SAQs File

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلّ الجهل طوال حياتهِ }

References:

Team work, Pathoma, First Aid Step 1 & Kaplan Pathology Lecture Notes.

Thyroglossal cyst:

A fibrous cyst that forms from a persistent thyroglossal duct. Presents as an anterior midline neck mass that moves with swallowing or protrusion of the tongue.

Hyperthyroidism:

- ↑ level of circulating thyroid hormone
  - ↑ basal metabolic rate (due to increased synthesis of Na+-K+ ATPase)
  - ↑ sympathetic nervous system activity (due to increased expression of receptors).
- Clinical features include:
  - Weight loss despite increased appetite & Heat intolerance and sweating.
  - Tachycardia with ↑ cardiac output.
  - Arrhythmia (e.g., atrial fibrillation), especially in the elderly.
  - Tremor, anxiety, insomnia, and heightened emotions.
  - Staring gaze with lid lag & Diarrhea with malabsorption.
  - Oligomenorrhea.
  - Bone resorption with hypercalcemia (risk for osteoporosis).
  - Decreased muscle mass with weakness & Hypocholesterolemia.
  - Hyperglycemia (due to gluconeogenesis and glycogenolysis).

TABLE 2-12. Causes of Hyperthyroidism

Cause	Etiology	Clinical Manifestations
Graves disease	▪ Thyroid-stimulating immunoglobulin (TSI) binds TSH receptor on thyroid gland → ↑ T_3/T_4 (diffuse uptake on thyroid scan). Type II hypersensitivity. ▪ Can be associated with other autoimmune disorders.	▪ Diffuse nontender goiter with or without bruit. ▪ Infiltrative ophthalmopathy (exophthalmos, extraocular muscle dysfunction). ▪ Pretibial myxedema.
Toxic multinodular goiter (Plummer disease)	▪ Hyperfunctioning areas that make ↑ T_3/T_4 (patchy uptake on thyroid scan). ▪ Due to a mutation in the TSH receptor. ▪ More common in the elderly.	▪ Similar to Graves disease, but less severe.
Subacute thyroiditis (de Quervain thyroiditis)	▪ Inflammation of thyroid gland → spilling of preformed thyroid hormones → transient hyperthyroidism. Pituitary inhibition causes transient hypothyroidism before return to euthyroid state. ▪ Usually preceded by upper respiratory infection.	▪ Thyroid gland firm, painful, tender. ▪ Fever. ▪ ↑ ESR. ▪ Pain radiating to ears, neck, and arm.
Struma ovarii	This is a very rare condition in which ectopic thyroid tissue develops as part of an ovarian tumor, causing hyperthyroidism.	

CHF = congestive heart failure; ESR = erythrocyte sedimentation rate; TSH = thyroid-stimulating hormone.

Graves Disease:

- Autoantibody (IgG) that stimulates TSH receptor (type II hypersensitivity)
- Leads to increased synthesis and release of thyroid hormone.
  - Most common cause of hyperthyroidism
  - Classically occurs in women of childbearing age (20- 40 years)
- **Clinical features include**
  - Hyperthyroidism
  - Diffuse goiter: Constant TSH stimulation leads to thyroid hyperplasia and hypertrophy.
  - Exophthalmos and pretibial myxedema:
    ⇒ Fibroblasts behind the orbit and overlying the shin express the TSH receptor.
    ⇒ Irregular follicles with scalloped colloid and chronic inflammation are seen on histology.
- **Laboratory findings include**
  - ↑ total and free T4; TSH (free T downregulates TRH receptors in the anterior pituitary to decrease TSH release).
  - Hypocholesterolemia & ↑ serum glucose.
- Treatment involves beta-blockers, thioamide, and radioiodine ablation.
- **Thyroid storm is a potentially fatal complication.**
  - Due to elevated catecholamines and massive hormone excess, usually in response to stress (e.g., surgery or childbirth)
  - Presents as arrhythmia, hyperthermia, and vomiting with hypovolemic shock
  - Treatment is propylthiouracil (PTU), beta-blockers, and steroids.

Multinodular Goiter:

- Enlarged thyroid gland with multiple nodules.
- Due to relative iodine deficiency, Usually nontoxic (euthyroid).
- Rarely, regions become TSH-independent leading to T release and hyperthyroidism ('toxic goiter').

Hypothyroidism:

Over 95% of cases of hypothyroidism result from failure of the thyroid gland itself (primary hypothyroidism).

Presentation:

⇒ Lethargy, fatigue, muscle weakness.
⇒ Cold intolerance, constipation, weight gain, coarse/dry skin, macroglossia.
⇒ Delayed recovery phase of deep tendon reflexes.
⇒ Slow mentation.
⇒ Diastolic hypertension.

⇒ **Myxedema coma:** Stupor, coma, and hypoventilation coupled with hypothermia, bradycardia, and hypotension. A life-threatening hypothyroid condition that results from long-standing, untreated hypothyroidism. Triggered by trauma, infections, and cold exposure. Treatment is with hormone replacement and supportive measures; mortality is high.

TABLE 2-13. Common Causes of Hypothyroidism

PRIMARY CAUSES	
Hashimoto thyroiditis	Autoimmune in origin (HLA-DR5). Antithyroid peroxidase antibodies confirm the diagnosis. Lymphocytic infiltrate with germinal centers seen on histology, as well as Hurthle cells.
Subacute (de Quervain) thyroiditis	Self-limited hypothyroidism following a flu-like illness. May have elevated ESR, jaw pain, and a tender thyroid gland. Histology shows granulomatous inflammation. Hyperthyroid earlier in course.
Iodine deficiency	Most common cause in the developing world.
Riedel thyroiditis	Rare disease in which thyroid tissue is chronically replaced by fibrosis. Rock-hard, fixed, painless goiter.
Lithium	Lithium toxicity may cause hypothyroidism.
Surgical resection and ^{131}I treatment	Surgical removal or radioactive iodine ablation may cause hypothyroidism.
SECONDARY CAUSE	
Sheehan syndrome	Postpartum pituitary necrosis secondary to postpartum hemorrhage. Decreased TSH.

ESR = erythrocyte sedimentation rate; TSH = thyroid-stimulating hormone.

TABLE 2-14. Signs and Symptoms of Abnormal Thyroid Hormone Levels

	HYPERTHYROIDISM	HYPOTHYROIDISM
Symptoms	Hyperactivity, irritability	Mental sluggishness
	Heat intolerance, sweating	Cold intolerance
	Palpitations	Dyspnea
	Fatigue, weakness	Fatigue, weakness
	Diarrhea	Constipation
	Hair loss, oily skin	Hair loss, dry skin
	Oligomenorrhea, loss of libido	Menorrhagia, loss of libido
	Weight loss, robust appetite	Weight gain, poor appetite
	Polyuria	Paresthesias
Signs	Tachycardia	Bradycardia
	Tremor	Delayed deep tendon reflex relaxation phase
	Goiter	Goiter
	Warm, moist skin	Dry, doughy skin
	Proximal muscle weakness	Carpal tunnel syndrome
	Exophthalmos	Periorbital edema
	Lid retraction, lid lag	Puffy face, hands, and feet (myxedema)
		Peripheral edema

TABLE 2-15. Types of Thyroid Cancer

Type	Prevalence (%)	Characteristics	Treatment
Papillary carcinoma	70–80%	▪ History of radiation exposure increases risk. ▪ Slow-growing, spreads by lymphatics in the neck. ▪ "Orphan Annie" nuclei (cells in papillary cancer have dispersed chromatin, giving appearance of empty nuclei). ▪ Psammoma bodies (concentric calcification of individual necrotic tumor cells).	Lobectomy or total thyroidectomy ± radioiodine
Follicular carcinoma	10–20%	▪ More aggressive than papillary carcinomas. ▪ Tends to invade into blood vessels → spreads to bone, lung, and liver (lymph node involvement rare).	Total thyroidectomy + postoperative iodine ablation
Medullary carcinoma	5%	▪ Arises from parafollicular "C" cells of thyroid. ▪ Produces calcitonin (can be used as tumor marker). ▪ Amyloid deposits (derived from altered calcitonin molecules). ▪ Associated with the MEN 2A and MEN 2B syndromes.	Total thyroidectomy
Anaplastic carcinoma	5%	▪ Older patients. ▪ Highly aggressive. Poor prognosis (death within a few months).	Chemotherapy and radiation

MEN = multiple endocrine neoplasia.

Adrenal Gland (Lecture 3)

Cushing syndrome:

Characterized by increased levels of glucocorticoids. It is investigated with lab and imaging studies (*see* Physiology Lecture Notes). The most com- mon cause is exogenous glucocorticoid administration. Endogenous causes include:

⇒ Cushing disease (hypersecretion of ACTH, usually due to a pituitary micro-adenoma)
⇒ Secretion of ACTH from nonpituitary tumors (e.g., small cell lung cancer)
⇒ ACTH-independent Cushing syndrome due to adrenal neoplasia Clinical manifestations include hypertension, weight gain (truncal obesity, "buffalo hump" and moon facies), cutaneous striae, hirsutism and mental disturbances.

Hyperaldosteronism may cause hypertension and hypokalemia.

- **Primary** (decreased plasma renin)
  - Adrenocortical neoplasm: adenoma (Conn syndrome)
    - Circumscribed yellow nodule with vacuolated cells
    - Carcinoma: poorly demarcated lesion with cystic change and pleomorphic cells
  - Bilateral nodular hyperplasia of the adrenal
- **Secondary** (increased plasma renin) (e.g., renal artery stenosis)

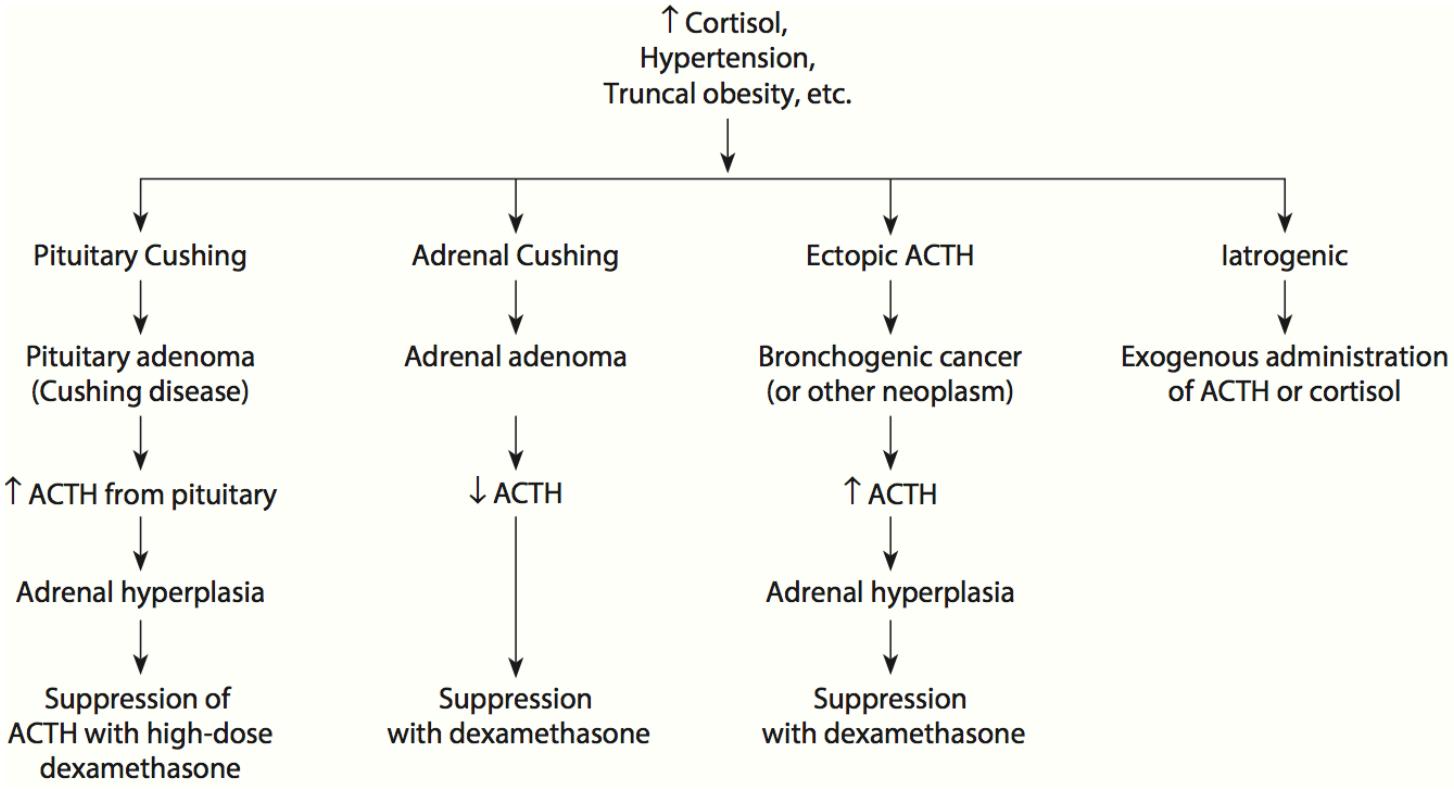
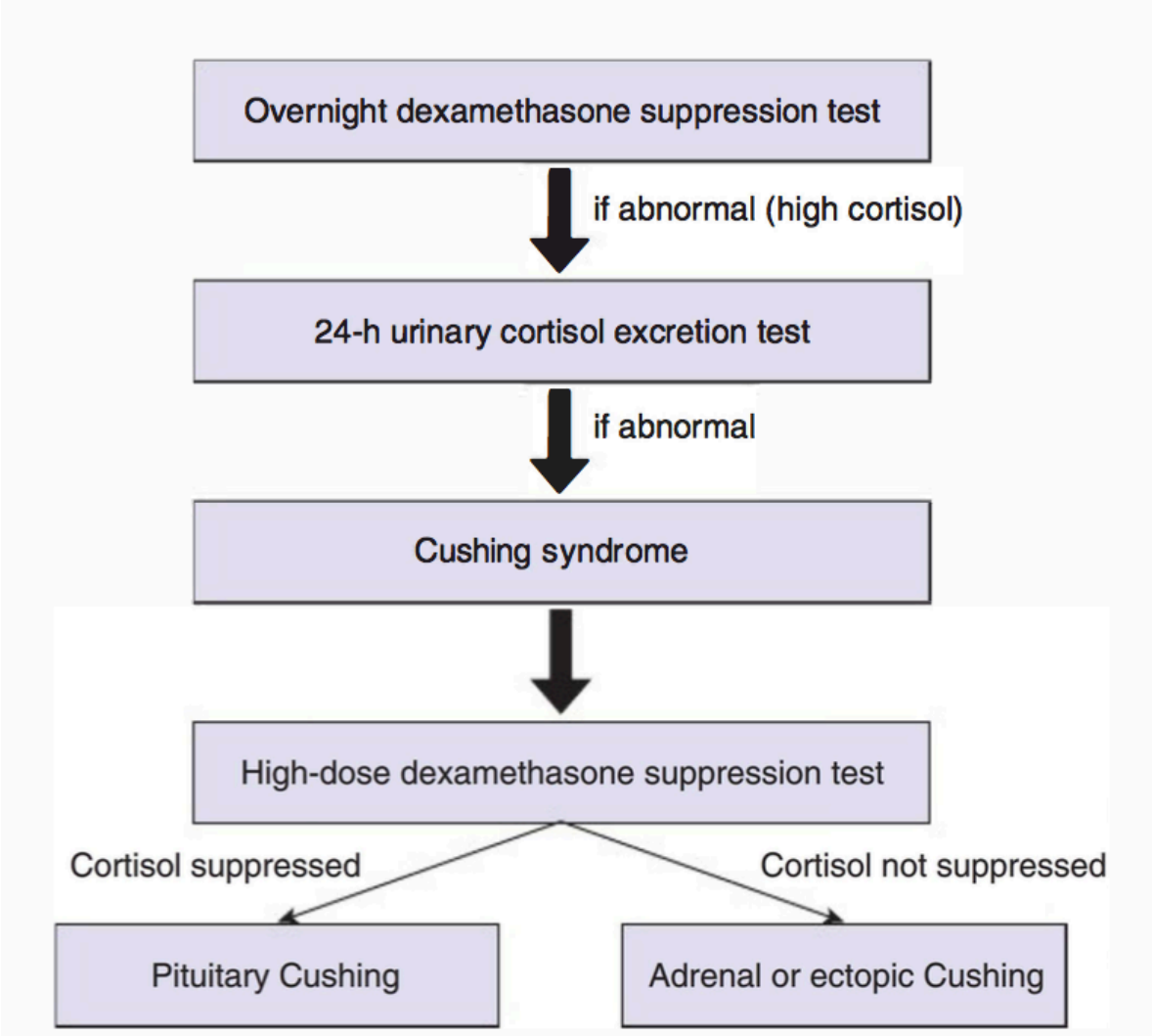


Figure 25-3. Cushing Syndrome and Its Effects



2-27. Diagnosis of Cushing syndrome.

Primary Hyperaldosteronism (Conn Syndrome):

Caused by excess secretion of aldosterone, resulting in increased sodium reabsorption and potassium secretion.

- Primary aldosteronism is most commonly due to a benign adenoma in the zona glomerulosa.
- Secondary causes include:
  - Renin-secreting tumors, renovascular disease and malignant hypertension.
  - Edematous state with decreased arterial volume (congestive heart failure [CHF], cirrhosis, nephrotic syndrome).
  - Diuretics & Excess non-aldosterone mineralocorticoid due to exogenous mineralocorticoids, CAH, and excessive ingestion of licorice (leads to build-up of precursors of cortisol).

Presentation:

- Sodium and water retention causes hypertension.
- Severe hypokalemia causes symptoms of muscle weakness and can cause arrhythmia.
- Excess aldosterone causes increased Na reabsorption and increased K+ and H- secretion mild hypernatremia, hypokalemia, and metabolic alkalosis.

Diagnosis:

Screen for hypertension.

Addison Disease:

Results from adrenal gland failure and is most commonly due to autoimmune destruction of the adrenal glands.

- **Primary causes** include **infection** (TB, cytomegalovirus, histoplasmosis, or disseminated meningococcemia in Waterhouse-Friderichsen syndrome), **vascular disorders** (hemorrhage or infarction), **metastasis**, **infiltrative disease** (hemochromatosis, amyloidosis, or sarcoidosis), and **drugs** such as ketoconazole and rifampin.
- **Secondary cortisol deficiency** results from **abrupt withdrawal** of corticosteroids or any cause of primary or secondary panhypopituitarism leading to decreased ACTH secretion.

Presentation:

- Weakness, fatigue, anorexia, nausea/vomiting, orthostasis, hyponatremia, and hypoglycemia, which stem from decreased cortisol and mineralocorticoid deficiency.
- Increased ACTH in primary adrenal insufficiency leads to skin hyperpigmentation (due to increased MSH) and hyperkalemia; decreased aldosterone leads to hypotension (due to salt loss), weakness, and hypoperfusion.

Secondary adrenocortical insufficiency:

May be caused by disorders of the hypothalamus or pituitary (cancer or infection, for example). Since ACTH levels are low, hyperpigmentation does not occur.

Pheochromocytoma:

("dark/dusky-colored tumor") is an uncommon benign tumor of the adrenal medulla, which produces catecholamines (norepinephrine and epinephrine). It can present with sustained or episodic hypertension and associated severe headache, tachycardia, palpitations, diaphoresis, and anxiety.

- **Note the rule of 10s:**
  - 10% occur in **children** • 10% are **bilateral** • 10% are **malignant**
  - 10% are **familial (MEN 2A and 2B)** • 10% occur **outside the adrenal gland**
- Urinary vanillylmandelic acid (VMA) and catecholamines are elevated.
- Microscopically, the tumor shows nests of cells (Zellballen) with abundant cytoplasm.
- Treatment is control of the patient's BP and surgical removal of the tumor.

Diabetes (Lectures 4 & 5)

Type 1	Type 2
Usually before 30	After 30
Abrupt; symptomatic (polyuria, polydipsia, dehydration); often severe with ketoacidosis	Gradual; usually subtle
Normal weight; recent weight loss is common	Overweight
Genetics <20%	>60%
Monozygotic Twins 50% concordant	90% concordant
HLA Association, ABS to islet cell AG +	No
Histopathology: Early—inflammation | Late—atrophy and fibrosis	Histopathology: Late- Fibrosis, amyloid
B-cell mass: Markedly reduced	Normal or slightly reduced
Insulin levels: Markedly reduced	Elevated or normal

TABLE 2-27. DM-1 and DM-2

Feature	DM-1	DM-2
Percentage of DM cases	10%	90%
Prevalence	0.2–0.5%	2–4%
Age of onset	< 30	> 40
Pathogenesis	Family history uncommon; HLA-B8, -B15, -DR3, and -DR4 association; autoimmune islet β-cell destruction	Family history common (90–100% concordance rate for identical twins)
Body habitus	Thin	Obese (fat reduces number of insulin receptors)
Treatment	Insulin	Diet; oral hypoglycemic drugs; insulin
Dreaded complications	Diabetic ketoacidosis	Hyperosmolar nonketotic coma

DM = diabetes mellitus; HLA = human leukocyte antigen.

Table 19–6 Type 1 Versus Type 2 Diabetes Mellitus

Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus
Clinical	
Onset usually in childhood and adolescence	Onset usually in adulthood; increasing incidence in childhood and adolescence
Normal weight or weight loss preceding diagnosis	Vast majority of patients are obese (80%)
Progressive decrease in insulin levels	Increased blood insulin (early); normal or moderate decrease in insulin (late)
Circulating islet autoantibodies	No islet autoantibodies
Diabetic ketoacidosis in absence of insulin therapy	Nonketotic hyperosmolar coma
Genetics	
Major linkage to MHC class I and II genes; also linked to polymorphisms in *CTLA4* and *PTPN22*	No HLA linkage; linkage to candidate diabetogenic and obesity-related genes
Pathogenesis	
Dysfunction in regulatory T cells (Tregs) leading to breakdown in self-tolerance to islet autoantigens	Insulin resistance in peripheral tissues, failure of compensation by beta cells Multiple obesity-associated factors (circulating nonesterified fatty acids, inflammatory mediators, adipocytokines) linked to pathogenesis of insulin resistance
Pathology	
Autoimmune "insulitis"	*Early*: inflammation; *late*: amyloid deposition in islets
Beta cell depletion, islet atrophy	Mild beta cell depletion

HLA, human leukocyte antigen; MHC, major histocompatibility complex.

Complications:

Vascular pathology:

Diabetes is a major risk factor for atherosclerosis and its complications, including myocardial infarction (most common cause of death), stroke (CVA), and peripheral vascular disease. The vascular disease can lead to atrophy of skin and loss of hair of the lower extremities, claudication, non-healing ulcers, and gangrene of lower extremities.

Diabetic nephropathy:

Includes glomerular lesions, arteriolosclerosis, and pyelonephritis.

Diabetic retinopathy:

Nonproliferative retinopathy is characterized by microaneurysms, retinal hemorrhages, and retinal exudates. Proliferative retinopathy is characterized by neovascularization and fibrosis. Diabetics also have an increased incidence of cataracts and glaucoma.

Diabetic neuropathy:

Can cause peripheral neuropathy, neurogenic bladder, and sexual impotence.

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قال صلى الله عليه وسلم: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق