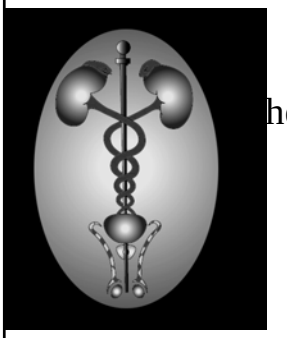
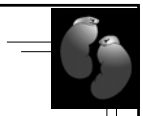


he Adrenal Glands

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



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

II. Hypoadrenalism

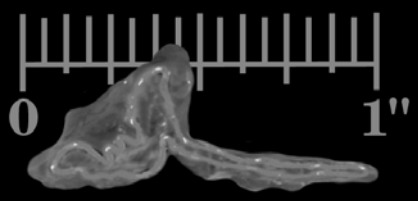
-- Break --

III. Hyperadrenalism; Adrenal cortical neoplasms

IV. Adrenal medulla

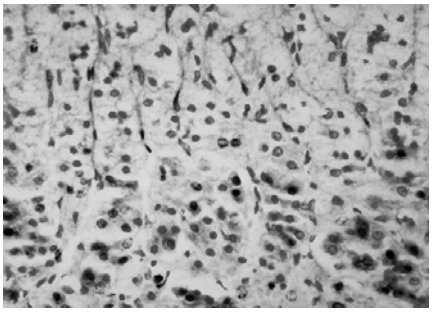
Normal Adrenal Gland

- Normal adult adrenal gland: 3.5 - 4.5 grams



Adrenal Cortex Morphology

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



Hormone synthesis, regulation, and measurements

Hypoadrenalism

Hypoadrenalism

- Primary Adrenocortical Insufficiency
- Secondary Adrenocortical Insufficiency

Hypoadrenalism
Clinical Manifestations

Hypoadrenalism
Clinical Manifestations

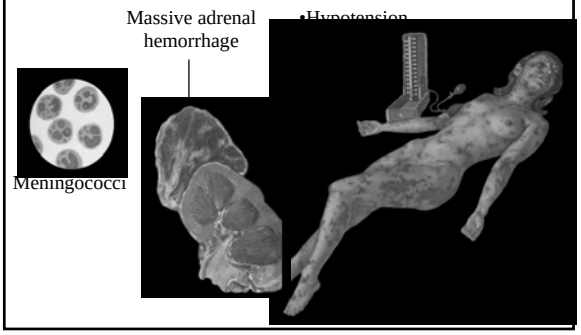
Hypoadrenalism
Clinical Manifestations

Hypoadrenalism
Clinical Manifestations

Pathology of Hypoadrenalism

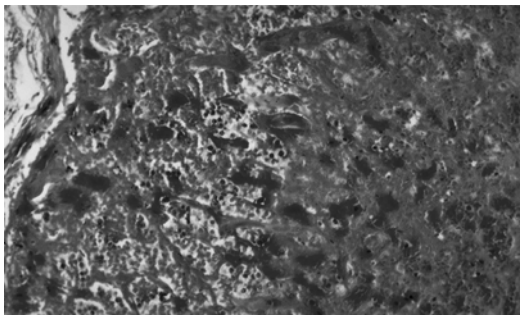
- Primary Adrenocortical Insufficiency
  - Acute
  - Chronic = Addison Disease
- Secondary Adrenocortical Insufficiency

Waterhouse-Friderichsen Syndrome



Waterhouse-Friderichsen Syndrome

Waterhouse-Friderichsen Syndrome



Pathology of Hypoadrenalism

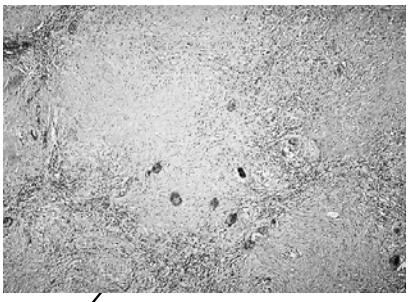
- Primary Adrenocortical Insufficiency
  - Acute
  - Chronic = Addison Disease

Addison Disease
Clinical findings

Autoimmune Adrenalitis

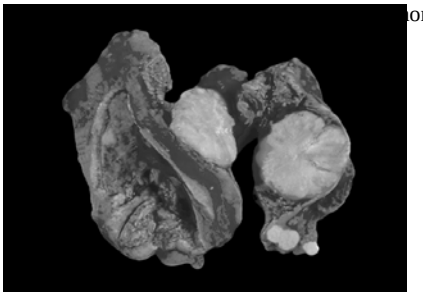
Pathologic Changes in Autoimmune Adrenalitis

- Gross:
  - Very small glands (1 - 1.5 grams)
  - Cortices markedly thinned
- Micro:
  - Diffuse atrophy of *all* cortical zones
  - Lymphoplasmacytic infiltrate
  - Medulla is unaffected



Multinucleated giant cells

Cortex and medulla are affected



Pathology of Hypoadrenalism

- Primary Adrenocortical Insufficiency
  - Acute
    - Waterhouse-Friderichsen Syndrome
  - Chronic = Addison Disease
- Secondary Adrenocortical Insufficiency

Diagnosis of Hypoadrenalism

Hyperadrenalism

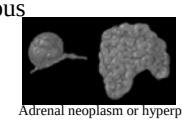
Hyperadrenalism

Hyperadrenalism

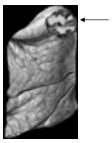
Cushing Syndrome

Endogenous

Pituitary adenoma



Adrenal neoplasm or hyperplasia



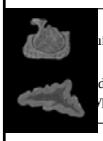
ACTH-producing tumor

Exogenous (Iatrogenic)

"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

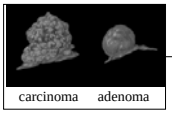
Cushing Syndro



itary adenoma

drenal cortical yperplasia

ACTH-producing tumor



carcinoma adenoma

C O R T I S O L

Dorsal f… n face

Ecchym…

Thin skin… triae

Thin ar… Pendulous abdomen

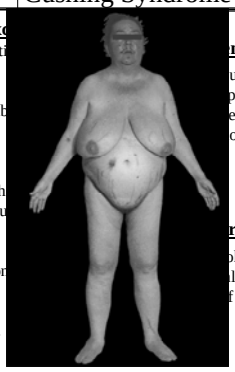
Poo… hea…

…d from Netter

Cushing Syndrome

Hydrocortisone Exc…

- •Abnormal fat distributi…
  - –Moon face
  - –Central obesity
- •Increased protein catab…
  - –Thin skin
  - –Easy bruisability
  - –Striae
  - –Osteoporosis with vertebral fractu…
  - –Impaired healing
  - –Muscle wasting
  - –Suppressed respon… infection
- •Diabetes
- •Psychiatric symptoms



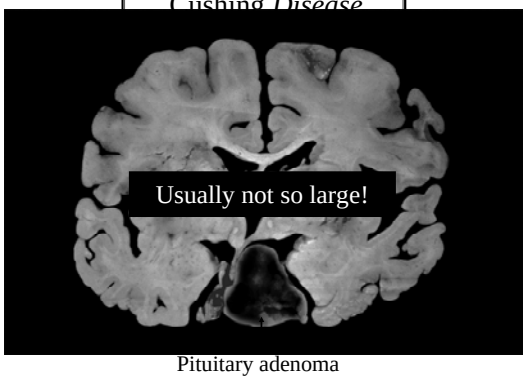
…nal Androgen Excess

- …utism
- …pened voice in women
- …e
- …ormal menses

…ralocorticoid Excess

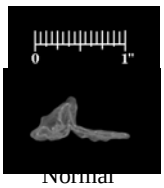
- …okalemia with alkalosis
- …lly occurs in cases …f ectopic ACTH production

Cushing *Disease*

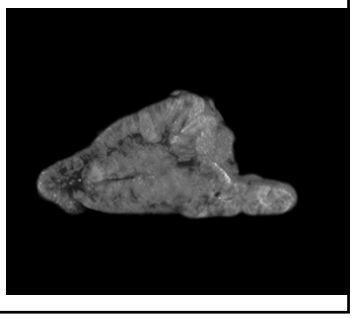


Pituitary adenoma

Adrenal cortical hyperplasia

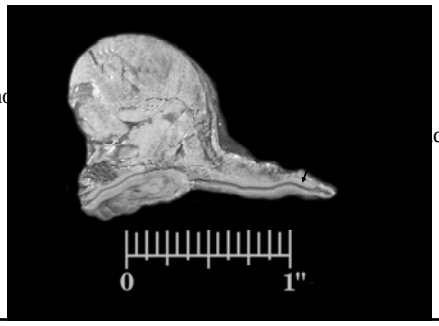


Normal



Adrenal cortical adenoma

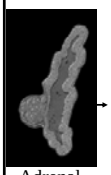
Tumo d



Pathology of Primary Hyperaldosteronism

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

Conn Syndrome



Adrenal adenoma

→ Aldosterone →

- Hypertension
- Polydipsia
- Polyuria
- Hypernatremia
- Hypokalemia

Adapted from Netter

Cortical Neoplasms

Adenomas and Carcinomas → Functioning *

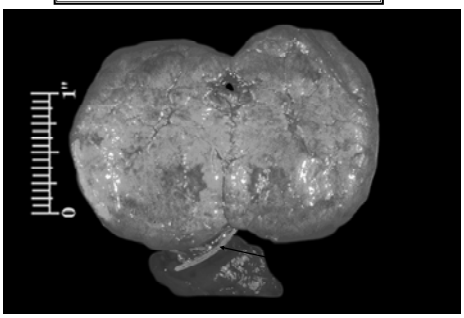
Adenomas and Carcinomas → Non-functioning

* May produce:
- Cortisol (Cushing Syndrome))
- Sex steroids
- Aldosterone (Conn Syndrome))

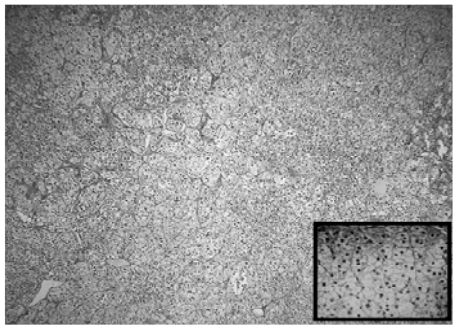
Cortical Neoplasms

- 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

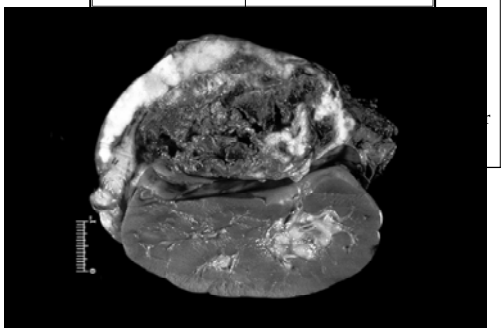
Adrenal cortical adenoma



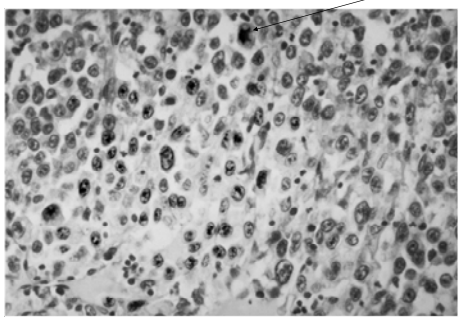
Adrenal cortical adenoma



Adrenal cortical carcinoma



Adrenal cortical carcinoma



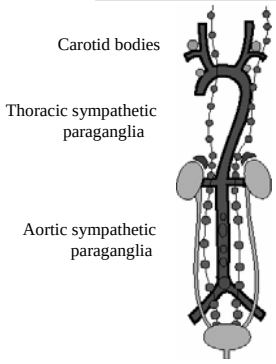
Diagnosis of Hyperadrenalism

Adrenal Medulla

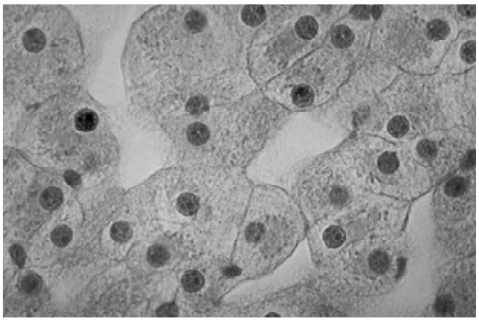
Adrenal Medulla

- Specialized neural crest (neuroendocrine) cells
- Part of the chromaffin system, which includes the adrenal medullae & paraganglia
- Major source of catecholamines (epi, norepi, & dopamine)

Paraganglion System

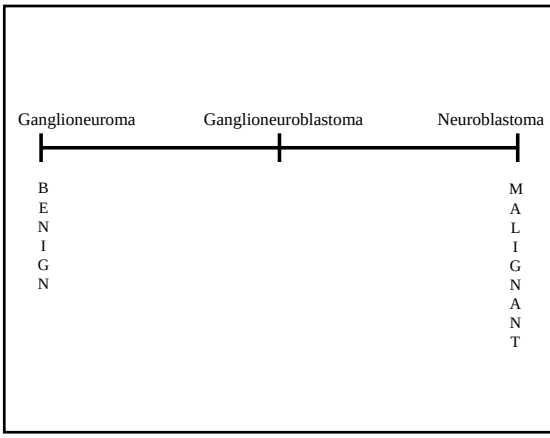


Adrenal Medulla



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

Rhabdomyosarcoma	Lymphoma
Retinoblastoma	Wilms tumor
Ewing sarcoma/PNET	Medulloblastoma

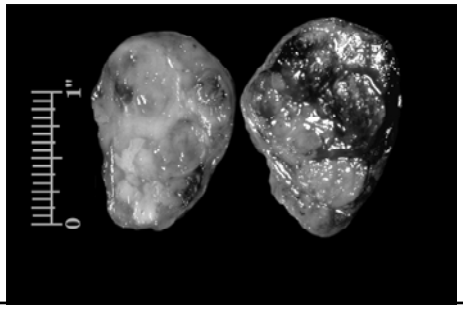
Neuroblastoma: primary sites

•Head	2%
•Neck	5%
•Chest	13%
•Adrenal	~ 40%
•Abdomen, nonadrenal	18%
•Pelvis	4%
•Other sites & unknown	21%

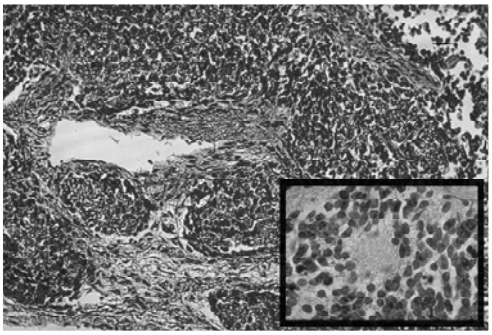
Neuroblastoma: Pathology

- Gross:
  - Large tumor with hemorrhage, necrosis, & calcification
- Micro:
  - Undifferentiated small cells resembling lymphocytes ("Small, round, blue cell tumor")
  - May show areas of *differentiation (larger cells with more cytoplasm and Schwannian stroma)*

Neuroblastoma



Neuroblastoma



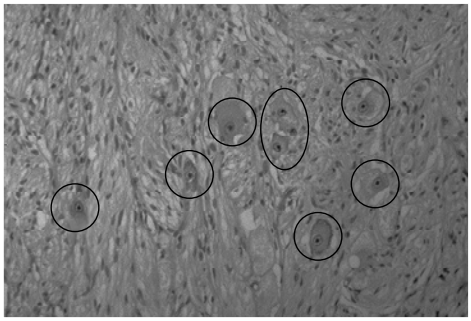
Neuroblastoma: Prognostic Factors

- Patient age
- Stage
- Site of 1^0 involvement
- Histologic grade
- DNA ploidy
- N-myc oncogene amplification
- Others: Chromosome 17q gain, Chromosome 1p loss, Trk-A expression, Telomerase expression, MRP expression, CD44 expression

Ganglioneuroma

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

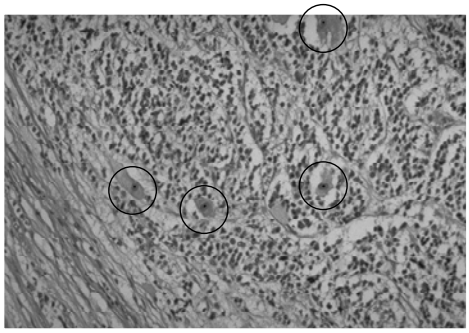
Ganglioneuroma



Ganglioneuroblastoma

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

Ganglioneuroblastoma



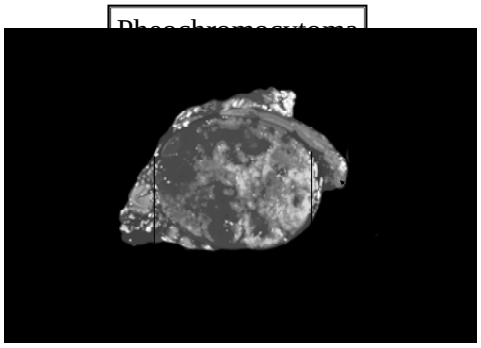
Pheochromocytoma

- 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": ~24% have germline mutations, including mutations of RET, VHL, SDH-B, and SDH-D genes
- Extra-adrenal tumors (e.g., carotid body) are called "paragangliomas"

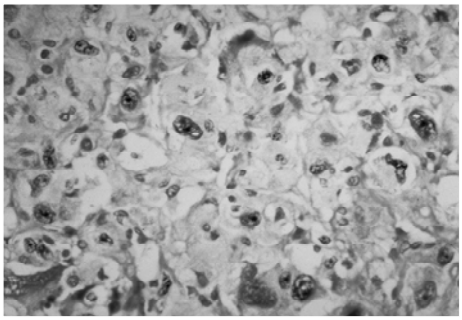
Pheochromocytoma: Pathology

- 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.*

Pheochromocytoma



Pheochromocytoma



Pheochromocytoma:
Clinical aspects