DRUGS USED FOR TREATMENT OF HYPO/HYPERTHYROIDISM

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The thyroid gland secretes three main hormones:

thyroxine (T4)

tri-iodothyronine (T3)

calcitonin

T4 and T3 are critically important for normal growth and development and for controlling energy metabolism.

Calcitonin is involved in the control of plasma [Ca^{2+}] and is used to treat osteoporosis.

The term ‘thyroid hormones’ will be used solely to refer to T4 and T3.

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MECHANISM OF ACTION

Thyroid hormones act mainly through a specific nuclear receptor, TR.

T4 may be regarded as a prohormone (when it enters the cell, it is converted to T3, which then binds with high affinity to TR).

When T3 is bound, these receptors change conformation, the co-repressor complex is released and a co-activator complex is recruited, which then activates transcription, resulting in generation of mRNA and protein synthesis.

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HYPERTHYROIDISM (THYROTOXICOSIS)

excessive secretion and activity of the thyroid hormones

high metabolic rate

increase in skin temperature and sweating

nervousness, tremor, tachycardia and increased appetite

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HYPOTHYROIDISM

decreased activity of the thyroid results in hypothyroidism, and in severe cases *myxoedema*

low metabolic rate, slow speech, deep hoarse voice, lethargy, bradycardia, sensitivity to cold and mental impairment

characteristic thickening of the skin

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HYPERTHYROIDISM – pharmacological tretment

RADIOIODINE

first-line treatment for hyperthyroidism

isotope ^{131}I (emits both β and γ radiation)

The γ rays pass through the tissue without causing damage, but the β particles have a very short range; they are absorbed by the tissue and exert a powerful cytotoxic action that is restricted to the cells of the thyroid follicles, resulting in significant destruction of the tissue.

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Hypothyroidism will eventually occur after treatment with radioiodine.

This is easily managed by replacement therapy with T4.

Radioiodine is best avoided in children and also in pregnant patients because of potential damage to the fetus.

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THYREOSTATIC DRUGS

related to thiourea: **carbimazole, methimazole, propylthiouracil**

Mechanism of action

They decrease the output of thyroid hormones from the gland, and cause a gradual reduction in the signs and symptoms

MoA: Not exactly clear, BUT:

There is evidence that they inhibit the iodination of tyrosyl residues in thyroglobulin.

It is thought that they inhibit the thyroperoxidasecatalysed oxidation reactions.

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AE

neutropenia and agranulocytosis (relatively rare, having an incidence of 0.1–1.2%), reversible on cessation of treatment

rashes (2–25%)

headaches, nausea, jaundice, pain in the joints

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IODINE/IODIDE

Iodine is converted in vivo to iodide (I^-), which temporarily inhibits the release of thyroid hormones.

The mechanism of action is not entirely clear (it may inhibit iodination of thyroglobulin).

OTHER DRUGS USED

The β-adrenoceptor antagonists (propranolol and nadolol), are not antithyroid agents as such, but they are useful for decreasing many of the signs and symptoms of hyperthyroidism – the tachycardia, dysrhythmias, tremor and agitation.

HYPOTHYROIDISM

There are no drugs that specifically augment the synthesis or release of thyroid hormones.

The only effective treatment for hypothyroidism, unless it is caused by iodine deficiency (which is treated with iodide), is to administer the thyroid hormones themselves as replacement therapy.

Synthetic T4 (**levothyroxine**) and T3 (**liothyronine**) given orally

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