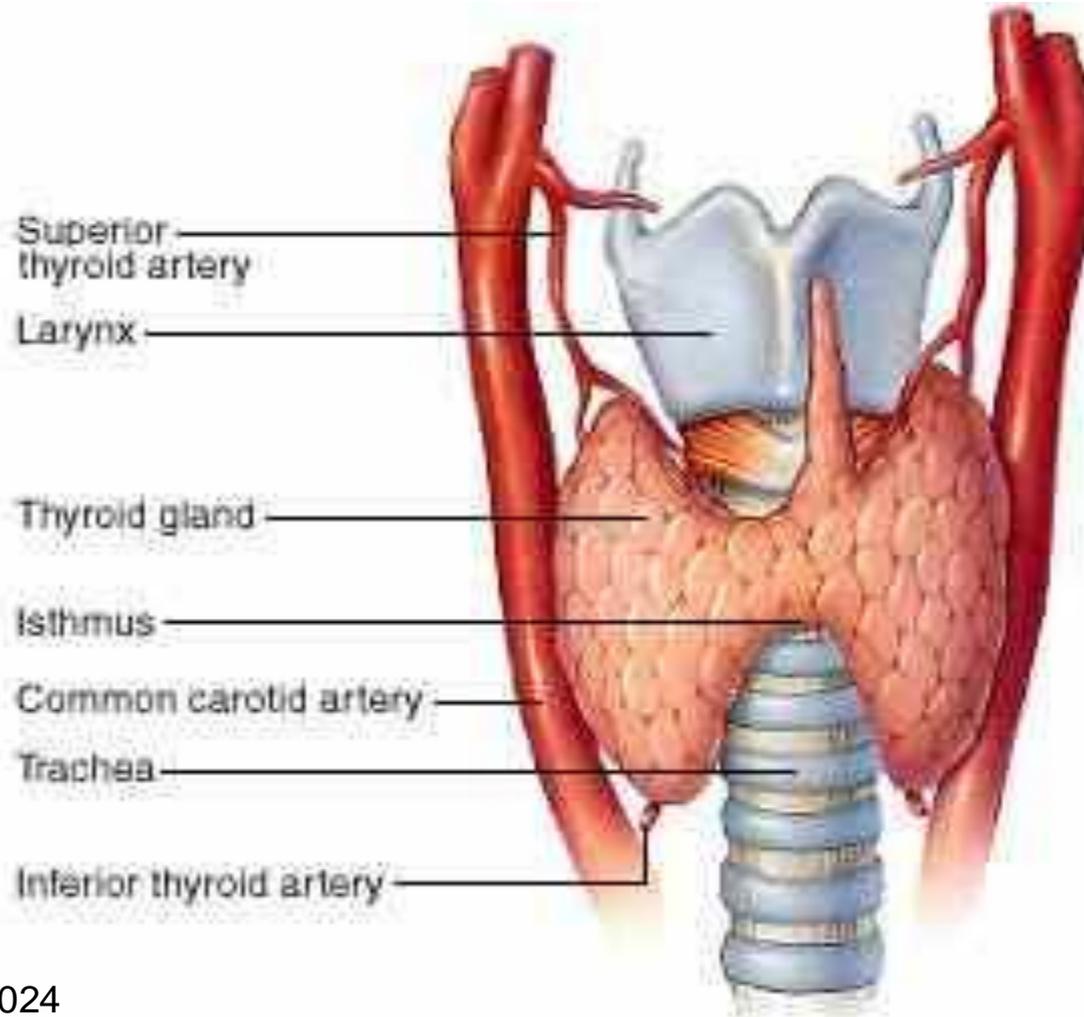


# **Thyroid hormones and Anti-thyroid drugs**

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# Thyroid gland

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# Thyroid Hormones

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- ❑ **Thyroxine (T4)**
- ❑ **Triiodothyronine (T3)**
- ❑ **Calcitonin**

# Thyroid Disorders

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- ❖ Hyperthyroidism
- ❖ Hypothyroidism
- ❖ Hashimoto's thyroiditis
- ❖ Goitre (thyroid enlargement)
- ❖ Malignancy

# Physiological considerations

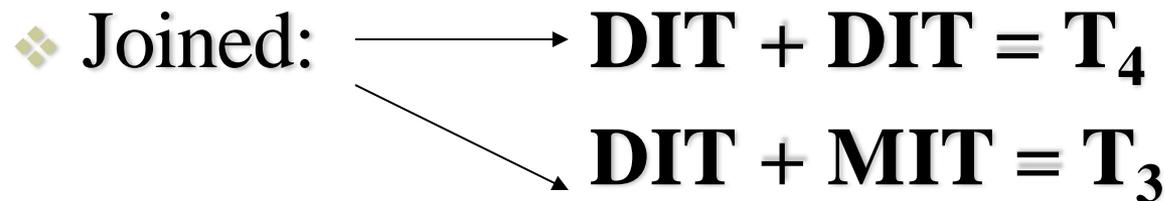
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- ❖ Dietary iodine is absorbed
- ❖ Circulates as iodide in blood
- ❖ Taken up by cells of the thyroid gland
- ❖ Concentrated up to 200 times

# In the thyroid gland

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- ❖ Iodide is oxidized & activated into iodine
- ❖ Combines with tyrosine on thyroglobulin
- ❖ Monoiodotyrosine & Diiodotyrosine are formed



# Physiological considerations

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- ❖ 2-month storage of  $T_4$
- ❖ Daily production:
  - $T_4$ : 75  $\mu\text{g}$
  - $T_3$ : 25  $\mu\text{g}$
- ❖ 80 % of circulating  $T_3$  are derived from  $T_4$  by deiodination in peripheral tissues

# Physiological considerations

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- ❖ Liberation of  $T_4$  and  $T_3$  :
  - Regulated by TSH
- ❖ TSH: regulated by TRH in hypothalamus
- ❖ TRH: affected by:
  - Stress, disease, food deprivation
  - Environmental temperature
  - Thyroid H level (-ve feedback inhibition)

# Comparison between T<sub>4</sub> & T<sub>3</sub>

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- T<sub>3</sub> has:
  - ❖ Rapid onset of action
  - ❖ Shorter duration
  - ❖ Five times more potent than T<sub>4</sub>
  - ❖ T<sub>4</sub> → t<sub>1/2</sub> about 7 days
  - ❖ T<sub>3</sub> → t<sub>1/2</sub> about 2 day

# Actions of thyroid hormones

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- ❖ Regulation of growth & development
- ❖ Calorigenic effect and body temp control
- ❖ Metabolic effects (catabolic):
  - Increase metabolism of Carbohydrate, fat, protein
- ❖ Effects on body systems:
  - ❖ **GIT**: excess causing diarrhea, deficiency causing constipation
  - ❖ **CVS**: positive chronotropic and inotropic effects
  - ❖ **CNS**: deficiency causes mental retardation

# Therapeutic uses of Thyroxine (T4)

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- ❖ Replacement therapy:
  - Hypothyroidism
- ❖ Diffuse non-toxic goiter:
  - Prevent TSH release & increase in size
- ❖ Hashimoto's thyroiditis: to correct hypothyroid state
- ❖ With anti-thyroid therapy:
  - Suppress increase in thyroid size secondary to increased TSH release

# Therapeutic uses of T3

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- ❖ Not used routinely
- ❖ Used sometimes carefully for rapid effects in:
  - Hypothyroid (Myxoedema) coma
  - Hypothyroid psychosis
  - Severe hypothyroidism
- ❖ Avoided in the presence of heart disease

# Adverse effects of thyroid hormones

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- ❖ Arrhythmias (tachycardia, ectopics)
- ❖ Anginal attacks
- ❖ Hyperthyroidism with high doses
- ❖ Muscle pain (myalgia)

# Anti-thyroid Drugs

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- ❖ Thiourea derivatives (Thionamide)
  - Carbimazole, Propylthiouracil, Methimazole
- ❖ Iodide
- ❖ Radioactive iodine I <sup>131</sup>

# Thiourea derivatives (thionamides)

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- ❑ Carbimazole
- ❑ Methimazole: it is a metabolite of carbimazol
- ❑ Propylthiouracil

# Carbimazole

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- ❖ Inhibits thyroid hormones synthesis:
  - Prevents binding of iodine to tyrosine to form iodotyrosines
  - Prevents coupling of iodotyrosines to form H
- ❖  $t_{1/2}$  about 6 hrs
- ❖ Crosses placenta
- ❖ Secreted in milk
- ❖ Once daily because its duration of action is 30h

# Adverse effects

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- ❖ Rash
- ❖ Arthralgia ( pain in a joint)
- ❖ Agranulocytosis & thrombocytopenia
  - Recognized idiosyncrotic adverse effect
  - May develop suddenly
- ❖ Liver damage

# Propylthiouracil

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- ❖ Similar to carbimazole but it also:
  - Inhibits peripheral metabolism of  $T_4$  into  $T_3$
- ❖  $t_{1/2}$  about 2 hrs
- ❖ Less placental crossing
- ❖ Less secretion in milk
  - Preferable in pregnancy & lactation

# Iodide

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- ❖ Oral iodide is well absorbed
- ❖ Daily requirement: 100 µg
  - Deficiency: → Non-toxic goiter because of reduction TH synthesis and activation of TSH
  - Excess: → Goiter: with increased function (decreases thyroglobulin proteolysis, thereby decreasing thyroid hormone secretion).
- ❖ Therapeutic uses of iodide:
  - Preparation for surgery: decrease TH
    - Less size, less vascular gland
  - Treatment of thyrotoxic crisis:
    - Inhibits thyroid H release

# Adverse effects

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- ❖ Allergy

- ❖ Iodism:

- Metallic taste, flu-like illness

- Pain in salivary glands

- Rashes

# Treatment of thyrotoxicosis

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## ❖ Medical:

- Anti-thyroid drug (carbimazole, propylthiouracil)
- Propranolol

## ❖ Surgical:

- Surgical preparation by propranolol & iodide

## ❖ Radioactive iodine I<sup>131</sup>

# Drug-induced goiter

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- ❑ Antithyroid drugs:

- ❖ Iodide

- ❖ Lithium

- ❖ Amiodarone

- ❑ Food-induced:

- ❖ Cabbage