Unit IV – Problem 4 – Pharmacology: Thyroid and Anti-thyroid Drugs



- What are the goals behind treatment:
 - To achieve euthyroid status (normal levels of thyroid hormones in the blood):
 - ✓ Inhibition of thyroid hormones synthesis (T3, T4).
 - ✓ Prevention of the release of thyroid hormones from thyroid gland.
 - To control the symptoms which result from increased thyroid hormones:
 - \checkmark This is achieved by blockade of β-adrenergic receptors.
- There are two important thyroid drugs which you must memorize:
 - Levothyroxine (T4):
 - ✓ Indicated for:
 - Hypothyroidism.
 - ❖ Prevention of mental retardation associated with congenital hypothyroidism (cretinism).
 - ❖ TSH suppression therapy after treatment for thyroid cancer.
 - ✓ <u>Half-life $(t_{1/2})$:</u> 7 days.
 - ✓ Adverse reactions:
 - * Tachycardia.
 - Heat intolerance.
 - **Tremors.**
 - Liothyronine (T3):
 - ✓ <u>Indicated for</u>: myxedema coma, which is a medical emergency characterized by: hypothermia, respiratory depression and unconsciousness. It is most commonly seen in elderly during winter months.
 - ✓ <u>Adverse reactions</u>: same as those mentioned for levothyroxine but this drug is more cardiotoxic.
- There are two important anti-thyroid drugs which you must memorize:
 - Methimazole (considered as the drug of choice).
 - ✓ <u>Mechanism of action</u>: inhibits T3 and T4 synthesis (in the thyroid gland) by inhibiting the peroxidase enzyme.
 - ✓ Why is it considered as the drug of choice?
 - ❖ Because it is more potent (thus given once daily) and causing less hepatotoxicity than propylthiouracil.
 - Propylthiouracil PTU (considered as a second line drug).
 - ✓ <u>Mechanism of action</u>: inhibits T3 and T4 synthesis (in the thyroid gland) by inhibiting the peroxidase enzyme. Also, it inhibits the conversion of T4 to T3 (a more potent form) in peripheral tissues by inhibiting the enzyme 5'-deiodinase.
 - ✓ PTU is only indicated in the 1st trimester of pregnancy (first three months) because it crosses the placenta less than methimazole. It is also indicated for thyroid storm (an emergency condition) since it has faster onset.
 - * Notice that thyroid storm it treated by the three P's: PTU, propranolol (β-blocker) and prednisolone (corticosteroid).
 - ✓ <u>Adverse reactions</u>: hepatotoxicity and agranulocytosis (which are both indications to stop therapy and refer the patient to hospital).
 - ❖ How the patient knows if he has agranulocytosis?
 - ➤ Once he notices that he is suffering from sore throat and fever.

In USA, the most common treatment modality of hyperthyroidism is by radioactive iodine. However, it acts slowly and is contraindicated in pregnancy and lactation:

- Radiation half-life (t 1/2) = 8 days and it emits both β and γ rays.
- Dosage of radiation is estimated based on the weight of thyroid gland and it functions by destroying follicular cells of the gland.
- Peak therapeutic effect is noticed after 3-6 months.
- Adverse effects:
 - ✓ Sore throat.
 - ✓ Sialitis (inflammation of salivary gland or duct).
 - ✓ Hypothyroidism.

- <u>β-blockers:</u>

- **Examples**: propranolol, metoprolol and atenolol.
- Theraputic benefit:
 - ✓ Control of palpitations, tremors and atrial fibrillation.
 - ✓ **Anti-thyroid effect**: by inhibiting peripheral conversion of T4 to T3 (by the enzyme deiodinase).
- Notice that β -blockers are always used in combination with other anti-thyroid medications.

