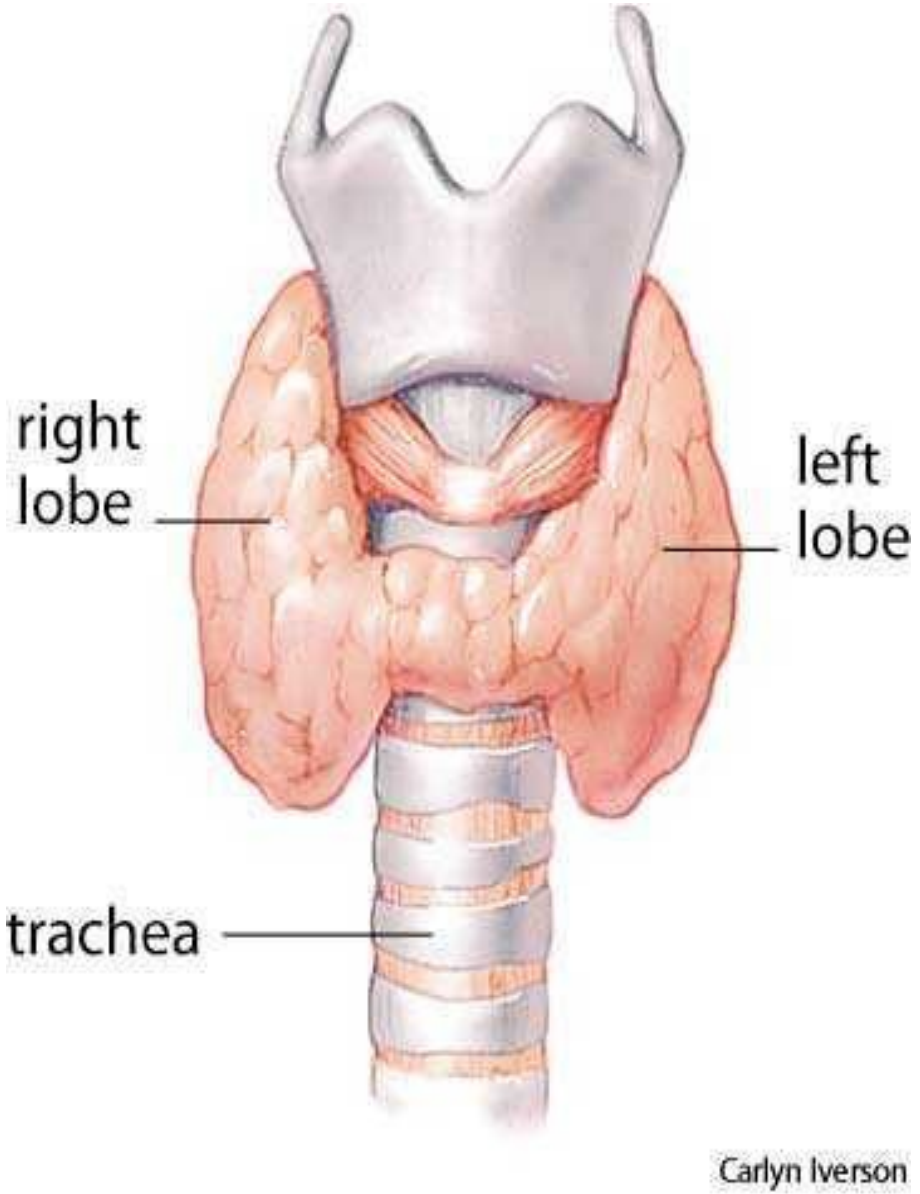
THYROID GLAND

By Dr. Dinesh Chouhan

INTRODUCTION

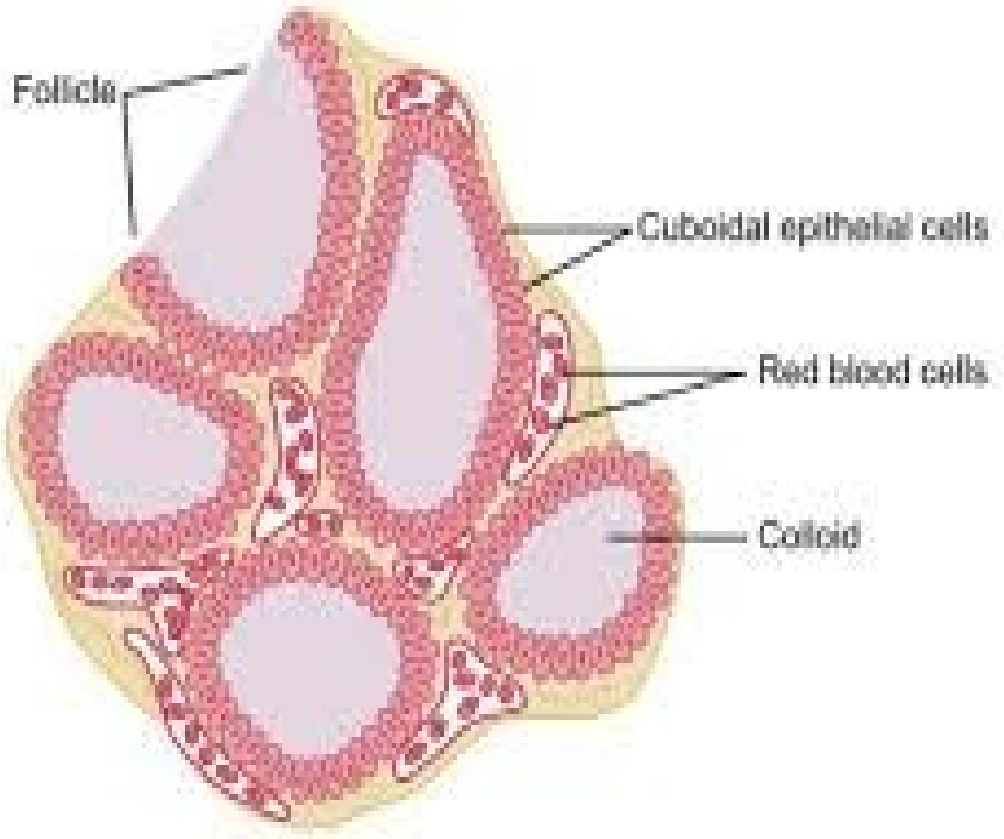
- Thyroid is an endocrine gland situated at the root of the neck on either side of the trachea.
- It has two lobes, which are connected in the middle by an isthmus.
- weighs about 20 to 40 g in adults.



- Thyroid is larger in females than in males during menstruation and pregnancy.
- The structure and the function of the thyroid gland change in different stages of the sexual cycle in females.
- Its function increases slightly during pregnancy and lactation and decreases during menopause.

HISTOLOGY

- Thyroid gland is composed of large number of closed follicles.
- These follicles are lined with cuboidal epithelial cells, called the follicular cells.
- Follicular cells secrete tetraiodothyronine (T4 or thyroxine) and tri-iodothyronine (T3).
- In between the follicles, the parafollicular cells are present. These cells secrete calcitonin.



HORMONES OF THYROID GLAND

Thyroid gland secretes three hormones:

1. **Tetraiodothyronine or T4 (thyroxine)**
2. **Tri-iodothyronine or T3**
3. **Calcitonin.**

- T4 is otherwise known as thyroxine and it forms about 90% of the total secretion, whereas T3 is only 9% to 10%.

CHEMISTRY

- Both T4 and T3 are iodine-containing derivatives of amino acid tyrosine.

POTENCY AND DURATION OF ACTION

- The potency of T3 is four times more than that of T4.
- T4 acts for longer period than T3.
- Duration of T4 action is four times more than T3 action.
- T3 has less affinity for plasma proteins and combines loosely with them, so that it is released quickly.
- T4 has more affinity and strongly binds with plasma proteins, so that it is released slowly.
- Therefore, T3 acts on the target cells immediately and T4 acts slowly.

HALF-LIFE

- Thyroid hormones have long half-life. T4 has a long halflife of 7 days. Half-life of T3 is varying between 10 and 24 hours.

RATE OF SECRETION

- Thyroxine = 80 to 90 µg/day
- Tri-iodothyronine = 4 to 5 µg/day

Plasma Level:

- Total T3 = 0.12 µg/dL
- Total T4 = 8 µg/dL

METABOLISM OF THYROID HORMONES

- Degradation of thyroid hormones occurs in muscles, liver and kidney.

SYNTHESIS OF THYROID HORMONES

- Synthesis of thyroid hormones takes place in thyroglobulin, present in follicular cavity.
- Iodine and tyrosine are essential for the formation of thyroid hormones.
- Iodine is consumed through diet. It is converted into iodide and absorbed from GI tract.
- Tyrosine is also consumed through diet and is absorbed from the GI tract.
- For the synthesis of normal quantities of thyroid hormones, approximately 1 mg of iodine is required per week or about 50 mg per year.
- To prevent iodine deficiency, common table salt is iodized with one part of sodium iodide to every 100,000 parts of sodium chloride.

STAGES OF SYNTHESIS OF THYROID HORMONES

Synthesis of thyroid hormones occurs in six stages:

1. Thyroglobulin synthesis
2. Iodide trapping
3. Oxidation of iodide
4. Transport of iodine into follicular cavity
5. Iodination of tyrosine
6. Coupling reactions

1. Thyroglobulin Synthesis

- Endoplasmic reticulum and Golgi apparatus in the follicular cells synthesize and secrete thyroglobulin continuously.
- After synthesis, thyroglobulin is stored in the follicle.

2. Iodide Trapping

- Iodide is actively transported from blood into follicular cell, against electrochemical gradient, this process is called iodide trapping.
- Iodide is transported into the follicular cell along with sodium by sodium-iodide symport pump, which is also called iodide pump. Normally, iodide is 30 times more concentrated in the thyroid gland than in the blood.

3. Oxidation of Iodide

- Iodide must be oxidized to elementary iodine, because only iodine is capable of combining with tyrosine to form thyroid hormones.
- The oxidation of iodide into iodine occurs inside the follicular cells in the presence of thyroid peroxidase. Absence or inactivity of this enzyme stops the synthesis of thyroid hormones.

4. Transport of Iodine into Follicular Cavity

- From the follicular cells, iodine is transported into the follicular cavity by an iodide-chloride pump called pendrin.

5. Iodination of Tyrosine

- Combination of iodine with tyrosine is known as iodination.
- It takes place in thyroglobulin.
- First, iodine is transported from follicular cells into the follicular cavity, where it binds with thyroglobulin, this process is called organification of thyroglobulin.
- Then, iodine (I) combines with tyrosine, which is already present in thyroglobulin. Iodination process is accelerated by the enzyme iodinase, which is secreted by follicular cells.
- Iodination of tyrosine occurs in several stages.
- Tyrosine is iodized first into monoiodotyrosine (MIT) and later into di-iodotyrosine (DIT). MIT and DIT are called the iodotyrosine residues.

6. Coupling Reactions

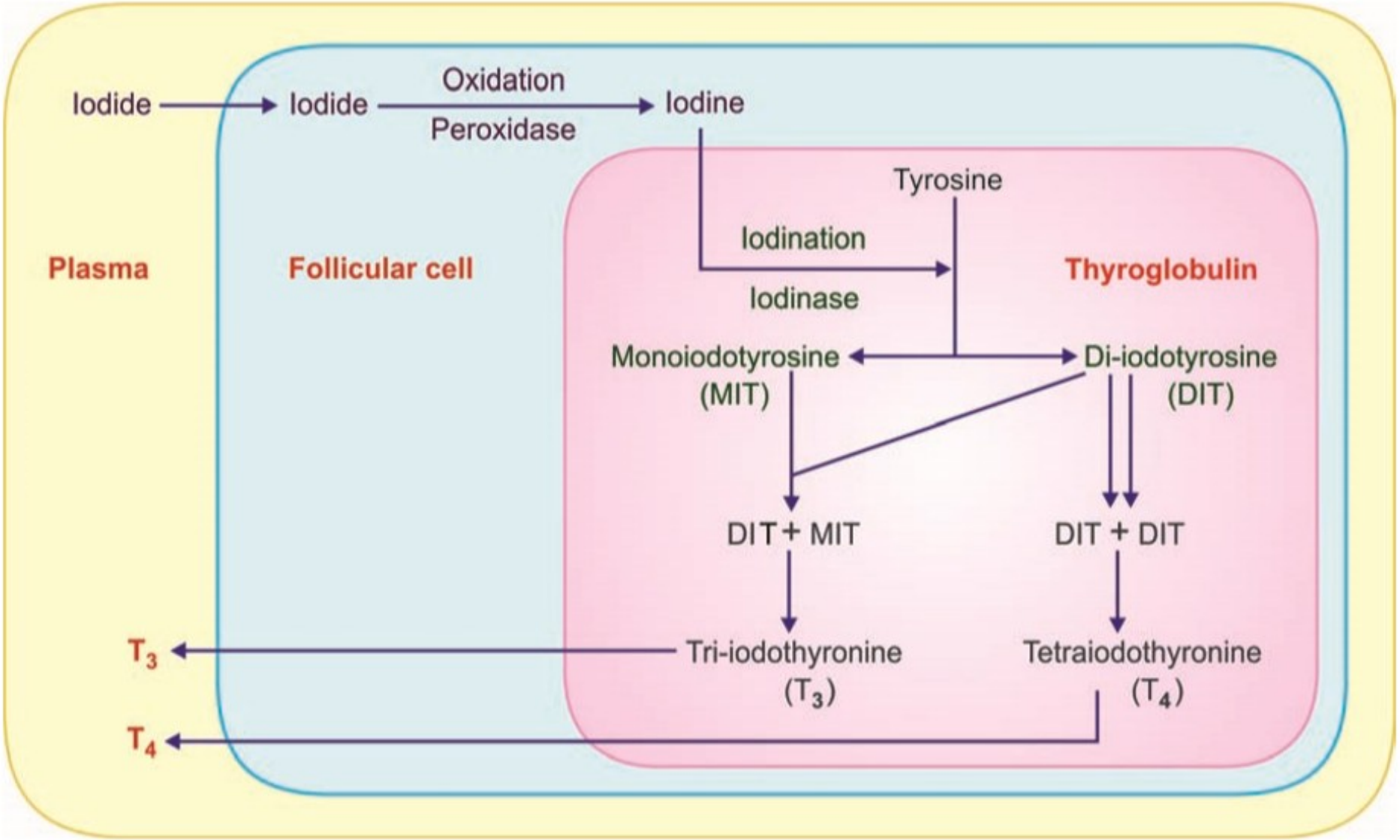
- Iodotyrosine residues get coupled with one another.
- The coupling occurs in different configurations, to give rise to different thyroid hormones.

- Tyrosine + I = Monoiodotyrosine (MIT)
- MIT + I = Di-iodotyrosine (DIT)
- DIT + MIT = Tri-iodothyronine (T3)
- MIT + DIT = Reverse T3
- DIT + DIT = Tetraiodothyronine or Thyroxine (T4)

STORAGE OF THYROID HORMONES

- After synthesis, the thyroid hormones remain in the form of vesicles within thyroglobulin and are stored for long period.
- The thyroid hormones can be stored for several months.
- Thyroid gland is unique in this, as it is the only endocrine gland that can store its hormones for a long period of about 4 months. So, when the synthesis of thyroid hormone stops, the signs and symptoms of deficiency do not appear for about 4 months.

SYNTHESIS OF THYROID HORMONES



TRANSPORT OF THYROID HORMONES IN THE BLOOD

Thyroid hormones are transported in the blood by three types of proteins:

1. Thyroxine-binding globulin (TBG)

- It has a great affinity for thyroxine and about one third of the hormone combines strongly with this protein.

2. Thyroxine-binding prealbumin (TBPA)

- Transports one fourth of the thyroid hormones. It is also called transthyretin (TTR).

3. Albumin

- Transports about one tenth of the thyroid hormones.

FUNCTIONS OF THYROID HORMONES

ACTION ON BASAL METABOLIC RATE (BMR)

- Thyroxine increases the metabolic activities in most of the body tissues, except brain, retina, spleen, testes and lungs.
- It increases BMR by increasing the oxygen consumption of the tissues.
- In hyperthyroidism, BMR increases by about 60% to 100% above the normal level and in hypothyroidism it falls by 20% to 40% below the normal level.

ACTION ON PROTEIN METABOLISM

- Thyroid hormone increases the synthesis of proteins in the cells.
- The protein synthesis is accelerated by the following ways:
  i. By Increasing the Translation of RNA
  ii. By Increasing the Transcription of DNA to RNA
  iii. By Increasing the Activity of Mitochondria In addition to acting at nucleus
  iv. By Increasing the Activity of Cellular Enzymes

ACTION ON CARBOHYDRATE METABOLISM

- Thyroxine stimulates almost all processes involved in the metabolism of carbohydrate.
  i. Increases the absorption of glucose from GI tract
  ii. Enhances the glucose uptake by the cells, by accelerating the transport of glucose through the cell membrane
  iii. Increases the breakdown of glycogen into glucose
  iv. Accelerates gluconeogenesis.

ACTION ON FAT METABOLISM

- Thyroxine decreases the fat storage by mobilizing it from adipose tissues and fat depots.
- The mobilized fat is converted into free fatty acid and transported by blood.
- Thus, thyroxine increases the free fatty acid level in blood.

ACTION ON VITAMIN METABOLISM

- Thyroxine increases the formation of many enzymes.
- Since vitamins form essential parts of the enzymes.
- Hence, vitamin deficiency is possible during hypersecretion of thyroxine.

ACTION ON BODY TEMPERATURE

- Thyroid hormone increases the heat production in the body,
- by accelerating various cellular metabolic processes and increasing BMR.
- It is called thyroid hormone induced thermogenesis.
- During hypersecretion of thyroxine, the body temperature increases greatly, resulting in excess sweating.

ACTION ON GROWTH

- Thyroid hormones have general and specific effects on growth.
- Increase in thyroxine secretion accelerates the growth of the body, especially in growing children. Lack of thyroxine arrests the growth.
- Thyroxine is more important to promote growth and development of brain during fetal life and first few years of postnatal life.
- Deficiency of thyroid hormones during this period leads to mental retardation.

ACTION 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.

ACTION ON BLOOD

- Thyroxine accelerates erythropoietic activity and increases blood volume.
- It is one of the important general factors necessary for erythropoiesis.
- Polycythemia is common in hyperthyroidism.

ACTION ON GASTROINTESTINAL TRACT

- Generally, thyroxine increases the appetite and food intake.
- It also increases the secretions and movements of GI tract.
- So, hypersecretion of thyroxine causes diarrhea and the lack of thyroxine causes constipation.

ACTION ON CENTRAL NERVOUS SYSTEM

- Thyroxine is very essential for the development and maintenance of normal functioning of central nervous system (CNS).

ACTION ON SLEEP

- Normal thyroxine level is necessary to maintain normal sleep pattern.
- Hypersecretion of thyroxine causes excessive stimulation of the muscles and central nervous system.
- So, the person feels tired, exhausted and feels like sleeping.
- But, the person cannot sleep because of the stimulatory effect of thyroxine on neurons.

ACTION ON SEXUAL FUNCTION

- Normal thyroxine level is essential for normal sexual function.
- In men, hypothyroidism leads to complete loss of libido (sexual drive) and hyperthyroidism leads to impotence.
- In women, hypothyroidism causes menorrhagia and polymenorrhea.
- In some women, it causes irregular menstruation and occasionally amenorrhea.
- Hyperthyroidism in women leads to oligomenorrhea and sometimes amenorrhea

REGULATION OF SECRETION OF THYROID HORMONES

Secretion of thyroid hormones is controlled by anterior pituitary and hypothalamus through feedback mechanism.

1. ROLE OF PITUITARY GLAND

- Thyroid-stimulating hormone (TSH) secreted by anterior pituitary is the major factor regulating the synthesis and release of thyroid hormones.
- It is also necessary for the growth and the secretory activity of the thyroid gland.

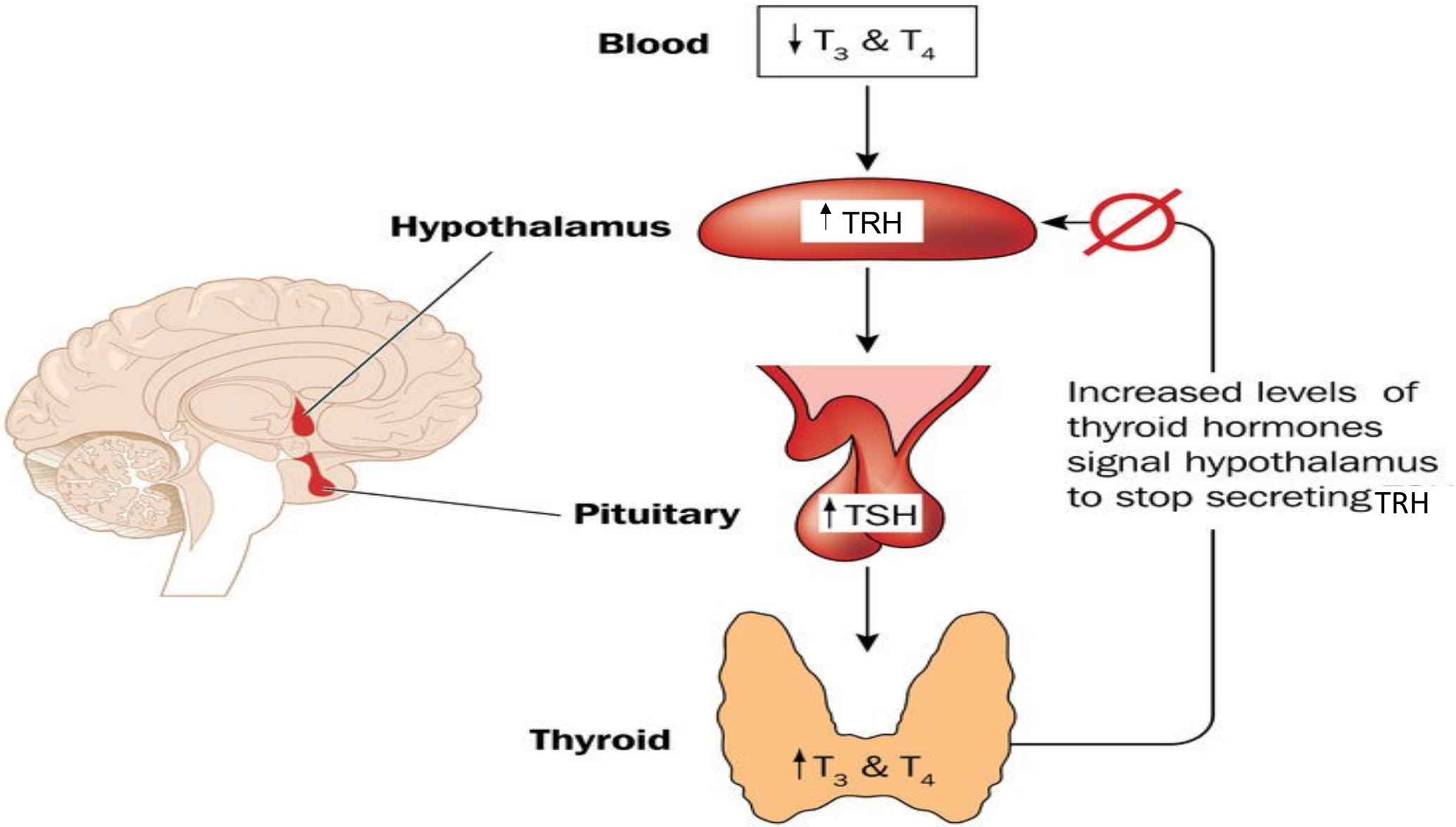
2. ROLE OF HYPOTHALAMUS

- Hypothalamus regulates thyroid secretion by controlling TSH secretion through thyrotropic-releasing hormone (TRH).
- From hypothalamus, TRH is transported through the hypothalamo-hypophyseal portal vessels to the anterior pituitary.

FEEDBACK CONTROL

- Thyroid hormones regulate their own secretion through negative feedback control, by inhibiting the release of TRH from hypothalamus and TSH from anterior pituitary

REGULATION OF SECRETION OF THYROID HORMONES



APPLIED PHYSIOLOGY

DISORDERS OF THYROID GLAND

1. **HYPERTHYROIDISM :** Increased secretion of thyroid hormones is called hyperthyroidism.

Signs and Symptoms of Hyperthyroidism

1. Intolerance to heat as the body produces lot of heat due to increased basal metabolic rate.
2. Increased sweating due to vasodilatation
3. Decreased body weight due to fat mobilization
4. Diarrhea due to increased motility of GI tract

5. Muscular weakness because of excess protein catabolism

6. Nervousness, extreme fatigue, inability to sleep, mild tremor in the hands.

7. Psychoneurotic symptoms such as hyperexcitability, extreme anxiety or worry.

8. Toxic goiter

9. Oligomenorrhea or amenorrhea

10. Systolic hypertension

2. HYPOTHYROIDISM:

- Decreased secretion of thyroid hormones is called hypothyroidism.
- Hypothyroidism leads to myxedema in adults and cretinism in children.

I. MYXEDEMA

- It is the hypothyroidism in adults, characterized by generalized edematous appearance, associated with the following symptoms:

1. Swelling of the face
2. Non-pitting type of edema, i.e. when pressed, it does not make pits and the edema is hard.

3. Atherosclerosis: It is the hardening of the walls of arteries because of accumulation of fat deposits and other substances.

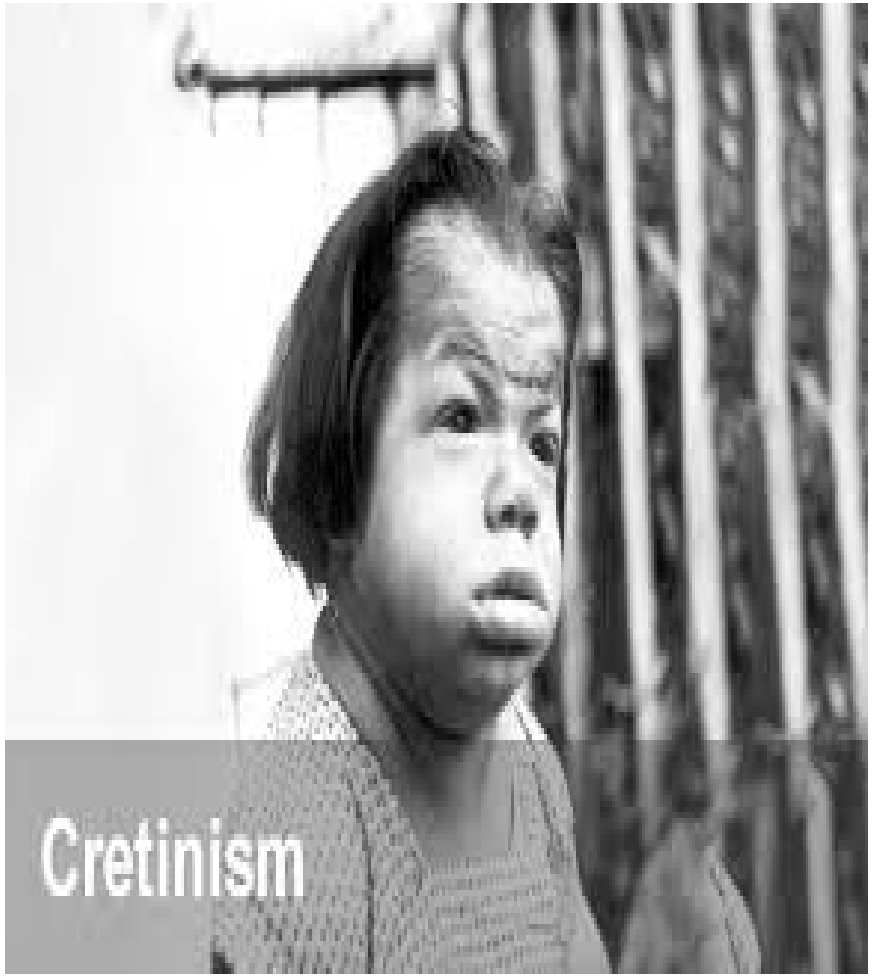
II. CRETINISM

- Cretinism is the hypothyroidism in children, characterized by stunted growth.

Features of cretinism:

1. A newborn baby with thyroid deficiency may appear normal at the time of birth because thyroxine might have been supplied from mother.
2. But a few weeks after birth, the baby starts developing the signs like sluggish movements and croaking sound while crying.

4. Unless treated immediately, the baby will be mentally retarded permanently.
5. Skeletal growth is more affected than the soft tissues. So, there is stunted growth with bloated body.
6. The tongue becomes so big that it hangs down with dripping of saliva.
7. The big tongue obstructs swallowing and breathing. The tongue produces characteristic guttural breathing that may sometimes choke the baby.



III. GOITER

Goiter means enlargement of the thyroid gland.
It occurs both in hypothyroidism and hyperthyroidism.

- **Goiter in Hyperthyroidism – Toxic Goiter**
  Toxic goiter is the enlargement of thyroid gland with increased secretion of thyroid hormones, caused by thyroid tumor.

- **Goiter in Hypothyroidism – Non-toxic Goiter**
  Non-toxic goiter is the enlargement of thyroid gland without increase in hormone secretion. It is also called hypothyroid goiter.

THANK YOU