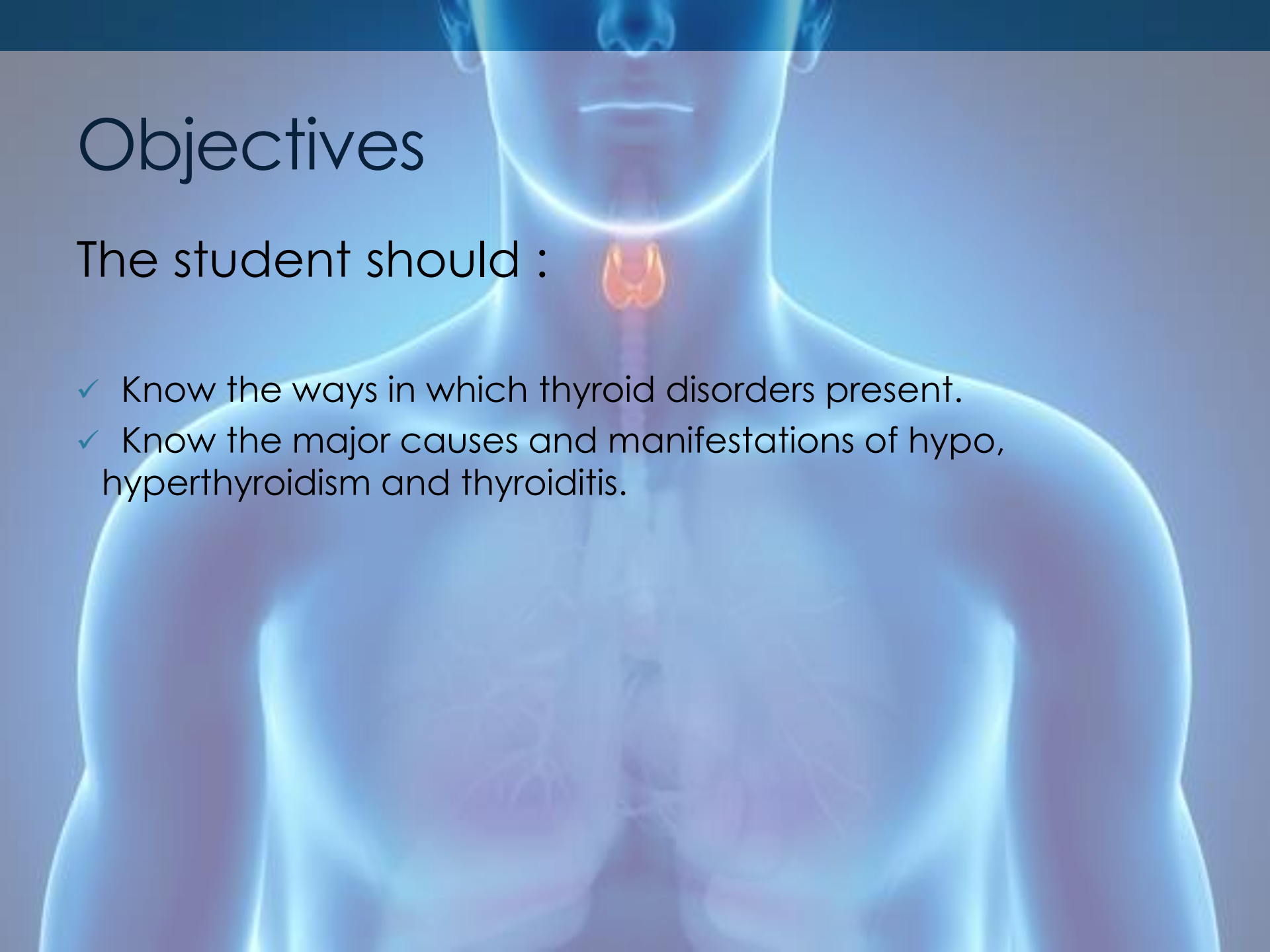
Lecture 1:
Hypo and Hyperthyroidism & Hashimoto's Thyroiditis

▫ Important ▫ Notes ▫ Explanation

Objectives

The student should :

- ✓ Know the ways in which thyroid disorders present.
- ✓ Know the major causes and manifestations of hypo, hyperthyroidism and thyroiditis.



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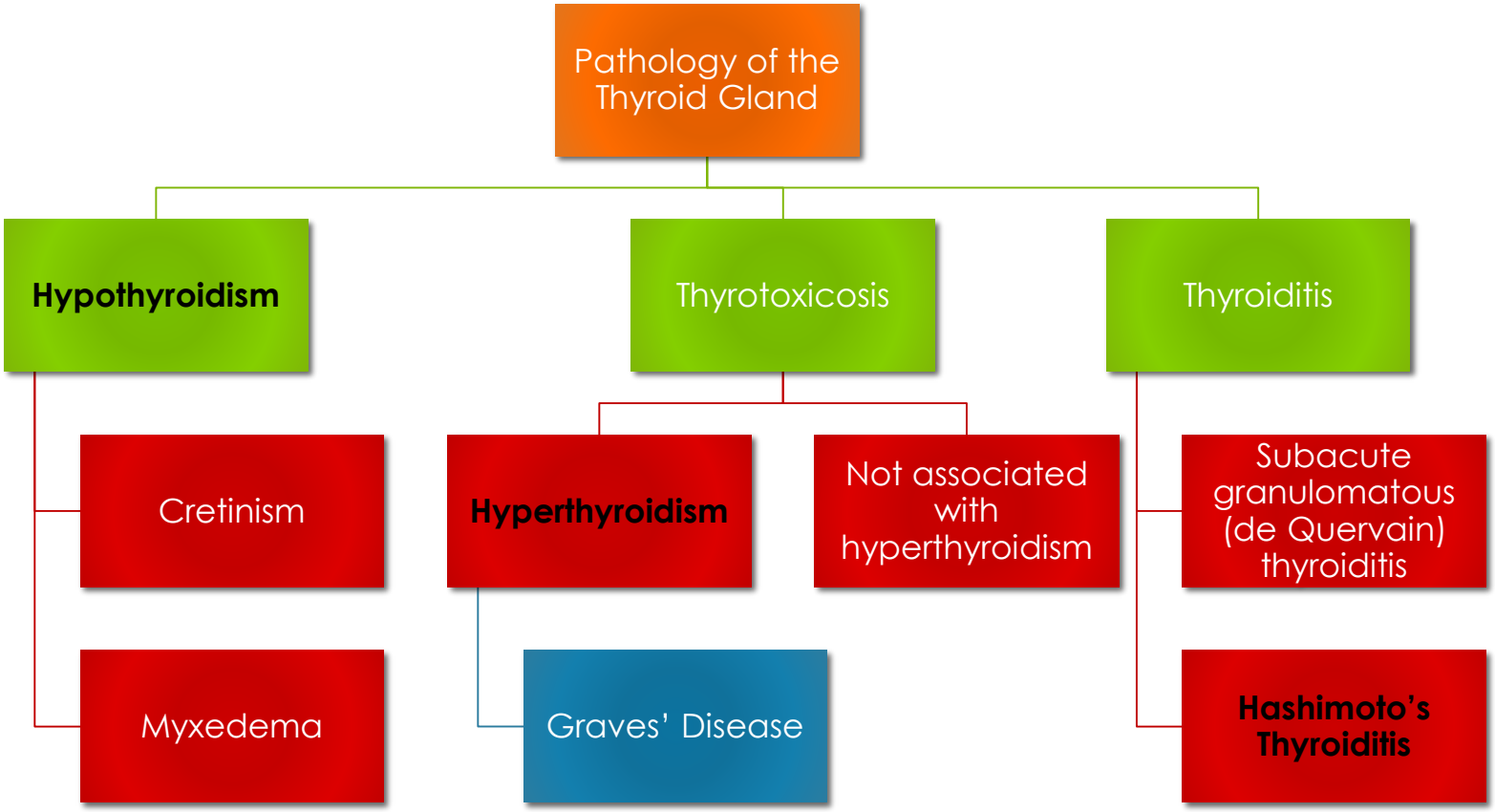

Pathology of the Thyroid Gland
Hypothyroidism
Thyrotoxicosis
Thyroiditis
Cretinism
Myxedema
Hyperthyroidism
Graves' Disease
Not associated with hyperthyroidism
Subacute granulomatous (de Quervain) thyroiditis
Hashimoto's Thyroiditis

Hypothyroidism

introduction:

- It is a **Decrease** in the levels of thyroid hormones in the circulation.
- Caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone
- Prevalence of overt (documented) hypothyroidism is 0.3%, while subclinical (not diagnosed) hypothyroidism can be found in greater than 4%.
- Increases with **age**, and more common in **females** than in males.

Causes classified into:

Primary (Majority) (related to the thyroid itself)	Secondary (Central) (related to hypothalamus & pituitary)
• **Developmental** (thyroid dysgenesis: *PAX8, FOXE1*, TSH receptor mutations) • **Postablative** (following radioactive ablation (destruction of thyroid tissue) in treatment for hyperthyroidism). • **Iodine deficiency** • **Acquired** Surgery, radioiodine therapy (radiation-induced ablation), or external irradiation • **Autoimmune hypothyroidism (Hashimoto's thyroiditis)** The most common cause of hypothyroidism in iodine sufficient area. • **Congenital biosynthetic defect** by: 1. endemic iodine deficiency in the diet 2. inborn errors of thyroid metabolism (dyshormonogenetic goiter) less common.	• **Pituitary failure** (deficiency of TSH) • **Hypothalamic failure** (deficiency of TRH) * Both are rare.

Clinical manifestation:

Cretinism	• In infants or early childhood • Sever mental retardation, short stature, coarse facial features, protruding tongue and umbilical hernia.
Myxedema	• In older child or adult. • slowing of physical and mental activity, mental sluggishness-overweight. • Histologically: accumulation of matrix substances such as: **Glycosaminoglycans** and **hyaluronic acid**, in skin, subcutaneous tissue, visceral sites, results in: Non-pitting edema, a broadening and coarsening of facial features, enlargement of the tongue, deepening of the voice.

Thyrotoxicosis

Hyperthyroidism

- Hypermetabolic state caused by elevated circulating levels of free **T3 and T4**
- Caused most commonly by **hyperfunction** of the thyroid gland
- Thyrotoxicosis is the increase the amount of thyroid hormone whatever the cause, and hyperthyroidism is the major cause of it.

Thyrotoxicosis, Causes:

ASSOCIATED WITH HYPERTHYROIDISM:

Primary:

- Diffuse hyperplasia of the thyroid associated with Graves' disease (accounts for 85% of cases)
- Hyperfunctional multinodular goiter (most of cases are associated with normal thyroid hormone).
- Hyperfunctional adenoma of the thyroid (most of cases the nodules are nonfunctional or cold nodules)

Secondary:

- TSH-secreting pituitary adenoma (rare)

NOT ASSOCIATED WITH HYPERTHYROIDISIM:

- Granulomatous (de Quervain) thyroiditis (painful)
- Sub-acute lymphocytic thyroiditis (painless)(sub acute: 1-2 weeks granuloma, fibrous thyroiditis: fibrosis in the neck **compressing the airway** that's why we need to remove it.)
- Struma ovarii (ovarian teratoma with ectopic thyroid) (presence of thyroid follicles in ovaries → secretion of thyroid hormones. Shown in radioactive iodine uptake test.)
- Factitious thyrotoxicosis (exogenous thyroxine intake)

Graves' Disease

- Graves: "violent and long continued palpitations in females" associated with enlargement of the thyroid gland.

Pathogenesis:

- An autoimmune disorder: (autoantibodies to the TSH receptor):
- LATS* proved to be an IgG antibody that binds to the TSH receptor and mimics the action of TSH = increase release of thyroid hormones.
- Coexistence of stimulating & inhibiting immunoglobulins in the serum of the same patient, a finding that could explain why some patients with Graves' disease spontaneously develop episodes of hypothyroidism.

**long-acting thyroid stimulator (LATS), so named because it stimulated thyroid function more slowly than TSH*

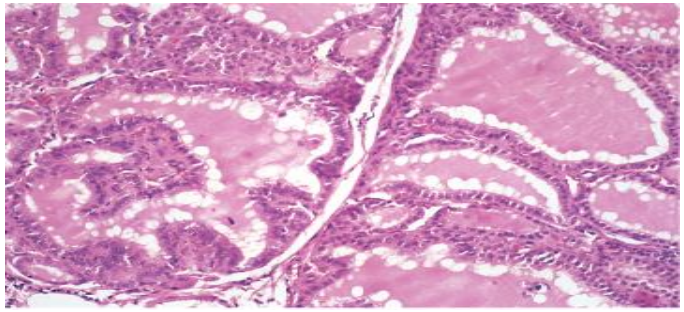
Characterized by:

- Thyrotoxicosis, caused by a diffusely enlarged, hyperfunctional thyroid.
- Infiltrative ophthalmopathy (exophthalmos).
- A localized, infiltrative dermopathy (pretibial myxedema).

Exophthalmos (bulging eyes)

Diffuse goiter

pretibial myxedema



Microscopically:

- Diffusely hyperplastic thyroid
- The follicles are lined by tall columnar epithelial cells that project into the lumina resulting in "scalloped" appearance of the edges of the colloid.
- Pseudo-papillary like formation (due to hyper activity of the gland). & vacuolated colloid.

Thyroiditis

inflammation of the thyroid gland, include diverse group of diseases characterized by some form of thyroid inflammation.

These diseases include conditions that result in:

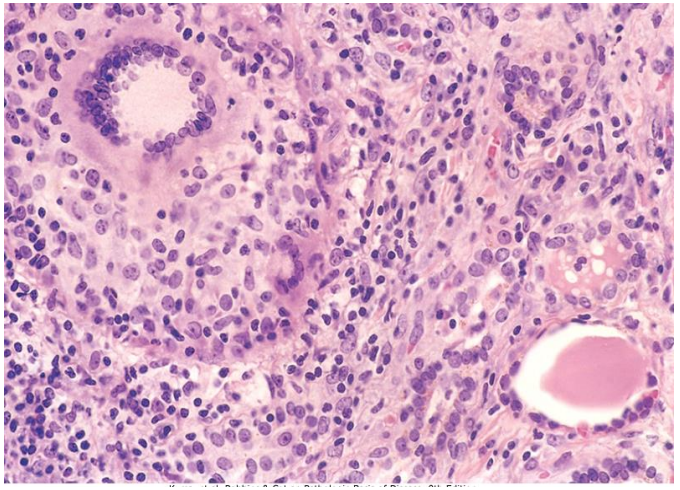
- **Acute illness** with severe thyroid pain (e.g., infectious thyroiditis, subacute granulomatous thyroiditis)
- Disorders with little inflammation, manifested by thyroid dysfunction (subacute lymphocytic thyroiditis and fibrous [Reidel] thyroiditis).

Subacute granulomatous (de Quervain) thyroiditis:

- Viral infection (e.g., coxsackie virus, mumps)
- Occurs most often in women 40 to 50 years old

Clinical findings:

- Most common cause of painful thyroid gland
- Often preceded by an upper respiratory infection
- Cervical adenopathy is *not* prominent.
- Initial thyrotoxicosis from gland destruction:
  Increased serum T4, decreased serum TSH
- Permanent hypothyroidism is uncommon.
- Self-limited; does *not* require treatment



Microscopically:
Granulomatous inflammation with giant cells.

Hashimoto's Thyroiditis: (chronic lymphocytic thyroiditis)

- The **most common** cause of hypothyroidism in areas of the world where iodine levels are sufficient.
- The name Hashimoto thyroiditis report by Hashimoto, describing patients with goiter & intense lymphocytic infiltration of the thyroid (struma lymphomatosa).
- **Hashimoto thyroiditis** and **Graves disease** are the two most common immunologically mediated disorders of the thyroid.
- **Female** predominance of 10:1 to 20:1. Age 45-65 .
- Hashimoto thyroiditis is characterized by **gradual thyroid failure** because of autoimmune **destruction** of the thyroid gland.
- It is a major cause of **non-endemic goiter in the pediatric population**.
- Strong genetic component, **40% of monozygotic twins**, as well as the presence of circulating antithyroid antibodies in approximately 50% of asymptomatic siblings.

Pathogenesis:

It is an **autoimmune** disease in which the immune system reacts against a variety of thyroid antigens (thyroglobulin & thyroid peroxidase)

Features:

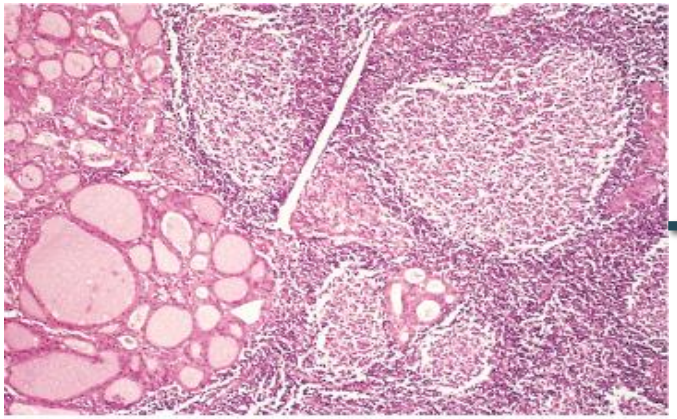
Progressive depletion of thyroid epithelial cells (**thyrocytes**), replaced by mononuclear cell infiltration and fibrosis.

Clinically:

- Painless enlargement of the thyroid, usually associated with the degree of hypothyroidism develops gradually. (Hyperthyroidism followed by Hypothyroidism episode)
- The enlargement is usually symmetric and diffuse.

Morphology:

- The thyroid is often **diffusely enlarged**.
- The cut surface is **pale**, **yellow**, **tan**, **firm**, and somewhat **nodular**.
- **Microscopic examination** reveals extensive infiltration of the parenchyma by a mononuclear inflammatory infiltrate containing small lymphocytes, **plasma cells**, and well-developed germinal centers.
- The thyroid follicles are atrophic and are lined in many areas by epithelial cells distinguished by the presence of abundant eosinophilic (pinkish), granular cytoplasm, termed **Hürthle cells.**



The thyroid parenchyma contains a dense lymphocytic infiltrate with germinal centers. Residual thyroid follicles lined by deeply eosinophilic Hürthle cells are also seen.

Summary (from Robbin's basic pathology)

SUMMARY

Graves Disease

- Graves disease, the most common cause of endogenous hyperthyroidism, is characterized by the triad of thyrotoxicosis, ophthalmopathy, and dermopathy.
- Graves disease is an autoimmune disorder caused by autoantibodies to the TSH receptor that mimic TSH action and activate TSH receptors on thyroid epithelial cells.
- The thyroid in Graves disease is characterized by diffuse hypertrophy and hyperplasia of follicles and lymphoid infiltrates; glycosaminoglycan deposition and lymphoid infiltrates are responsible for the ophthalmopathy and dermopathy.
- Laboratory features include elevations in serum free T_3 and T_4 and decreased serum TSH.

SUMMARY

Thyroiditis

- Chronic lymphocytic (Hashimoto) thyroiditis is the most common cause of hypothyroidism in regions where dietary iodine levels are sufficient.
- Hashimoto thyroiditis is an autoimmune disease characterized by progressive destruction of thyroid parenchyma, Hürthle cell change, and mononuclear (lymphoplasmacytic) infiltrates, with or without extensive fibrosis.
- Multiple autoimmune mechanisms account for Hashimoto disease, including cytotoxicity mediated by CD8+ T cells, cytokines (IFN-γ), and antithyroid antibodies.
- Subacute granulomatous (de Quervain) thyroiditis is a self-limited disease, probably secondary to a viral infection, and is characterized by pain and the presence of a granulomatous inflammation in the thyroid.
- Subacute lymphocytic thyroiditis is a self-limited disease that often occurs after a pregnancy (postpartum thyroiditis), typically is painless, and is characterized by lymphocytic inflammation in the thyroid.

Thank You!

We hope you found this helpful and informative.

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