Overview of Today’s Lecture

- Review of normal endocrine gland anatomy & physiology
- Pancreatitis
- Diabetes mellitus
- Pancreatic neoplasms

Overview of the Endocrine System

The endocrine system consists of collections of cells located in tissues scattered throughout the body that produce substances released into the blood (hormones) to ultimately affect the activity and metabolism of target cells.
Pituitary Gland (Hypophysis)

Two distinct portions
- anterior pituitary (adenohypophysis)
- posterior pituitary (neurohypophysis)

Overview of the Pituitary Hormones

All anterior and posterior pituitary hormones bind to membrane receptors and use 2nd messengers (cAMP)

Pituitary Gland Control

- Hypothalamic releasing hormones stimulate cells of anterior pituitary to release their hormones
- Nerve impulses from hypothalamus stimulate nerve endings in the posterior pituitary gland to release its hormones

Note the hypophyseal portal system (two capillaries in series)
Hormones of the Anterior Pituitary (SeT GAP)

Tropic hormones (in black) control the activity of other endocrine glands

All anterior pituitary hormones use second messengers

Feedback for Hormone Regulation

Recall that homeostasis is the maintenance of STABLE (not constant) internal conditions

Hormone Summary Table I – Pituitary Hormones
### Hormone Summary Table II

<table>
<thead>
<tr>
<th>Name</th>
<th>Origin</th>
<th>Destination</th>
<th>Action on Target Tissue</th>
<th>Control of Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIIODOTHYRONINE (T3) &amp; THYROXINE (T4)</td>
<td>Thyroid (follicular cells)</td>
<td>all cells</td>
<td>increases rate of metabolism (BMR)</td>
<td>Thyroid Stimulating Hormone (TSH)</td>
</tr>
<tr>
<td>CALCITONIN</td>
<td>Parafollicular C cells</td>
<td>Intestine, bone, kidney</td>
<td>decreases plasma $\text{Ca}^{2+}$ (↓ intestinal absorption; ↓ action of osteoclasts; ↑ excretion of Ca by kidney)</td>
<td>Calcium (Ca²⁺)</td>
</tr>
<tr>
<td>PARRATHYROID HORMONE (PTH)</td>
<td>Parathyroid glands</td>
<td>Intestine, bone, kidney</td>
<td>increases plasma $\text{Ca}^{2+}$ (↑ intestinal absorption; ↑ action of osteoclasts; ↓ excretion of Ca by kidney)</td>
<td>PTH</td>
</tr>
<tr>
<td>ADRENAL CORTEX HORMONE (ADRENALINE)</td>
<td>Adrenal Cortex</td>
<td>Kidney, smooth muscle</td>
<td>stimulation of motor and sympathetic neural pathways (increases blood pressure)</td>
<td>Adrenal Cortex (ACTH)</td>
</tr>
<tr>
<td>INSULIN</td>
<td>β-cells of pancreatic islets</td>
<td>all cells</td>
<td>pushes glucose into cells from blood, glycogen formation (decreases blood glucose)</td>
<td>Insulin (SNS)</td>
</tr>
<tr>
<td>GLUCAGON</td>
<td>α-cells of pancreatic islets</td>
<td>Liver and skeletal muscle</td>
<td>breakdown of glycogen (increase in blood glucose)</td>
<td>Glucagon (SNS)</td>
</tr>
<tr>
<td>TESTOSTERONE</td>
<td>Testes</td>
<td>secondary sex organs</td>
<td>development and maintenance</td>
<td>Testosterone (LH)</td>
</tr>
<tr>
<td>ESTROGEN</td>
<td>Ovaries</td>
<td>secondary sex organs</td>
<td>development and maintenance</td>
<td>Estrogen (LH)</td>
</tr>
<tr>
<td>NATRIURETIC PEPTIDES</td>
<td>atria and ventricles of heart</td>
<td>all cells</td>
<td>increased excretion of sodium and water from kidneys, ↓ blood volume, ↓ blood pressure</td>
<td>Angiotensin II, aldosterone (Angiotensin II)</td>
</tr>
</tbody>
</table>

### Major Types of Endocrine Disorders

- **Over- or underproduction of hormone**
  - Has a corresponding effect on target organ
  - Remember, this can apply to hypothalamus, pituitary, or other endocrine organ (recall ‘axis’)

- **Lesions that exert their effect by pressing on other structures**
  - Called ‘mass effect’
  - Some of these do not produce hormone
  - Some produce hormones (functional)

### Major Mechanisms of Hormone Dysfunction

- **Inappropriate amount of hormone**
  - Increased/Decreased hormone synthesis
  - Failure of feedback systems
  - Inactive hormones
  - Dysfunction of delivery system

- **Inappropriate response by target cell**
  - Cell surface receptor anomalies
  - Intracellular anomalies
Manifestations of Pituitary Disease

- Hyperpituitarism
  - Much more common than hypo
  - Hyperplasia, adenoma, carcinoma
  - Adenomas most common (30% of pituitary adenomas)
    - can affect any cell type in pituitary
    - Common cause of hyperpituitarism

- Hypopituitarism
  - Usually due to local destructive process
  - Infarction, surgery, radiation, inflammation, non-functional adenoma (mass effect)

- Mass effect
  - Pituitary mass presses on surrounding structures
  - ‘Stalk effect’ when tumor blocks PIF

Types of Pituitary Adenoma

<table>
<thead>
<tr>
<th>Pituitary Cell Type</th>
<th>Tumor Type</th>
<th>Effects</th>
</tr>
</thead>
</table>
| Lactotrophs | Prostate | Tumor or stalk effect
| Corticotrophs | ACTH adenoma | Cushion disease; Nelson syndrome
| Somatotrophs | GH cell adenoma | Gigantism in children; acromegaly in adults
| Gonadotrophs | LH, FSH adenoma | Hypogonadism, mass effect, hypogonadism
| Thyrotrophs | TSH | TSH adenoma

*Table from McConnell, The Nature of Disease, 2nd ed., LWW, 2014

Common manifestations:
- Headache and fatigue
- Visual changes
- Hyposecretion of neighboring anterior pituitary hormones
Prolactinoma

- Hypersecretion of prolactin due to adenoma
  - In females, increased levels of prolactin cause amenorrhea, infertility, galactorrhea, hirsutism, and osteopenia
  - In males, increased levels of prolactin cause hypogonadism, erectile dysfunction, impaired libido, oligospermia, and diminished ejaculate volume

Diseases of the Anterior Pituitary (cont’d)

- Acromegaly
- Dwarfism (R), Gigantism (L)

Diseases of the Anterior Pituitary (cont’d)

- Hypopituitarism
  - Pituitary infarction
    - Sheehan syndrome (Obstetrical)
    - Hemorrhage (apoplexy)
    - Shock
  - Others:
    - Head trauma
    - Surgery/Radiation
    - Infections
    - Tumors
    - Rathke’s Pouch cyst
    - Empty sella syndrome
    - Hypothalamic lesions
### Diseases of the Posterior Pituitary

- **Syndrome of inappropriate antidiuretic hormone secretion (SIADH)**
  - Hypersecretion of ADH
  - For diagnosis, normal adrenal and thyroid function must exist
  - Clinical manifestations are related to enhanced renal water retention, hyponatremia, and hypo-osmolality

### Diseases of the Posterior Pituitary (cont’d)

- **Diabetes insipidus**
  - Insufficiency of ADH
  - Polyuria and polydipsia
  - Partial or total inability to concentrate the urine
  - Neurogenic
    - Insufficient amounts of ADH
  - Nephrogenic
    - Inadequate response to ADH
  - Psychogenic
  - Manifestations are related to enhanced water excretion, hypernatremia, and hyper-osmolality

### Disorders of the Thyroid Gland

- Several types of disorders
  - Over- and underproduction of hormones
  - Inflammation (thyroiditis)
  - Tumors (functional or non-functional)

- **Goiter** – any enlargement of the thyroid

- **Euthyroid sick syndrome**
  - Nonthyroidal illnesses
  - May show hypothyroidism
  - But no S&S – appear to have normal function
Disorders of the Thyroid Gland - Thyrotoxicosis

- Hypermetabolic state
- Caused by presence of excess thyroid hormone (T3/T4)
  - Hyperthyroidism = Overproduction of T hormones
    - Primary – Intrinsic overproduction by thyroid
    - Secondary – TSH-secreting adenoma of pituitary
  - Not hyperthyroidism
    - Most commonly: overmedication
    - Sometimes release of already stored T hormone
- Most common types
  - Diffuse glandular (usually Graves disease; 70-80% cases)
  - Multinodular (toxic goiter)
  - Adenoma
- Usually: women, 20-40 years of age, no ethnic difference

Disorders of the Thyroid Gland - Thyrotoxicosis

Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Lab Value (Common)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td>T1 &lt; 0.02, T2 &lt; 0.03</td>
<td></td>
</tr>
<tr>
<td>Primary hyperthyroidism</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03</td>
<td>Thyroid-stimulating hormone (TSH) elevated</td>
</tr>
<tr>
<td>Secondary hyperthyroidism</td>
<td>T1 &lt; 0.02, T2 &lt; 0.03</td>
<td>TSH normal</td>
</tr>
<tr>
<td>Hyperthyroidism from other causes</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03</td>
<td>TSH normal</td>
</tr>
<tr>
<td>Thyrotoxic crisis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graves disease</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03, TSH elevated</td>
<td></td>
</tr>
<tr>
<td>Hyperthyroid goiter</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03, TSH elevated</td>
<td></td>
</tr>
<tr>
<td>Ophthalmopathy</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03, TSH elevated</td>
<td></td>
</tr>
<tr>
<td>Pretibial infiltrative dermatitis</td>
<td>T1 &gt; 0.02, T2 &gt; 0.03, TSH elevated</td>
<td></td>
</tr>
</tbody>
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Table from McConnell, The Action of Disease, 2nd ed., LWW, 2014

Hyperthyroidism

- Graves disease
  - Autoimmune – TSI (Ig)
  - Hyperthyroid goiter
  - Ophthalmopathy (exophthalmos)
  - Pretibial infiltrative dermatopathy
- Hyperthyroidism resulting from nodular thyroid disease
  - Toxic Goiter
- Thyrotoxic crisis

General Hyperthyroidism

- high metabolic rate
- weight gain
- hyperactivity
- protruding eyes

Figure from Huether & McCance, Understanding Pathology, 5th ed., Elsevier, 2012
Hypothyroidism

- Primary hypothyroidism
  - Subacute thyroiditis
  - Autoimmune thyroiditis (Hashimoto disease)
  - Painless thyroiditis
  - Postpartum thyroiditis
  - Manifestations due to hypometabolic state
    - Myxedema coma
    - Congenital hypothyroidism
    - Thyroid carcinoma

Neoplasms of Thyroid

- Common; usually not aggressive
- Most likely neoplastic are:
  - Solitary, cold, young, male, history of neck/head radiation
- Thyroid adenomas (follicular)
- Thyroid carcinoma
  - Papillary (85%) — solitary nodule, coffee bean nuclei
  - Follicular — follicular epithelium
  - Medullary (moderately aggressive; MEN2A/B)
  - Anaplastic (highly aggressive; < 5% of cases)

Summary of Thyroid Disorders

Hyperparathyroidism

- Hyperparathyroidism
  - “Stones, bones, groans, with psychiatric overtones”
  - Primary hyperparathyroidism
    - Excess secretion of PTH from one or more parathyroid glands
  - Secondary hyperparathyroidism
    - Increase in PTH secondary to a chronic disease
  - Manifestations:
    - Hypercalcemia
    - Hypophosphatemia
    - Hypercalcemia: kidney stones (Stones)
    - Pathologic fractures (Bones)
    - Peptic ulcers, pancreatitis (Groans)
    - Depression, lethargy, fatigue (Psychiatric overtones)

Hypoparathyroidism

- Hypoparathyroidism
  - Abnormally low PTH levels
  - Much less common than hyperparathyroidism
  - Usually caused by parathyroid damage in thyroid surgery
  - Manifestations:
    - Hypocalcemia
    - Hyperphosphatemia
    - Intermittent muscle aches and spasms (tetany), hyperspasticity, hyperreflexia

Adrenocortical Hyperfunction
Pathogenesis of Cushing Syndrome

Androgenital Syndromes

- Hypersecretion of adrenal androgens and estrogens
  - Feminization
  - Virilization
  - Salt wasting
Adrenocortical Failure

Disorders of Adrenal Function

- Adrenal medulla hyperfunction
  - Caused by tumors derived from the chromaffin cells of the adrenal medulla
    - Pheochromocytomas most common
      - Rule of Tens – 10% are: outside, bilateral, malignant, in children, no hypertension
    - Secrete catecholamines on a continuous or episodic basis
    - **Main clinical sign: hypertension**
  - Outside medulla in paraganglion system – called paragangliomas

Multiple Endocrine Neoplasia Syndromes (MEN)

- Heritable genetic defects causing hyperfunction due to hyperplasia, adenoma, or carcinoma
  - MEN-1 syndrome (Wermer)
    - Abnormal function of parathyroid, pancreas, pituitary, and duodenal gastrin-secreting cells
    - Associated with MEN-1 gene (menin)
  - MEN-2 syndrome
    - Several subvarieties according to the glands involved
    - Associated with RET gene
• Heritable genetic defects causing hyperfunction due to hyperplasia, adenoma, or carcinoma
• MEN-1 syndrome (Wermer)
  – Abnormal function of parathyroid, pancreas, pituitary, and duodenal gastrin-secreting cells
• MEN-2 syndrome
  – Several subvarieties according to the glands involved