.

5. Pain – They may be extremely sensitive to even a touch because they may have excruciating pain even while we touch.
6. Charcot joint in their foot- Disfigured joints on ankle and knees.

The symptoms follow a **stock glove pattern**- start from the toe and then proceed to the ankle, knee and upwards.

Autonomic neuropathy

The autonomic nervous system consists of sympathetic and parasympathetic nervous system.
Symptoms are-

- Orthostatic hypertension- due to damage to nerves caused due to ischemia- person goes to syncope.

Neurogenic bladder

Patients develop urinary retention because of nerve damage. The alpha 1 nerves at the urethra and the cholinergic nerves of the bladder have undergone damage due to which no message is passed to contract and the bladder remains full.

Gastroparesis

Delayed gastric emptying.
Nerves working on stomach for peristalsis may not be working.
They can get hypoglycemic coma.
Symptoms

- Constipation or diarrhoea
- Nausea and vomiting

Severe autonomic neuropathy can cause impotence in men as S2, S3 and S4 are affected.

Mono neuropathy

- Ulnar nerve- If this nerve is affected patient will have claw like hands where they are not able to flex the last 2 digits.
- Radial nerve- the hand may just drop at the level of the wrist due to neuropathy of radial nerve.
- Common perineal nerve- foot drop due to damage to common perineal nerve. They are not able to dorsiflex their foot.

Cranial nerve palsy

- Occulomotor nerve is the most affected.
- It innervates all the muscles of the eye except the inferior oblique and the lateral rectus muscles of the eye
- Pupils are innervated by parasympathetic branch of cranial nerve. Pupils are spared. Pupils have parasympathetic nerves which are the last to get affected. The motor nerves which are in the inner circle get affected first and hence there are problems with the eyelids. Pupils will constrict but will not be able to adduct.
- They will have symptoms like diplopia, ptosis and pain.

Treatment

1. **Gastroparesis**
   - metachlopramide
   - erythromycin

2. Peripheral neuropathy- pregobulin
    - Gaba pentin
    - Duloxetin
3. **Diabetic foot ulcers**
    - They can't feel anything on their toes hence they develop a lot of foot ulcers. They apply pressure on their nerves causing pressure necrosis. This can cause foot infections like cellulitis and osteomyelitis. They develop hammer toes.
    - This is the leading cause for below the knee amputation in the U.S.
4. **Delayed wound healing**
5. **Immunocompromised**

Management

1. Check HbA1c every 3 months (life span of RBC is 120 days). Check if it is below 7.0 or not.
2. Check for microalbuminuria in urine.
3. BUN/ creatnine
4. Yearly eye examination
5. Podiatrist consultation every year for foot exams
6. Cholesterol level- Check if the LDL is less than 100. For diabetics it should be below 70mg/dl.
7. Check the B.P. it is good if it is below than 130/80-85.

6. Diabetic ketoacidosis

Definition

It is a type of metabolic acidosis seen in diabetic patients in which the ketone bodies are produced excessively.

Causes

The main cause is stress and stress can be caused due to-

- Sepsis
- Myocardial infection
- GI bleeding
- Infections

Pathophysiology

↓insulin→↑ blood sugar

glycogen→ glucose (in presence of glucagon)

↑↑↑ blood sugar as a result, but body cannot use the glucose and is still starving,

Fatty acids→ acetyl coA→ beta hydroxylate, acetylcetate, acetone (the ketone bodies or ketoacids)

The cycle can be written as-

↓insulin and ↑glycogen → ↑blood sugar→ Tmax → osmotic dieresis →water is lost→ dehydration (volume depletion) →labs → high BUN/creatnine and presence of glucose in urine.

Signs and symptoms

- Nausea and vomiting
- Acetone breath
- Hyperventilation- rapid short breath to eliminate the excess of CO_2 in their body
- Dry mouth due to dehydration

Diagnosis

1. Blood glucose $\geq$ 250mg/dl- They are diabetic
2. ABG
3. Low pH which shows acidosis
   $pH=HCO_3^-$(if less than 15)/ Pa CO_2 .
   the pH is lower than 7.3

4. Beta hydroxybutrate and acetylacetate levels will be high. Nitroprusside agent is used to measure the levels. Test the urine and the serum as it will be seen in both.

Labs

1. Hyperosmolality
2. Hyponatremia- If the blood glucose rises by 100mg/dl the sodium lowers by 1.6mEq/l
3. Hyperkalemia- Patients look hyperkalemic but they are actually not.

Treatment

1. Plenty of fluids because patient is dehydrated
2. Insulin administration
3. Potassium is given to counter the lowering of potassium level due to insulin administration

Title : Acromegaly

Definition –

It is a condition that occurs due to excess of growth hormone. In children, excess of growth hormone causes gigantism. In adults, it causes acromegaly as the growth plates have got already fused. The adults start manifesting the features of acromegaly at the age of 40 to 50 years usually.

{Mnemonic for hormones produced from anterior pituitary- FLAT PiG

F – FSH

L- LSH

A – ACTH

T – TSH

P – PROLACTIN

G – GROWTH HORMONE}

Causes

Macro-adenoma is the cause for acromegaly. This adenoma is more than 1 cm in dimension.

Clinical features

- They have skeletal and soft tissue changes mainly
- Big and thick hands and feet
- Very coarse voice
- Enlarged mandible
- Obstructive sleep apnea- They snore heavily due to enlargement of soft tissues of the larynx. They may even choke to death due to excessive enlargement.
- Enlarged heart so they develop restrictive cardiomyopathy. They may develop systolic or diastolic dysfunction or both.
- Develop hypertension
- Enlarged liver, kidney and spleen.
- Impaired glucose tolerance- They are not able to clear their glucose level so they become hyperglycemic and develop diabetes.

Diagnosis

- Biochemical- Check IGF-1 (insulin growth like factor-1) level. Growth hormone is processed in the liver to produce IGF-1.
- If you find the level elevated, it indicates acromegaly.
- To confirm, give 100gm of glucose and check the level of GH. If GH is high, it means that the person has acromegaly.
- Imaging technique- MRI to check macro-adenoma inside the brain.

Treatment

Medical management

1. Octreotide-
    - A somatostanin analogue
    - Inhibits the release of growth hormone releasing hormone. The release of growth hormone is inhibited.
2. Peguisonent-

- Growth hormone receptor blocker

Surgical management

- Transphenoidal resection of the tumor.

Complications

- Cardiac arrhythmias
- Diabetes

Pheochromocytoma

Definition

It is a rare tumour of adrenal medulla which affects chromaffin cells formed from neural crest cells primarily. They produce a lot of catecholmines.

Formation of catecholamines

Tyrosine →L-Dopa→ dopamine → norepinephrine → epinephrine

↓ ↓ mao ↓ mao

HVA VMA Metanephrine mao=mono

mao=mono amino oxidase

Symptoms

5 Ps

1. **P**ressure (high B.P.)
2. **P**alpitations- tachycardia
3. **P**erspiration
4. **P**allor
5. **P**ain- headaches

Diagnosis

1. Urine screen- check urine metanephrine/ normetanehrine (Vaniller Mendelic Acid- VMA)
2. Urine epinephrine/ norepinephrine level- this test is done to confirm if the urine epinephrine is coming from adrenal medulla or other external agents like oragn of Zukerlandl (which is seen next to aorta).
3. Imaging- CTscan or MRI of abdomen to locate the tumor.
4. I-metaiodobenzylguanidine scan to locate the tumor.
5. I-131 can be used as the tumour takes it up.

Treatment

- Administration of non-selective alpha blockers which can reduce adrenergic response- phenoxybenzamine.
- Surgical resection of tumour after giving phenoxybenzamine

Rule of ten

10% - bilateral

10% - malignant

10% - extra-adrenal

10%- calcify

10% - kids

10% - familial

Neuroblastoma- a tumour found in children. It affects the adrenal medulla but it can also happen anywhere in sympathetic chain. Check for HVA. It can be the reason for hypertension in children.

Title:-Cushing syndrome

Cushing syndrome is related to ACTH which is produced by the anterior pituitary gland under the influence of CRH (corticotrophin releasing hormone- produced in hypothalamus). The function of ACTH is to produce cortisol so it moves to the adrenal cortex and acts on desmolase to start the process of conversion of cholesterol to cortisol. Cortisol is also called *glucocorticoid*. This is because cortisol is involved in gluconeogenesis in liver when the body is under stress. Under stress or starvation, our body needs energy in the form of glucose.

Definition

Cushing syndrome is defined as the state of the body caused by an elevated amount of cortisol.

Cushing disease occurs due to pituitary adenoma that leads to excess production of ACTH which in turn leads to excess of cortisol.

Causes

1. **Iatrogenic Cushing Syndrome-** For almost all types of inflammations like COPD, dermatitis, lupus or asthma, steroids like prednisolone are the drug of choice. Steroids are just like cortisol so the patient starts manifesting symptoms of Cushing Syndrome.
2. **ACTH producing adenoma-** The pituitary gland adenoma causes increased secretion of ACTH and, therefore, increased level of cortisol.
3. **Adrenal gland adenoma-** The adrenal gland itself starts producing excess of cortisol.
4. **Ectopic source-** Usually, it is ATCH-producing cancer like small cell lung carcinoma, bronchio-carcinoma or thymoma.

{Adrenal gland is called so as it is an **ad**ded component of the **renal** gland or kidney.**}**

Symptoms

1. Central obesity- Fat deposition on abdomen
2. Purplish striae on abdomen- Cortisol thins out collagen fibers and allows them to stretch making the dermis thin and the blood vessels beneath prominent in the form of purple striae.
3. Moon-like faces
4. Buffalo-hump
5. Easy bruising due to defective collagen fibers.
6. Muscle loss in extremities – Person may have skinny hands as cortisol causes muscle breakdown.
7. Glucose intolerance- Cortisol causes gluconeogenesis and produce excess of glucose. They are predisposed to diabetes.
8. Masculanization in females- This is due to excess of testosterone.
9. Hirsutism- Excess of facial hair.
10. Oligomenorrhea or amenorrhea
11. Osteoporosis
12. Depression- They may even go manic.
13. Immunosuppresion- Impaired immunity due to neutrophil dysfunction.

Case

A 22-year old female, with Cushing syndrome had her vital signs taken. Her B.P, was 148/90, RBS was 250mg/dl.

- The high blood sugar is due to gluconeogenesis caused by cortisol.
- The high B.P. is due to the activation and conversion of epinephrine into norepinephrine and due to the mineralocorticoid like activity of cortisol.

Diagnosis

1mg of dexamethasone administered in the night and the level of cortisol is checked in the morning.

- In **normal** cases, dexamethasone causes inhibition of ACTH secretion from pituitary leading to normal level of cortisol. 24 hour urine cortisol level can also be checked.

- If the cortisol level is **abnormally** high, check the level of ACTH.

- If the level of ACTH is high, it can be due to pituitary adenoma or small cell carcinoma of lung. Administer a high dose of Dexamethasone. If the ACTH level drops down, there is pituitary adenoma which can be confirmed by MRI but if it remains the same, it is small cell carcinoma of lung which can be confirmed by CT scan, X-ray and biopsy (best way).

- If the level of ACTH is low, it can be due to adrenal gland adenoma. To confirm, carry out an abdominal CT.

Treatment

1. **Iatrogenic**
   Taper the dose of steroid. Abrupt discontinuation can be fatal. No hyperpigmentation in cases if iatrogenic induced Cushing Syndrome.
2. **Pituitary adenoma**
   POMC (pro-opio-melano-corticotropin) is produced in patients with pituitary adenoma which causes hyperpigmentation of skin.
   Medical treatment- ketoconazole (inhibits desmolase activity), metapyrone (inhibits 11 beta hydroxylase)
   Surgical treatment – transphenoidal resection of adenoma (best for patient)
3. **Adrenal tumor**
   Surgical resection
4. **Small cell carcinoma of lung**
   Radiotherapy

10. Diseases of the Parathyroid Glands: Hyperparathyroidism

Definition

It is the elevated level of parathormone.

Causes

- Adenoma -80% of the cases have parathyroid adenoma as the cause
- Hyperplasia- All 4 parathyroid glands produce excess of PTH.
- Carcinoma- RARE cause like 1% only.

Clinical features

Mnemonic used is '**stones, bones, abdominal groans and psychiatric moans**'.

- Bone pain- due to destruction of bone
- Osteitis Fibrosis Cystica- also called Brown Tumors. They have pathological fractures.
- Nephrolithiasis (kidney stones)
- Nephrocalcinosis
- Abdominal groans due to hypercalcemia due to constipation, radiating to the back
- Predisposition to peptic ulcer and pancreatitis.
- Psychiatric overtones
- Lethargic
- Confused
- Sleeping problems, anxiety
- Polyuria and polydipsea- symptoms of D. Insipidus

Lab

- High PTH
- High Ca
- Low phosphate
- Hypercalciuria
- Chloride/phosphate ratio- 33:1- very sensitive

X-Ray

Sub-periosteal resorption- mainly on the radial aspect of 2^{nd} and 3^{rd} upper phalanges

Treatment

1. **Surgical**

- PTH adenoma- surgical removal
- Hyperplasia- take all 4 out. Bury one gland in your muscle so that PTH production continues.

2. **Medical**

- Increase fluids to treat high Ca
- Loop diuretic like furosemide
- Thiazides should not be given for hypercalcemic patients.

- Medical treatment is for non-symptomatic patients.

Hypoparathyroidism

Definition

The parathormone level is less.

Causes

- Thyroidectomy
- Radical surgery for thyroid cancer on head and neck.

Case

39 year old female comes into the emergency complaining of Grand mal seizures. First benzodiazepines were administered. Lab reports show that calcium level is 6.0 which is quite low or hypocalcemia.

In EKG prolonged QT seen which is about 500 which normally should be 440.

Low calcium, magnesium and potassium- prolonged QT

Clinical features

- Prolonged QT on EKG it will cause Torsades, and later ventricular fibrillation or cardiac arrhythmia.
- Grand mal seizures due to hypocalcemia
- Tetany –
    1. Chvostek's sign- tapping the facial nerve causes spasm on that side
    2. Trousseau sign- Put a BP cuff and pump it over patient's systolic pressure and hold it for 3 minutes there will be carpo-petal spasm. It is not practised in the hospital generally.
    3. Tingling sensation and numbness

Physical examination

- The signs of tetany are tested.
- Hyperactive Deep tendon reflexes

Diagnosis

1. Level of PTH- it will be low.
2. Low calcium level
3. Hyperphospotamia
4. Low urine cyclic AMP

Treatment

1. IV Calcium gluconate.
2. Vitamin D- calcium reabsorption

Hyperthyroidism

Definition

Abnormal excessive production of thyroid hormones (T3 and T4) due to hyperactivity of thyroid gland is hyperthyroidism.

What are the causes?

1) Graves disease- It is the most common cause. It is actually diffuse thyrotoxicosis or toxic diffuse goiter (hypoplasia of thyroid gland in which the entire gland is hyperfunctioning causing excess hormone production). This disease is an autoimmune disorder where numerous antibodies (TSI- Thyroid Stimulating Immunoglobulins) bind to the TSH (Thyroid Stimulating Hormone) receptors. TSH receptors respond to TSH under the action of which the gland keeps on producing more and more of thyroid hormones. TSI are actually IgG immunoglobulin. These immunoglobulins cause a lot of damage to the gland and cause the condition thyrotoxicosis as there is a toxic production of thyroid hormones.
2) Toxic adenoma- Only a small mass of cells of the thyroid gland produces thyroid hormones abnormally.
3) Drugs like Amiodarone – it is given when a person undergoes Ventricular tachycardia. This causes hyperthyroidism as there is an excess consumption of iodine.
4) Toxic multinodular adenoma – There are multiple nodules within the gland which act as separate factories that produce thyroid hormone excessively. This disease is also called Plummer's disease and these patients are at an increased risk of having CHF and arrhythmias. As thyroid hormones increase the beta1 receptors in the heart, there will be increase in heart contractility due to sympathomimetic effect. This leads to CHF. Atrial fibrillation, which leads to arrhythmias, is because of increased thyroid hormones.

   Clinical manifestations-

   - Exophthalmos and pretibial myxedema- The most common and prominent feature is exophthalmos and pretibial myxedema. These are the classic signs of Graves disease. Exophhalomos is the bulging of eyeballs and widening of pupils. The patients seem to be staring at a particular object. It is caused by the phenomenon of proptosis that is caused by glycosaminoglycans (produced by the antibodies that cause hyperthyroid) deposition in the eyelids. The leg has edema in front of the tibia so there will be indentations when the finger is pushed on that part of the leg. The same can appear on the dorsum of the hands.
   - Lack of sleep.
   - Develop tremors and have a shaking or trembling hand.
   - Frequent bowel movements
   - Excessive sweating
   - Palpitations
   - Weight loss in spite of having a good appetite- the increased level of T3 and T4 cause increased rate of metabolism.
   - Osteoporosis- the osteoclasts break down bone under the action of thyroid hormones. This leads to hypercalcemia.

Diagnosis

- TSH test- The level of TSH will be low because of negative feedback to the pituitary gland. The body senses that the level of thyroid hormones is high so there is no need for TSH. Hence the level will be low.
- The level of T3 and T4 will be high.
- The uptake of radioiodine will be high.
- Antimicrosomal antibodies
- Antithyroglobulin antibodies

Treatment

1. Propiothiouracil/ methimazole- inhibit the coupling and organification of T4 or T3 by acting on Iodide Peroxide
   Side effects- skin rashes, agranulocytosis
   Propiothiouracil is safe during pregnancy.
2. Propanolol- Beta blocker
3. Radioablation therapy- I131 can be used to destroy the tissue when used in Grave's disease. In case of a single nodule, the nodule gets eliminated under the action of I-131 isotope.
4. Surgical removal of the gland- In that case, levothyroxine hs to be given, otherwise, the body can go into hypothyroidic state.

13. Hypothyroidism

Definition

In this case, there is low level of T4 and T3 and there is increased level of TSH. It is primary type. Secondary is when TSH is not produced. Tertiary is when TRH is not produced.

Causes

1. Hashimoto's disease (chronic thyroiditis)- order antimicrosomal antibodies to know if they have this disorder or not.
2. Surgery/ Radioiodine therapy
3. Drugs- lithium,

Symptoms

i. **In newborns**- thyroid hormone is important for brain development. Order TSH level to find if it is low or normal. Absence of thyroid hormone causes-

1. cretinism (mentally retarded)
2. Dwarfism is another problem
3. Flat noses
4. Poor dentition
5. Wide spaced eyeballs
6. Pot belly
7. Umbilical hernia
8. Dry skin
9. Delayed bone development

ii. **In adults-**

1. Lethargy
2. Constipation
3. Depression
4. Carpal tunnel syndrome
5. Hyponatremia/anemia
6. Decreased deep tendon reflex
7. Cold intolerance

Diagnosis

1. TSH level- increased level
2. T3 and T4 free levels are low

Treatment

1. Levothyroxine

Complications

1. Myxedema coma- respiratory depression- CO_2 retention- respiratory acidosis

Thyroid storm

Definition

This is a decompensated state of thyroid hormone induced severe hypermetabolism. This is an extreme case of thyrotoxicosis.

- They usually have a history of hyperthyroidism. They have high T3 and T4 but low TSH.

Pathophysiology

- Not fully understood.

- increased adrenergic receptor activation because sympathetic nerves innervate thyroid gland.

- elevated thyroid hormone so high metabolism

History- thyrotoxicosis

Clinical features

- Voracious appetite but no gain in weight
- Anxiety, seizures, trembling, tremors
- Agitation, palpitations
- Excess sweating
- Heat intolerance
- Hyperpyrexic – 38.5-41 degree Celsius
- Increase in oxygen and energy consumption.
- Poor attention span
- Hypertension
- Heart failure
- Pulmonary oedema
- Tachycardia- may proceed to supraventricular arrhythmia- atrial fibrillation
- Nausea, vomiting, diarrhoea, abdominal pain, jaundice

Physical examination

- Sweaty patient
- Feverish
- Orbitary signs- Grave's Disease
- Neck – goitre

Causes

- Hyperthyroidism (Grave's disease- thyroid stimulating immunoglobulins)
- Stress from
    1. Sepsis
    2. Surgery
    3. Anaesthetic induction
    4. DEA

5. Drugs- anticholinergic
6. Direct trauma to thyroid

- Pregnant women transfer through placenta and affect the baby.

Diagnosis

- purely clinical diagnosis
- thyroid studies – increased T3 and T4 but low TSH
- CBC- mild leucocytosis with a small left shift.
- Change in LFTs , LDH, Creatinine, increased bilirubin

Imaging

- Chest X-ray- big heart- CHF
- EKG- due to Atr. Fibrillation

Treatment

1. Beta blockers-they prevent the peripheral conversion of T4 to T3. Eg. Propanolol- decrease heart rate and contractility.
2. Antithyroid medications- propiothiouracil (prevents organification and coupling) and methimazole (prevents organification and coupling). PTU inhibits peripheral conversion.
3. Glucocorticoids- prevent transformation of T4 to T3
4. Iodides like potassium iodide- inhibit the release of thyroid hormone from the thyroid gland.
5. Acetaminophen and Tylenol to bring down fever.
6. Fluids to control diarrhoea

15. Thyroiditis

Definition

It is the inflammation of the thyroid gland.

Forms:

i) Subacute viral thyroiditis or subacute granulomatous thyroiditis.
ii) Subacute lymphocytic thyoiditis
iii) Fibrous thyroididtis (Riedel's thyroiditis)

I. Subacute viral thyroiditis or subacute granulomatous thyroiditis

Causes:

It is caused by virus.

Symptoms

- Fever, flu like symptoms or illness
- Transient hyperthyroidism due to excess production of T3 and T4 due to inflammation.
- After some time, they become euthyroid and then due to draining out of thyroid hormones they become hypothyroid.
- They have painful tender thyroid gland

Diagnosis

Give radioiodine which is I 123

-the uptake is quite low as they are inflamed

- TSH level is low

- T3 and T4 is going to be high

- The ESR will be high.

Treatment

- Mild cases- NSAIDS like aspirin can be given
- Severe cases- corticosteroids like prednisone has to be given.

II. Subacute lymphocytic thyroiditis

It is painless or silent in nature.

Symptoms

- Transient thyrotoxicosis
- Hyperthyroid

Diagnosis

- Radioiodide uptake is low
- Hypothyroid – will be the only difference.

III. Fibrous thyroiditis (Riedel's thyroiditis)

- Fibrous collage tissue replaces the thyroid gland tissue
- Thyroid becomes firm
- Hypothyroid

Hyperosmolar hyperglycaemic non-ketotic syndrome HHNS

Definition

One of the acute complications of diabetes mellitus.

Cause

They have elevated blood sugar which causes osmotic dieresis and so dehydration.

Population affected

It is seen in type II DM

Pathogenesis

1. Low insulin- this causes hyperglycemia-so dehydration
2. Thirst response decreased- worsens dehydration

Symptoms

- Thirsty/Oliguria
- Decreased intravascular volume- low BP, (hypotension, tachycardia)
- Predisposed to seizures
- Lethargic
- Confused
- May go to coma

Diagnosis

- Finger stick and check RBS> 600mg/dl
- Osmolality>320mg/dl (normal-290)
- Check pH. If pH is 7.4, it means the person is not acidotic. Check bicarb>15 then the person is not acidotic
- Elevated BUN

Treatment

- Replace fluids- normal saline in 1st water and then I litre in next 2 hours.
- 2-4 units of Insulin for high blood sugar
- If glucose becomes low as much as 250mg/dl then we give 5% glucose (B5 1/2 NSS).
- Careful about CHF and renal insufficiency

Hypoglycaemia

Definition

Low level of glucose in blood is called hypoglycaemia.

Causes

1. Drugs like insulin
2. Factitious hypoglycaemia- due to exogenous insulin- high insulin and low blood glucose
   - C peptide is low
3. Sulfonylureas like glimeparide, gliburide- check urine to find drug metabolite
4. Insulinoma
5. Ethanol ingestion- no glycogen storage – they undergo glycogenolysis- they don't have enough NADH required for gluconeogenesis
6. Surgery
7. Adrenal insufficiency- under stress- reactive hyoglycemia
8. Liver failure

Clinical features

1. Glucose level< 50 mg/dl
2. Tachycardia
3. Palpitations
4. Anxiety
5. Sweating
6. Tremors

} epinephrine activation of alpha1 and beta1 receptors

7. Brain symptoms- confusion, lethargy, drowsy, coma and death

Diagnosis

1. Finger-stick test to know the blood sugar<50mg/dl
2. C- peptide
3. Serum insulin
4. Anti-insulin antibody levels

Treatment

1. Eat good food
2. D50W through IV- then D10 if it reaches to a level of 100mg/dl
3. Wernicke encephalopathy has to be avoided.
4. Thiamine (B1) has to be given first and then glucose.

Insulinoma

Definition

It is the tumour of beta cells of the pancreas. It is mostly benign.

It is associated with MEN 1(multiple endocrine nuclear-1)

Clinical features:

- Due to increased insulin there is hypoglycaemia
- The **epinephrine** is also high so there will be symptoms like –
- Sweating/diaphoresis
- Tachycardia
- Tremors
- Palpitations
- The **CNS symptoms** like-
- Headache
- Confusion
- Lethargy
- Coma
- Death in severe cases

Diagnosis

1. Fasting blood sugar- hypoglycaemia and elevated levels of insulin in serum
2. Whipple's triad- i) decreased glucose due to fasting
   ii) Blood sugar< 50 mg/dl- symptoms start
   iii) glucose- on giving glucose they feel normal.

Treatment

Surgical resection of the tumour is done. The prognosis is quite good generally.

	Insulin	**C-peptide**	**Glucose**	**Pro-insulin**
Insulinoma	↑↑↑	↑↑↑	↓↓	↑
Factitious insulin used	↑↑	↓	↓	↓

MULTIPLE ENDOCRINE NEOPLASIA(MEN)

MEN I -Werner's syndrome

Associated with the 3P's

- Pituitary tumour (prolactinoma)
- Parathyroid tumour
- Pancreatic tumour

Symptoms

- Chronic peptic ulcer
- Gastrinoma (Zolliger Ellison syndrome)
- Parathyroid hyperplasia (Hyper PTH)

MEN IIA- Sipple's syndrome (MPH)

Associated with

- Pheochromocytoma
- Hyperparathyrodism
- Medullary thyroid carcinoma

Symptoms-

- High blood pressure 180/100
- Palpitation
- Hypercalcemia
- High PTH level

MEN IIB (MMMP)

They have

- Pheochromocytoma
- Marfenoid habitus (tall and lanky)
- Mucosal neuromas (nasopharynx/oropharynx/ larynx)
- Medullary thyroid carcinoma

Symptoms-

- High blood pressure 220/100

Parathyroid gland physiology

Location- they are located behind the thyroid gland and are 4 in number.

- Produce parathormone
- Acts on bone and kidneys

On taking Vit. D (endogenous) it moves to

- liver where it is converted to 25-OH2 Vit.D
- In kidney, it is converted to 1, 25-OH2 Vit.D in the presence of 1, alpha hydroxylase.
- This way 1,25 dihydroxycholecalciferol is formed which is the active form of Vitamin D.
- The active form moves to duodenum to reabsorb calcium and phosphate.
- 400mg of calcium absorbed.

Functions

- Parathormone stimulates osteoclasts to cause bone destruction and release Ca ions
- Increases production of 1,25 (OH)2
- Decreases phosphate reabsorption by kidneys
- Increases the distal convoluted tubule reabsorption of calcium.

Vitamin D functions

- Increases reabsorption of calcium and phosphate
- Increase proximal tubular reabsorption of phosphate

Calcium regulation- occurs in bone, kidney and intestine

Too low/hypocalcemia	Too high/ hypercalcemia
Parathyroid hormone is released	Calcitonin (made by parafollicular cells of thyroid gland) is released
Activate Vit. D for calcium reabsorption	
Osteoclast destroy bone to release Ca	Osteoblasts are stimulated causing bone deposition

Pituitary gland physiology

Anterior lobe of pituitary produces FLAT PIG

- FSH
- LH
- ACTH
- TSH
- Prolactin
- Growth hormone

Posterior lobe produces

- Vasopressin, ADH- supraoptic
- Oxytocin- paraventricular

Prolactinoma

A tumour producing too much prolactin.

Microadenoma	Macroadenoma
<1cm	>1cm
Women	Men

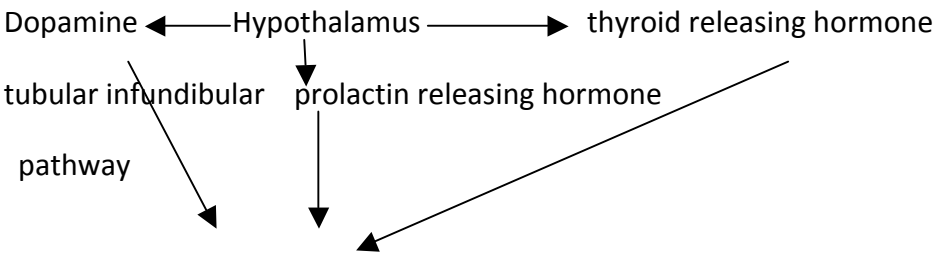
Case

23 year old female missed her periods from the past 3 months and has a milky secretion from her breasts.

1. b-HCG- not pregnant
2. TSH- normal
3. No drugs
4. This might be a prolactinoma

Causes

1. Pregnant
2. Stressed out
3. Seizures – increased prolactin level



Drugs to block dopamine action causing from increased release of prolactin

Phenothiazine

Metoclopromide (drug given for diabetics)- hyperprolactinemia is side effect

They are dopamine antagonist blockers

Patients with hypothyroidism have hyperprolactinemia.

History

C/o of galactorrhea and amenorrhoea

This is because of the prolactin inhibitory effect on hypothalamus in producing GnRH whic in turn is responsible for the release of LH and FSH. This is the reason for amenorrhoea.

Clinical features

- Osteoporosis/ osteopenia-due to lack of FSH which is responsible for oestrogen production
- In men, lowered libido
- Lowered erectile dysfunction
- Gynecomastia

Diagnosis

1. Check pregnancy- beta HCG
2. TSH level if she is hypothyroid or no
3. Rule out drugs
4. Check prolactin level>100mg/ml (normal is <20mg/ml)
5. MRI- to check if it is micro or macro adenoma

Treatment

1. Bromocriptene or Cabergoline (dopamine2 agonists)
2. Transphenoidal resection surgery

Primary aldosteronism

Definition

There is a tumour producing increased levels of aldosterone. This will cause increased activation of Na+/K+ATPase pump- increased Na reabsorption- increased K excretion- metabolic alkalosis and hypokalemic.

Causes

1. Single adrenal adenoma- Conn's syndrome
2. Bilateral adrenal hyperplasia
3. Adrenal carcinoma

Symptoms

1. High blood pressure- due to increased intravascular volume
2. Headache due to hypertension
3. Fatigue and weakness due to hypokalemia
4. Polydipsia/ polyuria
5. Do not have peripheral oedema.

Diagnosis

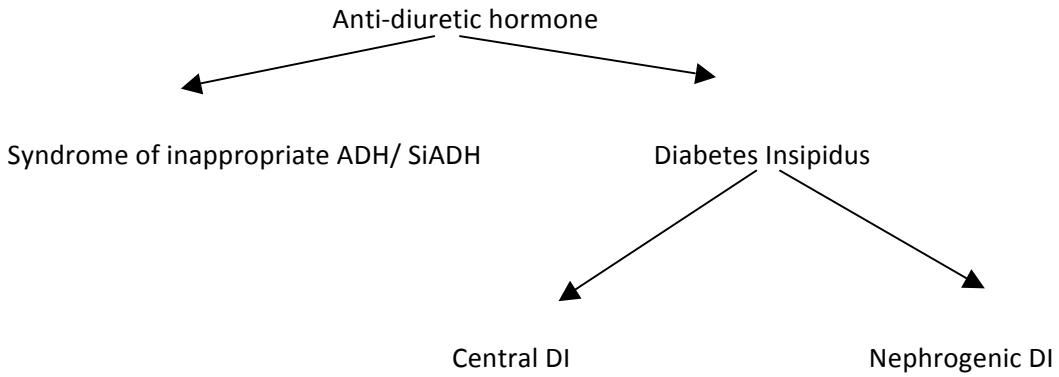
1. Check plasma aldosterone level/plasma rennin ratio>30 plasma aldosterone is very very high
2. Saline infusion test (NaCl)- in normal cases the level of aldosterone should decrease but in case of primary aldosteronism it increases.
3. Imaging- CT/MRI may show adrenal tumour.
4. Adrenal venous sampling- if the aldosterone level is high on one side only then it is adrenal adenoma, if both the sides then bilateral hyperplasia

Treatment

1. Isolated adrenal adenoma- surgical excision
2. B/L hyperplasia- spiranalactone is given

SiADH

POSTERIOR PITUITARY LOB E DISORDERS



Definition

It is the excess production of ADH which causes excess water absorption form collecting tubule of nephron. This causes volume expansion/hypervolumic and hyponatremia. In the atrium, ANP (atrial natriuretic peptide) is reeased which acts on kidneys to eliminate sodium ions. This worsens the hyponatremic condition.

They **do not** have oedema. So SiADH is different.

Causes

1. Cancer (neoplasm)- lung cancer (small cell/oat cell carcinoma)
2. Stroke
3. Trauma
4. Infections like meningitis or encephalitis
5. Drugs like Vincristin, SSRIs, Morphine, Desmopressin
6. TB, pneumonia

Clinical features

1. Acute state- swelling in brain due to hyponatremia- causes lethargic, weak, seizures, coma, somnolent

Diagnosis

1. Diagnosis of exclusion- labs
   i. Hyponatremia<135
   ii. Decreased BUN/Cr

Treatment

Treat the underlying cause

Asymptomatic	**Symptomatic**
Water restriction	Water restriction
Normal saline + loop diuretic (furasemide)	Isotonic saline
Lithium bicarbonate (inhibit ADH)or	Hypertonic saline 3%- titrate it at 0.5

demicocycline	meQ/hr. If too much concentration is given- central pontine myelolysis- it can cause brain damage

18.Insulinoma

Hyperthyroidism

- Excess of T3 and T4 are produced.
- **Perchlorate/ petechnate**- They are anion inhibitors which block the iodide pump by blocking the re-uptake of iodine into thyroid gland.
- **Methimazole or propythiouracil –** They inhibit the activity of IPO (iodine peroxidase) which is responsible for organification and coupling. Propythiouracil differs from methimazole because it goes outside and prevents the peripheral conversion of T3 and T4
- **Side effects of these drugs-** skin rashes, agranulocytosis (low WBC count). Such patients need to get their CBC (complete blood count) checked quite often to ensure that they don't have neutropenia. If they have neutropenia, a slight fever can cause their death.

Thyroid gland physiology

Thyroid releasing hormone TRH produced by hypothalamus- induces pituitary gland to form thyroid stimulating hormone TSH- which stimulates thyroid gland to produce T4/T3/thyroxine

Inside the follicular cells of thyroid gland

- Iodine molecules trapped by follicular epithelium- iodide pump
- Iodide peroxidase- oxidation of I molecules to form I_2
- In the cell membrane I_2 is added to tyrosine in the presence of iodide peroxidise- organification
- MIT and DIT are formed.
- 1MIT + 2DIT= T3 } Coupling process
- 2DIT + 2DIT = T4 }
- IPO catalyses organfication and coupling
- Thyroid globulin stores T3 and T4
- Under the impact of TSH , T4 and T3 are released
- T4 forms T3 in the presence of 5'iodase.
- T3 is the most active form and reverse T3 is less active form of T4.
- They are bound to thyroxine binding globulin formed by liver

Functions of T3

1. Metabolism – catabolic hormone
2. Growth hormone + T3 for bone formation
3. CNS- mental retardation if there is no T4 and T3
4. Autonomic nervous system- stimulate the increase of Beta1 receptors of heart. So beta blockers are given for hyperthyroidism
5. BMR maintenance- Na-K ATPase pump does not function in the absence of Oxygen
6. Metabolism-
    i. Glycogenolysis
    ii. Gluconeogenesis
    iii. Lipolysis
    iv. Protein synthesis

Mainly required for growth and metabolism.

VIP-oma

Definition- It is a malignant pancreative tumour that produces vaso-active intestinal peptide in excess. It is extremely rare. Another name is Verner Morrison syndrome or WDHAS (watery diarrhoea hypokalemia with achlohydria syndrome)

Symptoms

- Watery diarrhoea – this can lead to hypokalemia.
- Dehydration
- Achlohydria- the person is unable to produce HCl. VIP inhibits gastric acid production so no HCl produced.
- Hypoglycaemia and hypercalcemia

Treatment

Surgical resection of the tumor.

Zollinger Ellison syndrome

It is also known as gastrinoma. It is a tumor of pancreatic islet cells which produce excess gastrin.

It is associated with MEN I syndrome.

Gastrinoma triangle points are

- Cystic duct
- Neck of pancreas
- 2^{nd} and 3^{rd} portion of duodenum

Symptoms

- Peptic ulcer disease-
  i. epigastric pain and burning sensation,
  ii. GI bleed (hemorrhage),
  iii. GI perforation,
  iv. stricture formation due to fibrosis,
  v. metastasis into liver.
- Abdominal pain
- Diarrhoea
- Weight loss

Diagnosis

i. Gastrin level- fasting gastrin level.
ii. Secretin inhibitory test- secretin inhibits gastrin. If the level of gastrin is high even after administration of secretin, it is due to adenoma.
iii. Stomach Basal Acid Output- Normal level is <10mEq/hr. In case of these patients it will be higher than 15mEq/hr.

Treatment

- PPI- proton pump inhibitors- H K ATPase pump is inhibited. Omeperazole can be given.
- Surgical resection