
بسم الله الرحمن الرحيم
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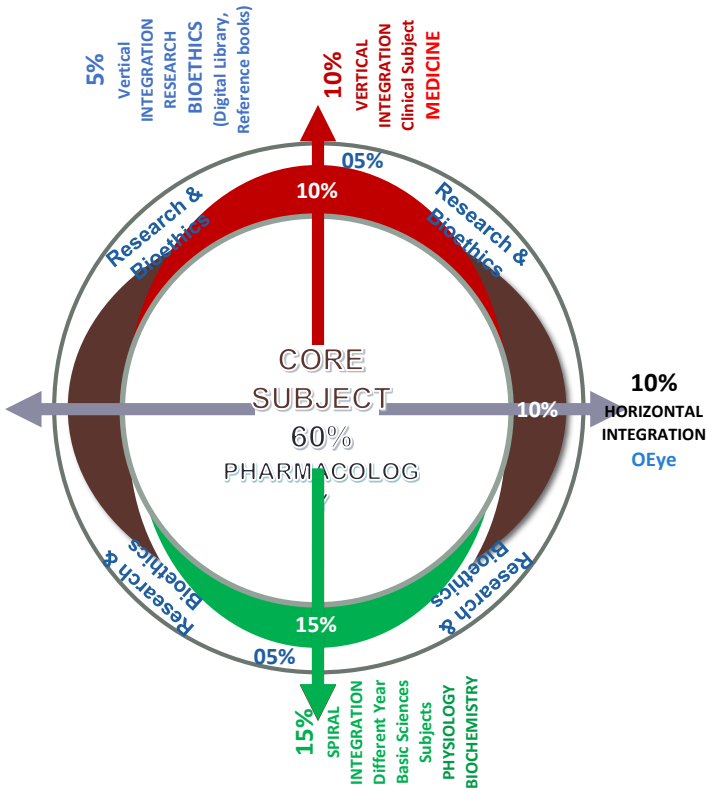
THYROID AND ANTI-THYROID DRUGS

Dr.Attiya Munir

MOTTO AND VISION

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

Prof. Umar's Clinically Oriented Integration Model
For Basic Sciences Interactive Lectures



4rd Year Pharmacology LGIS	
Core Subject – 60%	
Pharmacology	
Horizontal Integration – 10%	
Same Year Subjects	• Eye • Pathology
Vertical Integration – 10%	
Clinical Subjects	• Medicine • Surgery
Spiral Integration – 15%	
Different Year Basic Sciences Subjects	• Physiology (10%) • Biochemistry (5%)
Research & Bioethics, Digital library – 05%	

LEARNING OBJECTIVES

- At the end of the session, the students should be able to:

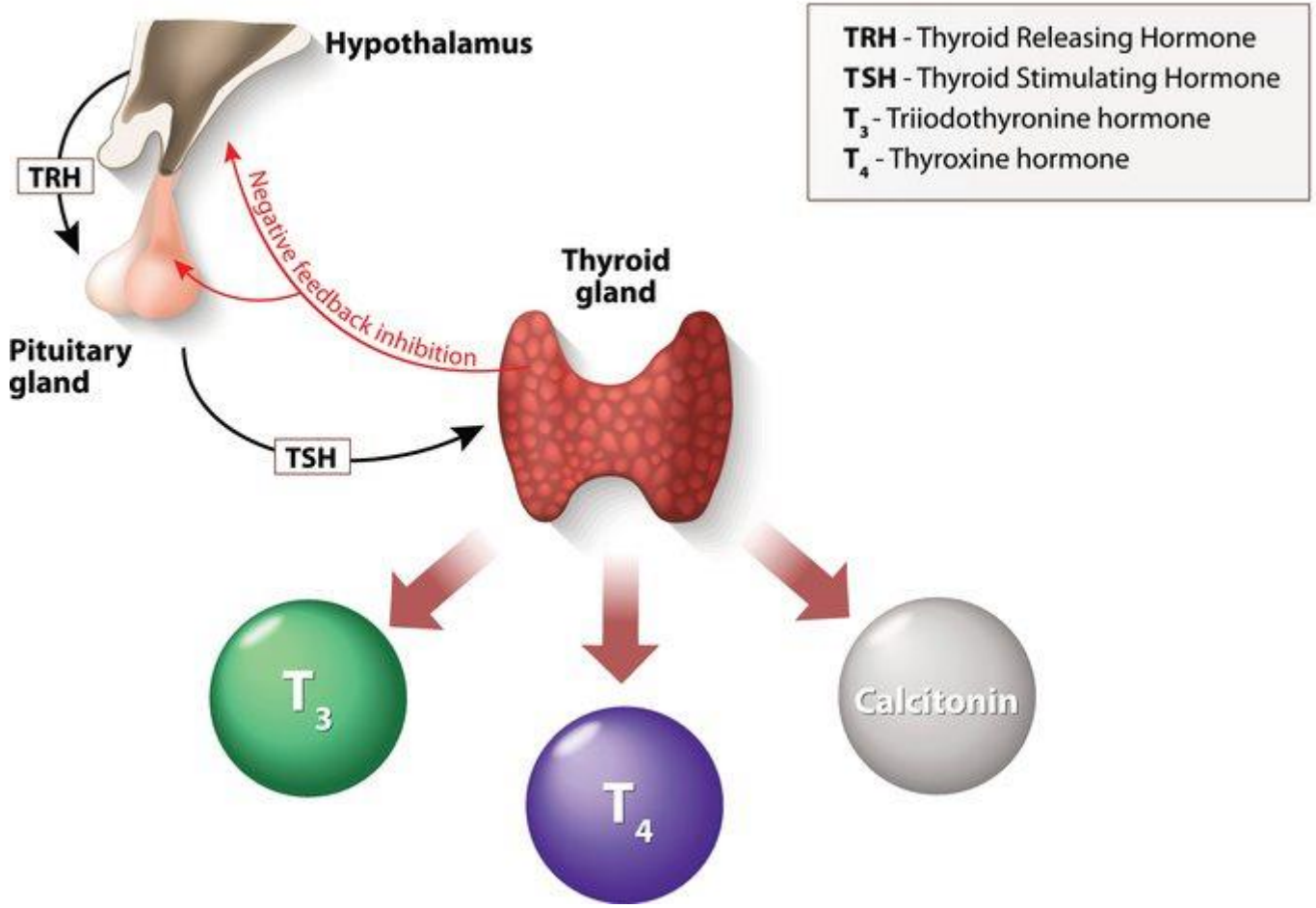
- Recall thyroid biosynthesis, feedback mechanism and major physiological roles of thyroxine

- Classify the antithyroid drugs

- Discuss pharmacodynamics and pharmacokinetics of each drug group.

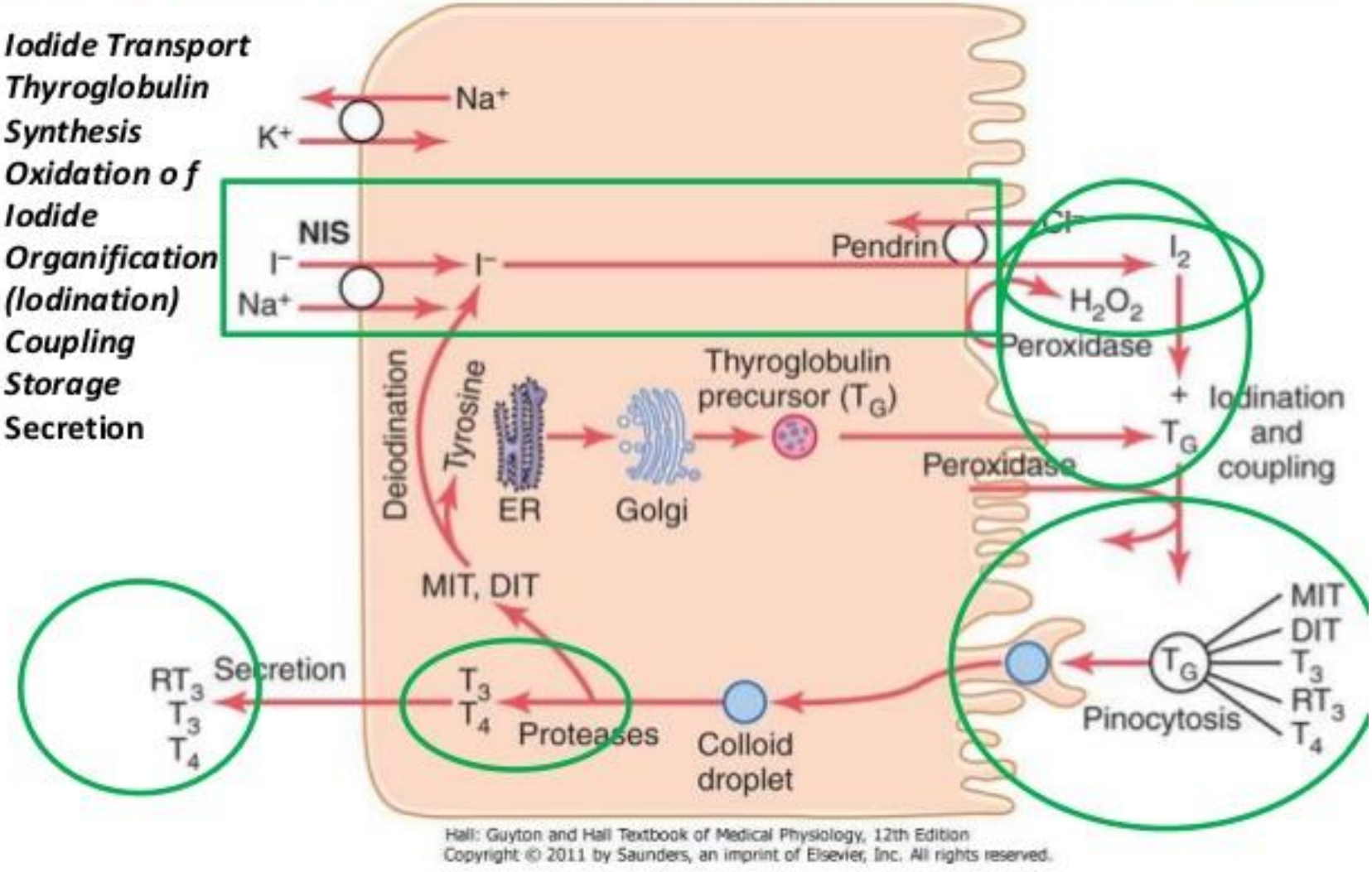
Spiral Integration- Physiology, Biochemistry

THYROID HORMONES

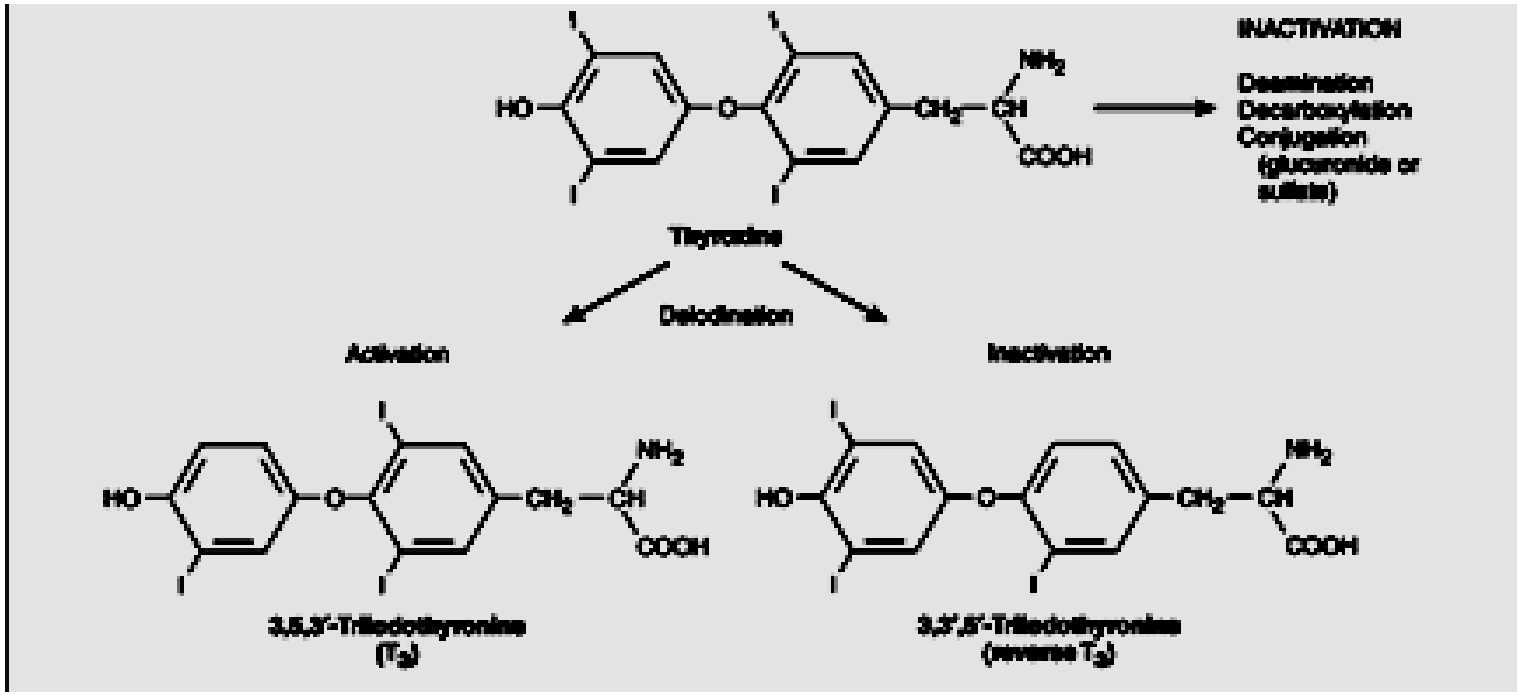


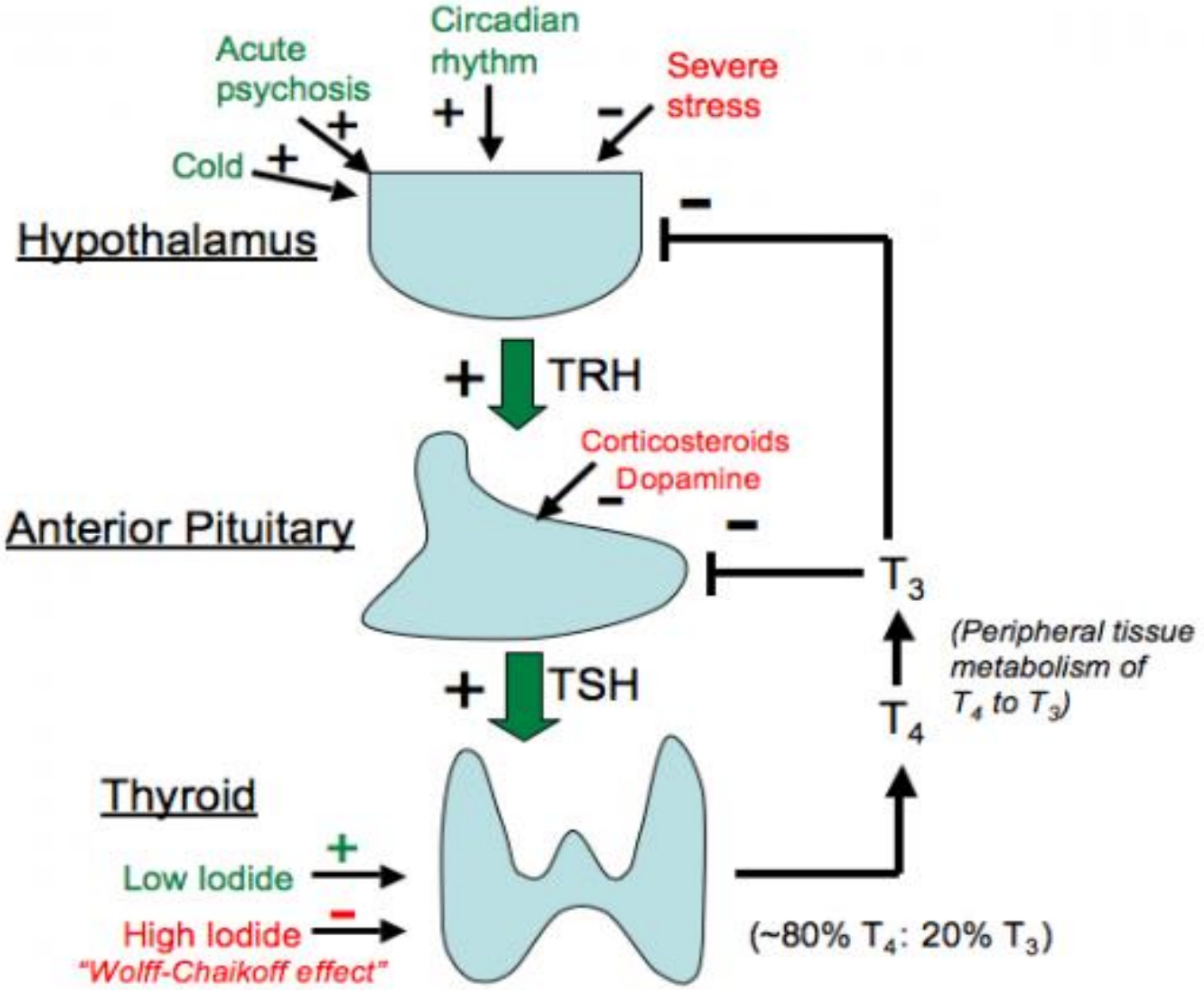
Bio-synthesis and Secretion of Thyroid Hormone

1. *Iodide Transport*
2. *Thyroglobulin Synthesis*
3. *Oxidation o f Iodide*
4. *Organification (Iodination)*
5. *Coupling*
6. *Storage*
7. *Secretion*



PERIPHERAL METABOLISM OF THYROXIN




Acute psychosis
Circadian rhythm
Severe stress
Cold
Hypothalamus
TRH
Corticosteroids
Dopamine
Anterior Pituitary
T3
(Peripheral tissue metabolism of T4 to T3)
TSH
T4
Thyroid
Low Iodide
High Iodide
"Wolff-Chaikoff effect"
(~80% T4: 20% T3)

THYROID HORMONES

- PREPARATIONS
  - Levothyroxine
  - Liothyronine
  - Liotrix
  - Desiccated thyroxine (animal origin)

THYROXINE

- Oral Absorption – L thyroxine 80 % , T3 95 %
- IV route
- Binding-99%
- Metabolism (effect of enzyme inducers)
- excretion

Actions of thyroid hormones

- Brain----growth&development of nervous system
- Bone&tissue growth– linear growth & maturation of bones
- CVS-- increased contractility,heart rate &cardiac output
- GUT—increased absorption of nutrients, increased motility
- Liver -increased gluconeogenesis&glyco genolysis
- Adipose tissue –increased lipolysis
- Muscle –increased protein catabolism in skeletal muscle
- Kidney -increased erythropoietin synthesis
- Respiration- increased central stimulation of respiration
- Energy metabolism -increased BMR,increased oxygen consumption,increased heat production stimulation of Na-K-ATP ase

levothyroxine

- It is the treatment of choice in replacement therapies and suppression therapies

USES

- Hashimoto’s thyroiditis
- Cretinism
- Iodine deficiency goiter
- Benign thyroid nodule
- Papillary CA of thyroid
- Infertility
- Myxedema coma
- Refractory anemias menstural disorders
- Chronic non healing ulcers

Call your doctor at once if you have a serious side effect such as:

- headache;
- sleep problems (insomnia);
- feeling nervous or irritable;
- fever, hot flashes, sweating;
- pounding heartbeats or fluttering in your chest;
- changes in your menstrual periods; or.
- appetite changes, weight changes.

Short list of side effects from levothyroxine

Common Side Effects of Levoxyl (Levothyroxine Sodium) Drug Center ...

www.rxlist.com/levoxyl-**side-effects**-drug-center.htm RxList

CORE SUBJECT

ANTI-THYROID DRUGS

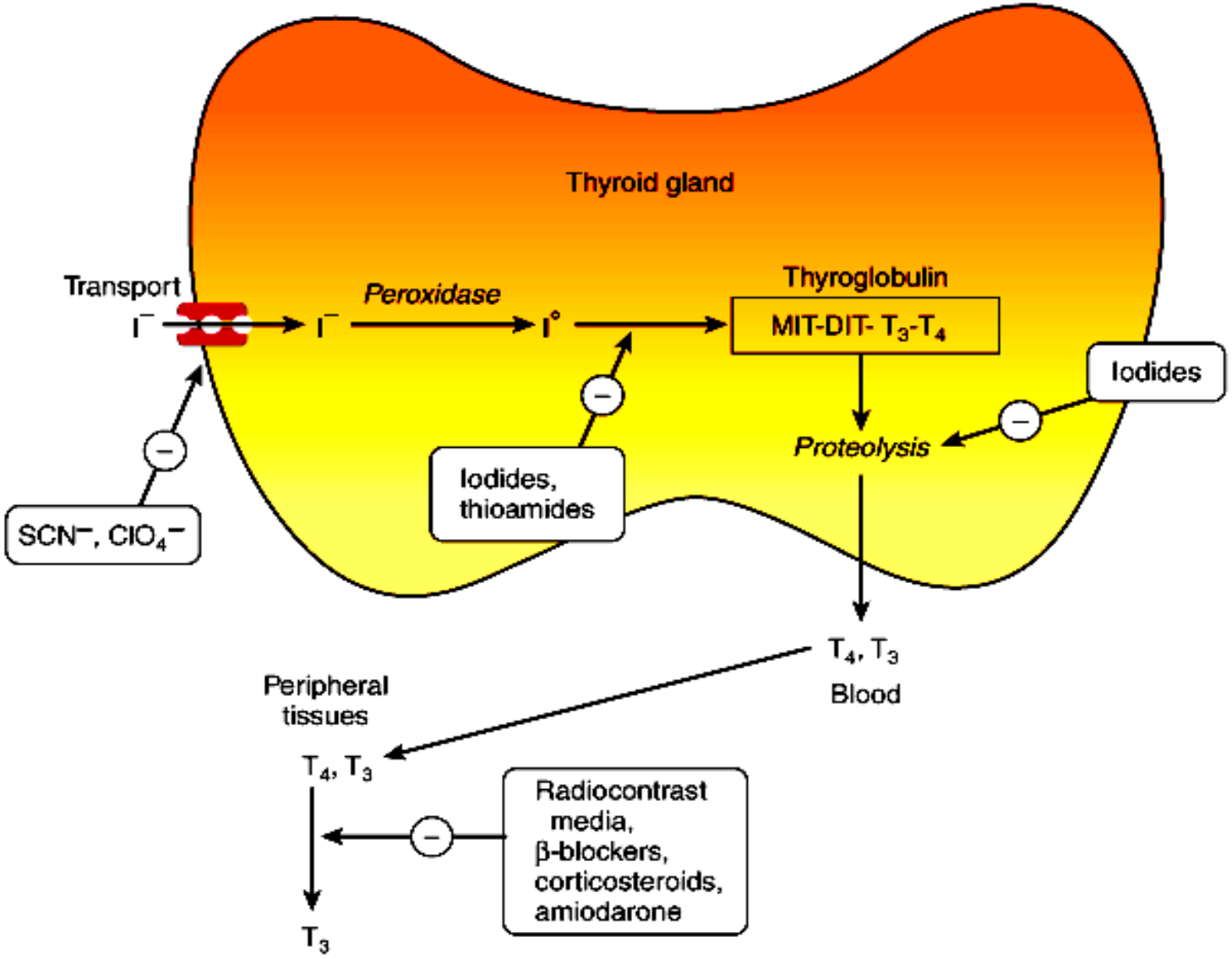
CLASSIFICATION

Chemical classification

- Thioamides
  - Carbimazole
  - Methimazole
  - Propylthiouracil
- Anion inhibitors
  - Perchlorate
  - Pertechnetate
  - Thiocyanate

- Iodides
  - Lugol’s iodine
  - Potassium iodine
- Iodinated contrast media
  - Ipodate
  - Iopanoic acid
  - Diatrizoate
- Radioactive iodine
- Misc.
  - Beta blockers
  - Corticosteroids

Anti-thyroid Drugs On Basis Of Mechanism Of Action



THIOAMIDES

Pharmacokinetics

Methimazole

- completely absorbed at variable rates
- Rapidly accumulated by thyroid gland
- Vd similar to propylthiouracil
- Excretion slower than propylthiouracil
- 65-70% dose is recovered in urine in 48 hours

Continued…

- ***Propylthiouracil***
- rapidly absorbed
- Peak serum level in 1hr
- Bioavailability 50-80%
- Large 1st pass effect
- Vd equals total body water
- Ingested dose excreted through kidneys within 24 hours

Continued…

- Plasma t ½ ---1.5 hours propylthiouracil
  6 hours methimazole
- Both drugs cross placental barrier and are concentrated by fetal thyroid
- Propylthiouracil can be used in 1st trimester of pregnancy
- Both secreted in low quantities in breast milk but are considered safe for the nursing infant
- Methimazole is 10 times more potent

PHARMACODYNAMICS

- Prevent hormone synthesis by inhibiting thyroid peroxidase catalyzed reactions
- Blocks iodine organification
- Blocks coupling of iodotyrosines
- Inhibit peripheral deiodination of T3 and T4(propylthiouracil)
- Onset of thioamides is slow

CLINICAL USES

- Grave's disease
- Toxic uninodular goiter
- Toxic multinodular goiter
- Thyrotoxicosis in pregnancy
- Preoperatively
- Thyroid storm

TOXICITY

- Nausea
- GIT distress
- Altered sense of smell and taste
- Maculopapular rash
- Lupus like reaction
- Agranulocytosis
- Severe hepatitis
- Cholestatic jaundice
- Cross sensitivity

ANION INHIBITORS

- MOA
  - Competitive inhibitors of iodide transport mechanism
- Use
  - Iodide induced hyperthyroidism
- Adverse effect:
  - Aplastic anemia

IODIDES

PHARMACOKINETICS

- Inhibits organification, hormone release and decrease size and vascularity of gland
- Inhibits hormone release through inhibition of thyroglobulin proteolysis
- Improvement in thyrotoxic symptoms occur within 2-7 days

CLINICAL USES

- Thyroid storm
- Preoperative preparation for surgery
- Iodide therapy include an increase in intraglandular stores of iodine

TOXICITY

- Iodism(reversible)
- Acneiform rash
- Swollen salivary glands
- Conjuctivitis
- Fetal goiter
- Jod-basedow phenomenon

RADIOACTIVE IODINE

- ^{131}I only isotope for treatment of thyrotoxicosis
- Administered orally as sodium ^{131}I
- Rapidly absorbed and concentrated by the thyroid follicles
- Therapeutic effect is by emission of beta rays with half life of 5 days
- Cause destruction of thyroid parenchyma

CLINICAL USES

- Hyperthroidism due to Grave's disease
- Toxic nodular goiter
- Partial ablation of thyroid
- Response after 2 weeks, reaching peak at 3 months

TOXICITY

- Contraindicated in pregnant and nursing mothers

ADRENOCEPTOR BLOCKING AGENTS

- Beta blockers without ISA activity are used
- Main function to reduce hyperthyroid symptoms
- Inhibits peripheral conversion of T4 to T3
- Used in

✓Thyroid storm

✓While waiting response to carbimazole

✓Preoperatively

Vertical integration-Medicine

CLINICAL PHARMACOLOGY

- **HYPOTHYROIDISM**
- It is characterized by slowing of all body functions
- Most commonly used preparation is ***levothyroxine***
- Combination therapies with leothyronine is not superior to alone therapy
- Infants and children require T4 with respect to their body weight

MYXEDEMA COMA

- End stage of untreated hypothyroidism
- Patient have large pool of empty receptors
- Loading dose of levothyroxine is given
- I.V T3 is also given
- I.V hydrocortisone

Continued…

- **Hypothyroidism and pregnancy:**

- **Subclinical hypothyroidism:**

- **Drug induced hypothyroidism:**

GRAVE'S DISEASE

- Antithyroid therapy
- Near total thyroidectomy
- Destruction of gland by radioactive iodine
- Adjuncts to antithyroid therapy
  - Beta-blockers
  - Diltiazem
  - Barbiturates
  - Bile acid sequestrants

SUBACUTE THYROIDITIS

- In acute viral infections destruction of thyroid parenchyma with transient release of thyroid hormone
- Beta blockers without ISA activity
- Aspirin or NSAIDs
- Corticosteroids

THYROID STORM

- Sudden acute attack
- Propanolol I.V or orally
- Diltiazem
- Saturated solution of potassium iodide
- Hormone synthesis blocked by propylthiouracil
- Hydrocortisone
- Plasmapheresis or peritoneal dialysis

OPHTHALMOPATHY

- ^{131}I ablation of gland or total surgical excision
- Oral prednisolone
- Elevation of head to reduce edema
- Artificial tears to relieve corneal drying due to exophthalmos
- Smoking cessation
- Irradiation of posterior orbit
- Surgical decompression of orbit
- Eyelid or eye muscle surgery

Vertical Integration- Peads

NEONATAL GRAVE'S DISEASE

- TSH-R Ab passage to the neonate
- Genetic transmission of the trait
- Elevated FT4
- Elevated T3
- Low TSH
- If caused by maternal Ab,subsides over the period of 4-12 weeks
- Propylthiouracil
- Lugol's solution
- Prednisolone

AMIODARONE INDUCED THYROTOXICOSIS

- 3% of patients

- Type I
- Type II

Artificial intelligence

- Aversano, L., Bernardi, M.L., Cimitile, M., Iammarino, M., Macchia, P.E., Nettore, I.C. and Verdone, C., 2021. Thyroid disease treatment prediction with machine learning approaches. Procedia Computer Science, 192, pp.1031-1040

Research

- He, Q., Dong, H., Gong, M., Guo, Y., Xia, Q., Gong, J. and Lu, F., 2022. New therapeutic horizon of Graves' hyperthyroidism: treatment regimens based on immunology and ingredients from traditional Chinese medicine. Frontiers in Pharmacology, 13.

End of Lecture Assessement (EOLA)

1. Which drug is currently approved to treat hypothyroidism and myxedema coma

a. Levothyroxine
b. Liothyronine
c. Liotrix
d. Desiccated thyroxine

2. Agranulocytosis, a rare but serious adverse event, usually occurs within three months after the start of

a. Carbimazole
b. Methimazole
c. Propylthiouracil
d. Percholate
e. Iodides

3. Which drug displaces thyroid hormone from binding proteins, consequently affecting the measurement of both fT4 and fT3

a. Glucocorticoids
b. Ketamine
c. Heparin
d. Ketoconazole
e. Rifamycin

4. Which of the following would be preferred for treatment of arrthymias associated with thyroid strom?

a. Esmolol
b. Hydrocortisone
c. Potassium Iodide
d. Propranolol
e. Propylthiouracil