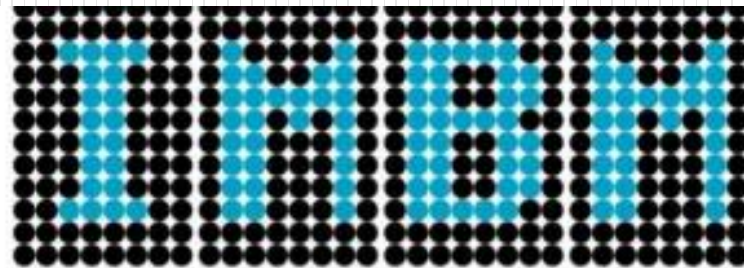


Thyroid gland

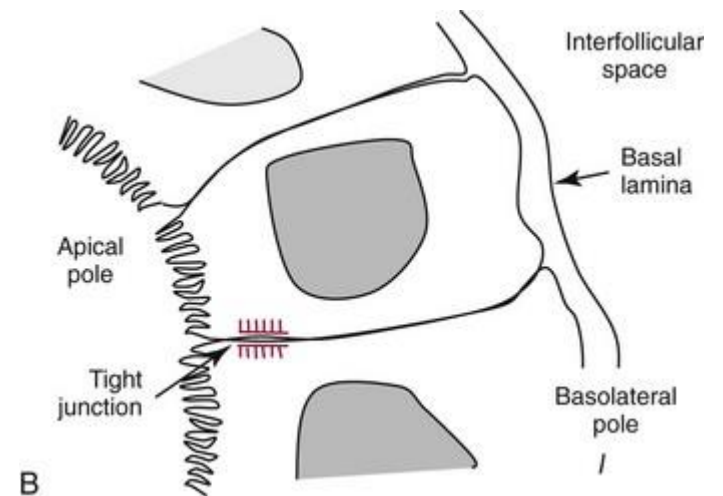
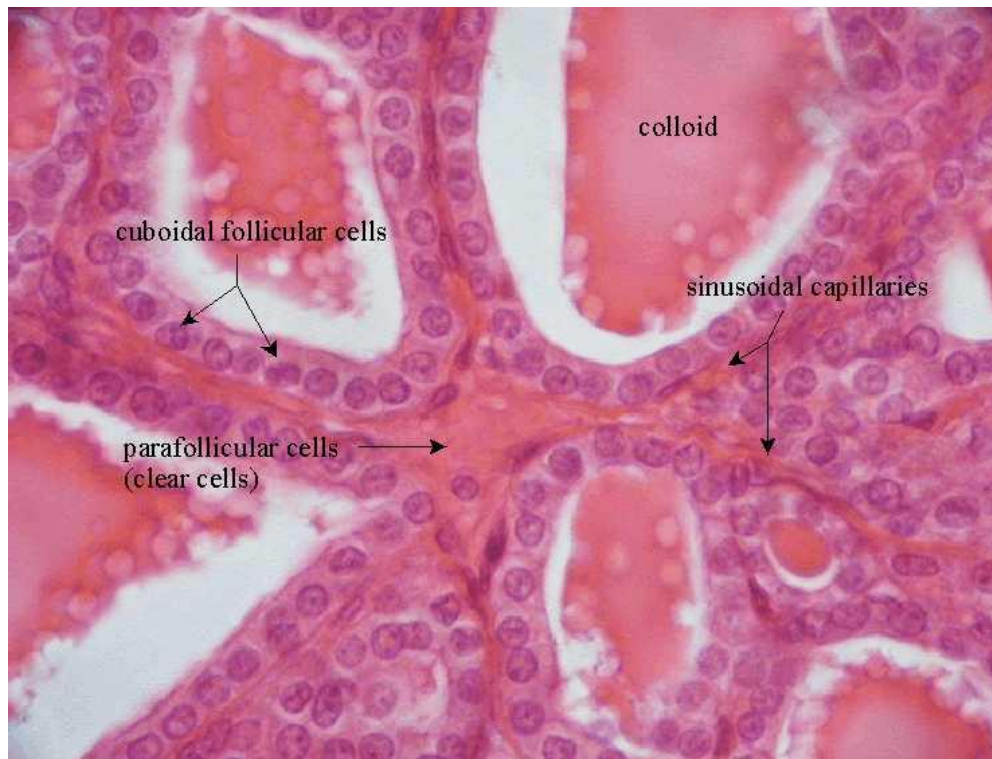
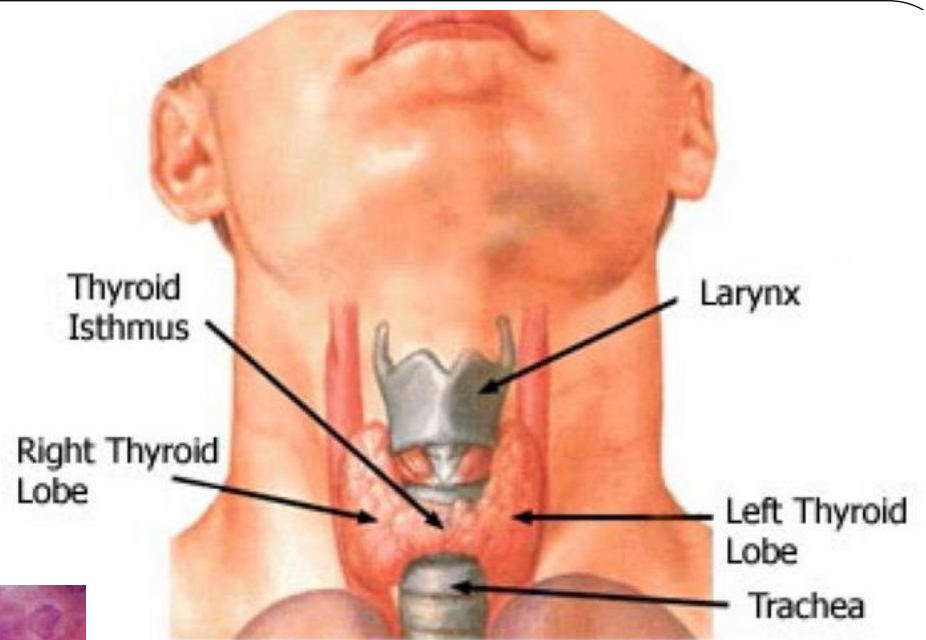
Mgr. Veronika Borbélyová, PhD.
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INSTITUTE OF MOLECULAR BIOMEDICINE

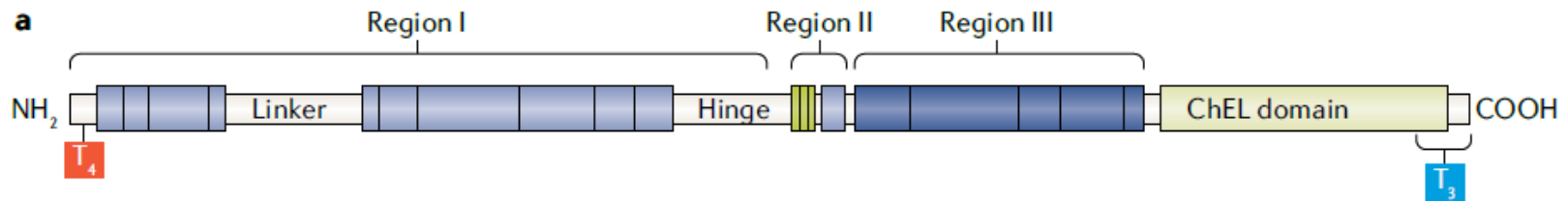
www.imbm.sk

Morphology



Biosynthesis of thyroid hormones

- **Thyroxine (T_4)**
- **Triiodothyronine (T_3)**



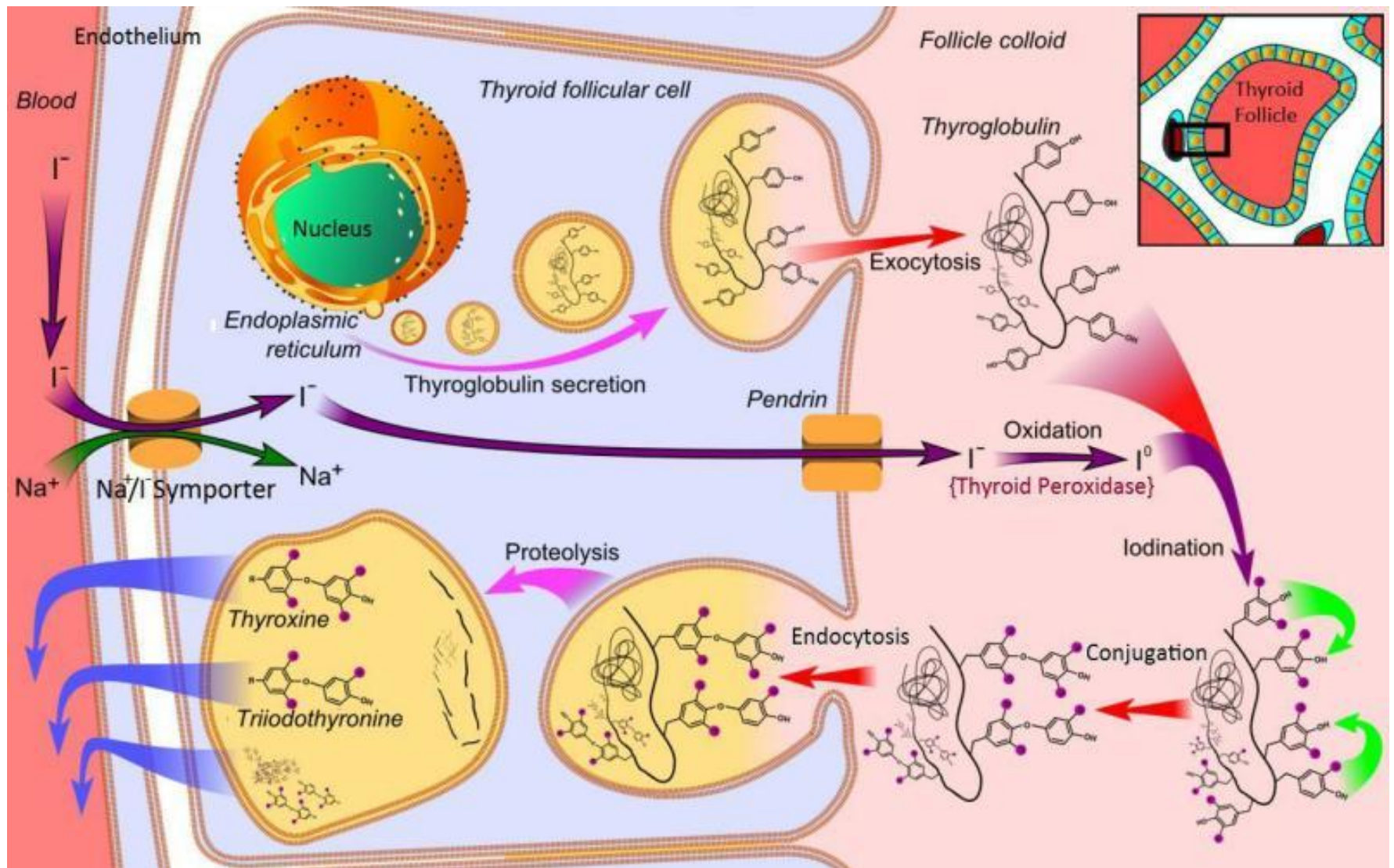
Iodination

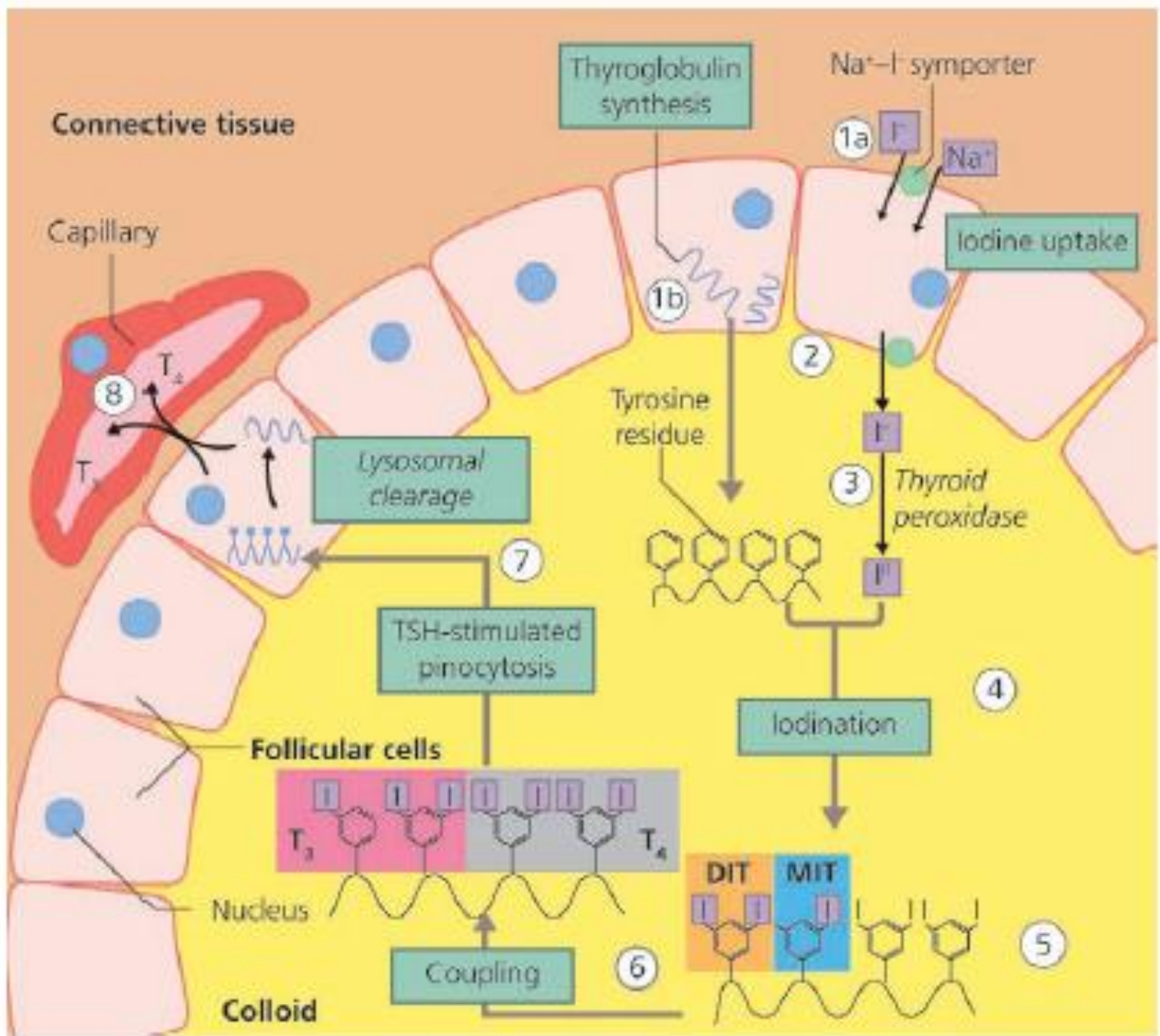
- iodine intake – 150 $\mu\text{g}/\text{day}$
- deiodination of thyroid hormones
- iodide supplementation of salt



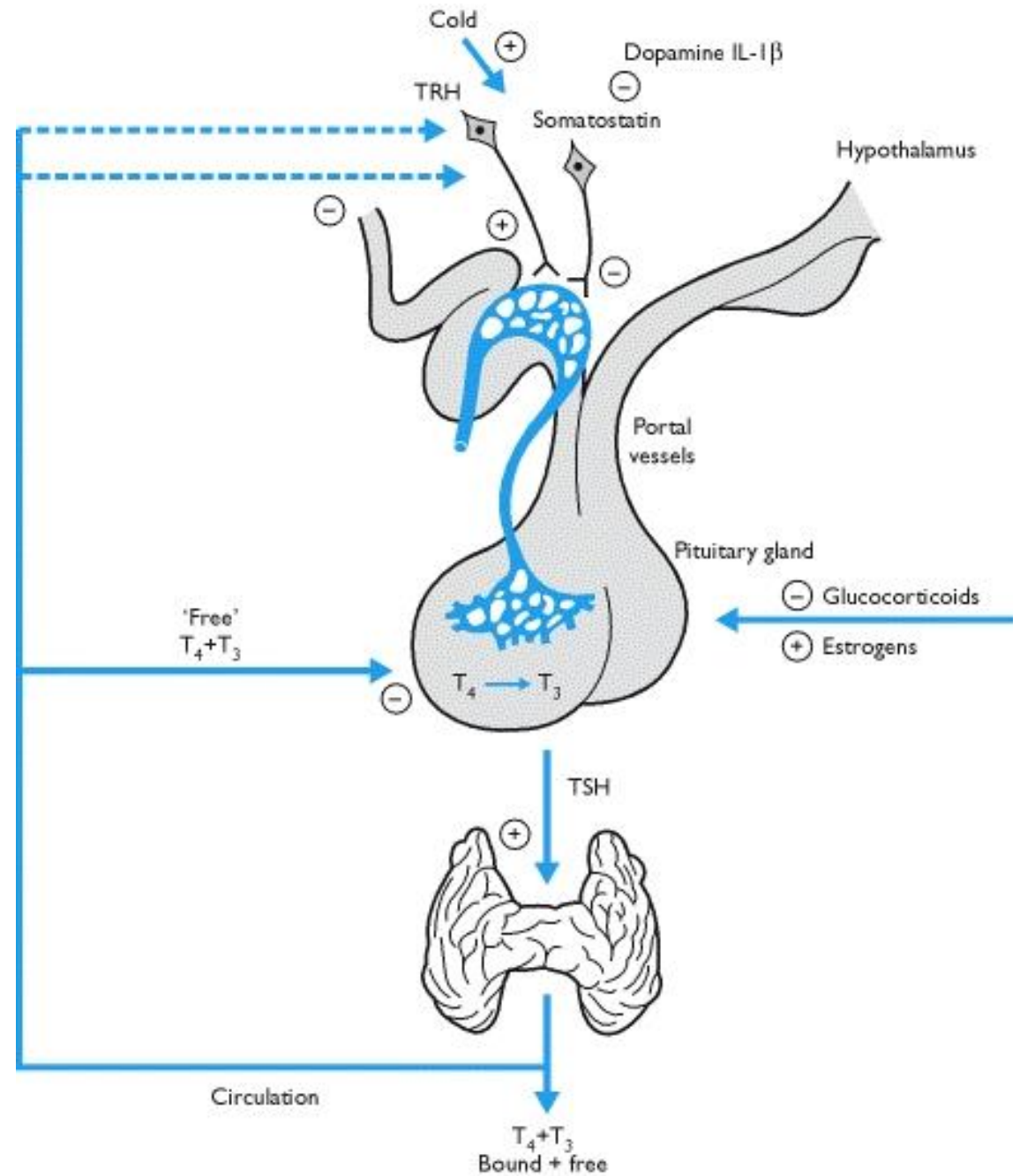
Biosynthesis of thyroid hormones

- Thyroglobulin synthesis – ER, GA
 - Iodide trapping – NIS
 - Transport of iodide into follicular cavity - pendrin
 - Oxidation of iodide – thyroid peroxidase
 - Iodination of tyrosine - iodinase
 - Coupling reactions
-
- Transport of thyroidal hormones to the blood





Regulation

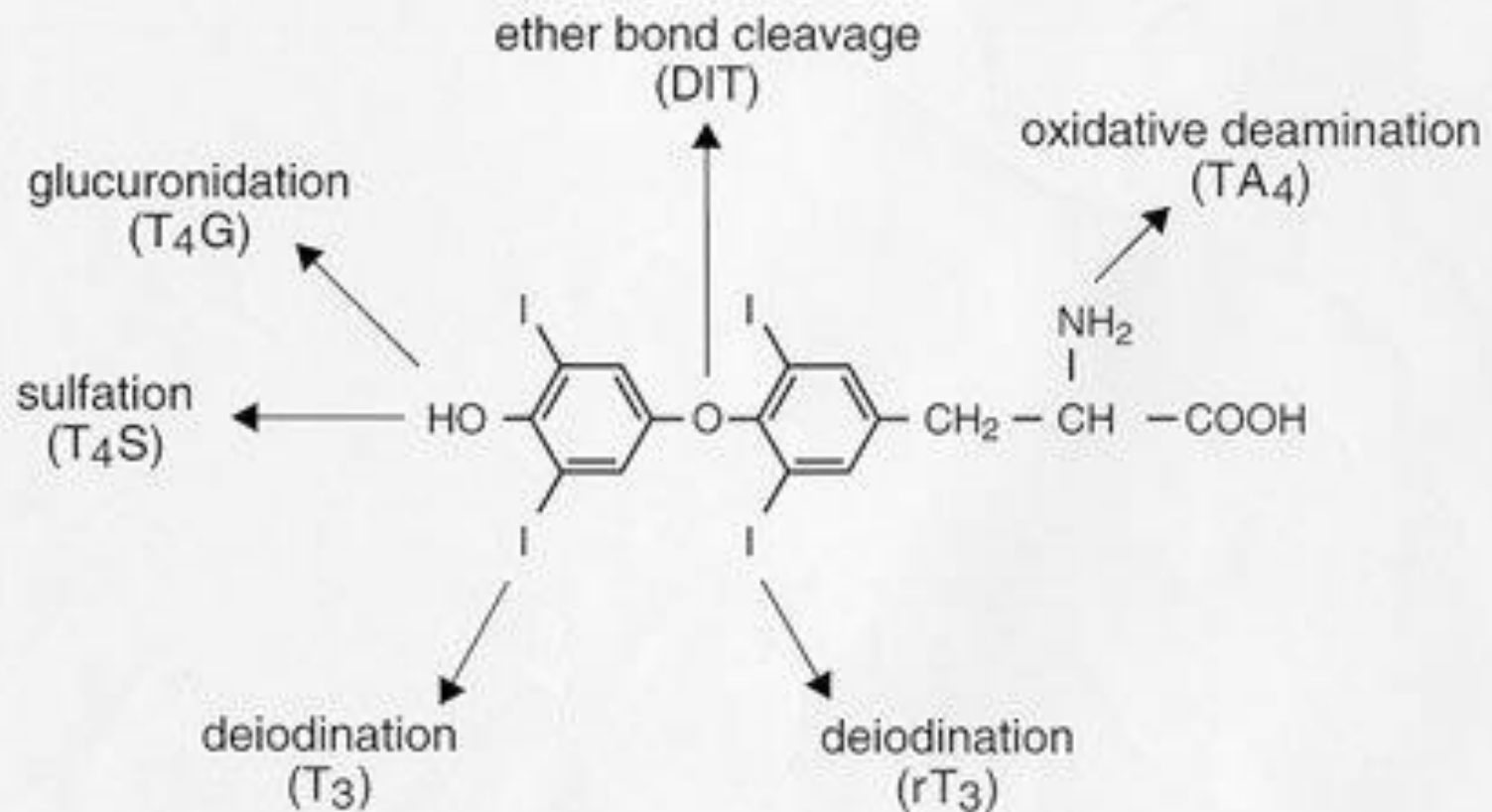


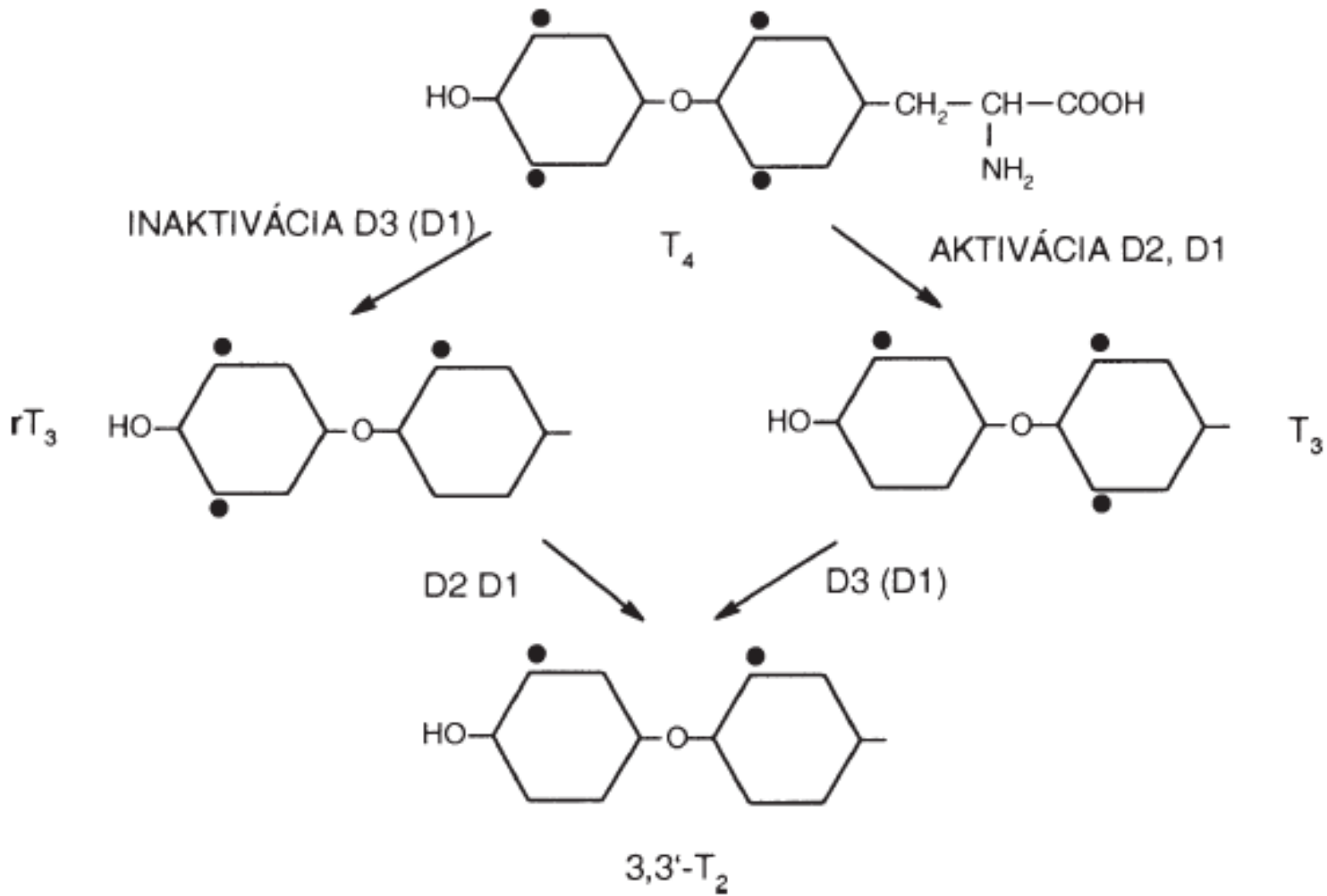
Transport and metabolism

- Transport proteins:
 - TBG (75%)
 - transthyretin (15%)
 - albumin (10%)
- In the **circulation**
 - **90% T₄**
 - 10% T₃
- In the **periphery**
 - **80% T₃**
 - 10% T₄
 - 10% rT₃

Comparison of T ₃ and T ₄		
Property	T ₃	T ₄
Activity	Active hormone	Inactive pro-hormone
Relative quantity produced by the thyroid gland	1	10
Free in blood (%)	0.2	0.02
Relative potency	4	1
Half-life (days)	1	7
Speed of action	Rapid (hours)	Slow (days)

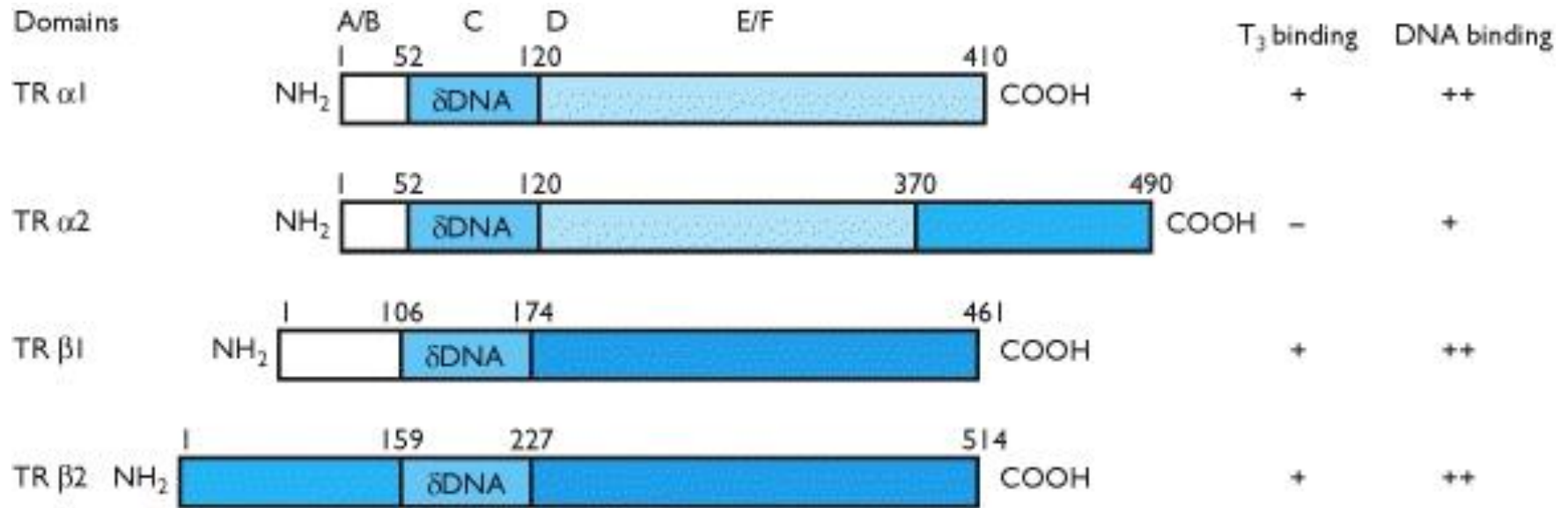
Pathways of Thyroid Hormone Metabolism





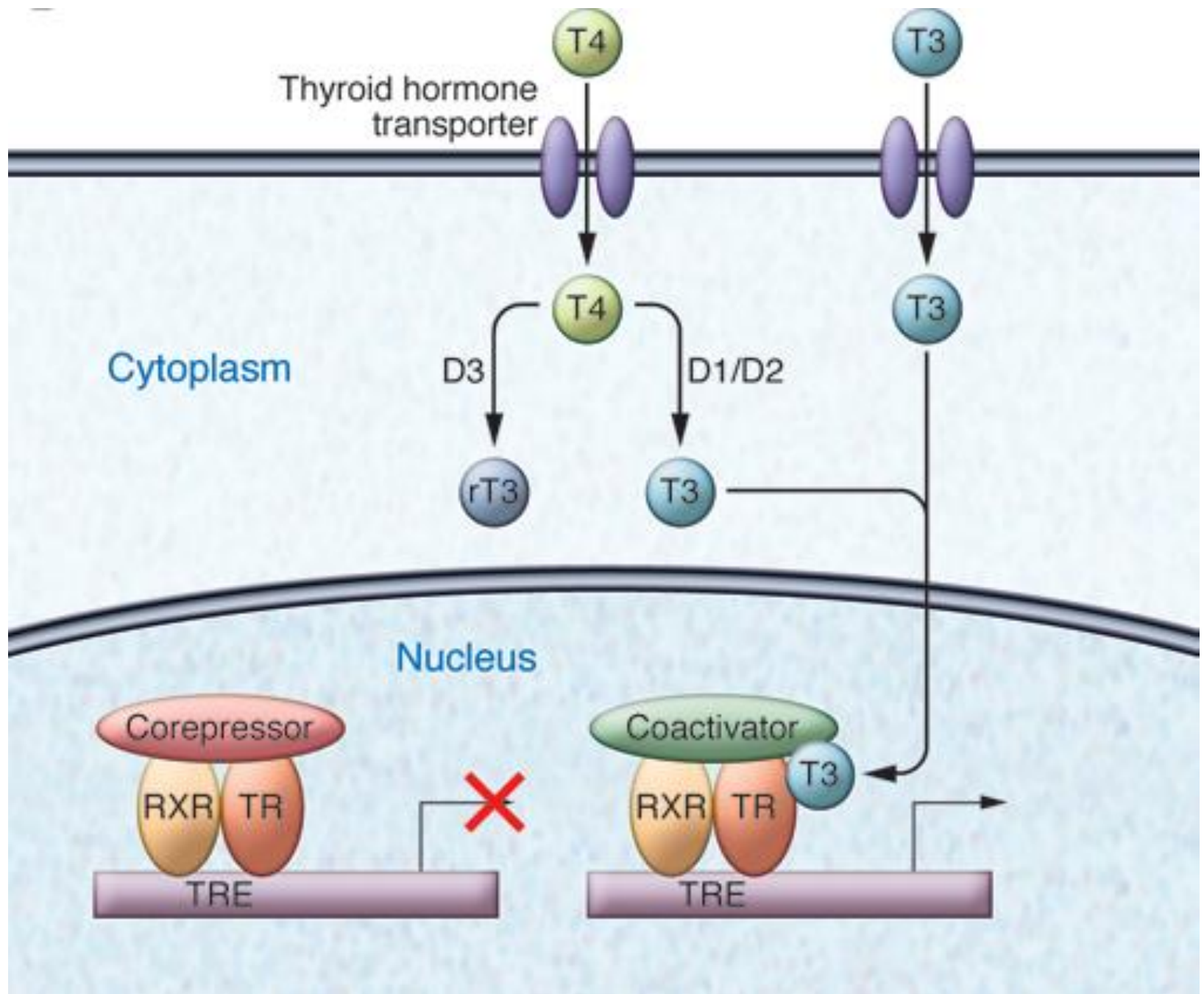
Black dots = I

Mechanism of action



- TR α 1 + α 2: brain, heart, kidney, gonads and skeletal muscle
- TR β 1 + β 2: pituitary, liver, brain, retina, and inner ear





Actions

- Increase of number and size of mitochondria
- Synthesis of respiratory chain enzymes
- $\text{Na}^+ \text{K}^+ \text{ATPase}$
- Uncoupling proteins

Actions of thyroid hormones

Category	Effect(s)
Metabolism	Increase basal metabolic rate and heat production
	Increase lipolysis
	Increase cellular uptake of triglycerides and cholesterol
	Increase gluconeogenesis, glycogenolysis and insulin-dependent glucose uptake
Development	Essential to fetal and neonatal brain development
Cardiovascular system	Increase heart rate, cardiac contractility and cardiac output
	Increase peripheral vasodilation
Central nervous system	Increase alertness
Reproductive system	Essential for normal reproductive function

Common thyroid gland diseases - Hypothyroidism

- the thyroid gland does not produce enough thyroid hormones
- more common in females
- **Causes:**
 - inadequate function of the gland itself (primary hypothyroidism) – TSH ↑
 - iodine deficiency in diet (primary hypothyroidism)
 - iatrogenic causes (treatment of hyperthyroidism, radiotherapy, surgery) (primary hypothyroidism)
 - congenital – thyroid aplasia and dysmorphogenesis (primary hypothyroidism)
 - inadequate stimulation by TSH from the pituitary gland (secondary/central hypothyroidism) - TSH ↓
 - inadequate release of TRH from the hypothalamus (secondary/central hypothyroidism) - TSH ↓

Hypothyroidism

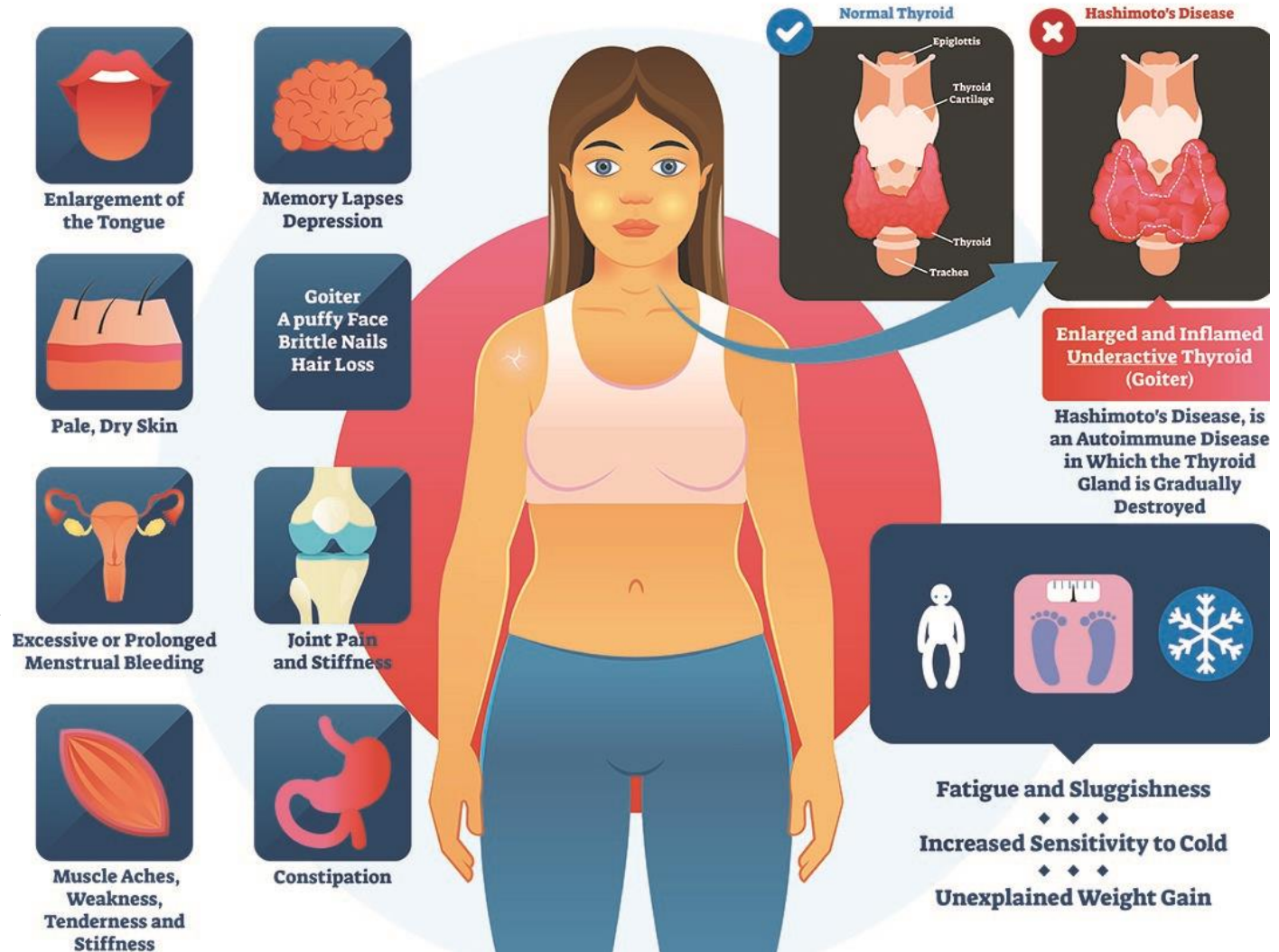
Chronic lymphocytic thyroiditis (Hashimoto's disease)

- anti-thyroid autoantibodies

- Thyroid peroxidase

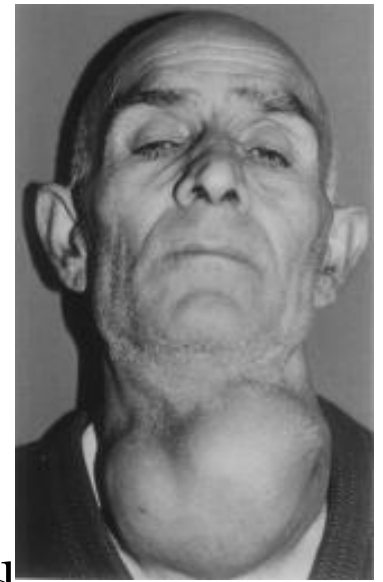
- Thyroglobulin

- TSH receptor



Hypothyroidism

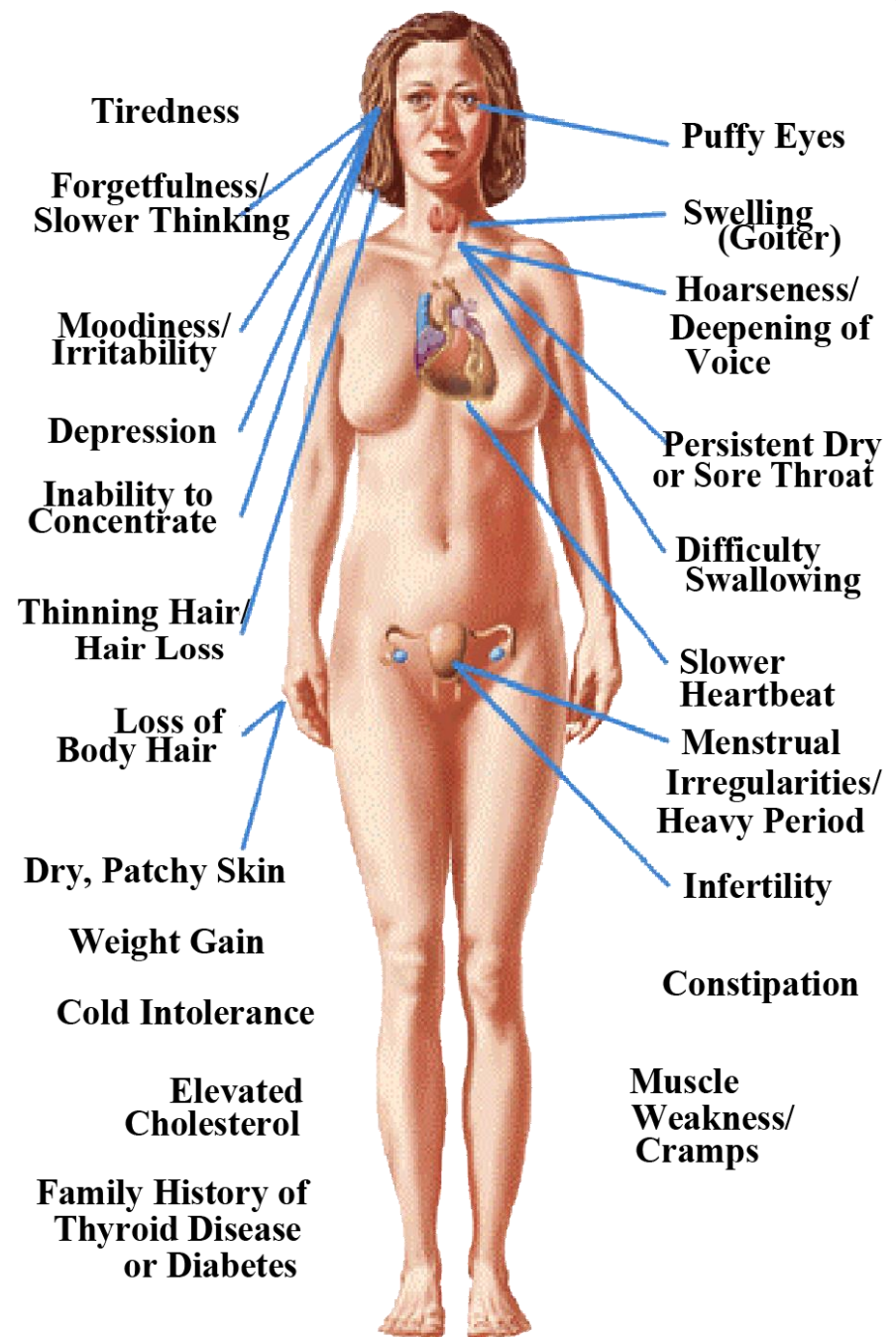
Iodine deficiency disorder - Goiter



- **Cause:** in 90% of case - iodine deficiency
- TSH, IGF-I – main regulators of growth of thyroid gland
- Iodine deficiency – TSHR hyperstimulation

Grade	Definition
0	No palpable or visible goiter
1	Palpable goiter
	A Only palpable
	B Palpable and visible with the neck extended
2	Goiter visible with neck in normal position
3	Very large goiter visible from distance

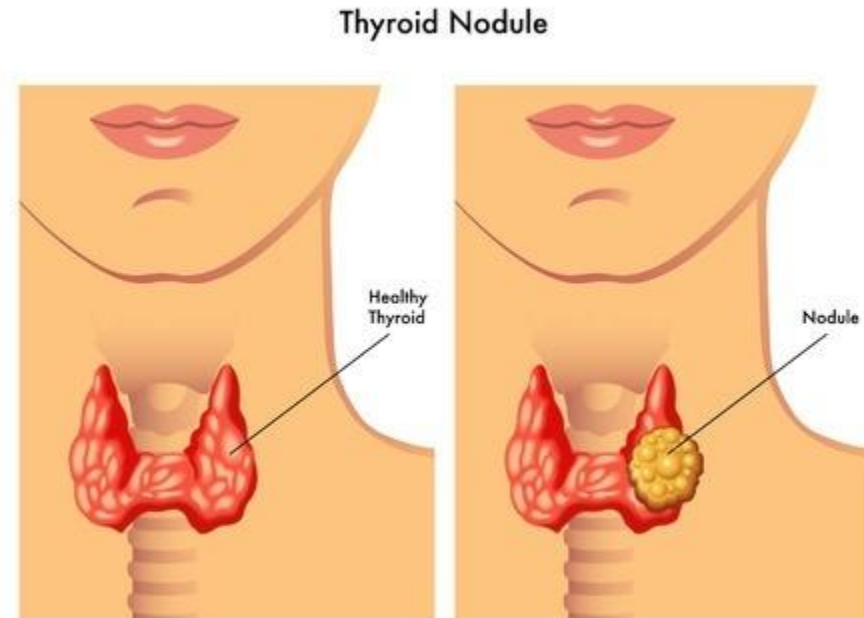
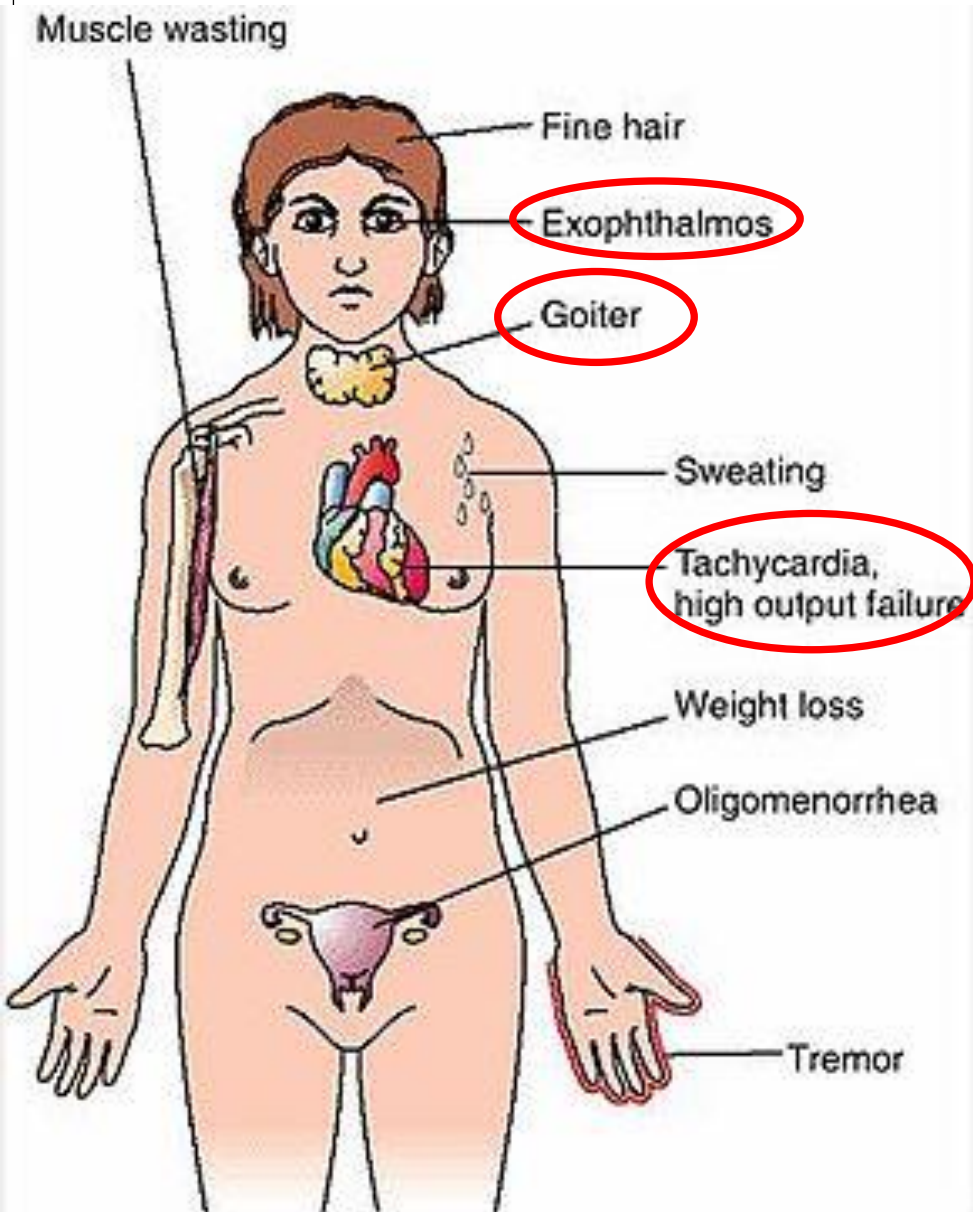
Common symptoms of hypothyroidism



Common thyroid gland diseases - Hyperthyroidism

- **Hyperthyroidism** = excessive production of thyroid hormones by the thyroid gland
- **Thyrotoxicosis** = occurs due to excessive thyroid hormone of any cause and therefore includes hyperthyroidism
- **Causes** (in 90%):
 - 1) **immunogenic thyrotoxicosis (Grave's disease)** - auto-antibodies bind to TSH receptor as a ligand
 - Goiter
 - Exophthalmus
 - Tachycardia
 - 2) **toxic adenoma** – autonomously functioning thyroid nodule(s) in a healthy thyroidal gland

Grave's disease Toxic thyroid adenoma

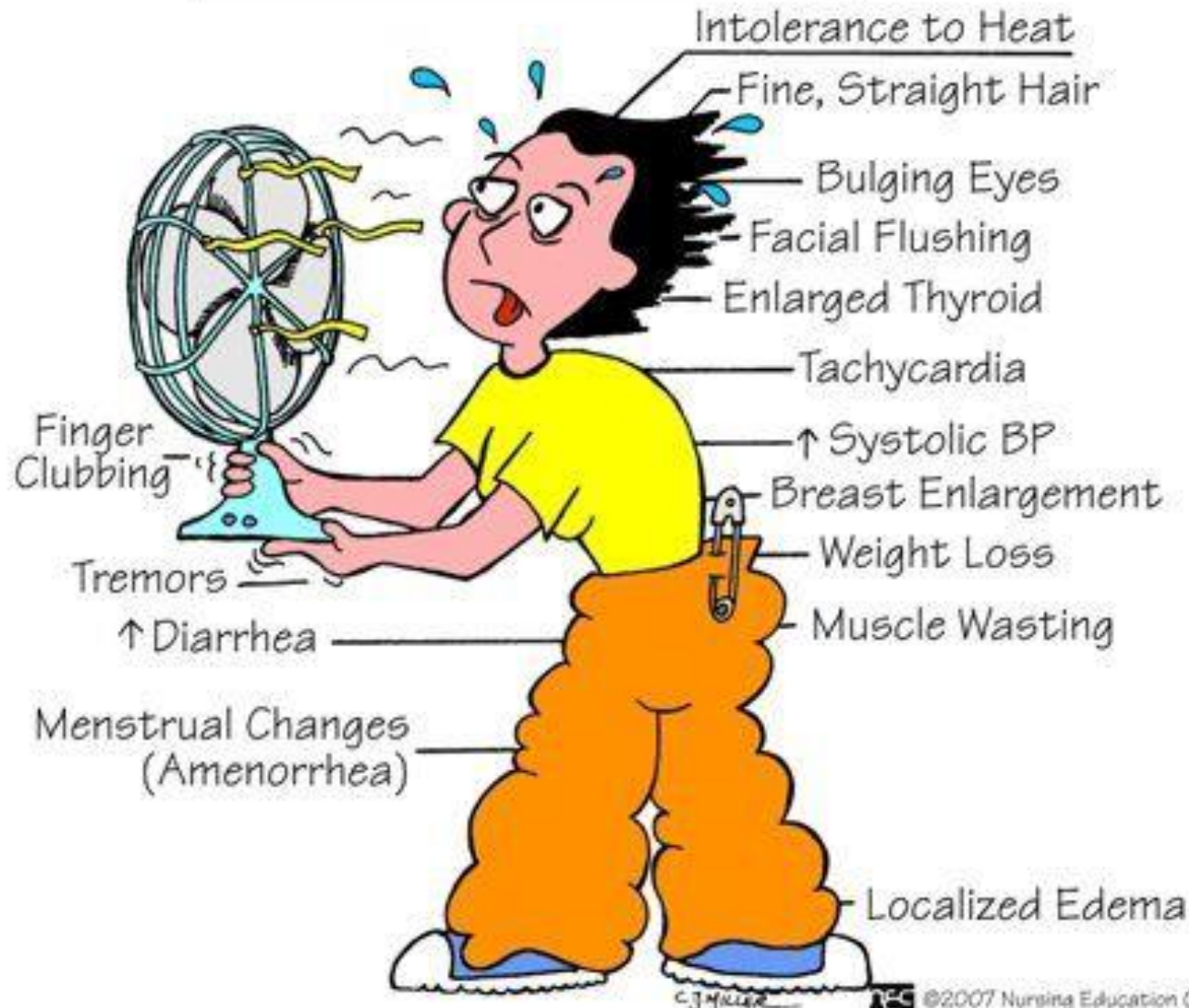


Causes and pathogenesis of thyrotoxicosis

Cause	Pathogenesis
Graves' disease	Stimulation of thyroid follicular cells by TSH receptor antibodies
Toxic multinodular goitre	Multiple autonomous nodules secreting excess thyroid hormone
Toxic nodule	Single autonomous nodule secreting excess thyroid hormone
Thyroiditis (including subacute or de Quervain's thyroiditis, silent thyroiditis and post-partum thyroiditis)	Release of preformed thyroid hormone following inflammatory destruction of thyroid follicles
Certain drugs (e.g. amiodarone, excessive intake of thyroxine, iodine, lithium or interferon α)	Different mechanisms including excess thyroid hormones or iodine, autoimmunity and thyroiditis
Gestational hyperthyroidism	β -chorionic gonadotrophin stimulating thyroid follicular cells
Hydatidiform mole and choriocarcinoma	β -chorionic gonadotrophin stimulating thyroid follicular cells
Struma ovarii (a teratoma of the ovary, containing thyroid tissue)	Excess thyroid hormone secretion from thyroid tissues within the ovarian tumour
Thyroid-stimulating hormone–secreting pituitary adenoma	Excess TSH from pituitary adenoma stimulating secretion of thyroid hormones

Common symptoms of hyperthyroidism

HYPERTHYROIDISM



Features of hypothyroidism and hyperthyroidism

