Disease of the Adrenals
Zona Glomerulosa

- Mineralocorticoids: aldosterone
- Angiotensin II/renin regulation by sympathetic tone; High potassium will stimulate and ACTH
- Increase in aldosterone leads to salt and water retention
- Increase in Angiotensin II leads to vasoconstriction
Zona Fasiculata and Reticularis

- Glucocorticoids: Cortisol
- Androgen: DHEAS
- Regulated by ACTH
Steroid Production Pathway (steroidogenesis)

- Begin with cholesterol
- Precursors: DHEAS
  - 17-OH progesterone
- End products: estradiol, cortisol, aldosterone
20 year old female

- Weight loss, easy tanning, nausea, vomiting, abdominal pain, weakness, dizzy

- BP=70/30, tan, confusion
Laboratory

- Hyponatremia
- Hyperkalemia
- Low glucose
- Elevated BUN/Cr
- Vitiligo

- Deficiency of all steroids
Diagnosis

Primary Adrenal Insufficiency
**Laboratory**

- AM cortisol, ACTH
- Cortrosyn (ACTH) stimulation IV or IM
  Baseline, 30 min and 60 minute values for cortisol
- If Aldosterone drawn with Cortrosyn stimulation, response blunted
- **Cortisol Goal > 20 micrograms/dl with Cortrosyn Stimulation, assuming a normal baseline cortisol**
Etiology

- 80% Autoimmune/Idiopathic
- 20% Tuberculosis
- Other: Vascular, infectious, AIDS, trauma, mets, meds, congenital adrenal hyperplasia
Autoimmune Etiology

- Addison Disease
- May be associated with other autoimmune conditions, as in Hashimoto or vitiligo
50 year old female

- Similar symptoms to index patient: low to low normal BP, fatigue weakness
- No change in skin color
- COPD
Laboratory

- Low sodium
- Normal potassium—{Suggests normal aldosterone production}
- Low ACTH or inappropriately normal when the end organ value is low
Additional History

- History of long term steroid use IV and oral treatment
- Recent change in pharmacy
- Prednisone not renewed
- Presents with fever and lung infiltrate
Diagnosis

Secondary Adrenal Insufficiency
Etiology

- Steroid dependent
- Tumor, infection, radiation, surgery, trauma involving hypothalamic region or pituitary
Consider CT of the adrenals for primary adrenal insufficiency

MRI of the brain for secondary adrenal insufficiency unless the cause is evident

CT Adrenals: primary----small adrenal glands
Treatment at diagnosis in Crisis

- IV hydrocortisone 100 mg q 6-8 hrs wean as tolerated to daily oral dose of 25 mg daily/divided
- Saline and glucose
- Supportive and correcting precipitating factors
- Primary adrenal insufficiency: Florinef as aldosterone replacement
- If steroids < 30 days in general medical treatment, do not necessarily need to wean slowly
Crisis Intervention

- Surgery
- Acute illness
- Additional steroids IV and/or PO
- Home illness: short course of double dose steroids
- Observe sodium, potassium and BP; Pt can follow BP at home for crisis intervention
25 Year Old Female

- Weight gain, hirsutism, diabetes, osteoporosis
- Centripetal obesity, striae, acne, hypertension, capillary fragility, amenorrhea
Diagnosis

Cushing Syndrome
Laboratory

- 1 mg overnight dexamethasone suppression testing; 1 mg Dex 11 pm with 8 am cortisol next day---may identify subtle with normal urine free cortisol---goal suppression < 3 to 5 some endocrinologists say less than 2
- 24 hour urine free cortisol
- Hypokalemia, hyperglycemia
- Some false positives
Pregnancy Striae
Differential Diagnosis

- Cushing disease: Cushing syndrome due to pituitary adenoma/high ACTH-dependent
- ACTH Independent vs ACTH Dependent
- Exogenous steroids
- Adrenal adenoma or hyperplasia
- Ectopic: lung tumor
Differential Diagnosis

- Cushing disease and ectopic have higher ACTH
- Adrenal disease is ACTH independent
- Clarification required with additional dexamethasone urinary testing
Imaging

- Cushing disease: MRI of the pituitary

- Cushing syndrome: CT or MRI of (adenoma vs hyperplasia) adrenals

- Ectopic: localize source
Treatment

- Pituitary: surgery, radiation, anti-adrenal drugs
- Ectopic: surgery, drugs
- Adrenal: surgery, drugs
Adrenal Carcinoma

- Metastatic at diagnosis
- Presents with weight loss
- Rapid onset
- Typical excessive activity of steroidogenesis pathway, not typical insufficiency
35 Year Old female

- Hypertension
- Hypokalemia
- Thin
- Metabolic alkalosis
Diagnosis

Hyperaldosteronism
Hyperaldosteronism

- Biochemical work-up first
- Low renin/high aldosterone is primary
- High renin/high aldosterone is secondary
- Elevated 24 hour urine aldosterone on high sodium diet and off diuretics
- Saline Suppression Testing
Hyperaldosteronism

- Adrenal adenoma (Conn Syndrome) “APA” Aldosterone Producing Adenoma
- Idiopathic Hyperaldosteronism “IHA” with bilateral disease
Secondary Hyperaldosteronism

- Sodium restriction
- Renal disease
- High Potassium intake
- Pregnancy
- Diuretics
Localization testing

- Cat Scan
- Nuclear imaging with Iodocholesterol
- Adrenal venous sampling
# Adrenal Venous Sampling Summary

**RE:** Male  
**DOB:** 1942

<table>
<thead>
<tr>
<th></th>
<th>Aldosterone (ng/dL)</th>
<th>Cortisol (ug/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basal:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right adrenal vein</td>
<td>1</td>
<td>4.3</td>
</tr>
<tr>
<td>Left adrenal vein</td>
<td>221</td>
<td>10.2</td>
</tr>
<tr>
<td>Peripheral Arm</td>
<td>12</td>
<td>12.3</td>
</tr>
<tr>
<td><strong>POST ACTH:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right adrenal vein</td>
<td>4</td>
<td>108.1</td>
</tr>
<tr>
<td>Left adrenal vein</td>
<td>16430</td>
<td>&gt;150</td>
</tr>
<tr>
<td>Peripheral Vena Cava</td>
<td>71</td>
<td>14.4</td>
</tr>
<tr>
<td>Peripheral Femoral Vein</td>
<td>46</td>
<td>18.9</td>
</tr>
</tbody>
</table>
Treatment

- Aldosterone producing adenoma: surgery; takes 6 months for final htn results, may have underlying essential HTN but hypokalemia should resolve; Spironolactone in patients with poor surgical risk

- Bilateral adrenal disease: restrict sodium, spironolactone use, no surgery
40 Year Old Male

- Hypertension unresponsive to meds
- Normal electrolytes
- Thin
- Headache, palpitations
Diagnosis

Pheochromocytoma
Laboratory

- Check 24 hour urine fractionated catecholamines, fractionated metanephrines, VMA
- 24 hour urine testing off meds if possible
- Some endocrinologists recommend serum catecholamine/metanephrine testing
Imaging

- MRI or CT: MRI may help with difference in signal intensity T1/T2—bright signal in pheo

- MIBG (Metaiodobenzylguanidine) nuclear imaging tracer concentrates in catecholamine producing cells
Treatment

- Alpha blockers preferred
- Avoid Beta Blockers, which can precipitate a pheo crisis without alpha blockade on board
- Avoid adrenal biopsy of a lesion that is not yet evaluated for pheochromocytoma
Incidental Adrenal Adenoma

- Benign adenomas common
- Avoid imaging until biochemical diagnosis
- Evaluation important with coexisting HTN, hypokalemia, hirsutism
Adrenal Incidentaloma

- Lesions discovered “inadvertently in the course of diagnostic testing or treatment for other clinical conditions that are not related to the suspicion of adrenal disease”
Prevalence

- In autopsy series 2.1 %
- More identified with better imaging
- Prevalence of 4.3 % in patients with a previous diagnosis of cancer
- Higher with aging at 7 % in 70 +
- More lesions in women—related to who is being tested
Causes

- **Pathology:** Cancer patients \( \frac{3}{4} \) mets, No history of cancer \( \frac{2}{3} \) benign
- 70 % non-functioning in patients without endocrine symptoms
- 5-10 %------Cushing Syndrome, subclinical
Natural History of lesion size

- 25% of lesions larger than 6 cm represent adrenal cancer
- Up to 25% of adrenal lesions may grow 1 cm, but the significance of size change is not known
- Adrenal Cancer rapid growth “doubling time”
Natural History of function

- Up to 20% may develop a functional component.
- Development of function more common in larger neoplasms (3 cm)—this evidence can depend on study follow-up length and methods.
- Less than 3 cm neoplasms rarely change in function.
Adrenal Incidentaloma Diagnosis

- Function
- Surgical resection vs non-surgical treatment
- Malignant vs benign