THE PHYSIOLOGY OF THE ENDOCRINE SYSTEM

Professor Dr. Ghalib Al Sharefi

Endocrine glands

1. No ducts
2. Highly vascular
3. Secret hormones
4. Distant targets

Hormones are ch. by :

1. Chemical substances
2. very low concentrations
3. Not utilized by the target cells
4. Act on specific receptors
5. they are either peptides ,amines or steroids

Endocrine Glands

- **Hypothalamus**

  CRF, GRF, GHIH, Dopamine,TRH, GnRH

- **Pituitary**

  ACTH, GH, Prolactin, TSH, FSH, LH

  ADH, Oxytocin

- **Thyroid**

  T4, T3, Calcitonin

- **Parathyroid**

  Parathyroid Hormone

- **Adrenal**

  Cortisol, Aldosterone, Androgens

  Catecholamines

- **Pancreas**

  Insulin, Glucagon, Somatostatin

- **Gonads**

  Oestrogen/Testosterone

- **GIT tract**

  Gastrin, Neurotensin, Secretin,

  GIP, GLP

- **Kidney**

  Renin, Erythropoietin, 1,25-

  dihydroxyvitamin D

- **Placenta**

  HCG, HPL

COMPARISON OF ENDOCRINE AND NERVOUS SYSTEMS

- **NERVOUS SYSTEM**
- "WIRED"
- CHEMICAL SIGNAL AT TARGET CELL
- RAPID
- BRIEF DURATION
- CLOSE ANATOMICAL PROXIMITY

- **ENDOCRINE SYSTEM**
- "WIRELESS"
- CHEMICAL SIGNAL AT TARGET CELL
- SLOW
- LONG DURATION
- SPECIFIC RECEPTORS

CATEGORIES OF HORMONES

- PEPTIDES
- AMINES
- STEROIDS

PEPTIDES

- HYDROPHILIC, DISSOLVED IN PLASMA
- RECEPTOR ON CELL SURFACE
- cAMP OR CALCIUM AS SECOND MESSENGERS
- ACTIVATE SPECIFIC GENES TO INITIATE PROTEIN SYNTHESIS

- HYPOTHALAMIC
- PITUITARY
- PANREATIC
- PARATHYROID

- GI
- KIDNEY
- LIVER
- HEART

AMINES

- ALL DERIVED FROM AMINO ACID TYROSINE
- UNIQUE SYNTHETIC AND SECRETORY PATHWAYS

- THYROID HORMONE
- CATECHOLAMINES

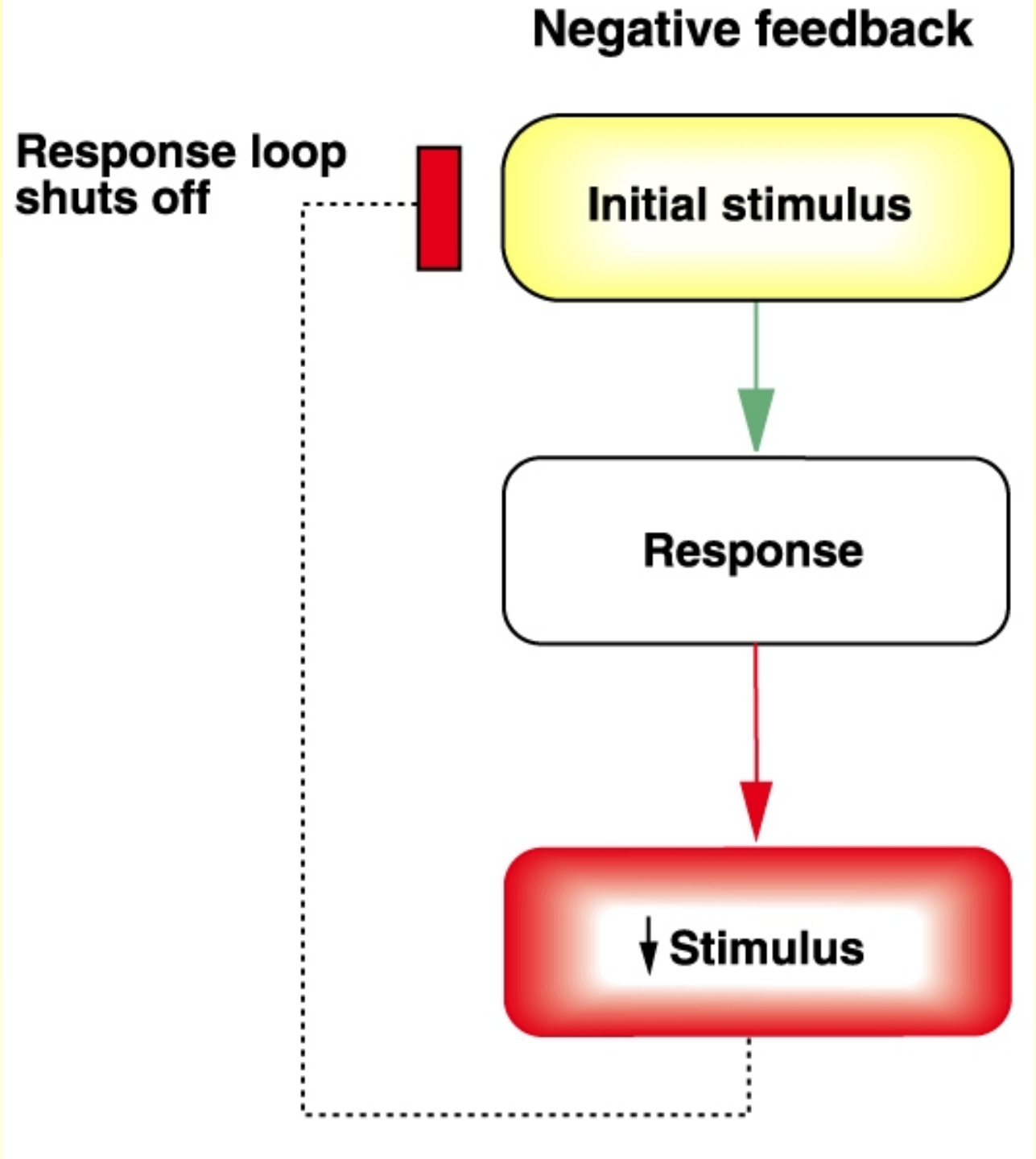
STEROIDS

- LIPOPHILIC
- RECEPTOR IN CYTOPLASM
- ACTIVATE SPECIFIC GENES TO INITIATE PROTEIN SYNTHESIS

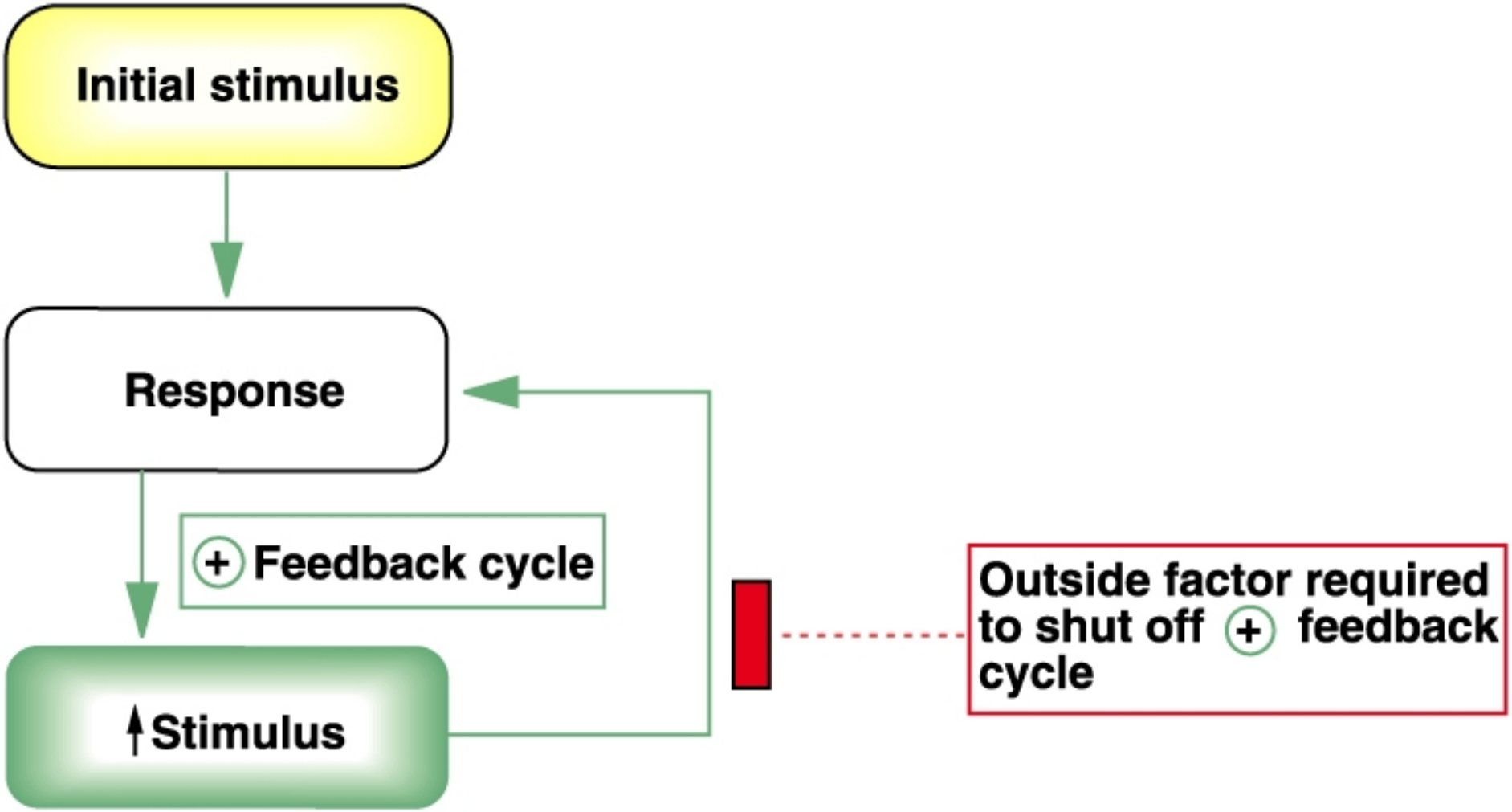
- ADRENAL CORTICAL
- GONADAL
- PLACENTAL

PLASMA CONCENTRATION OF HORMONES

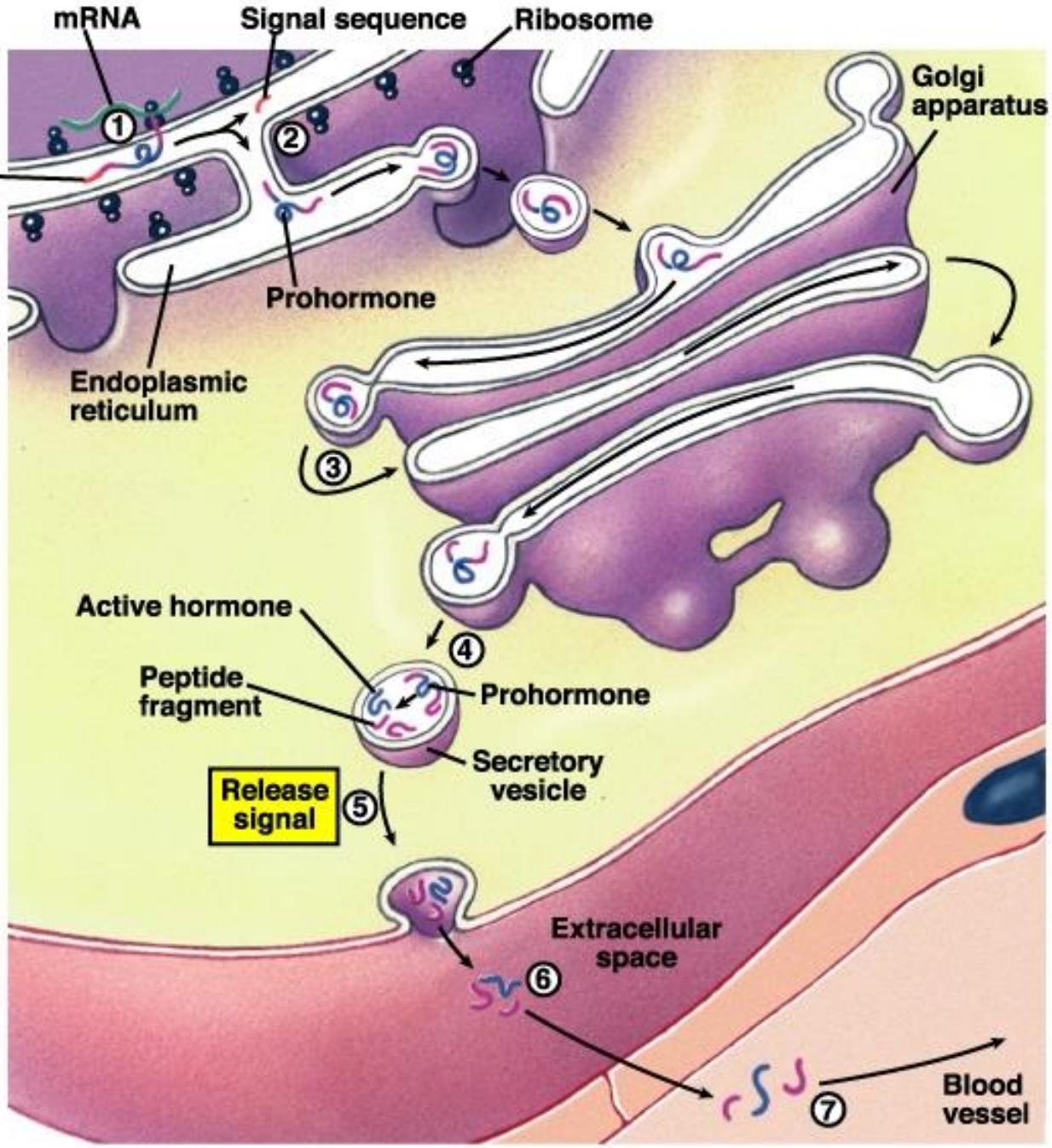
- DEPENDS ON RATE OF SECRETION
- NEGATIVE FEEDBACK
- NEUROENDOCRINE REFLEXES
- DIURNAL RHYTHMS


Negative feedback
Response loop shuts off
Initial stimulus
Response
Stimulus

Positive feedback

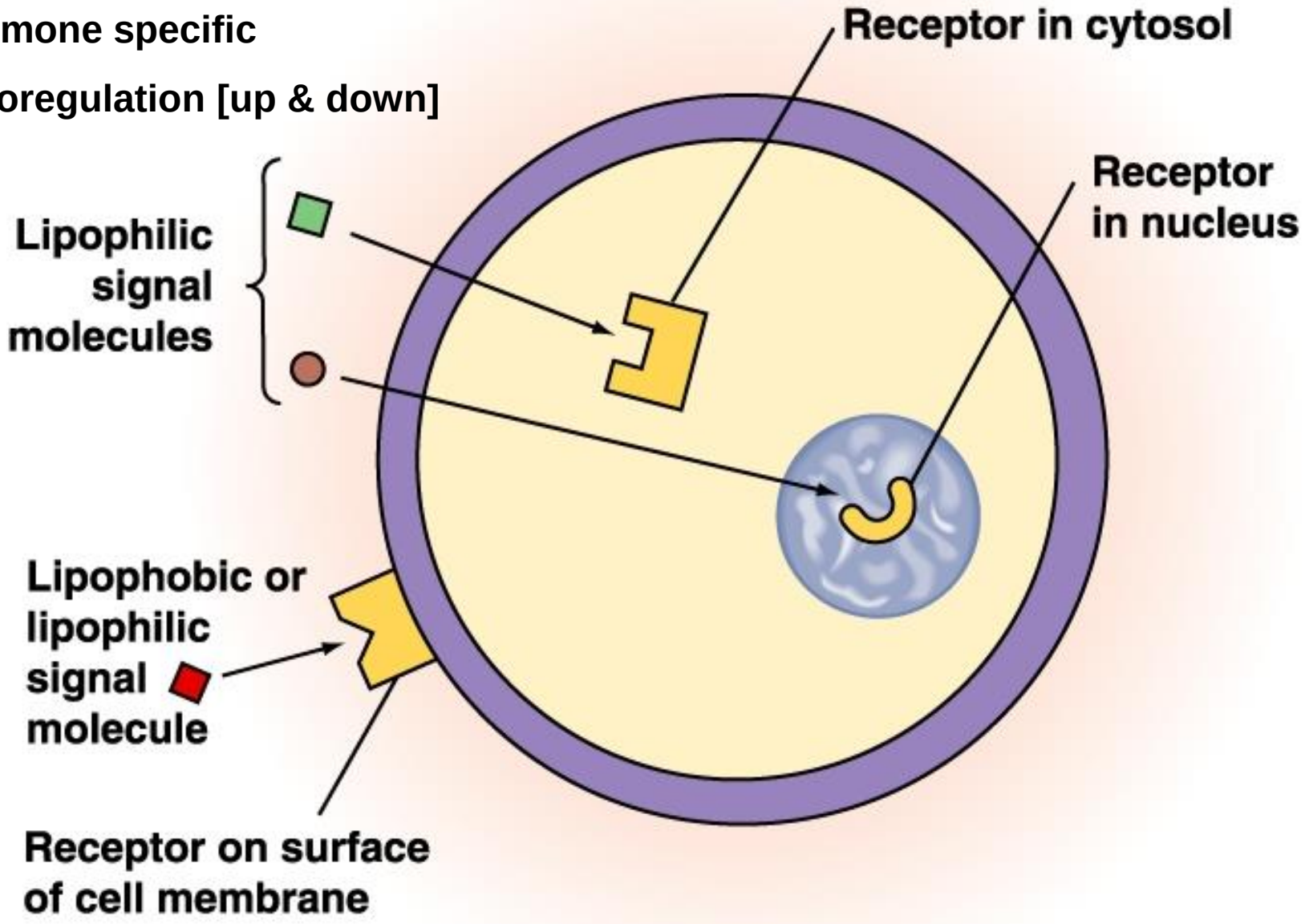


Transcription and translation



•High mol.wt

- Hormone specific
- Autoregulation [up & down]



Auto Regulation of receptors :

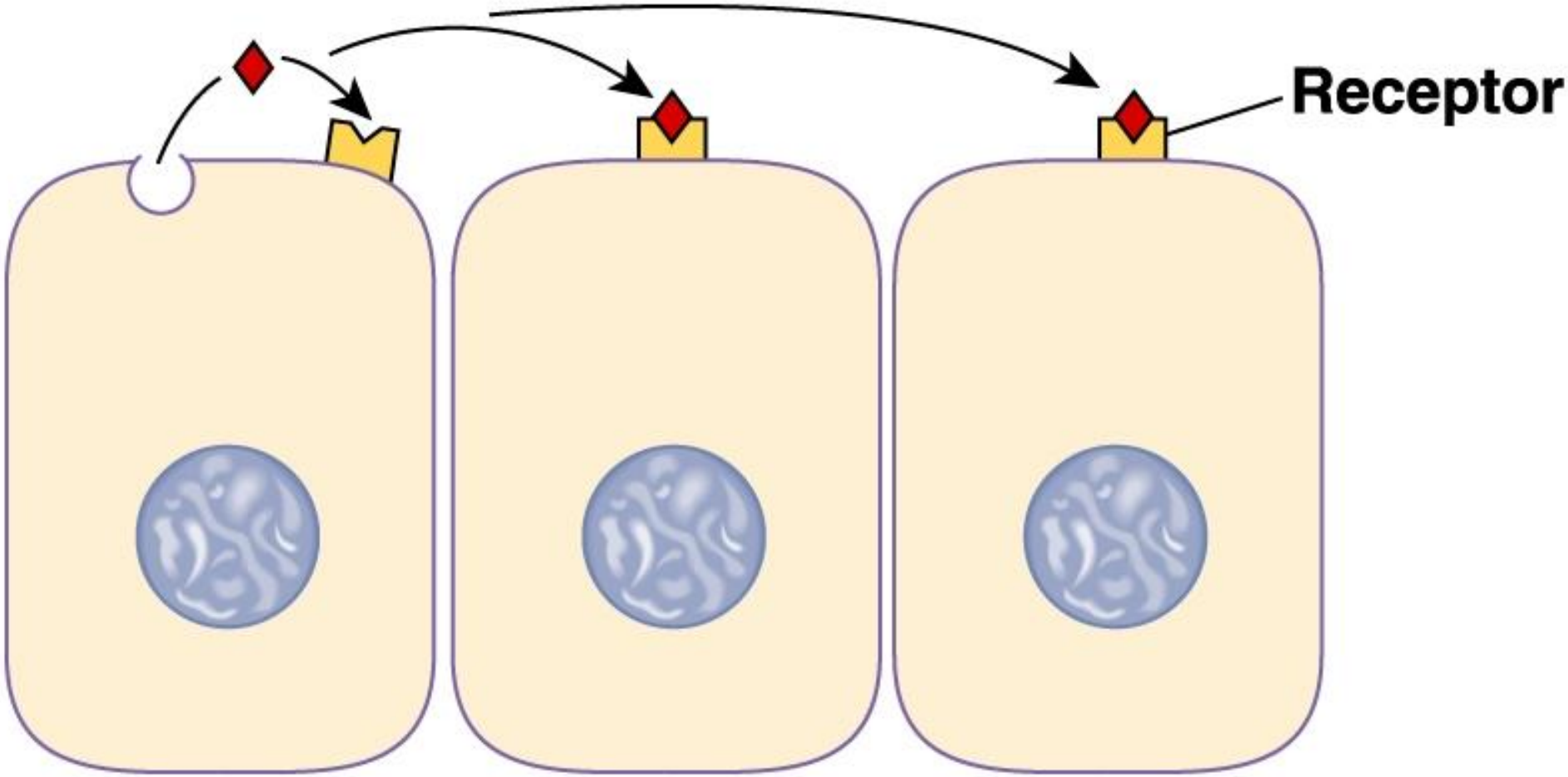
↑ Hormone conc. → ↓ Number and affenity of receptors

DOWN REGULATION

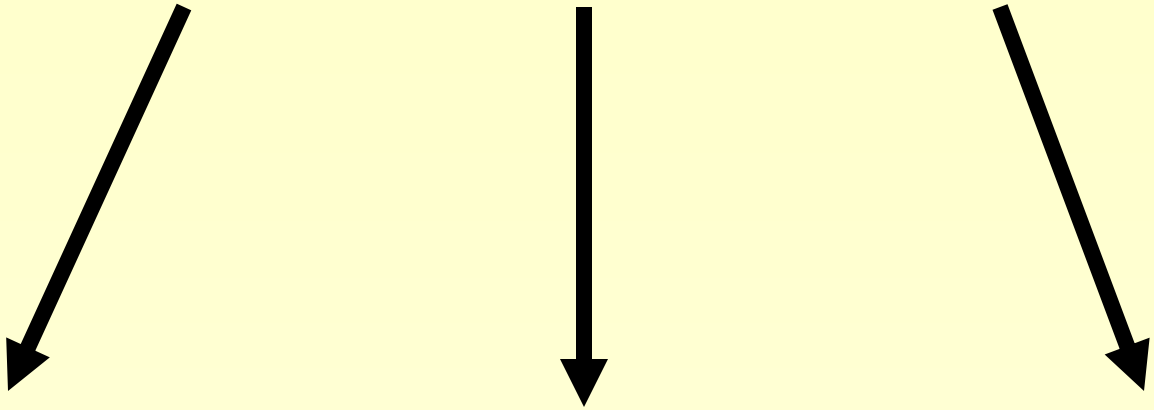
↓ Hormone conc. → ↑ Number and affenity of receptors

UP REGULATION

Autocrine and paracrine signals



Mechanism of action of hormones



Change in membrane permeability

e.g. Catecholamines

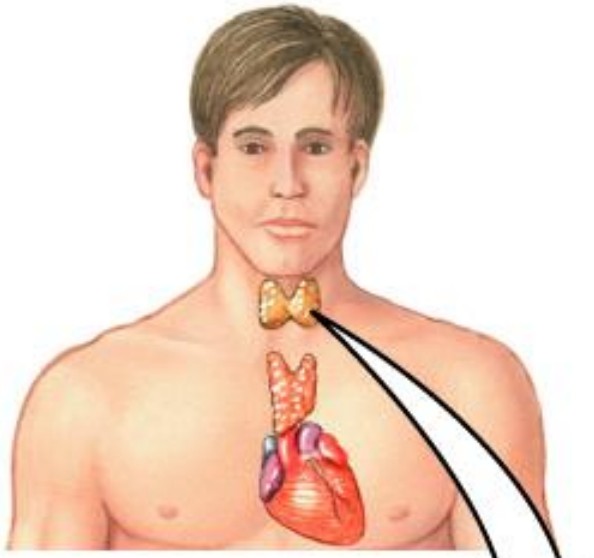
Activation of gene formation by H-R complex

e.g. Insulin& Growth hormone

Acrtivation of IC enzymes (second messanger)

e.g. Sex hormones

The Thyroid Gland

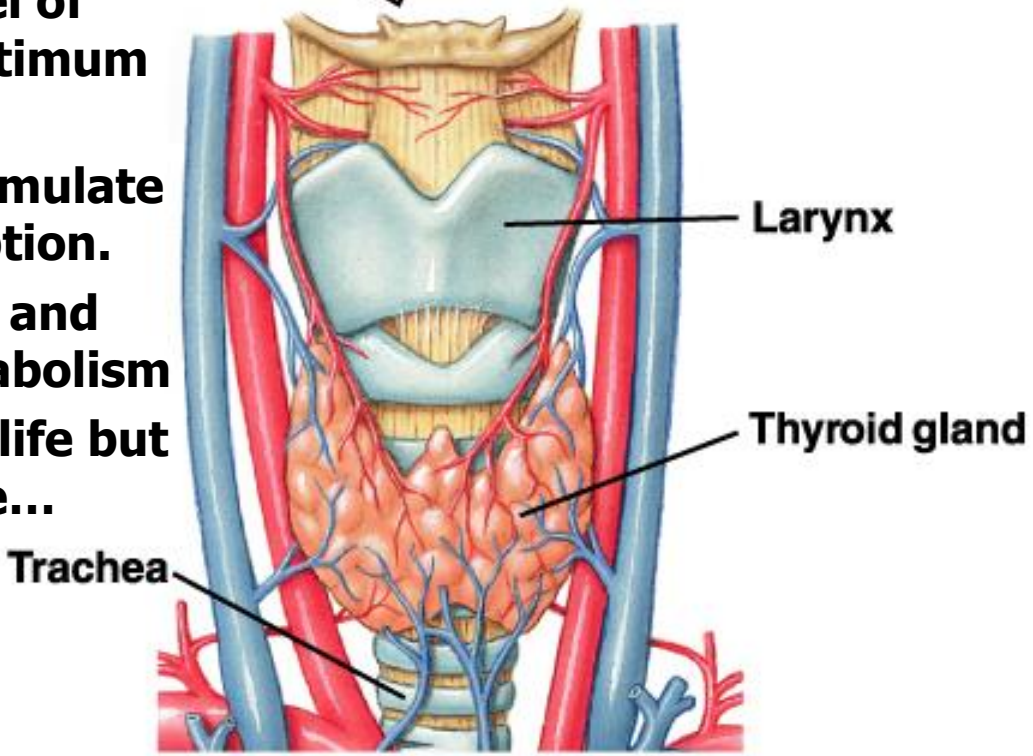


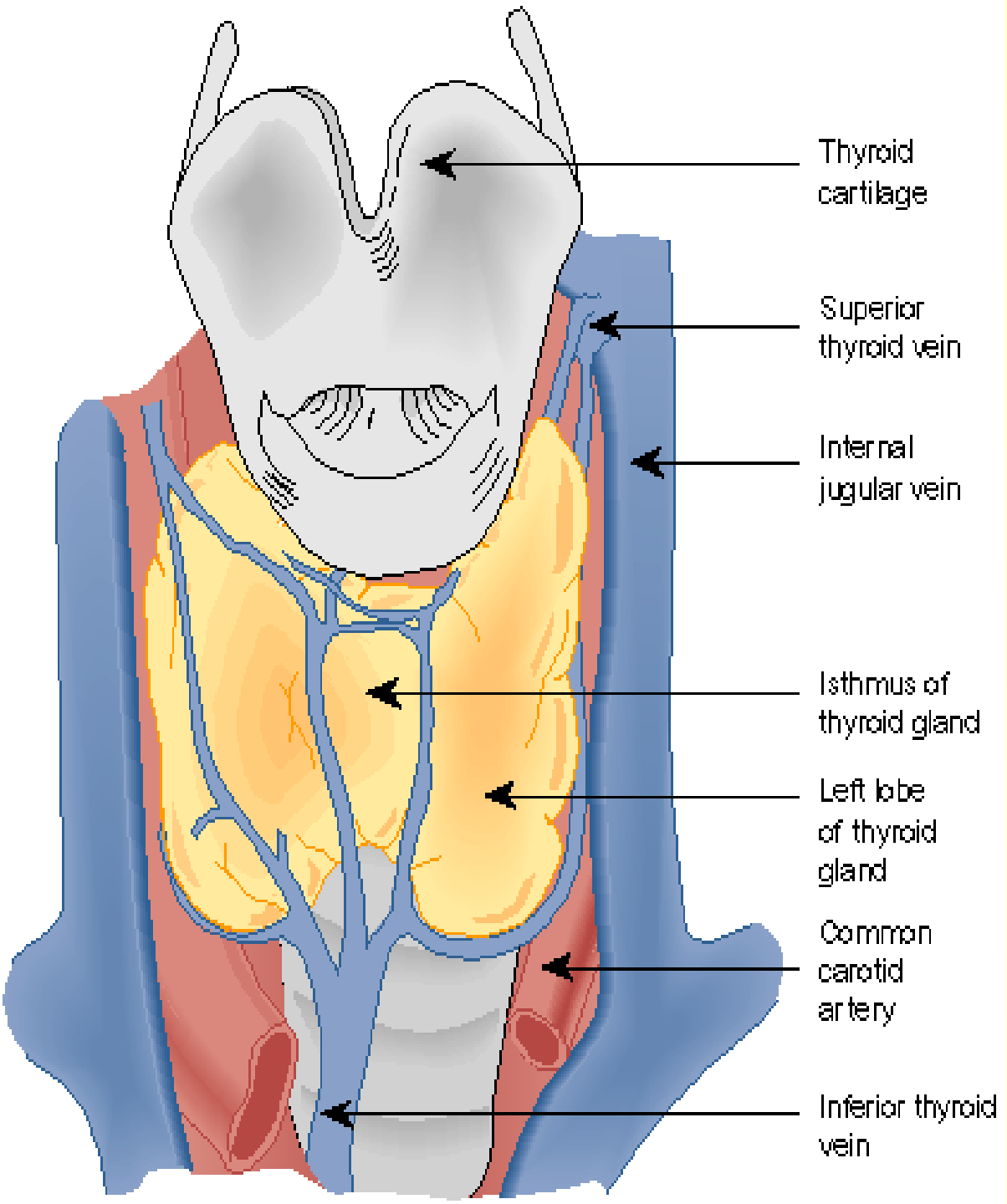
Maintains the level of metabolism at optimum level

Thyroid hormones stimulate the O2 consumption.

Regulation of lipid and carbohydrate metabolism

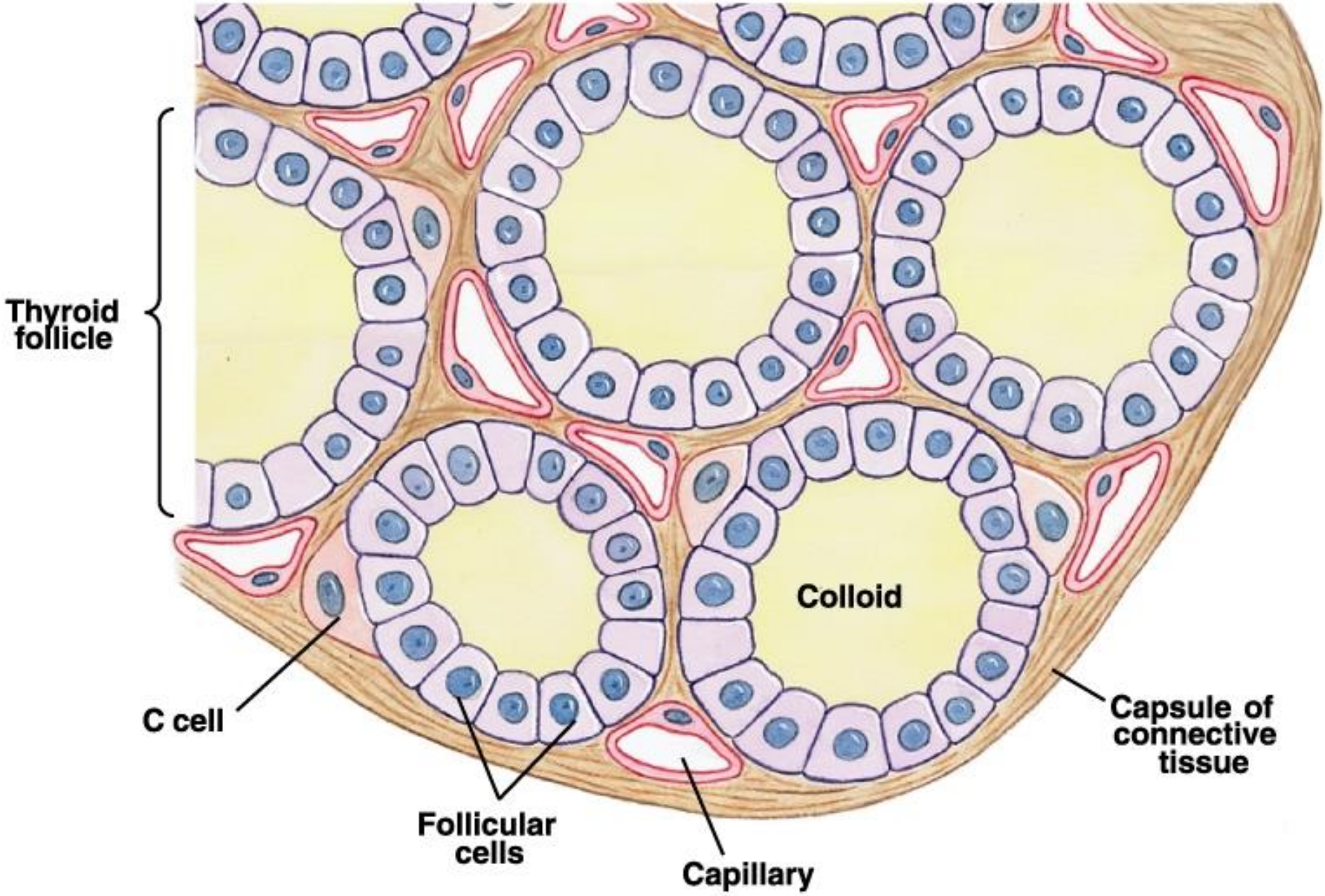
It is not essential for life but in it's absence…





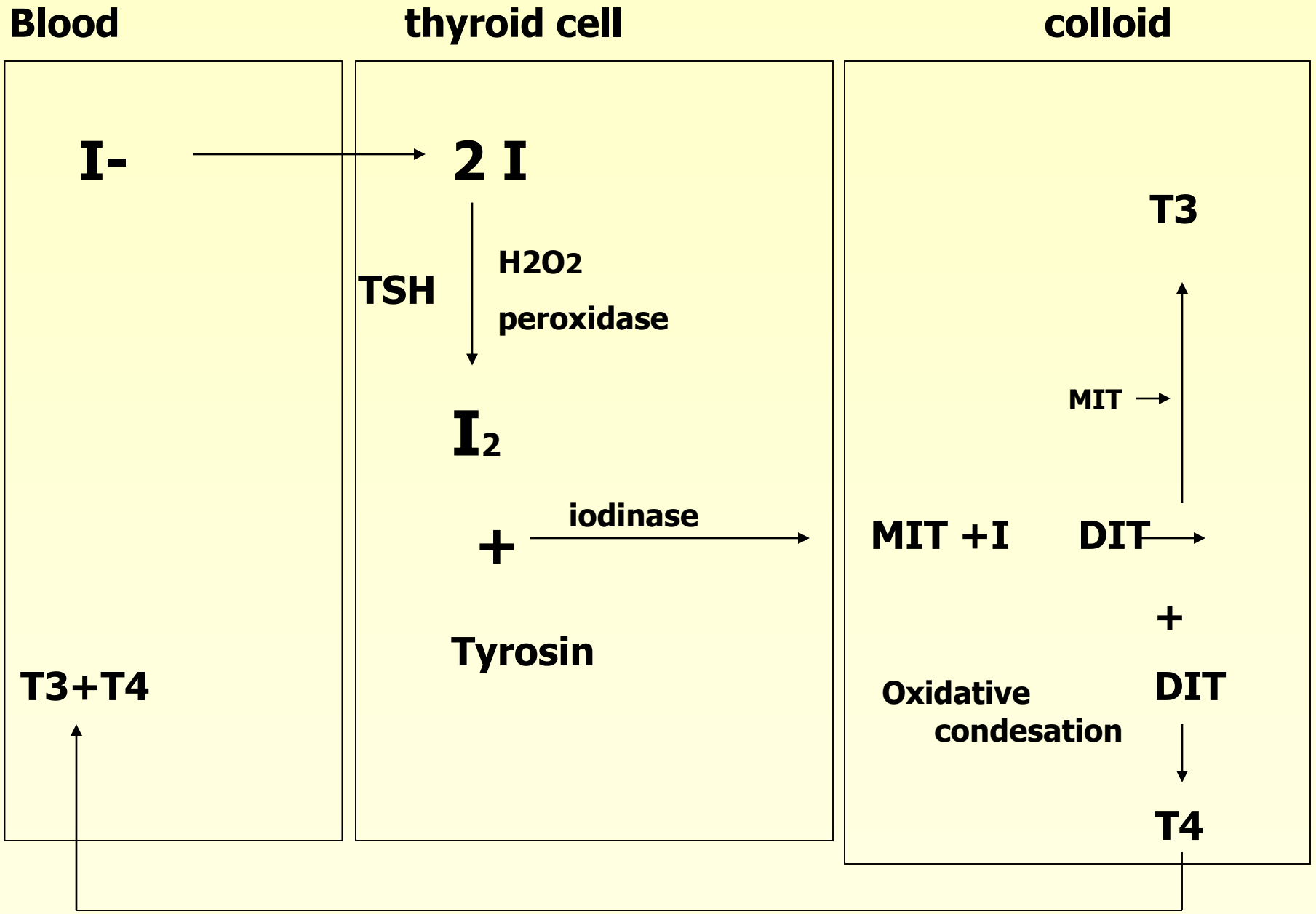
- **In adults**
- **Two lateral lobes**
- **Isthmus;**
  level of 2nd – 3rd tracheal rings.
- **The highest rate of blood flow**

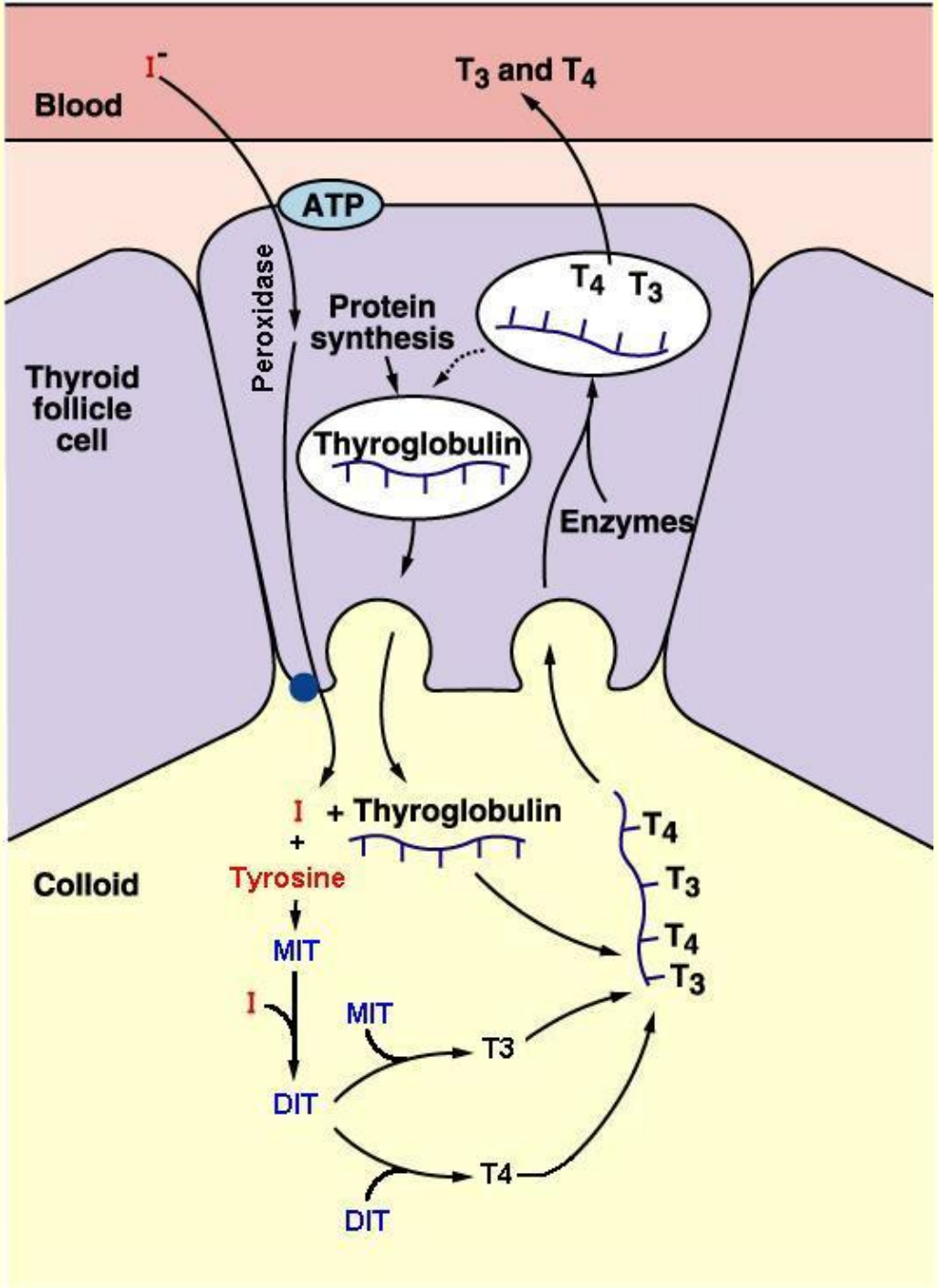
Section of thyroid gland

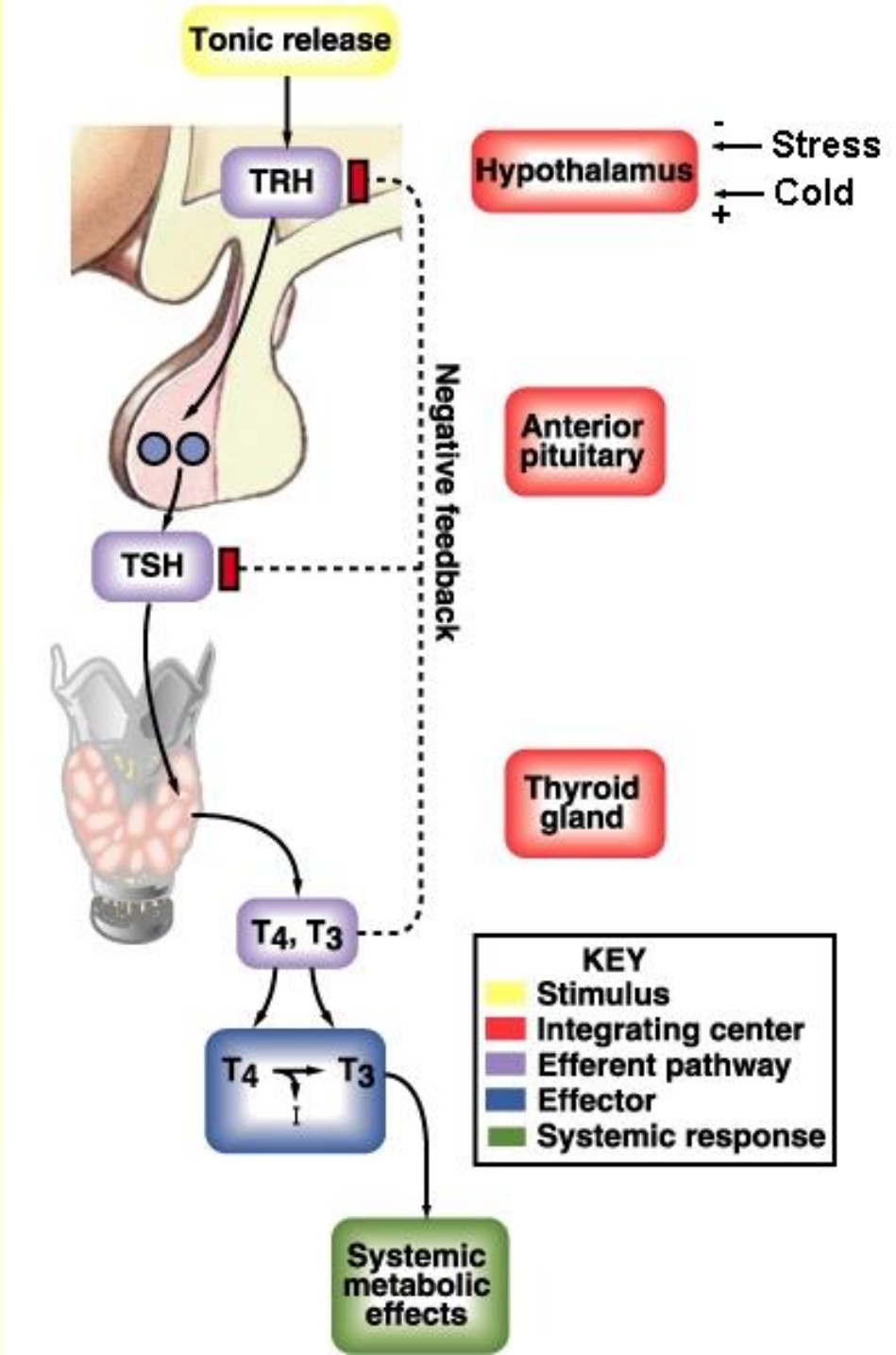


Functions of thyroid cells:

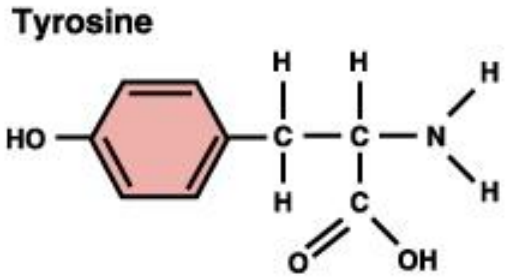
1. Collect and transport of iodine(iodine pump).
2. Synthesize and secrete thyroglobulin into the colloid .
3. Remove T3 and T4 from thyroglobulin back to the circulation.
4. Formation of thyroid hormones.


Blood
thyroid cell
colloid
I-
2 I
TSH
H2O2
peroxidase
I2
+
iodinase
Tyrosin
T3+T4
T3
MIT
MIT +I
DIT
+
DIT
Oxidative
condesation
T4


Blood
I⁻
T3 and T4
ATP
Peroxidase
Protein synthesis
T4 T3
Thyroid follicle cell
Thyroglobulin
Enzymes
I + Thyroglobulin
+
Tyrosine
Colloid
MIT
I
MIT
T3
DIT
T4
DIT
T4
T3
T4
T3


Tonic release
TRH
Hypothalamus
-
Stress
Cold
+
Negative feedback
Anterior pituitary
TSH
Thyroid gland
T4, T3
KEY
Stimulus
Integrating center
Efferent pathway
Effector
Systemic response
T4
T3
Systemic metabolic effects

T4



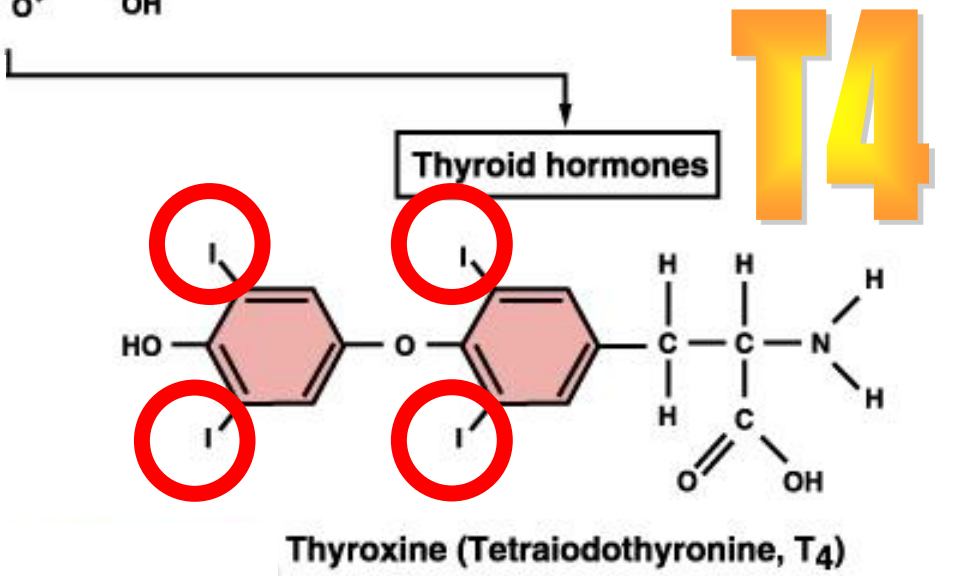
•Less **potent** than T3

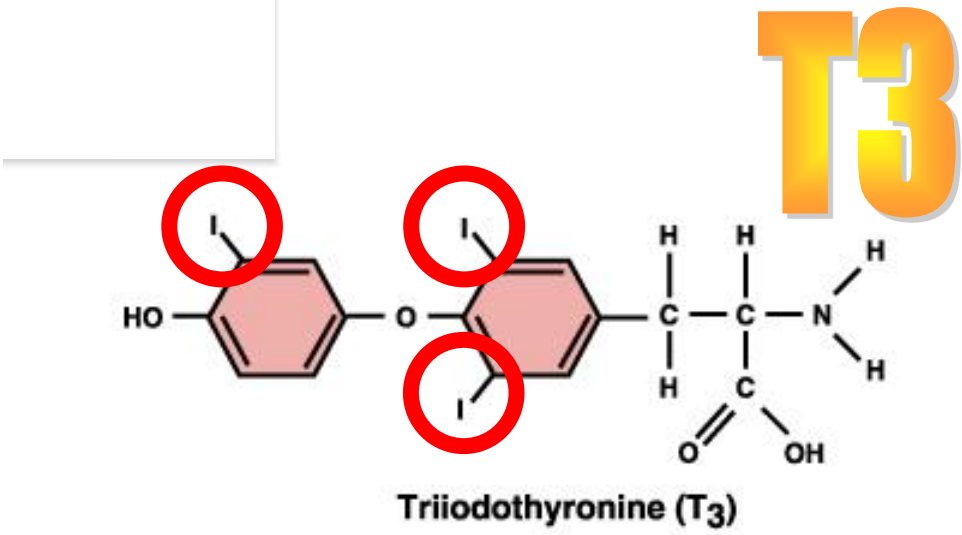
•**inert metabolically**

•Mostly **converted** to T3 and RT3 (Reversed T3, inactive) in tissue.

•T4 is the **major precursor** of T3.

•T4 has the major role in **feedback mechanism**



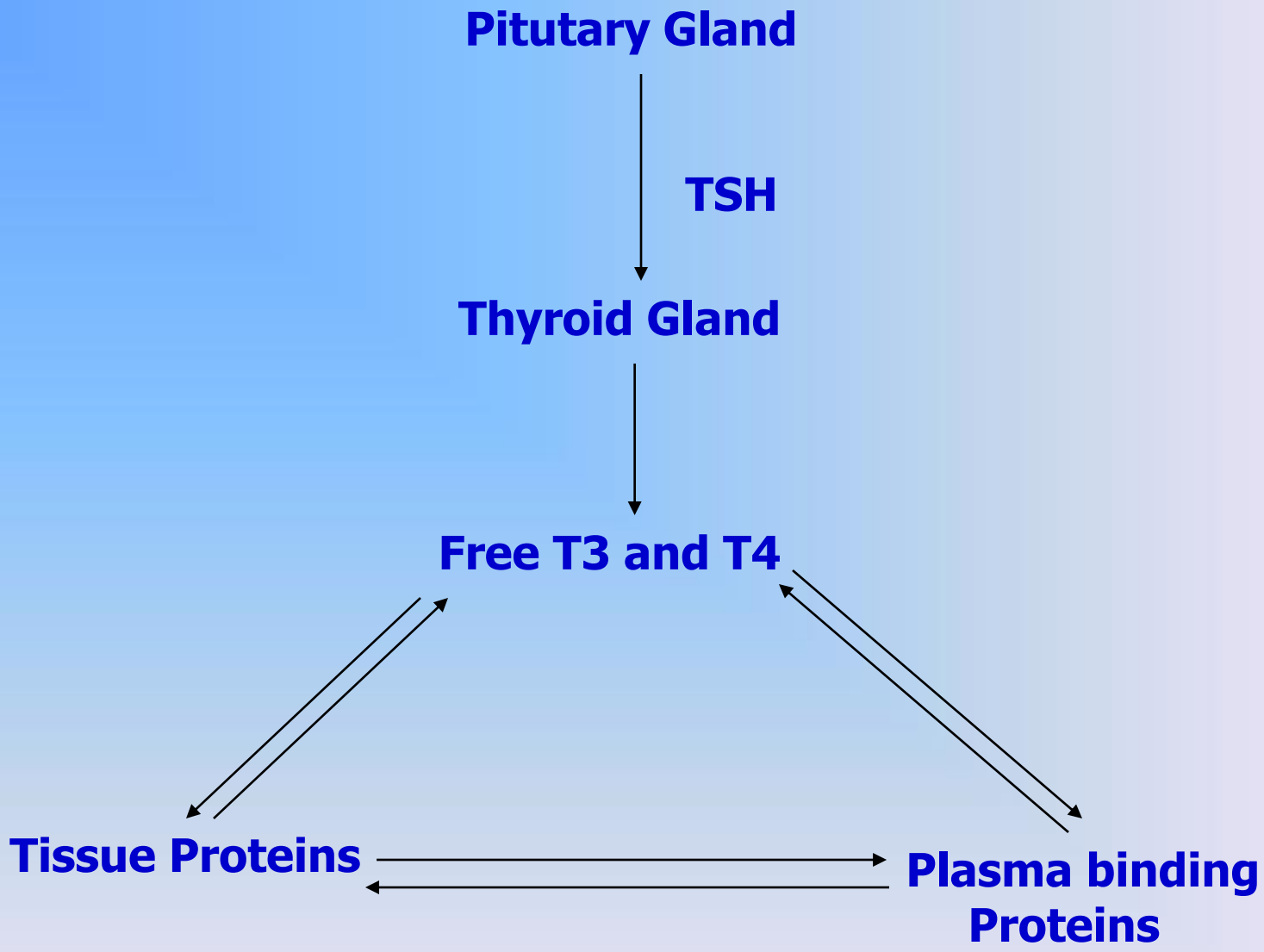


The total normal plasma T4 level is **8 μg/dl** and for T3 is **0.15 μg/dl.**

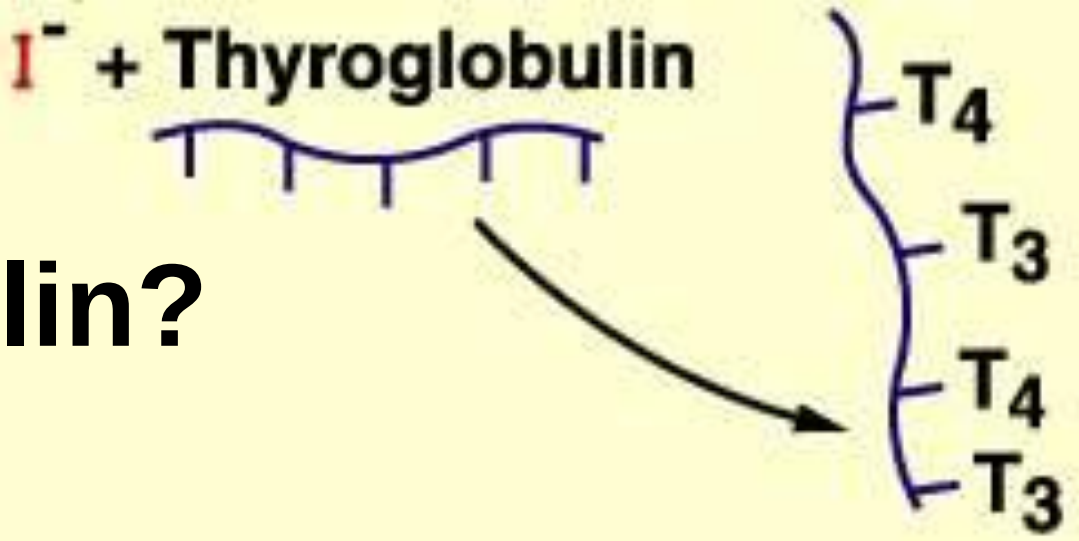
However,

the free circulating levels of T3 and T4 are much less than the total levels,

this is because most (99%) of T4 and T3 are bound to plasma proteins (albumin, thyroxine binding prealbumin [TBPA] and thyroxine binding globulin [TBG]).


Pitutary Gland
TSH
Thyroid Gland
Free T3 and T4
Tissue Proteins
Plasma binding Proteins

What is Thyroglobulin?



- Is a **glycoprotein** made up of two subunits, with 140 tyrosine residue.
- It is synthesized in the **thyroid cells** and secreted into the colloid by exocytosis of granules that also contain thyroid peroxidase.
- **Thyroid hormones remain bound to Thyroglobulin until secreted**.

TSH Control of Thyroid Gland

- Rapid Effects (2-5 min.):
  - +Ca++, +cAMP
  - + Colloid Reabsorption
- Intermediate Effects (10-30min.):
  - +Blood Flow to thyroid (vasodilatation)
  - +Na+-K+-ATPase Activity
  - +Na+ Transport into Thyroid
- Slow Effects (+/- 2 hours)
  - +Glucose Uptake & Utilization
  - +Iodide Transport
  - +O2 Uptake & Utilization
  - +A. A. Uptake, + RNA, +DNA, +Prot. Synt.

TSH Control of Thyroid Gland

- Long Term Effects (Days, Weeks, Months):
  - +Blood Supply
  - +Number of Cells (hyperplasia)
  - +Size of Cells (hypertrophy)
  - +Amount of Colloid
- SUMMARY
  - +TH output, +TH Synthesis & Storage

THYROID HORMONE'S EFFECTS

1. **CALOROGENIC: INCREASED HEAT PRODUCTION**

Due to increase O2 consumption (by increasing synthesis & activity of Na-K pump)

Except

Adult brain, retina, uterus, testes, LN, spleen, & lungs

THYROID HORMONE'S EFFECTS

2. METABOLIC EFFECTS: INCREASED BMR

- **Increase protein anabolism & catabolism ➔ Inc. N2 exc.**
- **Increase fat catabolism**
- **Decrease levels of cholesterol, phospholipids, & TG (increase LDL)**

THYROID HORMONE'S EFFECTS

- **Increase Glucose absorption by GIT, stimulates its uptake, Inc. glycolysis and gluconeogenesis (diabetic OGTT curve)**

3. Effect on nervous system:

Blood flow, O2 consumption, & glucose are not affected by Thyroid Hormones. The effect of Thyroid H. on the brain is due to increase responsiveness to catacholamines (increrase Reticular System Activity)

3. Effect on nervous system:

- Restlessness, crowds of thought, irritability , excess of activity and movment , increase tendon reflexes , nervousness .
- In opposite decrease thyroid hormones leads to slow movment , fatique , slow mantation , reduced and prolong reflexes and deppression .

4. Effect on CVS:

Increase number and affinity of beta receptors leading to increase response to catecholamines ➔ increased heart rate (tachycardia & palpitation) , increase systolic BP, increase cardiac output, decrease diastolic BP(wide pulse pressure),tremer, increase sleeping pulse ,

5. Other effects:

- **Enhances GH secretion(timming)**
- **Increases insulin secretion**
- **Increases 2,3 diphospho glycerol(DPG) , Increases rate & depth of respiration**
- **Increases milk secretion, stimulates metabolism of uterus (amenorrhea in thyrotoxicosis & menorrhagia in hypothyrodisim)**
- **In male changes in thyroxin level lead to loss of libido & imputance**

Goiter

Defined as any increase in the size of the thyroid gland which could be diffuse goiter or nodular goiter irrespective to the level of thyroid hormone secretion .

GOITER

- Normal thyroid secretion:
  - 1-Physiological
  - 2-Endemic
  - 3- Multinodular goiter
- Low thyroid secretion :
  - 1-Hashitmoto thyroiditis
- Increased thyroid secretion:
  - 1- Graves' disease

Physiological Goiter

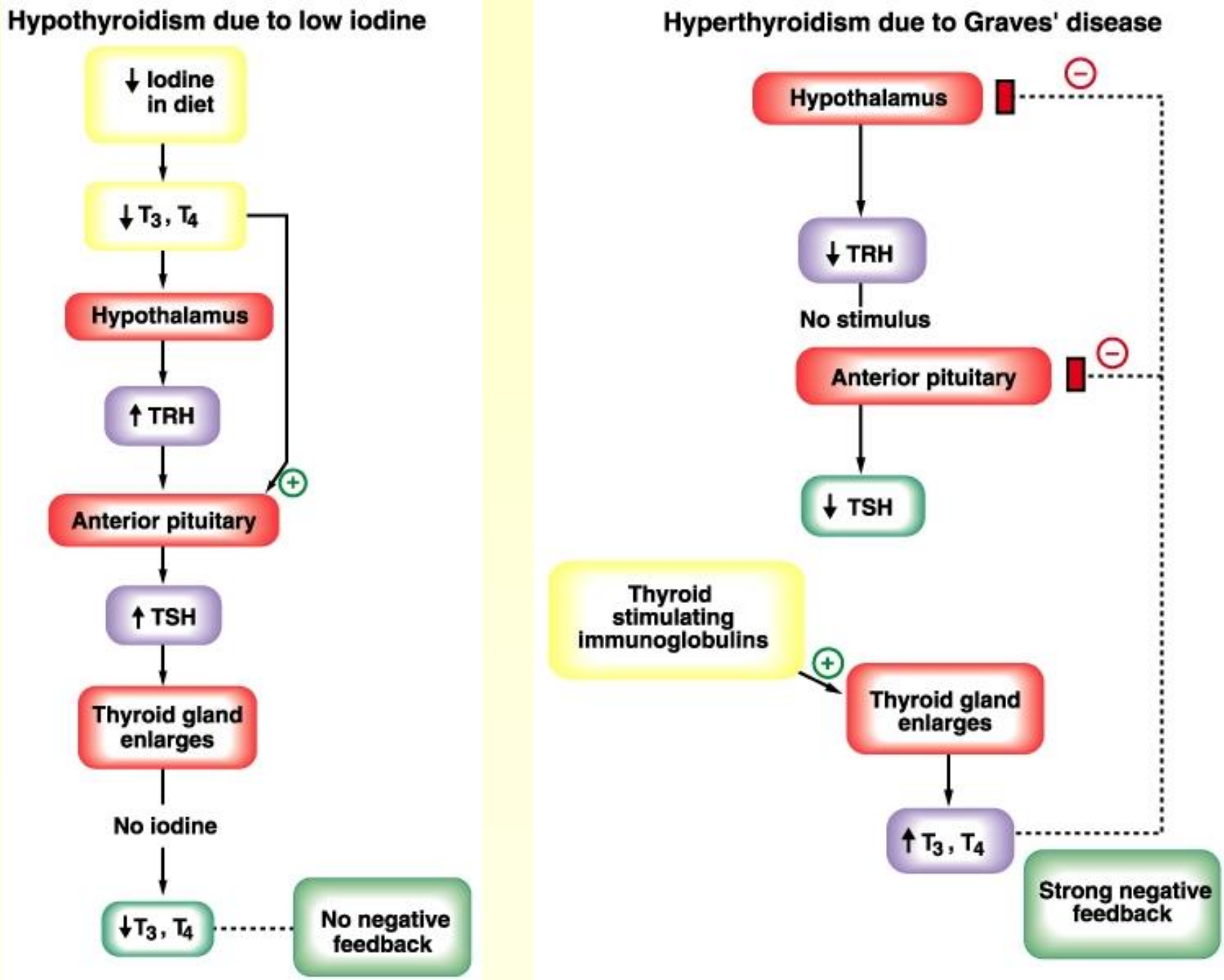
Occurs due to increase stress and increase demand for T3 and T4 necessary for growth.

e.g. puberty &

Pregnancy

Endemic Goiter

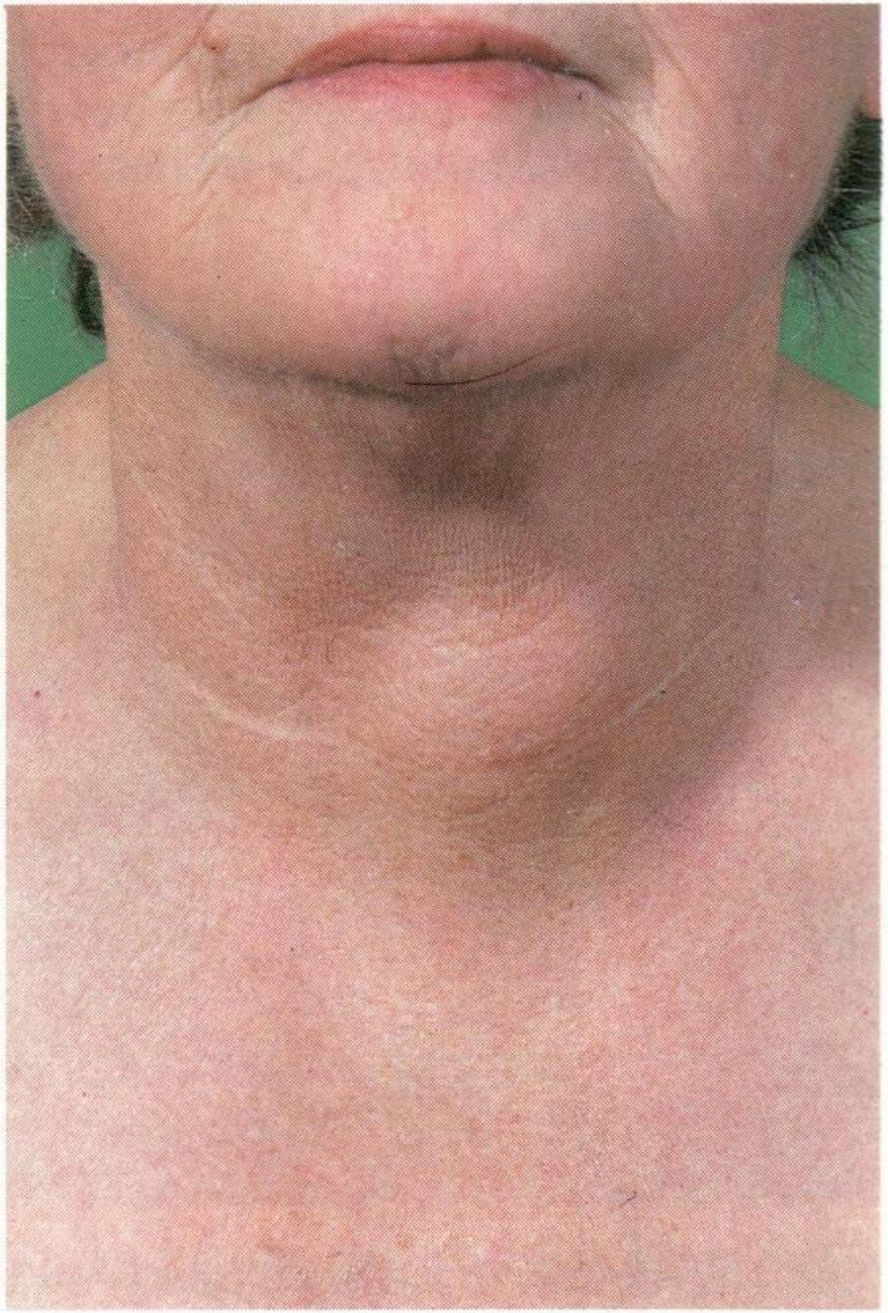
When the dietary intake is less tan 10 μg/day, the thyroid hormone synthesis is inadequate and T3 and T4 levels decline. As a resul TSH is stimulated leading the thyroid to be hypertrophied producing an iodine deficiency endemic goiter which may be very large. It occurs in certain areas around the great lakes and in inlands where the iodine is leached out of the soil by the rain so food will be grown in the soil is iodine deficient.


Hypothyroidism due to low iodine
↓ Iodine in diet
↓ T_3, T_4
Hypothalamus
↑ TRH
Anterior pituitary
↑ TSH
Thyroid gland enlarges
No iodine
↓ T_3, T_4
No negative feedback
Hyperthyroidism due to Graves' disease
Hypothalamus
↓ TRH
No stimulus
Anterior pituitary
↓ TSH
Thyroid stimulating immunoglobulins
Thyroid gland enlarges
↑ T_3, T_4
Strong negative feedback

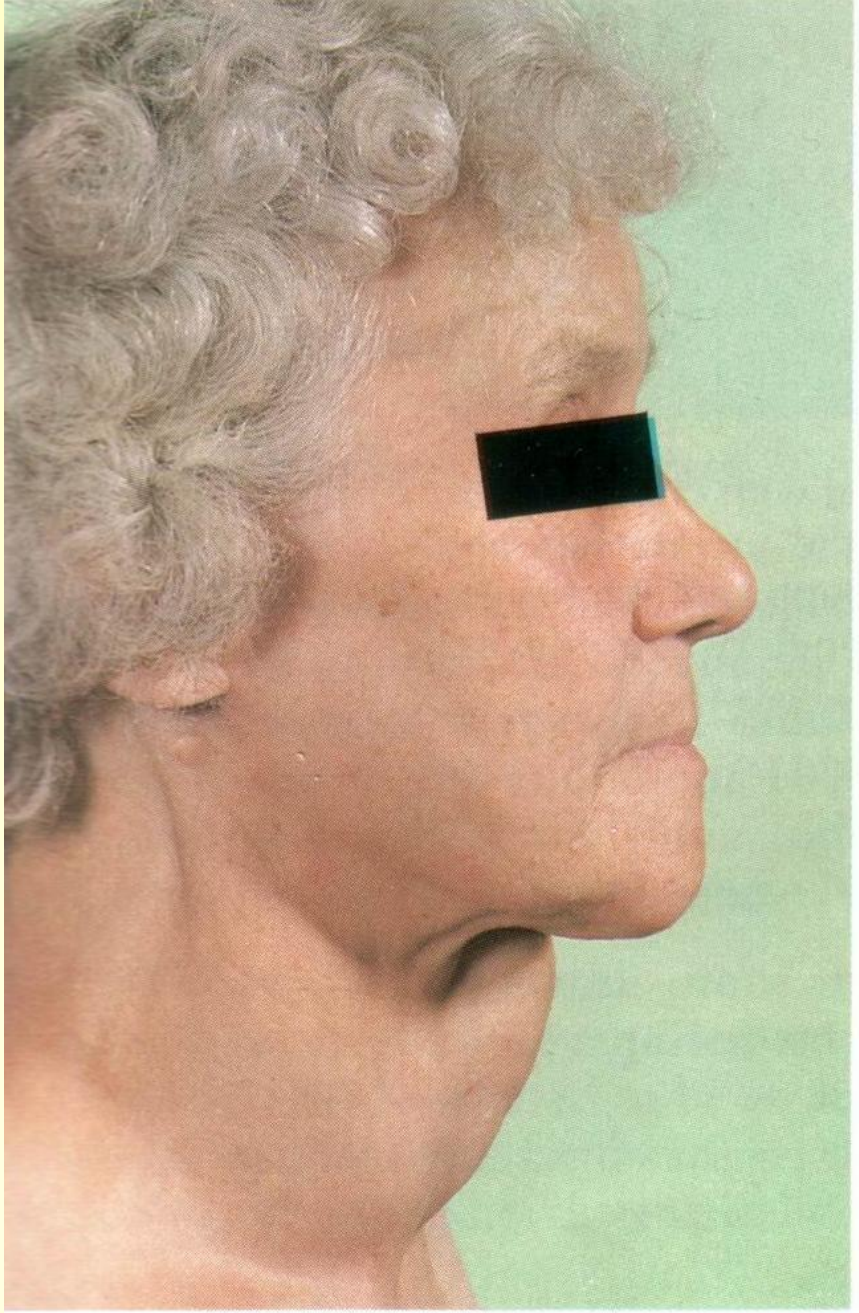
ABNORMALITIES OF THYROID FUNCTION

- HYPO
- REDUCED BMR
- POOR TOLERANCE OF COLD
- GAIN OF WEIGHT
- FATIGUE
- SLOW, WEAK PULSE
- SLOW REFLEXES AND MENTATION
- MYXEDEMA
- GOITER
- CRETINISM

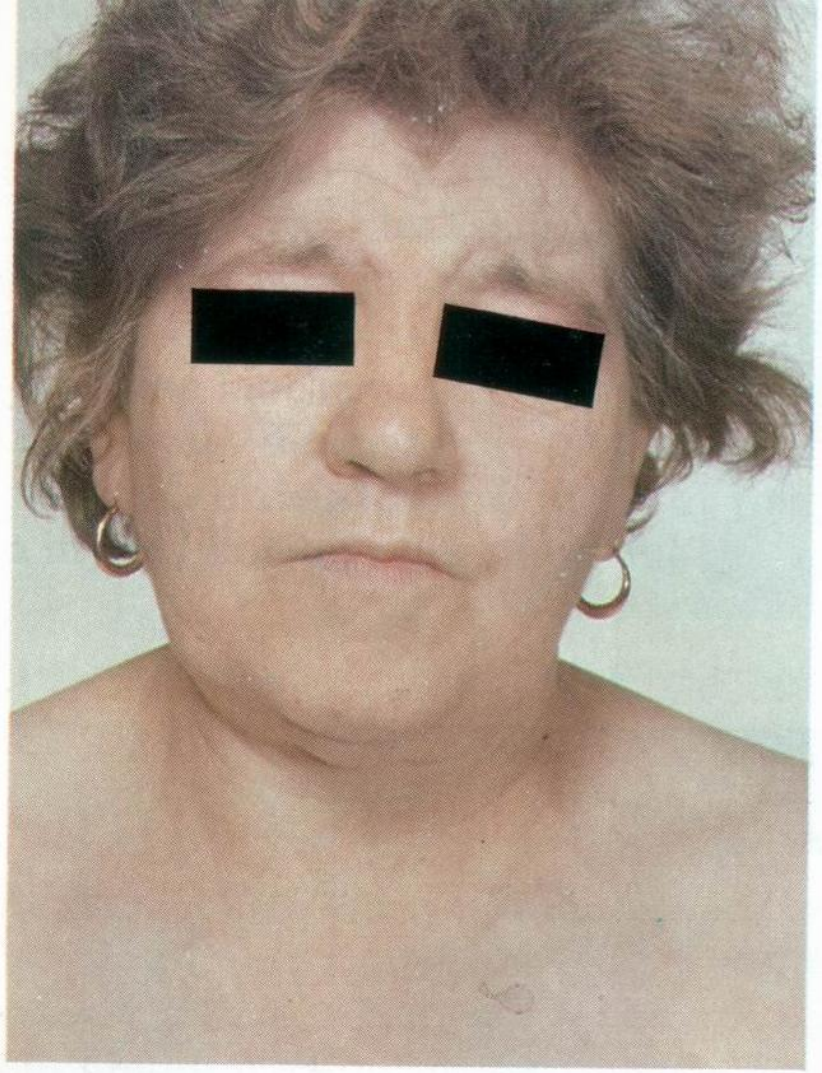
- HYPER
- GRAVE'S DISEASE:TSI
- EXOPHTALMOS
- GOITER



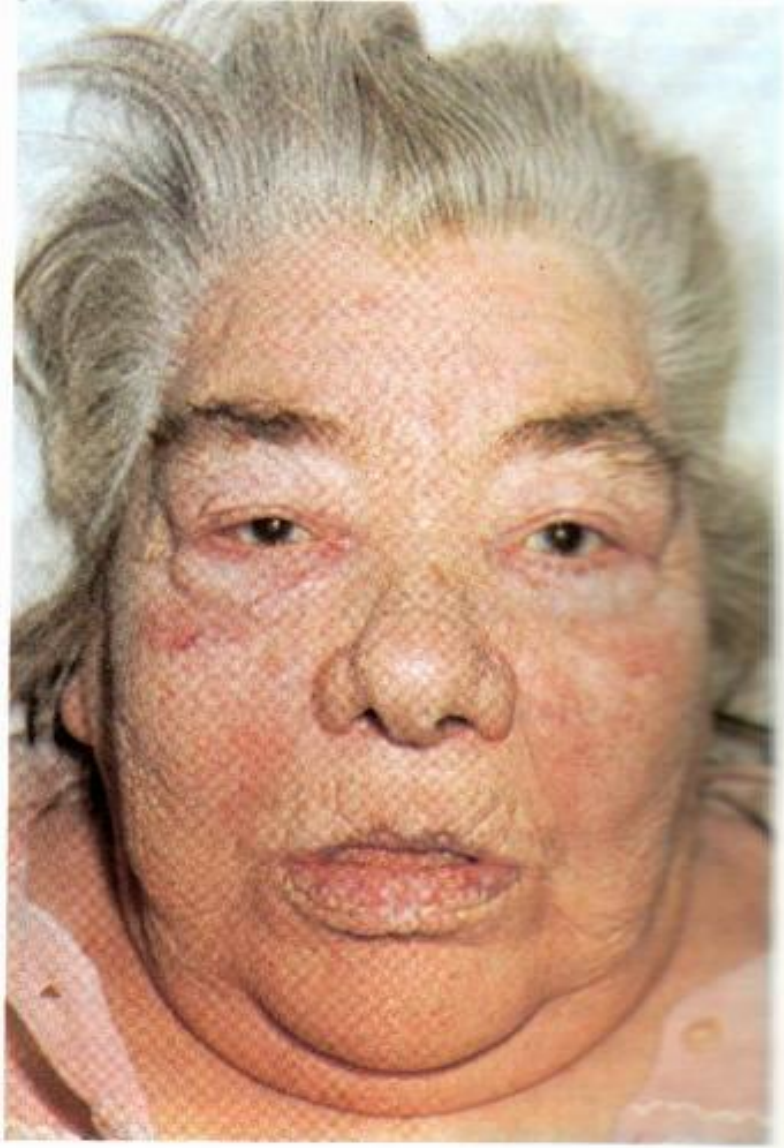
7.64 Toxic adenoma causing hyperthyroidism. This patient had a partial thytoidectomy 20 years previously, and a toxic nodule has now recurred. This was confirmed by isotope scanning.



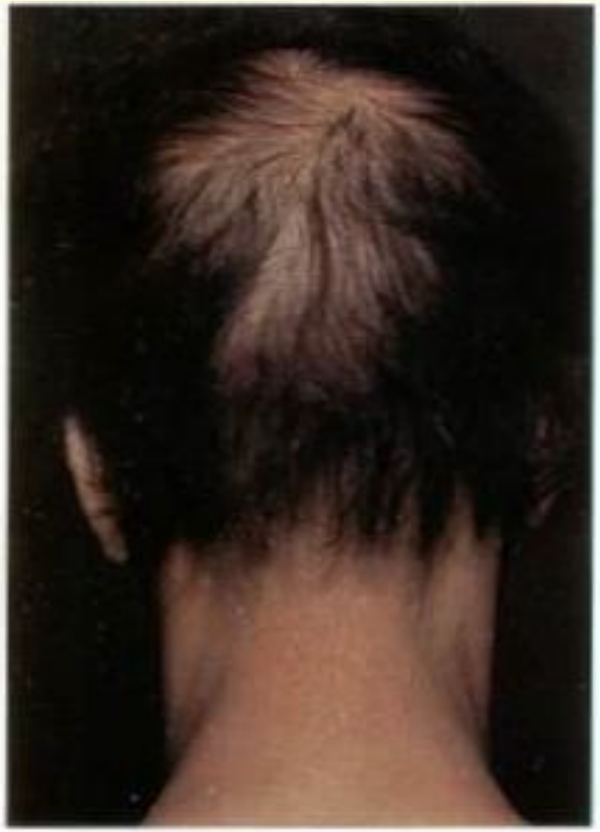
7.71 Multinodular goitre. The patient was euthyroid, but surgical treatment was ultimately required because of retrosternal extension with tracheal compression.



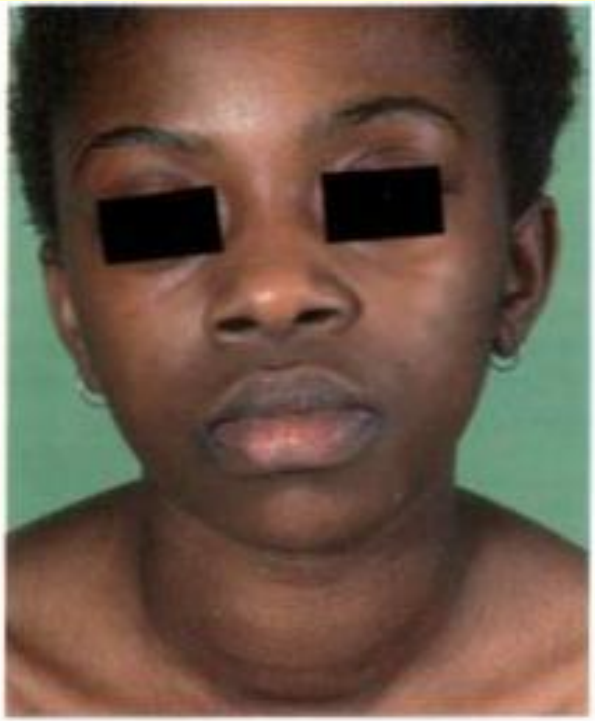
7.66 Hypothyroidism is not always clinically obvious. This patient shows some facial features, with a generalised pallor, puffiness andcoarsening of the features, and coarse , uncontrollable hair. She was grossly hypothyroid on biochemical testing.



7.67 Gross clinical hypothyroidism produces characteristic non-pitting oedematous changes in the skin of the face, giving rise to a characteristic clinical appearance. Note the dry, puffy facial appearance and the coarse hair. This patient was admitted with hypothermia. Her skin was cold and she showed mental apathy.



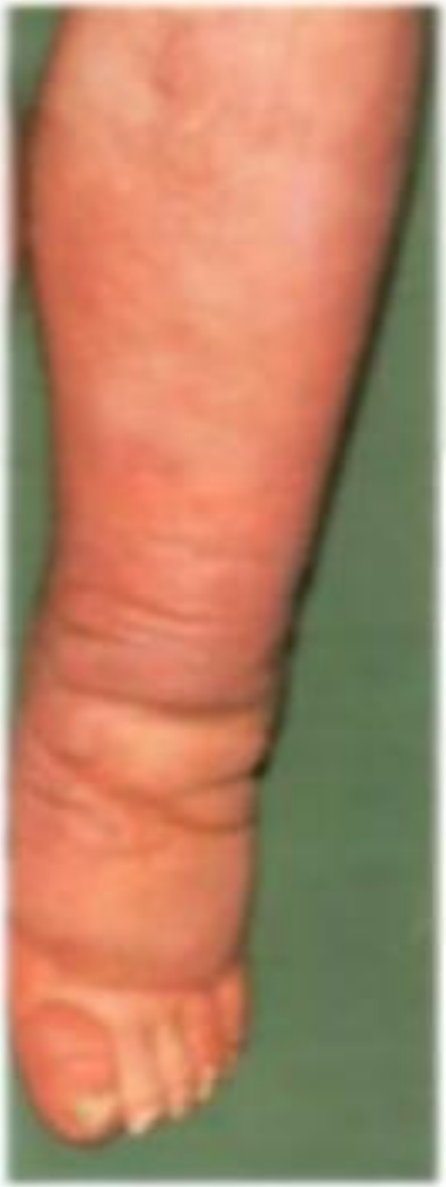
7.68 Hair loss is a common feature of hypothyroidism, as in this 48-year-old woman.



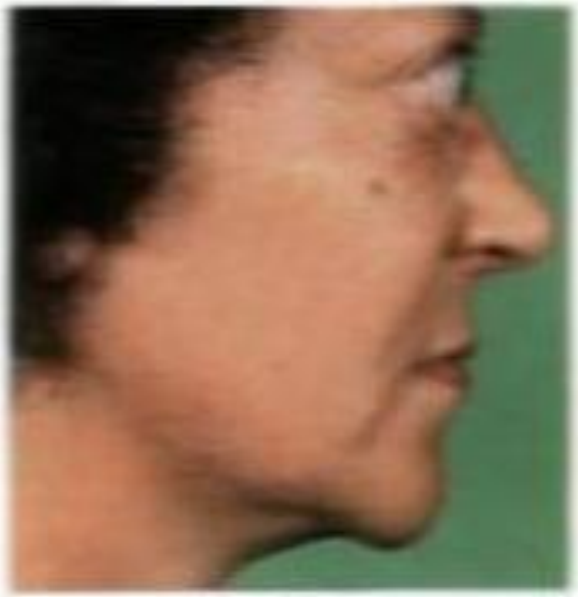
7.69 Hashimoto's disease is the most common cause of goitrous hypothyroidism in the world and is much more common in women than in men. This teenage patient has a marked goitre but few obvious signs of hypothyroidism. She is rather unusual, as the condition is much more common in older women.

7.70 Endemic goitre. Large goitres like this are not unusual in areas of iodine deficiency, but they are not always associated with hypothyroidism. This African patient was euthyroid.

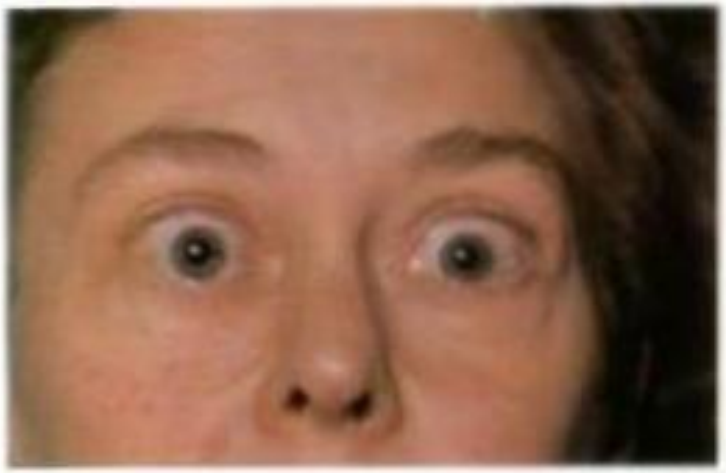
7.56 Graves' disease. This usually affects women between the ages of 20 and 40 years. This patient presented classically with a diffuse goitre over which a vascular bruit could be heard, and with eye signs.



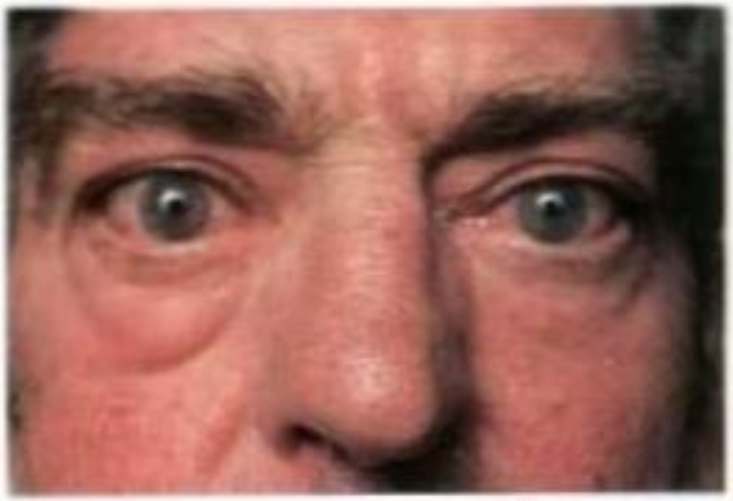
7.57 Pretibial myxoedema in Graves' disease. When this sign occurs, it may be combined with thyroid acropachy, in which there is oedema of the nail folds, producing a condition resembling clubbing.



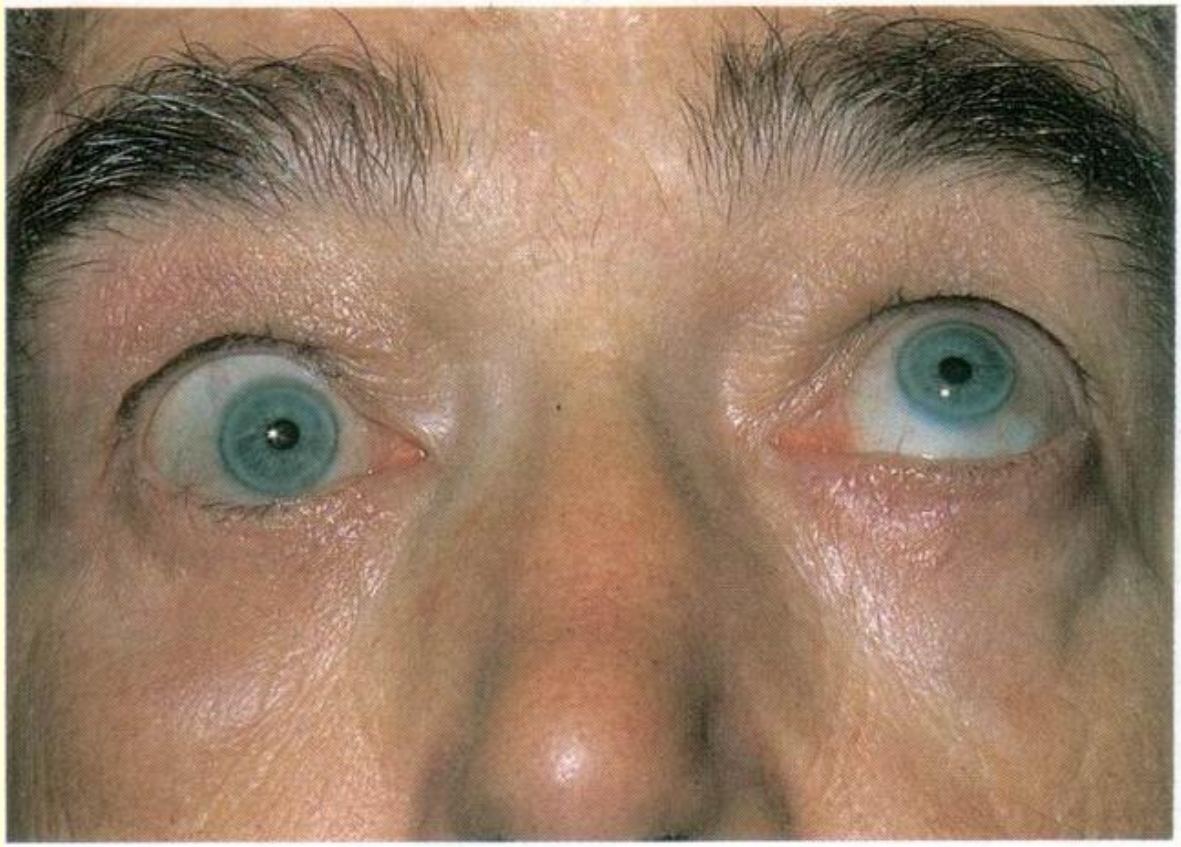
7.58 Exophthalmos (proptosis) in Graves' disease. This results from enlargement of the muscles, and fat within the orbit as a result of mucopolysaccharide infiltration.



7.59 Lid retraction is a common eye sign in Graves' disease, which can be recognised when the sclera is visible between the lower margin of the upper lid and the cornea. Lid retraction is usually bilateral, but may be unilateral.



7.60 Periorbital swelling may be associated with other eye signs, giving an erythematous and oedematous appearance to the eyelids. Note that this patient also has chemosis, seen as reddening of the sclera.



7.62 Ophthalmoplegia in Graves' disease. This is not caused by nerve palsy, but is the long-term result of swelling and infiltration of the extrinsic muscles of the eye. In this case, there is impaired upward and outward gaze in the patient's right eye. Ophthalmoplegia is usually accompanied by other eye signs. Note the presence of lid retraction. This patient also has markes corneal arcus.