Chapter 13: Thyroid Hormones

Lecture 20

Solubility

I. hydrophilic
- **1) peptide hormones**
- **2) catecholamines**

II. lipophilic
- **1) steroid hormones**
- **2) thyroid hormone**

I. Growth Hormone

A. growth indirectly: stimulating liver ↑ somatomedin production

B. somatomedin: insulin-like growth factor (IGF-1)

1) acts directly on bone & soft tissues:
   - a) protein synthesis
   - b) cell division
   - c) lengthening & thickening of bones

2) exerts metabolic effects unrelated to growth
   - a) ↑ blood fatty acid:
     breakdown triglyceride fat stored in adipose tissue
   - b) ↑ blood glucose: ↓ glucose uptake by muscles

Other hormones essential for normal growth

II. Thyroid hormone

growth severely stunted in hypothyroid children
hypersecretion not cause excessive growth

III. Insulin

deficiency often blocks growth
hyperinsulinism often spurs excessive growth

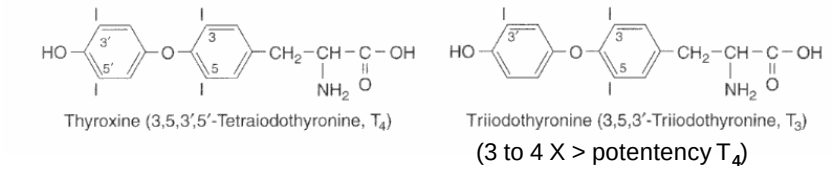
IV. Androgens

↑ pubertal growth spurt: ↑ protein synthesis
effects depend on presence of GH

V. Estrogens

growth prior to bone maturation ???

Thyroid Hormones



Thyroxine (3,5,3′,5′-Tetraiodothyronine, T_4)

Triiodothyronine (3,5,3′-Triiodothyronine, T_3)

(3 to 4 X > potentency T_4)

1) major form of thyroid hormone in blood thyroxine (T_4)

2) ratio of T_4 to T_3 released in the blood is roughly 20 to 1

mostly bound to transport proteins

70% thyroxine binding globulin (TBG)

10-15% thyroxine-binding prealbumin (TTR or TBPA)

15-20% albumin

small fraction free (unbound) & biologically active

0.03% T_4

0.3 % T_3

titers of free T_3 /T_4 important diagnostic value

total thyroxine in the blood can be misleading.

3) T_4 (precursor) to T_3 (active hormone) within cells by deiodinases (5'-iodinase)

cross cell membranes via amino acid importins

nuclear envelopes through receptors

4) further processed by decarboxylation & deiodination → iodothyronamine ($\mathbf{T_{1a}}$) and thyronamine ($\mathbf{T_{0a}}$)

Hormonal Effects

1) basal metabolic rate

2) protein synthesis

3) body's sensitivity to catecholamines (e.g. cortisol by permissiveness)

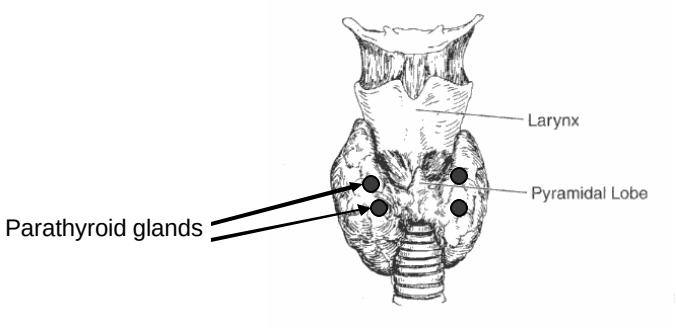
4) proper cellular development & differentiation

5) regulate protein, fat & carbohydrate metabolism

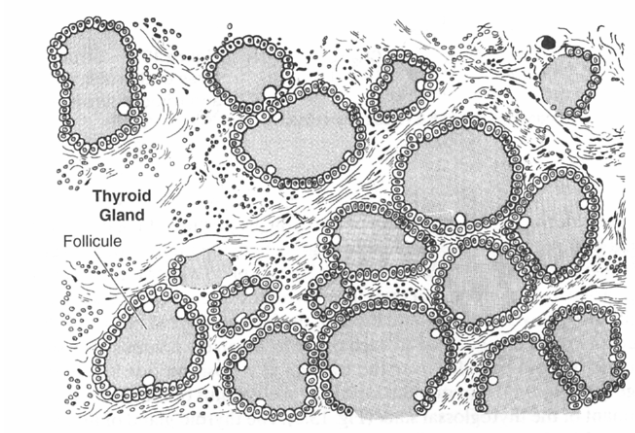
6) thyronamines function ?? mechanism to inhibit neuronal activity

e.g. mammalian hibernation cycles ?

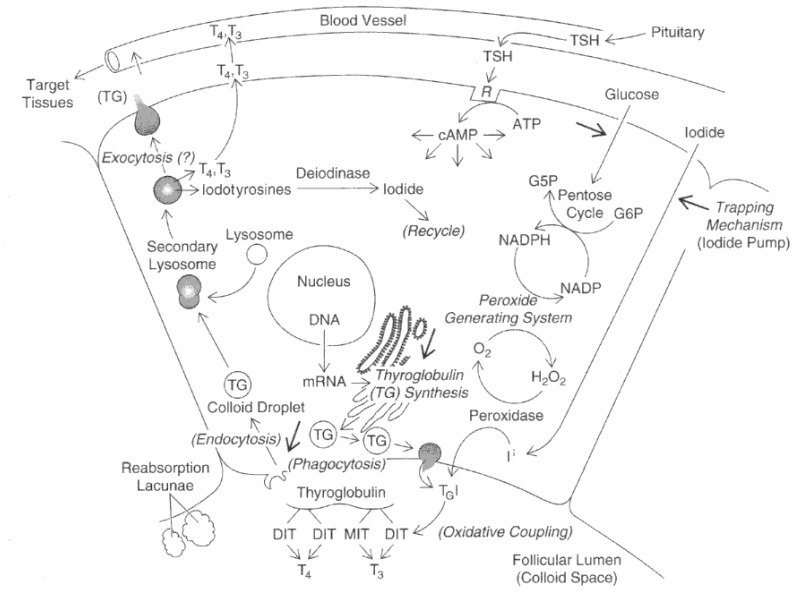
administering the thyronamines: severe drop in body temperature



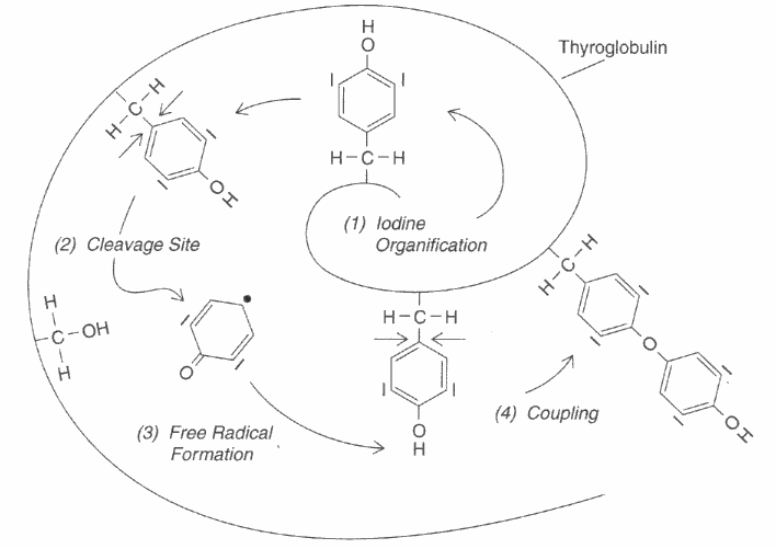
Thyroid gland



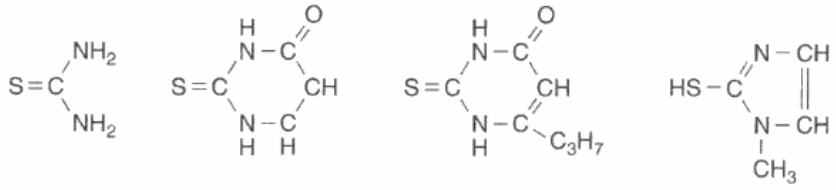
Histological diagram of human thyroid gland



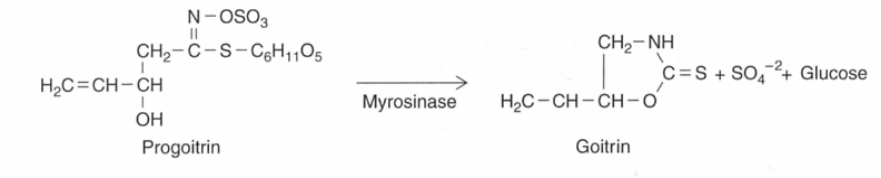
Thyroid hormone biosynthesis & secretion



Hypothetical coupling scheme for iodothyronine formation

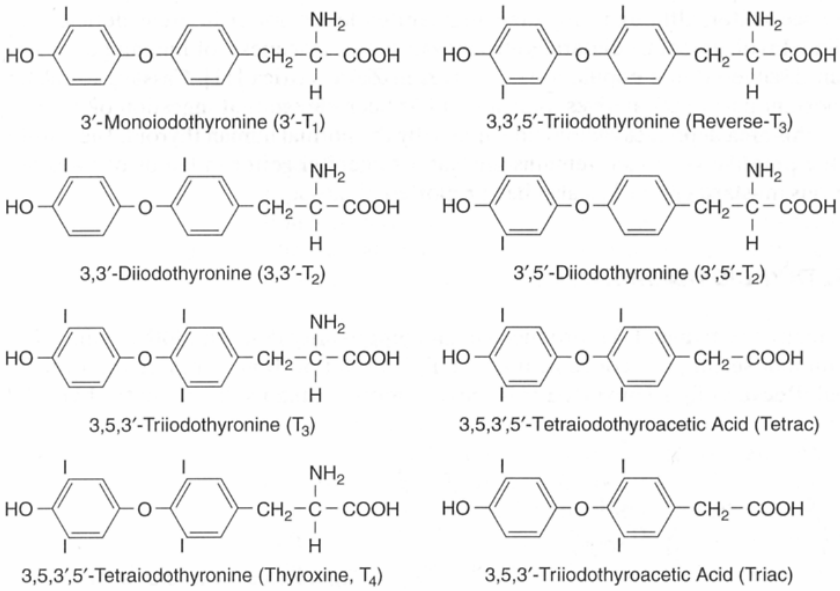


Thionamide type of anthithyroid drugs

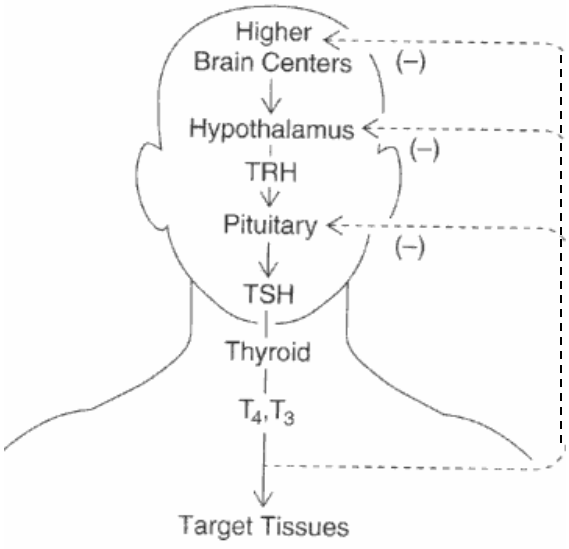


Synthesis and structure of goitrin

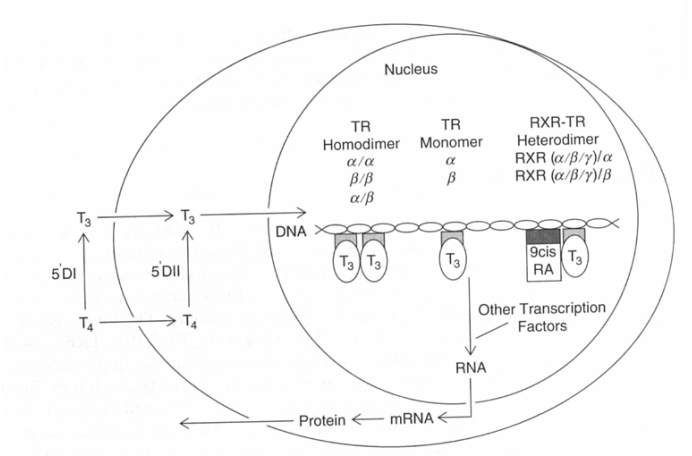
Goitrin: antithyroid compound in cabbage, rutabaga, turnip & brassicaceous weeds



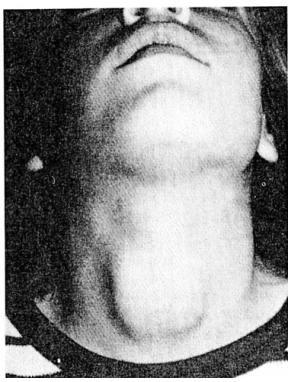
Structural formulas of iodothyronines in human plasma



CNS-Pituitary-Thyroid Axis

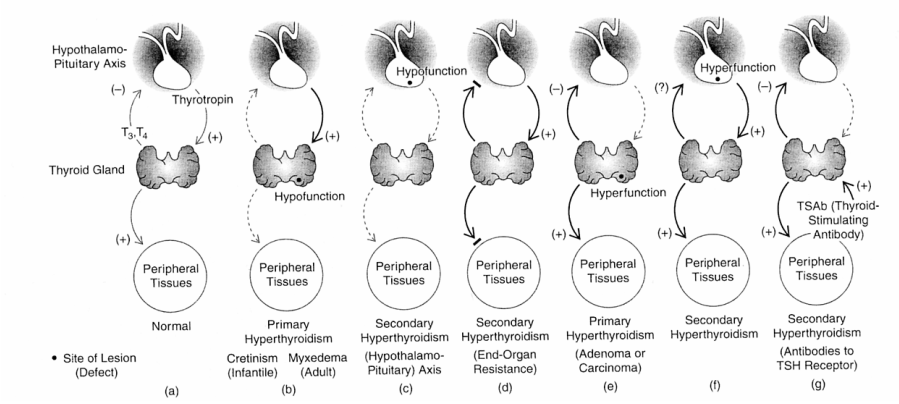


Model for action of mechanism of thyroid hormone on target tissues



Goiter: swollen thyroid gland

↓titers of T_4 & T_3: ↑titers of TSH



Pathophysiology: symptoms relating to:

1) ↑ or ↓ production of TSH or
2) inadequate thyroid gland or peripheral tissue response to TSH or thyroid hormones