Thyroid Gland

Part - I

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For UG Students

Thyroid Gland

- Thyroid gland is a unique gland as its' only tissue in the body, which is able to **accumulate iodine in great quantities and combine it in to a hormone.**
- Located immediately below the larynx on either side and anterior to trachea.
- Composed of large number of follicles, filled with secretary substance called colloid and lined with the cuboidal epithelial cells that secrete into the interior of the follicles.

Thyroid Gland ----

- **Major constituent of the colloid is the large quantities of glycoprotein thyroglobulin, which contains the thyroid hormones with in its molecules.**
- **Once the secretions has entered the follicles, it must be absorbed back through the follicular epithelium in to the blood before it can function in the body.**
- **Thyroid gland has blood flow about five times the weight of the gland each minute, which makes it maximum vascularized area, with exception to adrenal cortex.**

Iodine requirement for formation of thyroxine

- Approximately 50 mg of ingested iodine is required

  OR

- 1 mg/week in human beings for formation of optimum quantity of thyroxine.
- The main function of the thyroid gland is to accumulate iodine (I_2) and cause its attachment to tyrosine in order to form thyroid hormones.

Iodine metabolism

- The main function of the thyroid gland is to accumulate I_2 and cause its attachment to tyrosine in order to form the thyroid hormones.
- This process takes place under influence of TSH.
- The use of ^{131}I has helped in further investigating iodine metabolism. As ^{131}I has half life of 8 days and emits gamma radiation, which can be monitored externally.

Iodine Pump

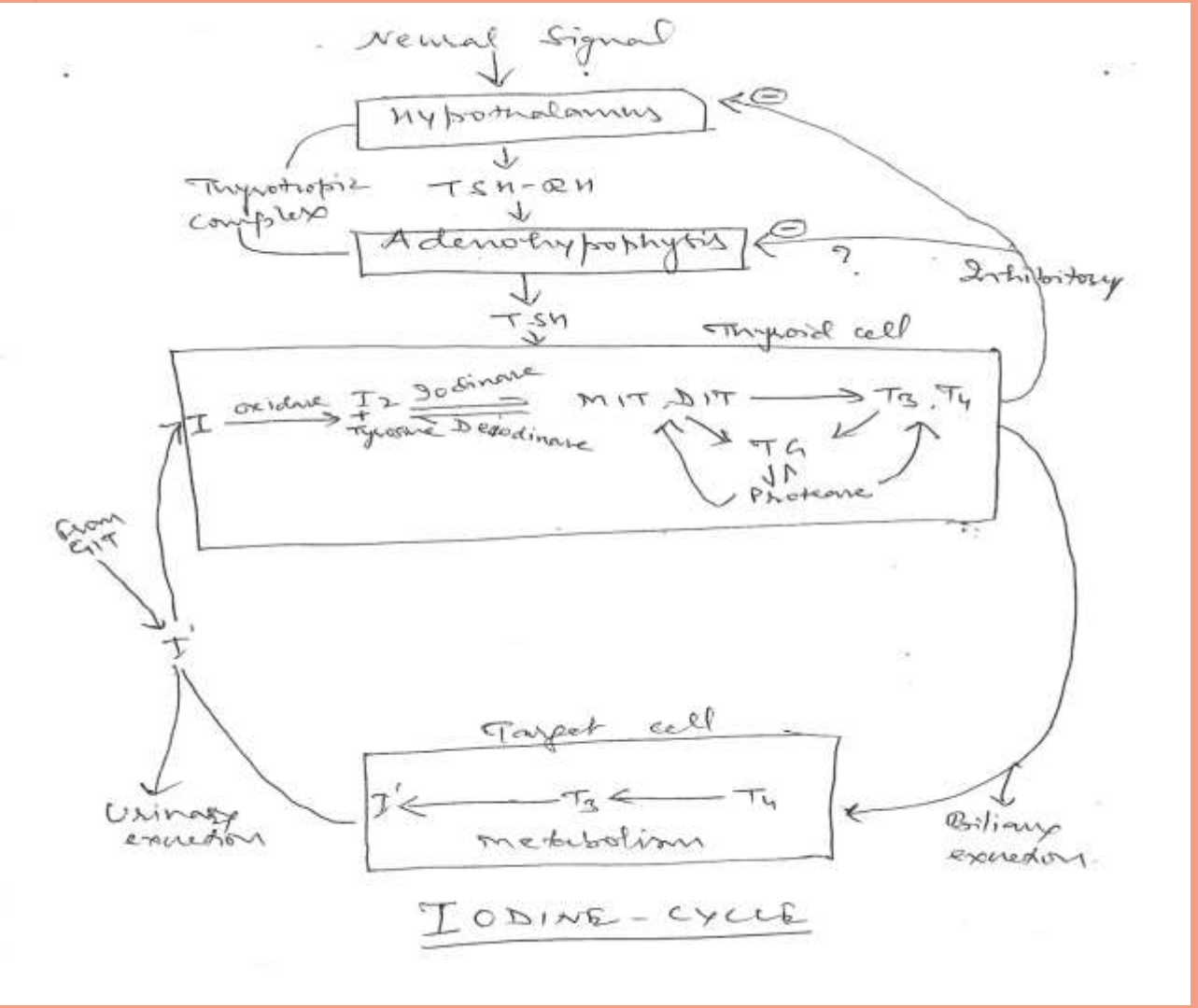
- The concentration of inorganic iodine (I^-) is ordinarily very low in plasma but is transported to thyroid gland against concentration gradient, to the ratio of 20:1 in normal animals
- And after TSH stimulation the concentration with in the thyroid gland may be 300 to 500 times that of plasma.
- Accumulation of iodine in the thyroid gland is called as trapping of iodine. The ability of the thyroid gland to trap iodine may be increased 10 to 20 times by maintaining the animal on iodine fee diet, that helps the animal to overcome the iodine deficiency.

cont……..

Iodine Pump…..

- Whereas administration of **excess of iodine will depress the iodine trapping** and similarly certain anti thyroidal drugs can inhibit the iodination of tyrosine thus inhibit the iodine trapping.
- The animal body contains only **one part of iodine to 3 million pasts of body weight,** hence its referred as trace mineral. Most of iodine is concentrated inthyroid gland and remaining in circulation as thyroxine.

Iodine Cycle



Biosynthesis of thyroglobulin (TG)

- Thyroglobulin is an iodine containing glycoprotein with molecular weight of 6,70,000.
- Molecule contains about 5800 amino acids residues plus about 350 carbohydrate residues.
- In addition thyroglobulin contains four types of iodoamino acids

  3-monoiodotyrosine,

  3,5 diiodotyrosine

  3, 5 , 3' triiodothyronine (T_3)

  tetraiodothyronine (T_4).

Biosynthesis of thyroglobulin (TG) …….

- TG is synthesized from endoplasmic reticulum and golgi apparatus.
- Synthesis of thyroglobulin is a complex process, which involves first the building of protein portion of TG.
- This consist of amino acids entering the basal end of the thyroid cell, where they assembled into polypeptide chains on the endoplasmic reticulum.

Biosynthesis of thyroglobulin (TG) .....

- From there the protein migrates to the apical portion of the cell, while CHO moieties are added by ER and gogli apparatus.
- At the apical end of the thyroid cell, the iodination of the tyrosyl group of thyroglobulin molecule occurs.
- Thyroglobulin acts as substrate for iodination reaction, which first leads to formation of MIT, then DIT followed by coupling of MIT and DIT or DIT and DIT, with in the thyroglobulin molecule.

THYROID HORMONE TRANSPORT

- Protease in the follicle cells acts to break the T4 and T3 from thyroglobulin complex stored in the follicular colloid cells.
- Hormones then moves through the cells, enters the blood stream and quickly bound by serum proteins (TBG).
- Proteins to which it is bound and the degree of binding vary from species to species.
- In cattle, swine, sheep and equines it is bound primarily to the a – globulin. Variation in activity of T3 as compared to thyroxine appears to be dependent on the strength of union between the respective hormones and plasma proteins.

THYROID HORMONE TRANSPORT……

- Only the free hormones are able to diffuse into cell and exert its effect.
- Strength of binding interferes with passage of the hormone to the site of the tissue activity, thereby determining, which hormone is more effective in a particular species. Ex. T_3 is more active in rats than T_4, as TBG is more than T_3.
- Determination of PBI in blood is used as test for amount of circulating T_3 and T_4, which reflect thyroid gland activity, however with advent of RIA, PBI estimation has become obsolete.

Mode of action of thyroxine

- Not well understood.
- important effect of T4 is stimulation of oxygen utilization, hence its also related with increased BMR.
- causes increase in mitochondria per unit body tissue, thus more metabolic activity per cell in the body.
- In addition thyroxine is known to cause an increased permeability of mitochondrial membranes (by causing swelling) which facilitates certain phosphorylation reactions.
- Receptors for thyroid hormones are on chromatin material of cell nucleus, where as for steroid hormones its cytoplasm.

Control/regulation of thyroid functions

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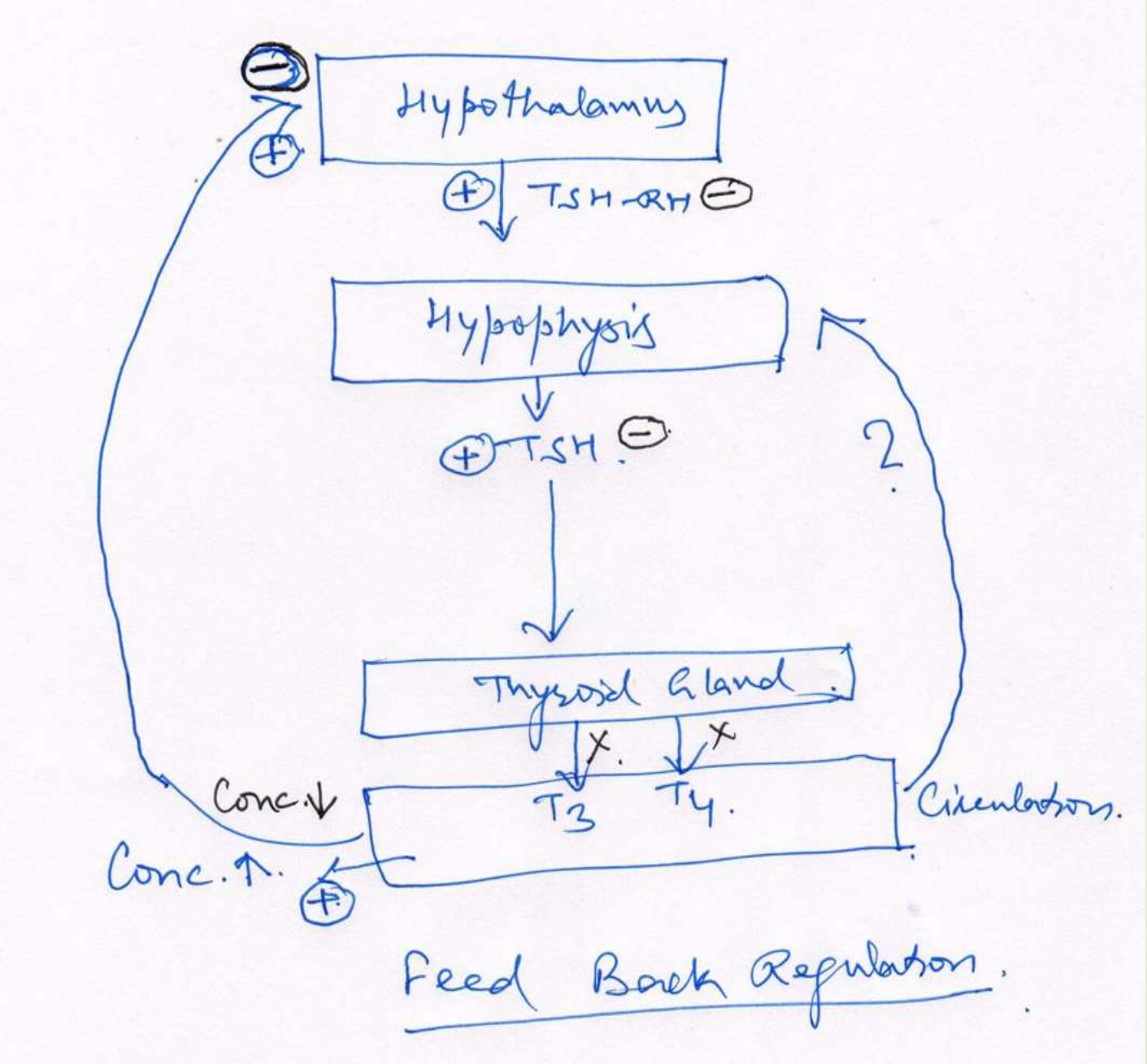
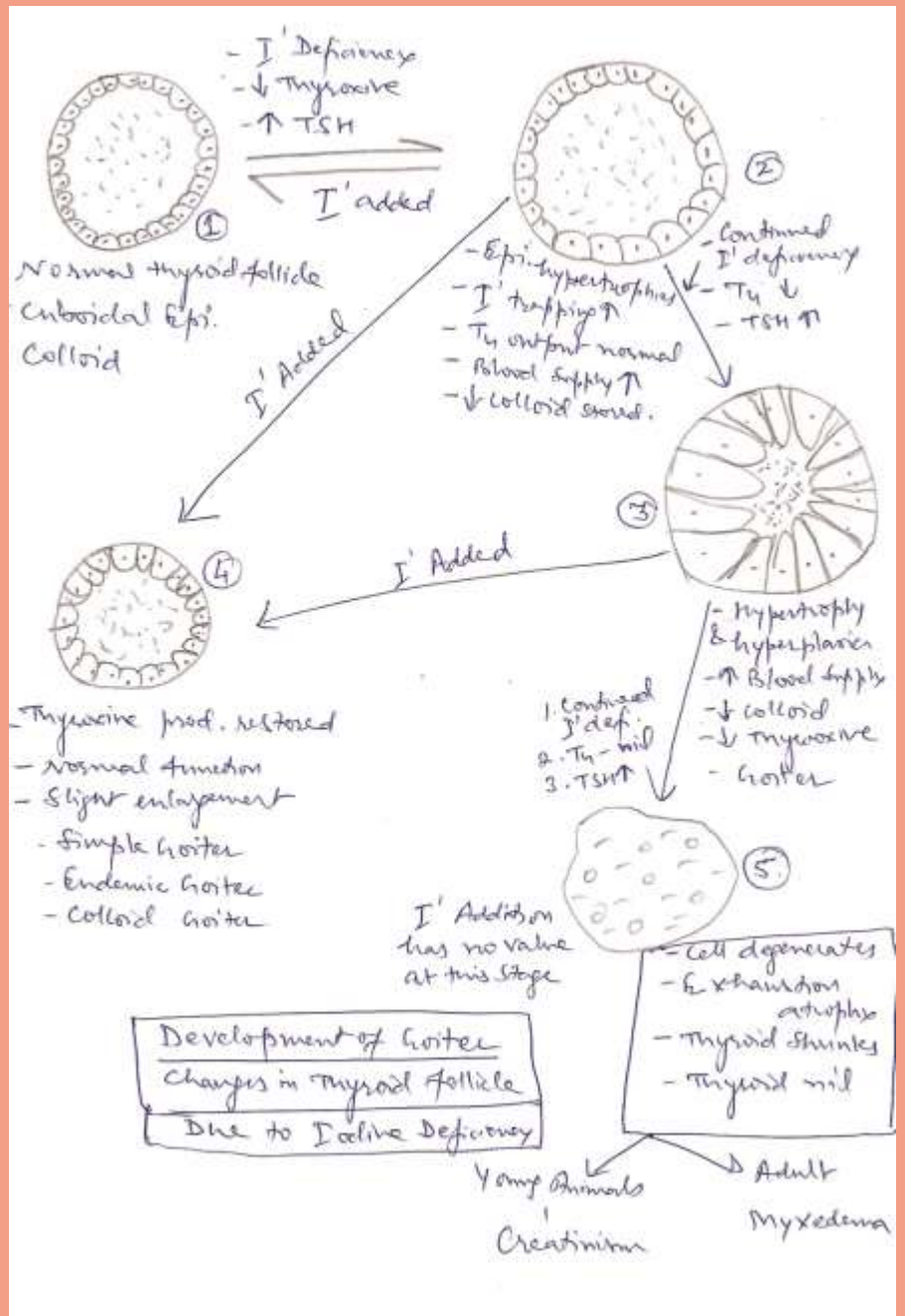

Hypothalamus
TSH-RH
Hypophysis
TSH
2
Thyroid Gland
X
X
Conc.↓
T3
T4.
Circulation.
Conc.↑.
Feed Back Regulation.

Goitre


- I' Deficiency
- ↓ Thyroxine
- ↑ TSH
I' added
1
Normal thyroid follicle
Cuboidal Epi.
Colloid
2
- Epi. hypertrophies
- I' trapping ↑
- T4 output normal
- Blood supply ↑
- ↓ colloid stored.
- Continued I' deficiency
- T4 ↓
- TSH ↑
I' Added
3
- Hypertrophy & hyperplasia
- ↑ Blood supply
- ↓ colloid
- ↓ Thyroxine
- Goiter
I' Added
4
Thyroxine prod. restored
- Normal function
- Slight enlargement
- Simple Goiter
- Endemic Goiter
- Colloid Goiter
1. Continued I' def.
2. T4 - mild
3. TSH ↑
5
I' Addition has no value at this stage
- Cell degenerates
- & exhaustion atrophies
- Thyroid shrinks
- Thyroid mild
Development of Goiter
Changes in Thyroid follicle
Due to Iodine Deficiency
Young Animals
Cretinism
Adult
Myxedema

Functions of thyroid hormones

- Molting
- Hibernation
- Growth
- Reproduction and lactation

Thyroid Dysfunctions

- **Hypothyroidism :** It means lower functioning of thyroid leading to decrease in circulating thyroid hormones T_4 and/or T_3. This could lead to at least 3 deficiencies/diseases:
- - Iodine deficiency
- - Primary Hypothyroidism
- - Secondary Hypothyroidism

Primary Hypothyroidism

- Decreased Secretion of thyroid hormones due to malfunctioning of the gland.
- Several factors like thyroiditis, neoplasms that destroy the follicle cells or alterations in biochemical mechanism involved in formation of T_4.
- **Clinical signs of primary hypothyroidism in dogs are inactiveness, sleepy, lack of vigour, seek warm places and may gain weight if appetite is good and thickening of skin particularly in face region is there.**
- Reproductive dysfunctions are also observed.

Treatment of hypothyroidism

-Desicated thyroid

-Thyroglobulin

- T_4 (Synthroid)

- T_3 Sodium leothyronine (Cytobin)

@ 0.2 to 0.3 mg for 10-15 Kg for dog.

Effects are seen with in a week or so.

Secondary Hypothyroidism

- It is relatively rare in domestic animals. It is caused by hypothalamic or pituitary defect leading to release of insufficient TSH-RH or TSH, resulting in low production or lack of stimulation of thyroid follicles.
- Usually it is due to tumors of adenohypophysis. Symptoms are dwarfism, which can be diagnosed with TSH response test and treated with thyroid preparations.

Hyperthyroidism

- It is less common in domestic animals, in comparison to hypothyroidism. Its due to overproduction of TSH due to pituitary tumors excess production of thyroxine due to thyroid gland tumors.
- In dogs mostly primary hypothyroidism is due to malignant tumors and treatment is not so successful.

- Clinical signs are : weight loss, Polyphagia, muscle weakness, fatigue, nervousness, heat tolerance and polyurea.

Compounds/Goitrogens

- Defined as those, which interferes with basal metabolic rate by altering the synthesis release or peripheral action of thyroid hormone. Cabbage contain goitrogens.
- Other anti thyroid drugs are : thiourea, thiouracil and their derivatives.

Classification of antithyroid drugs according to their mode of action is

- **Drugs inhibit iodide trapping :**
  - **Thiocynates (Raw soybeans & cabbage)**
  - **Perclorates.**
- **Inhibition of T_4 synthesis**
  - **Thiouracil**
  - **Propylthiouracil**
  - **Methy thiouracil**
  - **Thiourea**
  - **Methimazole**

- Destruction of thyroid tissue

  ^{131}I in large doses

- Mode of action unknown

  Iodine is much higher doses than required

Thyroid function tests

- **BMR** : O_2 consumption – not practical in animals.
- **^{131}I uptake** : method and external monitoring.
- **PBI reflects** T_3 & T_4 levels in circulation. But is subject to take reports due to dietary iodine etc.
- **T_3,T_4** : RIA, ELISA etc.
- **TSH Response test** : It consist of administration of 10 units of TSH (Dermathycin) and measuring T_4 at 0 & 10 hrs after TSH injection. In normal dog T_4 level doubles to resting stage. If T_4 at 10 hrs is less than double then dog is suffering from secondary hypothyroidism.
- **Cholesterol level is elevated** above 300 mg/dl in many hypothyroid dogs, but still diet can also cause elevation.
- Thyroid biopsy

Thanks