Pathophysiology of Adrenal Disorders

PHCL 415
Hadeel Alkofide
April 2010

Some slides adapted from Rania Aljizani MSc
Learning Objectives

• Describe the roles of the various zones of the adrenal cortex in hormone synthesis

• Explain the regulation of glucocorticoid, adrenal androgen, and mineralocorticoid secretion

• Describe and differentiate the various etiologies of some adrenal disorders

• Interpret the results of laboratory tests used to diagnose some adrenal disorders
Outline

• Introduction

• Disorders of Adrenal gland

• Causes/Classification

• Pathophysiology

• Manifestations

• Diagnosis
Introduction
Introduction

• Adrenal Gland

• Adrenal Cortex & Adrenal Medulla

• Physiology of Normal Adrenal Cortex:
  - Glucocorticoids: Regulation of Secretion & Effects
  - Mineralocorticoids: Regulation of Secretion & Effects

• Common Disorders of Adrenal Cortex
Adrenal Gland


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Adrenal Gland

• The adrenal gland is actually 2 endocrine organs

1. The outer adrenal cortex secretes steroid hormones

2. The inner adrenal medulla secretes catecholamines
Adrenal Cortex

- Occupies 90% of the total adrenal gland
- It consists of three zones (cell):

<table>
<thead>
<tr>
<th>Zone</th>
<th>Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zona glomerulosa</td>
<td>Mineralocorticoids (aldosterone)</td>
</tr>
<tr>
<td>Zona fasciculata</td>
<td>Glucocorticoids (cortisol)</td>
</tr>
<tr>
<td>Zonareticularis</td>
<td>Sex steroids (androgen, estrogen)</td>
</tr>
</tbody>
</table>
Adrenal Cortex

Zona glomerulosa

• 15% of the total adrenal cortex

• Responsible for mineralocorticoid (aldosterone)

• Aldosterone maintains electrolyte & volume homeostasis by altering potassium and magnesium secretion & renal tubular sodium reabsorption
Adrenal Cortex

**Zona fasciculata**

- The middle zone
- Makes up 60% of the cortex
- High in cholesterol
- Responsible for basal & stimulated glucocorticoid production
- Glucocorticoids, mainly cortisol, are responsible for the regulation of fat, carbohydrate, & protein metabolism
Adrenal Cortex

**Zona reticularis**

- Occupies 25% of the adrenal cortex
- Responsible for all adrenal androgen production
- The androgens, testosterone and estradiol, are the major end products and have influence within the reproductive system as well as affecting primary & secondary sex characteristics
Adrenal Medulla

• The adrenal medulla occupies 10% of the total gland

• Responsible for production of catecholamines which are:
  - Epinephrine
  - Nor epinephrine

• The regulation of these hormones by sympathetic nerves system
Physiology of Normal Adrenal Cortex

**Glucocorticoids: Regulation of Secretion**

- Glucocorticoid secretion is regulated by Adrenocorticotropic Hormone (ACTH), secreted by anterior pituitary

- ACTH regulates both basal secretion of glucocorticoids & increased secretion provoked by stress

- ACTH, in turn, is regulated by hypothalamic corticotropin-releasing hormone (CRH), secreted into the median eminence of the hypothalamus

- CRH secretion is regulated by a variety of neurotransmitters in response to physical & emotional stressors
Physiology of Normal Adrenal Cortex

Glucocorticoids: Regulation of Secretion

Various stimuli → Hypothalamus

CRH → + Anterior pituitary

ACTH → + Adrenal cortex

Cortisol
Physiology of Normal Adrenal Cortex

*Glucocorticoids: Regulation of Secretion*

- **Episodic & Diurnal Rhythm of ACTH Secretion**

- ACTH is secreted in episodic bursts throughout the day, after a diurnal (circadian) rhythm, with bursts most frequent in the early morning & least frequent in the evening.

- The peak level of cortisol in the plasma normally occurs between 6:00 and 8:00 AM (during sleep, just before awakening) and the nadir at around 12:00 AM.
Physiology of Normal Adrenal Cortex

**Glucocorticoids: Regulation of Secretion**

- **Episodic & Diurnal Rhythm of ACTH Secretion**

- The diurnal rhythm of ACTH secretion persists in patients with adrenal insufficiency who are receiving maintenance doses of glucocorticoids but is lost in Cushing's syndrome.

- The diurnal rhythm is altered also by changes in patterns of sleep, or food intake; physical stress, surgery, trauma, psychologic stress, CNS & pituitary disorders; liver disease & other conditions that affect cortisol metabolism.
Physiology of Normal Adrenal Cortex

*Glucocorticoids: Regulation of Secretion*

- **Stress Response**

- Plasma ACTH & cortisol secretion are also triggered by various forms of stress. Emotional stress (such as fear & anxiety) & bodily injury (such as surgery or hypoglycemia) release CRH from the hypothalamus.

- ACTH secretion induced by these hormones, in turn, stimulates a transient increase in cortisol secretion.

- If the stress is prolonged, it may abolish the normal diurnal rhythm of ACTH and cortisol secretion.
Physiology of Normal Adrenal Cortex

Glucocorticoids: Regulation of Secretion

- **Negative Feedback**

  - A rising level of plasma cortisol inhibits release of ACTH from the pituitary by inhibiting CRH release from the hypothalamus

  - The fall in plasma ACTH leads to a decline in adrenal secretion of cortisol

  - Conversely, the loss of negative feedback resulting from a drop in plasma cortisol induces a net increase in ACTH secretion

  - In untreated chronic adrenal insufficiency, there is a marked increase in the rate of ACTH synthesis & secretion
Physiology of Normal Adrenal Cortex

**Glucocorticoids: Regulation of Secretion**

- **Negative Feedback**

- ACTH & CRH secretion are also inhibited by chronic pharmacologic treatment with exogenous corticosteroids

- When prolonged corticosteroid treatment is stopped, the adrenal is unresponsive & the patient is at risk for acute adrenal insufficiency

- Chronic suppression of the HPA axis by exogenous steroids take some time to recover after cessation of treatment

- Abrupt glucocorticoid withdrawal can be life threatening
## Physiology of Normal Adrenal Cortex

### Glucocorticoids: Effects

<table>
<thead>
<tr>
<th>Target Tissue</th>
<th>Effect</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>Catabolic</td>
<td>Inhibit glucose uptake &amp; metabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decrease protein synthesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increase release of amino acids, lactate</td>
</tr>
</tbody>
</table>
### Physiology of Normal Adrenal Cortex

**Glucocorticoids: Effects**

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<tr>
<th>Target Tissue</th>
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<tbody>
<tr>
<td>Fat</td>
<td>Lipolytic</td>
<td>Stimulate lipolysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increase release of FFAs and glycerol</td>
</tr>
</tbody>
</table>

- **Fat**: Lipolytic
  - Stimulate lipolysis
  - Increase release of FFAs and glycerol
Physiology of Normal Adrenal Cortex

**Glucocorticoids: Effects**

<table>
<thead>
<tr>
<th>Target Tissue</th>
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<th>Mechanism</th>
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<tbody>
<tr>
<td>Liver</td>
<td>Synthetic</td>
<td>Increase gluconeogenesis</td>
</tr>
<tr>
<td></td>
<td>Increase glycogen synthesis, storage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increase glucose-6-phosphatase activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increase blood glucose</td>
<td></td>
</tr>
</tbody>
</table>
## Physiology of Normal Adrenal Cortex

### Glucocorticoids: Effects

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<thead>
<tr>
<th>Target Tissue</th>
<th>Effect</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system</td>
<td>Suppression</td>
<td>Reduce number of circulating lymphocytes, monocytes, eosinophils, basophils</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhibit T-lymphocyte production of interleukin-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interfere with antigen processing, antibody production and clearance</td>
</tr>
</tbody>
</table>
### Physiology of Normal Adrenal Cortex

#### Glucocorticoids: Effects

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<th>Target Tissue</th>
<th>Effect</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system</td>
<td>Anti-inflammatory</td>
<td>Decrease migration of neutrophils, monocytes, lymphocytes to injury sites</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>Stimulate release of neutrophils from marrow</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interfere with neutrophil migration out of vascular compartment (produces a relative neutrophilia during glucocorticoid therapy)</td>
</tr>
</tbody>
</table>
## Physiology of Normal Adrenal Cortex

### Glucocorticoids: Effects

<table>
<thead>
<tr>
<th>Target Tissue</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Increase cardiac output</td>
</tr>
<tr>
<td></td>
<td>Increase peripheral vascular tone</td>
</tr>
<tr>
<td>Renal</td>
<td>Increase glomerular filtration rate</td>
</tr>
<tr>
<td>Other</td>
<td>Aid in regulating water, electrolyte balance</td>
</tr>
<tr>
<td></td>
<td>Insulin antagonism</td>
</tr>
</tbody>
</table>
Physiology of Normal Adrenal Cortex

*Mineralocorticoids: Regulation of Secretion*

- **Regulation by Renin-Angiotensin System**

- The renin-angiotensin system regulates aldosterone secretion in a feedback fashion

- Renin is excreted by the kidney in response to decreases in renal perfusion pressure

- Once in the circulation, renin acts on angiotensinogen, to form angiotensin I
Physiology of Normal Adrenal Cortex

Mineralocorticoids: Regulation of Secretion

- **Regulation by Renin-Angiotensin System**

- In the lung and elsewhere, angiotensin I is converted by angiotensin-converting enzyme (ACE) to angiotensin II

- Angiotensin II stimulates synthesis and secretion of aldosterone. Aldosterone promotes Na+ & water retention, causing plasma volume expansion, which then shuts off renin secretion
Physiology of Normal Adrenal Cortex

*Mineralocorticoids: Regulation of Secretion*

- **Regulation by Renin-Angiotensin System**

- The physiologic stimuli for the renin-angiotensin system to increase aldosterone secretion include factors that reduce renal perfusion such as volume depletion, & dietary Na+ restriction

- Other disease states that cause reduced renal perfusion include renal artery stenosis, congestive heart failure, & cirrhosis of the liver,

- These disorders increase renin secretion, producing secondary hyperaldosteronism
Physiology of Normal Adrenal Cortex

Mineralocorticoids: Regulation of Secretion

- Regulation by Renin-Angiotensin System

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Physiology of Normal Adrenal Cortex

Mineralocorticoids: Regulation of Secretion

- **Regulation by ACTH**
- ACTH also stimulates mineralocorticoid output
- More ACTH is needed to stimulate mineralocorticoid than glucocorticoid secretion
Mineralocorticoids: Regulation of Secretion

- **Regulation by Plasma Electrolytes**

- An increase in plasma K+ concentration—or a fall in plasma Na+—stimulates aldosterone release

- Although minor changes of plasma K+ (~1 mEq/L) have an effect, major changes in plasma Na+ (drops of about 20 mEq/L) are needed to stimulate aldosterone secretion
Physiology of Normal Adrenal Cortex

**Mineralocorticoids: Effects**

- The target organs for the mineralocorticoids include the kidney, colon, duodenum, salivary glands, & sweat glands

- In the distal renal tubules and collecting ducts, aldosterone acts to promote the exchange of Na+ for K+ and H+, causing Na+ retention, K+ diuresis, & increased urine acidity

- It acts to increase the reabsorption of Na+ from the colonic fluid, saliva, & sweat

- In the heart, aldosterone has been shown to induce heart remodeling & interstitial & perivascular fibrosis of the myocardium
Disorders of Adrenal Gland
Disorders of Adrenal Gland

Hyperfunction of cortex
- Cushing's syndrome
- Aldosteronism
- Androgen Excess

Hypofunction of cortex
- Addison's disease

Hyperfunction of medulla
- Pheochromocytoma
Cushing's syndrome
Cushing's Syndrome

• Results from the combined metabolic effects of persistently elevated blood levels of glucocorticoids

• Can occur:

  ➢ Excessive cortisol secretion caused by a disturbance in the hypothalamic-pituitary adrenal axis (spontaneous)

  ➢ Long term Administration of pharmacologic doses of glucocorticoids (iatrogenic)
Cushing's Syndrome

Causes/Classification

Major Causes

Noniatrogenic

- ACTH dependent
  - Ectopic ACTH syndrome
  - ACTH-secreting pituitary adenoma

- ACTH independent
  - Functioning adrenocortical tumor

Iatrogenic

- Exogenous glucocorticoid
## Cushing's Syndrome

### Causes/Classification

<table>
<thead>
<tr>
<th>NONIATROGENIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH dependent</td>
</tr>
<tr>
<td>ACTH-secreting pituitary adenoma (Cushing’s disease)</td>
</tr>
</tbody>
</table>

**Epidemiology:** 68% of cases of noniatrogenic Cushing's syndrome
More common in women (F-M ratio of approximately 8:1)
Age at diagnosis usually 20–40 years

**Course:** Slow progression over several years
## Causes/Classification

### NONIATROGENIC

**ACTH dependent**

**Ectopic ACTH syndrome**

**Epidemiology:** 15% of cases of Cushing's syndrome
- More common in men (M-F ratio of approximately 3:1)
- Age at diagnosis usually 40–60 years
- Occurs most commonly in patients with small cell carcinoma of lung and bronchial carcinoid tumors

**Course:** With underlying carcinoma, hypercortisolism is of rapid onset, steroid hypersecretion is frequently severe, with equally elevated levels of glucocorticoids, androgens, & deoxycorticosterone
- With underlying benign tumor, more slowly progressive course
## Causes/Classification

<table>
<thead>
<tr>
<th>NONIATROGENIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH independent</td>
</tr>
</tbody>
</table>

### Functioning adrenocortical tumor

**Epidemiology:** 17% of cases of Cushing's syndrome
- Adrenal adenoma in 9%, adrenal carcinoma in 8%
- More common in women
- Adrenal carcinoma occurs in about 2 per million population per year
- Age at diagnosis usually 35–40 years

**Course:** Adrenal adenoma slow course, adrenal carcinoma rapid course
Causes/Classification

<table>
<thead>
<tr>
<th>IATROGENIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exogenous glucocorticoid administration</td>
</tr>
</tbody>
</table>

Glucocorticoid administered in high doses in the treatment of nonendocrine disorders.
Cushing's Syndrome

Pathophysiology

*Cushing's Disease*

- Persistent overproduction of ACTH by the pituitary adenoma
- The ACTH hypersecretion is disorderly, episodic, and random; the normal diurnal rhythm of ACTH & cortisol secretion is usually absent
- Plasma levels of ACTH and cortisol vary and may at times be within the normal range
- The excessive cortisol does not suppress ACTH secretion by the pituitary adenoma
Pathophysiology

**Ectopic ACTH Syndrome**

- In the ectopic ACTH syndrome, hypersecretion of ACTH and cortisol is random and episodic and quantitatively greater than in patients with Cushing's disease.

- Plasma levels & urinary excretion of cortisol, adrenal androgens, and other steroids are often markedly elevated.

- Ectopic ACTH secretion by tumors is usually not suppressible by exogenous glucocorticoids such as dexamethasone.
Pathophysiology

Adrenal Tumors

- Primary adrenal adenomas & carcinomas hypersecret cortisol
- The hypercortisolism suppresses pituitary ACTH production
- Steroid secretion is random & episodic & not usually suppressible by dexamethasone
- With adrenal carcinomas, overproduction of androgenic precursors is common, resulting in hirsutism or virilization of adult women or children of either sex
- With adrenal adenomas, production of androgenic precursors is relatively limited. Thus, their clinical manifestations are chiefly those of cortisol excess
Cushing's Syndrome

Clinical Manifestations

- Psychiatric effects
  - "Steroid encephalopathy," depression (50–80%)
- Growth retardation
  - (in child) (85%)
- Androgen excess
  - (in female)
    - Virilism (in adrenal carcinoma) (20%)
    - Acne (50%)
    - Menstrual irregularity (70%)
    - Infertility (70%)
- Increased mineralocorticoid effect
  - Hypertension (80%)
  - Hypokalemic alkalosis (in ectopic ACTH) (85%)
- Diabetes mellitus (80%)
  - Cortisol is insulin antagonist
- Redistribution of body fat
  - Central obesity (80%)
  - Moon facies (80%)
  - Thick neck (80%)
- Fat trunk or abdomen (80%)
- Thin extremities (80%)
- Atrophy of skin and dermal connective tissue (striae) (70%)
- Thinning of bones (osteoarthritis) (50%)
- Muscle wasting and weakness (steroid myopathy) (70%)
- Easy bruising (50%), delayed healing (40%)


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Cushing's Syndrome

Clinical Manifestations

- Abdominal striae
- Central fat deposition
- Thinning of limbs
- Bruising

HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA
Clinical Manifestations

Cushing's Syndrome
Clinical Manifestations
Cushing's Syndrome

Diagnosis

1. 24-Hour Urinary Free Cortisol Level (free scanning)
2. Dexamethasone Suppression Test
3. Basal Plasma ACTH Concentration
4. CRH Stimulation Test
5. Metyrapone Test
6. Radiologic Imaging
Cushing's Syndrome

Diagnosis

24-Hour Urinary Free Cortisol Level

• Urinary free cortisol measurement is the most sensitive & specific test to screen for & confirm Cushing's syndrome

• The patient's urine is collected over 24 hour period & tested for the amount of cortisol

• The cortisol reference range is less than 80 to 120 μg/24 hrs; free cortisol less than 10 μg/24 hrs excludes Cushing's syndrome

• Once Cushing's syndrome has been diagnosed, other tests are used to find the exact location of the abnormality that leads to excess cortisol production
Diagnosis

*Dexamethasone Suppression Test*

• Useful for differentiating pituitary from ectopic ACTH secretion

• Patients with Cushing's syndrome lack normal negative feedback cortisol regulation

• Dexamethasone, used to test for negative feedback control

• Patients with either ectopic ACTH or primary adrenocortical disease do not suppress ACTH or cortisol level
Diagnosis

*Basal plasma ACTH concentration*

- ↑ In pt with ACTH dependent Cushing’s syndrome
  - A plasma ACTH more than 20 pg/mL indicates ACTH-dependent Cushing's syndrome

- ↓ In pt with ACTH independent Cushing’s syndrome
  - A plasma ACTH less than 5 pg/mL indicates ACTH-independent Cushing's syndrome
Diagnosis

*Corticotropin-Releasing Hormone Stimulation Test*

- It helps to distinguish between pituitary adenomas & ectopic ACTH Syndrome or cortisol-secreting adrenal tumors
- CRH stimulates ACTH secretion in patients with Cushing's disease but not ectopic ACTH-secreting tumors
Diagnosis

*Metyrapone Test*

- Metyrapone blocks the synthesis of 11-deoxycortisol to cortisol at the level of the adrenal enzyme leading to decreased circulating cortisol.

- Plasma 11-deoxycortisol increases in response to increased pituitary ACTH secretion.

- Patients with Cushing's disease have a supra normal increase in plasma 11-deoxycortisol.

- Patients with ectopic ACTH-secreting tumors show little or no response.
Diagnosis

Radiologic Imaging

- CT is used to determine the location and size of tumors and to differentiate between adrenal adenomas and carcinomas
Cushing's Syndrome

Diagnosis

Cushing's syndrome suspected

24-hour urine free cortisol; low-dose dexamethasone suppression test

Abnormal

Plasma ACTH; high-dose dexamethasone suppression test

ACTH undetectable; no suppression
Adrenal tumor

ACTH elevated; no suppression
Ectopic ACTH syndrome

ACTH normal to elevated; dexamethasone suppression < 50% of baseline
Cushing's disease

Normal

Excludes Cushing's syndrome

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Disorders of Adrenal Gland

Hyperfunction of cortex
- Cushing's syndrome
- Aldosteronism

Hypofunction of cortex
- Androgen Excess
- Addison's disease

Hyperfunction of medulla
- Pheochromocytoma
Hyperaldosteronism
Hy珀aldosteronism

• Aldosterone (the mineralocorticosteroid hormone of the adrenal cortex):
  - Is major regulator of extracellular fluid volume by causing Na & H2o retention and is controlled by renin-angiotensin-aldosterone mechanism
  - It is also major determinant of K balance

• Results from excessive production of aldosterone
Causes/Classification

Types

Primary Hyperaldosteronism

Secondary Hyperaldosteronism

Occurs as a result of excessive aldosterone tumor or hyperplasia of the adrenal cortex

Occurs in conditioning the activation of reninangiotension system (CHF, liver cirrhosis)
Pathophysiology

- In primary hyperaldosteronism, there is a primary increase in aldosterone production by the abnormal zona glomerulosa tissue (adenoma or hyperplasia)

- However, circulating levels of aldosterone are still modulated to some extent by variations in ACTH secretion

- The chronic aldosterone excess results in expansion of the extracellular fluid volume and plasma volume
Pathophysiology

- This expansion is registered by stretch receptors of the juxtaglomerular apparatus and Na+ flux at the macula densa, leading to suppression of renin production & low circulating plasma renin activity.

- Patients with secondary hyperaldosteronism also produce excessively large amounts of aldosterone but, in contrast to patients with primary hyperaldosteronism, have elevated plasma renin activity.
Clinical Consequences

- Excess aldosterone cause Na & H2O retention

- Expansion of the ECF volume which lead to hypertension, hypernatremia, hypokalemia, metabolic alkalosis & edema
Diagnosis

1. Inc. levels of aldosterone in plasma, urine.

2. Measurements of plasma renin
   - In primary aldosteronism renin level is low
   - In secondary aldosterone levels renin level is high

3. Abnormal electrolyte levels (↑ Na, ↓ K, metabolic alkalosis)

4. CT scan or MRI can help detect & localized an adrenal lesion in patient with primary aldosteronism
Disorders of Adrenal Gland

- Hyperfunction of cortex
  - Cushing's syndrome
  - Aldosteronism
  - Androgen Excess

- Hypofunction of cortex
  - Addison's disease

- Hyperfunction of medulla
  - Pheochromocytoma
Androgen Excess
Syndromes of Androgen Excess

- Not discussed in class
Disorders of Adrenal Gland

- Hyperfunction of cortex
  - Cushing's syndrome
  - Aldosteronism
  - Androgen Excess

- Hypofunction of cortex
  - Addison's disease

- Hyperfunction of medulla
  - Pheochromocytoma
Addison's disease
Addison's Disease

• Deficiency of all three hormone groups produced by the adrenal gland (glucocorticoids, mineralcorticoids and androgens)

• Adrenocortical hormones secretion insufficient because:

1. Insufficiency of the adrenal cortex (Primary adrenal insufficiency)

2. Deficient secretion of ACTH (Secondary adrenal insufficiency)

• More 80% of gland destroyed before signs & symptoms occur
Addison's Disease

Causes/Classification

*Primary Insufficiency*

- Due to destruction of adrenal cortex by:
  1. Autoimmune diseases >50%
  2. Tuberculosis, AIDS
  3. Adrenal hemorrhage secondary to anticoagulant therapy
Causes/Classification

Secondary Insufficiency

- Due to disease or drug that decrease ACTH:
  1. Panhypopituitarism
  2. Sudden withdrawal of exogenous corticosteroid drugs
Addison's Disease

Clinical Manifestations

• Weight loss
• Vomiting
• Abdominal pain
• Diarrhea
• Nausea
• Hypoglycemia
• Hypotension
• Amenorrhea
• Dec. libido
• Dec. Axillary & pubic hair

• Hyperpigmentation (important characteristic of primary adrenocortical insufficiency)
• Dehydration
• Dec. cardiac output
• Tachycardia
• Metabolic acidosis,
• Hyponatremia
• Hyperkalemia
• Depression
Addison's Disease

Diagnosis

*Primary Insufficiency*

1. ↓ Plasma cortisol level

2. ↓ Urinary excretion of the degradation products or metabolites of cortisol (urinary 17-hydroxycorticoid)

3. ↑ Plasma ACTH level

4. Serum electrolyte levels are abnormal (↓ Na, ↑ K)

5. ↑ Serum renin

6. ↓ Serum aldosterone
Addison's Disease

Diagnosis

*Secondary Insufficiency*

1. ↓ Plasma ACTH level
2. ↓ Level of cortisol & it's urinary metabolites
3. Aldosterone levels is normal
Addisonian Crisis

- Acute adrenal insufficiency
- An episode of severe hypotension, vascular collapse, acute renal failure and hypothermia caused by a combined lack of cortisol and aldosterone
- It may be precipitated by infection, trauma and dehydration in individuals with Addison’s disease and can be life-threatening
Iatrogenic Acute Adrenocortical (2ry) Failure

- Prolonged high dose therapeutic corticosteroids then abruptly stopped leads to acute adrenocortical failure with hypovolimic, hypotensive shock, hypoglycemia, and risk of sudden death

- Corticosteroids drug dosage must be tapered before complete withdrawal to allow time for adrenocortical function to recover
Disorders of Adrenal Gland

- Hyperfunction of cortex
  - Cushing's syndrome
  - Aldosteronism
  - Androgen Excess

- Hypofunction of cortex
  - Addison's disease

- Hyperfunction of medulla
  - Pheochromocytoma
Pheochromocytoma
Pheochromocytoma

- A rare cause of secondary hypertension, is an adrenal medullary tumor that releases excessive amounts of catecholamines
Clinical Manifestations

- Mainly hypertension; With:
  1. Headaches on the top of the head
  2. Palpitations
  3. Pallor
  4. Diaphoresis
  5. Arhythmia
Diagnosis

- Basal plasma Catecholamines ↑
- 24-Hour Urinary catecholaminestest ↑
- Clonidine suppression test: fail to suppress Catecholamines secretion
- CT scan: help locate the tumor
References

• Pharmacotherapy: A Pathophysiologic Approach, 7e

• Pathophysiology of Disease: An Introduction to Clinical Medicine, 6e

• Applied Therapeutics: The Clinical Use of Drugs, 9e

• Some slides adapted from Rania Aljizani MSc
Thank You