

بنام خداوند جان و خرد

# ***Thyrotoxicosis***

*Thyrotoxicosis is defined as the state of thyroid hormone excess and is not synonymous with hyperthyroidism, which is the result of excessive thyroid function.*

***The major etiologies of thyrotoxicosis are:***

- *Graves' disease*
- *Toxic multinodular goiter*
- *Toxic adenomas*

# ***Causes of Thyrotoxicosis***

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## ***Primary hyperthyroidism***

***Graves' disease***

***Toxic multinodular goiter***

***Toxic adenoma***

***Functioning thyroid carcinoma metastases***

***Activating mutation of the TSH receptor*** (autosomal dominant)

***Struma ovarii***

***Drugs: iodine excess*** (Jod-Basedow phenomenon)

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# ***Causes of Thyrotoxicosis***

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## ***Thyrotoxicosis without hyperthyroidism***

***Subacute thyroiditis***

***Silent thyroiditis***

***Other causes of thyroid destruction:*** amiodarone,  
radiation, infarction of adenoma

***Ingestion of excess thyroid hormone (thyrotoxicosis  
factitia) or thyroid tissue***

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# ***Causes of Thyrotoxicosis***

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## ***Secondary hyperthyroidism***

***TSH-secreting pituitary adenoma***

***Thyroid hormone resistance syndrome:*** *occasional patients may have features of thyrotoxicosis*

***Chorionic gonadotropin-secreting tumors<sup>a</sup>***

***Gestational thyrotoxicosis<sup>a</sup>***

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<sup>a</sup> *Circulating TSH levels are low in these forms of secondary hyperthyroidism.*

# ***GRAVES' DISEASE***

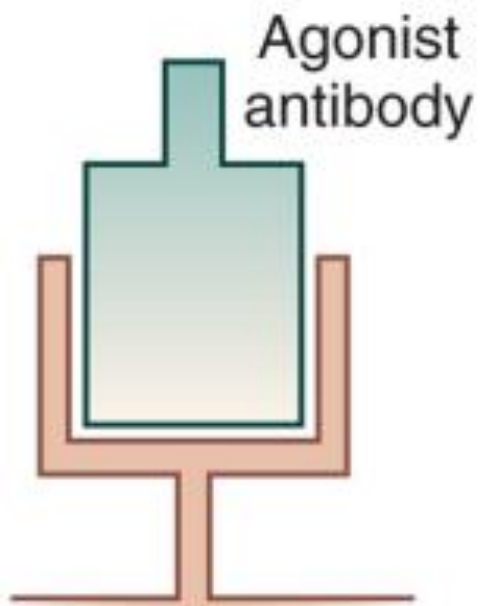
# *Epidemiology*

- *60 to 80% of thyrotoxicosis*
- *Depending mainly on iodine intake*
- *Occurs in up to 2% of women*
- *Is one-tenth as frequent in men*
- *Rarely begins before adolescence*
- *Typically occurs between 20 and 50 years*

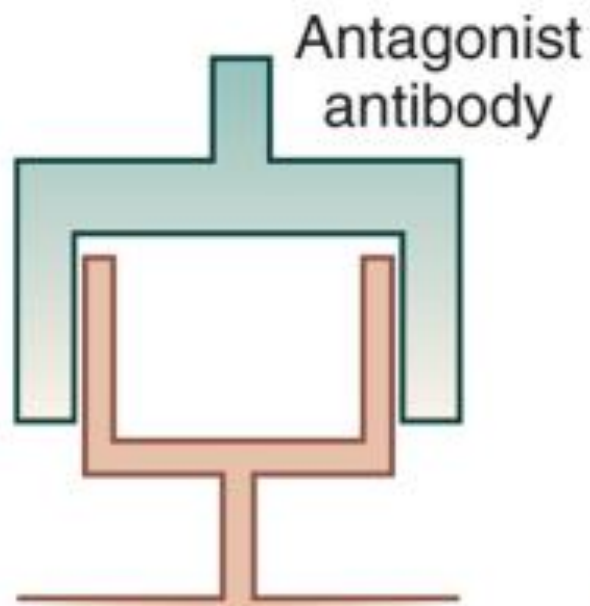
# Pathogenesis

- *The hyperthyroidism of Graves' disease is caused by TSI that are synthesized in the thyroid gland as well as in bone marrow and lymph nodes.*
- *Cytokines appear to play a major role in thyroid-associated ophthalmopathy.*
- *There is infiltration of the extraocular muscles by activated T cells; the release of cytokines such as IFN- $\gamma$ , TNF, and IL-1 results in fibroblast activation and increased synthesis of glycosaminoglycans that trap water, thereby leading to characteristic muscle swelling.*
- *Late in the disease, there is irreversible fibrosis of the muscles. Orbital fibroblasts may be particularly sensitive to cytokines, perhaps explaining the anatomic localization of the immune response.*

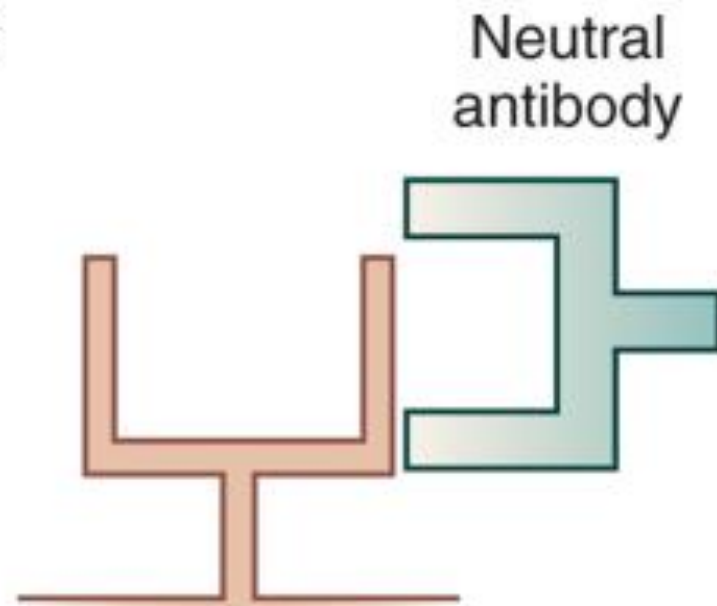




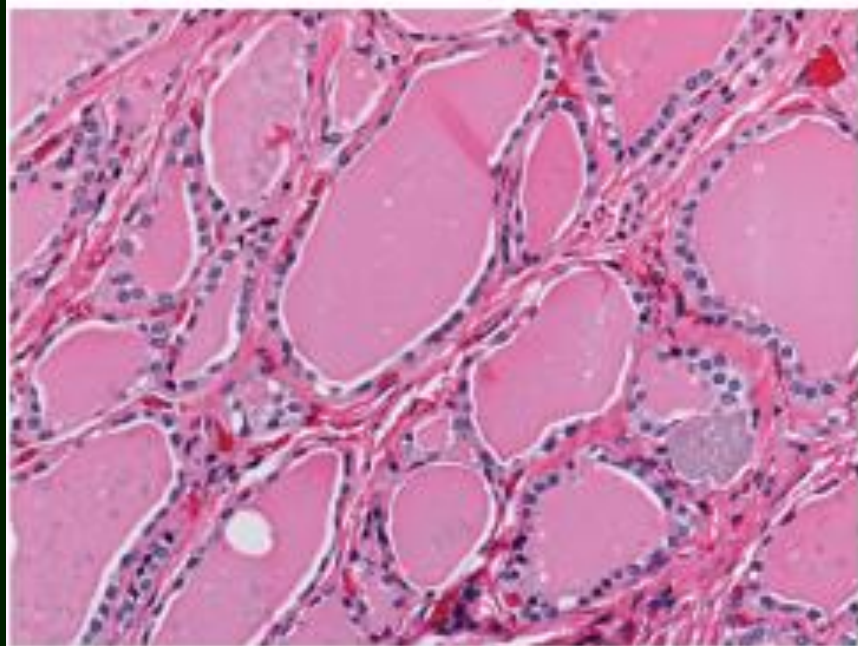
**Cell  
stimulation**



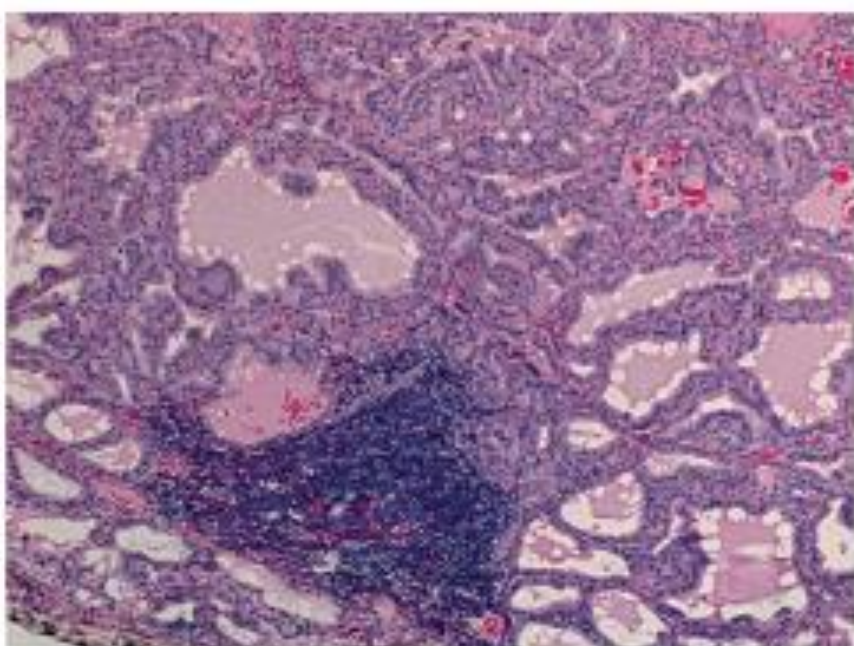
**Cell  
blockade**



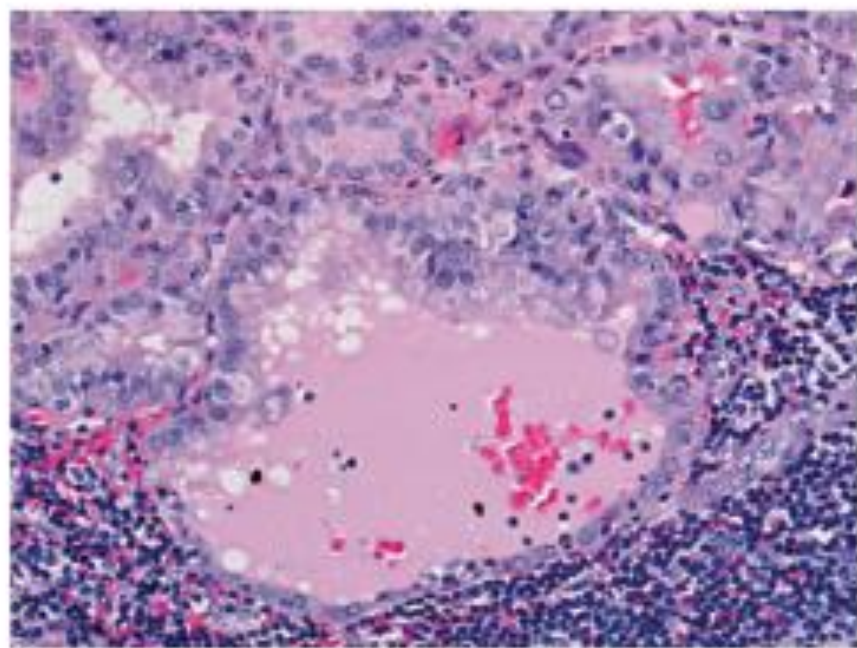
**Normal signal  
transduction**



A



B



C

# ***Clinical Manifestations***

# ***Signs and Symptoms of Thyrotoxicosis (Descending Order of Frequency)***

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## **Symptoms**

***Hyperactivity, irritability, dysphoria***

***Heat intolerance and sweating***

***Palpitations***

***Fatigue and weakness***

***Weight loss with increased appetite***

***Diarrhea***

***Polyuria***

***Oligomenorrhea, loss of libido***

## **Signs<sup>a</sup>**

***Tachycardia; atrial fibrillation in the elderly***

***Tremor***

***Goiter***

***Warm, moist skin***

***Muscle weakness, proximal myopathy***

***Lid retraction or lag***

***Gynecomastia***

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<sup>a</sup> Excludes the signs of ophthalmopathy and dermopathy specific for Graves' disease.

# ***The clinical presentation depends on the:***

- *Severity of thyrotoxicosis*
- *The duration of the disease*
- *Individual susceptibility to excess hormone*
- *The age of the patient*



*In the elderly, features of thyrotoxicosis may be subtle or masked, and patients may present mainly with fatigue and weight loss, leading to apathetic hyperthyroidism.*

*Common neurologic manifestations include hyperreflexia, muscle wasting, and proximal myopathy without fasciculation.*

*Thyrotoxicosis is sometimes associated with a form of hypokalemic periodic paralysis; this disorder is particularly common in Asian males with thyrotoxicosis.*

# ***common cardiovascular manifestations :***

- *Sinus tachycardia*
- *Palpitation*
- *Supraventricular tachycardia*
- *High cardiac output*
- *Bounding pulse*
- *Widened pulse pressure*
- *Aortic systolic murmur*
- *Worsening of angina or heart failure*

# ***Skin manifestations :***

- *Usually warm and moist*
- *Complains of sweating and heat intolerance*
- *Palmar erythema*
- *Onycholysis*
- *Pruritus, urticaria*
- *Diffuse hyperpigmentation*
- *Hair texture may become fine & alopecia*

# *Gastrointestinal manifestations:*

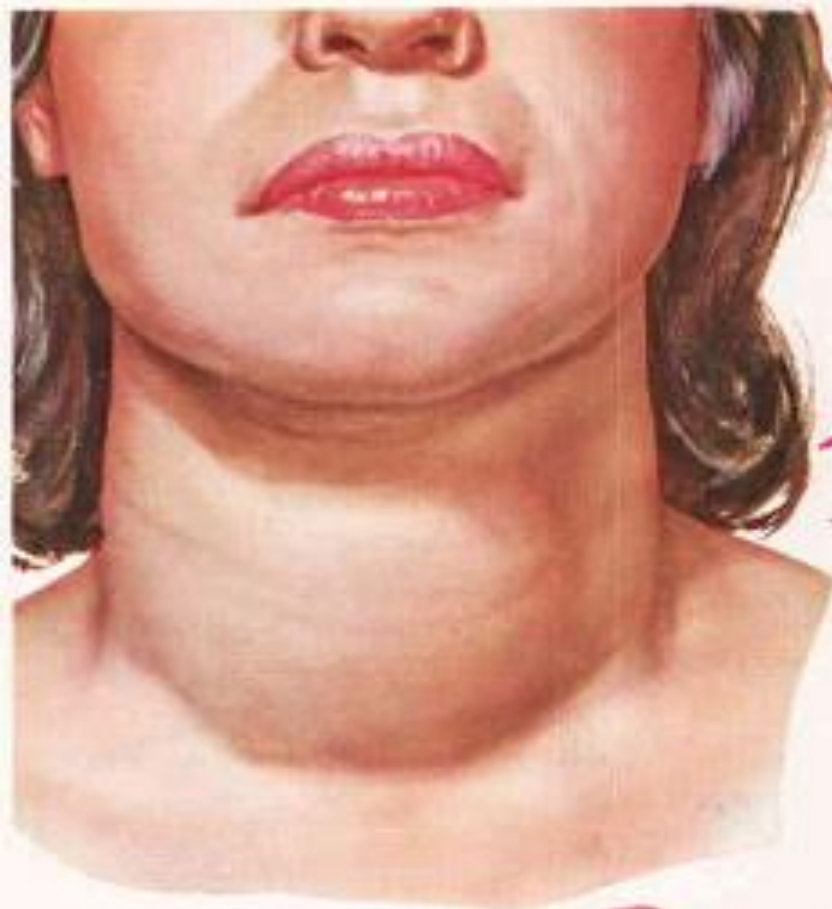
- *Increased appetite*
- *Decreased body weight*
- *Decreased transit time*
- *Increased stool frequency*
- *Diarrhea and occasionally mild steatorrhea*

*Women frequently experience oligomenorrhea or amenorrhea; in men there may be impaired sexual function and, rarely, gynecomastia.*

# ***Bone manifestations :***

- *Osteopenia*
- *Mild hypercalcemia*
- *Hypercalciuria*
- *Increased fracture rate*





DIFFUSE GOITER OF  
MODERATE SIZE



SCINTIGRAM



DIFFUSE  
ENLARGEMENT  
AND ENGORGEMENT  
OF THYROID GLAND  
(BROKEN LINE  
INDICATES NORMAL  
SIZE OF GLAND)

*F. Netter*  
M.D.  
CIBA

# *Graves' ophthalmopathy*

- *Lid lag and retraction*
- *Sensation of grittiness*
- *Eye discomfort*
- *Excess tearing*
- *Proptosis*
- *Corneal exposure and damage*
- *Periorbital edema*
- *Scleral injection and chemosis*
- *Diplopia*
- *Papilledema, field defects, loss of vision*



MODERATELY  
SEVERE  
EXOPHTHALMOS

*F. Netter  
M.D.*  
© CIBA

SEVERE  
PROGRESSIVE  
EXOPHTHALMOS



TESTING FOR  
RESILIENCY





# *scoring system for ophthalmopathy :*

## **NO SPECS :**

*0 = No signs or symptoms*

*1 = Only signs (lid retraction or lag), no symptoms*

*2 = Soft-tissue involvement (periorbital edema)*

*3 = Proptosis (>22 mm)*

*4 = Extraocular-muscle involvement (diplopia)*

*5 = Corneal involvement*

*6 = Sight loss*



# *Thyroid dermopathy*

*A noninflamed, indurated plaque with a deep pink or purple color and an "orange-skin" appearance in the pretibial or trauma sites*





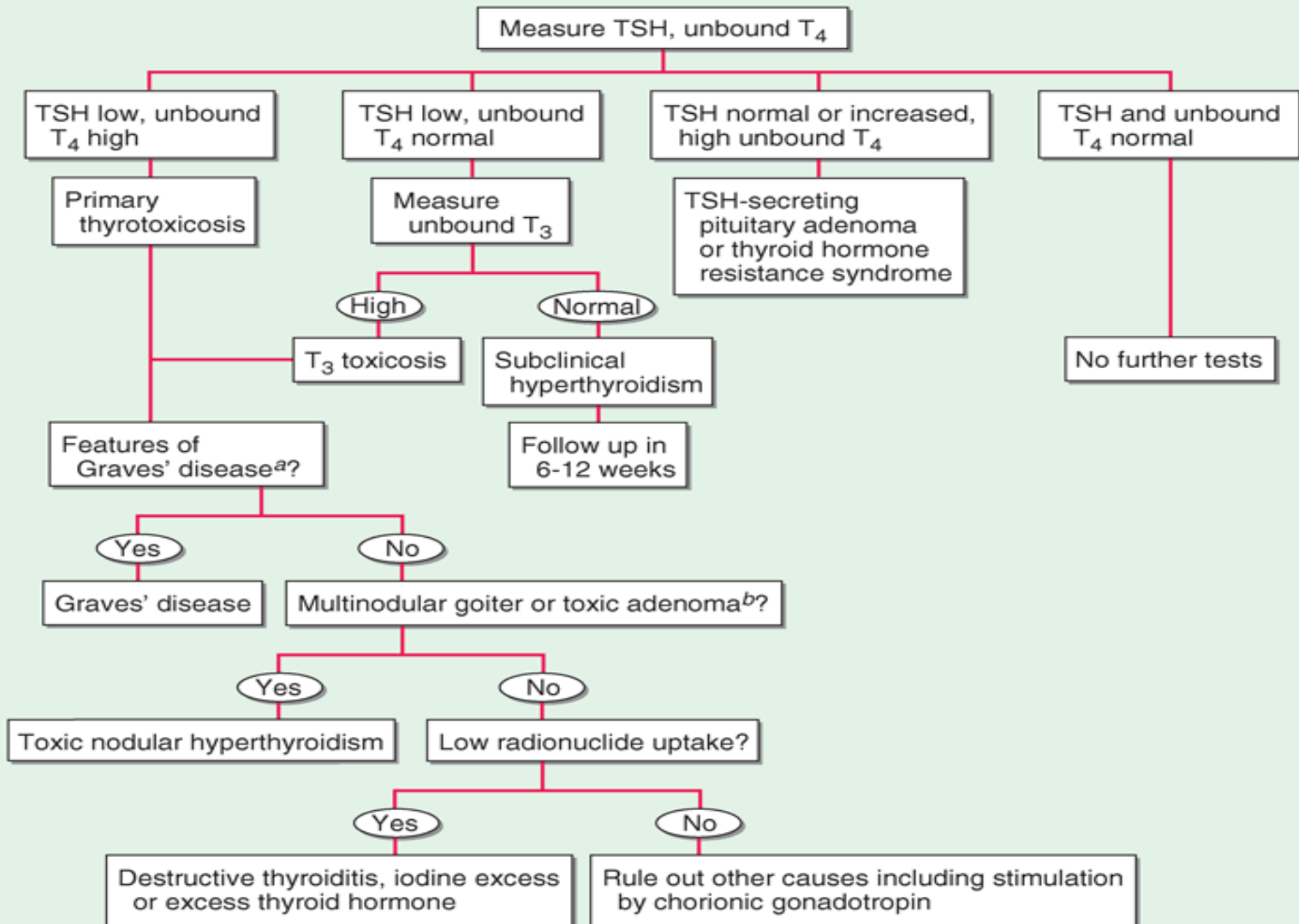
# *Laboratory Evaluation*

- *TSH , Free T4 , Free T3*
- *TPO antibodies*
- *TSH-R antibodies*

*Associated abnormalities that may cause diagnostic confusion include :*

- *Elevation of bilirubin*
- *Elevation liver enzymes*
- *Elevation of ferritin*
- *Microcytic anemia*
- *Thrombocytopenia*

# EVALUATION OF THYROTOXICOSIS



# *Differential Diagnosis*

- *Nodular thyroid disease*
- *Destructive thyroiditis*
- *Ectopic thyroid tissue*
- *Factitious thyrotoxicosis*
- *TSH-secreting pituitary tumor*
- *Panic attacks, mania*
- *Pheochromocytoma*
- *Malignancy*



# *Clinical Course*

- *Generally worsen without treatment*
- *Mortality was 10 to 30%*
- *Spontaneous relapses and remissions*
- *May be fluctuation between hypo and hyper*
- *Ophthalmopathy worsens over the initial 3 to 6 m*
- *Followed by a plateau over the next 12 to 18 m*
- *Diplopia may appear late*
- *Radioiodine worsens the eye disease in a small proportion of patients (especially smokers)*



# ***TREATMENT***

- *Antithyroid drugs*
- *Radioiodine ( $I_{131}$ ) treatment*
- *Subtotal thyroidectomy*

# *Antithyroid drugs are the thionamides*

*Such as propylthiouracil, carbimazole, and the active metabolite of the latter, methimazole*

## *Mechanisms of thionamides*

*Inhibit the function of TPO*

*Reduce thyroid antibody levels*

*Propylthiouracil inhibits deiodination of T4 to T3*

*Thyroid function tests and clinical manifestations are reviewed 3 to 4 weeks after starting treatment, and the dose is titrated based on free T4 levels. Most patients do not achieve euthyroidism until 6 to 8 weeks after treatment is initiated. TSH levels often remain suppressed for several months and therefore do not provide a sensitive index of treatment response.*

*Maximum remission rates (up to 30 to 50% in some populations) are achieved by 18 to 24 months. Patients with severe hyperthyroidism and large goiters are most likely to relapse when treatment stops.*

# *Side effects of antithyroid drugs are*

- *Rash and urticaria*
- *Fever and arthralgia*
- *Hepatitis*
- *SLE like syndrome*
- *Agranulocytosis*

# *Radioiodine*

*5 mCi to 15 mCi*

*I<sub>131</sub>*

# *Subtotal thyroidectomy*

- *Young individuals*
- *When the goiter is very large*
- *Relapse after antithyroid drugs and  $I_{131}$*



# *Major complications of surgery*

- *Bleeding*
- *Laryngeal edema*
- *Damage to the recurrent laryngeal nerves*
- *Hypoparathyroidism*
- *Hypothyroidism*
- *Recurrence*

# *Thyrotoxic crisis or thyroid storm*

- *Fever*
- *Delirium*
- *Seizures*
- *Coma*
- *Vomiting*
- *Diarrhea*
- *Jaundice*

# ***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 of thyroid storm*

- *Supportive care*
- *Identification and treatment of the precipitating cause*
- *Large doses of propylthiouracil*
- *A saturated solution of potassium iodide*
- *Propranolol*
- *Glucocorticoids (dexamethasone)*
- *Antibiotics if infection is present*
- *Cooling and intravenous fluids*

# *Treatment of Ophthalmopathy*

- *Meticulous control of thyrotoxicosis*
- *Cessation of smoking*
- *Artificial tears*
- *Use of dark glasses with side frames*
- *Upright sleeping position*
- *Taping the eyelids shut*
- *Prednisone 40 to 80 mg daily ; Cyclosporine*
- *Methylprednisolone*
- *Surgery and external beam radiotherapy*

# ***Nontoxic Multinodular Goiter***

- *MNG occurs in up to 12% of adults. MNG is more common in women than men and increases in prevalence with age.*
- *It is more common in iodine-deficient regions but also occurs in regions of iodine sufficiency, reflecting multiple genetic, autoimmune, and environmental influences on the pathogenesis.*



# *Clinical Manifestations*

- *Asymptomatic and euthyroid*
- *Symptoms including difficulty swallowing, respiratory distress (tracheal compression), or plethora (venous congestion) : Pemberton's sign*
- *Sudden pain*
- *Hoarseness*

# *Diagnosis*

- *Examination*
- *TSH level*
- *Pulmonary function testing*
- *CT or MRI*
- *barium swallow*
- *sonography*

# *Treatment*

- *MNGs can be managed conservatively*
- *T4 suppression is rarely effective*
- *Contrast agents and other iodine-containing substances should be avoided*
- *Radioiodine (Repeat treatment )*
- *Surgery remains highly effective but is not without risk, particularly in older patients with underlying cardiopulmonary disease*

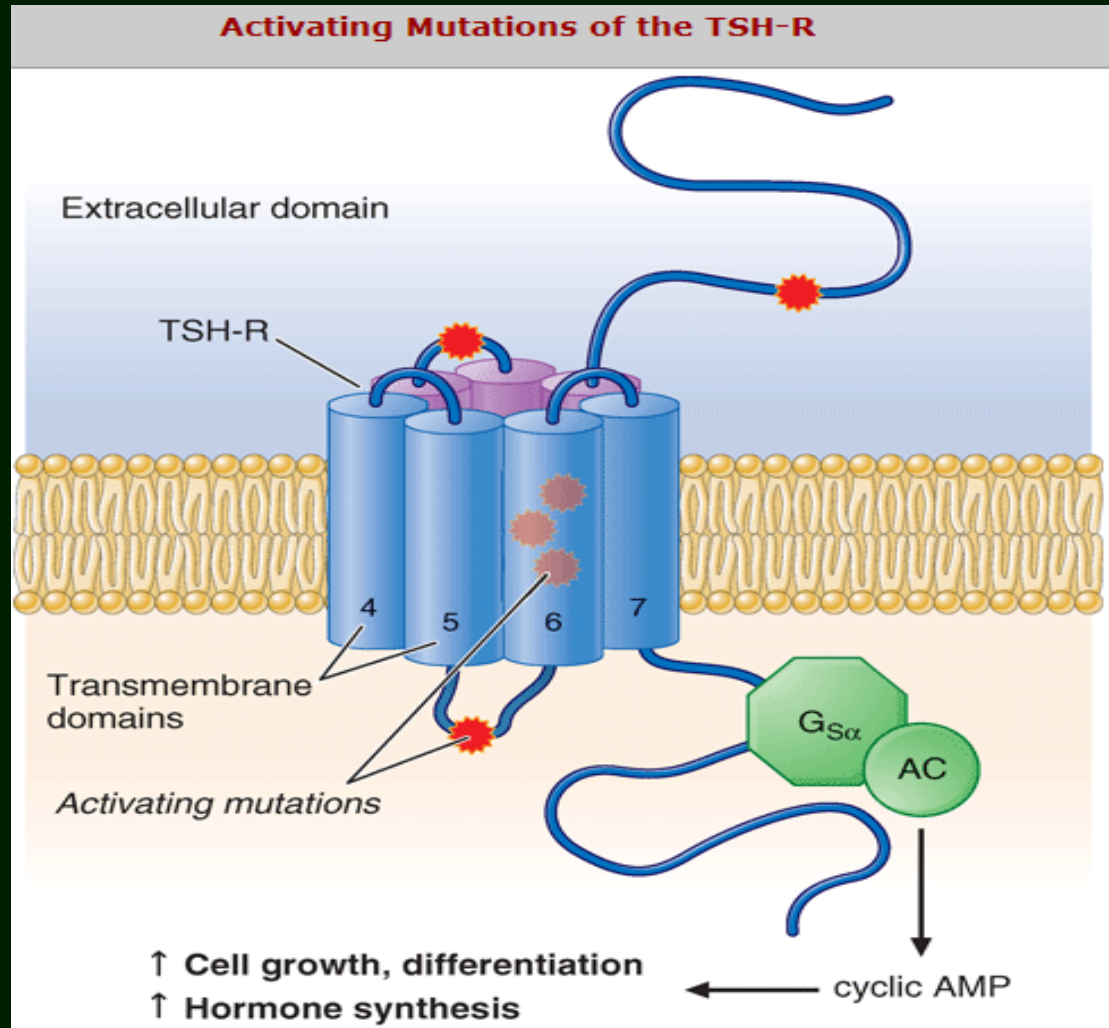
# ***TOXIC MULTINODULAR GOITER***

- *The patient is usually elderly and may present with atrial fibrillation or palpitations, tachycardia, nervousness, tremor, or weight loss.*
- *Recent exposure to iodine, from contrast dyes or other sources, may precipitate or exacerbate thyrotoxicosis.*

# ***TREATMENT***

- *Antithyroid drugs in combination with beta blockers*
- *Radioiodine*
- *Surgery*

# Toxic adenoma





- *Thyrotoxicosis is usually mild. The disorder is suggested by the presence of the thyroid nodule, which is generally large enough to be palpable, and by the absence of clinical features suggestive of Graves' disease or other causes of thyrotoxicosis.*
- *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***

- *Antithyroid drugs and beta blockers*
- *Radioiodine ablation is usually the treatment of choice*
- *Surgical resection is also effective*





**THANKS for YOUR  
ATTENTION**