

Thyroid gland

Dr. K.Medagoda

Department of Physiology

Thyroid gland

- Develops from thyroglossal duct

Has Two lateral lobes

Isthmus

Pyramidal lobe +/_

- Made up of acini (follicles)

- Single follicle

Lined by single cell layer- thyroid cells

Filled by colloid-contains thyroglobulin

- In between acini are Para follicular cells secreting calcitonin

Thyroid gland

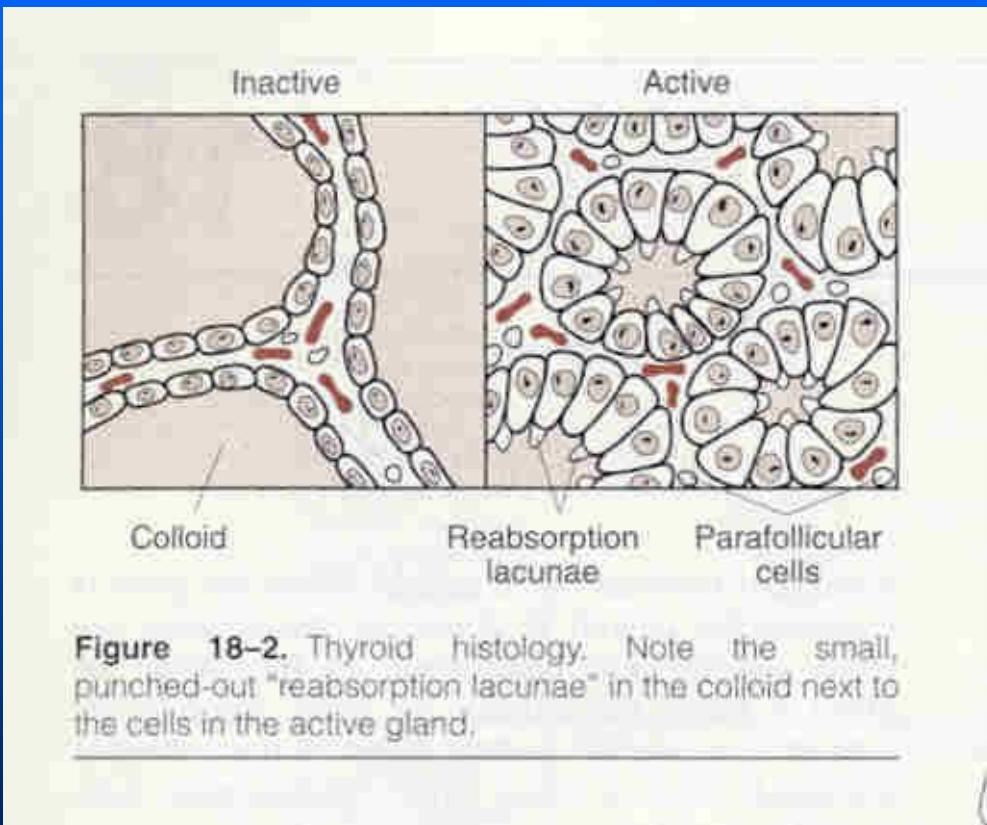
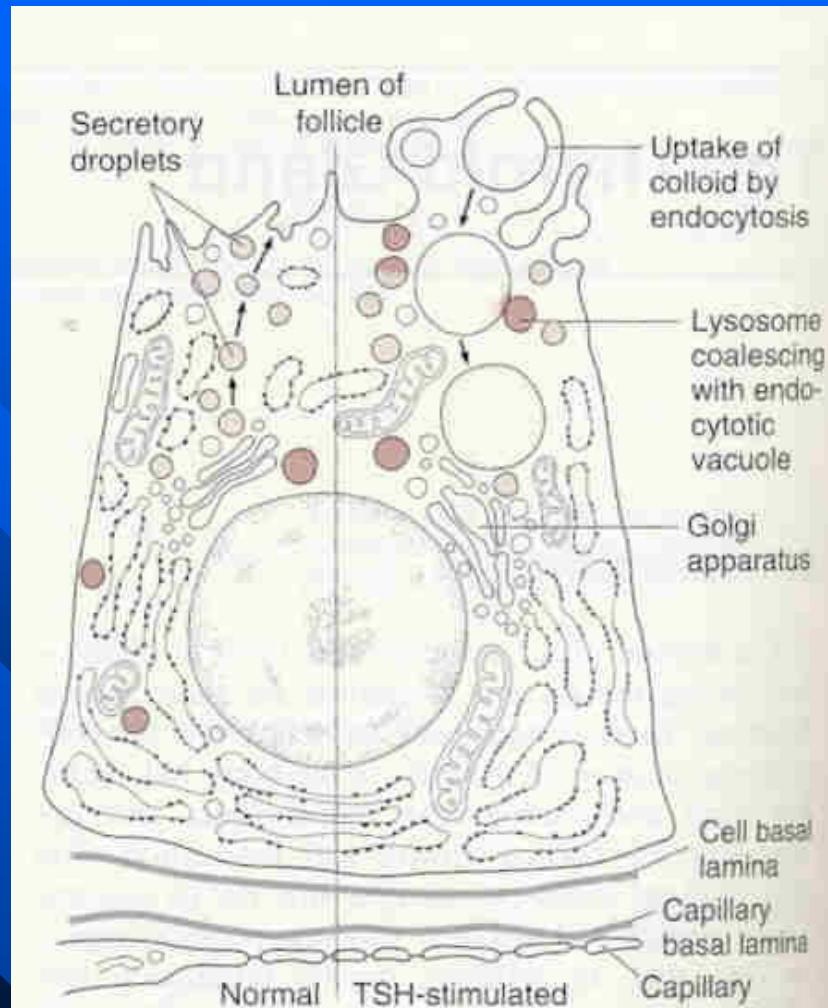


Figure 18–2. Thyroid histology. Note the small, punched-out "reabsorption lacunae" in the colloid next to the cells in the active gland.



Thyroid gland

■ Gland secrets

Thyroid hormones-Iodinated amino acids

Thyroxine-T₄

Triiodothyronine-T₃

■ Calcitonin

■ Thyroglobulin

A glycoprotein with tyrosine residues

Synthesised in thyroid cells

Secreted in to colloid by exocytosis from apical membrane

Iodine

- Needs for thyroid hormone synthesis
- Dietary iodine absorbed in the small intestine
- Thyroid –the principal organ takes iodine
- Excreted mainly from kidney

Synthesis of thyroid hormones and secretion-STEPS

1. *Iodide trapping (Iodide Pump)*
2. *Oxidation*
3. *Iodination*
4. *Coupling*
5. *Endocytosis of the colloid*
6. *Proteolysis*
7. *Deiodination*
8. *Secretion*

Synthesis of thyroid hormones

1. Iodide trapping (Iodide Pump)

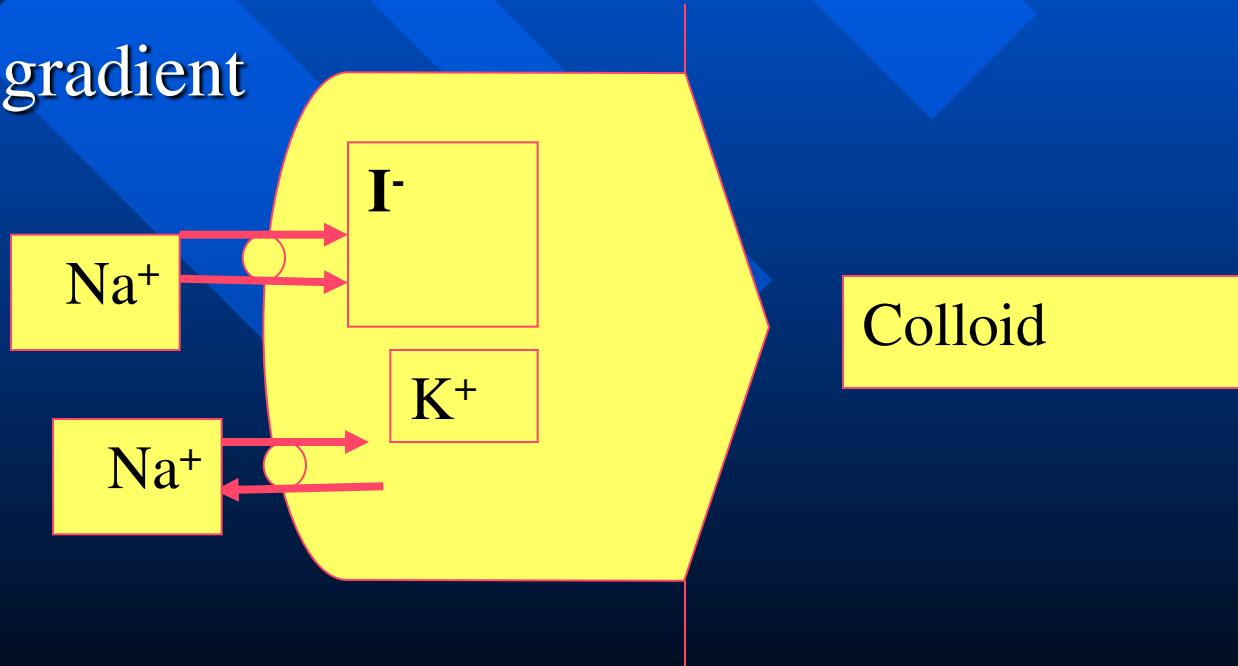
■ Thyroid gland concentrates iodine

By secondary active process of $\text{Na}^+ - \text{K}^+$ ATPase

Iodide (I^-) crosses the basal membrane against

An electrical gradient

A concentrate gradient



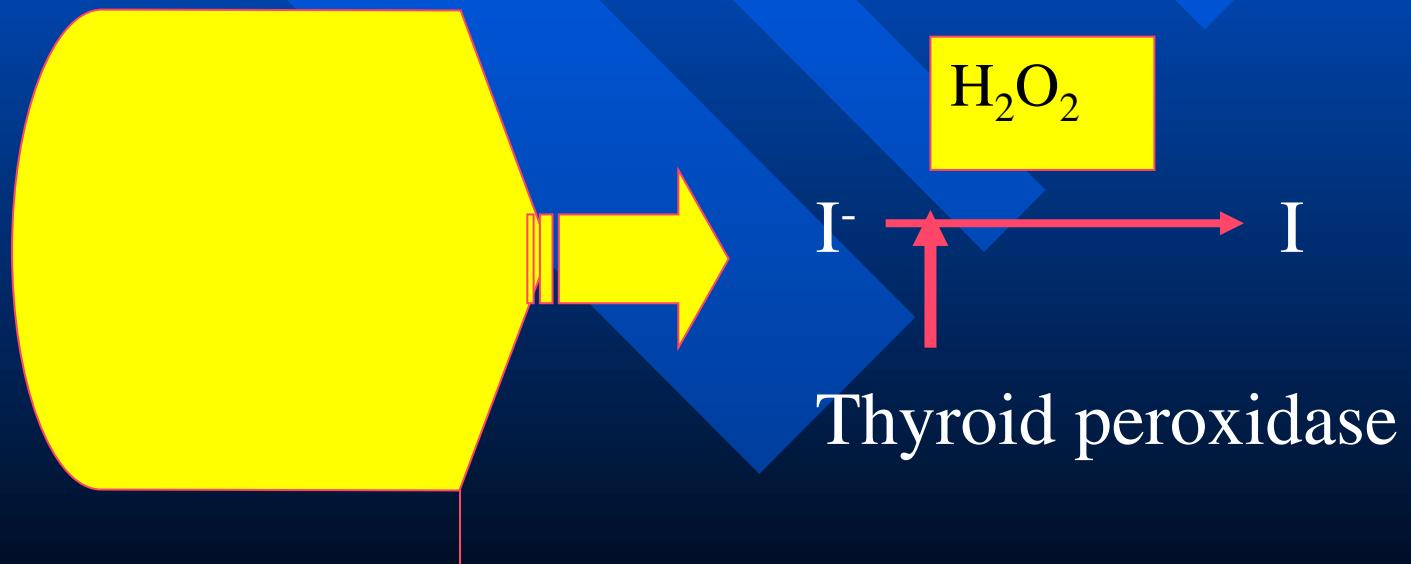
Synthesis of thyroid hormones

- *Iodide trapping (Iodide Pump)*
- Stimulated by TSH
 - LATS (long acting thyroid stimulators)
- Blocked by
 - perchlorate
 - Thiocynate

Synthesis of thyroid hormones

2. Oxidation

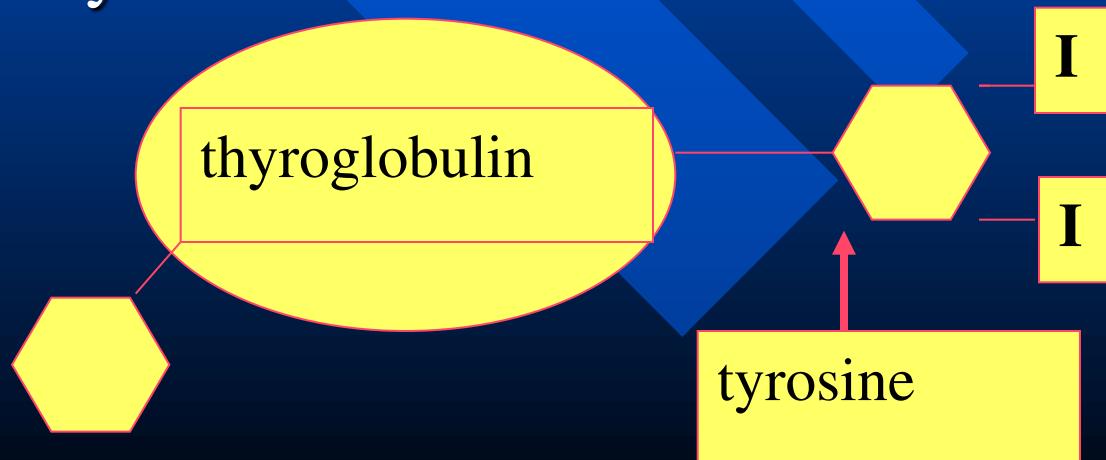
- Forms free iodine in the microvilli of cells at the apex
- Stimulated by TSH
- Inhibited by propylthiouracil



Synthesis of thyroid hormones

3. Iodination

- Free iodine rapidly get attached to tyrosine residues in thyroglobulin at 3 position
- Catalysed by Thyroid peroxidase
- Forms –Mono iodothyrosine-MIT
- Further iodination of MIT at 5 positions results Di-iodotyrosine
- Stimulated by TSH



Synthesis of thyroid hormones

4. Coupling

- Coupling of two iodinated tyrosine molecules forms
- DIT+DIT → Tetra iodothyronine(T_4)
(Thyroxine)



T_3 & T_4 stored in the colloid attached to thyroglobulin

Secretion of thyroid hormones

1. Endocytosis of the colloid

- Thyroid cells ingest colloid at apex by phagocytosis
- In the cell colloid globules fuse with the lysosomes → Phagolysosomes

2. Proteolysis

- Inside phagolysosome proteolytic degradation of thyroglobulin occurs
- Releases T_3 , T_4 , MIT, DIT and amino acids

Secretion of thyroid hormones

3. Deiodination

- Removal of iodide from MIT and DIT occurs by iodothyrosine deiodinase

4. Secretion

- T_3 and T_4 relatively immune to the deiodination
- Diffuse out to the blood along a concentrate gradient
- Partial deiodination of T_4 occurs to form T_3
- TSH stimulates steps 1,2 and 4

Transport of thyroid hormones in blood

- >99% are protein bound
- Only unbound fraction is physiologically active
- Protein binding

Transports hormone

Acts as a pool

Prevents rapid clearance

Buffer rapid fluctuations

- Binding proteins
 - i. Thyroxin binding globulin
 - ii. Thyroxin binding prealbumin
 - iii. Albumin

Transport of thyroid hormones in blood

Protein bound

- T_4 99.98%
- T_3 99.8%

Free

- 0.02% (2ng/dl)
- 0.2% (0.3ng/dl)

- T_4 half life- 6-7 days
- T_3 half life- 30 minutes

Regulation of secretion

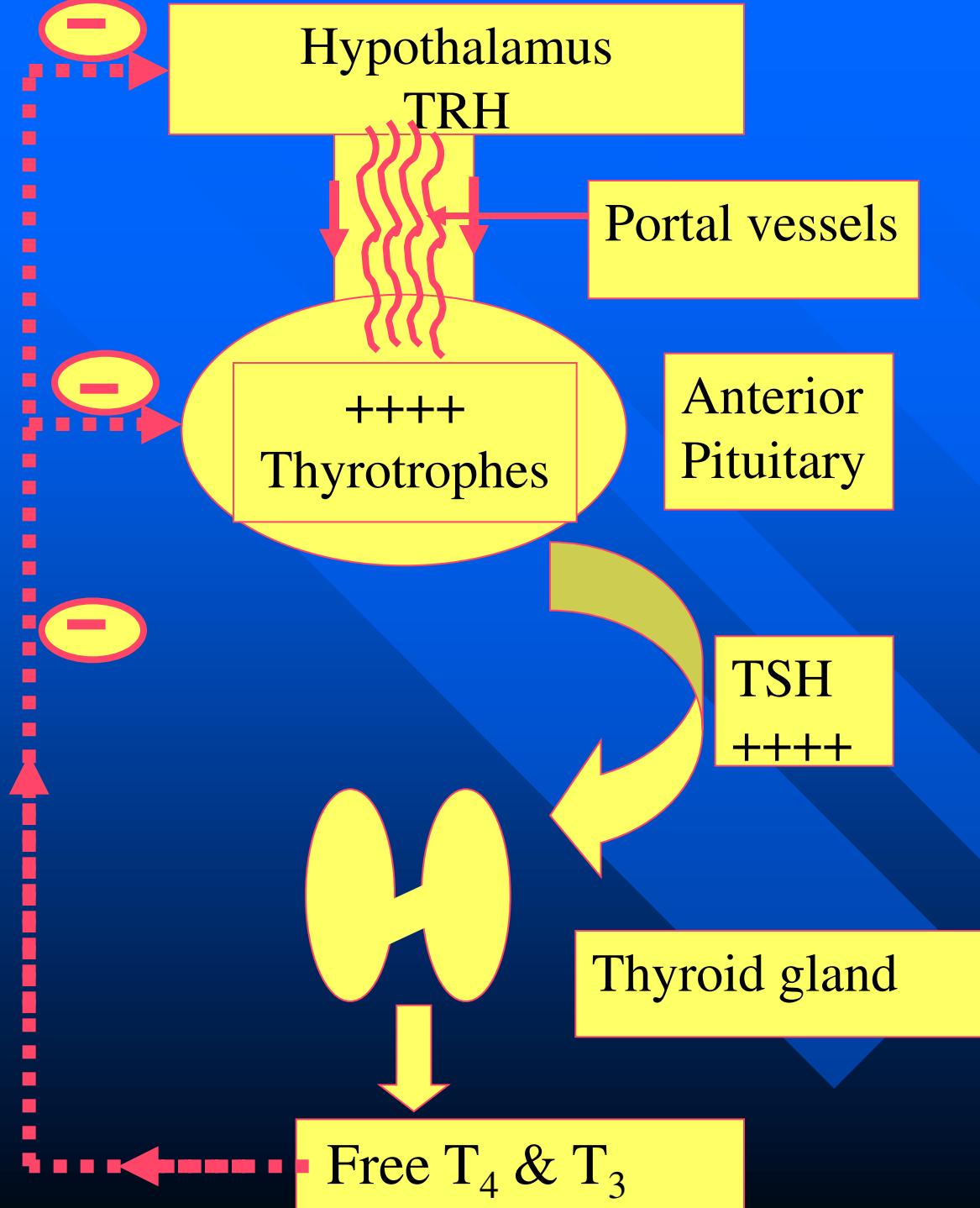
- By hypothalamo-pituitary thyroid axis
- A delicate feed back mechanism
- TRH
 - Tri peptide from hypothalamus
 - TRH stimulates TSH secretion from anterior pituitary

- TSH
 - a glycoprotein
 - Two subunits α and β
 - Short half life of 60 min

- Stimulates Adenylate cyclase
- Growth of the gland
- All steps in hormone synthesis

TSH secretion inhibits by free T_4 and T_3

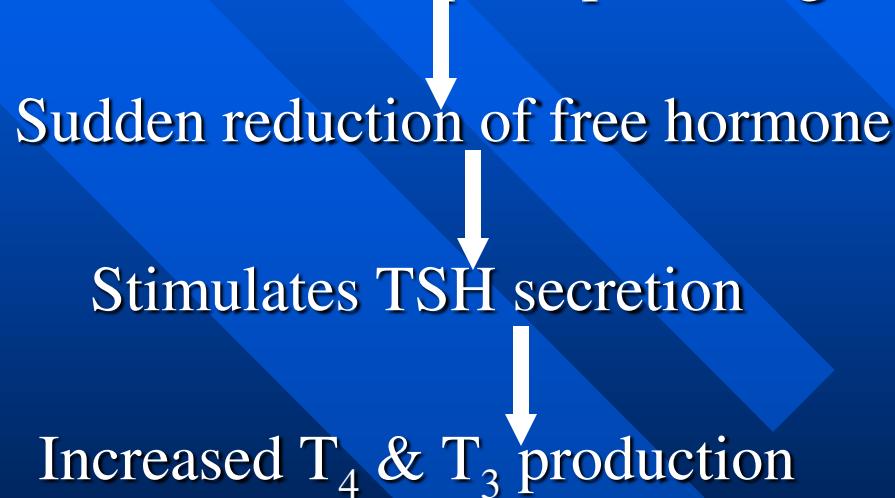




Regulation of
thyroid
hormone
secretion

Fluctuation of plasma proteins

- Alteration of plasma protein alters the thyroid hormone levels in plasma
- Increase plasma protein with
 - Oestrogen therapy
 - Oral contraceptive pills/Pregnancy



Normalises free hormone level with increased total hormone levels- but person is euthyroid

Fluctuation of plasma proteins

- Decreased plasma protein with

Nephrotic syndrome

Androgen therapy

Glucocorticoid therapy

Sudden increase in free hormones

Inhibits TSH secretion

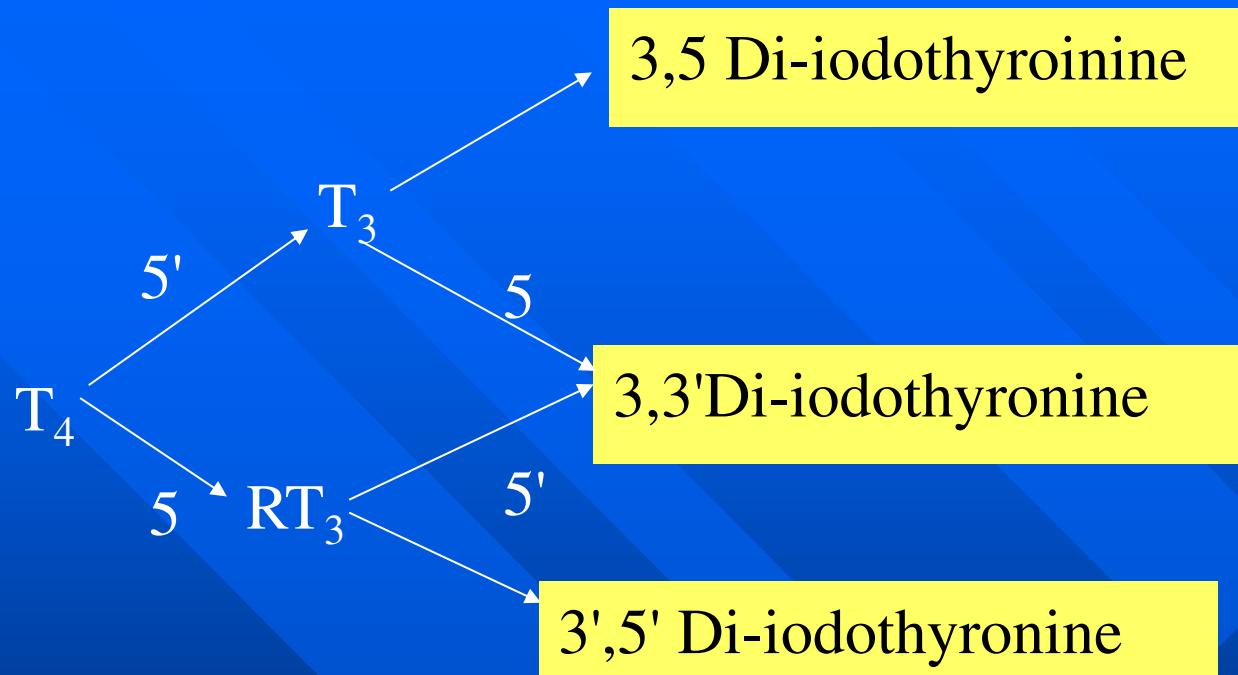
Decreased T_4 and T_3 production

- Normalises free levels with decreased total levels
- Patient is euthyroid

Metabolism of thyroid hormones

- T_4 is a prohormone
- T_4 is converted to T_3 in peripheral tissue by 5'iodinase
- T_3 is more active than T_4
- 87% of T_3 formed by peripheral conversion
- T_4 is converted to Reverse T_3 (RT_3) by 5 iodinase - an inactive metabolite
- T_3 and RT_3 is converted to other metabolites
- T_4 , T_3 , RT_3 conjugated in the liver and are excreted

Metabolism of thyroid hormones



- 5'iodinase activity
- Decreased in
- fever/burns/Myocardial infarction
cirrhosis/ renal failure
starvation
- Increased in overfeeding

Action of thyroid hormones

- T_3 and T_4 are active hormones
- T_3 more active (3-5 times)
- **Mechanism of action**
 - T_3 enters the cell
 - Binds to a nuclear receptor
 - T_3 + receptor complex binds to DNA
 - **Increase expression of specific genes**
- Resulting mRNA trigger protein synthesis

Effects of thyroid hormones

1. Calorigenic action

- Increases

- Basal metabolic rate

- Heat production

- Tissue O₂ consumption

- Except Brain/Testes/uterus/LN/spleen

- Ant.Pituitary

2. Carbohydrate metabolism

- Increases plasma glucose by

- Glycogenolysis

- Increased absorption

- Insulin break down

- Glycogenolytic action of catecholamines

- All catabolic/dibetogenic

Effects of thyroid hormones

3. Fat metabolism

Increased lipolysis

Increased free fatty acids oxidation

Promotes other lipolytic hormones

Increased triglyceride synthesis in liver

- ***Lowers plasma cholesterol

Effects of thyroid hormones

4. Protein metabolism

- In physiological doses

Increases

Protein synthesis

Amino acid uptake

Decreases nitrogen excretion

- Excess hormone results

Protein catabolism

Nitrogen excretion

5. Vitamin metabolism

Converts carotene to vitamin A

Deficiency leads to accumulation of carotene

How do you differentiate jaundice from carotinaemia?

Effects of thyroid hormones

6. Cardiovascular system

Direct action on the myocardium

Increase

the number of β_1 receptors
affinity to catecholamines

Indirect - Via catecholamines

positive chronotropic and positive inotropic action
increase the heart rate and the cardiac output

via increase heat production leads to vasodilatation
results decreased total peripheral resistance

Effects of thyroid hormones

7.Central nervous system

In late foetal and early post natal life stimulates

Development of CNS

Myelination of nerve fibers

In Adults

Stimulates mentation results rapid
mentation

Effects of thyroid hormones

8.Growth and development

- Early foetal growth is not dependent on thyroid hormones
- After foetal thyroid formation- thyroid hormones stimulates

Differentiation & Maturation of foetal tissue

CNS development
Skeletal growth

- After birth thyroid hormones stimulates

CNS development

Linear growth

Skeletal growth

Epiphyseal closure

Potentiate Growth hormone action

Effects of thyroid hormones

9. Interrelated with catecholamine actions

- Increases

- Number of Beta-receptors

- Affinity of beta receptors towards catecholamines

Abnormalities of thyroid function

Excess activity is known as Hyperthyroidism or (thyrotoxicosis)

- Reduced activity is known as Hypothyroidism
- Normal activity- Euthyroid

Any endocrine problem could either be

- Primary -due to a problem in the gland itself
- Secondary - a problem in the regulatory mechanism

Thyroid function tests

■ *Clinical*

Weight

Sleeping pulse

■ *Biochemical tests*

Total hormone levels

Total T_3 and T_4 is of less value because of protein binding

■ Free hormone levels

Free T_4 and T_3

Measured by - RIA(Radio immuno assay)

■ TSH assay

very sensitive test – 3rd generation TSH

■ TRH stimulation test

Not widely used

Imaging of the thyroid gland

■ Thyroid Scan

I^{131} concentrated in thyroid

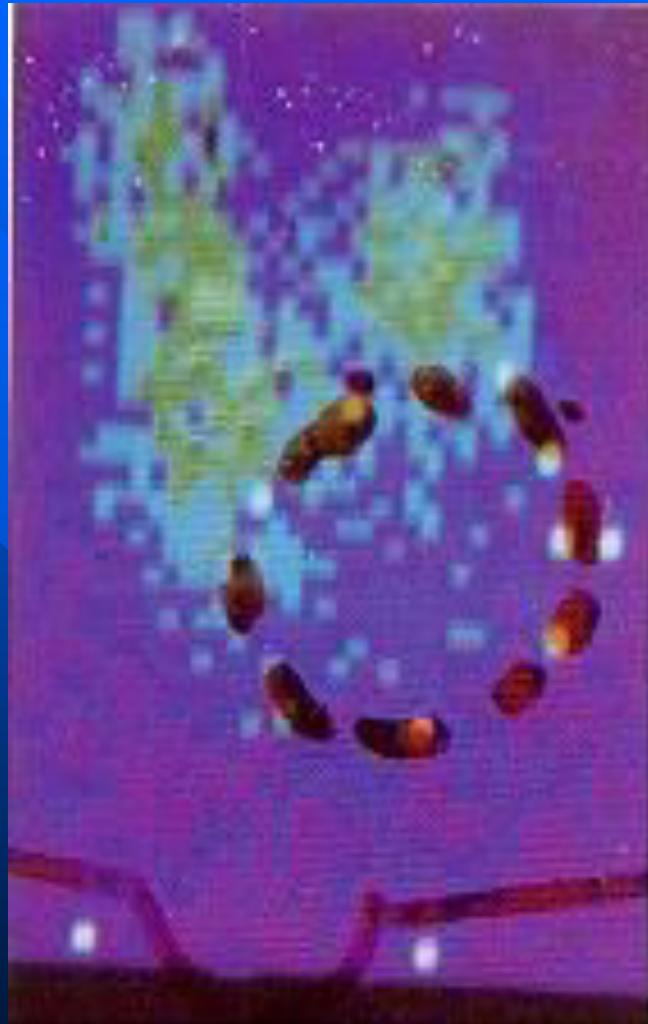
Radioactivity of thyroid measured after oral
 I^{131}

■ Uptake increased in

Hyperthyroidism

Hot nodule

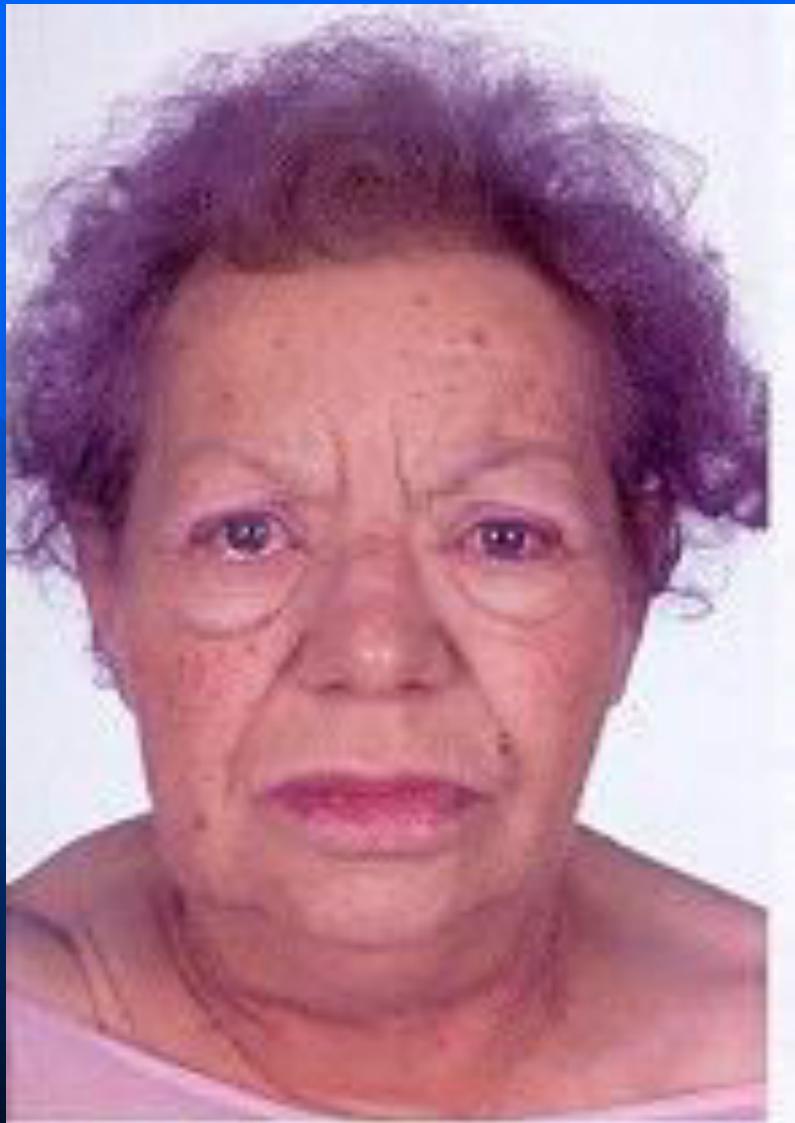
Imaging of the thyroid gland



Hypothyroidism (myxoedema)

- causes
- Primary -
 - Agenesis of gland
 - Dyshormogenesis
 - Autoimmune gland destruction
 - Iodine deficiency
- Secondary -
 - Pituitary failure- lack of TSH
 - Hypothalamic failure-lack of TRH

Hypothyroidism (myxoedema)



Hypothyroidism (myxoedema)

■ Clinical features

■ GIT

Decreased Appetite

Slow Gut motility- constipation

Decreased Glucose absorption

■ CVS

Sinus bradycardia

Decreased cardiac out put

■ CNS

Slow mentation

Slow speech/Horse voice

Slow reflexes

■ Skin

Lustreless hair

Hair loss

■ Decreased BMR

Lethargy

Low heat production

Cold intolerance

Diagnosis

■ Primary

Free T₄/T₃-reduced

TSH markedly elevated

■ Secondary

Free T₄/T₃-reduced

TSH also reduced

Cretinism

- Thyroid deficiency from birth
- Stunting of linear growth-Dwarf
- Mentally retarded
- Pot belly
- Large tongue

- Early detection very important
- Treatment with T_4 prevents

Mental and physical growth retardation

Cretinism



Hyperthyroidism

■ Causes

Graves' disease

Toxic adenoma of the thyroid gland

TSH secreting tumour (rare)

■ Graves disease

Autoimmune condition

Auto antibodies stimulates TSH receptor

Tsab antibodies

Acts similar to TSH

Hyperthyroidism

■ Clinical features

Increased BMR- excess heat production

Weight loss

Increased appetite

■ CNS

Restless/Irritability

Tremors/muscle weakness

■ Eye signs

Peculiar to Graves disease

Exophthalmos (Protrusion of eye ball)

Lid Lag/Lid retraction

■ CVS

Increased pulse rate

Sinus tachycardia

Atrial fibrillation

Increased cardiac output

Increased systolic BP

Vasodilatation

Decreased diastolic BP

Increased pulse pressure

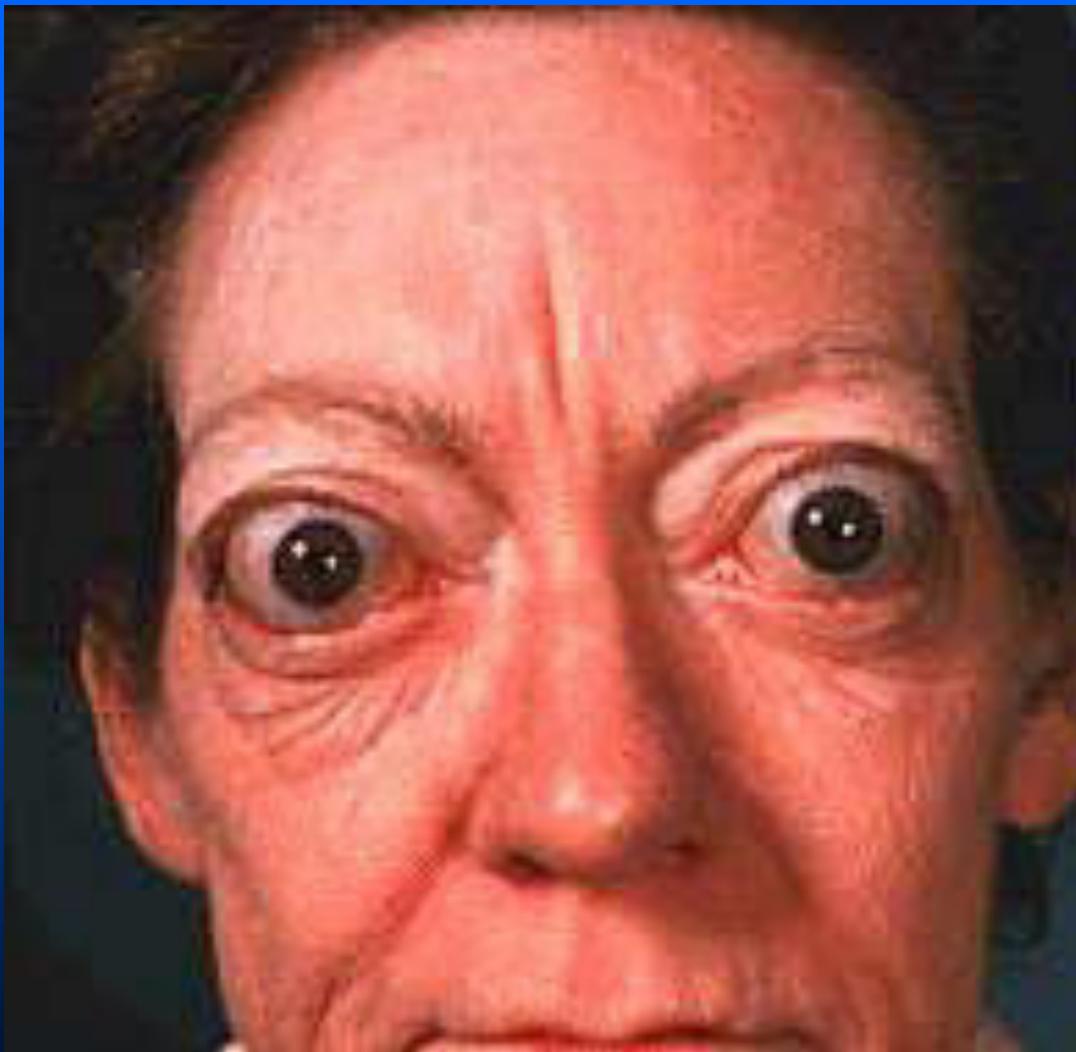
High output failure

Thyroid bruit

Hyperthyroidism

- Exophthalmos is thought to be due to
 - Immune complex deposition
 - Intra ocular muscle inflammation
- Pre tibial myxoedema
 - deposition of mucopolysacharaides
 - results non pitting ankle oedema

Graves disease



Hyperthyroidism

■ Diagnosis

Free T4 and T3 elevated
TSH markedly reduced

Treatment

Anti thyroid drugs

Beta Blockers

- Inhibits action of beta 1 receptors
- Inhibits conversion of T4 to T3

Goitre

- Enlargement of thyroid gland
- Can be Euthyroid/Hypothyroid/Hyperthyroid
- Causes

Physiological- Puberty/Pregnancy

- Other causes

Iodine deficiency

Lack of dietary Iodine

Presence of goitrogens (Cabbage)

- Autoimmune conditions (Graves disease)
- Tumours/cysts