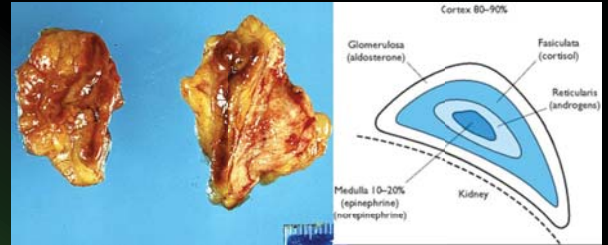


ADRENAL INSUFFICIENCY & ADRENAL CRISIS

新光急診 張志華醫師

Adrenal gland



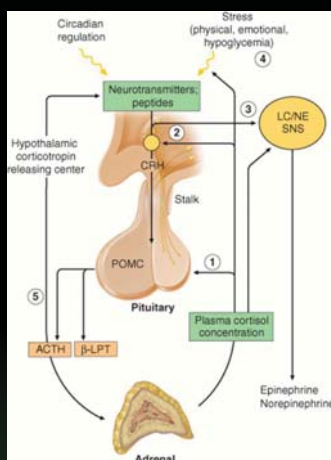
Two glands in one!

- **Cortex** – corticosteroids
 - Glomerulosa – mineralocorticoids
 - Fasciculata – glucocorticoids
 - Reticularis – hormones
- **Medulla** – epinephrine and norepinephrine
 - Sympathetic functions

Adrenal Physiology

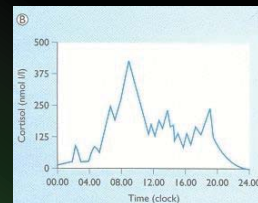
- Cyclic secretion controlled by time of day, HPA axis, renin-angiotensin system, serum potassium levels
- Stress increases basal glucocorticoid and mineralocorticoid levels 5-10 fold
 - Occurs within minutes

HPA axis

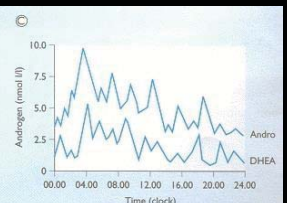


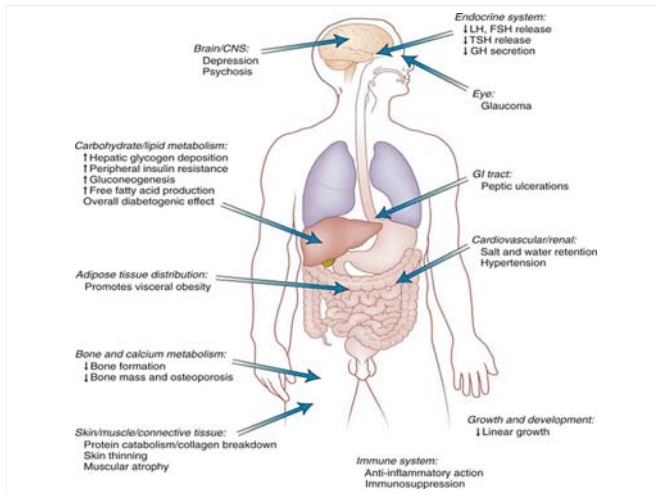
Cortisol secretion is circadian

Cortisol



Androgens





Adrenal Failure

- Basal failure results in *adrenal insufficiency*
 - Leads to insidious wasting disease
- Stress failure results in *adrenal crisis*
- Life-threatening
- Absence of glucocorticoids is most critical

Corticosteroids

- Three classes (by effect):
 - Glucocorticoids
 - Mineralcorticoids
 - Androgenic steroids

Glucocorticoids

- Regulate fat, glucose, protein metabolism
- Catecholamine and β -adrenergic receptor synthesis
- Maintain vascular tone and cardiac contractility
- Control endothelial integrity/vascular permeability

Glucocorticoids

- Cortisol
 - Controlled by HPA axis
 - Hypothalamus → CRH and arginine vasopressin in circadian rhythm (max 2-4am)
 - Anterior Pituitary → ACTH
 - Adrenal cortex → cortisol
 - Peak @ 8am; declines throughout day

Glucocorticoids

- Cortisol
 - 25mg produced daily (non-stressed)
 - 5-10% free and physiologically active
 - Remainder bound to cortisol-binding globulin
 - Becomes uncoupled in times of stress
 - Negatively feeds back to control hypothalamus
 - Role in adrenal insufficiency

Mineralcorticoids

- Regulated via renin-angiotensin system & serum potassium levels
 - Diminished GFR → juxtaglomerular apparatus release of prorenin
 - Aldosterone release → Na & H₂O resorption at distal tubules (K is lost)
 - Minor hyperkalemia can stimulate aldosterone secretion directly

Adrenal Androgens

- Controlled by ACTH
- Diurnal pattern (like cortisol)
- Significant source of androgens in females
 - Can cause signs/symptoms seen in adrenal insufficiency

Adrenal Insufficiency

- Primary = failure of adrenal glands
- Secondary = failure of HPA axis
 - Usually due to chronic exogenous glucocorticoid administration
 - pituitary failure
- Tertiary = Hypothalamic dysfunction

Primary Adrenal Insufficiency

- Loss of all three types of adrenal steroids
- 90% of glands must be destroyed to manifest clinically
 - High functional reserve
- Adrenoleukodystrophy = X-linked inherited d/o of very-long-chain fatty acid metabolism
 - Progressive neurological symptoms from demyelination

Primary Adrenal Insufficiency

- Addison disease = m.c. autoimmune dz
- Thrombosis/hemorrhage
 - Sepsis, DIC, antiphospholipid syndrome
- Infiltrative diseases
 - Bilateral cancer metastasis
 - Amyloidosis, hemosiderosis (rare)

Primary Adrenal Insufficiency

- TB = m.c. infectious cause worldwide
- HIV = m.c. infectious cause in US
 - 50% have degree of destruction
 - Only 5% have clinical symptoms of A.I.
 - CMV infection, ketoconazole use, macrophage-released cytokines are risk factors

Secondary Adrenal Insufficiency

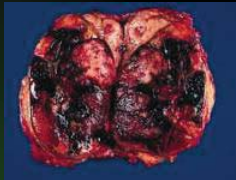
- HPA axis failure
 - deficiency of glucocorticoids and adrenal androgens
 - mineralcorticoids are unaffected
- #1 cause=chronic exogenous glucocorticoid
 - suppresses diurnal CRH/AV release
 - both time- and dose-related
 - reversible, recovery may take up to a year

Secondary Adrenal Insufficiency

- Less common causes
 - Postpartum necrosis (Sheehan syndrome)
 - Adenoma hemorrhage(s)
 - Pituitary destruction from head trauma
 - typically have associated focal neurological changes, visual deficits, diabetes insipidus or panhypopituitarism



Massive adrenal haemorrhage resulting in primary acute adrenal insufficiency



Metastatic breast carcinoma affecting the adrenal gland and causing primary chronic adrenal insufficiency



Caseating granuloma of tuberculosis

Secondary Adrenal Insufficiency

MYTHBUSTERS!

- Short course (2-3 weeks) is unlikely to suppress the HPA axis
- Daily doses of prednisone 5mg or less are unlikely to cause secondary insufficiency

Chronic Insufficiency

CLINICAL PRESENTATION

- Nonspecific
 - Fatigue, anorexia, weight loss, loss of libido
- Neurological
 - Headaches, visual changes, diabetes insipidus
- Gastrointestinal
 - Pain, nausea, vomiting, diarrhea

Chronic Insufficiency

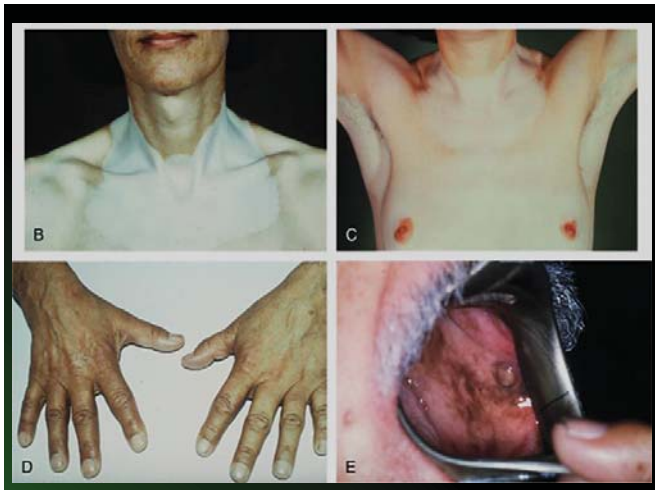
CLINICAL PRESENTATION

- Hypotension/Orthostasis
- Cachexia
 - Thin axillary and pubic hair in women
- Hypoglycemia
- Normocytic anemia, lymphocytosis, eosinophilia

Chronic Insufficiency

CLINICAL PRESENTATION

- Hyperpigmentation
 - Pressure points, axillae, sun-exposed area, palmar creases, perineum, oral mucosa
 - Usually seen early in primary AI
- Pallor out of proportion to anemia
 - Seen in secondary AI



Addison's disease:

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

- She was treated many years ago for pulmonary TB. What are the other causes of this condition?



Chronic Insufficiency

CLINICAL PRESENTATION

- Hyponatremia
 - Primary = lack of aldosterone & Na wasting
 - Secondary = vasopressin secretion & H₂O loss
- Hyperkalemia
 - Only occurs in primary
 - mild with associated azotemia & met acidosis

Adrenal Crisis

CLINICAL PRESENTATION

- Life-threatening emergency
- May be primary or secondary
- **HYPOTENSION**
 - Typically resistant to catecholamine and IVF resuscitation

Adrenal Crisis

CLINICAL PRESENTATION

- Abrupt adrenal failure usually from gland hemorrhage or thrombosis
 - Anticoagulation
 - DIC
 - Sepsis (Waterhouse-Friderichsen syndrome)
 - Usually have abdominal and flank pain
 - Can resemble ruptured AAA!!!

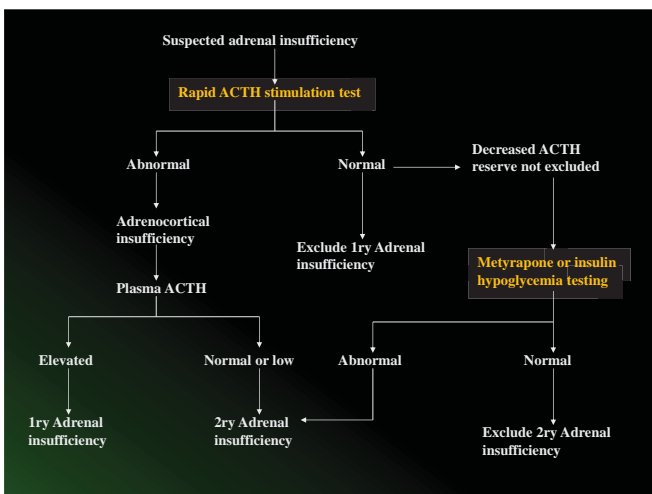
Adrenal Crisis

CLINICAL PRESENTATION

- Catastrophic HPA axis failure
 - Head trauma
 - Hemorrhage of pituitary adenoma
 - Post-partum herniation (Sheehan syndrome)
 - Usually neurological deficits, headaches, visual field cuts and diabetes insipidus

Diagnosis

- Short corticotropin stim test
 - Get baseline level
 - Inject 250µg cosyntropin (IV or IM)
 - Measure plasma cortisol level in 60 minutes
 - Excluded if basal or test level is > 525 nmol/L
- Plasma cortisol levels between 8am-9am
 - Level <83 nmol/L rules IN
 - Level >525 nmol/L rules OUT



Treatment – stable patient

- Admit to internist for stimulation test

“Other tests of adrenal function are much too time-consuming and cumbersome to warrant their use in the ED”

Treatment – stress or rescue

- Base the dose of steroid on the severity of the stressful event
- Use glucocorticoids only (no mineralcorticoids)
- 100mg bolus of IV hydrocortisone followed by infusion of 200mg IV over next 24 hours
- Correct volume and sugar deficits with D5NS
- Dexamethasone is recommended before stimulation test

Summary

- “Unexplained *hyponatremia* and *hyperkalemia* in the setting of *hypotension* unresponsive to catecholamine and fluid administration... should receive 100mg hydrocortisone intravenously.”

Before & after treatment



Questions

1. Failure of the adrenal gland to secrete basal levels of steroids results in adrenal insufficiency. T/F
2. TB is the most common infectious cause of adrenal insufficiency in the US. T/F
3. Chronic excessive exogenous cortisol inhibits CRH and AV secretion leading to adrenal failure. T/F
4. Hyponatremia and hyperkalemia are only seen in adrenal crisis and not in chronic adrenal insufficiency. T/F
5. High dose steroids for treatment of adrenal crisis should only be given after a positive corticotropin stimulation test. T/F

Answers

1. T
2. F – TB is most common worldwide but it is HIV in the US (less than 5% with failure will have clinical AI).
3. T
4. F – hyponatremia and hyperkalemia are common in both insufficiency and acute crisis – vitals and history dictate acute versus chronic.
5. F – takes too long. Give steroids to the unstable patient with high suspicion.

Before & after treatment

