# ENDOCRINOLOGY FOR COMMUNITY PRACTICE

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# A&G, C&B REFERRALS:

- 44 Yr old female referred by her GP
- Result requested by bariatric team given patient had blood test PTH and ALP raised with normal calcium and vitamin D. Patient previously took vitamin D.
- Reports intermittent neck hand and feet pain as well as occasional throat hoarseness eating drinking normally bowel and bladder normal
- Blood test result explained to patient. Referral to endocrinology is required for further assessment and Management.

- Key question: What exactly this patient needs for raised PTH?

# A&G AND C&B REFERRAL:

- On 19th Sept PTH 16.1 was 24.4 in early Sept. Her Adj calcium 2.34, Vit D not done and was 71 in May. ALP now 146 was 133

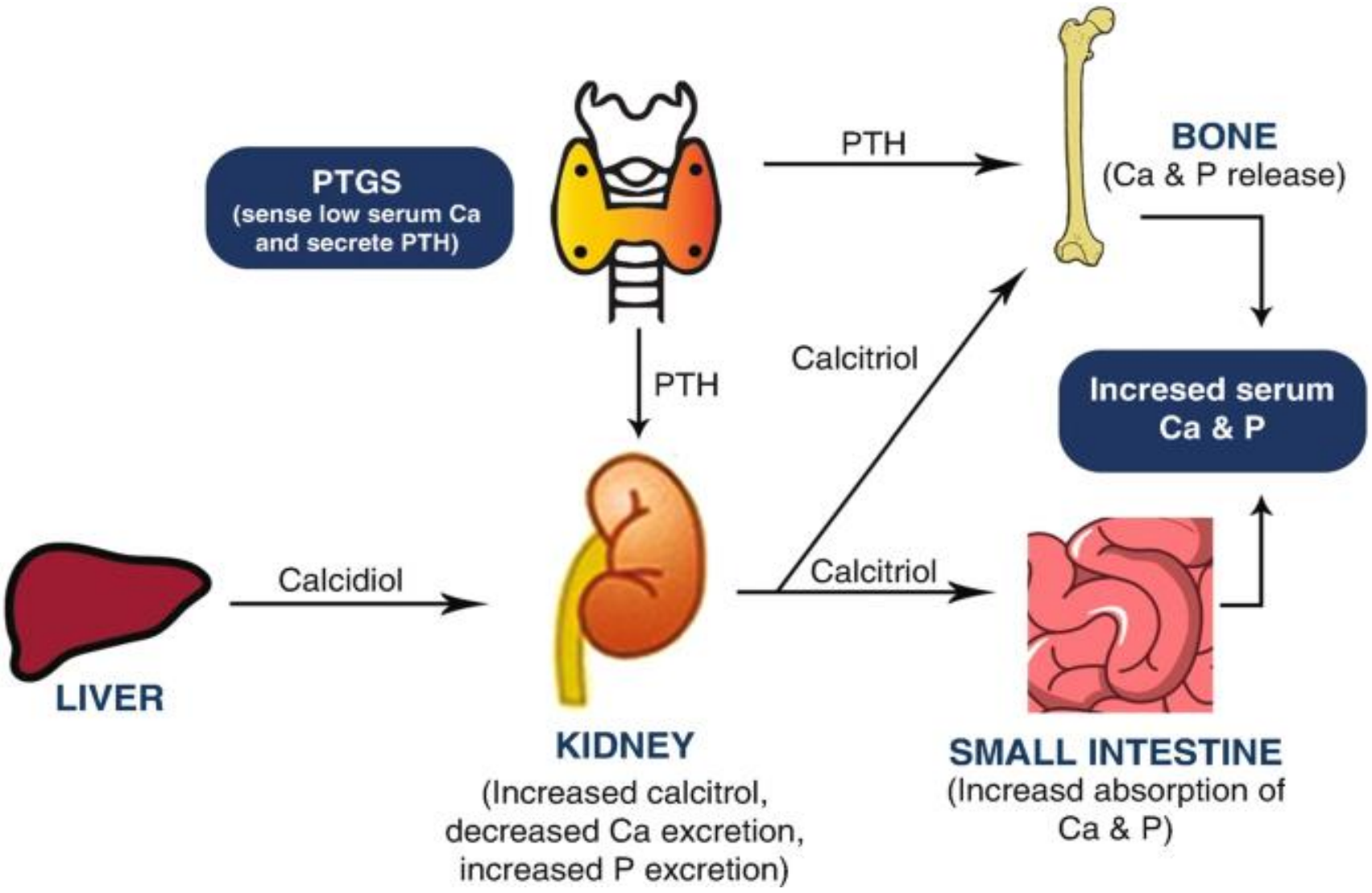
- Tier3 obesity clinic in Feb, PTH 24, Cal 2.34, Vit d 29 and raised ALP
- Recall the causes of elevated ALP

- ?Liver diseases, low vit D/osteomalecia and or stone diseases
- Or cholestasis, hepatitis, recent fracture and other bone diseases primary and metastatic

- Another one sent by physician associate via A&G
- I will be grateful for your review of this 68-year-old who has recent result of raised PTH with normal calcium and vitamin D and TSH.
- I confirm patient takes Calcium and Alendronic acid as per DEXA report which reported as osteopenia
- I wonder if any further investigation are needed for PTH or this is this acceptable

- PTH is 9.7 in December and was 8.75 in Nov. Calcium is 2.36 in Dec and was 2.42 in Nov and her Vid D was 52 in Nov. Vit D Not done on this occasion.

# CA HOMEOSTASIS AND PTH ACTION:



- **Secretion**:
- The parathyroid glands contain chief cells that produce and store PTH. When blood calcium levels drop, these cells release PTH into the circulation.
- **Calcium-sensing receptors**:
- The parathyroid cells have calcium-sensing receptors (CaSR). High calcium levels activate these receptors, which signal the cells to inhibit PTH release. Low calcium levels have the opposite effect.
- **PTH action**: On bones, Kidney and in Intestine
- It stimulates bone resorption and release calcium. It helps to retain calcium through renal tubule and excrete phosphate and also increase formation of Active D/Cacitriol (1, 25 OH Vit D3)

# PRACTICAL POINTS:

- Now let’s talk about practical points in relation to Calcium and Vit D metabolism
- PTH is not a test as first line investigation
- I would recommend to check PTH only if Calcium comes abnormal. Such as raised calcium or the level is lower than reference range.

- If Adj calcium is low or borderline low all that you need is Vit D level.
- If vit D low or borderline then will need treatment along with Calcium replacement

- This condition is most likely secondary hyperparathyroidism. Associated biochemical abnormality is raised PTH with low Vit D and or low/low normal Calcium
- This should be treated in community
- If Calcium level remain low despite treatment with Calcium and Vit D then consider testing PTH and referral to Endo

- Often this could be due to in appropriately low PTH consistent with hypoparathyroid.
- When Calcium is high then PTH must be checked along with Vit D. We are likely dealing with PHPT therefore referral to Endo is necessary

- PHPT = Raised Calcium and raised PTH.
- Please ensure no evidence of advanced CKD and patient is not on Calcium/Vit D. Other meds such as Lithium or Thiazide
- SHPT = Low/low-normal Calcium and raised PTH and usually low Vit D
- If likely PHPT then Please refer case to Endocrinology
- If PTH is low or low-normal with high calcium then potential malignant cause should be investigated. Needs further investigations and scans.

- Cases with hypocalcemia as a result for surgery causing iatrogenic hypoparathyroid which needs treatment with Calcium and activated Vit D (Alfacalcidol or calcitriol)

- Target Calcium level should be lower end of normal in ref range or slightly below normal. To avoid calcium level above mid point in ref range.
- Please review Bisphosphonate treatment annualy. Consider stopping Bisphosphonate treatment after 3-5 year.

- Continuing bisphosphonate treatment beyond 5 years may offer continued fracture protection but also increases the risk of rare, serious side effects, particularly Atypical femur fracture (AFFs) and ONJ

# MALE HYPOGONADISM:

- 41 Yr old c/o tiredness, fatigue and low mood
- With these symptoms had blood test and showed low Testosterone at 4.3 and 6.8. His LH 2.8, FSH 1.4 and SHBG 20.
- I believe issue is BMI
- Another case:
- 32 Yr old c/o Generally unwell, poor concentration, poor libido and weight gain as well as poor energy.
- FT in June was 10.1 and in Sept dropped to 9.0. LH 2.1, FSH 1.8, PRL 120 and SHBG16. His other medical conditions include OSA, HTN and GORD.

- Treatment for biochemical hypogonadism may not help with tiredness and poor energy level. It helps hypo gonadal symptoms with PDE5 medications.
- We carry out calculated free testosterone if Total testosterone is in borderline range (8-12) taking into account SHBG.
- Lower the SHBG higher the free testosterone level and is commonly seen in obese/overweight patient

- Cut off level for treatment is 225 pmol.

- It is very important to address Obesity/BMI.

# TIREDNESS AND RANDOM CORTISOL:

- Want to highlight classic example for referral with so called high cortisol
- First key Q is why are we checking Cortisol?
- Interpreting cortisol is not similar to most other result such as Hb. If high it is polycythemia and low means anemia
- Routine blood test can only confirm cortisol sufficient or not.

- Receiving referral as high cortisol when the value is 650/780/850 etc. These values are just normal.

- Time of the day, stress, illness or even medication specially OCP/Estrogen.

# CLINICAL CONTEXT OF HIGH CORTISOL:

- Referral with concern of high cortisol state such as Cushing's should be mainly on clinical context or with clinical suspicion.
- Not just due to obesity and or patient not feeling well. Presence or absence of Cortisol related complications such as Proximal myopathy and muscle wasting, central obesity, DM/Glucose intolerance, HTN and easy bruising etc are important.
- This condition is very rare and not for routine test/screen
- The necessary screening test is Overnight dexamethasone test. This can be carried out in community.

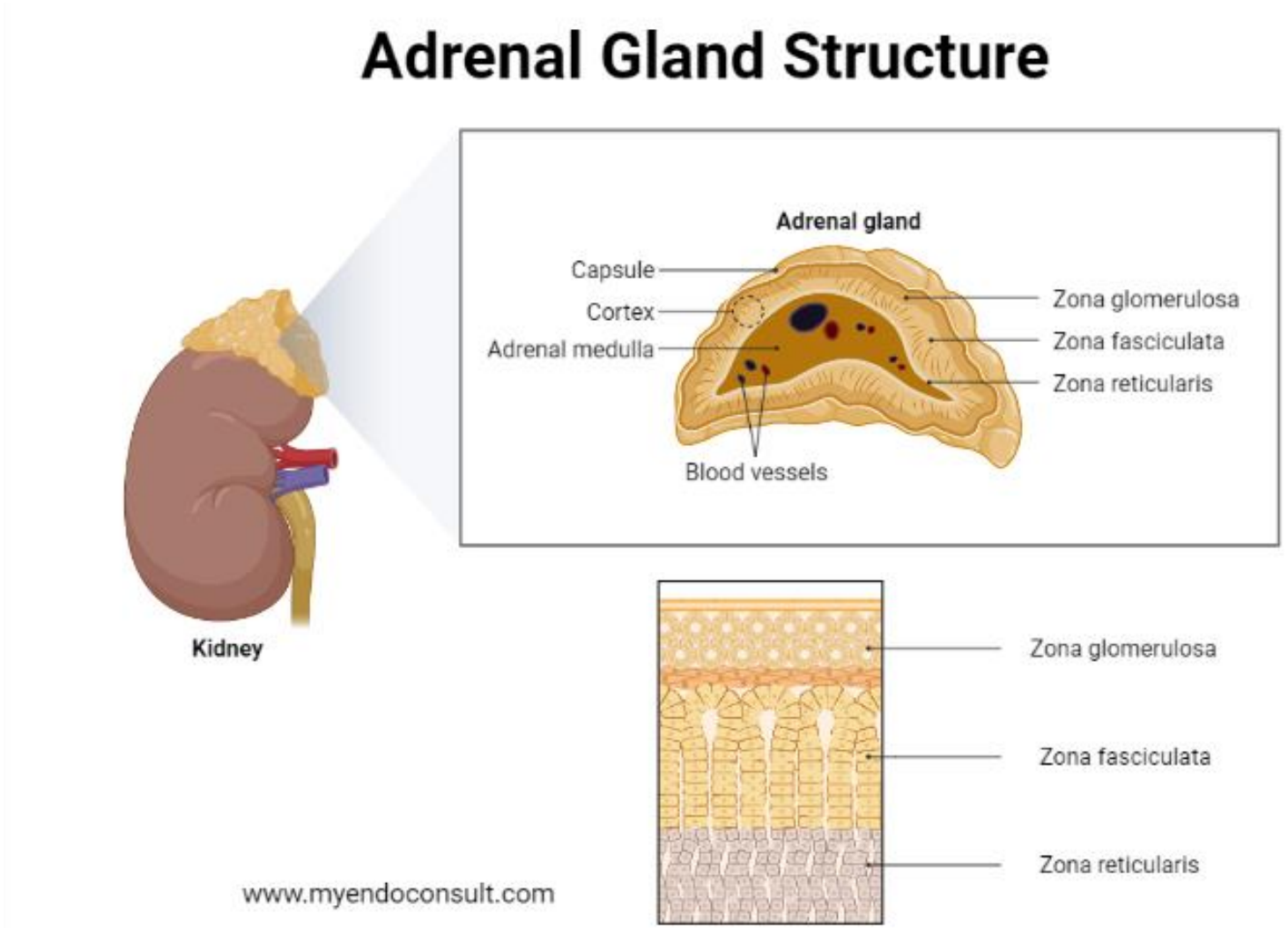
- Pt has Sjogren’s and PMR on regular Prednisolone 10mg od
- I would appreciate your advice regarding this 72-year-old lady who is feeling dizzy and faint. This problem is happening every day now. She does not pass out but is unable to do anything until BP gets to a normal range. BP was down to 87/69 yesterday and after an hour went to 113/70. Has had BP Meds reviewed.
- The dizziness is mainly when bending down to pick something up. BG of Addison's disease and is on Prednisolone 10mg OM

- What is the likely cause of her symptoms here?

- 10mg Pred is equivalent to 50mg Hydrocortisone daily
- Please recall the physiology of Hypothalmic-Pituitary-adrenal axis with ACTH
- This case is not Addison's but had secondary adrenal failure or iatrogenic adrenal insufficiency as a result of Chronic steroid treatment.
- Mineralocorticoid production is intact in adrenal suppression.

- The zona glomerulosa produces mineralocorticoids, the zona fasciculata produces glucocorticoids, and the zona reticularis produces androgen precursors

# ADRENAL GLAND PHYSIOLOGY:



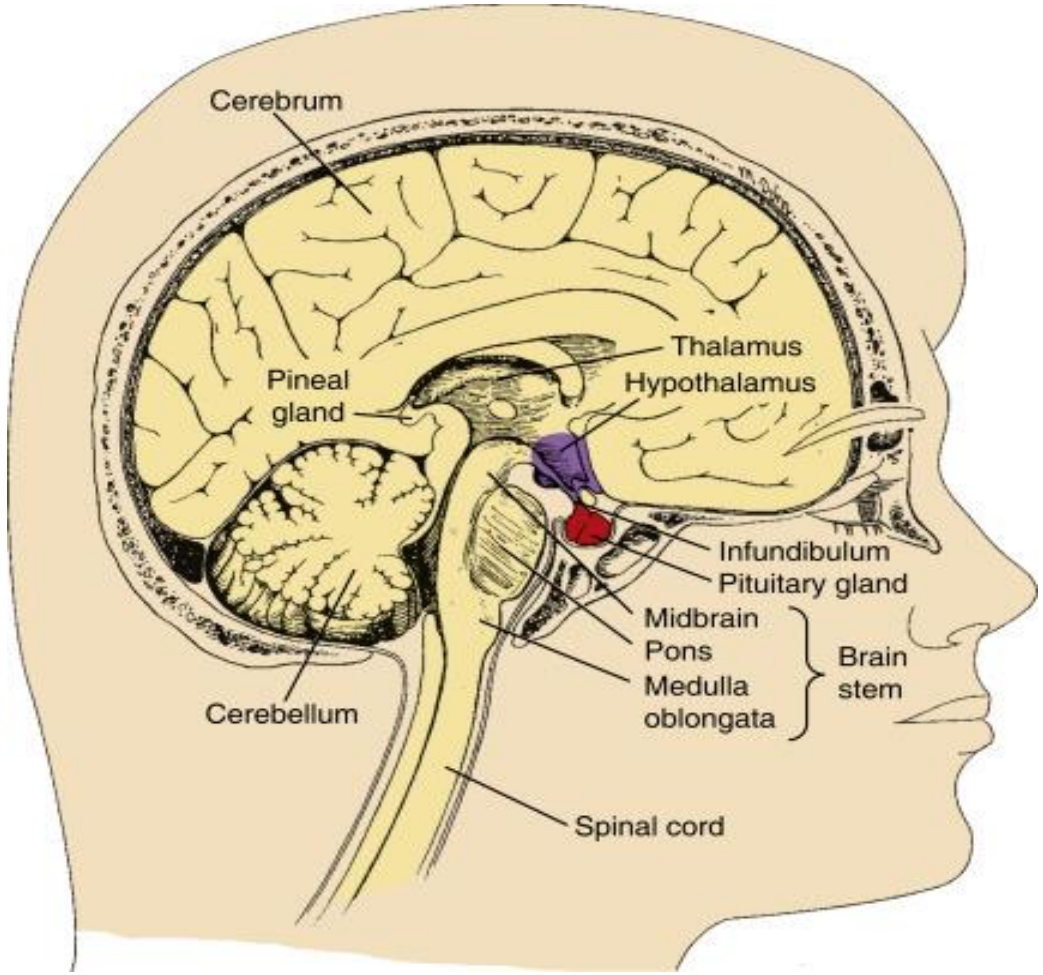
# CLINICAL CONTEXT OF HIGH CORTISOL:

- Another case: Dear endocrinologist. I am writing in regards to advice for so-and-so. she is 18-year-old with buffalo hump moon facies and abdominal striae obesity irregular. She denied any changes to the physical activity level no facial hirsutism no proximal muscle weakness.
- she is now waiting to see gynaecologist for irregular. These findings raise concern about endocrine disorders such as Cushing’s
- Add other case.

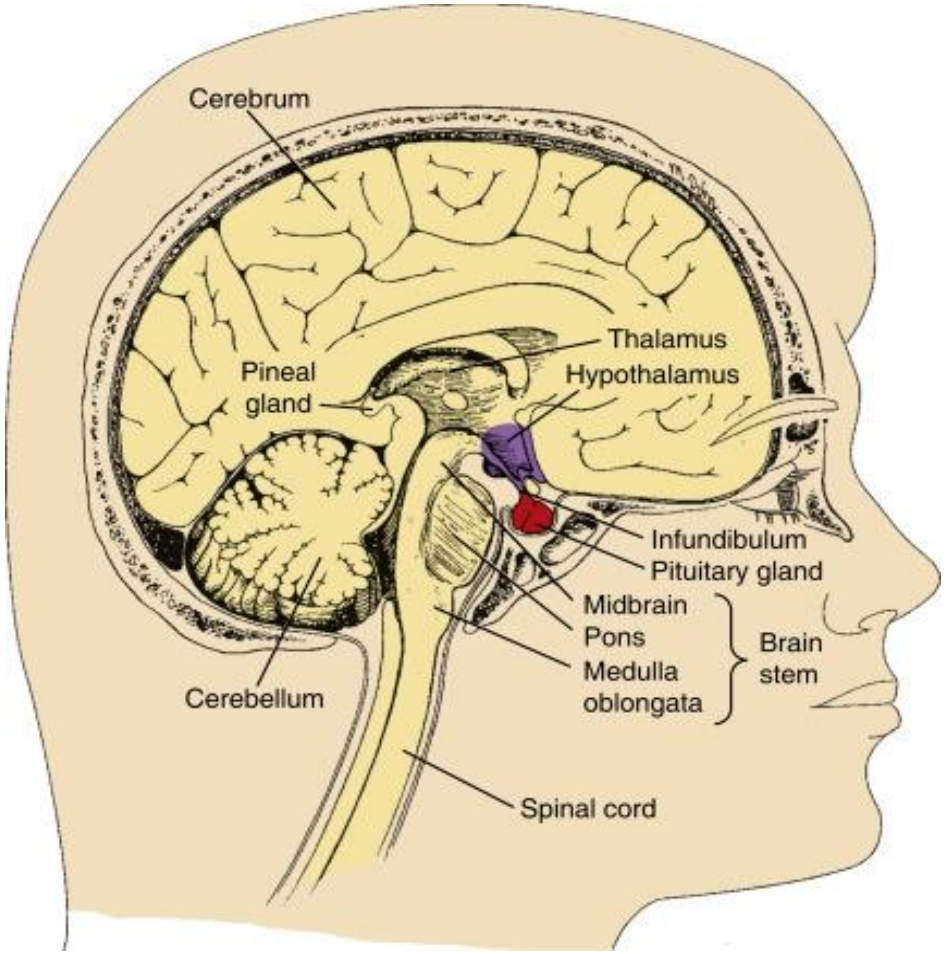
- The above patient has hypothyroidism, treated with 100micrograms levothyroxine.
- Repeat bloods still show a raised T4 despite us lowering the dose from July, but her TSH is now at upper end of normal. Patient describes profound symptoms of hypothyroidism despite the raised T4 and only a marginally lowered dose.
- Please could you review bloods on ICE and advise on next steps, as TSH and T4 don't really correlate? Patient compliant with her medications.

# PITUITARY:

- Pituitary function test
- Indication to carry out
- Pituitary function test



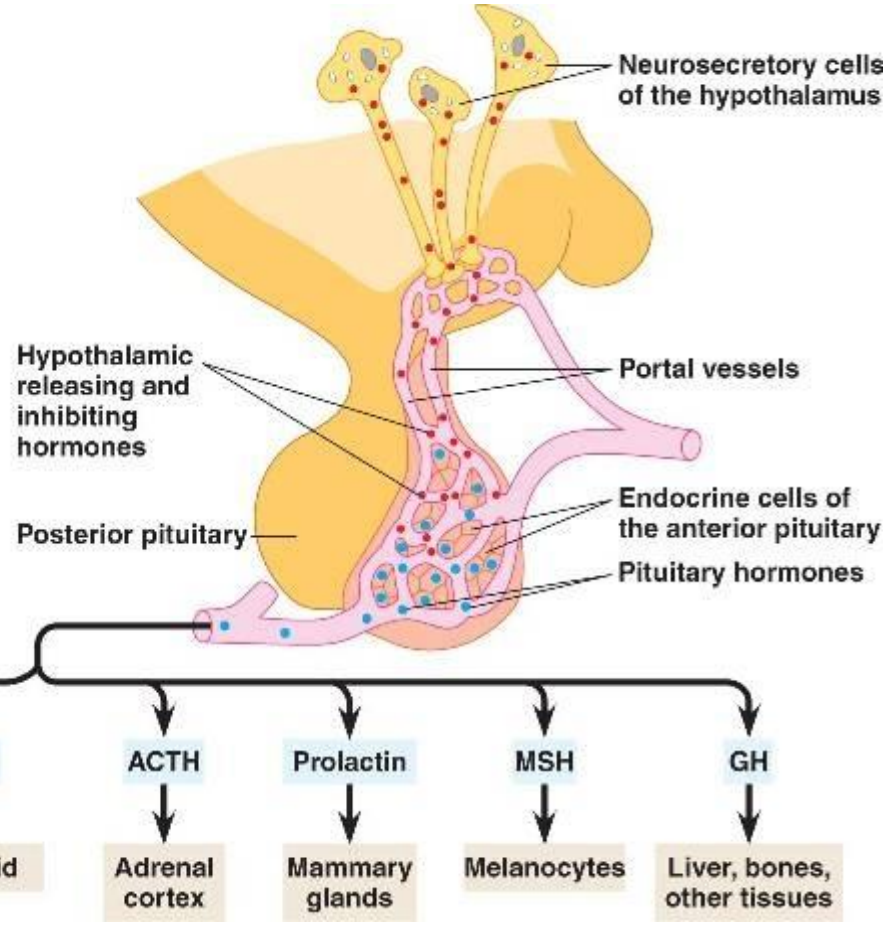
- Tumor in Pituitary or structural abnormality in Sella Turcica
- Empty sella
- Hx of radiation to brain (previously treated for brain tumor)
- Raised prolactin
- Reduced of suppressed any tropic hormone



Tropic effects only:
FSH
LH
TSH
ACTH

Nontropic effects only:
Prolactin
MSH

Nontropic and tropic effects:
GH



- A case referred to endocrinology

- 21 Yr old with 10 months hx of secondary amenorrhea. Blood test carried out and results are as follows:
- LH 1.1, FSH 1.5, Estrogen 110, PRL 160 and TSH 0.3

- Patient has Hx of Eating disorder and we made referral to Psychiatrist.

- This is functional/hypothalmic amenorrhea. There is a need for checking Pituitary function test. Plus minus MRI.

- Important fact to remember is to recognize Pituitary apoplexy in the context of patient with known pituitary micro/macroadenoma
- How to address raised Prolactin level
- Review of medication is important
- Two case who were on Metoclopramide and other one was on prochlorperazine

- It is very important to review medication before ordering hormone tests. It is very common that drugs and food can interfere test result. Specially Prolactin and Cortisol

# ENDOCRINOLOGY AND ELECTROLYTE:

- Please be aware that Endocrinology is not by default electrolyte specialty
- We can deal with Na related issue provided no clear non endo causes present such as HF, Renal dysfunction, CLD/Alcohol or GI causes, acute or chronic. Needs reviewing medication
- All type of calcium abnormalities belongs to Endo. Certain cases of K and Mg issues can be related to endocrinopathy. I shall talk about Na in the later slides.
- Hyperkalemia almost always renal dysfunction related
- Chronic and or intermittent hypokalemia on the context of Hypertension can be rerefer to Endo for screening.

- There are certainly many causes of low K.
- If you recall physiology to see how K homeostasis is maintained. Key role are with Acid-base and Renin-angiotensin-aldosterone system

- Only one cause that is Primary mineralocorticoid excess ie Primary Hyperaldosteronism (or in condition with hyper cortisol state) can result in low K.
- Most patient will have Hypertension. It is important to refer early and or test can be carried out in community.

# PHA/PRIMARY HYPERALDOSTERONISM:

- Recent studies suggest that more than 10% of hypertensive patients have primary hyperaldosteronism. Screening for PA is advised in the following circumstances:
- Resistant hypertension, Young onset of Hypertension and family history of early onset HTN
- Medication needs to stop for 4 weeks such as a. Spironolactone, epelerone, amiloride, and triamterene b. Potassium-wasting diuretics c. Liquorice
- And 2 weeks for Beta blockers, ACEi, ARB and NSAID
- Blood test 15 min after remain seated and patient needs to ambulatory for at least 2 hr. Test for Renin and aldosterone plus U&E (K needs to be within normal limit).
- Ideally screening for secondary HTN includes TFT and Pheo screen

# HYPOMAGNESEMIA:

- Often associated with low Calcium and or low K.
- Needs treating above

- But be aware that hypomagnesemia can be present in the following proportion of patient in certain setting:

  2%-4% normal population

  up 20% hospitalized patient

  up to 50%-60% of ICU patient

  30%-80% of people with alcohol related disorder

  up to 25% of patient with poorly managed diabetes

- Starvation.
- Alcohol use disorder with poor nutritional intake.
- Critically ill people who cannot take food by mouth and must receive all their nutrients by IV.
- Diarrhoea, Malabsorption
- Coeliac diseases, IBD and Gastric bypass surgery
- Acute pancreatitis
- Medication such as PPI, Diuretics (Hydrochlorthiazide, Bumetanide, Furosemide
- Other drugs, Gerntamycin, Neomycin, streptomycin, Cisplatin, Cyclosporin, Tacrolimu, Digoxin etc

- Familial hypomagnesemia with hypercalciuria and nephrocalcinosis
- Bartter/Gitelman
- Autosomal dominant hypocalcemia
- And EAST syndrome

# SUB CLINICAL THYROID DYSFUNCTION/THYROIDITIS

- Add the thyroiditis case; PPT and 245336
- Please see this 61-year-old lady with very low TSH and ongoing since April. Normal T4 and T3. Patient reports multiple symptoms related to hyperthyroidism (anxiety and irritability, mood swings, difficulty sleeping, feeling tired all the time, sensitivity to heath, needing to pee more often, excessive sweating, trembling).
- I would be grateful if you would kindly review this lady in your clinic
- Since Jan 2021 her T4 is around 10-12 with T3 around 5.0-6.2
- TSH has been normal to 0.11 was 0.3 on Jan 2021 and was intermittently lowish to normal in between.

# PCOS:

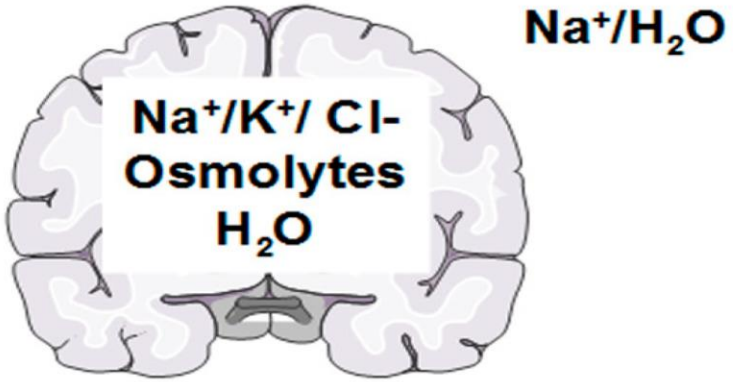
- May I ask what do you expect when referring cases for investigation of possible PCOS
- Want to clarify few points and some of misconception
- Roterdam criteria (Presence of two out of three signs from clinical, test and USS)
- Biochemical hyperandrogenism
- Female pattern baldness/androgenic alopecia, Acne and Hirsutism
- Biochemical hyperandrogenism are raised Total or free Testosterone, FAI, Androstenedione or DHEAS.
- Other abnormalities can be raised LH 9altered LH/FSH), low shbg and mild prolactin raise.

- We can carry out the screening test and to rule out secondary cause of PCOS
- Secondary causes are Thyroid dysfunction, Acromegaly, CAH, Cushing's, Ovarian hyperthecosis and androgen producing tumors

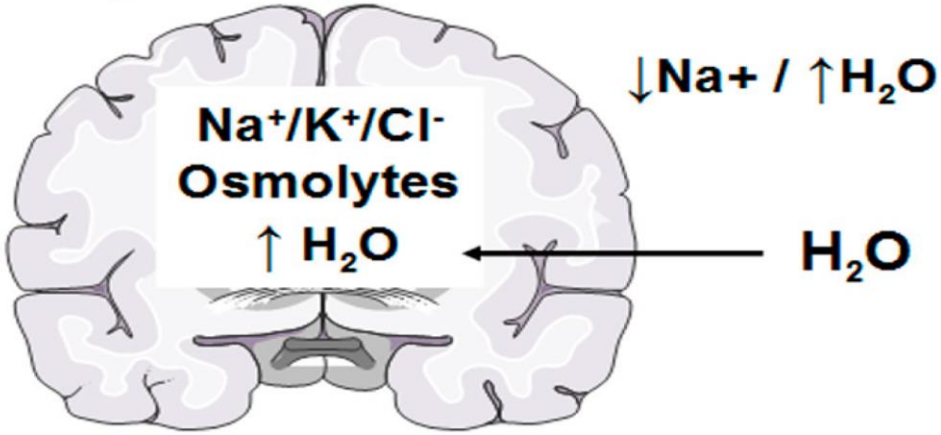
- Rotterdam criteria, NIH criteria and AES criteria (Exclusion of other androgen excess or ovulatory disorders)
- The oestrogen component increases sex hormone binding globulin, thus reducing free testosterone and improving hyperandrogenism.
- The progestogen component reduces ovarian androgen production by inhibiting secretion of luteinising hormone and protects the endometrium from hyperplasia.
- Lifestyle modification is first line. OCP with CPA with newer estrogenic compound (not ethinylestradiol; DVT risk). One with CPA plus Ethinylestradiol is more effective compare to the conventional ones.
- Treatment is based on area of concern or need (Hirsutism, Sub/infertility or oligoamenorrhoea)
- 17-hydroxyprogesterone in the early follicular phase in all women with possible PCOS to rule out non-classic congenital adrenal hyperplasia (NCCAH) due to 21-hydroxylase deficiency.

- Please see result. Elevated T4 and lowish TSH
- TSH 0.12, Was 0.38 in Nov, was 0.46 in Dec. Since 2010 lowish to normal. Very much chronic. This occasion T4 19.6 was 19.3 in 2023 and was 2/3 times in 19 otherwise all other time within the ref range
- Why this is an issue now
- You mention patient is okay. But sometime you would say some symptoms could be related. But possibly not as this has been very long standing
- Criteria for treatment

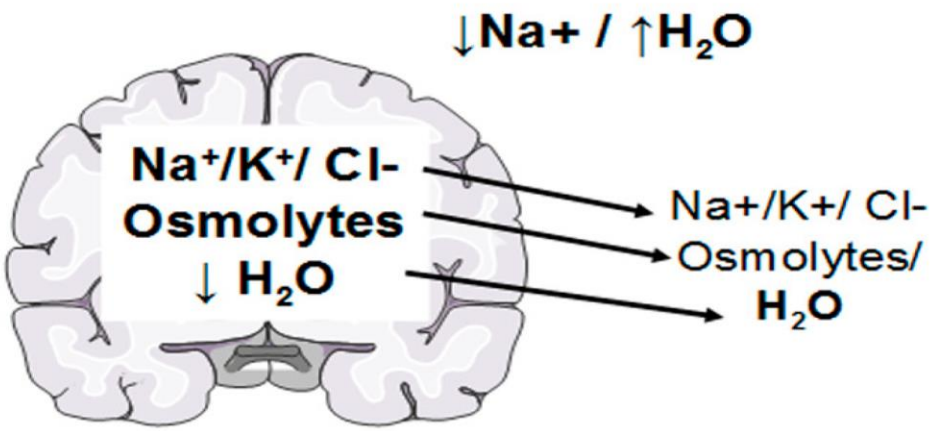
a) Normonatremia



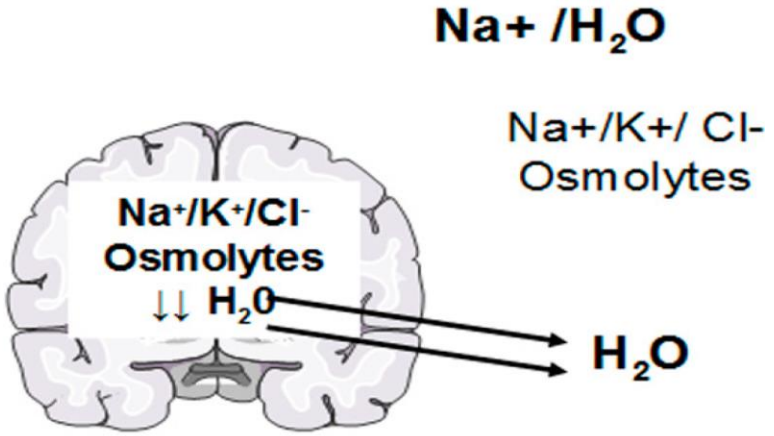

b) Acute hyponatremia



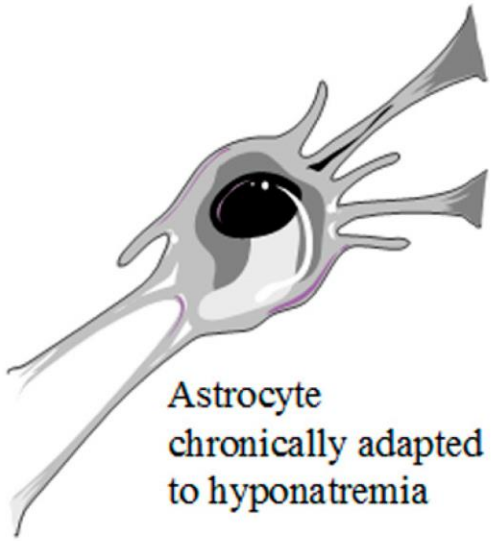

c) Chronic hyponatremia




d) Osmotic demyelination



- **1.** Effects of hyponatremia on the brain and adaptive mechanism. (**a**) Normonatremia: brain osmolality is in equilibrium with extracellular fluid osmolality; (**b**) Acute hyponatremia: water moves into the brain in response to an osmotic gradient, causing brain swelling; (**c**) Chronic hyponatremia: within a few hours cells loss electrolytes (rapid adaption) and later on organic osmolytes (slow adaption); the consequent loss of osmotically obligated water reduces cellular swelling and normalizes brain volume (**d**) Osmotic demyelination: an overly rapid correction of hyponatremia causes an inverse osmotic gradient with an excessive loss of water from the cells causing brain dehydration and demyelination of white matte



Astrocyte
chronically adapted
to hyponatremia

Overly rapid correction
of hyponatremia

Astrocyte apoptosis

Disruption of
blood-brain barrier

Exposure to
inflammatory cytokines
Microglia activation

**Osmotic demyelination**

# MAJOR CAUSES OF HYPOTONIC HYPONATREMIA

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|---|
| **Disorders with impaired urine dilution but normal suppression of ADH** |
| Advanced renal impairment |
| Diuretic-induced hyponatremia |
| **Disorders with impaired urine dilution due to unsuppressed ADH secretion** |
| Reduced effective arterial blood volume |
| True volume depletion (hypovolemic hyponatremia) |
| Heart failure and cirrhosis (hypervolemic hyponatremia) |
| Addison's disease |
| SIADH (euvolemic hyponatremia) |
| CNS disturbances |
| Malignancies |
| Drugs |
| Surgery |
| Pulmonary disease |
| Hormonal deficiency (secondary adrenal insufficiency and hypothyroidism)* |
| Hormone administration (vasopressin, desmopressin, oxytocin) |
| Acquired immunodeficiency syndrome |
| **Impaired urine dilution due to abnormal V2 receptor (nephrogenic SIADH)** |
| **Abnormally low osmostat** |
| Acquired reset osmostat of chronic illness |
| Genetic reset osmostat |
| Reset osmostat of pregnancy |
| **Exercise-induced hyponatremia** |
| **Cerebral salt wasting** |

ANY QUESTIONS?

THANK YOU FOR LISTENING