Ch 7: Introduction to the Endocrine System

- Hormones (classification & control of)
- Endocrine Pathologies
  - Too much or not enough?

Running Problem: Grave’s Disease

 Developed by John Gallagher, MS, DVM
The endocrine system

A. releases chemicals into the bloodstream for distribution throughout the body.

B. releases hormones that alter the metabolic activities of many different tissues and organs simultaneously.

C. produces effects that can last for hours, days and even longer.

D. Both A and B are correct.

E. A, B and C are correct
Endocrinology

= The study of hormones, their receptors, the intracellular signaling pathways they invoke, and the diseases and conditions associated with them.

What are hormones?

- Where do they come from?

Major endocrine glands?

Physiological processes controlled by hormones?
Hormones:

- Known since ancient times
- Secreted by cells into the blood
  - Not always from a gland
  - Pheromones?
  - Releasing Factors? Paracrines?
- Transported to distant targets
- Effective at very low concentration
  - Often measured in ng/ml
More Hormones:

- Bind to receptors
  - (differing effects on some tissues)
- Hormone action must be of limited duration
  - Some method of stopping activity
  - $t_{1/2} = \text{half life, usually measured in minutes}$
- Some are stored, others are manufactured as needed.
Chemical Classification of Hormones

4 main types:

1. Peptides and proteins
   1. Most common
2. Steroids
3. Amines
4. Eicosanoids

Differ on basis of synthesis, storage, release, transport and cellular mechanism of action
(review Table 7-1)
1. Peptide (Protein) Hormones

- Synthesis as **preprohormone** → post-translational modification to **prohormone** → then **hormone**

- Storage – release?

- Short half-life (mins.)

- Most common type

*Fig 7-3*
Peptide Hormone Processing

(a) PreproTRH (thyrotropin-releasing hormone) has six copies of the 3-amino acid hormone TRH.

(b) Prohormones (such as pro-opiomelanocortin, the prohormone for ACTH) may contain several peptide sequences with biological activity.

(c) The peptide chain of insulin’s prohormone folds back on itself with the help of disulfide (S-S) bonds. The prohormone cleaves to insulin and C-peptide.

Fig 7-4
Cellular Mechanism of Action for Peptide Hormones

- Peptides are usually lipophobic ⇒ how does message get into cell?
- Usually rapid cellular response because existing proteins are modified
- cAMP 2nd messenger system most common
2. Steroid Hormones

- Only gonads, adrenals, placenta
- Derived from cholesterol (lipophilic)
  - Cross membranes (no storage)
- SER, on-demand synthesis
- Usually Bound to Carrier proteins
  - May extend $t_{1/2}$
  - May block entry to target cell
- Activity is usually intracellular
  - Occasional surface receptors
  - Next slide
Steroid Hormone Mechanism of Action

- Lipophilic when unbound
- Cross membranes
- New DNA Replication
- *De novo* synthesis or response
3. Amine Hormones

- Derived from tyrosine or tryptophan
- 3 groups
  - Tryptophan $\Rightarrow$ Melatonin
  - Tyrosine $\Rightarrow$ Catecholamines
    behave like peptide hormones
  - Tyrosine $\Rightarrow$ Thyroid hormones
    behave like steroid hormones

Fig 7-8
Tyrosine and Hormone Derivatives

Tyrosine
is the parent amino acid for catecholamines and thyroid hormones.

Catecholamines
are made by modifying the side groups of tyrosine.

- **Dopamine**
- **Norepinephrine**
- **Epinephrine**

Thyroid hormones
are synthesized from two tyrosines and iodine (I) atoms.

- **Thyroxine (Tetraiodothyronine, T4)**
- **Triiodothyronine (T3)**
4. Eicosanoids (Fig 6-16)

- Derivatives of arachidonic acid
  - Unsaturated FA
- Produced by MANY cells
- Unclear if hormone is the proper term
  - May be autocrine/paracrine, too
- Produced by COX in response to cell damage
  - Mediators of inflammation
    - NSAIDS are COX inhibitors
  - Many other activities
Control of Hormone Release (p 222)

All endocrine reflex pathways have similar components

- Similar to PNS/CNS reflex pathway
  - Stimulus / input signal
  - Integration (where?)
  - Output signal (hormone / neurohormone)

- Physiological action

- Negative feedback – turns off reflex

One Hormone may follow > 1 reflex pathway pattern
Note: 2 different reflex patterns! (multiple stimuli for release)
Simple Endocrine Reflex

Endocrine cell acts as sensor AND integrating center ⇒ no afferent pathway ⇒ responds by secreting hormone

Example: PTH → increases [Ca\(^{2+}\)] in plasma

Fig 7-10
Neurohormone Reflex

NH release by modified neurons upon NS signal

► 3 major groups of Neurohormones:
  - Catecholamines from adrenal medulla
  - Hypothalamic neurohormones from posterior pituitary
  - Hypothalamic neurohormones acting on anterior pituitary
Neurohormones of Posterior Pituitary

► Other name of gland?

► 2 neurohormones
  - Oxytocin
  - ADH (vasopressin)

► Both are peptides (9 aa) transported in secretory vesicles via axonal transport

Fig 7-12
Anterior Pituitary

- Other name of gland?

- Secretes 6 Hormones (names?)

- A trophic (tropic) hormone controls the secretion of another hormone

- Hypothalamic trophic hormones and the hypothalamic-hypophyseal portal system
  - Growth, metabolism, repro
The Pituitary
Hypothalamus

**Ant. pituitary**

**Endocrine gland**

**Target tissue**

**Hypothalamus**

**IC1**

**Ant. pituitary**

**IC2**

**Endocrine gland**

**IC3**

**Response**

**Examples:**
Thyroxin, cortisol, testosterone etc

**Example:**
Thyrotropin RH
*Also inhibiting hormones (IH)*

**Examples:**
TSH
Gonadotropins (FSH & LH)
Adrenocorticotrop(h)ic hormone
Somatotropin
Hormone Interactions

Multiple hormones can affect a single target simultaneously

*Three types of hormone interactions:*

1. Synergism
2. Permissiveness
3. Antagonism
1. Synergism

- Combined action of hormones is more than just additive!

- Example: Blood glucose levels & synergistic effects of glucagon, cortisol and epinephrine

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![Graph showing blood glucose levels over time for different hormone combinations](Fig 7-18)
2. Permissiveness

► One hormone allows another hormone to have its full effect
  - Especially during growth
  - Hypothyroidism reduces effect of steroids

3. Antagonism

Antagonistic hormones have opposing physiological actions
  – Hormone B diminishes the effect of hormone A

Hormone Antagonists and Cancer:
Tamoxifen blocks estrogen receptors
Endocrine Pathologies

“Unbalance leads to disease”

Due to:

1. Hypersecretion (excess)
   1. See Running Problem
   2. Iatrogenic

2. Hyposcretion (deficiency)
   1. 1° vs. 2°

3. Abnormal target tissue response
   1. Receptor anomaly

Hyperadrenocorticism or Cushing’s disease
1. Hypersecretion:

- Due to?
  - Iatrogenic (could lead to gland atrophy)
  - Tumor

- Symptoms: Exaggerated Effects

Examples:
- **Graves disease** (Running Problem)
- Gigantism in child (acromegaly in adult)
- Cushing’s Syndrome
Example: Hyperthyroidism
(Review Running Problem)

Most common cause: **Graves' disease**

Autoantibodies (TSI) bind to TSH receptor and stimulate thyroid hormone production.

This activation by TSI is not subject to the normal negative feedback loop.

**exophthalmos**
2. Hyposecretion:

- Due to ?
- Symptoms: Normal effects of hormone diminished or absent

Examples:
- Hypothyroidism
- Dwarfism
- Addison’s disease
- DM
Example: Hypothyroidism

Most common cause in US: chronic autoimmune thyroiditis (Hashimoto's thyroiditis = Chronic thyroiditis)

Other causes
- surgical removal of the thyroid gland
- radioactive iodine treatment
- external radiation (Chernobyl)
- a deficiency in dietary iodide consumption (= endemic or primary goiter)
Symptoms:
During childhood:
stunted growth
retardation
lethargy
low body temp.

In adulthood:
Bradycardia
weight gain
lethargy
low body temp.
3. Abnormal Tissue Responsiveness

Hormone levels normal, target unresponsive. Usually inherited

*Due to:*

- Abnormal hormone / receptor interaction
  - E.g., Down-regulation
- Abnormal signal transduction
Diagnosis of Endocrine Pathologies

► Primary Pathology
  - Defect arises in last integration center in the reflex, i.e. the secretory cells.
  - Examples?

► Secondary Pathology
  - Defect arises in one of the trophic integration centers, i.e., where the trophic hormones are secreted
  - Examples?

► Sometimes the pathology is not simply an excess or a deficiency
  - Inability to respond to a stimulus
  - Specialized tests are necessary
Dx of Hyperadrenocorticism (Cushing’s)

Fig 7-20