Adrenal Insufficiency

Description & Epidemiology
A reduction in the output of adrenal hormones i.e. glucocorticoids and/or mineralocorticoids.
- Primary - adrenal cortex failure (insufficient glucocorticoid ± mineralocorticoid)
  o Requires >90% gland destruction before detectable clinically or biochemically
  o Rare 0.8 per 100,000; M=F, any age
- Secondary - there is inadequate pituitary ACTH or hypothalamic CRH.
  o Relatively common compared as exogenous steroid use is frequent

Aetiology
Primary adrenal insufficiency
- Anatomic destruction (acute or chronic) - Addison’s (autoimmune; >80% cases); Surgical removal; Trauma; Infections e.g. TB, CMV, HIV; Haemorrhage e.g. anticoags, Waterhouse-Fridreichsen syndrome; Infarction e.g. antiphospholipid syndrome; Invasion e.g. neoplastic, sarcoidosis, amyloidosis, haemochromatosis
- Metabolic failure in hormone production - ↑Hepatic metabolism of cortisol e.g. phenytoin, barbiturates, rifampicin; CAH e.g. 21-hydroxylase deficiency; Enzyme inhibition e.g. ketoconazole; ACTH/glucocorticoid resistance ; Cytotoxic agents
- Other causes - ACTH blocking antibodies; Mutation in ACTH receptor gene; Adrenal hypoplasia congenital; Familial adrenal insufficiency; Metabolic (e.g. ALD), Smith-Lemli-Opitz, Wolman disease; Mitochondrial disorders e.g. Kearnes-Sayre syndrome

Secondary adrenal insufficiency
- Hypothalamic-pituitary axis suppressed - Exogenous steroids; Tumour steroid release
- Pituitary - Congenital e.g. aplasia; Tumours e.g. craniopharyngioma; Panhypopituitarism e.g. Sheehan’s; ACTH suppression by valproate; Lymphocytic hypophysitis; Radiotherapy; Trauma; Isolated ACTH deficiency
- Hypothalamic related - Congenital; CRH deficiency; Trauma; Radiotherapy; Surgery; Neoplasm; Infiltration e.g. sarcoidosis

Children and adrenal insufficiency
- Adrenal insufficiency is rare in children
- Presentation is nonspecific and thus often there is a delay in diagnosis
- Commonest causes are CAH (72%), ALD (15%) and autoimmune adrenalitis (13%)

Critically ill patients
- Patients who are critically ill are at risk of adrenal dysfunction
- Non-survivors more often have higher baseline cortisol levels so less responsive to ACTH
- Considered insufficiency if pressor dependent or have biochemical clues
- Etomidate influences ACTH results

AIDS patients
- Can have CMV necrotizing adrenalitis, also M. avium intracellulare and Cryptococcus
- Adrenal tests are commonly abnormal in patients with HIV (may also be due to drugs)

Associated diseases: Other autoimmune illnesses. Consider polyglandular autoimmune syndrome.

Presentation
- Presentation may be precipitated by a stressful event - surgery, trauma, etc.
- Acute - e.g. Waterhouse-Friderichsen syndrome (infarction secondary to septicaemia e.g. meningococcal); presents with collapse and shock
- Chronic - symptoms develop insidiously and may be mild
Symptoms
- Fatigue and weakness
- Anorexia & weight loss
- Nausea & vomiting
- Abdominal pain
- Diarrhoea or constipation
- Syncope, dizziness, or confusion
- Personality change, Irritability
- Amenorrhoea

Signs
- Cutaneous and mucosal pigmentation
- Hypotension & in crisis: shock, coma
- Postural hypotension

Investigations (Routine tests may be normal)
**Bloods:** UEC (↓Na, ↑K, ↓Cl, ↑Ur. If secondary then electrolytes may be normal.), BSL (↓), CMP (↑Ca), ABG (normal anion gap met. acidosis), LFT, FBC.

**Hormones:** baseline cortisol (↓), ACTH (↑ in 1°, ↓ in 2°), renin and aldosterone levels, ± others e.g. 17-hydroxyprogesterone if CAH suspected.

**Other:** Adrenal autoantibodies, antiphospholipid antibodies, short synACTHen stimulation test, TB detection tests, insulin tolerance test (?unsafe-induce low BSL & measure cortisol response)

**ECG:** PR and QT interval prolongation

**Imaging:** CXR - ?lung neoplasm, AXR - any adrenal TB calcification, CT scan of adrenals

Management

**Adrenal/Addisonian crisis**
- May be life-threatening following a physiological stress (trauma, burns, pregnancy, anaesthesia, MI, sepsis) or withdrawal of exogenous steroids.

**Resuscitation ABCDs which may include:**
- Oxygen, IV Normal Saline fluid boluses (500-1000 ml for adult, 10-20 ml/kg for a child)
- 50% Dextrose 25-50 ml IV (child: 10% Dextrose 2-5 ml/kg) PRN

**Dehydration - continued IV replacement of estimated dehydration:**
- Usually 5%+ over 8+ hours using 5% dextrose in normal saline
- Take into account age, volume, cardiac & renal function. Unlikely to need K+ initially

**Steroids**
- If 1st presentation can give dexamethasone 10mg IV stat then IV q6h until cortisol level done (unlike HC doesn’t interfere with assay, but has little mineralocorticoid activity).
- Else Hydrocortisone 200mg (child 4mg/kg) IV stat then 100mg (child 2mg/kg) IV q4-6h
- Halve dose after 24hrs if stable and then add fludrocortisone 0.05-0.2 mg/day.

**Other**
- Consider ↑corticosteroids or vasopressors e.g. dopamine if persistent hypotension.
- Reversal of coagulopathy should be attempted with FFP.
- Hyperkalaemia usually responds to rehydration, treat specifically if >6.5mmol/L.
- Treat underlying precipitating disorder e.g. infection with antibiotics.

Prognosis
- Depends on the underlying cause but replacement Rx can result in normal life expectancy.
- Addison’s has ↑mortality due to cardiovascular, malignant and infectious disease.

Prevention
- Early dose adjustments (e.g. doubling usual maintenance dose) to cover increased stress.
- Patient education.
- Illness stress/vomiting episode action plan
- Avoid exposure to chickenpox or measles. If exposed seek medical advice without delay.