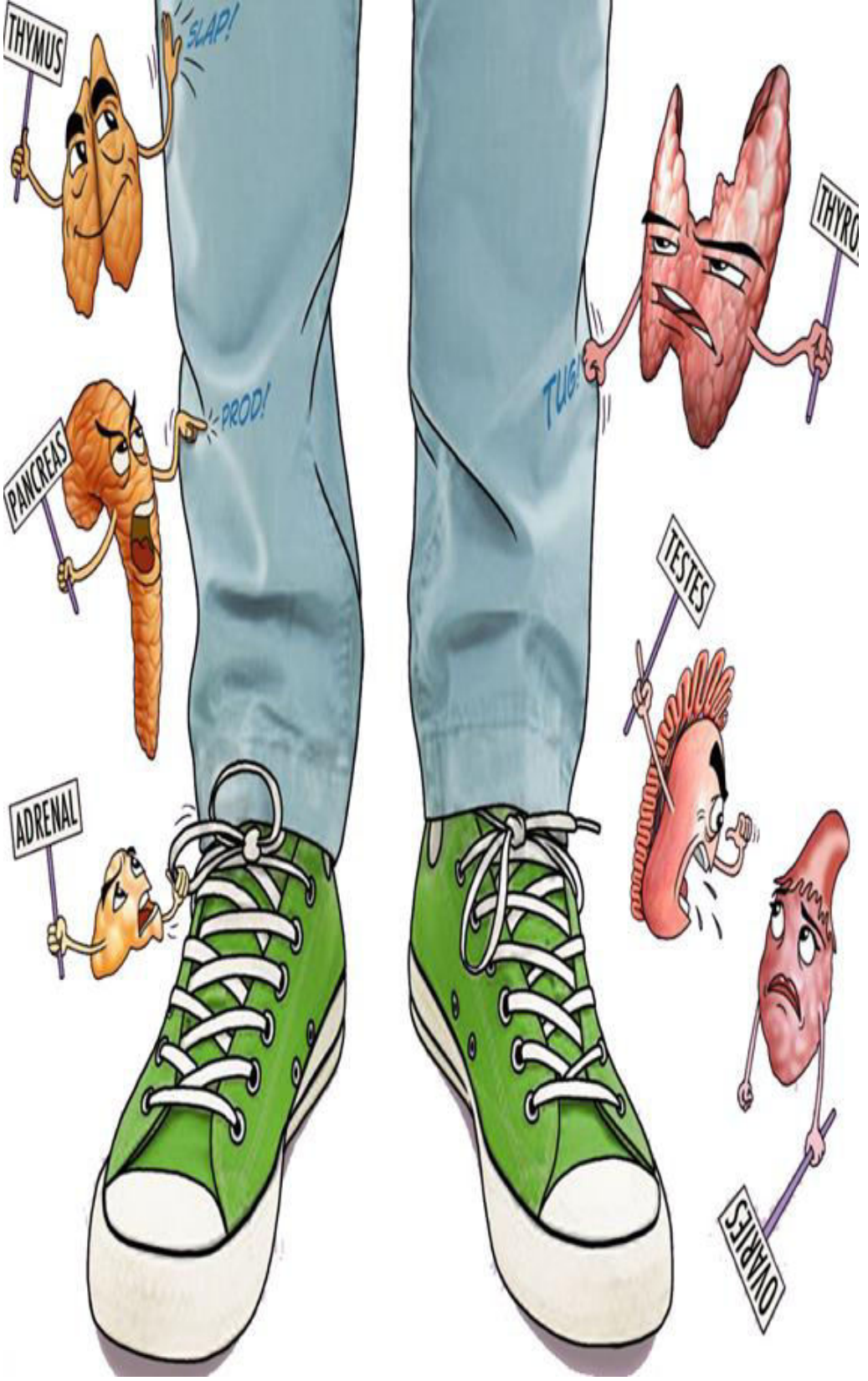
PATHOLOGY
TEAM 436

MEDICINE
KING SAUD UNIVERSITY



Pathology review file

- *Please keep in mind that this work is done by students , so if there are any mistakes please inform us*
- *This work is not by any means a reference*

	Hyperthyroidism	Hypothyroidism
Causes	Primary ➢ Diffuse toxic hyperplasia (Graves disease) ➢ Hyperfunctioning (“toxic”) multinodular goiter ➢ Hyperfunctioning (“toxic”) adenoma ➢ Iodine-induced hyperthyroidism ➢ Neonatal thyrotoxicosis associated with maternal Graves disease Secondary ➢ TSH-secreting pituitary adenoma (rare)	Primary ➢ Developmental (thyroid dysgenesis5: PAX8, FOXE1, TSH receptor mutations) ➢ Thyroid hormone resistance syndrome (THRB mutations) ➢ Postablative Surgery, radioiodine therapy, or external irradiation ➢ Autoimmune hypothyroidism (Hashimoto thyroiditis) ➢ Iodine deficiency ➢ Drugs6 (lithium, iodides, p-aminosalicylic acid) ➢ Congenital biosynthetic defect (dyshormonogenetic goiter) Secondary (CENTRAL) ➢ Pituitary failure ➢ Hypothalamic failure (rare)
Diagnosis	✓ The measurement of serum TSH is the most useful single screening test for hyperthyrodisim ✓ Free thyroid hormone assays ✓ Measurement of radioactive-iodine uptake by the thyroid gland (Increased)	✓ Measurement of serum TSH is the most sensitive screening test for this disorder ✓ The serum TSH is increased in primary hypothyroidism . ✓ Serum T4 is decreased in patients with hypothyroidism of any origin.
Extra Notes	Graves disease is the most common cause of endogenous hyperthyroidism. It is characterized by a triad: ➢ Thyrotoxicosis ➢ An infiltrative ophthalmopathy with resultant exophthalmos ➢ localized,infiltrative dermopathy(pretibial myxedema) Antibodies against the TSH receptors : (Activating it without regulation) ➢ Thyroid-stimulating immunoglobulin ➢ Thyroid growth-stimulating immunoglobulins ➢ TSH-binding inhibitor immunoglobulins (What causes episodes of hypothyrodisim)	➢ Cretinism refers to hypothyroidism developing in infancy or early childhood , impaired development of the skeletal system and central nervous system, with severe mental retardation. Hypothyroidism developing in older children and adults results in a condition known as myxedema. _____ ➢ Chronic Lymphocytic (Hashimoto) Thyroiditis: is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient. thyroid failure secondary to autoimmune destruction of the thyroid gland. May be associated with polymorphisms in multiple immune regulation–associated genes, which is the linkage to cytotoxic T lymphocyte–associated antigen-4gene (CTLA4)

	Morphology: ➢ The thyroid gland is enlarged (usually symmetrically. ➢ The gland is usually smooth and soft, and its capsule is intact. ➢ the follicular epithelial cells in untreated cases are tall, columnar, and more crowded than usual. Forms small papillae . ➢ colloid within the follicular lumen is pale, with scalloped margins. ➢ Lymphoid infiltrates, are present throughout the interstitium; germinal centers are common.	Symptoms: Painless – Hashitoxicosis - Increased risk of B-cell non-Hodgkin lymphoma Morphology: ➢ Diffuse and symmetrical enlargement The cut surface is pale and gray-tan in appearance, and the tissue is firm and somewhat friable. ➢ The most important triad –mononuclear infiltrate- ✓ Hurthle cells ✓ Plasma cells ✓ Lymphocytes (well developed germinal centers)

Thyroiditis

Diffuse and multinodular goiter

Definition of goiter

Enlargement of the thyroid, is the most common manifestation of thyroid disease

Pathogenies of goiter

- impaired synthesis of thyroid hormone, most often caused by dietary iodine deficiency.
- Which leads to a compensatory rise in the serum TSH, causes hypertrophy and hyperplasia of thyroid follicular cells and, ultimately, gross enlargement of the thyroid gland.

The compensatory increase in functional mass of the gland is enough to overcome the hormone deficiency, ensuring a euthyroid metabolic state.
If the underlying disorder is sufficiently the compensatory responses may be inadequate to overcome the impairment in hormone synthesis, resulting in goitrous hypothyroidism .

Types

- (diffuse goiter): The follicles are lined by crowded columnar cells, which may pile up and form projections. All long-standing diffuse goiters convert into multinodular goiters.
- colloid-rich gland (colloid goiter).
- Multinodular goiters typically are hormonally silent, although a minority (approximately 10% over 10 years) can manifest with thyrotoxicosis secondary to the development of autonomous nodules that produce thyroid hormone independent of TSH stimulation. This condition, known as toxic multinodular goiter or Plummer syndrome.

Features and morphology of Multinodular goiter

- Multinodular goiters are multilobulate, asymmetrically enlarged glands, which may attain massive size.
- On cut surface brown,
- gelatinous colloid are evident .
- Older lesions often show areas of fibrosis, hemorrhage, calcification, and cystic change.

Clinical features :

- In addition to the obvious cosmetic problem of a large neck mass, goiters also may cause airway obstruction, dysphagia, and compression of large vessels in the neck .
- a hyperfunctioning (toxic) nodule may develop within a long-standing goiter, resulting in hyperthyroidism.
- The incidence of malignancy in long-standing multinodular goiters is low and concern for malignancy arises with goiters that demonstrate sudden changes in size or associated symptoms (e.g., hoarseness).

Riedel thyroiditis

- Rare disorder of unknown etiology
- characterized by extensive fibrosis involving the thyroid and contiguous neck structures.
- Clinical evaluation demonstrates a hard and fixed thyroid mass, simulating a thyroid neoplasm.

Granulomatous Subacute (Quervain de) Thyroiditis:

- caused by a viral infection or an inflammatory process triggered by viral infections.
- patients have a history of an upper respiratory infection just before the onset of thyroiditis.
- acute onset , characterized by pain in the neck (particularly with swallowing), fever, malaise, and variable enlargement of the thyroid.
- typically is self-limited.
- Transient Hyperthyrodisim followed by transient hypothyrodisim

Morphology :

- The gland is firm
- with an intact capsule
- unilaterally or bilaterally enlarged.

- disruption of thyroid follicles
- extravasation of colloid leading to a polymorphonuclear infiltrate, which is replaced over time by lymphocytes, plasma cells, and macrophages.

- The extravasated colloid provokes an exuberant granulomatous reaction with giant cells.

Subacute lymphocytic thyroiditis

- disease follows pregnancy (postpartum thyroiditis). autoimmune in etiology.
- Painless neck mass or features of thyroid hormone excess.

Morphology:

The histologic features consist of lymphocytic infiltration and hyperplastic germinal centers within the thyroid parenchyma.

Thyroid carcinomas

	Papillary thyroid carcinoma	Medullary thyroid carcinoma *The only tumor that is derived from parafollicular (or C-cells) of thyroid
Genetic alteration	✓ Rearrangement of the tyrosine kinase OR ✓ NTRK1 OR ✓ Activating point mutations in BRAF	✓ Familial medullary thyroid carcinoma occur in multiple endocrine neoplasia type 2 (MEN-2A or 2B) RET protooncogene mutation OR ✓ Familial tumors without an associated MEN syndrome
Pathogenesis	○ The major risk factor is exposure of ionizing radiation ○ Most often between the ages of 35 -50 ○ Solitary or multifocal lesions	
Prognosis	➢ Dependent on several factors: 1. Age (less favorable in older patients) 2. Presence of extra-thyroidal extension 3. Presence of distant metastasis (stage)	-
Morphology	➢ Nuclear features: 1. Finely dispersed chromatin, with an optically clear appearance, giving rise to the designation ground glass or **orphan annie eye** nuclei. 2. Grooves 3. Intranuclear inclusions (pseudoinclusions) 4. Papillary architecture 5. Psammoma bodies 6. There may be a variant: follicular variant of papillary thyroid carcinoma	1. Polyglonal to spindle cells 2. Amyloid deposition 3. Bilaterally (both lobes) 4. Multicentricity 5. Necrosis 6. Hemorrhage

	Follicular carcinoma	Anaplastic carcenoma
Prognosis	✓ These neoplasms tend to metastasize through the bloodstream to the lungs, bone, and liver.	✓ Lethal
Morphology	✓ Usually solitary, cold nodule ✓ Composed of uniform cells forming small follicles, reminiscent of normal thyroid ✓ Follicular carcinomas may be : ▪ widely invasive, infiltrating the thyroid parenchyma and extrathyroidal soft tissues. ▪ or minimally invasive. are sharply demarcated lesions	✓ Undifferentiated tumor ✓ large, pleomorphic giant cells, including: ▪ occasional osteoclast-like multinucleate giant cells ✓ spindle cells with a sarcomatous appearance ✓ mixed spindle and giant cells ✓ Small cells
Notes	✓ Associated with dietary iodine deficiency. ✓ to distinguish FC from follicular adenomas on gross examination.it requires extensive histologic sampling of the tumor capsule–thyroid interface, to exclude capsular and/or vascular invasion	Can be arise from a more differentiated carcinoma(papillary)

Thyroid adenoma

	Follicular Adenoma
Prognosis	✓ Excellent , no recurrency nor metastisis
Morphology	✓ Usually solitary ✓ Usually Compresses adjacent structures ✓ Has a well-defined intact capsule ✓ Hurthle , Oxyphil cell change
Notes	✓ Careful evaluation is important to evaluate the integrity of the capsule to distinguish it from follicular carcinoma which demonstrate capsular/vascular Invasion . ✓ They appear as cold nodules ✓ We have to surgically remove the adenoma to exclude malignancy .

اللهم ليس بجدي و لا اجتهادي و إنما بتوفيقك و رحمتك و عظمتك و عطفك علي

القاده:
حنين السبكي.

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هبه الناصر.

Thank you for checking our work❤

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