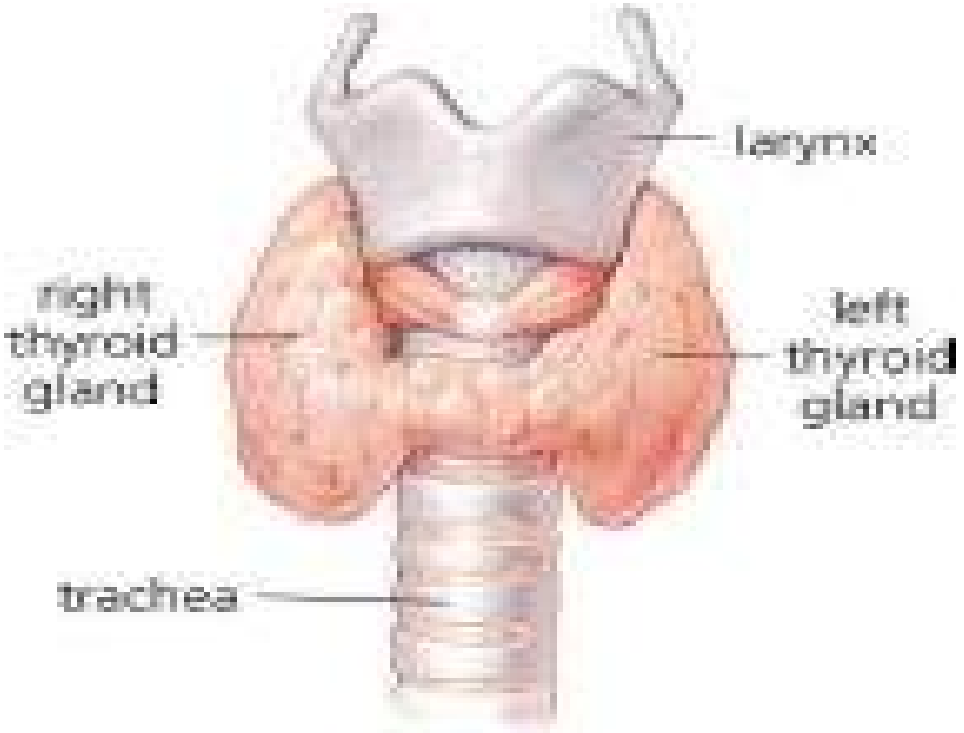
Pathophsiology

Disorder of thyroid function: Hypothyroidism and Hyperthyroidism

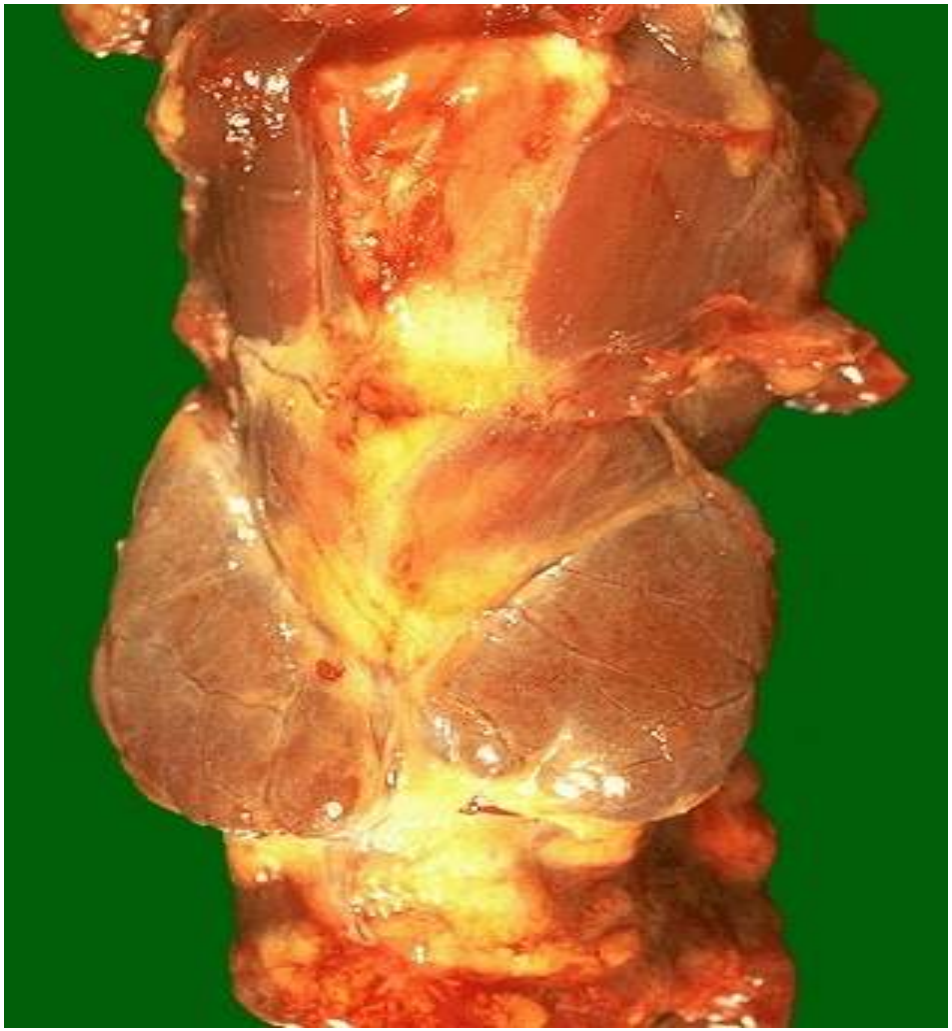
4-11-2018

Lecturer: M. Khaleel
Department of Clinical Laboratory Science
College of Pharmacy
University of Basrah

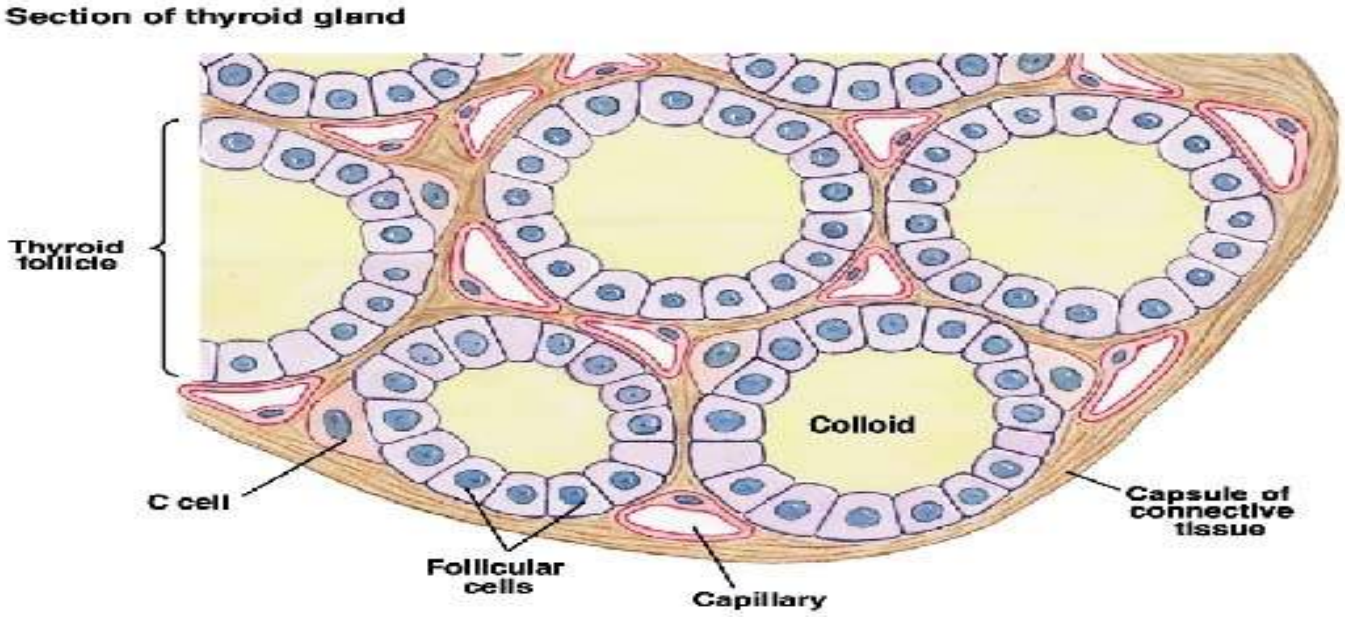
The thyroid gland is a shield-shaped structure located below the larynx in the anterior middle portion of the neck. It is composed of a large number of tiny, saclike structures called follicles, these are the functional units of the thyroid.



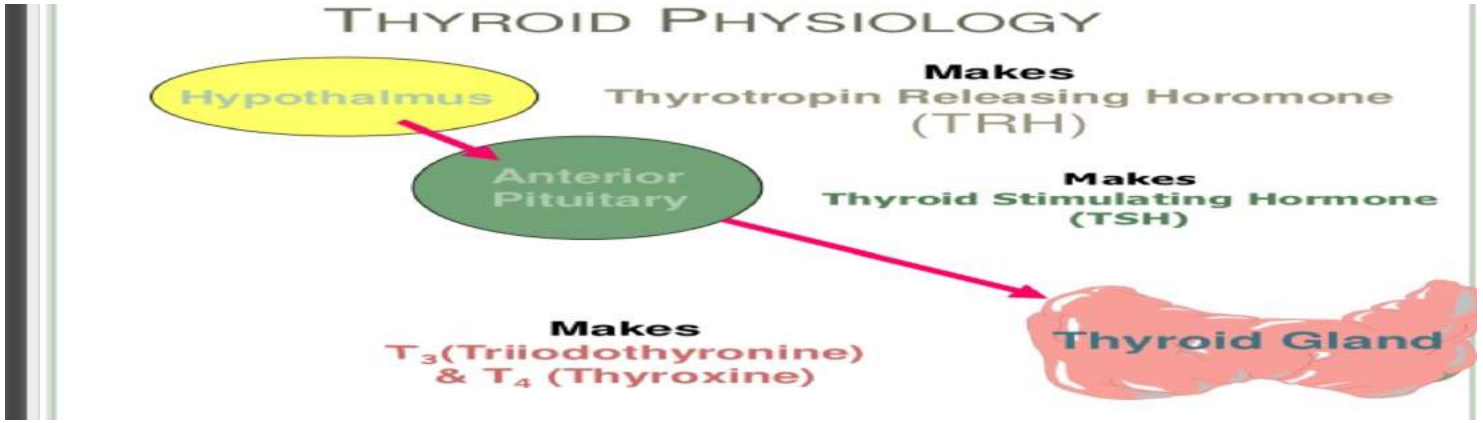
Macroscopic normal appearance of the thyroid gland in the middle of neck.



The thyroid produces and secretes two metabolic hormones. Thyroxin(T4) and triiodothyronine(T3), these hormones act throughout the body, influencing metabolism, growth and development , and body temperature. It also is necessary for brain development and growth in infants and small children.



Production and regulation of thyroid hormones



The secretion of thyroid hormone is regulated by the hypothalamic-pituitary-thyroid feedback system . In this system, thyrotropin-releasing hormone(TRH), which is produced by the hypothalamus, controls the release of TSH from the anterior pituitary gland. TSH increases the overall activity of the thyroid gland by increasing thyroglobulin breakdown and the release of thyroid hormone from follicles into the bloodstream, When blood level of thyroid hormone increase, they inhibit both TSH and TRH , leading to "shutdown" of the thyroid epithelial cells. Later , when blood level of thyroid hormoen have decreased , the negative feedback system wakes up again.

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.

Disorders of thyroid function

Hypofunction

↓ in level of hormone → impair development in infants and slowing of physical and mental ability in adults

Due to:

- Postablation
  - Surgery
  - Radiation
- Autoimmune thyroiditis
- Drugs
- Dyshormonogenetic

The clinical manifestation of hypothyroidism include :-

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:an accumulation of a hydrophilic mucopolysaccharide substance in the connective tissues of skin, subcutaneous tissue, visceral sites, results innon-pitting mucous edema, a broadening and coarsening of facial features, enlargement of the tongue, deepening of the voice.

Disorders of thyroid function

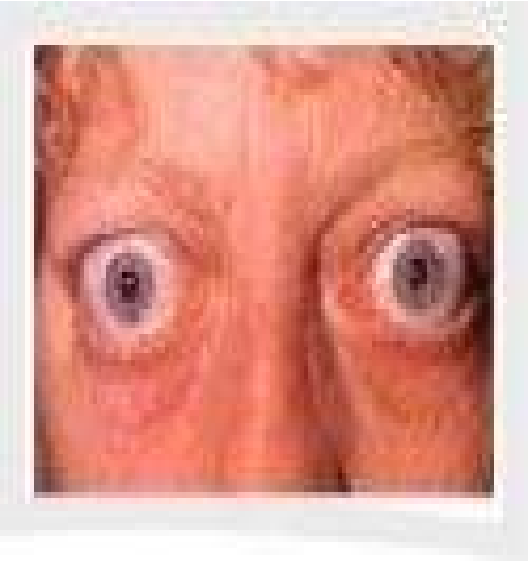
Hyperfunction

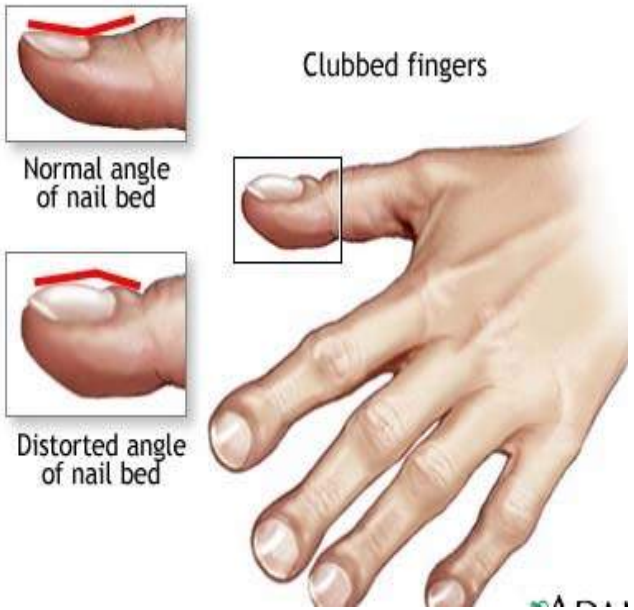
↑ in level of hormone → toxic effects

Due to:

- Diffuse hyperplasia
- Hyperfunctioning multinodular goiter
- Hyperfunctioning adenoma
- Subacute lymphocytic (painless) thyroiditis

Many of the manifestations of hyperthyroidism are related to the increase in oxygen consumption and use of metabolic fuels associated with the hypermetabolic state, as well as to the increase in sympathetic nervous system activity that occurs . These signs are:- diarrhea and weight loss, eye problems, enlarged thyroid gland, hair and skin changes , heart palpitations, clubbing, menstrual cycle changes, muscle weakness and easily bruised.





Thyrotoxicosis is the increase the amount of thyroid hormone whatever the cause, and hyperthyroidism is the major cause of it. The hyperthyroidism and thyrotoxicosis terms are not synonymous.

Causes of Thyrotoxicosis:-

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)and 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 thyroiditis (painful), sub-acute lymphocytic thyroiditis (painless) and factitious thyrotoxicosis (exogenous thyroxine intake).

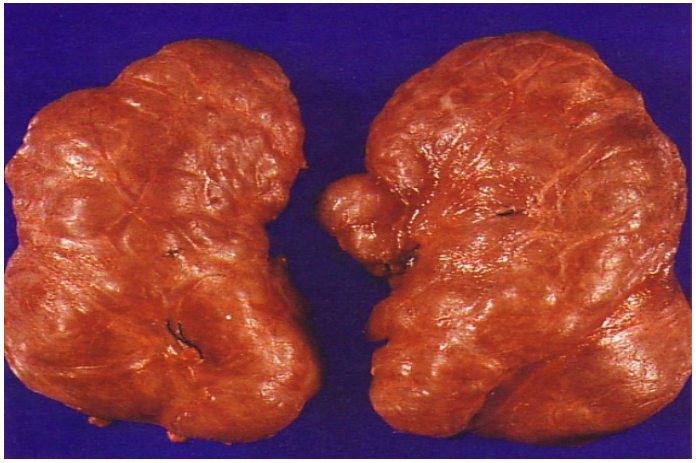
Graves disease:

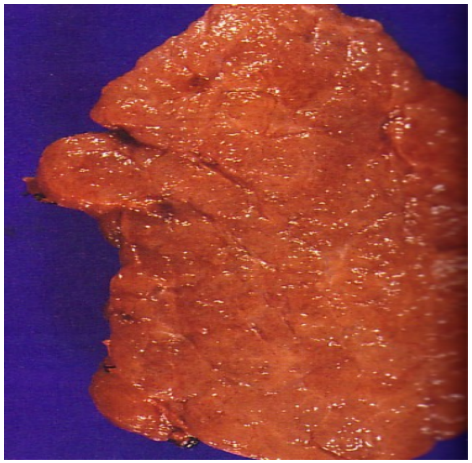
Graves disease is a state of hyperthyroidism, goiter, ophthalmopathy, or, less commonly, dermopathy. The onset usually is between the ages of 20 and 40 years, and women are five times more likely to develop the disease than men. Graves disease is an autoimmune disorder characterized by abnormal stimulation of the thyroid gland by thyroid-stimulating antibodies(TSH-receptor antibodies) that act through the normal TSH receptors.

Graves disease:

The ophthalmopathy, which occurs in up to one third of persons with Graves disease, is thought to result from a cytokine-mediated activation of fibroblasts in orbital tissue behind the eyeball. The ophthalmopathy of Graves disease can cause severe eye problems, including abnormal positioning of the extraocular muscles resulting in diplopia; involvement of the optic nerve, with some visual loss; and corneal ulceration because the lids do not close over the protruding eyeball (due to the exophthalmos).

Graves Disease





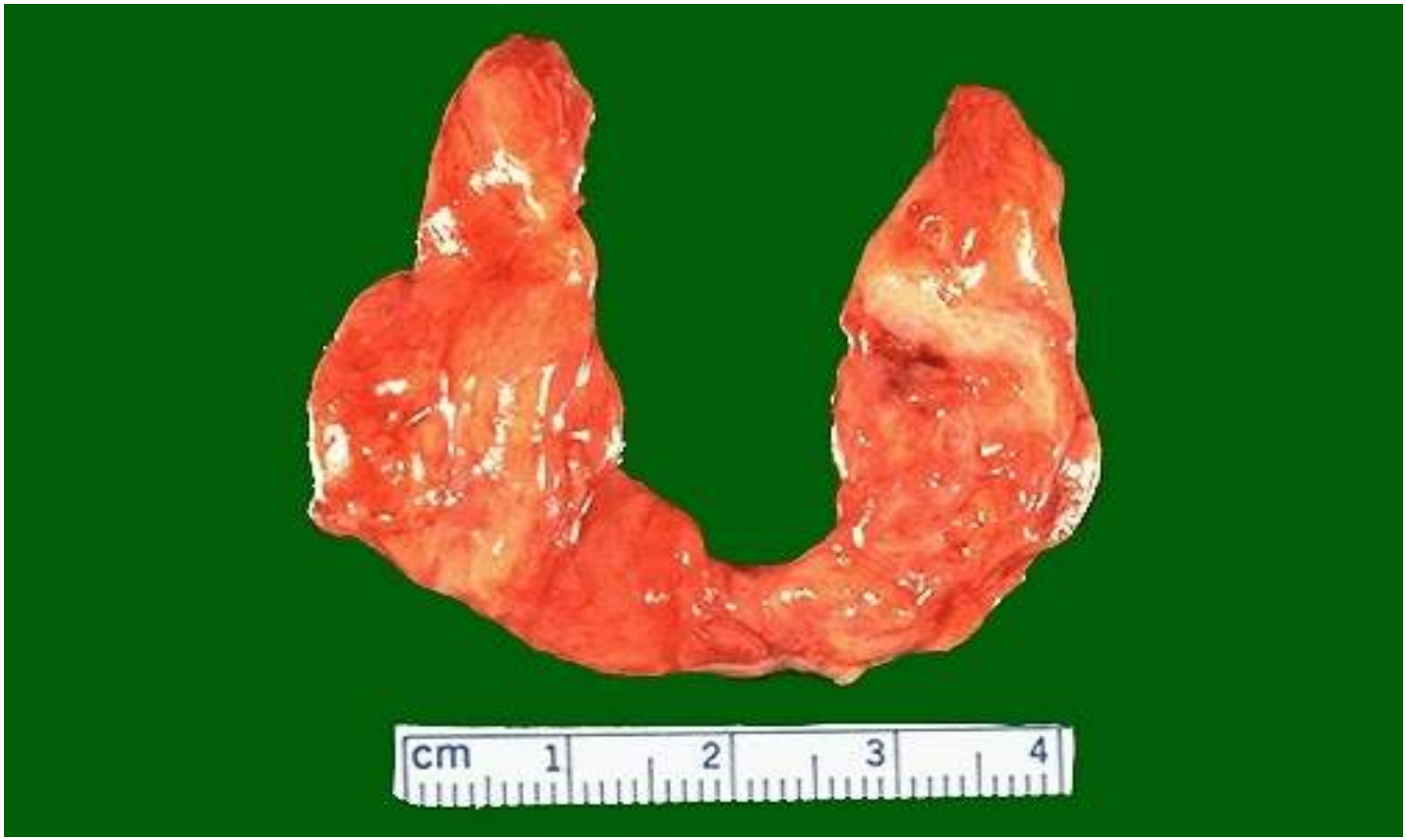
- **Symmetrical enlargement of thyroid gland**
- **Cut-surface is homogenous, soft and appear meaty**
- **Hyperplasia and hypertrophy of follicular cells**

Hashimoto's Thyroiditis: (chronic lymphocytic thyroiditis)

Hashimoto thyroiditis is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient. It is characterized by gradual thyroid failure secondary to autoimmune destruction of the thyroid gland. It is most prevalent between the ages of 45 and 65 years and is more common in women than in men.

Pathogenesis

Hashimoto thyroiditis is caused by destruction of the thyroid gland by auto antibodies against (thyroglobulin , thyroid peroxidase and other thyroid tissue components. Thus, demonstrate progressive depletion of thyroid epithelial cells (thyrocytes) and their replacement by mononuclear cell infiltration and fibrosis.



This symmetrically small thyroid gland demonstrates atrophy. This patient was hypothyroid. This is the end result of Hashimoto's thyroiditis.

Goiter is an increase in the size of the thyroid gland. It can occur in hypothyroid, euthyroid, and hyperthyroid states. Goiters may be :-

Diffuse & Multinodular goiters

- Reflects impaired synthesis of thyroid hormone most often caused by iodine deficiency
- Impairment leads to compensatory ↑ in TSH levels → hypertrophy and hyperplasia of follicular cells → gross enlargement of gland
- Euthyroid metabolic state
- Degree of enlargement is proportional to level and duration

Diffuse nontoxic goiter

- Diffuse non-toxic (simple) goiter
  - colloid goiter
  - Endemic
  - sporadic (dyshormonogenetic)

Multinodular goiter

•Recurrent episodes of hyperplasia and involution leads to irregular enlargement

•Causes most extreme enlargement and may be mistaken for neoplasm

•May arise due to variable response of follicular cells to external stimuli such as trophic hormones

•With uneven follicular hyperplasia, generation of new follicles and uneven accumulation of colloid → rupture of follicle and vessels →hemorrhage, scarring & calcification → nodularity

Goiter

goiter simply means enlarged thyroid