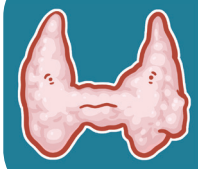

NOTES
HYPERTHYROIDISM & HYPOTHYROIDISM

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Imbalance in thyroid hormones triiodothyronine (T_3), thyroxine (T_4) → alterations in metabolism

CAUSES

Hyperthyroidism

- Thyroid gland hyperfunction → overproduction of thyroid hormones
  - *Primary*: dysfunction of thyroid gland
  - *Secondary*: ↑ thyroid-stimulating hormone (TSH) secretion by pituitary gland

Hypothyroidism

- Thyroid hormone deficiency
  - *Primary*: dysfunction of thyroid gland
  - *Central (secondary)*: pituitary/hypothalamic gland dysfunction → ↓ thyrotropin-releasing hormone (TRH)/TSH

COMPLICATIONS

- *Hyperthyroidism*: thyroid storm
- *Hypothyroidism*: myxedema, cretinism (infants, young children)

SIGNS & SYMPTOMS

- *Hyperthyroidism*: hypermetabolic state, related to sympathetic nervous system stimulation
- *Hypothyroidism*: hypometabolic state

DIAGNOSIS

DIAGNOSTIC IMAGING

Radioiodine uptake scan (RAIU)

- Measures thyroid function
  - Ability to absorb radioactive iodine (^{123}I)

Ultrasound

- Size of thyroid; characteristics of nodules/cysts

Color flow Doppler sonography (CFDS)

- Thyroid blood flow velocity, vascularity

LAB RESULTS

- Serum levels of TSH, total T_4, free (unbound) T_4, total T_3, thyroid-stimulating immunoglobulins (TSI), TSH-receptor antibodies (TRAb)

TREATMENT

MEDICATIONS

Hyperthyroidism

- Antithyroid medication
- Beta blockers for symptomatic thyrotoxicosis

Hypothyroidism

- Exogenous thyroid hormone replacement

SURGERY

- Hyperthyroidism
  - Radioactive thyroid ablation
  - Thyroidectomy

EUTHYROID SICK SYNDROME

osms.it/euthyroid-sick-syndrome

PATHOLOGY & CAUSES

- Older term; describes acquired, transient central hypothyroidism in severely sick
  - Thought to be euthyroid despite ↓ T_3 +/- T_4 concentrations
  - Transient central hypothyroidism coincident with peripheral T_3 metabolism/production abnormalities
- ↓ 5'-monodeiodinase activity → ↓ peripheral (skeletal muscle, liver, kidney) T_4 → T_3 conversion → ↓ T_3 serum concentration
- ↑ 5'-monodeiodinase (D3) activity → ↑ conversion of T3 → rT_3 → ↓ T_3 serum concentration (↑ rT_3, T_2 breakdown products)

CAUSES

- Poor caloric intake
- High endogenous serum cortisol in setting of exogenous glucocorticoid therapy
- Circulating inhibitors of deiodinase activity (e.g. free/nonesterified fatty acids)
- Medications (e.g. amiodarone; propranolol, in high doses)
  - Inhibit 5'-monodeiodinase activity
- Cytokines
  - Tumor necrosis factor (TNF), interferon-alpha (IFN-α), nuclear factor kappa-beta (NF-kB), interleukin 6 (IL-6)
- Impaired peripheral T_4 uptake → ↓ T_3 production

RISK FACTORS

- Severe illness, intensive care unit (ICU) hospitalization

COMPLICATIONS

- Myxedema coma

SIGNS & SYMPTOMS

- Similar to hypothyroidism, not attributable to critical illness
  - Fatigue, cold intolerance, weight loss/gain, constipation, muscle cramps, headache, hair loss/brittleness, menstrual irregularities

DIAGNOSIS

LAB RESULTS

- Serum TSH (required for diagnosis)
  - Detects TSH suppression

TREATMENT

OTHER INTERVENTIONS

- Standard replacement therapy (e.g. levothyroxine)
  - No benefit, unless diagnosis of preceding hypothyroidism/progression to myxedema coma

GRAVES' DISEASE

osms.it/graves-disease

PATHOLOGY & CAUSES

- Autoimmune disease; production of antibodies against TSH receptor
- Most common cause of hyperthyroidism (80%)
- Thyroid-stimulating immunoglobulin (TSI) antibody binds to TSH receptors, acts as analog

RISK FACTORS

- Genetic; polymorphisms in CTLA4, PTPN22, HLA-DR3 allele
- Peak incidence occurs at 20–40 years old
- Individuals who are biologically female affected 10 times more often

COMPLICATIONS

- Congestive heart failure, osteoporosis
- Thyroid storm
- Autoimmune conditions
  - Rheumatoid arthritis, systemic lupus erythematosus, pernicious anemia, diabetes mellitus Type I
- Radioiodine treatment → hypothyroidism

SIGNS & SYMPTOMS

- Effects of TSI
  - Thyroid hypertrophy, hyperplasia → diffuse goiter
  - Increased synthesis, release of T3, T4
  - Follicular cells express molecules on surface, attract nearby T cells → T cells bind to follicular cells, infiltrate interstitium of thyroid tissue
  - TSI stimulation of fibroblasts in eye orbit → increased production of glycosaminoglycans → local inflammation, swelling → exophthalmos, lid retraction
  - Exophthalmos dries eyes → corneal ulcers; weakens muscles controlling eye, upper lid
- Infiltrative dermopathy
  - Glycosaminoglycan builds up → pretibial myxedema → non-pitting edema
- Pretibial myxedema

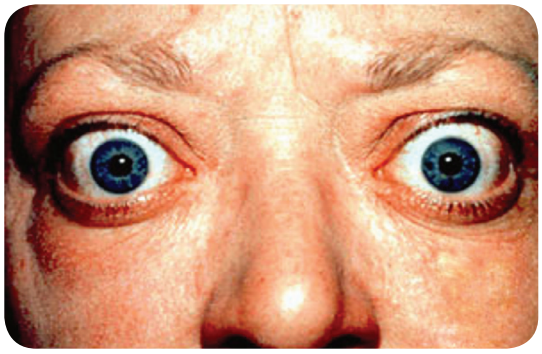

Figure 19.1 The clinical appearance of Graves' disease. There is proptosis and lid retraction bilaterally.

DIAGNOSIS

DIAGNOSTIC IMAGING

- Radioiodine scans, measurements of iodine uptake
  - Diffusely increased

LAB RESULTS

- ↓ TSH, ↑ T3, ↑ T4, ↑ TSI

TREATMENT

MEDICATION

- Antithyroid medication
  - Thioamides
- Beta-blockers

SURGERY

- Thyroidectomy
- Radioiodine radioisotope surgery
  - Partially/completely destroy thyroid gland with radiation

OTHER INTERVENTIONS

- Ophthalmopathy
  - Steroids, radiation and surgery

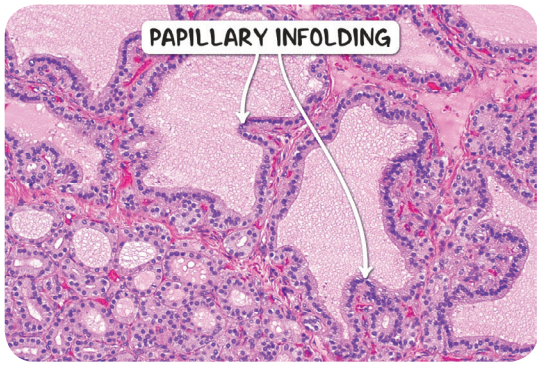

Figure 19.3 The histological appearance of the thyroid gland in Graves' disease. There are enlarged thyroid follicles lined by hyperplastic follicular epithelium. The epithelium demonstrates papillary infolding.

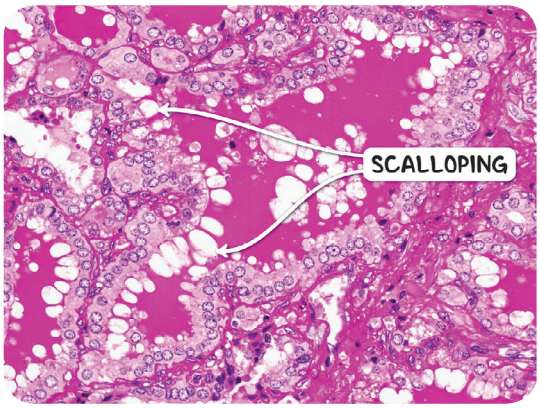

Figure 19.2 The histological appearance of scalloped colloid within a hyperplastic thyroid follicle; a classic sign of Graves' disease.

HYPERTHYROIDISM

osms.it/hyperthyroidism

PATHOLOGY & CAUSES

- Disorder caused by excessive amount of thyroid hormone produced by overactive thyroid gland
- ↑ thyroid hormone synthesis, secretion → thyrotoxicosis (↑ circulating thyroid hormones)

CAUSES

- Autoimmune
  - Graves' disease (most common cause)
- TSH-related disease
  - TSH-secreting pituitary adenoma; stimulation of TSH receptors due to excess hCG (e.g. trophoblastic tumors, hyperemesis gravidarum)
- Solitary autonomous adenoma
- Excessive iodine ingestion

RISK FACTORS

- More common in individuals who are biologically female
- Smoking, genetic inheritance (Graves' disease)

COMPLICATIONS

- Thyroid storm

SIGNS & SYMPTOMS

- Thyroid
  - Normal/enlarged, with/without palpable nodules (may be diffusely firm, tender)
- Cardiovascular
  - Bounding, rapid pulse; hypertension; palpitations
- Respiratory
  - Tachypnea, dyspnea on exertion
- Gastrointestinal (GI)
  - ↑ appetite/↓ weight; hyperdefecation
- Integumentary
  - Warm, flushed, moist skin; patchy hair loss; thyroid acropachy (digital clubbing); infiltrative dermopathy (pretibial myxedema)
- Musculoskeletal
  - Osteoporosis (↑ bone resorption); skeletal muscle atrophy
- Neurological
  - Heat intolerance, fine tremor, agitation, insomnia
- Reproductive
  - Menstrual irregularities, ↓ libido, infertility
- Ocular changes (Graves' disease)
  - Wide, staring gaze; lid lag, exophthalmos

DIAGNOSIS

DIAGNOSTIC IMAGING

RAIU

- ↑ ^{123}I uptake confirms hyperthyroidism

CFDS

- ↑ blood flow due to thyroid hyperactivity

Ultrasound

- Benign/malignant nodules (e.g. microcalcifications, hypoechogenicity in malignant nodules)

LAB RESULTS

- ↓ TSH, ↑ free T_4, total/free T_3
  - Confirms hyperthyroidism with suppressed TSH
- ↑ TSH, free T_4, total/free T_3
  - Confirms TSH-induced hyperthyroidism
- ↑ TRAb/TSI

TREATMENT

MEDICATIONS

- Antithyroid drugs

SURGERY

- Thyroidectomy

OTHER INTERVENTIONS

- Radioactive thyroid ablation

HYPOTHYROIDISM

osms.it/hypothyroidism

PATHOLOGY & CAUSES

- Hypometabolic state caused by underproduction of thyroid hormones T_3, T_4
- ↓ availability of thyroid hormone → general slowing of thyroid hormone-induced cell metabolism
- Accumulation of matrix glycosaminoglycans in interstitial space → myxedema

TYPES

Primary hypothyroidism (thyroid gland dysfunction)

- Iodine deficiency
- *Autoimmune:* Hashimoto's thyroiditis
  - Autoantibodies against thyroglobulin (Tg), thyroid peroxidase (TPO), TSH receptor → bound antibodies facilitate T-cell, complement-mediated immune destruction of thyroid cells; steric hindrance at TSH receptor
- Congenital
  - Inborn errors of thyroid hormone metabolism
  - Thyroid agenesis/hypoplasia
- Iatrogenic
  - Treatment of hyperthyroidism, thyroid neoplasm (radiation, surgical)
- Medication-induced
  - Overdose of antithyroid drugs (propylthiouracil, methimazole)
  - Agents ↓ T_4 absorption (cholestyramine, iron salts)
  - Agents ↓ T_4 → T_3 conversion (amiodarone)
  - Agents ↓ clearance of T_4 (phenytoin, carbamazepine)
  - *Others:* lithium carbonate, interferon alpha, IL-2, tyrosine kinase inhibitors (esp. sunitinib), *P*-aminosalicylic acid

Secondary, tertiary hypothyroidism (central hypothyroidism)

- Disorder of pituitary/hypothalamus/hypothalamic-pituitary communication → ↓ TSH/TRH
  - *Hypopituitarism:* surgical resection/radiation for adenoma, trauma, postpartum pituitary necrosis (Sheehan's syndrome), infiltrative disease
  - *Hypothalamic damage:* radiation, granulomas, neoplasms

RISK FACTORS

- ↑ age
- More common in individuals who are biologically female

COMPLICATIONS

- Myxedema coma
  - Common in older individuals who are biologically female with longstanding hypothyroidism; precipitated by acute event (e.g. trauma, infection, myocardial infarction)
- Dyslipoproteinemias
- Dilated cardiomyopathy; ↓ thyroid hormone → dysregulation of myocardial enzymes → ↓ myocardial contractility
- Anemia
  - Hypoproliferative (normochromic, normocytic)/pernicious anemia (most common in chronic autoimmune thyroiditis)
- Hyperprolactinemia → galactorrhea
- ↓ clearance of drugs (e.g. antiepileptic, anticoagulant, opioids) in setting of hypothyroidism → ↑ accumulation of drugs → potential drug toxicity
- Congenital hypothyroidism
  - Failure to thrive, intellectual disability

SIGNS & SYMPTOMS

- Fatigue, cold intolerance, constipation, muscle weakness, headache, weight gain, brittle hair/loss of eyebrow hair, menstrual irregularities, goiter (primary hypothyroidism)
- Neurologic manifestations
  - Difficulty concentrating, poor memory, peripheral neuropathy, carpal tunnel syndrome, ↓ deep tendon reflexes
- Myxedema (nonpitting edema)
  - Periorbital edema, tongue enlargement, puffy facies
- Myxedema coma
  - Altered mental status, hypothermia, multi-organ failure, hypotension, bradycardia, hyponatremia, hypoglycemia, hypoventilation

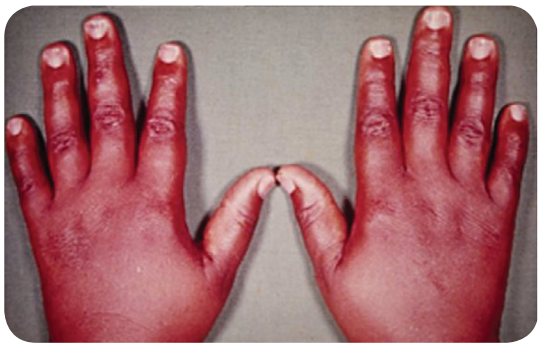

Figure 19.4 Myxedema of the hands in an individual with hypothyroidism.

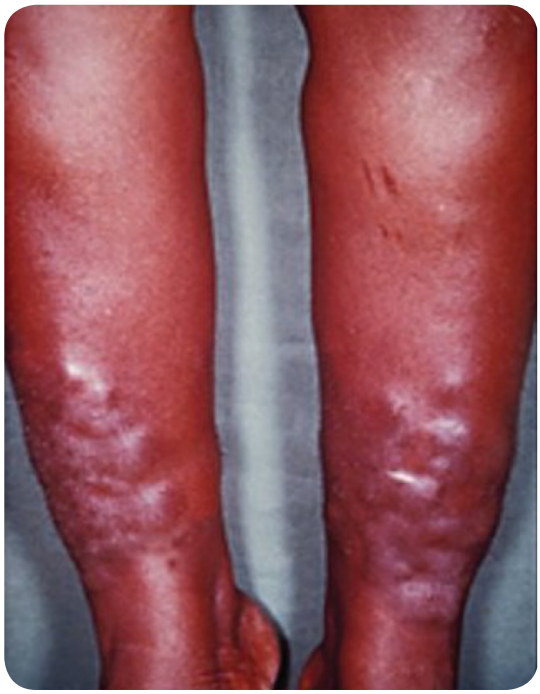

Figure 19.5 Pretibial myxedema in an individual with hypothyroidism.

DIAGNOSIS

LAB RESULTS

- Primary hypothyroidism
  - ↑ TSH, ↓ free T_4
- Central hypothyroidism
  - ↓ free T_4, ↓/↔/↑ TSH
- Autoimmune autoantibody detection (Hashimoto's thyroiditis)
  - ↑ ↑ anti-TPO/Tg/TSH receptor antibodies

OTHER DIAGNOSTICS

- History, physical examination

TREATMENT

MEDICATIONS

- Synthetic T_4 (levothyroxine) replacement therapy

THYROID STORM

osms.it/thyroid-storm

PATHOLOGY & CAUSES

- Severe, acute, life-threatening complication of hyperthyroidism

CAUSES

- Abrupt termination of hyperthyroidism therapy
- Complication of hypothyroid treatment
- Diabetic ketoacidosis
- Stressors (surgery, infection, trauma, childbirth)
- Increased sensitivity of tissues to thyroid hormone, catecholamines

COMPLICATIONS

- Myocardial infarction (MI), heart failure; coma, death

SIGNS & SYMPTOMS

- Exaggerated hyperthyroidism symptoms
  - Heat intolerance → fever
  - Hyperactivity, anxiety → agitation, confusion, seizures, coma
  - Tachycardia → cardiac arrhythmias, high-output heart failure

DIAGNOSIS

LAB RESULTS

- ↓ TSH, ↑ T3, ↑ T4

OTHER DIAGNOSTICS

ECG

- Confirmation

TREATMENT

MEDICATION

- Beta blockers
- Thyroid hormones reduction
  - Thioamides, iodine preparations, glucocorticoids, bile acid sequestrants

OTHER INTERVENTIONS

- Plasmapheresis

TOXIC MULTINODULAR GOITER

osms.it/toxic-multinodular-goiter

PATHOLOGY & CAUSES

- Excess thyroid hormone production from multiple autonomous thyroid nodules, without stimulation of TSH
- Second most common cause of hyperthyroidism; AKA Plummer's disease
- Starts as non-toxic multinodular goiter caused by chronic lack of dietary iodine
  - Lack of iodine → low levels of thyroid hormones→ anterior pituitary releases TSH → thyroid hypertrophy, hyperplasia → some parts of thyroid gland more responsive to TSH than others → uneven growth → most responsive follicular cells grow quickly, develop into nodule → multiple nodules appear
  - More follicular cells compensate for low thyroid hormone production → euthyroid state
- Non-toxic multinodular goiter becomes toxic when genetic mutation for TSH receptor occurs in one of dividing follicular cells → cell becomes constitutively active without TSH → overstimulation of thyroid to divide, produce thyroid hormone → toxic multinodular goiter

COMPLICATIONS

- Malignancy (rare)

SIGNS & SYMPTOMS

- Increased synthesis, release of T_3, T_4 → hyperthyroidism
  - Increased basal metabolic rate, catabolism of proteins, carbohydrates, bone resorption
  - Exacerbation of sympathetic nervous system
  - Impairment of reproductive system
- Thyroid hypertrophy, hyperplasia → goiter
  - Difficulty swallowing, airway obstruction
  - Compression of recurrent laryngeal nerve → hoarse voice
  - Superior vena cava syndrome → facial, arm swelling

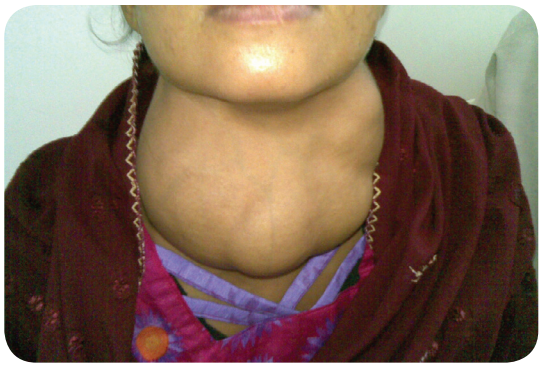

Figure 19.6 The clinical appearance of a goiter.

DIAGNOSIS

DIAGNOSTIC IMAGING

- Radioiodine scans, measurements of iodine uptake
  - Uneven ("hot" autonomous nodules)

LAB RESULTS

- ↓ TSH, ↑ T3, ↑ T4

TREATMENT

MEDICATION

- Beta blockers
- Antithyroid medication
  - Thioamides
  - If radioiodine therapy, surgery not appropriate

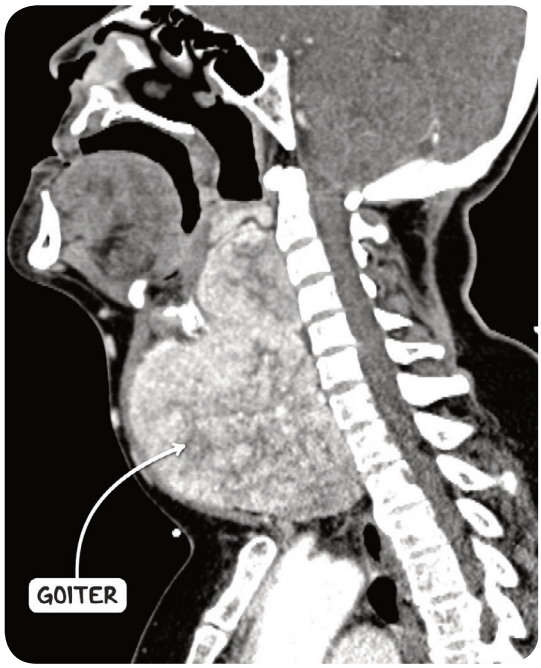

Figure 19.7 A CT scan of the head and neck in the sagittal plane demonstrating a massive goiter extending from the mandible to the suprasternal notch.

SURGERY

- Thyroidectomy
- Radioiodine radioisotope surgery
  - Partially/completely destroy thyroid nodules with radiation

OTHER INTERVENTIONS

- Inject ethanol into nodules