Endocrinology

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F year

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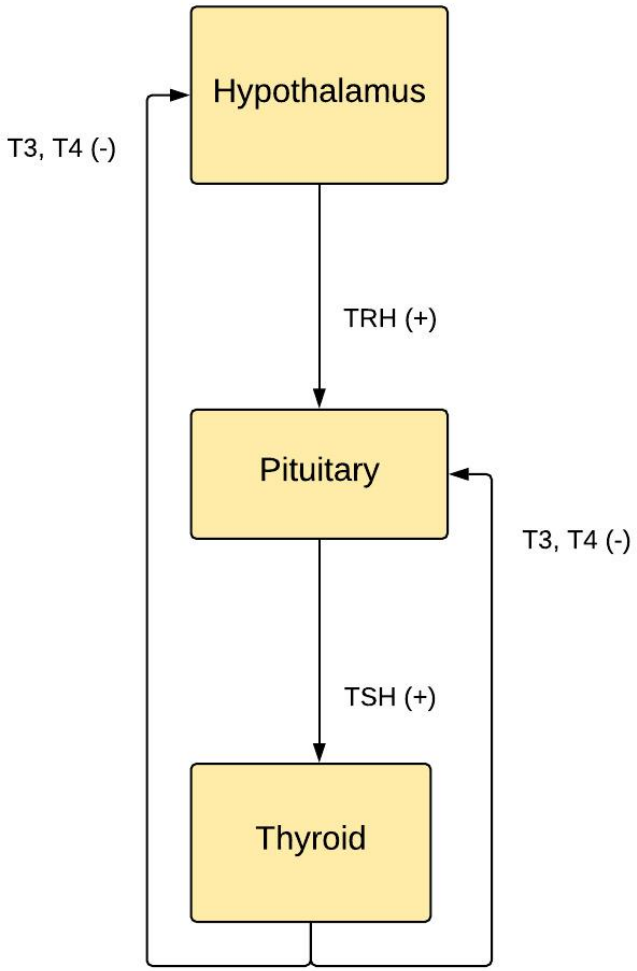
Thyroid Disease



Effect of thyroid hormone on end organs

T3 is the more active form
T4 is converted into T3 in peripheral tissues – liver, kidneys, etc by selenodeiodinases
T4 is also converted to rT3 = deactivated form

CVS: ++HR and CO
Bone: increases bone turnover and resorption
Blood: increases RBC 2,3 DPG – more oxygen released to tissues
Neuromuscular: increases speed of muscle contraction + relaxation
Carbohydrate metabolism: + hepatic gluconeogenesis and glycolysis; +intestinal glucose absorption
++SNS activity
Lipid metabolism: ++lipolysis

Case 1

Patient details: Yzma, 35yo

PCx: Feeling anxious and occasional fluttering in her chest.

HPCx: 2-month hx of feeling more anxious and irritable.

Change in bowel habits – diarrhoea but not sure if this is due to anxiety.

Sometimes gets “flutters” in her chest – no known triggers

Also says that she “runs hot” all the time.

6kg weight loss noted despite increased appetite

Periods have become lighter and irregular – worried that she may be going through the menopause

PMHx: asthma

DHx: salbutamol, COCP. NKDA

FHx: mum had SLE, grandma had bowel cancer aged 80y

SHx: works as a lawyer. Lives alone. Smoker – 10/d since 18. Non-drinker.

O/E:

Unable to sit still, inappropriately dressed for cold weather

HR 120bpm regular, warm peripherally.

Fine tremor noted in hands

Neck exam: smooth diffuse swelling, no cervical lymphadenopathy

Neuro: brisk reflexes. Otherwise normal

Cranial nerves – II, III, IV, VI: some pain and double vision on eye movement. Able to see sclera above pupils and eyes appear to be protruding out.

Investigations

What investigations would you like to do next?

a. Nothing. Reassure her that her anxiety is due to her high stress job and send her home.
b. ECG, FBC, U+E, TFTs + thyroid antibody screen, USS neck, iodine uptake scan
c. FBC, U+E, LFTs, faecal immunochemical testing and refer for colonoscopy
d. ECG, FBC, TFTs, menopause screen – FSH and LH

Results

ECG: sinus tachycardia

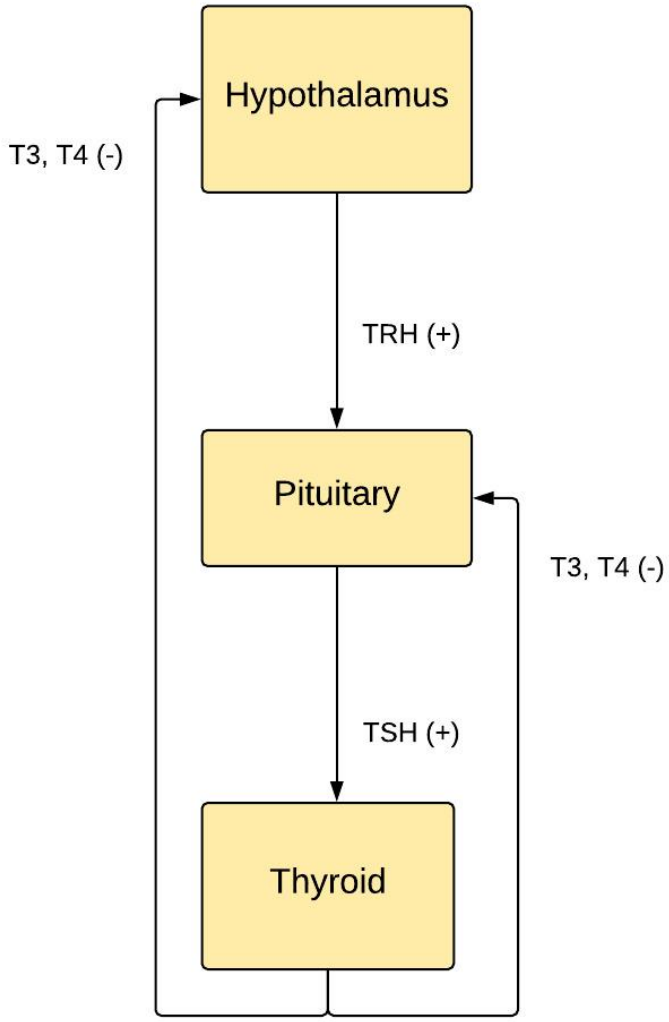
Bloods:
FBC – all within normal limits
U+E – all within normal limits

TFTs:
TSH <0.1mU/L (0.4 – 4)
Free T4: 45pmol/L (9-24)
TSH receptor antibodies +ve

What do these results show?

a. Toxic multinodular goitre
b. Graves' disease
c. Hashimoto's thyroiditis
d. Secondary hyperthyroidism

Hyperthyroidism TFTs



Tertiary hyperthyroidism:
Problem is at the hypothalamus
Hormone panel:
High T3 and T4
High TSH
High TRH

Secondary hyperthyroidism:
Problem is at the pituitary gland
Hormone panel:
High T3 and T4
High TSH
Low TRH

Primary hyperthyroidism:
Problem is at the thyroid gland
Hormone panel:
High T3 and T4
Low TSH
Low TRH
Causes: Graves' disease, toxic multinodular goitre

Pathophysiology

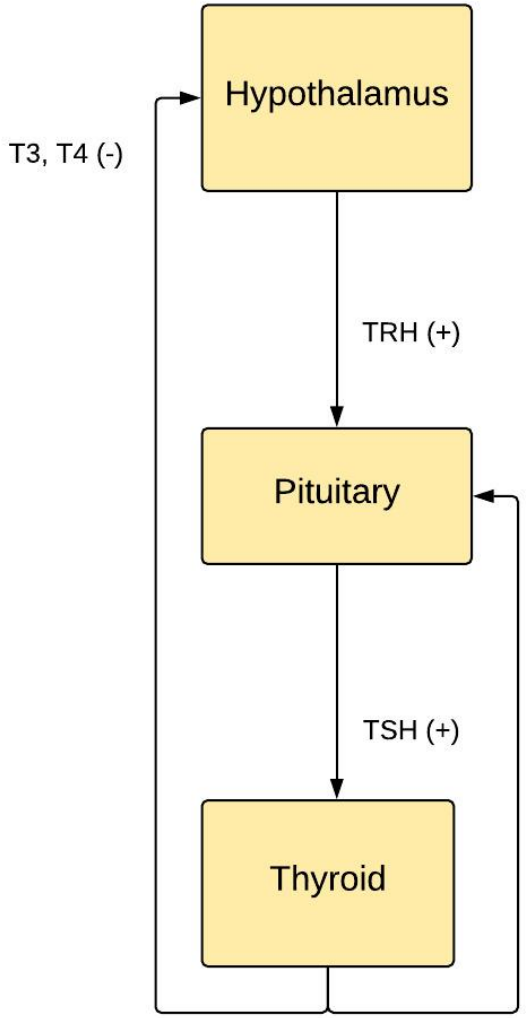
Toxic multinodular goitre – primary hyperthyroidism

This is when you have a couple of nodules within the thyroid gland which have +++functioning cells.

TFTs: no antibodies present

Iodine uptake scan: patchy areas of ++uptake

May be able to palpate nodules on neck exam



Pituitary tumour – secondary hyperthyroidism

Tumour of the thyrotrophic cells

++proliferation of thyrotrophs leads to increased TSH production.

This then increases T3 and T4 production

Graves' disease - primary hyperthyroidism

Autoimmune disease where antibodies are produced against TSH receptors in thyroid gland.

+++activation at TSH-r means ++T3 and T4 release

TFTs: TSH antibody positive

Iodine uptake scan – increase uptake throughout

Graves' disease signs:

Eye disease = exophthalmos + ophthalmopathy

Pretibial myxoedema = waxy discolouration + oedema on shins

Thyroid acropachy = clubbing + soft tissue swelling of hands and feet

Treatment

Medical management

Carbimazole – thyroid peroxidase enzyme inhibitor

Propylthiouracil - thyroid peroxidase enzyme inhibitor and acts at peripheral tissue to stop T4 to T3 conversion

Safer for use in pregnancy

Important SE: agranulocytosis

So you need to tell the patient that if they feel unwell, they need to be seen by a doctor ASAP + check WCC

Repeat TFTs in 6-8w to see effect of treatment and review dose accordingly

Radioiodine therapy

Surgery – total thyroidectomy

Case 2

Patient details: Hades, 40yo

PCx: tiredness

HPCx: 3 month hx of feeling tired all the time – feels lethargic

Has also noticed that he's been putting on weight despite going on a diet.

Change in bowel habits - constipation

Feels cold a lot of the time

Low mood

PMHx: depression in late 20s and was on sertraline.

DHx: none. NKDA

FHx: nil of note

SHx: lives with wife who complains that he has the heating on all the time, unable to take his dogs out for a walk as very tired and achey

O/E:

Dressed in 3 jumpers and a massive coat.

Slow to follow instructions

HR: 60bpm regular. Cool dry peripheries

Neuro: slow reflexes. Otherwise normal

Face: appears quite puffy. Loss of outer 1/3rd of eyebrows

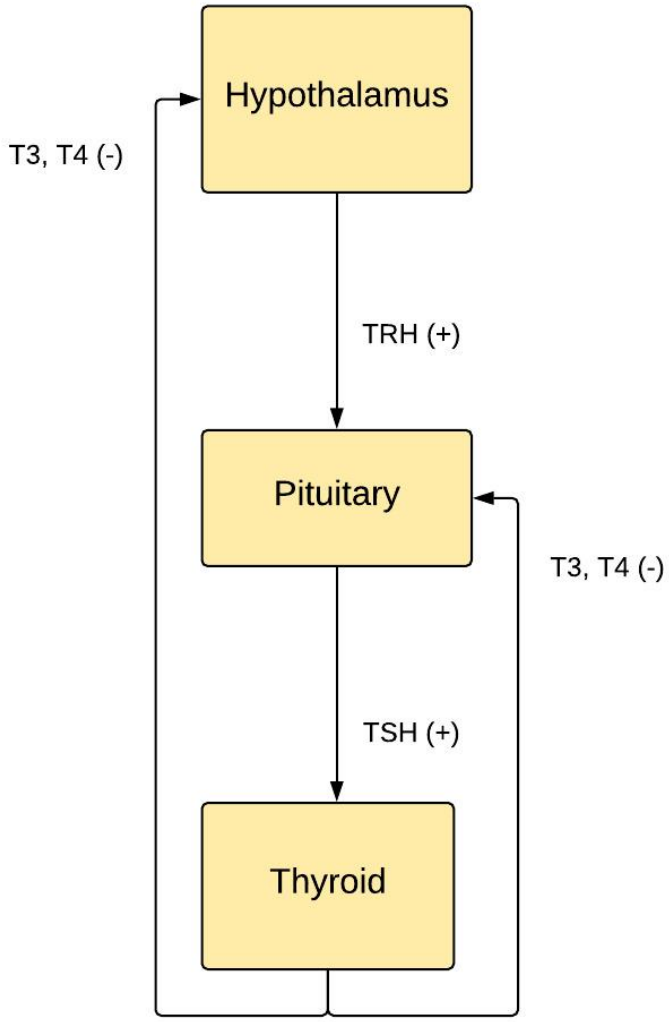
Lower limbs: very dry skin with patchy hair loss

Investigations

What investigations would you like to do for Hades?

a. FBC with iron studies + vitamin B12 and folate, TFTs + thyroid antibody screen, LFTs, lipid profile, U+Es
b. Urine dip, fasting glucose and HbA1c , TFTs
c. PHQ-9 questionnaire for depression, FBC, U+E, LFTs

Hypothyroidism TFTs



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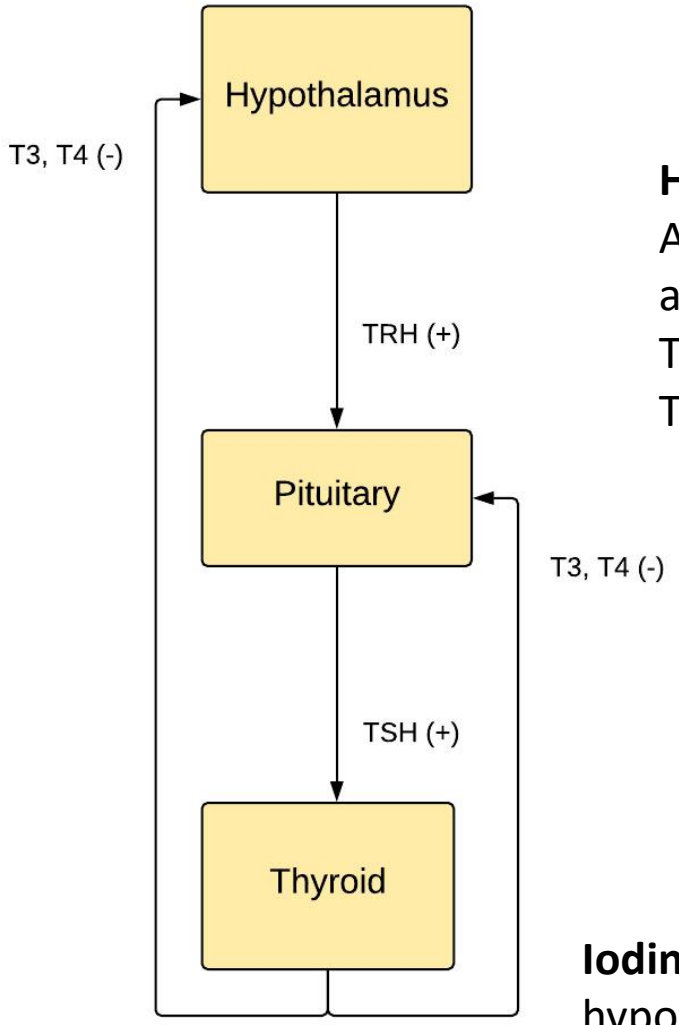
Pathophysiology



Hashimoto's thyroiditis
Autoimmune disorder where autoantibodies are generated against:
Thyroid peroxidase enzyme
Thyroglobulin

Riedel's thyroiditis
Normal thyroid tissue is replaced by dense fibrous tissue
Hard, fixed, painless goitre
Common in middle aged women

Iodine deficiency – common cause of hypothyroidism in developing countries.
Not so much in developed countries due to iodine supplementation in food

Treatment

Thyroid replacement therapy – levothyroxine for life

Monitor TFTs 6-8w initially until TSH normalizes or after any dose changes

Follow up with yearly TFTs

Pancreas problems

Case 3

Patient details: Aurora, 18yo

PCx: confusion and feeling incredibly drowsy

HPCx: brought into A+E by boyfriend who says that she has been acting very strange.

Went to a party last night where they had a few drinks – but Aurora woke up this morning feeling more hungover than usual.

Complaining of headache, stomach pains and feeling very nauseous – ?hungover

Was also drinking lots of water and complaining of being thirsty despite this.

He also noticed that her breath smelled a bit weird – like nail polish remover.

Becoming more and more confused – didn't know where she was

PMHx: nil of note

Unable to get any more info from Aurora and boyfriend doesn't really know much more

O/E:

Patient struggling to keep eyes open – says she just wants to go to sleep and that everyone should leave her alone.

Very confused – not orientated to time / place / person

HR 120bpm, BP 110/65mmHg, RR 35

Dry mucous membranes

Abdo exam: generalized tenderness

Investigations

WHAT WOULD YOU DO NOW?

a. Bedside glucose measurement, urine dip, ABG, ECG, FBC, U+E
b. Bedside glucose + ABG
c. Leave her alone! – she just wants to sleep..
d. Urine dip, FBC, U+Es, HbA1c, LFTs

ABG interpretation

pH 7.20 (7.35 – 7.45)

PO2 11.5 (11-13)

PCO2 3.2 (4.5-6)

HCO3 10 (22-26)

Glucose 30.2mmol/L

Lactate 4

K+ 5.5 (3.5-5.3)

Na+ 132 (133-146)

Other results:

Urine dip :

WCC ++

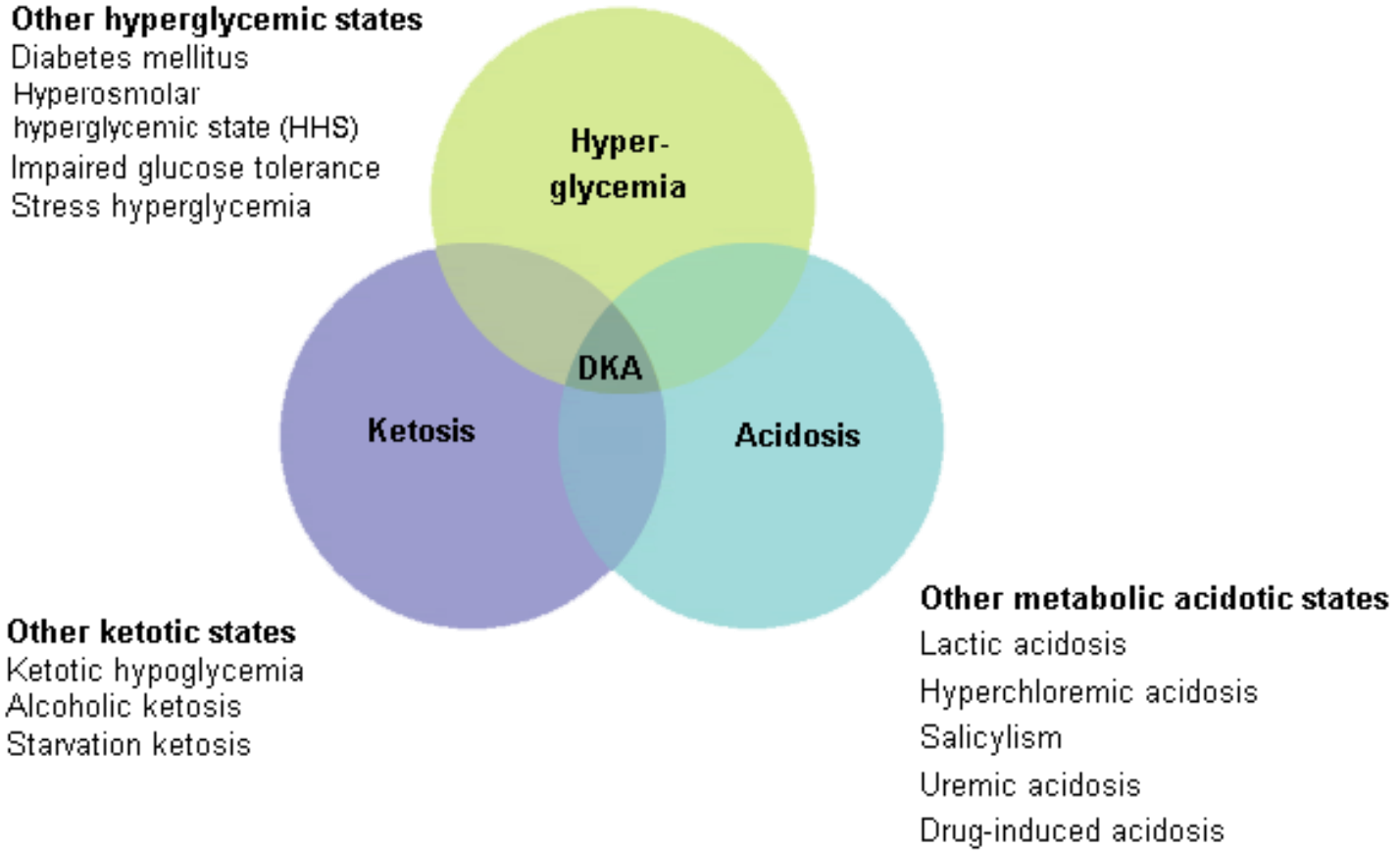
ketones +++

Glucose ++

What does this ABG show?

a. Metabolic acidosis with partial respiratory compensation
b. Metabolic acidosis with complete respiratory compensation
c. Respiratory acidosis because of the high lactate
d. Metabolic alkalosis

** DKA – diabetic emergency **



Precipitants for DKA:
Infection, surgery, MI, pancreatitis, MI, chemotherapy, antipsychotics, wrong insulin dose or non-compliance

What happens in DKA?

T1 diabetics have insulin deficiency = their beta cells do not produce insulin due to autoimmune destruction.

Without insulin, the glucose they take in cannot be used. It remains in the bloodstream. = HYPERGLYCAEMIA

So the body switches to free fatty acid and amino acid metabolism. An important by product of free fatty acid metabolism are ketone bodies - these are acidic. Bicarbonate ions are used to buffer this. = METABOLIC ACIDOSIS + KETOSIS.

Body tries to compensate for this metabolic acidosis by increasing respiratory rate to blow off the CO2.

Another important thing about the HYPERGLYCAEMIA is that it can cause something called OSMOTIC DIURESIS. Glucose in the extracellular compartment has an osmotic draw – draws out water from the intracellular compartments. Results in POLYURIA and POLYDIPSIA.

Treatment

Aims of treatment:

Fluid replacement: IV 0.9% saline – gradual rehydration to prevent cerebral oedema

Insulin replacement: fixed rate insulin infusion of 0.1units / kg /h

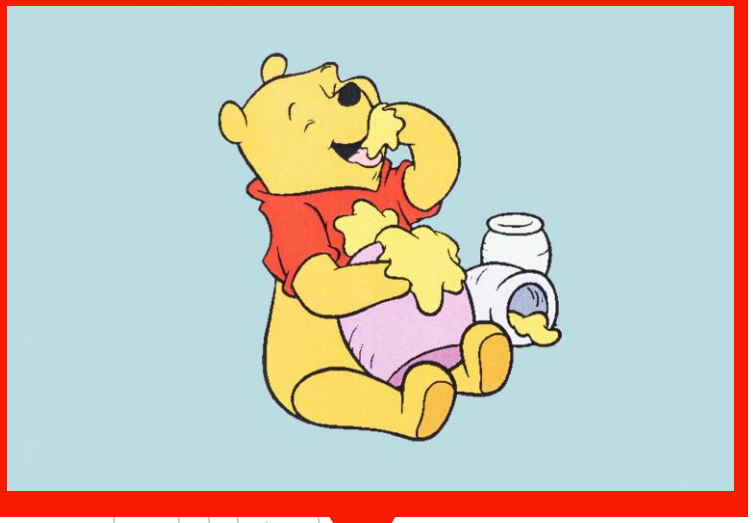
Stop ketogenesis: once blood glucose falls < 14mmol/L, add IV 5% glucose

Correct electrolyte abnormalities

Identify and treat underlying precipitating factors - in Aurora's case, this is a UTI – Abx treatment + sepsis 6 protocol

Monitor K+, blood glucose, fluid status throughout

Case 4



Patient details: Winnie, 60yo

PCx: nocturia

HPCx: 6 month hx of waking up multiple times at night to go to the toilet – has been disrupting his sleep. Feels very tried

Also feels thirsty all the time and is having to drink loads of water throughout the day

Sometimes his vision goes a bit blurry but he hasn't got round to visiting his optician yet.

Worried that this might be prostate cancer as his friends has recently been diagnosed with it.

PMHx: hypertension, high cholesterol

DHx: atorvastatin, ramipril, amlodipine

FHx: dad had an MI at 55

SHx: ex-smoker of 30 pack years, drinks 3 pints of beer at the weekends. Works as an office manager.

O/E:

Height: 154cm, weight: 90kg. BMI: 37.9kg/m2

HR 80bpm, regular. BP 137/100mmHg

Skin exam – darkening of skin in the armpits

Eye exam: CN II, III, IV VI normal

Neuro: sensation intact

Investigations

What investigations would you like to do for Winne?

a. Bedside glucose monitoring, urine dip, BP, FBC, U+E, LFTs, fasting blood glucose, HbA1c

b. Urine dip, ECG, DRE, PSA

c. FBC, U+E, TFTs, MSU

d. DRE, bedside glucose measure.

Pathophysiology

T2DM = beta cells are producing insulin but there is an INSULIN RESISTANCE at peripheral tissues due to persistently raised levels of glucose in the blood.

Initially, your beta cells work overtime to address this high [glucose].

But over time, they become exhausted and insulin secretion decreases.

If this carries on, the beta cells deteriorate even more until they final stop producing insulin.

Again, glucose exerts an osmotic draw – so you get water pulled out of the intracellular compartment into the extracellular compartment. POLYDIPSIA + POLYURIA.

Glucose lost in urine = GLYCOSURIA – more prone to infections. Screen for recurrent UTIs and thrush infections

Treatment

Conservative Mx:

Lifestyle modification – eat healthy, exercise more, smoking cessation, good control of co-morbidities (HTN), cut down alcohol intake

Medications:

Metformin = increases insulin sensitivity + decreases hepatic gluconeogenesis + decreased GI absorption of lucose

Sulfonylureas (gliclazide) = increases pancreatic insulin secretion

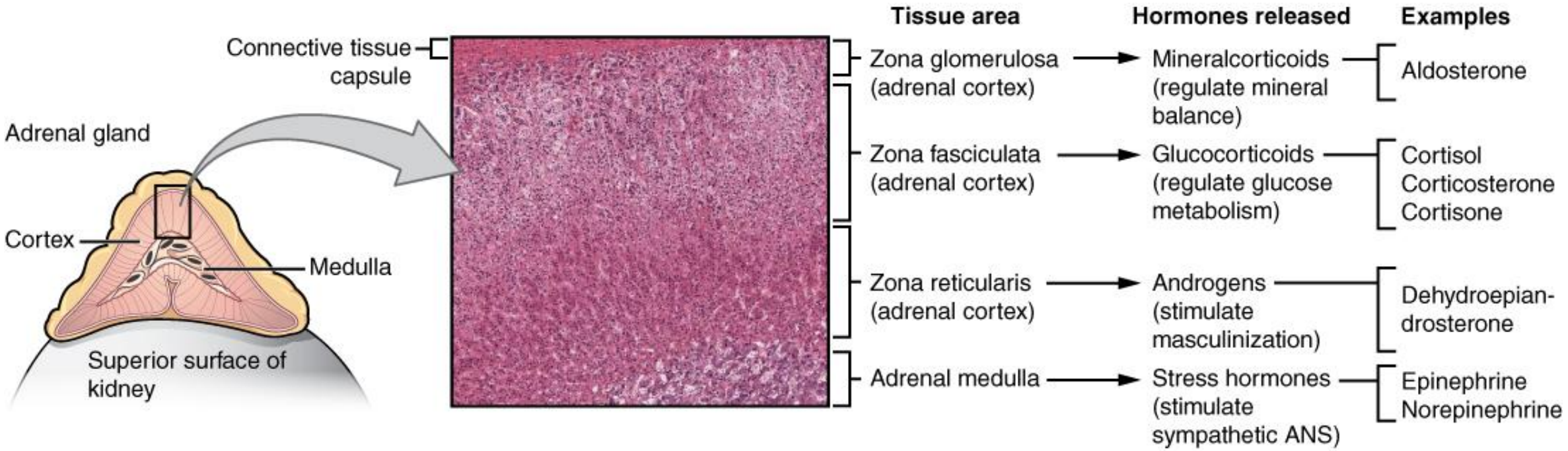
Glitpin (sitagliptin) = DDP4 inhibitor – inhibits incretin activation to increase insulin synthesis and suppress glucagon release

Thiazolidinediones (pioglitazone) = PPARy inhibitor – decreases peripheral insulin resistance

SGLT2 inhibitors (dapagliflozin) = reduce glucose reabsorption from glomerular filtrate + increase urinary excretion of glucose

GLP-1 agonists (exenatide) = increase insulin secretion and inhibit glucagon secretion

Screen for diabetic complications – retinopathy, nephropathy, neuropathy



Adrenal problems

Case 5

Patient details: 40yo

PCx: 6month hx of feeling very weak

HPCx: Says that she doesn't have the strength to do anything anymore and thinks that her "muscles aren't working"

Has also been feeling quite low in herself and this is very unlike her. Has been getting headaches as well.

Feels very self conscious about herself as she thinks she may have more facial hair than normal and she's been getting lots of stretch marks on her abdomen and arms.

Also noticed that she has been gaining some weight – mainly around her midsection.

Has been bruising very easily as well – gets big bruises from accidentally knocking into stuff which she has been doing more often. Her peripheral vision isn't so good anymore.

PMHx: appendicectomy, well controlled asthma

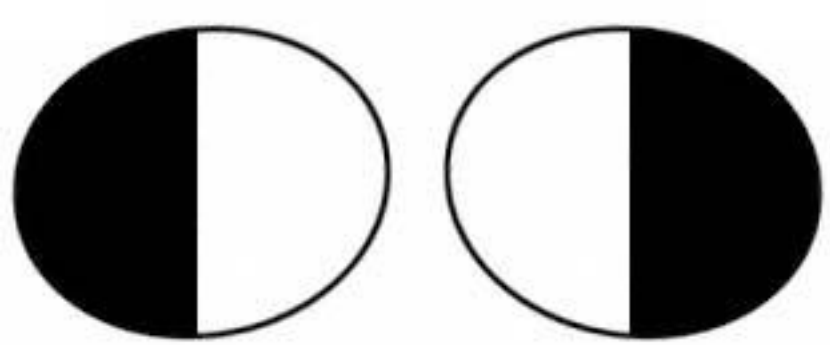
O/E:

Obs: HR 80bpm, BP 147/105mmHg, RR 18

Truncal obesity – weight distributed mainly around her mid section and her arms and legs are smaller in comparison

Moon shaped face and has supraclavicular and dorsocervical fat pads noted

Examination of visual fields reveal this:



What do you think the likely diagnosis here is?

a. Cushing's syndrome due to exogenous steroid use
b. ACTH secreting pituitary tumour – Cushing's disease
c. Acromegaly
d. Phaechromocytoma

Investigations

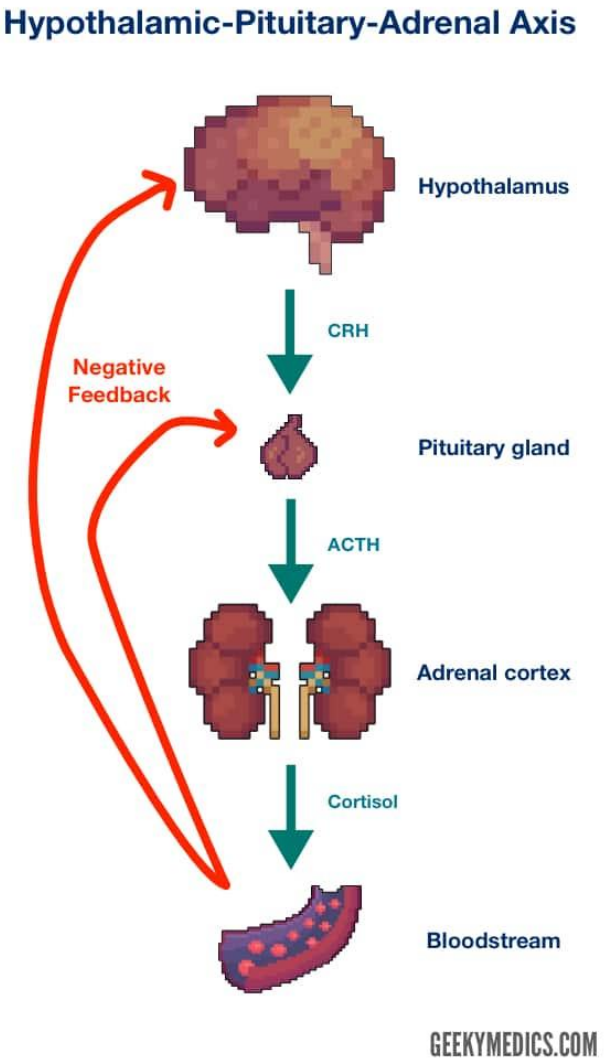
Stimulation and suppression tests in endocrinology:

If you've got hormone **EXCESS,** you want to see if you can **SUPPRESS PRODUCTION**

If you've got hormone **DEFICIENCY**, you want to see if you can **INCREASE PRODUCTION**

Cushing's = excess cortisol → DEXAMETHASONE SUPPRESSION TEST

Pathophysiology

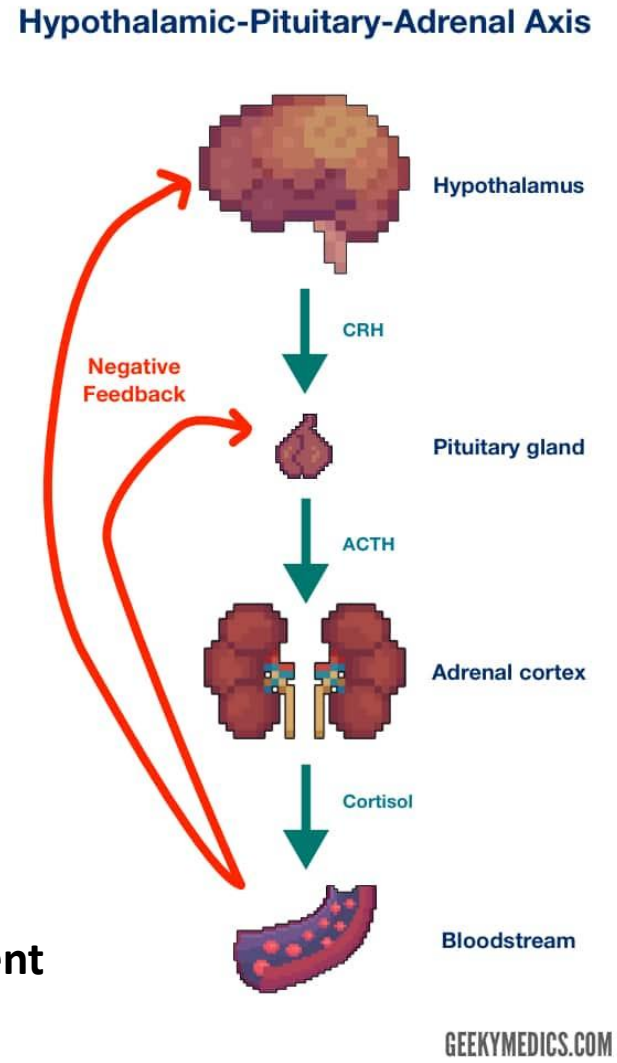


ACTH dependent Cushing's:
Pituitary adenoma that secreted ACTH – Cushing's disease
Ectopic ACTH producing tumours

Non - ACTH dependent Cushing's:
Adrenal adenomas / carcinomas
Exogenous steroid use

In patient with ectopic ACTH production
Give low dose dexamethasone
Body senses rise in cortisol
ACTH levels remain high because
+++production outside of pituitary
So ++cortisol

Dexamethasone suppression test



In patient with non-ACTH dependent Cushing's
Give low dose dexamethasone
Body senses rise in cortisol and ACTH is suppressed
But because they might be taking exogenous

In patient without Cushing's:
Give low dose dexamethasone
Body senses rise in cortisol
So negative feedback loop will suppress ACTH and CRH secretion
Cortisol measured after 24h = low

In patient with pituitary tumour:
Give low dose dexamethasone
Body senses rise in cortisol
But ACTH production not suppressed as +++corticotrophic cells in tumour – keep secreting ACTH
Cortisol measured after 24h = high

Give high dose dexamethasone
Pituitary still retains some feedback control, so you do get

Case 6

Patient details: Grandma Fa, 70yo

PCx: Feels very unwell and asked to speak to a doctor on the ward

HPCx: Feels very lightheaded, weak and tired - couldn't participate in her physio session on the ward

Had cholecystectomy 2d ago and was recovering well but unable to keep anything down this morning – vomited x2

PMHx: polymyalgia rheumatica

DHx: prednisolone 15mg PO. NKDA

SHx: lives with her son and his family, keeps as active as possible, ex-smoker of 40 pack years, drinks only on special occasions.

O/E:

Obs: BP 90/60mmHg, HR 100bpm, T 38.2

Not orientated to time, place or person → very confused and distressed

Holding stomach and saying that the pain is unbearable = unable to examine patient as she is very agitated and won't let you to do so.

Notice dry mucous membranes and catheter in situ but draining small amount of dark coloured urine.

Vomited again when you were in the cubicle with her

Investigations

Bedside glucose reading 2.5mmol

FBC: normal

CRP: 8 mg /L

U+Es:

Na+ 123 (133-146)

K+ 6.8mmol/L (3.5-5.3)

Urea 8 (2.5 -7.8)

Creatinine 100 (45-84)

What is going on?

******ADDISONIAN CRISIS******

Acute severe cortisol and aldosterone deficiency

Triggers: infection, surgery, severe dehydration, trauma, sepsis, MI, physical overexertion, sudden cessation of long-term steroid therapy, adrenal haemorrhage

When there is an environmental stressor:

++CRH release → ++ ACTH release → ++cortisol release

If someone is on long term steroids, their ACTH secretion will be suppressed. Low stimulation to adrenal glands causes them to shrink.

When meds are stopped / dose not increased, it can precipitate an ADRENAL CRISIS because adrenals are not able to appropriately respond.

As a result:

Low mineralocorticoids = aldosterone – normally helps with sodium reabsorption and potassium excretion.

If low = sodium excretion + potassium retention = HYPERKALAEMIA and HYPONATRAEMIA
Aldosterone is important in BP control – if sodium excreted, then water will also be excreted = HYPOVOLAEMIA + LOW BP

Low glucocorticoids = cortisol

Insufficient gluconeogenesis = hypoglycaemia

Addisonian crisis- emergency

Hydrocortisone 100mg IM or IV/8h

IV fluids – monitor clinical state and U+Es

May need IV glucose if hypoglycaemia

Search for and treat underlying cause