SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME : Pharmacology Pathology and Clinical Microbiology

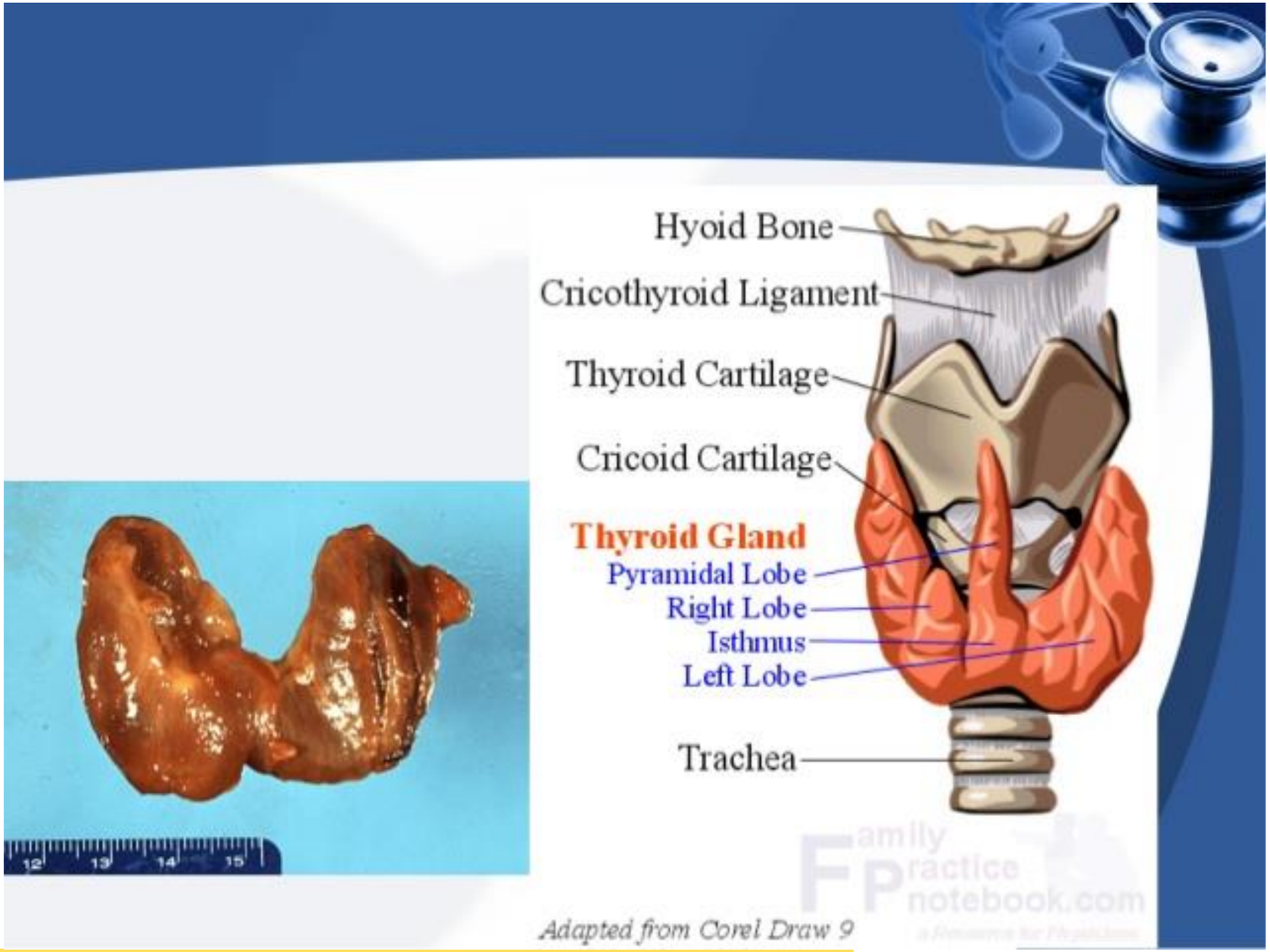
II nd YEAR

TOPIC : ANTI THYROID DRUGS

HISTOLOGY OF THE THYROID GLAND

- The thyroid gland contains numerous follicles, composed of epithelial follicle cells and colloid.

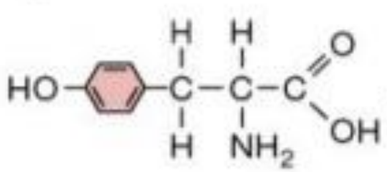
- Also, between follicles are Para-follicular cells, which produce Calcitonin.


Hyoid Bone
Cricothyroid Ligament
Thyroid Cartilage
Cricoid Cartilage
Thyroid Gland
Pyramidal Lobe
Right Lobe
Isthmus
Left Lobe
Trachea
Adapted from Corel Draw 9

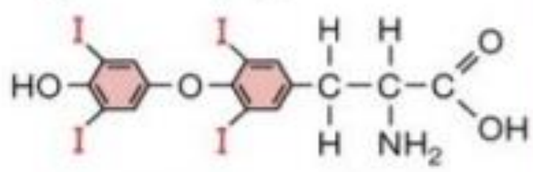
THYROID HORMONES:

- There are two biologically active thyroid hormones:
  - Tetraiodothyronine(T4; usually called thyroxine)
  - Triiodothyronine (T3)
- Derived from modification of tyrosine(amino acid).

Tyrosine

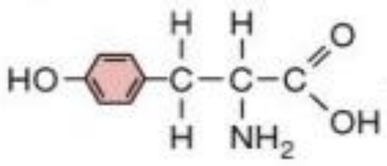


Thyroxine (T_4)

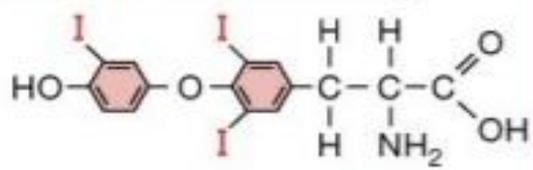


(2 tyrosine + 4 I)

Tyrosine



Triiodothyronine (T_3)



(2 tyrosine + 3 I)

MAJOR SOURCES OF IODINE:

- Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- Thus, adequate iodine intake either through diet or water is required for normal thyroid hormone production.
- Major sources of iodine are:
  - iodized salt
  - iodated bread
  - dairy products
  - shellfish
- Minimum requirement(RDA): 75 micrograms/day
- US intake: 200 - 500 micrograms/day

IODINE METABOLISM

- Dietary iodine is absorbed in the GI tract, then taken up by the thyroid gland (or removed from the body by the kidneys).
- About 80% of the iodine is lost in urine where as only 20 % is taken up by the Thyroid follicular cells.
- The transport of iodide into follicular cells is dependent upon a Na^{+}/I^{-} co-transport system.
- Iodide taken up by the thyroid gland is oxidized by peroxide in the lumen of the follicle:

$$I^{-} \xrightarrow{\text{Peroxidase}} I^{+}$$

- Oxidized iodine can then be used in production of thyroid hormones.

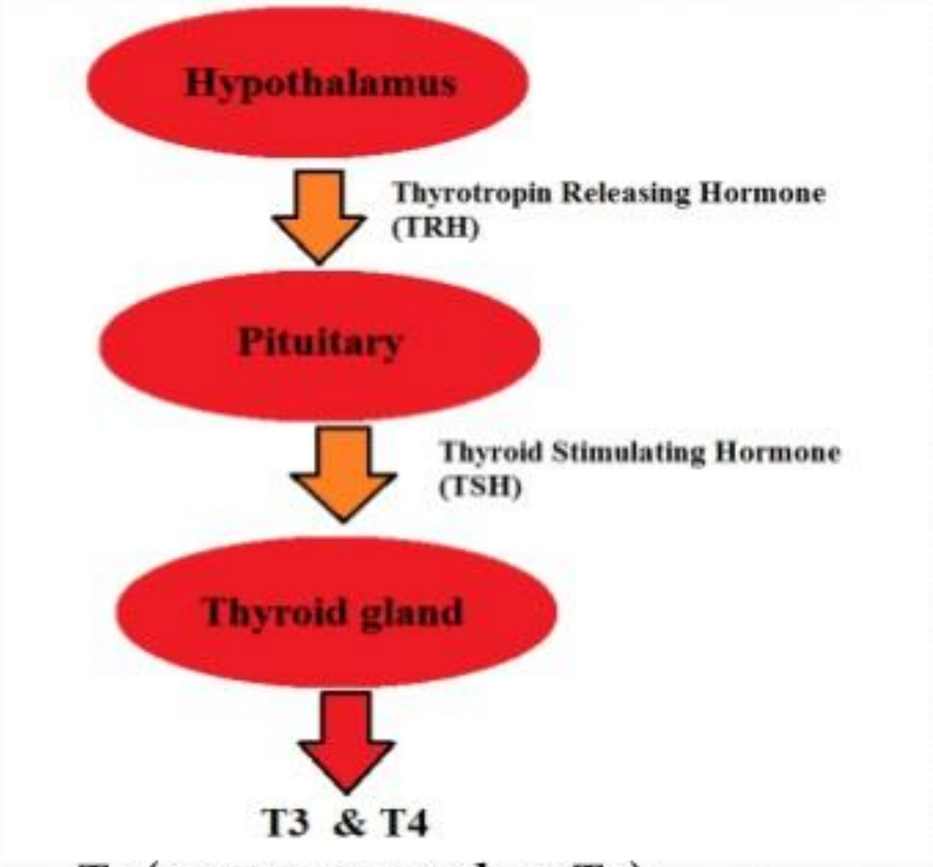
CONVERSION OF T4 TO T3

- T3 has much greater biological activity than T4.
- A large amount of T4 (25%) is converted to T3 in peripheral tissues.
- This conversion takes place mainly in the liver and kidneys. The T3 formed is then released to the blood stream.
- In addition to T3, an equal amount of "Reverse T3" may also be formed. This has no biological activity.

T3 ⟶ MIT + DIT

Reverse T3 ⟶ DIT + MIT

Regulation of thyroid hormone release



T3 (more potent than T4)

Mechanism of thyroid hormone secretion

1. Thyroglobulin synthesis
2. Iodide trapping
3. Oxidation of Iodide
4. Transport of Iodine
5. Iodination of Tyrosine
6. Coupling reactions

- **Thyroglobulin synthesis**:

  Endoplasmic reticulum and golgi bodies of follicular cells synthesize thyroglobulin and are secreted to the follicular cavity. Thyroglobulin contain tyrosine.

- **Iodide trapping:**

  Iodide from blood is transported to follicular cells by sodium-iodide symport, also called iodide pump.

- **Oxidation of iodide:**

  Iodide is oxidized to iodine in follicular cell in presence of enzyme thyroid peroxidase.

- **Transport of iodine**:

  Iodine is transported to follicular cavity by iodine-chloride pump, also called pendrin.

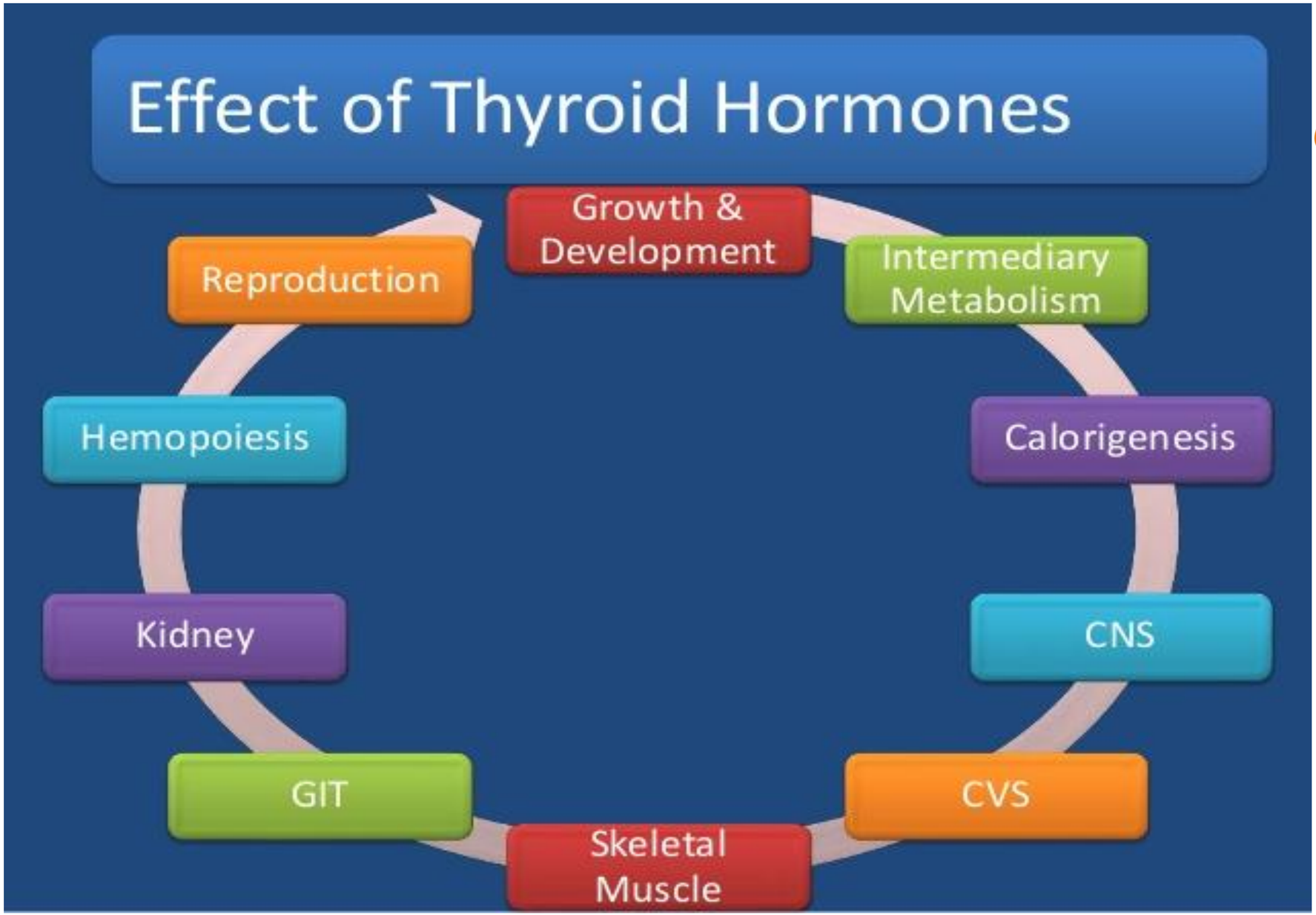
- **Iodination of tyrosine**:

  Iodine combines with tyrosine present in thyroglobulin in presence of enzyme iodinase to form MIT and DIT. This step is also known as organification of thyroglobulin.

- **Coupling reaction**:

  MIT+DIT= T_3 (more potent than T_4)

  DIT+DIT= T_4


Effect of Thyroid Hormones
Growth & Development
Reproduction
Intermediary Metabolism
Hemopoiesis
Calorigenesis
Kidney
CNS
GIT
CVS
Skeletal Muscle

Growth and development :

- Essential
- Exerted through the protein synthesis by translation of genetic code
- Cretinism in children and adults also impaired intelligence
- Affects nervous system

- On GIT:
  - ↑ appetite & food intake.
  - ↑ motility of GIT → diarrhea often result in hyperthyroidism

- On CVS:
  - Direct action on contractile elements and upregulation of beta receptors
  - Hyperdynamic circulation- due to demand and direct cardiac effect
  - ↑cardiac output, HR, contractility
  - Angina, AF, CHF, systolic BP increases

- On nervous system:
  - excitable effect.
  - Has role on development of brain in fetal & 1st few weeks of postnatal life

- Muscle weakness due to protein catabolism

- Haemopoiesis:

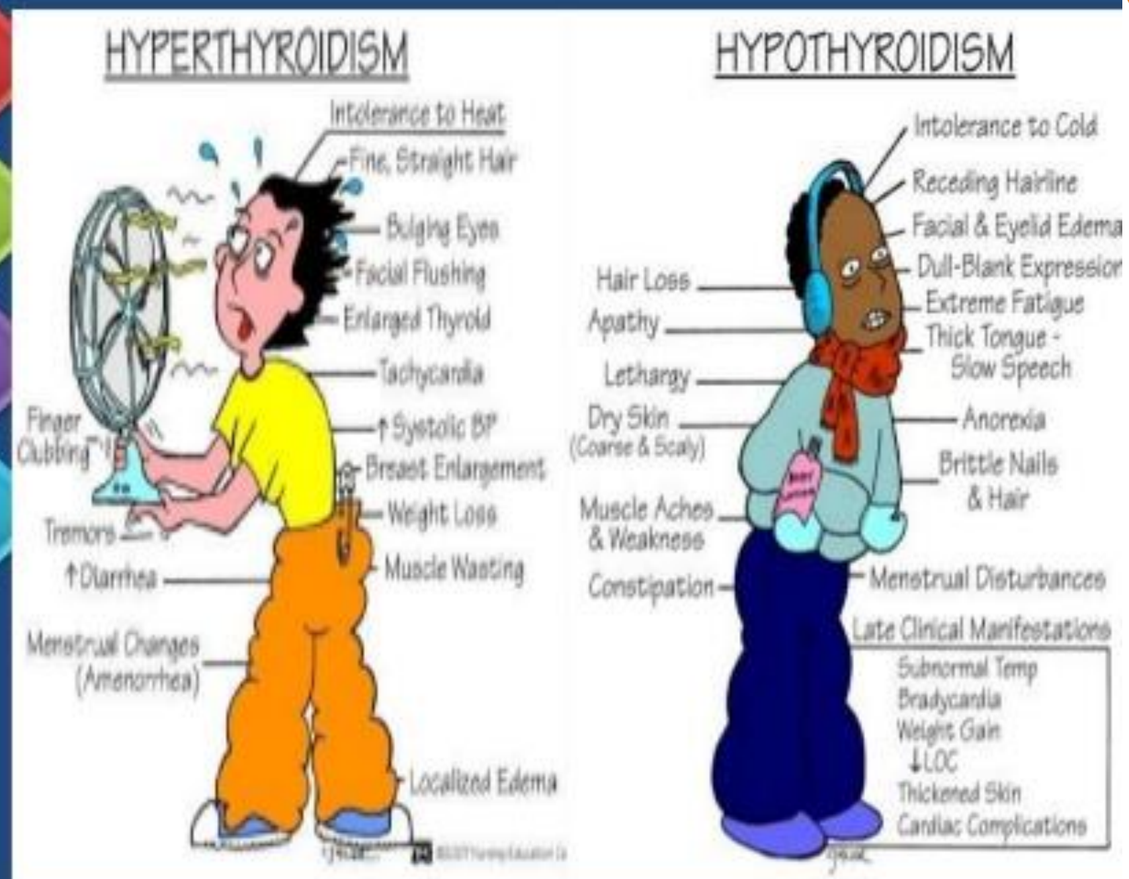
Anaemia in hypothyroidism

- Reproduction:

Indirect effect on reproduction

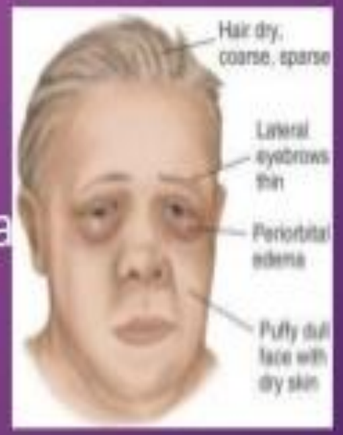
Thyroid Disorders

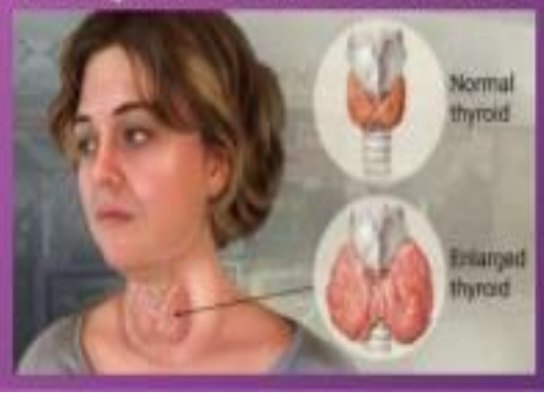
- Cretinism
- Hyperthyroidism
- Hypothyroidism
- Euthyroid Goiter



HYPOTHYROIDISM

- Hypothyroidism in early childhood and in the foetal stage results in Cretinism.
- The children become dwarf and are mentally retarded.
- Hypothyroidism in adults results in Myxedema. There is edema and puffiness in the face.
- Goitre or enlargement of the thyroid gland can occur due to deficiency of iodine in the diet.

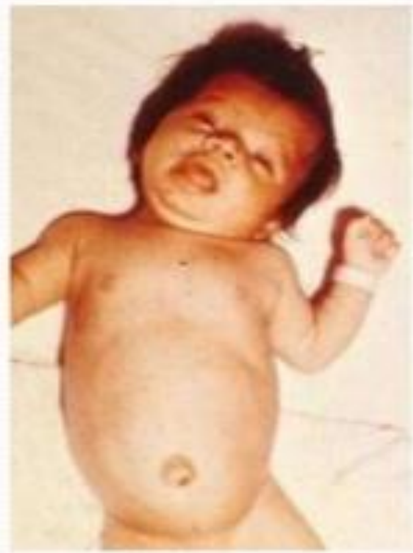




Disease related to hypothyroidism:

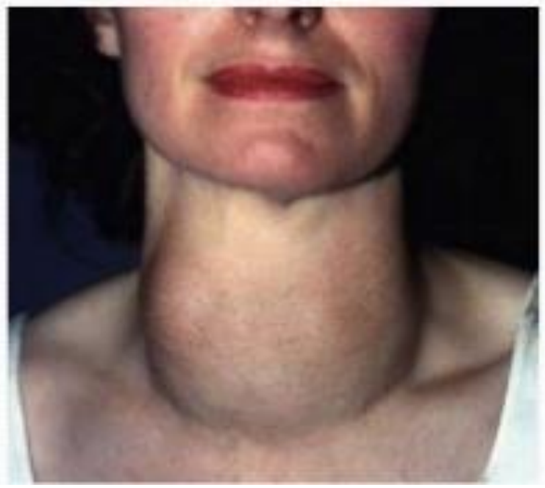
1. Cretinism:

- → Congenital disease
- → Occurs in child
- → Physical and mental growth is retarded
- → due to hypothyroidism



2. Simple goitre:

- → Enlargement of thyroid gland due to lower secretion of iodine containing thyroid hormone.
- → Can be treated by iodine intake.



3. Myxoedema/ Gull's disease:

→ Occurs in adults

→ Due to deficiency of thyroid secretion

→ Charecterized by bradycardia, decreased pulse, blood pressure, less resistant to cold.

4. Hashimoto's disease:

→ Auto-immune disease

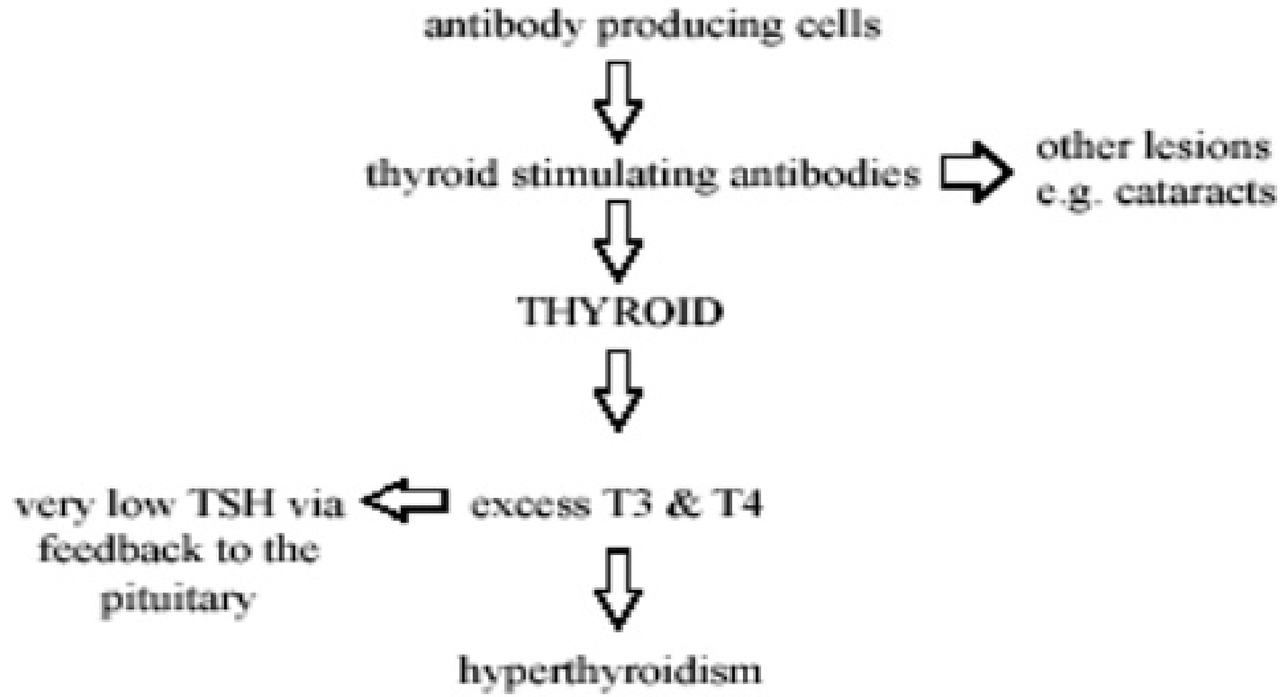
→ Thyroid gland is attacked by cell and antibody mediated immune response and results in decreased thyroid hormone secretion.

→ Charecterized by weight loss, thinning of hair, fatigue, slow heart rate, fall in blood presssure, depression.

HYPERTHYROIDISM

- Hyperthyroidism results in Grave's disease. There is enlargement of the gland and edema behind the eyes and the eyes protrude. This is Exophthalmic goitre.

GRAVE'S DISEASE



ANTI- THYROID DRUGS

- These are drugs used to lower the functional capacity of the hyperactive thyroid gland.

- Thyrotoxicosis is due to excessive secretion of thyroid hormones. Graves' disease(Autoimmune disorder) and toxic nodular goiter are two main causes.

Classification of Antithyroid Drugs

Inhibitor of hormone synthesis

- Carbimazole
- Methimazole
- Propylthiouracil

Inhibitor of hormone release

- Iodine
- Iodides of Na, k
- Organic iodides

Radioactive iodine

- ^{131}I (Radioactive iodine)

Ionic inhibitors

- Thiocynate(-SCN)
- Perchlorates($-ClO_4$)
- Nitrates(NO_3)

Inhibitor of hormone synthesis

- Methimazole (carbimazole)
- Propyl thiouracil (PTU)

✓ These 2 are the major drugs used in the treatment of thyrotoxicosis (Carbimazoles converted to methimazole in vivo).

MOA: These drug inhibit thyroid hormone production by

a) inhibiting thyroid peroxidase which is required in intrathyroidal oxidation of Iodide.

b) by inhibiting the iodination of tyrosine

c) by inhibiting coupling of MIT and DIT to form thyroid hormones

d) propylthiouracil also inhibits peripheral conversion of T_4 TO T_3 by inhibiting DID -1 enzyme

IODIDE SALTS AND IODINE:

- Iodide salts inhibit organification (iodination of tyrosine) and thyroid hormone release.
- These salts also decrease the size & vascularity of the hyperplastic thyroid gland.
- Since iodide salts inhibit the release as well as the synthesis of the hormone, their onset of action occurs rapidly within 2-7 days.
- This effect is transient because the thyroid gland escapes from iodide block after several weeks of treatment.

Radioactive iodine:

- Radioactive iodine (Mol. Mass 131) is readily absorbed in thyroid gland.
- This iodine undergoes disintegration along with emission of beta rays.
- These rays causes destruction of thyroid parenchyma without endangering other tissues.
- Produce permanent cure in thyrotoxicosis without surgery.
- Shouldn't be given to pregnant and nursing mothers because it crosses placental barriers and ejected in breast milk.

Ionic inhibitors

- Certain monovalent anions inhibit iodide trapping by NIS into thyroid because of similar hydrates ionic size.

- T4 ,T3 synthesized is inhibited.

- They are very toxic so they are not used.
- eg: Thiocyanates, Perchlorates

Anion inhibitors

- Includes:

→Thiocyante

→ Perchlorate

- Competitively blocks iodide pump and prevents uptake of iodide from blood to follicular cells.

Miscellaneous drugs:

- Includes:

→Beta blockers like Propanolol

→Anti-arrythmic drug like Amiodarone

→Iodinated contrast media like Ipodate, Diatrozate

- They all prevent de-ionization of T_4 to T_3.

- β-blockers are used in hyperthyroidism in following situations:

a) while awaitng response to propylthiouracil/carbimazole

b) along with iodide for preoperative preparation before subtotal thyroidectomy

c) thyrotoxic crisis

- Propranolol 1-2mg slow I.V may be followed by 40-80 mg oral every 6 hrly.

THANK YOU