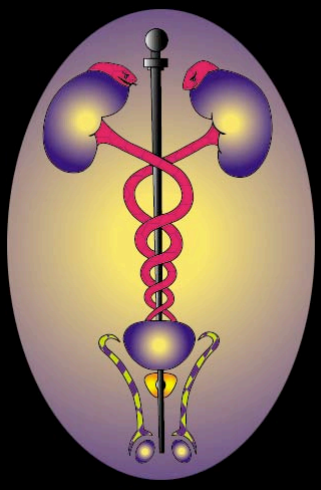
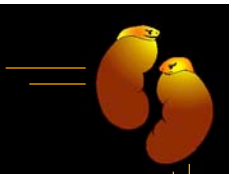


The Adrenal Glands

Thomas Jacobs, M.D.
Diane Hamele-Bena, M.D.



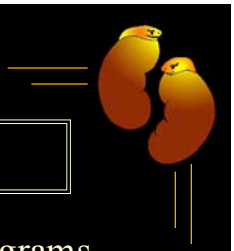
I. Normal adrenal gland
   A. Gross & microscopic
   B. Hormone synthesis, regulation & measurement

II. Hypoadrenalism

III. Hyperadrenalism; Adrenal cortical neoplasms

IV. Adrenal medulla

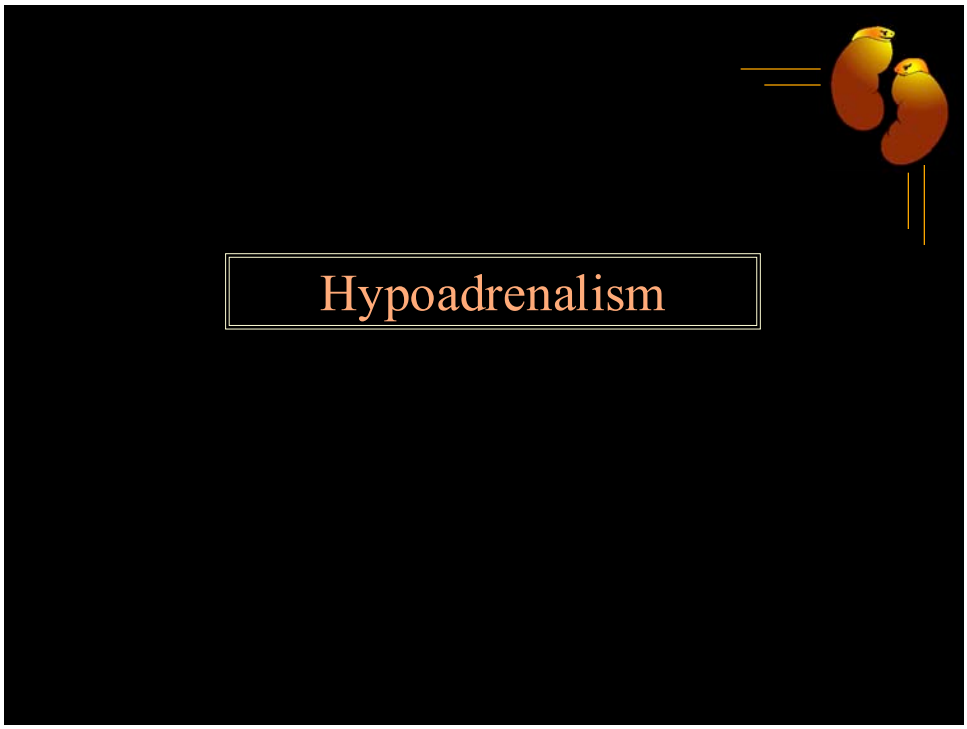
Normal Adrenal Gland



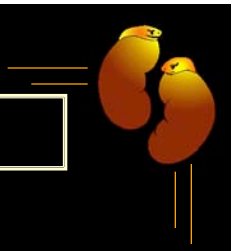
- Normal adult adrenal gland: 3.5 - 4.5 grams

Adrenal Cortex Morphology

- Cortex: 3 zones:
  - Glomerulosa
  - Fasciculata
  - Reticularis


Hypoadrenalism

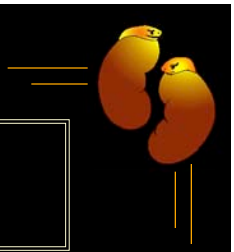
Hypoadrenalism



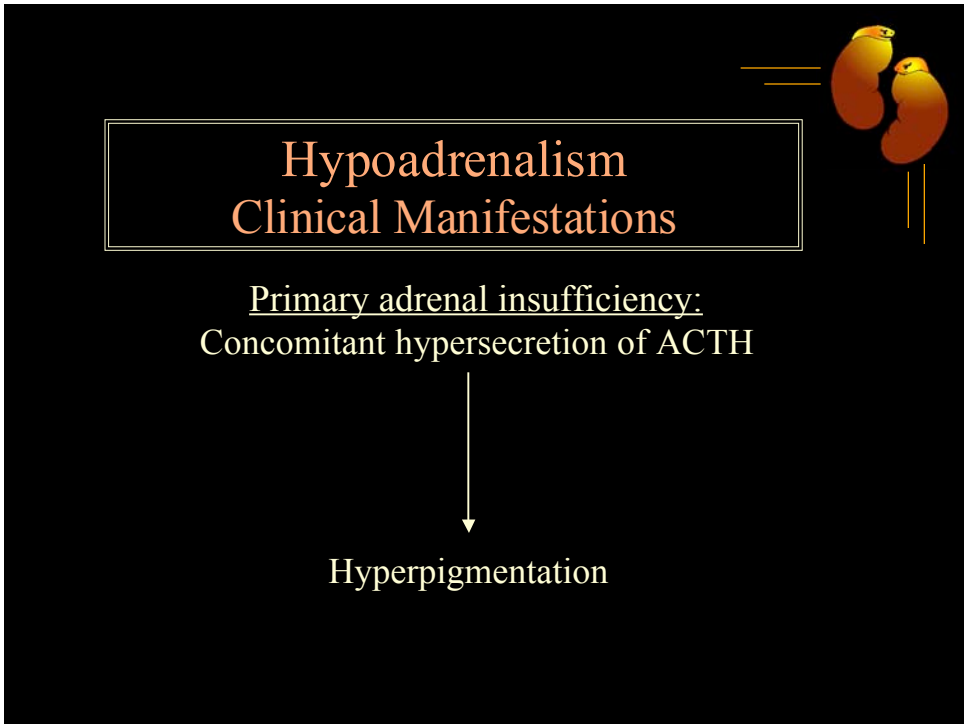
- Primary Adrenocortical Insufficiency

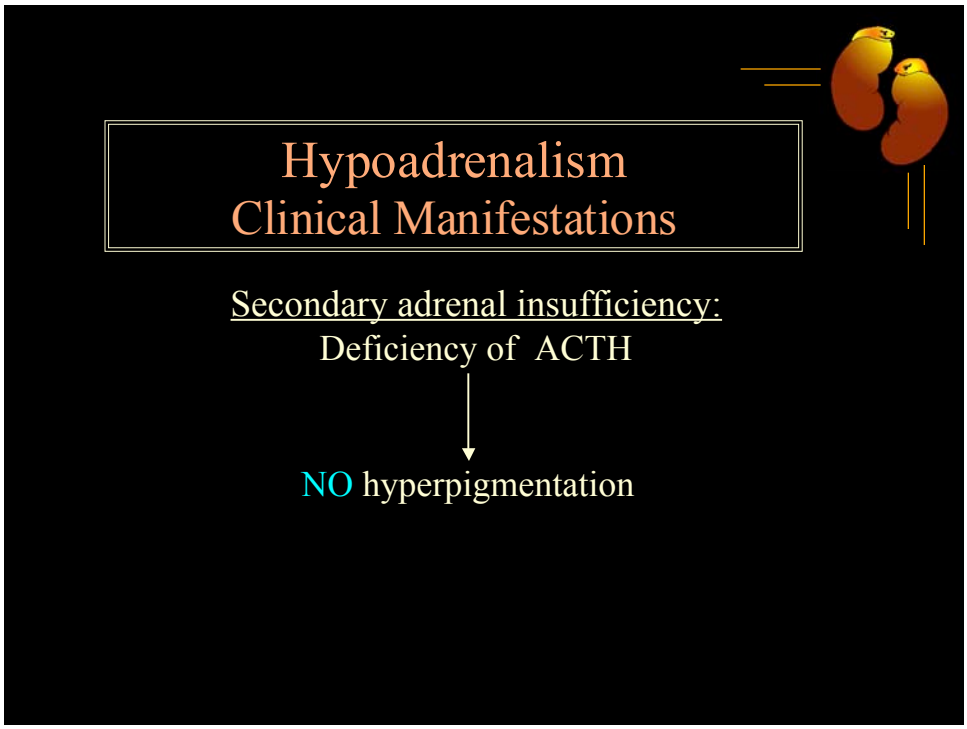
- Secondary Adrenocortical Insufficiency

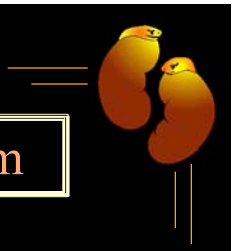
Hypoadrenalism
Clinical Manifestations



Primary adrenal insufficiency:
Deficiency of
glucocorticoids, mineralocorticoids, and androgens

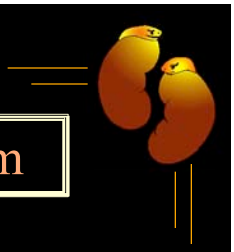

Hypoadrenalism
Clinical Manifestations
Primary adrenal insufficiency:
Concomitant hypersecretion of ACTH
Hyperpigmentation


Hypoadrenalism
Clinical Manifestations
Secondary adrenal insufficiency:
Deficiency of ACTH
NO hyperpigmentation



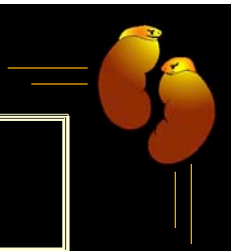
Pathology of Hypoadrenalism

- Primary Adrenocortical Insufficiency
  - Acute
  - Chronic = Addison Disease
- Secondary Adrenocortical Insufficiency



Pathology of Hypoadrenalism

- Primary Adrenocortical Insufficiency
  - Acute
  - Chronic = Addison Disease
    - Autoimmune adrenalitis



Addison Disease
Clinical findings

Mineralocorticoid deficiency

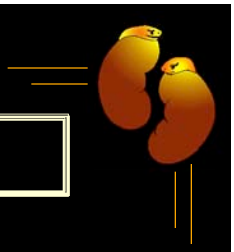
- Hypotension
- Hyponatremia
- Hyperkalemia

Androgenic deficiency

- Loss of pubic and axillary hair in women

Glucocorticoid deficiency

- Weakness and fatigue
- Weight loss
- Hyponatremia
- Hypoglycemia
- Pigmentation
- Abnormal H_2O metabolism
- Irritability and mental sluggishness

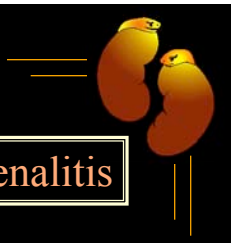


Autoimmune Adrenalitis

Three settings:

- Autoimmune Polyendocrine Syndrome type 1 (APS1) = Autoimmune Polyendocrinopathy, Candidiasis, and Ectodermal Dysplasia (APECED)
- Autoimmune Polyendocrine Syndrome type 2 (APS2)
- Isolated Autoimmune Addison Disease

Pathologic Changes in Autoimmune Adrenalitis



•Gross:

–Very small glands (1 - 1.5 grams)

–Cortices markedly thinned

•Micro:

–Diffuse atrophy of *all* cortical zones

–Lymphoplasmacytic infiltrate

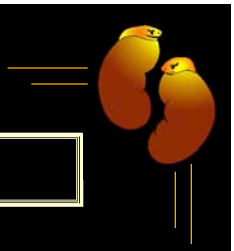
–Medulla is unaffected

Pathology of Hypoadrenalism

- Primary Adrenocortical Insufficiency
  - Acute
    - Waterhouse -Friderichsen Syndrome
  - Chronic = Addison Disease
- Secondary Adrenocortical Insufficiency
  - Any disorder of the hypothalamus or pituitary leading to diminished ACTH; e.g., infection; pituitary tumors, including metastatic carcinoma; irradiation


Hyperadrenalism

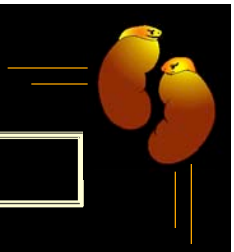
Hyperadrenalism



Three distinctive clinical syndromes:

- Cushing Syndrome
- Hyperaldosteronism
- Adrenogenital or Virilizing Syndrome

Hyperadrenalism



In clinical practice, most cases of Cushing Syndrome are the result of administration of exogenous glucocorticoids ("exogenous" or iatrogenic Cushing Syndrome).

"Endogenous" Cushing Syndrome

Etiology	Pathology
I. ACTH-dependent:	
•Cushing *Disease*	Pituitary adenoma or hyperplasia ↓ Adrenal cortical hyperplasia
•Ectopic ACTH production	Extra-adrenal ACTH-producing tumor ↓ Adrenal cortical hyperplasia
II. ACTH-independent:	
•Hypersecretion of cortisol by adrenal neoplasm or autonomous adrenal cortical hyperplasia	Adrenal neoplasm or cortical hyperplasia

Cushing Syndrome

Hydrocortisone Excess

- •Abnormal fat distribution
  - –Moon face
  - –Central obesity
- •Increased protein catabolism
  - –Thin skin
  - –Easy bruisability
  - –Striae
  - –Osteoporosis with vertebral fractures
  - –Impaired healing
  - –Muscle wasting
  - –Suppressed response to infection
- •Diabetes
- •Psychiatric symptoms

Adrenal Androgen Excess

- •Hirsutism
- •Deepened voice in women
- •Acne
- •Abnormal menses

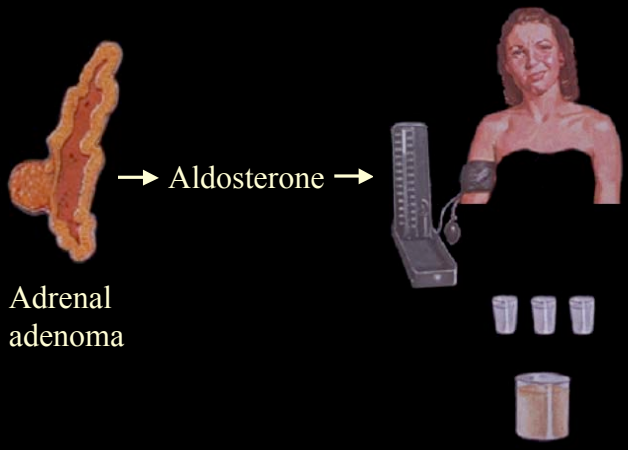
Mineralocorticoid Excess

- •Hypokalemia with alkalosis
- •Usually occurs in cases of ectopic ACTH production

Pathology of Primary Hyperaldosteronism

- Aldosterone-secreting adenoma
  - *Conn Syndrome*
- Bilateral idiopathic cortical hyperplasia
- Adrenal cortical carcinoma
  - Uncommon cause of hyperaldosteronism

Conn Syndrome



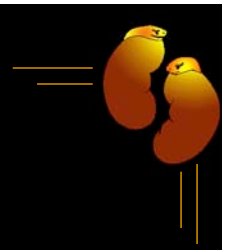
- Hypertension
- Polydipsia
- Polyuria
- Hypernatremia
- Hypokalemia

Adapted from Netter

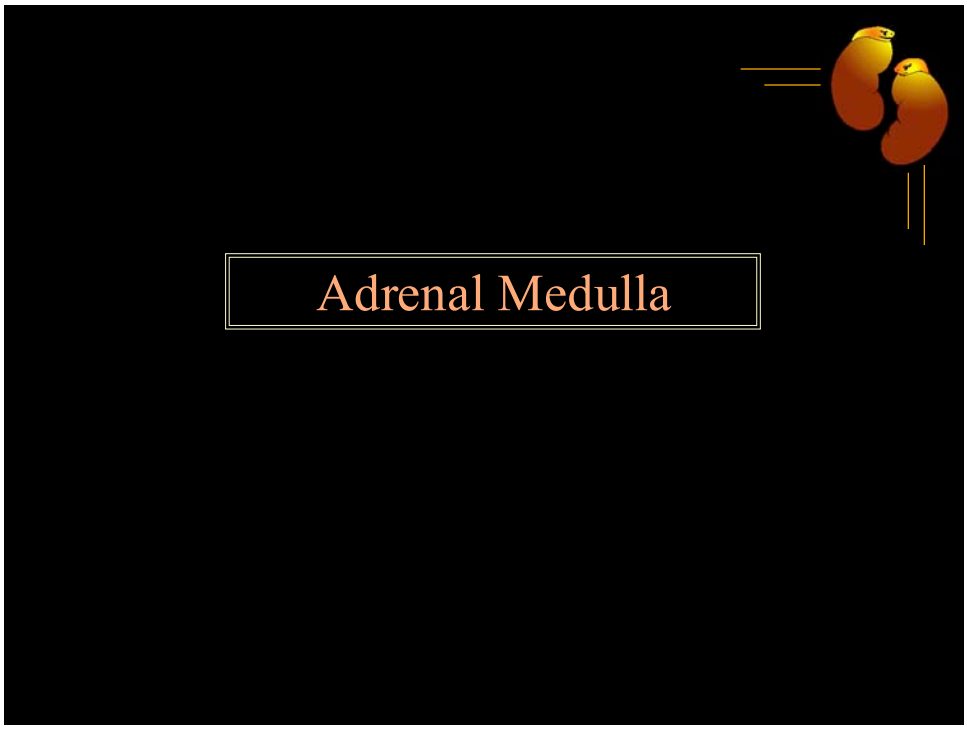
Cortical Neoplasms

Adenomas and Carcinomas → Functioning
Adenomas and Carcinomas → Non-functioning

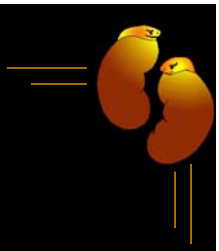
Cortical Neoplasms



- Adenomas
  - Gross:
    - Discrete, but often unencapsulated
    - Small (up to 2.5 cm)
    - Most <30 grams
    - Yellow-orange, usually without necrosis or hemorrhage
  - Micro:
    - Lipid-rich & lipid-poor cells with little size variation
- Carcinomas
  - Gross:
    - Usually unencapsulated
    - Large (many >20 cm)
    - Frequently > 200-300 grams
    - Yellow, with hemorrhagic, cystic, & necrotic areas
  - Micro:
    - Ranges from mild atypia to wildly anaplastic

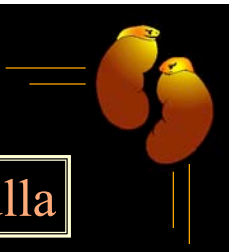

Adrenal Medulla

Adrenal Medulla



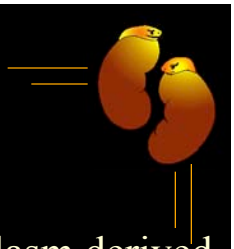
- Specialized neural crest (neuroendocrine) cells
- Part of the chromaffin system
- Major source of catecholamines

Tumors of the Adrenal Medulla



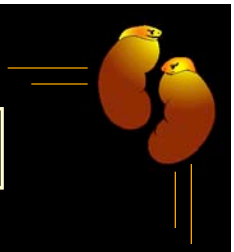
- Neuroblastoma
- Ganglioneuroblastoma
- Ganglioneuroma
- Pheochromocytoma

Neuroblastoma



- *Poorly differentiated* malignant neoplasm derived from neural crest cells
- Usually occurs in infants & small children
- "Small round blue cell tumor" of childhood

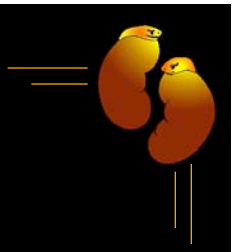
Neuroblastoma: Pathology



- Gross:
  - Large tumor with hemorrhage, necrosis, & calcification
- Micro:
  - Undifferentiated small cells resembling lymphocytes
  - May show areas of *differentiation*

Neuroblastoma: Prognostic Factors

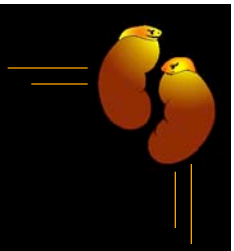
- Patient age
- Stage
- Site of 1^0 involvement
- Histologic grade
- DNA ploidy
- N-myc oncogene amplification



Ganglioneuroma

- *Differentiated* neoplasm of neural crest origin
- Benign
- Occurs in older age group
- Pathology:
  - Gross: Encapsulated, white, firm
  - Micro: Ganglion cells & Schwann cells

Ganglioneuroblastoma

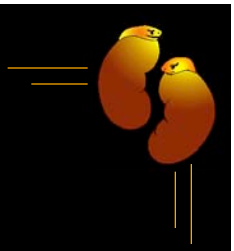


- Composed of malignant neuroblastic elements & ganglioneuromatous elements
- Prognosis depends on % of neuroblasts

Pheochromocytoma

- Catecholamine-secreting neoplasm: HYPERTENSION
- Rare, but important: surgically curable form of hypertension
- May arise in association with familial syndromes, e.g., MEN2, von Hippel-Lindau, von Recklinghausen (NF1)
- May be "sporadic"
- Extra-adrenal tumors (e.g., carotid body) are called "paragangliomas"

Pheochromocytoma: Pathology



- Gross:
  - 1 - 4000 grams (average = 100 grams)
  - Areas of hemorrhage, necrosis, & cystic degeneration
- Micro:
  - Balls of cells resembling cells of medulla, with bizarre, hyperchromatic nuclei; richly vascular stroma
- Benign & malignant tumors are histologically identical; the only absolute criterion for malignancy is *metastasis*.