Endocrine Emergencies

WHY ???

- Uncommon
- Potentially lethal
- Diagnostic dilemmas
- Emergency treatment may be life-saving

Objectives:

- How (un)common?
- What defines these conditions?
- What are the main clinical features?
- When should these dx be considered?
- Which investigations are pertinent?
- What is the emergency management?

Spectrum of Endocrine Emergencies

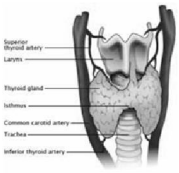
- Myxoedema coma
- Thyroid storm
- Acute adrenal insufficiency
- Pituitary apoplexy
- Pheochromocytoma crisis
- Acute hypercalcaemia
- Acute hypocalcaemia

Myxoedema Coma

End stage of untreated or insufficiently treated hypothyroidism

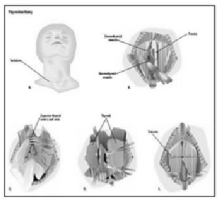
What is Myxoedemic Coma?

- Myxoedema = swelling of hands, face, feet, periorbital tissues
- Myxoedemic coma = decreased level of consciousness, associated with severe hypothyroidism



Myxoedema Coma

- Typical clinical picture:
  - Elderly obese female
  - Becoming increasingly withdrawn, lethargic, sleepy and confused
  - Slips into a coma
- History:
  - Previous thyroid surgery
  - Radio iodine
  - Default thyroid hormone therapy



Etiology of Myxoedemic Coma

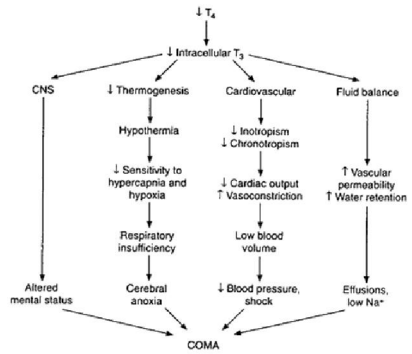
Undiagnosed Undertreated → Acute Precipitant → Myxoedemic Coma

Hashimoto's thyroiditis
Post surgery/ablation

Precipitating Events

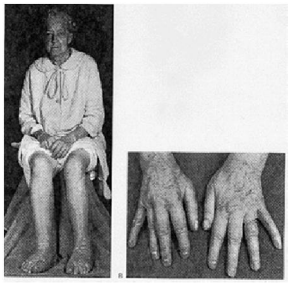
- CVI
- Myocardial infarction
- Infection
  - UTI
  - Pneumonia
- Gastrointestinal hemorrhage
- Acute trauma
- Administration of sedative, narcotic or potent diuretics

Pathogenesis



Physical Findings

- Comatose or semi comatose
- Dry coarse skin
- Hoarse voice
- Thin dry hair
- Delayed reflex relaxation time
- Hypothermia
- Pericardial, pleural effusions, ascites



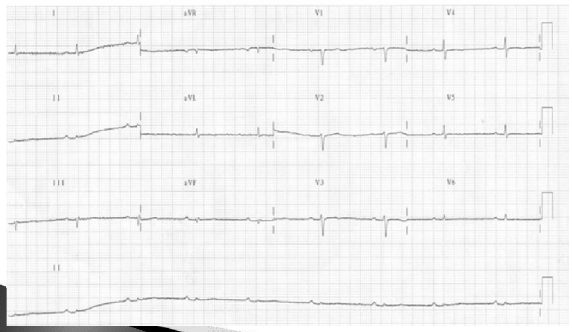
When should it be considered?

- Altered LOC
  - Structural vs metabolic causes of decreased LOC
- Hypoventilatory/ Respiratory Failure
  - Narcotics, Benzodiazepines, EtOH intoxication, OSA, obesity hypoventilation, brain stem CVA, neuromuscular disorders (MG, GBS)
- Hypothermia
  - Environmental
  - Medical: pituitary or hypothalamic lesion, sepsis

Laboratory

- Free T4 low and TSH high
- If the T4 is low and TSH low normal consider pituitary hypothyroidism
- Blood gasses
- Electrolytes and creatinine
- Distinguish from euthyroid sick syndrome
  - Low T3, Normal or low TSH, normal free T4

ECG in Patient with Myxoedema Coma



Slow Releasing Reflexes

Management (1)

- ICU admission may be required for intubation, ventilatory support and IV medications
- Levothyroxine is the cornerstone of Mx

→Parenteral thyroxine (T4)
(not readily available in SA)

  - Loading dose of 300 – 400 µg
  - Then 50 µg daily

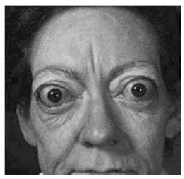
  - If no IV available, give tablets via NG tube or PO

Management (2)

- Electrolytes
  - Water restriction for hyponatraemia
  - Avoid fluid overload
- Avoid sedation
- Glucocorticoids
  - Controversial but necessary in hypopituitarism or multiple endocrine failure
  - Dose: Hydrocortisone 40 – 100 mg 6 hly for 1 week, then taper
- Treat precipitating illness

Prognosis of Myxoedema

- Mortality is 20%, and is mostly due to underlying and precipitating diseases



Thyroid Storm

Acute life threatening exacerbation of thyrotoxicosis

Clinical Setting

- Patient with Grave's disease who has discontinued antithyroid medication OR is previously undiagnosed
- Hyperpyrexia (>40 ^{0}C)
- Sweating
- Tachycardia with or without AF
- Nausea, vomiting and diarrhea
- Tremulousness and delirium, occasionally apathetic

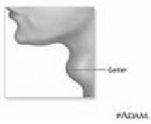
Precipitating factors

- Withdraw of antithyroid drugs
- Severe infection
- DKA
- CVI or AMI
- Cardiac failure
- Surgery
- Trauma
- Radio iodine
- Drug reaction
- Iodinated contrast medium

Etiology of Thyroid Storm

Undiagnosed
Undertreated
Grave's disease
Mulitnodular toxic goiter

→ Acute Precipitant → Thyroid Storm

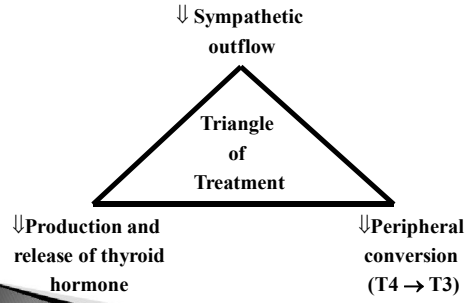


Diagnosis

- Free T4, free T3 elevated
- TSH suppressed

Note that findings are not different than that of hyperthyroidism, but the difference is in the setting

Treatment of Thyroid Storm



Management (1)

- **Specific Measures:**
  - Propylthiouracil 150 mg 6 hly or Methimasole 20 mg 6 hly (pr of po),
    then
  - Lugol's Iodine 5 drops (250 mg) orally bd
  - Propranolol 40 – 80 mg 6 hly, or 0.5-1mg IV 3hly
  - Dexamethasone 2 mg 6 hly
  - Cholestyramine or colestipol 20-30mg dly

Management (2)

- **Supportive care**
  - Adequate fluids, containing Glucose
  - Oxygen
  - Digoxin for atrial fibrillation or cardiac failure
  - Cooling
  - Phenobarbital
  - Parenteral water soluble multivitamins
  - If indicated antibiotics

Avoid Aspirin

Why Lugol's?

Jod-Basedow effect

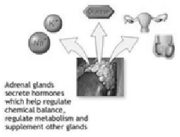
- Iodine induced hyperthyroidism
- Following administration of iodine
  →supplement/dietary/contrast medium
- Underlying thyroid disease
  - Patient with endemic goitre → relocates to iodine abundant area
  - Side effect of amiodarone

Wolff-Chaikoff effect

- Reduction in thyroid hormone levels caused by ingestion of large amount of iodine
- Autoregulatory phenomenon → inhibits formation of thyroid hormones inside thyroid follicle, and release of thyroid hormones into the bloodstream

Prognosis

- Mortality dropped since the 1920's from 100% to 20 – 30%
- Mortality most frequently associated with serious underlying medical conditions



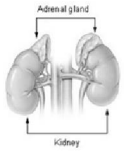
Acute Adrenal Insufficiency

Addison's crisis

Etiology of Adrenal Crisis

Usually presents as an acute illness in a patient with underlying chronic adrenal insufficiency

Underlying Adrenal Insufficiency (Addision's disease or Chronic Steriods) → Acute Precipitant → Adrenal Crisis



Causes (1)

- Causes of Primary adrenal insufficiency (Primary = Adrenal disease = Addison's)
  - Auto-immune
  - TB of adrenals
  - Metastatic malignancy to adrenals
  - Post surgery
- Causes of secondary adrenal insufficiency
  - Pituitary or hypothalamic disease (Pituitary infarct or hemorrhage)

Causes (2)

- Acute destruction of the adrenals can occur with bleeding in the adrenals
  - Overwhelming sepsis (Waterhouse-Frederichson syndrome)
  - DIC
  - Complication of anticoagulant therapy
- Functional = Exogenous steroids

Precipitating Events (1)

- Omission of medication
- Precipitating illness
  - Severe infection
  - Myocardial infarction
  - CVI
  - Surgery without adrenal support
  - Severe trauma

Precipitating Events (2)

- Withdrawal of steroid therapy in a patient on long term steroid therapy (adrenal atrophy)
- Administration of drugs impairing adrenal hormone synthesis e.g. Ketoconazole
- Using drugs that increase steroid metabolism e.g. Phenytoin and Rifampicin

Clinical Presentation

Non specific:

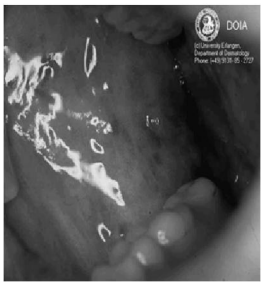
- Nausea and vomiting
- Hyperpyrexia
- Abdominal pain
- Dehydration

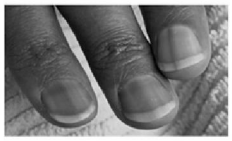
Hypotension and shock

- Consider adrenal insufficiency if hypotension does not respond to pressors

Clues to Underlying Chronic Adrenal Insufficiency

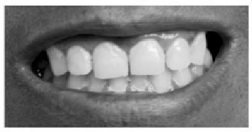
- Pigmentation in unexposed areas of the skin
  - Buccal mucosa
  - Creases of hands
  - Scars
- Other:
  - Abnormalities of GI function
  - Personality changes
  - Decreased pubic and axillary hair

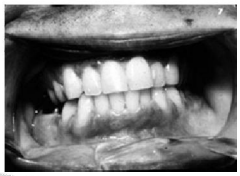




Addison's disease:

- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.





Lab Diagnosis (1)

- Hyponatraemia and hyperkalemia (Hyponatraemia might be obscured by dehydration)

PRIMARY ADRENAL INSUFF	SECONDARY / TERTIARY ADRENAL INSUFFICIENCY
Hyperpigmentation Hyponatremia Hyperkalemia Metabolic Acidosis	NO Hyperpigmentation Mild hyponatremia NO hyperkalemia NO met acidosis

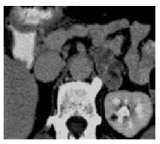
Lab Diagnosis (2)

- **Random cortisol**
  Not helpful unless it is very low (<5 mg/L) during a period of great stress
- **ACTH stimulation test**
  Failure of cortisol to rise above 552 nmol/L 30 min after administration of 0.25 mg of synthetic ACTH IV
- **Basal ACTH**
  Will be raised in primary adrenal insufficiency but not in secondary

CT of abdomen

May reveal enlargement of adrenals in patents with adrenal hemorrhage, active TB or metastatic malignancy

Adrenals may appear atrophic in autoimmune or idiopathic disease



Management of Acute Adrenal Insufficiency (1)

- **Hydrocortisone**
  - 100 mg IV stat then 50 mg 4 hly for 24 h
  - Taper slowly over the next 72 h
  - When oral feeds is tolerated change to oral replacement therapy
  - Overlap the first oral and last IV doses
- Replace salt and fluid losses with 5% dextrose in normal saline IV

Management of Acute Adrenal Insufficiency (2)

- Patients with primary adrenal insufficiency may require mineralocorticoid therapy (fludrocortisone) when shifted to oral therapy
- Treat precipitating diseases

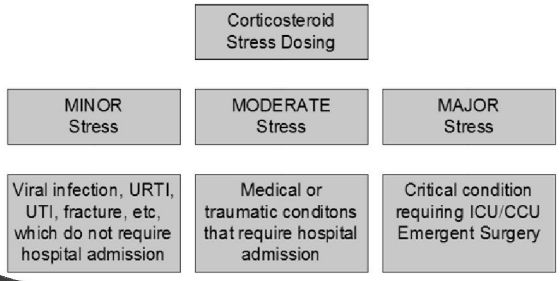
Prevention of crisis:

Failures of Adrenal Treatment

Indications:

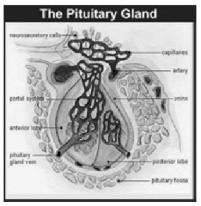
- Known adrenal failure
- Chronic steroid therapy
- Recent (1 year) steroid treatment (prednisone >5 mg/day for two months in the last twelve)

Corticosteroid Stress Dosing



Corticosteroid Stress Dosing

- MINOR
  - Double chronic steroid dose for duration of illness (only needs iv if can't tolerate po)
- MODERATE
  - Hydrocortisone 50 mg po/iv q8hr
- MAJOR
  - Hydrocortisone 100 mg iv q8hr

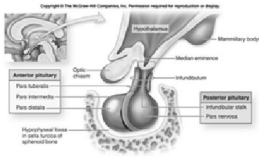


Pituitary Apoplexy

Hemorrhage or infarction of the pituitary gland

Clinical Setting

- Sudden crisis in a patient with known or previously unknown pituitary tumor
- It may occur in a normal gland during and after child birth, or with head trauma, or in patient on anticoagulation therapy



Symptoms and Signs

- Severe headache and visual disturbance
- Bitemporal hemianopia
- N III palsy
- Meningeal symptoms with neck stiffness
- Symptoms of acute secondary adrenal insufficiency
  - Nausea vomiting , hypotension and collapse

Diagnosis

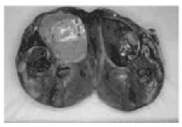
- CT scan of head and pituitary

- Hormonal studies only of academic interest
- Assessment of pituitary function after acute stage has settled

Management

- **Hormonal**
  - Dexamethasone 4 mg bd (glucocorticoid support and relief of cerebral edema)
- **Neurosurgical**
  - Transsphenoidal pituitary decompression

After the acute episode the patient must be evaluated for multiple pituitary deficiencies



Pheochromocytoma Crisis

Causes

- Neuroendocrine tumour
  - Catecholamine secreting
- Action of unopposed high circulating levels of atecholamines
  - α - receptors: Pressor response
  - β - receptors: positive ino- and chronotopic

Precipitating factors

- Spontaneous
- Haemorrhage into pheochromocytoma
- Exercise
- Pressure on abdomen
- Urination
- Drugs: glucagon, naloxone, metoclopramide, ACTH, cytotoxics, TAD

Clinical Features

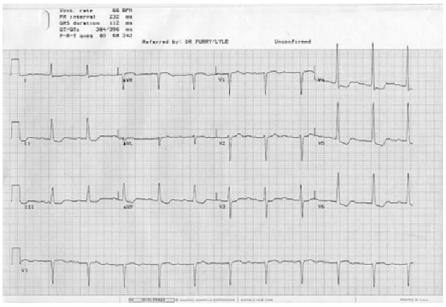
- History of poorly controlled or accelerated hypertension
- Symptoms → action of secreted catecholamines
  - Palpitations, sweating, pallor, pounding headache, anxiety or panic, tremulousness, pulmonary edema, feeling of impending death, hyperhydrosis, nausea and vomiting, abdominal pain, paralytic ileus, hyperglycaemia, hypertensive encephalopathy, myocardial infarction and stroke

Attacks:

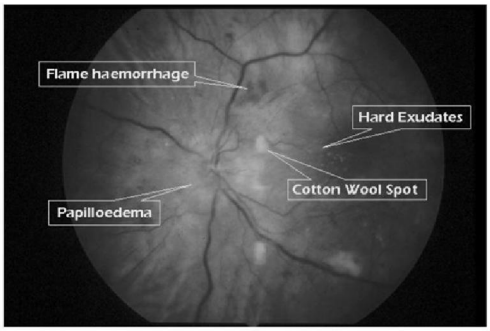
- Attacks build up over a few minutes and fade gradually over 15 min or can be more sustained (60 min).
- Hypertension with the classic triad of episodic headaches, sweating and palpitations.
- Paroxysms occur due to the episodic nature of catecholamine secretion

Signs of end organ damage

- Eyes
- Cardiac
- Renal



Hypertensive Retinopathy - Grade 4



Biochemical Diagnosis

- 24h urine collection for free catecholamines and metanephrines
- No use in acute stetting
- Confirm after stabilized
- CT/MRI/MIBG/PET

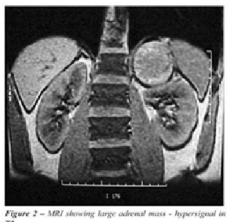
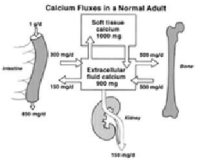


Figure 2 – MRI showing large adrenal mass - hyperignal in T2.

Treatment

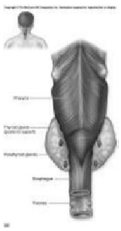
- Don't wait for biochemical confirmation of the diagnosis
- α - antagonists: Prazocin, Doxazosin
- Non selective β- antagonist: Propranolol
- Treatment with α - antagonists should precede β- antagonist treatment with 48 h to avoid exacerbation of the crisis
- Calcium channel blockers
- Be aware of postural hypotension



Acute Hypercalcaemia

Most Common Causes

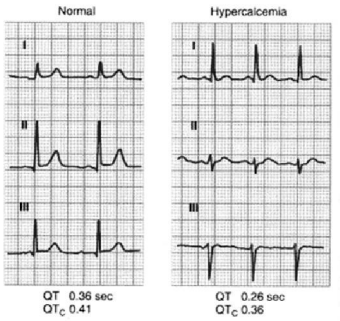
- **Endocrine:**
  - Hyperparathyroidism
  - MEN
  - PTHrp by solid tumors
- **Neoplastic:**
  - Ca with bone metastases
  - Myeloma
- **Granulomatous:**
  - Sarcoidosis
  - Tuberculosis



Clinical Features

- History of polyuria and polydipsia
- Dehydration
- Confusion / drowsiness / behavioural changes
- Anorexia / constipation / nausea and vomiting / abdominal pain
- Bradyarrhythmias / heart block
- Bone pain

ECG Hypercalcaemia



Workup

S – Ca high

PTH high → Primary hyperparathyroidism

PTH low → Malignancy or other Cause

S – Ca > 3.0 is 90% of the time of malignant origin

Treatment of Hypercalcaemia

- Volume repletion and diureses
  - NaCl 0.9% 4 L in first 24 h
  - Loop diuretics (furosemide has calciuretic effects)
- Bisphosphonates IV (Pamidronate)
- Corticosteroids (prednisone 30 – 60 mg daily)
  Drugs of choice if granulomatous disease or vit A or D intoxication is the cause
- Dialysis

Acute Hypocalcaemia

Causes (1)

- Hypoparathyroidism
  - Destruction of parathyroid glands
    - Most commonly surgical – parathyroid resection or accidental with neck surgery
  - Acute hypomagnesaemia
- Reduced 1,25(OH)vit D
  - Chronic renal insufficiency
  - Acute systemic illness
  - Drugs: ketoconazole, doxorubicin, cytarabine

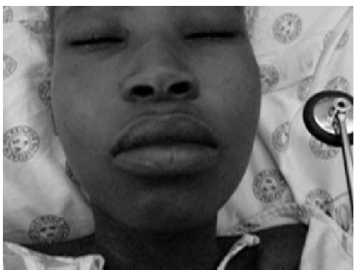
Causes (2)

- Increased uptake of Ca in bone
  - Osteoblastic metastases (breast or prostate CA)
  - Hungry bone syndrome (Osteitis fibrosis cystica)
- Complexing of Ca from the circulation
  - ↑ albumin binding in alkalosis
  - Acute pancreatitis with formation of Ca soaps
  - Transfusion related citrate complexing

Clinical Picture of Acute Hypocalcaemia

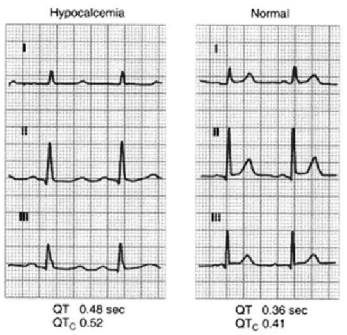
- **Symptoms**
  - Perioral numbness
  - Tingling parasthesias
  - Muscle cramps
  - Carpopedal spasm
  - Seizures
- **Signs**
  - Hyperreflexia
  - Chvostek sign
  - Trousseau sign
  - Hypotension
  - Bradicardia
  - Prolonged QT interval
  - Arrhythmias

Chvostek's Sign



Trousseau's Sign

ECG in Hypocalcaemia



Biochemical Workup

- S total Ca^{++}, Albumin and Ionized Ca^{++}
- S PO_4^{++}
- S Mg^{++}
- Plasma PTH
  - Low in hypoparathyroidism
  - High in hungry bones syndrome
- 25$(OH)D_3$ and 1,25 $(OH)D_3$
- S Amylase and Lipase

Treatment of Hypocalcaemia

- First correct low Mg^{++}
- Calcium gluconate 10 ml of 10% solution IV over 5 – 10 min and repeat as necessary in cases with frank generalized tetany
- Slower continuous infusion of Calcium gluconate in less acute cases

Summary

- Acute and chronic failure or hyper functioning of an endocrine gland can occasionally result in catastrophic illness or death
- It is important to recognizes these abnormalities and manage them appropriately

End