
KEEP CALM,
STUDY HARD,
AND BECOME A
GREAT DOCTOR.
medschool.inspiration

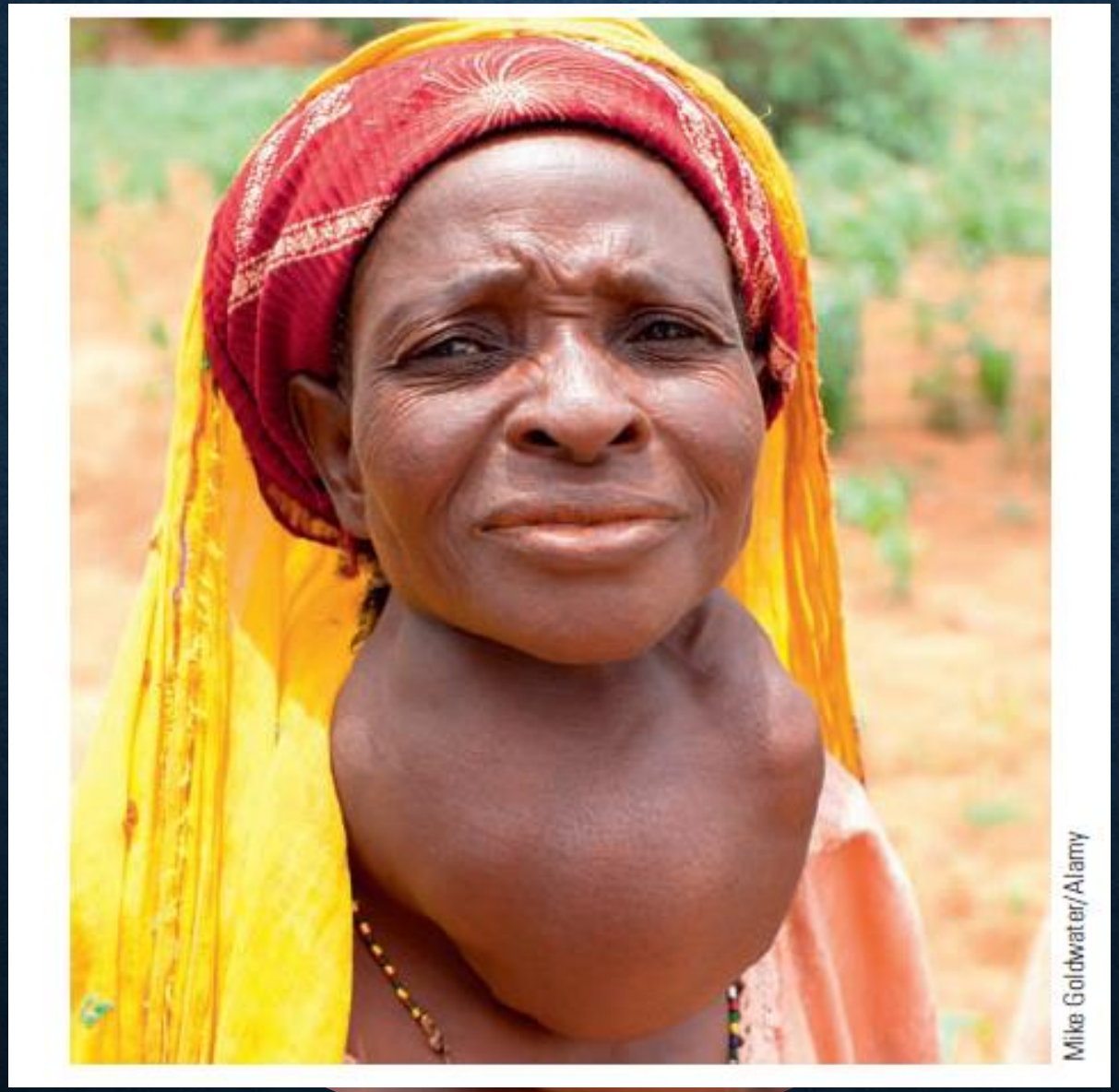

أعوذ بكلمات الله
التّامّات
من شرّ ما خلق
@8UTOOF

"I can't wait for Summer vacation, I have all these great plans!"

Meanwhile, during Summer vacation:


WHAT EVERYONE THINKS I DO OVER SUMMER BREAK...
VS.
WHAT I REALLY DO OVER SUMMER BREAK...
BORED TEACHERS©
TEACHERS

WHAT IS THE ABNORMALITY ?



GOITER

PHYSIOLOGY OF THYROID HORMONES

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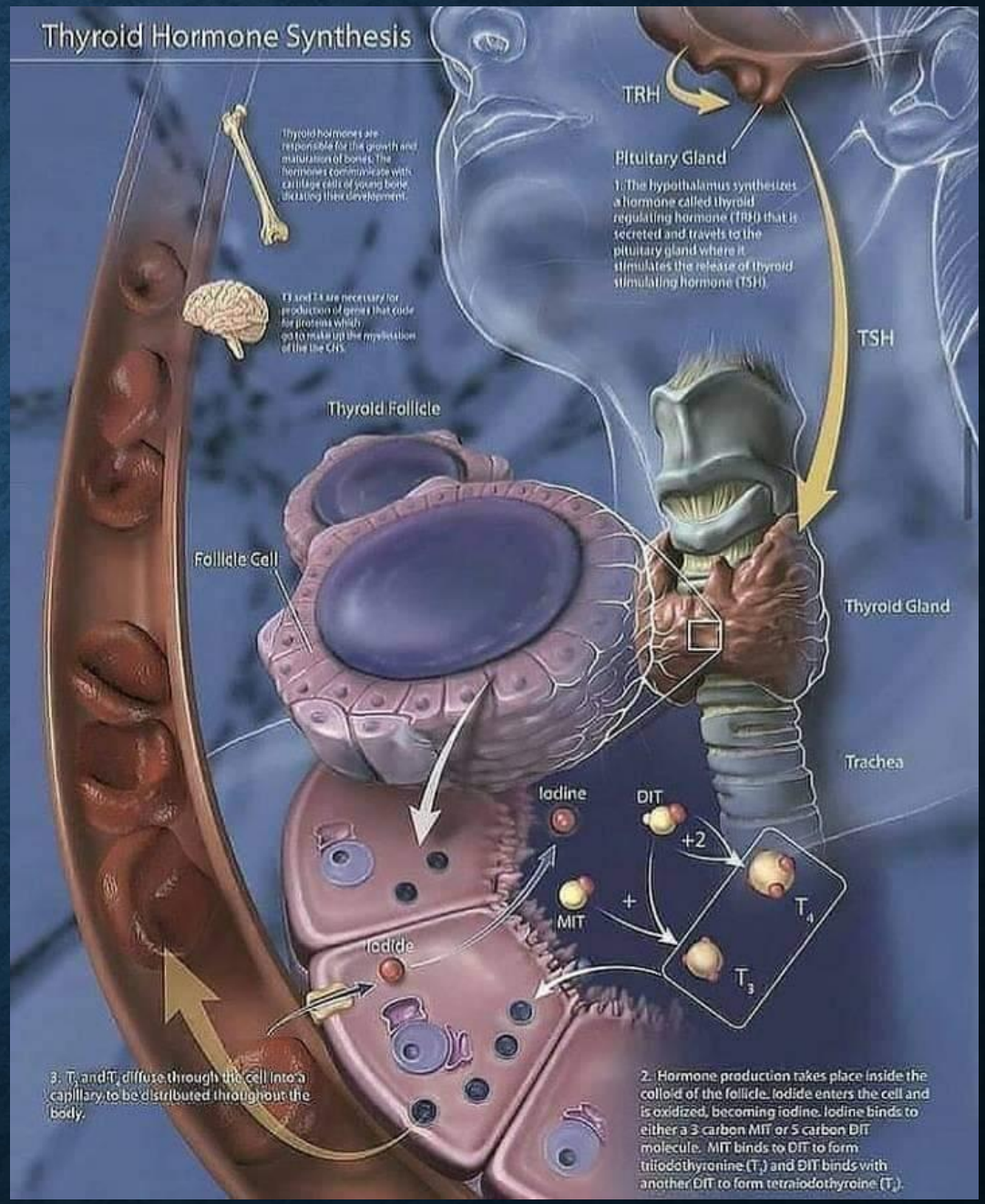
Assistant Professor

FCPS (Medicine)

M phil Physiology

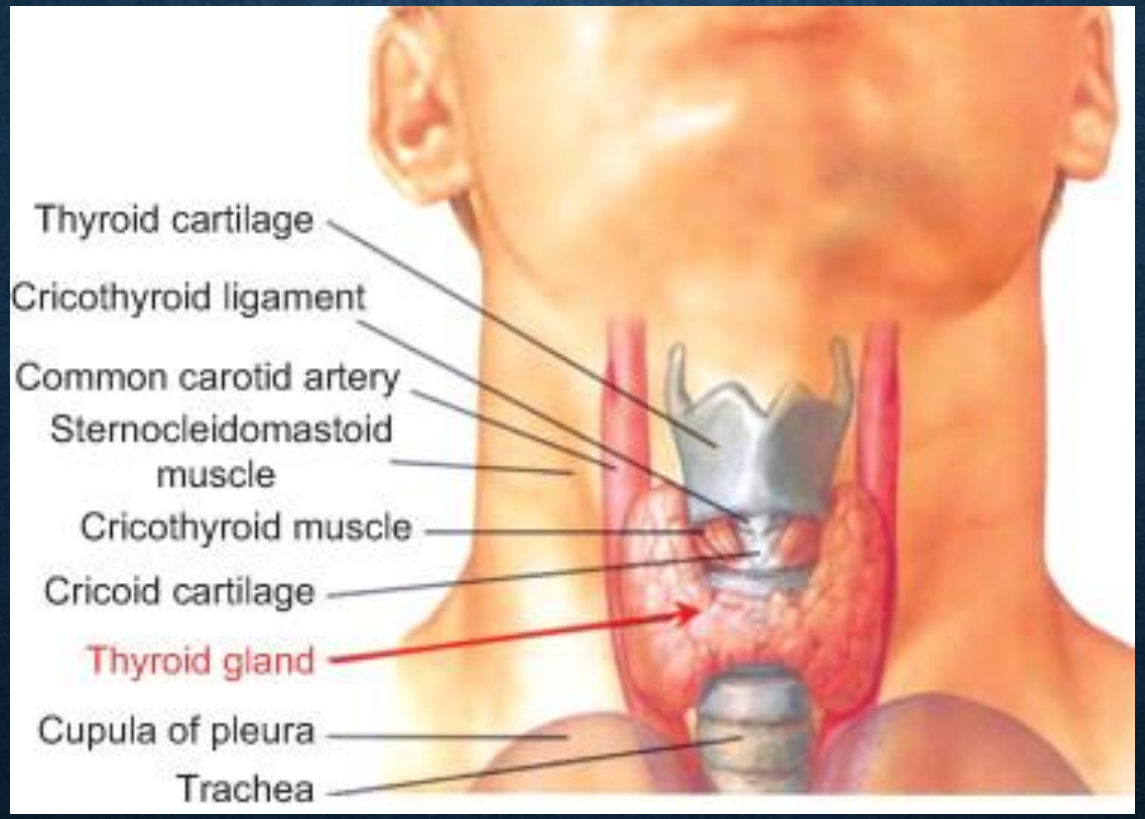



بسم الله الرحمن الرحيم

LEARNING OBJECTIVES

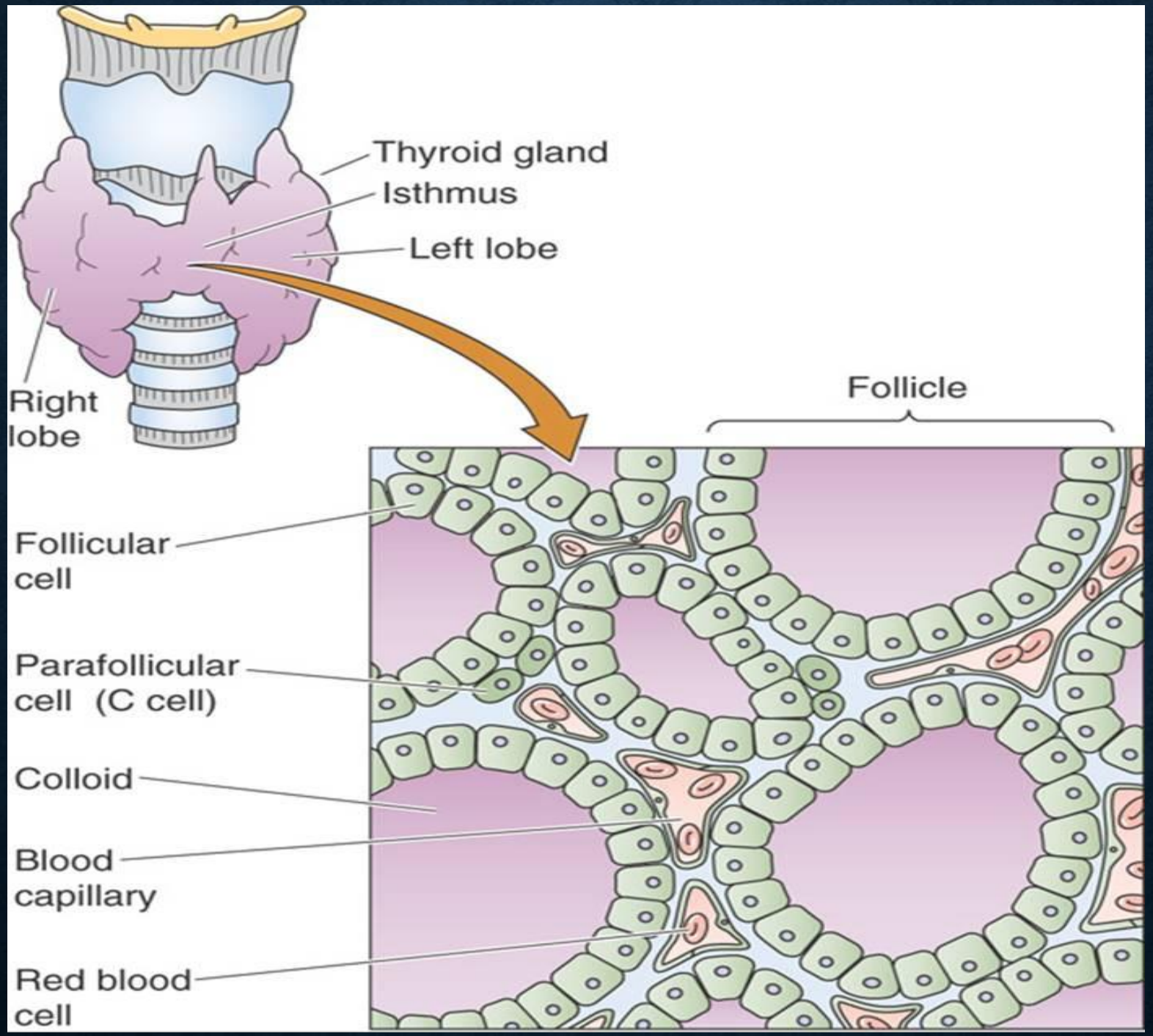
- Describe the thyroid hormones
- Describe formation, Secretion and transport of thyroid hormones
- Explain mechanism of action of thyroid hormones
- Explain the actions of thyroid hormones on cellular metabolism
- Describe Physiological effects of Thyroid Hormone on Growth, metabolism and body systems
- Describe Regulation of Thyroid Hormone Secretion

RECALL YOUR PREVIOUS KNOWLEDGE…



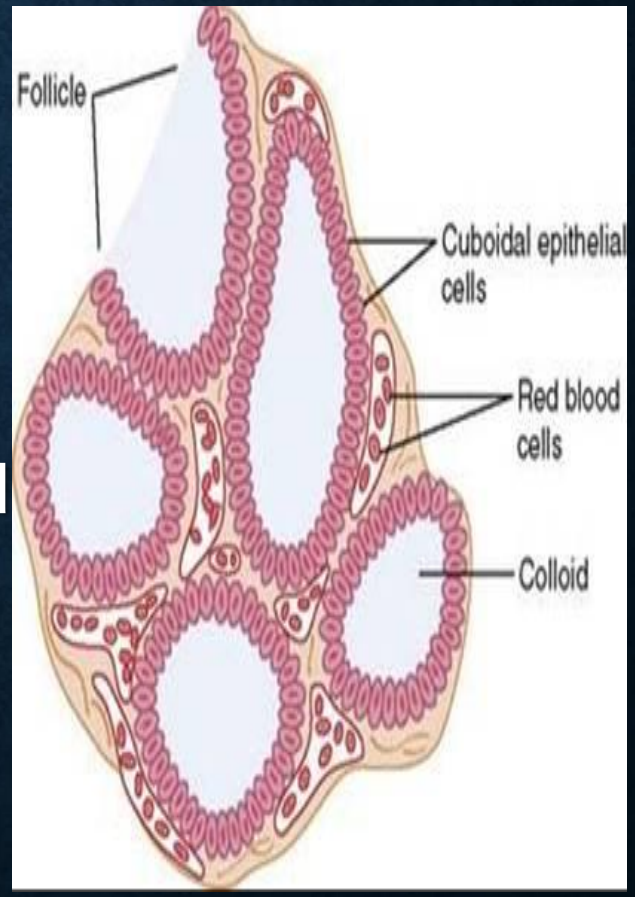
SYNTHESIS OF THYROID HORMONE

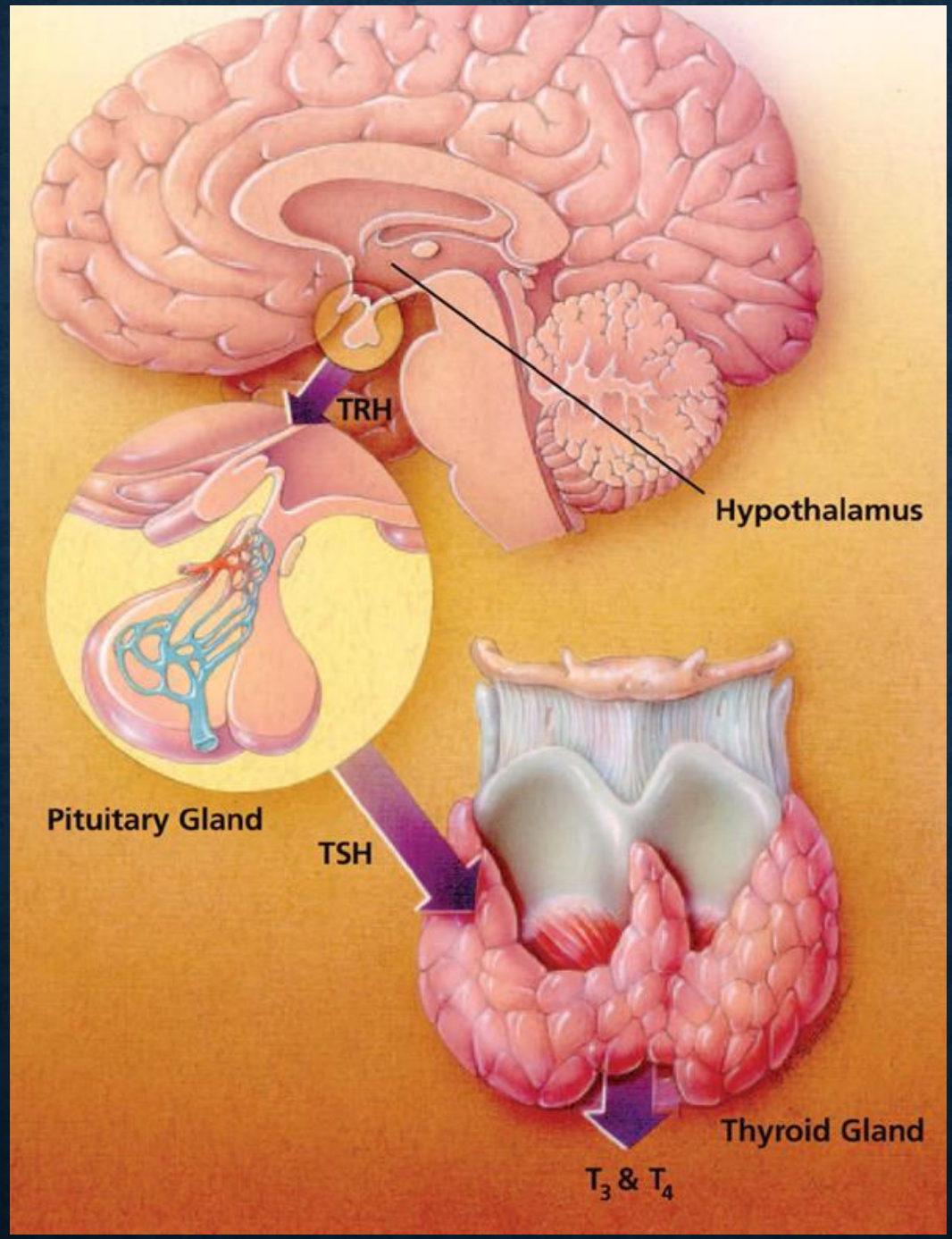
Lecture 1

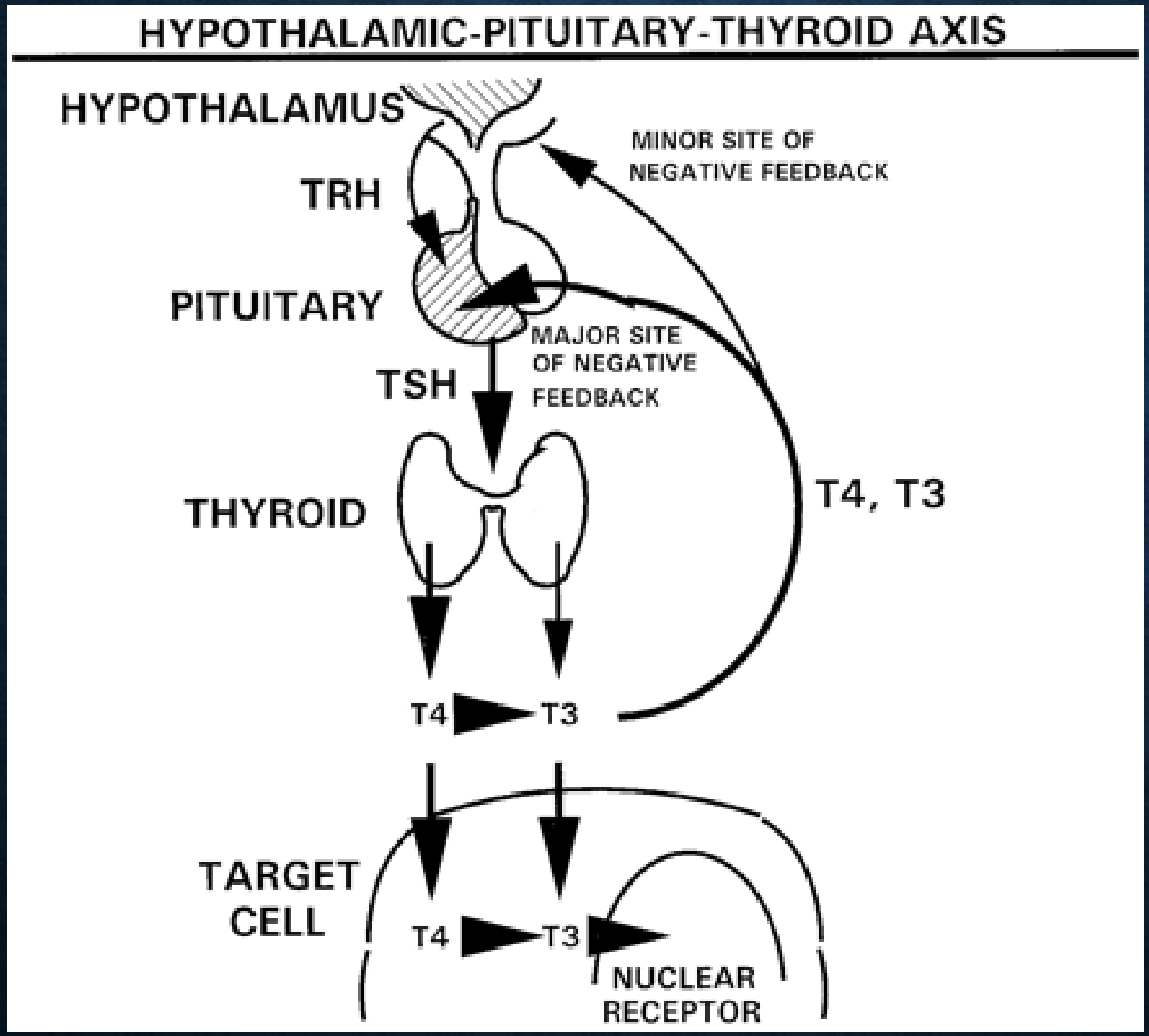

Thyroid gland
Isthmus
Left lobe
Right lobe
Follicle
Follicular cell
Parafollicular cell (C cell)
Colloid
Blood capillary
Red blood cell

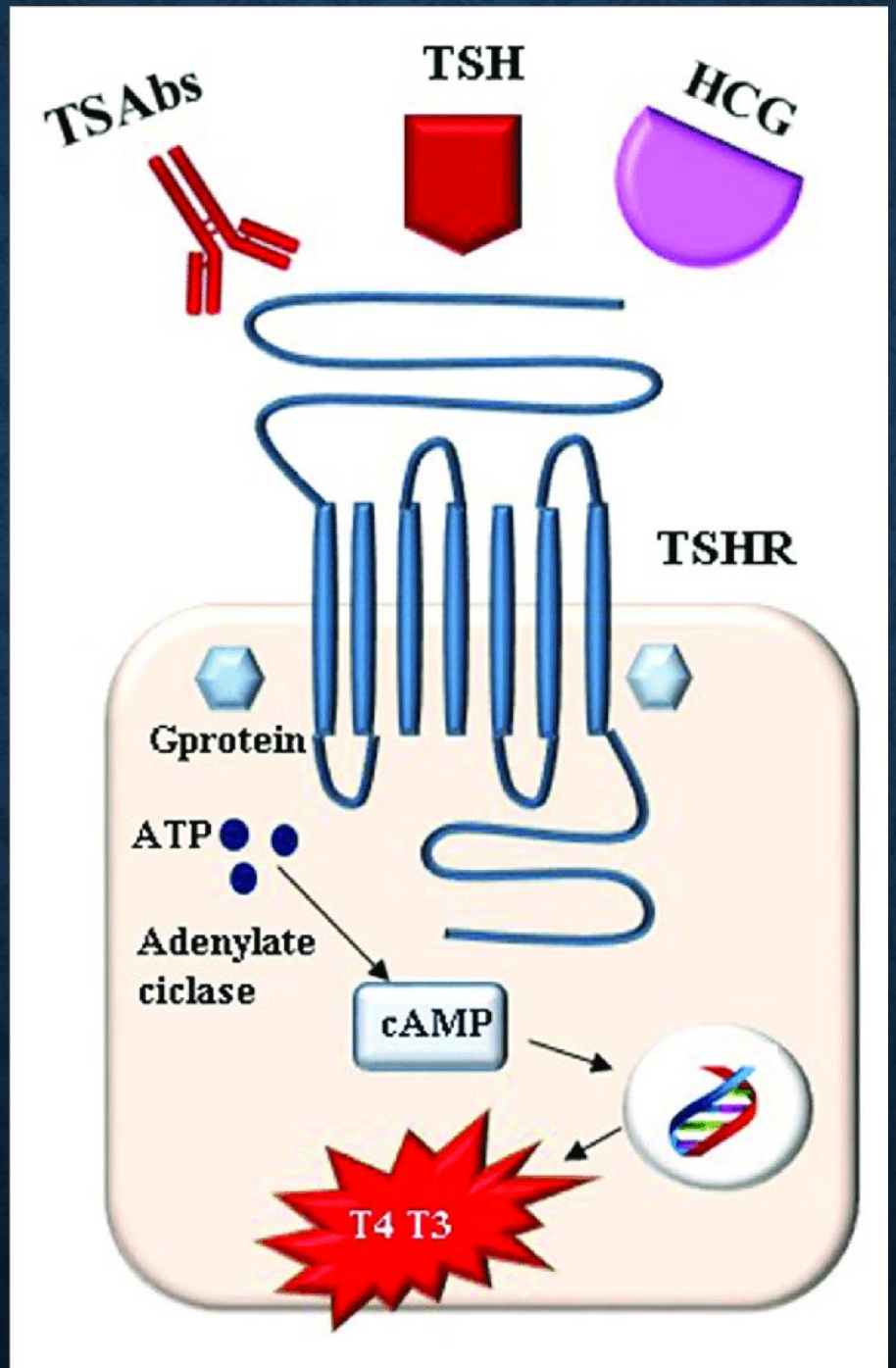
PHYSIOLOGIC ANATOMY OF THE THYROID GLAND

- Composed of large numbers of closed follicles (100-300 micrometers in diameter)
- filled with colloid (major component Thyroglobulin) and
- lined with cuboidal epithelial cells that secrete into the interior of the follicles
- The large glycoprotein Thyroglobulin contains the thyroid hormones within its molecule.
- Secretion enters the follicles →absorbed (through epithelium)back into the blood to function.
- Blood flow/min = 5 times its wt.



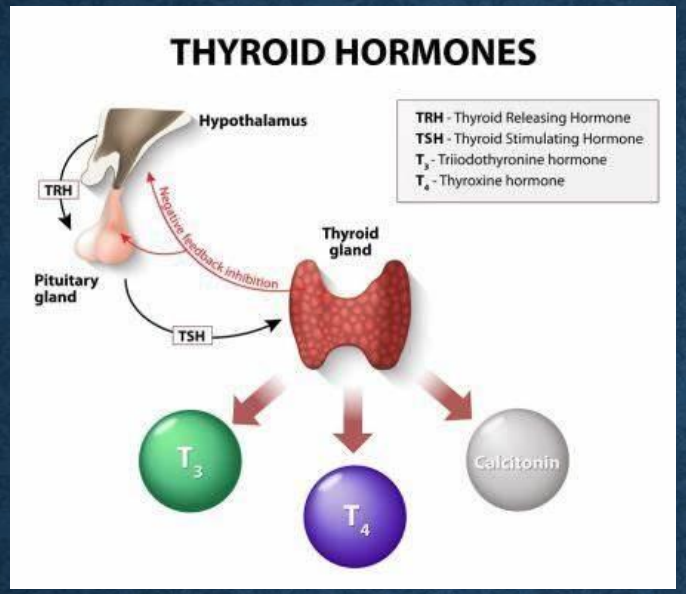

TRH
Hypothalamus
Pituitary Gland
TSH
Thyroid Gland
T_3 & T_4


HYPOTHALAMIC-PITUITARY-THYROID AXIS
HYPOTHALAMUS
TRH
MINOR SITE OF
NEGATIVE FEEDBACK
PITUITARY
MAJOR SITE
OF NEGATIVE
FEEDBACK
TSH
THYROID
T4, T3
T4
T3
TARGET
CELL
T4
T3
NUCLEAR
RECEPTOR


TSAbs
TSH
HCG
TSHR
Gprotein
ATP
Adenylate
ciclase
cAMP
T4 T3

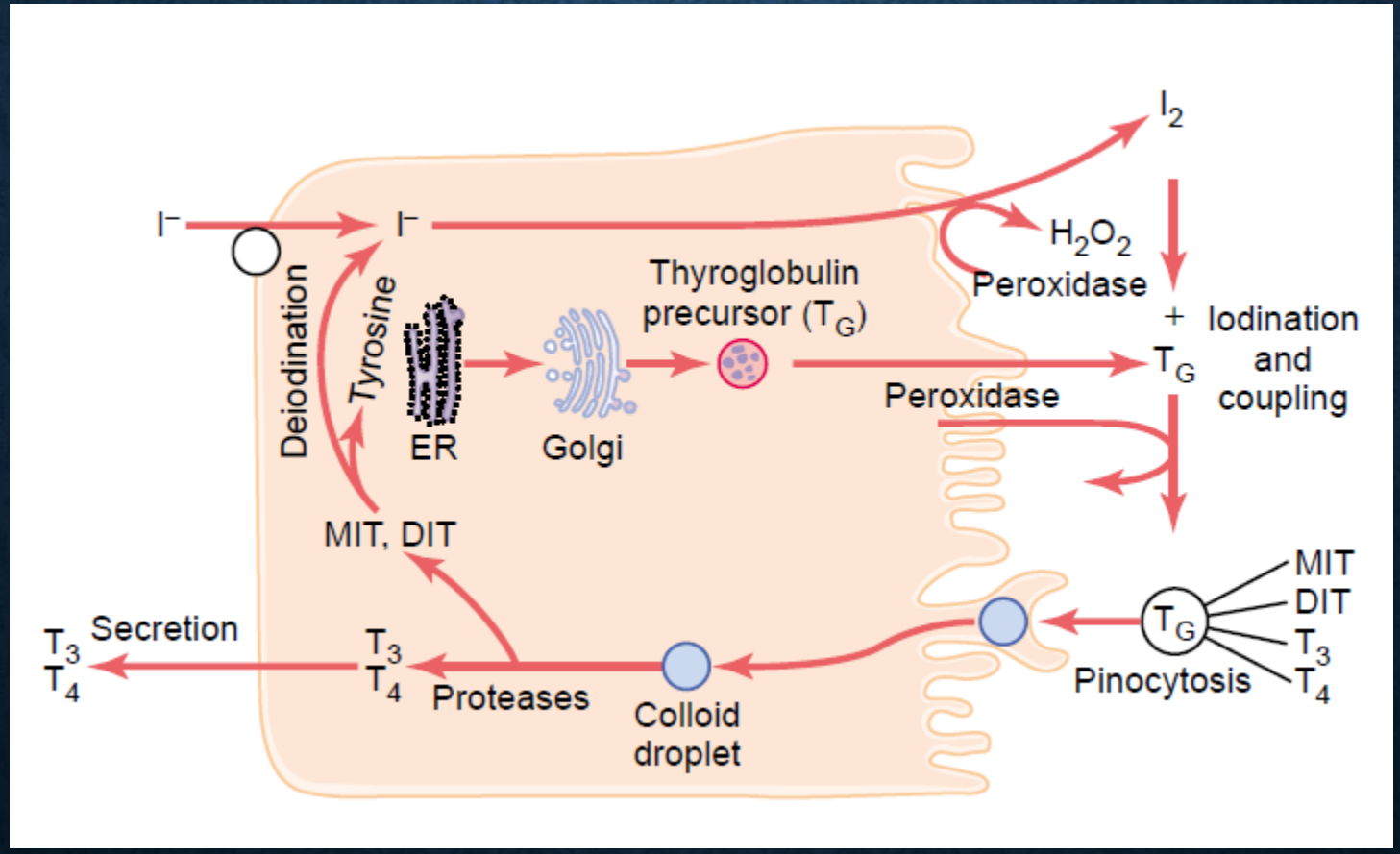
IODINE REQUIREMENT

- 50mg/year
- 1mg/week
- Common table salt is iodized with 1 part sodium iodide to every 100,000 parts NaCl.
- Iodides (absorbed from GIT)→⅕ removed from the blood by thyroid cells for synthesis of hormones;
- rest excreted through kidneys.



Synthesis of Thyroid Hormone

Thyroid cellular mechanisms for iodine transport, thyroxine and triiodothyronine formation , release and into the blood.



MIT, monoiodotyrosine; DIT, diiodotyrosine; T3, triiodothyronine; T4, thyroxine; TG, thyroglobulin.

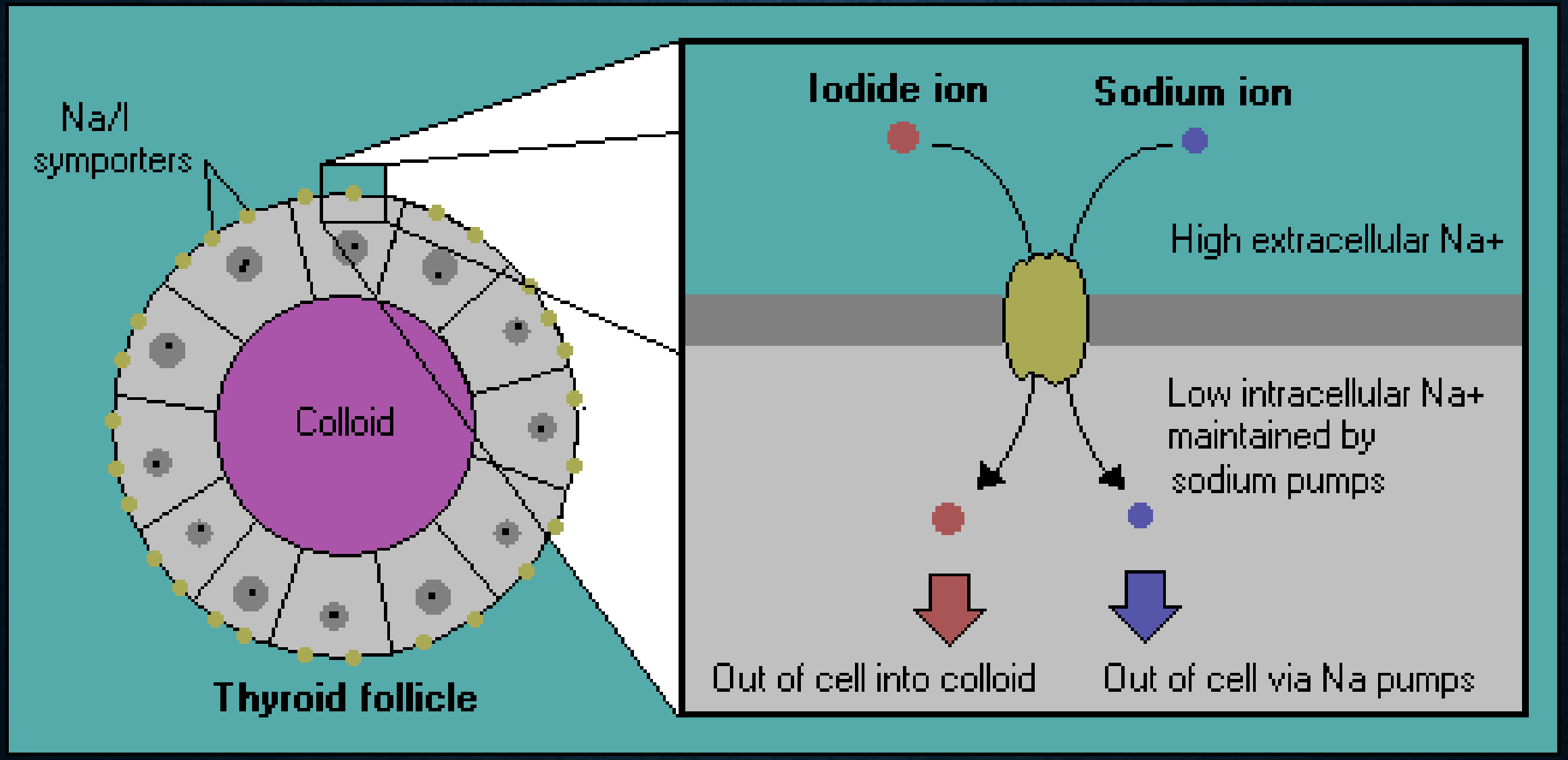
STEP 1: FORMATION AND SECRETION OF THYROGLOBULIN

- The thyroid epithelial cells also secrete into the follicle thyroglobulin that contains tyrosine amino acids to which the iodide ions will bind

- ER and Golgi apparatus synthesize and secrete in to the follicles a large glycoprotein molecules called “Thyroglobulin”
- Each mol. Of Thyroglobulin contain 70 tyrosine amino acids
- Tyrosine + Iodide = Thyroid hormone within Thyroglobulin.

STEP 2: IODIDE TRAPPING

- Transport of iodides from the blood in to the thyroid follicles.
- This is achieved by the action of sodium-iodide symporter (NIS)
- Which cotransport one iodide ion along with two sodium ions.
- the energy for transporting iodide against a concentration gradient comes from the sodium-potassium ATPase pump, which pumps sodium out of the cell, thereby establishing a low intracellular sodium concentration and a gradient for facilitated diffusion of sodium into the cell
- Iodide is transported out of the thyroid cells across the apical membrane into the follicle by a chloride-iodide ion counter-transporter molecule called *pendrin*


Na/I
symporters
Colloid
Thyroid follicle
Iodide ion
Sodium ion
High extracellular Na+
Low intracellular Na+
maintained by
sodium pumps
Out of cell into colloid
Out of cell via Na pumps

STEP 3: OXIDATION OF IODIDE

Conversion of Iodides to oxidized form of Iodine

Oxidized form of iodine is capable of combining directly with amino acid Tyrosine.

Oxidation is promoted by enzyme Peroxidase & Hydrogen Peroxide (H_2O_2)

Peroxidase is in apical membrane of the cell or attached to it

STEP 4: ORGANIFICATION OF THYROGLOBULIN

The Iodination of Tyrosine and Formation of the Thyroid Hormones

The binding of iodine with the thyroglobulin molecule is called *organification* of the thyroglobulin

This reaction is catalyzed by the enzyme TPO

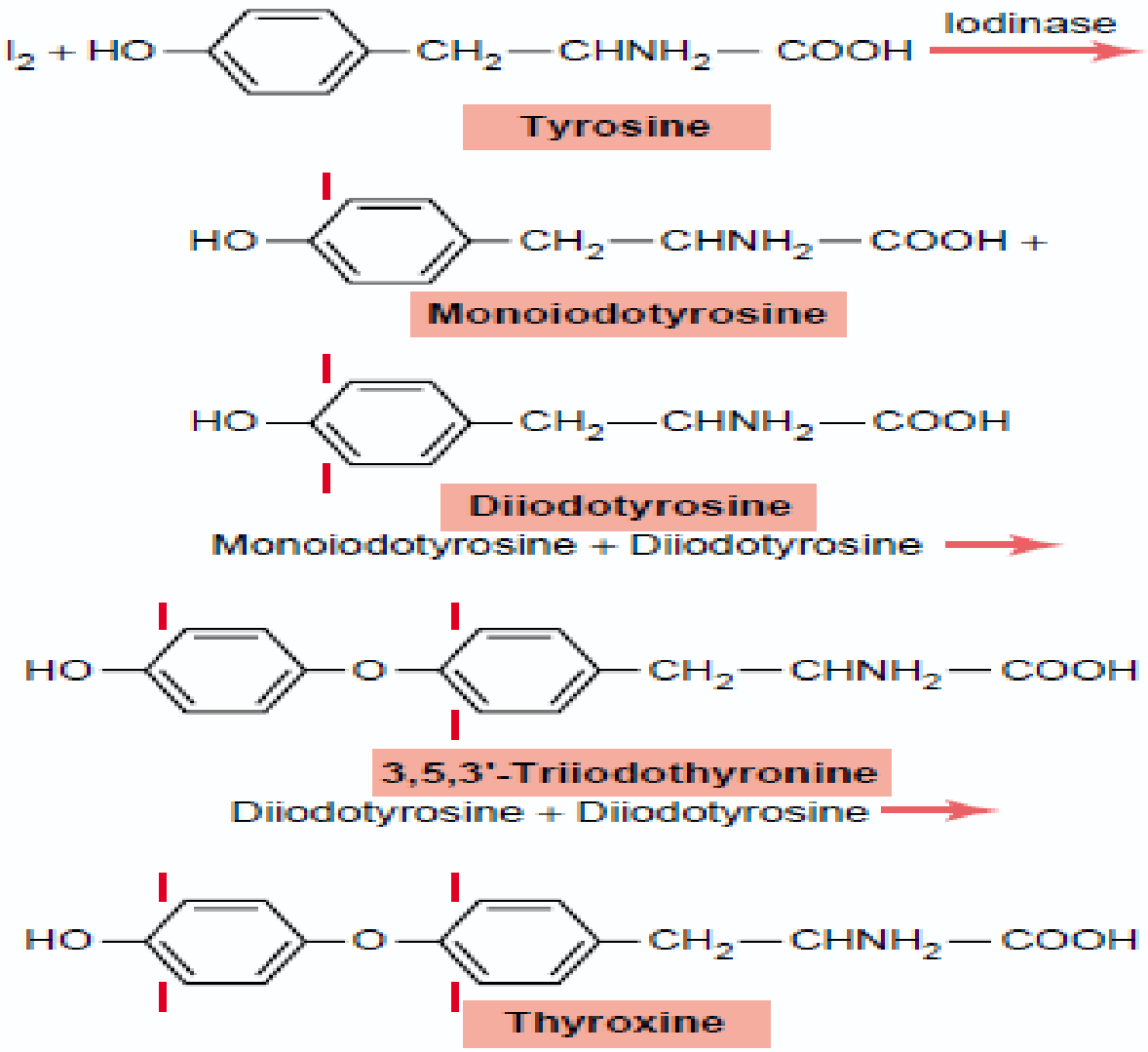
If Peroxidase is not present→Thyroid hormone formation falls to zero.

Iodine is first iodized to monoidotyrosine and then to diidotyrosine

STEP 5: COUPLING REACTION

- Then one molecule of iodine couples with one molecule of diidotyrosine to form triidothyronine T3
- MIT + DIT = T3
- Two molecules of Diidotyrosine couple together to form tetraiodothyronine T4
- DIT + DIT =T4
- Coupling reactions are also activated by TPO enzymes

CHEMISTRY OF THYROXINE AND TRIIODOTHYRONINE FORMATION



STEP 6: STORAGE OF THYROID HORMONE

After synthesis of thyroid hormone, they are stored in the thyroglobulin molecule,

Each Thyroglobulin mol. has 30 thyroxine molecules and a few T3.

Storage sufficient for body requirements for 2-3 months.

STEP 7: RELEASE OF THYROXINE AND TRIIODOTHYRONINE IN THE BLOOD

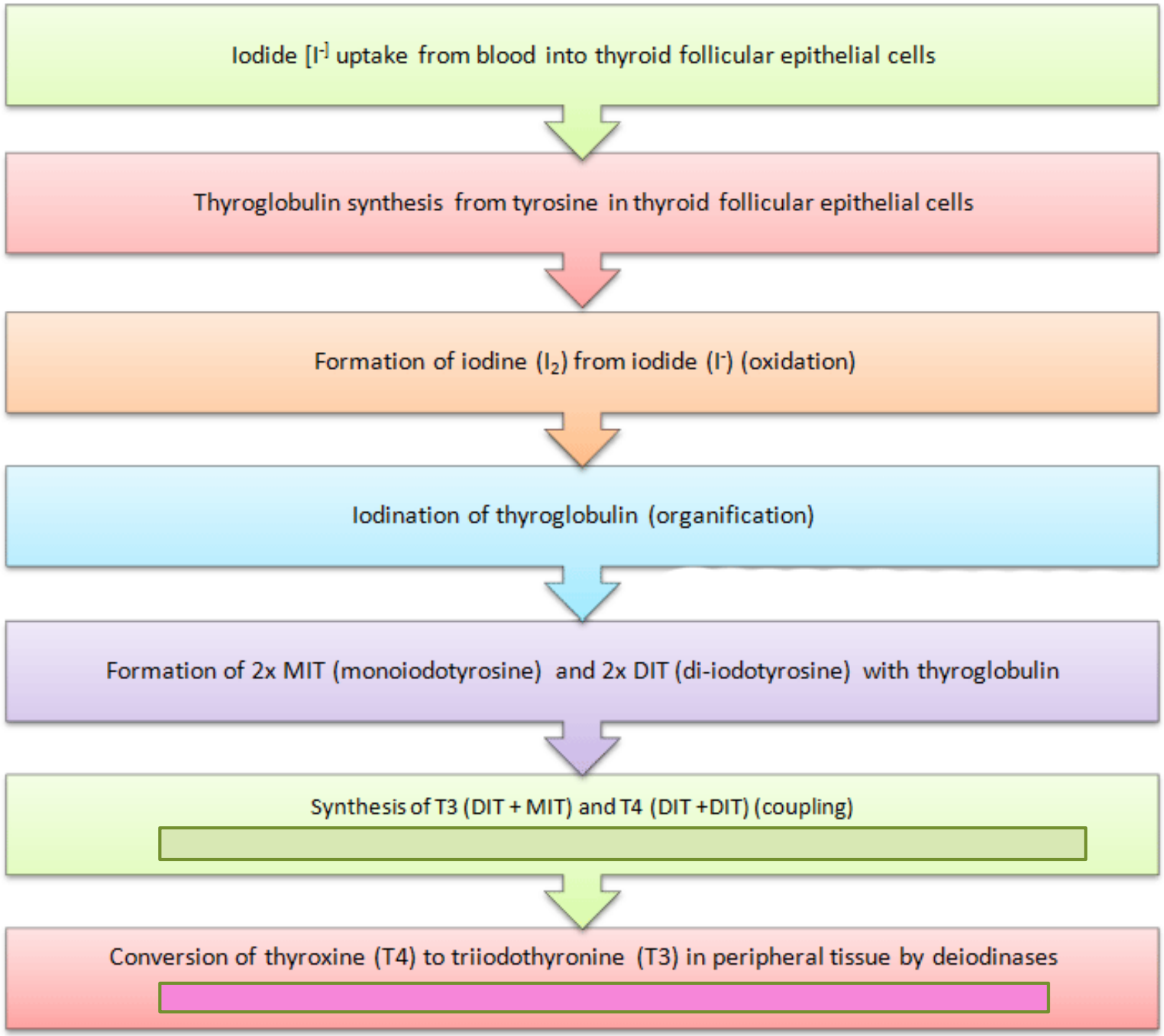
- Cleavage required for the release.
- Pseudopod extensions from the apical surface of the thyroid cells that close around small portions of the colloid → *pinocytic vesicles formed* → *enter the apex of* thyroid cell —lysosomes→ digestive vesicles —proteases→ release T4 & T3 in free form→
- diffuse through the base of the thyroid cell into the blood.
- ¾ of iodinated tyrosinase never forms hormone, remains as mono or di ido-MIT, DIT released from Thyroglobulin —deiodinase→ Tyrosine + I^-.
- 75% MIT, DIT is recycled.
- ↓↓↓ of enzyme deiodinase can cause defficiency of

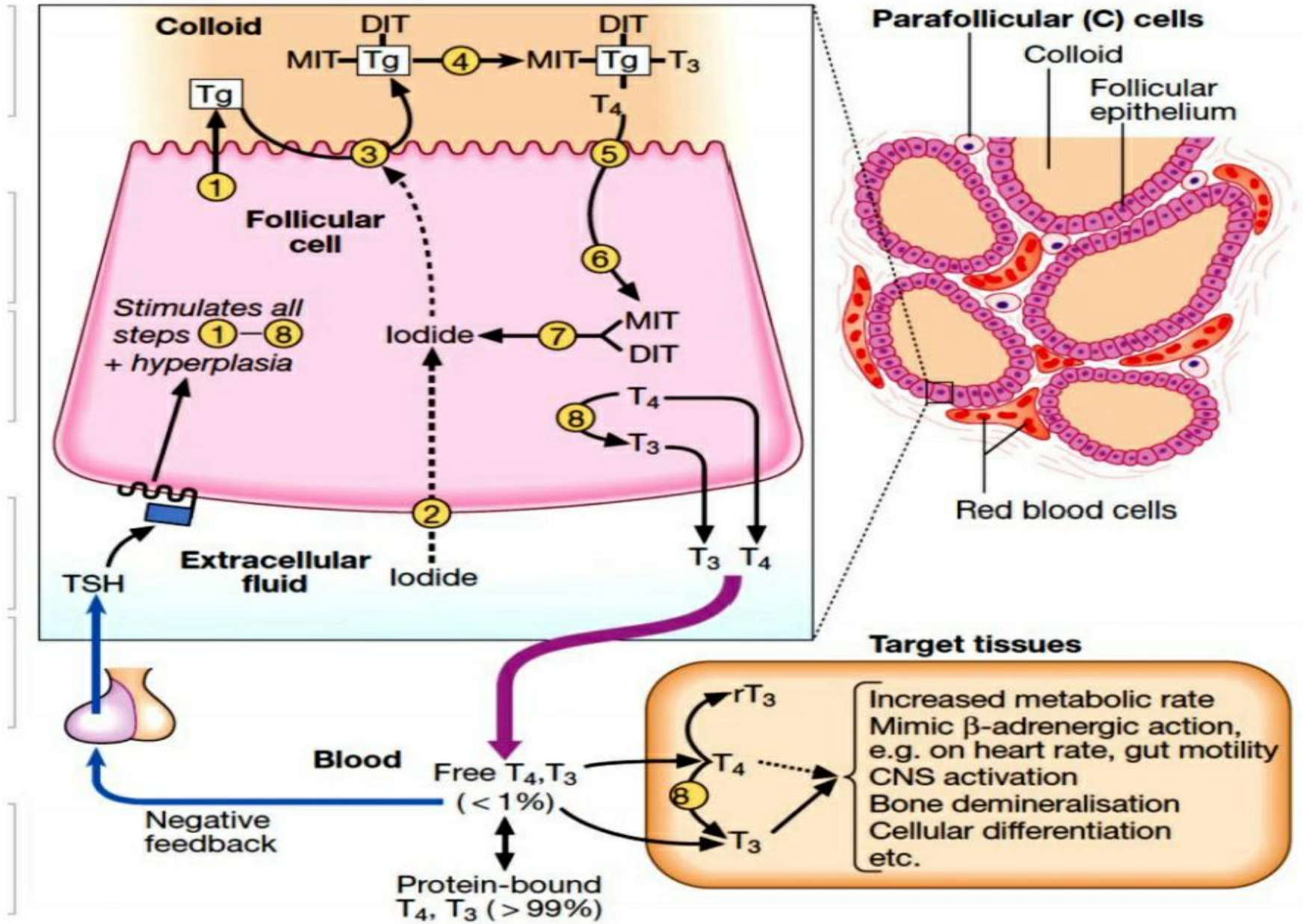
TRANSPORT IN BLOOD

- 99% of T3 & T4 combines with plasma proteins on entering blood.
  - Thyroxine binding globulin
  - Thyroxine binding prealbumins
  - Thyroxine binding albumin

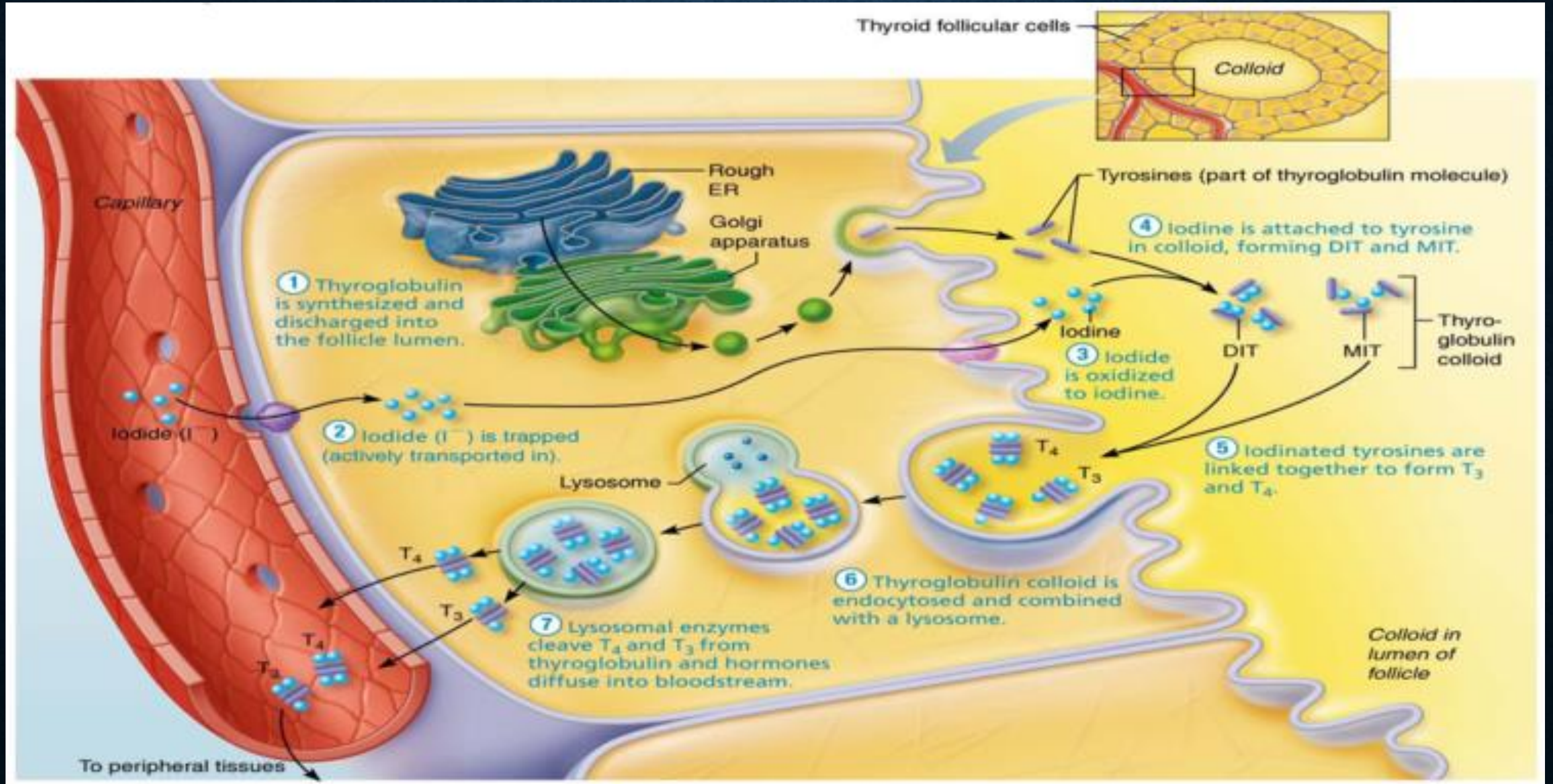
TARGET TISSUES

- Hormone used by tissues is Triidothyroxine 35 µgm/day

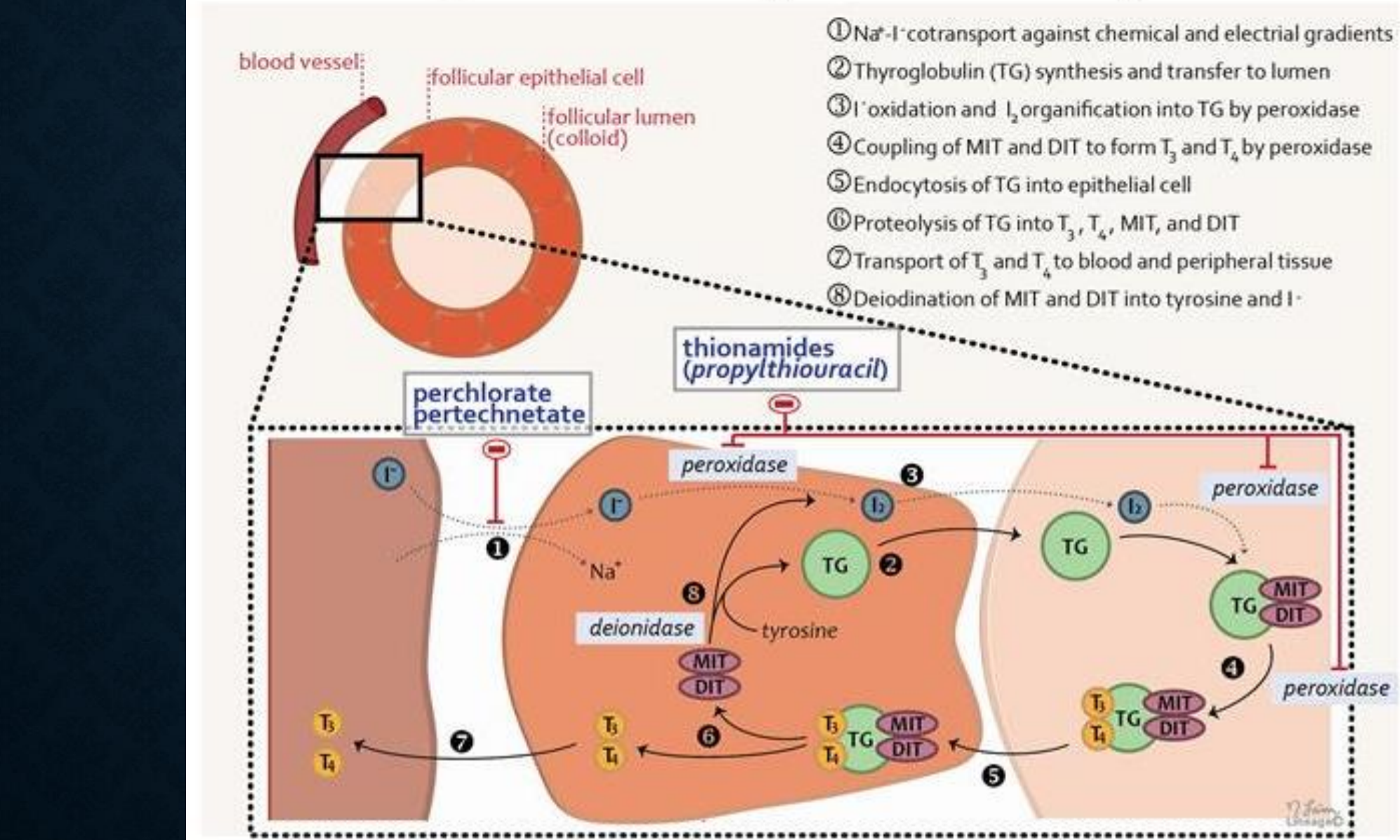

Iodide [I^-] uptake from blood into thyroid follicular epithelial cells
Thyroglobulin synthesis from tyrosine in thyroid follicular epithelial cells
Formation of iodine (I_2) from iodide (I^-) (oxidation)
Iodination of thyroglobulin (organification)
Formation of 2x MIT (monoiodotyrosine) and 2x DIT (di-iodotyrosine) with thyroglobulin
Synthesis of T3 (DIT + MIT) and T4 (DIT +DIT) (coupling)
Conversion of thyroxine (T4) to triiodothyronine (T3) in peripheral tissue by deiodinases



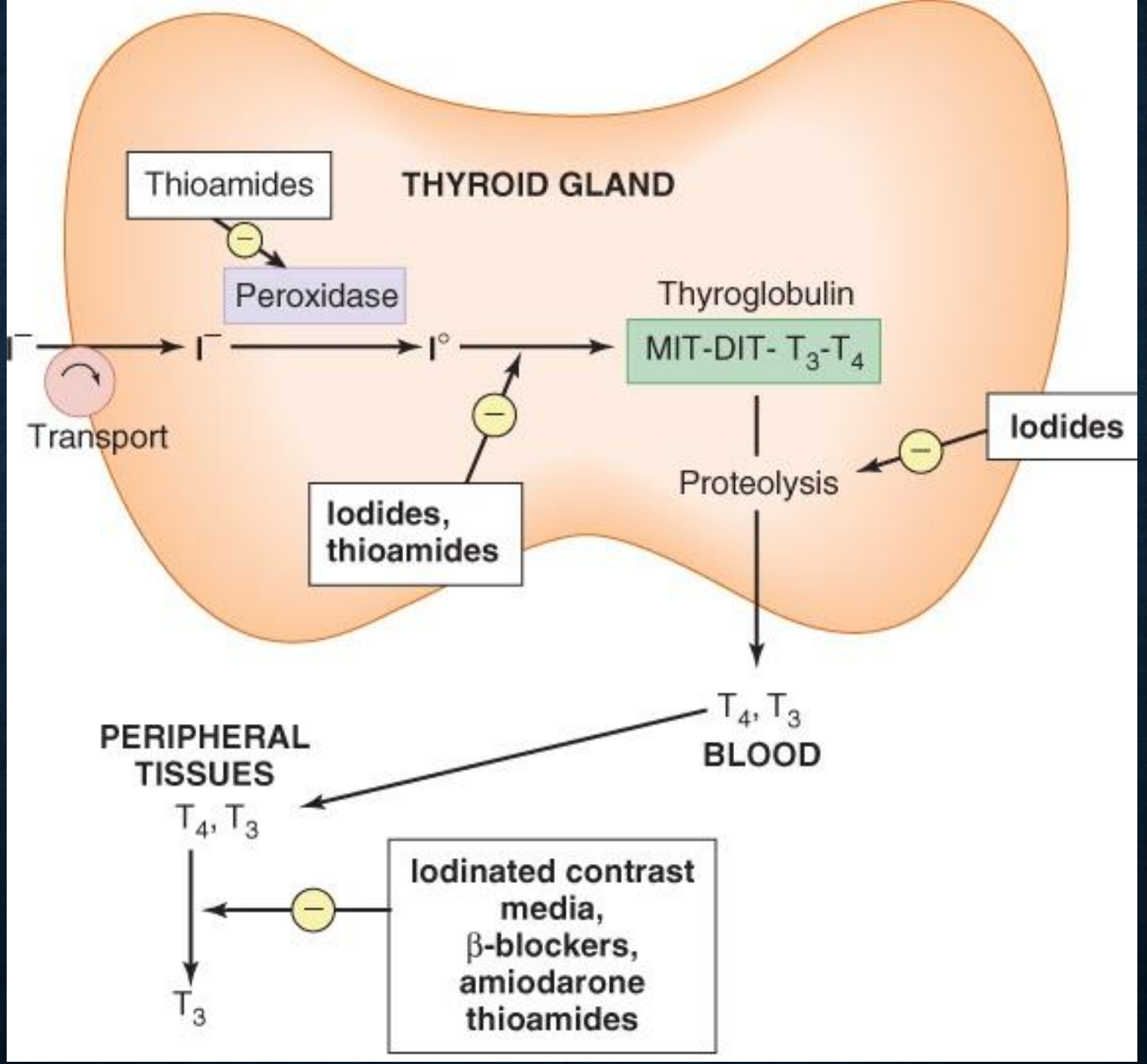
Synthesis and action of Thyroid hormones (T3 and T4)


Thyroid follicular cells
Colloid
Capillary
Rough ER
Golgi apparatus
1 Thyroglobulin is synthesized and discharged into the follicle lumen.
Tyrosines (part of thyroglobulin molecule)
4 Iodine is attached to tyrosine in colloid, forming DIT and MIT.
Iodine
3 Iodide is oxidized to iodine.
DIT
MIT
Thyro-globulin colloid
Iodide (I⁻)
2 Iodide (I⁻) is trapped (actively transported in).
Lysosome
T4
T3
5 Iodinated tyrosines are linked together to form T3 and T4.
6 Thyroglobulin colloid is endocytosed and combined with a lysosome.
7 Lysosomal enzymes cleave T4 and T3 from thyroglobulin and hormones diffuse into bloodstream.
Colloid in lumen of follicle
To peripheral tissues

Thyroid Hormone Synthesis and Transport



Key steps in thyroid hormone synthesis.


Thioamides
THYROID GLAND
Peroxidase
Thyroglobulin
MIT-DIT- T_3-T_4
Transport
Iodides
Iodides, thioamides
Proteolysis
T_4, T_3
BLOOD
PERIPHERAL TISSUES
T_4, T_3
Iodinated contrast media, β-blockers, amiodarone thioamides
T_3

SECRETION, TRANSPORT & MECHANISM OF ACTION

WHAT ARE THE THYROID HORMONES?

- **Thyroxine :** {3,5,3',5' – Tetra-Iodothyronine} (T4)

· **Tri-Iodothyronine**: {3,5,3' – Tri-Iodothyronine} (T3)

· T4 contains Four Iodine atoms, · T3 contains Three Iodine atoms

· T3: Biological active form of Thyroid hormones, because it binds to receptors and trigger end-organ effects

· **Reverse T3: {**3,3',5'-Tri-Iodothyronine} (rT3):
· Is the Biological Inactive form of Thyroid hormones

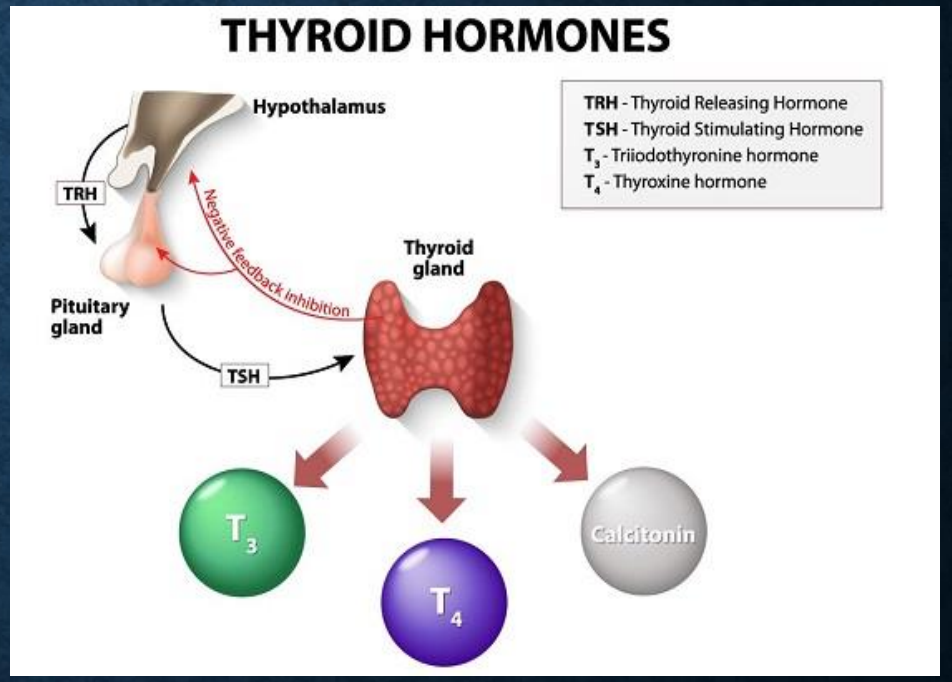


TABLE 4-4 Chemical Classification of Hormones

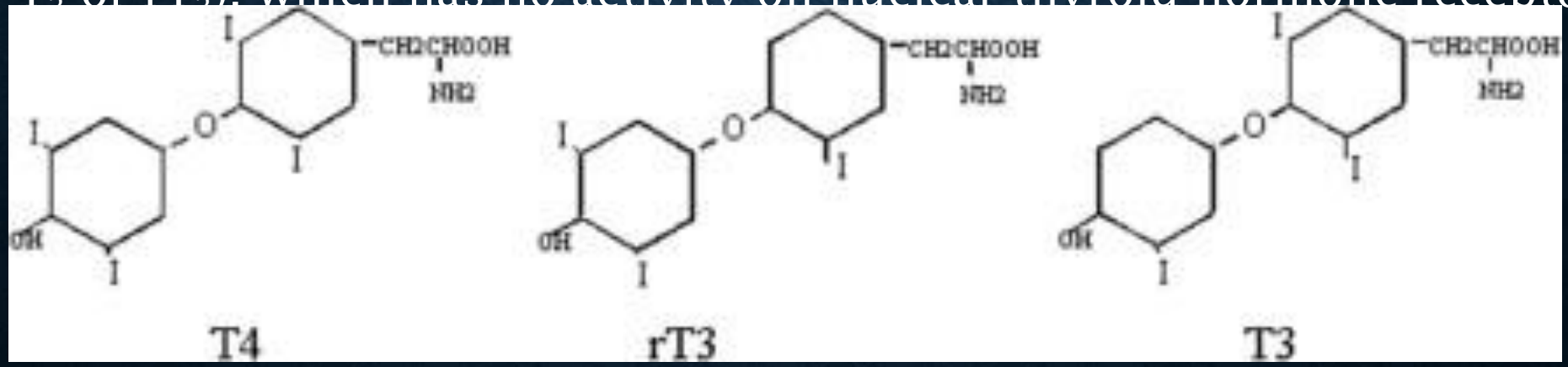
Properties	Peptides	AMINES: Catecholamines and Indoleamines	AMINES: Thyroid Hormone	Steroids
Solubility	Hydrophilic	Hydrophilic	Lipophilic	Lipophilic
Structure	Chains of specific amino acids	Tyrosine derivative (catecholamines) or tryptophan derivative (indoleamines)	Iodinated tyrosine derivative	Cholesterol derivative
Synthesis	In rough endoplasmic reticulum; packaged in Golgi complex	In cytosol	In colloid within thyroid gland (see p. 691)	Stepwise modification of cholesterol molecule in various intracellular compartments
Storage	Large amounts in secretory granules	In secretory granules	In colloid	Not stored; cholesterol precursor stored in lipid droplets
Secretion	Exocytosis of granules	Exocytosis of granules	Endocytosis of colloid	Simple diffusion
Transport in Blood	As free hormone	Half bound to plasma proteins	Mostly bound to plasma proteins	Mostly bound to plasma proteins
Receptor Site	Surface of target cell	Surface of target cell	Inside target cell	Inside target cell
Mechanism of Action	Activation of second-messenger pathway to alter activity of preexisting proteins that produce the effect	Activation of second-messenger pathway to alter activity of preexisting proteins that produce the effect	Activation of specific genes to make new proteins that produce the effect	Activation of specific genes to make new proteins that produce the effect
Hormones of This Type	Majority of hormones	Catecholamines: hormones from the adrenal medulla, dopamine from hypothalamus. Indoleamines: melatonin from pineal	Only hormones from the follicular cells of the thyroid	Hormones from the adrenal cortex and gonads and some placental hormones; vitamin D (a hormone) is steroidlike

Differences between T3 and T4

T3	T4
Four time more potent than T4	Less potent
Peak effect reaches with in 24-48 hrs.	Peak effect reaches in 6-8 hrs
Plasma protein binding capacity is less	It bind more tightly to plasma proteins
It is active in vitro	It is inactive invitro
Thyroid gland produce 20% of T3	Thyroid gland produces 80% of T4
T3 is the active form	T4 is less active than T3

CHEMICAL STRUCTURE OF THYROID HORMONES

- Thyronines may contain iodine atoms at the 3 and 5 positions on the inner ring as well as at the 3′ and 5′ positions on the outer ring.
- If all four sites are iodinated, the molecule is called 3′,5′,3,5-tetraiodothyronine (thyroxine or T_4).
- If a single iodine is missing from the outer ring, the result is 3′,3,5-triiodothyronine (T_3),
- whereas if one is missing from the inner ring, it yields 3′,5′,3-triiodothyronine (reverse T_3 or rT_3), which has no activity on nuclear thyroid hormone receptors (TRs)



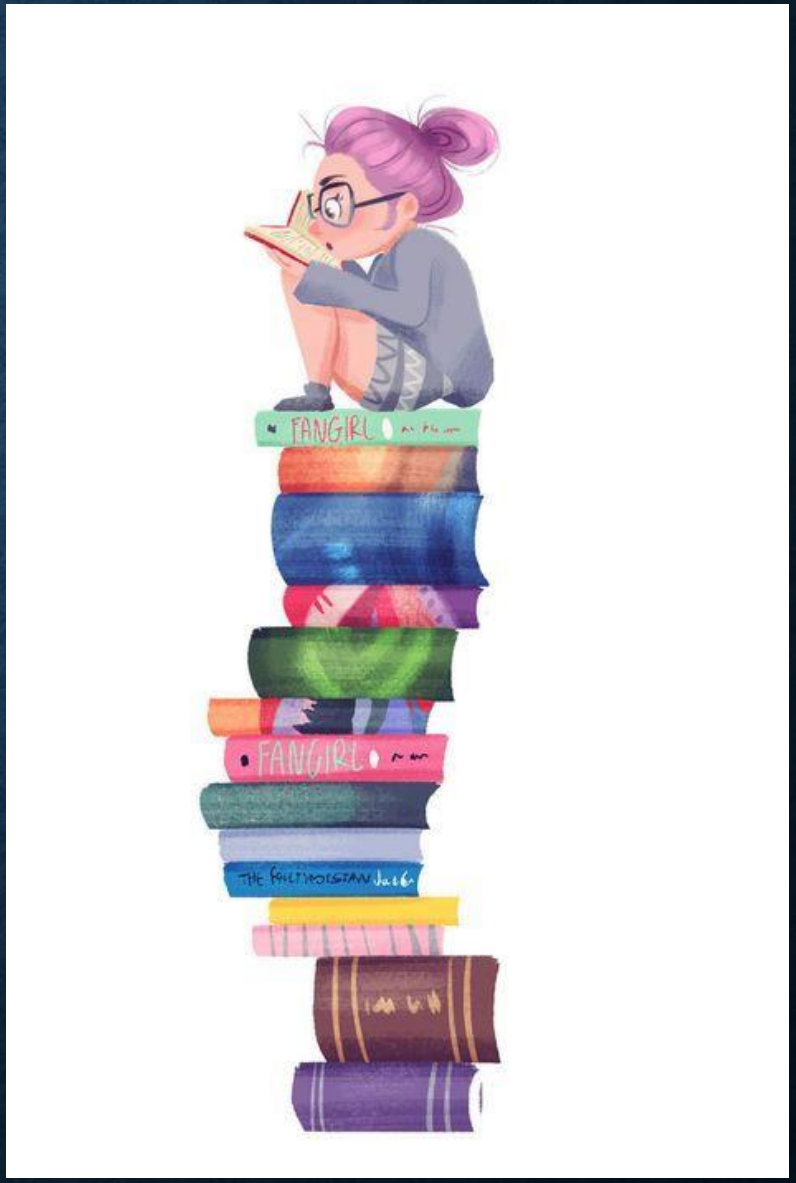
THE REACTION

When someone asks a medical Student.... "How is life in Medical School"?

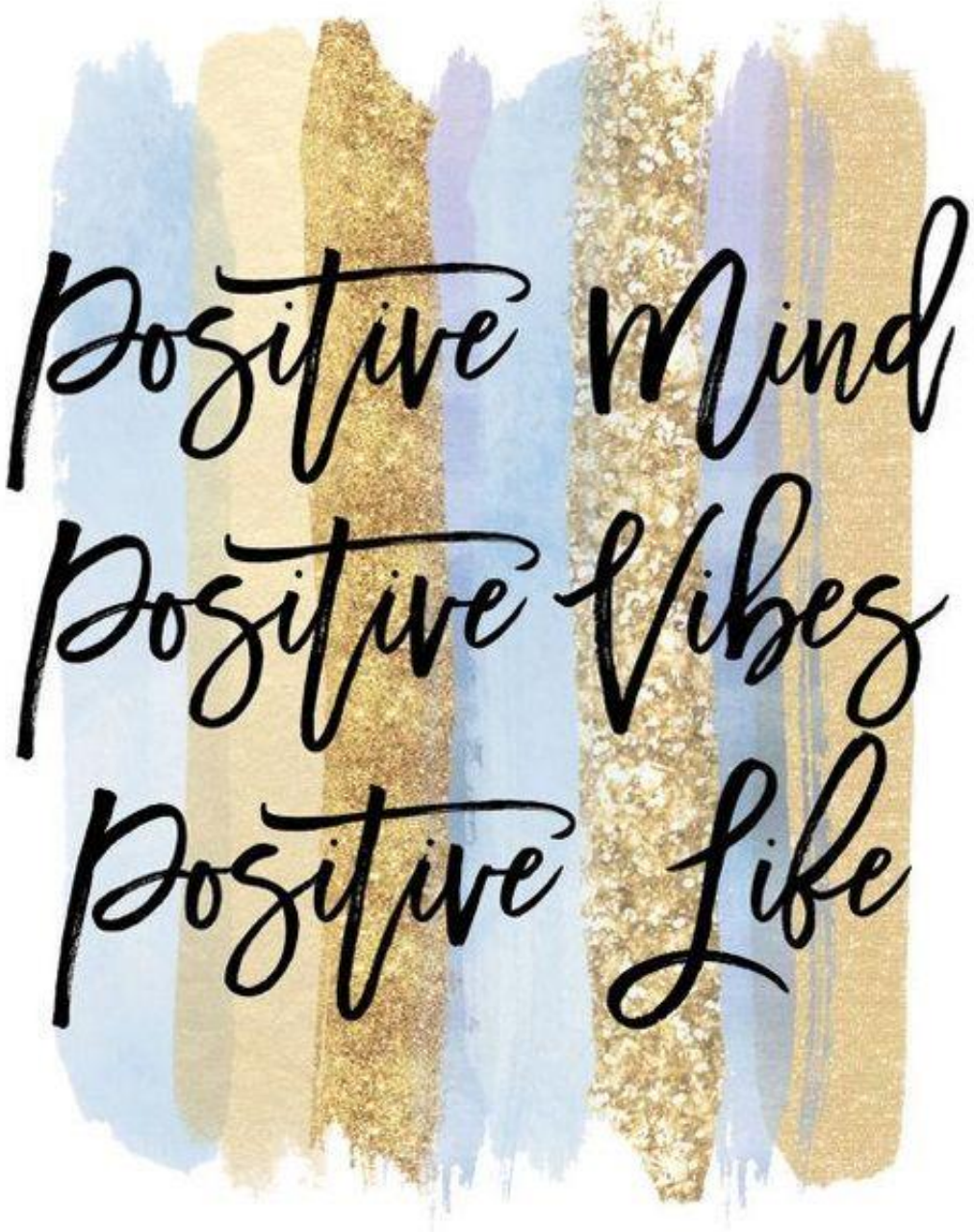
RECOMMENDED BOOKS

- Text book of Medical Physiology-Guyton and Hall
- Principles of human Physiology- Lauralee Sherwood
- Color Atlas of human Physiology

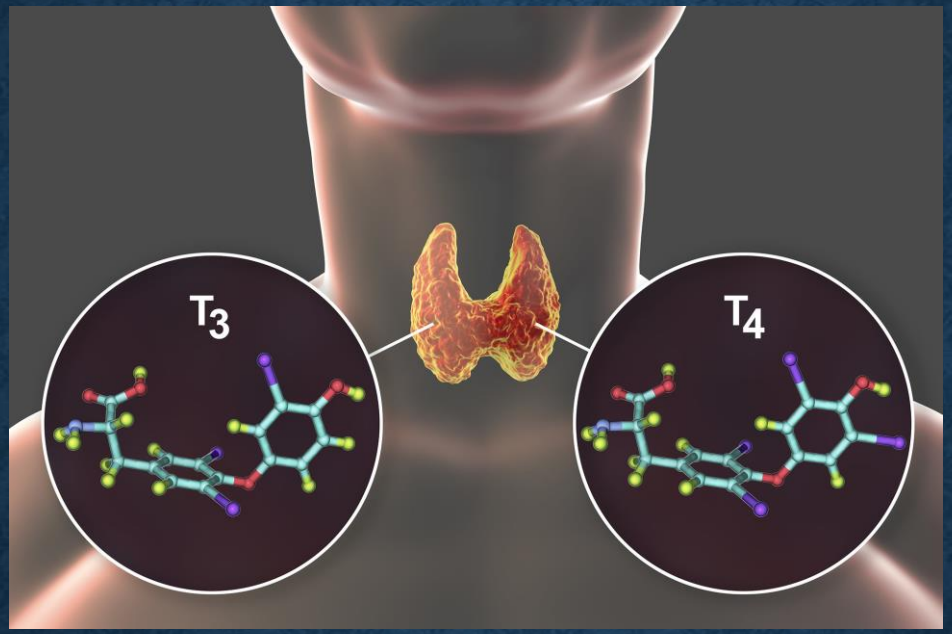
- https://www.youtube.com/watch?v=BeI0-xw_cSQ




That's all Folks!
SUPERB wallpapers


Positive Mind
Positive Vibes
Positive Life

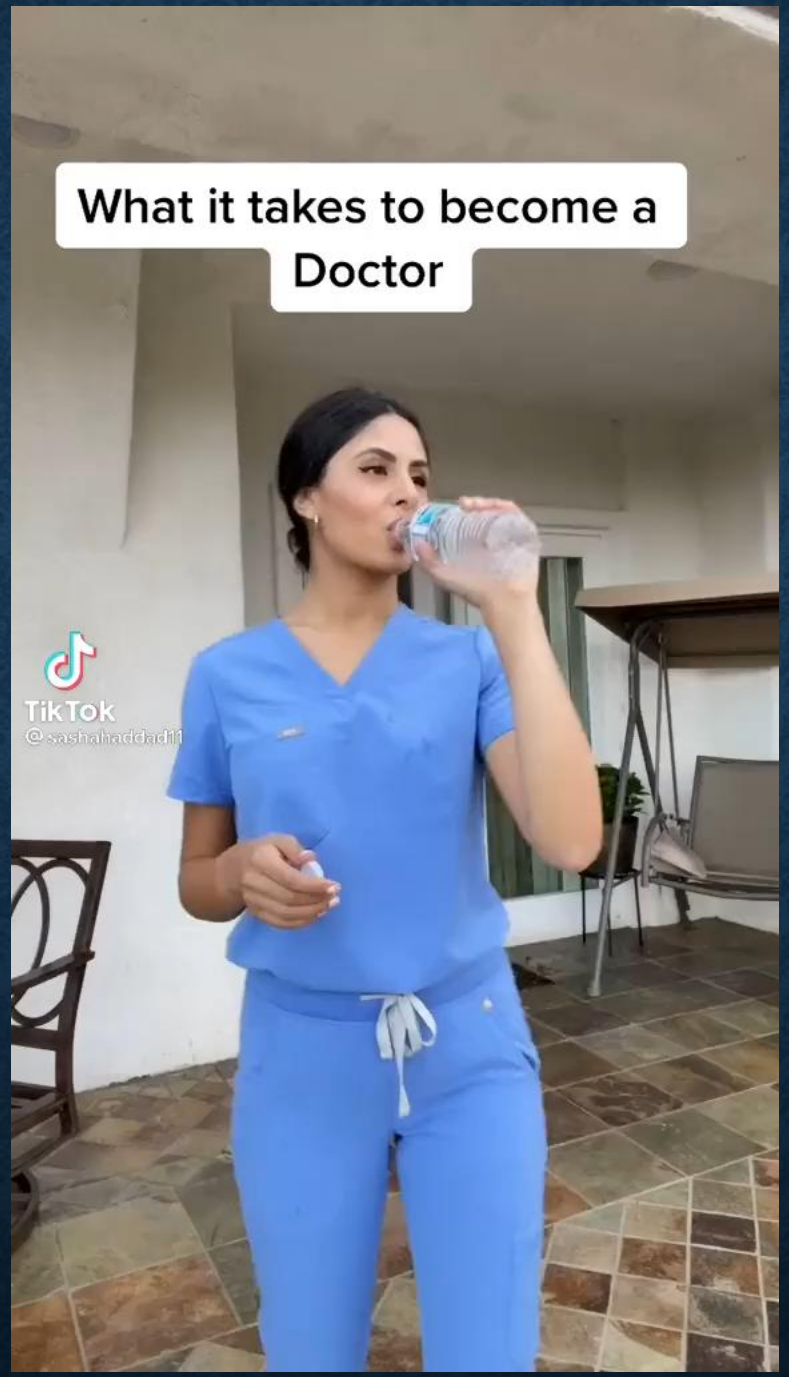

إِنَّ ٱللَّهَ
وَمَلَٰٓئِكَتَهُۥ
يُصَلُّونَ عَلَى ٱلنَّبِيِّۚ
يَٰٓأَيُّهَا ٱلَّذِينَ ءَامَنُواْ صَلُّواْ عَلَيْهِ
وَسَلِّمُواْ تَسْلِيمًا ٥٦ سورة الأحزاب
GHAJARALALFI



FUNCTIONS OF THYROID HORMONES

Lecture 2

I want this Book 😂😂

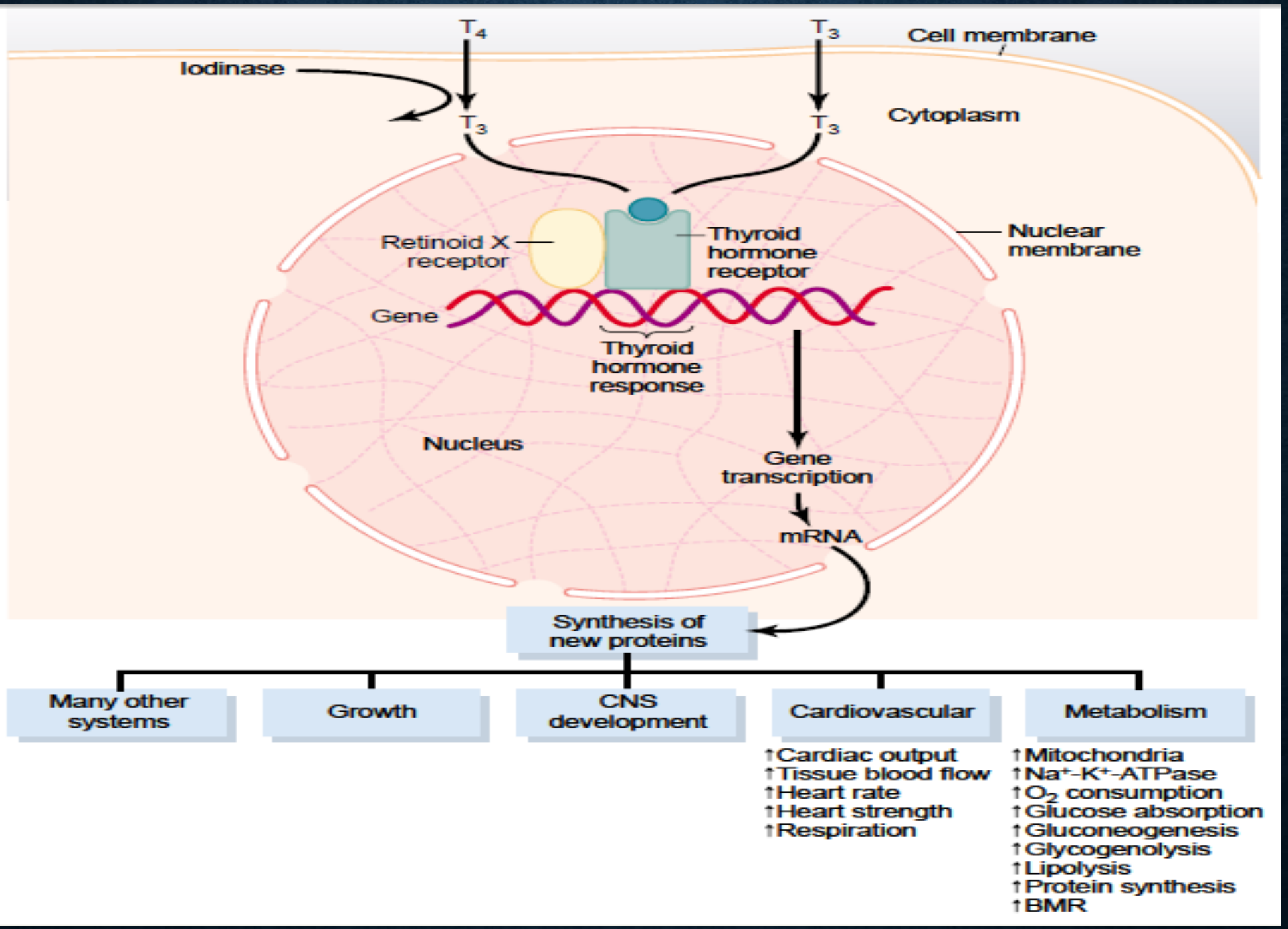

What it takes to become a Doctor
TikTok

MECHANISM OF ACTION

PHYSIOLOGIC FUNCTIONS OF THE THYROID HORMONES

Thyroid Hormones Increase the Transcription of Large numbers of Genes

- Activates Nuclear Transcription→ Protein synthesis → Generalised increase in function.
- Almost all cells in the body are targets for thyroid hormones and have thyroid receptors
- Thyroid Hormone Receptor usually forms a heterodimer with Retinoid X receptor r(RXR) at specific thyroid hormone response element on DNA.
- Receptor+Hormone →Messenger RNA→ Translation


T_4
T_3
Cell membrane
Iodinase
T_3
T_3
Cytoplasm
Retinoid X receptor
Thyroid hormone receptor
Nuclear membrane
Gene
Thyroid hormone response
Nucleus
Gene transcription
mRNA
Synthesis of new proteins
Many other systems
Growth
CNS development
Cardiovascular
Metabolism
↑Cardiac output
↑Tissue blood flow
↑Heart rate
↑Heart strength
↑Respiration
↑Mitochondria
↑Na^+-K^+-ATPase
↑O_2 consumption
↑Glucose absorption
↑Gluconeogenesis
↑Glycogenolysis
↑Lipolysis
↑Protein synthesis
↑BMR

Action of thyroid hormones

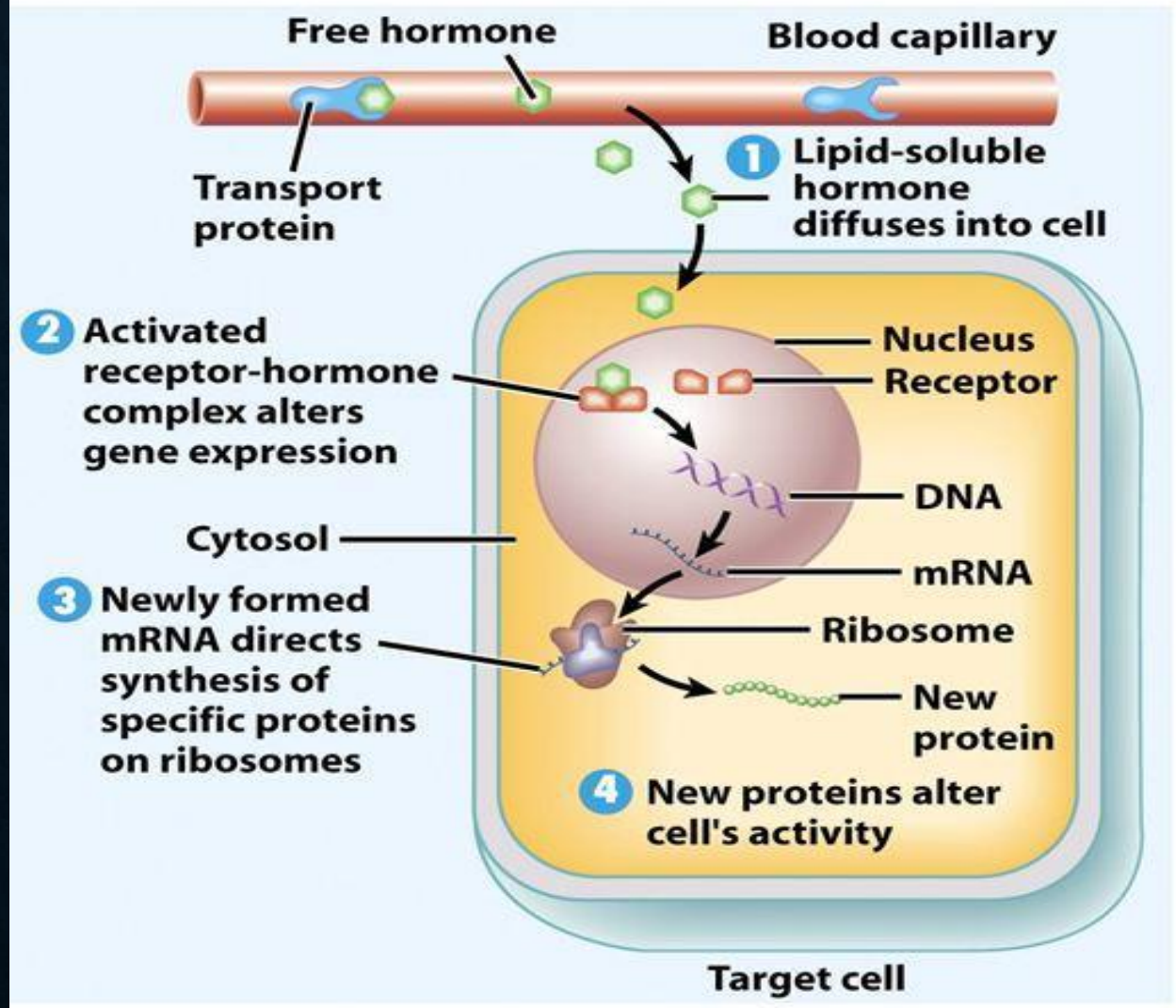
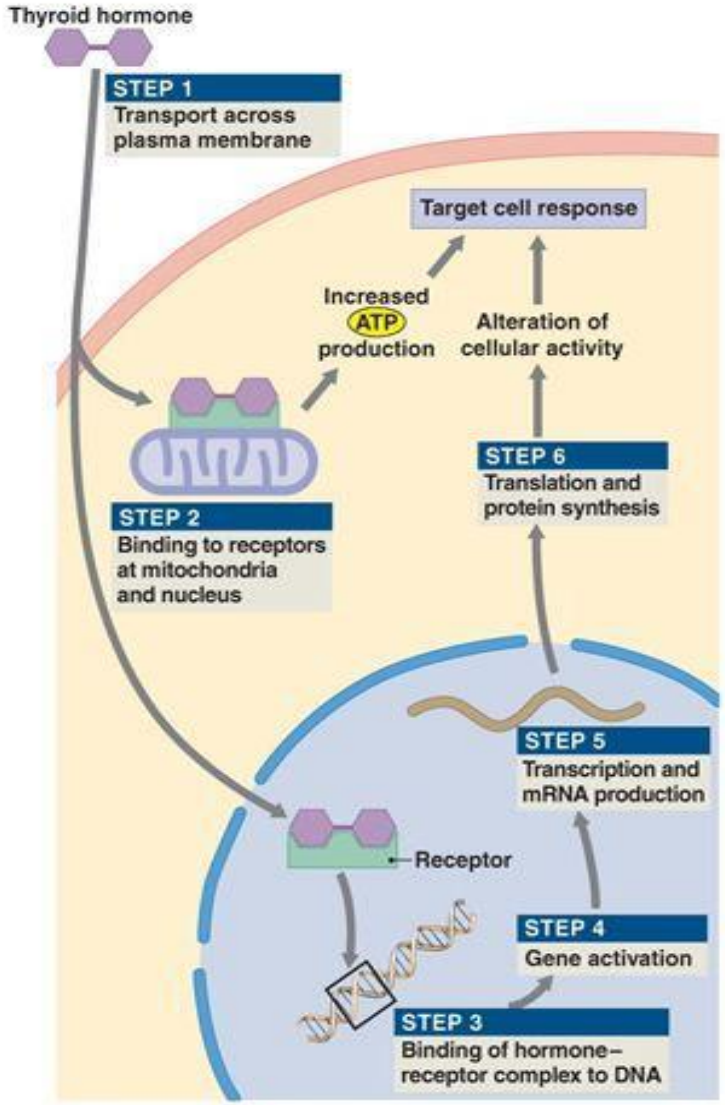


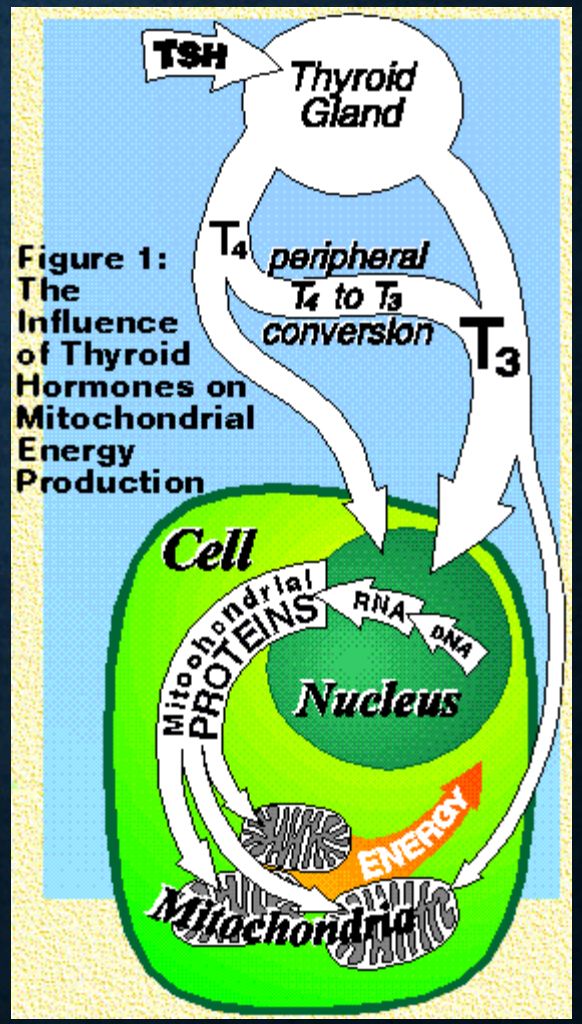
Figure 18-3 Principles of Anatomy and Physiology, 11/e



(b)

EFFECTS ON MITOCHONDRIA

- Increases the number and size of mitochondria.
- Increases the activity of mitochondria.
- Increases ATP formation.
- Increases intracellular enzymes, such as the oxidative enzymes of mitochondria. Due to an in Increase in protein synthesis.



EFFECT ON BMR & HEAT PRODUCTION

- Thyroid hormones stimulate diverse metabolic activities in most tissues, leading to an increase in basal metabolic rate.
- It increases the oxygen consumption in metabolically active tissues
- BMR can ↑ by 60 – 100%
- Increase in metabolism results in increase heat production- calorigenesis

EFFECTS ON INTERMEDIARY METABOLISM

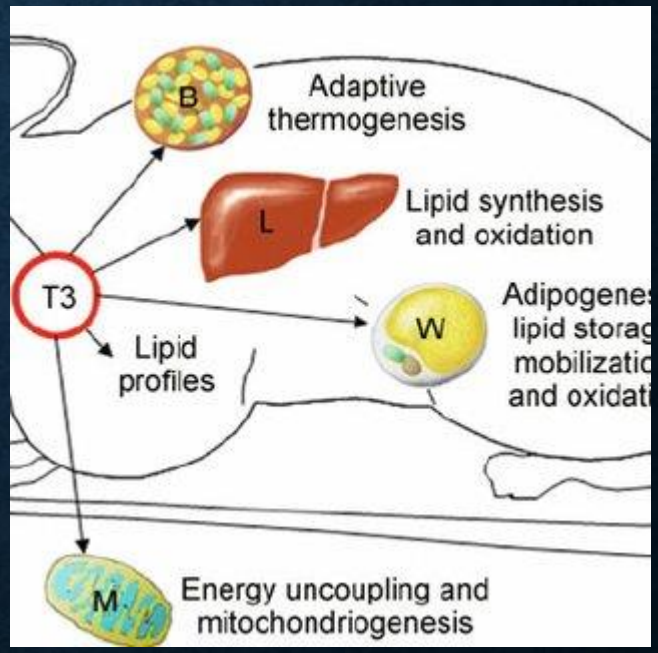
The effects on the metabolic fuels are multifaceted;

- ***Influences the synthesis and degradation of carbohydrate, fat, and protein***
- **small or large amounts of the hormone may induce opposite effects.**
  - the conversion of glucose to glycogen, is facilitated by small amounts of thyroid hormone,
  - the breakdown of glycogen into glucose, occurs with large amounts of the hormone
  - Adequate amounts of thyroid hormone are essential for the protein synthesis needed for normal bodily growth,
  - high doses favors protein degradation.

In general, the overall metabolic effect of thyroid hormone at normal physiologic levels is to favor the consumption rather than storage of body fuels.

EFFECT ON LIPID METABOLISM

- Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma.
- They also enhance oxidation of fatty acids in many tissues.
- Plasma concentrations of cholesterol and triglycerides are inversely correlated with thyroid hormone levels



EFFECT ON CARBOHYDRATE METABOLISM:

- Thyroid hormones stimulate almost all aspects of carbohydrate metabolism
- enhancement of insulin-dependent entry of glucose into cells
- increased gluconeogenesis
- Increased glycogenolysis to generate free glucose.
- Increased absorbtion from GIT
- Increased insulin production

EFFECTS ON PROTEIN METABOLISM:

Increases the synthesis of proteins in the cells.

The protein synthesis is accelerated by the following ways:

1.By Increasing the Transcription of DNA to RNA

2. By Increasing the Translation of RNA

3. By Increasing the Activity of Mitochondria

4. By Increasing the Activity of Cellular Enzymes

Though thyroxine increases synthesis of protein, it also causes catabolism of proteins

EFFECTS ON VITAMIN METABOLISM

Thyroid hormone increases quantities of hormones i.e increase in Formation of enzymes & coenzymes → increase need for vitamins

A relative vitamin deficiency can occur when excess thyroid hormone is secreted, unless at the same time increased quantities of vitamins are made available.

EFFECT ON GROWTH & DEVELOPMENT

- Thyroid hormones are clearly necessary for normal growth in children and young animals, as evidenced by the growth-retardation observed in thyroid deficiency.
- the growth-promoting effect of thyroid hormones is synergistic with that of growth hormone
- Normal levels of thyroid hormone are essential to the development of the fetal and neonatal brain.

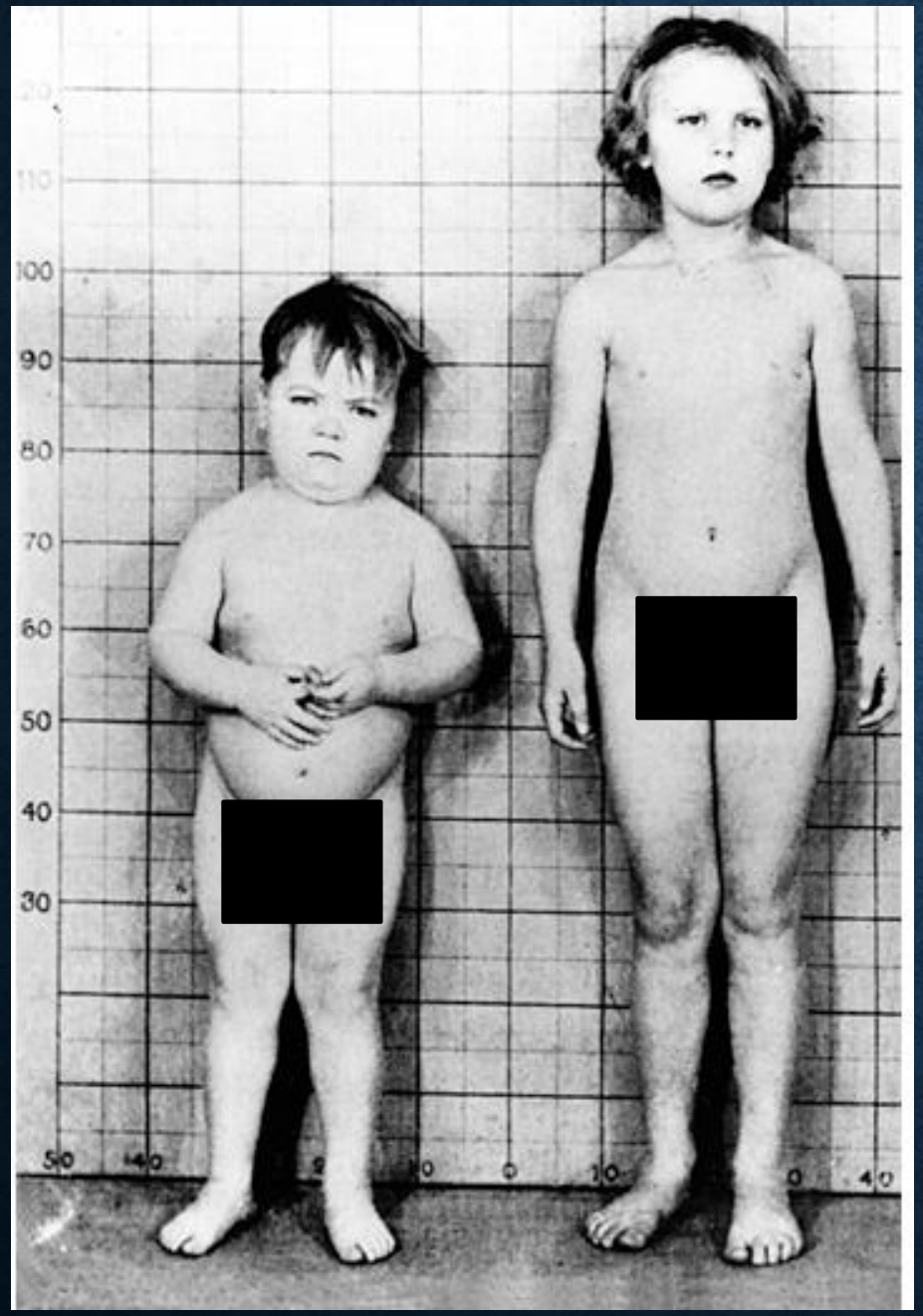


Figure 18-13. Fraternal twins, age 8 years. The boy has congenital hypothyroidism. (Reproduced, with permission, from Wilkins L in: *Clinical Endocrinology I*. Astwood EB, Cassidy CE [editors]. Grune & Stratton, 1960.)

EFFECT ON CARDIOVASCULAR SYSTEM:

Increased number and affinity of beta-adrenergic receptors in the heart → increase its sensitivity to inotropic and chronotropic effects of catecholamines.

- thyroid hormone ***increases heart rate and force of contraction, thus increasing cardiac output.***

- in response to the heat load generated by the calorigenic effect of thyroid hormone, ***peripheral vasodilation*** occurs to carry the extra heat to the body surface for elimination to the environment

EFFECT ON CENTRAL NERVOUS SYSTEM:

- Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state.
- Too little thyroid hormone, and the individual tends to feel mentally sluggish, while too much induces anxiety and nervousness.

EFFECT ON REPRODUCTIVE SYSTEM:

- Normal reproductive behavior and physiology is dependent on having essentially normal levels of thyroid hormone. Hypothyroidism in particular is commonly associated with infertility.

- **EFFECTS ON RESPIRATION:**
  - Causes increased utilization of O_2 and formation of CO_2.
  - Increases pulmonary ventilation.
  - Increases the rate and depth of respiration.
  - Increased the formation of surfactant.
- **EFFECTS ON GIT:**
  - Increases the rate of absorption.
  - Increases appetite.
  - Increases food intake.
  - Increases secretion of digestive juices.
  - Increases motility of GIT.
  - Causes diarrhea.

EFFECTS ON MUSCLE

- A muscle weakness occurs in most patients with hyperthyroidism called thyrotoxic myopathy. When the hyperthyroidism is severe and prolonged, the myopathy may be severe.
- Hypothyroidism is also associated with muscle weakness, cramps, and stiffness.

EFFECT ON BODY WEIGHT

- Thyroxine is essential for maintaining the body weight.
- Increase in thyroxine secretion decreases the body weight and fat storage.
- Decrease in thyroxine secretion increases the body weight because of fat deposition.

7.65 **Gross clinical hypothyroidism** produces characteristic non-pitting oedematous changes in the skin of the face, giving

PHYSIOLOGICAL EFFECTS OF THYROID HORMONES

TABLE 1 ■ Physiologic Effects of Thyroid Hormones[1,4,7]

System	Effects
Cardiovascular	Increases heart rate Increases the force of cardiac contractions Increases cardiac output as a result of the previous two effects Promotes peripheral vasodilation
Central nervous	Essential for normal brain development, such as cerebellar growth and nerve myelination Necessary for normal intellectual development in infants Necessary for emotional stability in adults
Gastrointestinal	Increases appetite Increases secretion of "digestive juices" Increases gastric motility
Hematopoietic	Influences erythropoiesis
Metabolic	Profoundly affects oxidative metabolism Increases oxygen consumption in all tissues except the brain, gonads, and spleen Promotes heat production Influences synthesis and degradation of carbohydrate, fat, and protein
Respiratory	Influences lung development Necessary for surfactant production Increases rate and depth of respirations
Skeletal	Indirectly promotes growth formation by actions on the pituitary gland Acts synergistically with growth hormone and other growth factors that promote bone formation Directly affects skeletal maturation **Necessary** for progression of tooth development and eruption
Skin	Necessary for growth and maturation of the epidermis and hair follicles

Factors that Affect Thyroid Function

T4

Factors that contribute to proper production of thyroid hormones

- Nutrients: iron, iodine, tyrosine, zinc, selenium vitamin E, B2, B3, B6, C, D

Factors that inhibit proper production of thyroid hormones

- Stress
- Infection, trauma, radiation, medications
- Fluoride (antagonist to iodine)
- Toxins: pesticides, mercury, cadmium, lead
- Autoimmune disease: Celiac

Factors that increase conversion of T4 to RT3

- Stress
- Trauma
- Low-calorie diet
- Inflammation (cytokines, etc.)
- Toxins
- Infections
- Liver/kidney dysfunction
- Certain medications

Factors that increase conversion of T4 to T3

- Selenium
- Zinc

RT3 T3

T3 and RT3 compete for binding sites

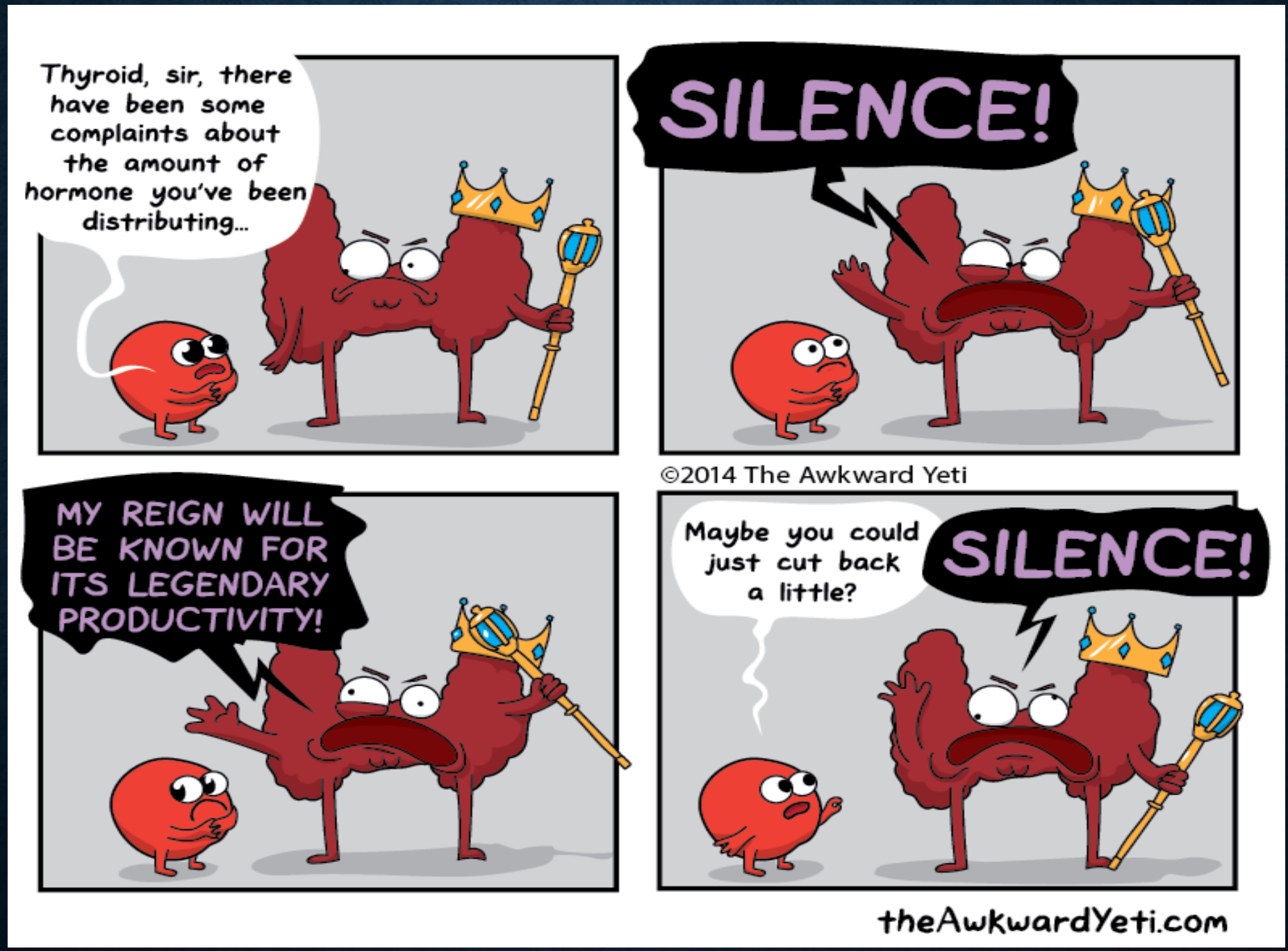
Nucleus/ Mitochondria

Cell

Factors that improve cellular sensitivity to thyroid hormones

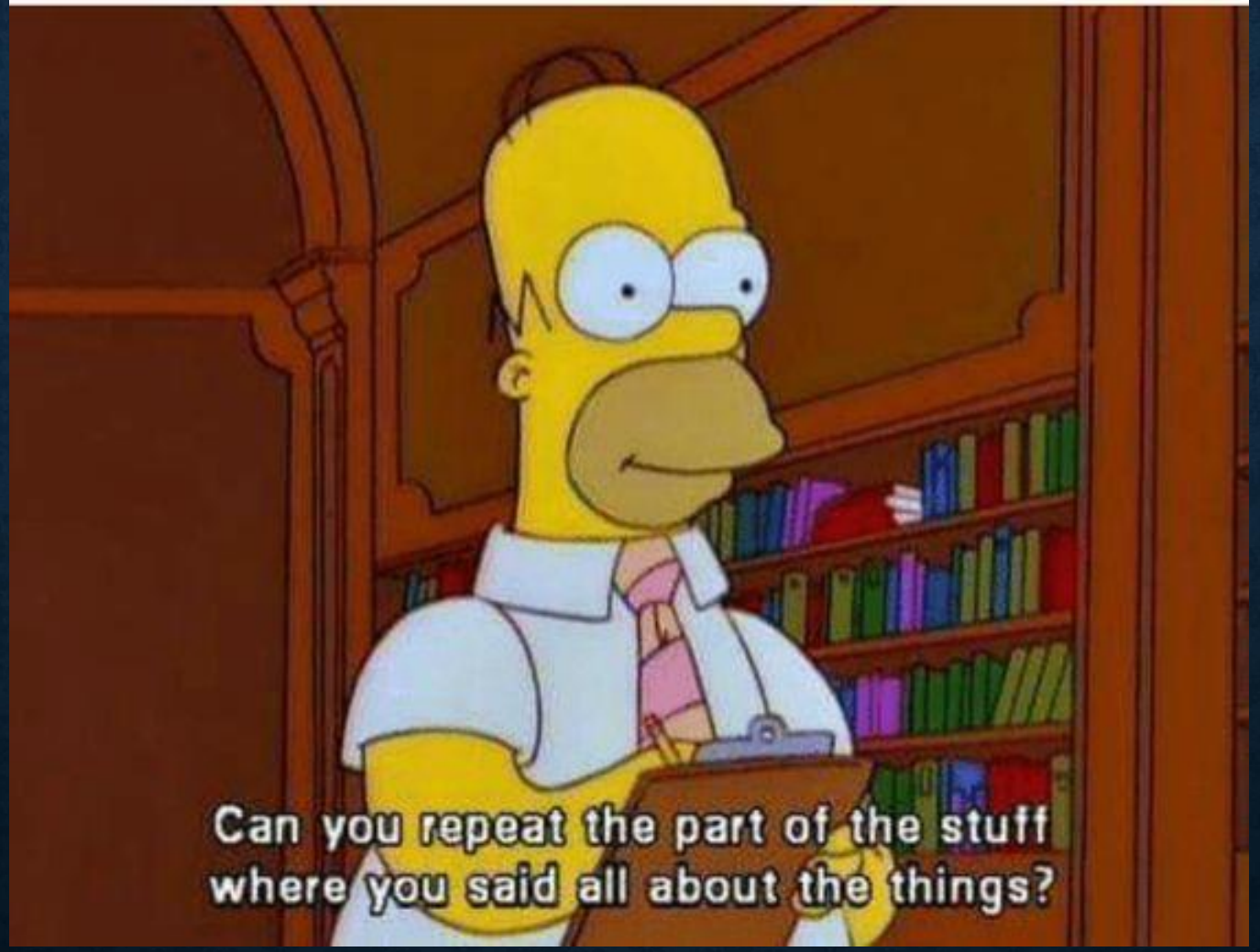
- Vitamin A
- Exercise
- Zinc

No one
Me after choosing Medical:


Thyroid, sir, there have been some complaints about the amount of hormone you've been distributing...
SILENCE!
©2014 The Awkward Yeti
MY REIGN WILL BE KNOWN FOR ITS LEGENDARY PRODUCTIVITY!
Maybe you could just cut back a little?
SILENCE!
theAwkwardYeti.com

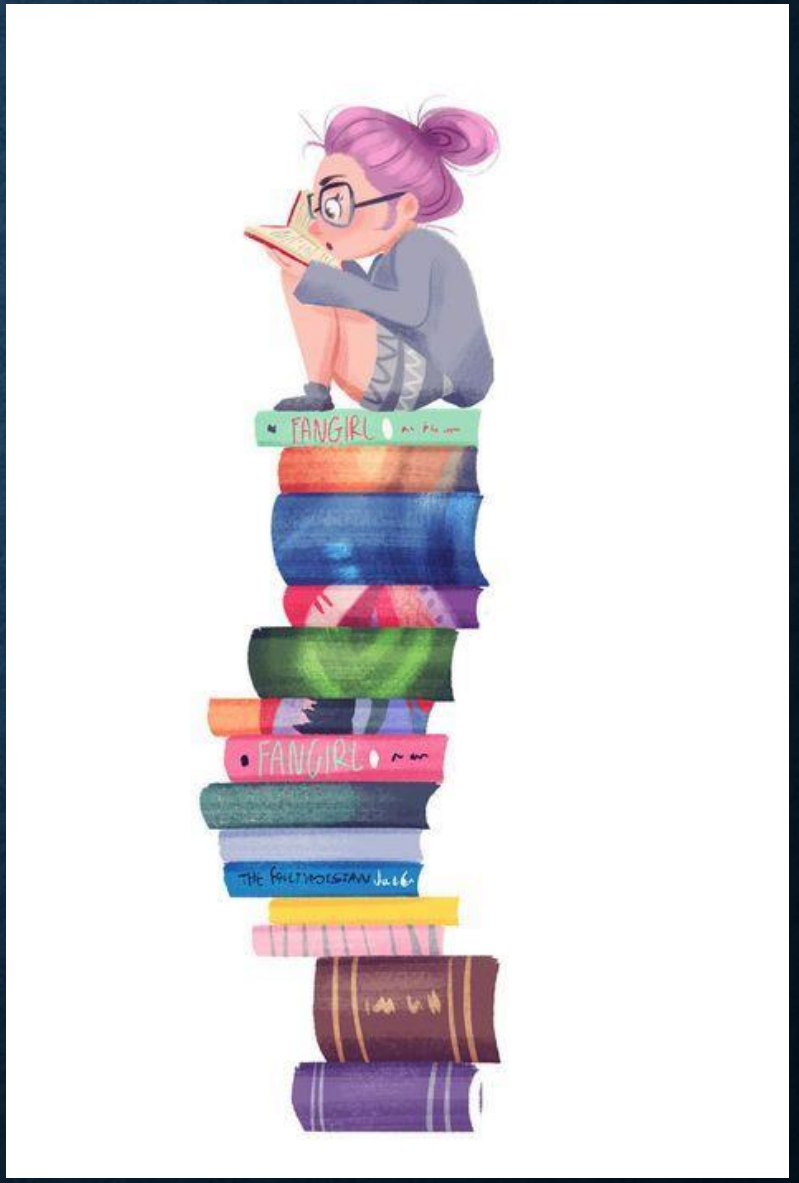
My class after I give very clear instructions:

BORED TEACHERS



RECOMMENDED BOOKS

- Text book of Medical Physiology-Guyton and Hall
- Principles of human Physiology- Lauralee Sherwood
- Color Atlas of human Physiology

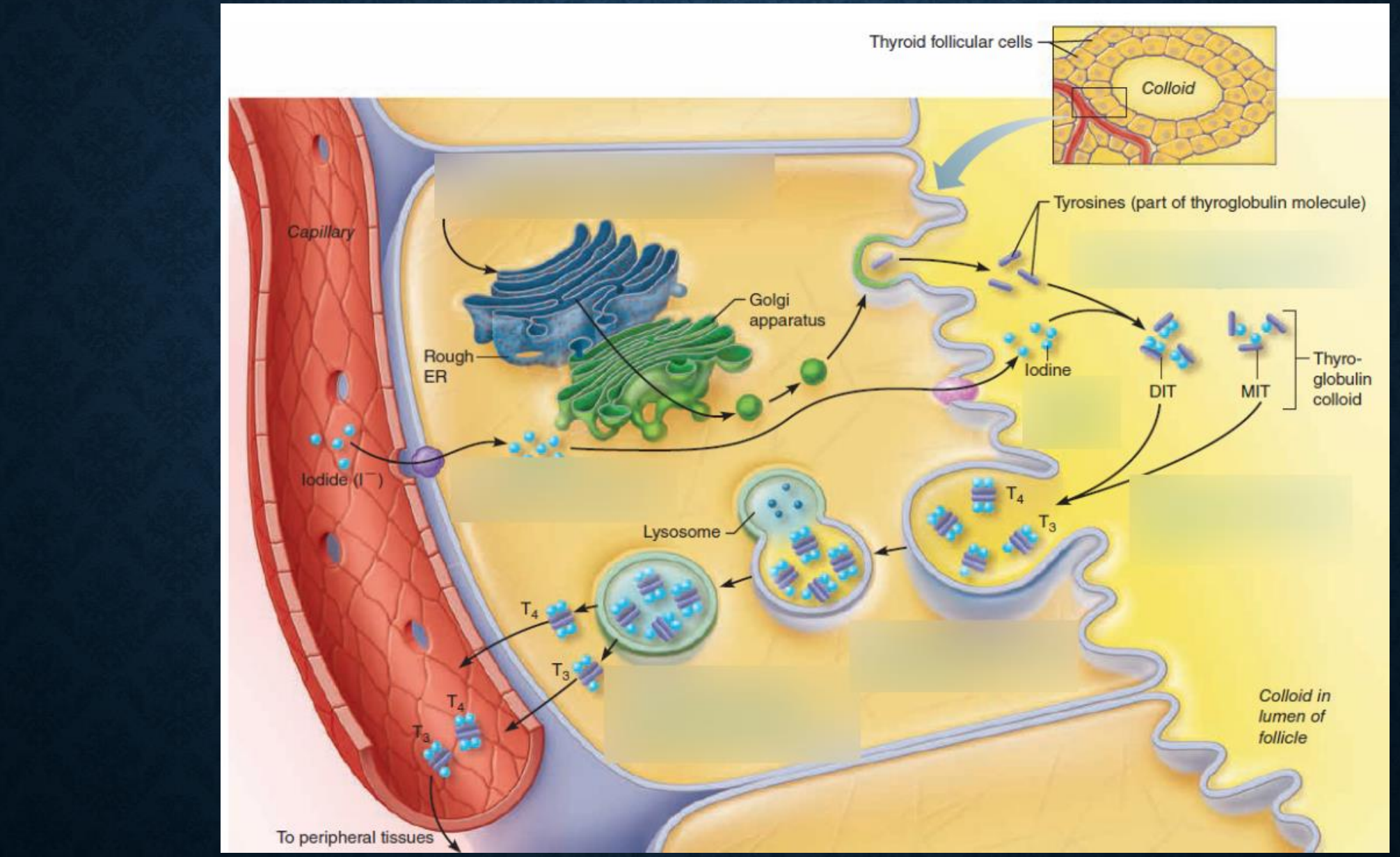


FOR FEEDBACK

If you have any questions or confusion regarding this topic plz contact me at:

dr_sarah@yahoo.com


That's all Folks!
SUPERB wallpapers


Thyroid follicular cells
Colloid
Capillary
Tyrosines (part of thyroglobulin molecule)
Golgi apparatus
Rough ER
Iodine
DIT
MIT
Thyro-globulin colloid
Iodide (I^-)
T_4
T_3
Lysosome
T_4
T_3
T_4
T_3
Colloid in lumen of follicle
To peripheral tissues