Diseases of the Endocrine Glands – Introduction

The Endocrine System

Definition: The endocrine system consists of glands and organs that synthesize and secrete hormones directly into the bloodstream to regulate target tissues, including:

- Metabolism
- Growth and development
- Reproduction
- Mood and stress response
- Fluid, electrolyte, and glucose balance

Unlike the nervous system (which uses electrical signals for rapid communication), the endocrine system acts slowly but persistently to maintain homeostasis.

Major Endocrine Glands:

The key endocrine glands include:

Gland	Main Hormones	Primary Functions
Hypothalamus	TRH, CRH, GnRH, ADH, oxytocin	Controls pituitary; links brain to endocrine system
Pituitary	TSH, ACTH, FSH, LH, GH, prolactin, ADH	"Master gland"—regulates other endocrine organs
Thyroid	T3, T4, calcitonin	Controls metabolism, heart rate, temperature
Parathyroids	Parathyroid hormone (PTH)	Regulates calcium and phosphate
Adrenals	Cortisol, aldosterone,	Stress response, blood pressure,

	adrenaline	salt balance
Pancreas (islets)	Insulin, glucagon	Blood sugar regulation
Gonads	Testosterone (testes), estrogen/progesterone (ovaries)	Sexual development, reproduction

Note: ADH and oxytocin are made in the hypothalamus but stored/released from the posterior pituitary.

Key Hormone Types:

- Peptide/protein hormones (e.g., insulin, ACTH): act via cell surface receptors → activate second messengers
- Steroid hormones (e.g., cortisol, estrogen): lipid-soluble → cross membranes → bind intracellular receptors → affect gene transcription
- Amine hormones (e.g., T3/T4, epinephrine): derived from tyrosine; T3/T4 act like steroids, catecholamines act like peptides

Principles of Endocrine Regulation:

1. Negative Feedback Loops

- Most common (e.g., HPA axis: CRH → ACTH → cortisol → inhibits CRH/ACTH)
- Maintains hormonal homeostasis

2. Positive Feedback (rare)

- Example: LH surge during ovulation

3. Pulsatile Secretion

- Hormones often released in pulses (e.g., GnRH); disruption → pathology (e.g., hypothalamic amenorrhea)

4. Circadian Rhythms

- Cortisol peaks in the morning; melatonin at night

Core Principles of Endocrine Physiology:

Understanding disease starts with understanding normal control:

1. Hormone Regulation via Feedback Loops

- Most endocrine axes use negative feedback: Example: High thyroid hormone (T4) → tells pituitary to reduce TSH.
- Disruption leads to disease (e.g., low T4 + high TSH = primary hypothyroidism).

2. General Mechanisms of Endocrine Disease

Category	Examples
Hypofunction	Autoimmune destruction (e.g., Hashimoto's, T1DM), surgical removal, infarction (Sheehan syndrome), enzyme defects
Hyperfunction	Adenomas (e.g., pituitary prolactinoma), autoimmune stimulation (Graves'), ectopic hormone production (e.g., ACTH from lung cancer)
Hormone Resistance	Type 2 DM (insulin resistance), androgen insensitivity syndrome
Receptor/Post-receptor Defects	Pseudohypoparathyroidism (end-organ resistance to PTH)
Iatrogenic Causes	Exogenous steroid use → adrenal suppression

3. Common Causes of Endocrine Disorders

- Autoimmune (most common—e.g., type 1 diabetes, Graves', Addison's)
- Tumors (benign or malignant—e.g., pituitary adenoma, pheochromocytoma)
- Genetic/congenital (e.g., congenital adrenal hyperplasia)
- Iatrogenic (e.g., steroid-induced Cushing's syndrome)
- Infiltrative diseases (e.g., hemochromatosis damaging the pancreas)

Clinical Approach to Endocrine Disorders:

A. Common Presentations

- Metabolic: weight change, fatigue, glucose abnormalities
- Reproductive: amenorrhea, infertility, libido changes
- Growth: short stature, gigantism, acromegaly
- Electrolyte disturbances: hyponatremia (SIADH), hypercalcemia (hyperparathyroidism)
- Pigmentation changes: hyperpigmentation (Addison's), vitiligo (autoimmune polyglandular syndromes)

B. Diagnostic Strategy

1. **Clinical suspicion based on signs/symptoms**

2. **Initial hormone testing:**

- ✓ Measure peripheral hormone and upstream regulator (e.g., TSH + free T4; cortisol + ACTH)

3. **Dynamic testing if basal levels inconclusive:**

- ✓ Stimulation (e.g., ACTH stimulation test for adrenal insufficiency)
- ✓ Suppression (e.g., dexamethasone suppression test for Cushing's)

4. Imaging:

- ✓ Ultrasound (thyroid), CT/MRI (adrenals, pituitary)

5. Autoantibodies:

- ✓ TPO antibodies (Hashimoto's), TSH receptor antibodies (Graves')

C. Localization of Lesion

- Primary: problem in the gland itself → abnormal hormone ± compensatory change in upstream hormone
  - ✓ Example: Primary hypothyroidism → ↑ TSH, ↓ T4
- Secondary: problem in pituitary → ↓ stimulating hormone → ↓ target hormone
  - ✓ Example: Secondary adrenal insufficiency → ↓ ACTH, ↓ cortisol
  - ✓ Tertiary: hypothalamic dysfunction → ↓ releasing hormone → ↓ pituitary hormone → ↓ target hormone