

**The Nature of Disease**  
**Pathology for the Health Professions**

Thomas H. McConnell

**Chapter 14**  
**Disorders of the Endocrine Glands**  
**Lecture 14**

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**Overview of Today's Lecture**

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

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

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

From: *Pathophysiology: A Clinical Approach*, Braun & Anderson, Lippincott, 2011

From: *Hole's Human Anatomy & Physiology*, Hole, McGraw-Hill, 2008

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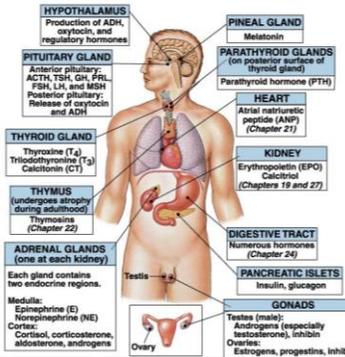
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**Overview of the Endocrine System**



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.**

Figure from: Martini, *Anatomy & Physiology*, Prentice Hall, 2001

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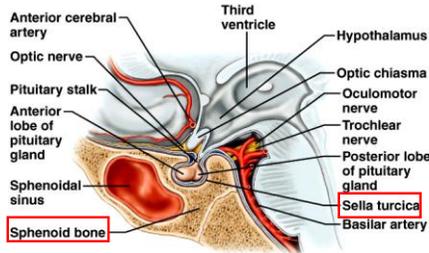
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## Pituitary Gland (Hypophysis)

Two distinct portions

- anterior pituitary (adenohypophysis)
- posterior pituitary (neurohypophysis)

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Figure from: Holt's Human A&P, 12<sup>th</sup> edition, 2010




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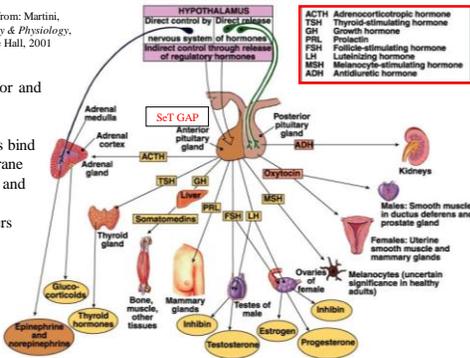
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## Overview of the Pituitary Hormones

Figure from: Martini, Anatomy & Physiology, Prentice Hall, 2001

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




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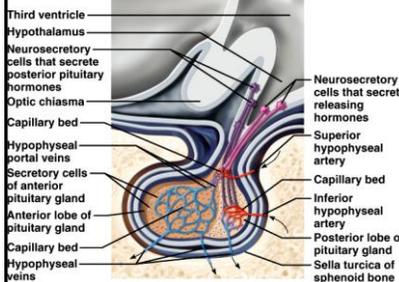
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## Pituitary Gland Control

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Figure from: Holt's Human A&P, 12<sup>th</sup> edition, 2010



- 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)

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## Alterations of the Hypothalamic-Pituitary System

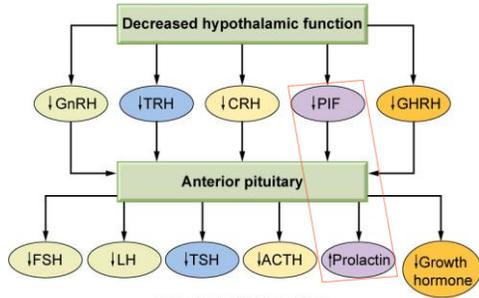


Figure from: McConnell, *The Nature of Disease*, 2nd ed., LWW, 2014

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## 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

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## Types of Pituitary Adenoma

Pituitary Cell Type*	Hormone	Approximate Percent of all Adenomas	Tumor Type	Effects
Lactotroph	Prolactin	~30%	Prolactinoma	Females: unexpected milk secretion or amenorrhea Males or females: sexual dysfunction, infertility
Various cells	None	~25–30%	Null cell adenoma	Mass effect or stalk effect
Corticotroph	ACTH MSH	~15%	ACTH adenoma	Cushing disease; Nelson syndrome
Somatotroph	GH	~15%	GH cell adenoma	Gigantism in children; acromegaly in adults
Gonadotroph	LH, FSH	~10%	Gonadotroph adenoma	Hypogonadism, mass effect, hypopituitarism
Thyrotroph	TSH	~1%	TSH adenoma	Hyperthyroidism

\*Each cell type may produce nonfunctioning adenomas that present with mass effect and hypopituitarism due to destruction of the gland. Some adenomas may produce more than one hormone (most commonly a combination of GH and prolactin).

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

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

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## 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

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## Diseases of the Anterior Pituitary (cont'd)

Acromegaly →



← Dwarfism (R), Gigantism (L)

Figures from: *Hole's Human Anatomy & Physiology*, Hole, 12<sup>th</sup> ed., McGraw-Hill, 2008

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## 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

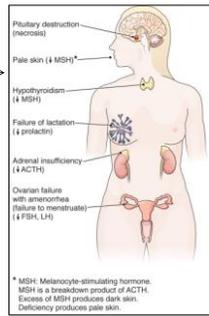


Figure from: McConnell, *The Nature of Disease*, 2<sup>nd</sup> ed., LWW, 2014

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### 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

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### 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

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### 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

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## Disorders of the Thyroid Gland - Thyrotoxicosis

- Hypermetabolic state
- Caused by presence of excess thyroid hormone ( $T_3/T_4$ )
  - 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

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## Disorders of the Thyroid Gland - Thyrotoxicosis

### Diagnosis

**Table 14.3 Laboratory Tests of Thyroid Function\***

Condition	Total T4 (µg/dL)	Total T3 (ng/dL)	TSH (mIU/mL)	% Radioactive Iodine Uptake by Thyroid in 24 hours	Comment
Normal range	5-12	95-190	0.3-5	10-30	
<b>THYROTOXICOSIS</b>					
Primary hyperthyroidism, untreated	↑	↑	↓	↑	Thyroid-stimulating immunoglobulin in Graves disease
secondary hyperthyroidism, untreated	↑	↑	↑	↑	
Thyrotoxicosis from overtreatment with T4	↑	↓	↓	↓	
T3 toxicosis	↓	↑	↓	Normal to ↑	Uncommon
<b>HYPOTHYROIDISM</b>					
Primary, untreated	↓	↓	↑	↓	
Secondary to pituitary failure, untreated	↓	↓	↓	↓	
<b>EUTHYROID</b>					
Euthyroid patient treated with T4	Normal	Varies to ↓	Normal to ↓	↓	Correct dosage determined by clinical effect
Patient taking iodine	Normal	Normal	Normal	↓	
Euthyroid sick syndrome	Normal to ↓	↓	Varies	↓	No clinical evidence of hypothyroidism

Table from: McConnell. *The Nature of Disease*, 2<sup>nd</sup> ed., LWW, 2014

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## Hyperthyroidism

### General Hyperthyroidism

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

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

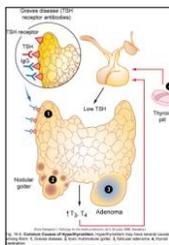


Figure from: Hauber & McCance, *Understanding Pathology*, 5<sup>th</sup> ed., Elsevier, 2012

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## Hypothyroidism

Figures from: Huether & McCance, *Understanding Pathology*, 5<sup>th</sup> 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




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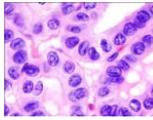
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## Neoplasms of Thyroid

- 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)



From: <http://commons.wikimedia.org>

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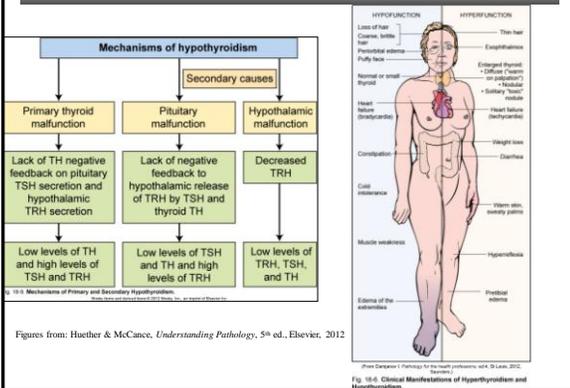
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## Summary of Thyroid Disorders




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## 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
    - Hypercalciuria: kidney stones (Stones)
    - Pathologic fractures (Bones)
    - Peptic ulcers, pancreatitis (Groans)
    - Depression, lethargy, fatigue (Psychiatric overtones)

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## 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

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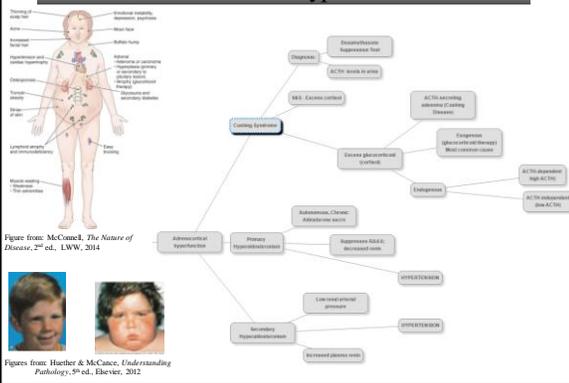
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## Adrenocortical Hyperfunction




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## Pathogenesis of Cushing Syndrome

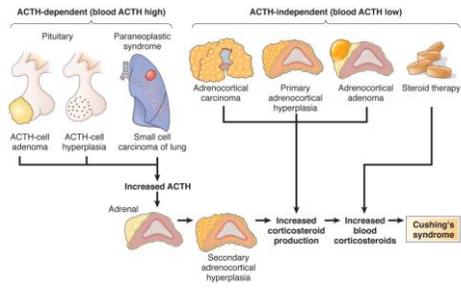


Figure from McConnell, *The Nature of Disease*, 2<sup>nd</sup> ed., LWW, 2014

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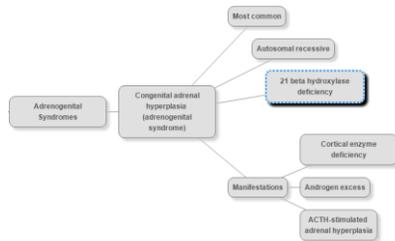
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## Androgenital Syndromes

– Hypersecretion of adrenal androgens and estrogens

- Feminization
- Virilization
- Salt wasting

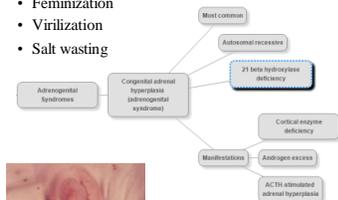


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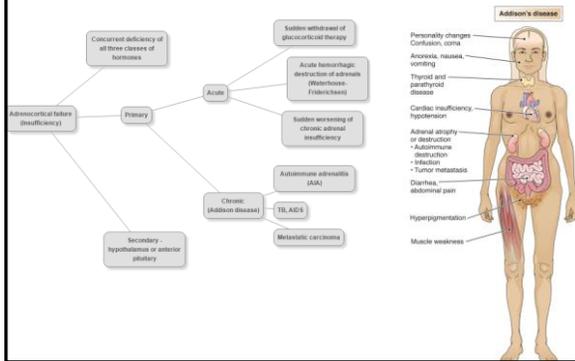
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## Adrenocortical Failure




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## 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

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## 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

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- 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
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