# Disorders of the Thyroid Gland

# Thyrotoxicosis

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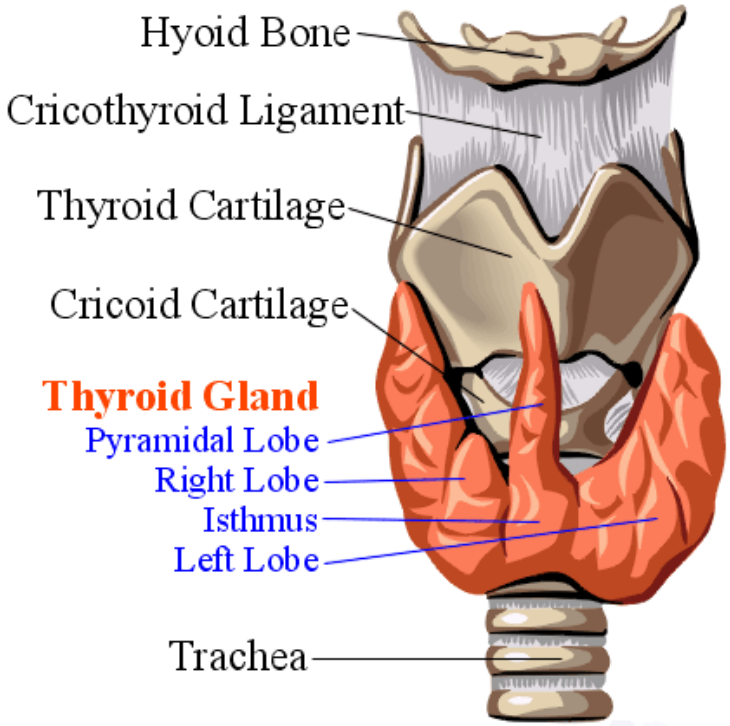
2020

# Anatomy of the thyroid gland



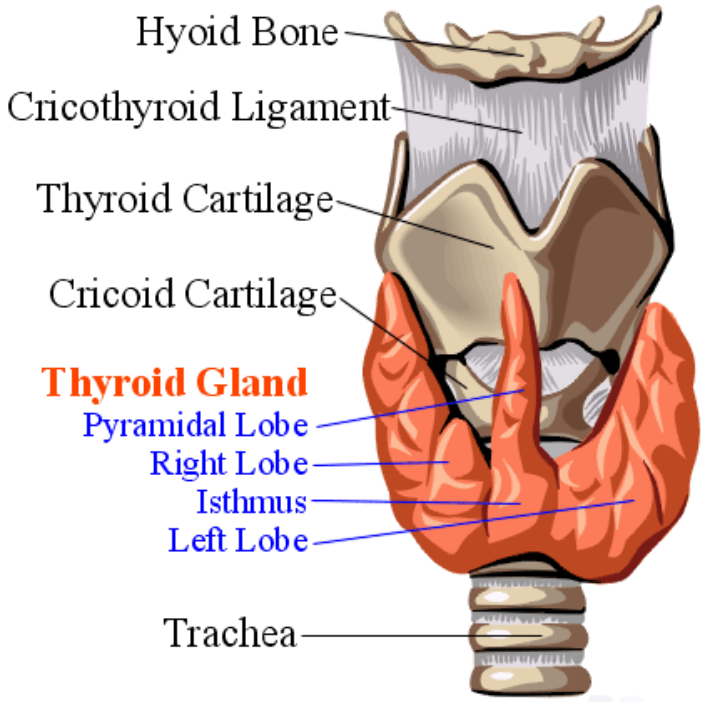

*Adapted from Corel Draw 9*

The thyroid gland is situated in the anterior surface of the neck at the region of the 2nd-4th tracheal rings.

It consists of two lateral lobes (right and left) and one intermediary part between them called the isthmus.

In adult the thyroid gland weighs from 25 to 30 gr on the average.

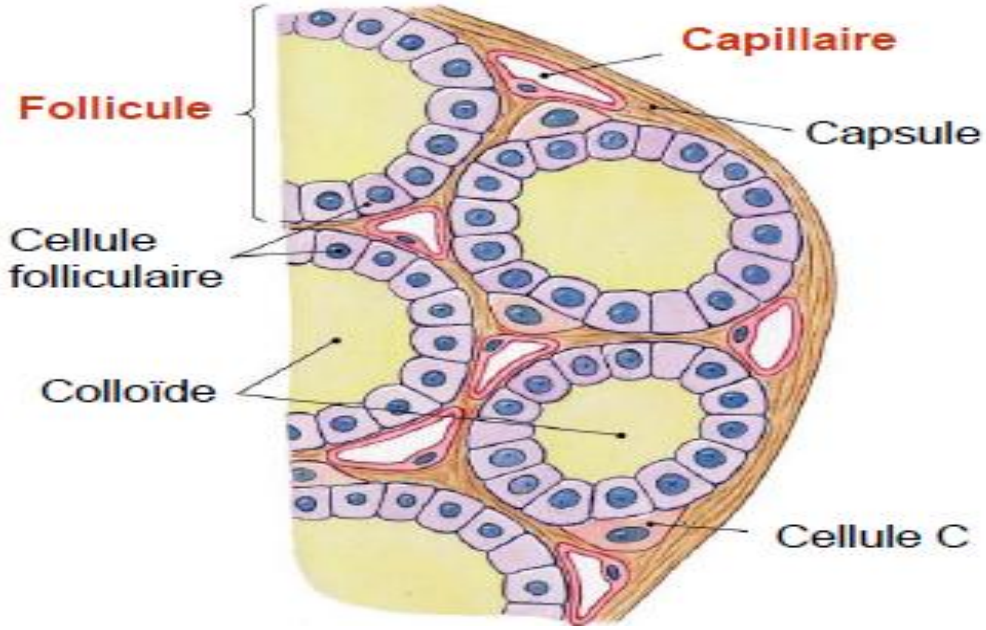
Each lobe is pear-shaped and measures about 2.5-4 cm in length, 1.5-2 cm in width and 1-1.5 cm in thickness.




*Adapted from Corel Draw 9*

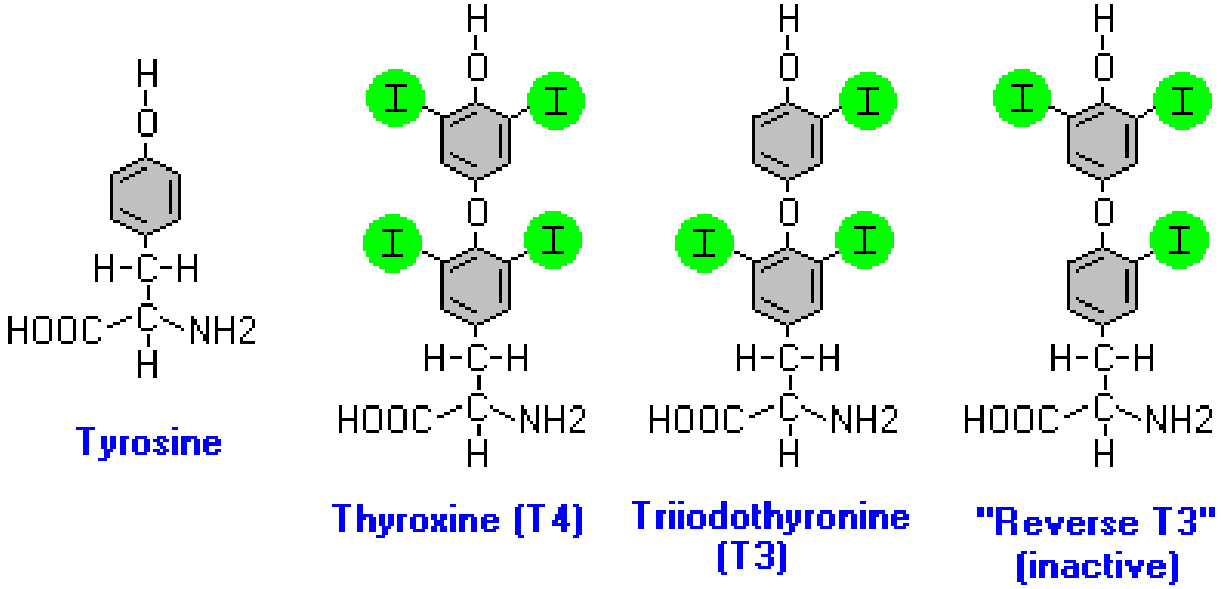
**The structural and functional unit of the thyroid gland is the follicle. The follicle's walls are lined with one layer of cubical epithelium (thyroid follicular cells). The cavity of each follicle is filled with colloid, composed by the thyroglobulin.**

**Except the follicular cells, the thyroid gland contains parafollicular cells (C-cells), which are responsible for calcitonin production.**



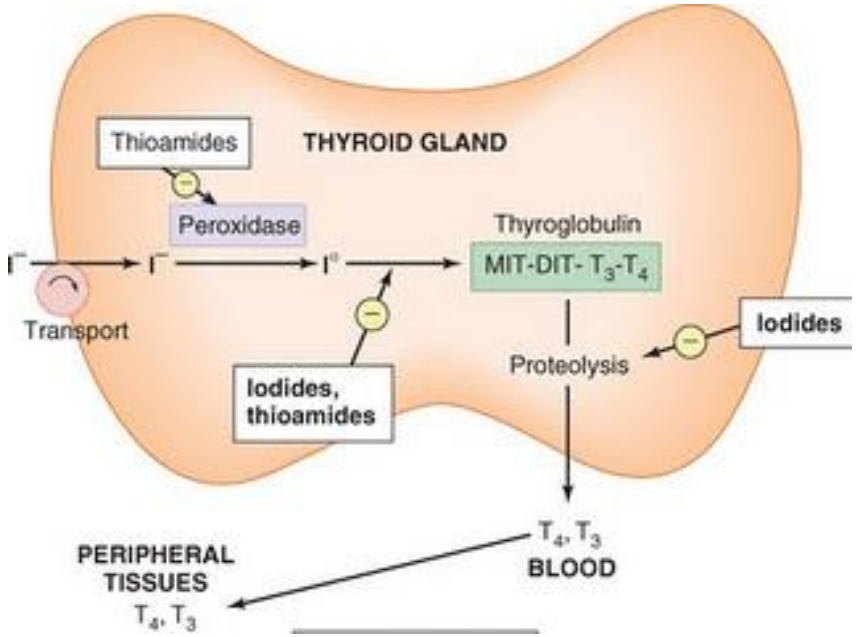
**The thyroid gland produces several hormones:**

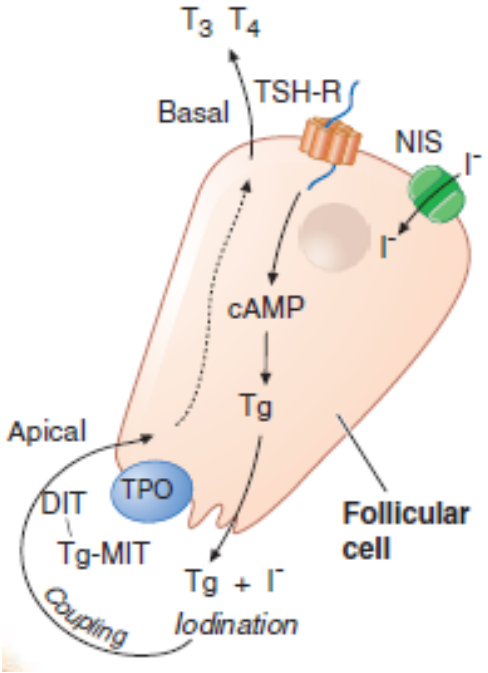
- **<u>T4 (thyroxine)</u> and <u>T3 (triiodothyronine) –</u> iodine-containing hormones - by follicular cell.**
- **<u>Calcitonin</u> – by parafollicular cell. This hormone regulates calcium homeostasis.**



The process of the thyroid hormones synthesis includes four steps:

1. Uptake of the iodine in the thyroid gland.
2. Organification (oxidation) of the iodide and iodination of the thyrosine in thyroglobulin.
3. Condensation of the iodo-thyrosines into the iodo-thyronines (coupling of iodothyrosine molecules within thyroglobulin to form T3 and T4)
4. Realeasing (secretion) of the thyroid hormones.

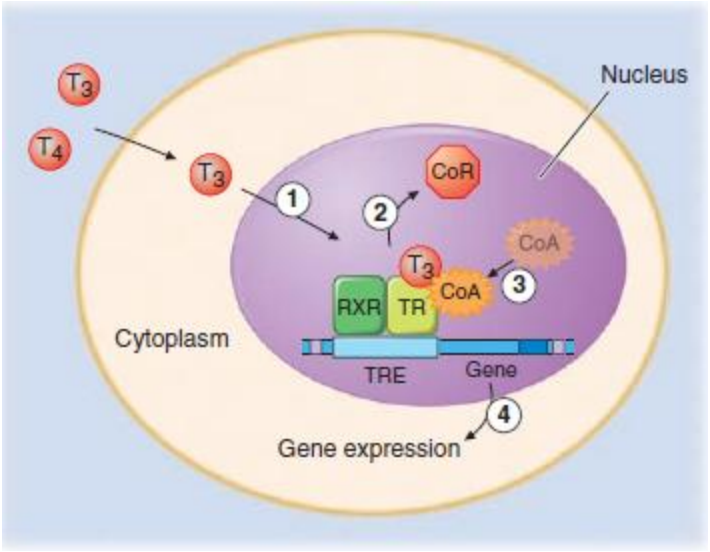


**Thyroid hormones are transported in serum bound to carrier proteins (globulins, albumins, prealbumins).**

**Only 0.04% of T4 and 0.4% of T3 are 'free', but the free fraction are responsible for hormonal activity.**

**Thyroid hormones action is associated with T3, that is 4 to 5 times more active than T4. 20% of T3 is formed in the thyroid gland, 80% is formed from T4.**



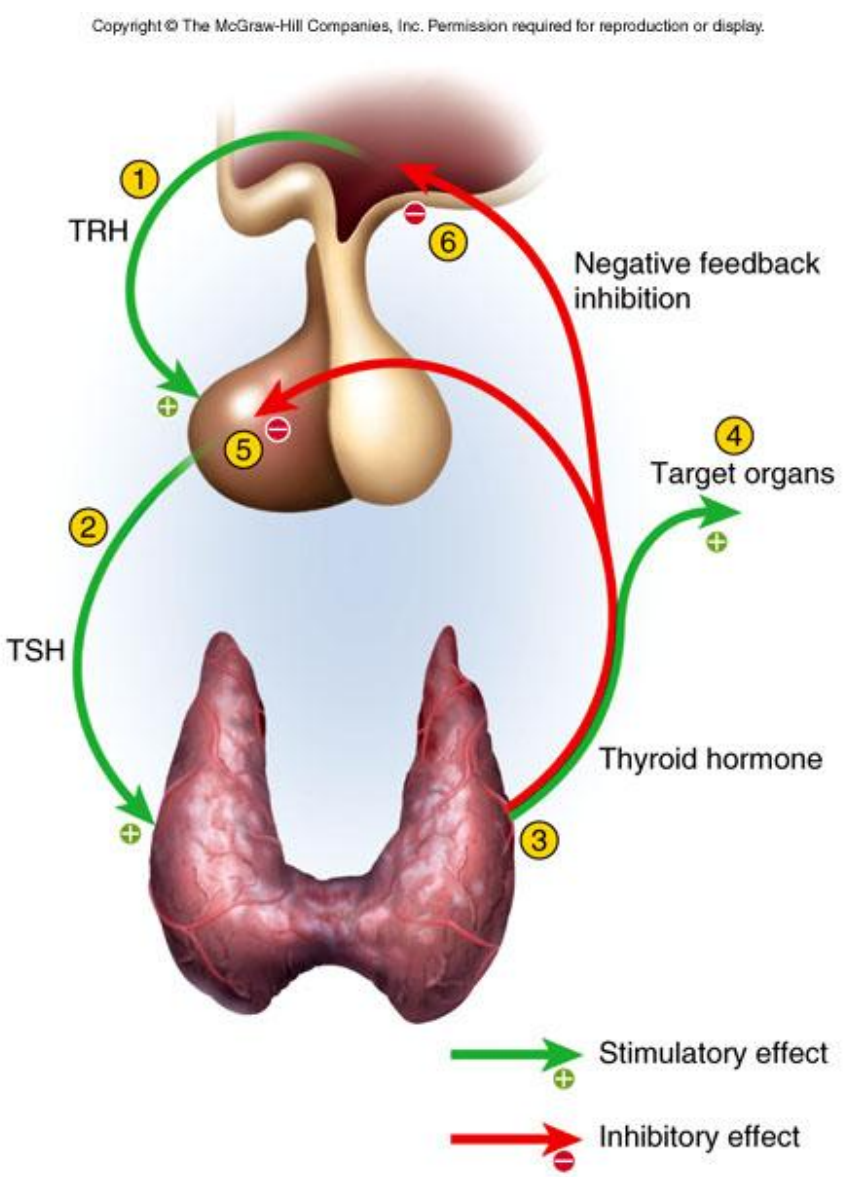

**Mechanism of thyroid hormone receptor action.**

The growth and function of thyroid gland are controlled by 2 mechanism:

- The classic hypothalamic – pituitary -thyroid axis
- Autoregulation of hormone synthesis by the thyroid gland itself in relationship to its iodine supply

The hypothalamic TRH stimulates the synthesis and release of anterior pituitary TSH, which in turn stimulates hormone secretion by the thyroid gland.

TSH has many actions on the thyroid cell. It also stimulate diffuse hyperplasia of the thyroid tissue.



TSH synthesis and release are inhibited by high serum levels of T4 and T3 (hyperthyroidism) and stimulated by low levels of thyroid hormone (hypothyroidism).

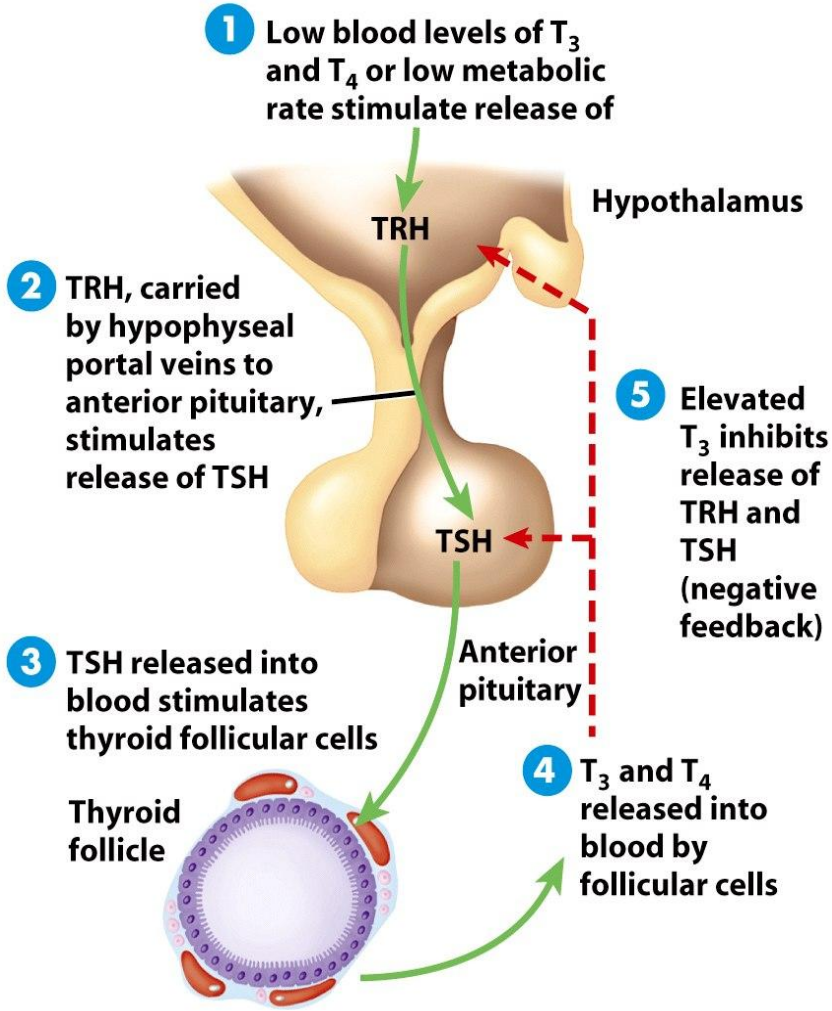
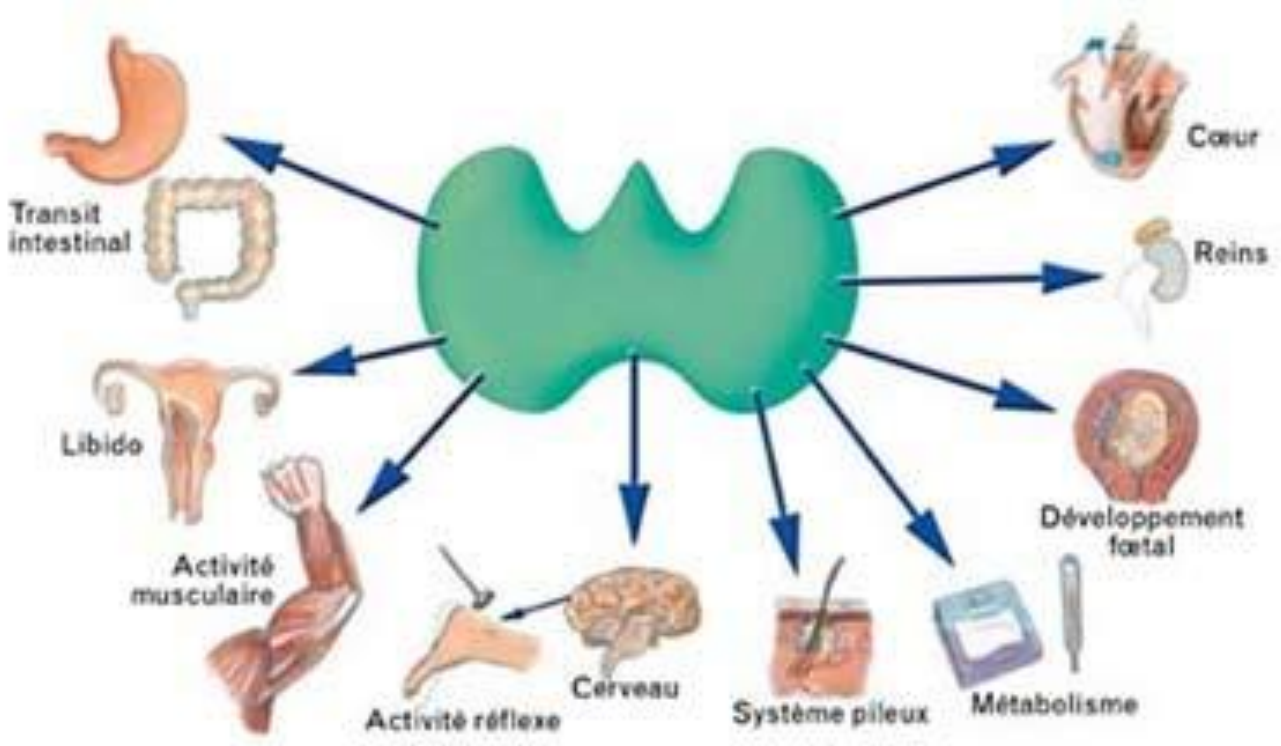



Figure 17-11 Anatomy and Physiology: From Science to Life

## The action of thyroid hormones.

**Thyroid hormones have a lot of physiological effects.**

**They exert actions in all tissues and affect essentially every metabolic pathway. Mechanism of the thyroid hormone action is intracellular.**



# Physiologic effects of thyroid hormones

- **Stimulate thermogenesis**
- **Intensify oxygen consumption and oxidative processes in the body, heat production. This contributes to the increased basal metabolic rate.**
- **Stimulate contractive cardiac muscle activity; have marked positive inotropic and chronotropic effects on the heart.**

# Physiologic effects of thyroid hormones

- **They may amplify catecholamine action at a postreceptor site.**
- **Stimulate intestinal motility.**
- **Intensify synthetic processes. Stimulate increased synthesis of many structural proteins. Increase the speed of muscle contraction and relaxation. Are essential for normal development and function of the central nervous system.**

# Physiologic effects of thyroid hormones

- **Intensify the erythropoiesis**
- **Stimulate increased bone turnover, increasing bone resorption and, to a lesser degree, bone formation.**
- **Influence the carbohydrate metabolism – hyperglycemic effect.**
- **Cholesterol synthesis and degradation are both increased by thyroid hormones.**

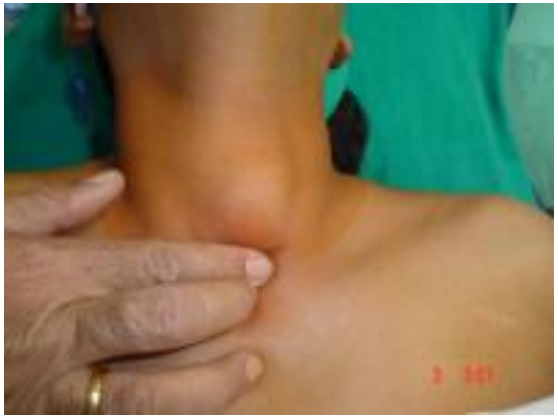
# Classification of Thyroid Diseases

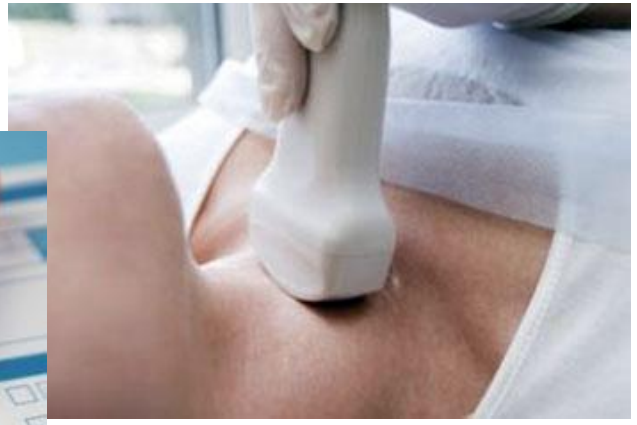
- **It is based largely on thyroid function. The functional behavior of the thyroid is fundamental in most thyroid diseases and represents the basis for diagnosis and therapy.**

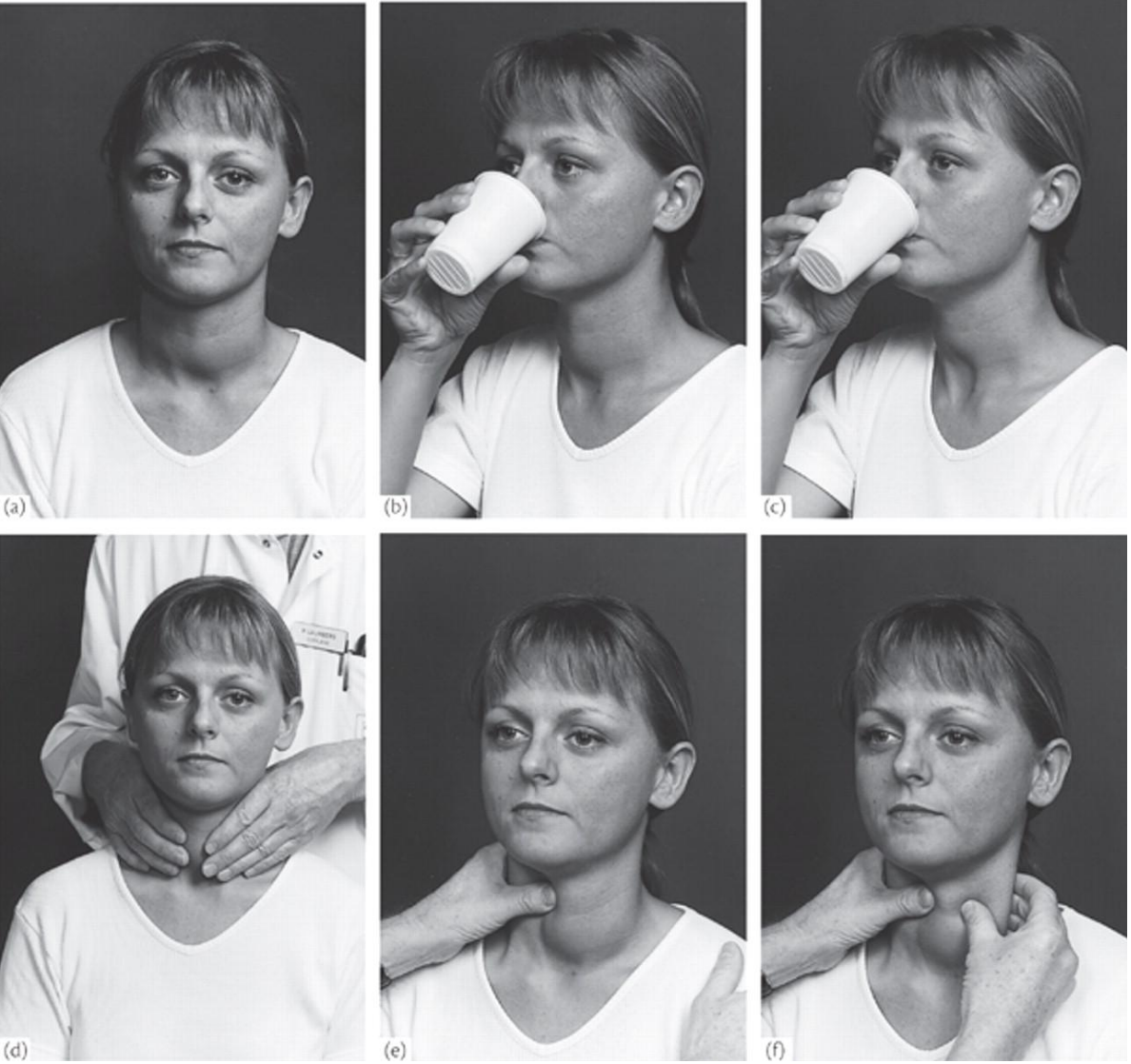
- **Euthyroidism – normal levels of thyroid hormones**
- **Thyrotoxicosis – excessive levels of thyroid hormones**
- **Hypothyroidism – deficiency of thyroid hormones**

| Diseases characterized by (tissue) hyperthyroidism (or by Thyrotoxicosis) | Diseases characterized by (tissue) hypothyroidism | Diseases characterized by (tissue) euthyroidism |
|---|---|---|
| Graves' disease<br><br>Toxic multinodular goiter<br><br>Toxic adenoma | Primary hypothyroidism<br><br>Pituitary (or secondary) hypothyroidism<br><br>Hypothalamic (or tertiary) hypothyroidism | Euthyroid Diffuse goiter (Sporadic goiter)<br><br>Nodular goiter<br><br>Tumors<br><br>Thyroiditis |

# Tests of thyroid function






**A goiter in a patient is determined by direct examination and palpation of a gland.**

**The palpation of a thyroid gland must be carried out in front, observing a patient's reaction.**

**The first fingers of both hands are put on an isthmus and palpate it.**

**Than the right finger examines the left lobe and the left one examines the right lobe.**

# Thyroid gland

**During palpation of a gland it is determined:**

- ✓ **Mobility**
- ✓ **A consistence**
- ✓ **Presence or absence of nodes**
- ✓ **Size, shape**
- ✓ **Painfulness**

# Classification of sizes of the thyroid gland

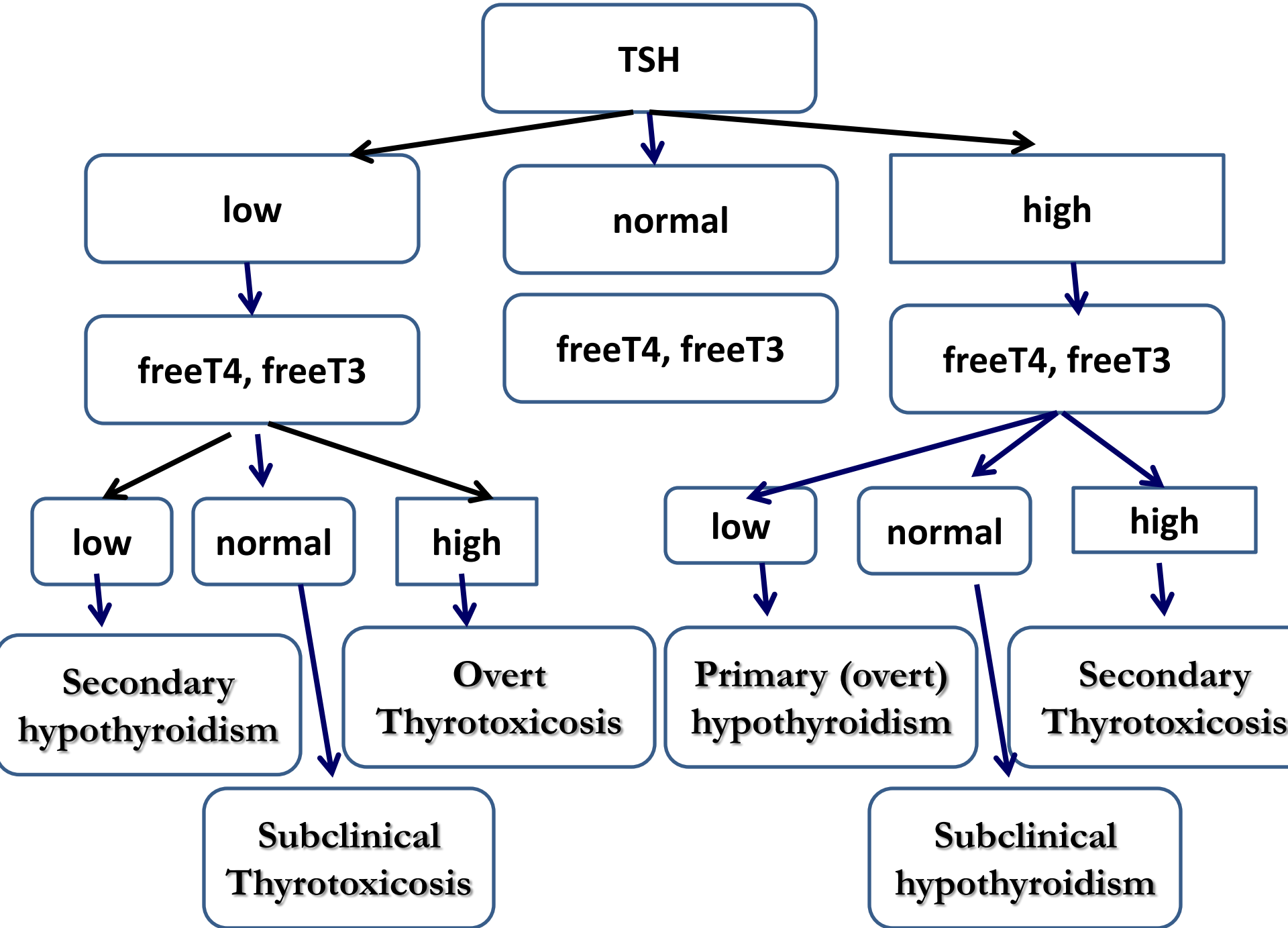
## (WHO 1994)

| | |
|---|---|
| **0** | **Goiter is hidden and not palpable** |
| **I** | **Goiter is palpable, but hidden** |
| **II** | **Goiter is palpable and visible** |

# LABORATORY EVALUATION

**Measurement of thyroid hormones**

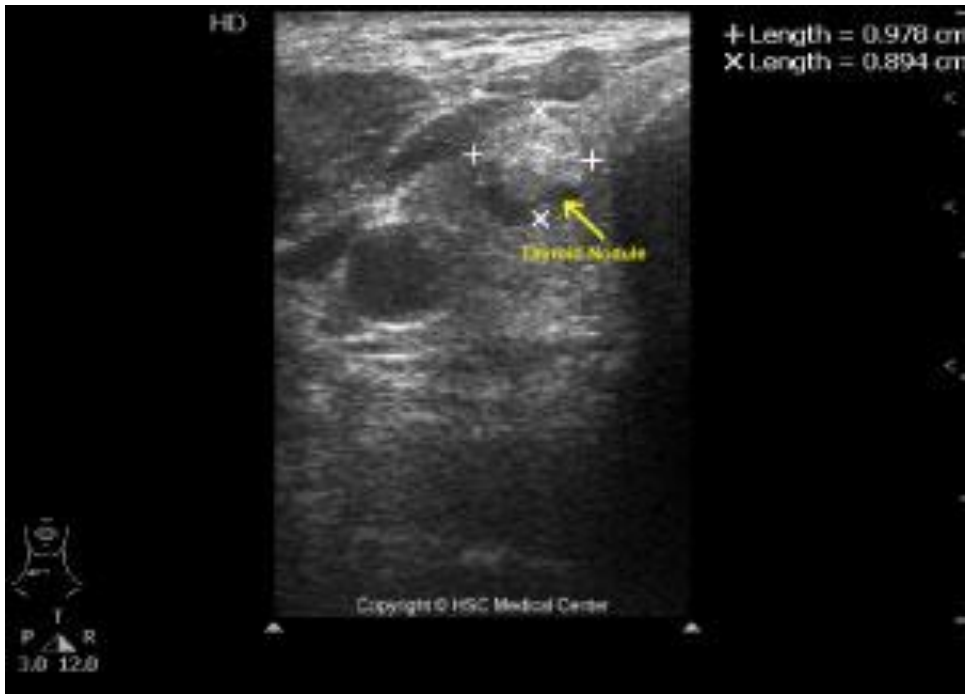
- free T4 and free T3
- TSH
- total T4 and total T3

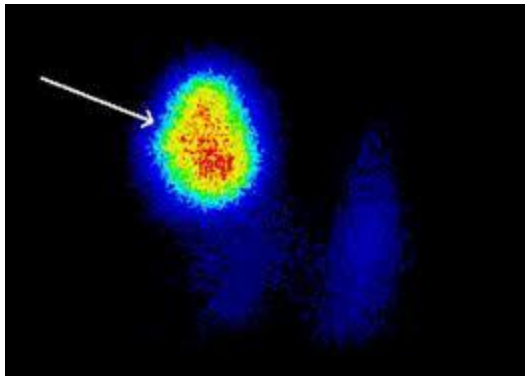

TSH
low
normal
high
freeT4, freeT3
freeT4, freeT3
freeT4, freeT3
low
normal
high
low
normal
high
Secondary hypothyroidism
Overt Thyrotoxicosis
Primary (overt) hypothyroidism
Secondary Thyrotoxicosis
Subclinical Thyrotoxicosis
Subclinical hypothyroidism

**Tests to determine the etiology of thyroid dysfunction**

- **antibodies against TPO (Thyroperoxidase)**
- **antibodies against Tg (Thyroglobulin )**
- **antibodies against TSH receptor**

# Thyroid Imaging



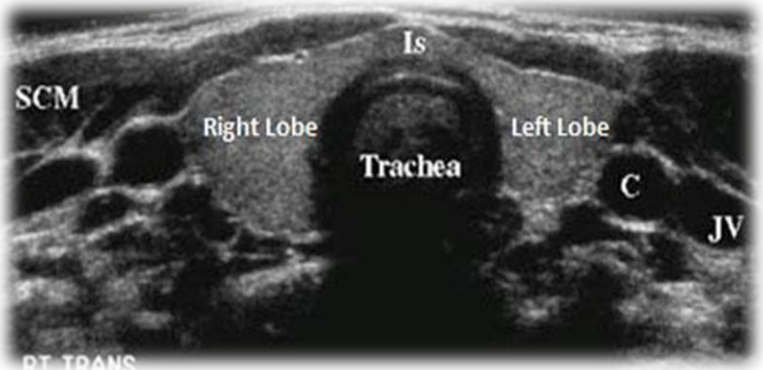



# Thyroid ultrasonography:

- **Thyroid ultrasonography is particularly useful for measuring the size of the gland or individual nodules and for evaluating the result of therapy.**

- **It is useful also for differentiating solid from cystic lesions and to guide the operator to a deep nodule during fine-needle thyroid aspiration biopsy.**

- **ultrasound is useful for monitoring nodule size and for the aspiration of nodules or cystic lesions.**



# Thyroid volume

**The volume of each thyroid lobe Is calculated using expression:**

$$V = L\,(\text{length}) * W(\text{width}) * T(\text{thickness}) * 0.479$$

**Total volume is obtained as the sum of two thyroid lobes.**

**The isthmus is not included into the sum.**

$$V_{thyroid} = V_{rl} + V_{ll}$$

**Thyroid Volume (ml):**

- **Female <18 ml**
- **Male <25 ml**

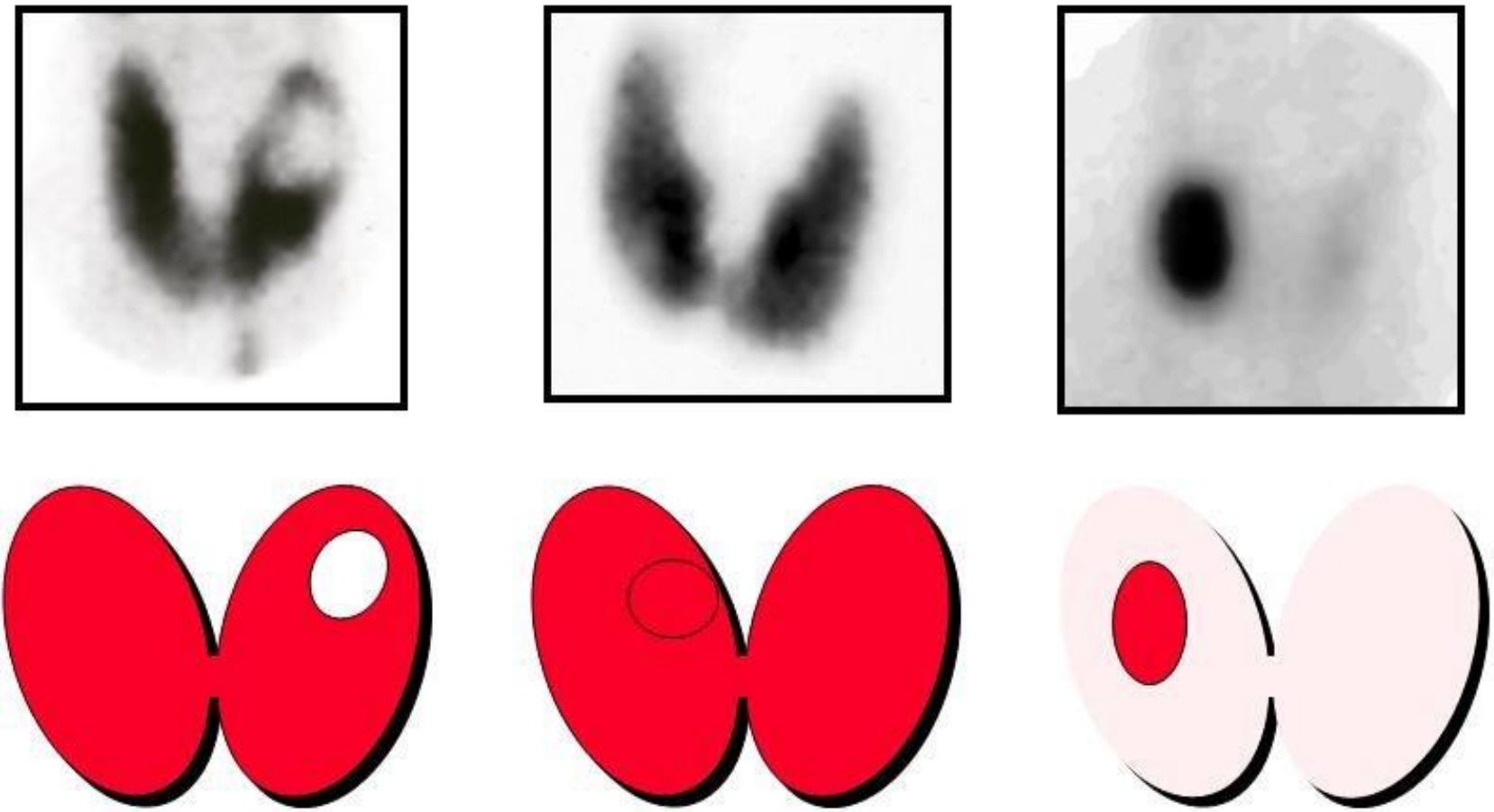
# Radioiodine scanning and uptake

## Thyroid Scan.

- **I123 and Technetium Tc 99m pertechnetate are useful for determining the functional activity of the thyroid gland.**

- **Radionuclide scans provide information about size and shape of the thyroid gland and the geographic distribution of functional activity in the gland. Functioning thyroid nodules are called «hot» nodules, and nonfuctioning ones are called «cold» nodules.**

Figure 7. Potential Radionuclide Scan Findings in Individuals with a Thyroid Nodule



Cold Warm Hot

Numele pacientului : [redacted]

BON Nr. 0754129

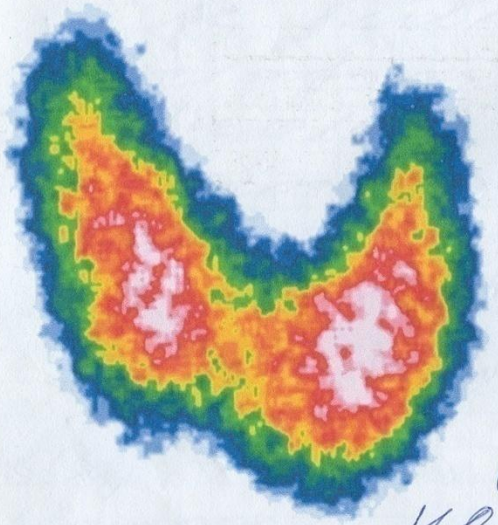
Data investigatiei: 12/21/2007 10:21:28 AM

PRF: TC-99M 50.09 MBq

# Ministerul Sanatatii al RM
# Centrul Republican de Diagnosticare Medicala
# Laboratorul Medicina Nucleara

tel: 888-389, 888-382, 888-381

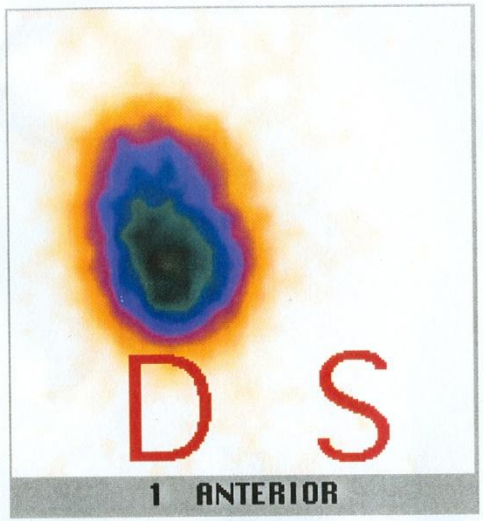
## Scintigrafia glandei tiroide



| Aria si parametrii functionali | | | | | | |
|---|---|---|---|---|---|---|
| | Aria cm2 | Norma cm2 | % Acumulare | Norma % | %/Aria | Norma |
| Glanda tiroida | 45.5 | 20 | 20.71% | 1.8-4.0 | 0.46 | 0.09-0,20 |
| Lobul sting | 23.2 | 10 | 11.02% | 0.9-2.0 | 0.48 | 0.09-0,20 |
| Lobul drept | 22.8 | 10 | 9.69% | 0.9-2.0 | 0.43 | 0.09-0,20 |

Щитовидная железа расположена в типичном месте. Контуры четкие, увеличена в размерах. Паренхима железы неравномерно накопление РФП, асимметричное по долям с повышением накопления в левой доле. Очагов дефектов накопления РФП не выявлено.

**Comentariu:**

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or.Chișinău , Republica Moldova , 729-296

I [redacted]

Scintigrafia glandei tiroide

Gama- camera „DIACAM - SIEMENS"

RF - 99mTc pertehn. Doza uzuală 150 MBq

Doza iradiere 4,5 mSv

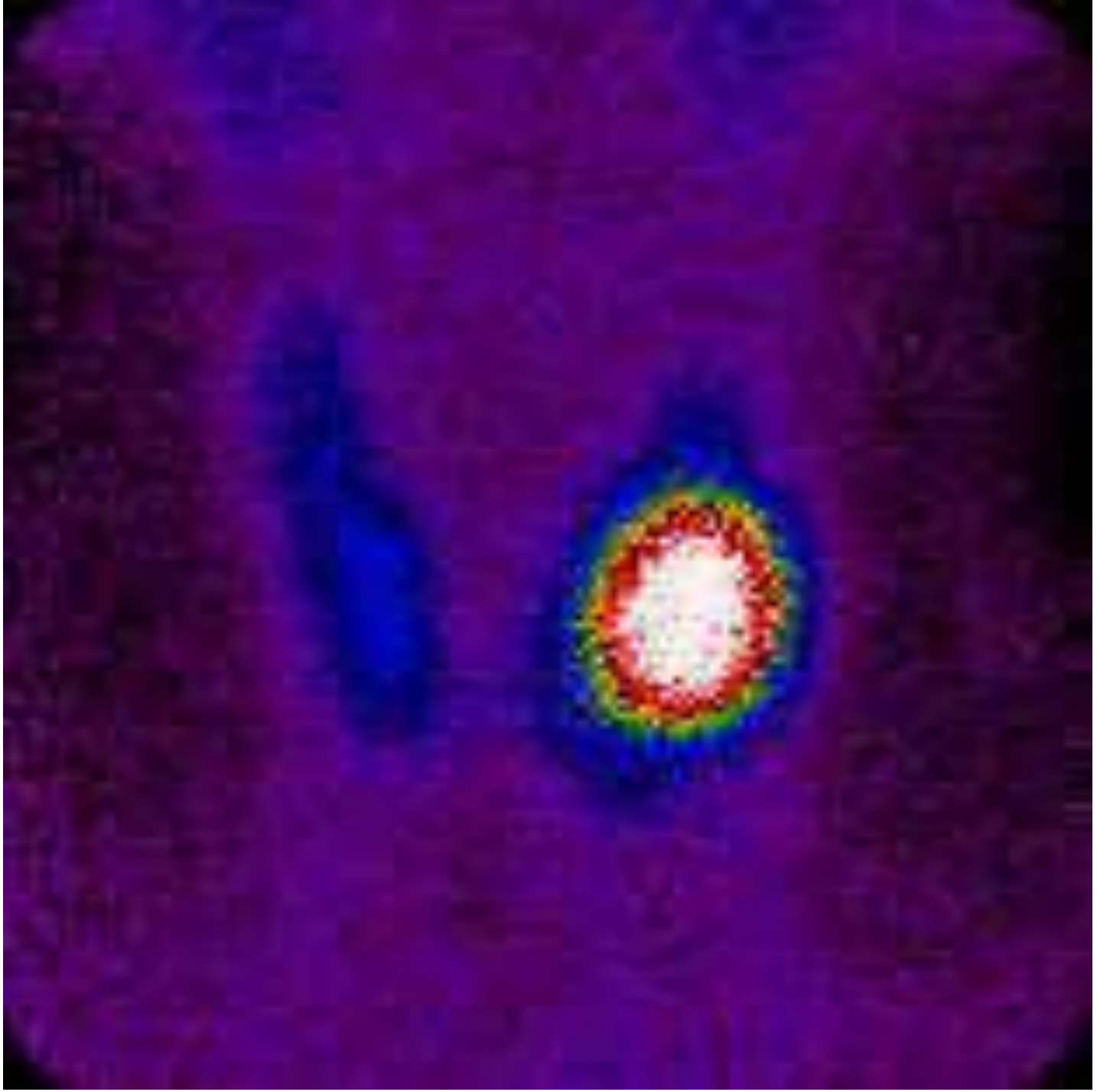
Rezumat: Imaginea scintigrafică a glandei tiroide prezintă o arie de formă oval-circulară de acumulare maximală a RF-ului cu aspect de nucleu de radioactivitate, pe fundalul căruia, lobul stîng nu se vizualizează.

Scintigrafic: sugestii pentru adenom al lobului D.

ds. VC

*Medic mediicina nucleara*
***Valeri Draciov***

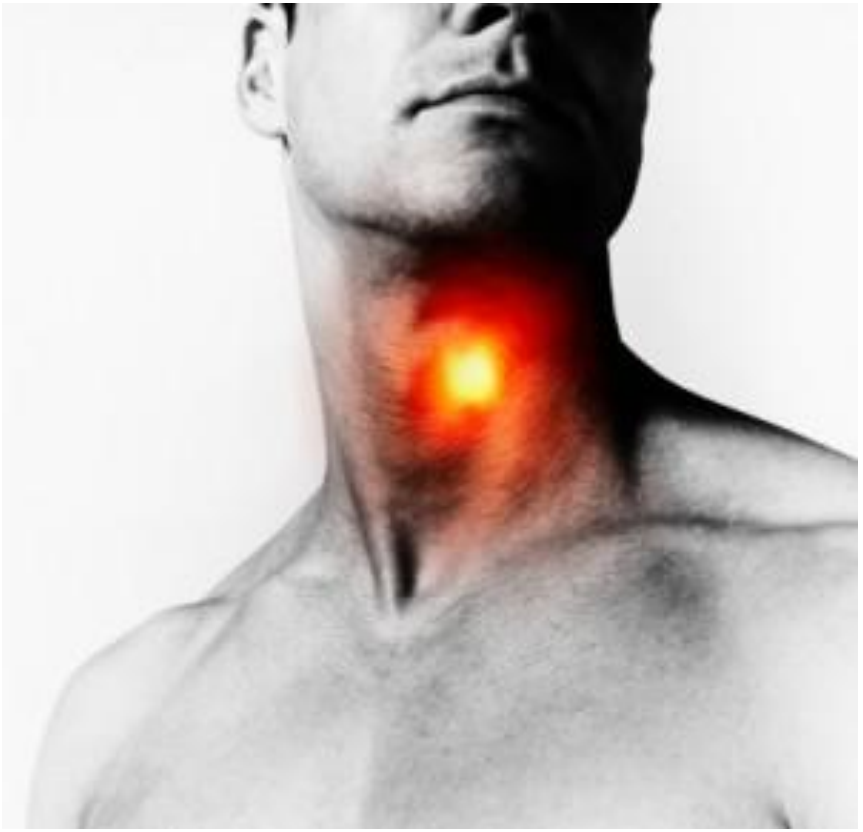
D-r



## Patients with thyroid disease will complain of:

1. Symptoms of thyroid deficiency, or hypothyroidism
2. Symptoms of thyroid hormone excess or thyrotoxicosis
3. Thyroid enlargement, which may be diffuse or nodular
4. Complications/symptoms of a specific form of thyroid disease – exophthalmos and dermopathy in Graves'disease; pain in Subacute thyroiditis.

# Thyrotoxicosis



***Thyrotoxicosis*** **is the clinical syndrom that results when tissues are exposed to high levels of circulating thyroid hormone.**

***Thyrotoxicosis*** **is defined as the state of thyroid hormone excess and is not synonymous with *hyperthyroidism*, which is the result of excessive thyroid function. However, the major etiologies of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic MNG, and toxic adenomas.**

**Occasionally, thyrotoxicosis may be due to other causes such as excessive ingestion of thyroid hormone or excessive secretion of thyroid hormone from ectopic sites.**

# Conditions associated with thyrotoxicosis

1. Diffuse toxic goiter (Graves disease)
2. Toxic adenoma
3. Toxic multinodular goiter
4. Hyperthyroid phase of subacute thyroiditis
5. Hyperthyroid phase of Hashimoto's thyroiditis
6. Thyrotoxicosis factitia (caused by self-administration of thyroid hormone)
7. Rare forms: metastatic thyroid carcinoma, TSH-secreting pituitary tumor

**Clinical manifestations of thyrotoxicosis -** include Signs and symptoms that are common to any cause of thyrotoxicosis

# The cardiovascular system

- **The most typical clinical symptoms of thyrotoxicosis are changes in cardiovascular system.**
- **Tachycardia is one of the most constant and early symptoms. It is not relieved at rest or during sleep. Sometimes extrasystole or atrial fibrillation in severe cases may appear.**
- **The systolic blood pressure increased and diastolic blood pressure is reduced. There are a considerable increase of the stroke volume and the minute volume of bloodstream.**
- **Heart insufficiency develops in 15-20% of cases, mainly in patients with atrial fibrillation.**
- **The excess of thyroid hormones cause increased sensitivity of adrenoreceptors to catecholamines.**

# Psychic and nervous symptoms

- **Psychic and nervous symptoms are a prominent part of a clinical picture.**
- **Patients appear to be nervous, anxious, irritate with no reason. Changes of mood are often.**
- **The trembling of the whole body is very characteristic.**
- **Tremor of the extended fingers of a relaxed hand it is easily observed. Tremor is constant, it is not stopped by detracting attention.**

# Muscular system

- Change of muscular system appear as a result of the increase of the catabolic processes in the muscular tissue.

- Chronic thyrotoxic myopaty: significant muscular weakness, up to that a patient can hardly move or get up from a chair.

# Digestive system

- Weight loss is one of the most typical symptom of thyrotoxicosis.
- Many patients complain of an increase of appetite.
- Defecation becomes more frequent, it can be up to 20 times a day.
- The liver in toxic goiter is affected quite often.

# Skin

- **The skin is warm and moist, thin.**
- **Subcutaneous fatty layer is often diminished.**
- **In some patients an uneven hyperpigmentation of all body is observe.**

# Endocrine system

- **Function of adrenal glands is intensified in mild forms of the disease, and decrease in severe forms (the insufficiency of the adrenal cortex).**

- **In women the menstrual cycle is disturbed. Sometimes we can observe atrophic changes of a uterus, a vagina, mammary glands. Males has atrophic change in testis, prostate gland, reduced libido and potency.**

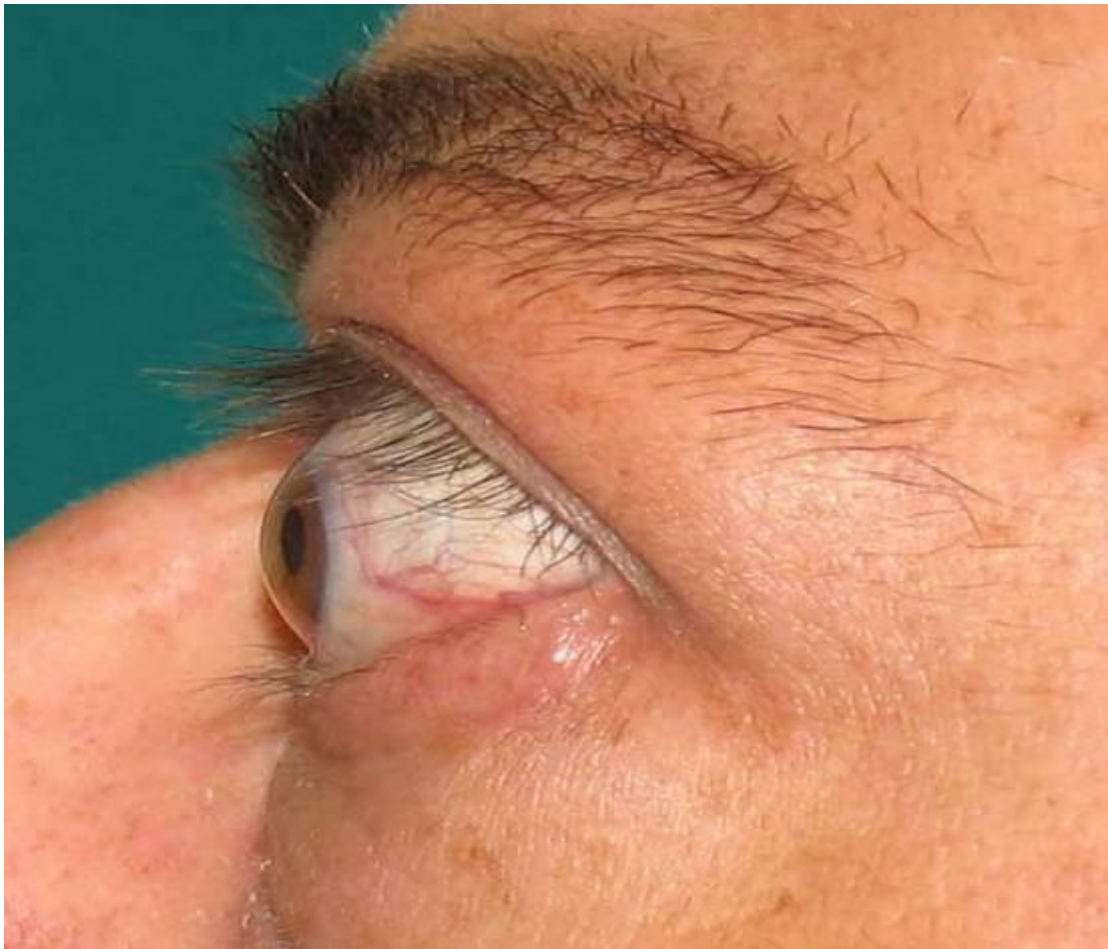
- **Patients with thyrotoxicosis may have diabetes mellitus.**

- **Respiratory organs – There are no essential disorders of respiration.**
- **The kidneys and urinary tract are not affected as a rule.**
- **On the part of skeletal system an intensification of osteoporosis is possible.**

# The eyes signs (ocular symptoms).

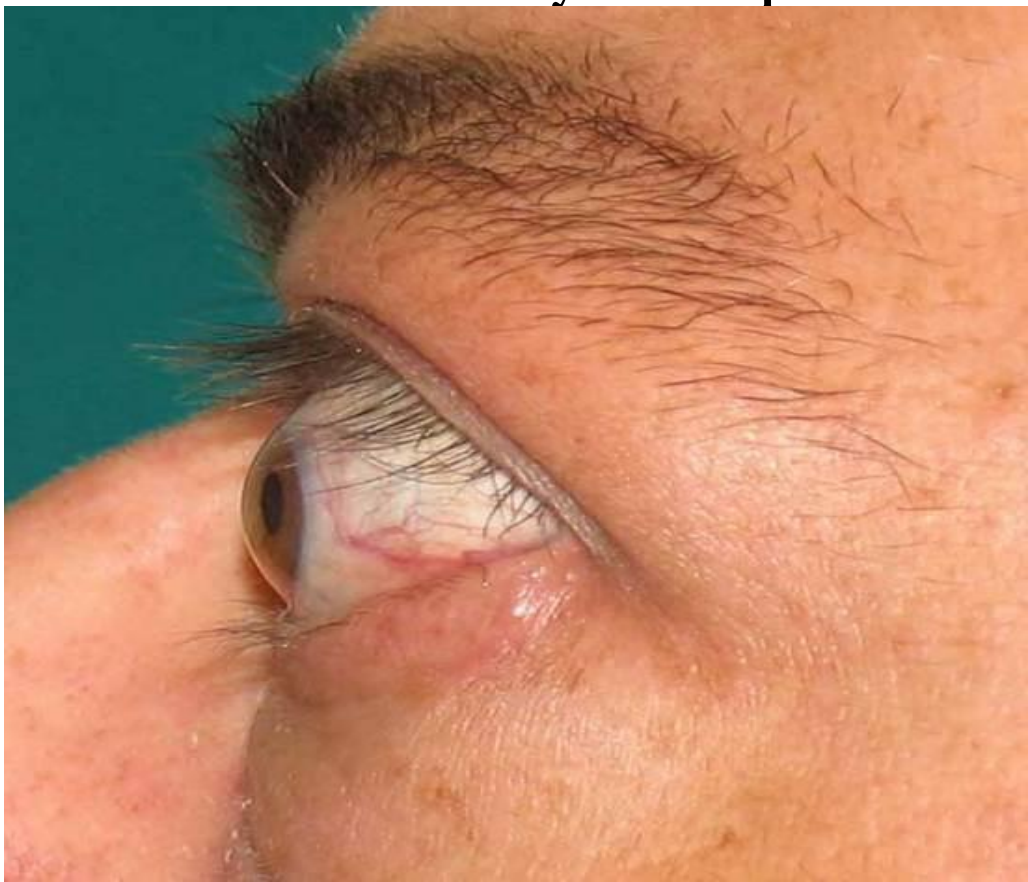
**They are mainly connected with the increased activity of the *sympathoadrenal system.***

- **Delremplin's symptom – palpebral fissures are widely opened with expression of surprise.**
- **Shtelwag's symptom – rare winking**



# The eyes signs (ocular symptoms).

- **Graefe's symptom – a white strip of the sclera is seen between the upper lid and the iris during the movement of an eyeball downwards.**
- **Coher's symptom - a white strip of the sclera is seen between the upper lid and the iris during the movement of an eyeball upwards.**
- **Moebius symptom – impairment of convergence of eyeballs.**
- **Ellineck's symptom – pigmentation around the eyes**



# Stages of the thyrotoxicosis

## Mild form

- The clinical symptoms are less pronounced
- Tachycardia no more than 100 beats per minute
- Weight loss up to 10%

# Stages of the thyrotoxicosis

## Moderate form

- The clinical symptoms are well manifested
- Tachycardia from 100 to 120 beats per minute
- Weight loss up to 20%

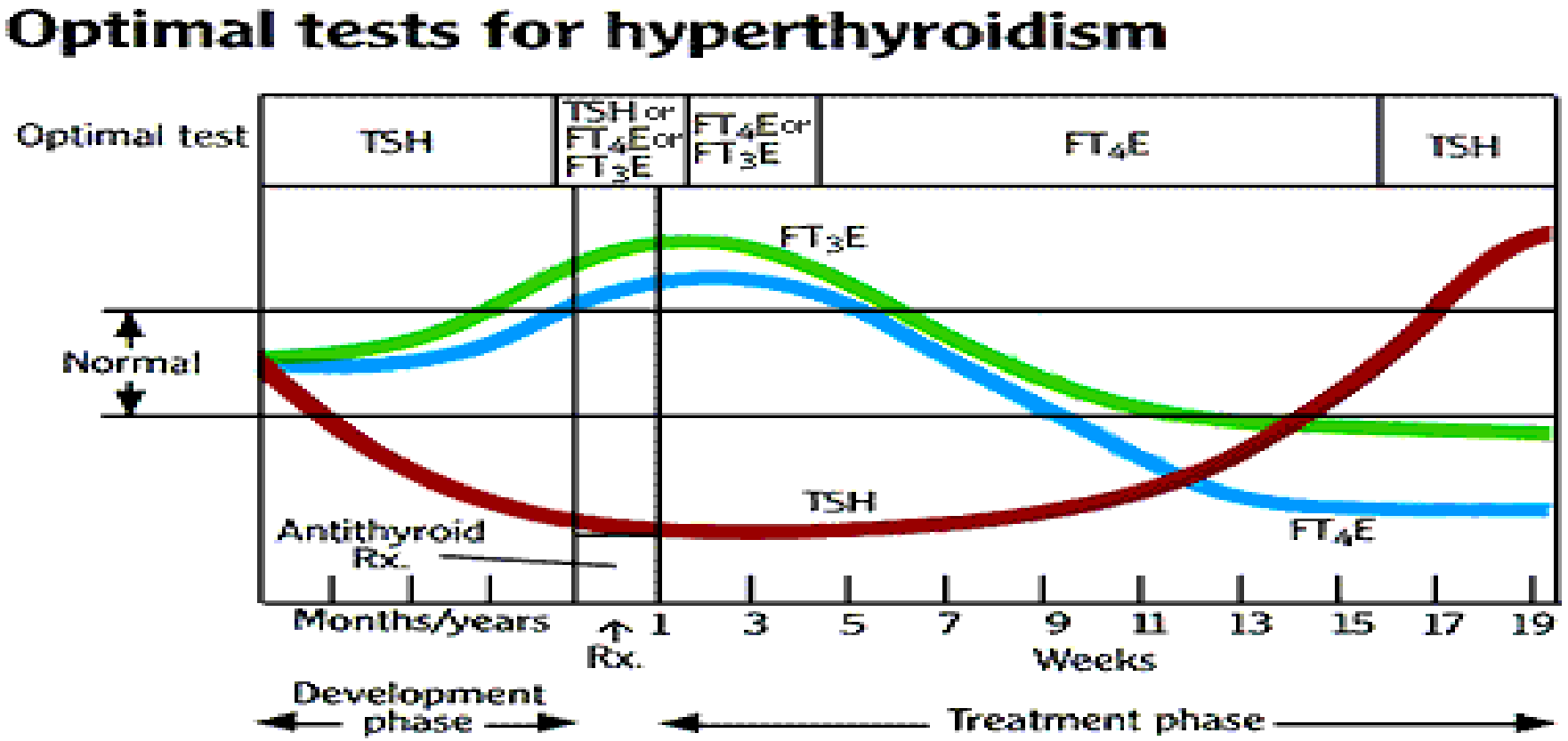
# Stages of the thyrotoxicosis

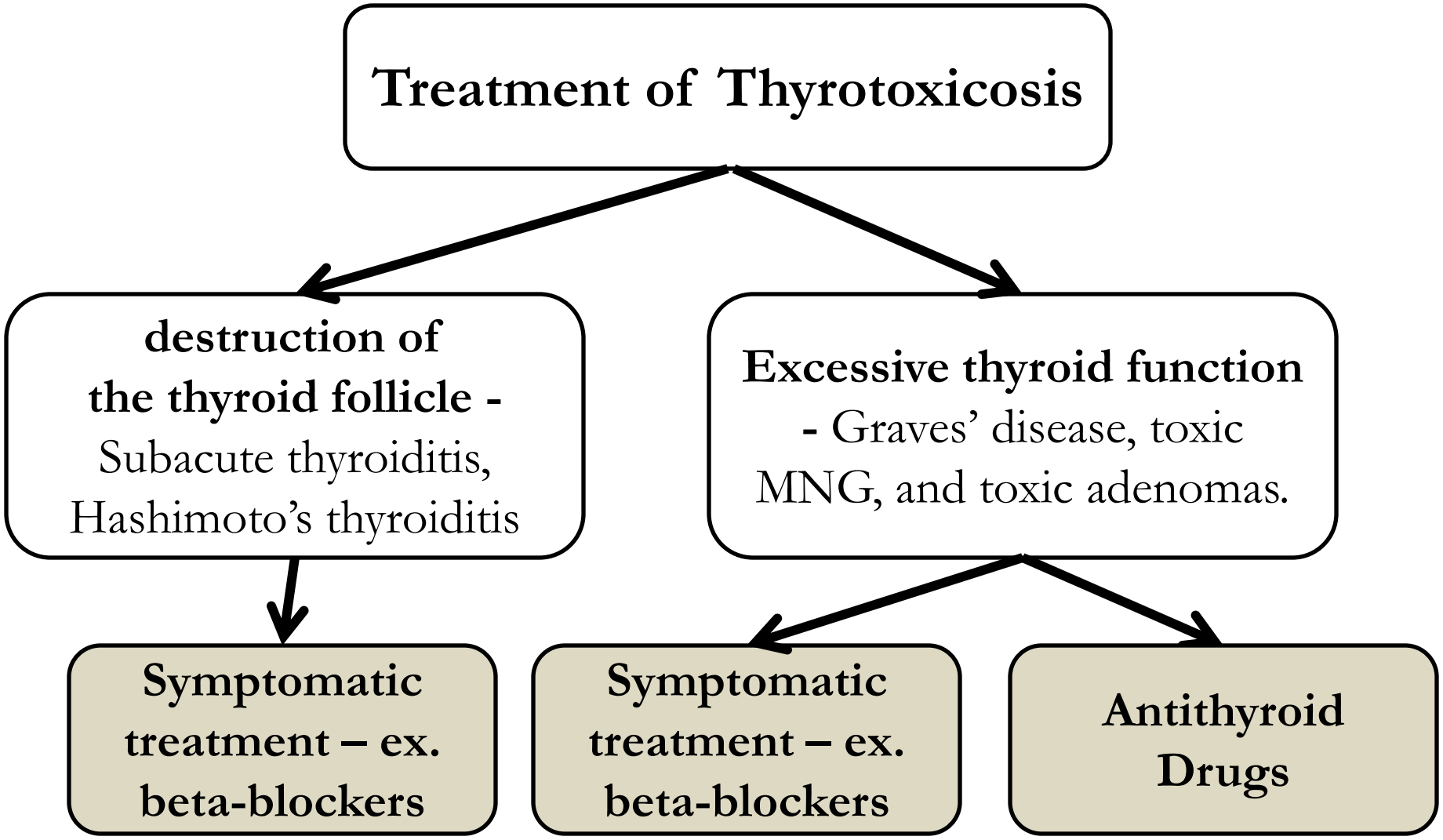
## Sever form

- The clinical symptoms significantly pronounced
- Tachycardia more than 120 beats per minute
- Weight loss more than 20%
- There are complications. Frequently atrial fibrillation, blood circulation insufficiency, adrenal insufficiency

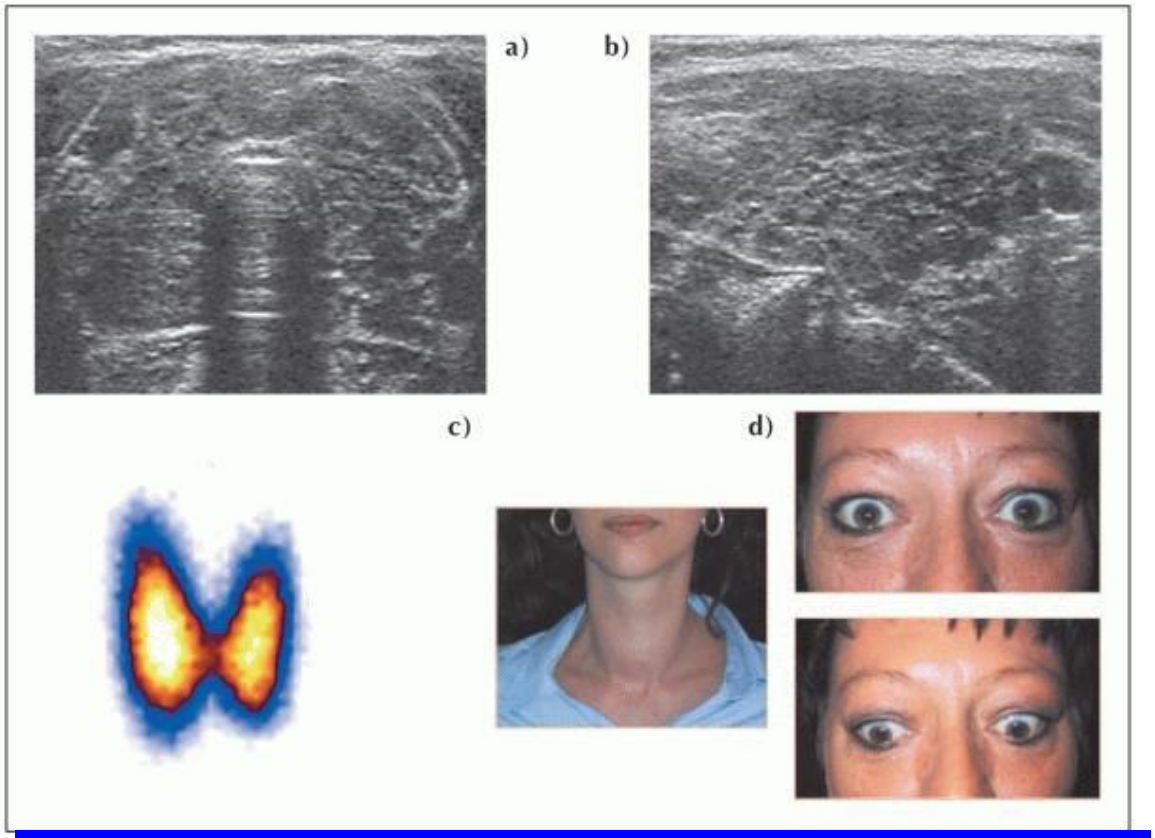
# Laboratory findings

- Plasma levels of freeT4, freeT3, are elevated
- Plasma level of TSH is low




Treatment of Thyrotoxicosis
destruction of the thyroid follicle - Subacute thyroiditis, Hashimoto's thyroiditis
Excessive thyroid function - Graves' disease, toxic MNG, and toxic adenomas.
Symptomatic treatment – ex. beta-blockers
Symptomatic treatment – ex. beta-blockers
Antithyroid Drugs

# Diffuse toxic goiter (Graves' Disease)



# Diffuse toxic goiter (Graves disease)

**Is an endocrine disease which is characterized by:**

- **excessive production of thyroid hormones (hyperthyroidism) and**
- **diffuse enlargement of the thyroid gland.**

**Hyperthyroidism determines the development of the thyrotoxicosis and causes the metabolic disturbances and pathological changes in all organs, systems and tissues of the organism.**

**The disease may occur at any age, most commonly between 20 to 50 years.**

**Women being affected more frequently (about five times) than men.**

# Etiology

**Graves'disease is an autoimmune disease of unknown cause.**

**The hereditary factors predispose to the development of the disease.**

**Factors that can lead to autoimmune disorders can be:**

- **pregnancy, particularly the postpartum period**
- **Iodine excess, particularly in geographic areas of iodine deficiency**
- **Viral or bacterial infections**

# Pathogenesis

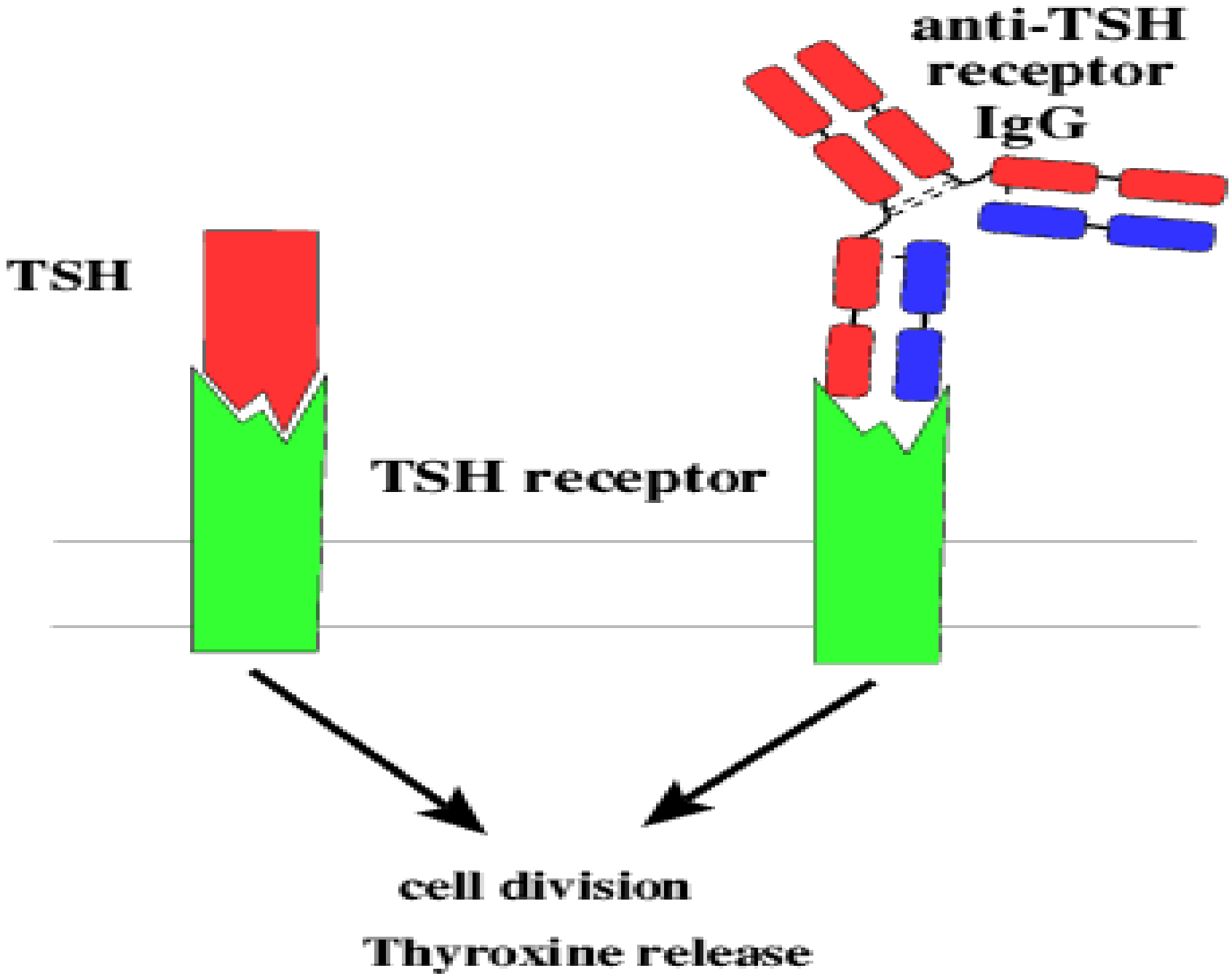
- **Pathogenesis of the GD is not yet sufficiently clear. Nowadays the GD is considered as a genetic autoimmune disease.**

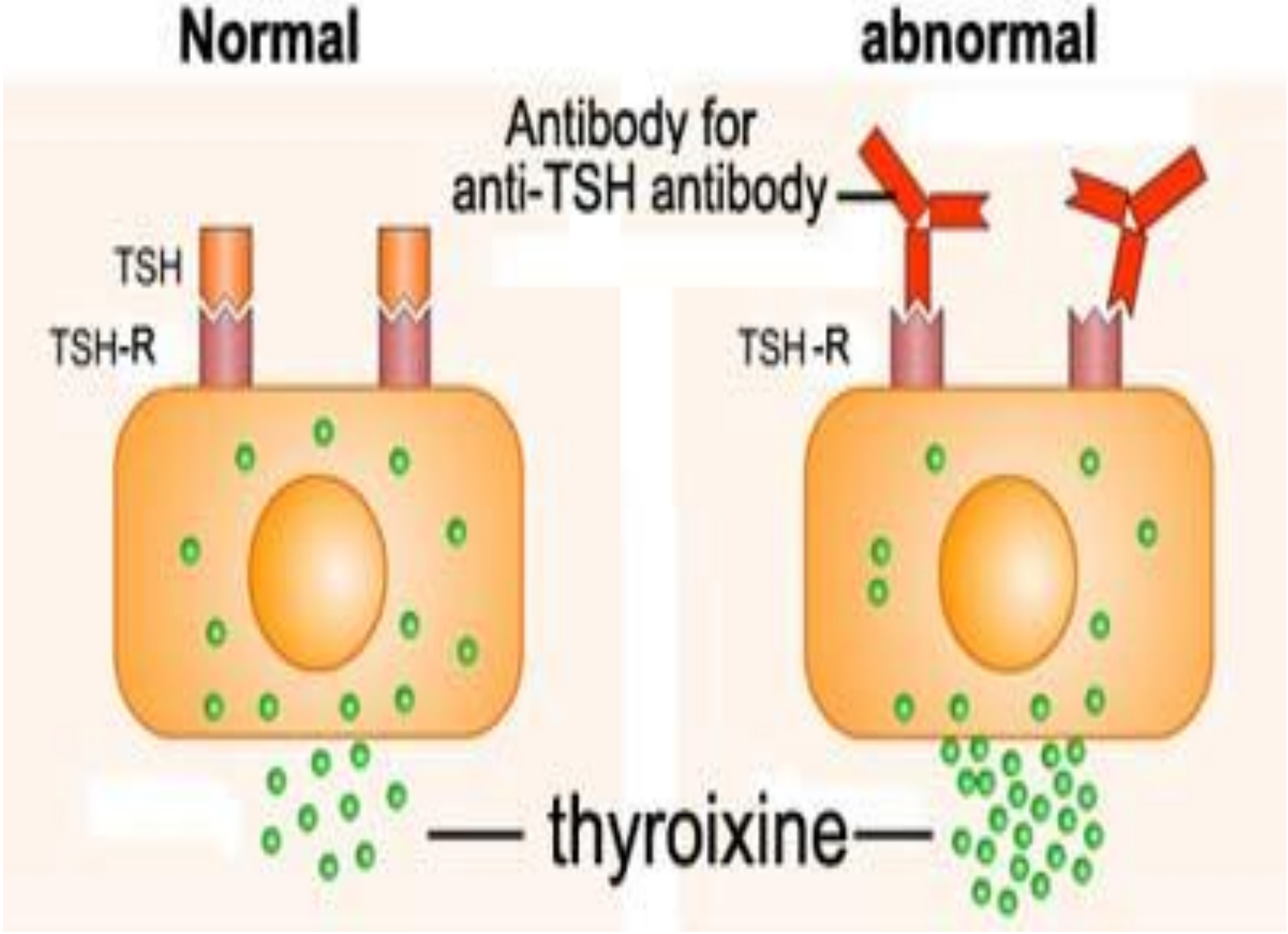
- **As a result of genetic defect in the system of immunological survival, forbidden lymphocyte clones are not suppressed and they interact with the organ specific antigen of the thyroid.**

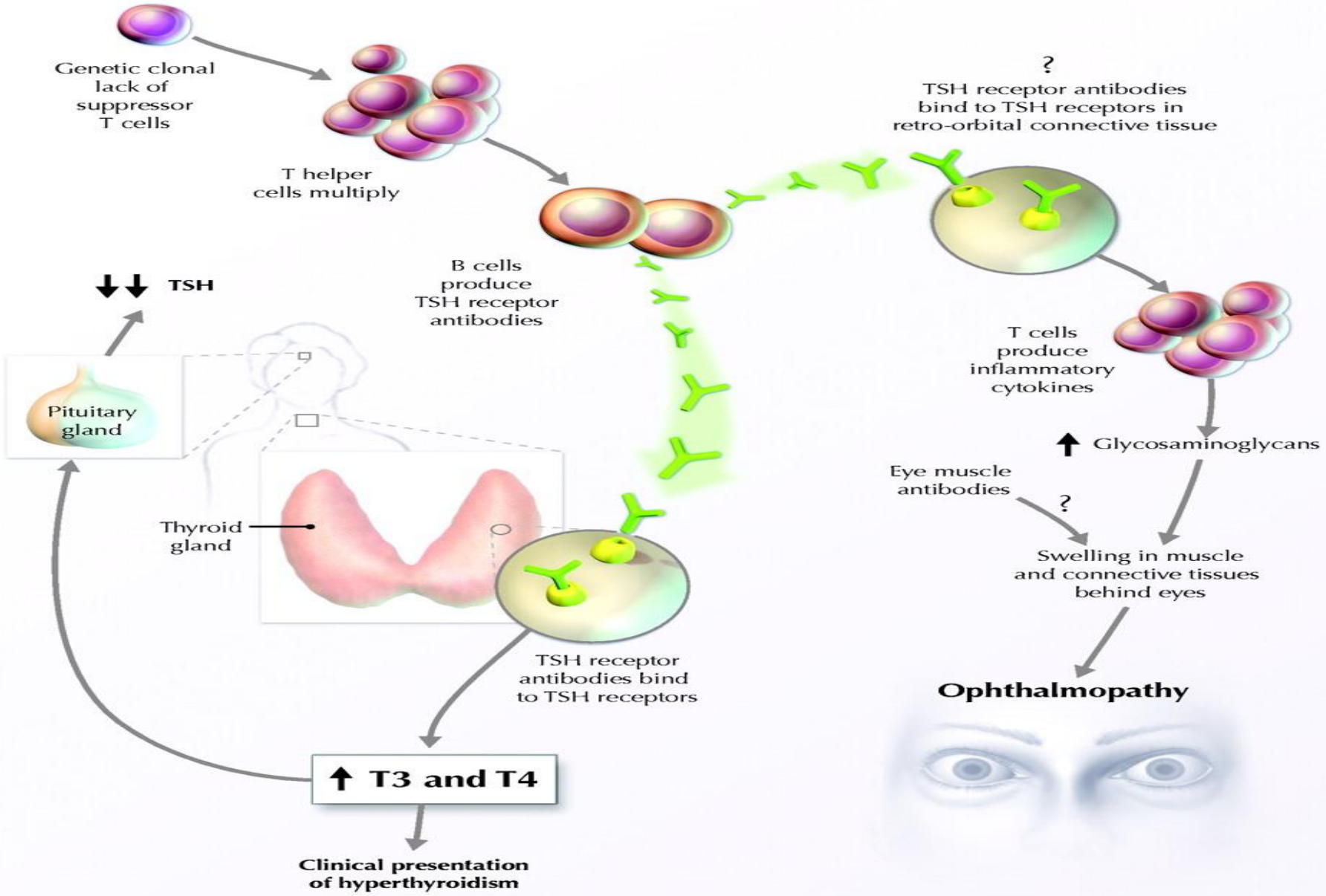
- **As a consequence, B-lymphocytes stimulates synthesis of thyroidstimulating immunoglobulins.**

- **These immunoglobulins react with the TSH-receptors.**

- **As a result increased production of thyroid hormones and growth of the thyroid gland.**


anti-TSH
receptor
IgG
TSH
TSH receptor
cell division
Thyroxine release


Normal
abnormal
Antibody for
anti-TSH antibody
TSH
TSH-R
TSH-R
— thyroixine—


Genetic clonal lack of suppressor T cells
T helper cells multiply
B cells produce TSH receptor antibodies
?
TSH receptor antibodies bind to TSH receptors in retro-orbital connective tissue
T cells produce inflammatory cytokines
Glycosaminoglycans
Eye muscle antibodies
?
Swelling in muscle and connective tissues behind eyes
Ophthalmopathy
TSH
Pituitary gland
Thyroid gland
TSH receptor antibodies bind to TSH receptors
T3 and T4
Clinical presentation of hyperthyroidism

# Clinical features

**The clinical manifestations of GD consists of one or more of the following features:**

1. **Thyrotoxicosis**
2. **Goiter**
3. **Ophthalmopathy**

# Complaints:

***Thyrotoxicosis:***

- Weakness, fatigability
- Irritability, nervousness, tearfulness
- Palpitation
- A tremor of all body
- Sweating
- Heat intolerance
- Weight loss with normal nourishment
- Diarrhea
- Disturbance of menstrual cycle

***Goiter:***

- Sensation of pressure in the region of the neck

***Ophthalmopathy:***

- Exophtalmos

# Clinical features

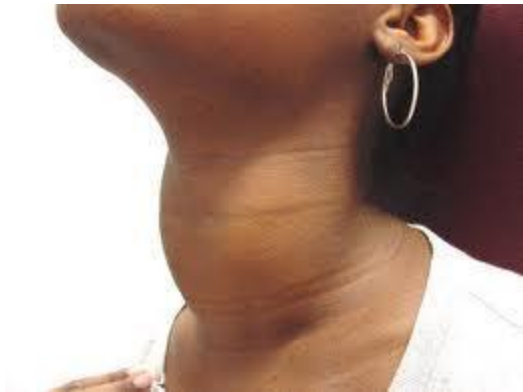
1. **Thyrotoxicosis** - Signs and symptoms that are common to any cause of thyrotoxicosis
2. Goiter
3. Ophthalmopathy

# Clinical features

1. Thyrotoxicosis
2. **Goiter**
3. Ophthalmopathy

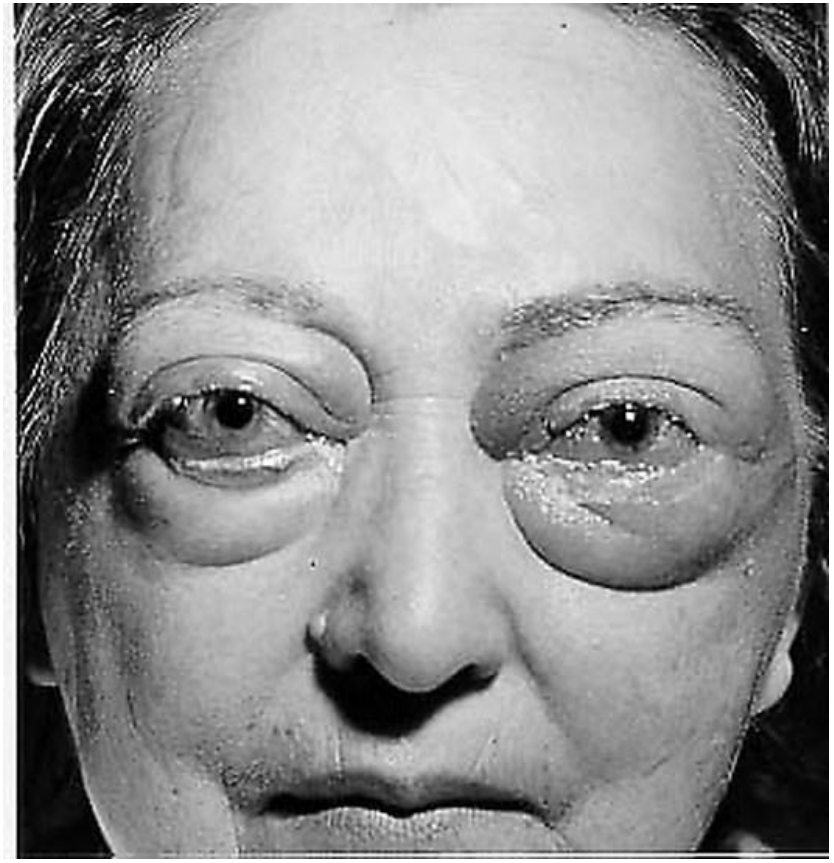
## The thyroid gland

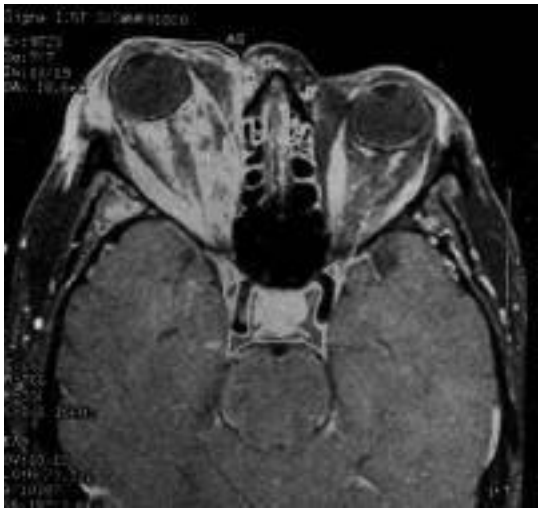
- **Is enlarged diffusely, although in some cases the increase of one lobe may be greater than of another.**
- **Is usually of soft or moderately firm consistency, mobile and not fused with underlying tissues.**



# Clinical features

1. Thyrotoxicosis
2. Goiter
3. **Ophthalmopathy**





# Endocrine ophthalmopathy

# Endocrine ophthalmopathy

**Ophthalmopathy is one of the most characteristic symptoms of GD.**

**EO occurs in 50% of patients with GD.**

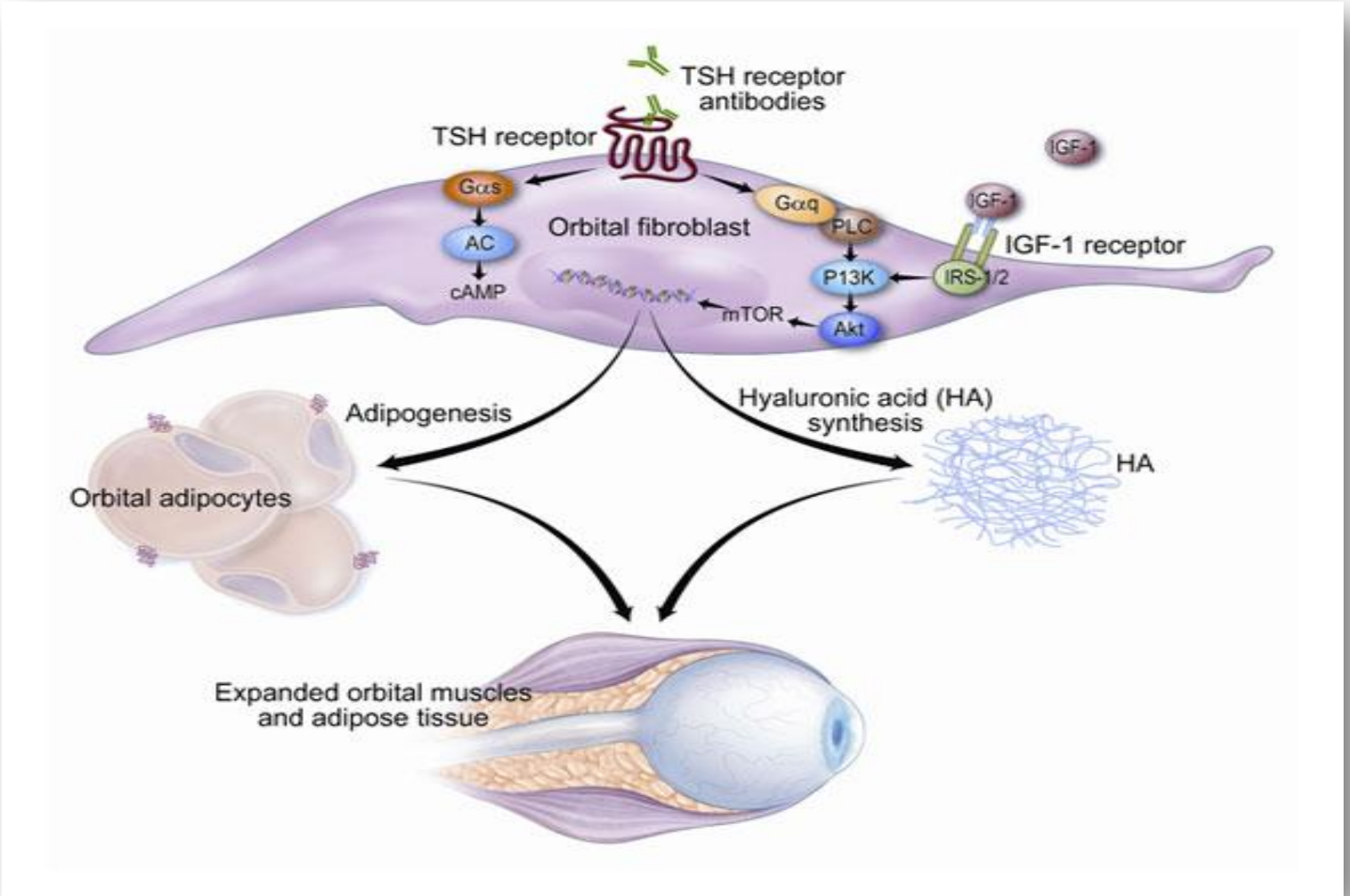
**The EO is determined more often on both eyes.**

**The EO can affect only one eye.**

# Pathogenesis of the ophthalmopathy

- **The pathogenesis of the ophtalmophathy is determined by cytotoxic lymphocytes and cytotoxic antibodies sensitized to a common antigen such as the TSH-R found in orbital fibroblasts, orbital muscle and thyroid tissue. Cytokines from these lymphocytes would cause inflammation of orbital fibroblast and orbital myositis.**

# "Exophthalmos by Hypertrophia of the Tissue in the Orbita"



# Pathogenesis of the ophthalmopathy

**In the base of ophtalmophathy are:**

- **the oedema and the proliferation of the retrobulbar tissue**
- **the oedema and the proliferation of the extraocular muscles.**

  **(This is caused by the accumulation in these muscles of acid mucopolysaccharides containing hyaluronic and chondroitinsulfuric acids, possessing marked hydrophily.)**
- **Increase adiposogenesis.**

**There are distinguished more stages of ophthalmopathy depending on:**

- **subjective symptoms,**
- **exophtalm's expression,**
- **oedema of the eyelids**
- **disorders of the function of the oculomotor muscles.**

# Classification of ophthalmopathy

**Several classification systems have been conceived to assess the clinical manifestations of GO.**

1. ***Severity*** **–** NOSPECS Classification - by Werner in 1969, 1977

2. ***Activity*** – Clinical Activity Score (CAS) – by Mourits in 1989

Table 1: NO SPECS modified classification [22].

| Class | Grade | Suggestions for grading |
|---|---|---|
| 0 | | No physical signs or symptoms |
| I | | Only signs |
| II | | Soft tissue involvement |
| | 0 | Absent |
| | a | Minimal |
| | b | Moderate |
| | c | Marked |
| III | | Proptosis (3 mm or more of normal upper limits with or without symptoms) |
| | 0 | Absent |
| | a | 3 or 4 mm over upper normal |
| | b | 5 to 7 mm increase |
| | c | 8 mm increase |
| IV | | Extraocular muscle involvement (usually with diplopia) |
| | 0 | Absent |
| | a | Limitation of motion at extremes of gaze |
| | b | Evident restriction of motion |
| | c | Fixation of a globe or globes |
| V | | Corneal involvement (primarily due to lagophthalmos) |
| | 0 | Absent |
| | a | Stippling of cornea |
| | b | Ulceration |
| | c | Clouding, necrosis, and perforation |
| VI | | Sight loss (due to optic nerve involvement) |
| | 0 | Absent |
| | a | Disc pallor or choking, or visual field defect, vision 20/20–20/60 |
| | b | The same, but vision 20/70–20/200 |
| | c | Blidness, vision less than 20/200 |

The currently grading systems used for the assessment of GO are

- the **VISA Classification** (vision, inflammation, strabismus, and appearance)
- the **EUGOGO Classification** (European Group of Graves' Orbitopathy)

Both systems are grounded in the NOSPECS and CAS classifications and use indicators to assess the signs of ***activity*** and the degree of ***severity***.

They allow the clinician to guide the treatment of the patient with GO.

VISA is more commonly used in North America and Canada while EUGOGO is in Europe.

Since the two protocols are not interchangeable, only one of them should be employed as a reference in a specific patient.

# Why is it important to distinguish activity and severity when evaluating patients?

**Determining the phase of GO at each clinical assessment is fundamental to formulating an appropriate management plan.**

**This is because immunomodulatory therapies can only be effective while there is active inflammation.**

**On the other hand, certain surgical treatment should only be undertaken when GO is inactive.**

Table 2: Clinical Activity Score (CAS) (amended by EUGOGO after Mourits et al.). One point is given for the presence of each of the parameters assessed. The sum of all points defines clinical activity: active ophthalmopathy if the score is above 3/7 at the first examination or above 4/10 in successive examinations.

| | For initial CAS, only score items 1–7 |
|---|---|
| 1 | Spontaneous orbital pain |
| 2 | Gaze evoked orbital pain |
| 3 | Eyelid swelling that is considered to be due to active GO |
| 4 | Eyelid erythema |
| 5 | Conjunctival redness that is considered to be due to active GO |
| 6 | Chemosis |
| 7 | Inflammation of caruncle OR plica |
| | Patients assessed after follow-up (1–3 months) can be scored out of 10 by including items 8–10 |
| 8 | Increase of >2 mm in proptosis |
| 9 | Decrease in uniocular ocular excursion in any one direction of >8° |
| 10 | Decrease of acuity equivalent to 1 Snellen line |

Table 3: VISA Inflammatory Index (I) (Dolman and Rootman 2006 [25], ITEDS modified). Patients with moderate inflammatory index (less than 4 of 10) are managed conservatively. Patients with high scores (above 5 of 10) or with evidence of progression in the inflammation are offered a more aggressive therapy.

| Sign or symptom | Score |
|---|---|
| Caruncular edema | 0: absent<br>1: present |
| Chemosis | 0: absent<br>1: conjunctiva lies behind the grey line of the lid<br>2: conjunctiva extends anterior to the grey line of the lid |
| Conjunctival redness | 0: absent<br>1: present |
| Lid redness | 0: absent<br>1: present |
| Lid edema | 0: absent<br>1: present but without redundant tissues<br>2: present and causing bulging in the palpebral skin, including lower lid festoon |
| Retrobulbar ache<br>At rest<br>With Gaze | <br>0: absent; 1: present<br>0: absent; 1: present |
| Diurnal variation | 0: absent; 1: present |

# Severity classifications in GO (EUGOGO)

**Mild GO:** patients whose features of GO have only a minor impact on daily life, insufficient to justify immunosuppressive or surgical treatment.

**They usually have only one or more of the following:**

- minor lid retraction (<2 mm),
- mild soft tissue involvement,
- exophthalmos < 3 mm above normal for race and gender,
- transient or no diplopia,
- corneal exposure responsive to lubricants.

# Severity classifications in GO (EUGOGO)

**Moderate-to-severe GO:** Patients whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive).

**Patients with moderate-to-severe GO usually have any one or more of the following:**

- Lid retraction >2 mm,
- moderate or severe soft tissue involvement,
- exophthalmos >3 mm above normal for race and gender,
- inconstant, or constant diplopia.

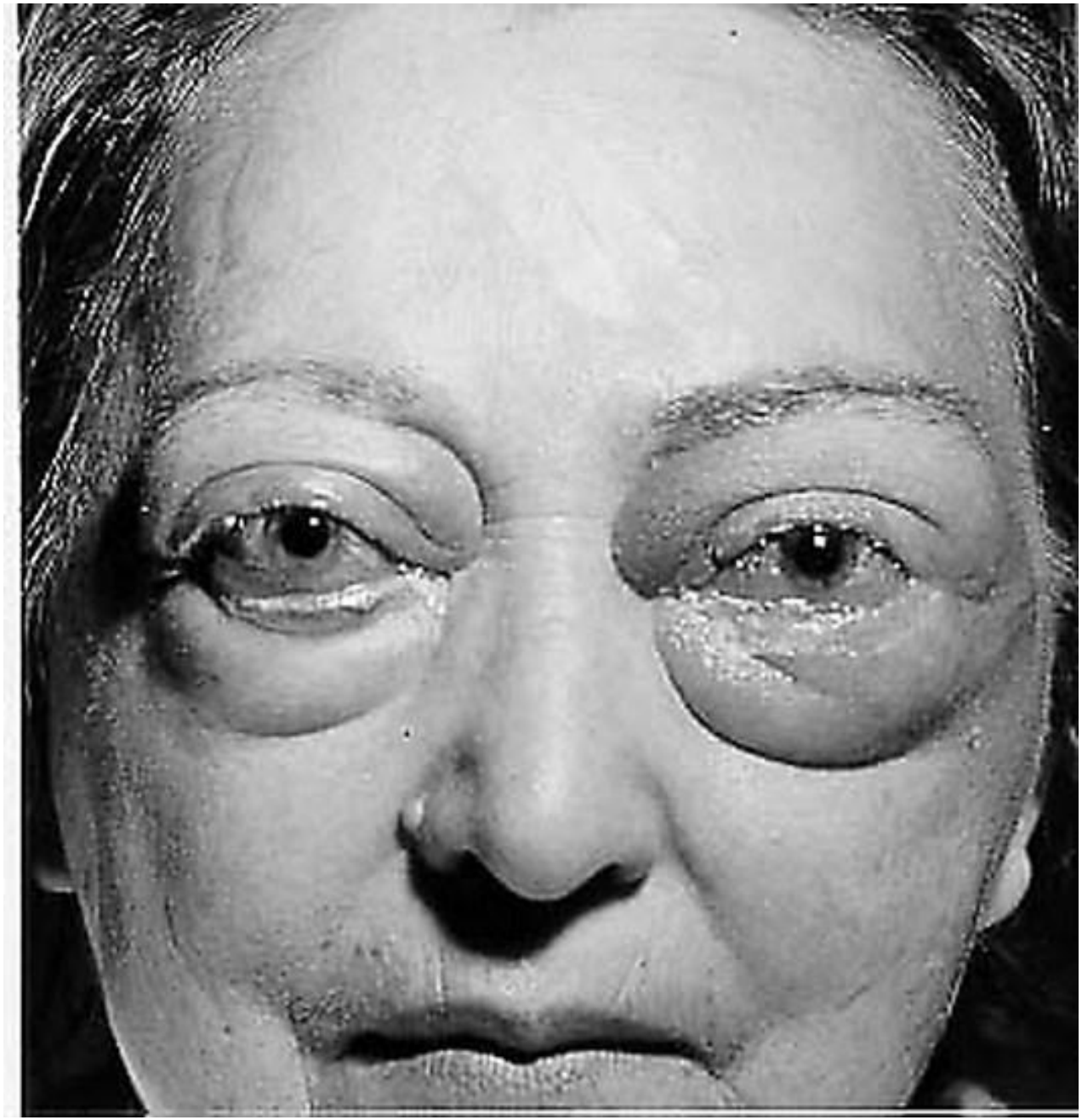
# Severity classifications in GO (EUGOGO)

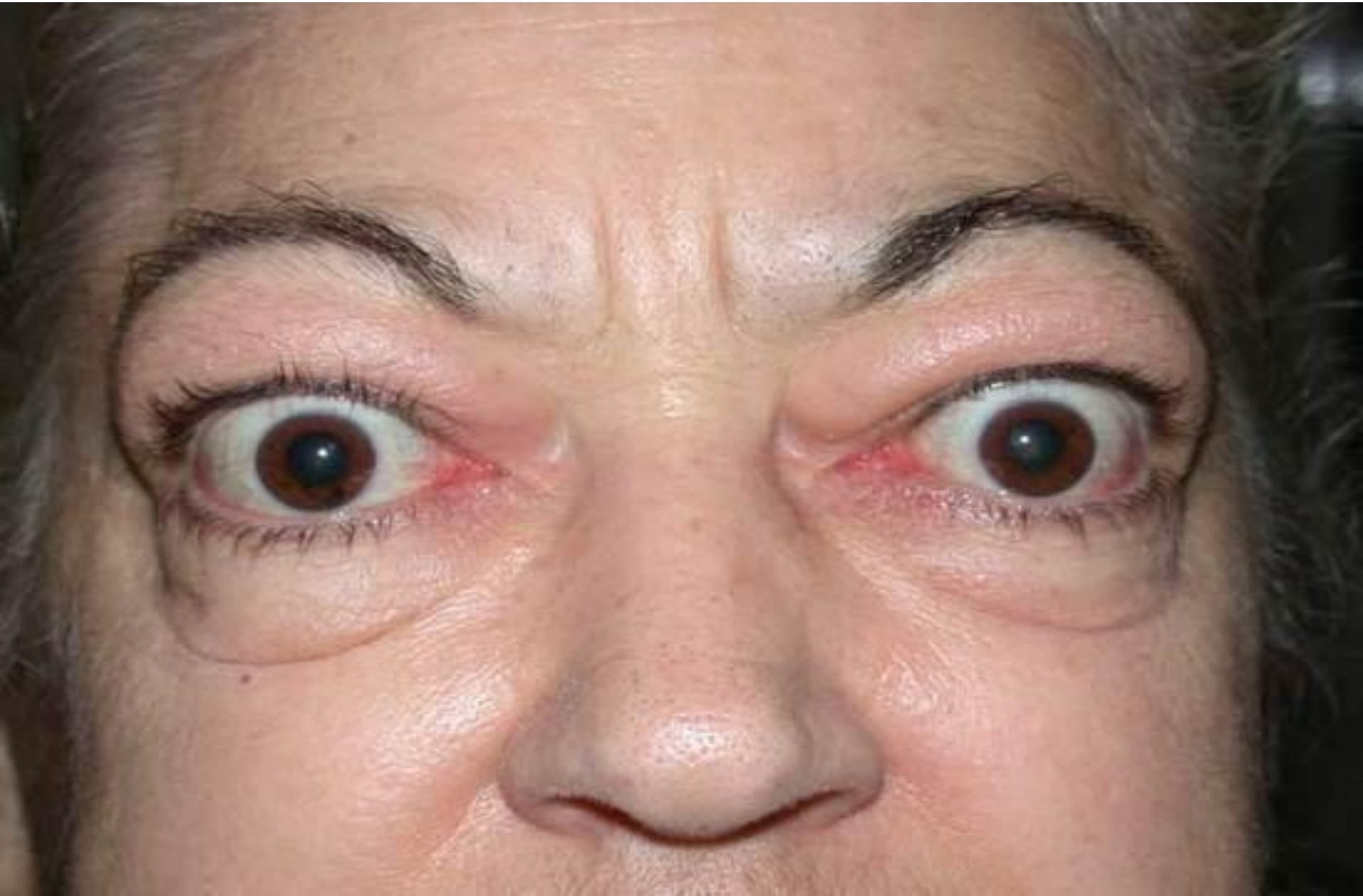
**Severe GO:**

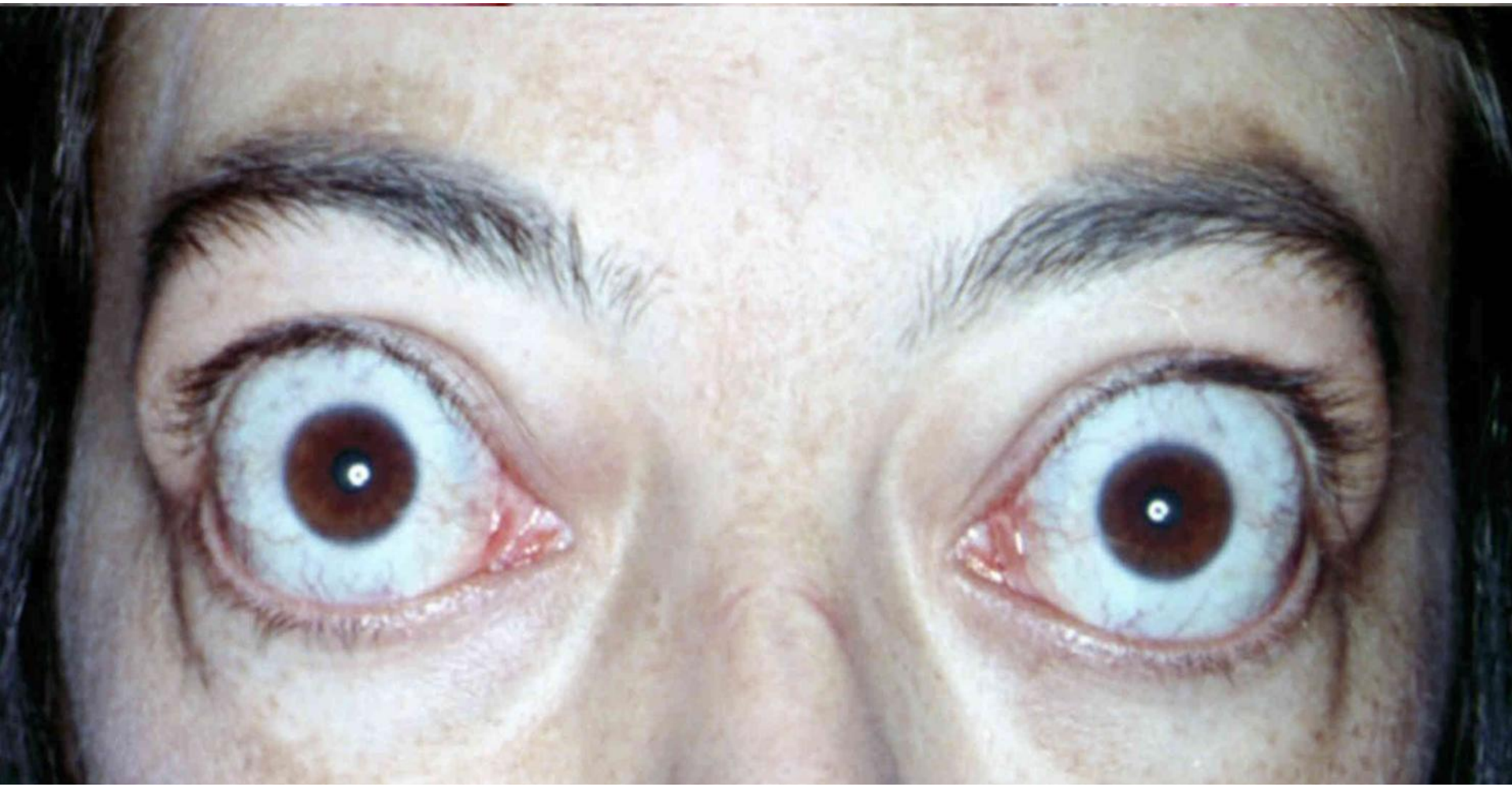
Patients with:

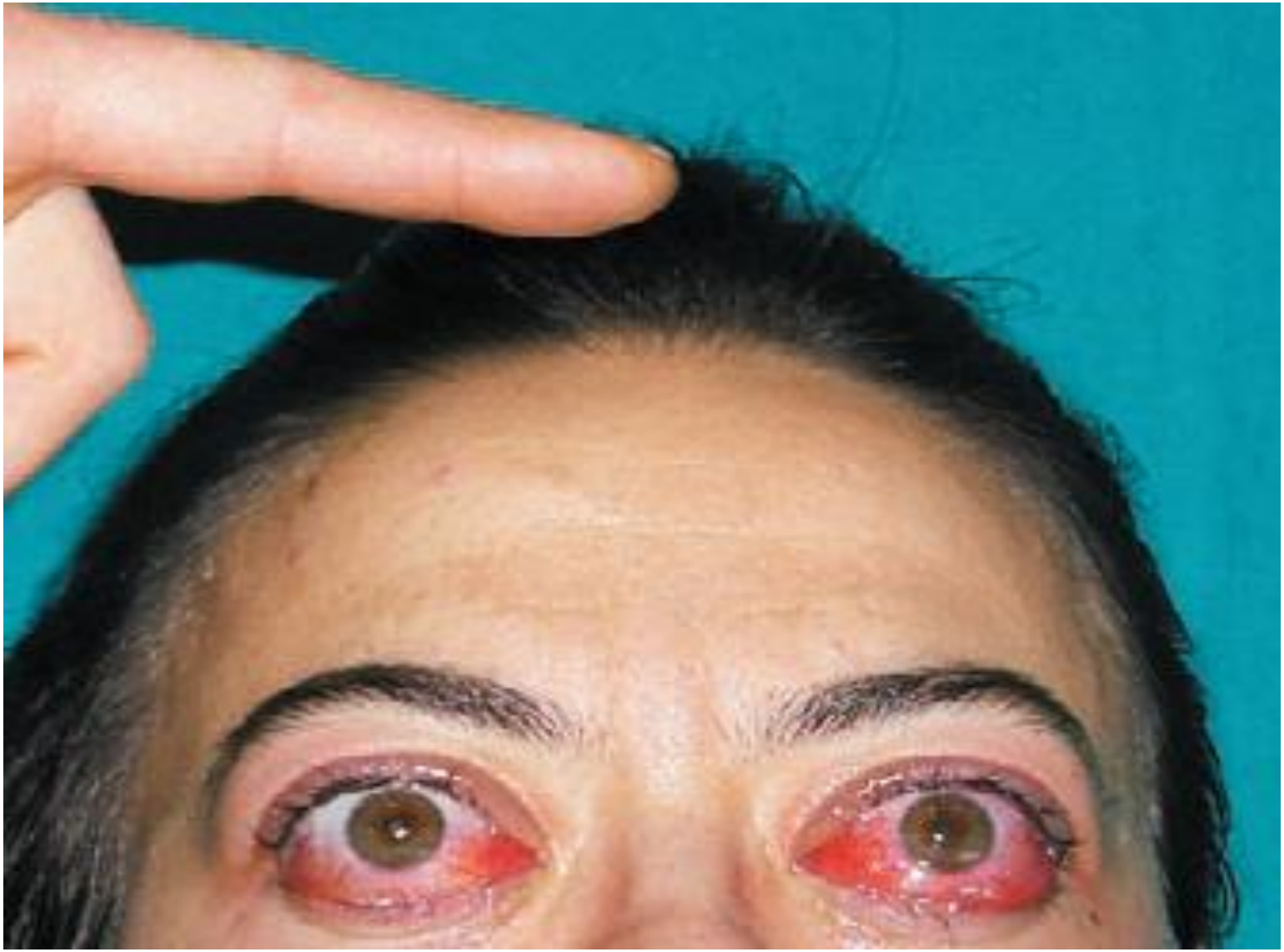
- dysthyroid optic neuropathy (DON)
- corneal breakdown due to severe exposure
- ocular globe subluxation,
- severe forms of frozen eye,
- choroidal folds
- postural visual darkenings.

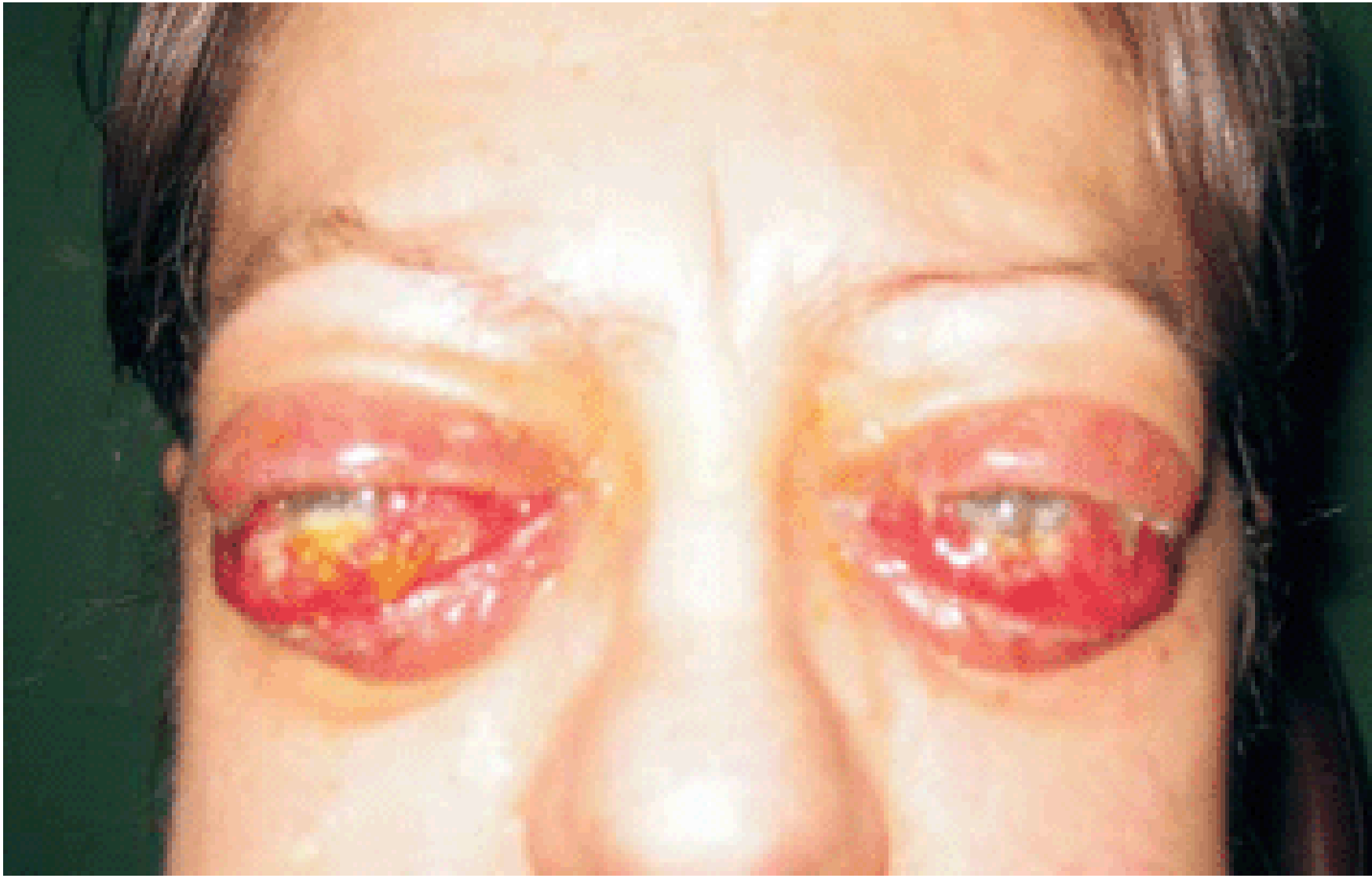
This category warrants immediate intervention.











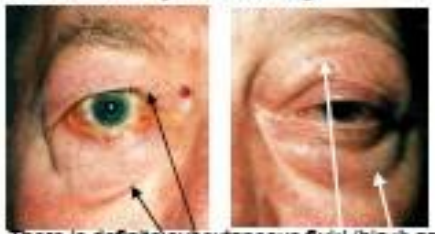
EUGOGO
EUropean Group of Graves' Orbitopathy

# EYELID SWELLING
HOW TO SCORE

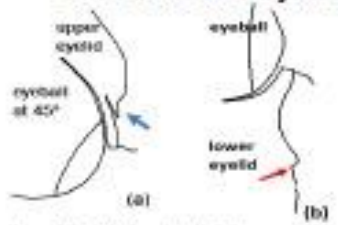
**MILD eyelid swelling**

Patient may be aware of changed appearance, but appearance is similar to these photographs. CAS negative

**MODERATE eyelid swelling**

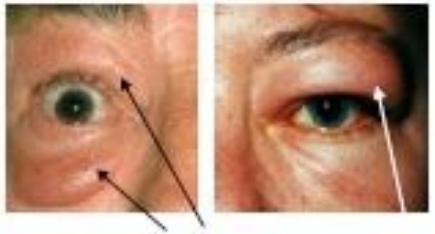


**cross-sections of eyelids**

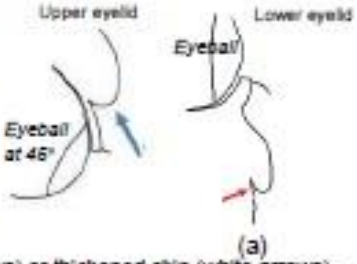



There is definite subcutaneous fluid (black arrows) or skin thickening (white arrows).
(a) When patient to looks down at 45°, the skin fold in the central upper eyelid forms as angle (blue arrow).
(b) Swelling in lower eyelid, does not fold skin to form festoon (red arrow).

**SEVERE eyelid swelling**



**cross-sections of eyelids**




There is tense subcutaneous fluid (black arrows) or thickened skin (white arrows).
(a) When patient to looks down at 45°, the skin fold in the central upper eyelid remains rounded (blue arrow).
(b) Swelling in lower eyelid folds skin to form festoon (red arrow).

EUGOGO
EUropean Group of Graves' Orbitopathy

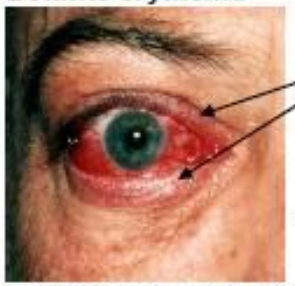
# EYELID ERYTHEMA
HOW TO SCORE

*Note: If patient only shows preseptal erythema, then exclude blepharitis.*
*Redness must exceed generalised facial redness to score*

**No erythema**

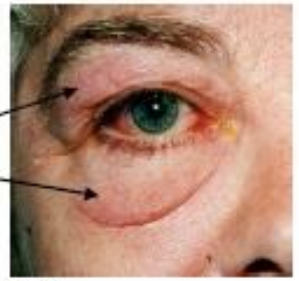
This degree of redness may be normal: score as "no"
= CAS negative

**Definite erythema**



**pretarsal** erythema

**preseptal** erythema



Pretarsal or preseptal erythema suggests **active** GO.
Score either as "yes" = CAS positive.

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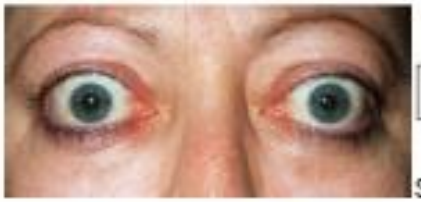
# CONJUNCTIVAL REDNESS

## HOW TO SCORE

*Examine patient from 1 metre without prior drops or handling eyelids*

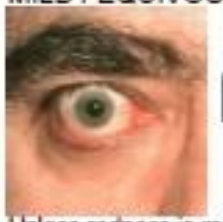
NO redness



normal appearance

Score as "no" = CAS negative

MILD / EQUIVOCAL redness

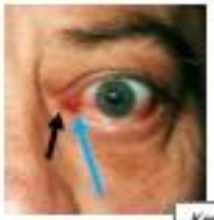


equivocal redness

Unless redness is more obvious than this, score as "no" = CAS negative

DEFINITE redness can be subdivided if helpful into moderate or severe. Both score "yes" = CAS positive.

MODERATE < 50% redness excluding plica and caruncle



Key: plica = ; caruncle =

SEVERE ≥ 50% redness excluding plica and caruncle

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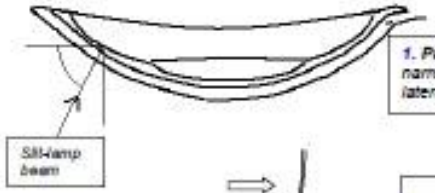
# CHEMOSIS: HOW TO SCORE

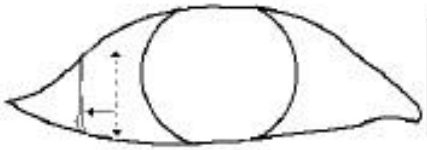
*Method: examine on slit-lamp*




*1. Patient adopts primary gaze. Use vertical narrow slit-lamp beam at 60°, midway between lateral canthus and limbus.*


Cross sectional slit-lamp view

*2. Assess where sclera (i) separates from conjunctiva (ii):see arrow*
*Note whether chemosis prolapses in front of "grey" line (this is the line formed by the orifices of the meibomian glands as shown as a dotted line in this diagram), or not*

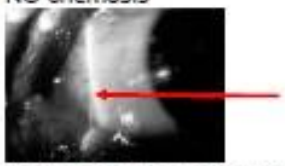


*3. Assess whether separation point of sclera and conjunctiva (horizontal arrow) is higher than a third of the total height of the palpebral aperture (broken arrow)*

Mild chemosis (<1/3 total palpebral aperture height) is hard to distinguish from conjunctival folds common in elderly patients and known as conjunctivochalasis.

**SCORING** *(slit lamp view)*

NO chemosis



1. Conjunctiva and sclera separate ≤1/3 of total height of palpebral aperture (arrow)
2. Chemosis does not prolapse in front of grey line: Score is "no" CAS negative

DEFINITE chemosis

1. Conjunctiva and sclera separate >1/3 of total height of palpebral aperture (arrow) OR
2. Conjunctiva prolapses in front of greyline: Score is "yes" CAS positive

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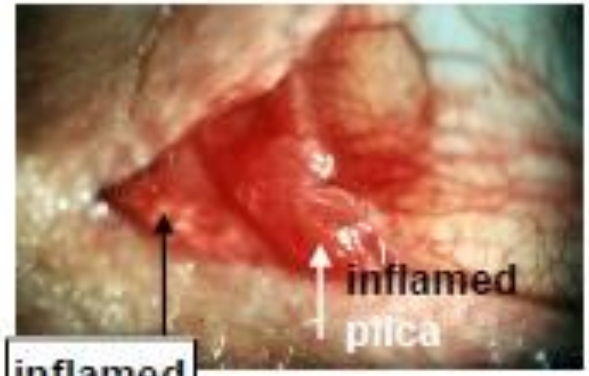
# CARUNCLE AND PLICAL INFLAMMATION:

## HOW TO SCORE

*Caruncle is normally yellowish pink and lies medial to plica, which is normally pink. Proptosis can prolapse caruncle forwards – this is not the same as inflamed*

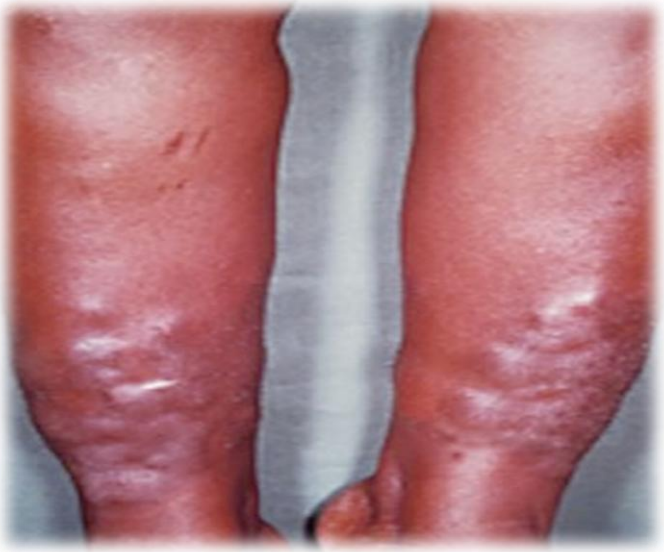




## SCORING

| | |
|---|---|
| prominent or prolapsed caruncle, but **not** inflamed | score "no" |
| plica prolapses through closed eyelids | score "yes" |
| inflamed plica OR caruncle | score "yes" |

Yes = CAS positive

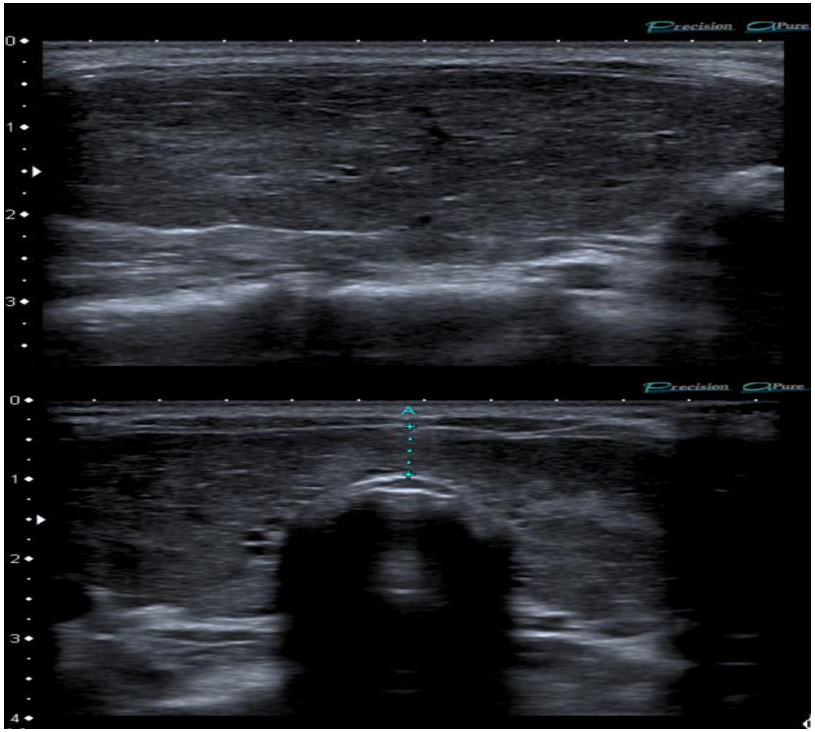
- **Pretibial Mixidema -** a pretibial swelling. Occurs in <5% of patients with GD. Most frequent over the anterior and lateral aspects of the lower leg. The skin is characterized by swelling of pretibial areas, indurated plaque, brownish in color and an "orange skin" appearance.



# Diagnosis of Graves' Disease

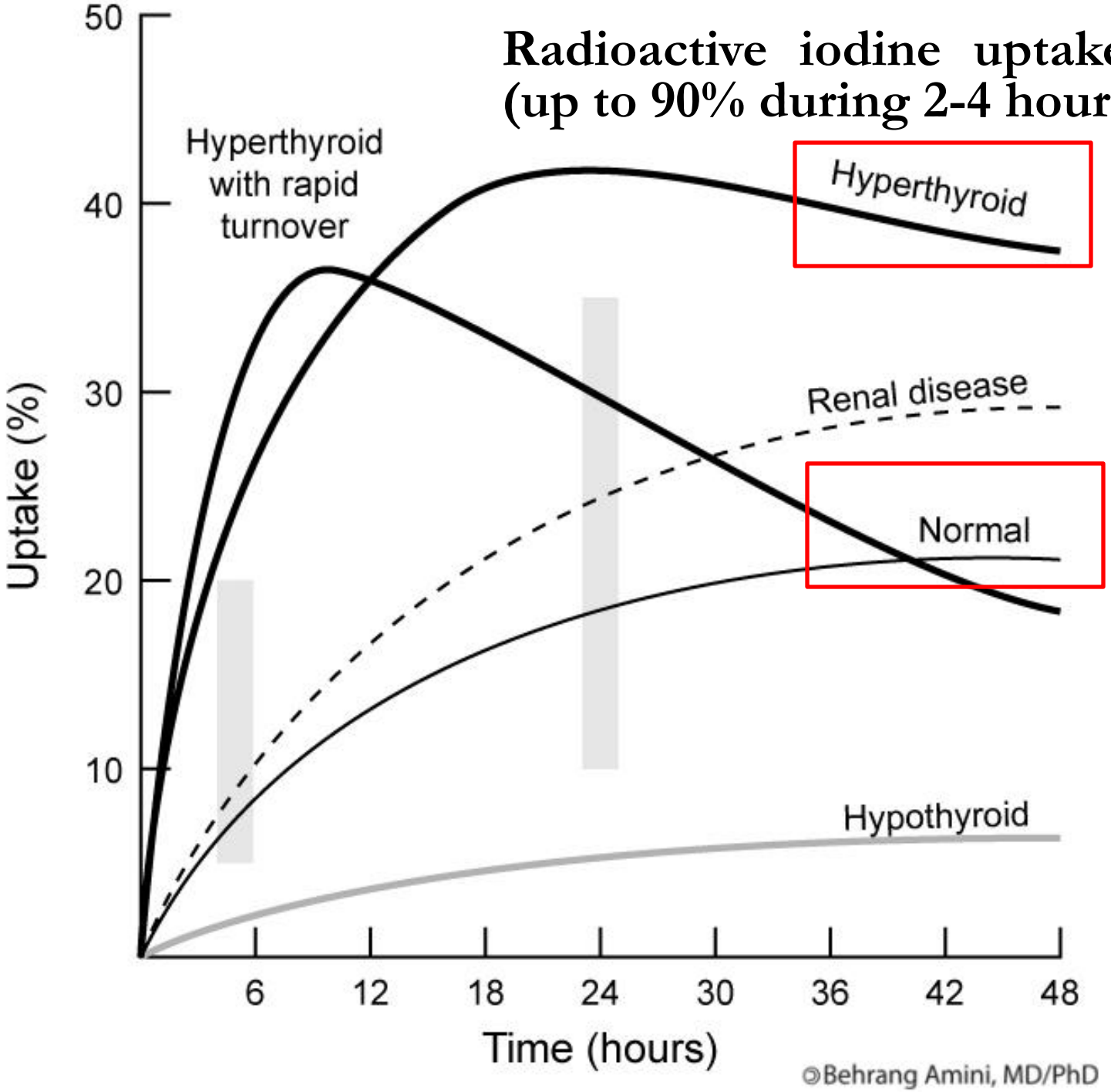
# Laboratory findings

- **freeT4, freeT3 - are elevated**
- **TSH - is low**
- **Thyroid autoantibodies:**
  - ✓ **TSH-R Ab (TRAB) is specific for Graves'disease.**
  - ✓ **Tg Ab and TPO Ab – are usually present in both Crave's disease and Hashimoto's thyroiditis**



- Ultrasound studies – thyroid gland is diffusely enlarged, its parenchyma is hypoechogenic, structure is homogeneous, boundary is clear, the bloodstream in a gland is increased.

**Radioactive iodine uptake: is increased (up to 90% during 2-4 hours.)**



Numele pacientului : [redacted]

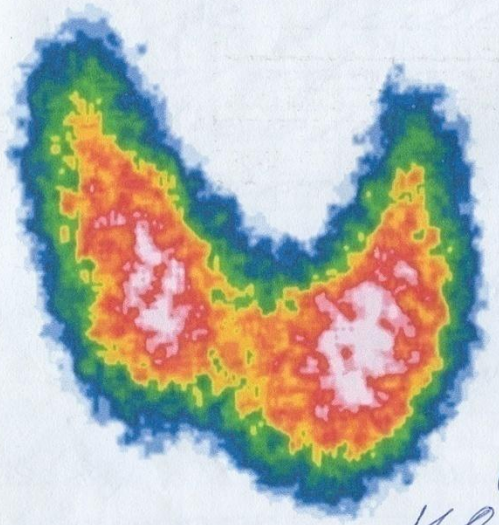
BON Nr. 0754129

Data investigatiei: 12/21/2007 10:21:28 AM

PRF: TC-99M 50.09 MBq

Ministerul Sanatatii al RM
Centrul Republican de Diagnosticare Medicala
Laboratorul Medicina Nucleara
tel: 888-389, 888-382, 888-381

## Scintigrafia glandei tiroide



| Aria si parametrii functionali | | | | | | |
|---|---|---|---|---|---|---|
| | Aria cm2 | Norma cm2 | % Acumulare | Norma % | %/Aria | Norma |
| Glanda tiroida | 45.5 | 20 | 20.71% | 1.8-4.0 | 0.46 | 0.09-0,20 |
| Lobul sting | 23.2 | 10 | 11.02% | 0.9-2.0 | 0.48 | 0.09-0,20 |
| Lobul drept | 22.8 | 10 | 9.69% | 0.9-2.0 | 0.43 | 0.09-0,20 |

**Scan - reveals increased iodine uptake by the whole gland, diffuse enlargement of the gland**

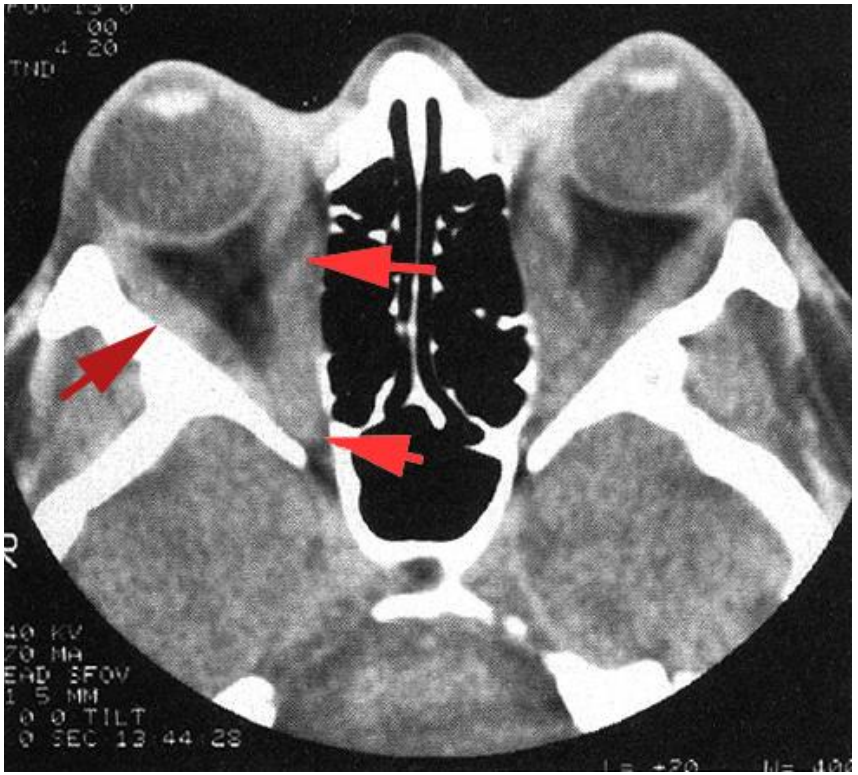
Comentariu:

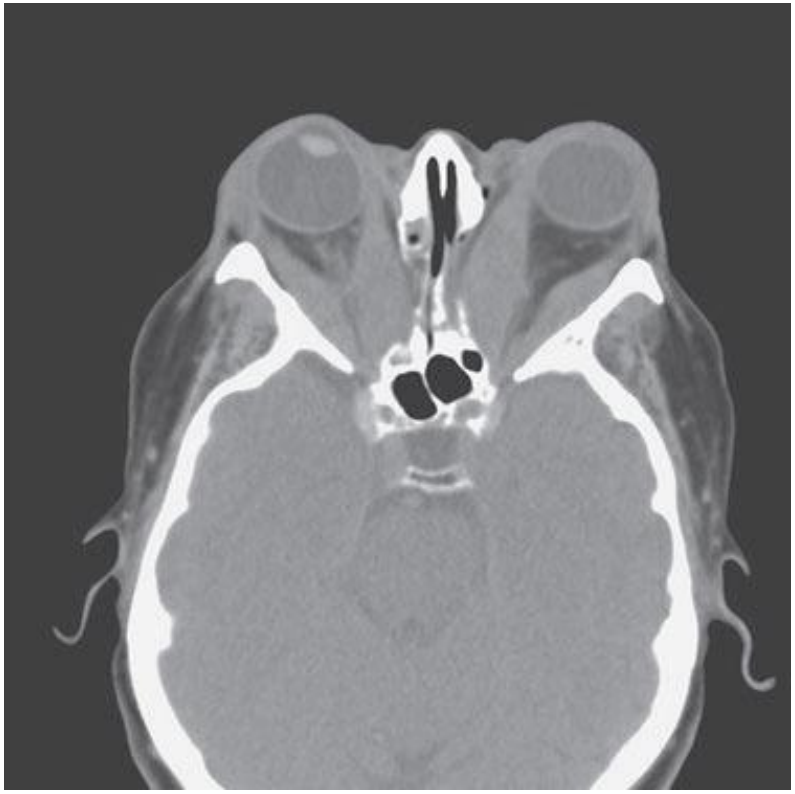
# Diagnosis of ophthalmopathy

- **CT and MRI scans of the orbit have revealed muscle enlargement.**

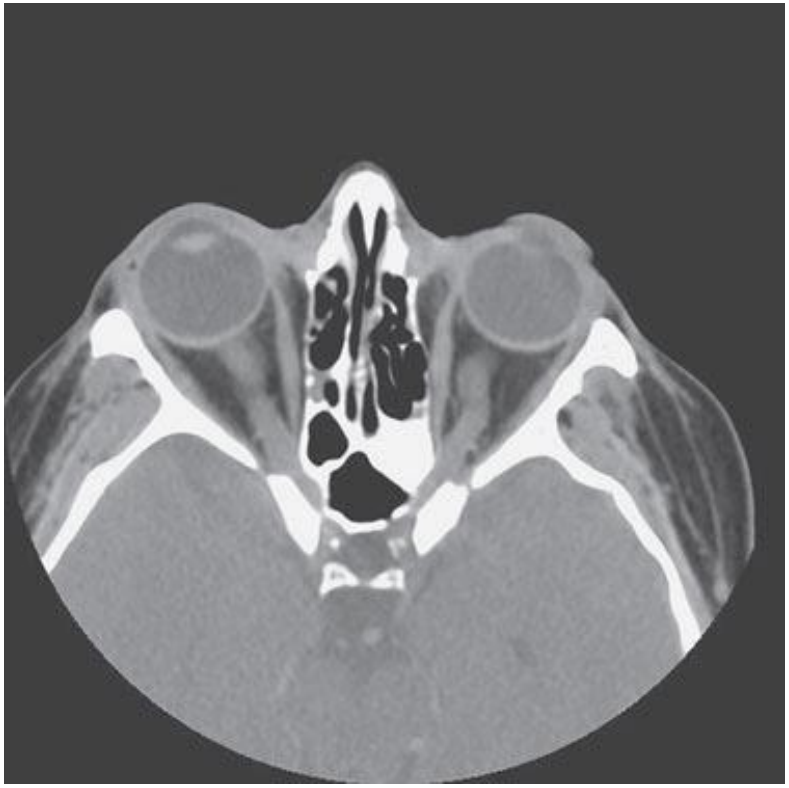
# Diagnosis of ophthalmopathy

**Marked enlargement of extraocular muscles, with compression of the optic nerve**





**CT scan – enlargement of extraocular muscles, bilateral exophtalmus**



**CT scan – healthy people**

**A 35 -year-old female with symptoms of:**

- fatigue, palpitations, 27 kg weight loss over last 2 months (from 82 kg – to 55), heat intolerance, tremor;
- Puffy eyelids, Diplopia, Visual loss, ocular pressure and pain, protrusion of both eye balls for last 2 months.
- The thyroid gland is diffusely enlarged and smooth.
- The skin is warm with increased sweating.
- There are mild conjunctival hyperemia, lid lag and mild proptosis (4 mm) in both eyes. Periorbital edema around the lids; Conjunctiva is congested nasally and temporally, with mild chemosis, inflamation of caruncle
- Cardiovascular: atrial arrhythmia with pulse 128/min, arterial pressure 160/60 mmHg.

**diagnosis:** Graves disease

**A 35 -year-old female with symptoms of:**

- fatigue, palpitations, 27 kg weight loss over last 2 months (from 82 kg – to 55), heat intolerance, tremor;
- Cardiovascular: atrial arrhythmia with pulse 128/min, arterial pressure 160/60 mmHg.
- The skin is warm with increased sweating.

**Thyrotoxicosis**

- The thyroid gland is diffusely enlarged and smooth.

**Goiter**

- Puffy eyelids, Diplopia, Visual loss, ocular pressure and pain, protrusion of both eye balls for last 2 months.
- There are mild conjunctival hyperemia, lid lag and mild proptosis (4 mm) in both eyes. Periorbital edema around the lids; Conjunctiva is congested nasally and temporally, with mild chemosis, inflamation of caruncle

**Ophthalmopathy**

- fatigue, palpitations, 27 kg **weight loss** over last 2 months **(from 82 kg – to 55 – 33%),** heat intolerance, tremor;
- Cardiovascular: atrial arrhythmia with **pulse 128/min,** arterial pressure 160/60 mmHg.
- The skin is warm with increased sweating.

**diagnosis Graves disease Sever thyrotoxicosis**

- Puffy eyelids, Diplopia, Visual loss, **ocular** pressure and **pain**, protrusion of both eye balls for last 2 months.
- There are mild **conjunctival hyperemia,** lid lag and mild proptosis (4 mm) in both eyes. **periorbital edema around the lids; Conjunctiva is congested** nasally and temporally, with mild **chemosis, inflamation of caruncle.**

**5/7**

TABLE 2: Clinical Activity Score (CAS) (amended by EUGOGO after Mourits et al.). One point is given for the presence of each of the parameters assessed. The sum of all points defines clinical activity: active ophthalmopathy if the score is above 3/7 at the first examination or above 4/10 in successive examinations.

| | For initial CAS, only score items 1–7 |
|---|---|
| 1 | Spontaneous orbital pain |
| 2 | Gaze evoked orbital pain |
| 3 | Eyelid swelling that is considered to be due to active GO |
| 4 | Eyelid erythema |
| 5 | Conjunctival redness that is considered to be due to active GO |
| 6 | Chemosis |
| 7 | Inflammation of caruncle OR plica |
| | Patients assessed after follow-up (1–3 months) can be scored out of 10 by including items 8–10 |
| 8 | Increase of >2 mm in proptosis |
| 9 | Decrease in uniocular ocular excursion in any one direction of >8° |
| 10 | Decrease of acuity equivalent to 1 Snellen line |

diagnosis Graves disease Sever hyrotoxicosis. Endocrine opthalmopathy. Activ - CAS 5/7.

- Puffy eyelids, **Diplopia,** Visual loss, ocular pressure and pain, protrusion of both eye balls for last 2 months.
- There are mild conjunctival hyperemia, lid lag and mild **proptosis (4 mm) in both eyes.** periorbital edema around the lids; Conjunctiva is congested nasally and temporally, with mild chemosis, inflamation of caruncle.

**Moderate-to-severe GO**

- **Lid retraction >2 mm,**
- **moderate or severe soft tissue involvement,**
- **exophthalmos >3 mm above normal for race and gender,**
- **inconstant, or constant diplopia.**

# Examples of diagnosis

**Graves disease. Sever tirotoxicosis Thyrotoxic opthalmopathy. Activ - CAS 5/7. Moderate-to-severe.**

# Investigation

- **freeT3 26 (2.4 - 6.8)** - high,
- **freeT4 82 (10 - 22)** - high,
- **TSH 0.001 (0.27 - 4.05)-** low
- **antibodies against TSH receptor – 34 (Nr < 1.75) -** present
- **USG -** diffusely enlarged, the bloodstream increased.
- **MRI scans of the orbit -** muscle enlargement

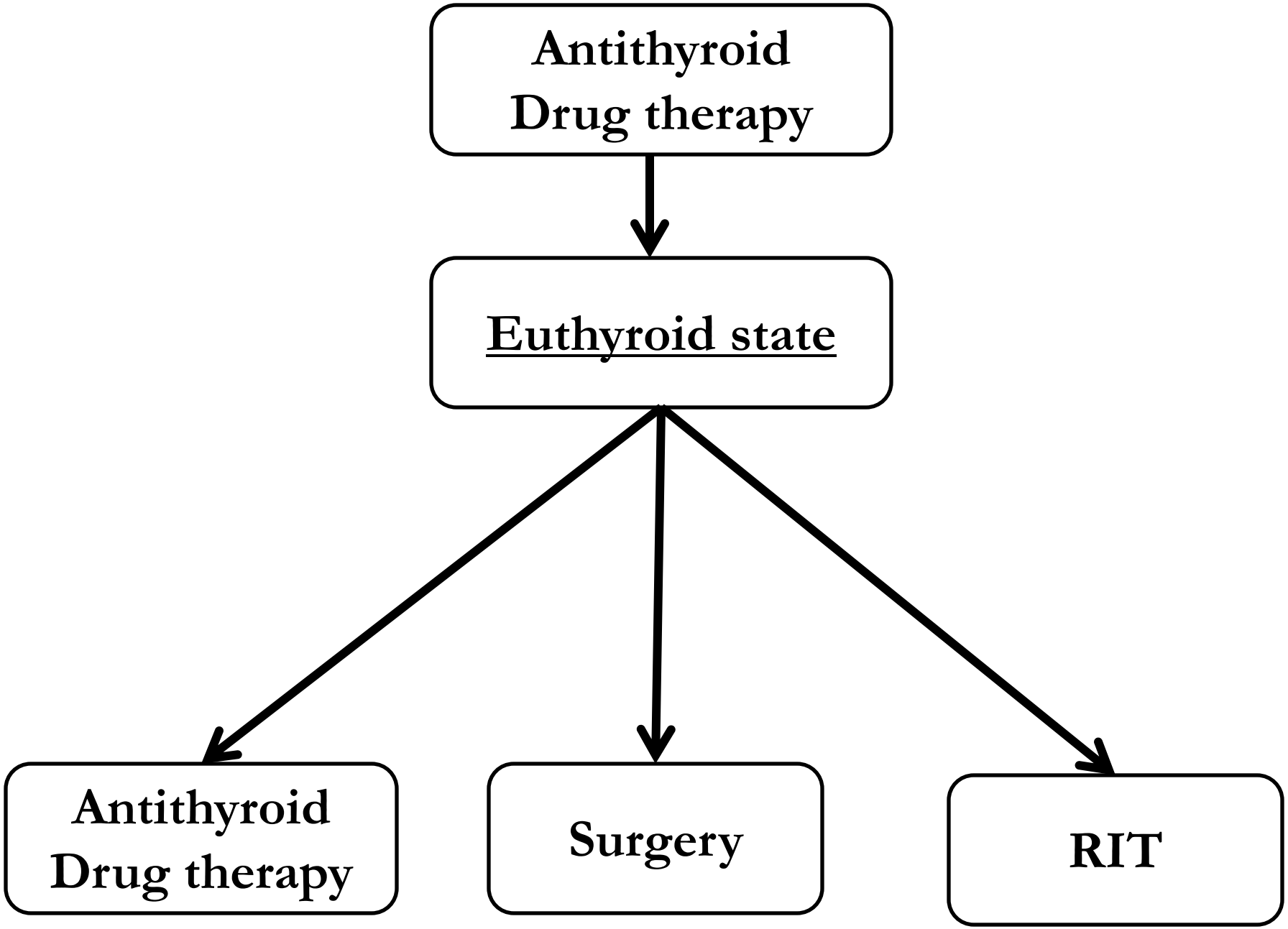
# Treatment of GD

**Three methods are available:**

1. **<u>Antithyroid drugs:</u>** using thionamides, such as propylthiouracil, carbimazole, methimazole.

2. **<u>Surgery</u> –** total thyroidectomy.

3. **<u>Radioactive iodine therapy (</u>**with 131I)


Antithyroid
Drug therapy
Euthyroid state
Antithyroid
Drug therapy
Surgery
RIT

# Thyrotoxic crisis, or thyroid storm

- is rare and presents as a life-threatening exacerbation of hyperthyroidism, accompanied by fever, delirium, seizures, coma, vomiting, diarrhea, and jaundice.
- The mortality rate due to cardiac failure, arrhythmia, or hyperthermia is as high as 30%, even with treatment.
- Thyrotoxic crisis is usually precipitated by acute illness (e.g., stroke, infection, trauma, diabetic ketoacidosis), **surgery (especially on the thyroid), or radioiodine treatment of a patient with partially treated or untreated hyperthyroidism.**
- Management requires intensive monitoring and supportive care, identification and treatment of the precipitating cause, and measures that reduce thyroid hormone synthesis.

# Antithyroid drugs

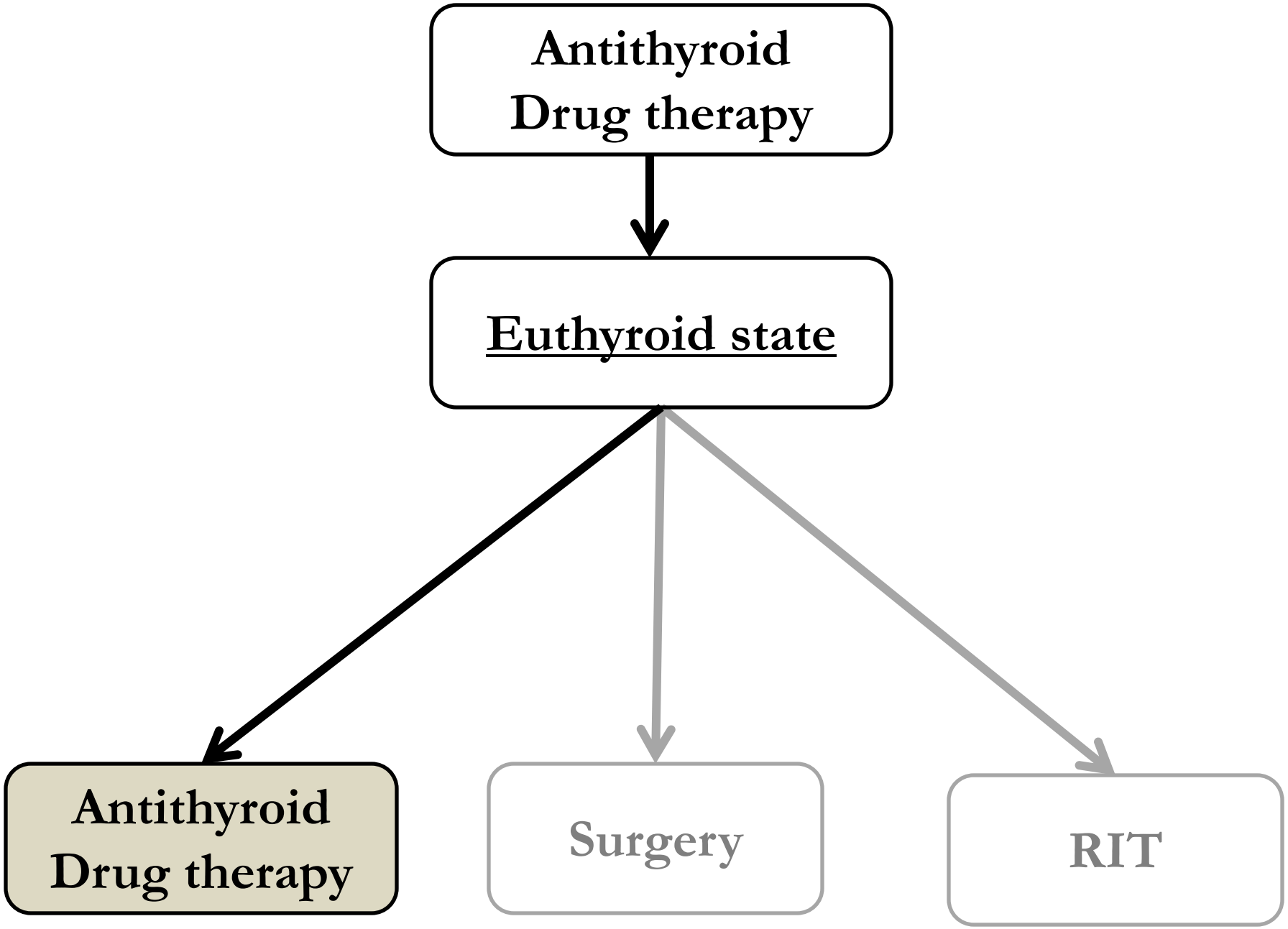
**Antithyroid drugs is always used. It can be an independent method of treatment or precede surgery or radioiodine therapy. These medicaments block formation of triiodothyronine and thyroxine.**

**Are used:**

- **Derivatives of imidazolum – carbimazole (Thiamazol, mercasolile).**
- **Thiouracil derivatives (propylthiouracil).**

- **Antithyroid drug therapy is generally started with large divided doses.**
- **The initial dose of methimazole depending on seriousness of clinical course of thyrotoxicosis.**
- **In the mild form is prescribed in doses 20-30 mg per day (10 mg two or three times a day). In the moderate and severe form – 40-60 mg per day.**

**Higher doses is prescribed until achieving a stable euthyroid state (lack of clinical symtpoms, reduction of the thyroid gland sizes, achievement of normal amounts of freeT4, free T3 and TSH).**


Antithyroid
Drug therapy
Euthyroid state
Antithyroid
Drug therapy
Surgery
RIT

**Then the dose is gradually reduced and the patient is transferred to maintenance doses (5-10 mg once a day).**

**The maintenance doses are prescribed over long periods of time (up to 2 years).**

- **The laboratory test of most value in monitoring the course of therapy are serum freeT3, freeT4 and TSH.**

- **Clinical remission of thyrotoxicosis is possible in case of achievement of stable euthyroid during one or one and a half year and vanishing of antithyroid antibodies from blood.**

**Adverse reaction from treatment of antithyroid drugs are:**

- **Nausea**
- **Allergic reaction**
- **Skin rash**
- **Agranulocytosis – the most serious.**

**As a result it is recommended to control the white blood cell each 10 days during first 2-3 months of treatment and later – montly.**

**If agranulocytosis arises, methimazole is decreases. A glucocorticoids, stimulators of leucopoesis are prescribed.**

# Beta-adrenergic blocking agents

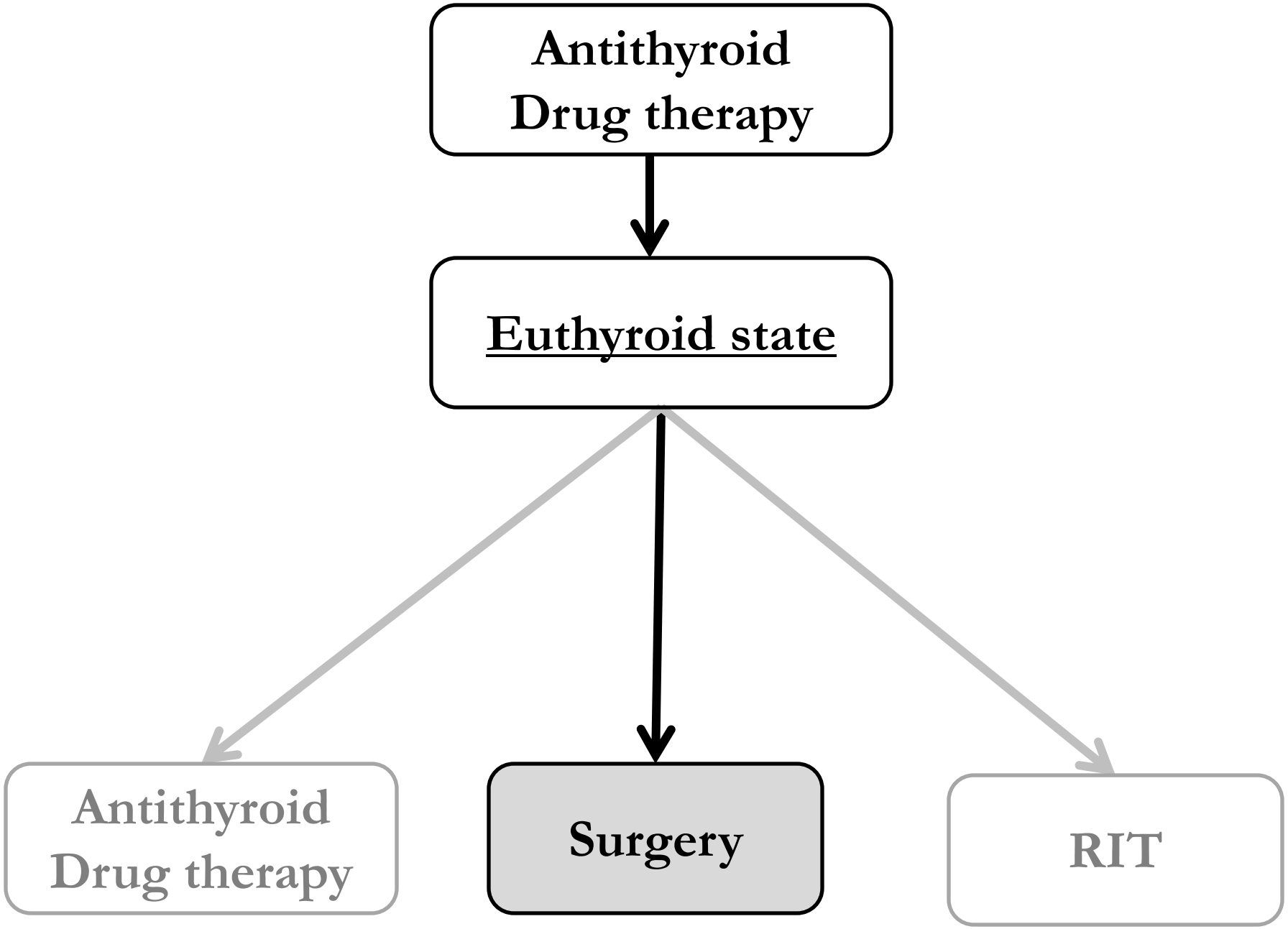
- Are prescribed with antithyroid medicaments.
- Block the increased sensitivity of adrenoreceptors.
- Quickly ameliorate tachycardia, palpitation, hypertension.
- Initial dose of propranolol is 10-40 mg every 6 hours. The dose is gradually reduced after the complete relief of tachycardia. Selective beta-blockers can also be used: metoprolol 100-200 mg per day.

# Other medical measures

- **Glucocorticoids also used, especially in case of relative adrenal insufficiency in patients with severe form of the disease or in case of argranulocytosis. Prednisone is prescribed in an initial dose of 20-30 mg, reducing each 7 days to 5 mg.**

- **Barbiturates (phenobarbital) may be helpful both for its sedative effect an to accelerate T4 metabolism.**

- **Anabolic steroids are used in malnutrition.**


Antithyroid
Drug therapy
Euthyroid state
Antithyroid
Drug therapy
Surgery
RIT

# Surgical Treatment

- It is rather physiological method of treatment.
- **Surgical treatment** is carried out **in the condition of stable medicamental euthyrosis.**

**Indications:**

- Goiter of big size (> 40 ml)
- Nodular forms of a goiter
- Retrosternal location of a goiter
- An inefficiency of medicinal treatment
- Leucopenia
- A goiter with a compression of organs of the neck or mediastinum

**Crontraindications:**

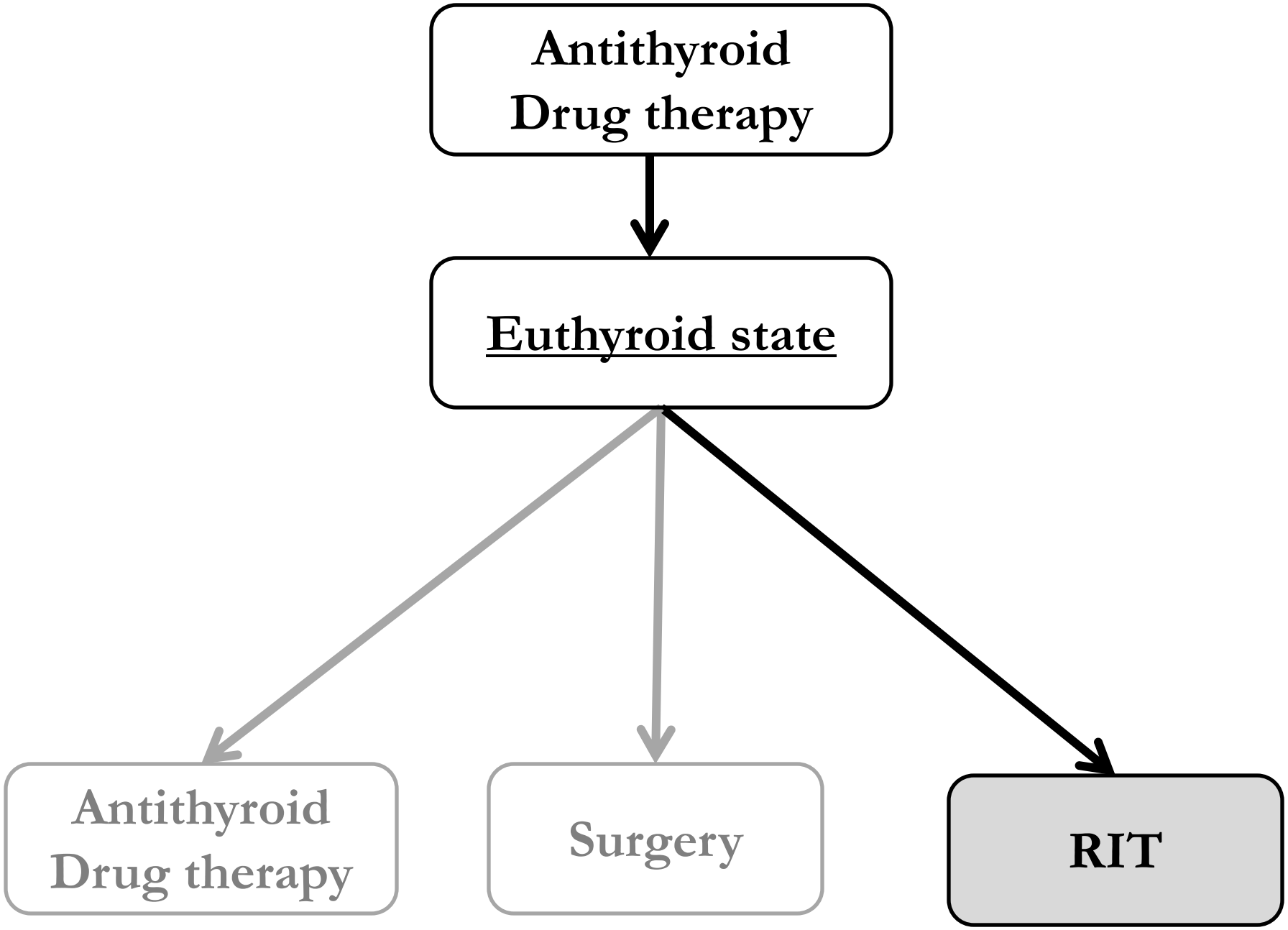
- **Severe somatic condition of a patient when the risk of surgical intervention raises risk of illness.**

**Early complications are:**

- **Acute hypoparathyrosis with a storm**
- **Postoperative bleeding**
- **Paresis of throat**
- **Postoperative thyroid crisis**

**Late complications are:**

- **Suppurations**
- **Postoperative hypothyrosis**
- **Hypoparathyrosis**
- **Relapse of a toxic goiter**


Antithyroid
Drug therapy
Euthyroid state
Antithyroid
Drug therapy
Surgery
RIT

# Treatment by radioactive iodine

**Radioiodine therapy should be carried out in the condition of stable medicamental euthyrosis.**

**Indications:**

- **GD with low sensitivity to medicinal treatment**
- **Severe changes in the internal organs when there is a high risk of surgical interventions**
- **Relapses of a GD after surgical treatment**

**Crontraindications:**

- **Young age of patients**
- **Retrosternal goiter, Nodular forms of a goiter**
- **Pregnancy, breast-feeding**
- **Diseases of blood, kidneys, digestive organs.**

# Treatment of Ophthalmopathy

**How does the phase of the disease influence choice of treatment?**

**For the clinician it is helpful to assess the degrees of activity and severity independently; both are important in deciding whether a patient requires treatment and if so which type of treatment is indicated.**

# Treatment of Ophthalmopathy

**Three methods are available:**

1. **Drugs:** symptomatic (local) and pathogenetic (GCS) treatment.
2. **Surgery**
3. **Orbital radiotherapy**

# Treatment of Ophthalmopathy

**If the disease is mild, no treatment is necessary even though there may be some evidence of activity.**

**If the disease is moderate to severe and in the active phase - anti-inflammatory or immunomodulatory treatment (corticosteroids) or orbital radiotherapy may be indicated.**

**If the patient has severe orbital involvement, with little evidence of activity there is unlikely to be a response to medical treatment, and then surgical treatment (orbital decompression or rehabilitative surgery) may be indicated.**

# Treatment of Ophthalmopathy

**Simple measures that may alleviate symptoms in GO:**

- **Lubricant eye drops during the day and/or lubricant ointments at night-time**
- **Artificial tears**
- **Taping of lids at night**
- **Sunglasses**
- **Patients with symptomatic diplopia should be given prisms**
- **Achieve and maintain euthyroidism**
- **Smoking cessation**

# Treatment of Ophthalmopathy

**What are the non-surgical treatments of choice for moderate-to-severe GO?**

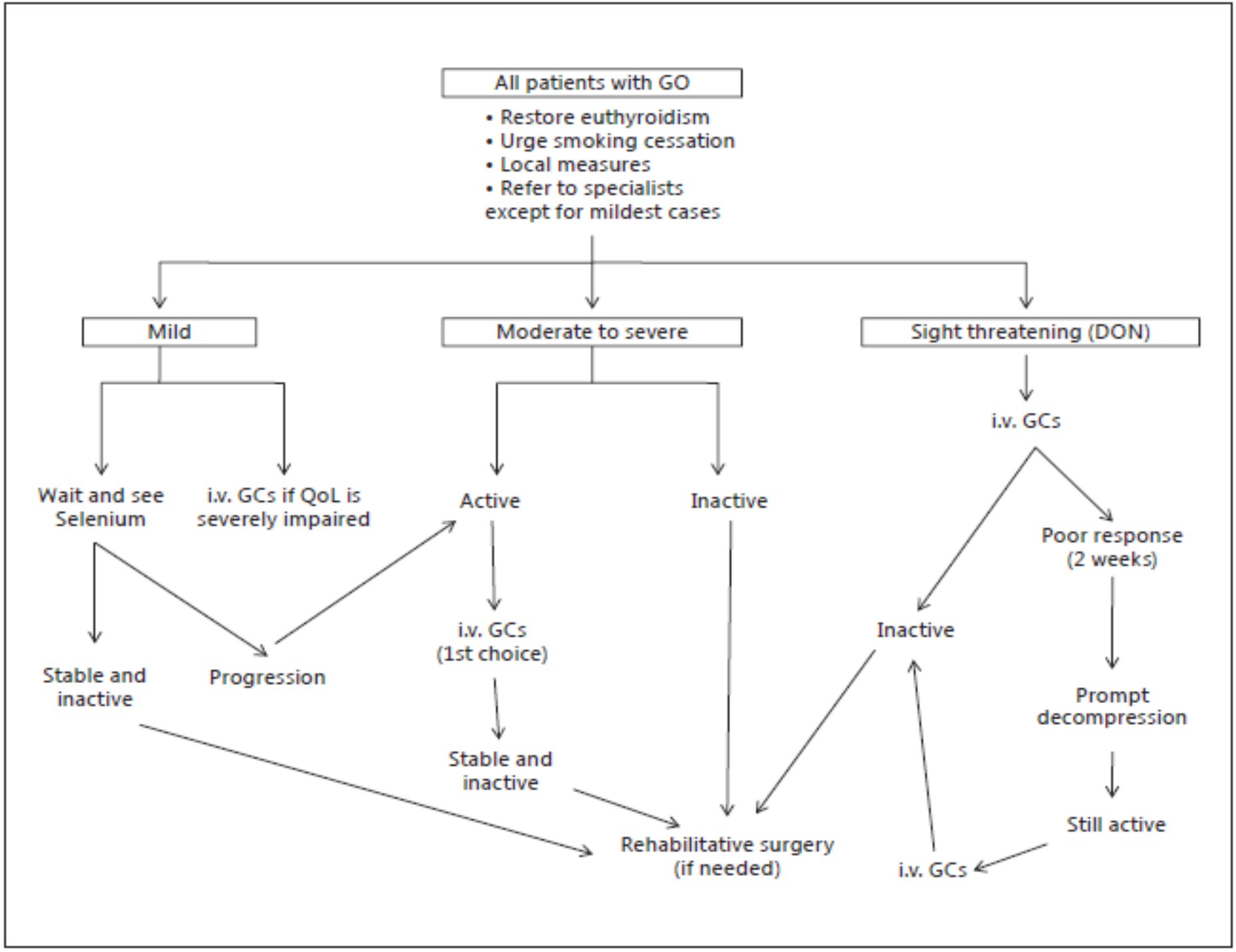
**Glucocorticoids.**

GC therapy has been used in the management of GO through oral, local (retrobulbar or subconjunctival), or i.v. routes.

Oral GC therapy (starting dose, 80–100 mg prednisone (or 1 mg/kg) or equivalent) requires high doses for prolonged periods of time.

Retrobulbar or subconjuctival GC therapy is less effective than oral GCs.

**Intravenous GC pulse therapy is more effective than oral GC.**


All patients with GO
• Restore euthyroidism
• Urge smoking cessation
• Local measures
• Refer to specialists
except for mildest cases
Mild
Moderate to severe
Sight threatening (DON)
Wait and see
Selenium
i.v. GCs if QoL is
severely impaired
Active
Inactive
i.v. GCs
Poor response
(2 weeks)
Stable and
inactive
Progression
i.v. GCs
(1st choice)
Inactive
Prompt
decompression
Stable and
inactive
Still active
Rehabilitative surgery
(if needed)
i.v. GCs

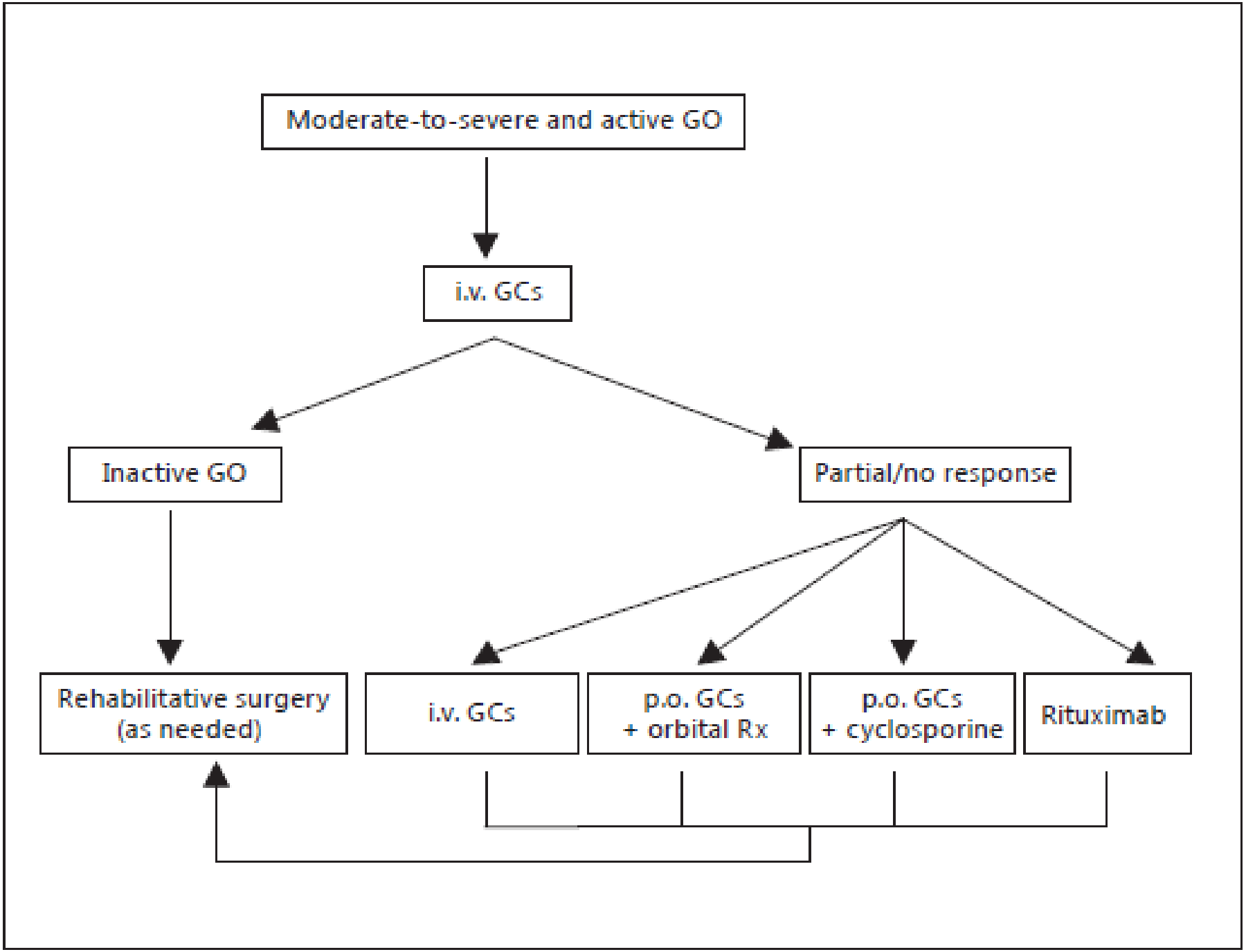

Moderate-to-severe and active GO
i.v. GCs
Inactive GO
Partial/no response
Rehabilitative surgery (as needed)
i.v. GCs
p.o. GCs + orbital Rx
p.o. GCs + cyclosporine
Rituximab

Table 6: Orientative therapeutic protocol for Graves' ophthalmopathy (see text for bibliographic references).

| All patients | Restore euthyroidism<br>Avoid smoking<br>Conservative local measures | |
|---|---|---|
| Severity | Activity | |
| | Active | Nonactive |
| Mild | (i) Artificial tears<br>(ii) Sunglasses<br>(iii) Head of the bed slightly elevated<br>(iv) Selenium (200 $\mu$/g daily × 6 months)<br>(v) Fresnel-type prisms<br>(vi) Botulinum toxin in Müller muscle | (i) Artificial tears<br>(ii) Prisms<br>(iii) Botulinum toxin in Müller muscle<br>(iv) Surgical Müllerectomy<br>(v) Blepharoplasty |
| Moderate-severe | (i) Intravenous methylprednisolone:<br>1st, 500 mg/week × 6 weeks<br>2nd, 250 mg/week × 6 weeks<br>3rd, if activity persists: consider prolongation of treatment up to 8 g of maximum cumulative dosage<br>4th If non responsive after 6 weeks, change the treatment<br>(ii) Patients resistant to glucocorticoids:<br>(a) Association of cyclosporin A (5 mg/kg/day in 2 doses) plus oral glucocorticoids, methotrexate (7,5–10 mg/week), tocilizumab (8 mg/kg/every 4 weeks), and Rituximab (500 mg–1000 mg),<br>(b) If muscular involvement predominates: orbital radiotherapy (20 Gy) (not in <35 years or diabetic patients)<br>(iii) Consider botulinum toxin in extraocular muscles if with diplopia (medial rectus or inferior rectus) | 1st, orbital decompression (2 or 3 walls depending on the degree of exophthalmos)<br>2nd, surgery for strabismus (stability of 6-month deviation angle. Muscular recessions)<br>3rd, palpebral surgery<br>(i) Palpebral retraction: levator recession surgery, retractors for the lower eyelid.<br>(ii) Blepharoplasty of upper eyelids, lower eyelids, or both. |
| Threat to vision | | |
| Dysthyroid optic neuropathy | Methylprednisolone 1 g intravenously × 3 days, repeat after a week<br>If nonresponsive: urgent orbital decompression. (+/– glucocorticoids intravenously if still active +/– radiotherapy) | Urgent deep orbital medial wall decompression |
| Severe exposure keratopathy | Intravenous methylprednisolone when relevant orbital inflammation; palpebral closure, lubrication, tarsorrhaphy, botulinum toxin in Müller muscle, and orbital decompression if other measures are inefficient | Lateral tarsorrhaphy, orbital decompression, amniotic membrane transplant, and corneal transplant |

# Examples of treatment

**Graves disease. Sever tirotoxicosis Thyrotoxic opthalmopathy. Activ - CAS 5/7. Moderate-to-severe.**

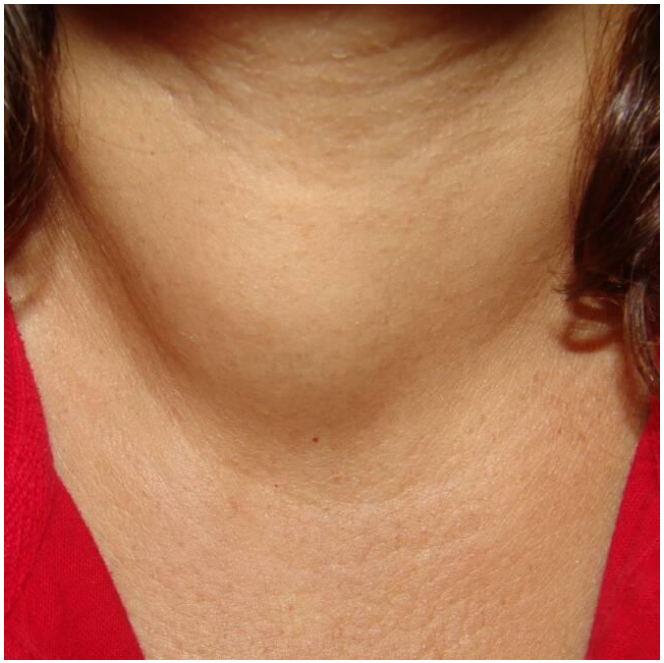
**Sever tirotoxicosis:**

- Thiamazole 50 mg per day until normal freeT4, freeT3 and TSH
- Propranolol 120 mg per day until normal BP and HR
- Fenobarbital 100 mg per day

**Thyrotoxic opthalmopathy. Activ - CAS 5/7. Moderate-to-severe:**

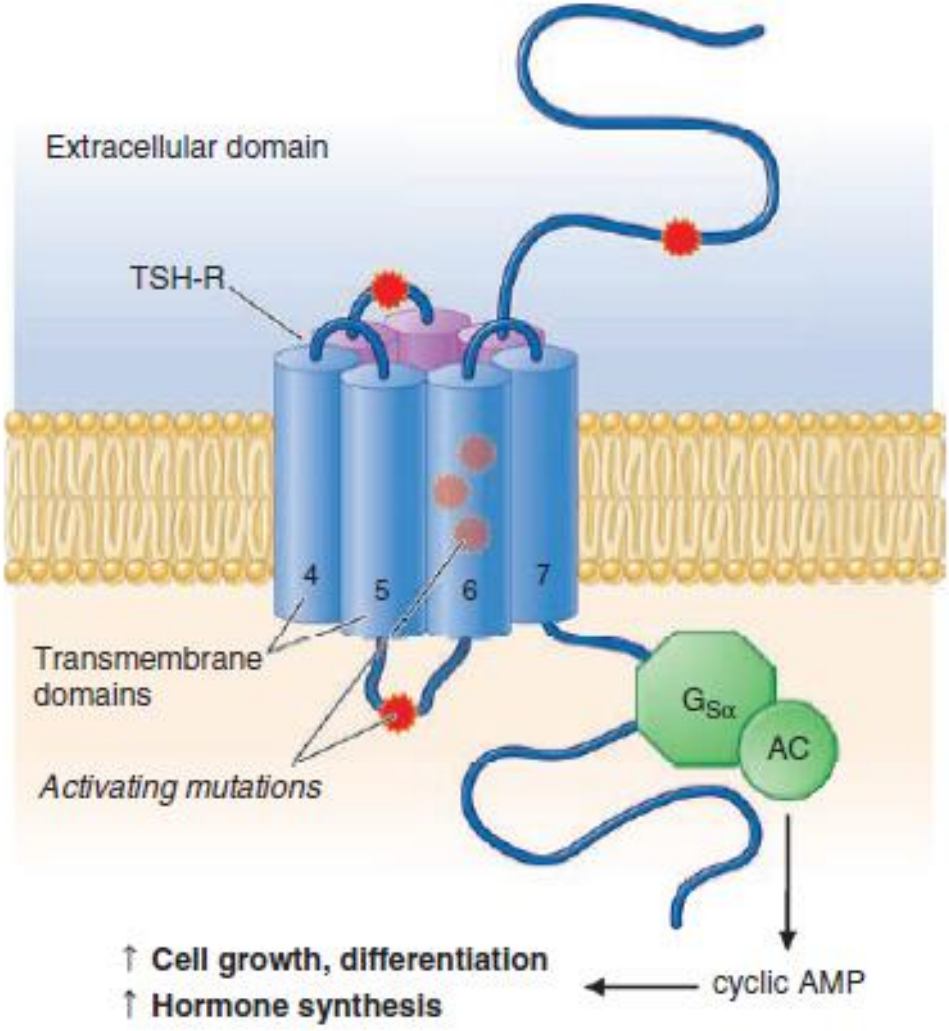
- Local therapy
- i/v methylprednisolon 500 mg/week – 6 weeks, 250 mg/week – 6 weeks
- with or without Orbital radiotherapy

# Toxic adenoma



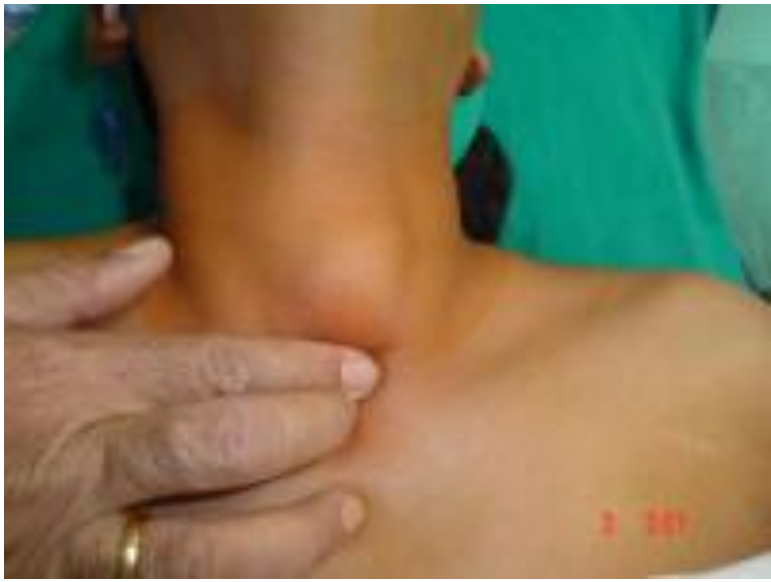
**A solitary, autonomously functioning thyroid nodule.**

**The pathogenesis** of this disorder has been unraveled by demonstrating the functional effects of **mutations that stimulate the TSH-R** signaling pathway. Most patients with solitary hyperfunctioning nodules have acquired somatic, activating mutations in the TSH-R.



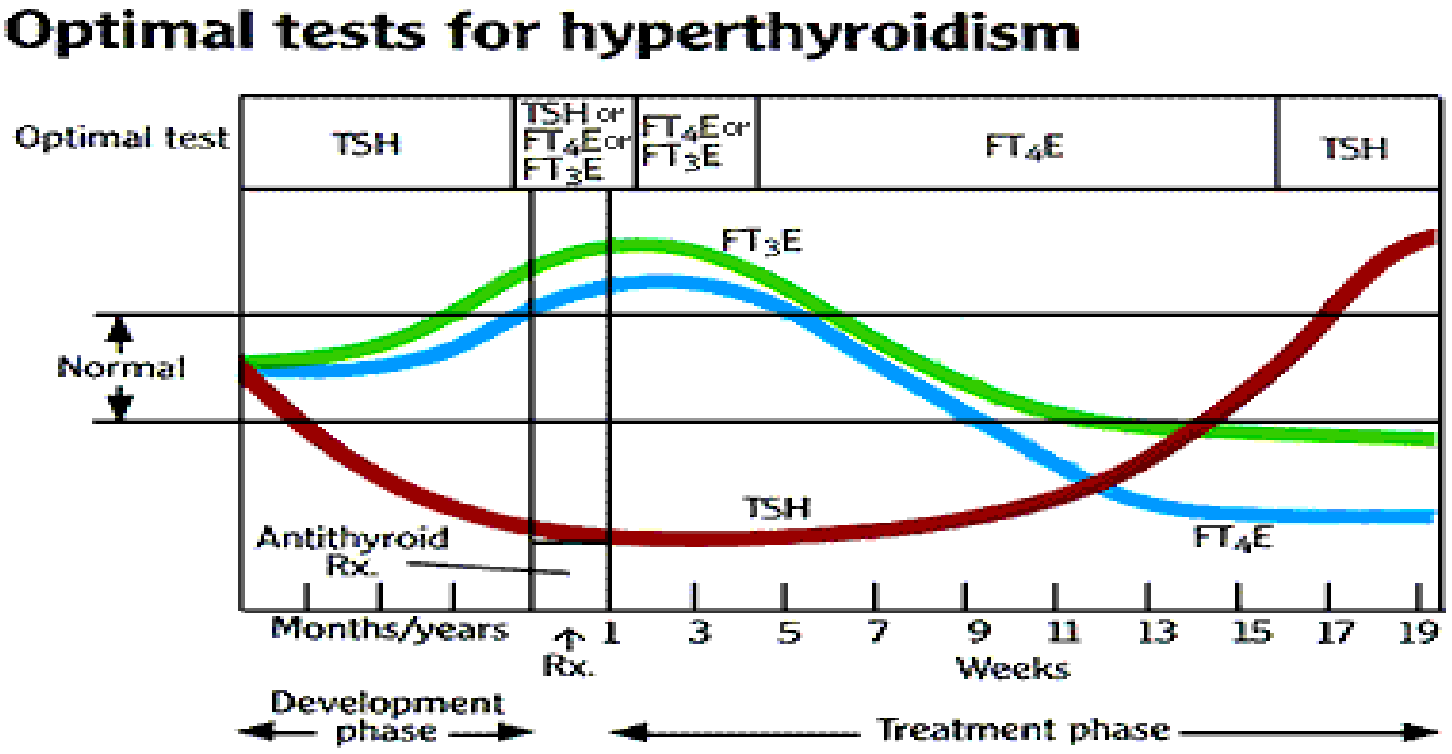
# Clinical features

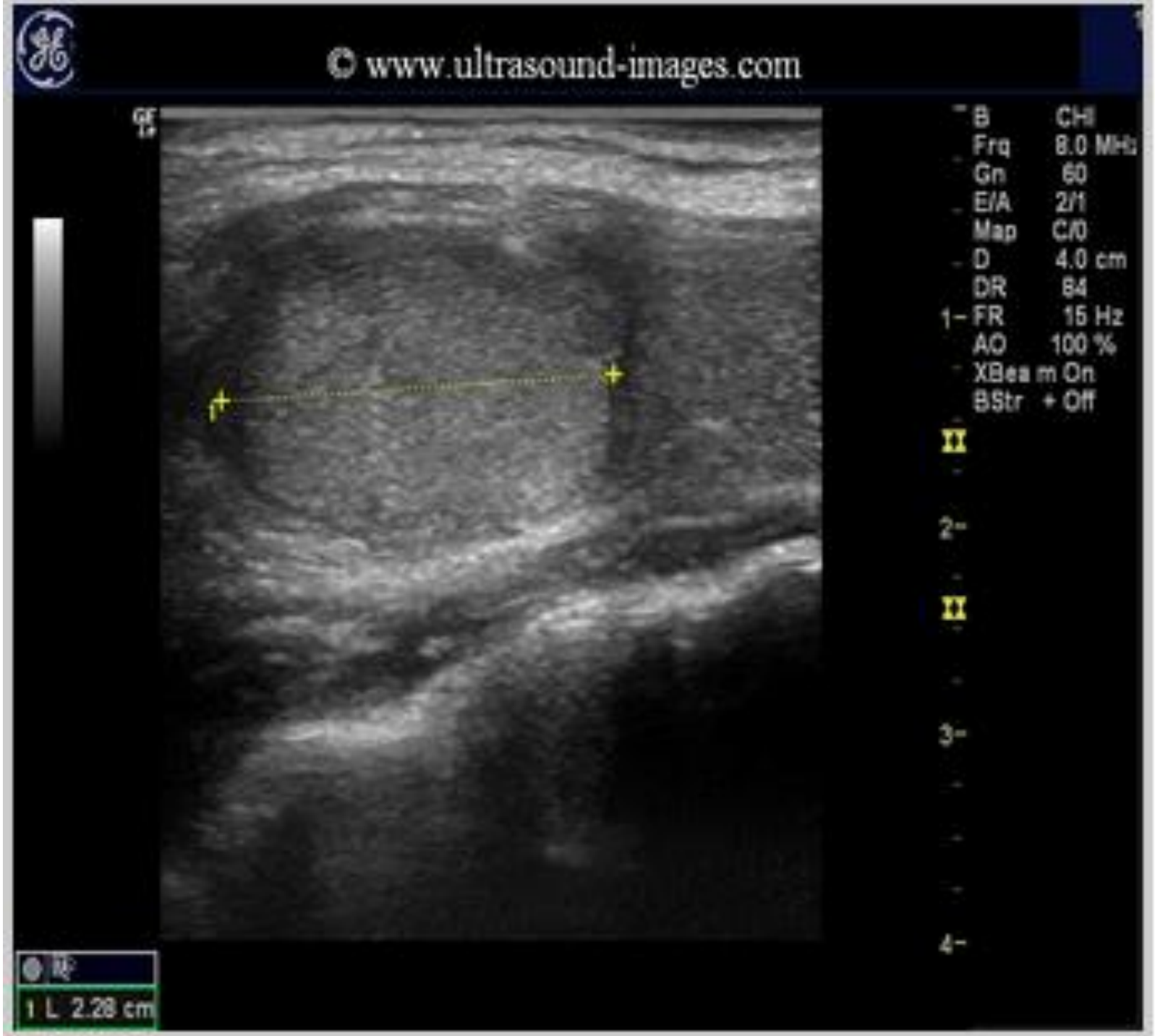
1. **Thyrotoxicosis -** is usually mild.
2. **Presence of the thyroid nodule**, which is generally large enough to be palpable.
3. No clinical features suggestive of Graves' disease **(no ophthalmopathy)**



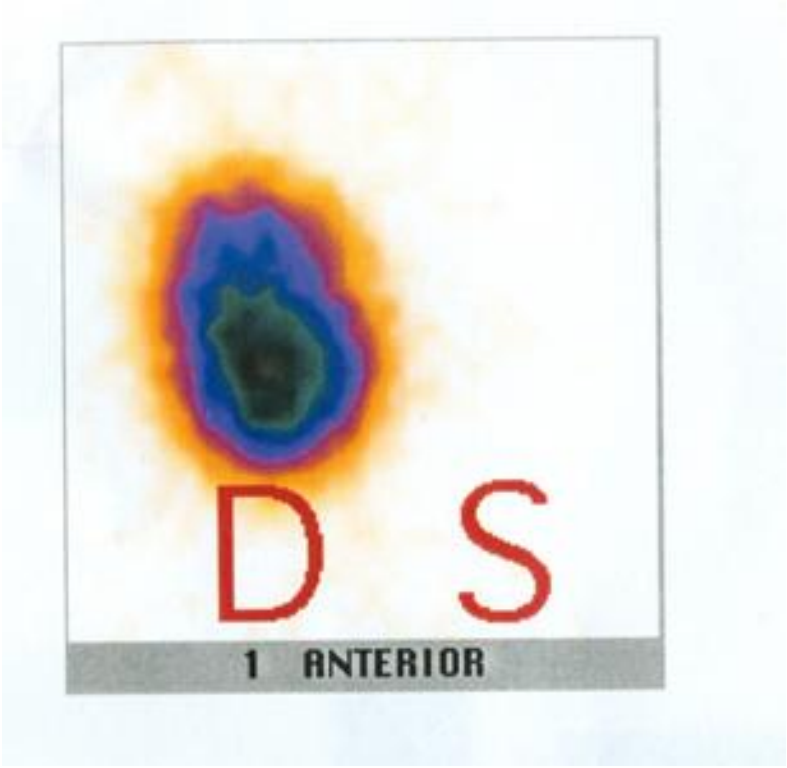
# Laboratory findings

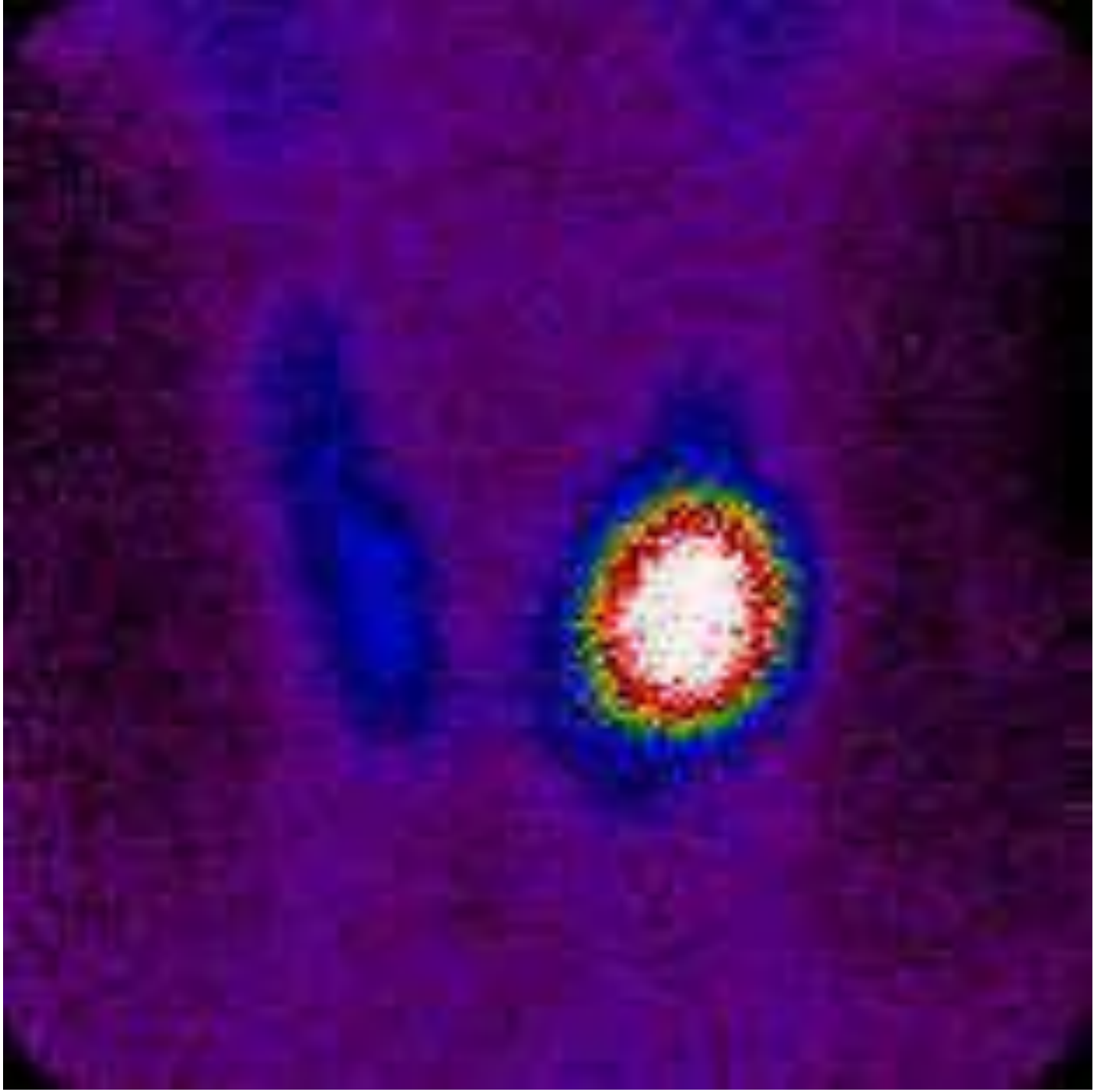
- Plasma levels of freeT4, freeT3 are elevated
- Plasma level of TSH is low
- No Thyroid autoantibodies




© www.ultrasound-images.com
B CHI
Frq 8.0 MHz
Gn 60
E/A 2/1
Map C/0
D 4.0 cm
DR 84
FR 15 Hz
AO 100 %
XBeam On
BStr + Off
1
2
3
4
1 L 2.28 cm

**A thyroid scan** provides a definitive diagnostic test, demonstrating **focal uptake in the hyperfunctioning nodule and diminished uptake in the remainder of the gland**, as activity of the normal thyroid is suppressed.





# Treatment of TA

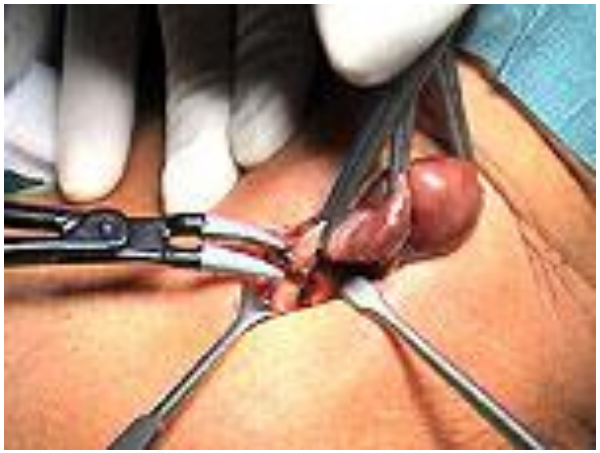
Antithyroid
Drug therapy

↓

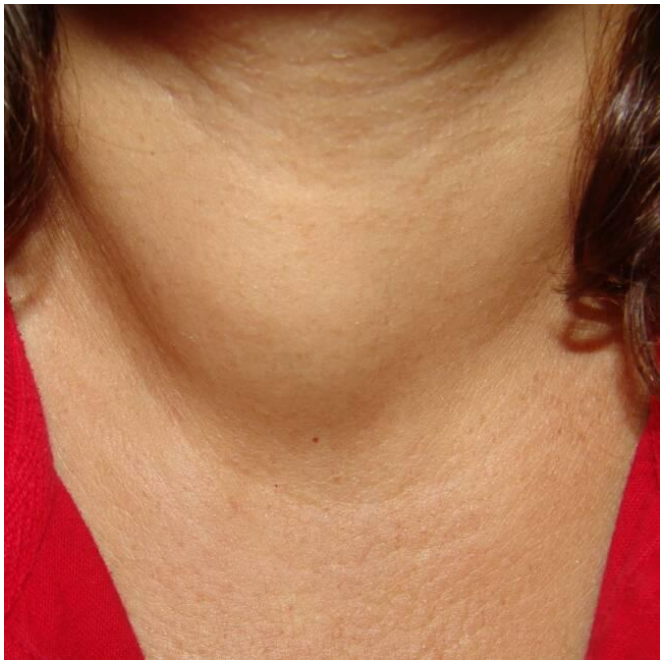
**Euthyroid state**

↓

Surgery

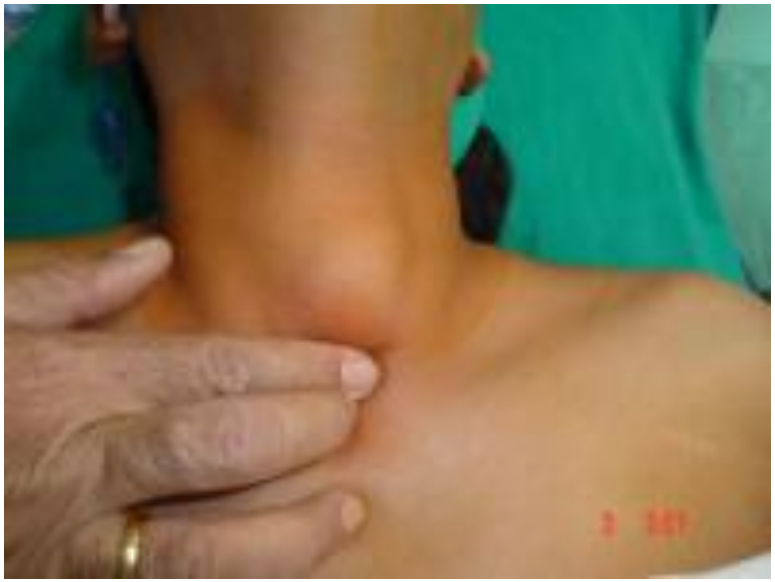


# Toxic multinodular goiter



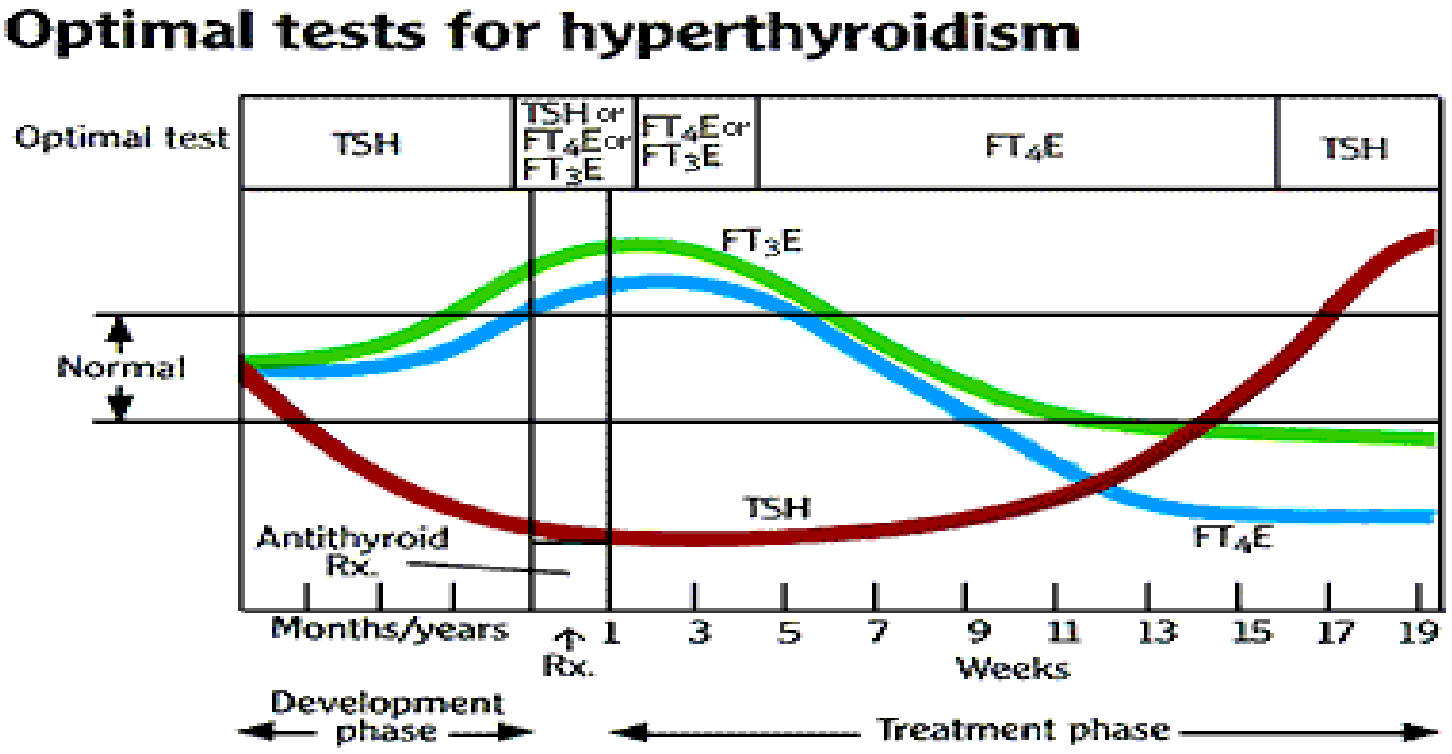
# Clinical features

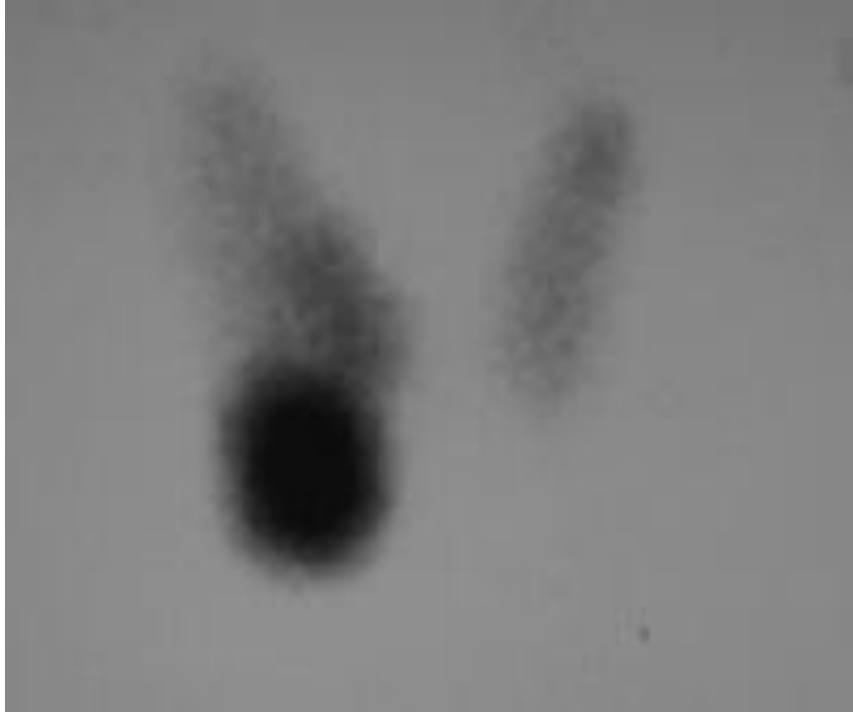
1. **Thyrotoxicosis –** subclinical or mild
2. **Multi Nodular Goiter -** an enlargement in the neck.
3. No clinical features suggestive of Graves' disease **(no ophthalmopathy)**

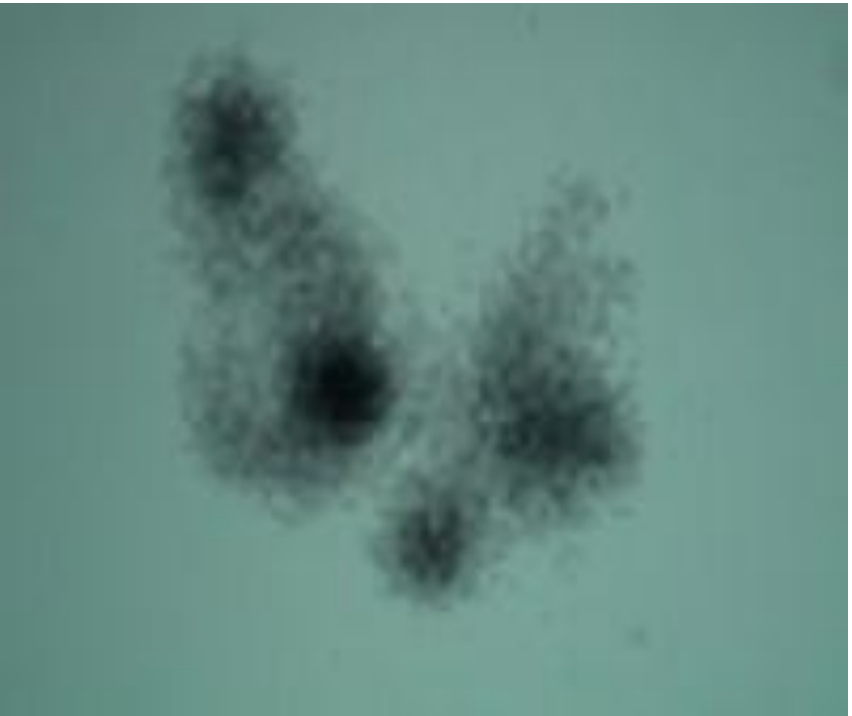


# Laboratory findings

- Plasma levels of freeT4, freeT3 are elevated
- Plasma level of TSH is low
- No Thyroid autoantibodies







**Thyroid scan** shows heterogeneous uptake with **multiple regions of increased and decreased uptake**

# Treatment of TA

**Antithyroid Drug therapy**

↓

**Euthyroid state**

↙ ↘

**Surgery**

**Radioactive iodine therapy**