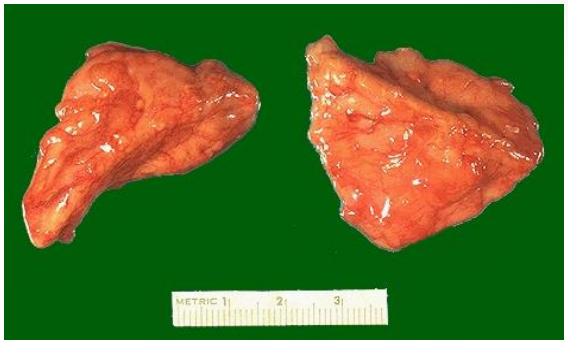
Primary Adrenal Disease

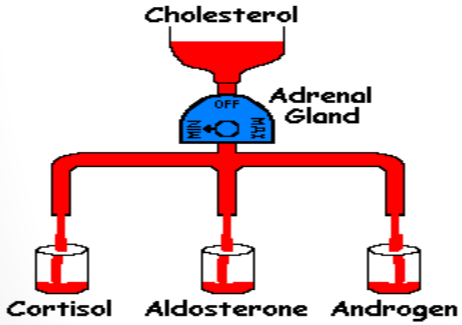
Adrenal Cortex

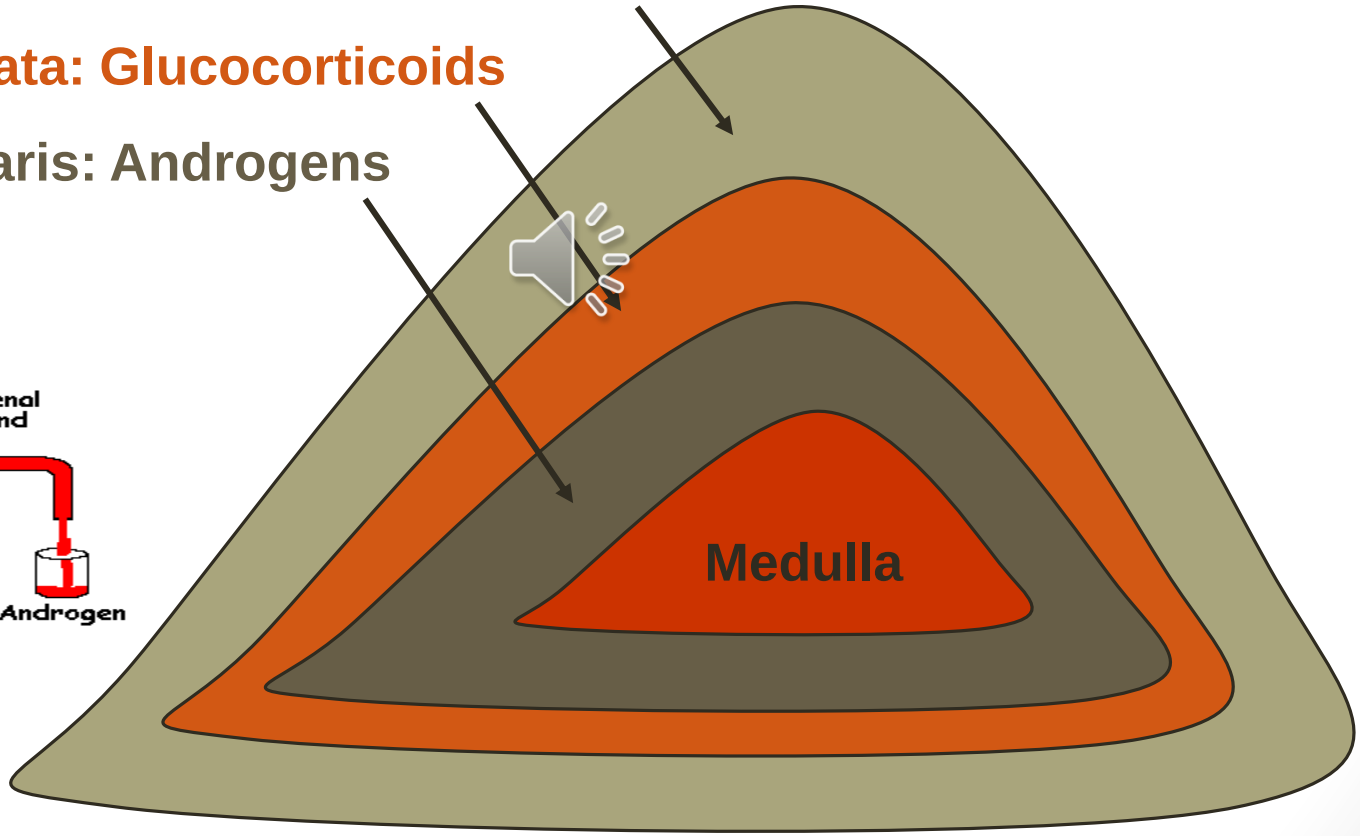


Zona Glomerulosa: Mineralocorticoids

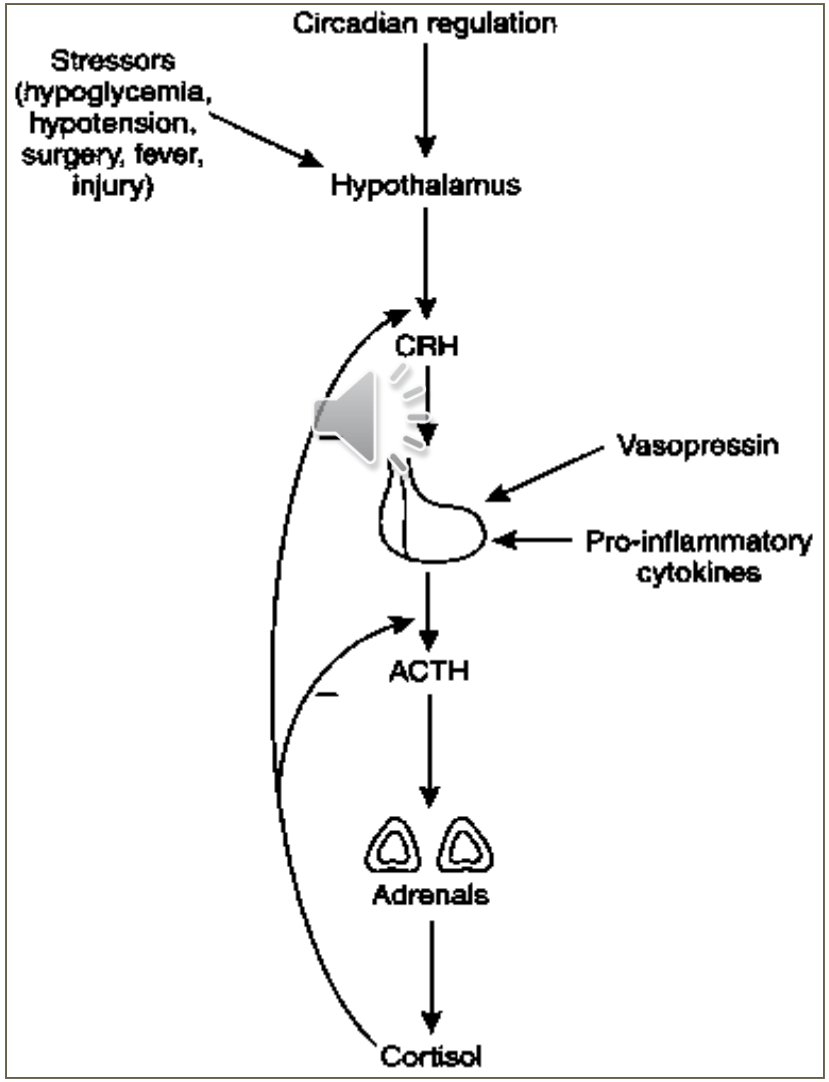
Zona Fasiculata: Glucocorticoids

Zona Reticularis: Androgens





Adrenal physiology 1:
HPA axis



Primary adrenal insufficiency: Etiologies

Acquired

- Autoimmune
- AIDS
- Tuberculosis
- Bilateral injury
  - Hemorrhage
  - Necrosis
  - Metastasis
- Idiopathic

Congenital

- Congenital adrenal hyperplasia
- Wolman disease
- Adrenal hypoplasia congenita
- Allgrove syndrome (AAA)

Syndromes

- Adrenoleukodystrophy
- Kearns-Sayre
- Autoimmune polyglandular syndrome 1 (APS1)
- APS2

When to consider AI: Patients at risk…Secondary AI

- Pituitary trauma/surgery
- Brain tumor
  - Craniopharyngioma
  - Suprasellar germ cell tumor
- Infiltrative pituitary disease
  - Sarcoidosis
  - Histiocytosis
- Congenital pituitary abnormalities
  - May have progressive loss of corticotroph function
- Chronic glucocorticoid therapy

Primary adrenal insufficiency: Etiologies

Acquired

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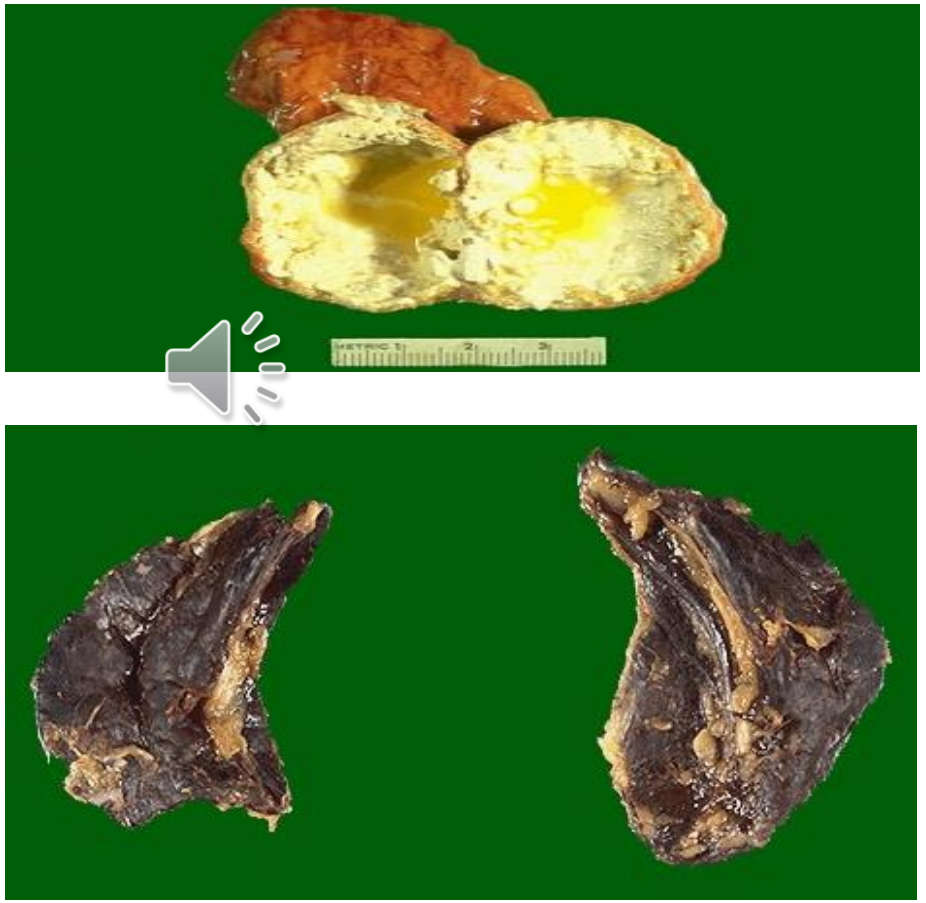
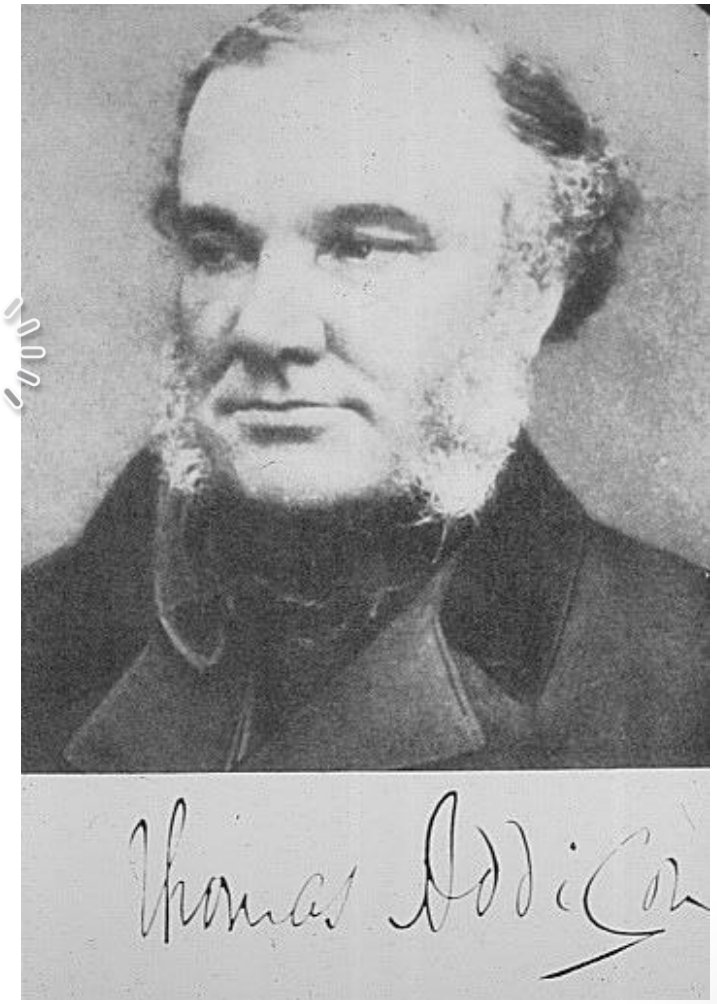
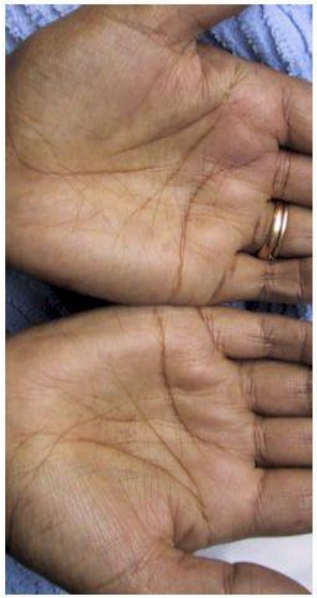
- AIDS
- **Tuberculosis**
- Bilateral injury
  - **Hemorrhage**
  - Necrosis
  - Metastasis
- Idiopathic

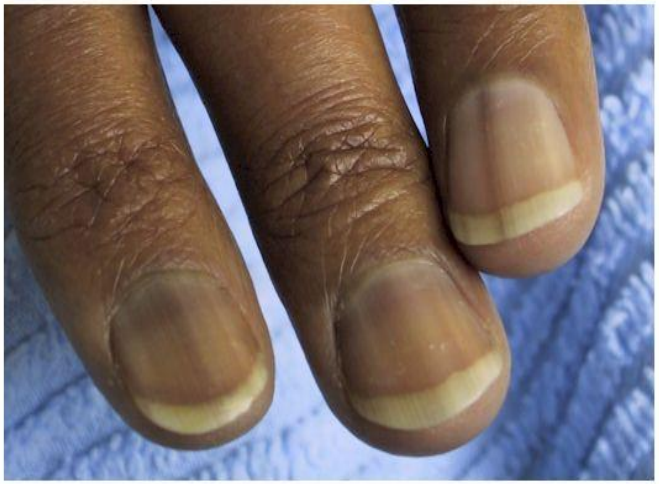


Addison's Disease

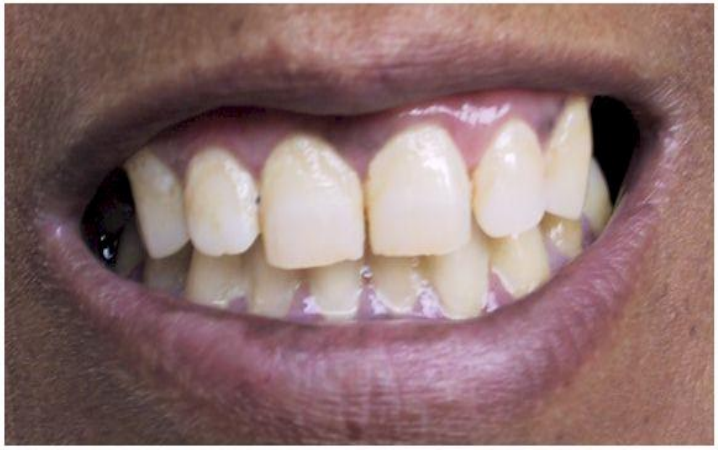
- 1st described in 1855 by Dr. Thomas Addison
- Refers to acquired primary adrenal insufficiency
- Does not confer specific etiology
  - Usually autoimmune (~80%)





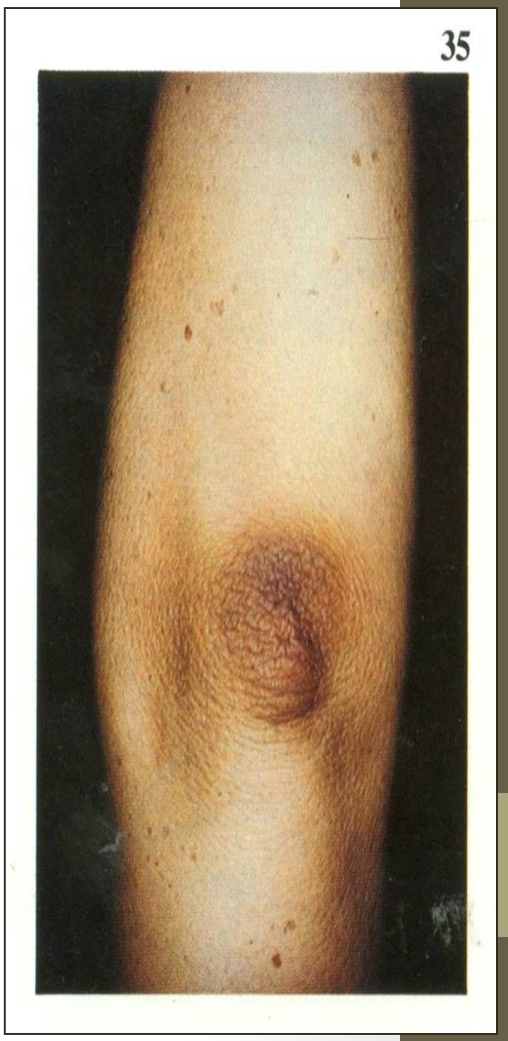


Addison's disease:

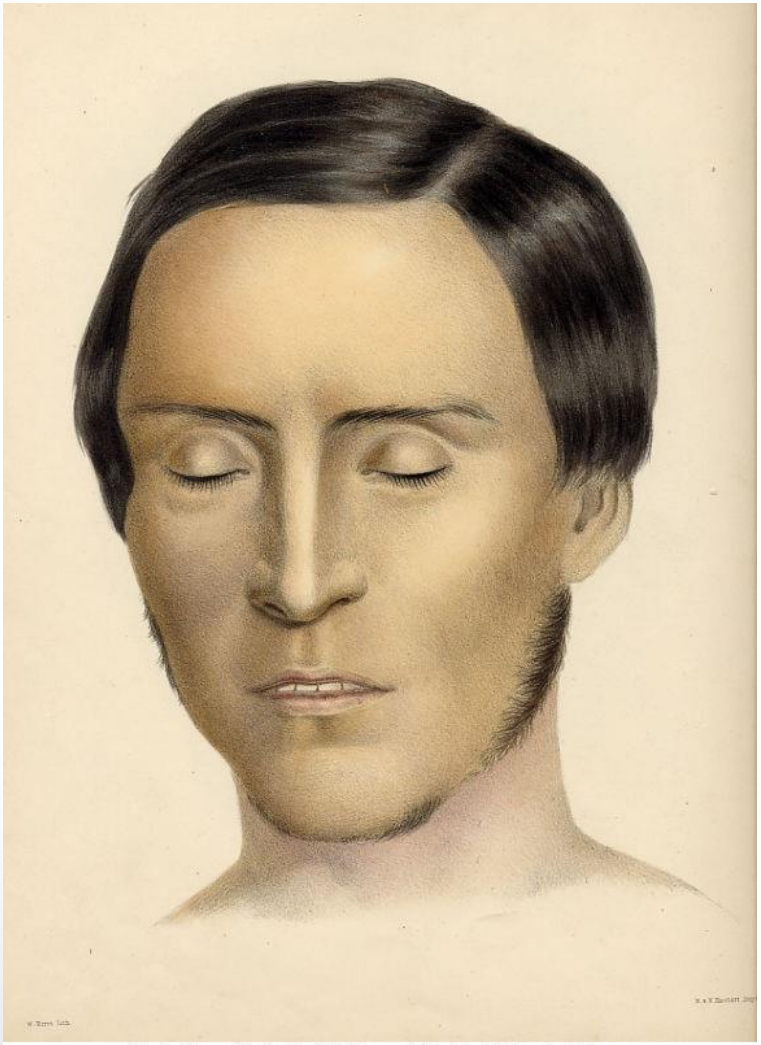


- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.

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



Primary adrenal insufficiency: Symptoms



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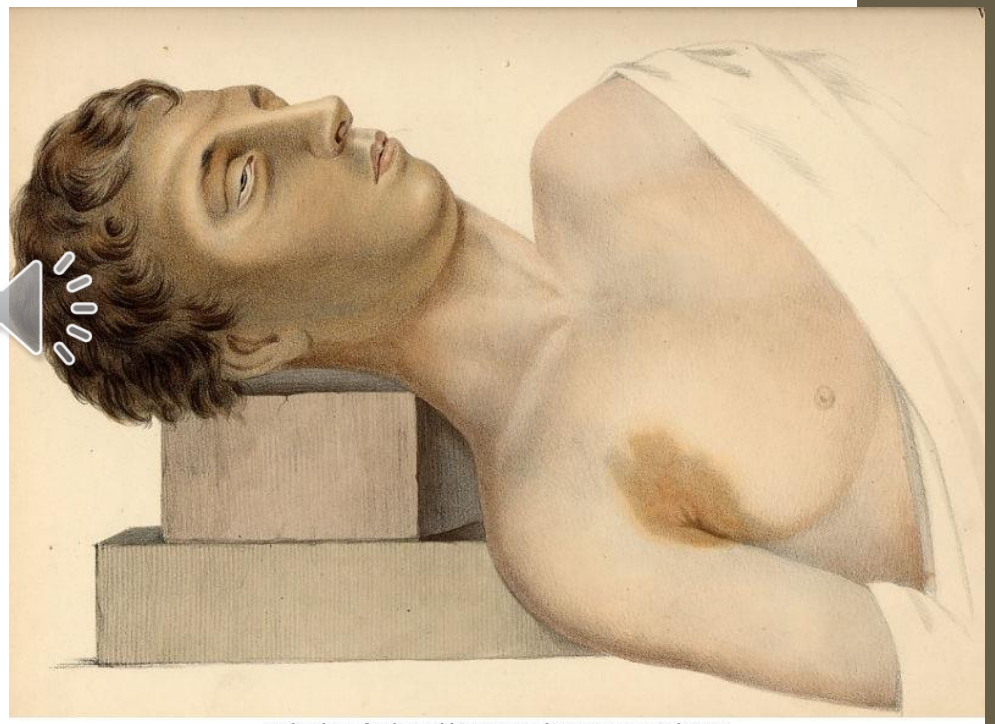
- Fatigue
- Weakness
- Orthostatsis
- Weight loss
- Poor appetite
- Neuropsychiatric
  - Apathy
  - Confusion
- Nausea, vomiting
- Abdominal pain
- Salt craving

Primary adrenal insufficiency: Physical findings

- Hyperpigmentation
- Hypotension
- Orthostatic changes
- Weak pulses
- Shock
- Loss of axillary/pubic hair (women)



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Primary adrenal insufficiency: Laboratory findings

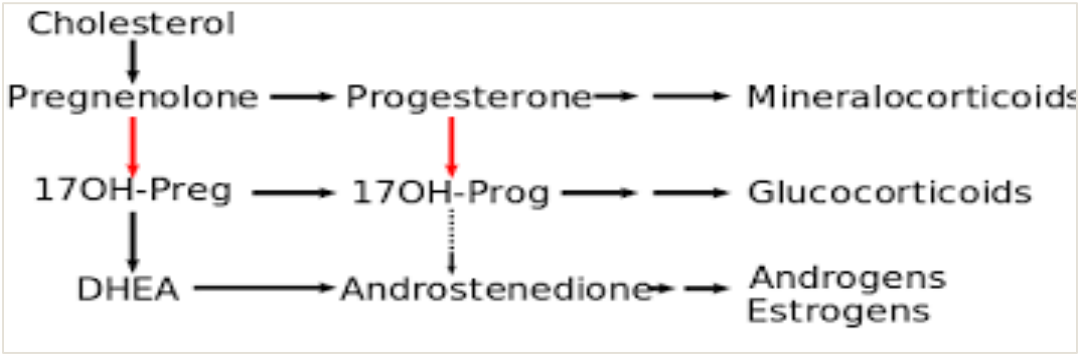
- Hyponatremia
- Hyperkalemia
- Hypoglycemia
- Narrow cardiac silhouette on CXR
- Low voltage EKG

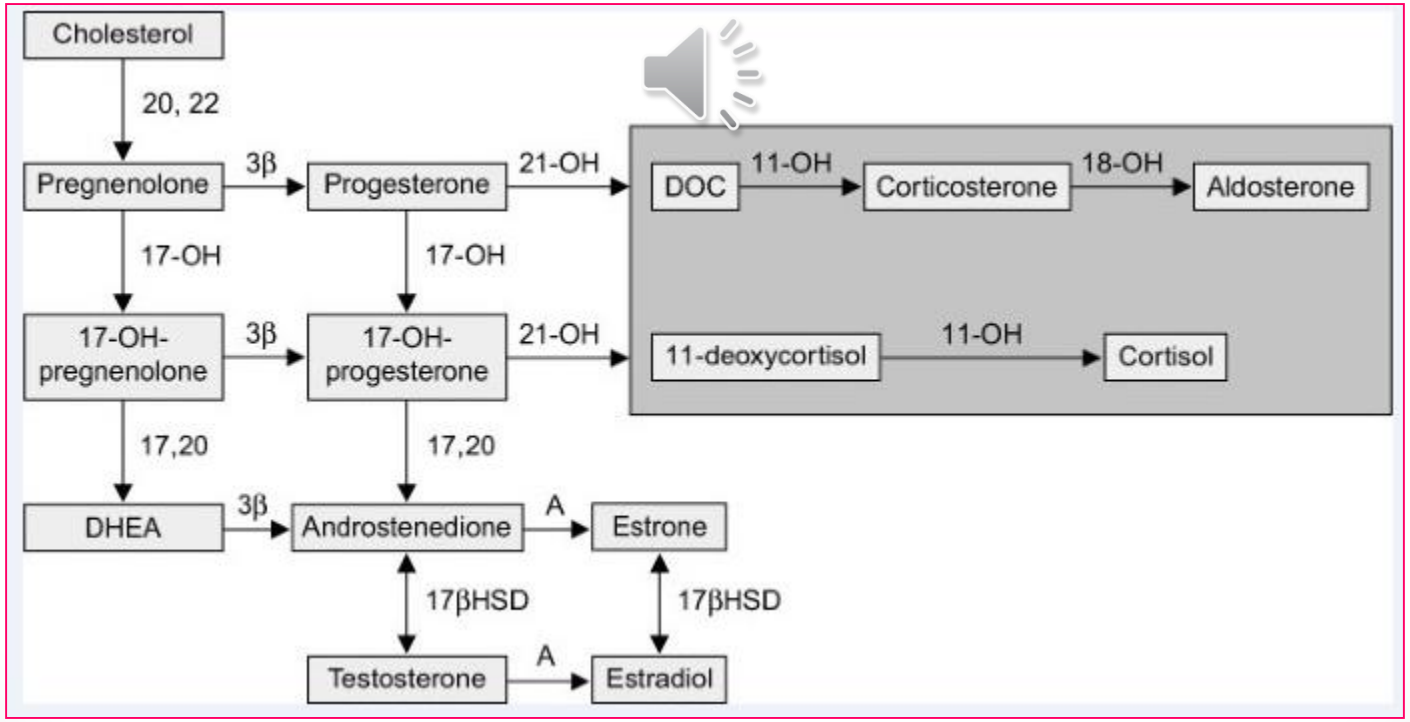
Primary adrenal insufficiency: Etiologies

Congenital

- **Congenital adrenal hyperplasia**
- Wolman disease
- Adrenal hypoplasia congenita
- Allgrove syndrome (AAA)

CAH: Pathophysiology

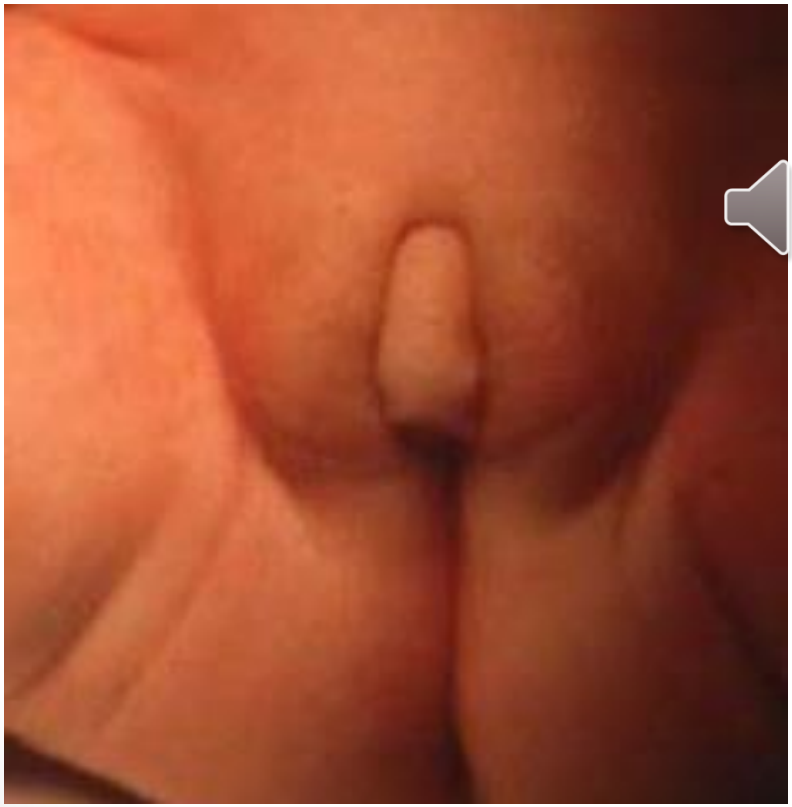




Congenital Adrenal Hyperplasia

- The first case was described in 1865
- Family of inherited disorders of adrenal steroidogenesis
- Each disorder results from a deficiency of one of several enzymes necessary for steroid synthesis
- Autosomal Recessive (M=F)
- 21-hydroxylase ↓ is the commonest form

21-hydroxylase deficiency: Physical exam



- Females are unremarkable other than genitalia
- GU exam – Clitoromegaly, posterior labial fusion, no vaginal opening
- Males appear normal

Primary adrenal insufficiency: Etiologies

Syndromes

- Adrenoleukodystrophy
- Kearns-Sayre
- **Autoimmune polyglandular syndrome 1 (APS1)**
- **APS2**

Evaluation

Primary adrenal insufficiency: Evaluation

- 0800 cortisol level
- ACTH level
- Random cortisol in ill patient
- ACTH stimulation test
- Suspected CAH
  - Needs special evaluation

Primary adrenal insufficiency: Evaluation

- 0800 cortisol level
  - Levels less than 3 mcg/dL are suggestive of AI
  - Levels greater than 11 mcg/dL exclude AI
- ACTH level
  - Elevated in adrenal insufficiency
  - ACTH readily degraded if not properly processed

Primary adrenal insufficiency: Evaluation

- Random cortisol in ill patient
  - >20 mcg/dL reassuring
- Adrenal Autoantibodies
  - ACA—adrenal cortex antibody
  - Anti-21-OH-hydroxylase antibody

Primary adrenal insufficiency: Evaluation—ACTH Stimulation

- Low dose (1 mcg) test
  - Baseline and 30 minute cortisol levels
  - More physiological ACTH level/stimulation
  - Useful in central AI
  - Useful for assessing recovery after chronic steroid treatment
- High dose (250 mcg) test
  - Baseline, 30 and 60 minute levels
  - Can be done IM
  - Stronger stimulation than 1 mcg test

Primary adrenal insufficiency: Evaluation—ACTH Stimulation

- Cortisol peaks are controversial
  - Reported normals range between 16-25 mcg/dl
  - Some providers also look at the magnitude of rise
- Also use ACTH to help differentiate primary vs secondary deficiency
  - Secondary may respond to high dose, but not low
  - Primary should fail both high and low dose

Treatment

Primary adrenal insufficiency: Acute treatment

- NS volume resusitation
  - Reverse shock
- Look for/treat hypoglycemia
  - 5cc/kg dextrose10%
- New problem, suspected AI
  - Labs→steroids
- Established patient with AI
  - Steroids

Stress dose steroids

- Loading dose
  - 50-100 mg/M2 hydrocortisone IV/IM
  - Small/medium/large approach
    - Infants: Hydrocortisone 10mg
    - Toddler : Hydrocortison 25 mg
    - children: Hydrocortisone 50 mg
    - teens: Hydrocortisone 100 mg
- Continue hydrocortisone with 100 -150mg/M2/day
  - Divide q6-8 hours
  - May be 2-3x home dose

Primary adrenal insufficiency: Long term treatment

- Daily glucocorticoid replacement (hydrocortisone)
  - 10-15 mg/m2/day divided TID
  - Option to change to prednisone in teen years
- Daily mineralocorticoid replacement
  - Fludrocortisone 0.05-0.2 mg daily
- Patient education
  - Stress coverage
  - Emergency steroid administration
    - IM hydrocortisone (Solucortef Actovial)
  - Medic Alert ID

Adrenal Insufficiency Summary

- May be primary or secondary
- May be congenital or acquired
- Treatment is relatively simple
- Diagnosis is often controversial
  - Baseline cortisol/ACTH before steroids
  - ACTH stim test if possible
  - Additional testing if CAH is suspected
- Don’t forget to check the blood sugar!


Thank
You