

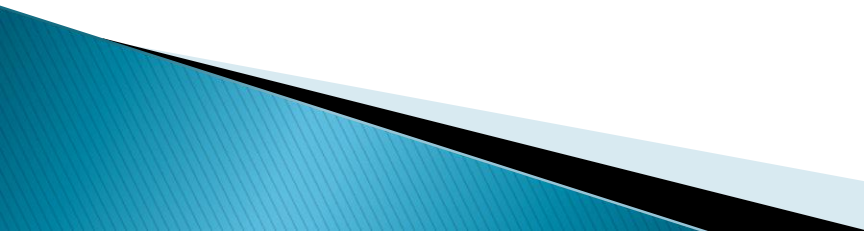
Animal physiology

Endocrinology

MSc.Students

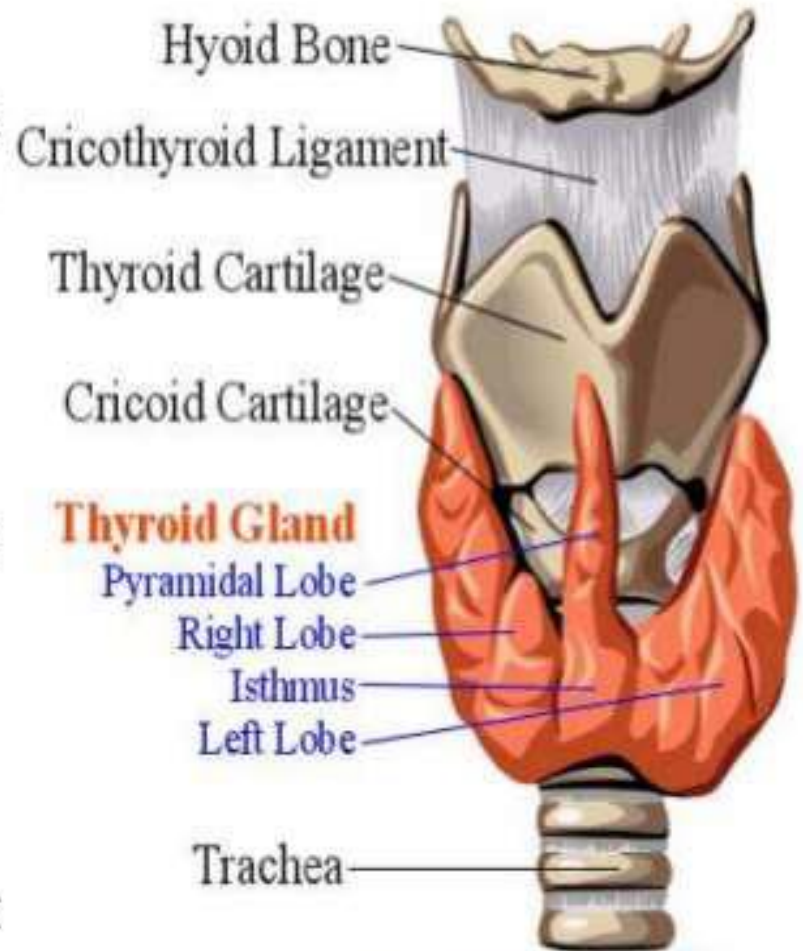
Assistant Prof. Dr.Heba Th.Yser

Thyroid gland

- ▶ Largest Endocrine organ in the body
 - ▶ ▪ Involved in production, storage, and release of thyroid hormone
 - ▶ ▪ Function influenced by
 - ▶ ▪ Central axis (TRH)
 - ▶ ▪ Pituitary function (TSH)
 - ▶ ▪ Comorbid diseases (Cirrhosis, Graves, etc.)
 - ▶ ▪ Environmental factors (iodine intake)
- 

Anatomy

- ▶ **Location:** lower part of the front and side of the neck opposite to the C5, C6, C7 and T1 vertebrae.
- ▶ Each lateral lobe extends upwards to oblique line of thyroid cartilage and below up to the 5th or 6th tracheal ring.
- ▶ The isthmus extends across the midline in front of the 2nd, 3rd and 4th tracheal ring.



Adapted from Corel Draw 9

Histology

THYROID GLAND

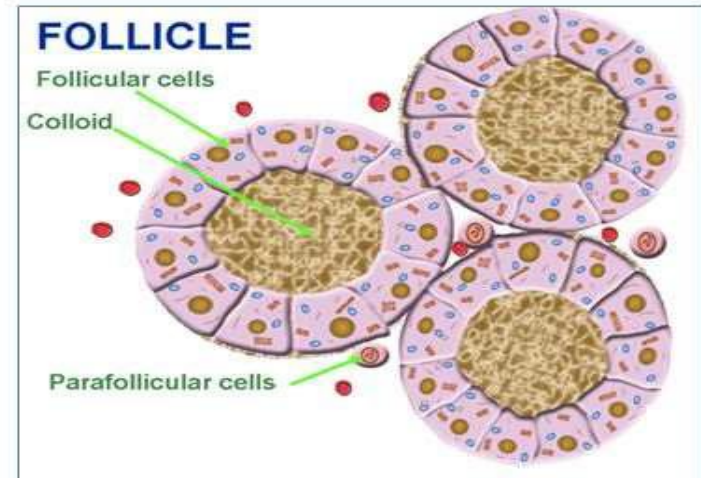
Cells of Thyroid gland:

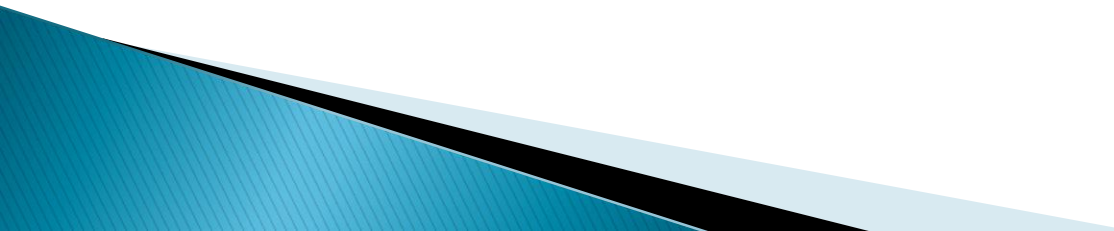
- 1- **Follicular A Cells** secrete Thyroxine (T_4) & Triiodothyronine (T_3).
- 2- **Parafollicular C Cells** secrete **ThyroCalcitonin**.

Functions of Thyroid gland:

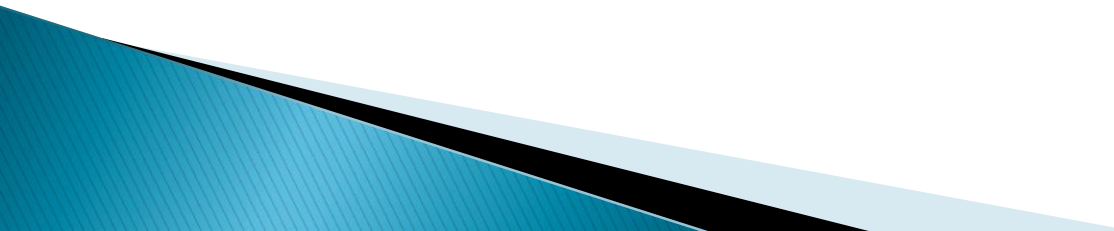
Required for

- 1- Normal metabolism.
- 2- Growth & maturation.
- 3- Ca^{+2} regulation.

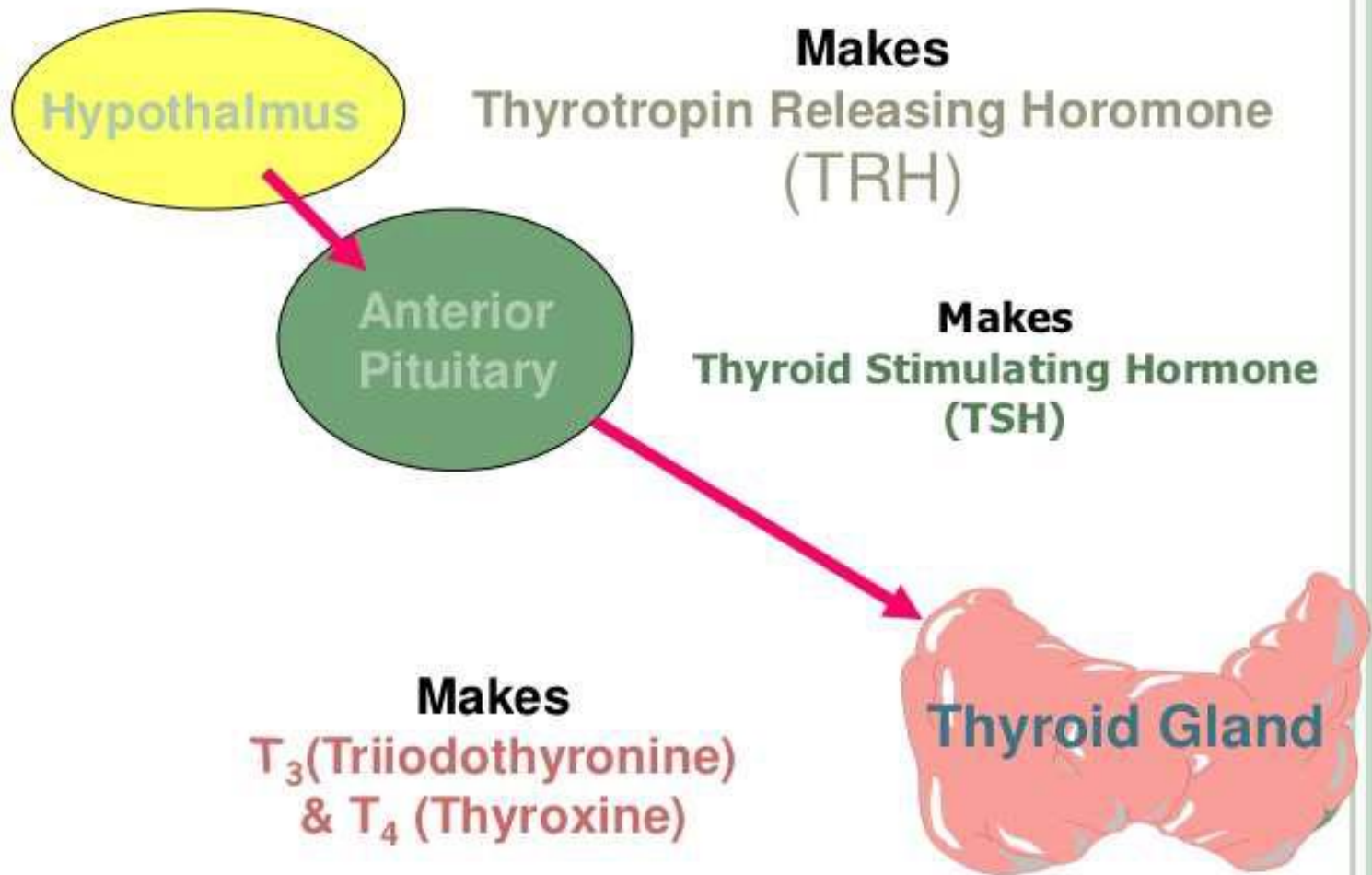


- ▶ Regulates basal metabolic rate
 - ▶ ▪ Improves cardiac contractility
 - ▶ ▪ Increases the gain of catecholamines
 - ▶ ▪ Increases bowel motility
 - ▶ ▪ Increases speed of muscle contraction
 - ▶ ▪ Decreases cholesterol (LDL)
 - ▶ ▪ Required for proper fetal neural growth
- 

Thyroid Physiology

- ▶ Uptake of Iodine by thyroid
 - ▶ ▪ Coupling of Iodine to Thyroglobulin
 - ▶ ▪ Storage of MIT / DIT in follicular space
 - ▶ ▪ Re-absorption of MIT / DIT
 - ▶ ▪ Formation of T3, T4 from MIT / DIT
 - ▶ ▪ Release of T3, T4 into serum
 - ▶ ▪ Breakdown of T3, T4 with release of Iodine
- 

THYROID PHYSIOLOGY



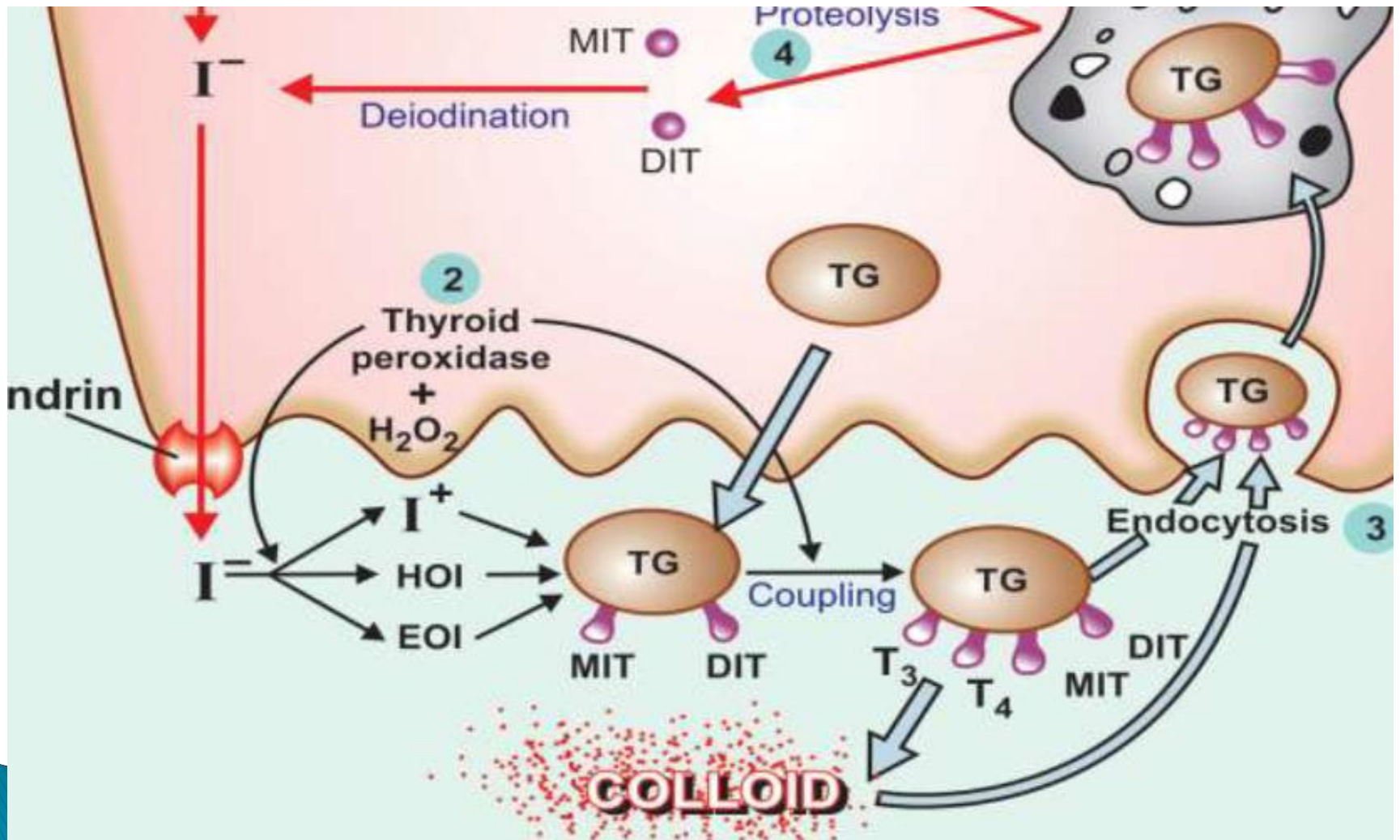
Iodine uptake

- ▶ ▪ Na^+/I^- symport protein
- ▶ controls serum I^- uptake
- ▶ ▪ Based on Na^+/K^+
- ▶ antiport potential
- ▶ ▪ Stimulated by TSH
- ▶ ▪ Inhibited by Perchlorate

MIT / DIT formation

- ▶ Thyroid Peroxidase (TPO)
 - ▶ ▪ Apical membrane protein
 - ▶ ▪ Catalyzes Iodine organification to Tyrosine residues of
- ▶ Thyroglobulin
 - ▶ ▪ Antagonized by methimazole
 - ▶ ▪ Iodine coupled to Thyroglobulin
 - ▶ ▪ Monoiodotyrosine (Tg + one I-)
 - ▶ ▪ Diiodotyrosine (Tg + two I-)
 - ▶ ▪ Pre-hormones secreted into follicular space

Synthesis, storage, secretion

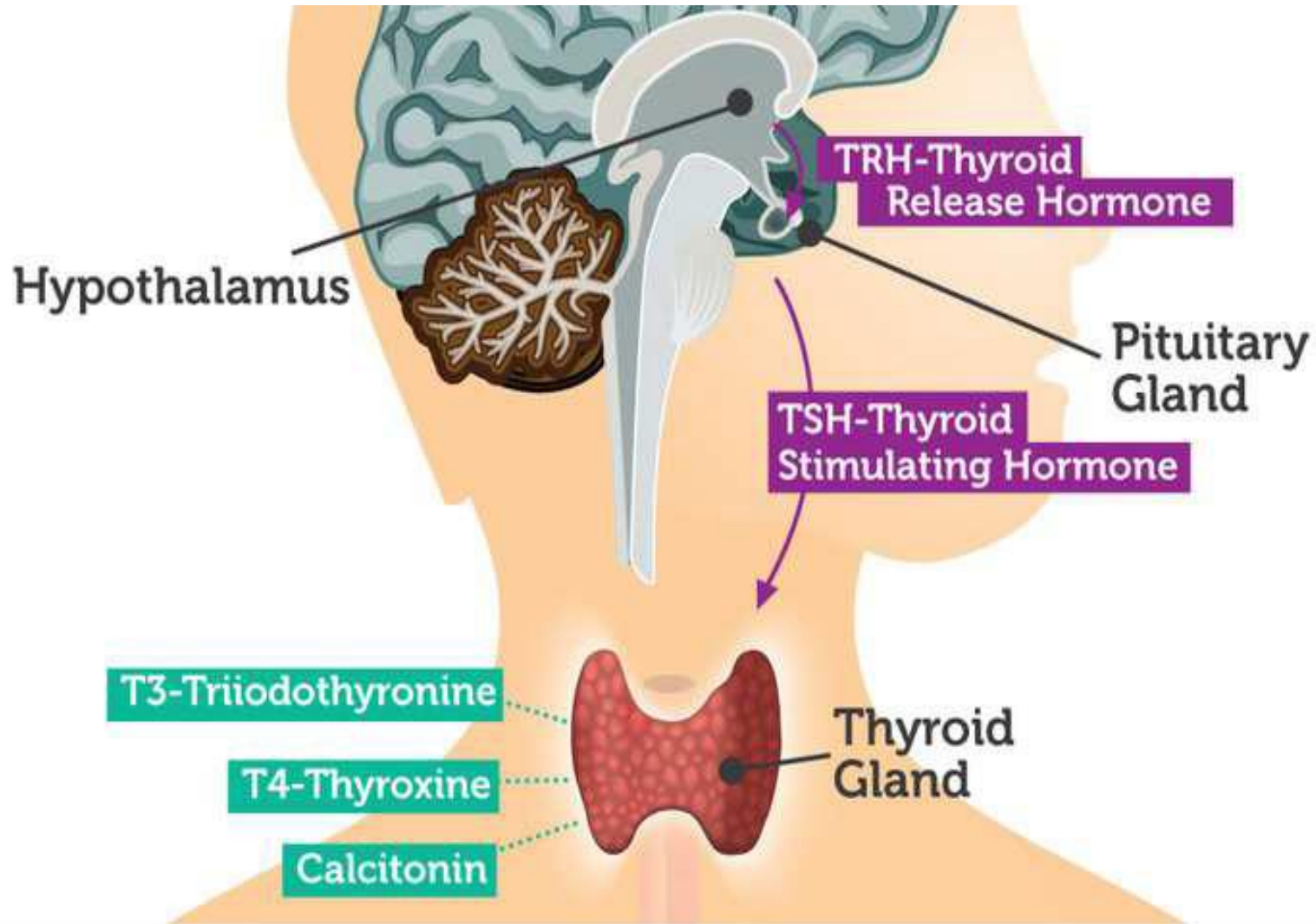


Secretion of Thyroid Hormone

- ▶ Stimulated by TSH
- ▶ ▪ Endocytosis of colloid on apical membrane
- ▶ ▪ Coupling of MIT & DIT residues
- ▶ ▪ Catalyzed by TPO
- ▶ ▪ $\text{MIT} + \text{DIT} = \text{T}_3$
- ▶ ▪ $\text{DIT} + \text{DIT} = \text{T}_4$
- ▶ ▪ Hydrolysis of Thyroglobulin
- ▶ ▪ Release of T₃, T₄

Thyroid Hormone

- ▶ Majority of circulating hormone is T4
 - ▶ ▪ 98.5% T4
 - ▶ ▪ 1.5% T3
- ▶ ▪ Total Hormone load is influenced by serum binding proteins (TBP, Albumin, ??)
- ▶ ▪ Thyroid Binding Globulin 70%
- ▶ ▪ Albumin 15%
- ▶ ▪ Transthyretin 10%
- ▶ ▪ Regulation is based on the free component of thyroid hormone



THYROID HORMONES

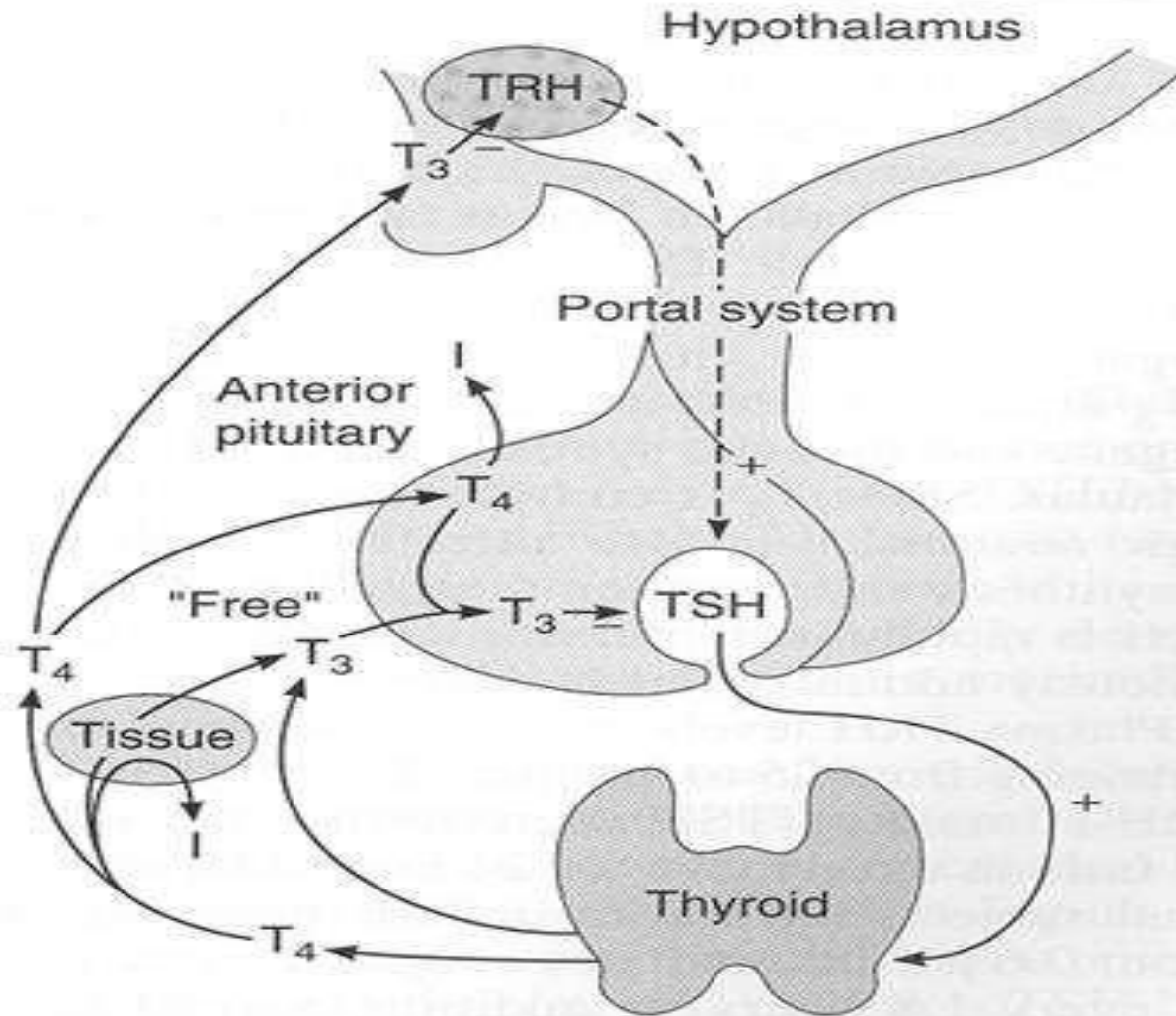
Hormone Binding Factors

- ▶ Increased TBG
 - ▶ ▪ High estrogen states (pregnancy, OCP, HRT, Tamoxifen)
 - ▶ ▪ Liver disease (early)
- ▶ Decreased TBG
 - ▶ ▪ Androgens or anabolic steroids
 - ▶ ▪ Liver disease (late)

Hormone Degredation

- ▶ T4 is converted to T3 (active) by *5' deiodinase*
- ▶ ▪ T4 can be converted to rT3 (inactive) by *5 deiodinase*
- ▶ ▪ T3 is converted to rT2 (inactive) by *5 deiodinase*
- ▶ ▪ rT3 is inactive but measured by serum tests

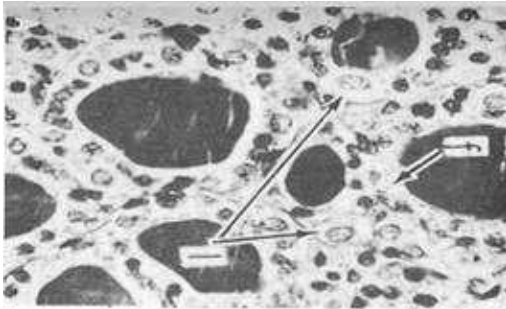
Thyroid Hormone Control



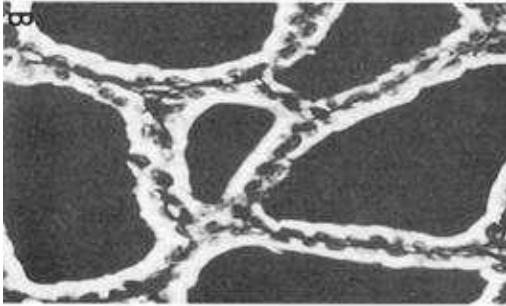
TRH and TSH

- ▶ Produced by Hypothalamus
 - ▶ ▪ Release is pulsatile, circadian
 - ▶ ▪ Downregulated by T4, T3
 - ▶ ▪ Travels through portal venous system to adenohypophysis
 - ▶ ▪ Stimulates TSH formation
- ▶ **TSH**
- ▶ Produced by Adenohypophysis Thyrotrophs
 - ▶ ▪ Upregulated by TRH
 - ▶ ▪ Downregulated by T4, T3
 - ▶ ▪ Travels through portal venous system to cavernous sinus, body.
 - ▶ ▪ Stimulates several processes
 - ▶ ▪ Iodine uptake
 - ▶ ▪ Colloid endocytosis
 - ▶ ▪ Growth of thyroid gland

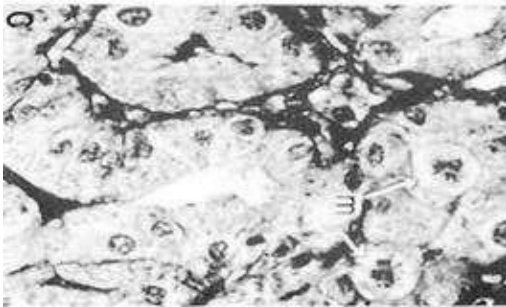
Iodine states



Normal Thyroid



▪ Inactive Thyroid



▪ Hyperactive Thyroid

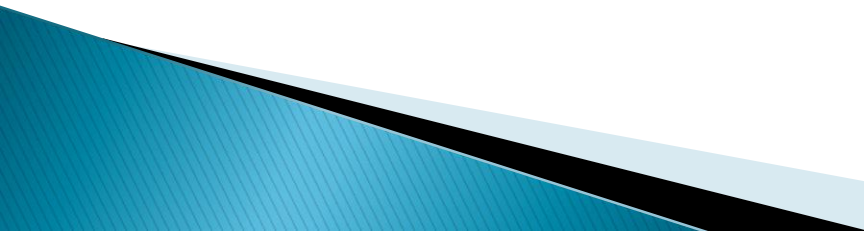
Hypothyroid

- ▶ Symptoms – fatigability, coldness, weight gain, constipation, low voice
 - ▶ ▪ Signs – Cool skin, dry skin, swelling of face/hands/legs, slow reflexes, myxedema
 - ▶ ▪ Newborn – Retardation, short stature, swelling of face/hands, possible deafness
 - ▶ ▪ Types of Hypothyroidism
 - ▶ ▪ Primary – Thyroid gland failure
 - ▶ ▪ Secondary – Pituitary failure
 - ▶ ▪ Tertiary – Hypothalamic failure
 - ▶ ▪ Peripheral resistance
- 

Hypothyroid

- ▶ Cause is determined by
- ▶ geography
- ▶ ▪ Diagnosis
- ▶ ▪ Low FT4, High TSH
- ▶ (Primary, check for
- ▶ antibodies)
- ▶ ▪ Low FT4, Low TSH
- ▶ (Secondary or Tertiary, TRH
- ▶ stimulation test, MRI)
- ▶ ▪ Treatment
- ▶ ▪ Levothyroxine (T4) due to longer half life
- ▶ ▪ Treatment prevents bone loss, cardiomyopathy,
- ▶ myxedema

Hashimoto's (Chronic, Lymphocytic)

- ▶ Most common cause of hypothyroidism
 - ▶ ▪ Result of antibodies to TPO, TBG
 - ▶ ▪ Commonly presents in females 30–50 yrs.
 - ▶ ▪ Usually non-tender and asymptomatic
 - ▶ ▪ Lab values
 - ▶ ▪ High TSH
 - ▶ ▪ Low T4
 - ▶ ▪ Anti-TPO Ab
 - ▶ ▪ Anti-TBG Ab
 - ▶ ▪ Treat with Levothyroxine
- 

Hashimoto's (Chronic, Lymphocytic)

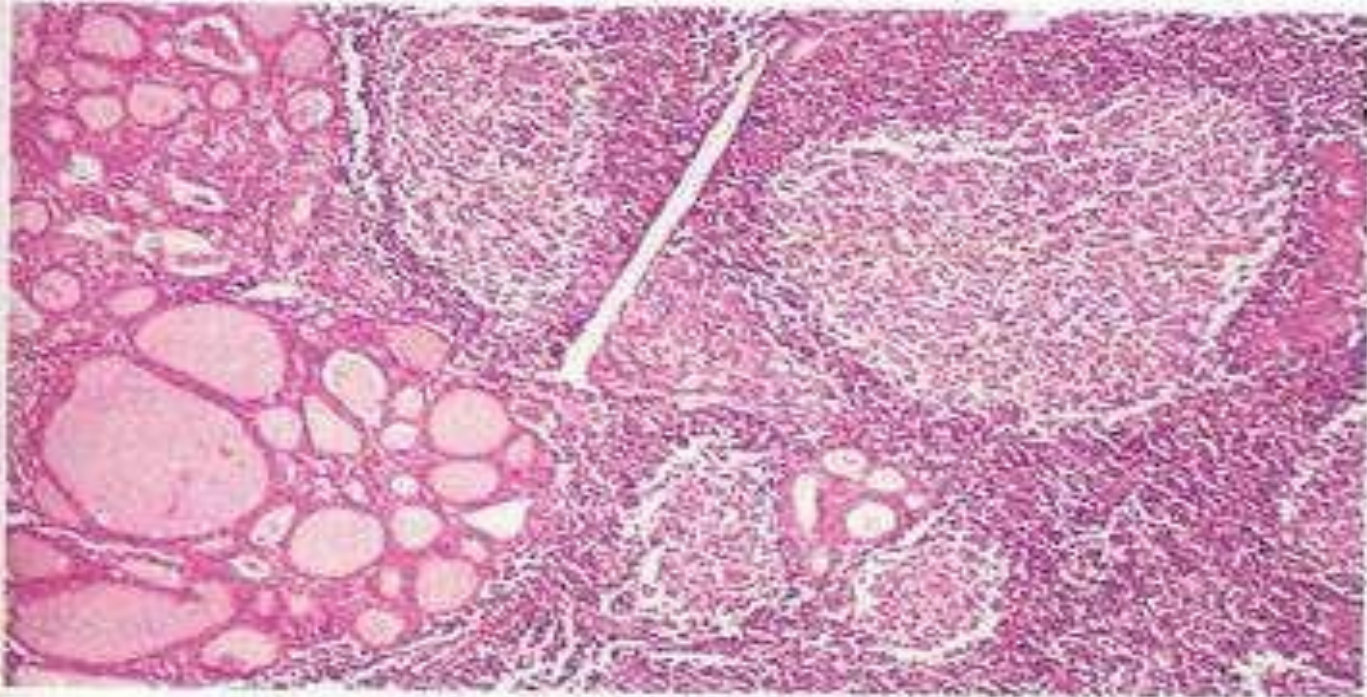


Figure 26-8

Photomicrograph of Hashimoto thyroiditis. The thyroid parenchyma contains a dense lymphocytic infiltrate with germinal centers. Residual thyroid follicles lined by deeply eosinophilic *Hürthle* cells are also seen.

Goiter

- ▶ Endemic goiter
 - ▶ ▪ Caused by dietary deficiency of Iodide
 - ▶ ▪ Increased TSH stimulates gland growth
 - ▶ ▪ Also results in cretinism
 - ▶ ▪ Goiter in developed countries
 - ▶ ▪ Hashimoto's thyroiditis
 - ▶ ▪ Subacute thyroiditis
 - ▶ ▪ Other causes
 - ▶ ▪ Excess Iodide (Amiodarone, Kelp, Lithium)
 - ▶ ▪ Adenoma, Malignancy
 - ▶ ▪ Genetic / Familial hormone synthesis defects

Hyperthyroid

- ▶ Symptoms – Palpitations, nervousness, fatigue, diarrhea,
- ▶ sweating, heat intolerance
- ▶ ▪ Signs – Thyroid enlargement
- ▶ ▪ Lab workup
- ▶ ▪ TSH
- ▶ ▪ FT4
- ▶ ▪ RAIU
- ▶ ▪ Other Labs
- ▶ ▪ Anti–TSH–R Ab, Anti–TPO Ab, Anti–TGB Ab
- ▶ ▪ FT3
- ▶ ▪ FNA
- ▶ ▪ MRI, US

Hyperthyroid

- ▶ Common Causes
 - ▶ ▪ *Graves
 - ▶ ▪ Adenoma
 - ▶ ▪ Multinodular Goiter
 - ▶ ▪ *Subacute Thyroiditis
 - ▶ ▪ *Hashimoto's Thyroiditis
 - ▶ ▪ Rare Causes
 - ▶ ▪ Thyrotoxicosis factitia, struma ovarii, thyroid metastasis, TSH-secreting tumor, hamburger

Graves

- ▶ Most common cause of hyperthyroidism
- ▶ ▪ Result of anti-TSH receptor antibodies
- ▶ ▪ Diagnosis
- ▶ ▪ Symptoms of hyperthyroidism
- ▶ ▪ Clinical exophthalmos and goiter
- ▶ ▪ Low TSH, normal/high FT4, anti-TSH Ab (Optional)
- ▶ ▪ If no clinical findings I123 may demonstrate increased uptake.
- ▶ ▪ Treatments
- ▶ ▪ Medical – Propylthiouracil, Methimazole, Propranolol
- ▶ ▪ Surgical – Subtotal Thyroidectomy
- ▶ ▪ Radiation – RAI ablation [I^{131} (mCi/g) x weight / %RAIU]



Treatment for Hyperthyroidism

- Anti-thyroid drugs—Inhibits thyroid hormone synthesis by irreversibly binding to TPO inhibiting its ability to break down iodine ($I_2 \rightarrow I^-$) and covalently attach it to the tyrosine residue of thyroglobulin.
 - Propylthiouracil
 - Methimazole
 - Carbamazepine—Degraded to methimazole in the body.
- Radioactive Iodine.
- Thyroidectomy.
- β -Blockers used in the treatment of thyrotoxicosis to treat symptoms.

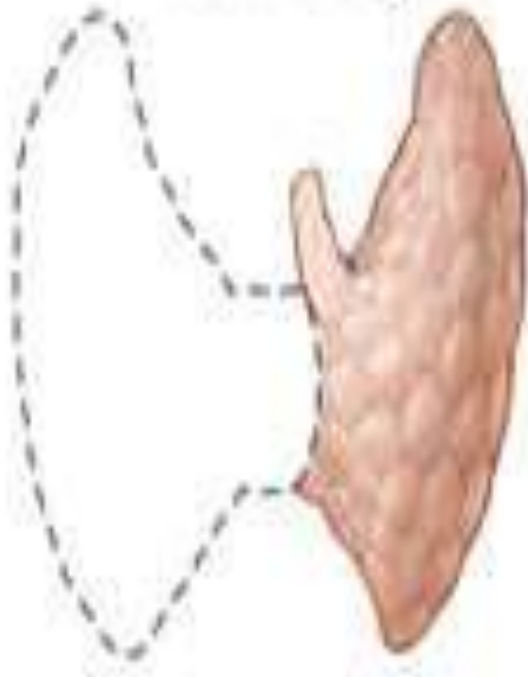


Radioactive Iodine Therapy

- Used for definitive therapy or ablation
- The only isotopes used for treatment of thyrotoxicosis
- Uses the ff radioisotopes: I_{123} or I_{131}
- Side- effects are minimal: avoid in children (may inhibit bone growth) and pregnant women or those intending pregnancy
- Contraceptives are encouraged among those who are sexually active:

surgery

Thyroid lobectomy



Subtotal thyroidectomy



Total thyroidectomy

