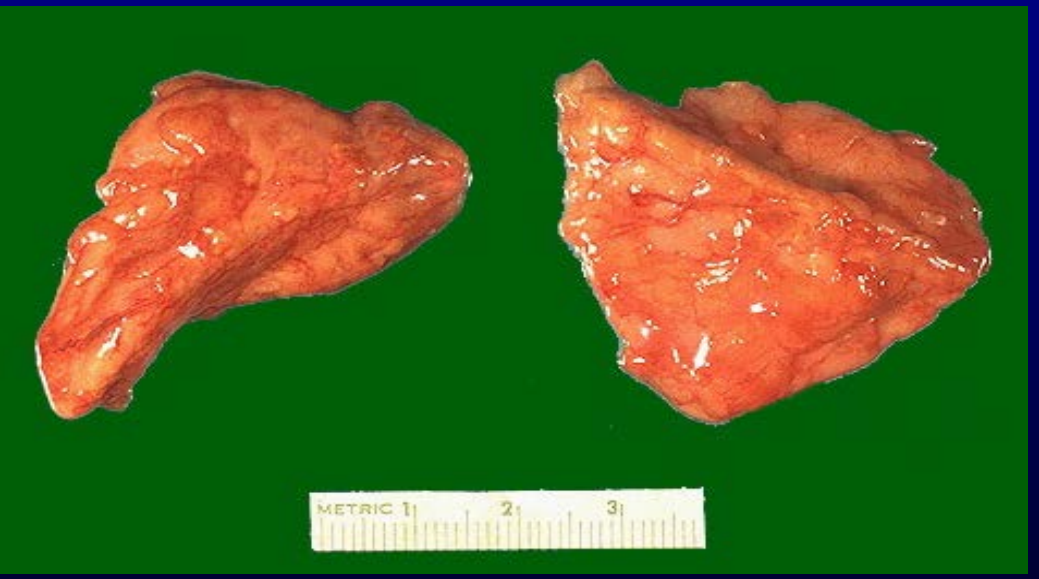
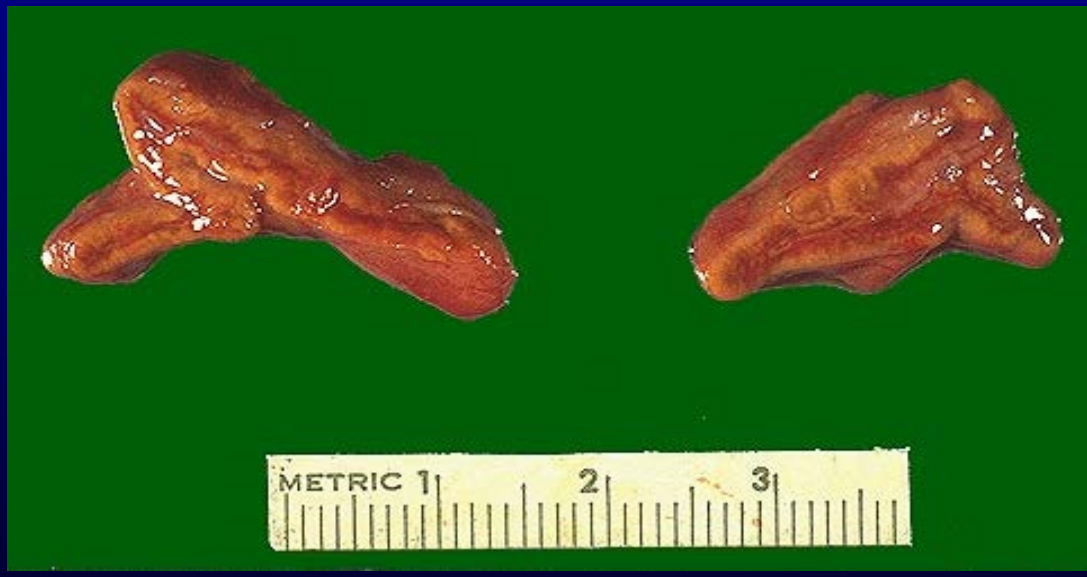
Adrenal Insufficiency

- Normal adrenal physiology
- Clinical features, Laboratory findings
- Common causes of primary adrenal insufficiency
- Evaluation of suspected adrenal insufficiency
- Acute and chronic management issues

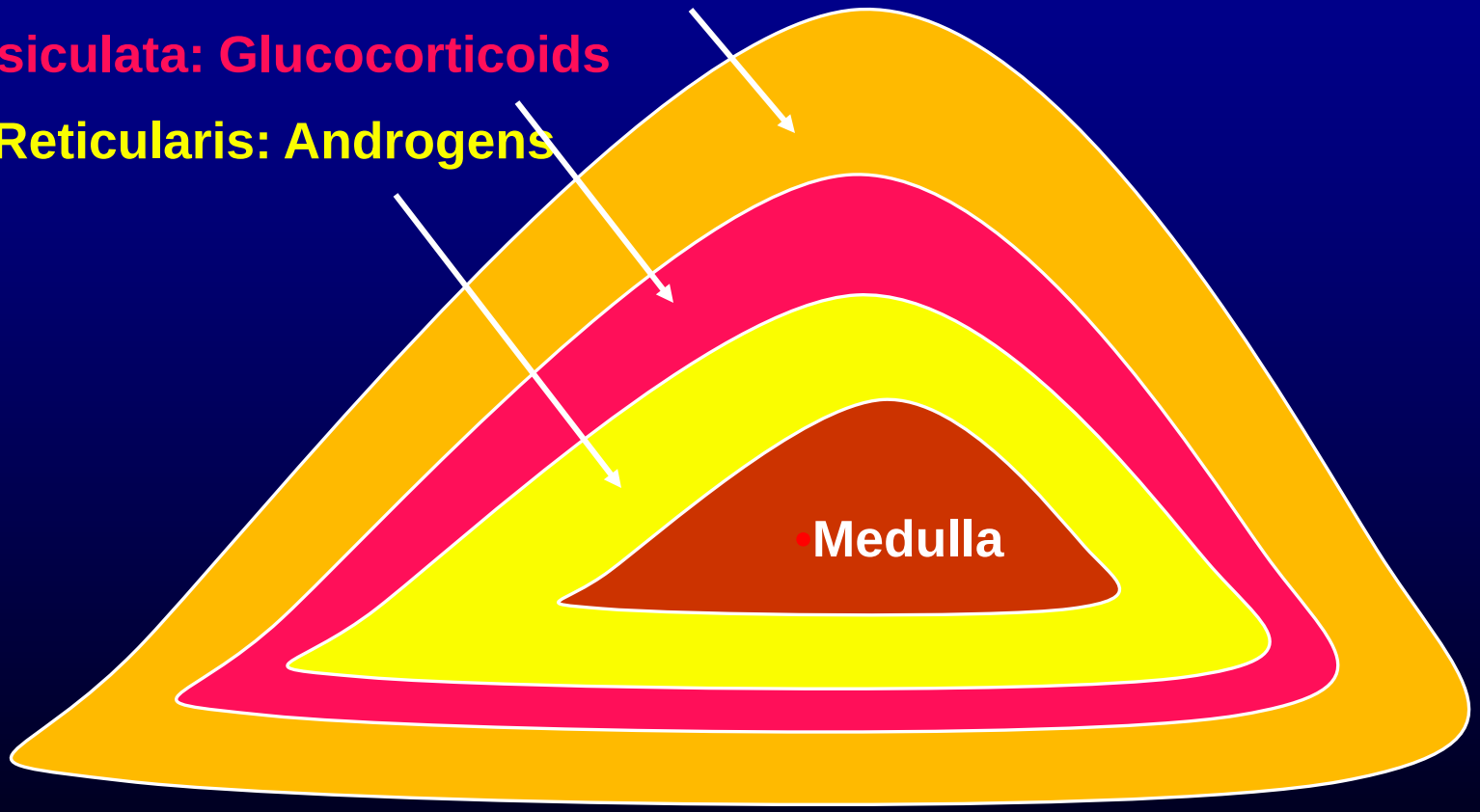
Normal Adrenals



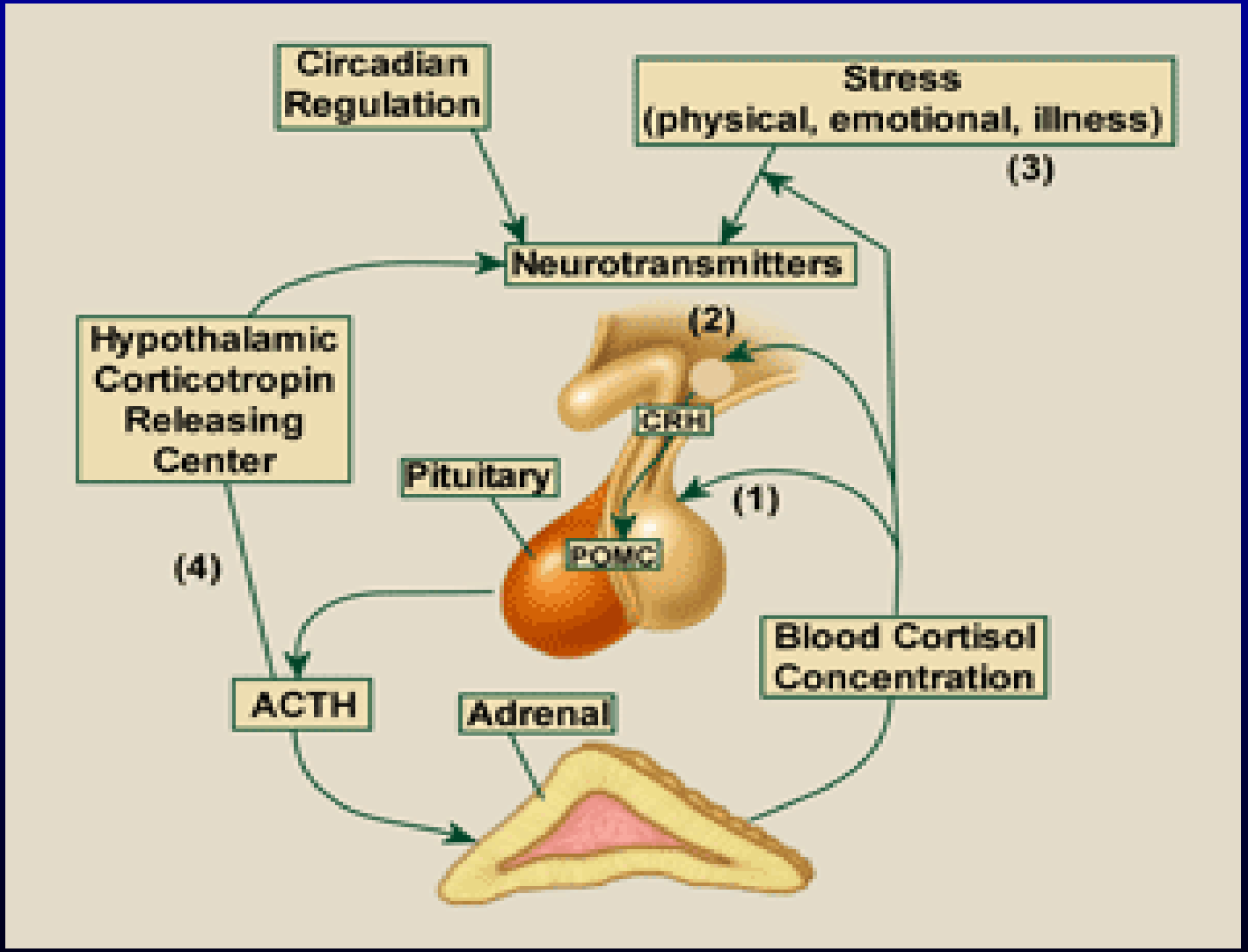


Adrenal Cortex

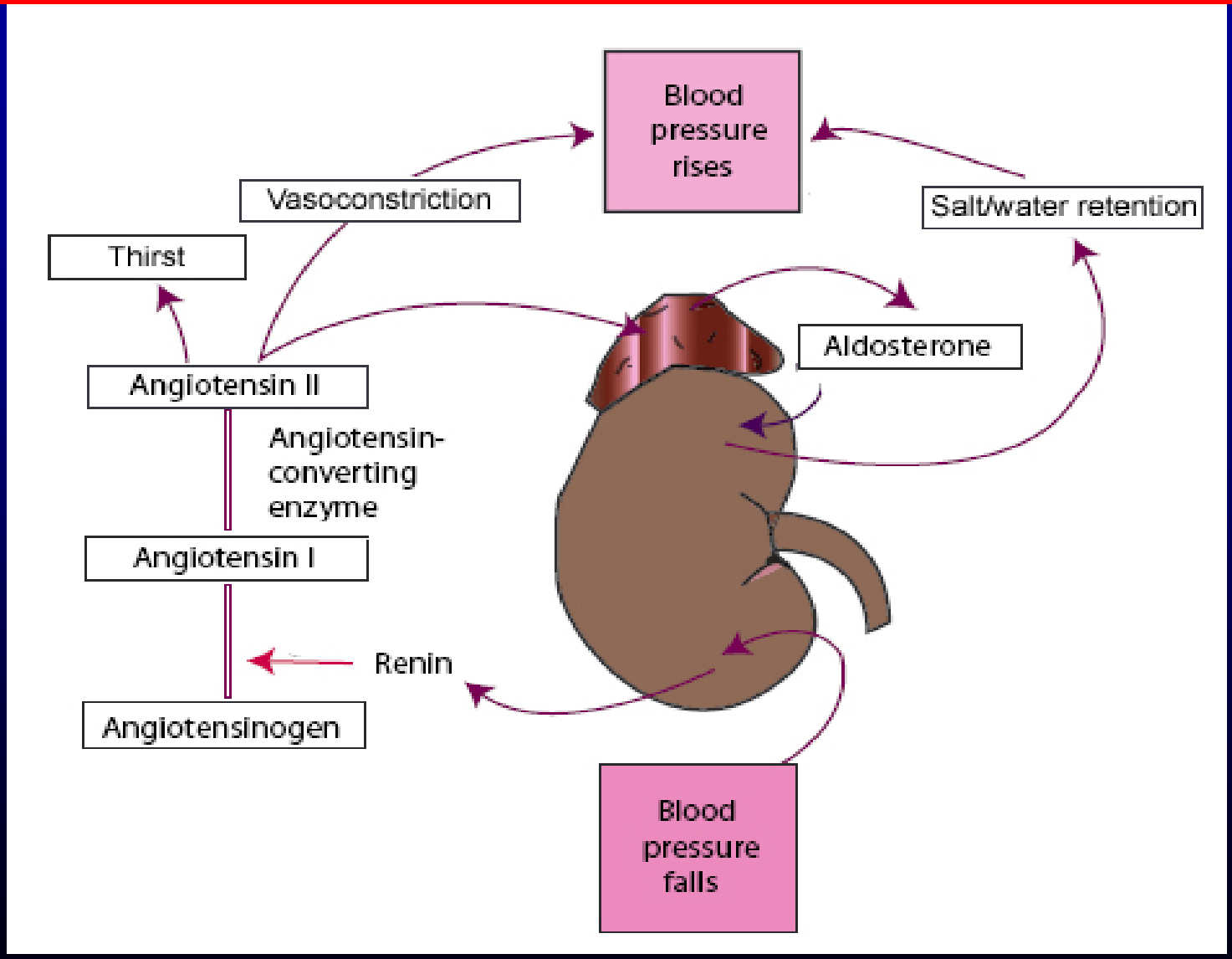
- Zona Glomerulosa: Mineralocorticoids
  - Zona Fasiculata: Glucocorticoids
    - Zona Reticularis: Androgens



Adrenal physiology: HPA axis



Adrenal physiology: Renin-angiotensin system



Causes of Primary adrenal insufficiency:

Acquired

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

Congenital

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

Syndromes

- Adrenoleukodystrophy
- Autoimmune polyglandular syndrome 1 (APS1)
- APS2 (Schmidt syndrome)

Aetiology of Primary adrenal insufficiency:

Acquired

- Autoimmune
- AIDS
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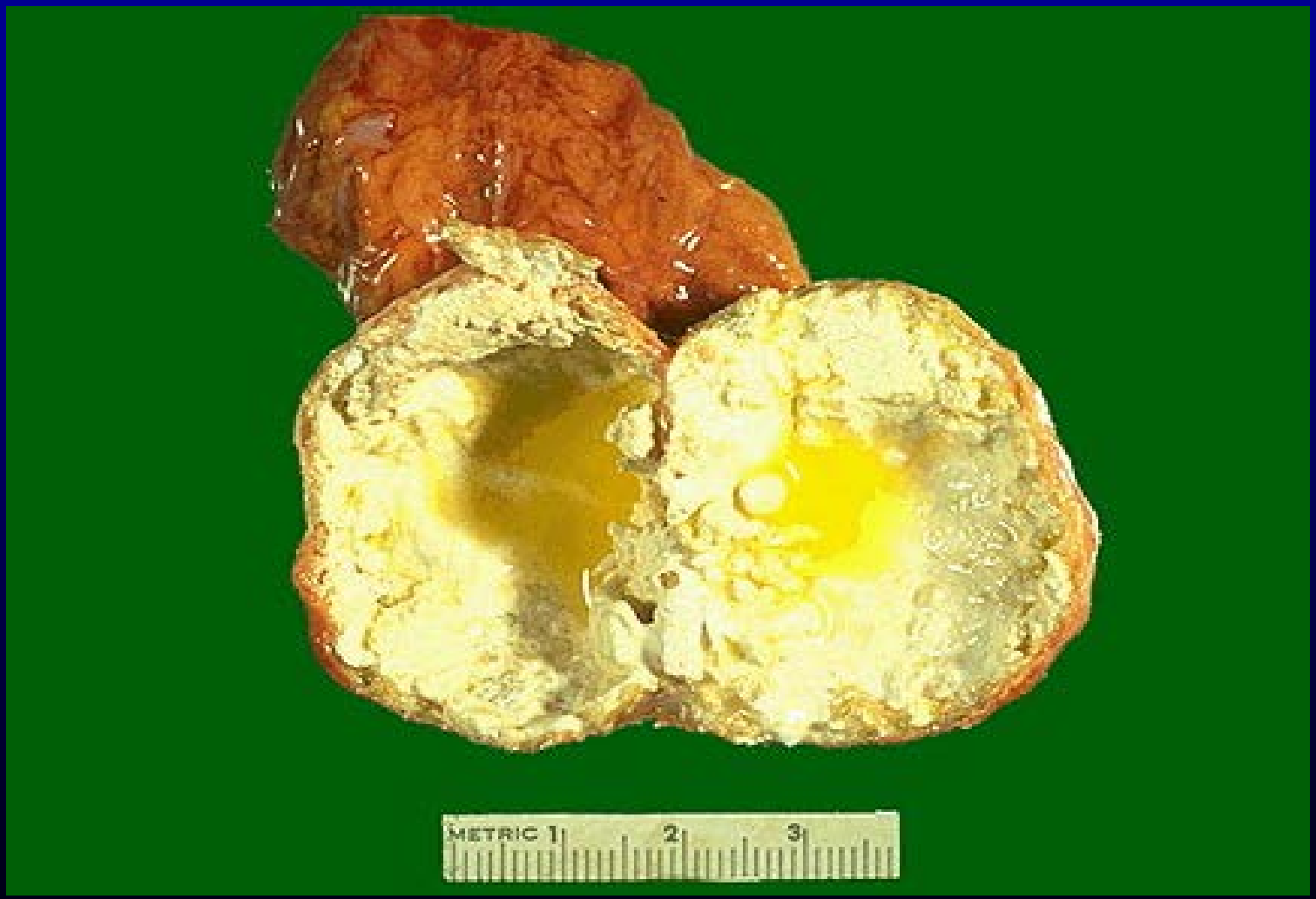
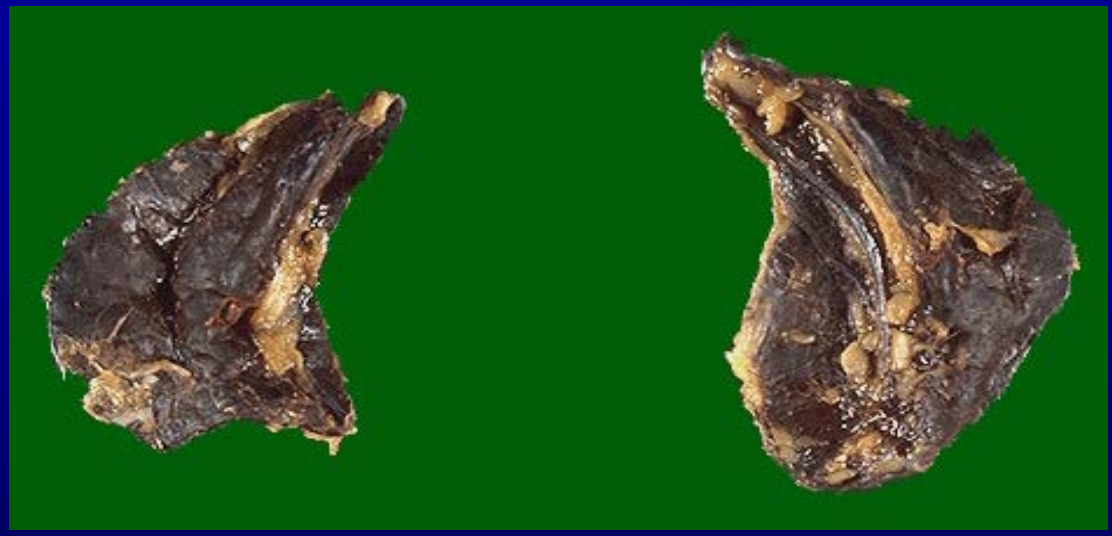
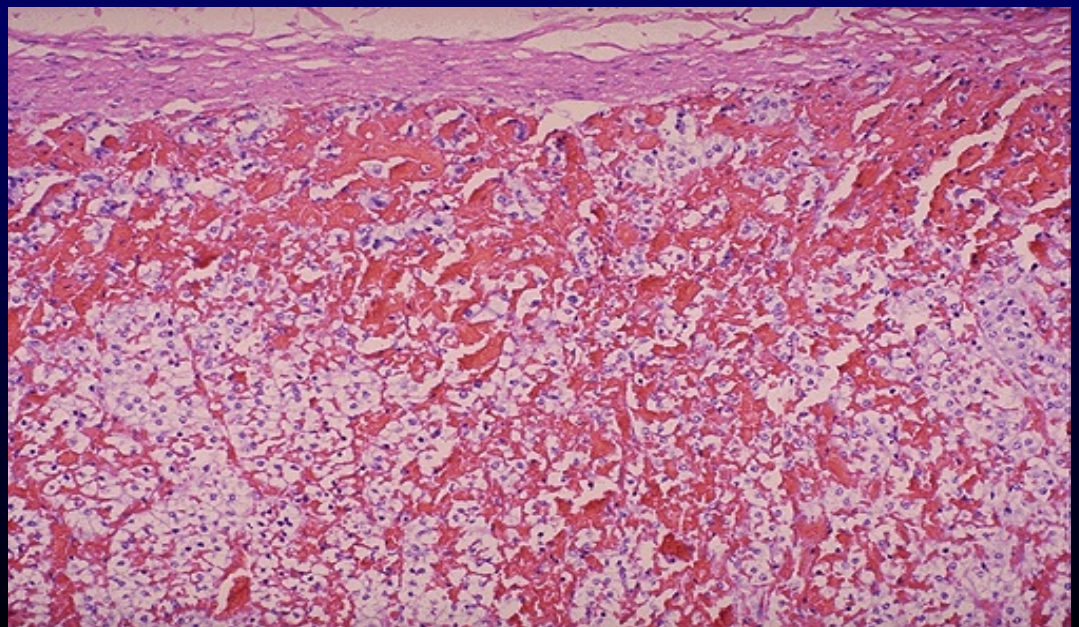
Tuberculosis



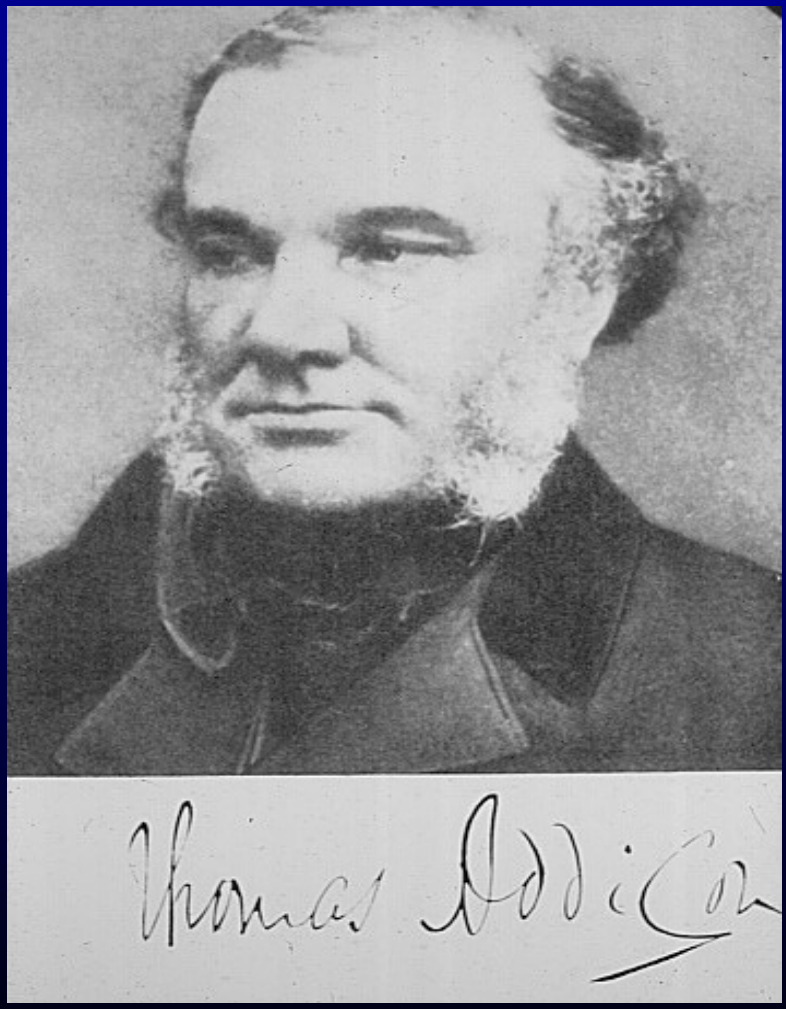
Adrenal Hemorrhage: Meningococcemia Waterhouse-Friderichsen Syndrome





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%)



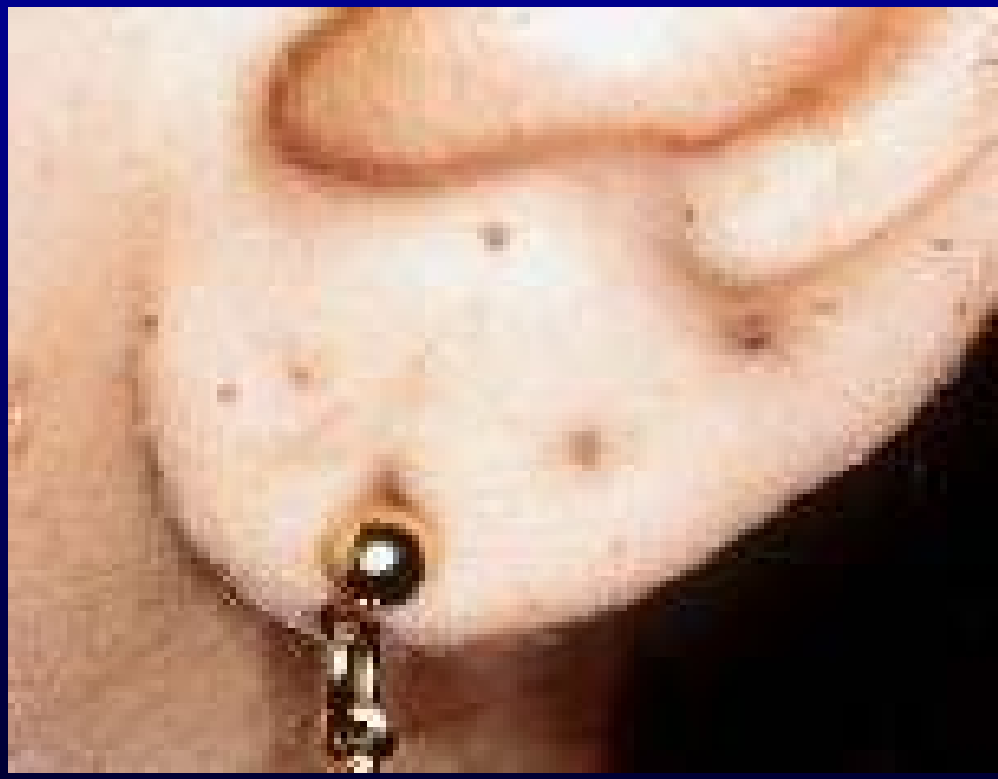
Primary adrenal insufficiency: Symptoms

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

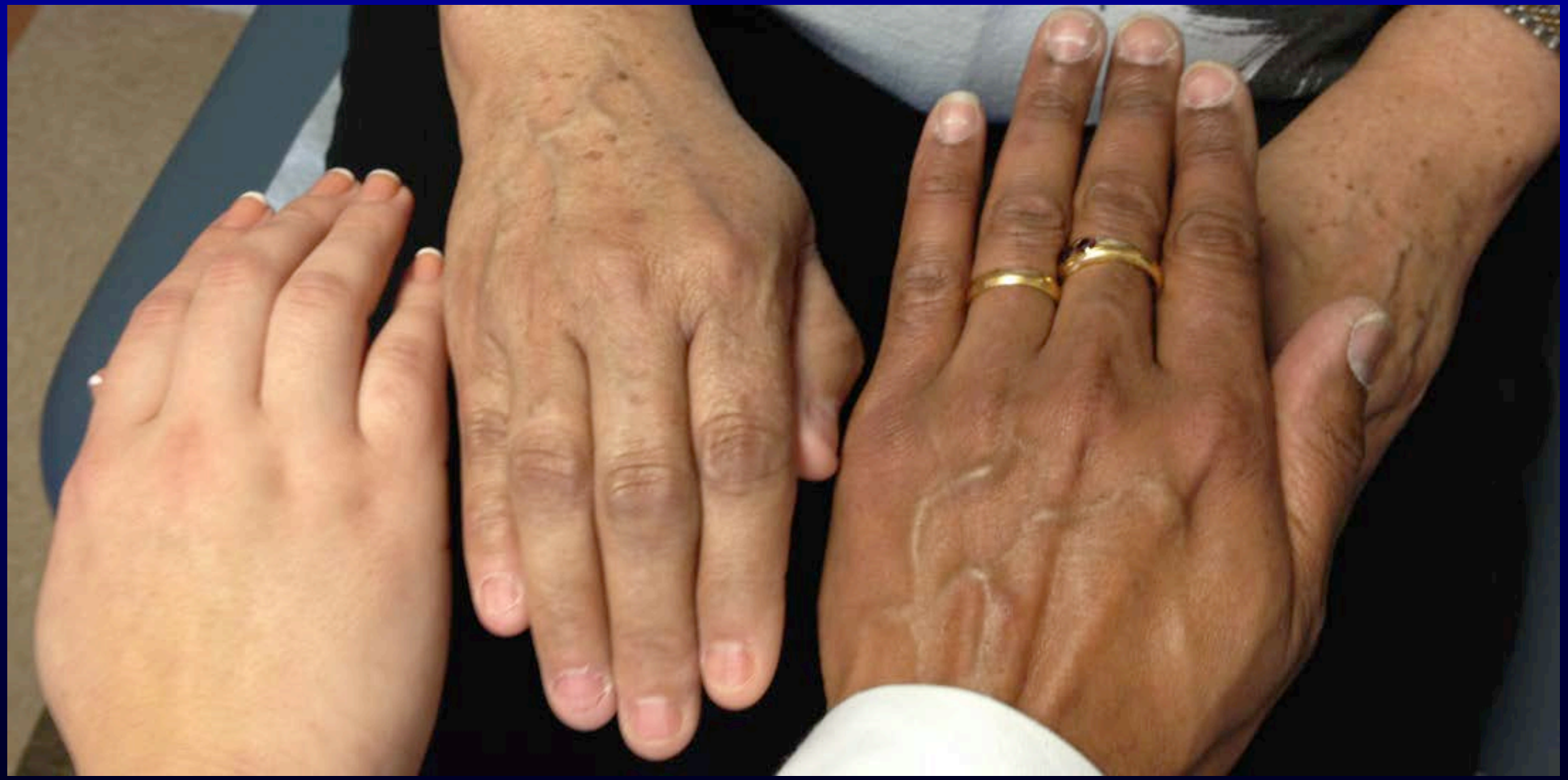
Primary adrenal insufficiency: Physical findings

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

Primary adrenal insufficiency: Physical findings



Adrenal Insufficiency - hyperpigmentation



Primary adrenal insufficiency: Laboratory findings

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

Primary adrenal insufficiency:

Congenital

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

21-hydroxylase deficiency CAH

- Classification based on enzyme activity
  - Classic
    - Salt wasting (Complete deficiency)
    - Simple virilizing (Significant but partial defect)
  - Non Classic
    - Elevated enzyme levels (Mild deficiency)

Primary adrenal insufficiency:

Syndromes

- Adrenoleukodystrophy
- **Autoimmune polyglandular syndrome 1 (APS1)**
- **APS2 (Schmidt Syndrome)**

Primary adrenal insufficiency: Associated conditions

- Autoimmune Polyglandular Syndrome I
  - Hypoparathyroidism
  - Chronic mucocutaneous candidiasis
  - Atrophic gastritis
  - Adrenal insufficiency in childhood
  - Pernicious anemia
  - Vitiligo
  - AIRE mutation
    - Transcription factor
    - Affects immune regulation

Primary adrenal insufficiency: Associated conditions

- Autoimmune Polyglandular Syndrome II
  - Autoimmune thyroiditis
  - Type I diabetes mellitus
  - Adrenal insufficiency
  - Pernicious anemia
  - Premature ovarian failure
  - Genetic associations
    - HLA haplotype, CLTA4

- 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 15 mcg/dL unlikely to be AI
- ACTH level
  - Elevated in adrenal insufficiency
  - ACTH readily degraded if not properly processed [frozen]

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, 30 and 60 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 18-25 mcg/dl
  - Some providers also look at the degree of increase
- 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

- Normal Saline volume resuscitation
  - Reverse shock
- Look for/treat hypoglycemia
  - 25% dextrose
- New problem, suspected AI
  - Labs→steroids
- Established patient with AI
  - Steroids

Stress dose steroids

- Loading dose
  - 100mg IV and then 100mg SQ q 8hr
- Continue hydrocortisone with 50-100 mg/sq. m/day
  - Divide q6-8 hours
  - May be 2-3x home dose

Primary adrenal insufficiency: Long term treatment

- Daily glucocorticoid replacement (hydrocortisone)
  - 15-30 mg/day divided BID

  Daily mineralocorticoid replacement
  - Fludrocortisone 0.05-0.2 mg daily

- Patient education
  - Stress coverage
  - Emergency steroid administration
    - IM hydrocortisone (Solucortef Actovial)
  - Medic Alert ID

Relative Steroid Potencies

	Glucocorticoid	Mineralocorticoid
Hydrocortisone	1	++
Prednisone/ Prednisolone	3-5	+
Methylprednisone	5-6	0
Dexamethasone	25-50	0
Fludrocortisone	15-20	+++++

Relative Steroid Potencies

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Dexamethasone	25-50	-
Fludrocortisone	15-20	+++++

When to consider AI: Patients at risk…Primary AI

- History of TB
- Refractory shock
  - Particularly meningococcal disease
- Dehydration/shock with hyperpigmentation
- Neonate with vomiting/dehydration/shock
- Other autoimmune endocrine disease
- History consistent with APS1
  - Immunodeficiency/chronic mucocutaneous candidiasis

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

Summary: Adrenal Insufficiency

- May be primary or secondary
- May be congenital or acquired
- Treatment is relatively simple
- Diagnosis is often controversial
  - Baseline cortisol/ACTH before steroids
  - ACTH stimulation test, if possible
  - Additional testing if CAH is suspected