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)
  - Requires >90% gland destruction before detectable clinically or biochemically
  - Rare 0.8 per 100,000; M=F, any age
- Secondary - there is inadequate pituitary ACTH or hypothalamic CRH.
  - 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. Avoid exposure to chickenpox or measles. If exposed seek medical advice without delay.