# THYROID DRUGS

General:

- Hashimoto →Anti-TPO Ab
- PTU/methimazole/elevated iodide->inhibit TPO iodination
- PTU/methimazole-> inhibit condensation of DIT/MIT
- Elevated iodide-> inhibit proteolytic release of hormones
- T3/T4 MOA ma3roofeh

# T3 & T4/HYPOTHYROIDISM

- **Pharmacokinetics**
  - Both T4 and T3 are **absorbed after** oral **administration**.
  - Food, calcium preparations, and aluminum-containing antacids can decrease the absorption of **T4**.
  - **Deiodination** is the major route of metabolism of T4.
  - T3 also undergoes sequential deiodination.
  - The hormones are also metabolised via **conjugation** with glucuronides and sulfates and excreted into the bile

- **Tx of Hypothyroidism**:
  - **Levothyroxine (T4)** is preferred over **liothyronine (T3)** or **liotrix (T3/T4 combo)** for the treatment of hypothyroidism.
  - **Levothyroxine (T4):**
    - is better tolerated than T3 preparations
    - longer half-life.
    - dosed once daily
    - steady state is achieved in 6 to 8 weeks.
  - **Toxicity** is directly related to T4 levels and manifests as nervousness, palpitations and tachycardia, heat intolerance, and unexplained weight loss.
  - **Drugs that induce cytP450**, such as phenytoin, rifampin, and phenobarbital, **accelerate metabolism of the thyroid hormones and may decrease the effectiveness**

# TX OF HYPERTHYROIDISM

**The goal of therapy is to decrease synthesis and/or release of additional hormone.**

## removing part or all of the thyroid gland

- Either:
  - surgically
  - destruction of the gland with **radioactive iodine ($^{131}$I),** which is selectively taken up by the thyroid follicular cells.

- Most patients become hypothyroid as a result of this drug and require treatment with levothyroxine.

## Inhibiting synthesis of the hormones

- **The thioamides, propylthiouracil (PTU) and methimazole**, are concentrated in the thyroid, where they inhibit both:
  - **oxidative** processes required for iodination of tyrosyl groups
  - **condensation** (coupling) of iodotyrosines
- **PTU** also blocks peripheral conversion of T4-> T3.
- These drugs have no effect on thyroglobulin **already stored** in the gland.
- Therefore, clinical effects of these drugs may be delayed until thyroglobulin stores are **depleted**.
- **Methimazole** is preferred over **PTU** bc:
  - **longer half-life,** allowing for ***once-daily*** dosing
  - **lower incidence of AE**
- **PTU** is:
  - recommended during the **first trimester** of pregnancy due to a greater risk of teratogenic effects with **methimazole**.
  - associated with **hepatotoxicity** and, rarely, **agranulocytosis**.

## Blocking release of hormones from follicles

- **A pharmacologic dose of iodide** inhibits the **iodination** of tyrosines
  - ("Wolff-Chaikoff effect")
  - lasts only a few days.
- Most imp, inhibits the **release** of thyroid hormones from thyroglobulin by mechanisms not yet understood.
- employed to treat **thyroid storm** or prior to surgery, because it decreases the **vascularity** of the thyroid gland.
- **not** useful for long-term therapy, because the thyroid ceases to respond to the drug after a few weeks.
- administered orally.
- **AE:** sore mouth and throat, swelling of the tongue or larynx, rashes, ulcerations of mucous membranes, and a metallic taste in the mouth.

# THYROID STORM

- Thyroid storm presents with extreme symptoms of hyperthyroidism.
- The treatment of thyroid storm is the same as that for hyperthyroidism, except that the drugs are given in **higher doses and more frequently.**
- **β-blockers**, such as **metoprolol** or **propranolol**, are effective in blunting the widespread sympathetic stimulation that occurs in hyperthyroidism.