Thyroid and parathyroid glands

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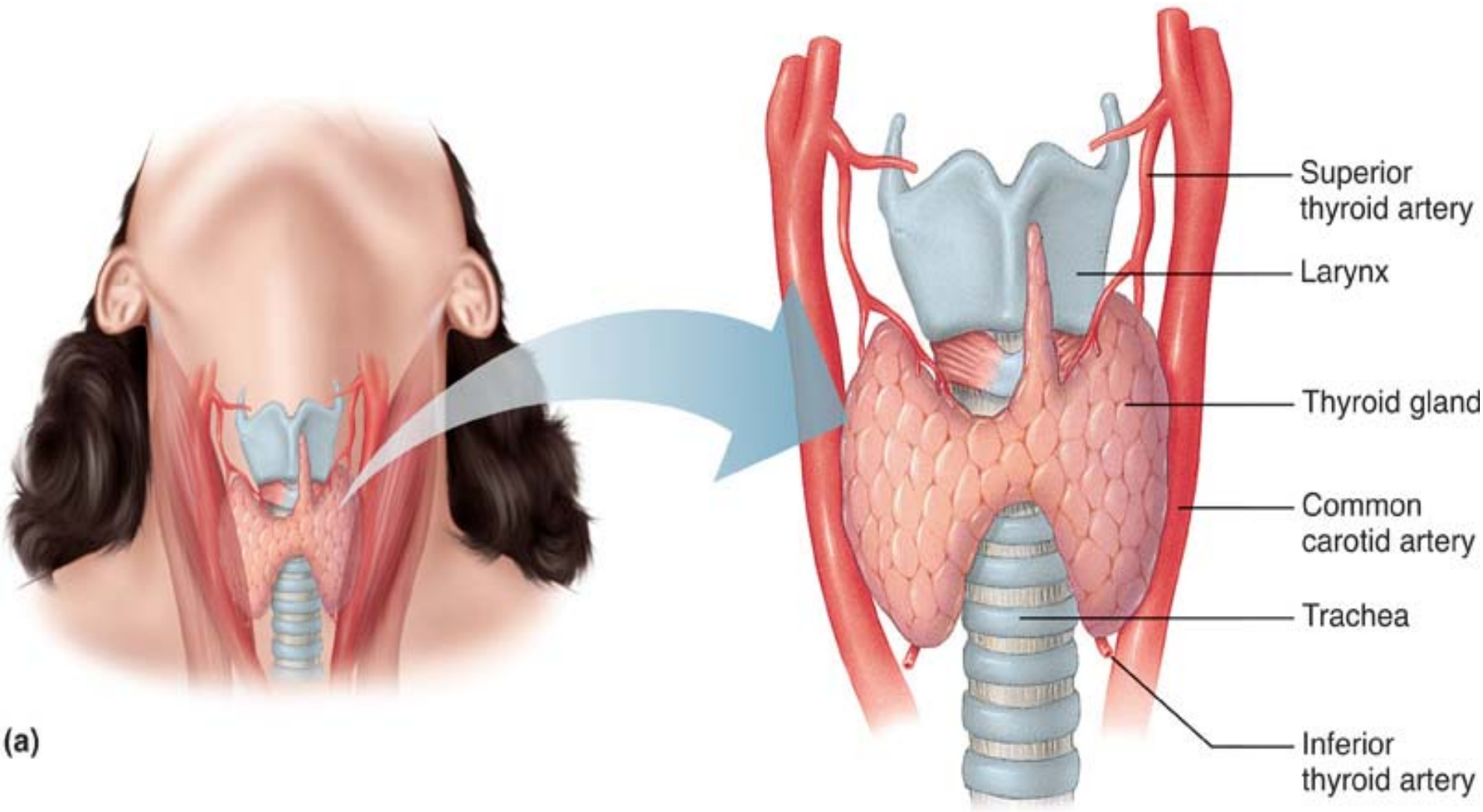
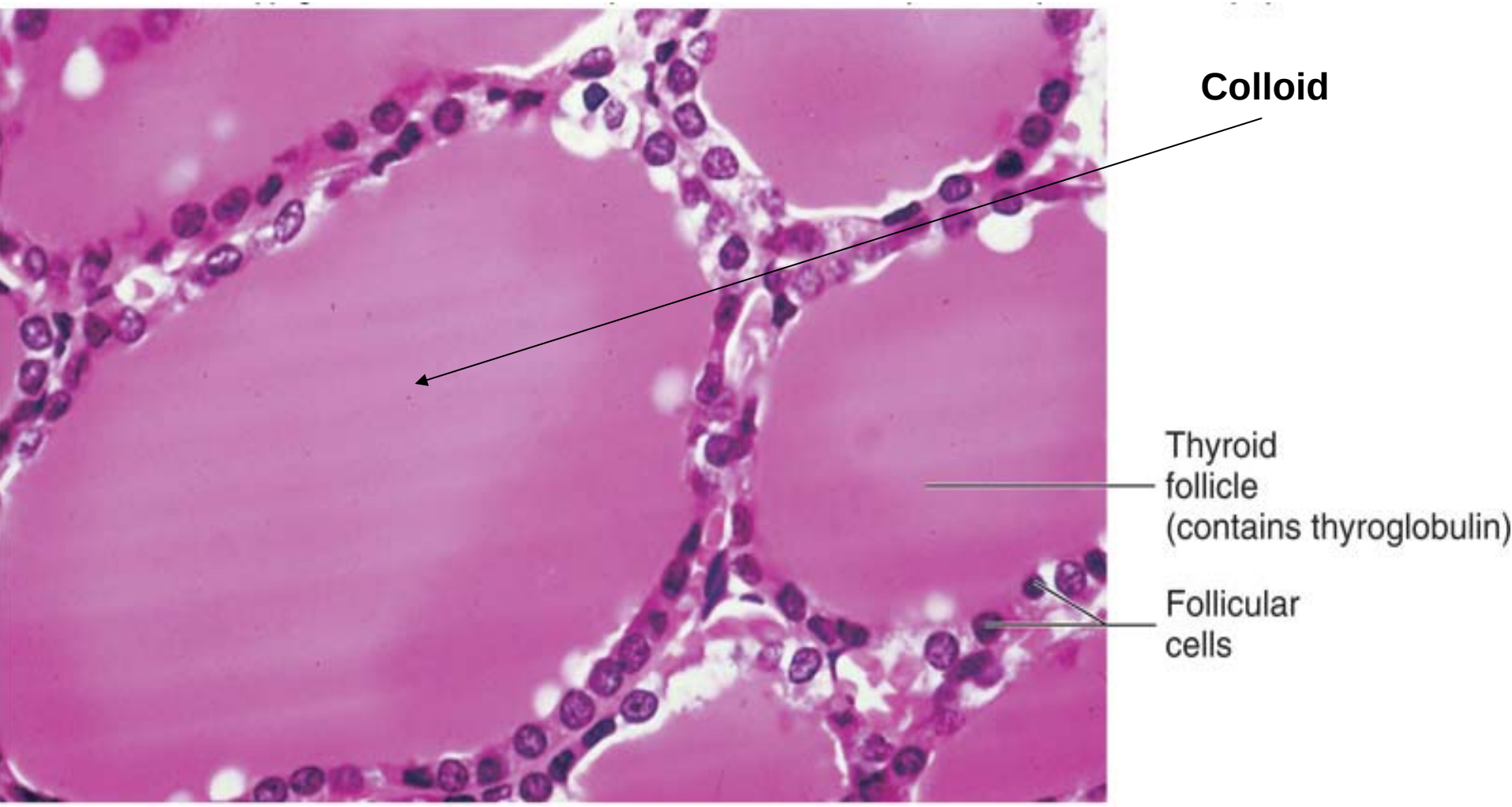
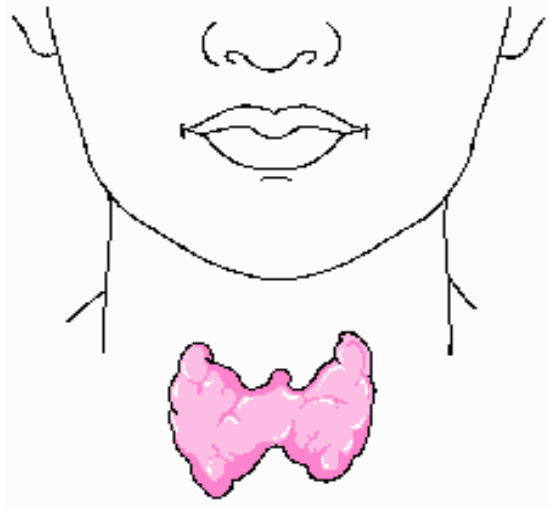
The thyroid gland straddles the esophagus, just below the larynx, in the neck.



Thyroid gland becomes functional early in fetal life as it plays a role in the development of brain cells (forming nerve terminals/ synapse/ dendrites/ myelin)
The follicular cells take part in almost all stages of TH synthesis and secretion



THYROID



Biosynthesis.

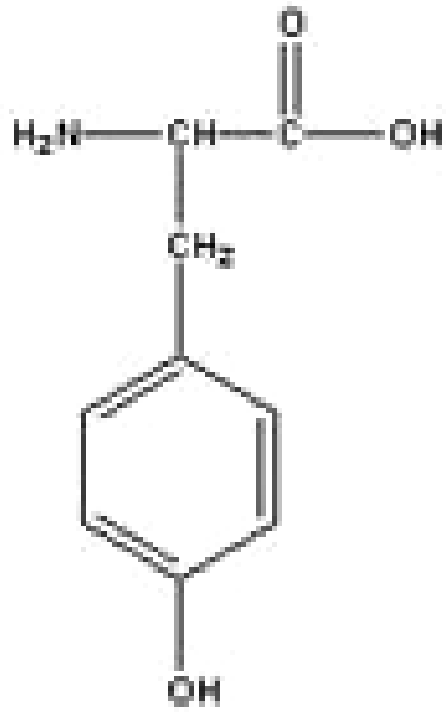
Iodine/iodide trapping
Oxidation of iodide
Incorporation (iodination)
Coupling

TSH affects all these steps
plus release of thyroid hormones

Bound to plasma proteins

Thyroid Hormone:

- **Amino acid hormones containing 2 tyrosine molecules each bound to iodine molecules;**
- **Regulates metabolic activities of all cell types, especially glucose oxidation (energy & heat production)**
- **Formed by joining 2 tyrosine-iodine complexes (MIT/DIT)**

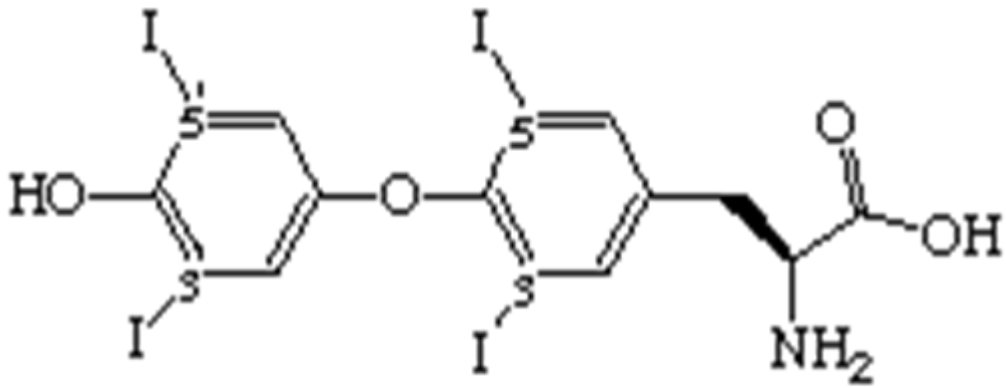


MIT-monoiodotyrosine
DIT-diiodotyrosine

2 Types of Thyroid Hormones

1. Thyroxine (T_4)

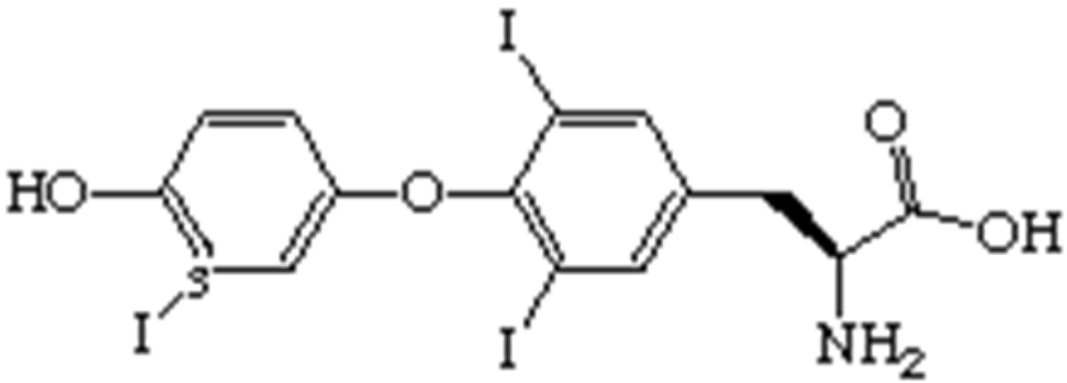
- Major hormone released from thyroid follicles
- Contains 4 iodine atoms
- More abundant than T_3
- Synthesis occurs in follicular cell colloid via the combination of DIT + DIT



T4 (thyroxine)

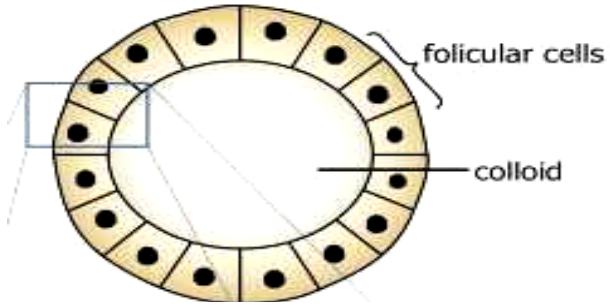
2. Triiodothyronine (T_3)

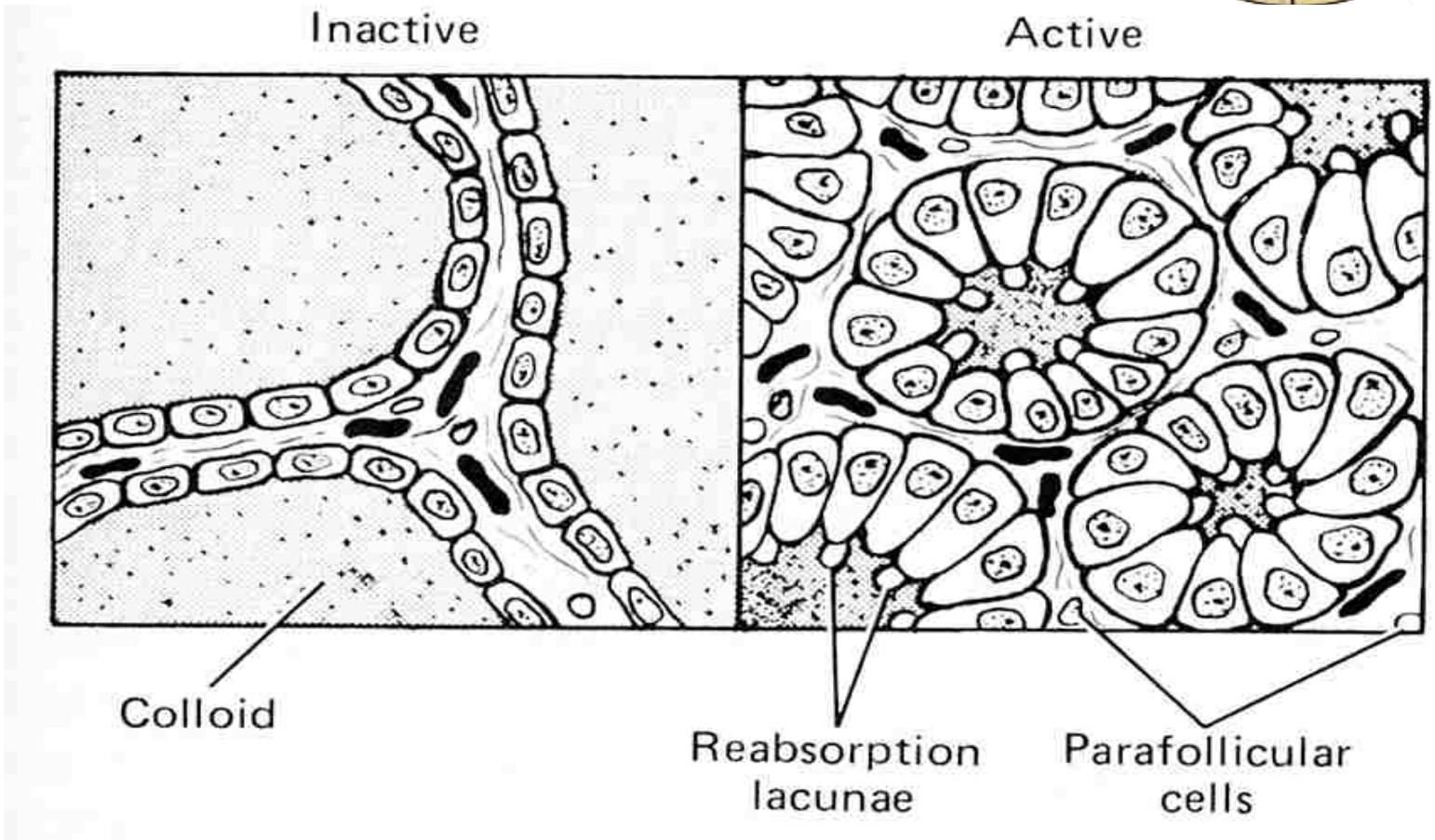
- Generally formed from T_4 by cleaving an iodine molecule (deiodinase in target cells)
- More potent than T_4
- Contains 3 iodine atoms
- Synthesis occurs in the follicular cell colloid via the combination of DIT + MIT



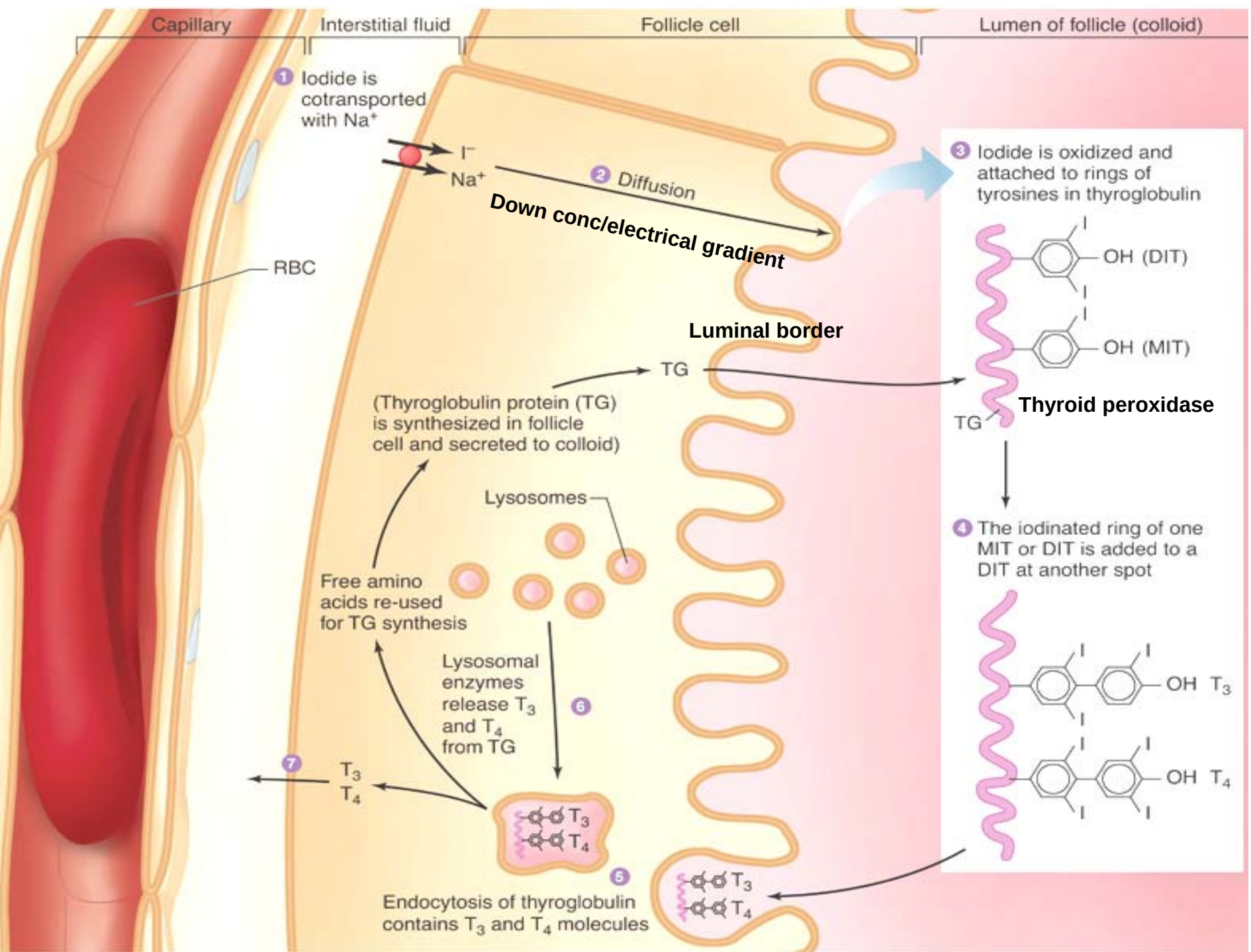
T3 (3,5,3'-triiodothyronine)

- **Thyroid follicles are sacs lined with follicular cells and containing a substance called *colloid***
- **Colloid contains *thyroglobulin***

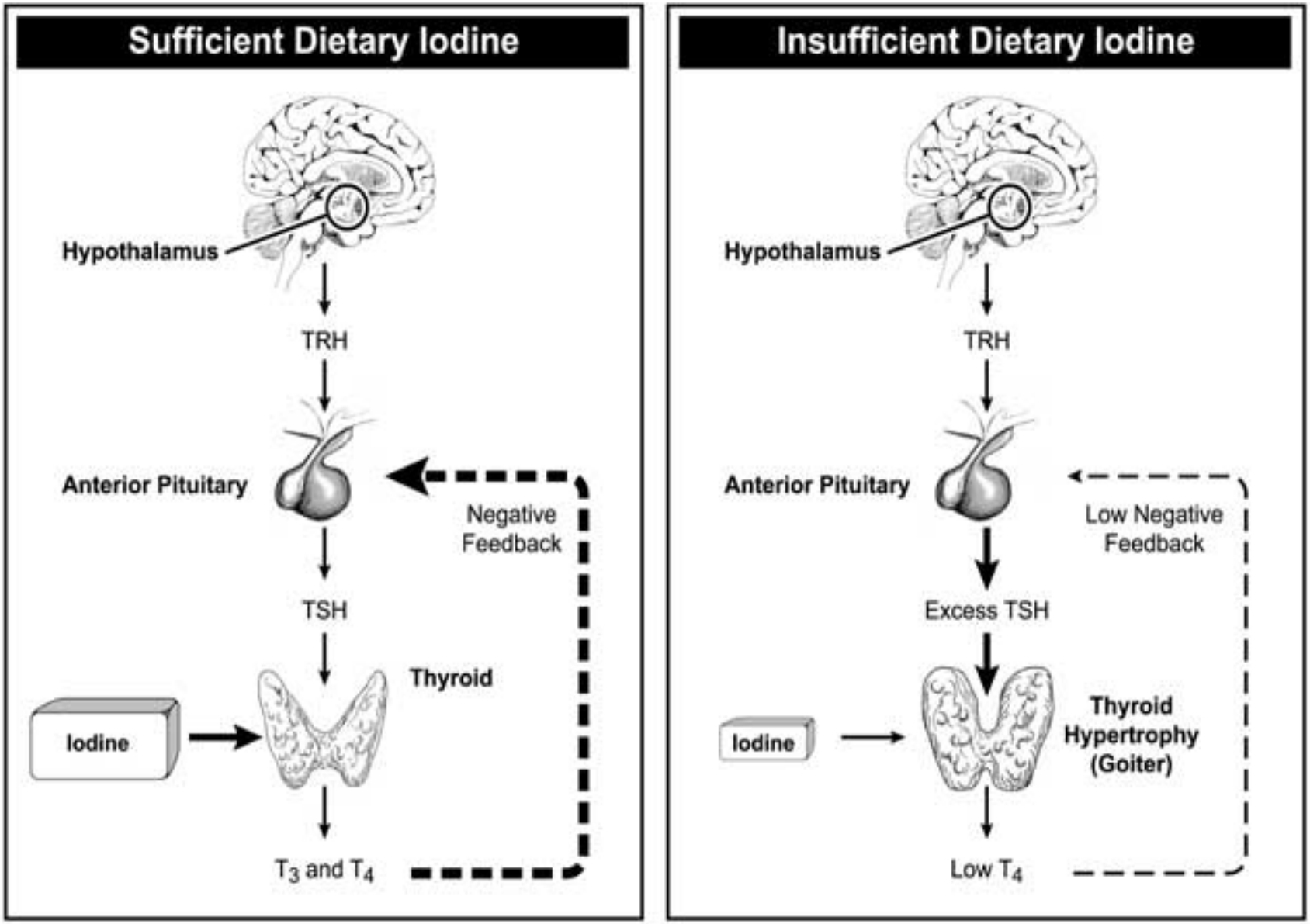




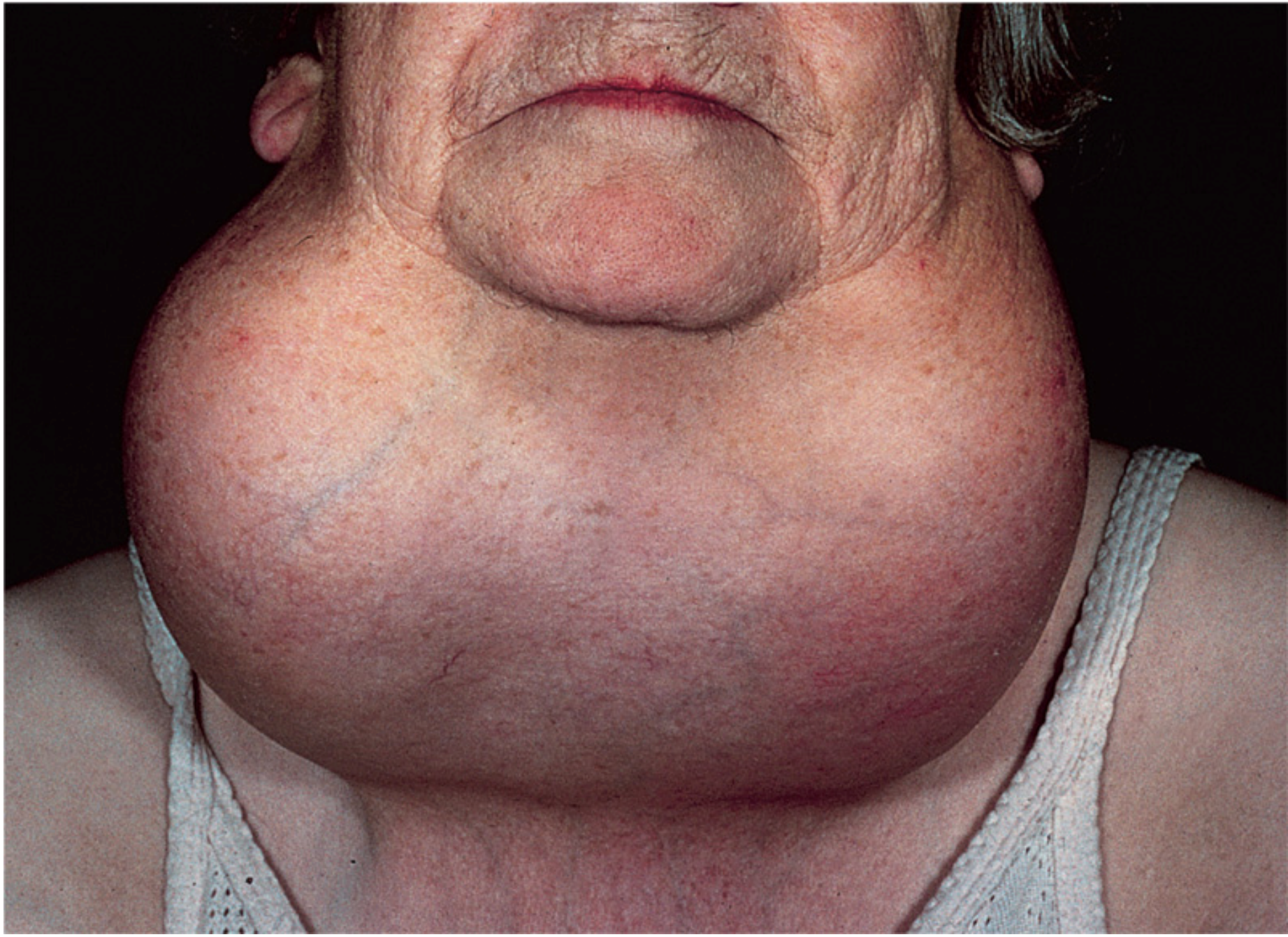
Thyroid Hormone Synthesis and Secretion


Capillary
Interstitial fluid
Follicle cell
Lumen of follicle (colloid)
1 Iodide is cotransported with Na+
I−
Na+
2 Diffusion
Down conc/electrical gradient
RBC
Luminal border
3 Iodide is oxidized and attached to rings of tyrosines in thyroglobulin
OH (DIT)
OH (MIT)
TG
Thyroid peroxidase
(Thyroglobulin protein (TG) is synthesized in follicle cell and secreted to colloid)
Lysosomes
4 The iodinated ring of one MIT or DIT is added to a DIT at another spot
OH T3
OH T4
Free amino acids re-used for TG synthesis
Lysosomal enzymes release T3 and T4 from TG
6
7
T3
T4
5
Endocytosis of thyroglobulin contains T3 and T4 molecules

Click here to play the Biosynthesis of Thyroid Hormones Flash Animation



TSH is a trophic hormone, it stimulates not only T_3/T_4 secretion but also protein synthesis in follicular cells. Therefore, ↑ exposure in thyroid ↑ size

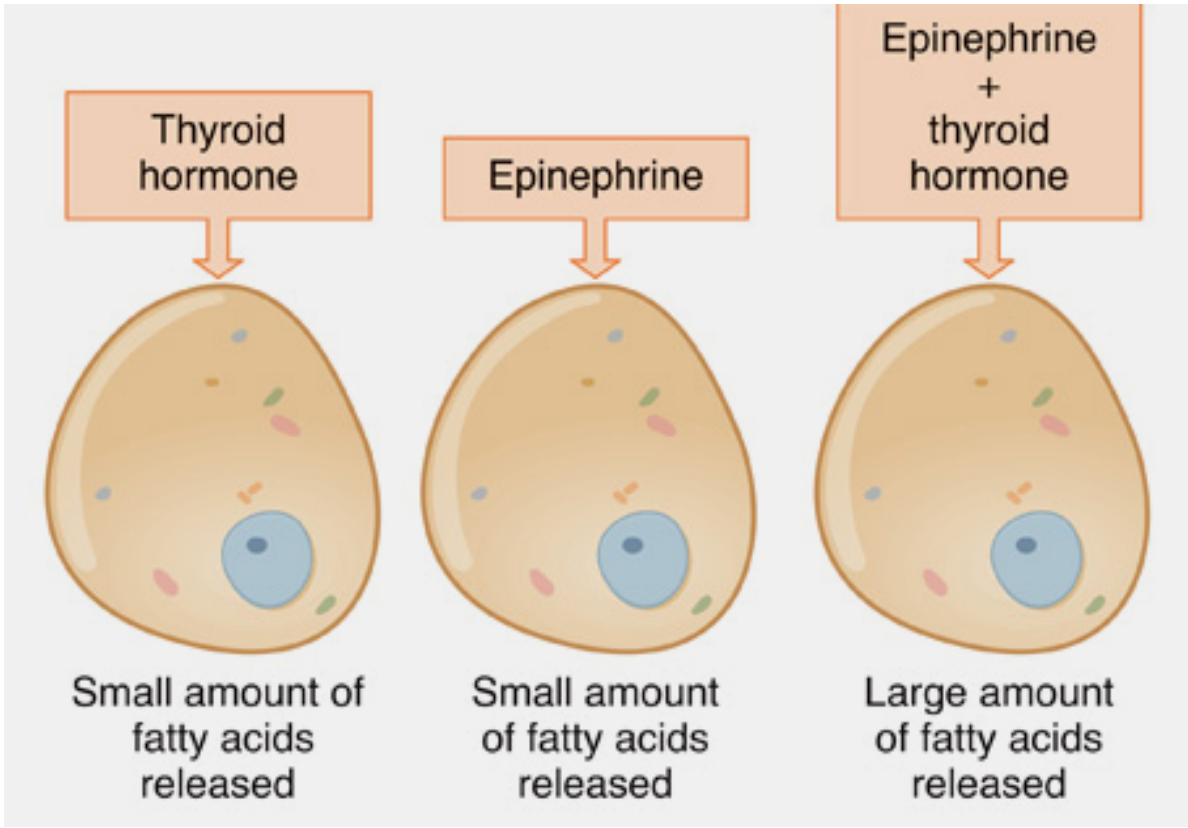


Physiological Effects of Thyroid Hormones

1. **Metabolic rate & Growth.**

↑ Basal metabolic rate (oxygen consumption)

Growth (TH is required for normal production of GH)
protein synthesis
skeletal maturation (ossification- prepubertal growth)



- **TH has permissive effects on catecholamines**
- **Upregulates beta-adrenergic receptors in many tissues (heart and nervous system)**
- **Potentiate (↑ the effect of, being synergistic) actions of catecholamines (i.e. hyperthyroid resemble symptoms of hypersecretion of epinephrine/ norepinephrine**

2. Carbohydrate metabolism

- ↑ glycogen breakdown
- ↑ gluconeogenesis
- ↑ glycolysis

Too much ⟶ blood glucose
(Diabetes)

↑ **Lipolysis (lipogenesis)**

Triglyceride ⟶ FFA + glycerol

↓ **serum cholesterol (excretion into GI)**

↓ **serum triglyceride (uptake into tissues)**

3. Cardiovascular system.
(contraction)

a. direct
b. ↑ response to adrenaline/ noradrenaline
(sympathetic nervous system)
c. metabolic effect
(vasodilation)
Oxygen
Heat

4. Effect on CNS.

Development (Critical period)

Behaviour (through catecholamine)

5. Temperature regulation.

Heat production

Oxidative phosphorylation (formation of ATP, needs O_2)

Regulation of secretion.

1. **Hypothalmico-pituitary-thyroid axis.**

   TRH $\rightarrow$ TSH $\rightarrow$ T_3/T_4

2. **Environmental factors cold, stress**

3. **Negative feed-back.**

4. **Excessive iodide. (anti-TSH)**

Thyroid disorders.

A. Hypothyroidism.

Causes: Primary (thyroid), secondary (pituitary gland) or tertiary (hypothalamus)

e.g. autoimmune disease, partial thyroidectomy, pituitary hypothyroidism rare.

Clinical features

– lack of energy,
cold intolerance (↓ metabolism),
dryness of skin and hair (↓ protein)
weight gain (↓ metabolism)
constipation (↓ GI motility)
acroparesthesia (numbness/tingling of hands)
Low sex drive
prolongation of tendon reflex
↓ cardiac output (remember permissive effect of TH to epinephrine/norepinephrine).

(Hypothyroidism in infants may be associated with *cretinism* (underdeveloped thyroid gland); symptoms are short, stocky stature & may lead to mental retardation

3. Diagnoses – low serum free T_4, usually greatly elevated serum TSH level;

4. Treatment – thyroxine (T_4) replacement.

B. **Hyperthyroidism.**

1. Causes – thyrotoxicosis*, due to Graves disease (presence of Ab called thyroid stimulating immunoglobulin (TSI) that bind and activate TSH receptor.

2. Clinical features – enlarged thyroid (goitre)
tachycardia (↑ heart rate, >100 per minute) & palpitation (subjective),
↑ cardiac output
excessive sweating (↑ metabolism)
weight loss (↓ protein)
nervousness, irritability, tremour (CNS)
exophthalmos (eye signs; extra-thyroidal)

(many of the effects are mediated by the sympathetic nervous system).

* **The condition resulting from excessive quantities of the thyroid hormones, if the excess results from overproduction by the thyroid gland (as in Graves disease), originated outside the thyroid or is due to loss of storage function and leakage from the gland.**

An abnormal protrusion of the eyeball in the orbit when observed from the side.

Swelling within the orbital cavities and enlargement of the perorbital muscles behind the eyes

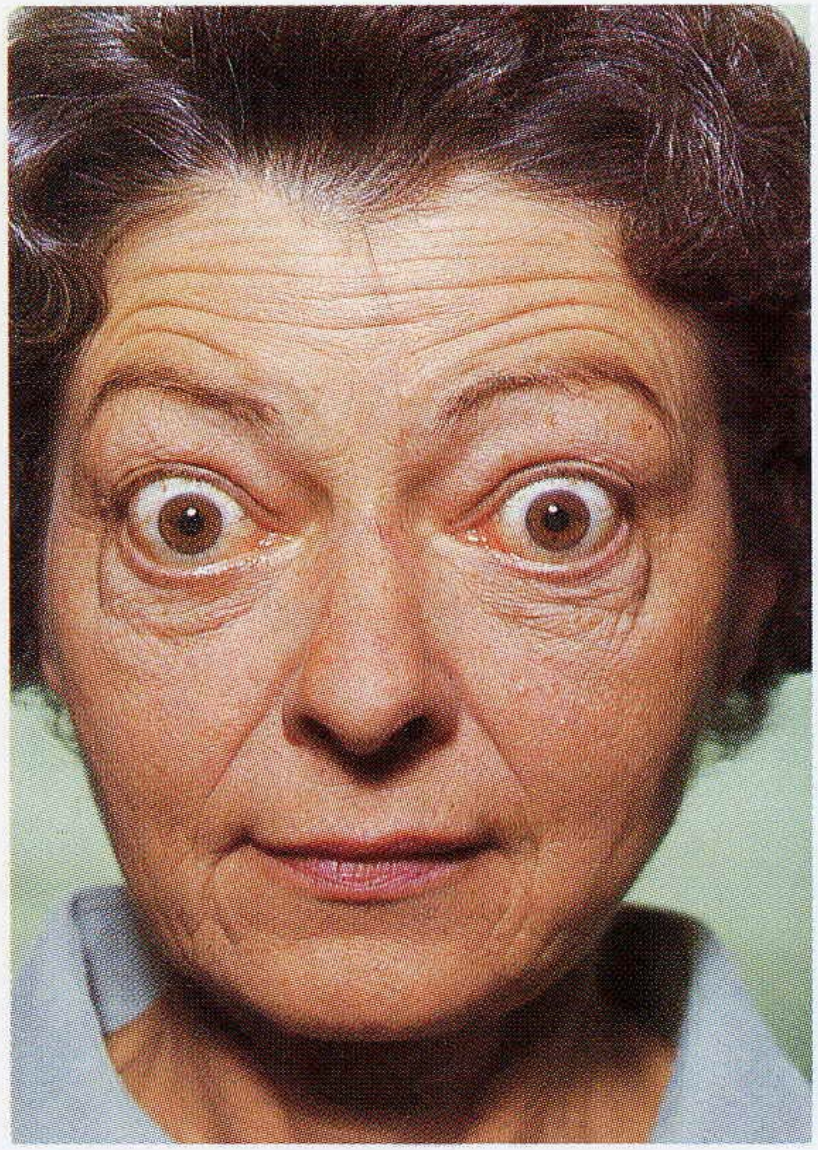
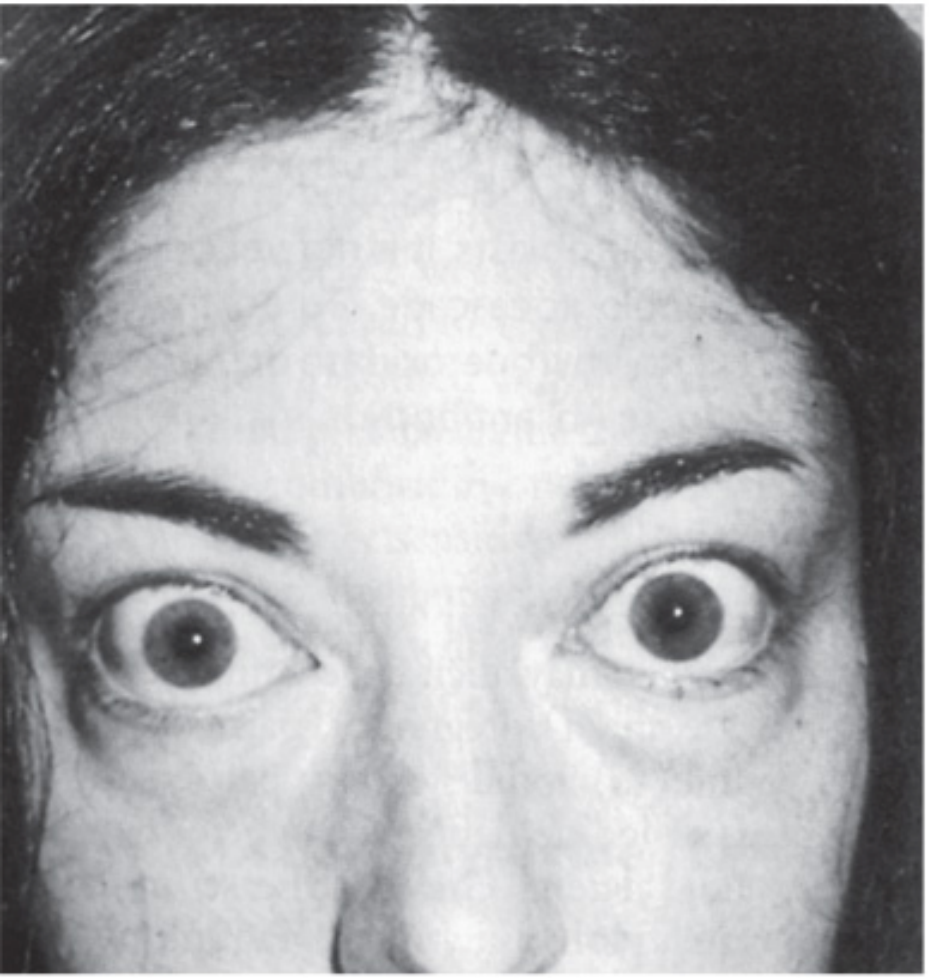
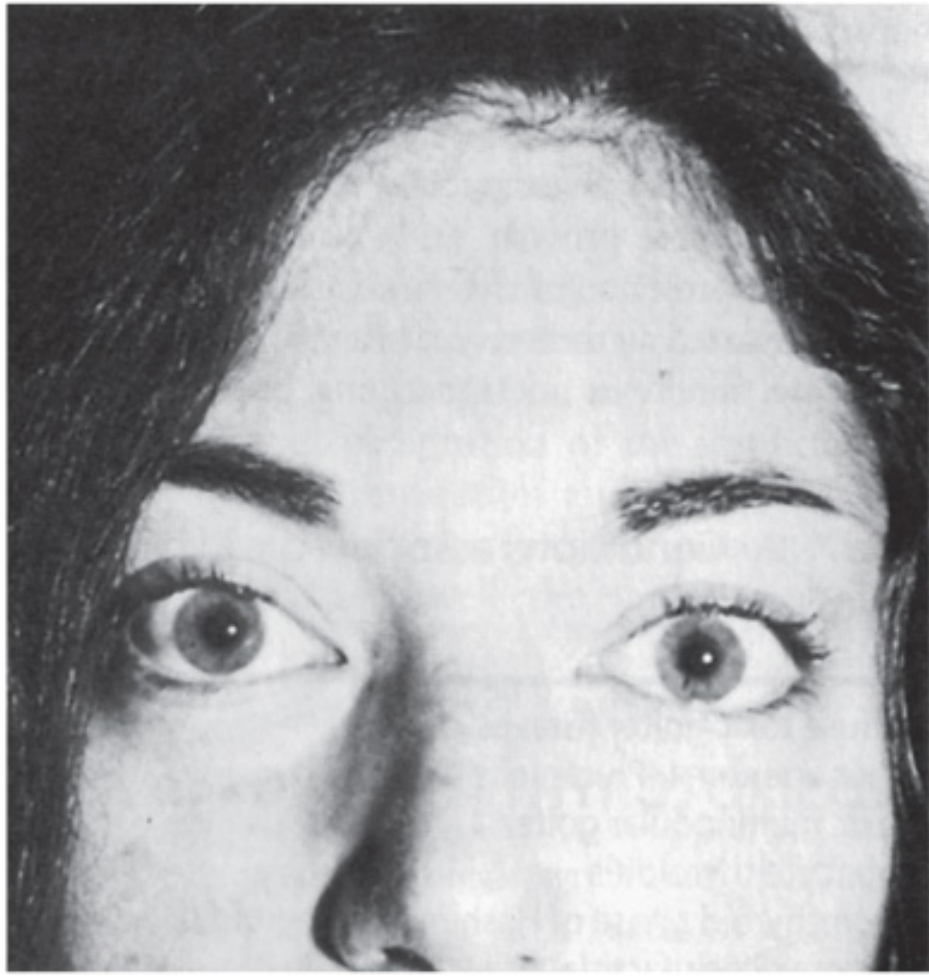


Fig. 13 Lid retraction and exophthalmos in patient with Graves' disease.



(a)

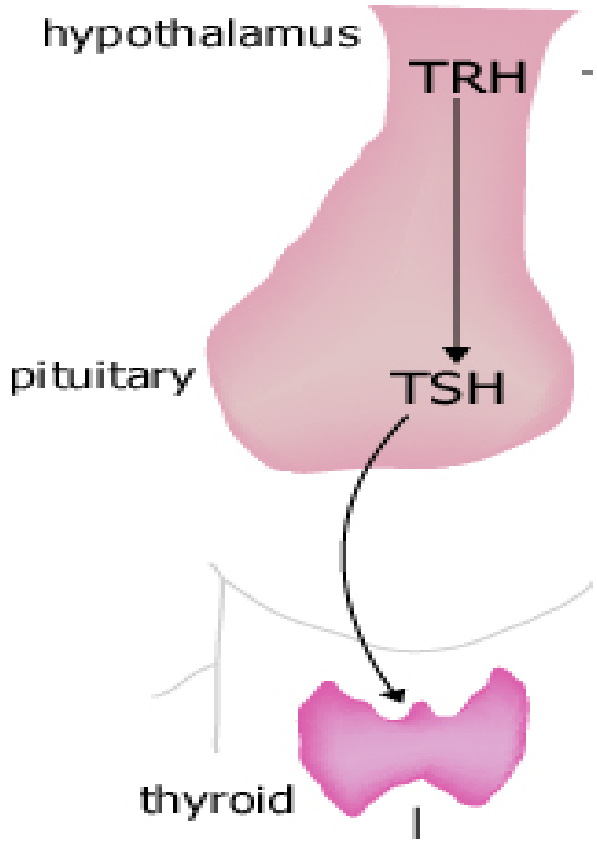


(b)

3. Diagnoses –

- **Free serum T_3 and T_4 tests;**

4. Treatments – anti-thyroid drugs, partial thyroidectomy, radioactive iodine (to radiate the gland with high energy gamma rays, 3 months max. effect)

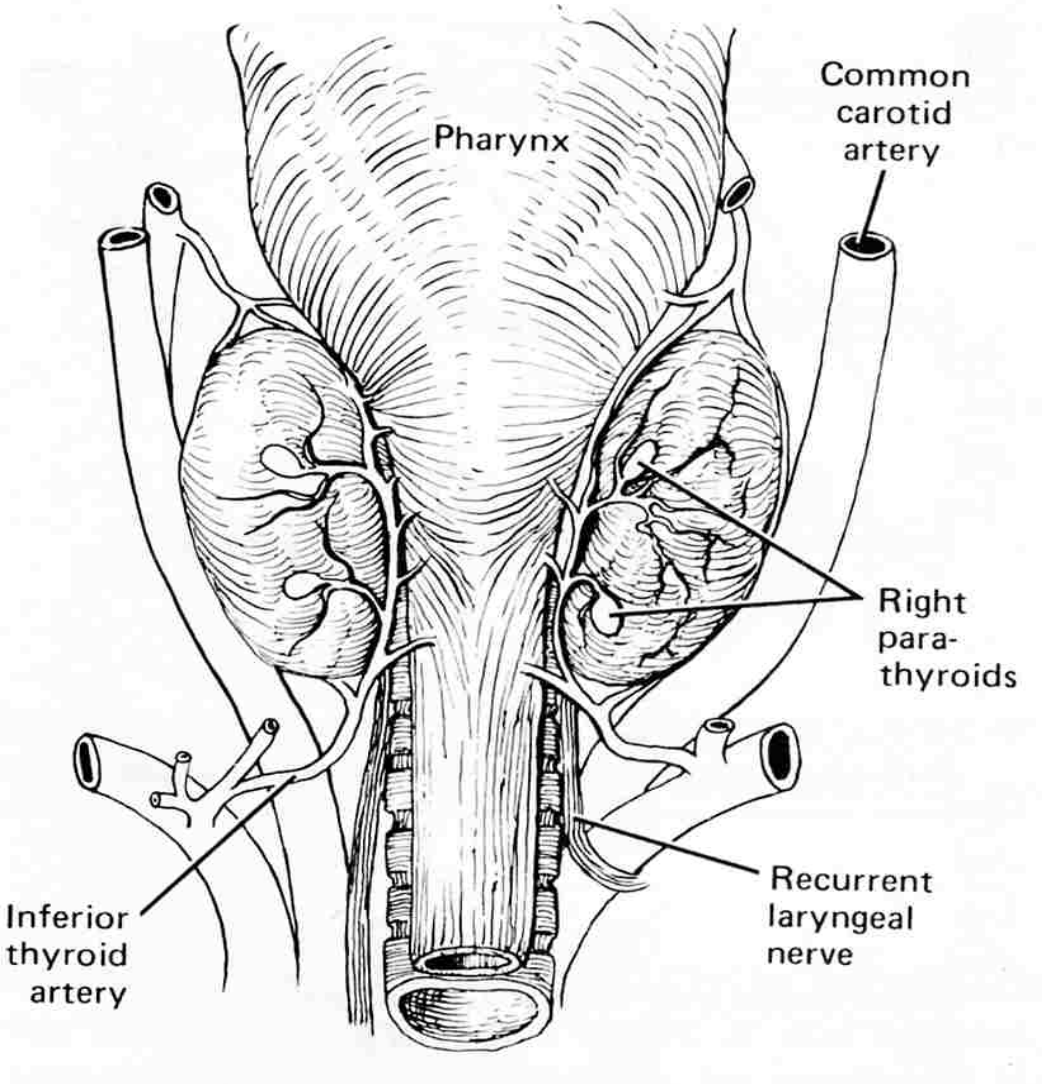


Calcitonin

- **Produced by parafollicular cells (C cells) of thyroid gland**
- **Lowers blood calcium levels by inhibiting osteoclasts (for bone resorption) & stimulating calcium uptake by bones**
- **Unlike parathyroid hormone and vitamin D, it plays no role in normal day-to-day regulation of plasma calcium regulation in humans**

Parathyroid glands

Parathyroid glands- paired glands on posterior aspect of thyroid gland



PARATHYORID HORMONE.

I. Parathyroid hormone.

1. Actions –

↑ bone resorption by stimulating osteoclasts and osteocytes and inhibiting osteoblasts

↑ kidney reabsorption of Ca^{++}.

excretion of phosphate

↑ vitamin D3 → GI absorption

— ↑ of Ca^{++}

2. Regulation by calcium

(negative feed-back)

serum Ca↓ → PTH↑ → Ca↑ →↓ PTH

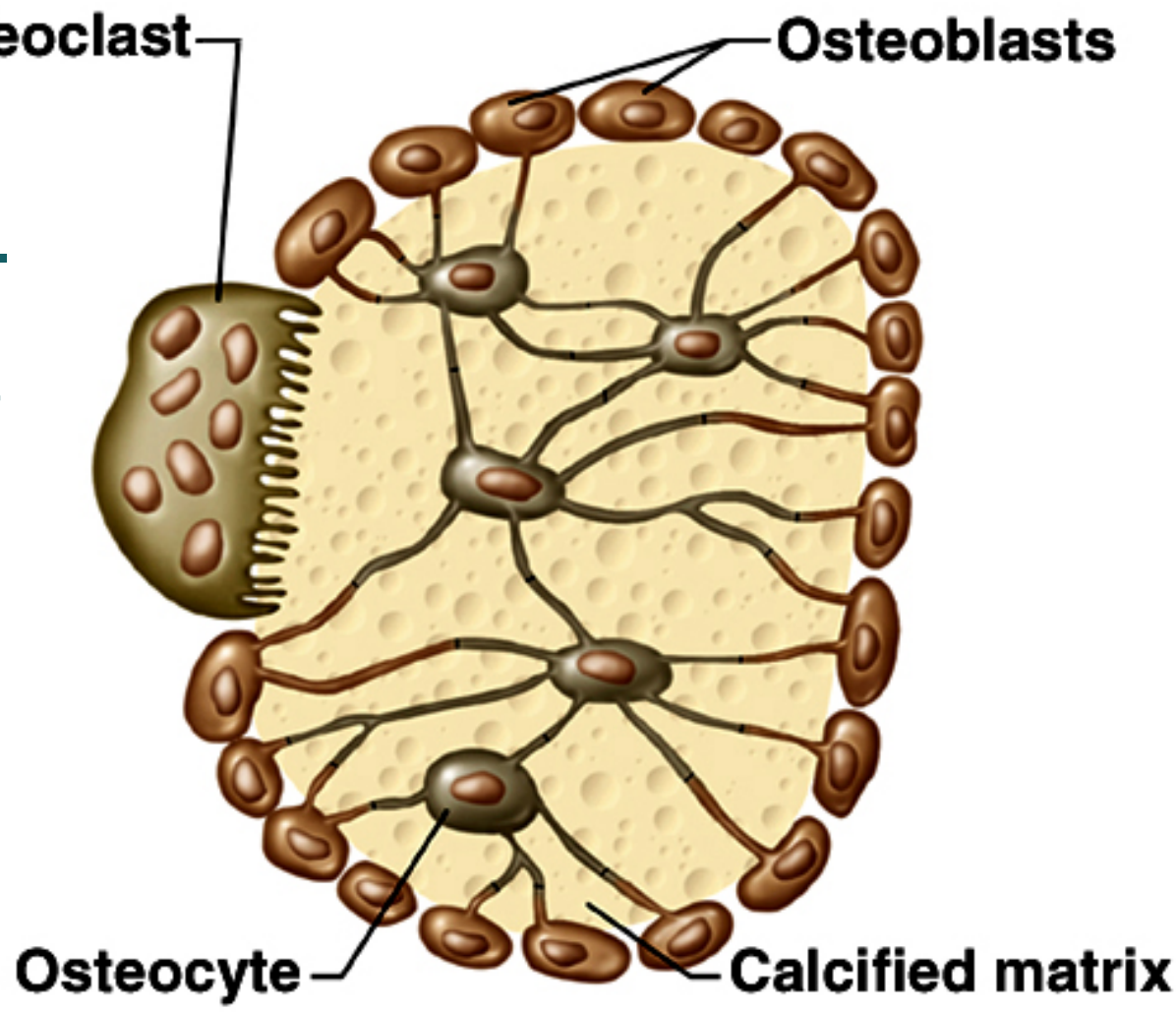
II. Bone resorption. (Breakdown)

osteoclasts mobilize

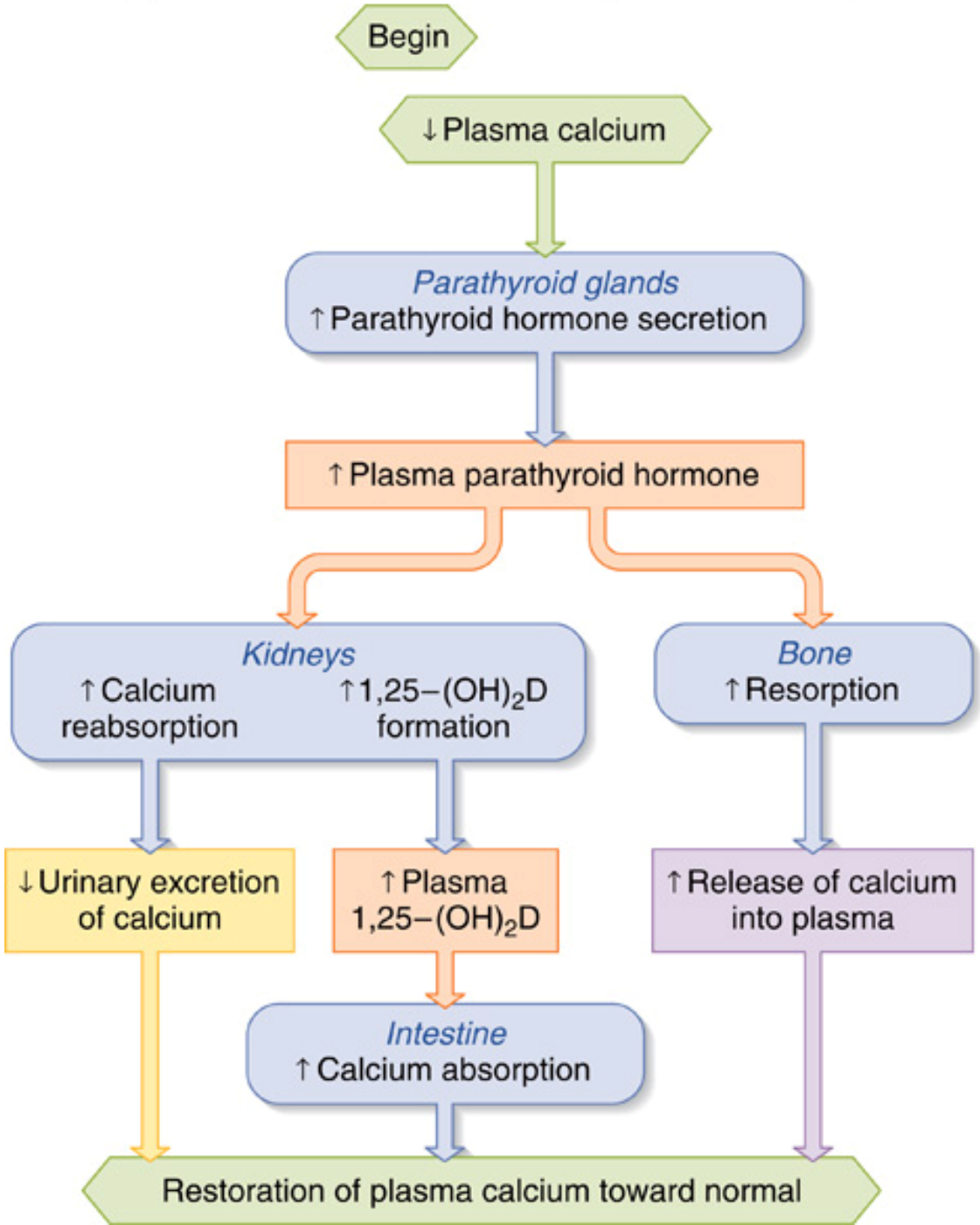
osteocytes (cell formed from osteoblast when surrounded by mineralised bone) transport

blood bone barrier of inactive osteoblasts (bone forming)

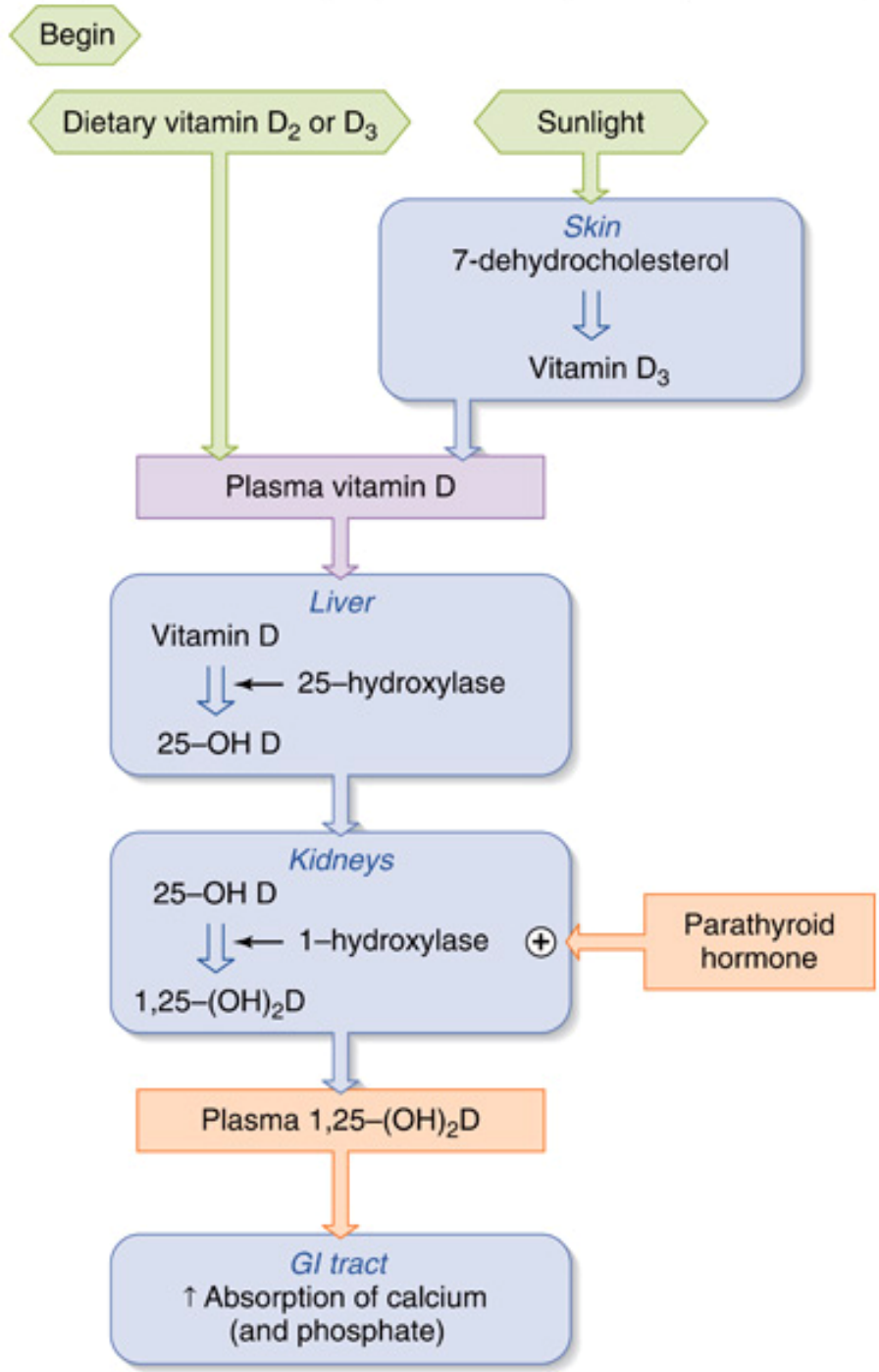
Osteo***b***lasts ***b***uild bone. Osteocytes have long processes that connect with each other and to osteoblasts via tight junctions.
Osteo***c***lasts ***c***atalyze bone degradation, when stimulated by parathormone (PTH).



Parathormone's action to restore normal calcium levels include increased calcium reabsorption in the kidneys, increased calcium-liberating activities of osteoclasts, and increased formation of vitamin D, which increases uptake of dietary calcium in the gastrointestinal tract.



Activated 1,25 $(OH)_2$D3 is a steroid hormone that causes cells in the gut to increase the expression of genes whose products take up dietary calcium.



III. Vitamin D.

1. **Source – UV irradiation of skin.**
   Diet

2. **Actions – GI absorption of Ca^{2+}**
   (& phosphate)
   Bone resorption

3. **Regulation –calcium**
   PTH

TABLE 14–7 *Summary of Major Hormonal Influences on Bone Mass*

Hormones that favor bone formation and increased bone mass

- Insulin
- Growth hormone
- Insulin-like growth factor I (IGF-I)
- Estrogen
- Testosterone
- Calcitonin

Hormones that favor increased bone resorption and decreased bone mass

- Parathyroid hormone
- Cortisol
- Thyroid hormones (T_4 and T_3)

IV. Disease of the parathyroids.

A. Hyperparathyroidism.

1. **Causes – parathyroid tumour (benign adenoma- glandular).**

2. **Clinical features - excessive bone resorption**
   (osteitis fibrosa cystica*)
   hypercalcaemia
   depression of CNS/PNS
   muscular weakness
   hypertension
   constipation
   peptic ulcer
   polyuria (↑ volume of urine per given time)
   formation of kidney stones

***Rarefying osteitis (bone inflammation) with fibrous degeneration and formation of cysts, and with the presence of fibrous nodules on the affected bones. It is due to marked osteoclastic activity secondary to hyperfunction of the parathyroid glands**

3. Diagnosis – plasma fasting calcium and plasma PTH level.

4. Treatment – surgical removal of tumour.

(Secondary hyperparathyroidism – result of hypocalcaemia e.g. caused by chronic renal failure due to ↓ active form of vitamin D production, decreases plasma Ca)

B. Hypoparathyroidism.

1. Causes – autoimmune disease; damage to blood supply during thyroidectomy.

2. Clinical features – hypocalcaemia

↑neuromuscular excitability

(tetany-muscular cramps)

3. Diagnosis – low serum calcium level and PTH level.

4. Treatment – vitamin D [$1,25(OH)_2D_3$] plus calcium supplementation.