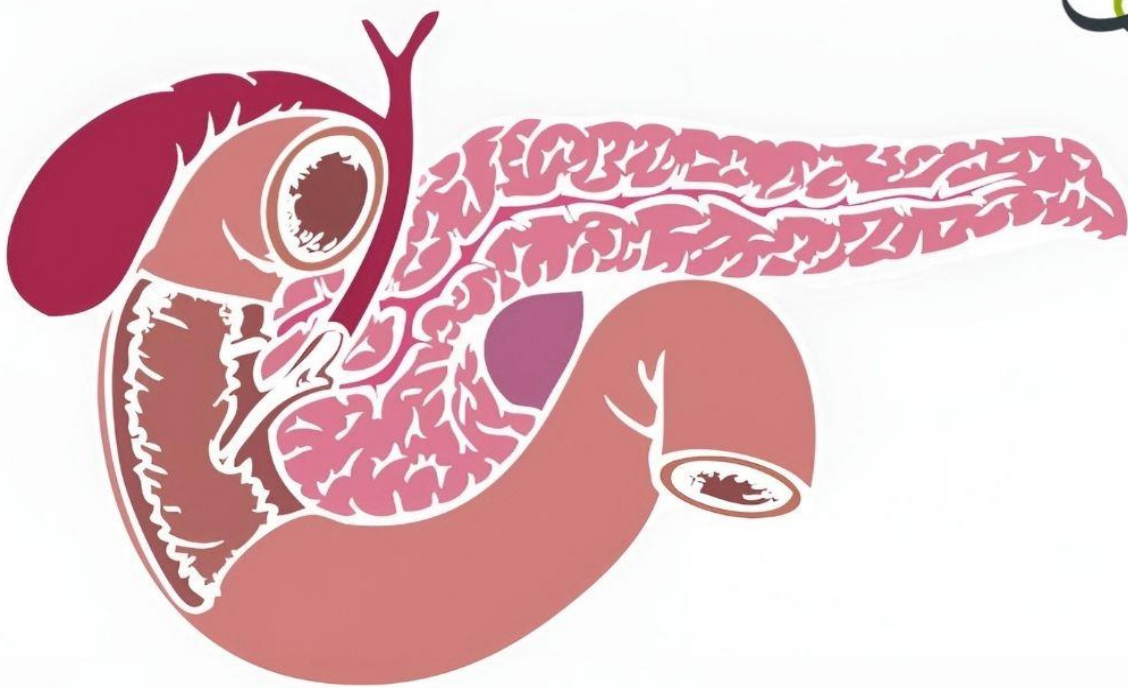


# Endocrine system

2

## Pathology



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# Hypothyroidism (low T3, T4 ,,, high TSH)

- Hypothyroidism: is decreased level of T4 (tetraiodothyronine/thyroxine), T3 (triiodothyronine) and elevated TSH.
- High TSH because of the positive feedback of the low T3, T4.
- TSH is probably the **best screening test** for thyroid disease.
- It's very serious that's why nowadays any newborn should have (T3, T4, TSH) test, so that hypothyroidism can be detected early on to avoid development of Cretinism: hypothyroidism in children, young patients.
- Thyroid gland is necessary in adults and children, growing up children need thyroid hormones for normal development and normal CNS function.
- Untreated hypothyroidism will end up being severe and patients may be mentally retarded.

❖ **Cretinism:** patient is obese, big tongue outside. We should not see it nowadays because all newborns are screened for it.



❖ **Myxedema:** hypothyroidism in adults at the age of 15-20.

- **Cold intolerance:** temperature is high, but patient still feels cold.
- **Overweight:** patient doesn't eat too much but gains weight because of the low metabolic rate, no energy expenditure.
- Cool pale thick skin especially in chin.
- **Opposite of hyperthyroidism.** (For example; here we have constipation while in hyperthyroidism it is diarrhea).

# Hypothyroidism

## ■ Cretinism (child)

- Impaired CNS & bone growth
- Mental retardation
- Short stature
- Coarse facial features
- Protruding tongue
- Umbilical hernia

## ■ Myxedema (adult)

- Slow physical and mental activity
- Cold intolerance
- Over weight
- Low cardiac output
- Constipation and decreased sweating
- Cool pale thick skin

## Causes of hypothyroidism:

Primary    The disease in the thyroid itself		
<ul style="list-style-type: none"><li>● Postablative Surgery, radioiodine therapy, or external irradiation</li><li>● Autoimmune hypothyroidism Hashimoto thyroiditis*</li><li>● Iodine deficiency*</li><li>● Drugs (lithium, iodides, p-aminosalicylic acid)*</li><li>● Congenital biosynthetic defect (dyshormonogenetic goiter) (rare)*</li><li>● Genetic defects in thyroid development (rare)</li><li>● Thyroid hormone resistance syndrome (rare) End organ resistance</li></ul>	} <b>MOST COMMOM</b>	
Secondary (Central)    Normal thyroid		
<ul style="list-style-type: none"><li>● Pituitary failure (rare)</li><li>● Hypothalamic failure (rare)</li></ul>		

### Notes about the table above:

- **Ablation**(تدمير) (**most common cause**): damage either by surgery, radioiodine therapy or external irradiation in the neck, for example: carcinoma of the larynx.
- If Hashimoto thyroiditis is not treated it ends up with fibrosis and hypothyroidism.
- Areas away from the sea may have iodine deficiency, rare to see nowadays because we have iodinated salts.
- Lithium: A drug used for bipolar disorders to stabilize mood.
- In the case of pituitary adenoma: remove pituitary gland → no TSH → secondary hypothyroidism → long life thyroxine replacement therapy.
- Hypothalamic failure: TRH is not secreted → TSH is not secreted → T3 and T4 are not secreted.



**\*Extremely important to differentiate between both of them.**

# Hypothyroidism

## Symptoms:

Extreme Tiredness/Lethargy/  
Lack of Stamina/Motivation  
Memory Loss/'Brain Fog'  
Depression/  
Mood Swings  
Hearing Loss

Weight  
Gain

3pm  
crash

Broken  
Sleep

Brittle/  
Ridged  
Nails

Joint/  
Muscle  
Pain

Hair  
Loss

Constipation

Prmenstrual Tension

Intolerance to Cold/Heat/  
Sweating/Low Body Temperature

Tingling & Numbness in Extremities

## Signs:

Sparse Eyebrows  
Especially outer ends  
Swelling of the Face  
Especially around Eyes  
(Oedema)  
Changes at the back of  
the Eye (at Fundus Oculi)  
Wasting of Tongue  
Listless, dull to look Eyes  
Hoarseness

Rapid Heart  
Rate with  
weak force  
of contraction  
Slow Thinking  
Slow Pulse  
Rate

Non pitting oedema of ankles

Cold/dry/sore/scaly skin/brittle nails  
Low basal activity level temperature  
Dry/course/brittle hair or hair loss  
Unexplained Weight Gain

Pounding Heart Beat

Nervousness  
Sluggish  
Movement

# Hyperthyroidism

## Symptoms:

Protusion of one or both  
eyeballs (exophthalmos)  
Breathlessness  
Nervousness  
Difficulty  
Sleeping/  
Insomnia

Fatigue

Itching  
-overall

Heartbeat  
Sensations  
Palpitations

Weakness

Diarrhoea

Increased Bowel Movements

Heat Intolerance

Light or Absent  
Menstrual Periods

## Signs:

Protruding Eyes  
(exophthalmos)

Hair Loss

Staring Gaze

Nausea & Vomiting  
Warm Moist Skin

Goitre

Fast  
Heart  
Rate

Trembling  
Hands

Skin Blushing/ Flushing

Blood Pressure- high

Pulse- Pounding

Weight Loss

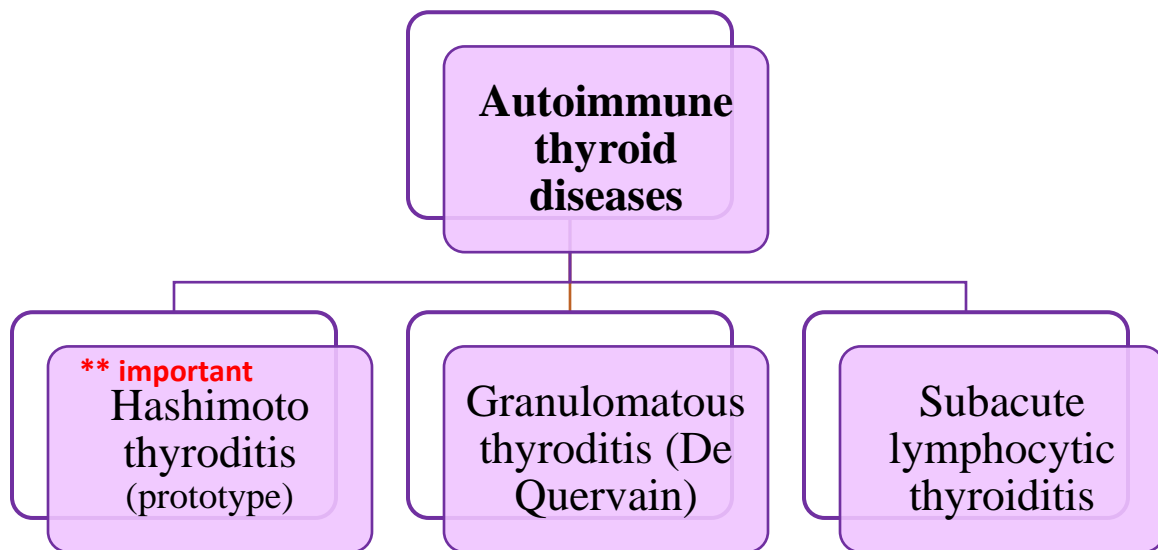
Muscle Weakness

Breast Development in Men

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- Severe untreated hypothyroidism is one of the causes of depression.
- 3pm crash: afternoon those patients feel extremely tired.
- When you see these symptoms, you start to investigate to diagnose the patient with hypothyroidism or hyperthyroidism.

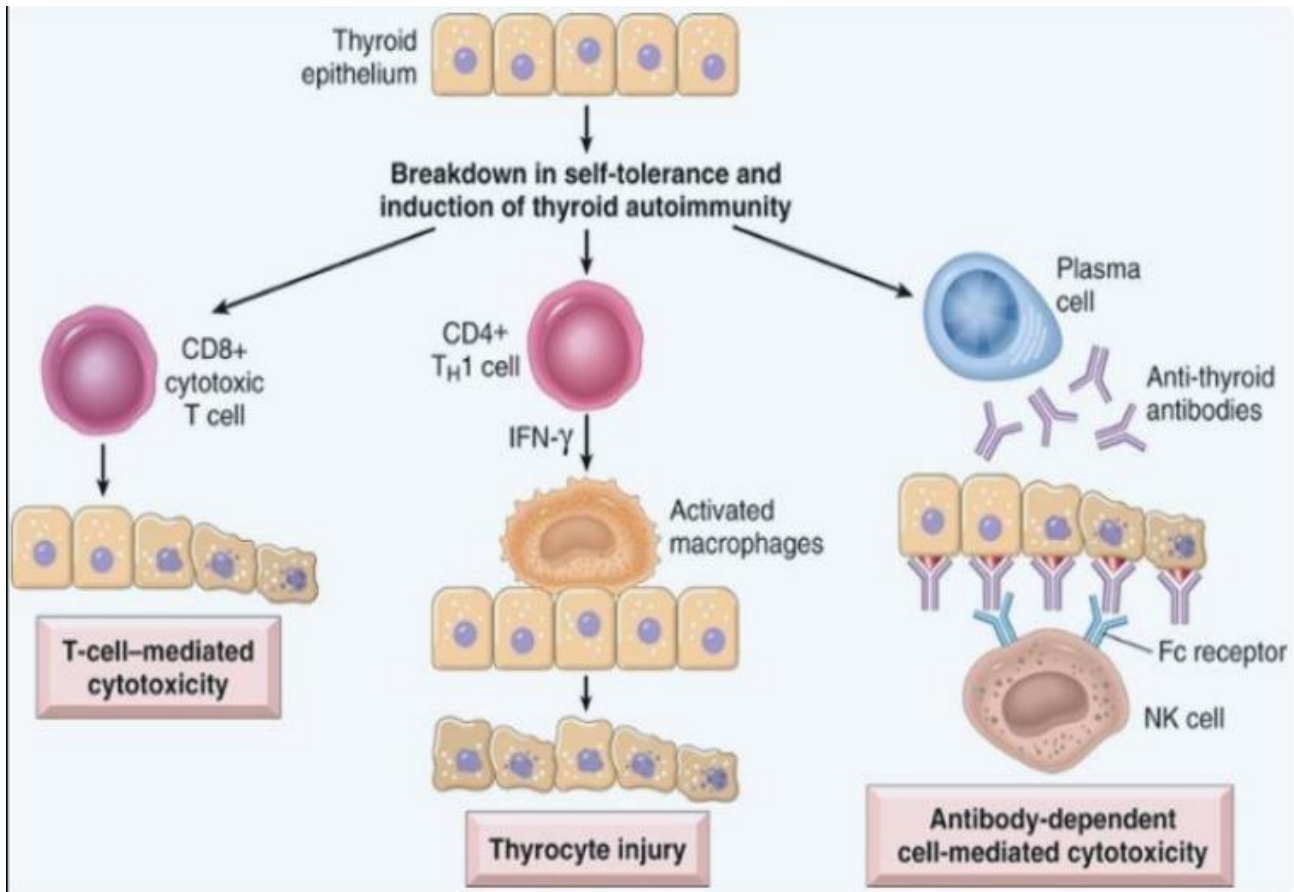


- Read the paper, doctor said there are questions about it in the exam:  
[Hashimoto-review.pdf \(jumedicine.com\)](https://www.jumedicine.com/Hashimoto-review.pdf)

## Hashimoto Thyroiditis (Chronic Lymphocytic Thyroiditis)

- It's a common **chronic** disease.
- Most common cause of hypothyroidism in areas with no iodine deficiency. (Considering that there is no iodine deficiency in the world, it's **the most common cause of hypothyroidism**).
- **Gradual** hypothyroidism (rarely initial transient Hashitoxicosis).  
It doesn't happen suddenly, starts with the inflammatory response → increased T3, T4 → euthyroid → hypothyroid → chronicity (repair and fibrosis) thyroid become fibrotic no secretion of T3, T4 → hypothyroidism.  
(Hashitoxicosis → initial thyrotoxicosis due to Hashimoto)
- More common in middle aged females (45-60 years).
- **Autoimmune** destruction of thyroid epithelial cells, **anti-thyroid antibodies** (serological test: anti-thyroid antibodies)
- 4-6 times increased risk for **papillary thyroid carcinoma** (most common malignancy in thyroid) and **B-cell NH lymphoma** (primary non-Hodgkin).

## Pathogenesis:



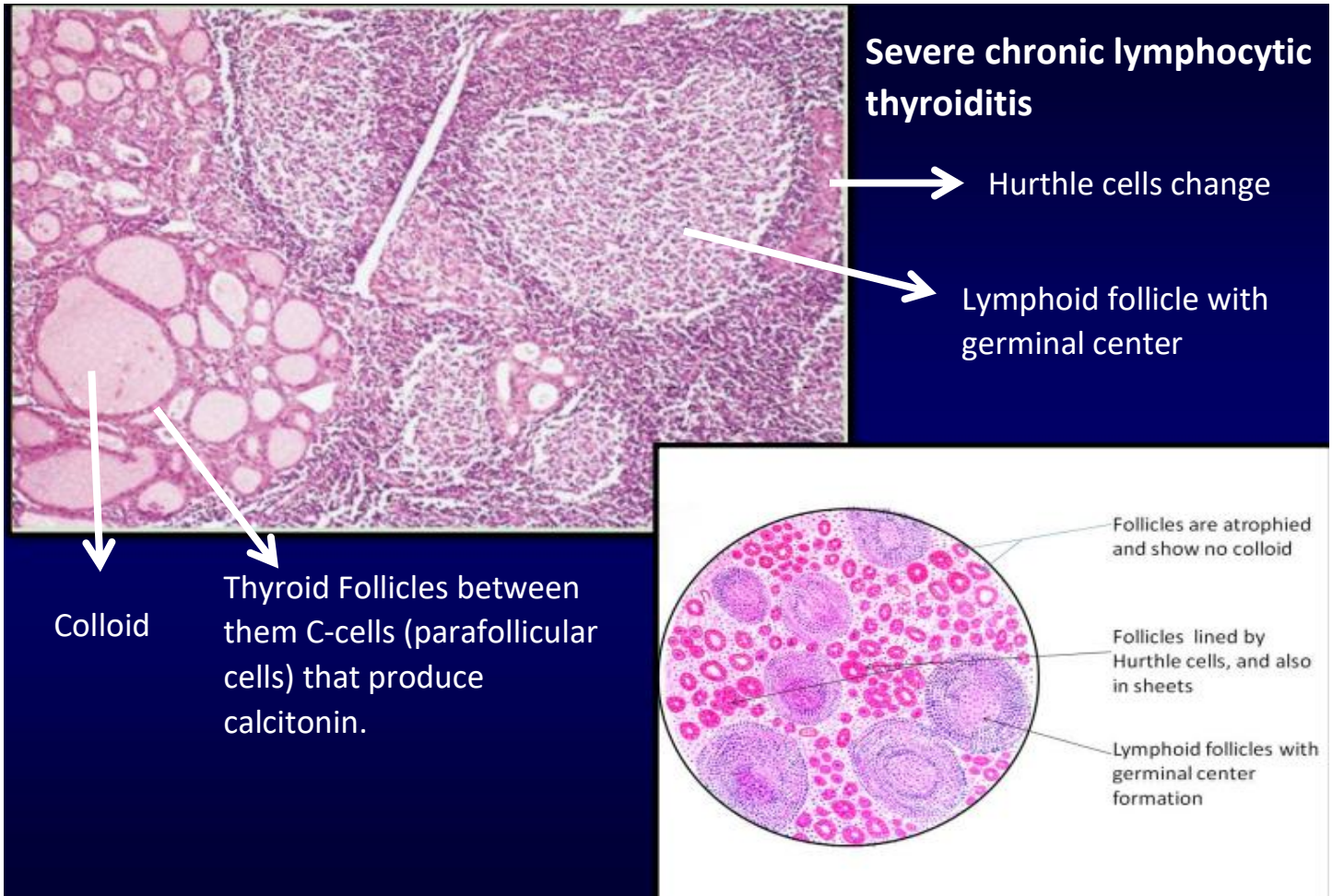
- ❖ Some factors that induce autoimmunity causes your immune system to get stimulated to damage your own thyroid cells.
- ❖ **Anti-thyroid antibodies** are not the only mechanism leading to Hashimoto thyroiditis there are also **T cell mediated cytotoxicity (CD8+ T cells)** and **thyrocyte injury (CD4+ TH1 cells)** but there is no test for these two.
- ❖ That's why sometimes the anti-thyroid antibodies test is negative, but the patient has Hashimoto thyroiditis because of one of the other mechanisms.

\*\*\*\***not all Hashimoto thyroiditis patients are anti-thyroid antibodies positive.**

\*\*\*\* **T/F: 100% of Hashimoto patients have circulating antibodies ← FALSE**



## Histologically:



### ❖ **Thyroid endocrine organ secretes 2 major hormones:**

- 1) T3, T4 together from follicular and epithelial cells.
- 2) Calcitonin from parafollicular cells.

### ❖ **2 different cancers can happen in the thyroid gland:**

- 1) Thyroid cancer → cell of origin: follicular cells.
- 2) Medullary thyroid carcinoma (MTC) → cell of origin: para-follicular cells.

### ❖ **Colloid:** pink material (eosinophilic) where there are no cells only proteins and raw materials (iodine one of them) used to synthesize hormones (T3, T4).

### ❖ **Hurthle cell change (oncocytic cell change)** in the epithelial cells of thyroid cytoplasm becomes larger and granular and full of mitochondria; that's why it's pink (eosinophilic) can be seen in histology and fine needle aspiration (FNA).



## Histological features of Hashimoto thyroiditis:

- 1- Lymphocytic thyroiditis
- 2- Hurthle cell change.

**Diagnosis:** clinical presentation → serological test → histology.

## Subacute Granulomatous (de quervain) Thyroiditis

- Subacute implies that it's somewhere between acute and chronic.
- Granulomatous thyroiditis, more acute with **neck pain, firm thyroid**.  
(Differs from Hashimoto that it's **painful**), Patient came with painful anterior neck swelling and fine needle aspiration revealed colloid and granulomas → subacute granulomatous.
- Could be virally associated or induced but the etiology is unknown.
- More common in middle aged females, 30-50 years.
- Maybe initial transient thyrotoxicosis (doesn't last long) followed by hypothyroidism
- Self-limiting disease (6-8 weeks), either self-limited or there will be thyroid damage and there will be hypothyroidism → replacement therapy and watch for future malignancy.

## OTHER LESS COMMON THYROIDITIS:

### 1- Subacute lymphocytic thyroiditis:

- Some believes that it's a variant of Hashimoto.
- Middle aged women.
- Post-partum.
- Initial transient thyrotoxicosis then gradual hypothyroidism.
- Autoimmune with circulating antibodies.
- Gland is usually normal size (no mass).
- Lymphocytic thyroiditis **no hurthle cells**; that's why Hashimoto is excluded.

## 2- Riedel thyroiditis:


- **IgG4 associated disease** can occur anywhere (pancreas, mesentery,...) there would be a lot of plasma cells full of IgG4 which cause **sclerosis (fibrosis)**.
- What's special about it is: **stony-hard thyroid** due to severe fibrosis, so thyroid is destroyed >> Hypothyroidism >> decreased T3, T4, increased TSH and no antibodies (even CD4, CD8 are negative).
- Very rare and not easy to diagnose.

## Graves Disease (diffuse toxic goiter)


- Described by Robert Graves in 1835.
- **Most common cause of endogenous hyperthyroidism.**
- Triad for the diagnosis: thyrotoxicosis (high T3, T4, low TSH) + ophthalmopathy (exophthalmos) + dermopathy (pretibial myxedema) specially in the chin.
- Autoimmune, HLA-DR3 and CTLA-4.
- High homogenous radioactive iodine uptake.
- Women, 20-40 years.

### GRAVES DISEASE


Autoimmune disease that destroys the thyroid gland




Women to men ratio is 8:1




1<sup>st</sup> described by Robert Graves in 1835




Affects 6 per 1000 persons in the US




Causes 50-80% cases of hyperthyroidism in the US




Fatigue is present in 70% of the patients




Palpitations and weight loss are seen in 50% of the patients




Other symptoms include heat intolerance, hair loss & hand tremor




Diagnosed by blood tests & radiography of thyroid gland

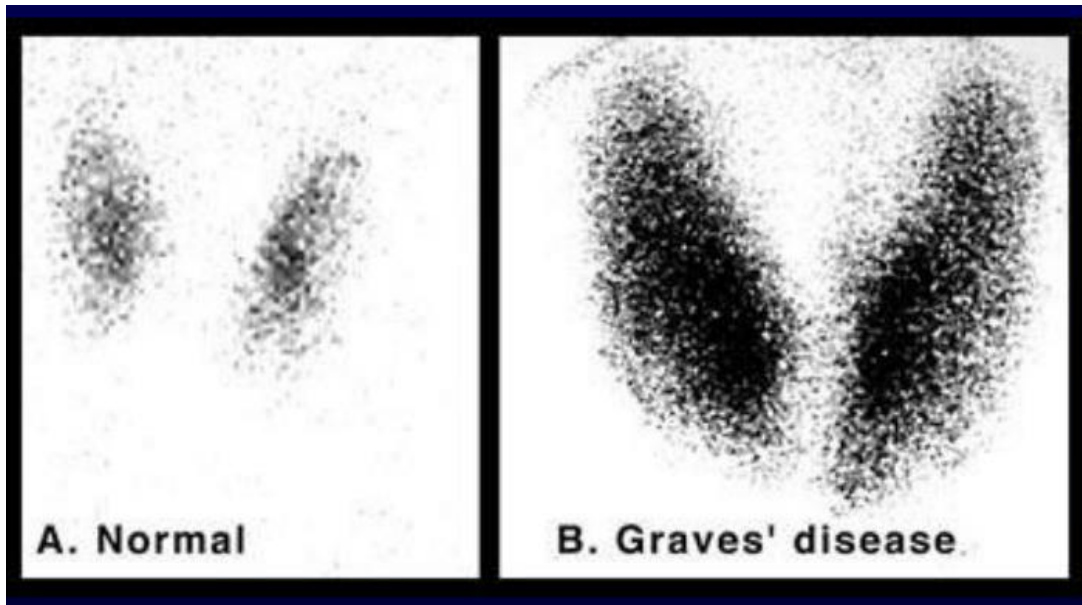


Treatment includes radioiodine therapy, medications & thyroid surgery

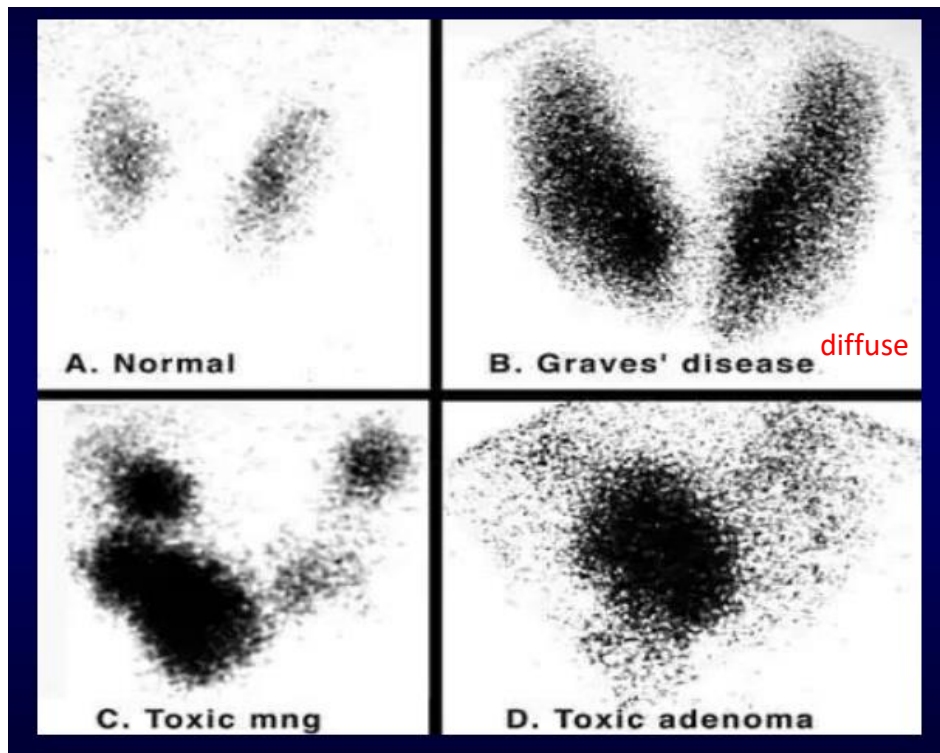


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## Radioactive Iodine Uptake (RAIU) Scan/Test



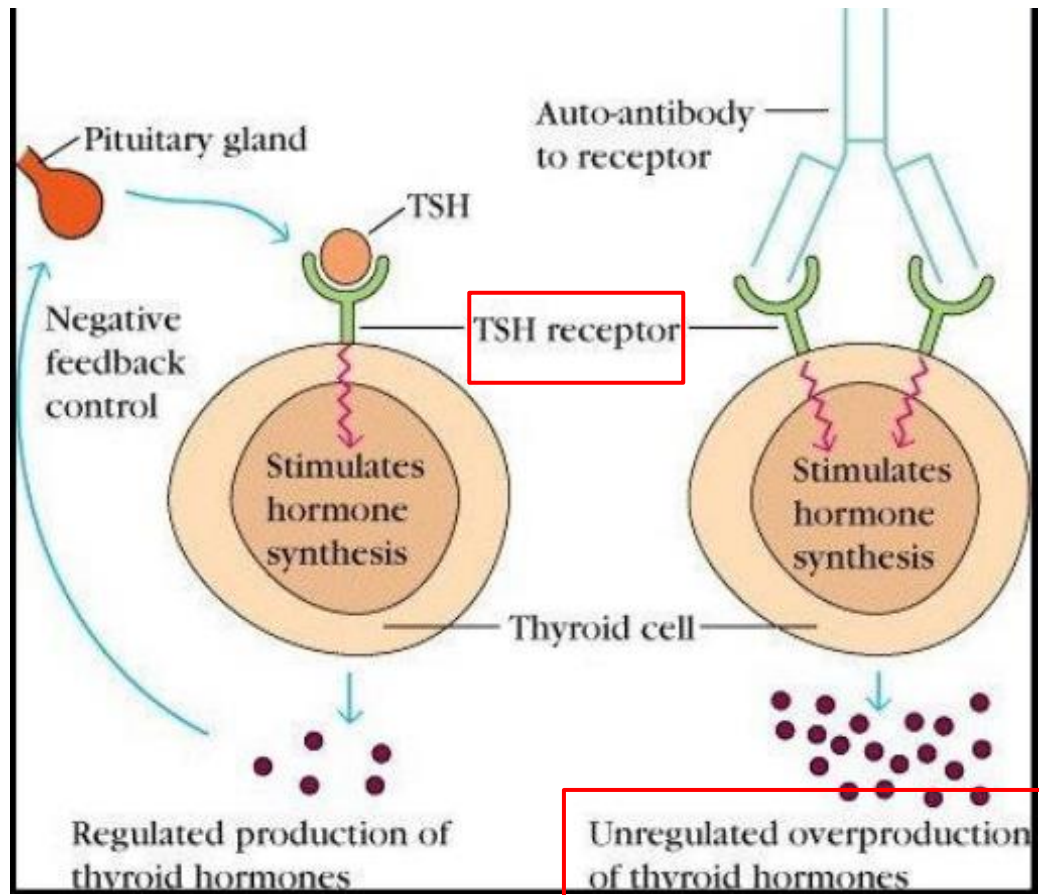
- If a patient came and doctors doubted that he has a problem in thyroid uptake, a **radioactive iodine** will be given in vein and then a camera will detect the **activity (black dots)**.
- Comparing A(normal) and B (grave's disease), B has high uptake and it's diffuse (in all the thyroid), increased uptake in both lobes.
- Questions doctor would ask:
  - 1- Scenario: A female patient came with heat intolerance, palpitation, short temper, irritable, shivering, sweating, diarrhea, and menstrual cycle abnormality, and the T3, T4 test showed high T3, T4 and low TSH and the iodine uptake was as the picture above then the diagnosis is → Graves disease.
  - 2- If a patient was diagnosed with graves disease what is the RAIU expected? Figure B.
  - 3- What is the T3, T4 levels depending on figure B? High T3, T4 low TSH.



- In figure C (toxic MNG) the increase in uptake isn't in the whole lobe. (rare)
- In figure D (toxic adenoma): hot nodules, risk of malignancy is almost zero.

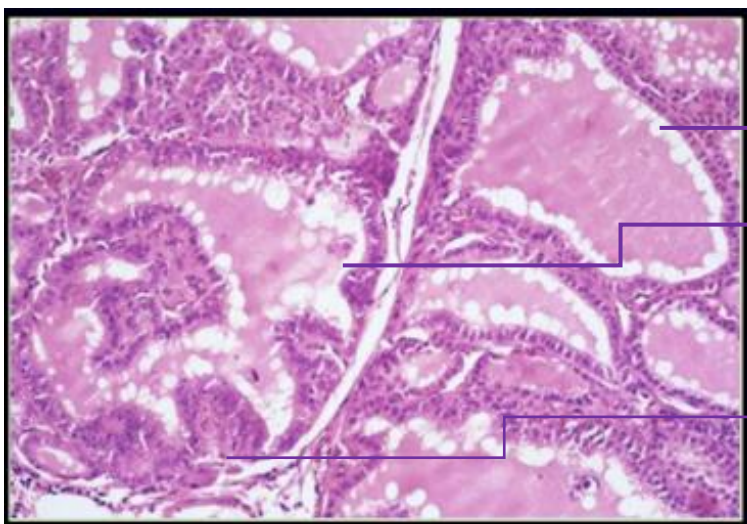


## Autoantibodies for Graves disease:



- ❖ Autoantibodies bind to TSH receptor and inhibit the negative feedback → continuous secretion of T<sub>3</sub>, T<sub>4</sub>.

+Sometimes TSH-binding inhibitor Ig, may cause hypothyroidism (written in the slides but doctor said forget about it)



Scalloping follicles (colloid is white) indicates hyperactivity, a characteristic of thyroid disease

Follicular epithelial cells take the colloid to synthesize T<sub>3</sub>, T<sub>4</sub>.

Papillary hyperplasia

- ❖ Complications should not be seen nowadays; because of early detection.

### Exophthalmos



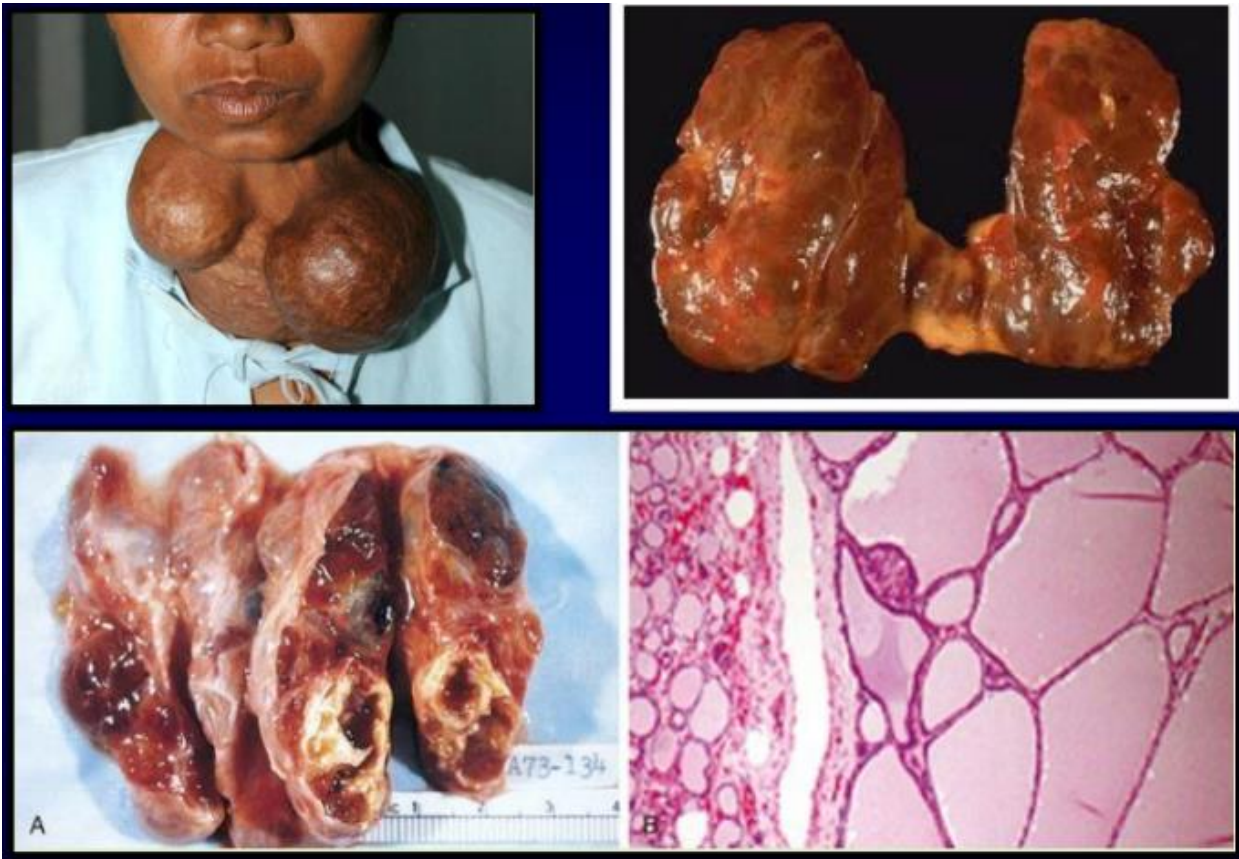
### Pretibial myxedema



## Diffuse and Multinodular Goiter:

- Very common; **most common thyroid disease (euthyroid MNG).**
- Thought to be caused because of impaired hormone synthesis, iodine deficiency, but the etiology is unknown.
- Sometimes high TSH, hyperplasia & hypertrophy.
- In most cases; **euthyroid** no problem in T3, T4 or TSH; rarely goitrous hypothyroidism.
- Endemic or sporadic.
- More common in Females
- **Initially diffuse then multinodular.**
- Clinically: mass effects, pressure symptoms (difficulty in swallowing, drinking, and snoring at night) and cosmetic.
- Rare: toxic MNG (Plummer syndrome).

## euthyroid



## Nodules and hemorrhage

**A FINAL NOTE:** almost all thyroid diseases are more common in females, reason unknown.

# The End.