

The Nature of Disease
Pathology for the Health Professions

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Chapter 14
Disorders of the Endocrine Glands
Lecture 14

Overview of Today's Lecture

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

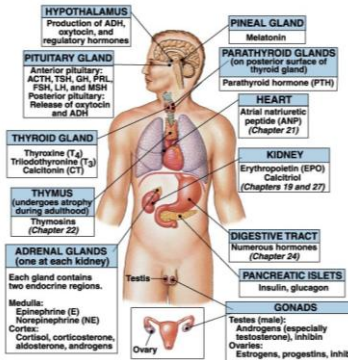
Figure from: McConnell, *The Nature of Disease*, 2nd ed., LWW, 2014

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

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.**

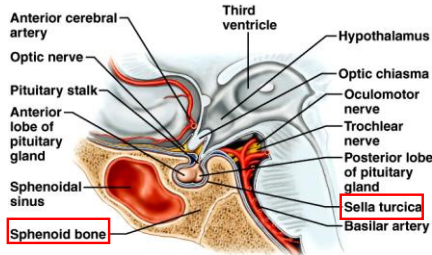
Figure from: Martini, *Anatomy & Physiology*, Prentice Hall, 2001

Pituitary Gland (Hypophysis)

Two distinct portions

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

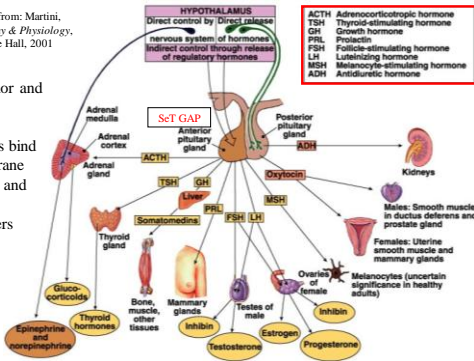
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Overview of the Pituitary Hormones

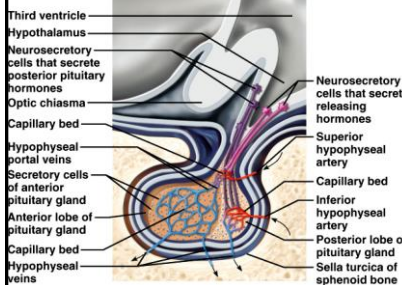
Figure from: Martini, Anatomy & Physiology, Prentice Hall, 2001

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



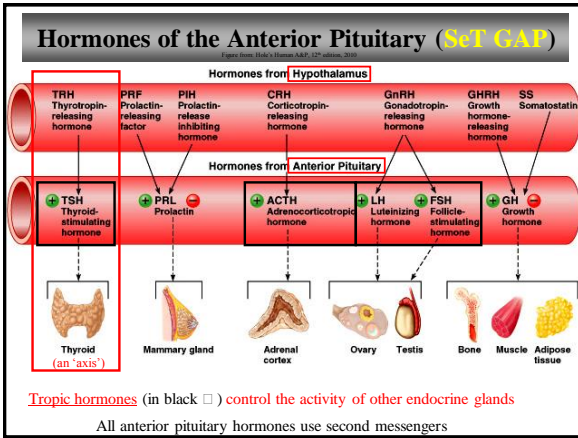
Pituitary Gland Control

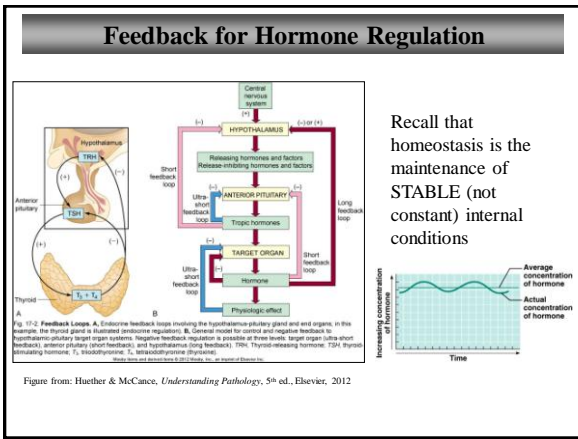
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- Hypothalamic releasing hormones stimulate cells of anterior pituitary to release their hormones
- Nerve impulses from hypothalamus stimulate nerve endings in the posterior pituitary gland to release its hormones

Note the **hypophyseal portal system** (two capillaries in series)





Hormone Summary Table I – Pituitary Hormones

	Tissue					
	Name	Origin	Destination	Action on Target Tissue	Control of Release ^a	
Se	c	Anterior pituitary	FOLLICLE STIMULATING HORMONE (FSH)	males: seminiferous tubules of testes; females: ovarian follicle	males: sperm production; females: follicle/ovum maturation	Gonadotropin Releasing Hormone (GnRH)
			LUTEINIZING HORMONE (LH)	In males: interstitial cells in testes; in females: mature ovarian follicle	males: testosterone secretion; females: ovulation	Gonadotropin Releasing Hormone (GnRH)
T	G	Anterior pituitary	THYROID STIMULATING HORMONE (TSH)	thyroid	secrete hormones	Thyrotropin Releasing Hormone (TRH)
			GROWTH HORMONE (GH)	bone, muscle, fat	growth of tissues	Growth Hormone Releasing Hormone (GHRH)
A	P	Anterior pituitary	ADRENOCORTICOTROPIC HORMONE (ACTH)	adrenal cortex	secrete adrenal hormones	Corticotropin Releasing Hormone (CRH)
			PROLACTIN (PRL)	mammary glands	produce milk	Prolactin Releasing Hormone (PRH)
		Posterior pituitary	ANTI-DIURETIC HORMONE (ADH) (VASOPRESSIN)	Collecting ducts of kidneys	reabsorption of water; increases blood pressure	increase in osmolarity of plasma or a decrease in blood volume
			OXYTOCIN (OT)	uterine smooth muscle; breast	contraction during labor; milk letdown	Stretching of uterus; infant sucking

Hormone Summary Table II

Name	Tissue		Action on Target Tissue	Control of Release
	Origin	Destination		
TRIHODOTHYRONINE (T ₃) & THYROXINE (T ₄)	Thyroid (follicular cells)	all cells	increases rate of metabolism (BMR)	Thyroid Stimulating Hormone (TSH)
CALCITONIN	Thyroid (C cells)	Intestine, bone, kidney	Decreases plasma [Ca ²⁺] (↓ intestinal absorp of Ca; ↓ action of osteoclasts; ↑ excretion of Ca by kidney)	↑ plasma [Ca ²⁺]
PARATHYROID HORMONE (PTH)	Parathyroids	Intestine, bone, kidney	Increases plasma [Ca ²⁺] (↑ intestinal absorp of Ca; ↑ action of osteoclasts; ↓ excretion of Ca by kidney)	↓ plasma [Ca ²⁺]
EPINEPHRINE/ NOREPINEPHRINE (Catecholamines)	Adrenal Medulla	cardiac muscle, atriole and bronchiole smooth muscle, diaphragm, etc	increases heart rate and blood pressure... (fight or flight)	Sympathetic Nervous System
ALDOSTERONE (Mineralocorticoids)	Adrenal Cortex	Kidneys; sweat glands; salivary glands; pancreas	reabsorption of water and Na (increases blood pressure) and excretion of K (mineralocorticoid)	Angiotensin II ↓ plasma [Na ⁺] ↑ plasma [K ⁺]
CORTISOL (Glucocorticoids)	Adrenal Cortex	all cells	Diabetogenic; anti-inflammatory (glucocorticoid)	ACTH
INSULIN	β-cells of Pancreatic Islets	all cells, liver and skeletal muscle	pushes glucose into cells from blood; glycogen formation (decreases blood glucose)	↑ plasma [glucose] SNS
GLUCAGON	α-cells of pancreatic islets	liver and skeletal muscle	breakdown of glycogen (increase in blood glucose)	↓ plasma [glucose]
TESTOSTERONE	Testes	secondary sex organs	development and maintenance	LH
ESTROGEN	Ovaries	secondary sex organs	development at puberty and maintenance throughout life	LH
NATRIURETIC PEPTIDES	atria and ventricles of heart	adrenal cortex, kidneys	increased excretion of sodium and water from kidneys; ↓ blood volume; ↓ blood pressure	Stretching of atria and ventricles

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

Alterations of the Hypothalamic-Pituitary System

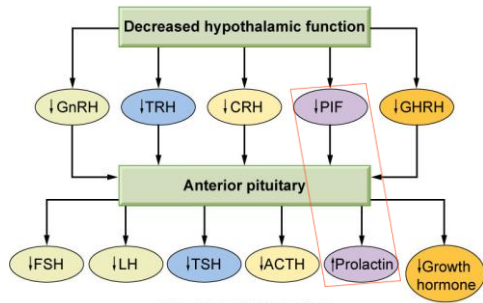


Figure from: McConnell, *The Nature of Disease*, 2nd ed., LWW, 2014

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

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

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)

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

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

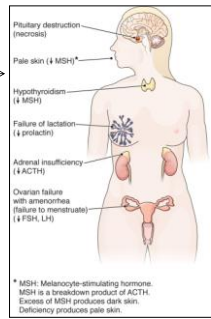


Figure from: McConnell, *The Nature of Disease*, 2nd ed., LWW, 2014

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 (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

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	
THYROTOXICOSIS					
Primary hyperthyroidism, untreated	↑	↑	↓	↑	Thyroid-stimulating immunoglobulin in Graves disease
secondary hyperthyroidism, untreated	↑	↑	↑	↑	
Thyrotoxicosis from overtreatment with T4	↑	↓	↓	↓	
T3 toxicosis	↓	↑	↓	Normal to ↑	Uncommon
HYPOTHYROIDISM					
Primary, untreated	↓	↓	↑	↓	
Secondary to pituitary failure, untreated	↓	↓	↓	↓	
EUTHYROID					
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*, 2nd ed., LWW, 2014

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

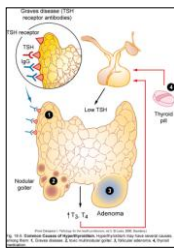


Figure from: Hauber & McCance, *Understanding Pathology*, 5th ed., Elsevier, 2012

Hypothyroidism

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

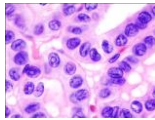
• Hypothyroidism

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



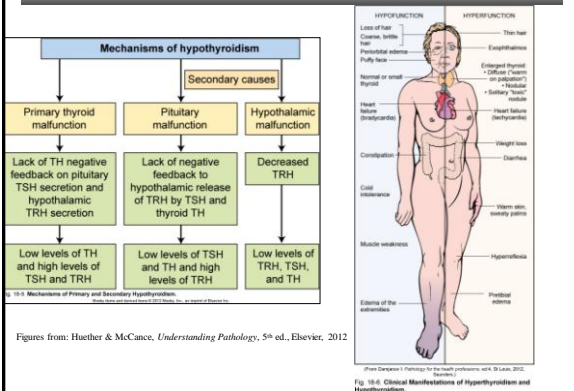
Neoplasms of Thyroid

- 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)



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

Summary of Thyroid Disorders



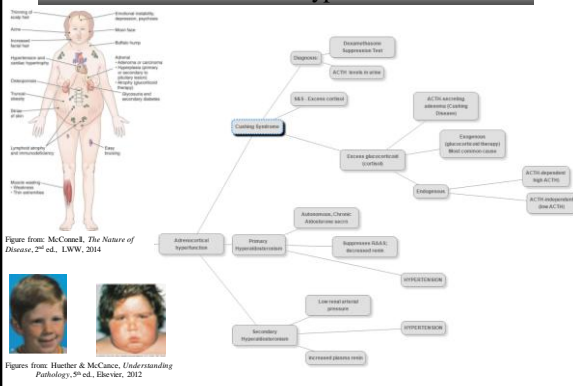
Hyperparathyroidism

- 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
 - Hypercalciuria: 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

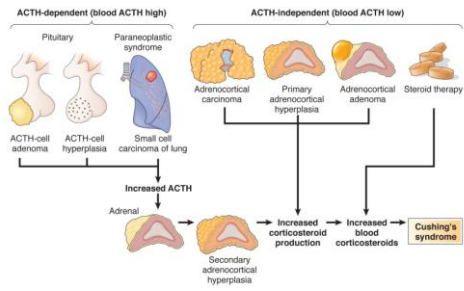
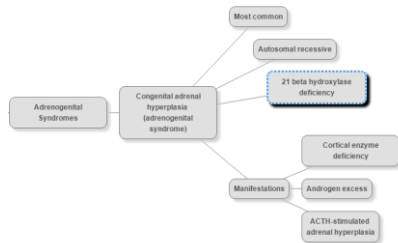


Figure from McConnell. *The Nature of Disease*, 2nd ed., LWW, 2014



Androgenital Syndromes

– Hypersecretion of adrenal androgens and estrogens

- Feminization
- Virilization
- Salt wasting

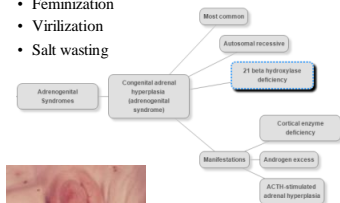
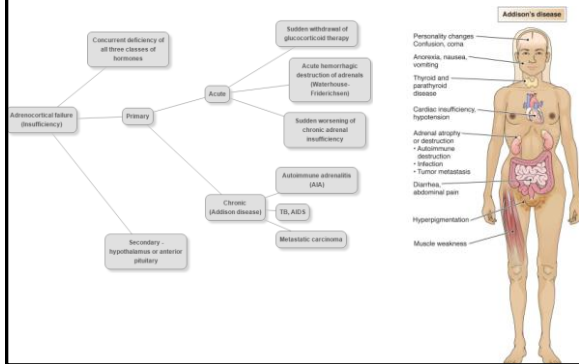


Figure from McConnell. *The Nature of Disease*, 2nd ed., LWW, 2014



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

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

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- MEN-1 syndrome (Wermer)
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 - Several subvarieties according to the glands involved
