Physical Activity and Health Promotion

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Lesson 5
The thyroid gland

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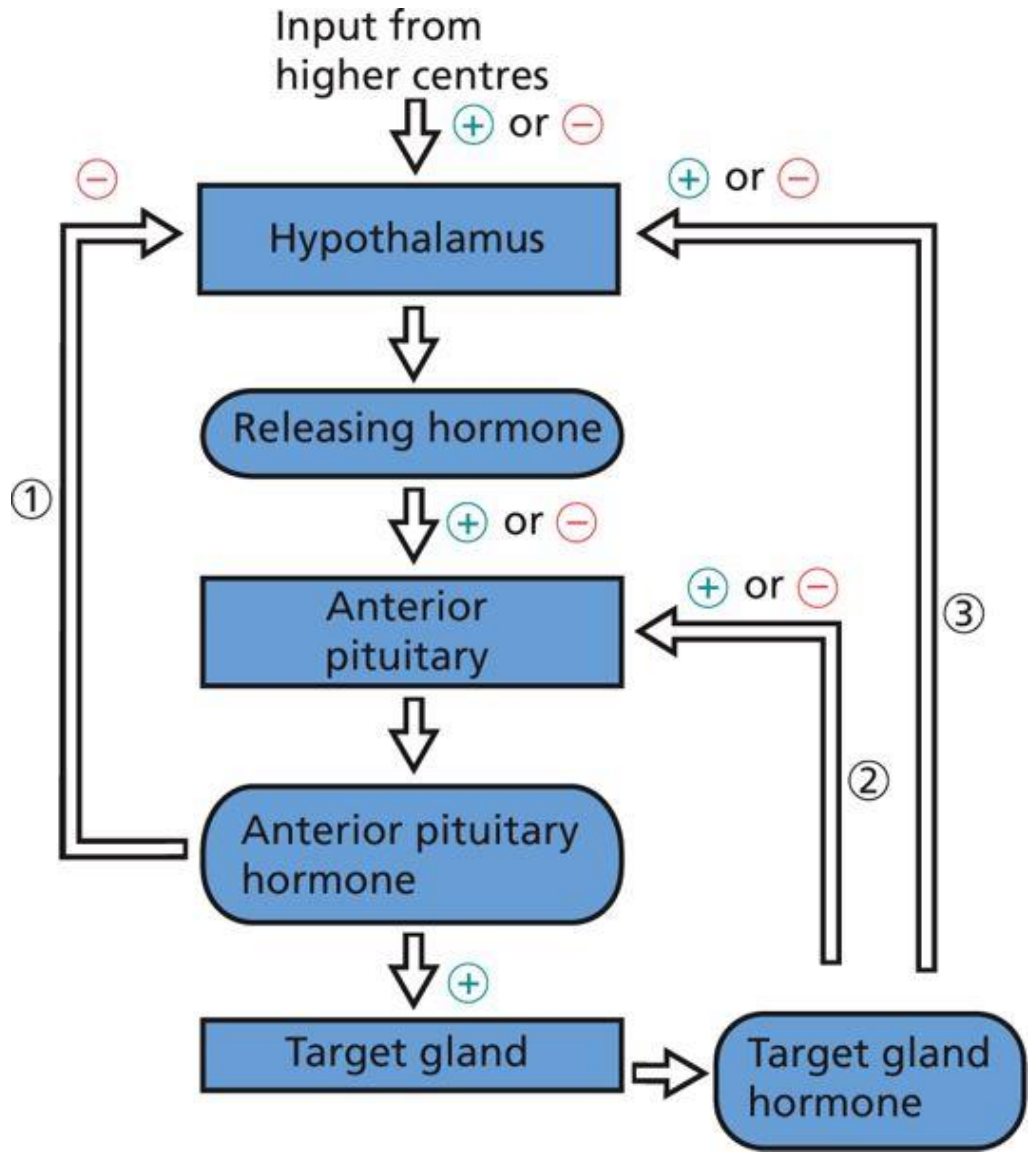
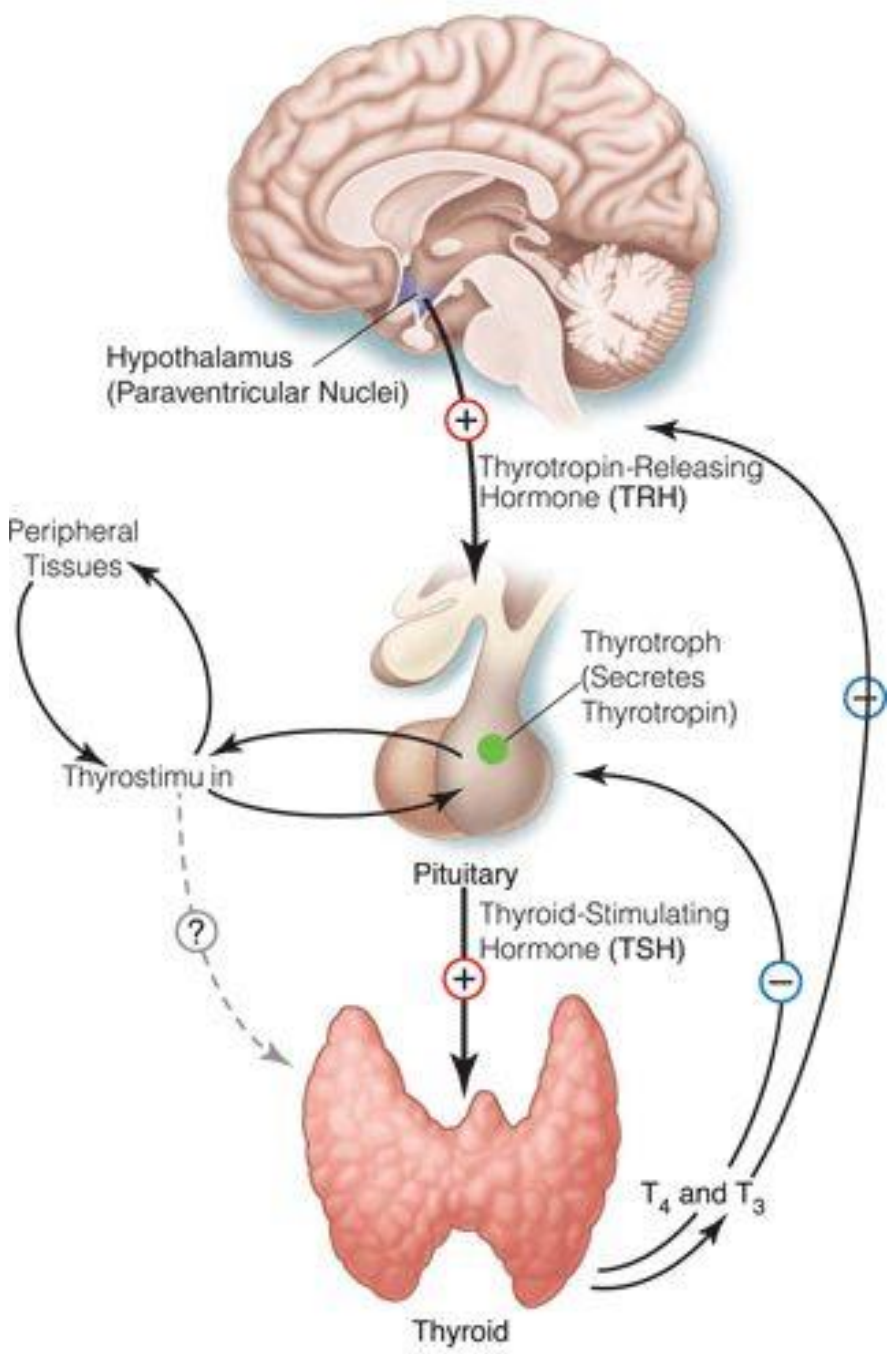
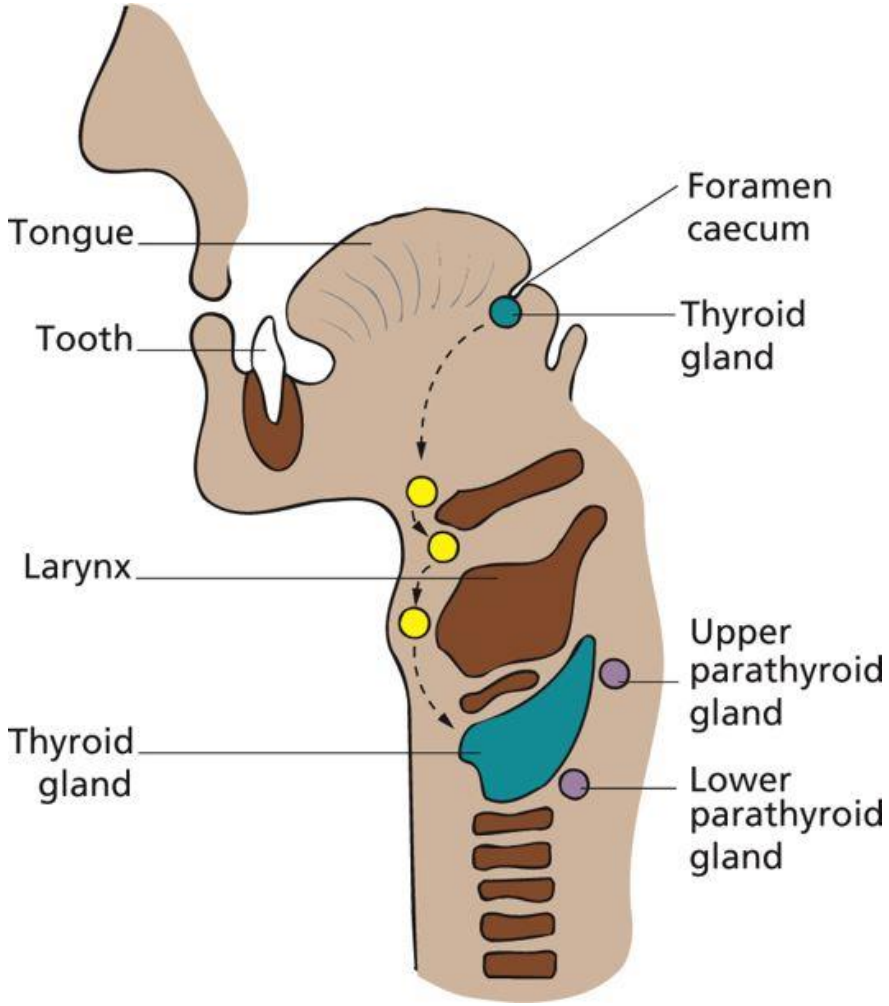

Input from higher centres
+ or −
Hypothalamus
Releasing hormone
+ or −
Anterior pituitary
Anterior pituitary hormone
+
Target gland
Target gland hormone
+ or −
+ or −
+ or −
−
①
②
③



The thyroid gland is responsible for making thyroid hormones by concentrating iodine and utilizing the amino acid tyrosine. The hormones play major metabolic roles, affecting many different cell types in the body.

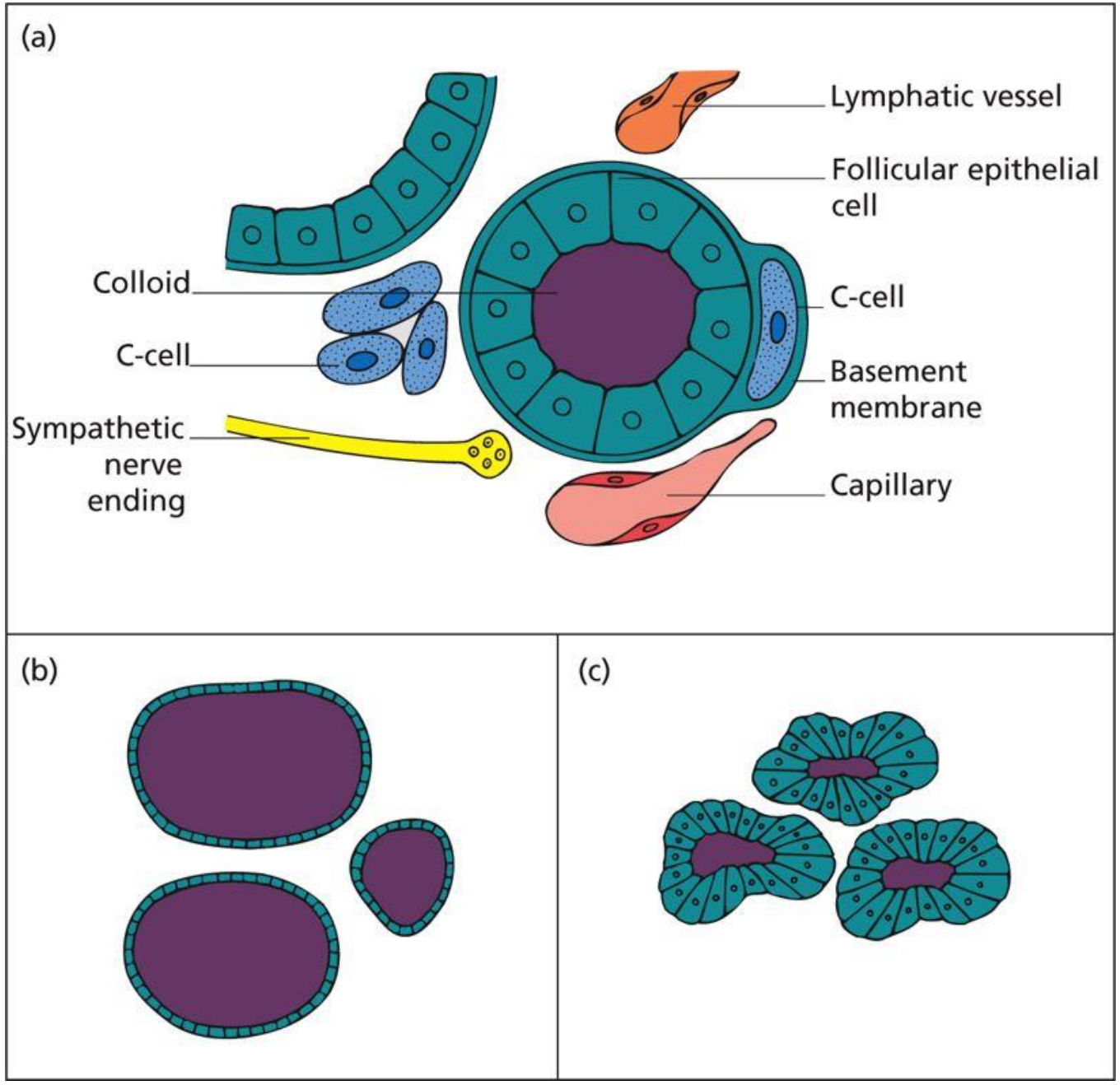
	ACTIONS	FACTORS
1	Neuroendocrine regulation	Hypothalamus and Pituitary TRH/TSH
2	Thyroid Hormones (TH)	T4 / T3 (TBG) – FT4/FT3
3	TH Transporters	Monocarboxylate transporter 8 (MCT8)
4	TH Receptors	Subunits α and β
5	Local activation	5’ Deiodinase type 2 (FT4 FT3)
6	Nutritional status of cells	Feed-back on TH signaling pathway

Embryology



In the fourth week of human embryogenesis, the thyroid begins as a midline thickening at the back of the tongue that subsequently invaginates and stretches downward. This creates a mass of progenitor cells that migrates in front of the larynx and comes into close proximity with the developing parathyroid glands. In adulthood, the pea-sized parathyroids located on the back of the thyroid as pairs of upper and lower glands regulate calcium by secreting parathyroid hormone (PTH). The lower parathyroids originate higher in the neck than the upper glands and only achieve their final position by migrating downwards. The migrating thyroid also comes into contact with cells from the lower part of the pharynx. These latter cells eventually comprise ~10% of the gland as future C-cells, which will secrete calcitonin.

The thyroid gland and its downward migration. The point of origin in the tongue persists as the foramen caecum. Common sites of thyroglossal cysts ( ) are shown. The final position of the paired parathyroid glands ( ) is also indicated.

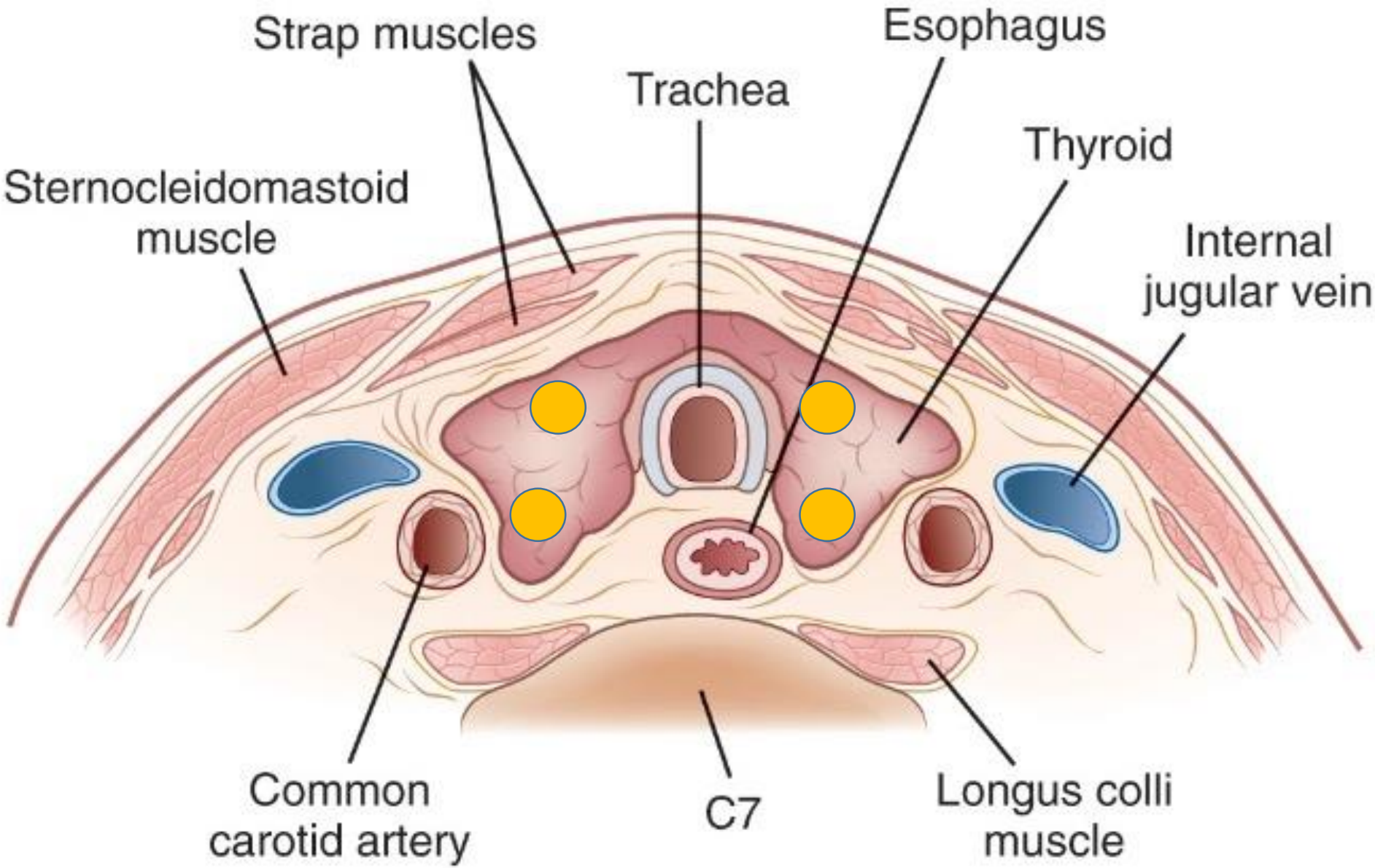


Histology of the human thyroid gland.

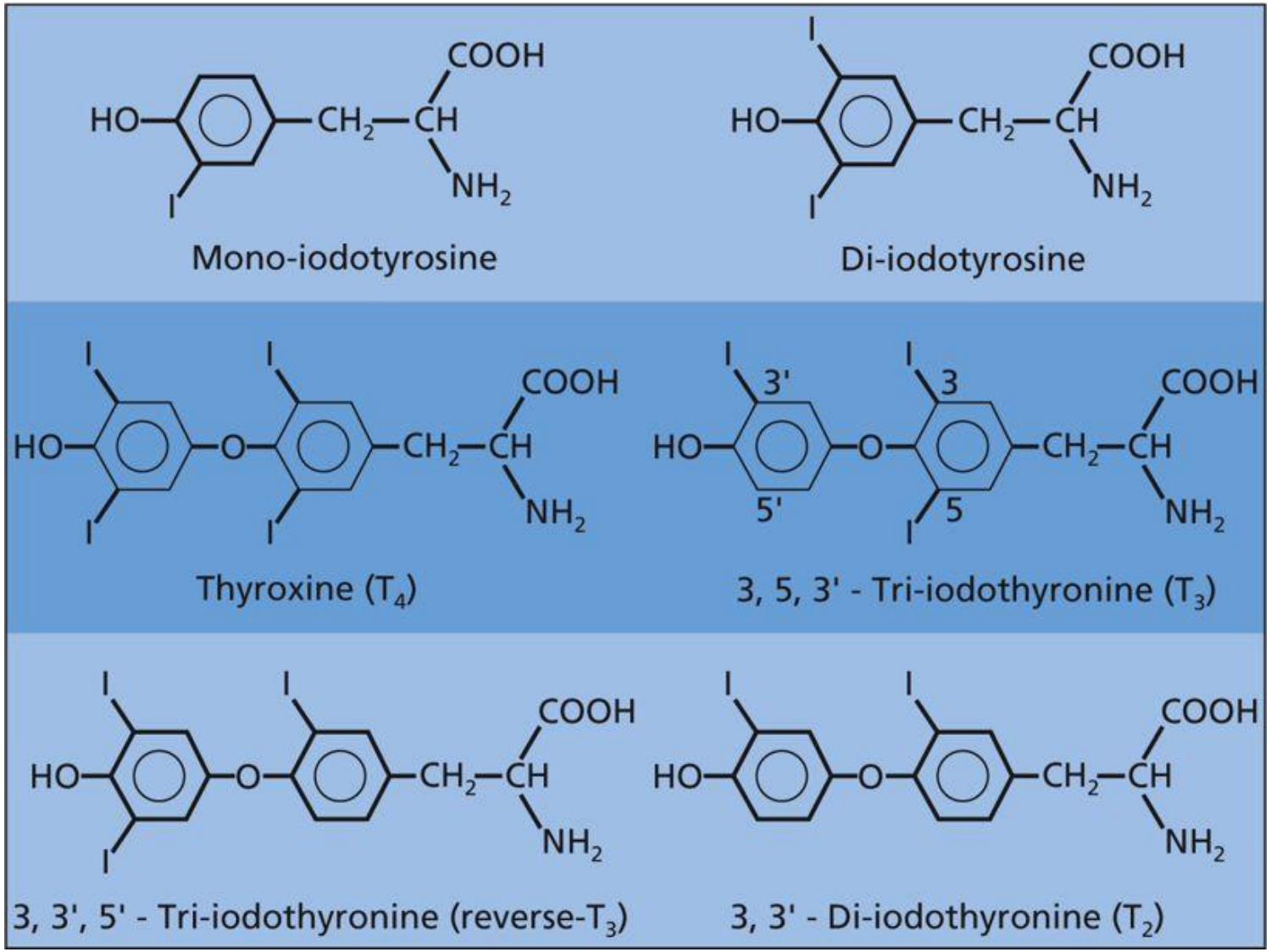
(a) Euthyroid follicles are shown lined with cuboidal epithelium and lumens filled with gelatinous colloid that contains stored thyroid hormone. Surrounding each follicle is a basement membrane enclosing parafollicular C-cells within stroma containing fenestrated capillaries, lymphatic vessels and sympathetic nerve endings.

(b) Underactive follicles with flattened epithelial cells and increased colloid.

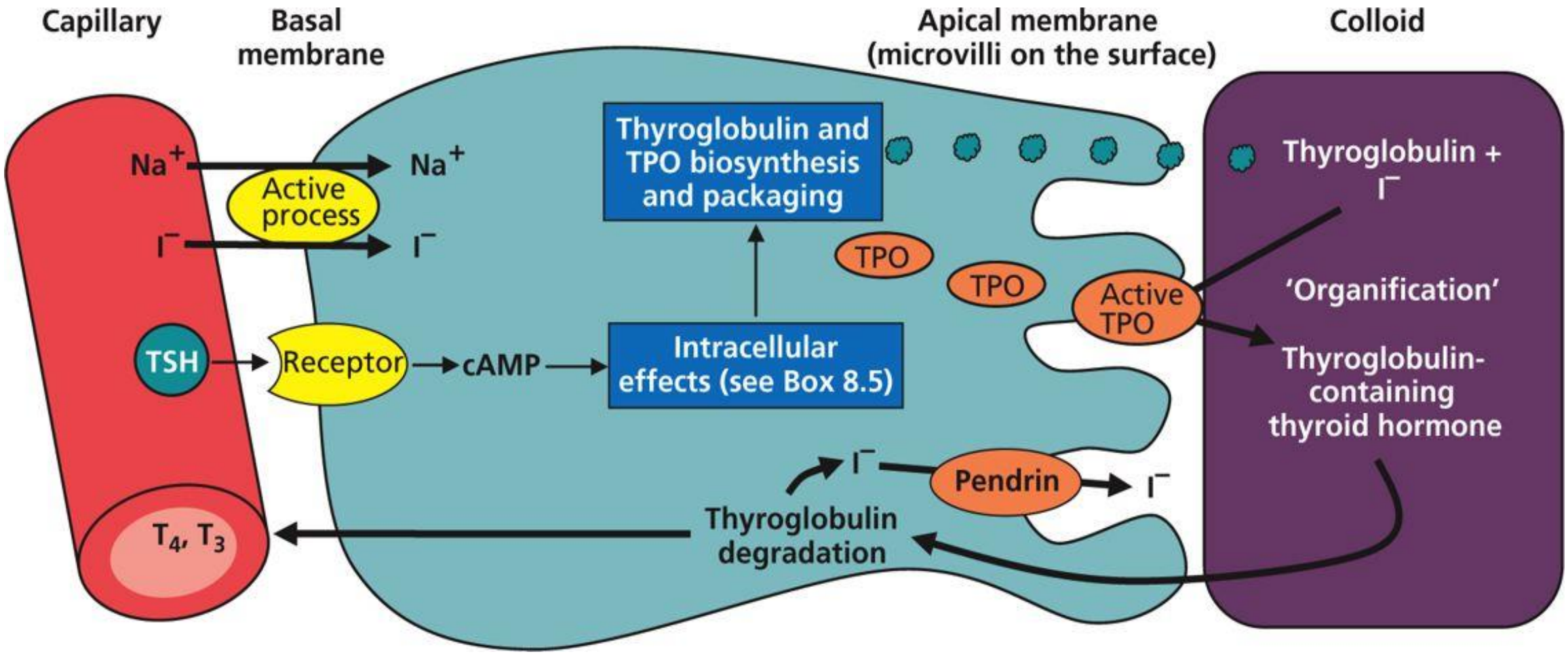
(c) Overactive follicles with tall, columnar epithelial cells and reduced colloid.


Strap muscles
Esophagus
Trachea
Thyroid
Sternocleidomastoid muscle
Internal jugular vein
Common carotid artery
C7
Longus colli muscle

Thyroid hormone biosynthesis

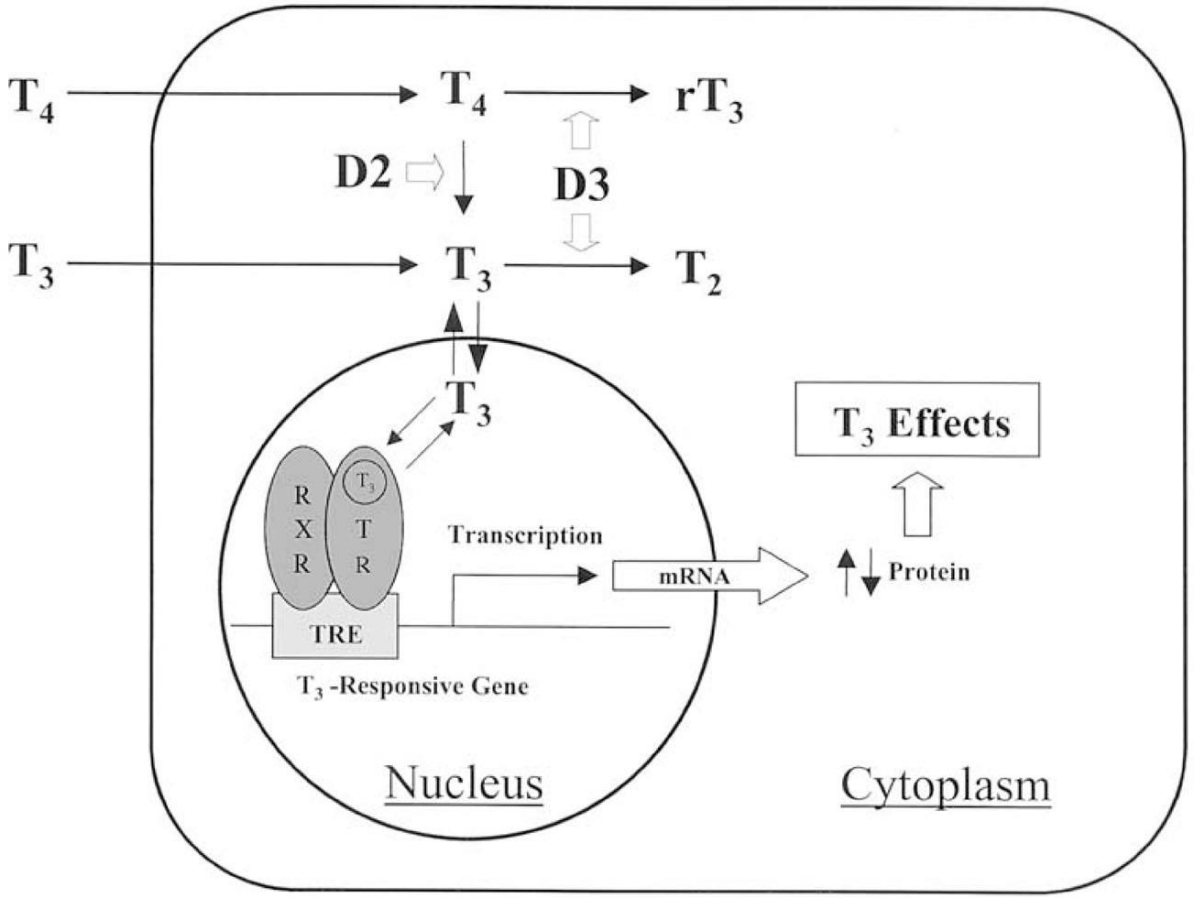


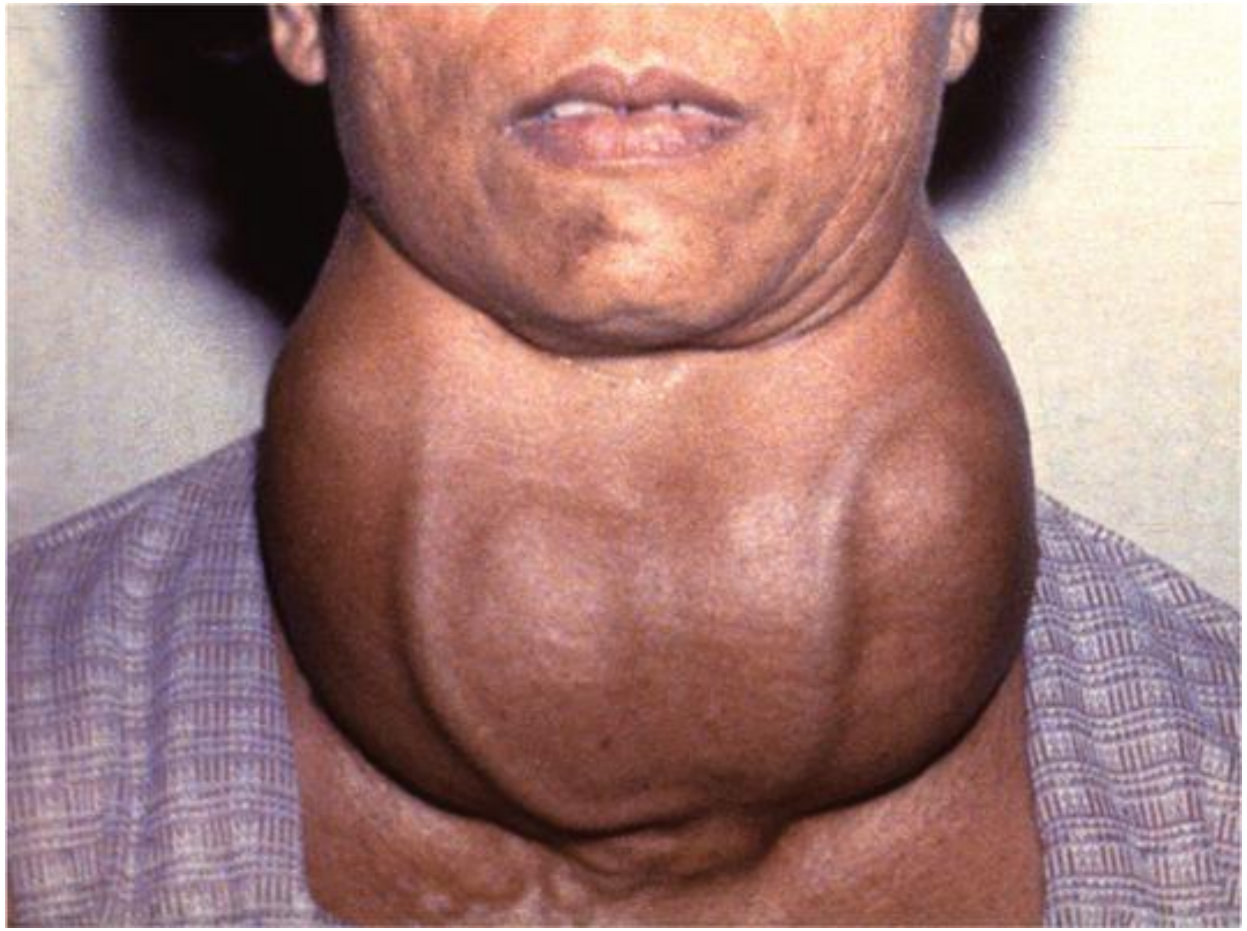
There are two active thyroid hormones: thyroxine (3,3′,5,5′-tetra-iodothyronine; abbreviated to T4) and 3,5,3′-tri-iodothyronine (T3); the subscripts 4 and 3 represent the number of iodine atoms incorporated on each thyronine residue. These hormones are generated from the sequential iodination and coupling of the amino acid tyrosine and inactivated by de-iodination and modification to 3,3′,5′-tri-iodothyronine [reverse T3 (rT3)] and di-iodothyronine (T2). The equilibrium between these different molecules determines overall thyroid hormone activity. Synthesis of thyroid hormone can be broken down into several key steps



Thyroid hormone biosynthesis within the follicular cell. Active iodide (I-) import is linked to the Na+/K+-ATPase pump. Thyroglobulin is synthesized on the rough endoplasmic reticulum, packaged in the Golgi complex and released from small, Golgi-derived vesicles into the follicular lumen. Its iodination is also known as 'organification'. Cytoplasmic microfilaments and microtubules organize the return of iodinated thyroglobulin into the cell as endocytotic vesicles of colloid, which is broken down to release thyroid hormone. TSH, thyroid-stimulating hormone; TPO, thyroid peroxidase; T4, thyroxine; T3, tri-iodothyronine.

Thyroid hormone action





The thyroid gland

Thyroid enlargement is called goitre

The gland is encapsulated:

Breaching the capsule is a measure of invasion in thyroid cancer

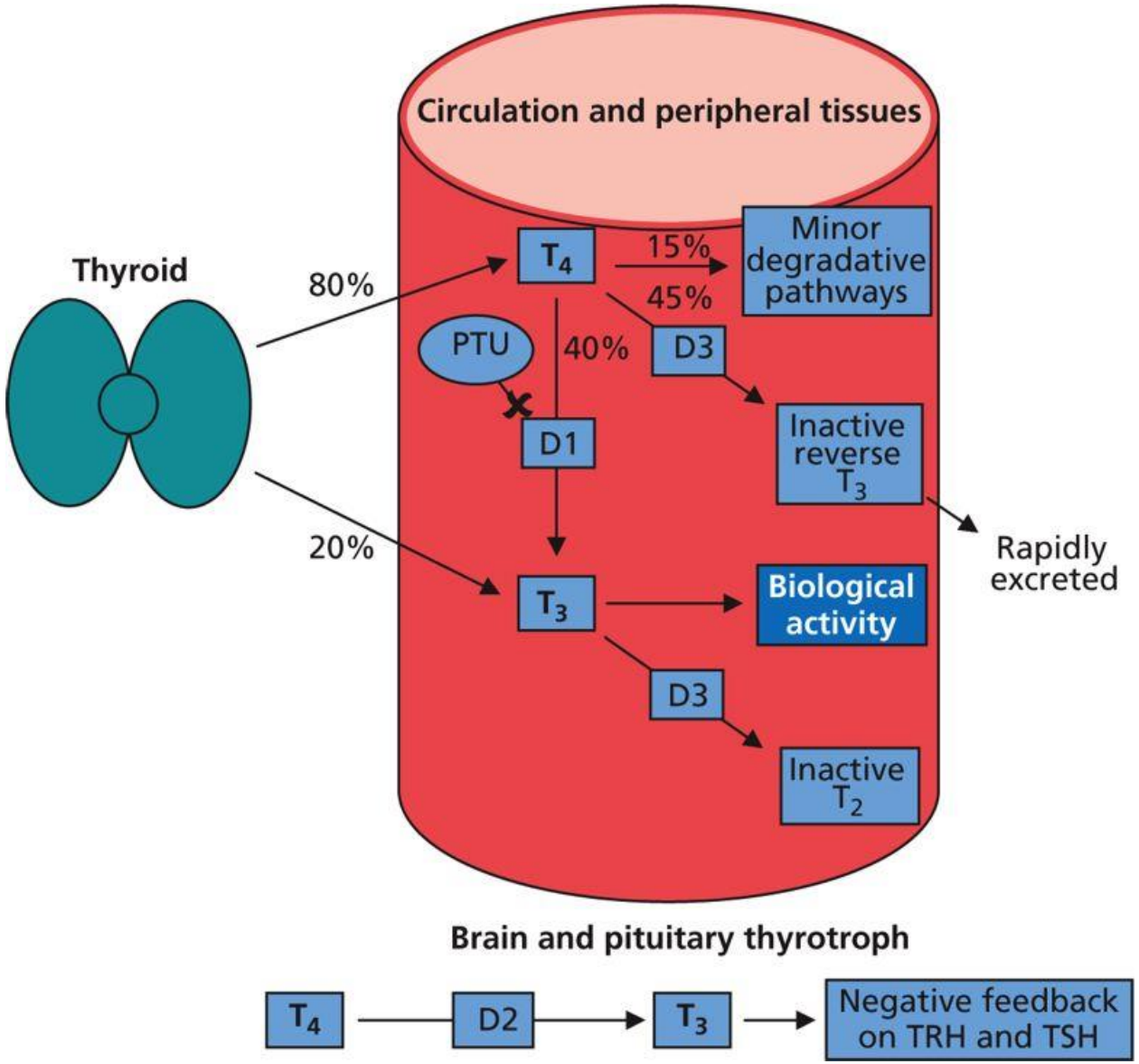
The thyroid receives a large arterial blood supply:

May cause a bruit in Graves disease

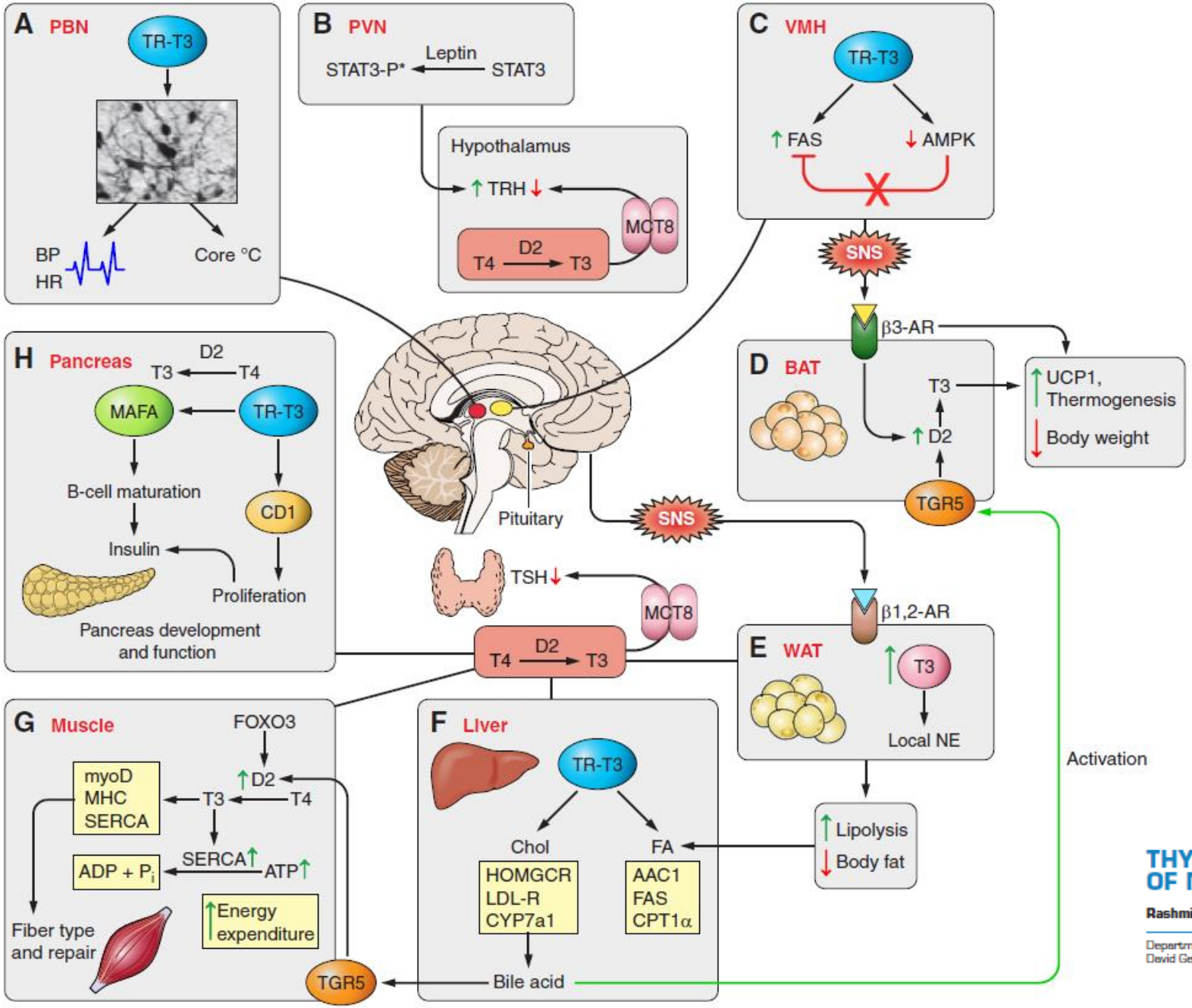
Metabolism of thyroid hormones, deiodinase's action

Conversion of T4 to T3 and rT3. T3 is the more active hormone, yet only 20% of thyroid hormone output. Most T3 is generated by removing one iodine atom from the outer ring of T4 (de-iodination). This step is catalyzed by selenodeiodinase enzymes, which contain selenium that accepts the iodine from the thyroid hormone. Selenium deficiency can be a rare contributory factor to hypothyroidism. Type 1 selenodeiodinase (D1) predominates in the liver, kidney and muscle, and is responsible for producing most of the circulating T3. It is inhibited by PTU. The type 2 enzyme (D2) is predominantly localized in the brain and pituitary, key sites for regulating T3 production for negative feedback at the hypothalamus and thyrotroph. The third selenodeiodinase, D3, de-iodinates the inner ring and converts T4 to rT3. rT3 is biologically inactive and cleared very rapidly from the circulation (half-life ~5h). D3 action on T3 is one method by which inactive T2 is generated. These combined steps are important: at least in part, T4 can be thought of as a 'prohormone'; when a given cell has sufficient T3, it can limit its exposure to further thyroid hormone action by switching to rT3 generation.

Metabolism of thyroid hormones in the circulation.



Four times more T4 is produced by the thyroid gland than T3. Under normal 'euthyroid' physiology, ~40% of circulating T4 is converted to active T3 by type 1 selenodeiodinase (D1; inhibited by propylthiouracil – see Box 8.4) and ~45% of T4 is converted to rT3 by the type 3 selenodeiodinase (D3). The remaining 15% of T4 is degraded by minor pathways, such as deamination. The conversion of T3 to T2 by D3 is shown, although other pathways also exist for this reaction. The type 2 selenodeiodinase (D2) is predominantly located in the brain and pituitary gland where it catalyzes the production of T3 for negative feedback at the hypothalamus and anterior pituitary. TRH, thyrotrophin-releasing hormone; TSH, thyroid-stimulating hormone.



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THYROID HORMONE REGULATION OF METABOLISM

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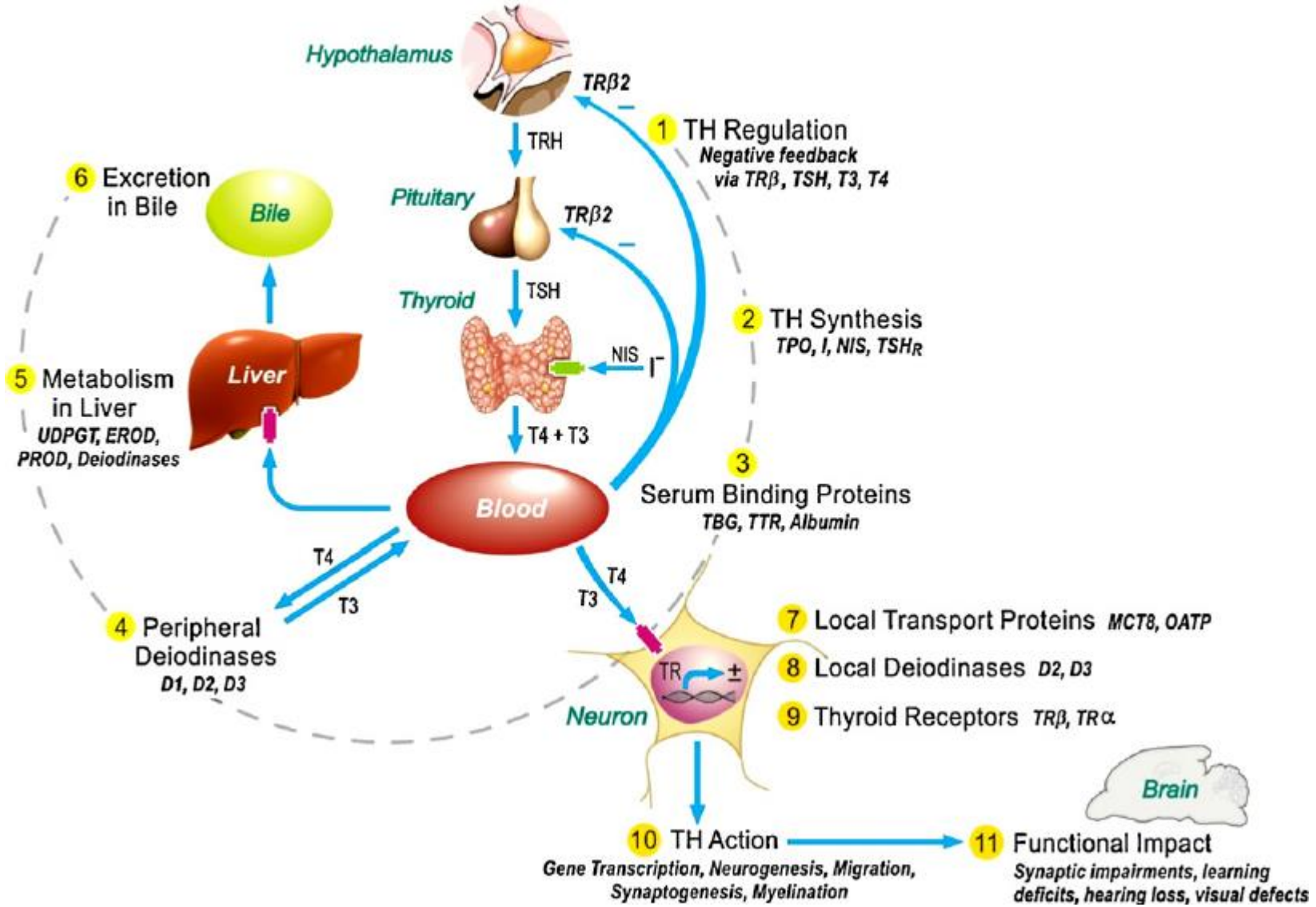
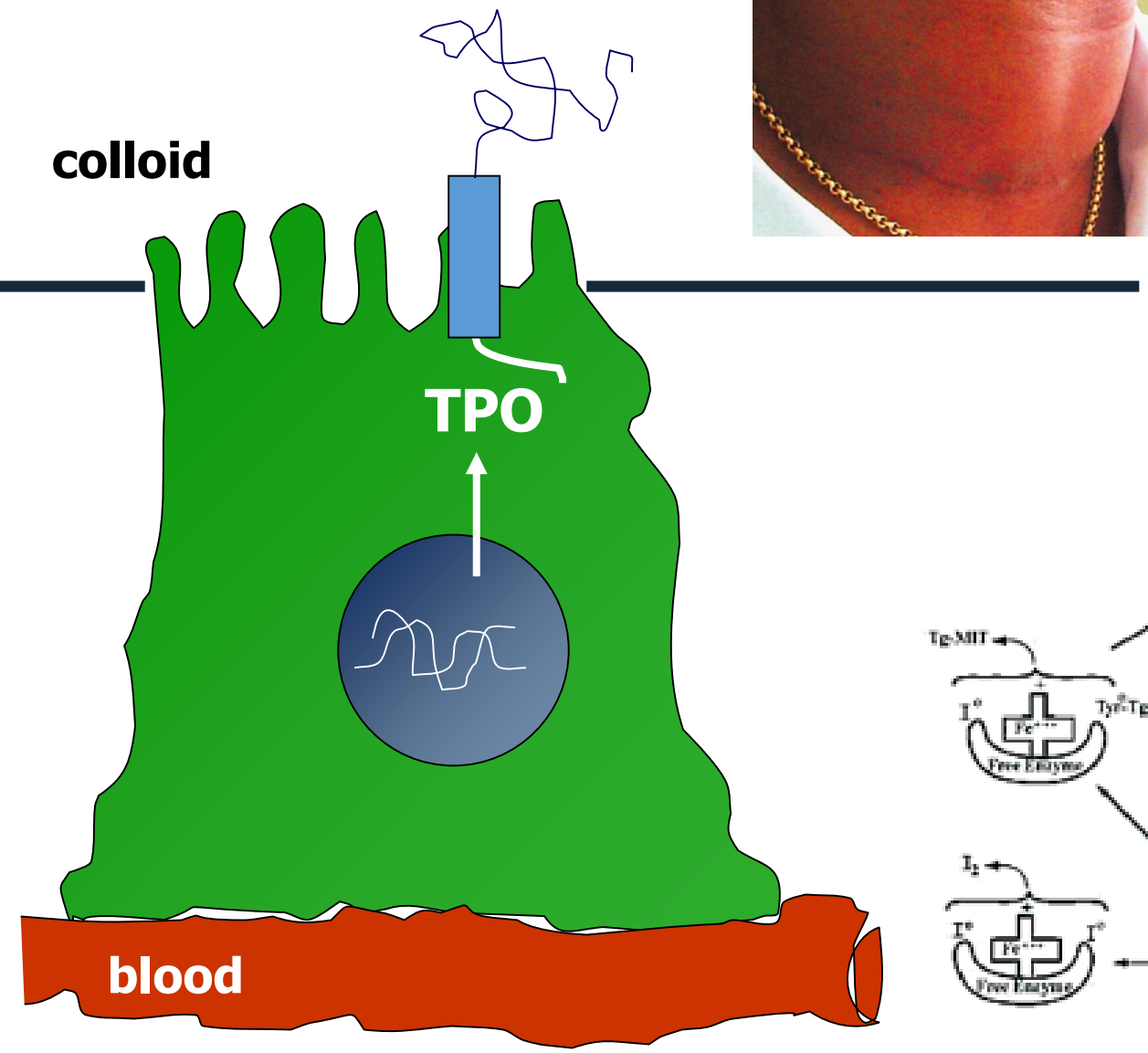
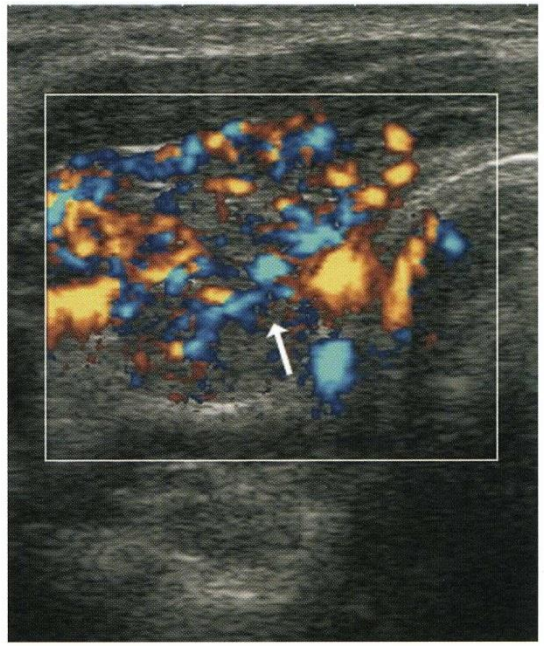
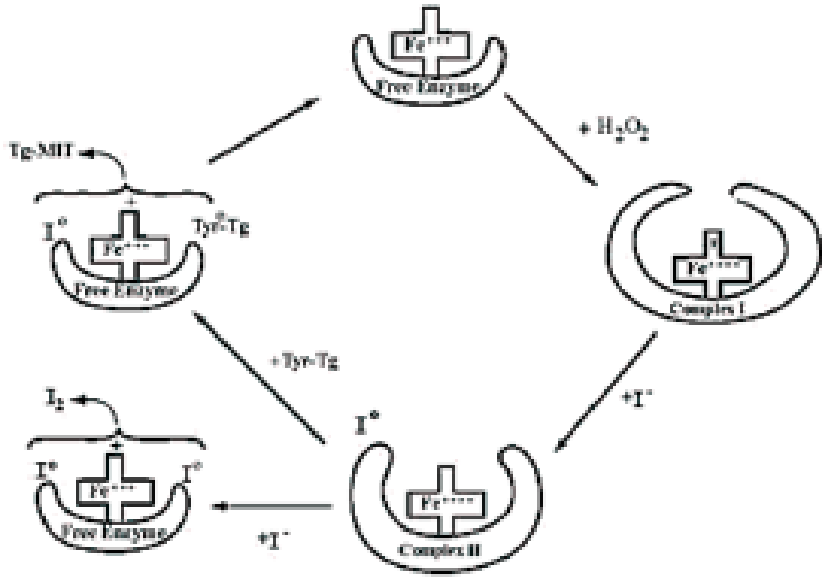
Possible Sites of Action of Environmental Contaminants on HPT Axis





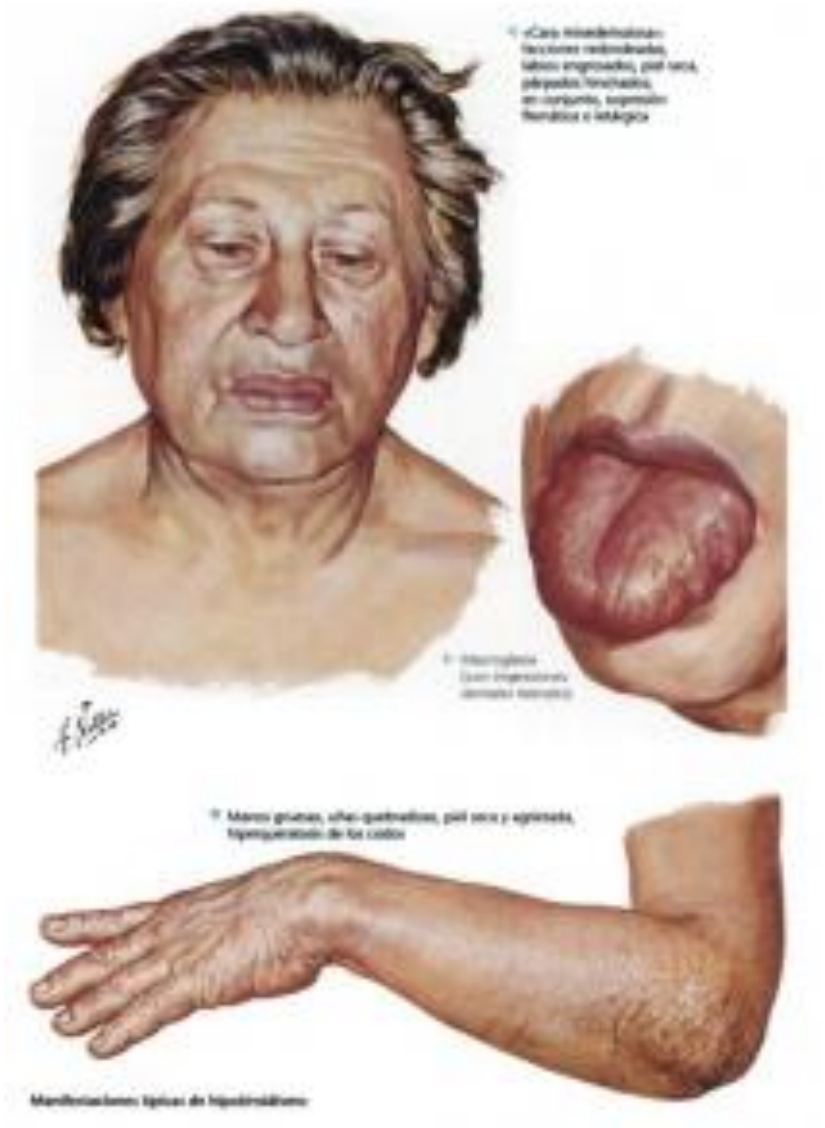




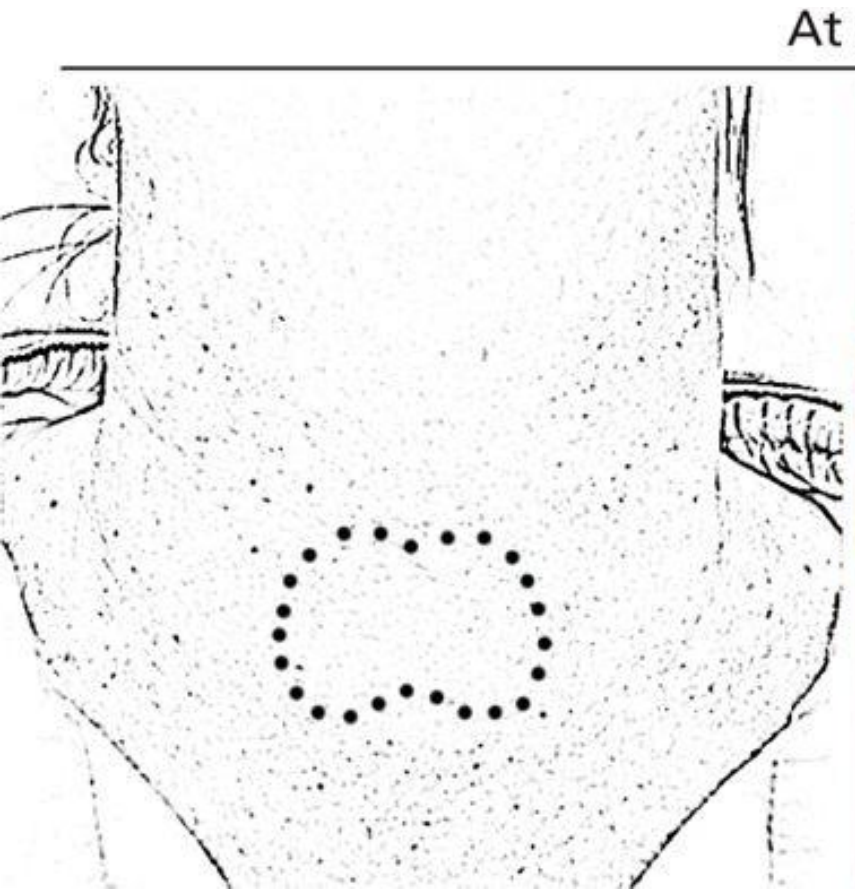
Causes of hypothyroidism
Primary

- *Goitre*
  - Autoimmune Hashimoto thyroiditis
  - Iodine deficiency
  - Drugs (e.g. lithium)
  - Riedel thyroiditis
  - Congenital hypothyroidism – dyshormonogenesis
- *No goitre*
  - Autoimmune atrophic thyroiditis
  - Post-radioiodine ablation or surgery (see treatment of hyperthyroidism)
  - Post-thyroiditis (hypothyroidism is transient)
  - Congenital hypothyroidism hypoplasia or aplasia

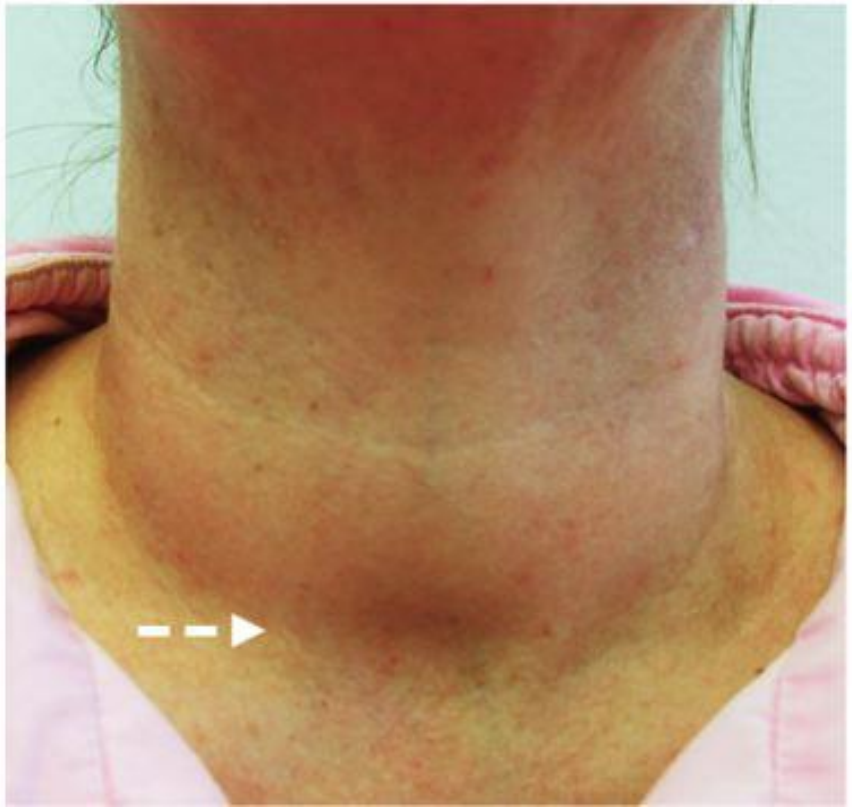
Hypothyroidism



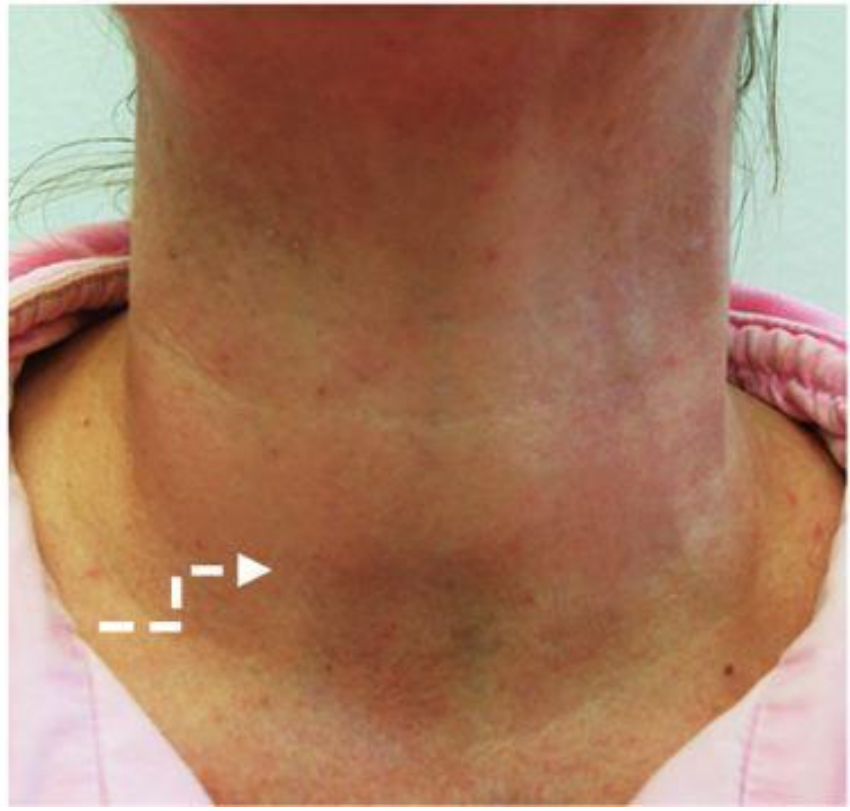
Graves-Basedow disease: thyrotoxicosis



At rest



On swallowing



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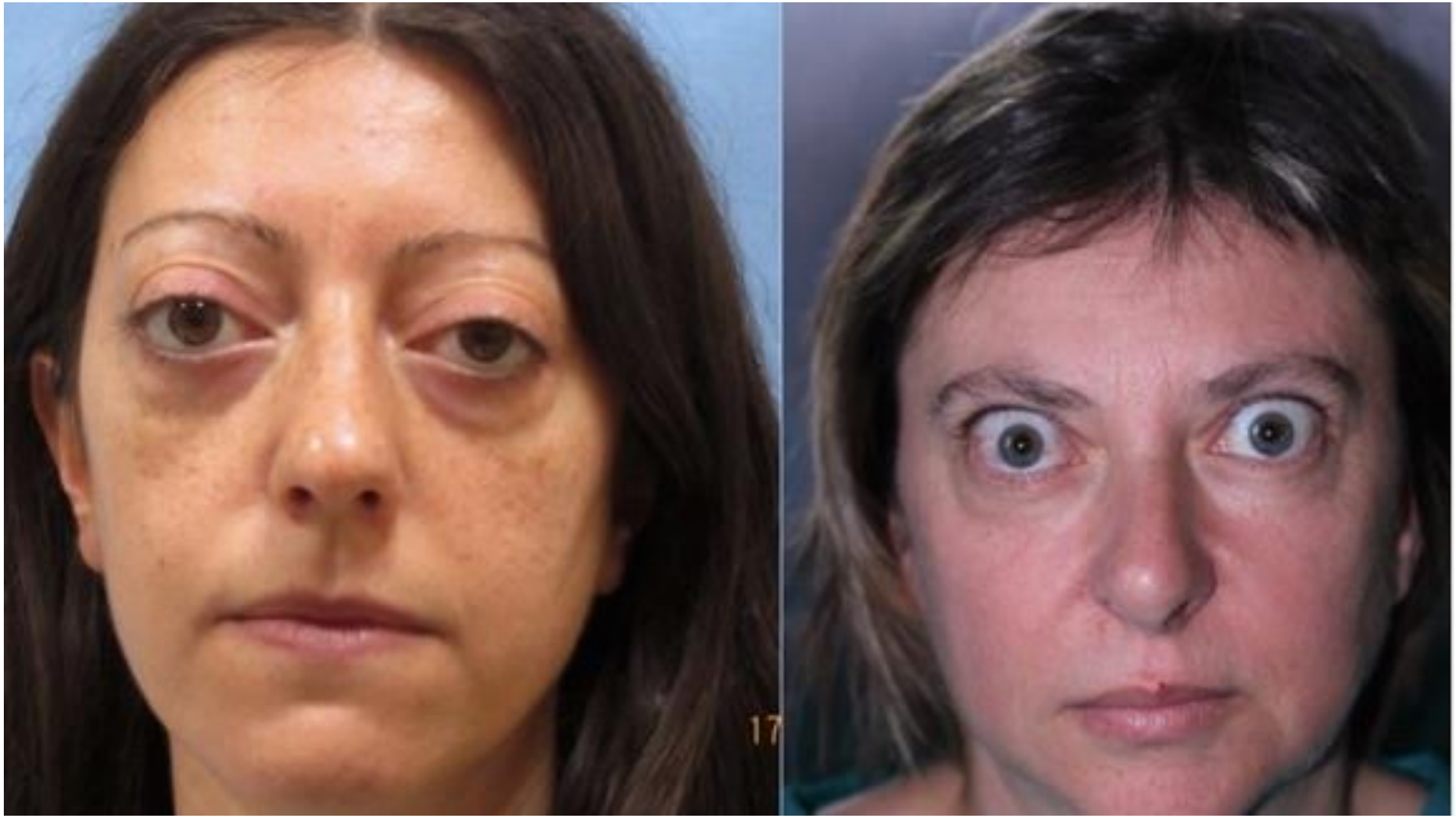

Symptoms and signs of thyrotoxicosis plus features associated with Graves-Basedow disease

- Weight loss despite full, possibly increased, appetite
- Tremor
- Heat intolerance and sweating
- Agitation and nervousness
- Palpitations, shortness of breath/tachycardia ± atrial fibrillation
- Amenorrhoea/oligomenorrhoea and consequent subfertility • Diarrhoea
- Hair loss
- Easy fatigability, muscle weakness and loss of muscle mass
- Rapid growth rate and accelerated bone maturation (children)
- Goitre, diffuse and reasonably firm ± bruit in Graves disease

Extra-thyroidal features associated with Graves disease

- Thyroid eye disease, also called Graves orbitopathy
- Pretibial myxoedema – rare, thickened skin over the lower tibia
- Thyroid acropachy (clubbing of the fingers)
- Other autoimmune features, e.g. vitiligo