Thyroid hormones and Anti-thyroid drugs

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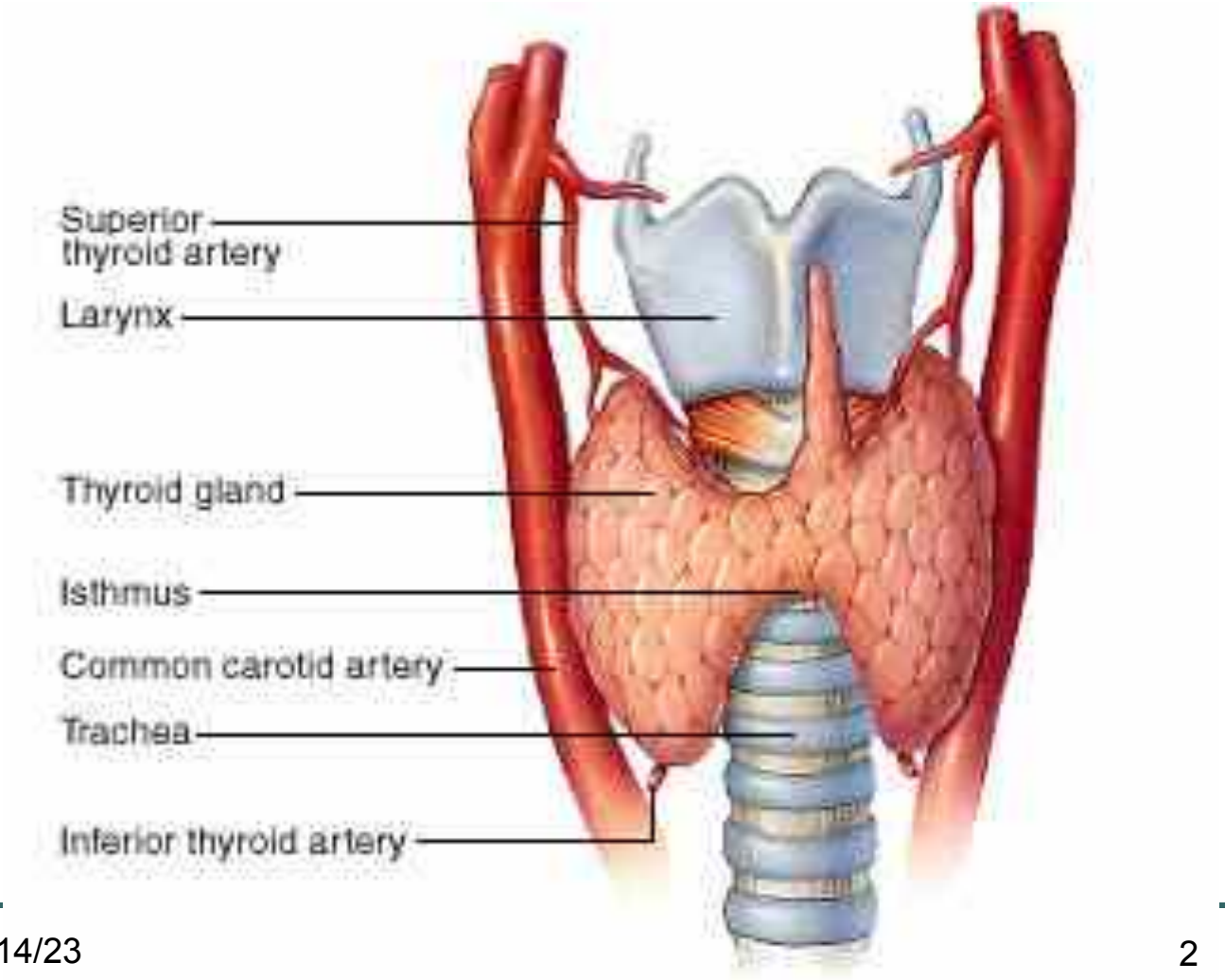
Thyroid gland



Thyroid Hormones

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

Thyroid Disorders

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

Physiological considerations

- 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

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

- Joined: → **DIT + DIT = T_4**
  → **DIT + MIT = T_3**

Physiological considerations

- 2-month storage of T_4
- Daily production:
  - T_4: 75 µg
  - T_3: 25 µg
- 80 % of circulating T_3 are derived from T_4 by deiodination in peripheral tissues

Physiological considerations

- 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_4 & T_3

- T_3 has:
- Rapid onset of action
- Shorter duration
- Five times more potent than T_4
- T_4 ⟶ t ½ about 7 days
- T_3 ⟶ t ½ about 2 day

Actions of thyroid hormones

- 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 cause mental retardation

Therapeutic uses of Thyroxine (T4)

- 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

- 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

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

Anti-thyroid Drugs

- Thiourea derivatives (Thionamide)
  - Carbimazole, Propylthiouracil, Methimazole
- Iodide
- Radioactive iodine I^{131}

Thiourea derivatives (thionamides)

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

Carbimazole

- Inhibits thyroid hormones synthesis:
  - Prevents binding of iodine to tyrosine to form iodotyrosines
  - Prevents coupling of iodotyrosines to form H
- t ½ about 6 hrs
- Crosses placenta
- Secreted in milk
- Once daily because its duration of action is 30h

Adverse effects

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

Propylthiouracil

- Similar to carbimazole but it also:
  - Inhibits peripheral metabolism of T_4 into T_3
- t½ about 2 hrs
- Less placental crossing
- Less secretion in milk
  - Preferable in pregnancy & lactation

Iodide

- 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

- Allergy
- Iodism:
  - Metallic taste, flu-like illness
  - Pain in salivary glands
  - Rashes

Treatment of thyrotoxicosis

- Medical:
  - Anti-thyroid drug (carbimazole, propylthiouracil)
  - Propranolol
- Surgical:
  - Surgical preparation by propranolol & iodide
- Radioactive iodine I^{131}

Drug-induced goiter

- Antithyroid drugs:
  - Iodide
  - Lithium
  - Amiodarone

- Food-induced:
  - Cabbage