

السمنه

تخفي

بداخلك

تخضع

اجمل

فحاول

اخرجه

*Medicine 341 MED-COURSE*

# Thyroid Disorders

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***KKUH-KSUMC***

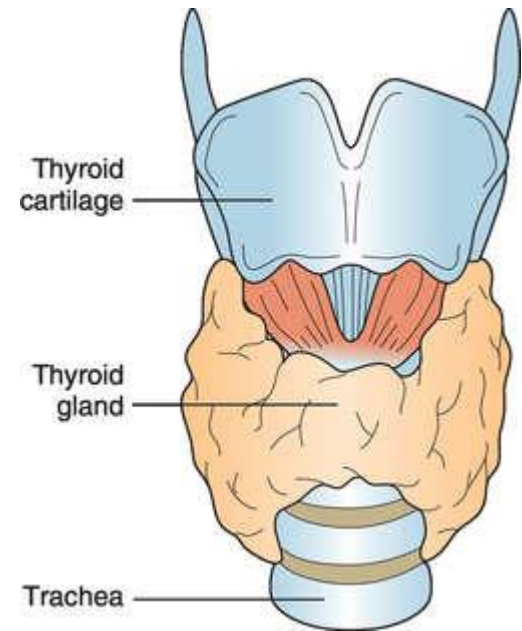
March 5, 2017

# Objectives

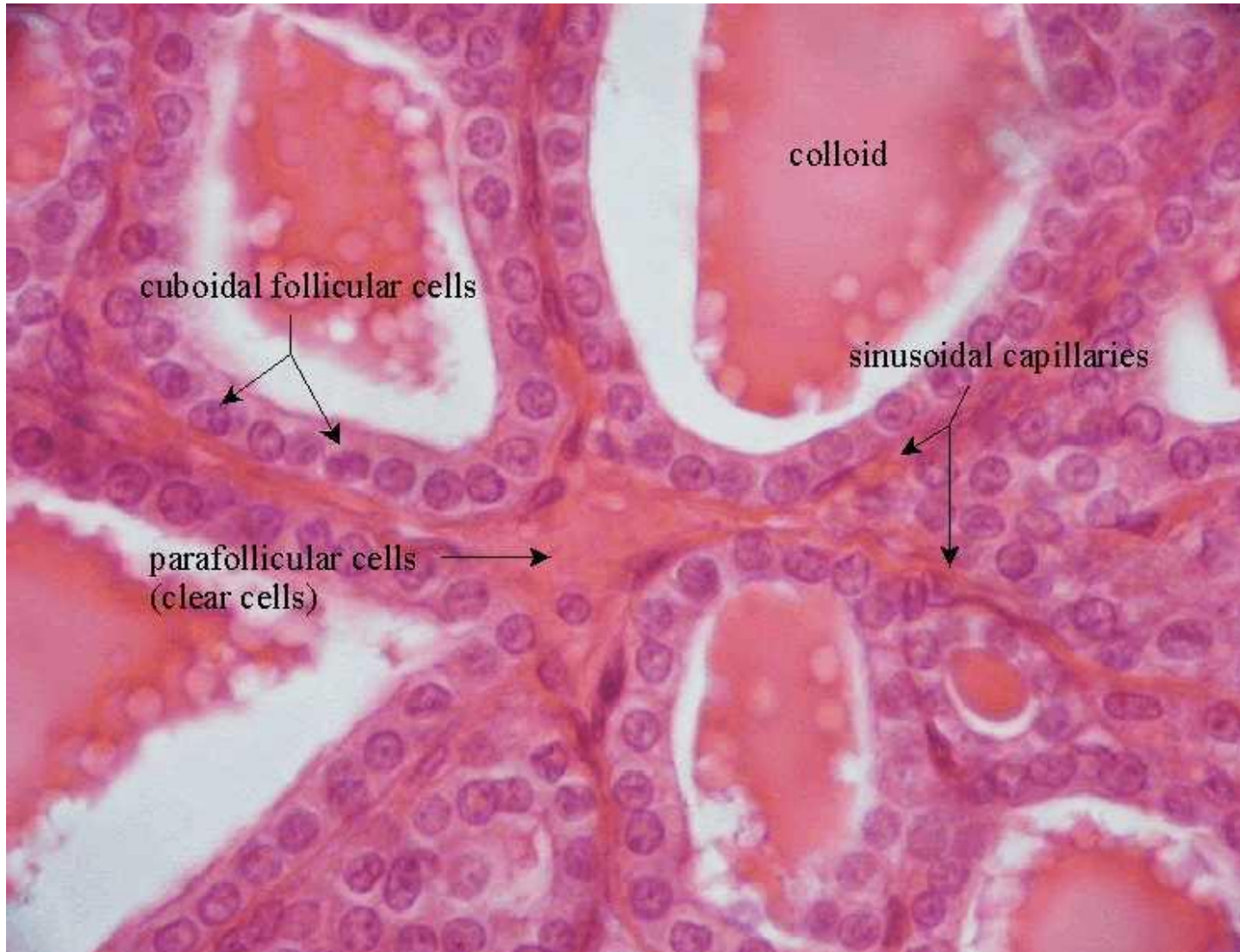
- Thyroid anatomy and physiology
- Action of thyroid hormones
- Thyroid function Tests
- Thyroid disorders:
  - **Function disorders:**
    - Hypothyroidism
    - Hyperthyroidism
  - **Structure disorders:**
    - Goiter
    - Nodule

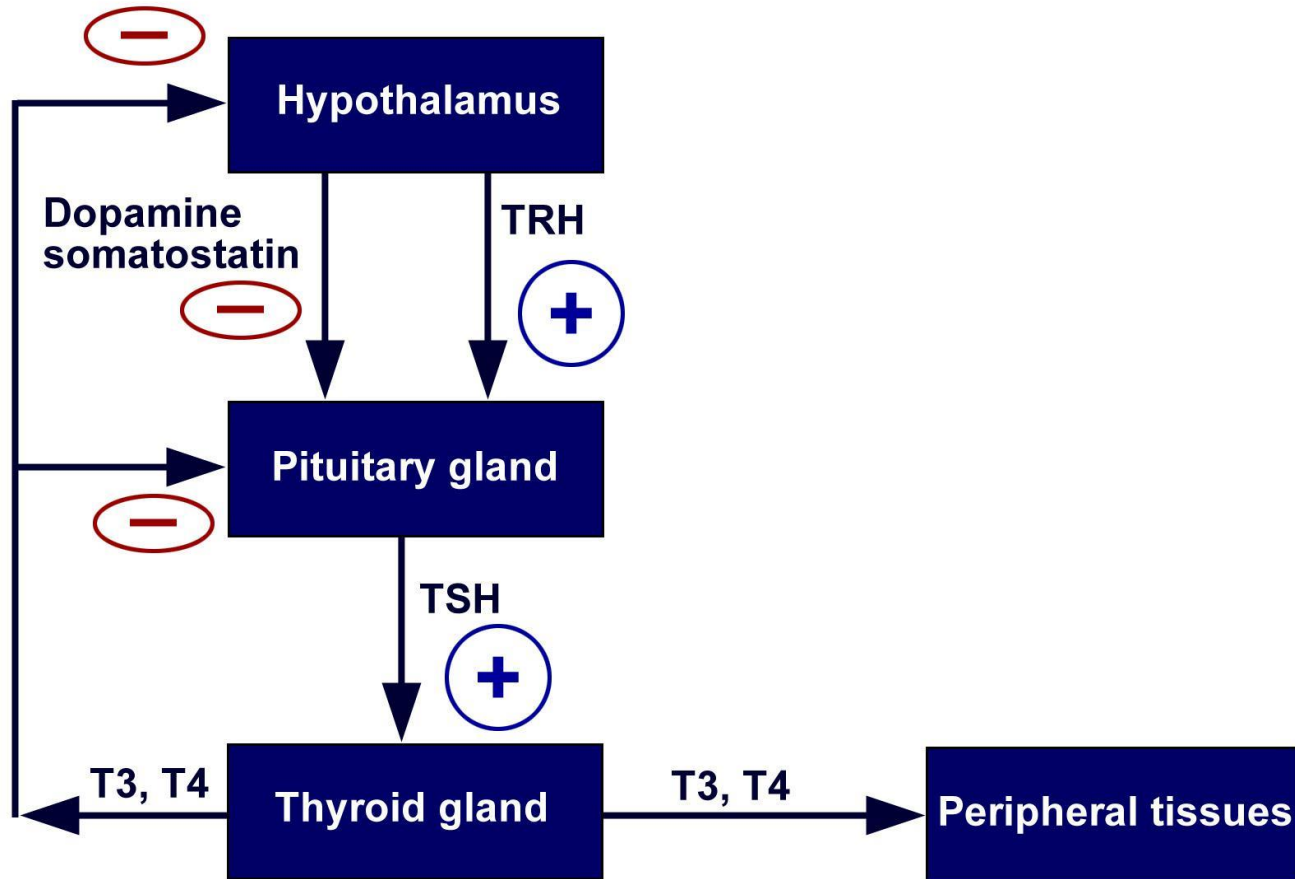
# Thyroid gland

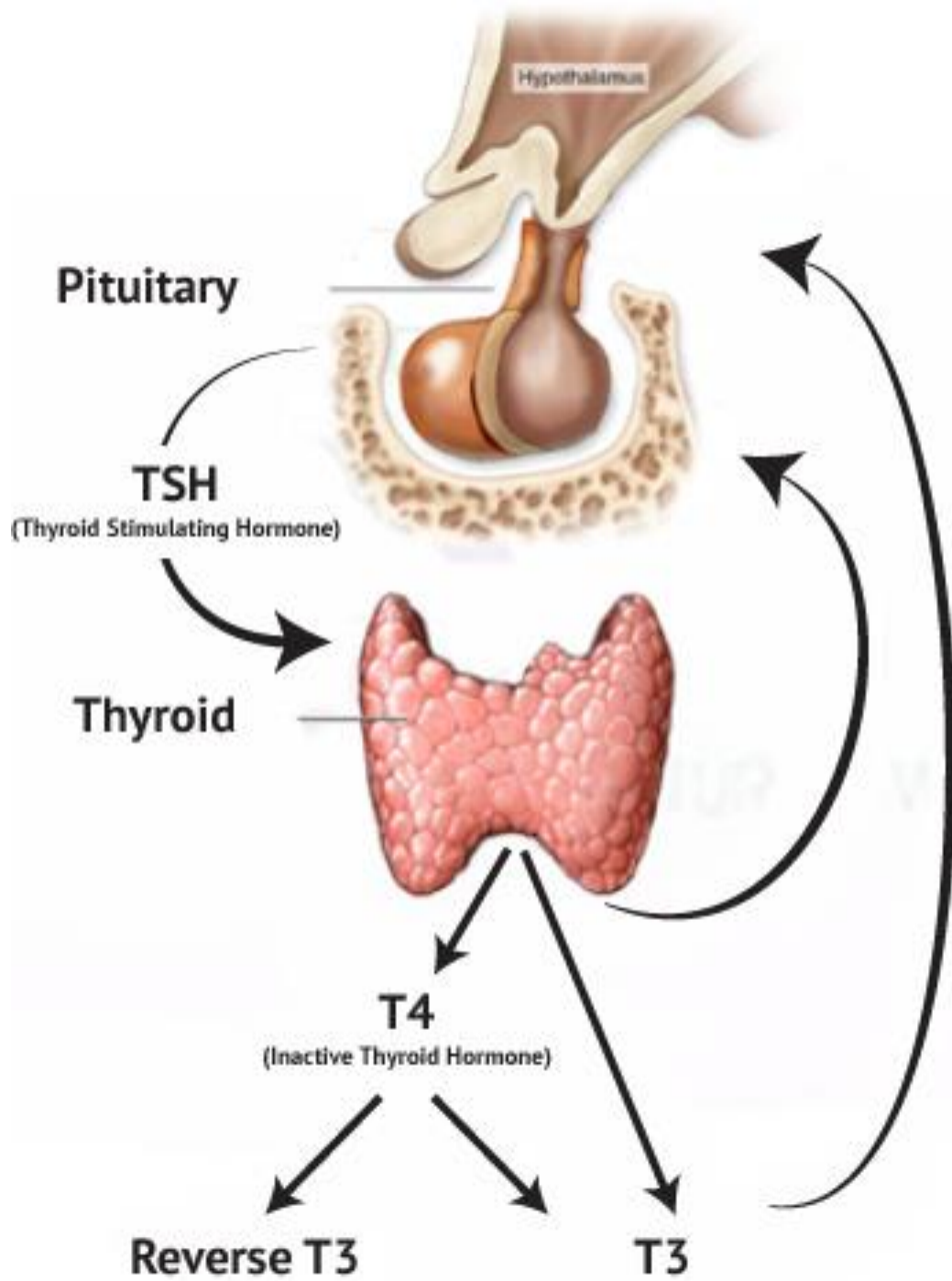
- **One** gland has:
  - 2 lobes ( Right thyroid lobe, Left thyroid lobe)
  - and connected by the isthmus
- Thyroid gland is made up of **follicles**
  - Thyroid hormone synthesis & storage
- Weigh 20 g, more volume in men, increase with age and bodyweight and decrease with iodine intake
- Located in front of larynx

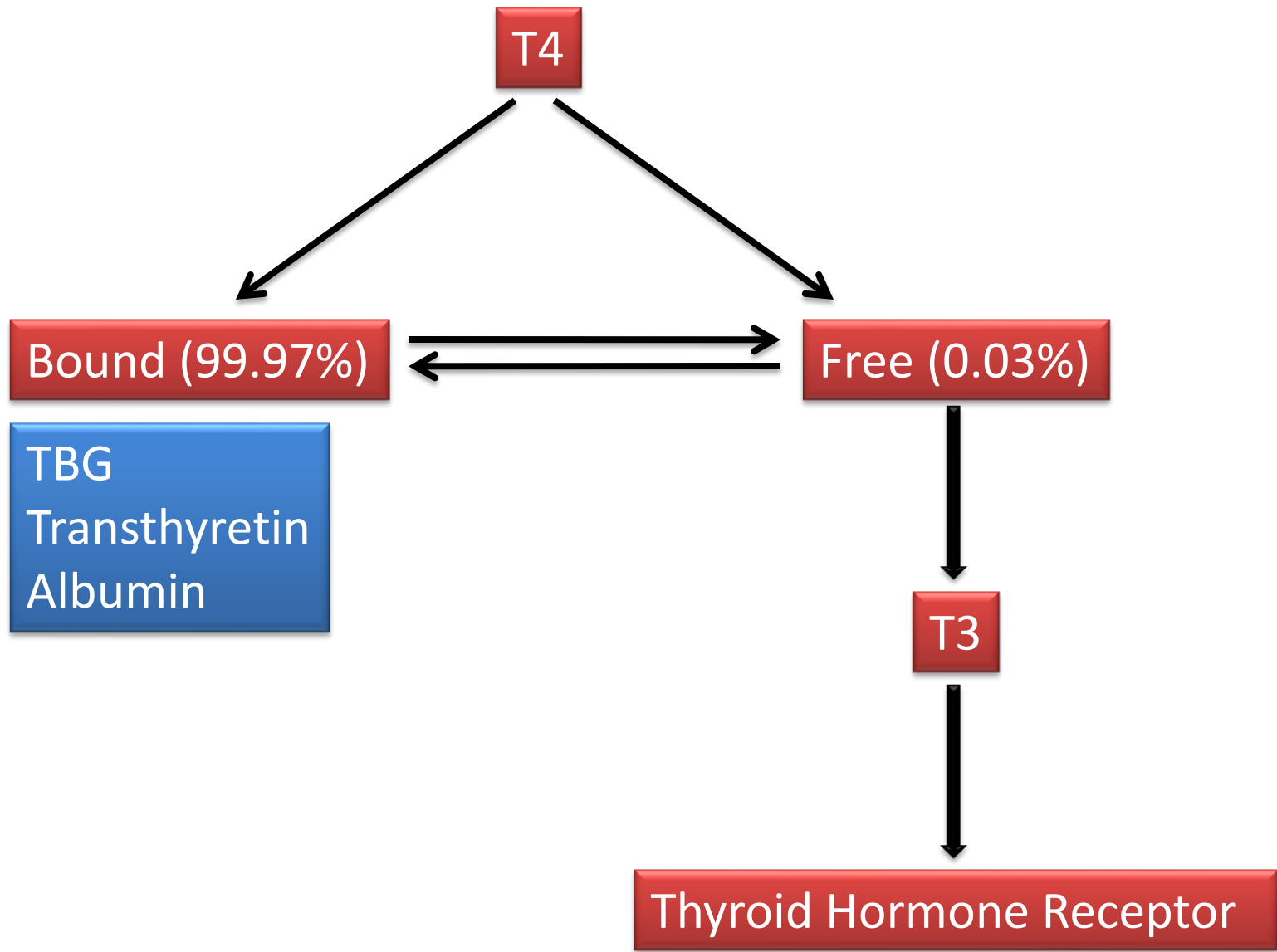


# Thyroid histology









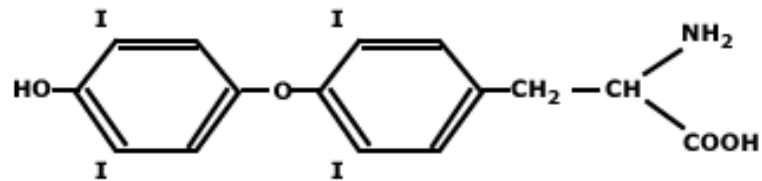


# Thyroid hormone

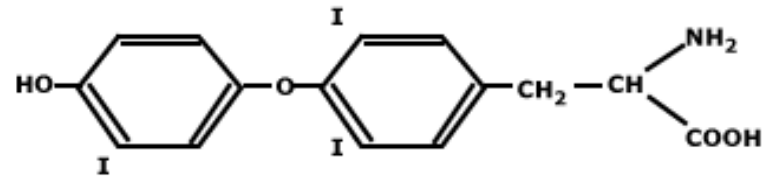
- Somatic development in adults
- Brain development in infants
- Fetal thyroid functions at 10-12th weeks of gestation
- Maternal T4 reaches the fetus during development
- if mother has hypothyroidism
  - miscarriage,
  - cognitive impairment of infant
  - preterm delivery
- Main action of thyroid hormones by T3 :
  - 80 % from peripheral conversion: T4 → T3
  - 20% produced by the thyroid itself

# Thyroid hormones

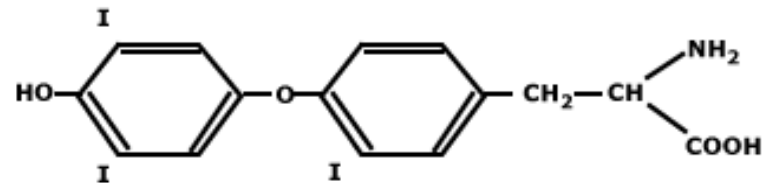
Thyroxine ( $T_4$ )



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



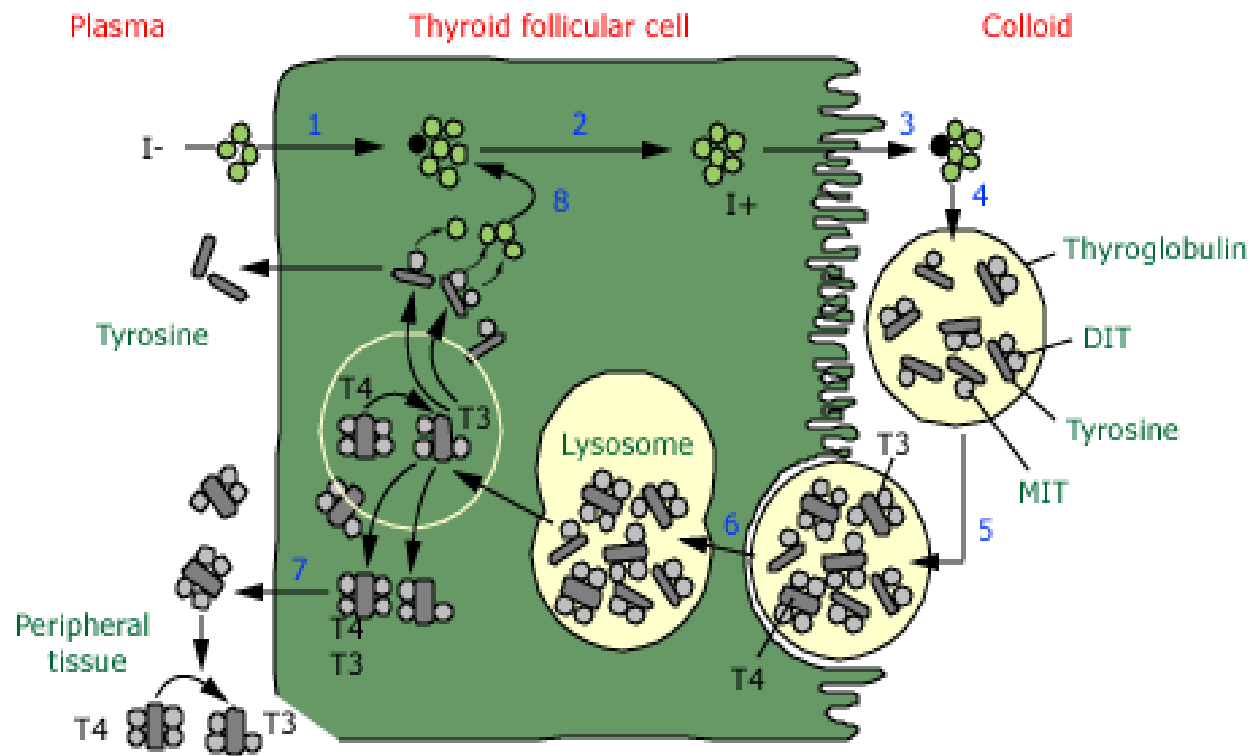
3,3,5-Triiodothyronine ( $rT_3$ )



# Thyroid hormones

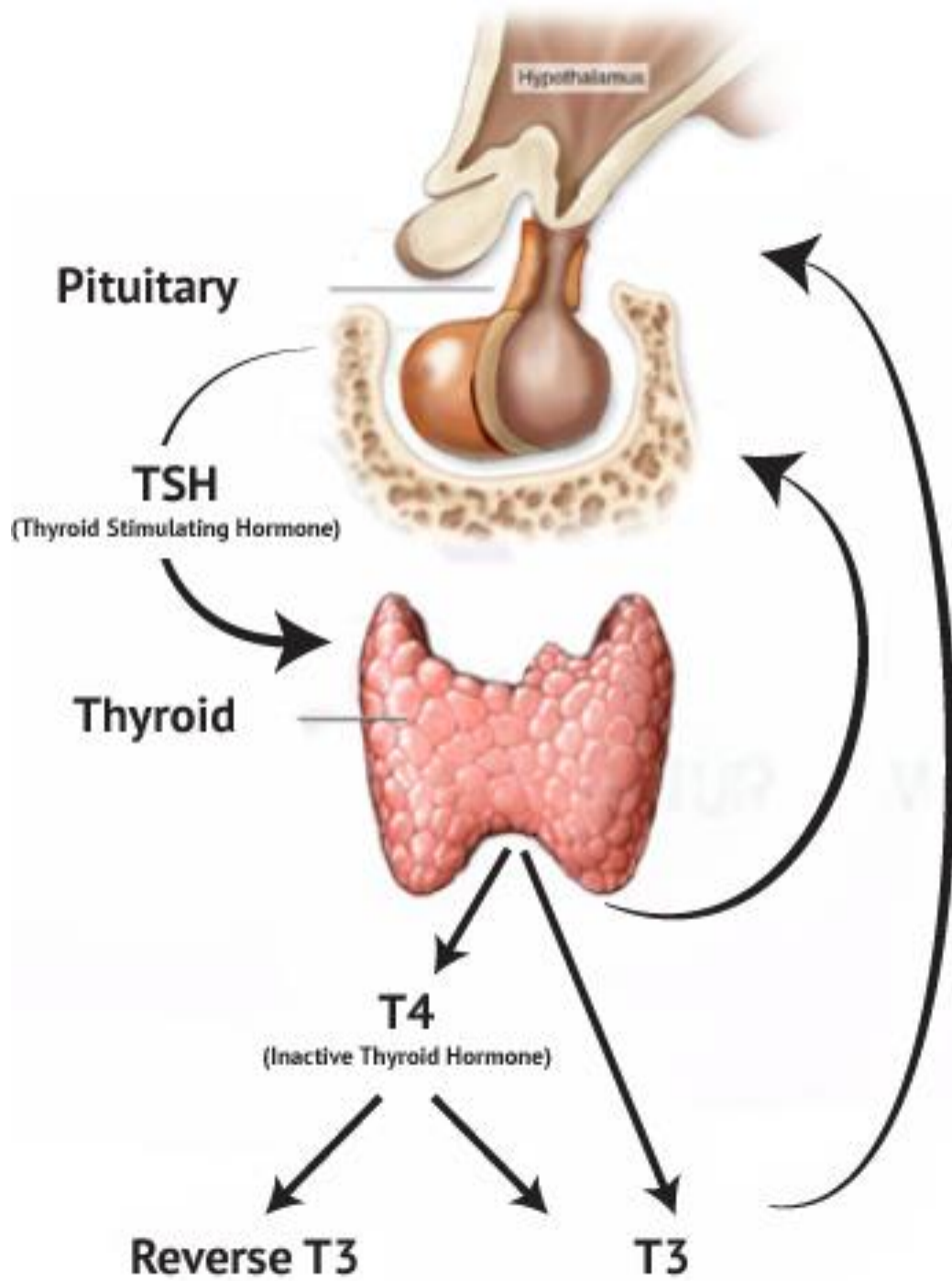
- **Follicular cells** of the thyroid is the main site of hormones **synthesis and storage**
- **Mainly T4** and small amount of T3
- **Iodine** is needed to produce thyroid hormones
- Average adult requirement of iodine is 150 mcg a day, 220 mcg for pregnant, 290 mcg for lactating
- Source of iodine:
  - dairy and seafood products

# Thyroid hormones synthesis



# Thyroid hormones

- Stored in the **thyroglobulin in follicular cells** of the thyroid gland
- **99.9 %** of T4 and T3 are **bound to protein** in the blood: TBG, albumin, lipoprotein
- T4 and T3 synthesis and secretion is regulated by **pituitary TSH**.
- TSH is inhibited by T4 and T3, stimulated by TRH
- Extrathyroidal conversion of T4 to T3 is regulated by nutrition, illness, hormonal factors



# Thyroid hormone action

- Thyroid hormones act on almost all the body systems
- Heart, bone, GI, Brain .....
- bone development and short stature
- Brain development , cognitive impairment
- Heart muscle: tachy and bradycardia
- Regulate metabolic rate and little change in bodyweight

# Thyroid function tests (**Biochemical**)

- Thyroid function tests
  - Free T4
  - TSH
  
- Autoantibody tests:
  - Anti- TPO
    - (most specific autoantibody test for autoimmune thyroiditis ), high titer
    - Could be mildly elevated in normal person
  - **TSI (TSH receptor Ab)**
    - GD



# Radiological imaging of thyroid ( Anatomical)

- **US neck:**

- The best radiological modality for assessment or suspected of **structural thyroid** disorders ( nodule, goiter in **eu or hypo**thyroid patient)

- **Radioactive uptake scan:**

- To differentiate the cause of thyrotoxicosis
  - **High** uptake = **active** thyroid **synthesis** = ( GD, Toxic MNG, Toxic adenoma)
  - **No** uptake = **no active** thyroid synthesis = thyroiditis

- **CT neck:**

- sometimes for **retrosternal** goiter and compression symptoms

# Thyroid disorders

```
graph TD; A[Thyroid disorders] --> B[Function disorders: Hypothyroidism, Hyperthyroidism]; A --> C[Structure disorders: Goiter, Nodule];
```

## *Function disorders:*

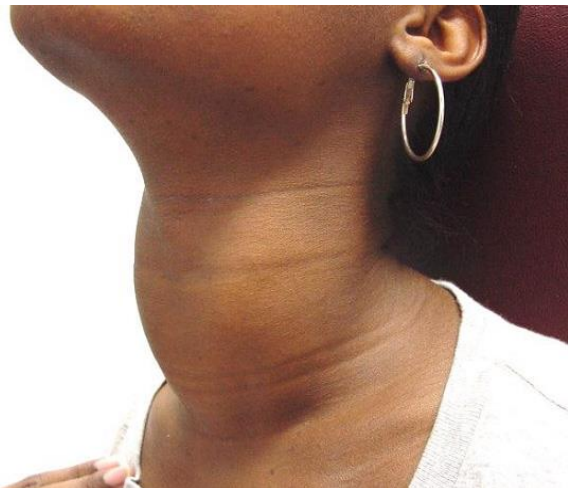
Hypothyroidism  
Hyperthyroidism

## *Structure disorders:*

Goiter  
Nodule

# Common thyroid disorders

- Goiter: chronic enlargement of thyroid gland
- Endemic Goiter: common in china and central africa
- Sporadic Goiter: multinodular goiter
- Familial



# Goiter

- Hashimoto's thyroiditis: in early stage
- Graves' disease: due to chronic stimulation of TSH receptor
- Diet: cabbage, Cauliflower
- Chronic iodine excess
- Medication: lithium in 6%
- neoplasm

# Goiter

- **C: Clinical**

- History & examination of lump, hyper or hypothyroidism, compression symptoms, change in voice, family history of thyroid tumors, history of irradiation.

- **B: Biochemical**

- TSH & T4

- **A: Anatomical**

- Ultrasound neck: if patient with eu or hypothyroidism
- Radioactive uptake scan: thyrotoxicosis

# Goiter - non Toxic

- Surgery (Thyroidectomy) if:
  - pressure symptoms
  - Malignancy
  - Cosmetic

# Thyroid disorders

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graph TD; A[Thyroid disorders] --> B[Function disorders: Hypothyroidism, Hyperthyroidism]; A --> C[Structure disorders: Goiter, Nodule];
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## **Function disorders:**

Hypothyroidism  
Hyperthyroidism

## **Structure disorders:**

Goiter  
Nodule

# Thyrotoxicosis

## – Hyperthyroidism

- There are increase synthesis and release of thyroid hormones
  - So, both T4,T3 will be high in same ratio
  - Thyroid uptake scan will be : high uptake (increase synthesis, need iodine)

## – Non-Hyperthyroidism (Other causes)

- There are NO increase in synthesis of thyroid hormones , but increase of release of stored thyroid hormones in vesicles
  - So, both T4 >> T3
  - Thyroid uptake scan will be : low uptake ( NO increase synthesis)

• .



**Thyrotoxicosis**



```
graph TD; A[Thyrotoxicosis] --> B[Hyperthyroidism]; A --> C["Non-Hyperthyroidism (Other causes)"]
```

**Hyperthyroidism**

**Non-Hyperthyroidism  
(Other causes)**

- Sometimes physician use term of hyperthyroidism = thyrotoxicosis

# C: Clinical

## History

- **Sympathetic activation**
  - Nervousness ,Anxiety ,Increased perspiration ,Heat intolerance ,Hyperactivity ,Palpitations
- **Cardiovascular symptoms**  
(SOB, atrial fibrillation) and unexplained weight loss
- **Ophthalmopathy (Graves disease )**

# C: Clinical

## History

- autoimmune disease
- Radiation exposure
- family history
- medications and dietary

# C: Clinical

## Examination

- Tachycardia or atrial arrhythmia ,Systolic hypertension with wide pulse pressure ,Warm, moist, smooth skin
- Lid lag ,Stare
- Hand tremor ,Muscle weakness

# C: Clinical

- **Thyroid examination**
- diffusely enlarged and slightly firm + bruit
  - **GD**
- enlarged (2 - 3 x) + soft
  - **MNG**
- enlarged and painful:
  - subacute painful or granulomatous **thyroiditis**
  - degeneration or hemorrhage into a nodule and suppurative thyroiditis

# Ophthalmologic examination

- 50% GD have **GO**
  - periorbital edema
  - conjunctival edema (chemosis)
  - Injection
  - poor lid closure
  - extraocular muscle dysfunction (diplopia)
  - Proptosis



# dermatologic examination

- **Pretibial myxedema**
  - deposition of glycosaminoglycans in the dermis of the lower leg
  - nonpitting edema, erythema and thickening of the skin, without pain or pruritus
  - **orange peel** in color and texture.



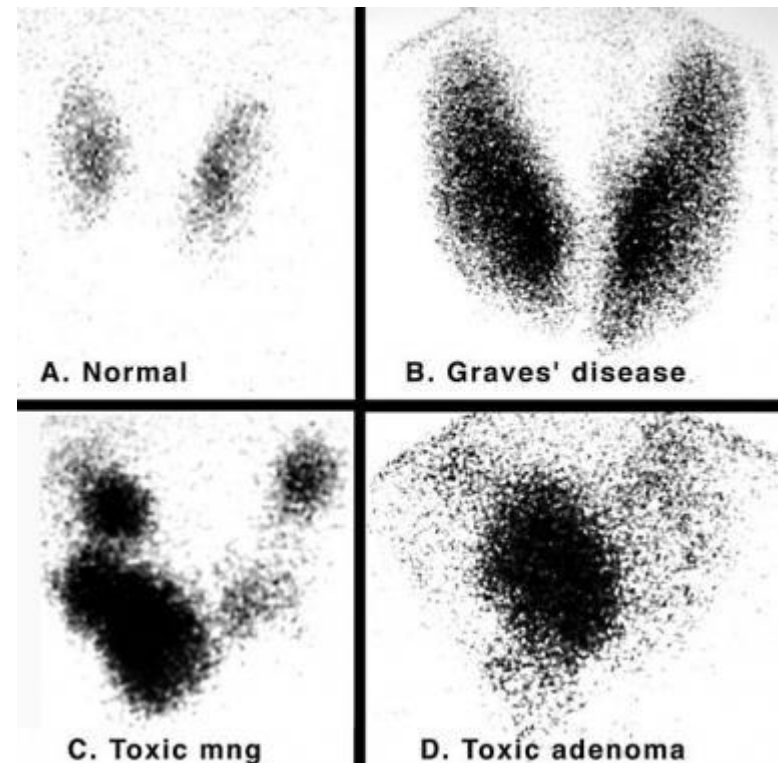


# B: Biochemical

- Thyroid function tests
  - Free T4
  - TSH
  
- Autoantibody tests:
  - Anti- TPO
    - (most specific autoantibody test for autoimmune thyroiditis ), high titer
    - Could be mildly elevated in normal person
  - **TSI (TSH receptor Ab)**
    - GD

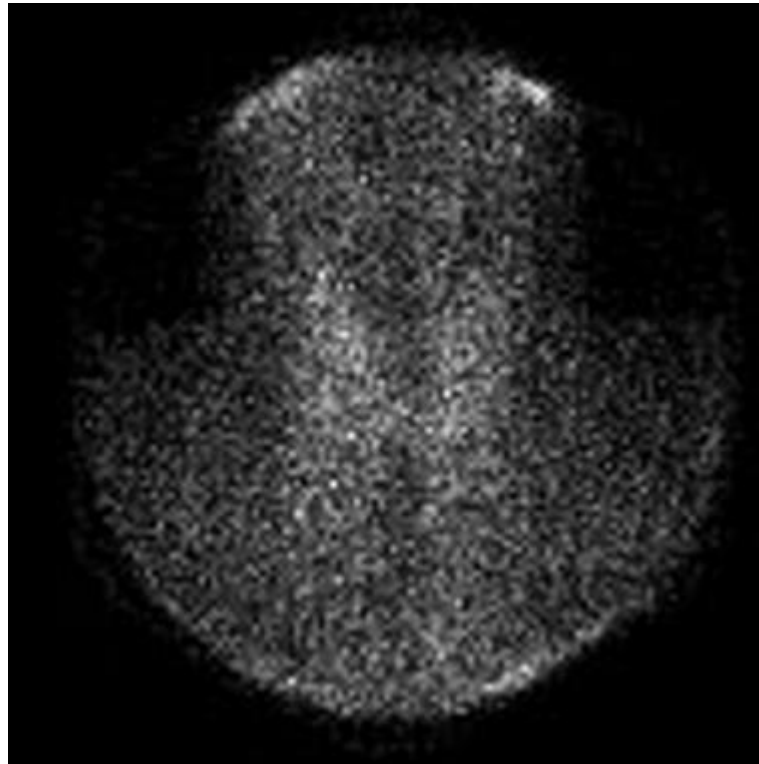
# A: Anatomical

- **Thyroid uptake scan:**
  - Technetium-99m ( $^{99m}\text{Tc}$ )
  - Iodine-123 ( $^{123}\text{I}$ )



**High** uptake = **active** thyroid **synthesis**  
= ( GD, Toxic MNG, Toxic adenoma)

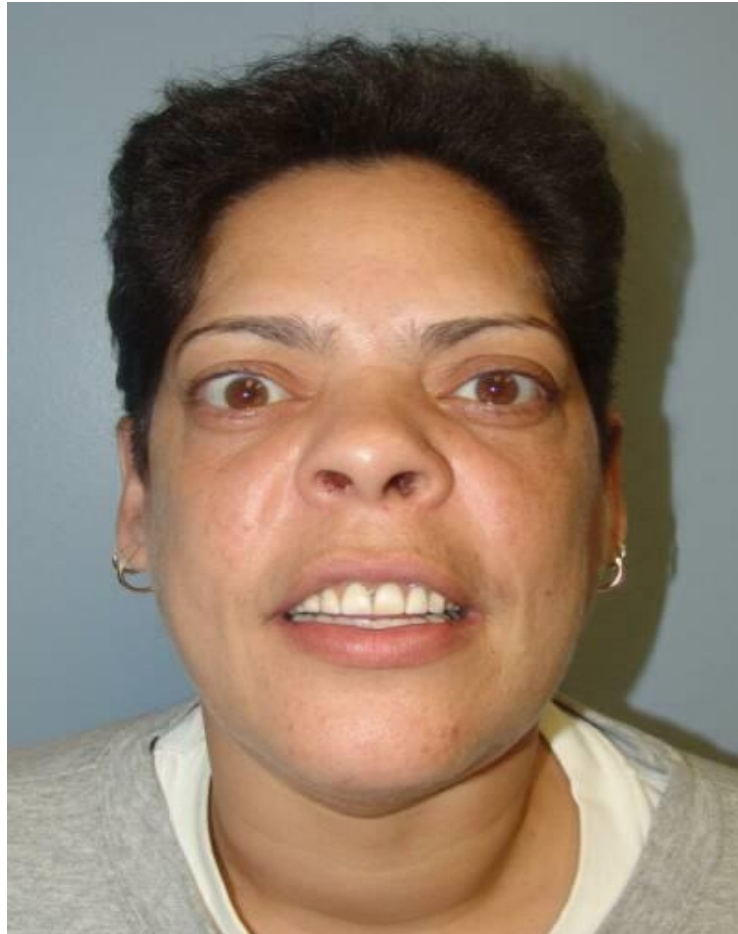
# Thyroid uptake scan



No uptake = no active thyroid synthesis = thyroiditis

# Hyperthyroidism

- Hypermetabolic state caused by increased availability of thyroid hormones



## Causes of hyperthyroidism

<b>Hyperthyroidism with a normal or high radioiodine uptake</b>
<b>Autoimmune thyroid disease</b>
Graves' disease
Hashitoxicosis
<b>Autonomous thyroid tissue (uptake may be low if recent iodine load led to iodine-induced hyperthyroidism)</b>
Toxic adenoma
Toxic multinodular goiter
<b>TSH-mediated hyperthyroidism</b>
TSH-producing pituitary adenoma
Non-neoplastic TSH-mediated hyperthyroidism
<b>Human chorionic gonadotropin-mediated hyperthyroidism</b>
Hyperemesis gravidarum
Trophoblastic disease
<b>Hyperthyroidism with a near absent radioiodine uptake</b>
<b>Thyroiditis</b>
Subacute granulomatous (de Quervain's) thyroiditis
Painless thyroiditis (silent thyroiditis, lymphocytic thyroiditis)
Postpartum thyroiditis
Amiodarone (also may cause iodine-induced hyperthyroidism)
Radiation thyroiditis
Palpation thyroiditis
<b>Exogenous thyroid hormone intake</b>
Excessive replacement therapy
Intentional suppressive therapy
Factitious hyperthyroidism
<b>Ectopic hyperthyroidism</b>
Struma ovarii
Metastatic follicular thyroid cancer

# Clinical features of hyperthyroidism

- Skin: warm, excessive sweating
- Onycholysis, hyperpigmentation
- Pruritus, vitiligo, alopecia, thinning of the hair
- Pretibial myxedema



# Hyperthyroidism

- Eyes: sympathetic overactivity
- Common in graves' disease
- Extraocular muscles dysfunction: diplopia, proptosis, lid retraction, corneal ulceration, optic neuropathy and blindness
- Periorbital and conjunctival edema



# Hyperthyroidism

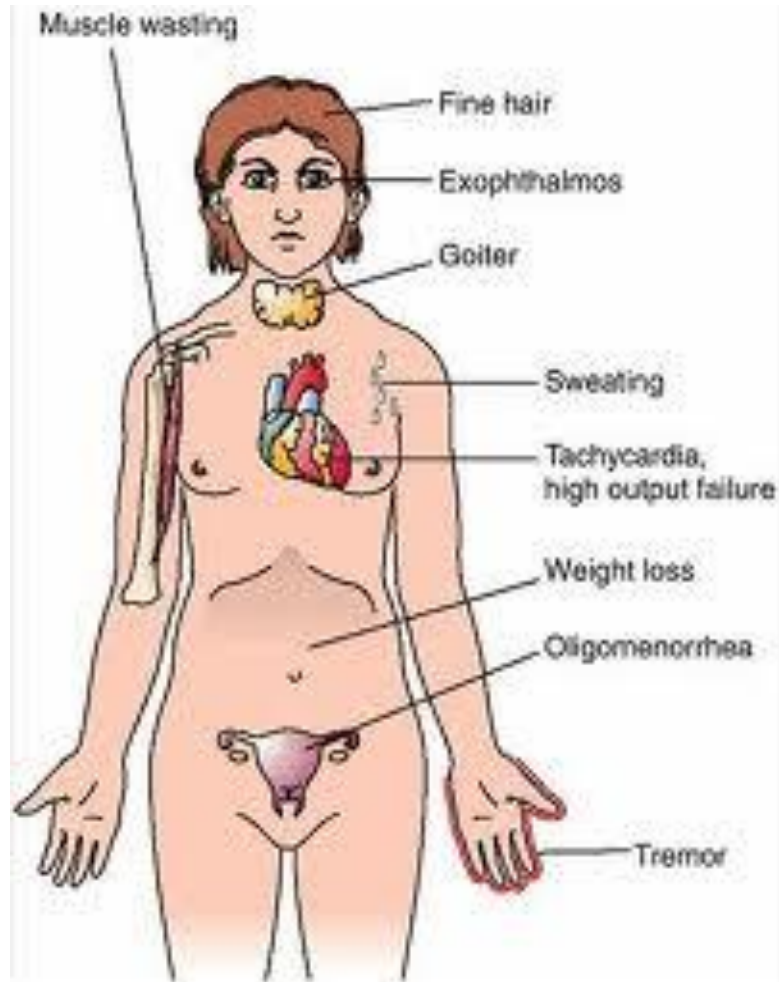
- Cardiac:
  - Atrial fibrillation in 10-20 %
  - High output cardiac failure
  - Wide pulse pressure, hypertension
- Respiratory:
  - Dyspnoea
- GI:
  - Weight loss, diarrhoea, increase liver enzyme



# Hyperthyroidism

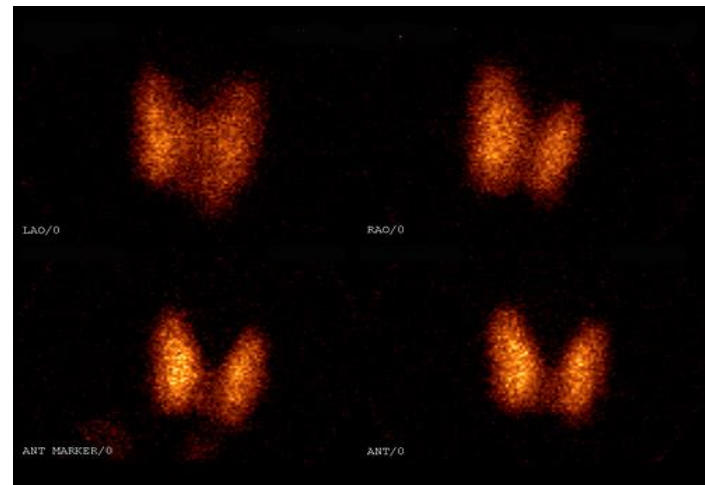
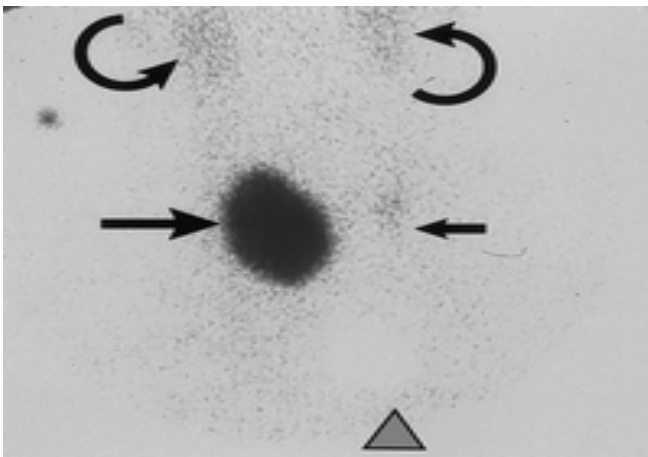
- Bone:
  - Bone turnover increased: osteoporosis
- Neuropsychiatry:
  - Behavioral and personality changes: irritability, depression
- Hyperactivity increased

# Hyperthyroidism




# Lab-hyperthyroidism

- Increased Free T4
- Increased Free T3
- Low TSH
- TSH-receptor antibodies
- Increased radioactive iodine uptake on scan



## Treatment of Graves' hyperthyroidism

Therapy	Advantages	Disadvantages
Thionamides	<p>Chance of permanent remission</p> <p>Some patients avoid permanent hypothyroidism</p> <p>Lower cost</p>	<p>Minor side effects: rash, hives, arthralgias, transient granulocytopenia, gastrointestinal symptoms</p> <p>Major side effects: agranulocytosis, vasculitis (lupus-like syndrome), hepatitis</p> <p>Risk of fetal goiter and hypothyroidism if pregnant</p> <p>Requires more frequent monitoring</p>
Radioiodine	<p>Permanent resolution of hyperthyroidism</p>	<p>Permanent hypothyroidism</p> <p>Patient must take radiation precautions for several days after treatment, avoiding contact with young children and pregnant women</p> <p>Rare radiation thyroiditis</p> <p>Patient concerns about long-term oncogenic effects of radiation</p>
Surgery	<p>Rapid, permanent cure of hyperthyroidism</p>	<p>Permanent hypothyroidism</p> <p>Risk of hypoparathyroidism, recurrent laryngeal nerve damage, and general anesthesia</p> <p>High cost</p>

Summary of the advantages and disadvantages of the three major therapeutic modalities used in the treatment of Graves' hyperthyroidism. 

# Hypothyroidism

- Causes
- Clinical features
- management

## Major causes of hypothyroidism

<b>Primary hypothyroidism</b>
Chronic autoimmune thyroiditis
Iatrogenic
Thyroidectomy
Radioiodine therapy or external irradiation
Iodine deficiency or excess
Drugs - thionamides, lithium, amiodarone, interferon-alfa, interleukin-2, perchlorate
Infiltrative diseases - fibrous thyroiditis, hemochromatosis, sarcoidosis
<b>Transient hypothyroidism</b>
Painless (silent, lymphocytic) thyroiditis
Subacute granulomatous thyroiditis
Postpartum thyroiditis
Subtotal thyroidectomy
Following radioiodine therapy for Graves' hyperthyroidism
Following withdrawal of suppressive doses of thyroid hormone in euthyroid patients
Congenital thyroid agenesis, dysgenesis, or defects in hormone synthesis
<b>Central hypothyroidism</b>
TSH deficiency
TRH deficiency
<b>Generalized thyroid hormone resistance</b>

## Drugs affecting thyroid function or function tests

<b>Drugs causing hypothyroidism</b>
Inhibition of thyroid hormone synthesis and/or release - thionamides, lithium, perchlorate, aminoglutethimide, thalidomide, and iodine and iodine-containing drugs including amiodarone, radiographic agents, expectorants (Organidin, Combid), kelp tablets, potassium iodine solutions (SSKI), Betadine douches, topical antiseptics
Decreased absorption of T4 - cholestyramine, colestipol, colesevelam, aluminum hydroxide, calcium carbonate, sucralfate, iron sulfate, raloxifene, omeprazole, lansoprazole, and possibly other medications that impair acid secretion, sevelemer, lanthanum carbonate, and chromium; malabsorption syndromes can also diminish T4 absorption
Immunedysregulation - interferon-alfa, interleukin-2
Suppression of TSH - dopamine
Possible destructive thyroiditis - sunitinib
Increased T4 clearance and suppression of TSH - bexarotene
<b>Drugs causing hyperthyroidism</b>
Stimulation of thyroid hormone synthesis and/or release - iodine, amiodarone
Immunedysregulation - interferon-alfa, interleukin-2, denileukin diftitox
<b>Drugs causing abnormal thyroid function tests without thyroid dysfunction</b>
Low serum TBG - androgens, danazol, glucocorticoids, slow-release niacin (nicotinic acid), l-asparaginase
High serum TBG - estrogens, tamoxifen, raloxifene, methadone, 5-fluouracil, clofibrate, heroin, mitotane
Decreased T4 binding to TBG - salicylates, salsalate, furosemide, heparin (via free fatty acids), certain NSAIDs
Increased T4 clearance - phenytoin, carbamazepine, rifampin, phenobarbital
Suppression of TSH secretion- dobutamine, glucocorticoids, octreotide
Impaired conversion of T4 to T3 - amiodarone, glucocorticoids, contrast agents for oral cholecystography (eg, iopanoic acid), propylthiouracil, propranolol, nadol

## Major symptoms and signs of hypothyroidism

Mechanism	Symptoms	Signs
Slowing of metabolic processes	Fatigue and weakness Cold intolerance Dyspnea on exertion Weight gain Cognitive dysfunction Mental retardation (infant) Constipation Growth failure	Slow movement and slow speech Delayed relaxation of tendon reflexes Bradycardia Carotenemia
Accumulation of matrix substances	Dry skin Hoarseness Edema	Coarse skin Puffy facies and loss of eyebrows Periorbital edema Enlargement of the tongue
Other	Decreased hearing Myalgia and paresthesia Depression Menorrhagia Arthralgia Pubertal delay	Diastolic hypertension Pleural and pericardial effusions Ascites Galactorrhea

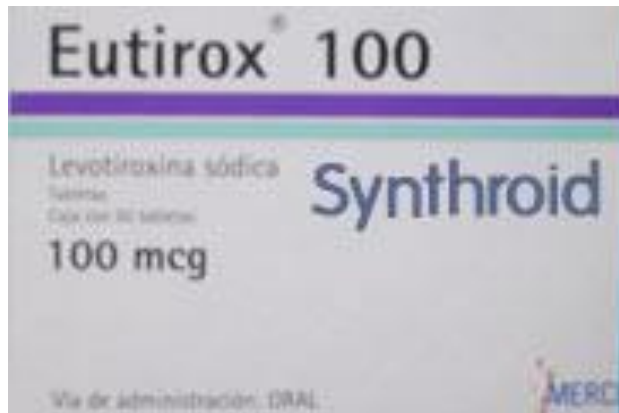


# Hypothyroid-Diagnosis

- High TSH
- Low Free T4 and T3
- Positive TPO antibodies

# Hypothyroidism- treatment

- Thyroxine replacement



- Half life of T4 is one week, so, we need 4-6 weeks before check T4, TSH to adjust thyroxine dose

## Patterns of thyroid function tests during assessment of thyroid function

Serum TSH	Serum Free T4	Serum T3	Assessment
<b>Normal hypothalamic-pituitary function</b>			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinemia
Normal	Low	Normal or high	Euthyroid: triiodothyronine therapy
Normal	Low normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
<b>Abnormal hypothalamic-pituitary function</b>			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low*	Low or low-normal	Low or normal	Central hypothyroidism

\* In central hypothyroidism, serum TSH may be low, normal or slightly high.

# Hypo and hyperthyroidism

## KNOW MORE

### HYPOTHYROIDISM

It is a disease affecting humans and vertebrates, caused by insufficient production of thyroid hormones by the thyroid gland

- Poor muscle tone (muscle hypotonia)
- Fatigue
- Cold intolerance, greater sensitivity to cold
- Constipation
- Depression
- Muscle cramps and joint pain
- Goiter
- Thin, brittle fingernails
- Coarse hair
- Paleness
- Decreased sweating
- Poor muscle tone (muscle hypotonia)



### HYPERTHYROIDISM

It is a condition in which an overactive thyroid gland produces excessive amount of thyroid hormones that circulate in the blood

- Palpitation
- Heat intolerance
- Nervousness
- Insomnia
- Breathlessness
- Increased bowel movements
- Light or absent menstrual periods
- Fatigue
- Fast heart rate
- Trembling hands
- Weight loss
- Muscle weakness
- Hair loss

