Adrenal Diseases

Adrenal Cortex
- Adrenal Hyperfunction
  - Hypercortisolism
    - Cushing's Syndrome
      - ACTH Dependent
        - Cushing Disease
        - Ectopic ACTH Secretion
      - ACTH Independent
        - Autonomous Secretion of ACTH by Adrenal
        - Prolonged Glucocorticoid Therapy
    - Pseudo-Cushing Syndrome
  - Conn's Syndrome / Primary
    - Secondary Hyperaldosteronism
    - Bilateral Zona Glomerulosa Hyperplasia
    - Adrenal Cancer

Adrenal Hypofunction
- Adrenal Medulla Hyperfunction
- Adrenal Medulla

Adrenal Medulla
- Adrenal Medulla Hyperfunction
- Pheochromocytoma
- Nueroblastoma

5 Diabetogenic Hormones
1. Glucagon
2. Growth Hormone
3. Thyroid Hormone
4. Cortisol
5. Catecholamine
   a. Norepinephrine
   b. Epinephrine
# Adrenal Cortex

## Adrenal Hyperfunction

### Hypercortisolism

<table>
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<tr>
<th>Disease</th>
<th>Causes</th>
<th>Laboratory Investigation</th>
<th>Clinical Manifestations</th>
<th>Complications</th>
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<tr>
<td>Cushing's Syndrome</td>
<td>ACTH Dependent</td>
<td>Hypercortisolism Confirmation Tests</td>
<td>Peripheral Fat Redistribution, Overt Diabetes Mellitus</td>
<td>Osteoporosis, Vertebral collapse, Hypertension, Secondary infection</td>
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<tr>
<td></td>
<td>• Hypersecretion of ACTH by Pituitary</td>
<td>• 24 hours Urinary free Cortisol</td>
<td>• Moon face, Buffalo hump, Trunkal Obesity</td>
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<tr>
<td></td>
<td>o Microadenoma</td>
<td>o &gt;700nmol/day</td>
<td>• Proximal myopathy, Muscle wasting, Purple striae, Thinning of the skin</td>
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<tr>
<td></td>
<td>o Macro adenoma</td>
<td>o Overnight Dexamethasone Suppression Test*</td>
<td>• Increase Plasma Glucose Level, Glucose intolerance, Diabetes mellitus</td>
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<td>o Diffuse Corticotrophic Hyperplasia</td>
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<td>• Ectopic secretion of ACTH</td>
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<td>o Small Cell Carcinoma of the Bronchus</td>
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<td>o Carcinoid Tumors of the Lungs</td>
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<td>o Medullary Thyroid Carcinoma</td>
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<td>ACTH Independent</td>
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<td>• Primary Adrenal Neoplasms</td>
<td>Causal Determination Test</td>
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<td></td>
<td>o Adrenal Adenoma</td>
<td>• High-dose Dexamethasone Suppression Test</td>
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<td></td>
<td>o Bilateral Nodular Adrenal Hyperplasia</td>
<td>• Plasma ACTH level</td>
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<td></td>
<td>• Prolong Glucocorticoid therapy</td>
<td>o ACTH Independent (Adrenal tumors)</td>
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<td></td>
<td>▪ Not detectable</td>
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<td>▪ Inappropriately normal</td>
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<td>▪ ACTH markedly high</td>
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<td>• Inferior Petrosal Sinus Sample</td>
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<td>• Imaging studies</td>
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### Complications
- Overt Diabetes Mellitus
- Osteoporosis
- Vertebral collapse
- Hypertension
- Secondary infection

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### ACTH Dependent

- Hypersecretion of ACTH by Pituitary
  - Microadenoma
  - Macroadenoma
  - Diffuse Corticotrophic Hyperplasia

### ACTH Independent

- Primary Adrenal Neoplasms
  - Adrenal Adenoma
  - Adrenal Carcinoma
  - Bilateral Nodular Adrenal Hyperplasia

- Prolong Glucocorticoid therapy

### Hypercortisolism Confirmation Tests

- 24 hours Urinary free Cortisol
  - >700nmol/day
- Overnight Dexamethasone Suppression Test*

### Causal Determination Test

- High-dose Dexamethasone Suppression Test
- Plasma ACTH level
  - ACTH Independent (Adrenal tumors)
    - Not detectable
    - Inappropriately normal
  - ACTH Dependent
    - ACTH markedly high
- Inferior Petrosal Sinus Sample
- Imaging studies

---

### Peripheral Fat Redistribution
- Moon face
- Buffalo hump
- Trunkal Obesity

### Increase Proteolysis
- Proximal myopathy
- Muscle wasting
- Purple striae
- Thinning of the skin

### Increase Plasma Glucose Level
- Glucose intolerance
- Diabetes mellitus

### Antiinflammatory Effects
- Delayed wound healing
- High risk of infections

### Electrolytes Imbalances
- Renal stones
- Hypertension
- Dependent edema

### Increase Androgens level
- Hirsutism
- Acne
- Loss of libido
- Infertility

### Increased osteoclastic activity, reduced osteoblastic activity
- Osteopenia
- Osteoporosis
- Pathological fracture

### Psychiatric Disturbances
- Mania
- Euphoria

### CYP450 Inducer, Pseudo-Cushing Syndrome
- 1mg of Dexamethasone given at 11.00pm
- Cortisol Plasma Level taken next morning at 9.00am
- >140nmol/L
  - False Positive
- <140nmol/L
  - Normal Response

### False Positive
- CYP450 Inducer, Pseudo-Cushing Syndrome
- Partially Suppress Pituitary Dependent

### Eliminate False Positive
- 2mg Dexamethasone given 4 times daily for 2 days
- Plasma Cortisol Level taken at 9.00am in 3 consecutive days
- <140nmol/L
  - Normal Response
- >140nmol/L
  - Eliminate False Positive

### Failure to Suppress Ectopic secretion of ACTH, Adrenal Tumors
- Over Night Dexamethasone Suppression Test
- 1mg of Dexamethasone given at 11.00pm
- Cortisol Plasma Level taken next morning at 9.00am
- >140nmol/L
  - False Positive
- <140nmol/L
  - Normal Response
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<td>Adrenocortical Adenoma</td>
<td>Diagnostic Tests</td>
<td>Salt Retention</td>
<td>Hypertension</td>
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<td></td>
<td>Adrenocortical Adenoma</td>
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<td>Heart failure</td>
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<td>Bilateral Zona Glomerulosa Hyperplasia</td>
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<td>Kidney failure</td>
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<td>Adrenal Carcinoma</td>
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**Diagnostic Tests**
- Plasma Aldosterone and Renin
  - Result
    - ↑Aldosterone
    - ↓Renin
  - Taken on 2 consecutive days
  - 8 hours after recumbency
  - Again with patient ambulatory

**Supportive Tests**
- Hypokalemia
- Metabolic Alkalosis
# Adrenal Hypofunction

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<tr>
<td>Adrenal Insufficiency</td>
<td>Primary Adrenal Hypofunction/ Addison’s Disease</td>
<td>Hypofunction Confirmation Test - Short Synacthen Test</td>
<td>Corticosteroid Deficiency - Weakness, Fatigue, Hypoglycemia, Anorexia, Craving for salty foods, Orthostatic Hypotension, Decreased cardiac output, Irregular pulse</td>
<td>• Addisonian Crisis&lt;br&gt; o Profound weakness&lt;br&gt; o High fever&lt;br&gt; o Hypotension&lt;br&gt; o Vomiting&lt;br&gt; o Nausea&lt;br&gt; o Dehydration&lt;br&gt; o Hyperpyrexia&lt;br&gt; o Psychotic reactions&lt;br&gt; o Inadequate or excessive steroid therapy&lt;br&gt; o Shock&lt;br&gt; o Profound Hypoglycemia</td>
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<td>Secondary Adrenal Hypofunction</td>
<td>Causal Determination Test - Long Synacthen Test</td>
<td>• Excessive ACTH (primary) - Hyperpigmentation of skin and mucosa, Conspicuous bronze color of creases at Skin, Metacarpalphalangeal joints</td>
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<td>Supportive Tests - Low random Plasma Cortisol level, Hyponatremia, Hyperkalemia, Metabolic Acidosis, Uremia, Hypoglycemia</td>
<td>• Reduction in Adrogens - Excessive loss of hair in women, Less prominent in men due to present of Testicular Androgen</td>
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### Laboratory Tests

- **Short Synacthen Test**
  - 250µg of iv Synacthen given
  - Basal Level is >190nmol/L
  - Plasma level taken before, 30 and 60 minutes after Synacthen
  - Normal Response: 200nmol/L increment, peak at 500nmol/L
  - Adrenal Hypofunction: Failure of increment

- **Long Synacthen Test**
  - 1mg of im Synacthen given for 3 days
  - Plasma Cortisol level taken during day 4
  - Primary Causes <200nmol/L
  - Secondary Causes >200nmol/L
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<tr>
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<th>Hyerp catecholaminism</th>
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<td>• Sporadic</td>
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<td></td>
<td>• Familial</td>
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<tr>
<td></td>
<td>o Multiple Endocrine Neoplasia (MEN) 2a</td>
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<td>• Bilateral Pheochromocytoma</td>
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<td>• Medullary Thyroid Carcinoma</td>
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<td>• Primary Hyperparathyroidism</td>
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<td>o MEN2b</td>
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<td>• Mucosal Neuroma</td>
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<td>• Marfanoid Habitus</td>
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