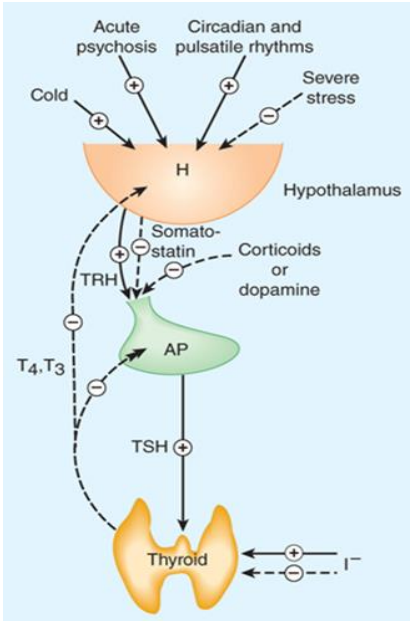
- **The thyroid gland secretes** thyroid hormones (T3 and T4:thyroxine) in addition to calcitonin (secreted by parafollicular cells). In thyroid replacement therapy, we consider the administration of T4 to the patient lacking the production of thyroid hormones.
- **In the peripheral tissue**, there will be conversion of T4 to T3 (by removing one iodine ion via deiodinase). T3 is more potent, absorbed better when given orally and is considered as the active form of the hormone.
- **Regulation of the production of thyroid hormones (figure).**
- **Measurement of TSH** is one of the main things to be done when thyroid replacement therapy is considered to be given to a patient. TSH is an indicator to show if the replacement therapy is working or not. We also use it to adjust the dose.
- **Thyroid preparations:**
  - **Synthetic:**
    - ✓ *Levothyroxine (T4).*
    - ✓ *Liothyronine (T3).*
  - **Animal origin:**
    - ✓ *Desiccated thyroid (الغدّة الدرقية المجفّفة).*



Levothyroxine (T4):

- This is the main drug and the preparation of choice because it is stable, uniformed, has a low cost, and a longer half life (t1/2) (7 days compared to 1-2 days for T3). Because of its longer (t1/2) it is given once daily. Administering levothyroxine will provide the body with both T4 and T3 (because normally T4 is converted to T3 in the periphery of the body).
- **There is some variability in the absorption** of this drug so you have to continue giving the same preparation when providing a patient with a refill (pharmacokinetics will change when changing the brand of the drug given to the patient).
- **The dose** in infants and children is higher. In addition, a pregnant female will require a higher dose of thyroid hormone.
- **Administration of the drug** is orally on an empty stomach (morning, bed time or 1 hour before a meal). It is given once a day because of its longer half life (which is lasting approximately 1 week). It would take the drug 4-6 weeks to reach the steady state (only then you can start to adjust the dose). In children, you have to monitor growth and development.
- **In elderly patient** especially those with cardiac disease, you have to start with a low dose (25 mcg/day) or even less and you have to monitor them (because there is a risk of cardiac toxicity with thyroid replacement therapy especially with an underlying cardiac disease or abnormality).
- **Toxicity** is directly related to the dose (as you increase the dose toxicity will be increased). In children, growth might be affected. Adults will have heat-intolerance, palpitations and tremors while in elderly there will be osteoporosis.

Liothyronine (T3):

- It is more potent than levothyroxine but has a shorter half life (t1/2). Because of its shorter (t1/2) it is given more frequent. In addition, liothyronine has a higher risk of cardiac toxicity.
- This drug is mainly used in myxedema coma (emergency situation of a decompensated hypothyroidism).

Desiccated thyroid:

- Not used because of allergies and it is not stable.
- It has a variable hormone concentration (T3 and T4).

Variable	T_4	T_3
Volume of distribution	10 L	40 L
Extrathyroidal pool	800 mcg	54 mcg
Daily production	75 mcg	25 mcg
Fractional turnover per day	10%	60%
Metabolic clearance per day	1.1 L	24 L
Half-life (biologic)	**7 days**	**1 day**
Amount bound	99.96%	99.6%
Biologic potency	**1**	**4**
Oral absorption	**70%**	**95%**