THYROID DISORDERS

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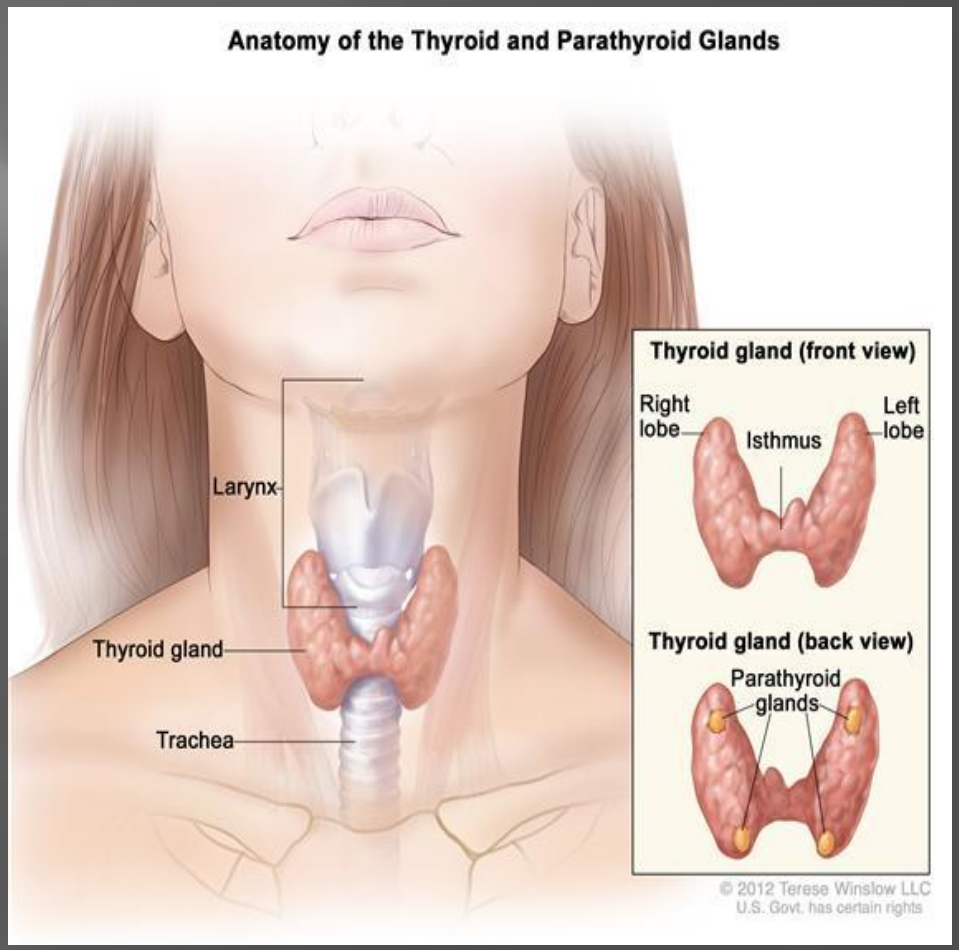
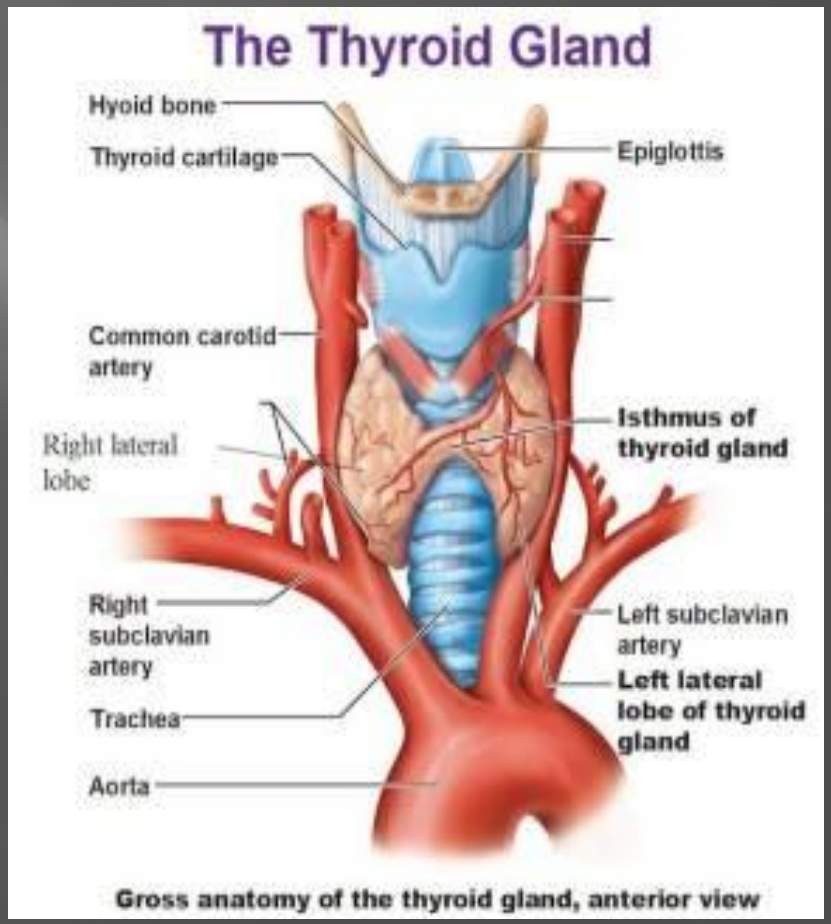
Introduction

- The thyroid is one of the largest of the endocrine organs, weighing approximately 15 to 20 g.
- It has a tremendous potential for growth → termed a *goiter,* can weigh many hundreds of grams.



- The normal thyroid is made up of two lobes joined by a thin band of tissue, the isthmus.
- Two pairs of vessels constitute the major arterial blood supply, the superior thyroid artery, arising from the external carotid artery, and the inferior thyroid artery, arising from the subclavian artery.

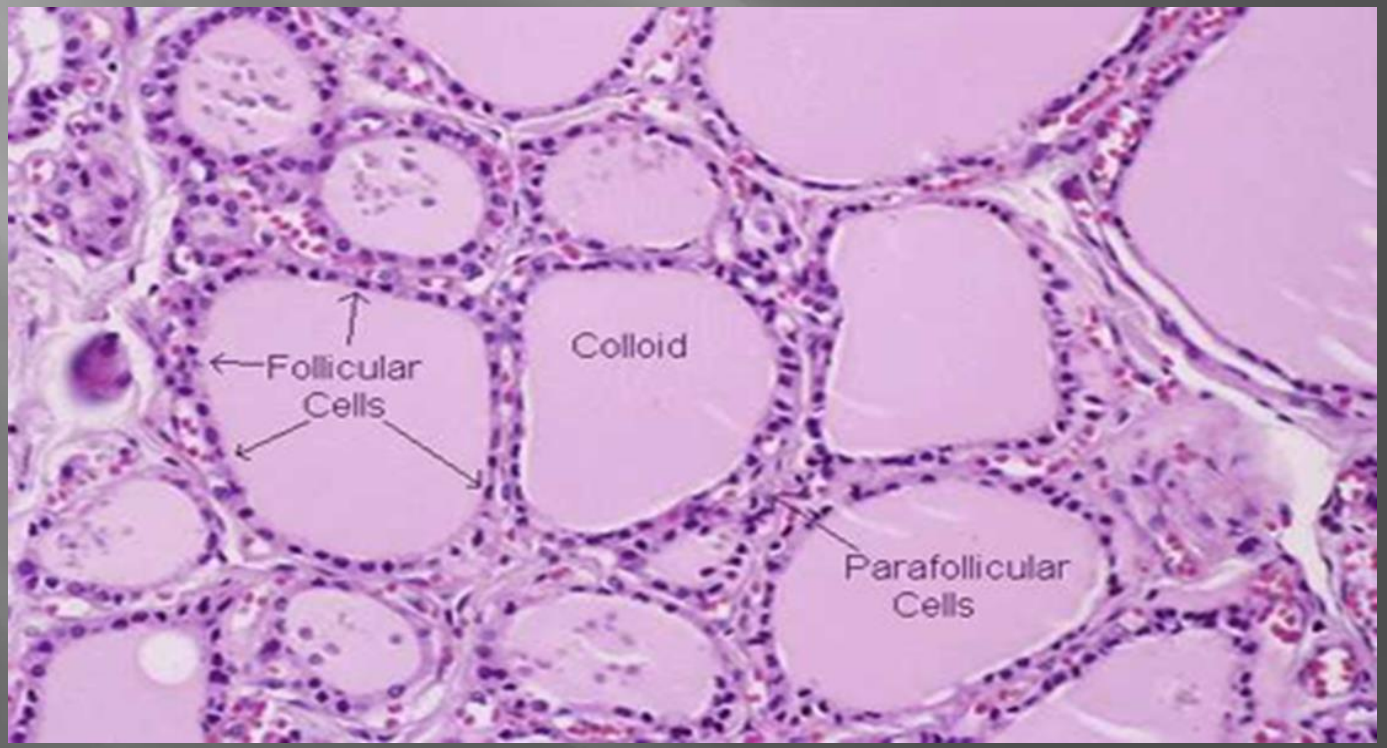


- Estimates of thyroid blood flow range from 4 to 6 mL/min/g, well in excess of the blood flow to the kidney (3 mL/min/g). In diffuse toxic goiter due to Graves' disease, blood flow may exceed 1 L/min and be associated with an audible bruit or even a palpable thrill.

- The gland is composed of closely packed spherical units termed *follicles,* which are invested with a rich capillary network. The interior of the follicle is filled with the clear proteinaceous colloid that normally is the major constituent of the total thyroid mass.

- On cross section, thyroid tissue appears as closely packed ring-shaped structures consisting of a single layer of thyroid cells surrounding a lumen.

- The thyroid also contains para-follicular cells, or C cells, that are the source of calcitonin.
- The C cells undergo hyperplasia early in the syndrome of familial medullary carcinoma of the thyroid (MEN2) and give rise to this tumor in both its familial and its sporadic forms



(A) Normal thyroid gland. (B) Normal thyroid follicles. (C) Parafollicular cells. Calcitonin immunostain.

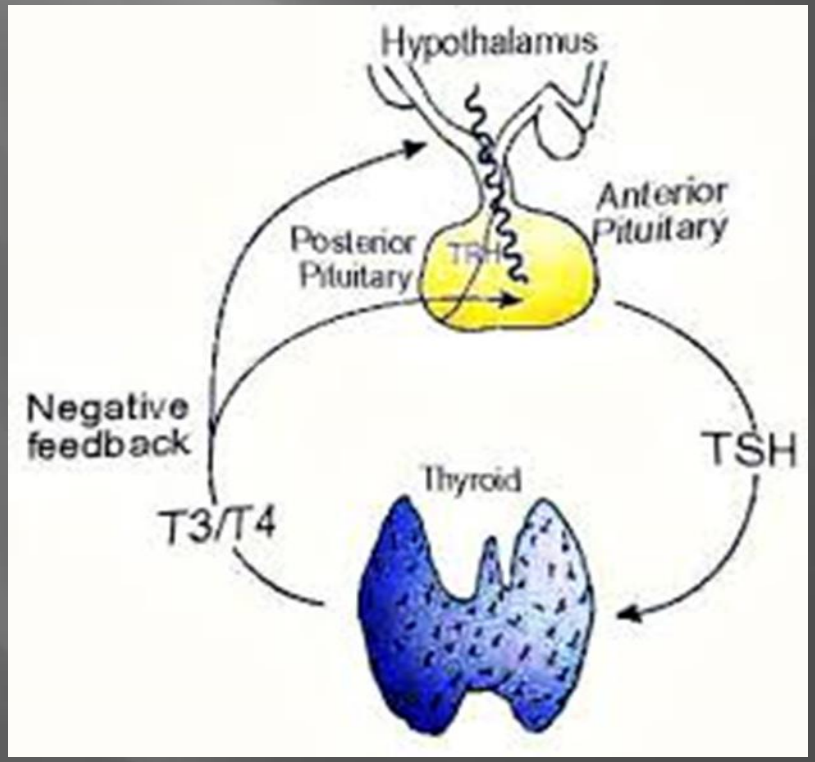
Laboratory/Radiologic assessment of thyroid Status

- Goal is to assess the functional and anatomic status.
- Laboratory determinations will confirm whether there is an excess, normal, or insufficient supply of thyroid hormone to verify the inferences from the clinical history and physical examination.

- Laboratory/radiologic tests can be divided into four major categories:

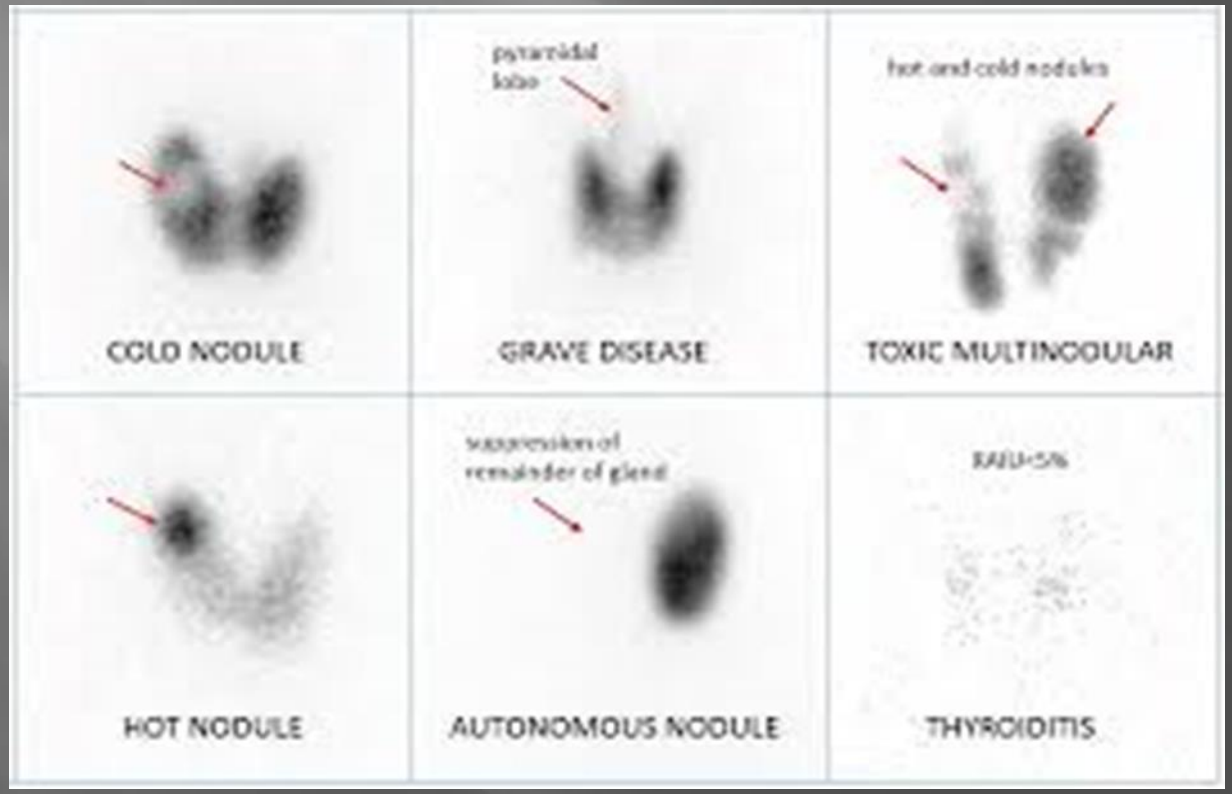
(1) Those that assess the state of the hypothalamic-pituitary-thyroid axis.

(2) Tests that reflect the impact of thyroid hormone on tissues.



(3) Tests for the presence of autoimmune thyroid disease.

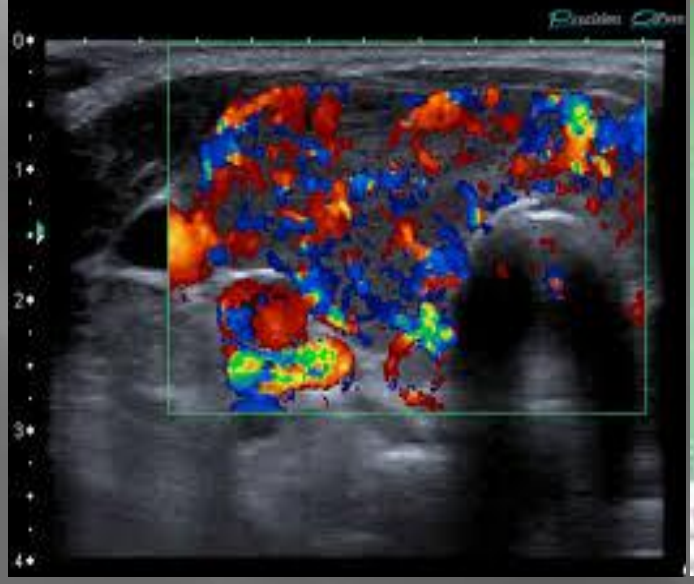
(4) Tests that provide information about thyroidal iodine metabolism. The use of iodine and other isotopes for scintiscanning.



Physiologic state	Serum TSH	Serum Free T4	Serum T3	24-h radioiodine uptake
Hyperthyroidism, untreated	Low	High	High	High
Hyperthyroidism, T3 toxicosis	Low	Normal	High	Normal or High
Primary Hypothyroidism, untreated	High	Low	Low or Normal	Low or Normal
Hypothyroidism secondary to pituitary disease	Low or Normal	Low	Low or Normal	Low or Normal
Euthyroid, on exogenous thyroid hormone	Normal	Normal on T4, Low on T3	High on T3, Normal on T4	Low

THYROTOXICOSIS


A
B


0
1
2
3
4


C

Causes of Thyrotoxicosis

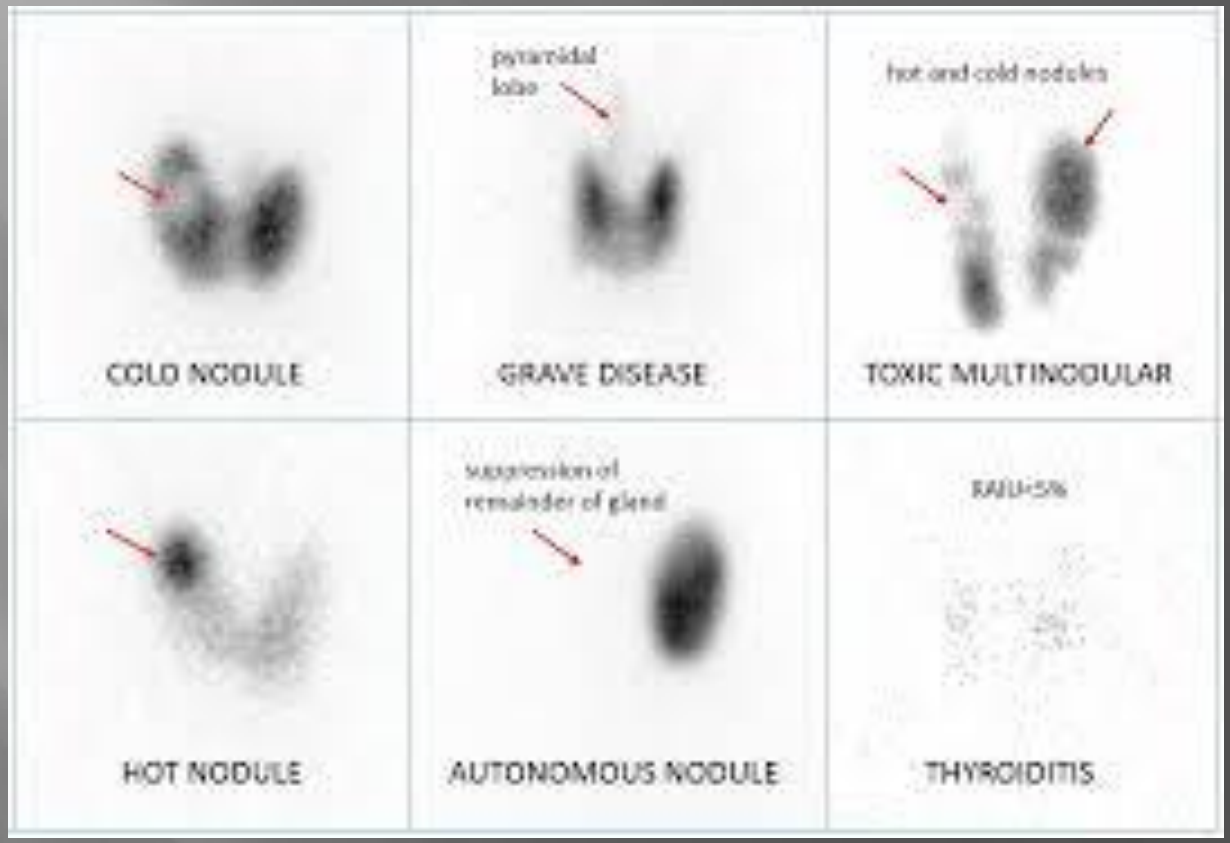
- **Disorders with increased Iodine uptake:**

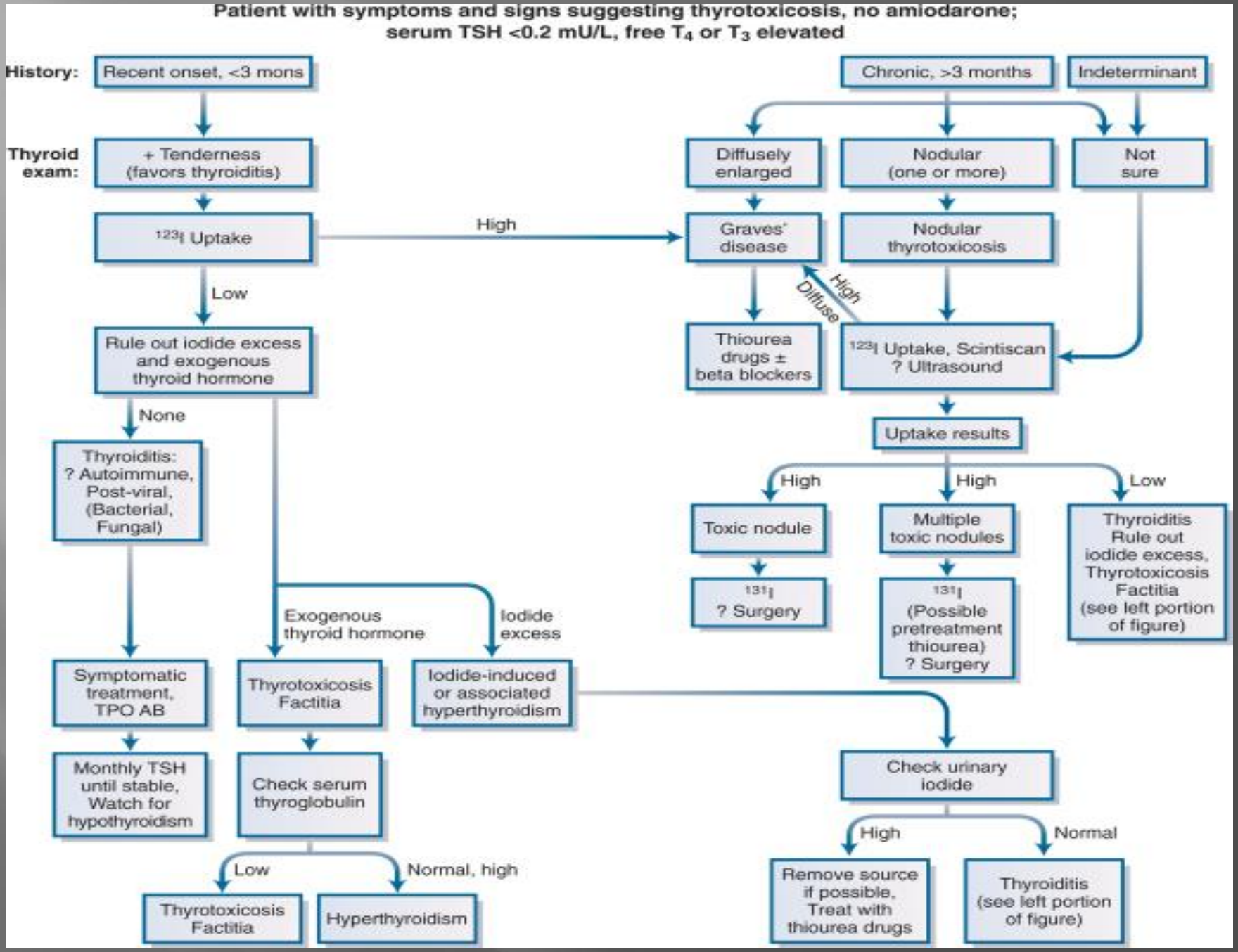
1. Graves' disease
2. Toxic MNG/adenoma
3. Inherited non-immune hyperthyroidism
4. Hyperthyroidism due to thyrotropin secretion (TSH-oma).
5. HCG-induced hyperthyroidism – Associated with pregnancy or Trophoblastic Tumors

DO NOT DO THYROID UPTAKE AND SCAN DURING PREGNANCY.

Disorders with decreased Iodine uptake:

1. Sub-acute thyroiditis.
2. Iatrogenic thyrotoxicosis
3. Strauma ovarii
4. Metastatic thyroid carcinoma


pyramidal lobe
hot and cold nodules
COLD NODULE
GRAVE DISEASE
TOXIC MULTINODULAR
suppression of remainder of gland
RAIU<5%
HOT NODULE
AUTONOMOUS NODULE
THYROIDITIS


Patient with symptoms and signs suggesting thyrotoxicosis, no amiodarone; serum TSH <0.2 mU/L, free T_4 or T_3 elevated
History:
Recent onset, <3 mons
Chronic, >3 months
Indeterminant
Thyroid exam:
+ Tenderness (favors thyroiditis)
Diffusely enlarged
Nodular (one or more)
Not sure
^{123}I Uptake
High
Graves' disease
Nodular thyrotoxicosis
Low
High
Diffuse
Rule out iodide excess and exogenous thyroid hormone
Thiourea drugs ± beta blockers
^{123}I Uptake, Scintiscan ? Ultrasound
None
Uptake results
Thyroiditis: ? Autoimmune, Post-viral, (Bacterial, Fungal)
High
High
Low
Toxic nodule
Multiple toxic nodules
Thyroiditis Rule out iodide excess, Thyrotoxicosis Factitia (see left portion of figure)
^{131}I ? Surgery
^{131}I (Possible pretreatment thiourea) ? Surgery
Exogenous thyroid hormone
Iodide excess
Symptomatic treatment, TPO AB
Thyrotoxicosis Factitia
Iodide-induced or associated hyperthyroidism
Monthly TSH until stable, Watch for hypothyroidism
Check serum thyroglobulin
Check urinary iodide
Low
Normal, high
High
Normal
Thyrotoxicosis Factitia
Hyperthyroidism
Remove source if possible, Treat with thiourea drugs
Thyroiditis (see left portion of figure)

Treatment?

- **In cases of Graves' disease, toxic MNG or adenoma:**

1. Anti-thyroid medications, i.e carbimazole
2. I131 treatment
3. Surgery
4. Temporary beta blockers for symptoms control.

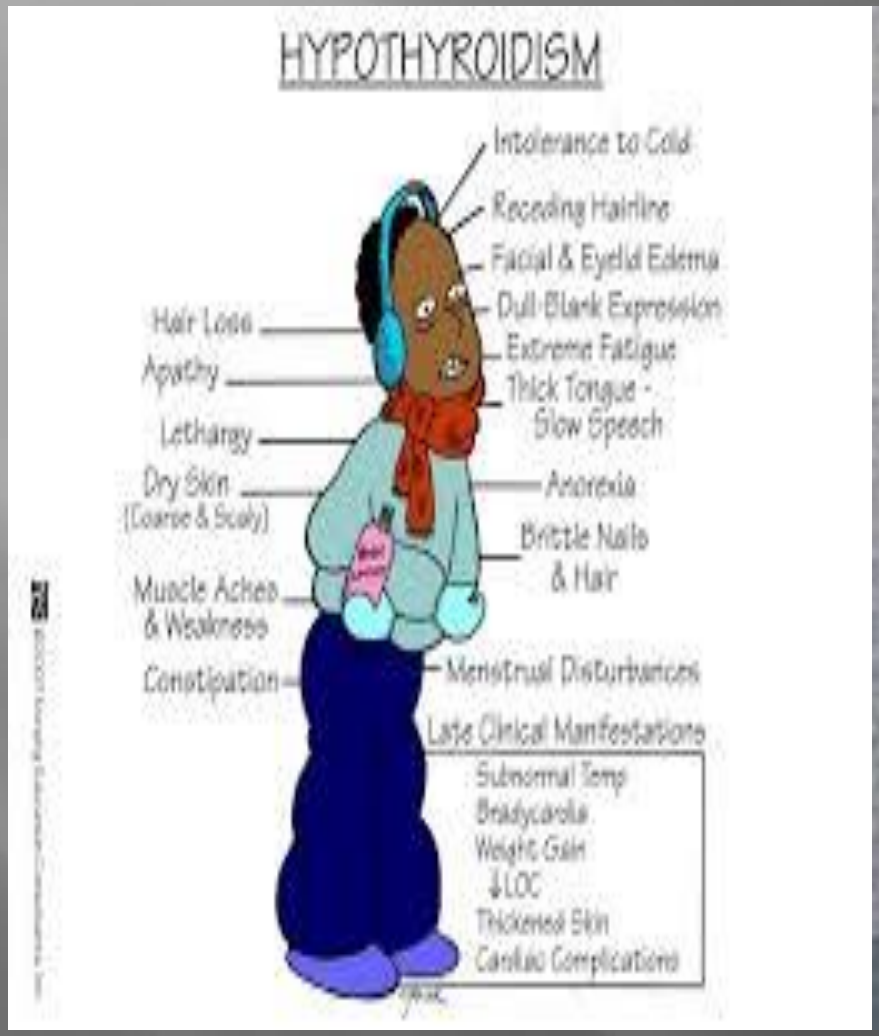
- **In cases of subacute thyroiditis** → Temporary beta blockers, NSAID's and/or steroids for symptoms control.

THYROID STORM/THYROID CRISES

- An acute, life-threatening, hypermetabolic state induced by excessive release of thyroid hormones.
- Presentation: Fever, tachycardia, HTN , and neurological and GI abnormalities.

- Rapid diagnosis and aggressive treatment are critical.
- Diagnosis is primarily clinical
- Management: Supportive measures, Propylthiouracil and Beta blockers.

Hypothyroidism



Typical appearance with moderately severe primary hypothyroidism or myxedema

Causes of hypothyroidism

1. Hashimoto's thyroiditis.
2. Post total thyroidectomy.
3. Post I131 treatment
4. Congenital, i.e Thyroid agenesis or dysplasia,
5. Medications, i.e Lithium and Amiodarone.
6. Iodine deficiency
7. Central hypothyroidism
8. Thyroid infiltration, i.e Riedel's struma, amyloidosis, and hemochromatosis

Physiologic state	Serum TSH	Serum Free T4	Serum T3	24-h radioiodine uptake
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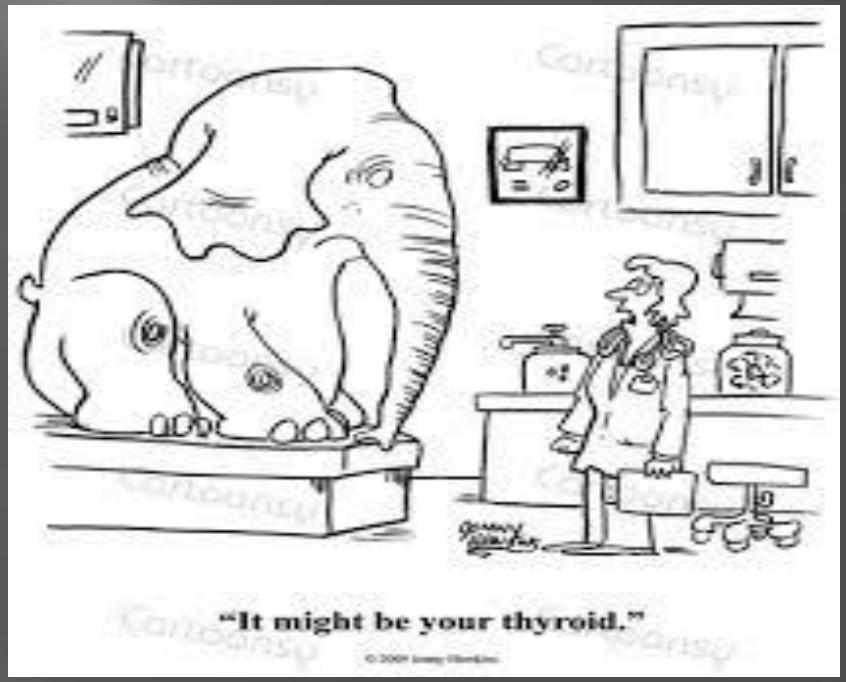
Treatment

- Levothyroxine replacement.
- No need for additional T3 replacement.
- In older people with history of CAD, start with a low dose and then titrate dose up slowly.



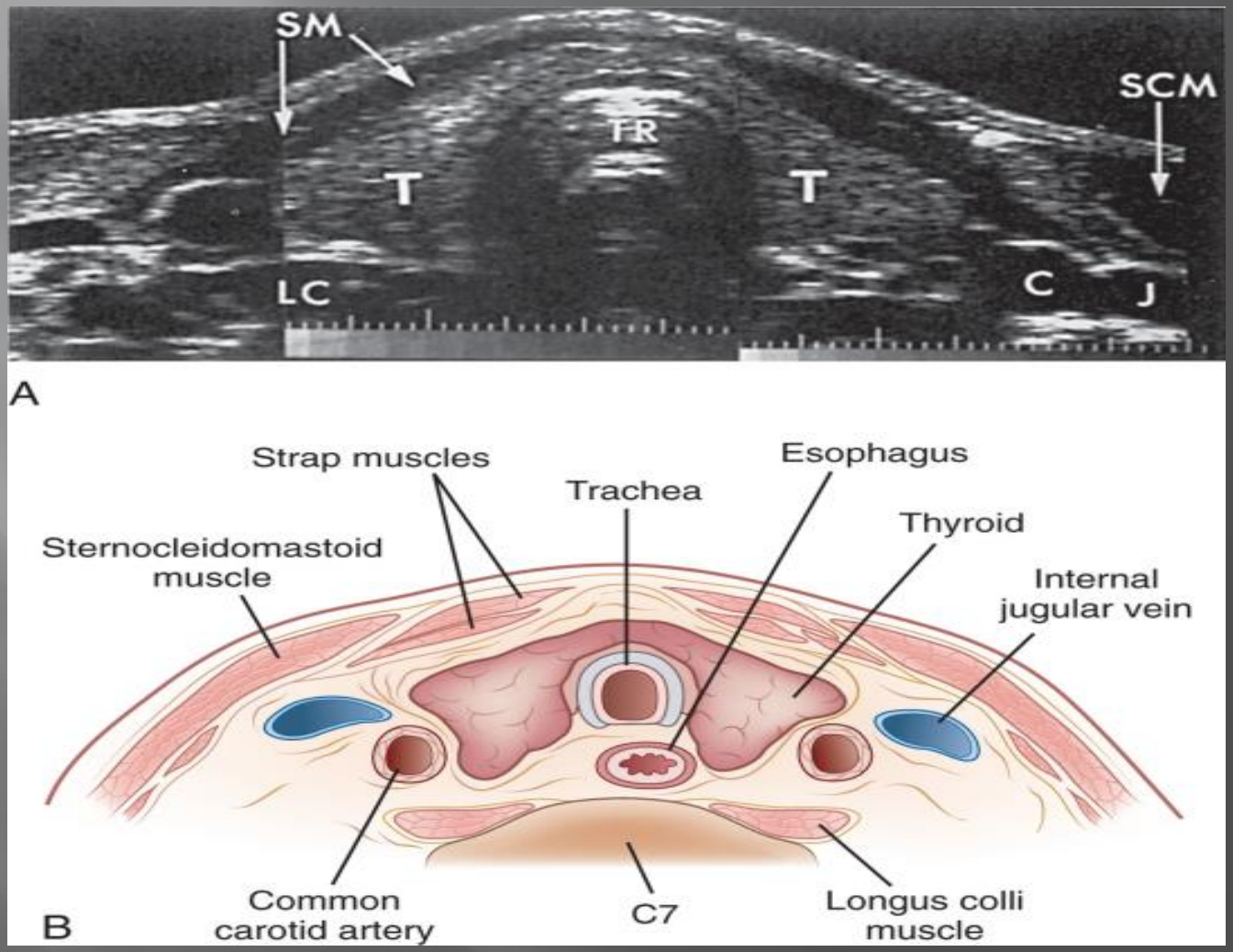
Myxedema coma/Myxedema crises

- An uncommon but a life-threatening form of untreated hypothyroidism with physiological decompensation.
- The condition occurs in patients with long-standing, untreated hypothyroidism and is usually precipitated by a secondary insult, such as climate-induced hypothermia, infection, or another systemic condition, or drug therapy.

- Patients with myxedema coma have changes in their mental status, including lethargy, stupor, delirium, or coma.
- Treatment:

- Supportive measures
- IV levothyroxine
- In light of the possibility of adrenal insufficiency, stress steroid replacement *after* a cortisol level is obtained.

NONTOXIC DIFFUSE AND NODULAR GOITER AND THYROID NEOPLASIA

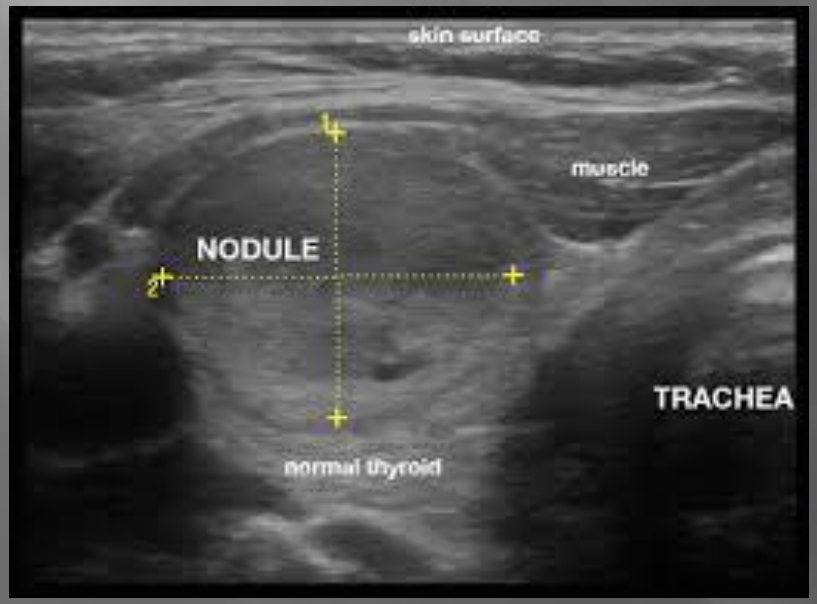


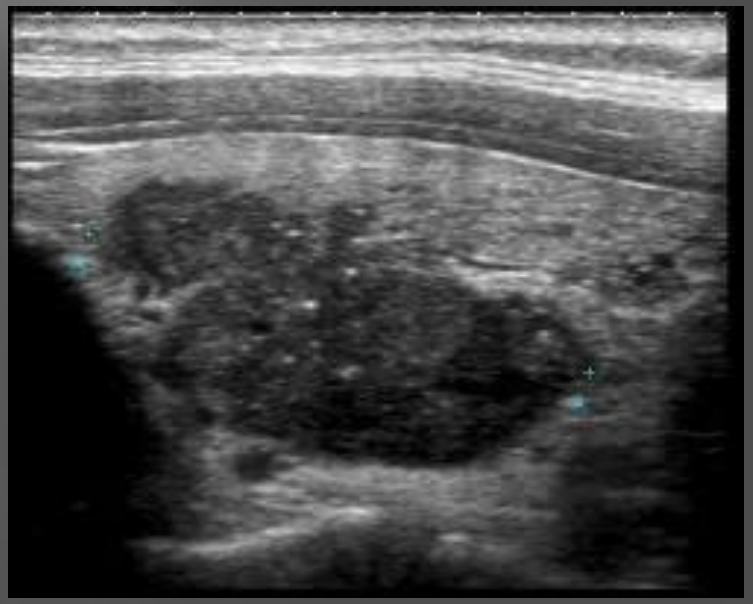
NONTOXIC GOITER: DIFFUSE AND NODULAR

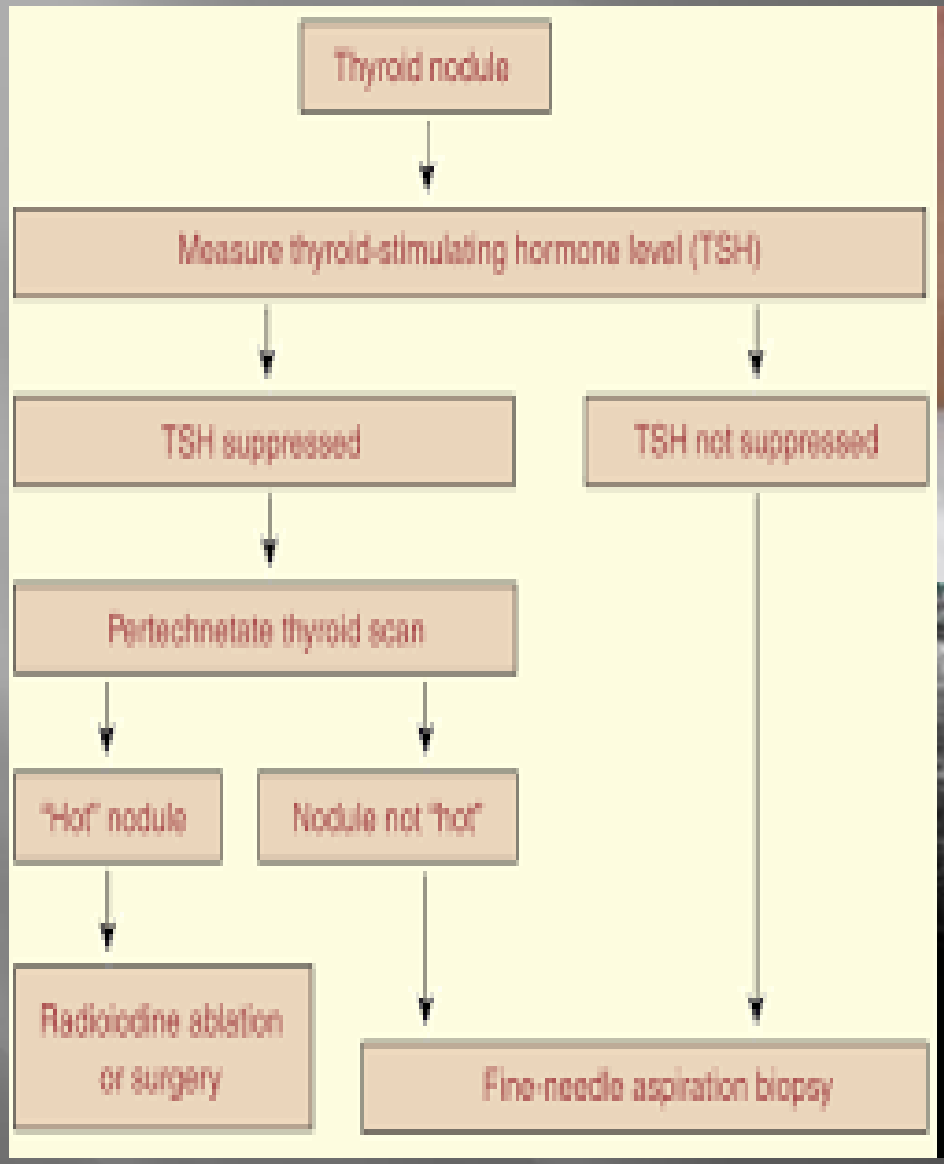
- Nontoxic goiter may be defined as any thyroid enlargement characterized by uniform or selective growth of thyroid tissue that is not associated with overt hyperthyroidism or hypothyroidism and that does not result from inflammation or neoplasia.
- A thyroid nodule is defined as a discrete lesion within the thyroid gland that is due to an abnormal focal growth of thyroid cells.
- **Risk factors:**

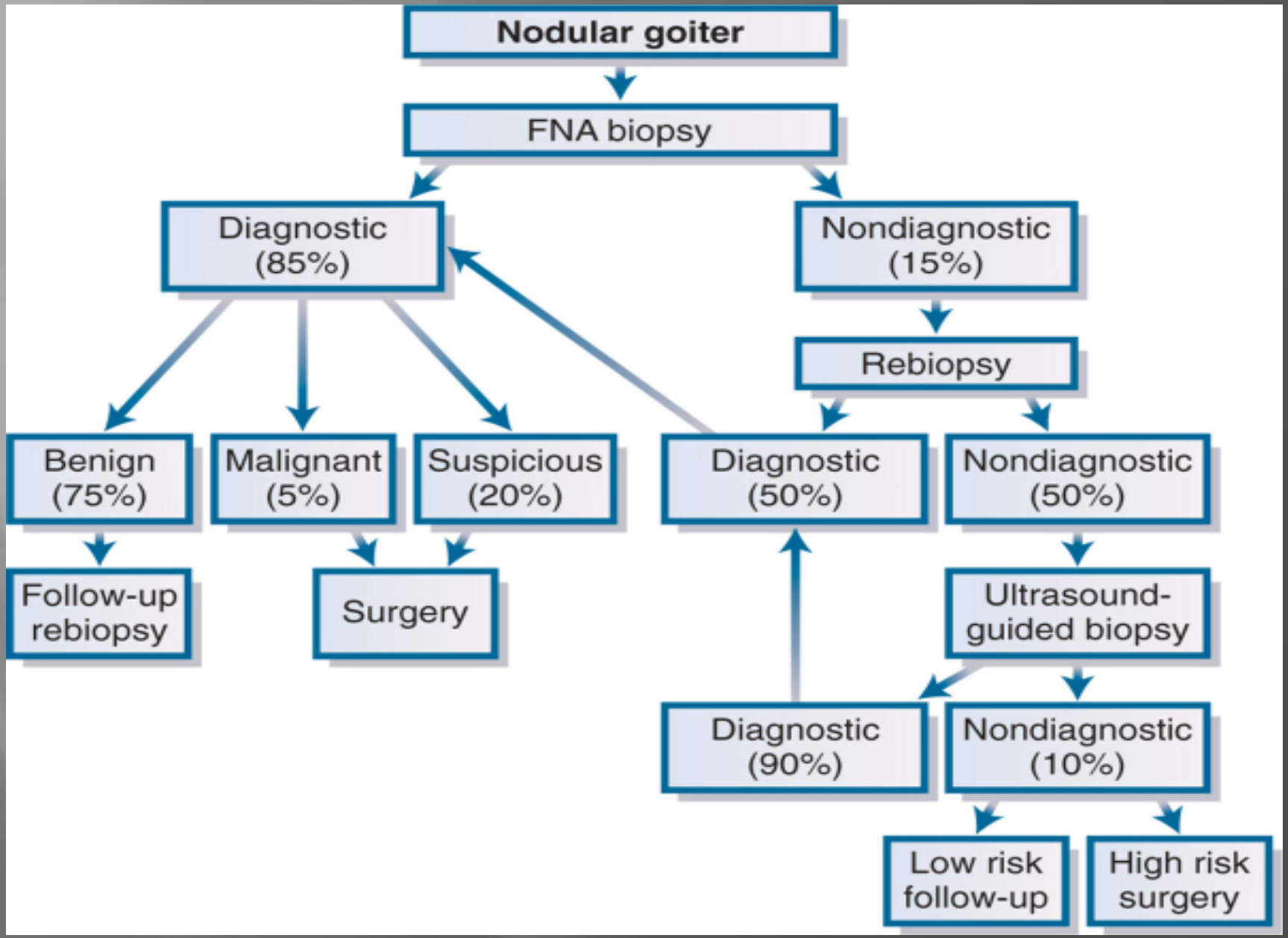
- Familial
- Iodine deficiency
- Smoking
- Alcohol
- Older age
- Female sex
- Hx of uterine fibroids


General
Chronic thyroiditis


skin surface
muscle
NODULE
TRACHEA
normal thyroid

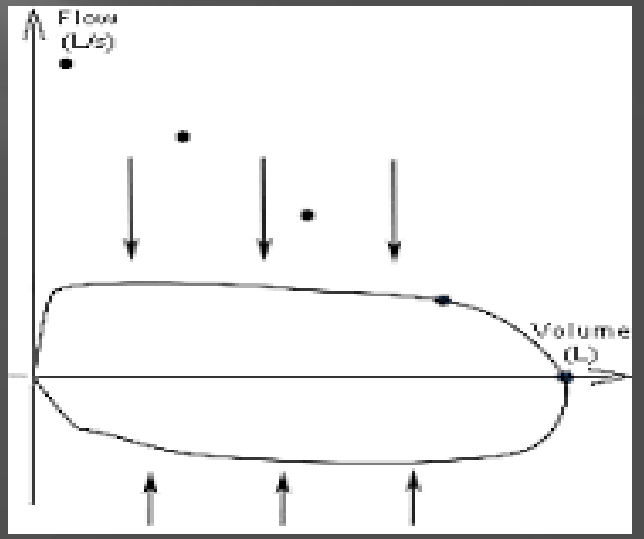



Thyroid nodule
Measure thyroid-stimulating hormone level (TSH)
TSH suppressed
TSH not suppressed
Pertechnetate thyroid scan
"Hot" nodule
Nodule not "hot"
Radioiodine ablation or surgery
Fine-needle aspiration biopsy


Nodular goiter
FNA biopsy
Diagnostic (85%)
Nondiagnostic (15%)
Rebiopsy
Benign (75%)
Malignant (5%)
Suspicious (20%)
Diagnostic (50%)
Nondiagnostic (50%)
Follow-up rebiopsy
Surgery
Ultrasound-guided biopsy
Diagnostic (90%)
Nondiagnostic (10%)
Low risk follow-up
High risk surgery

Indications for thyroid surgery

- Malignancy
- Indeterminate and/or repeatedly nondiagnostic FNA results
- Cosmetic, mostly in females
- Obstructive symptoms



Does levothyroxine treatment help in non-toxic diffuse or nodular goiter?

- The efficacy of thyroid hormone suppressive therapy in euthyroid patients with solitary benign thyroid nodules or sporadic nontoxic multinodular goiters is **controversial**.

- Most studies have shown that few thyroid nodules regress in patients taking thyroid hormone. However, suppressive therapy does appear to interfere with goitrogenesis in many patients.

- The American Thyroid Association does not recommend suppression therapy of benign thyroid nodules in iodine sufficient populations

Thyroid cancer

- The National Cancer Institute indicates that thyroid cancer is the most common type of endocrine-related cancer and estimates 60,220 new cases in 2013.
- Thyroid cancer represents approximately 3.6% of all new cancer cases.

- Although a diagnosis of thyroid or any type of cancer is frightening, the vast majority of thyroid cancers is highly treatable and in most cases curable with surgery and other treatments.

- Thyroid cancer is generally first suspected by a lump or nodule in the thyroid gland.

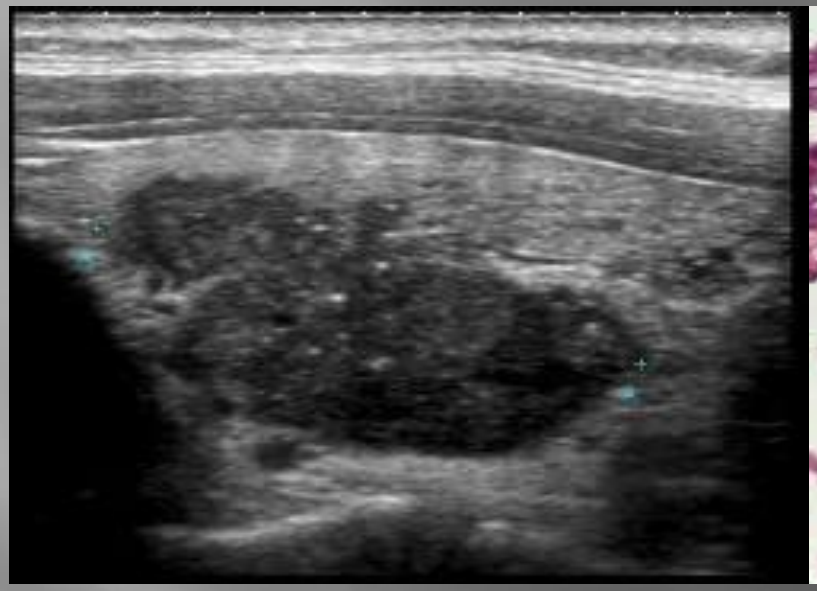
Table 1. Relative Frequencies and Mortality Rates of the Various Histological Types of Thyroid Cancer

Histological Type	Relative Frequency (%)	Cause-Specific Mortality Rates 20 Years (%)
Papillary	70 - 80	5 - 10
Follicular	15 - 25	25 - 30
Hürthie cell	2 - 5	20 - 35
Medullary	5 - 8	20 - 25
Anaplastic	4 - 10	> 95

1. Papillary Thyroid Cancer

- Most common type of thyroid cancer: 70% to 80% of all thyroid cancers are papillary thyroid cancer
- Commonly diagnosed between the ages of 30 and 50
- Females are affected 3 times more often than males
- Usually not aggressive
- May spread, but usually not beyond the neck

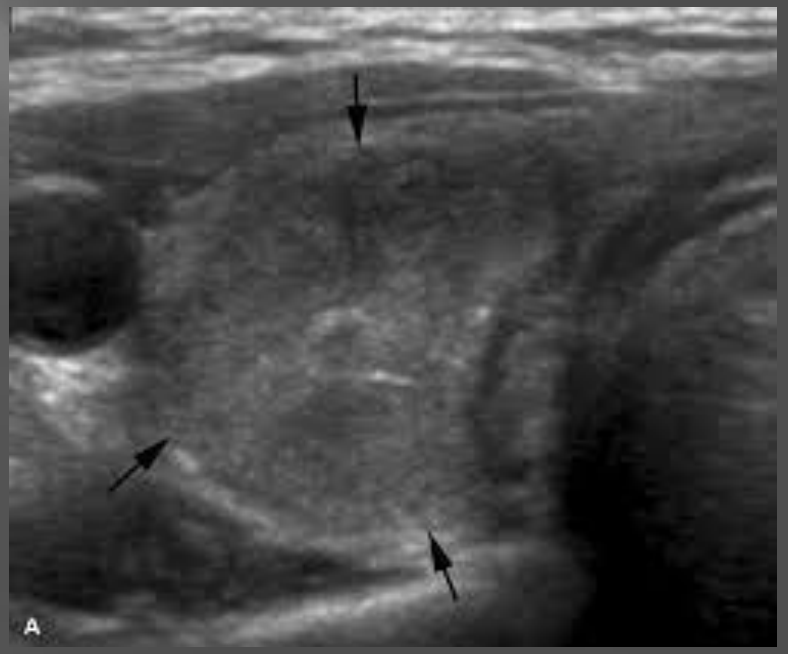
- Papillary cells resemble finger-like projections



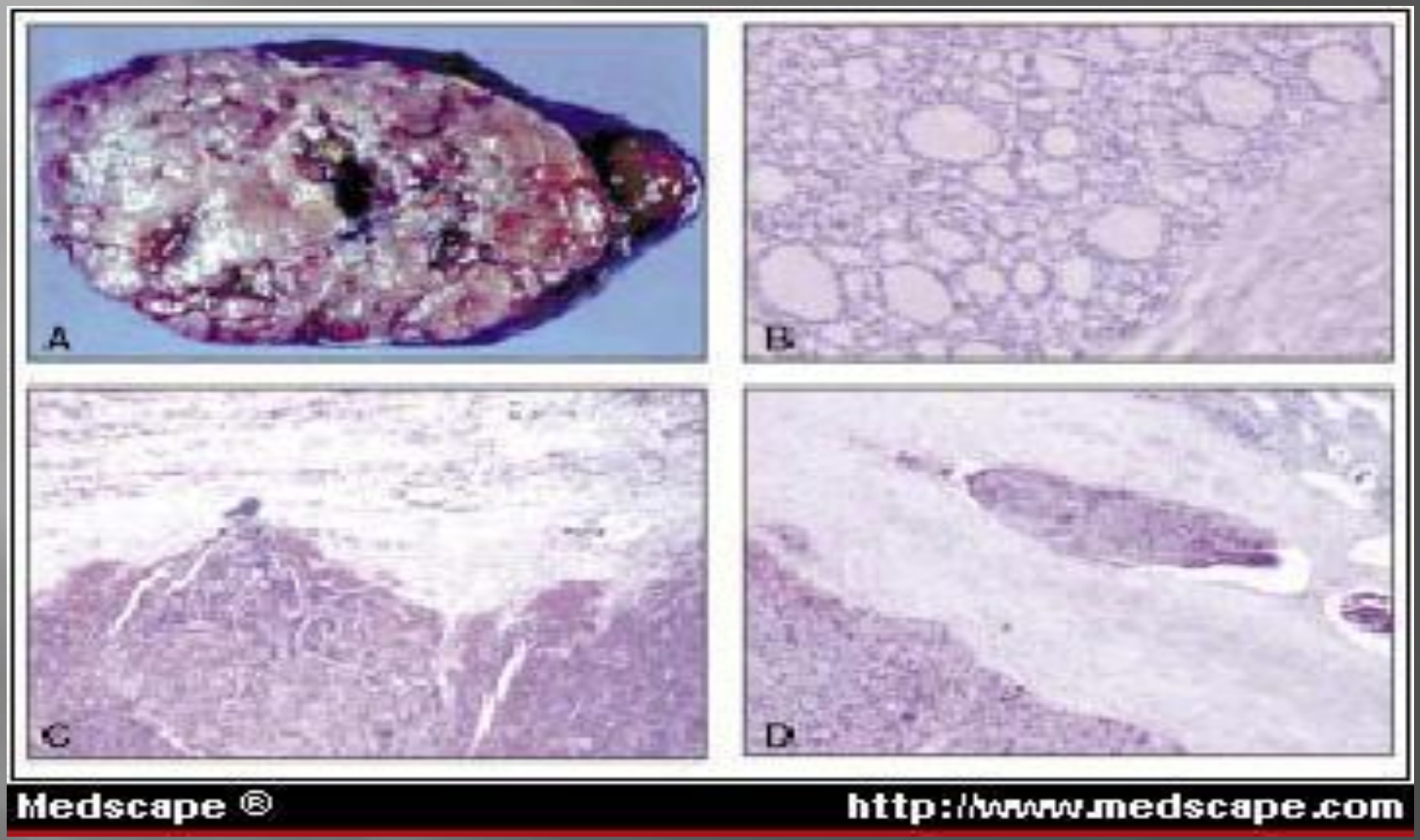
- Tumor development can be related to radiation exposure, such as radiation treatments for acne or adenoid problems as a child

2. Follicular Thyroid Cancer

- Makes up about 10% to15% of all thyroid cancers
- Often diagnosed between the ages of 40 and 60
- Females are affected 3 times more often than males
- Cancer cells may invade blood vessels and travel to other body parts such as bone or lung tissues



- Follicular cells are sphere-shaped

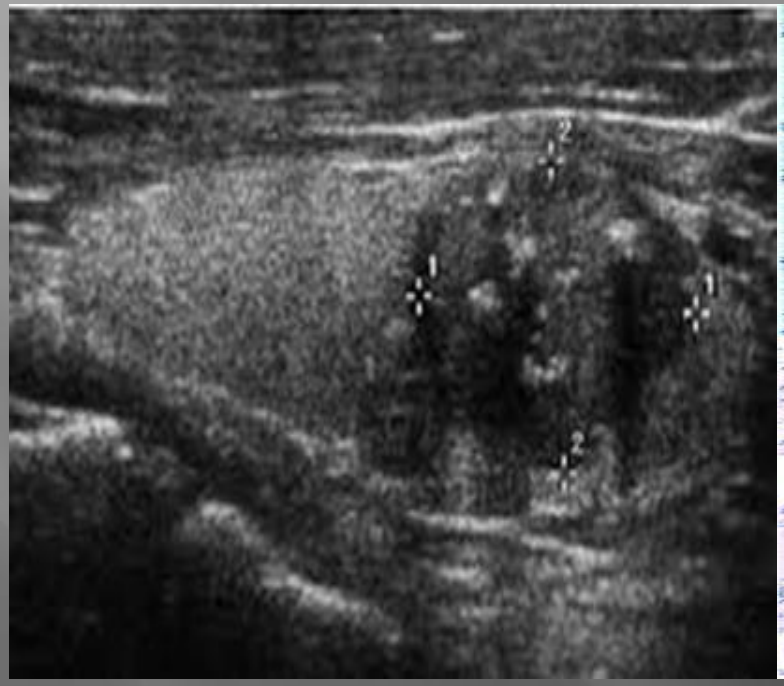


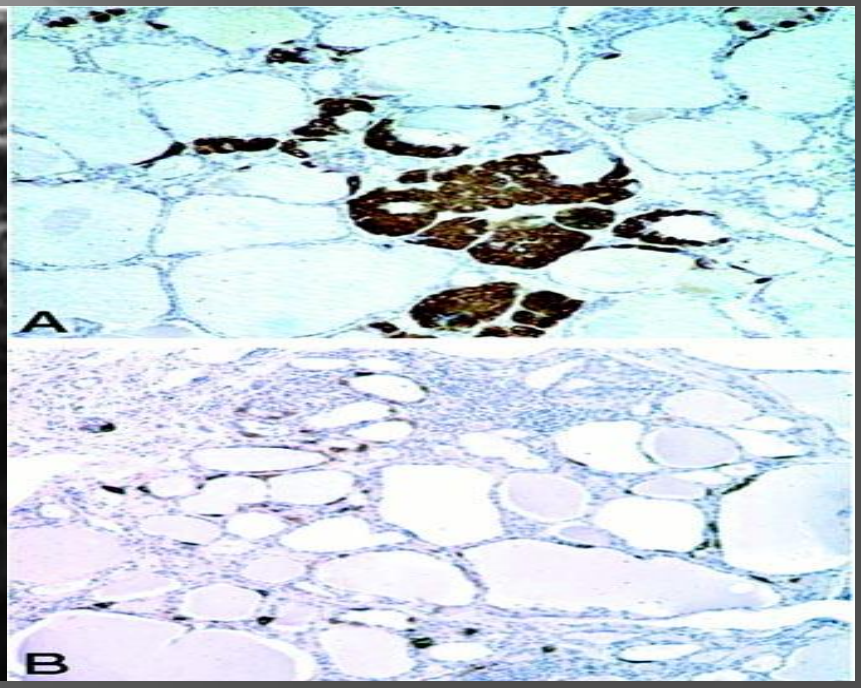
(A) Follicular adenoma with variegated gross appearance. (B) Follicular adenoma. The periphery of the tumor is surrounded by a fibrous capsule. (C) Follicular adenoma with indentation of the inner aspect of the tumor capsule. (D) Follicular carcinoma with vascular invasion with tumor attachment to the endothelium.

3. Medullary Thyroid Cancer

- Makes up about 5 % to 10% of all thyroid cancers
- More likely to run in families and associated with other endocrine disorders
- Develops from the *C Cells or parafolicullar cells* that produce calcitonin
- An elevated calcitonin level can indicate cancer

- Often diagnosed between the ages of 40 and 50
- Females and males are equally affected
- Forms of medullary thyroid cancer include sporadic (not inherited), MEN 2A and MEN 2B, and familial (genetic, but not linked to other MEN-related endocrine tumors)

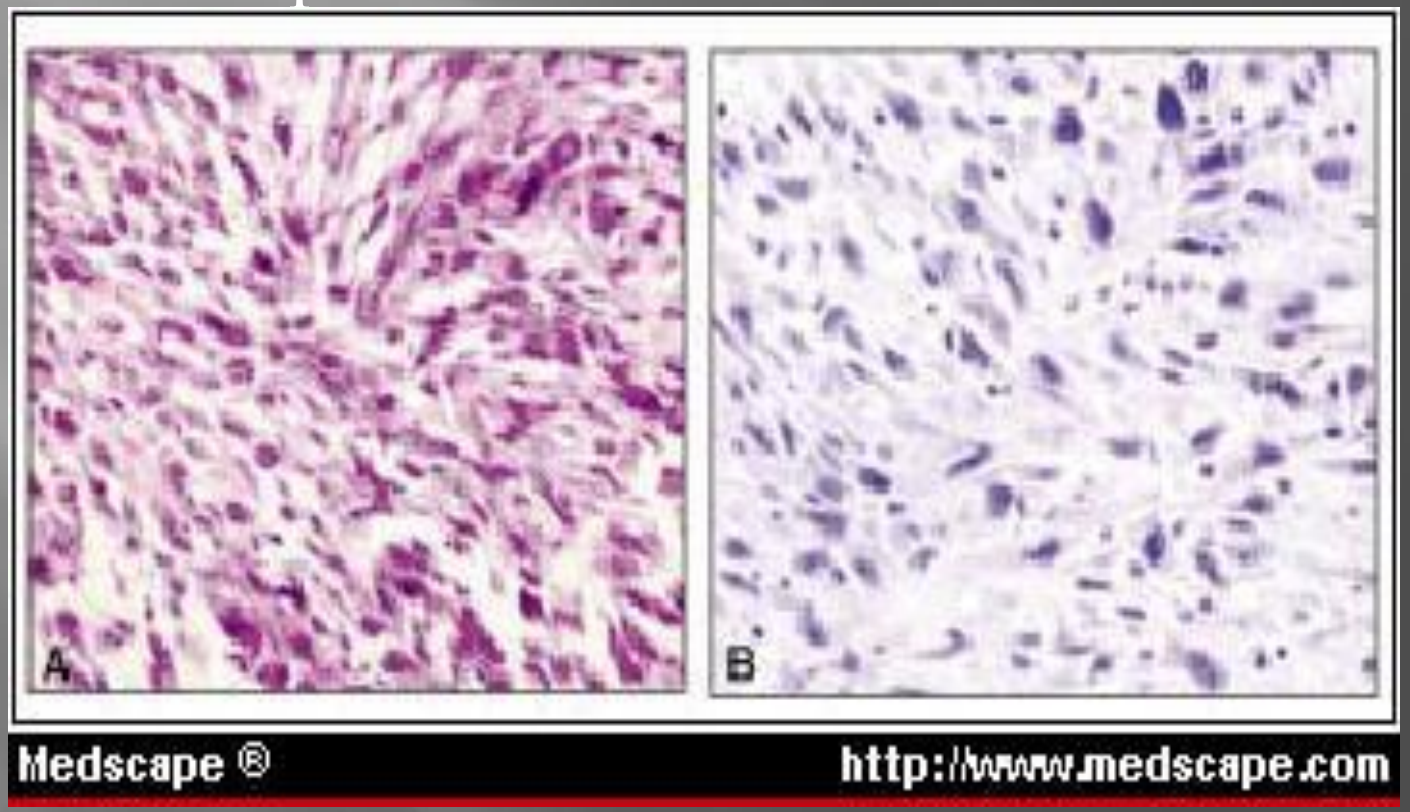




4. Anaplastic Thyroid Cancer

- Very rare—affects fewer than 5% of thyroid cancer patients
- Usually occurs in patients older than 65 years
- Females are affected more often than males

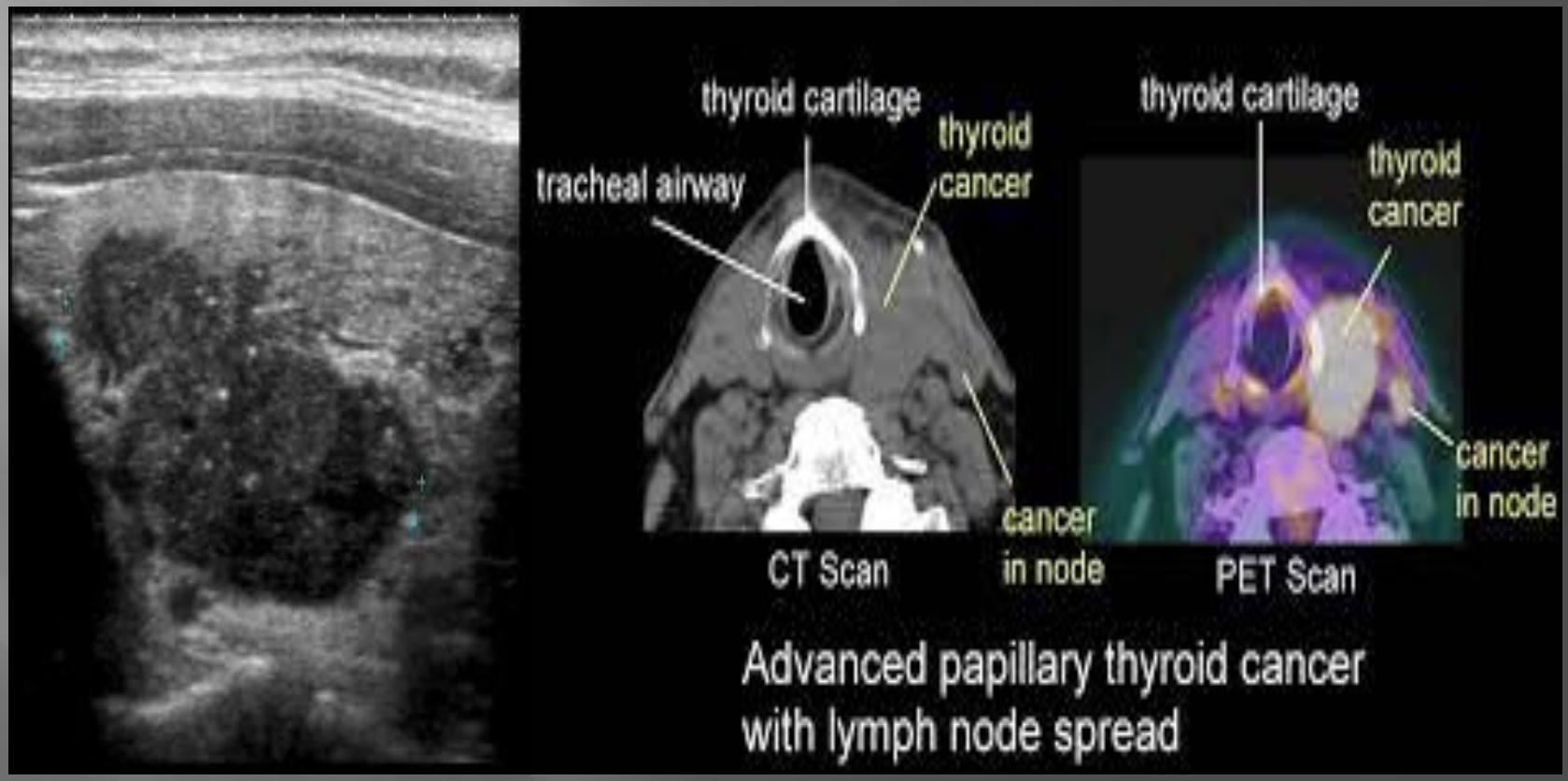
- Anaplastic means the cells lose normal structure and organization →Aggressive and invasive
- Least responsive to treatment



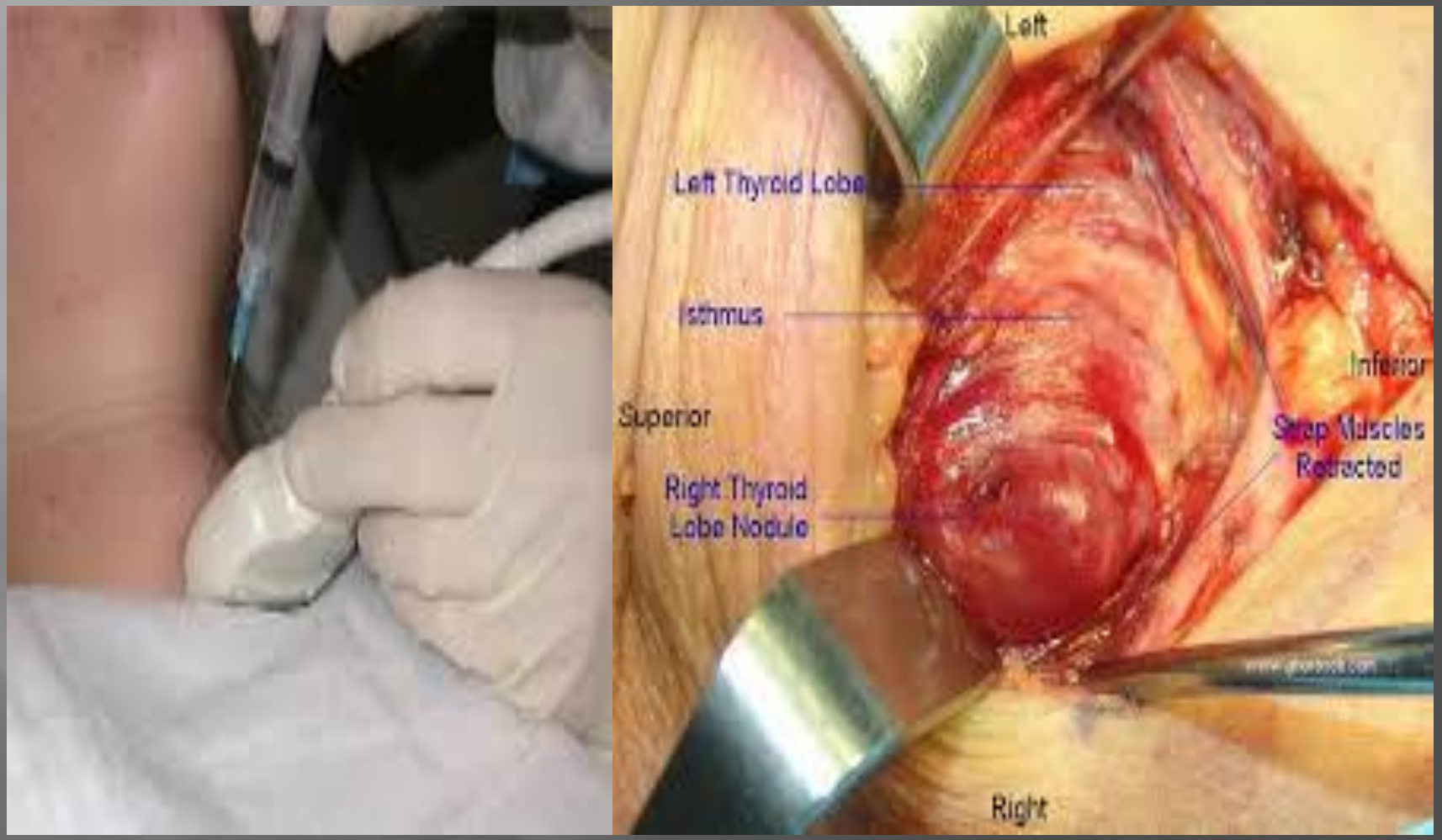
Undifferentiated (anaplastic) carcinoma. (A) Spindle cells in storiform growth pattern. (B) Prominent hyperchromatism and atypia of tumor cells

Diagnostic tests

1. Imaging studies (thyroid ultrasound, CT neck, PET scan).

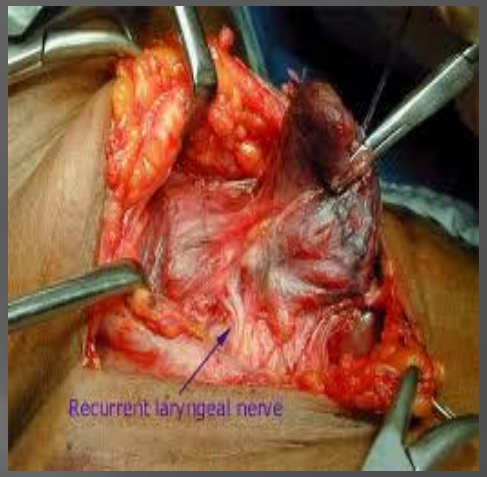


2. The gold standard is thyroid FNA or surgery.



Treatment

1. Surgery (total, subtotal or hemi-thyroidectomy)→ Need an experienced thyroid surgeon.



2. I131 ablation

3. External beam radiation

4. Chemotherapy

Secondary thyroid tumors

1. Thyroid lymphoma

2. Metastasis (Kidney, Lung, Bone, Melanoma)

1. Williams Textbook of Endocrinology
2. Medscape.com
3. UpToDate.com

Cases (Thyroid and adrenal disorders)

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Endocrinology

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Case#1

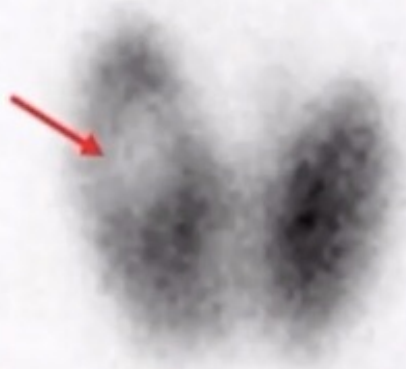
- All of the following etiologies of thyrotoxicosis can cause increased thyroid iodine uptake EXCEPT:

A. Graves' disease

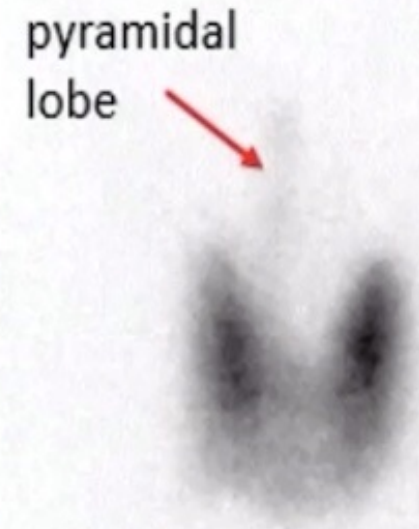
B. Toxic Multi-nodular goiter

C. Hyperthyroidism due to thyrotropin secretion (TSH-oma).

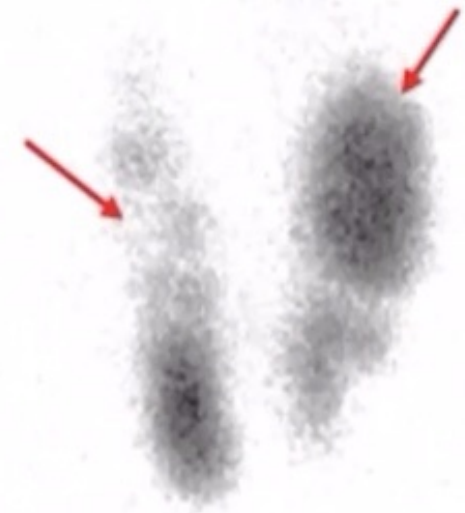
D. Iatrogenic thyrotoxicosis



COLD NODULE

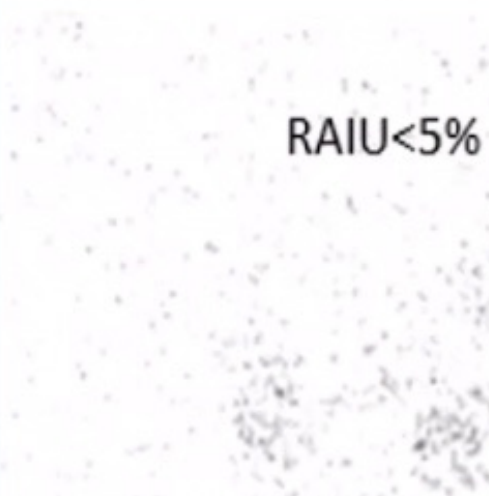


GRAVE DISEASE



TOXIC MULTINODULAR

HOT NODULE



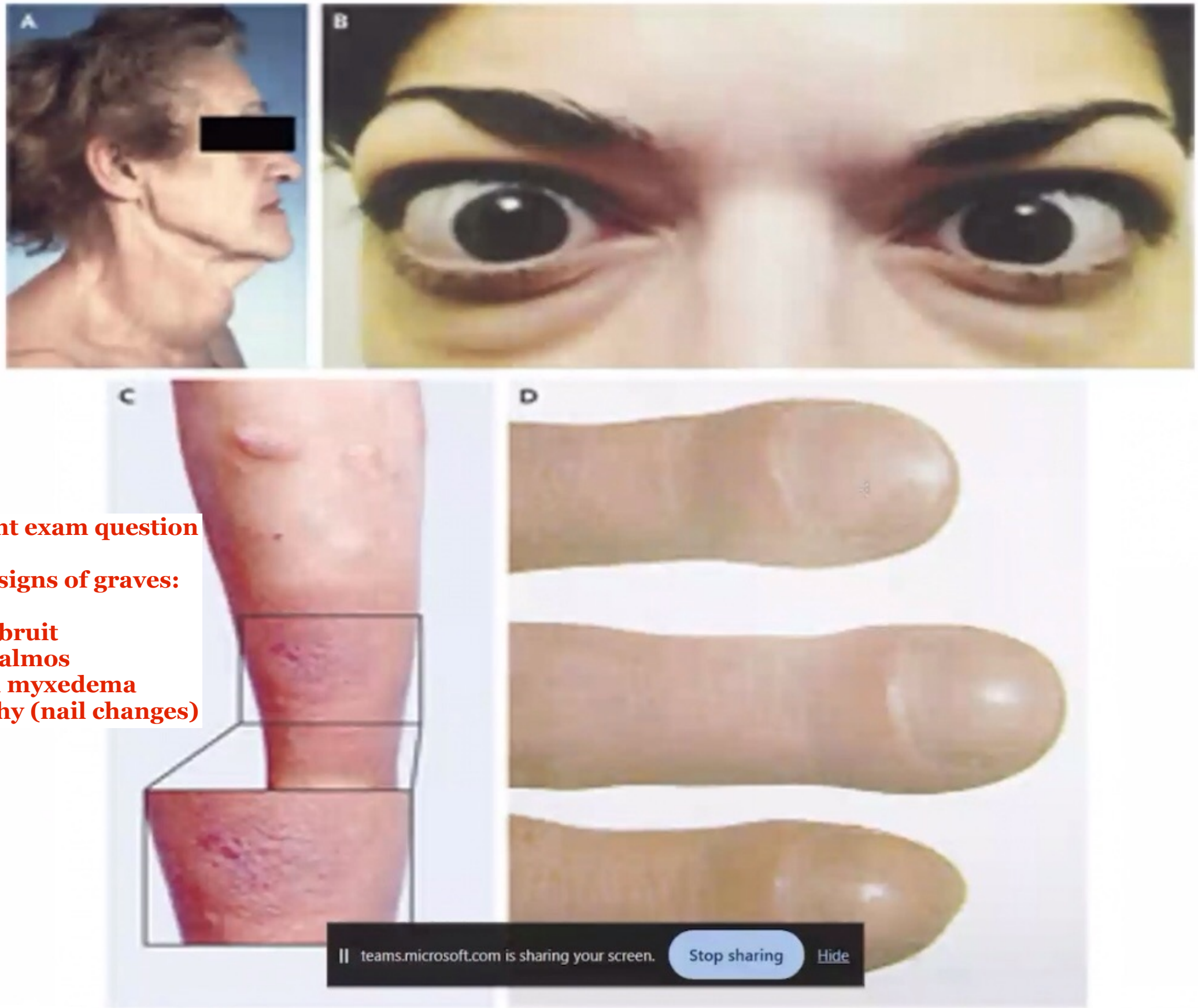
THYROIDITIS

A. Graves' disease
B. Toxic Multi-nodular goiter
C. Hyperthyroidism due to thyrotropin secretion (TSH-oma).
D. Iatrogenic thyrotoxicosis

Case#2

- 22 y/o female with no known medical problems, presented to endocrinology clinic for further evaluation of a newly diagnosed thyrotoxicosis which was confirmed per repeat labs, on PE she was noted to have a mild bilateral exophthalmus. The most likely cause of her thyrotoxicosis is:

A. Graves' Disease
B. Toxic MNG
C. Iatrogenic thyrotoxicosis
D. TSH-oma



***Frequent exam question**

Specific signs of graves:

Thyroid bruit
Exophthalmos
Pretibial myxedema
Acropachy (nail changes)

A. **Graves' Disease**

B. Toxic MNG

C. Iatrogenic thyrotoxicosis

D. TSH-oma

Case#3

- 18 y/o pregnant female, currently 8 weeks pregnant, presented with thyrotoxicosis, exam showed diffuse goiter and pretibial myxedema, labs with suppressed TSH and high Free T4. What is the best next step in management?

A. Proceed with thyroid uptake and scan.
B. Start her on propylthiouracil, repeat thyroid labs after 4 weeks.
C. Start her on carbimazole, repeat thyroid labs after 4 weeks.
D. Proceed with empiric I131 treatment.
E. Proceed with total thyroidectomy.

A. Proceed with thyroid uptake and scan.

B. Start her on propylthiouracil, repeat thyroid labs after 4 weeks.

C. Start her on carbimazole, repeat thyroid labs after 4 weeks.

Teratogenic in the first trimester

D. Proceed with empiric I131 treatment.

E. Proceed with total thyroidectomy.

Can't be done in the first trimester

Management of hyperthyroidism during pregnancy and lactation

Fereidoun Azizi [1], Atieh Amouzegar

Affiliations + expand

PMID: 21389085 DOI: 10.1530/EJE-10-1030

Abstract

Introduction: Poorly treated or untreated maternal overt hyperthyroidism may affect pregnancy outcome. Fetal and neonatal hypo- or hyper-thyroidism and neonatal central hypothyroidism may complicate health issues during intrauterine and neonatal periods.

Aim: To review articles related to appropriate management of hyperthyroidism during pregnancy and lactation.

Methods: A literature review was performed using MEDLINE with the terms 'hyperthyroidism and pregnancy', 'antithyroid drugs and pregnancy', 'radioiodine and pregnancy', 'hyperthyroidism and lactation', and 'antithyroid drugs and lactation', both separately and in conjunction with the terms 'fetus' and 'maternal.'

Results: Antithyroid drugs are the main therapy for maternal hyperthyroidism. Both methimazole (MMI) and propylthiouracil (PTU) may be used during pregnancy; however, PTU is preferred in the first trimester and should be replaced by MMI after this trimester. Choanal and esophageal atresia of fetus in MMI-treated and ma[illegible] of utmost concern.

Case#4

An 85 y/o man with known history of CAD s/p CABG one year ago, current weight is 70 kg, he was found to have primary hypothyroidism per recent routine labs, TSH was 18.0, Free T4 was slightly low, unremarkable thyroid exam, no previous TFTs were available for comparison. The best next step in management is:

A. Start levothyroxine 25 mcg daily
B. Start levothyroxine 100 mcg daily
C. Do not start levothyroxine and repeat TFTs after 4-6 weeks
D. Proceed with thyroid ultrasound before making decision on treatment

A. **Start levothyroxine 25 mcg daily**

B. Start levothyroxine 125 mcg daily

C. Do not start levothyroxine and repeat TFTs after 4-6 weeks

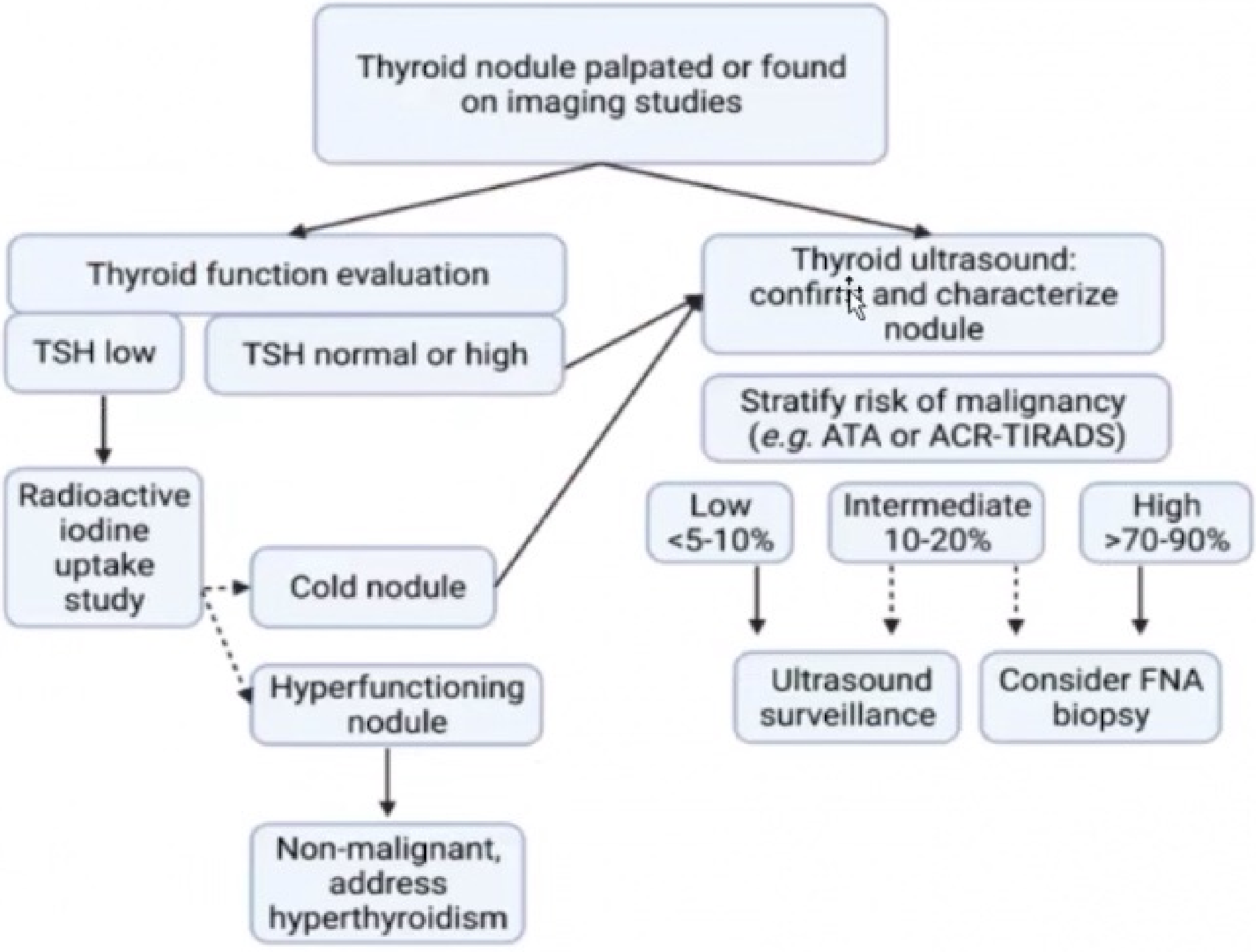
D. Proceed with thyroid ultrasound before making decision on treatment

Because he is an old male and has a history of cardiac disease, otherwise we would give 125mg.

Case#5

A 70 y/o man with history of colon cancer, presented with incidentally found 4 cm right thyroid nodule per carotid Doppler. The best next step in management is:

A. Check TSH
B. Proceed with CT neck
C. Proceed with right thyroid nodule FNA
D. PET/CT scan


Thyroid nodule palpated or found on imaging studies
Thyroid function evaluation
TSH low
TSH normal or high
Radioactive iodine uptake study
Cold nodule
Hyperfunctioning nodule
Non-malignant, address hyperthyroidism
Thyroid ultrasound: confirm and characterize nodule
Stratify risk of malignancy (e.g. ATA or ACR-TIRADS)
Low <5-10%
Intermediate 10-20%
High >70-90%
Ultrasound surveillance
Consider FNA biopsy

A. **Check TSH**

B. Proceed with CT neck

C. Proceed with right thyroid nodule FNA

D. PET/CT scan

Case#6

- 36 y/o female presented with palpable left thyroid nodule and hyperthyroidism, thyroid scan was as shown in the figure. The best next step in management:

A. I131 ablation

B. Left thyroid nodule FNA

C. No treatment but repeat thyroid US and scan after 6 months

D. Total thyroidectomy

A. **I131 ablation** Can then go back to euthyroid

B. Left thyroid nodule FNA

C. No treatment but repeat thyroid US and scan after 6 months

D. Total thyroidectomy

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Successful Treatment of Solitary Toxic Thyroid Nodules with Relatively Low-Dose Iodine-131, with Low Prevalence of Hypothyroidism

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Abstract

Forty-five patients with solitary toxic thyroid adenomas received ^{131}I (mean hypothyroidism, and none had a low serum thyroxine level associated with an elevated serum thyrotrophin level. Three patients developed minimal elevations in serum thyrotrophin levels: 1, 4, and 7. 5 years after ^{131}I treatment, their thyrotrophin levels were 8.4, 6.2, and 9.6 μU/mL, respectively. All 3 had normal serum thyroxine levels and were clinically euthyroid. Mean serum thyroxine concentrations of all patients were unchanged between 1 and more than 9 years of follow-up. These data suggest that solitary toxic adenomas may be treated with relatively low doses of ^{131}I (5 to 15 mCi), and that post-treatment hypothyroidism is very unusual.

Case#7

- The thyroid cancer type with the worst prognosis is:
  A. Papillary
  B. Follicular
  C. Medullary in the settings of MEN syndrome
  D. Anaplastic

A. Papillary

B. Follicular

C. Medullary in the settings of MEN syndrome

D. Anaplastic