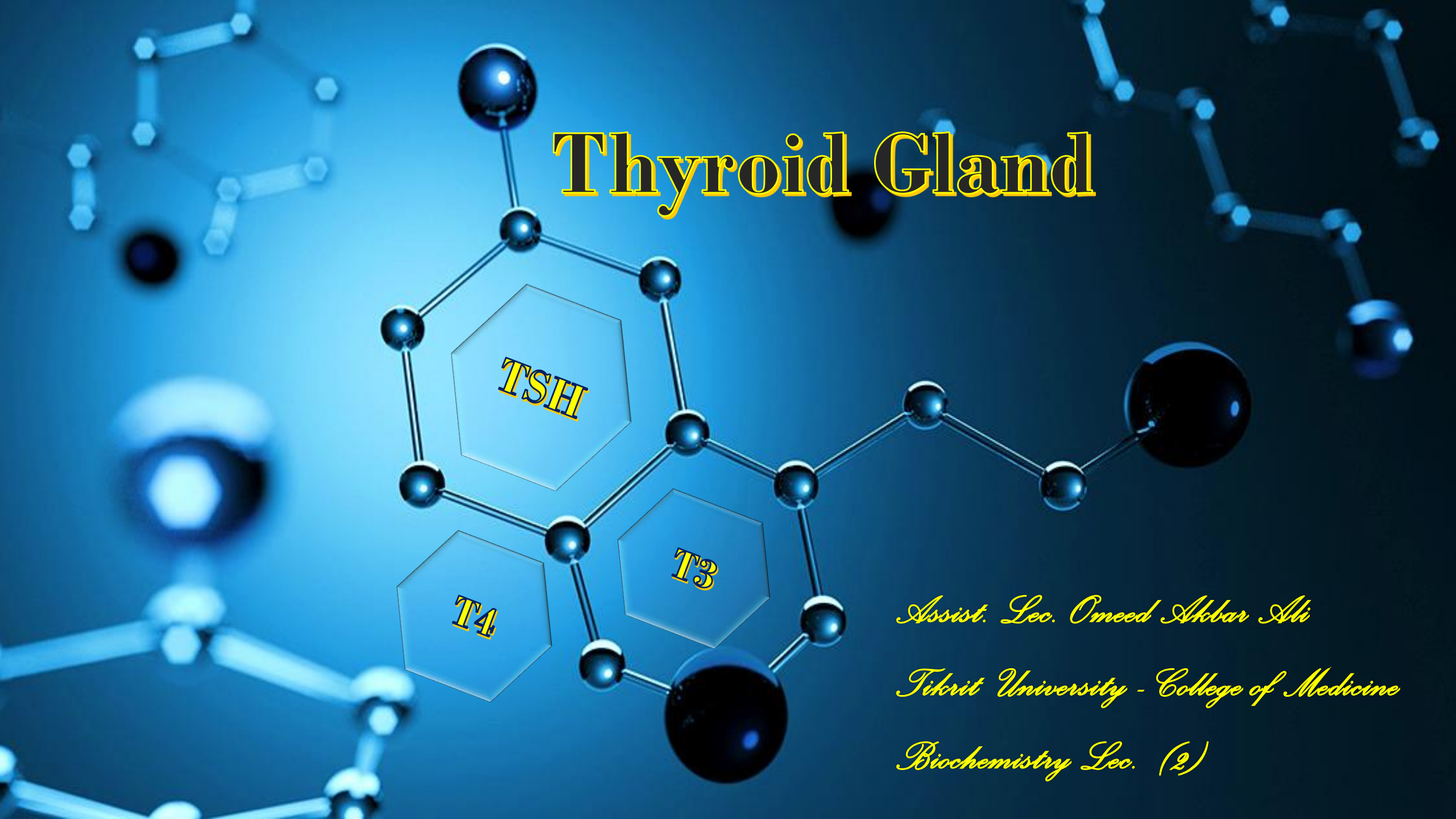


Thyroid Gland

The background of the slide features a complex, blue-toned molecular structure. It consists of various interconnected rings and spheres, resembling a chemical or biological model. Overlaid on this structure are three light blue hexagonal labels with yellow text. The label 'TSH' is positioned in the upper left, 'T3' is in the lower right, and 'T4' is in the lower left. The overall aesthetic is scientific and modern.

TSH

T3

T4

Assist. Lec. Omeed Akbar Ali
Tikrit University - College of Medicine
Biochemistry Lec. (2)

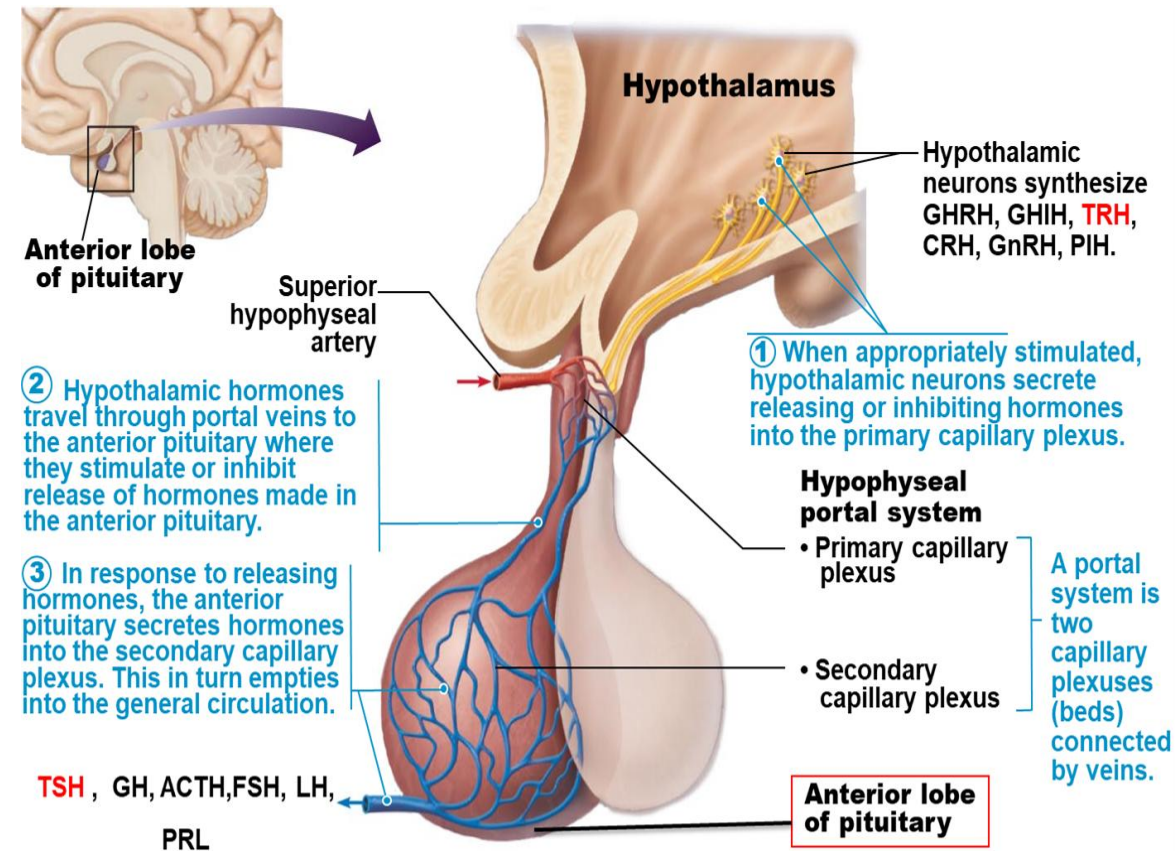
Overview

- Thyroid hormone synthesis and secretion
- Thyroid hormone action
- Regulation of thyroid hormones
- Thyroid function tests
- Thyroid gland disorders
 - - Goitre
 - - Hypo and hyperthyroidism
 - Causes
 - Diagnosis

Thyroid-stimulating hormone (TSH)

TSH is a glycoprotein hormone produced by the anterior pituitary.

- ✓ - It is the primary stimulus for thyroid hormone production by the thyroid gland.
- ✓ - Specifically, neurons in the **hypothalamus release TRH**, or **Thyroid-releasing Hormone**, which stimulates thyrotrophs of the anterior pituitary to secrete **TSH**.
- ✓ - **TSH**, in turn, stimulates **thyroid follicular cells** to release thyroid hormones in the form of **T3** or **T4**.



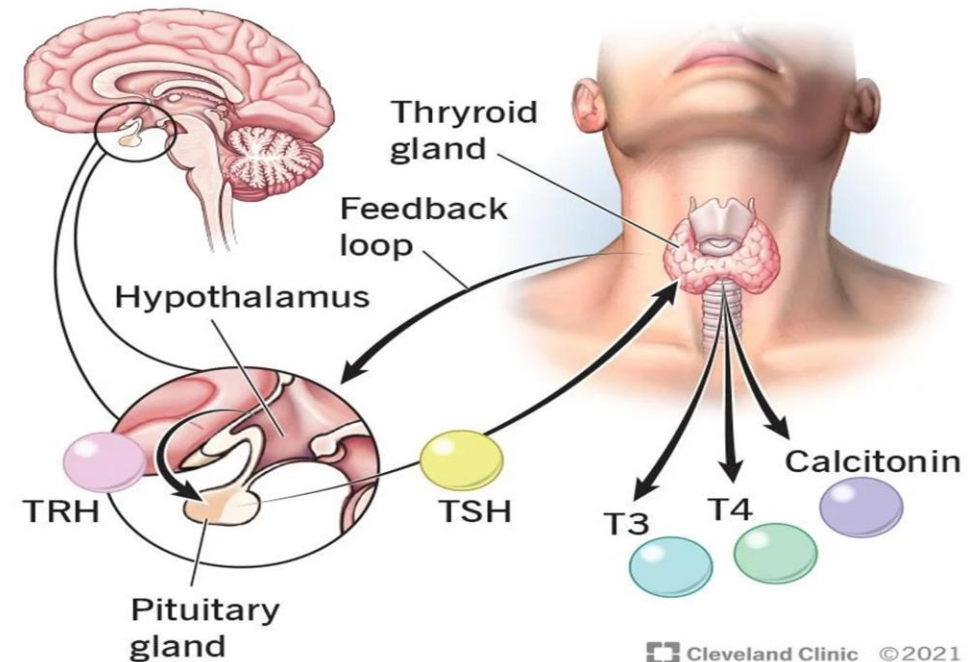
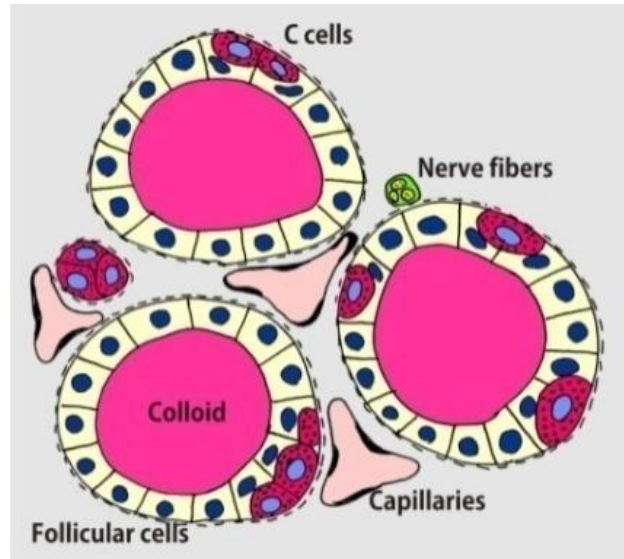
Thyroid Gland

- The thyroid gland is the largest butterfly shaped endocrine gland.
- Located at the base of the neck below larynx on each side and anterior to the trachea.

Consist two types of cell :-

1-Follicular cell secrete Triiodothyronine (T3) and Thyroxine (T4).

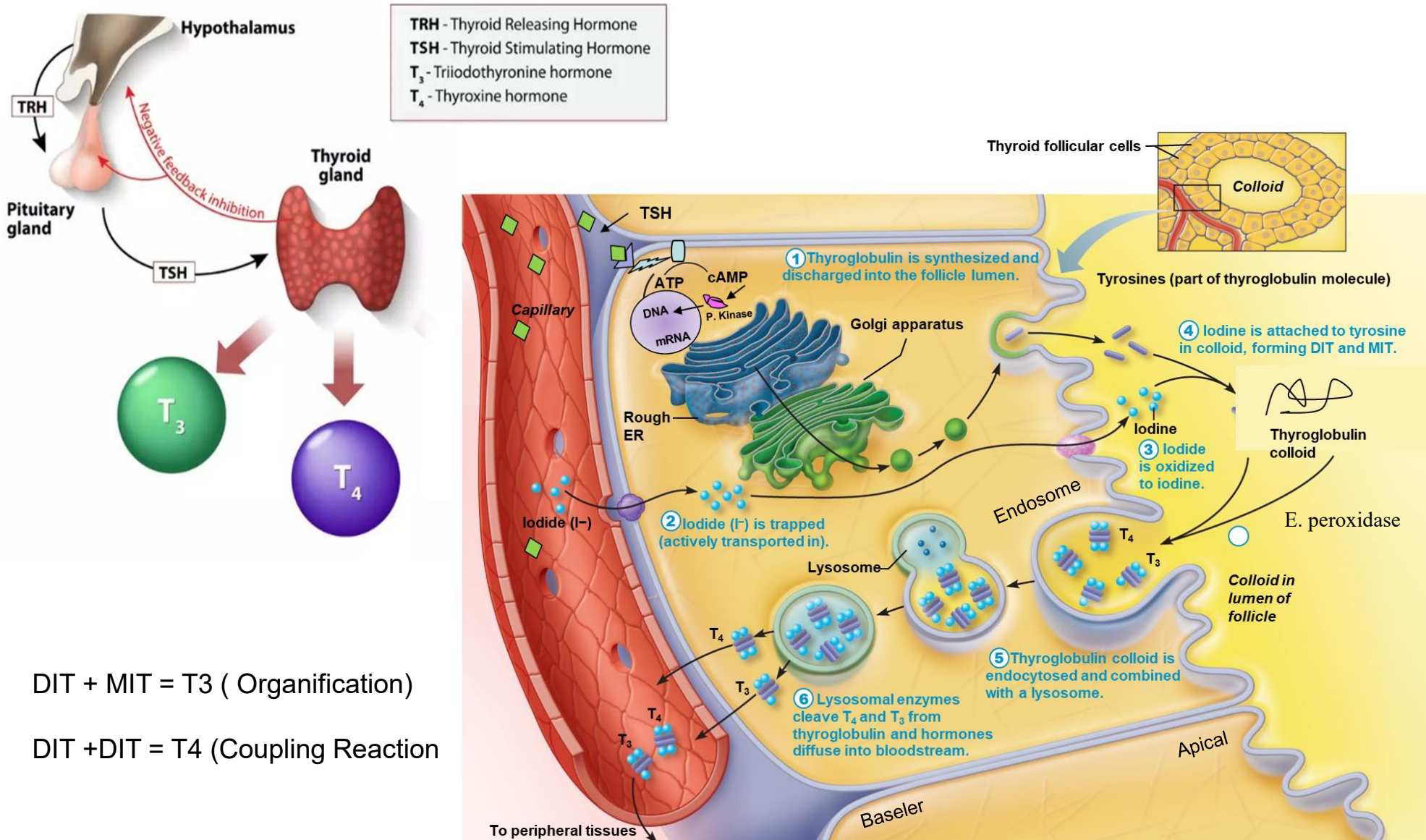
2-Parafollicular cell secrete Calcitonin.



Synthesis of thyroid hormones

- ✓ - Thyroglobulin is synthesized and discharged into the lumen
- ✓ - Iodides (I^-) are actively taken into the cell, oxidized to iodine (I_2), and released into the lumen
- ✓ - Iodine attaches to tyrosine, mediated by peroxidase enzymes, forming T1 (monoiodotyrosine, or MIT), and T2 (diiodotyrosine, or DIT)
- ✓ - Iodinated tyrosines link together to form T3 and T4
- ✓ - Colloid is then endocytosed and combined with a lysosome, where T3 and T4 are cleaved and diffuse into the bloodstream
 - - This process stimulates T4 and T3 are released into blood stream by **proteolytic enzyme**.
- ✓ - This process is stimulated by TSH. and inhibited by iodide.

Thyroid Hormones Secretion

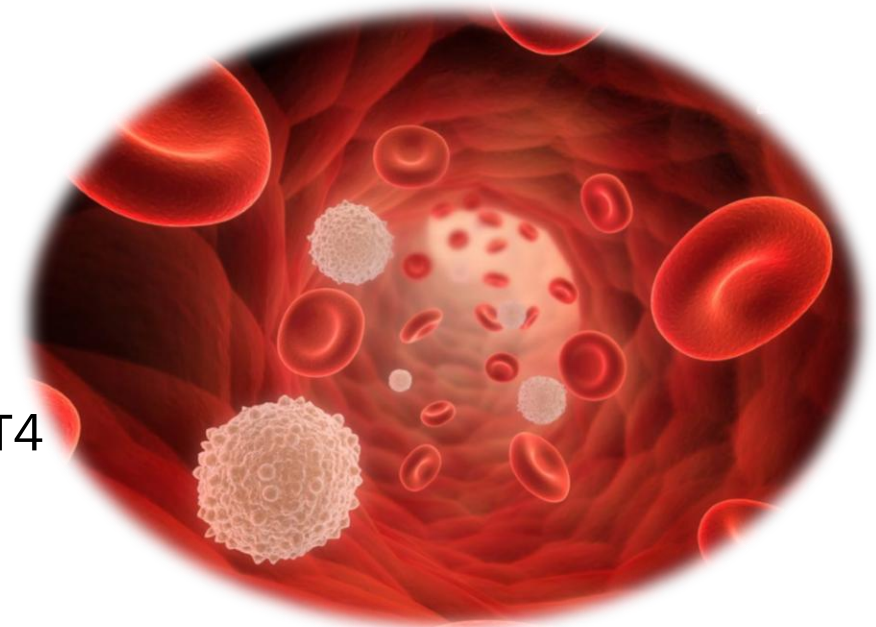


DIT + MIT = T₃ (Organification)

DIT +DIT = T₄ (Coupling Reaction

Transport And Regulation of TH

- - T3 is the more biologically active form
- - T4 can be converted to rT3 (reverse T3) – inactive form (this is a regulatory mechanism)
- - Bound form most of T4 & T3 is transported in plasma.
 - - Thyroxin Binding globulin (TBG)-bound (70%)
 - - Albumin-bound (25%)
 - - Transthyretin (prealbumin)-bound (5%).
- Both bind to target receptors, but T3 is **ten** times more active than T4
- Peripheral tissues convert T4 to T3



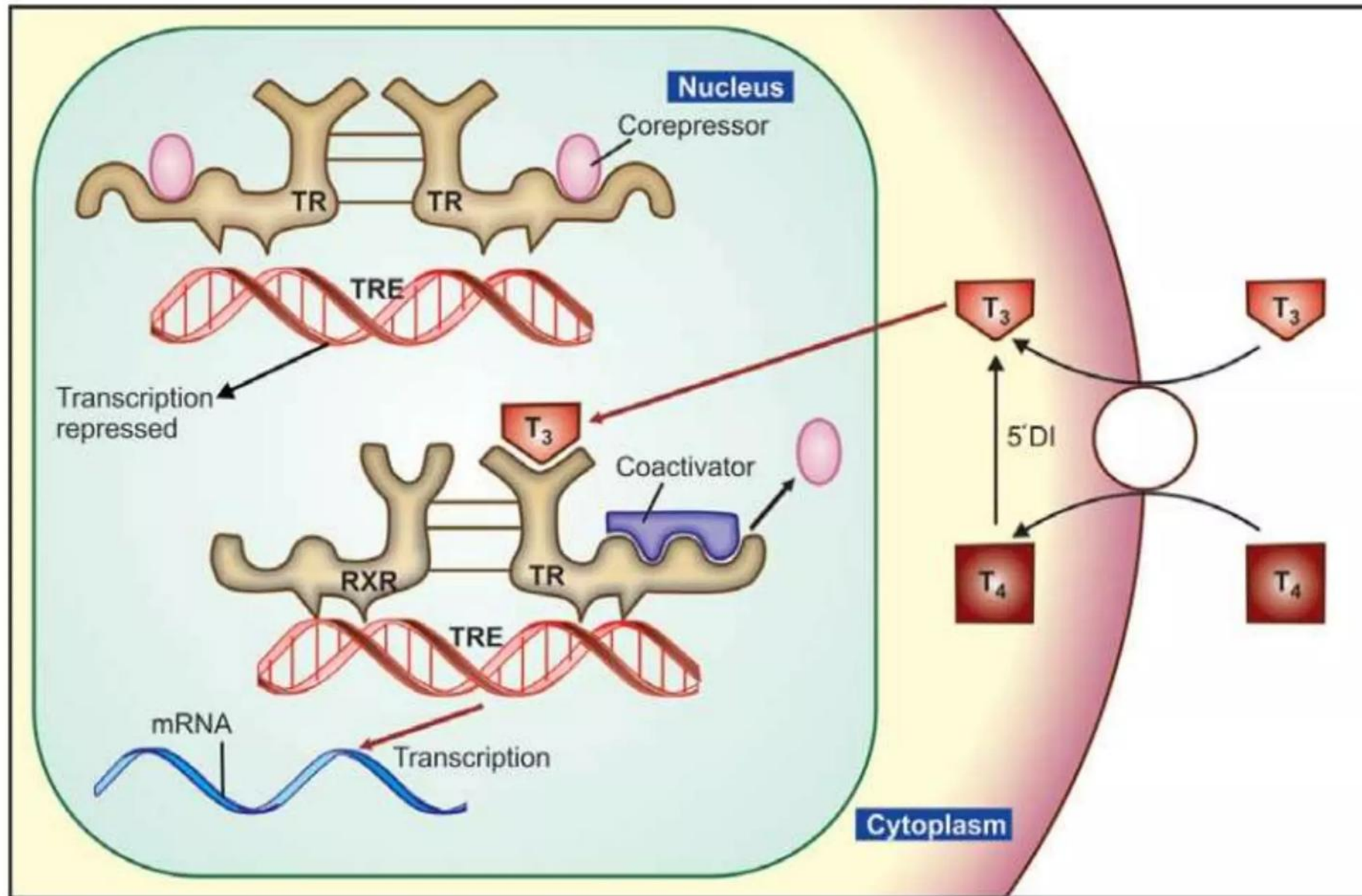
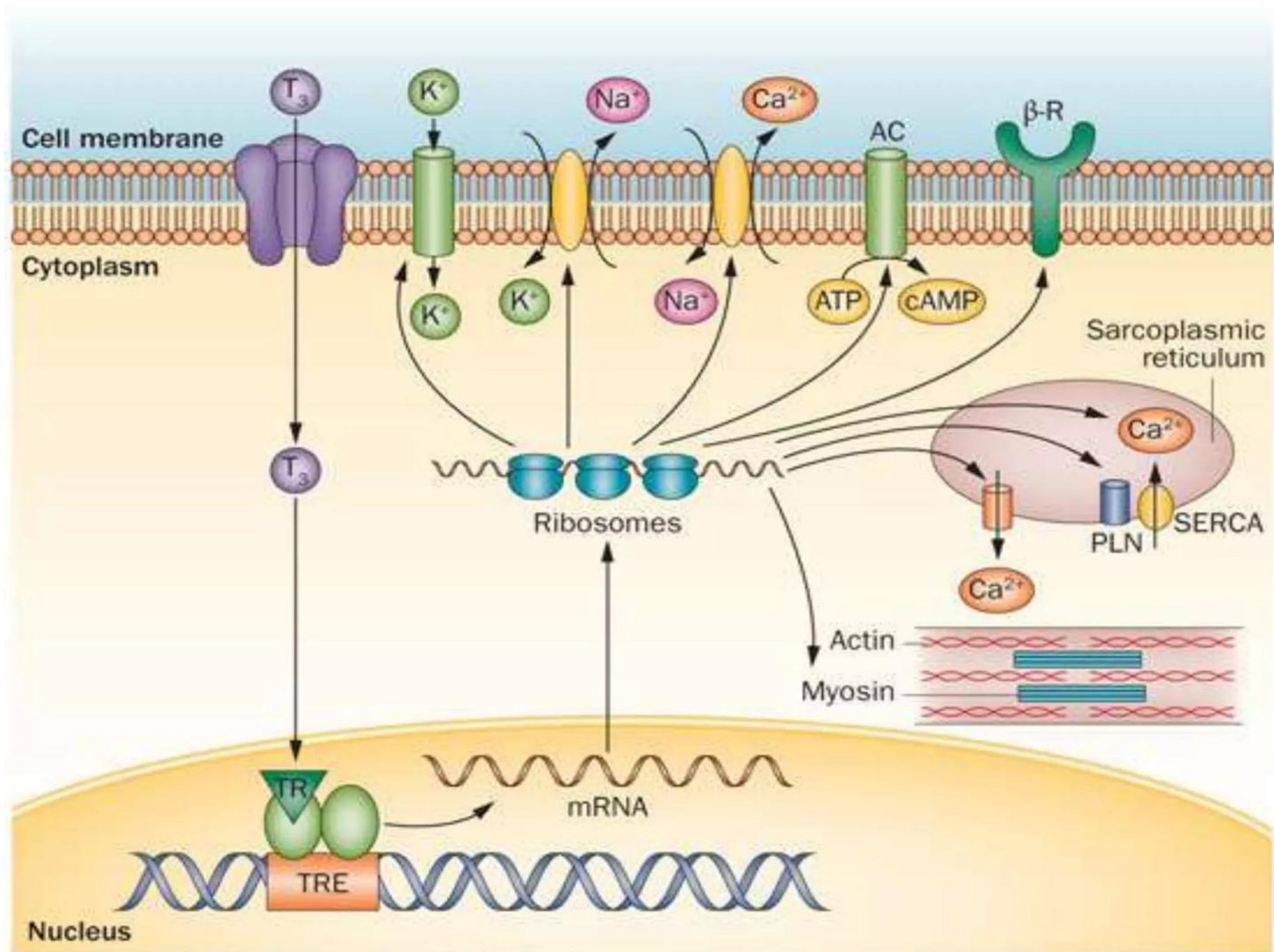


Fig. 18.4: Mechanism of action of thyroid hormone on nuclear thyroid hormone receptor (TR).
 T_3 —Triiodothyronine; T_4 —Thyroxine; TRE—Thyroid hormone response element; RXR—Retinoid X receptor;
 mRNA—Messenger ribonucleic acid; 5'DI—5'Deiodinase (See text for explanation)



Effects of Thyroid Hormone

- TH is concerned with:
 - Glucose oxidation / Glycogenolysis
 - Increasing metabolic rate
 - Heat production
- TH plays a role in:
 - Maintaining blood pressure
 - Regulating tissue growth
 - Developing skeletal and nervous systems
 - Maturation and reproductive capabilities

Actions of Thyroid Hormone

❖- The important actions performed by thyroid hormone are as follows:

1- Calorigenic Action.

- Thyroxine stimulates **metabolism in the tissues**, increases oxygen consumption and heat production.
 - It also increases the size of the cells.

2- Effects on Carbohydrate Metabolism.

- Increases absorption of glucose from GIT.
- Increases insulin secretion.
- Increases glycolysis in the liver.
- Increases breakdown of glycogen into glucose.

Actions of Thyroid Hormone Con..

3- Effects on Protein Metabolism.

- Thyroid hormone **increases the synthesis of protein in the cells.**
 - By increasing the translation of RNA.
 - By increasing the transcription of DNA and RNA.
 - By increasing the activity of Mitochondria.
 - By increasing the activity of cellular enzymes.

Actions of Thyroid Hormone Con..

4- Effects on Fat Metabolism.

- Thyroxine **increases the free fatty acid level in blood.**
- Decreases phospholipids, triglycerides, and cholesterol in blood.

5- Effects on Vitamin Metabolism.

- The metabolism of fat soluble vitamins is also affected by thyroid hormone.
 - T4 is necessary for the synthesis of vitamin A from carotene and the conversion of vitamin A to retinine.

Actions of Thyroid Hormone Con..

6- Effects on water and mineral Metabolism.

- Promotes demineralization of bones.
- Increases excretion of calcium and phosphates in the urine.
- Increases K^+ excretion.
- Causes diuresis

Actions of Thyroid Hormone Con..

7- Effects on Central Nervous System

- Increases the synaptic activity.
- Cerebration becomes very rapid.
- Development and maintenance of normal function of the CNS.

8- Effects on Cardiovascular.

- Heart rate increased.
- Cardiac output increased.
- Systolic blood pressure increased.
- Diastolic blood pressure decreased.

Actions of Thyroid Hormone Con..

9- Effects on Respiration.

- Causes increased utilization of oxygen and carbon dioxide.
- Increases pulmonary ventilation.
- Increases rate and depth of respiration.

10- Effects on GIT.

- Increases appetite.
- Increases food intake.
- Increases secretion of digestive juices.
- Increases motility of GIT.

Actions of Thyroid Hormone Con..

11- Effects on Blood.

- Increases the production of RBCs.
- Increases the blood volume.

12- Effects on Body Weight.

- Maintaining weight of the body.
- Increase in thyroxine secretion decreases the body weight and fat storage, and decrease in thyroxine secretion increase the body weight b/c of fat deposition.

Actions of Thyroid Hormone Con..

13- Effects on Muscle.

- A muscle weakness occurs in most
 - patients with hyperthyroidisms called thyrotoxic myopathy.
 - When hyperthyroidism is severe and prolonged, the myopathy may be severe.

14-Effects on other endocrine glands.

- Increased thyroid hormone increased the rates of secretion of **most of the other endocrine glands.**

Normal Reference Interval

- T3 : 0.8 - 2.0ng/ml
- T4 : 5.1 - 14.1μg/dl
- fT4 : 0.93 - 1.7ng/dl
- fT3 : 3.5 - 7.8pmol/L
- TSH : 0.27 - 4.1μIU/ml
- Anti-TPO : <34.0IU/ml
- Tg : 3-40 ng/mL

Thyroid Function Tests (TFT)

I. TSH measurement:

- Indicates thyroid status
- Sensitive, first-line test

II. Total T_4 or free T_4 :

- Indicates thyroid status
- Monitors thyroid treatment (both anti-thyroid and thyroid supplement treatment)
- TSH may take up to 8 weeks to adjust to new level during treatment

Thyroid Function Tests (TFT),

continued..

III. Total T_3 or free T_3 :

- In hyperthyroidism, the rise in T_3 is disproportionate of T_4
 - For earlier identification of **thyrotoxicosis**
 - In some patients only T_3 rises (T_4 is normal): **T_3 toxicosis**

IV. Antibodies:

- Diagnosis and monitoring of autoimmune thyroid disease (**Hashimoto's thyroiditis**); anti-thyroid peroxidase (anti-TPO) in **hypothyroidism**
- Diagnosis of **Grave's disease**: stimulating antibodies against TSH receptors on thyroid cells in **thyrotoxicosis**.

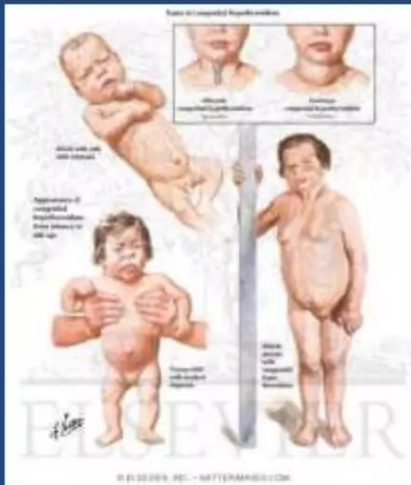
Thyroid Disorders

Cretinism

Hyperthyroidism

Hypothyroidism

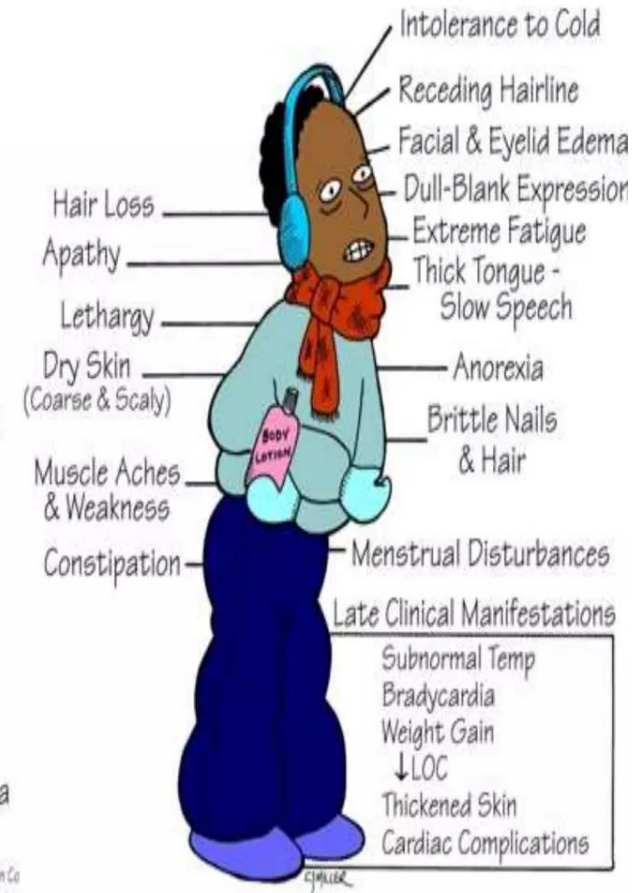
Euthyroid Goiter



HYPERTHYROIDISM



HYPOTHYROIDISM



Algorithm for Diagnosis of Thyroid Dysfunction

1 2 Sub

TSH ↑ ↓ ↑

T3, T4 ↓ ↓ ~



TSH

Decreased

Normal

Increased

FreeT4&T3

Euthyroid No further testing

FreeT4

Increased
Hyperthyroidism

Decreased Nonthyroidal
illness or drug effect
Secondary Hypothy.

Normal
Subclin hypothyroidism

Normal
Subclin hyperthyroidism
Glucocort.

Decreased
Primary
Hypothyroidism

Increased
Thyroid
Resistance or
Pituitary Tm.

Hypothyroidism

- Deficiency of thyroid hormones
- *Primary hypothyroidism:*
 - Failure of thyroid gland (Elevated TSH level is diagnostic)
- *Secondary hypothyroidism:*
 - Failure of the pituitary to secrete TSH (rare)
 - Failure of the hypothalamic-pituitary-thyroid axis (e.g. any pituitary disease)

Hypothyroidism, *continued*..

- **Causes:**

- Hashimoto's disease (autoimmune destruction of the thyroid gland)
- Radioiodine or surgical treatment of hyperthyroidism
- Drug effects (e.g. lithium)
- TSH deficiency (may be with panhypopituitarism)
- Congenital defects (e.g. defective synthesis of T4 & T3, or organ resistance to their actions)
- Severe iodine deficiency

Over 90% of
cases

- **Clinical features**

- Tiredness
- Cold intolerance
- Weight gain
- Dry & coarse skin and hair
- Others (constipation, bradycardia,...)

Hypothyroidism, *continued*..

- *Non-thyroidal illness (acute illness)*
 - In some systemic diseases, the normal regulation of TSH, T_3 and T_4 secretion and metabolism is disturbed & the concentrations of the transport proteins (albumin and transthyretin) are low.
 - Most of T_4 is converted to rT_3 (inactive) $\rightarrow$ $\downarrow$ thyroid hormone activity (low T_3 syndrome)
 - This does not increase TSH secretion (TSH is suppressed) $\rightarrow$ secretion of T_4 and T_3 is decreased

Hyperthyroidism

- **Hyperthyroidism** is over-activity of the thyroid gland → ↑ secretion of thyroid hormones
- Tissues are exposed to ↑ levels of thyroid hormones (**thyrotoxicosis**)
- ↑ pituitary stimulation of the thyroid gland (rare)
- **Causes:**
 - **Grave's disease** (the most common cause)
 - Toxic multinodular goitre
 - Thyroid adenoma
 - Thyroiditis
 - Intake of iodine / iodine-containing drugs e.g. amiodarone
 - Excessive intake of T_4 and T_3

Hyperthyroidism, *continued*..

Diagnosis

- Suppressed TSH level
- Raised thyroid hormones level

Confirms primary
hyperthyroidism

Problems in diagnosis

- Total serum[T₄] changes due to changes in binding protein levels
- In pregnancy, high estrogens → increase TBG synthesis in the liver
 - Total [T₄] will be high, free [T₄] will be normal
- Congenital TBG deficiency → problem in screening of thyroid hormones.

Hyperthyroidism, *continued*..

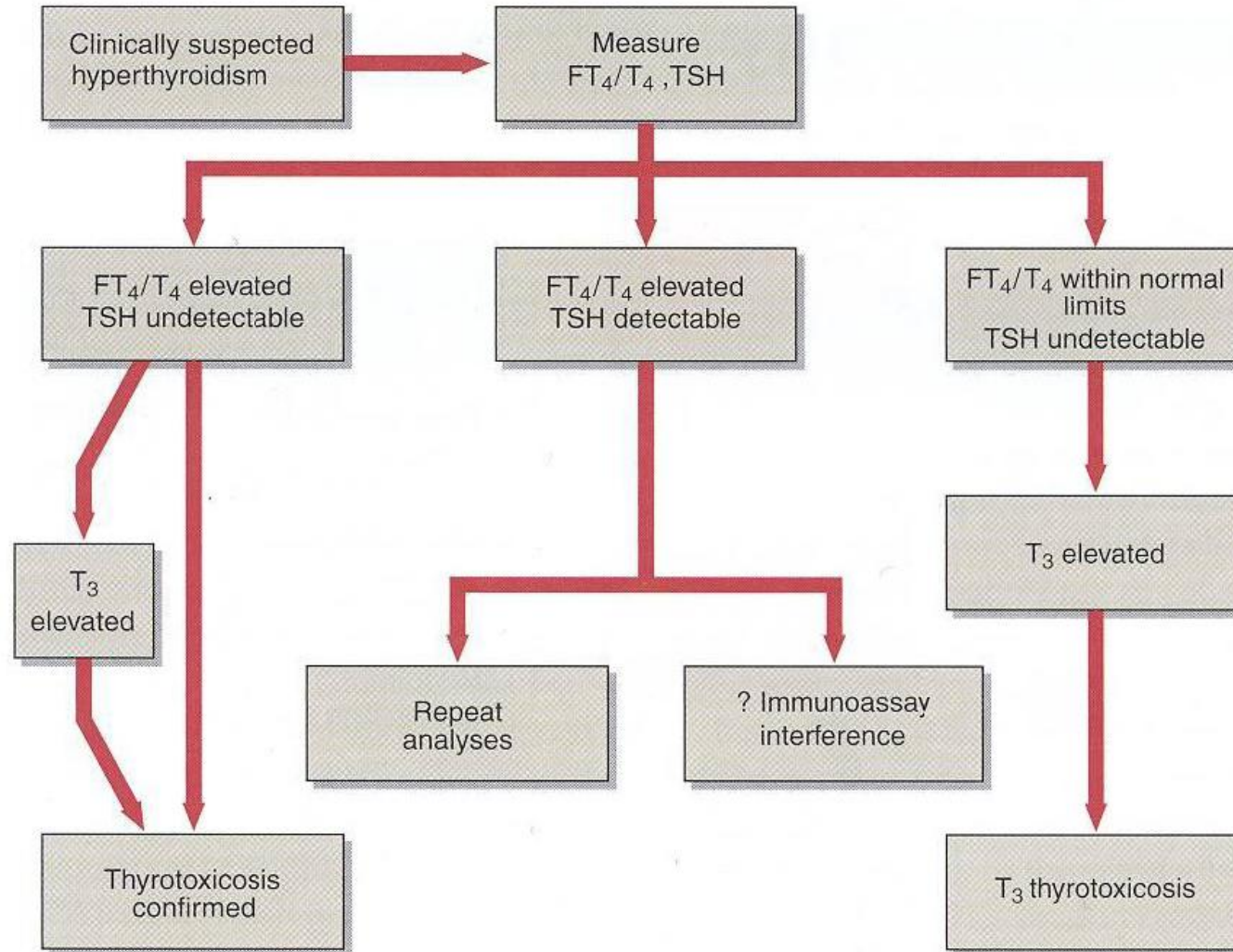


Fig. 2 **Strategy for the biochemical investigation of suspected hyperthyroidism.**

Hyperthyroidism, *continued*..

Clinical features:

- Weight loss with normal appetite
- Sweating / heat intolerance
- Fatigue & generalized muscle weakness, proximal myopathy
- Palpitation / agitation, tremor
- Angina, heart failure
- Diarrhea
- Eyelid retraction and lid lag
- Goiter
- Oligomenorrhoea & subfertility

Goitre

- Enlarged thyroid gland
- **Functionally**; Goitre may be associated with:
 - Hypofunction
 - Hyperfunction
 - Normal concentration of thyroid hormones (euthyroid)
- **Causes:**
 - Iodine deficiency
 - Selenium deficiency
 - Hashimoto's thyroiditis
 - Congenital hypothyroidism
 - Grave's disease (hyperthyroidism)
 - Thyroid cancer



Grave's Disease: Diffuse Toxic Goiter

- Most common cause of hyperthyroidism
- An **autoimmune** disease
- **Antibodies** against TSH receptors on thyroid cells mimic the action of pituitary hormone
- Normal regulation of synthesis/control is disturbed

Figure 16.11 Thyroid disorders.



(a)



(b)

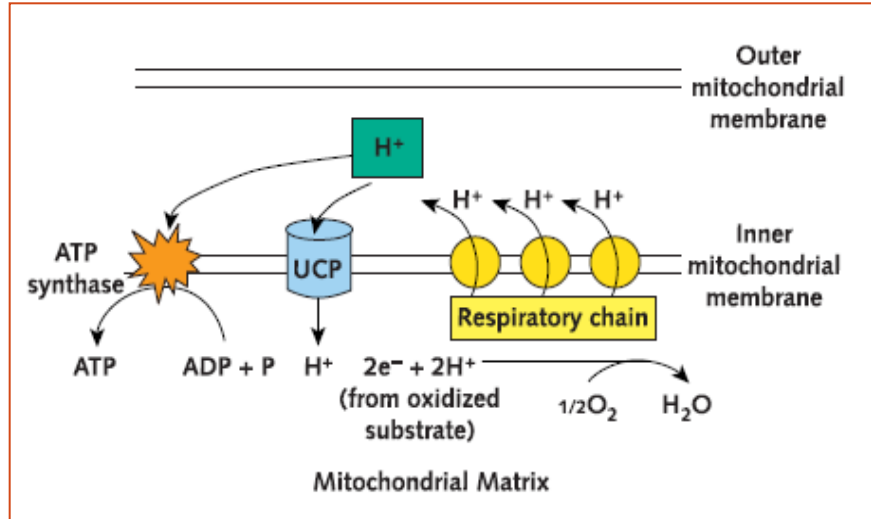
Thermogenesis

- Thyroid hormone has an active role in thermogenesis
- About 30% thermogenesis depends on thyroid
- Thyroid regulates metabolism and ATP turnover
- It increases ATP synthesis and consumption

Thermogenesis, *continued*..

- Na^+ / K^+ gradient requires ATP to maintain it
- The gradient is used to transport nutrients inside the cell
- Thyroid reduces Na^+ / K^+ gradient across the cell membrane by increasing metabolism (more nutrient transport in the cell)
- This increases the demand for ATP to maintain the gradient
- ATP synthesis and consumption is increased that produce heat

Mechanism of action of uncoupling proteins (UCP):



The energy released in the oxidation of substrates in the mitochondria → proton gradient

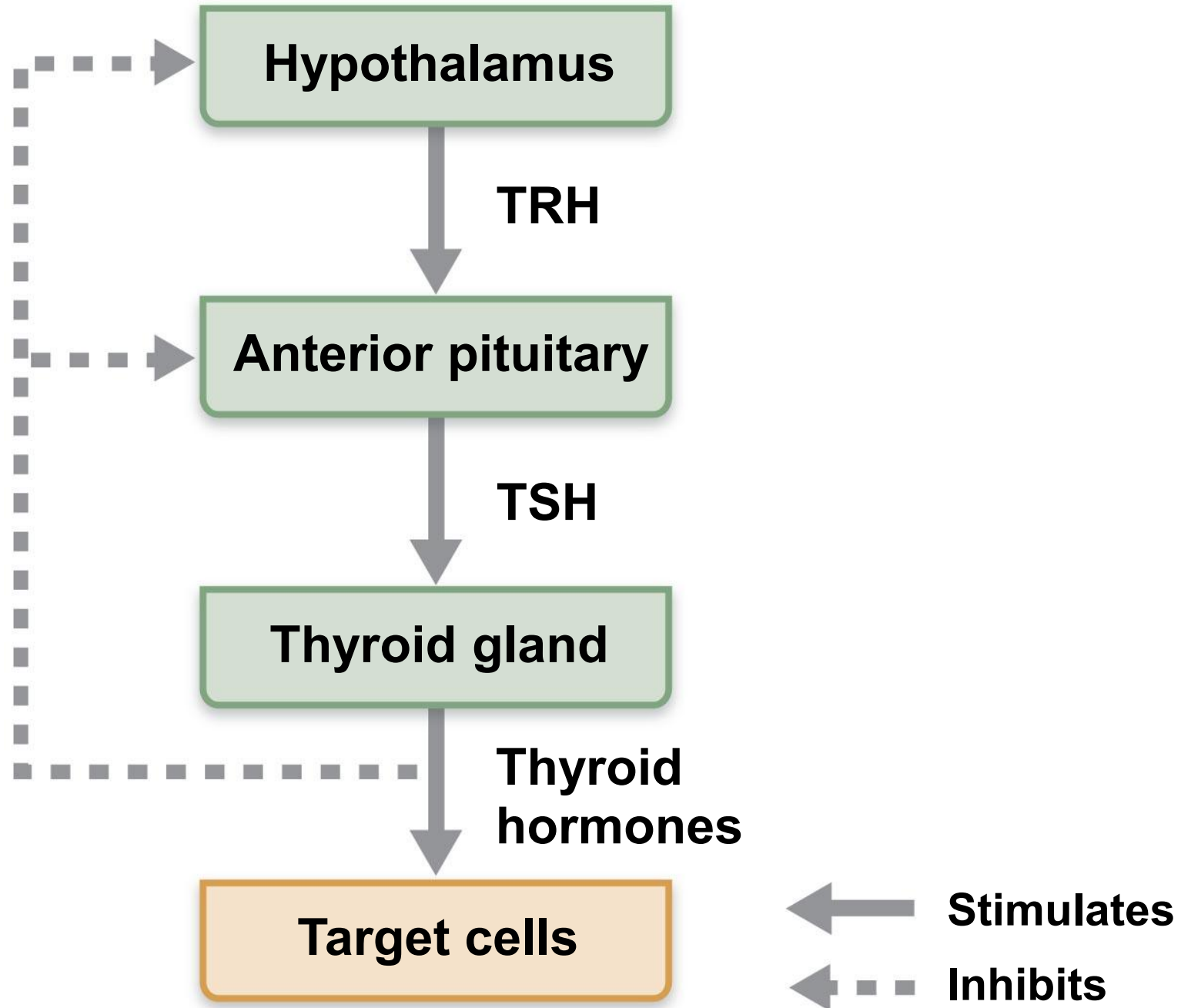


The energy accumulated in this gradient is used by the ATP Synthase to produce ATP



UCPs reduce the proton gradient, bypassing the ATP synthase → exothermic movement of protons down the gradient → heat

Figure 16.8 Regulation of thyroid hormone secretion.



A decorative arrangement of autumn leaves in shades of red, orange, and yellow, scattered across the left and bottom portions of the slide. Some leaves are large and detailed, while others are small and scattered. There are also soft, glowing light effects around some of the leaves.

Thanks For Listening ..