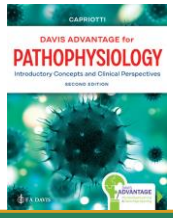

Chapter 24

Endocrine Disorders

1

Basic Concepts

- Endocrine glands secrete chemical messengers (hormones) into bloodstream
- Many endocrine processes involve several tissues
  - Hypothalamus
    - Sends signals to the pituitary gland
  - Anterior pituitary
    - Receives hormonal signals from hypothalamus

2

Basic Concepts (continued)

- Posterior pituitary
  - Releases hormones synthesized by hypothalamus
- End organs
  - Targets for pituitary hormones, may or may not secrete additional hormones

3

Hypothalamic-Pituitary-Hormonal Axis

- Link between hypothalamus-pituitary-end organ
- Pituitary (hypophysis)
  - Anterior pituitary (adenohypophysis)
    - Blood vessel connection with hypothalamus (hypothalamus-hypophyseal portal system)
    - Releases tropic hormones
  - Posterior pituitary (neurohypophysis)
    - Neural connection with hypothalamus
    - Hormones made by hypothalamus, stored and released by posterior pituitary

4

Pituitary as Master Gland

Anterior

- Growth hormone
- Prolactin
- Adrenocorticotropic hormone
- Thyroid-stimulating hormone
- Follicle-stimulating hormone
- Luteinizing hormone

Posterior

- Antidiuretic hormone
  - AKA: arginine vasopressin
- Oxytocin

5

Endocrine Regulation

- Negative feedback mechanism
  - End-product hormone negatively feeds back to prevent further stimulatory signals
    - *Example:* thyroid hormones suppress thyroid-stimulating hormone production
- Receptor activity
  - Upregulation
    - Increased receptor sensitivity and number
  - Downregulation
    - Decreased receptor sensitivity and number

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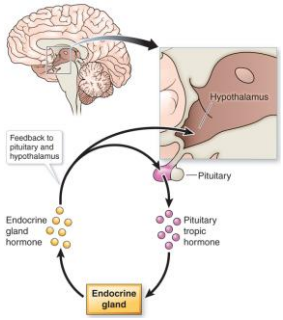
Endocrine Regulation (continued)



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Three Major Types of Endocrine Conditions

- Hormone deficiency
  - Gland destruction
    - Autoimmune, infection, tumor
- Hormone excess
  - Tumor, autoimmune, genetic mutation
- Hormone resistance
  - Usually genetic (lack hormone receptor or ability to respond)

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Endocrine Dysfunction

- Hypofunction
  - Inadequate amount of hormone
- Hyperfunction
  - Excessive amount of hormone
- Three levels of dysfunction
  - Primary
    - Endocrine gland itself
  - Secondary
    - Abnormal pituitary activity
  - Tertiary
    - Dysfunction of hypothalamic origin

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Endocrine Dysfunction Causes

- Autoimmune
  - Antibodies target endocrine gland, may cause hypofunction or hyperfunction
- Neoplasia
  - Hypofunction or hyperfunction of gland itself or any endocrine tissue the gland affects
  - Some cancers: paraneoplastic disorder in which cancer cells secrete hormone-like substances
- Endocrine-disrupting compounds (EDCs)
  - Chemical in environment that can alter endogenous hormone functions

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Assessment of Endocrine Disorders

- Current and past medical history
- Some endocrine disorders present with wide-ranging, multi-system signs and symptoms
- Endocrine dysfunction may affect mood and behavior, can be misinterpreted as psychological issues

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Diagnosis of Endocrine Disorders

- Immunoassays or blood levels of hormones most important
- Urinary hormone levels assessed in some instances
- Urinary collection over 24 hours
- Suppression/stimulation tests
- CT scan/MRI
- Ultrasound

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Treatments of Endocrine Disorders

- Hormone replacement therapy
  - Dosage schedules attempt to mimic physiological effects
  - Glucocorticoids, thyroid hormones, sex steroids, ADH most common replacements
- Suppression of hormone overproduction
  - Medications, surgery, radiation

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Hypopituitarism

- One or more of the pituitary hormones
  - Panhypopituitarism
    - Complete loss of all pituitary hormones
    - Rare
- Causes
  - Pituitary tumor, brain surgery, radiation of brain tumor, congenital disorder
  - Trauma, ischemia, and infarction can cause sudden loss of pituitary function
    - Sheehan's syndrome
      - Develops after childbirth with severe hemorrhage

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Hypopituitarism (continued_1)

- Primary adenoma
  - Most common cause
  - Benign neoplasm
  - With growth can compress pituitary gland in sella turcica
    - Interfere with pituitary function
- Craniopharyngioma
  - Benign neoplasm close to pituitary gland or pituitary stalk

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Hypopituitarism (continued_2)

- Pituitary apoplexy
  - Sudden destruction of the pituitary tissue due to infarction or hemorrhage into gland
  - Traumatic brain injury most common cause
- Sheehan's Syndrome
  - Ischemia or infarction of the pituitary after childbirth because of severe hemorrhage
  - Degree of necrosis correlates with hemorrhage
  - Develop deficiency of ACTH, TSH, FSH, LH, ADH, and PRL

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Other Causes of Hypopituitarism

- Empty sella syndrome
  - Herniation of meningeal membrane compresses pituitary gland against bone
- Traumatic brain injury
- Hypothalamic dysfunction
  - May impair pituitary function

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Signs and Symptoms of Hypopituitarism

- Depend on pituitary hormones suppressed
  - Most serious concerns are adrenal insufficiency, hypothyroidism, and diabetes insipidus
- Age of onset
  - Children with hypopituitarism will have different complications than adults
- If hypopituitarism acute, rapid deterioration of patient

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Signs and Symptoms of Hypopituitarism (continued)

Neonate and infant

- Dwarfism
- Developmental delay
- Various visual and neurological symptoms
- Seizure disorder
- Congenital malformation

Adults

- Weakness
- Weight loss or gain
- Hypotension caused by adrenal insufficiency
- Sluggishness
- Depression
- Excessive urination and dehydration

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Diagnosis

- Blood tests to assess hormone levels
  - Pituitary, hypothalamic, and end-organ levels may be needed
- Corticotropin stimulation test: give ACTH
  - Cortisol levels should rise
    - If cortisol levels rise with ACTH administration: pituitary problem
    - If cortisol levels do not rise with ACTH administration: adrenal gland problem
- MRI, CT scan

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Diabetes Insipidus (DI)

- Posterior pituitary hypopituitarism
- Lack of ADH or response to ADH
- Dilute, large volume urine
  - Plasma concentration increases
- Categories of disease
  - Central DI
    - Lack ADH from the posterior pituitary
  - Nephrogenic DI
    - Kidney fails to respond to ADH
    - Distinguish by administering ADH to see if kidneys can respond, if so, central DI

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Diabetes Insipidus (DI) (continued)

- Signs and symptoms
  - Frequent urination, thirst, dehydration, disorientation, seizures
  - Blood test will show high osmolarity and hypernatremia
  - Urine osmolarity and specific gravity will be low
- Diabetes insipidus differs from diabetes mellitus (no hyperglycemia in DI)
- Treatment
  - ADH administration (if central DI)

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Hyperpituitarism

- Pituitary adenoma
  - Most common cause
  - May produce ACTH, TSH, or GH
  - Prolactinoma most common form: secretes PRL
    - High PRL has antiestrogenic and antiandrogenic effects
- Large tumors may cause headaches and visual disturbances (because of proximity to optic nerves)

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Hyperpituitarism (continued_1)

- Children
  - ACTH-producing adenoma
  - Corticotropinomas, common before puberty
  - Cushing-like symptoms
- GH-secretion adenoma
  - Children
    - Gigantism
  - Adults
    - Acromegaly

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Hyperpituitarism (continued_2)

- Diagnosis
  - Serum hormone levels
  - Urine hormone levels may also be assessed
  - Dexamethasone suppression test to assess ACTH response
- Treatment
  - Depends on elevated hormone
  - Prolactinoma
    - Bromocriptine
  - Transsphenoidal surgery
  - Adrenal enzyme inhibitors
  - GH inhibitors

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Syndrome of Inappropriate ADH (SIADH)

- Excessive ADH
  - Causes: brain injury or neurosurgery
  - Paraneoplastic disorder
- Causes fluid retention
  - Concentrated urine, dilute plasma, hypervolemia
- Treatment
  - Fluid restriction
  - Slow correction of hyponatremia
  - ADH receptor antagonists may be used

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Thyroid

- Triiodothyronine (T3) and thyroxine (T4)
  - Iodine required for synthesis
  - Thyroxine
    - Regulate body metabolism
- Thyroid disorder more common in women
- Primary thyroid disorders most common
- Enlarged thyroid can indicate hypo- or hyperfunction

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Goiter

- Enlargement of the thyroid
- May or may not present with thyroid dysfunction signs and symptoms
- May develop with:
  - Excess TSH
  - Low iodine levels
  - Goitrogens
    - Foods or other substances that promote thyroid gland enlargement

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Hypothyroidism

- Hashimoto's thyroiditis
  - Autoimmune disorder
  - Anti-thyroglobulin antibody and anti-thyroperoxidase antibody
- Other causes
  - Drugs
  - Genetics
  - Thyroiditis (postpartum period especially high incidence)
  - Congenital hypothyroidism: cretinism

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Hypothyroidism: Signs and Symptoms

- Cold intolerance
- Weight gain
- Lethargy
- Fatigue
- Memory deficits
- Poor attention span
- Muscle cramps
- Constipation
- Decreased fertility
- Puffy face
- Hair loss
- Brittle nails

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Systemic Effects of Hypothyroidism

- Hyperlipidemia
- Yellow-orange skin (elevated carotene levels)
- Anemia
- Decreases filtration by kidney
- Pendred's syndrome: defective iodine incorporation into thyroid hormone
- Myxedema: Adult severe hypothyroidism
- Subclinical hypothyroidism: present in elderly

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Diagnosis of Hypothyroidism

- Primary: high TSH, low free T3, low free T4
- Secondary: low TSH, low free T3 and T4
- Hashimoto's thyroiditis antibodies
  - Antithyroglobulin (anti-Tg)
  - Antithyroperoxidase (anti-TPO)
- Ultrasound
- Recommended: thyroid test in women at age 35 and every 5 years after

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Treatment of Hypothyroidism

- Replacement hormone: levothyroxine
- Surgical intervention if necessary
- Myxedema coma
  - Severe hypothyroid condition
  - Will progress to confusion and coma if untreated

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Hyperthyroidism

- Elevated free T3 and free T4
- Graves' disease
  - Most common cause
  - Autoimmune stimulation of the thyroid gland

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Hyperthyroidism (continued)

- Other causes
  - Subacute thyroiditis
  - Thyroid adenoma
  - Excessive TSH
  - Subacute thyroiditis
  - Toxic multinodular goiter
  - Excessive iodine ingestion
    - Jod-Basedow syndrome
  - Secondary to pregnancy, HCG is similar to TSH

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Graves' Disease

- Thyroid-stimulating antibodies
  - Bind to thyrotropin receptors
  - Gland enlargement
  - Continual synthesis thyroid hormones

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Graves' Disease (continued)

- Nervousness
- Insomnia
- Sensitivity to heat
- Weight loss
- Enlarged thyroid gland
- Atrial fibrillation
- Increased HR
- Increased sympathetic nervous system sensitivity
- Exophthalmos
  - Wide-eyed stare
  - Extraocular area filled with mucopolysaccharides
  - Graves ophthalmopathy
    - Periorbital edema and bulging of the eyes

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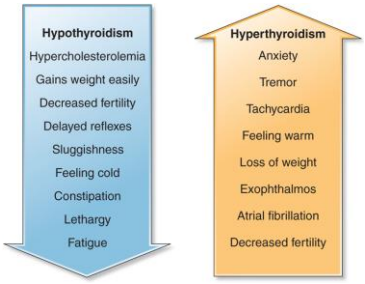
Hypothyroidism vs. Hyperthyroidism



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Hyperthyroidism Diagnosis

- Primary: low TSH, high free T3 and T4
- Secondary: high TSH, high free T3 and T4
- Antibodies for Graves' disease
  - Anti-thyroid peroxidase (anti-TPO)
  - Thyroid stimulating immunoglobulin
- Ultrasound with color-Doppler evaluation
- Radioactive iodine scanning and iodine uptake

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Treatment of Hyperthyroidism

- Antithyroid hormone medication propylthiouracil (PTU)
- Radioactive iodine treatment
- Surgery
  - If gland removed, replacement thyroid hormone (levothyroxine) needed for life

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Thyrotoxic Crisis (Thyroid Storm)

- *Overwhelming* release of thyroid hormones
- Stimulate metabolism
  - High fever, tachycardia, agitation, psychosis
- Often precipitated by surgery or trauma
- Medical emergency

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Thyroid Nodules

- Most asymptomatic
- Hypothyroidism or hyperthyroidism
  - Single nodule
    - Increased malignancy risk
  - Multiple nodules
    - Often benign

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Thyroid Nodules (continued)

- Ultrasound and needle biopsy for diagnosis
- Technetium scan
  - Uses radioactive isotope
  - Hot nodule
    - Hyperfunctioning tumor
  - Warm nodule
    - Normal tissue
  - Cold nodule
    - Hypofunctional tissue, sometimes malignant

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Malignant Thyroid Nodule

- Age younger than 20 years or older than 70 years
- Male sex
- History of neck irradiation
- Firm, hard, or immobile nodule
- Presence of cervical lymphadenopathy

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Parathyroid Gland

- Four pea-sized glands on posterior thyroid
- Secrete PTH (parathyroid hormone)
  - Released when blood calcium low
  - Activate bone resorption, intestinal calcium absorption by kidneys

45

Hypoparathyroidsm

- Rare
- Inadvertent damage with thyroid surgery, genetic disorders
- Presentation due to hypocalcemia
  - Trousseau's sign, Chvostek's sign
  - Muscle cramps, tetany
  - Convulsion
- Treatment
  - Replacement PTH, normalize serum calcium

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Hyperparathyroidism

- Usually due to parathyroid adenoma
- Primary
  - Elevated PTH and calcium
- Secondary
  - Elevated PTH, low to normal calcium
  - Any disorder that causes hypocalcemia can induce secondary hyperparathyroidism

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Hyperparathyroidism (continued)

- Presentation due to excess calcium
  - Muscle weakness
  - Poor concentration
  - Neuropathies
  - Kidney stones
  - Osteopenia
  - Pathological fractures
- Treatment
  - Surgery
  - Reduce serum calcium

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The Adrenal Gland: Cortex and Medulla

Medulla

- Glucocorticoids
  - Cortisol
- Androgens
- Mineralocorticoids
  - Aldosterone

Cortex

- Epinephrine
- Norepinephrine

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Adrenal Insufficiency

- Secondary
  - Decreased ACTH
- Primary
  - AKA: Addison's disease
  - Autoimmune destruction adrenal cortex
    - Antibodies to adrenal cortex
    - Antibodies to steroid enzymes

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Hypoadrenalism and Glucocorticoids

- Hypoadrenalism can also be due to exogenous glucocorticoids
  - With prolonged glucocorticoid use, CRF-ACTH signals to adrenal cortex suppressed
  - Adrenal gland down regulates receptors
  - Steroid usage should not be abruptly stopped
    - Individual may be unable to respond to stressor
- Smallest dosage of steroid needed should be given to patient to lessen adrenal atrophy

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Adrenal Insufficiency Symptoms

- Weakness
- Hypotension
- Easy fatigue
- Emotional lability
- Anorexia
- Hypoglycemia
- Electrolyte imbalances
  - Hyponatremia
  - Hyperkalemia
- Tanned appearance due to melanocyte-stimulating hormone (MSH)
- ACTH and MSH arise from same precursor molecule
- Women
  - Loss of pubic and axillary hair
  - Amenorrhea

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Adrenal Insufficiency (continued)

- Diagnosis
  - Rapid ACTH test
    - With ACTH administration, cortisol should rise within 30 minutes
    - No cortisol rise: adrenal cortex insufficiency
- Treatment
  - Daily replacement of glucocorticoid and mineralocorticoid
  - Parenteral steroid coverage in times of major stress, trauma, surgery

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Hyperadrenalism

- AKA: hypercortisolism
  - Cushing's disease
    - Elevated ACTH, tumor in pituitary
  - Cushing's syndrome
    - Elevated cortisol, hyperfunction of adrenal cortex
- *Exogenous steroids most common cause of Cushing's syndrome*

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Hyperadrenalism (continued)

- Causes
  - Pituitary adenoma
    - Cushing's disease
  - Cushing's syndrome
    - Adrenal hyperplasia, adrenal neoplasm
    - Carney complex
      - Genetic disorder
    - McCune-Albright syndrome
      - Cushing's syndrome and precocious puberty
    - Secretion of ACTH from tumors

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Hyperadrenalism Signs and Symptoms

- Weight gain
- Redistribution of body fat to the face, trunk, and abdomen
- Puffy face called "moon facies"
- Extra subcutaneous fat in the cervicothoracic area called "buffalo hump"
- Increase in the waist-to-hip circumference ratio
- Striae
- Easy bruising and poor wound healing
- Women
  - Hirsutism
  - Male pattern hair growth
  - Amenorrhea

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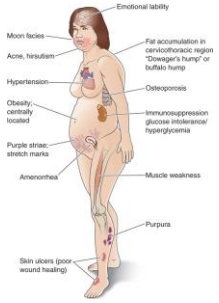
Hyperadrenalism Signs and Symptoms (continued)



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Effects of High Cortisol Levels

- Block the action of insulin
  - Glucose intolerance and hyperglycemia
- Inhibit bone formation and accelerates bone reabsorption
  - Osteopenia, osteoporosis
- Suppress immune response
- Hypertension

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Diagnosis of Hyperadrenalism

- Serum levels
  - Elevated WBCs, hyperglycemia, hypokalemia
- Salivary levels of cortisol, 24-hour urine cortisol
- Dexamethasone suppression test
  - Administer dexamethasone
  - Serum cortisol should be suppressed
  - Cushing's syndrome: no cortisol suppression with dexamethasone
- MRI, CT scan

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Treatment of Cushing's Syndrome

- Surgery
- Ketoconazole
  - Suppress cortisol

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Pheochromocytoma

- Adrenal medulla tumor
  - Secrete norepinephrine and epinephrine
  - Excessive sympathetic stimulation
- Hypertension, tremors, increased cardiac contractility, cardiac arrhythmias, tachycardia
- Diagnosis
  - 24-hour urine for catecholamine metabolites

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Multiple Endocrine Neoplasia (MEN)

- Several forms
- MEN1 is most common
- Defective tumor suppressor gene
- Allows tumor growth in several different endocrine glands
  - Parathyroid, pituitary, and pancreas most commonly affected

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Pineal Gland Dysfunction

- Produces melatonin with the phases of the light-dark cycle
- Tumor may place pressure on adjacent brain structures
  - Blockage of cerebrospinal fluid (CSF) flow
- Symptoms include headache, nausea and vomiting, seizures, memory disturbances, and visual changes

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