Endocrine Pathophysiology

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Endocrine system

- Central:
  - Hypothalamus
  - Pituitary
  - Pineal

- Peripheral:
  - Thymus
  - Thyroid
  - Parathyroid
  - Adrenal
  - Endocrine pancreas
  - Ovaries
  - Testes
Hormones

**Definition:** Hormones are chemical messengers secreted by endocrine organs and transported throughout the body where they exert their action on specific cells called target cells.

- Chemically hormones are of three basic types:
  - **Steroid** (glucorticoids and mineral corticoids).
  - **Monoacids** analog-derivated from amino acid tyrosine (T3 and T4)
  - **Peptides** (ACTH, TSH or ADH)

**Mechanism of hormonal action**

1. **Polypeptide hormones & catecholamines**
   - Membrane receptor, activating of G-protein and change in enzyme activity

2. **Steroid hormones & T3/T4**
   - Cytoplasmatic receptor influencing gene expression
Functional range of the endocrine system

- Response to stress and injury.
- Behavioral reactions.
- Growth and development.
- Reproduction.
- Homeostasis.
- Energy metabolism.

Modulation

Hormones
- Growth
- Development
- Reproduction
- Intelligence
Hypothalamus-pituitary-peripheral glands interactions

Hormones, released from the anterior pituitary

Anterior pituitary (Adenohypophysis)

- Prolactin
  - Mammary glands

- Gonadotropic hormones
  - Ovary

- Thyroid stimulating hormone
  - Thyroid gland

- ACTH
  - Adrenal cortex

- Growth hormone
  - Muscle, bone, and other tissues
Acromegaly

Occurs during adulthood

Gigantism

Begins during childhood

WHY are patients who suffer gigantism taller than those who suffer acromegaly?

Hormones released from the posterior pituitary:

- Antidiuretic hormone (ADH)
- Oxytocin
Feedback loop mechanism

Negative feedback mechanism
Possitive feed back mechanism
Primary endocrinopathy

- With hypofunction
  - Aplasia & Hypoplasia
  - Damage (autoimmune)
  - Yatrogenic
- With hyperfunction
  - Hyperplasia
  - Tumor
- With dysfunction
Secondary endocrinopathy

- Altered feedback loops
- Altered transport (Proteins, Ab)
- Receptor defects \((10^3-10^5)^*\)
- Altered hormonal interactions
  (permissive effects)

* up- and down- regulation
Endocrine dysfunctions
Can be divided into five broad categories

- **Subnormal hormonal production**, resulting from malformation, or absent of the endocrine glands, or the gland could be diseased, or destroyed or secretions are block.
- **Hormonal excess** tends to caused severe disease.
- **Production of abnormal hormone** cause by a gene mutation.
- **Disorder of hormonal receptors.**
- **Abnormality of hormonal transport** or metabolism (lack of protein to bind the hormones, results in increase free level of the hormone)

Mechanisms of endocrine disease

- Endocrine disorders result from hormone deficiency, hormone excess or hormone resistance
- Almost without exception, hormone deficiency causes disease
  - One notable exception is calcitonin deficiency
Mechanisms of endocrine disease

- Deficiency usually is due to destructive process occurring at gland in which hormone is produced — infection, infarction, physical compression by tumor growth, autoimmune attack

Adison’s disease

Mechanisms of endocrine disease

- Hormone excess may be due to overproduction by gland that normally secretes it, or by a tissue that is not an endocrine organ.

- Endocrine gland tumors produce hormone in an unregulated manner.

Cushing’s Syndrome
Mechanisms of endocrine disease

- Alterations in receptor number and function result in endocrine disorders
- Most commonly, an aberrant increase in the level of a specific hormone will cause a decrease in available receptors

Type II diabetes

Thyroid gland
Thyroid hormones

- The glands contain two types of cells
  - Follicular cells which produce T3 and T4
  - Parafolicular cells which secrete thyrocalcitonin

- T3=9% of the hormone secreted is in active form.
- T4=90% of the hormone secreted is bound to protein as a storage form; this form is inactive until converted to T3.

Thyroid hormones - functions

- Body tissues
- Metabolism: BMR
- CHO metabolism
- Fat metabolism
- Protein metabolism
- Body weight
- Body growth
- Cardiovascular function
- Pulmonary function
- Gastrointestinal function
- CNS
- Thyrocalcitonin: Bone Ca++
Pathophysiologic variants of hypofunction

Hypothyroidism - etiology

Primary (thyroid) hypothyroidism
Loss of functional thyroid tissue

- Chronic autoimmune thyroiditis
- Transitory autoimmune thyroiditis
- $^{131}$I and external radiation therapy
- Postoperative hypothyroidism
- Transitory hypothyroidism
- Infiltrative involvement of the thyroid gland
Hypothyroidism - etiology

Biosynthetic defects

- Hereditary defects
- Iodine deficiency
- Iodine excess
- Antithyroid factors

Hypothyroidism - etiology

Central (secondary) hypothyroidism

- Pituitary
- Hypothalamic
- Generalized resistance to thyroid hormones
- Drugs: Dopamine, Amiodarone, Lithium
Signs and symptoms of hypothyroidism

- Exhaustion
- Depression
- Dry coarse skin
- Cold intolerance
- Constipation
- Weight gain

Mental retardation (IQ<75)

<table>
<thead>
<tr>
<th>Class</th>
<th>IQ</th>
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</thead>
<tbody>
<tr>
<td>Profound mental retardation</td>
<td>Below 20</td>
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<tr>
<td>Severe mental retardation</td>
<td>20–34</td>
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<td>Moderate mental retardation</td>
<td>35–49</td>
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<td>Mild mental retardation</td>
<td>50–69</td>
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<tr>
<td>Borderline mental retardation</td>
<td>70–79</td>
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Hyperfunction of the thyroid gland

Thyrotoxicosis = T3 and T4 ↑

Hyperthyroidism
- Primary
- Secondary

Ectopic thyroid hormone production

Pathophysiologic variants of hyperfunction

NORMAL
- hypothalamus
- hypophysis
- thyroid gland
- peripheral tissues

Primary hyperthyroidism
- Peripheral tissues
- Thyroid cancer and tumors

Secondary hyperthyroidism
- Peripheral tissues
- Grave's disease
- Toxic Goblet
Hyperthyroidism

- Definition: Excess of TH in the body
- Causes increase in metabolic rate
  - Cardiac rate and stroke volume ↑
  - Peripheral blood flow ↑
  - Oxygen consumption ↑
  - Body temperature ↑

Hyperthyroidism

- Grave’s disease (Basedow)
- Toxic adenoma
- Iodine induced hyperthyroidism
- Hyperthyroidism due to ectopic TSH production
- Inappropriate TSH secretion
Disease of Graves (Basedow) - pathogenesis

- Fatigue
- Difficulty sleeping
- Hand tremors
- Weight loss despite increased appetite
- Skin = warm, moist, smooth, flushed
- Amenorrhea

Signs and symptoms of hyperthyroidism

- Hoarseness
- Dyspnea
- Tachycardia
- Increase blood volume
- Increased CO
- Palpitations
- Exophthalmos
Patients with hyperthyroidism

- Drug induced (yatrogenic) thyreotoxicois
- Functionally-active metastases of thyroid carcinoma
- Struma ovarii
The adrenal glands are bilaterally located above each kidney and consist of two tissues in one gland:

- **Cortex** - outer layer
- **Medulla** - inner portion
Adrenal medullary hormones

- **Epinephrine**
  - Fight or flight response
  - Increased HR, BP
  - Gluconeogenesis
  - Lipolysis

- **Norepinephrine**
  - Increased HR, BP
  - Neurotransmitter

- **Dopamine**
  - Increased BP

Disorder of the adrenal medulla

- Pheochromocytoma a benign tumor of the adrenal medulla leading to hyper production of epinephrine and nonepinephrin.

- Ectopic cells in the abdomen or along the ganglia
  - Excess of adrenal medulla hormones
Pheochromocytoma: An Overview

- Pathophysiology
- Etiology
- Clinical manifestations
  - ↑ BP with classic triad
  - Tachycardia
  - Headache
  - Diaphoresis
- Diagnostic findings

- Nursing interventions
  - Prepare for surgery
  - Administer adrenergic blockers
  - Administer catecholamine inhibitors
  - Patient education
  - Potential triggers
  - Drugs to avoid

Variants of adrenal gland abnormal function
Disorders of the adrenal cortex.

- **Cushing’s Syndrome**
  - Caused by excess of cortisol production or by excessive use of cortisol or other similar steroid (glucorticoid)

- **Addison’s Disease**
  - Addison’s disease is a severe or total deficiency of the hormones made in the adrenal cortex, cause by a destruction of the adrenal cortex.

**Etiology of Cushing’s Syndrome**

- Endogenous or exogenous.
  - Tumors: oat cell carcinomas, renal, ovarian, lungs, thymus, pancreas or other organs
  - Chronic administration of glucocorticoids or ACTH or iotrogenic cause.
Etiology of Cushing's Syndrome

- A pituitary tumor producing ACTH stimulating the adrenals to growth (hyperplasia) and to produce too much cortisol.

  - It is the most common type and is called Cushing's disease. It is the cause of 70% of spontaneous Cushing's syndrome.

Signs and Symptoms of Cushing's Syndrome

- Hypertension
- Hypervolemia
- Hyperglycemia
- Hypokalemia
- Ketosis
- Immunosuppression
- Osteoporosis
- Emotional liability
Cushing syndrome

Clinical signs of Cushing syndrome
Buffalo hump and moon face

Addison’s Disease

Hypofunction of the adrenal cortex.

- Autoimmune reaction in which the body immune system erroneously makes antibodies against the cells of the adrenal cortex and slowly destroys it.

- Other rare infections can cause Addison’s disease: TB, CMV, fungal infections, and adrenal cancer.

Rare disorder can occur at any age; most common among adult white women.
Addison’s Disease etiology

- **Primary** adrenal insufficiency is caused by gradual destruction of the outer layer of the adrenal glands by the body own immune system.
- Lack or decreased glucocorticoid and mineral corticoid.

Addison’s Disease etiology

- **Secondary** adrenal insufficiency results from deficient pituitary ACTH secretion from dysfunction or destruction of hypothalamus or the anterior pituitary gland.
Signs and symptoms of Addison’s:

- Chronic fatigue
- Muscle weakness
- Loss of appetite
- Weight loss
- Nausea/vomiting
- Low blood pressure
- Hyperpigmentation
- Irritability/depression

Adisson disease

J.F. Kennedy
## Diagnostic findings in Addison disease

### Primary disease
- Increased ACTH
- Decrease cortisol
- Abnormal ACTH stimulation test

### Secondary disease
- Decrease ACTH
- Decreased Cortisol
- Normal ACTH stimulation test

Thank you!