Endocrinology

Acromegaly
- Pituitary adenoma secreting excessive GH stimulating excessive IGF-I
  - ectopic GHRH/GH may rarely be produced by ca. of lung (SC), pancreas, ovary
- Symptoms (insidious) - headache, bitemporal hemianopia, back pain, OSA
  - musculoskeletal - large hands / feet, macroglossia, prognathism, OA, kyphosis, CTS
  - dermatological - skin tags, hyperhidrosis, hirsutism
  - visceral - organ hypertrophy, hypertension, HCM
- Diagnosis - OGGT (high GH / IGF-I) - GH normally inhibited by glucose
  - random IGF-1 useful for screening (long half-life, unlike GH)
- Management - trans-sphenoidal surgery; radiotherapy if refractory
  - somatostatin analogues (octreotide) inhibit GHRH; pegvisomant (anti-GH receptor)
- Complications - colorectal adenoma, IHD, CCF, DM, stroke - increased mortality

Addison’s disease
- Adrenal insufficiency - primary (productive - rare) or secondary (stimulatory - commoner)
  - Addison’s disease technically relates to autoimmune primary adrenal insufficiency
- Symptoms - fatigue, dizziness / syncope, confusion, mood disturbances, amenorrhea
  - GI - anorexia / weight loss, nausea / vomiting, abdominal pain, altered bowel habit
- Signs - postural hypotension, hyperpigmentation (esp. buccal, new scars)
- Investigations - cortisol, SST, U&Es (low sodium / glucose, high potassium / calcium)
  - cortisol - low at 9am (<100nm) suggestive; also low aldosterone:renin ratio (cf. Conn’s)
  - short Synacthen test - 250mcg Synacthen IV/IM, high 1hr serum cortisol excludes
- Management - PO hydrocortisone / fludrocortisone
- Acute adrenal insufficiency - due to infection, haemorrhage, drugs e.g. phenytoin
  - presents very similarly to thyrotoxic crisis (see below)
  - management - IVT, IV glucose, hydrocortisone 100mg IV followed by qds. dose IV / IM

Conn’s syndrome
- Benign adrenal adenoma secreting aldosterone leading to hypertension, hypokalaemia
- Symptoms (typically middle-aged women) - headaches, polydipsia, lethargy
- Investigations - renin (normal/high excludes Conn’s), high aldosterone:renin ratio
- Management - spironolactone for 4wks; laparoscopic adrenalectomy
Cushing’s syndrome
- Excessive cortisol levels - commonest in DM, obesity, HTN, osteoporosis
  - ACTH-dependent - pituitary adenoma (Cushing's disease), ectopic ACTH (SC lung ca.)
  - ACTH-independent - adrenal adenoma, exogenous steroids (commonest)
- Symptoms - facial ‘fullness’, acne, hirsutism, truncal obesity, striae, proximal myopathy
  - also IGT, PUD (prednisolone) recurrent infections, depression, oligomenorrhoea
- Investigations - 24-hour urinary cortisol, ACTH, MRI, dexamethasone suppression test
  - 1mg / 8mg dexamethasone at 11pm, high cortisol at 8am suggests ectopic ACTH
- Drug options - metyrapone (inhibits adrenal synthesis); etomidate if severe acute
- Complications - MI, stroke, HTN, metabolic syndrome, DM, osteoporosis, hypokalaemia

Diabetes insipidus
- Insufficient ADH either due to hypo-secretion (neurogenic) or insensitivity (nephrogenic)
  - neurogenic - cranial tumour / trauma / infection, granulomas, Wolfram (DIDMOAD)
  - nephrogenic - metabolic e.g. hypokalaemia, RTA, drugs e.g. lithium, antibiotics
- Symptoms - polyuria, nocturia, polydipsia; in children also FTT (ddx. for TIDM)
- Diagnosis - desmopressin suppression test (withhold fluids, desmopressin 2mcg IM)
  - urinary osmolarity initially low and remains low - nephrogenic DI (DDAVP ineffective)
  - urinary osmolarity significantly increases - neurogenic DI
- Management - correct underlying cause, maintain adequate hydration
  - if neurogenic DI - DDAVP 300mcg od. PO (regular monitoring required)

Diabetes mellitus (DM)
- Secondary causes - CF, chronic pancreatitis, Cushing’s, acromegaly, hyperthyroidism, HHC
- Diagnosis - HbA1c > 48 (6.5%); fasting > 7.0 (6.1 IFG), 2-hour post OGTT > 11.1 (7.8 IGT)
- Type I - associated with HLA-DR3 / 4 (RA)
  - regimes - basal bolus (ActRapid with e.g. NPH), twice-daily (NPH), long-acting (glargine)
  - target HbA1c - 48 (6.5%); aim for pre-prandial glucose < 7, post-prandial glucose < 9
- Type II - associated with obesity, PCOS, GDM, FH, South Asian / Afro-Caribbean
  - step 1 - lifestyle interventions
  - step 2 - metformin e.g. 500mg bd. (s/e GI upset inc. abdominal pain, lactic acidosis)
  - step 3 - add sulphonylurea e.g. gliclazide (s/e hypoglycaemia, weight gain, cholestasis)
    - if hypos or not tolerated - try DPP4-inhibitor (-gliptins); s/e cough, SJS, pancreatitis
    - also thiazolidinedione (e.g. pioglitazone); s/e oedema, bladder ca., hepatotoxicity
    - if BMI > 35 try exenatide; s/e GI upset / GORD, pancreatitis, alopecia
  - step 4 - add insulin
Complications - Acute

- **Hypoglycaemia** - blood glucose < 3.0, pathological if < 2.5
  - Whipple’s triad for diagnosis - low blood glucose, symptoms, resolution with correction
  - risk factors - tight glycaemic control, malabsorption, **alcohol**, renal disease, Addison’s
  - symptoms - shaking, sweating, mouth paraesthesia, hunger, diplopia, confusion, coma
  - management - PO / 80ml IV 20% glucose, or 1mg IM glucagon (if insulin-induced)
  - complications - convulsions, stroke, cognitive dysfunction, arrhythmias, MI, heart failure

- **DKA** - hyperglycaemia (variable degrees) with **ketonuria** and **metabolic acidosis**
  - risk factors - infection / intercurrent illness, low insulin, PE, **hypothyroidism**, pregnancy
  - symptoms - nausea, vomiting, **abdominal pain**, hyperventilation, polydipsia, polyuria
  - significant dehydration, plasma osmolality > 290, anion gap > 13, **Kussmaul breathing**
  - IVT - normal saline with **0.1 units/kg** insulin; reduce glucose by 3 mmol/L/hour
  - add 40mmol/L potassium while > 5.5; add IV 10% glucose when BM < 14
  - complications - cerebral / pulmonary oedema, **hypokalaemia**, VTE, MI, ARDS

- **HONK** - hyperglycaemia (substantial) causing hyperosmolar serum without ketosis
  - risk factors - dementia, sedatives, hot weather, **hyperthyroidism**, immunosuppression
  - symptoms - focal neurology / seizures, visual impairment, nausea, confusion, lethargy
  - glycosuria, plasma osmolality > 320, normal anion gap, mild metabolic acidosis
  - management - as above but **significantly less insulin needed** (1-4 units/hour)

Complications - Chronic

- Microvascular complications - **retinopathy**, **neuropathy** (inc. diabetic foot), **nephropathy**
- Macrovascular complications (**despite glycaemic control**) - IHD / HTN, PVD, **stroke** / TIA

- **Retinopathy** - retinal ischaemia, oedema, venous beads, IRMA
  - background - micro-aneurysms (like dot haemorrhages, due to weak capillary walls)
  - moderate - haemorrhages (dot / blot / flames, due to capillary rupture); cotton wool spots
  - severe - several of the above affecting **multiple retinal quadrants**
  - proliferative - **neovascularisation** around the optic disc; **retinal detachment** if severe

- **Neuropathy** - treat acutely with **duloxetine**; amitriptyline / pregabalin otherwise
  - chronic peripheral - **glove and stocking** sensory / reflex loss
  - acute neuritis - burning foot pain, worse at night
  - mono-neuropathy - **carpal tunnel syndrome**, ocular cranial nerve palsy
  - diabetic amyotrophy - proximal thigh weakness, muscle wasting, paraesthesia
  - autonomic - impotence, GI disturbances, **postural hypotension**
- **Diabetic foot** - abnormal forces on feet (neuropathy), ulceration on mild injury (PVD)
  - slow-healing, warm, dry, bounding pulses (cf. ischaemic - cool, absent pulses, pain)
- **ulcers** - soles/margins of feet around thick callus; painless, punched-out, infected
- **Charcot foot** - hot swollen foot after mild trauma - fracture, destruction, deformity
  - complications - *osteomyelitis*, septic arthritis, amputation
- **Nephropathy** - *proteinuria* (microalbuminuria to nephrosis), renal atherosclerosis, UTIs
  - albumin:creatinine ratio > 3 is microalbuminuria; > 30 is proteinuria (albumin 20 / 200)
  - high albumin excretion in type II diabetes suggests *general vascular damage* (PVD)
  - consider non-diabetic causes if no retinopathy, sudden heavy proteinuria / haematuria
  - management - **ACE inhibitors** for all, titrated to full dose even if normotensive

**Hyperprolactinaemia**
- Excess **prolactin** (anterior pituitary hormone) usually due to **prolactinoma**
  - in women - inhibits LH / FSH - oligo/*amenorrhoea*, galactorrhoea, subfertility, hirsutism
  - in men - reduced libido, erectile dysfunction, reduced hair growth
- Causes - physiological (pregnancy, breastfeeding), prolactinoma, PCOS, head injury
  - also hypothyroidism, Cushing’s, stress, verapamil, omeprazole, metoclopramide
- Investigations - prolactin (serial levels; > 5000 suggests prolactinoma), MRI (for tumour)
- Management - bromocriptine (dopamine agonist; s/e fibrosis, daytime somnolence)
  - consider osteoporosis prophylaxis, COCP, surgery, radiotherapy

**Hyperthyroidism**
- **Primary** (low TSH - check T3 if T4 normal) or **secondary** (high TSH - ectopic secretion; rare)
- Risks - FH, excessive iodine, smoking, childbirth, ART (HIV), amiodarone
- Symptoms - diarrhoea / **weight loss** despite high appetite, tremor, proximal myopathy
  - also irritability / psychosis, heat intolerance, hyperhidrosis, low libido, oligomenorrhoea
- Signs - palmar erythema, tachycardia / AF, diffuse alopecia, pruritis, brisk reflexes
- Grave’s - autoimmune, **anti-TSH receptor** / anti-thyroglobulin antibodies; HLA-B8
  - small diffuse firm goitre, ophthalmopathy, pretibial myxoedema, acropachy (clubbing)
  - radioiodine may trigger or exacerbate ophthalmopathy in up to 15%
- **Subacute** (De Quervain’s) **thyroiditis** - post-viral, *painful* goitre, high ESR; self-limiting
- Management - beta-blockers (symptomatic), **carbimazole** 10mg bd./tds. titrated accordingly
  - risk of *agranulocytosis* - mouth ulcers, sore throat etc. (uncommon)
  - if young (*not* pregnant), toxic adenoma - **radioiodine** (drink); sleep alone for 1wk
  - last resort - **subtotal thyroidectomy** (s/e hypoparathyroidism, vocal cord paralysis)
  - **smoking cessation** may prevent ophthalmopathy
- Complications - increased mortality from osteoporosis, IHD, stroke
  - **thyrotoxic crisis** - pyrexia, vomiting, jaundice, delirium, seizures; give propylthiouracil
Hypothyroidism

- 95% thyroid hormones protein-bound (TBG); T3 half-life of 1 day, T4 half-life of 7 days
  - subclinical - **high TSH**, normal T3/4
  - clinical - high TSH, **low T4**, often normal T3
- Aetiology - pregnancy, **autoimmune** (Hashimoto’s), iodine deficiency, amiodarone, lithium
- Symptoms - constipation / **weight gain** despite low appetite, **lethargy**, dry skin
  - also cold intolerance, memory impairment, hoarse voice, low libido, **menorrhagia**
- **Myxoedema** - expressionless facies, peri-orbital puffiness, sparse hair, cerebellar ataxia
- **Hashimoto’s** - painless irregular goitre; **anti-TPO** antibodies
- Management - **levothyroxine** (T4) 100-200 mcg od. (more in pregnancy, less if IHD)
- Complications - **hyperlipidaemia** (check lipid profile; statins unnecessary), **hyponatraemia**

Phaeochromocytoma

- Rare catecholamine-secreting tumour of the **adrenal medulla** causing **excess adrenaline**
  - associated with **MEN-II**, neurofibromatosis, von Hippel-Lindau
  - 10% malignant; 10% familial; 10% bilateral (MEN); 10% extra-adrenal (paraganglioma)
- Symptoms - **headache**, sweating, palpitations, tremor, nausea, constipation, weight loss
- Diagnosis - 24-hour urinary catecholamines / **metanephrines**, MRI
- Management - alpha-blockers (phenoxybenzamine) 1wk prior to **surgery**

SIADH

- **Euvolaemic hyponatraemia** - other electrolytes (particularly K+) are often normal
- Aetiology - pneumonia, asthma, malignancy (esp. SCLC), MS, SAH
  - drug causes - carbamazepine, SSRIs, tramadol, sulfonylureas
- Management - **fluid restriction** (< 1L / day) if not hypovolaemic (otherwise slow NaCl IV)
  - consider **furosemide** if urine osmolarity >> serum osmolarity