

Essentials of Diagnosis, Treatment and Prevention of Major Endocrine Diseases: Diseases of the Thyroid Gland. Goiter.

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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US MLE TEST

A 58-year-old Caucasian female presents to her primary care physician with concerns about several recent health changes. The patient has recently gained weight and can't seem to exercise like she used to. She also notes that her thinking seems slow. Physical examination shows thickened, dry skin. Serum analysis confirms the physician's suspicions. Which of the following findings was most helpful in the diagnosis?

1. High T4 and T3, 2. Low T4 and T3, 3. High TSH,
4. Hypercholesterolemia, 5. Low TSH

US MLE TEST

correct Answer 1: The patient in this question displays many of the common clinical findings of hypothyroidism, which is most commonly caused by primary hypothyroidism. The most sensitive test for diagnosis is an elevated serum TSH

Incorrect Answers:

1: Elevated thyroid hormones would be consistent with hyperthyroidism

2: Though decreased thyroid hormone is consistent with hypothyroidism, serum TSH levels are a better indication of primary hypothyroidism

4: Though hypercholesterolemia is a clinical finding sometimes seen with hypothyroidism, high serum TSH is the more specific diagnostic tool

5: Low TSH would be more consistent with hyperthyroidism

Plan of the Lecture



- Definition
- Epidemiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

Definition

Diseases of the Thyroid Gland

Diseases of the thyroid gland result from primary or secondary autoimmune (80%) and from non autoimmune (20%) processes that either stimulate the overproduction of thyroid hormones (*thyrotoxicosis*) or cause glandular destruction and hormone deficiency (*hypothyroidism*); in addition, benign nodules and various forms of thyroid cancer are relatively common and amenable to detection by physical examination; all of them have a large range of symptoms and affect all ages.

Definition

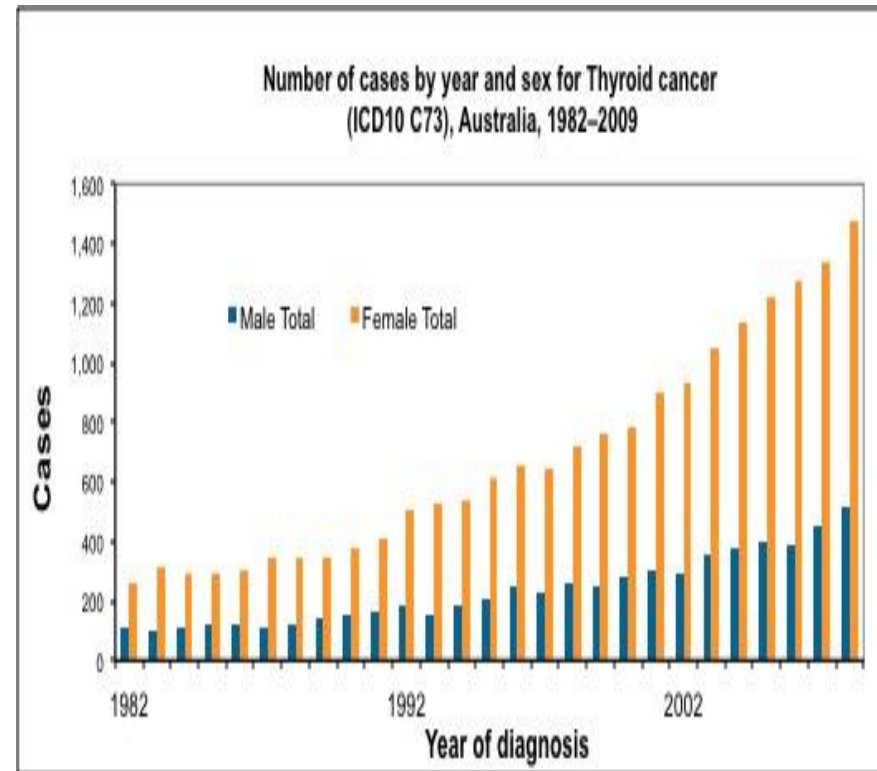
Goiter

- A goiter (American English) or goitre (British English) (from the Latin *gutteria*, *struma*) is a swelling of the neck or larynx resulting from enlargement of the thyroid gland (thyromegaly), that is not functioning properly
- Worldwide, over 90% cases of goitre are caused by iodine deficiency

Epidemiology

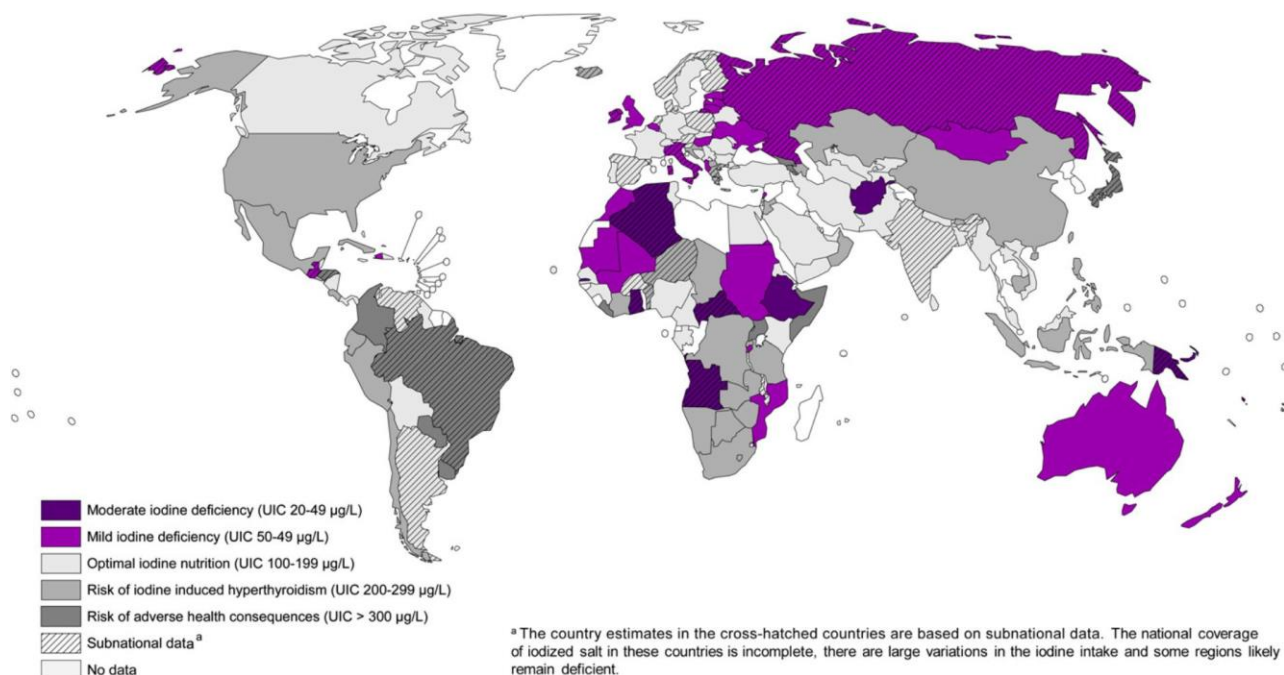
Diseases of the Thyroid Gland

- The prevalence of thyroid dysfunction in adults ranges from 1% to 10 %
- About 200 million people in the world have some form of thyroid disease
- Women are more susceptible than men: male ratio of 4:1
- The incidence increases by age



Epidemiology

Goiter



Countries classified by iodine nutrition according to degree of public health importance. Iodine intake is inadequate in 32 countries, adequate in 71, more than adequate in 36, and excessive in 11

Risk Factors

Diseases of the Thyroid Gland 1

- Gender (women are from 6 to 8 times more likely than men)
- Age (> 50)
- Personal history of thyroid disease
- Family history
- Thyroid surgery (hypothyroidism)
- Radioactive iodine treatment (RAI)
- Cigarette smoking (autoimmune thyroid disease)
- Use of iodine or supplements containing iodine (risk of autoimmune thyroid disease, hypothyroidism, and hyperthyroidism)

Risk Factors

Diseases of the Thyroid Gland 2

- Iodine deficiency
- Certain medical treatments and drugs (campath-1H), bone marrow transplant, lithium, amiodarone, etc.)
- Some foods (cabbage, Brussels sprouts, broccoli, turnips, rutabagas, kohlrabi, radishes, cauliflower, African cassava, millet, kale, and soy)
- Radiation exposure (increases the risk of autoimmune thyroid disease, and thyroid cancer)
- Distress
- Neck surgery/Trauma
- Other factors

Risk Factors

Goiter

Some common risk factors:

- A lack of dietary iodine in areas where iodine is in short supply and where people don't have access to iodine supplements
- Being female
- Age: chances of developing a goiter increase with age
- A personal or family history of autoimmune disease
- Pregnancy and menopause
- Certain medications (immunosuppressants, antiretrovirals, amiodarone, lithium)
- Risk increases with radiation exposure.

Etiology

Diseases of the Thyroid Gland 1

- Diseases of the thyroid gland sometimes result from inappropriate thyroid stimulating hormone (TSH) levels, or may be caused by problems in the thyroid gland itself
- The common causes of hypothyroidism are *Hashimoto's thyroiditis*, iodine deficiency , pituitary and hypothalamus problems
- The common causes of hyperthyroidism are *Graves' disease*, *toxic nodular goiter (toxic thyroid adenoma)*, *thyroiditis*

Etiology

Diseases of the Thyroid Gland 2

- Four types of thyroid cancers: *papillary, follicular, anaplastic, medullary*
- Most of thyroid cancers are associated with radiation treatment to the head, neck, or chest
- A genetic mutation might be associated with thyroid cancer, either alone or in conjunction with other types of cancers (e.g., multiple endocrine neoplasia, BRAF gene mutations)
- Other cancers might metastasize to the thyroid (e.g., lymphoma, breast cancer).

Etiology

Goiter

- Goiter refers to a condition where the thyroid gland is enlarged in size
- Goiter can result from autoimmune Hashimoto's and Graves' diseases, iodine excess and deficiency, and nodular thyroid disease.



Etiology 3

Goiter

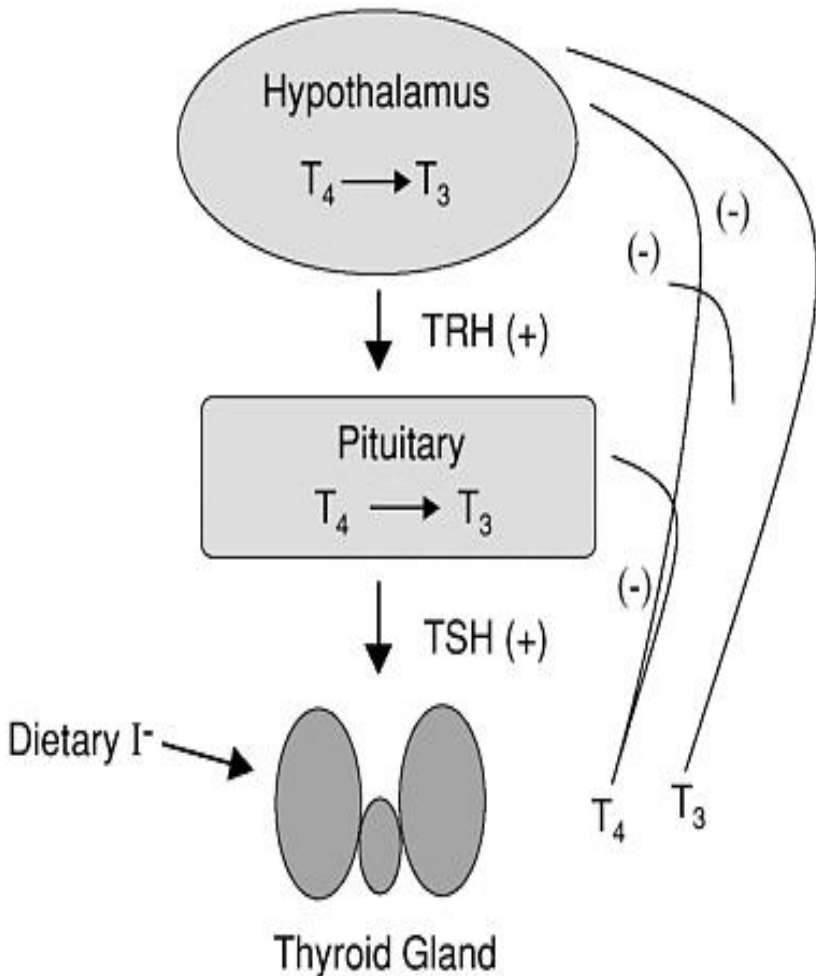
- The most common cause for goiter is iodine deficiency, usually seen in countries that do not use iodized salt
- Selenium deficiency is also considered a contributing factor
- In countries that use iodized salt, Hashimoto's thyroiditis is the most common cause
- Goiter can also result from cyanide poisoning (in tropical countries people eat the cyanide-rich cassava root as the staple food)



Cassava or manioc

Mechanisms

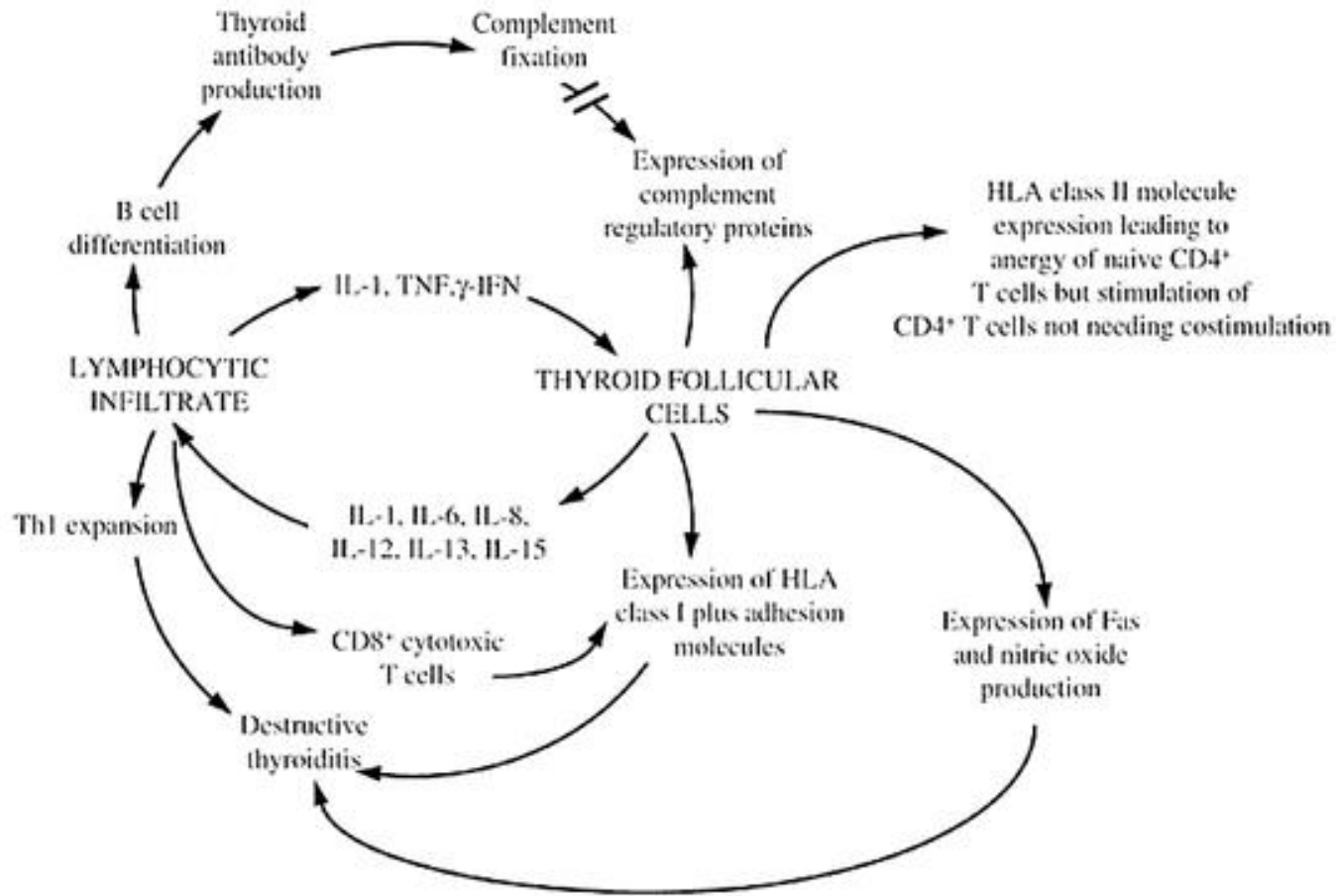
Pathological in Physiological



- TSH regulates thyroid gland function and hormone synthesis and release
- The pituitary secretion of TSH in turn is influenced by the releasing factor, thyrotropin-releasing hormone (TRH) produced in the hypothalamus
- The secretion of both TSH and TRH is regulated by negative feedback from thyroid hormone, predominantly T_3 , from the circulation and/or T_3 that is produced locally from intracellular conversion of T_4 to T_3 .

Mechanisms

Local Humoral Factors



Interactions between thyroid follicular cells and the immune system in autoimmune thyroid disease

Classification

International Classification of Diseases (ICD)

IV Endocrine, nutritional and metabolic diseases

(E00-E07) Disorders of thyroid gland

E00 Congenital iodine-deficiency syndrome

E01 Iodine-deficiency-related thyroid disorders and allied conditions

E02 Subclinical iodine-deficiency hypothyroidism

E03 Other hypothyroidism

E04 Other nontoxic goitre

E05 Thyrotoxicosis [hyperthyroidism]

E06 Thyroiditis

E07 Other disorders of thyroid

Classification

Goiter Morphology

Regarding morphology, goiter may be classified either as the growth pattern or as the size of the growth:

- Growth pattern
 - uninodular goiter: can be either inactive or a toxic
 - multinodular goiter: can likewise be inactive or toxic
- Diffuse goiter when the whole thyroid appearing to be enlarged;
 - Class I size: in normal posture of the head, it cannot be seen; it is only found by palpation
 - Class II size: the goiter is palpable and can be easily seen
 - Class III size: the goiter is very large and is retrosternal, pressure results in compression marks.

Classification

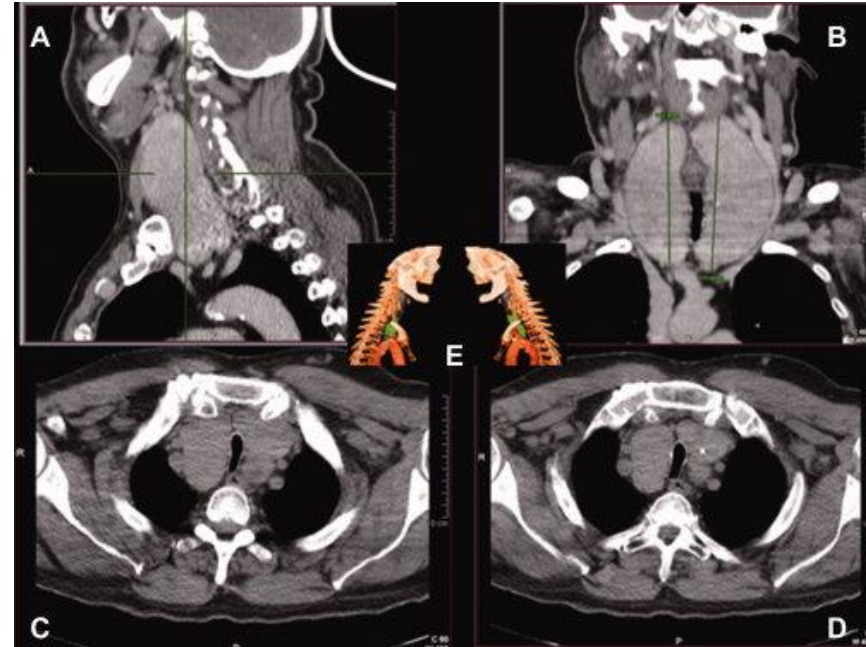
WHO of Goiter' Grade

Grade 0 – no goiter presence is found (the thyroid impalpable and invisible)

Grade 1 – neck thickening is present in result of enlarged thyroid, palpable, however, not visible in normal position of the neck; the thickened mass moves upwards during swallowing

Grade 1 includes also nodular goitre if thyroid enlargement remains invisible

Grade 2 – neck swelling, visible when the neck is in normal position, corresponding to enlarged thyroid – found in palpation



Substernal goiter, grade 1 type A bilateral.

(a) Cranio-caudal extension of the substernal goiter. (b) Substernal goiter with bilateral extension. (c,d) Substernal goiter with bilateral extension at the level of the thoracic inlet.

Classification

Inflammatory Forms

- Acute thyroiditis (a bacterial infection, fungal or parasitic infection, in an immunocompromised host)
- Subacute thyroiditis (the most common subacute granulomatous form, or de Quervain's)
- Silent thyroiditis (subacute lymphocytic thyroiditis, painless thyroiditis)
- Riedel's thyroiditis (Riedel's struma, IgG4-related disease) is one of manifestations of a inflammatory chronic systemic multi-organ disease
- Palpation thyroiditis refers to the development of thyroid inflammation due to mechanical damage to thyroid follicles by repeated palpation or surgical manipulation in neck area

Classification

Forms of Clinical Manifestation

- Functional disorders
 - Hypothyroidism (Hashimoto's thyroiditis / thyroiditis, Ord's thyroiditis, postoperative hypothyroidism, postpartum thyroiditis, silent thyroiditis, acute thyroiditis, iatrogenic hypothyroidism, thyroid hormone resistance, euthyroid sick syndrome)
 - Hyperthyroidism (thyroid storm, Graves' disease, toxic thyroid nodule, toxic nodular struma (Plummer's disease), Hashitoxicosis)
- Nodular abnormalities - Goitre
- Tumors (thyroid adenoma, thyroid cancer, lymphomas and metastasis from elsewhere (rare))
- Deficiencies (congenital hypothyroidism which untreated can lead to cretinism)

Classification

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Clinical Investigation

Common Symptoms and Signs

- Nervousness and tremor (hyperthyroidism)
- Mental fogginess and poor concentration (hyperthyroidism and hypothyroidism)
- Menstrual changes (hyperthyroidism and hypothyroidism)
- Feeling bloated (hypothyroidism)
- Racing heartbeat (hyperthyroidism)
- Aches and pains (hyperthyroidism and hypothyroidism)
- Weight gain (hypothyroidism)
- High cholesterol levels (hypothyroidism)
- Heat intolerance (hyperthyroidism)
- Feeling cold (hypothyroidism)

Clinical Investigation

Hypothyroidism

- Coarse and dry hair
- Confusion or forgetfulness (often mistaken for dementia in seniors)
- Constipation
- Depression
- Dry, scaly skin
- Fatigue or a feeling of sluggishness
- Hair loss
- Increased menstrual flow (women)
- Intolerance to cold temperatures
- Irritability
- Muscle cramps
- Slower heart rate
- Weakness
- Weight gain

US MLE TEST

A 53-year-old female presented to her primary care physician for an annual check-up. She does not smoke, use drugs, or consume alcohol. The patient currently takes no medications. Routine blood tests demonstrate a TSH level of 9.5 uU/mL (normal 0.35 to 5.0 uU/ml). Her T3/T4 levels are within normal limits. The initiation of treatment for hypothyroidism would be indicated for all EXCEPT which of the following findings?

1. Pretibial myxedema, 2. Presence of antithyroid peroxidase (anti-TPO) antibodies, 3. Hyperlipidemia, 4. Constipation, 5. Decreased sweating

US MLE TEST

Correct Answer 1: This patient's elevated TSH level coupled with normal T3/T4 levels indicates subclinical hypothyroidism. While patients with serum TSH levels greater than 10 uU/mL are generally treated with levothyroxine, asymptomatic patients with elevated TSH levels (but < 10) are not treated with thyroid supplementation

Incorrect answers:

2: The American Association of Clinical Endocrinologists recommends levothyroxine therapy for patients with positive anti-TPO antibodies, as this may indicate short-term worsening of hypothyroidism due to thyroid gland destruction

3: Hyperlipidemia is associated with hypothyroidism and patients should be treated with levothyroxine

4 and 5: Constipation and decreased sweating are clinical symptoms of hypothyroidism that warrant therapy

Clinical Investigation

Severe form of Hypothyroidism (Myxedema)

- Low body temperature
- Dulled mental processes
- Congestive heart failure
- Myxedema coma (loss of consciousness, seizures, slowed breathing)



Clinical Investigation

Hyperthyroidism

- Increased heart rate with abnormal rhythm or pounding (palpitations)
- High blood pressure
- Increased body temperature (feeling unusually warm)
- Increased sweating
- Clamminess
- Feeling agitated or nervous
- Tremors in the hands
- Feeling of restlessness even though the person is tired or weak
- Increased appetite accompanied by weight loss
- Interrupted sleep
- Frequent bowel movements, sometimes with diarrhea
- Puffiness around the eyes, increased tears, sensitivity to light, or an intense stare
- Bone loss (osteoporosis)
- Stopped menstrual cycles

Clinical Investigation

Life-Threatening Thyrotoxicosis or Thyroid Storm



- Confusion, coma
- Fever
- High blood pressure
- Irregular heartbeat, which can be fatal
- Jaundice associated with liver enlargement
- Mood swings
- Muscle wasting
- Restlessness
- Shock
- Weakness

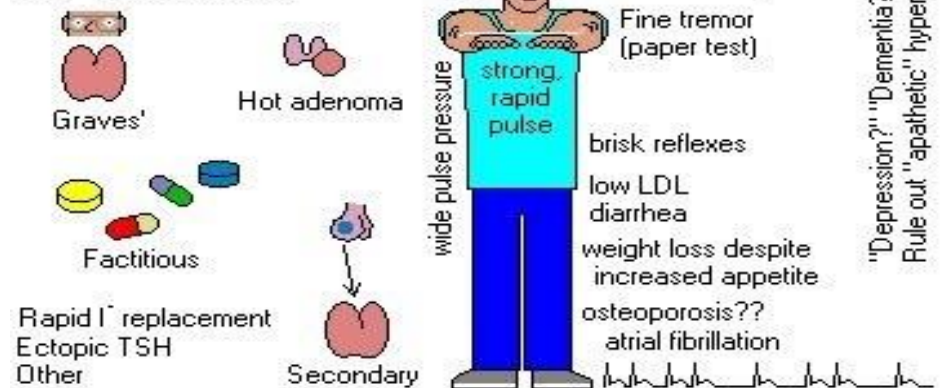
Clinical Investigation

Hyperthyroidism and Hypothyroidism in Charts

| Hypothyroidism | Hyperthyroidism |
|-----------------------------------|---------------------------|
| Dry, coarse hair | Hair loss |
| Loss of eyebrow hair | Bulging eyes |
| Puffy face | Sweating |
| Enlarged thyroid (goitre) | Enlarged thyroid (goitre) |
| Slow heartbeat | Rapid heartbeat |
| Weight gain | Weight loss |
| Constipation | Frequent bowel movements |
| Brittle nails | Soft nails |
| | Warm, moist palms |
| | Tremor of fingers |
| Further signs and symptoms | |
| Arthritis | Difficulty sleeping |
| Cold intolerance | Heat intolerance |
| Depression | Nervousness |
| Dry skin | Irritability |
| Fatigue | Muscle weakness |
| Forgetfulness | Infertility |
| Heavy menstrual periods | Scant menstrual periods |
| Infertility | |
| Muscle aches | |

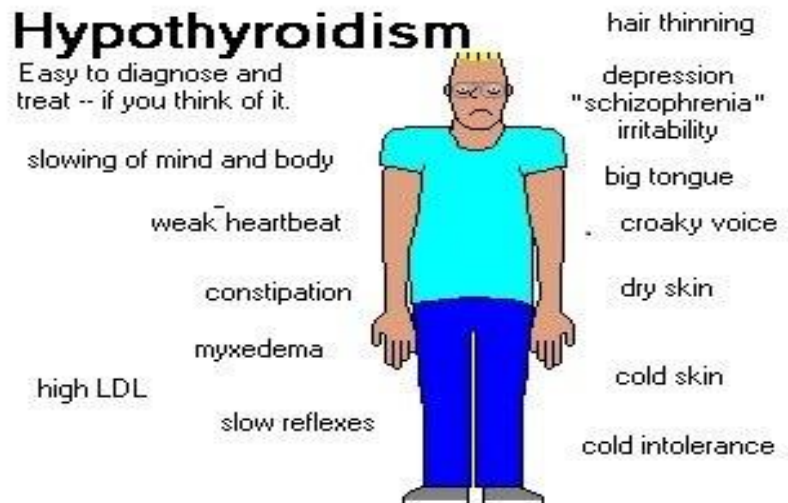
Hyperthyroidism

Easy to diagnose and treat -- if you think of it.



Hypothyroidism

Easy to diagnose and treat -- if you think of it.



US MLE TEST

A 40-year-old woman presents to her primary care physician for an annual check-up. She complains of intermittent fatigue. Laboratory tests are notable for the following: TSH, serum: 11.2 uU/mL (normal 0.5-5.0 uU/mL), Thyroxine (T4), serum: 9.8 ug/dL (normal 5-12 ug/dL). Which of the following other conditions, if present, would merit treatment with thyroxine?

1. Tender thyroid gland,
2. High erythrocyte sedimentation rate (ESR),
3. Hypercholesterolemia,
4. Proptosis,
5. Hand tremor.

US MLE TEST

Correct Answer 3: The patient presents with elevated TSH (normal range 0.5-5.0 uU/mL) and T4 levels within the normal reference range (5-12 ug/dL) consistent with subclinical hypothyroidism. Patients with subclinical hypothyroidism should be treated with thyroxine if hypercholesterolemia is present.

Incorrect answers:

1 and 2: Painful, tender thyroid gland and high ESR are associated with hypothyroidism from subacute thyroiditis. Subacute thyroiditis is managed with NSAIDs and aspirin for mild symptoms and corticosteroids for severe pain.

4: Proptosis is a hallmark of Graves' disease.

5: Hand tremor is a symptom of hyperthyroidism.

Clinical Investigation

Symptoms in the Neck and Thyroid Area

- Neck discomfort
- Visible thyroid enlargement or lump
- Discomfort with ties, scarves, turtlenecks, or necklaces
- Hoarseness
- Sore throat
- Soreness in neck
- Difficulty swallowing

In some cases, thyroid diseases and conditions can have no symptoms at all, such as thyroid cancer or certain types of thyroiditis

Clinical Investigation

Nodules

- Nodules usually are found in 4-7% in the thyroid gland
- The majority of nodules do not cause any symptoms
- Malignant nodules, which only occur in about 5% of nodules, include follicular, papillary, medullary carcinomas and metastases from other sites
- Nodules are more likely in females
- There can be many nodules, which is termed a multinodular goiter, and this can sometimes be a toxic multinodular goiter.

Clinical Investigation

Goiter

- Goiter which is associated with hypothyroidism or hyperthyroidism may be present with symptoms of the underlying disorder
- For hyperthyroidism, the most common symptoms are associated with adrenergic stimulation (tachycardia, palpitations, nervousness, tremor, increased blood pressure and heat intolerance), and clinical manifestations are often related to hypermetabolism (increased metabolism), excessive thyroid hormone, an increase in oxygen consumption, metabolic changes in protein metabolism, immunologic stimulation of diffuse goitre, and ocular changes (exophthalmos)
- For hypothyroidism, the most common symptoms are weight gain despite poor appetite, cold intolerance, constipation and lethargy, that are often non-specific and make diagnosis difficult.

Clinical Investigation

Goiter in Pictures



Diagnosis

Key Steps

- A clinical examination
- Blood testing: TSH test, free T4 and free T3 antibodies testing to diagnose Hashimoto's and Graves' disease, and testing for reverse T3 levels
- Imaging tests (the radioactive iodine uptake (RAI-U), computer tomography (CT) scans, magnetic resonance imaging (MRI), ultrasound) to evaluate the size, shape, and function of the thyroid gland, to evaluate the size and shape of the nodules or lumps, and evaluate whether or not they are suspicious for thyroid cancer and require further evaluation
- Fine needle aspiration biopsy (FNA) is done when thyroid nodules are considered suspicious and need to be tested for possible thyroid cancer.

Diagnosis

TSH testing of thyroid dysfunction

- The most sensitive test in an ambulatory population at risk for thyroid dysfunction is the serum TSH
- Among individuals with serious, acute illness, the serum TSH is less specific for thyroid disease because a serious illness alone can depress TSH secretion
- When an abnormal serum TSH value is obtained, the usual next step is to repeat the measurement of TSH and also measure a serum free T_4
- The most common cause of discordance between the TSH and free T_4 result occurs in patients with subclinical thyroid dysfunction with high or low serum TSH values and a normal serum free T_4 result
- Serum TSH measurements may yield misleading results for individuals with changing levels of thyroid hormones

Diagnosis

Hypothyroidism

- The most common cause of primary hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's disease)
- Other causes are radioactive iodine and surgical therapy for thyroid
- Hypothyroidism may occur rarely (<1%) as a result of deficiency of TRH or impaired TSH secretion
- People with primary hypothyroidism have high serum TSH levels, and the concomitant finding of a low free T_4 level confirms this diagnosis
- People with a high serum TSH concentration and a normal or low-normal serum free T_4 level have subclinical hypothyroidism
- The diagnosis of secondary hypothyroidism is based on the findings of a low serum free T_4 level and a serum TSH level that is normal or low

Diagnosis

Hyperthyroidism

- The most common cause is Graves' autoimmune disease with activation the TSH receptor, resulting in stimulation of T_4 and T_3 production and enlargement of the thyroid
- Other caused are a multinodular goiter, thyroid adenoma, thyroiditis, iodide- or drug-induced hyperthyroidism, and a TSH secreting pituitary tumor
- The diagnosis is based on the findings of a high serum free T_4 level and a low serum TSH concentration
- Occasionally, patients with hyperthyroidism have a normal serum free T_4 and high serum free T_3 concentrations with normal the serum TSH (T_3 -hyperthyroidism)
- Patients with a low serum TSH concentration and normal serum free T_4 and free T_3 levels have subclinical hyperthyroidism.

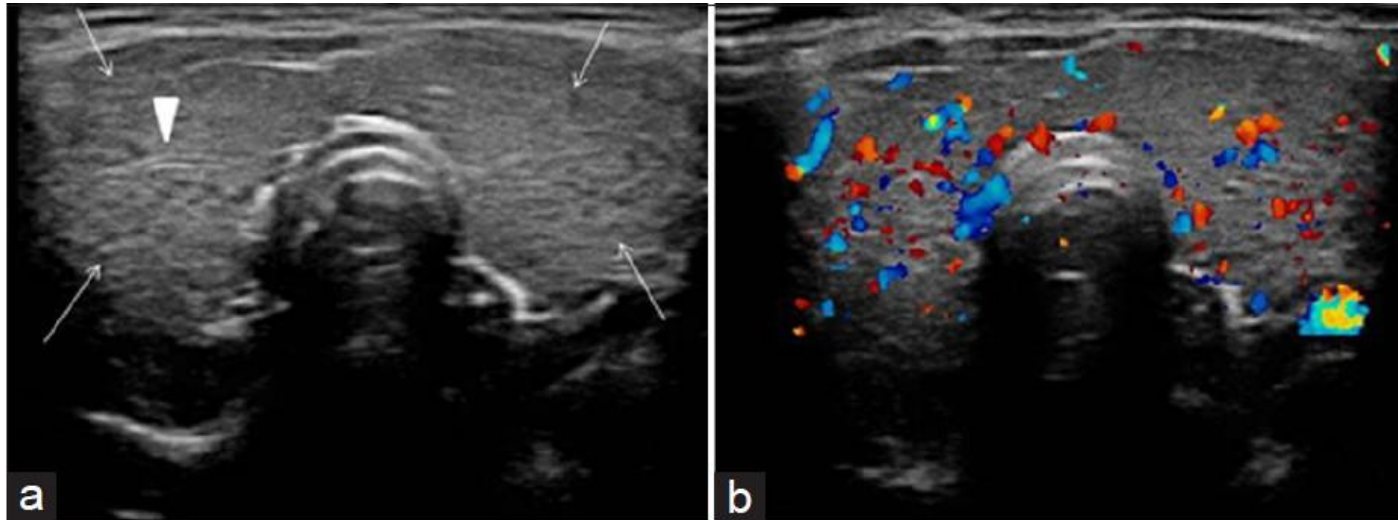
Diagnosis

Ultrasound

- Nodules of the thyroid may or may not be cancer
- Medical ultrasonography can help determine their nature because some of the characteristics of benign and malignant (irregular border, hypoechoic (less echogenic than the surrounding) tissue, microcalcifications, taller than wide shape on transverse study, significant intranodular blood flow by power Doppler) nodules differ
- Ultrasonography is not always able to separate benign from malignant nodules with complete certainty
- In suspicious cases, a tissue sample is often obtained by biopsy for microscopic examination.

Diagnosis

Ultrasound: Diffuse Hashimoto's Thyroiditis



Diffuse Hashimoto's thyroiditis in a 35-year-old female patient.

Transverse gray-scale ultrasound neck (a) demonstrates diffuse enlargement of thyroid gland with heterogeneous echotexture. Multiple tiny and discrete hypoechoic nodules (arrows) and few linear echogenic septae (arrowhead) are also noted. Color Doppler sonogram (b) demonstrates mildly increased parenchymal vascularity.

Diagnosis

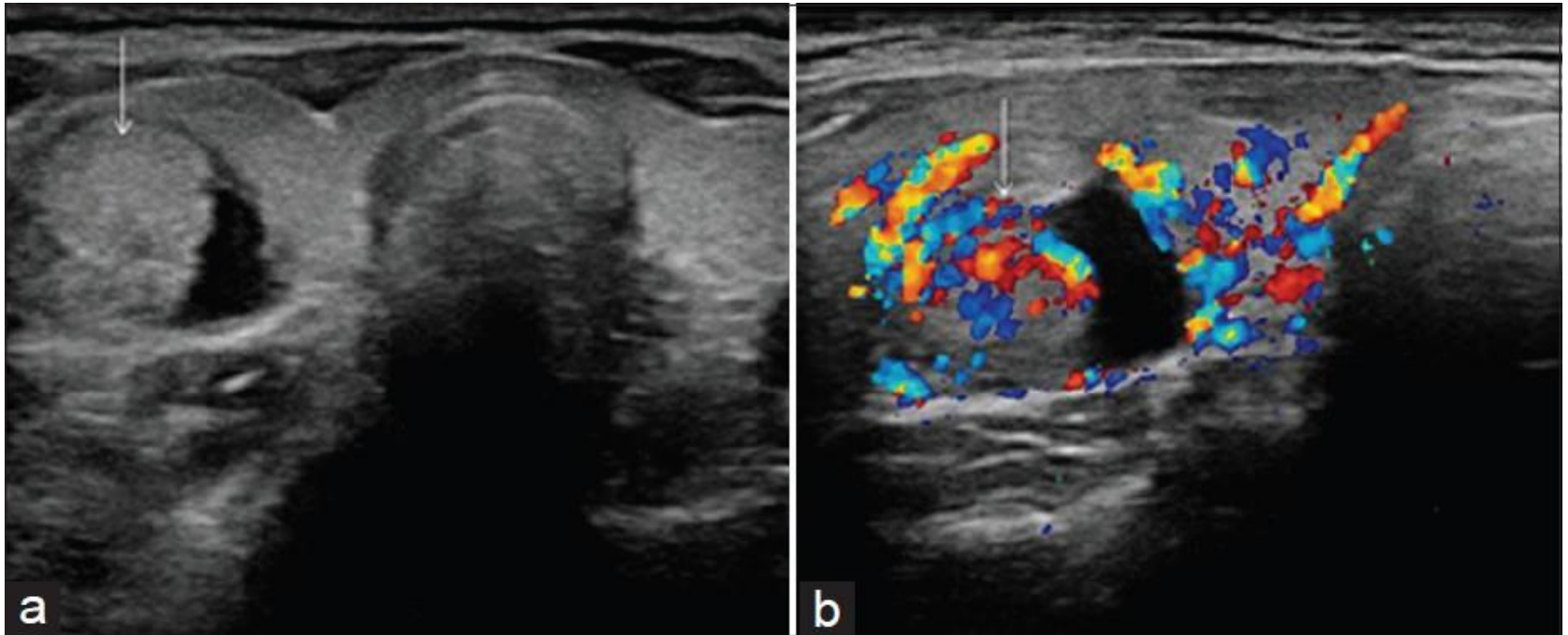
Ultrasound: Colloid Multinodular Goitre



Colloid multinodular goitre in a 50-year-old female patient. Transverse (a) and longitudinal (b) gray-scale ultrasound neck images reveal enlarged thyroid gland having multiple hyperechoic colloid nodules with internal cystic areas (arrows) showing 'ring down' sign. Color Doppler image (c) shows increased peripheral vascularity.

Diagnosis

Ultrasound: Malignant Thyroid Nodule



Malignant thyroid nodule in a 60-year-old woman. Transverse sonogram (a) of right lobe of the thyroid shows a partially cystic tumor with solid internal nodule (arrow) and thick walls. Color Doppler sonogram (b) depicts increased vascularity in solid parts of the tumor (arrow).

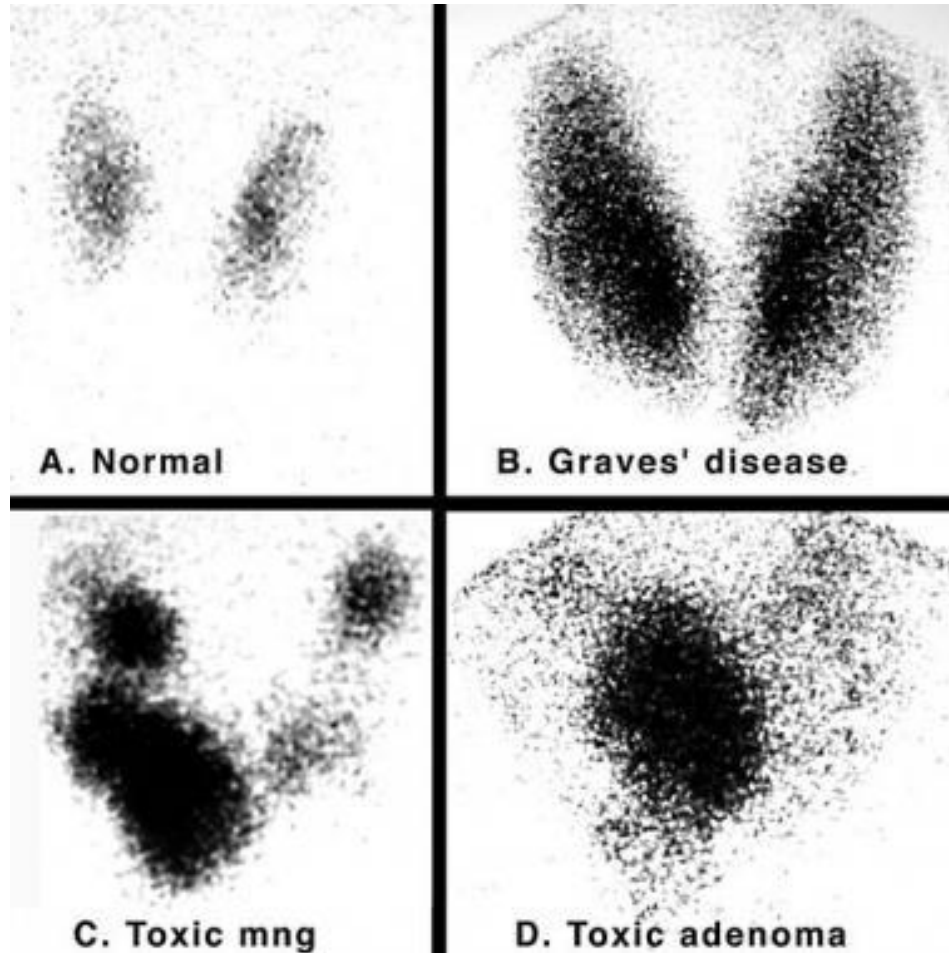
Diagnosis

Radioiodine Scanning and Uptake 1

- Thyroid scintigraphy, imaging of the thyroid with the aid of radioactive iodine (iodine-123)
- Radioiodine collects in the thyroid gland before being excreted in the urine
- A nodule that is overactive ("hot") to the point of suppressing the activity of the rest of the gland is usually a thyrotoxic adenoma, a surgically curable form of hyperthyroidism that is hardly ever malignant
- Finding that a substantial section of the thyroid is inactive ("cold") may indicate an area of non-functioning tissue such as thyroid cancer
- A normal quantitation of radioiodine uptake demonstrates that about 8 to 35% of the administered dose can be detected in the thyroid 24 hours later

Diagnosis

Radioiodine Scanning and Uptake 2



US MLE TEST

A 54-year-old woman comes to the physician for a routine health maintenance examination. She has had no weight loss, fever, cough, decreased appetite, chest pain, lower extremity swelling or blood in the stool or urine. She has a history of osteoarthritis in her right knee treated with ibuprofen. Her temperature is 36.5° C (97.7° F), blood pressure is 128/72 mm Hg and pulse is 75/min. Neck examination shows a solitary nodule in the thyroid gland that is readily palpable. The remainder of the examination shows no abnormalities. Laboratory studies show TSH 0.4 μ U/mL and free thyroxine (FT₄) 10 ng/L. Ultrasound of the thyroid shows a 1.5-cm hyperechoic nodule in the right lower lobe. Which of the following is the most appropriate next step in management?

A. Fine-needle aspiration (FNA), **B.** No further management is necessary, **C.** Radioactive iodine uptake (RAIU), **D.** Surgical resection, **E.** Thyroid replacement therapy, **F.** Treatment of subclinical hyperthyroidism.

US MLE TEST

Correct Answer C: The patient has a solitary thyroid nodule. Measuring TSH level is the next step in management. If serum TSH concentration is low, indicating hyperthyroidism, the nodule is most likely hot, and thyroid scintigraphy (RAIU scan) is the next step in diagnosis. Scintigraphy determines whether the nodule is hot cold. A cold nodule is more concerning for malignancy and surgical resection is recommended.

Incorrect answers:

A: FNA is indicated in patients with ultrasound findings that suggest malignancy.

D: Surgery is indicated for nodules that have features of malignancy.

E: Thyroid replacement therapy is appropriate with hypothyroidism.

F: A subclinical hyperthyroidism diagnosis is based on the combination of low serum TSH ($<0.5 \mu\text{U/mL}$) and normal serum T_4 and T_3 in an asymptomatic patient.

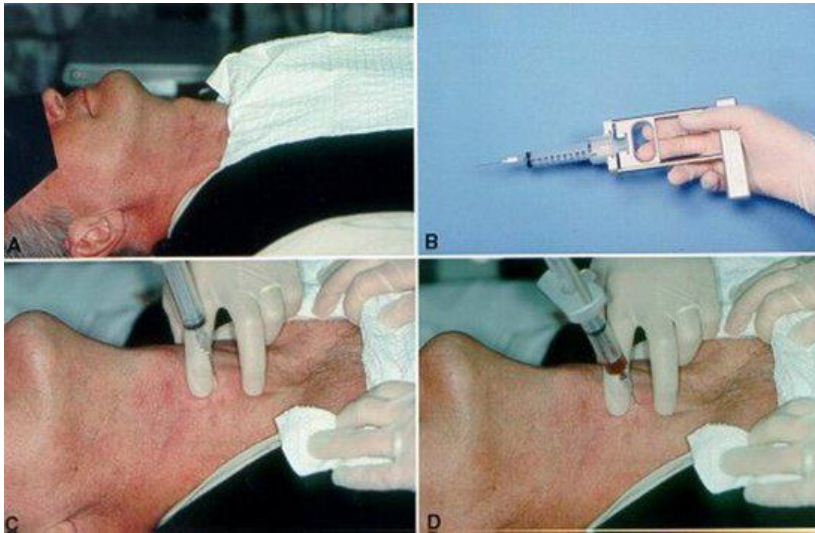
Diagnosis

Biopsy 1

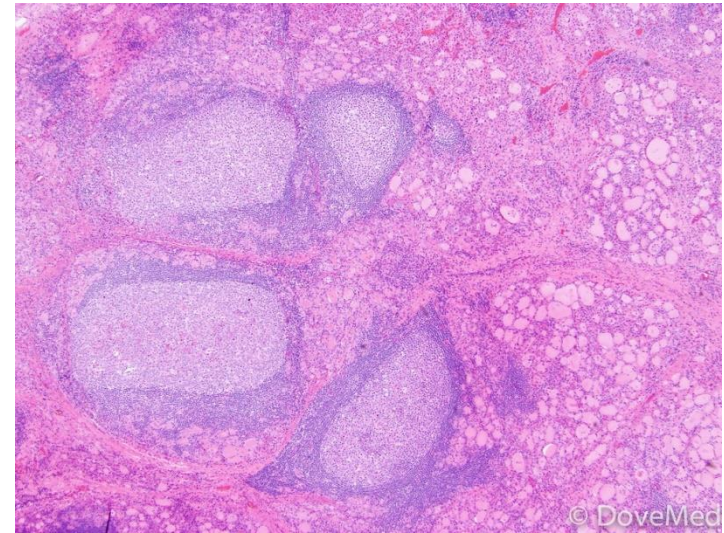
- Thyroid tissue may be obtained for biopsy by fine needle aspiration or by surgery
- Needle aspiration has the advantage of being a brief, safe, outpatient procedure that is safer and less expensive than surgery and does not leave a visible scar
- Needle biopsies became widely used in the 1980s, but it was recognized that accuracy of identification of cancer was good but not perfect
- The accuracy of the diagnosis depends on obtaining tissue from all of the suspicious areas of an abnormal thyroid gland
- The reliability of needle aspiration is increased when sampling can be guided by ultrasound, and over the last 15 years, this has become the preferred method for thyroid biopsy

Diagnosis

Biopsy 2



Fine-Needle Aspiration Biopsy



Autoimmune Thyroiditis

US MLE TEST

A 31-year-old female with a past medical history of follicular thyroid cancer treated two years prior with a total thyroidectomy followed by radioactive iodine ablation presents to her gynecologist with questions relating to pregnancy. She and her partner are thinking about getting pregnant, but she is concerned about her thyroid replacement hormone, specifically the complications of being hypothyroid during pregnancy. She wants to know how her levothyroxine dosing should be handled prior to conception and during her pregnancy. Which of the following would be an appropriate response to this patient's concerns?

Current dose will need to be increased: 1. before conception to reduce the potential fetal complications, 2. during pregnancy, 3. before pregnancy, 4. for mother and the fetus during pregnancy, 5. Pregnancy is at increased risk of complications because of hypothyroidism regardless of the dose.

US MLE TEST

Correct Answer 2: In hypothyroidism during pregnancy, the levothyroxine dose will only need to be increased during pregnancy, not before.

Incorrect answers:

1,3,4: These are not appropriate responses.

5: While this patient would be at increased risk if untreated, treating hypothyroidism adequately with thyroid replacement therapy reduces the risk dramatically.

Management

Key Nutrients

- Iodine deficiency is the main cause of thyroid diseases worldwide and has been considered rare in a lot of countries since the last century largely due to the widespread use of iodized salt, although supplemental iodine may cause symptom flare-ups in people with Hashimoto's disease because it stimulates autoimmune antibodies
- Vitamin D deficiency is linked to hyperthyroidism, Hashimoto's disease, and particularly Graves' disease
- The highest concentration of selenium is found in the thyroid gland, and it is necessary component of enzymes integral to thyroid function
- Vitamin B12 deficiency is the one of risk factors of autoimmune thyroid disease (ATD), so it's important for dietitians to suggest patients with thyroid disease have their levels tested

Management

Foods, Supplements, and Medication Interactions

- There are no specific foods or dietary supplements
- The medications can interact with common nutritional supplements
- Calcium supplements have the potential to interfere with proper absorption of thyroid medications
- Coffee and fiber supplements lower the absorption of thyroid medication
- Chromium picolinate (for blood sugar control and weight loss) impairs the absorption of thyroid medications and patients should take it three to four hours apart from thyroid medications
- Flavonoids in fruits, vegetables, and tea may suppress thyroid function

Management

Goitrogens

- Cruciferous vegetables (broccoli, cauliflower, cabbage) release a compound called goitrin when they're hydrolyzed, or broken down
- Goitrin can interfere with the synthesis of thyroid hormones, this is usually a concern only when coupled with an iodine deficiency
- Heating cruciferous vegetables denatures much or all of this potential goitrogenic effect
- Soy is another potential goitrogen, and the isoflavones in soy can lower thyroid hormone synthesis
- The potential exception is millet, a nutritious gluten-free grain, which may suppress thyroid function even in people with adequate iodine intake

Management Exercise

- With hypothyroid patients, exercise can help with weight gain, fatigue, and depression
- With hyperthyroidism, anxiety and sleep disturbances are so common, and exercise can help regulate both
- A structured exercise program in patients with Graves' disease is showing dramatic improvements in fatigue levels, and significantly more patients are able to successfully stop taking antithyroid medications without a relapse
- Since fatigue can be a barrier to exercise, it is recommended patients use a pedometer as a tool for a tangible source of structure and motivation.

Management Hypothyroidism

- Hypothyroidism is treated with thyroid hormone replacement drugs
- The most commonly prescribed thyroid hormone replacement drug is levothyroxine, a synthetic form of the thyroid hormone thyroxine
- There is also a synthetic form of the T3 hormone, known as liothyronine, that is sometimes added to levothyroxine for T4/T3 combination treatment
- There is a hormone replacement drug called natural desiccated thyroid (NDT) or thyroid extract; while it has been available for more than a century and is still in use today

Management

Hyperthyroidism and Graves' Disease

- There are three key ways that chronic hyperthyroidism and Graves' disease are treated:
 - Antithyroid drugs (methimazole, carbimazole and propylthiouracil) treatment, that can slow down the thyroid's production of thyroid hormone
 - Radioactive iodine treatment (RAI), that given in a single dose, either in a capsule or drink; this shrinks the thyroid, slows down its function, and reverses hyperthyroidism
 - Thyroid surgery/thyroidectomy in some cases, especially for patients who cannot tolerate antithyroid drugs or are pregnant and RAI is not an option.

Management Goiter

- Goitre is treated according to the cause
- If the thyroid gland is producing too much T3 and T4, radioactive iodine is given to the patient to shrink the gland
- If goitre is caused by iodine deficiency, small doses of iodide in the form of Lugol's Iodine or KI solution are given
- If the goitre is associated with an underactive thyroid, thyroid supplements are used as treatment
- In extreme cases, a partial or complete thyroidectomy is required

Management Thyroid Cancer

- Treatment for thyroid cancer almost always involves surgical removal of the thyroid gland
- For more aggressive types of thyroid cancer, this may be followed by RAI treatment to ensure that all thyroid cells are destroyed, a process known as remnant ablation
- Following surgical removal of the thyroid gland, patients are functionally hypothyroid and require lifelong thyroid hormone replacement treatment
- Less commonly, other treatments, including external beam radiation, chemotherapy, radiofrequency ablation, and percutaneous ethanol injections

Management

Autoimmunity and Hashimoto's

- Integrative and functional medicine practitioners sometimes treat autoimmune thyroid disease, especially Hashimoto's, with the drug low dose naltrexone (LDN) which may help lower antibodies
- Other treatment approaches include:
 - Supplementation with selenium to lower antibodies
 - Addressing related adrenal imbalances that may be complicating thyroid treatment
 - Dietary changes to reduce inflammation
 - Eliminating gluten from the diet due to a connection between gluten and autoimmunity
 - Stress reduction and management

Prognosis

- Most people with either hypothyroidism, hyperthyroidism, and benign and malignant thyroid nodules, with proper diagnosis and treatment, can control their condition with no long-term effects and a normal life expectancy
- Those with undiagnosed disease may progress to hypothyroid coma or thyrotoxic crisis (thyroid storm), with death rates approaching 50%
- Graves' eye disease has been treated with corticosteroid medication, radiotherapy, and surgery with varying success
- Patients with thyroid cancer have a very low mortality rate (<5%) but the overall risk depends on age, type of thyroid cancer, and the extent of spread of the tumor
- Endocrinologists will manage the evaluation and treatment of thyroid cancer, rather than an oncologist

Prophylaxis

- There is no known way to prevent hyperthyroidism or hypothyroidism
- In some countries, iodine deficiency is rare, so there is no way to prevent goiter or thyroid nodules
- Anyway, Iodide is essential for thyroid hormone synthesis, and the World Health Organization (WHO) recommends: 90 mcg of iodine daily for infants and children up to five years; 120 mcg for children 6 to 12 years; 150 mcg daily for children ≥ 12 years and adults; 250 mcg daily during pregnancy and lactation
- Radiation will induce both benign and malignant thyroid nodules, so individuals should avoid excess radiation or unnecessary CT scans of the head and neck and use a "thyroid shield" when dental X-rays are performed

Abbreviations

ATD - autoimmune thyroid disease

CT - computer tomography

FNA - fine needle aspiration biopsy

Free T4 - free thyroxine

Free T3 - free triiodothyronine

LDN - low dose naltrexone

MRI - magnetic resonance imaging

NDT - natural desiccated thyroid

RAI - radioactive iodine treatment

RAI-U - the radioactive iodine uptake

TSH - thyroid stimulating hormone

Diagnostic and treatment guidelines

- [American Thyroid Association Professional Guidelines](#)
- [European Thyroid Association Guidelines](#)