1. **Name the iodothyronine hormones synthesized by the thyroid gland.**

   The iodothyronine hormones synthesized by the thyroid gland are:

   - 3,5,3'-triiodothyronine (T3).
   - 3,5,3'5'-tetraiodothyronine (T4, thyroxine)

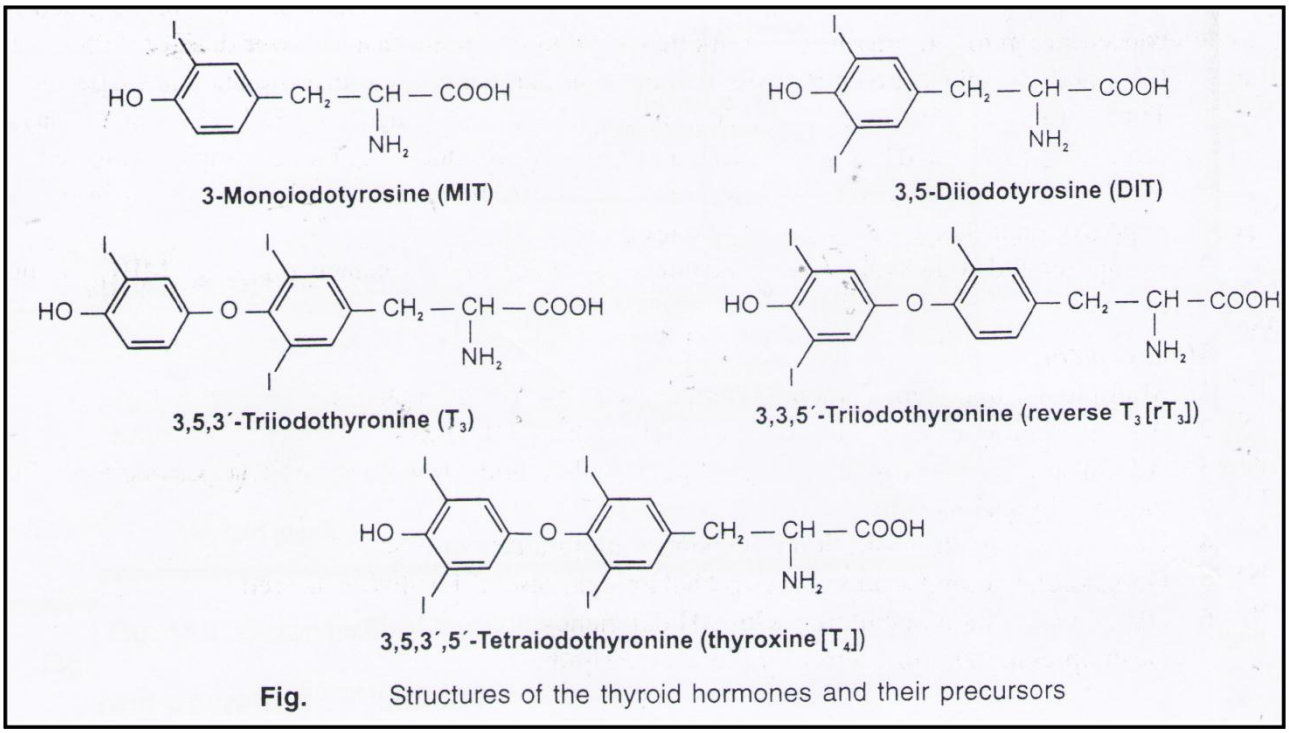

Fig. Structures of the thyroid hormones and their precursors

2. **Outline the steps involved in thyroid hormone synthesis**.

   The thyroid hormones are synthesized on the tyrosine residues of thyroglobulin, a protein present in the follicular cells of the thyroid surrounding a cavity termed the 'colloid'. Thyroid hormone synthesis involves the following step:

   1) **Iodide (I^-) uptake** from the blood by the follicular cells by an active transport mechanisims Iodide uptake is blocked by thiocyanate and perchlorate.
   2) **Oxidation of iodide** by thyroperoxidase, which uses hydrogen peroxide as an oxidizing agent.
      This step is inhibited by thiourea……..
   3) **Iodination of tyrosine residues** in thyroglobulin (organification) by *thyroperoxidase* to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). This step is inhibited by propylthiouracil and carbimazole……
   4) **Coupling** of MIT to DIT to form T3, and coupling of two residues of DIT to generate T4.
   5) **Proteolysis and secretion**. Thyroglobulin, the storage form of thyroid hormones, is taken up by the follicular cells followed by hydrolysis by lysosomal enzymes

with release of the thyroid hormones into circulation. This step is stimulated by thyroid stimulating hormone (TSH) and inhibited by iodide.

6) **Deiodination** of MIT and DIT by a *deiodinase*. The iodine is reutilized. The major hormone synthesized by the thyroid gland is T4, whereas T3 and reverse T3 are obtained by deiodination of T4 in the liver, kidney, and muscle.

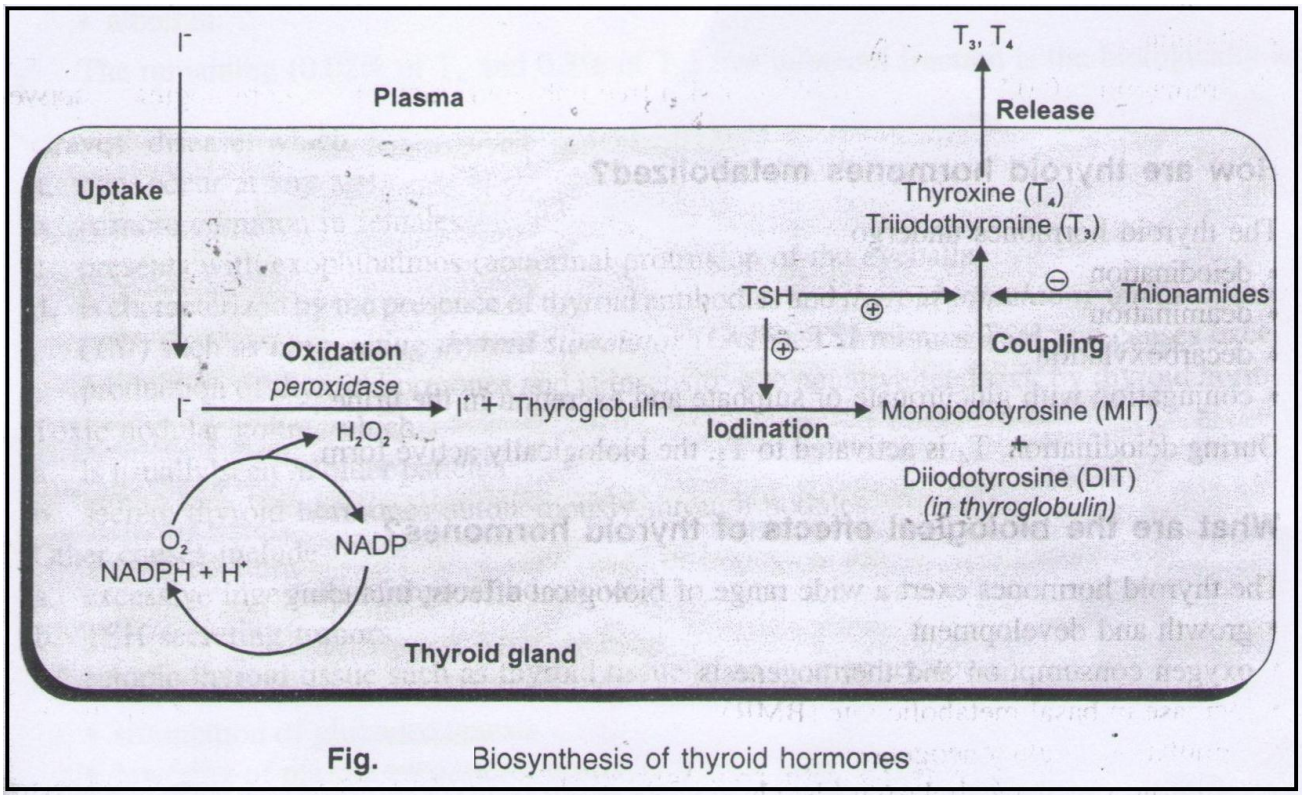

Fig. Biosynthesis of thyroid hormones

3. **How are thyroid hormones transported in circulation?**

More than 99% of thyroid hormones are transported in circulation, bound to:

- Thyroxine-binding globulin, TBG (predominant).
- Prealbumin
- albumin.

The remaining (0.02% of T4 and 0.3% of T3) free unbound fraction is the biologically active form.

4. **How are thyroid hormones metabolized?**

The thyroid hormones undergo:

- Deiodination.
- Deamination.
- Decarboxylation.
- Conjugation with glucuronate or sulphate and excretion in the urine.

During deiodination, T4 is activated to T3, the biologically active form.

5. **What are the biological effects of thyroid hormones?**

   The thyroid hormones exert a wide range of biological effects, including:

   - Growth and development.
   - Oxygen consumption and thermogenesis.
   - Increase in basal metabolic rate (BMR).
   - Stimulation of gluconeogenesis.
   - Lowering of plasma cholesterol levels.
   - Protein anabolic effects in physiological amounts.
   - Bone resorption and decalcification.

6. **Give a brief explanation of thyroid function tests.**

   The tests available for the assessment of thyroid function include the following:

   1) Direct tests of thyroid function (uptake of radioactive iodine and technetium)
      a. *Radioactive iodine uptake (RAIU) test* that assesses the amount of iodide accumulated by the thyroid using radioiodine $^{131}\mathbf{I}$ or $^{123}\mathbf{I}$. The uptake correlates inversely with the plasma iodide concentration and directly with the functional state of the thyroid.
      b. *Thyroid scintiscanning* that makes use of the isotope ^{99m}Tc to identify 'hot' (active) or 'cold' (inactive and malignant) nodules in the thyroid as well as in the differential diagnosis of hyperthyroidism.
   2) Measurement of total hormone levels by radioimmunoassay (RIA). This however, reflects the fraction bound to the protein TBG, which is increased by estrogens and decreased by severe illness, androgens, and glucocorticoids.
   3) Measurement of free hormone levels, which correlate better with the thyroid status.
   4) Tests of thyroid hormone regulation by:
      a. Measurement of TSH.
      b. TRH stimulation test based on the principle that TRH administration (200 ug in 2 mL saline I.V.) induces increased secretion of TSH with increase in plasma TSH levels that reach a peak in 20 minutes and subsequently decline rapidly.
   5) Miscellaneous tests
      a. Detection of antibodies to T3 and T4 is useful in autoimmune thyroid disease.
      b. Measurement of plasma TBG is useful in thyroid cancer.
      c. Detection of antithyroid peroxidase in Hashimoto's disease and Graves' disease.

7. **How is hyperthyroidism diagnosed in the laboratory?**

   Hyperthyroidism can be confirmed by the following laboratory findings:

   a. Increase in total and free thyroid hormone levels, with increase in T3 being greater and occurs earlier than T4.

b. Low plasma TSH levels.
c. TRH Test: The response of TSH to TRH stimulation is subnormal.

8. **What are the laboratory findings in hypothyroidism?**
   1) Plasma T4 is decreased.
   2) Plasma TSH is :
      a. Increased in primary hypothyroidism due to decreased negative feedback.
      b. Decreased in secondary hypothyroidism.
   3) **TRH test**
      a. *In primary hypothyroidism*, there is exaggerated rise in plasma TSH in response to TRH.
      b. *In secondary hypothyroidism of pituitary origin*, the response to TRH is reduced due to inability of the anterior pituitary to secrete TSH.
      c. *In secondary hypothyroidism of hypothalamic origin*, the response is delayed with higher concentrations of plasma TSH at 60 minutes than at 20 minutes.

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Good Luck

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ممثل المرحلة : حسين شاكر محمد

"Courage is what it takes to stand up and speak; courage is also what it takes to sit down and listen."

Winston Churchill, PM of UK