Lecture 51

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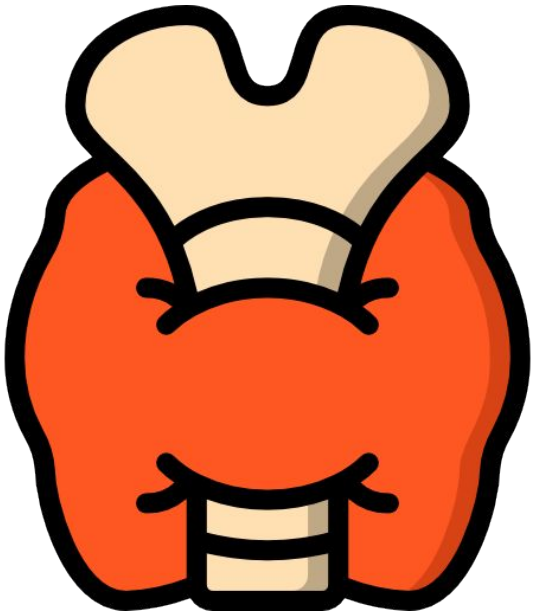

Medicine Team

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Thyroid disorders

Objectives:

- ★ Thyroid anatomy and physiology
- ★ Action of thyroid hormones
- ★ Thyroid function
- ★ How to evaluate a patient with thyroid disease
- ★ Goiter
- ★ Hypothyroidism and Hyperthyroidism: causes,pathogenesis,diagnosis and treatment
- ★ Other thyroid disorders

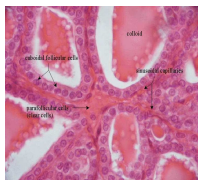
Color index:

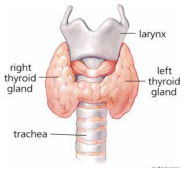
Original text Females slides Males slides
Doctor's notes Textbook Important Golden notes Extra

Introduction

◀ Thyroid Anatomy

- Thyroid gland is made up of follicles
- Has 2 lobes and connected by the isthmus
- Weigh 20 g, more volume in men,
- increase with age and body weight and decrease with iodine intake
- Located in front of larynx and moves on swallowing.





◀ Thyroid Hormone

1

- Somatic development in adults
- Brain development in infants
- Fetal thyroid functions at 10-12 weeks of gestation
- Maternal T4 reaches the fetus during development
- if mother has hypothyroidism this may lead to preterm delivery, miscarriage, cognitive impairment of infant

2

- Main action of thyroid hormones is done by T3[1] and 80 % from peripheral conversion and 20 % produced by the thyroid itself
- Follicular cells of the thyroid is the main site of hormones synthesis 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 pregnants, 290 mcg for lactating

3

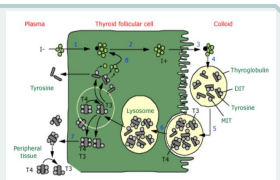
- Source of iodine: dairy and seafood products
- Stored in the thyroglobulin[2] in follicular cells of the thyroid gland 99.9%[3] of T4 and T3 are bound to protein in the blood: TBG, albumin, lipoprotein

4

- 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 synthesis

1- iodine is taken up by follicular cells
2- iodine is oxidized to I^+
3- I^+ moves to colloid
4- I^+ binds to thyroglobulin
5- now thyroglobulin contains T3 and T4 → taken up by follicular cells
6- broken down by lysosome → free T3 and T4
7- Release of T3 and T4 into peripheral tissues



◀ Thyroid Action and Function

Thyroid hormone action:

- Thyroid hormones act on the **bone** and bone development
- Low thyroid hormone **in children:**
  - **delayed growth** and epiphyseal growth
  - **In brain:** cognitive impairment
- Thyroid hormone in adults mainly affects the metabolism (body weight, fat tissue (lipolysis and lipogenesis)
- Act on **cardiac muscle:** tachy and bradycardia
- Regulate **metabolic rate** and little change in bodyweight

Thyroid hormone Function

- TSH • Free T4, Free T3 • TRH[4] • TBG[5]
- Thyroid antibodies:
  - (microsomal antibodies, TSH receptor antibodies, thyroglobulin antibodies)

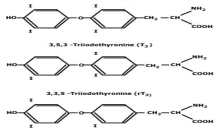
Radiological imaging of thyroid function

- US neck (to check the shape), Radioactive uptake scan (to check the function), CT neck sometimes for retrosternal goiter → usually in areas of endemic iodine deficiency

Box 21.25 Physiological effects of thyroid hormone

Target	Effect
Cardiovascular system	Increases heart rate and cardiac output
Bone	Increases bone turnover and resorption
Respiratory system	Maintains normal hypoxic and hypercapnic drive in respiratory centre
Gastrointestinal system	Increases gut motility
Blood	Increases red blood cell 2,3-BPG*, facilitating oxygen release to tissues
Neuromuscular function	Increases speed of muscle contraction/ relaxation and muscle protein turnover
Carbohydrate metabolism	Increases hepatic gluconeogenesis/glycolysis and intestinal glucose absorption
Lipid metabolism	Increases lipolysis and cholesterol synthesis and degradation
Sympathetic nervous system	Increases catecholamine sensitivity and β-adrenergic receptor numbers in heart, skeletal muscle, adipose cells and lymphocytes Decreases cardiac α-adrenergic receptors

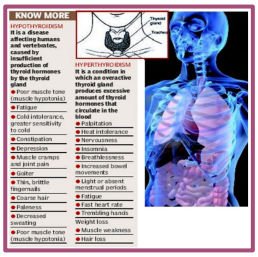
*2,3-BPG, 2,3-bisphosphoglyceric acid.

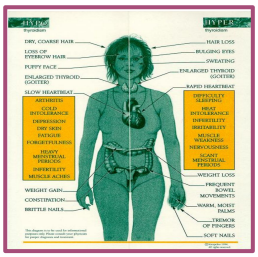


1- produced mainly by the conversion of T4 to T3
2- reflects the thyroid reserve
3- the 0.01% that is free is the active thyroid hormone
4- usually not available
5- done when thyroid hormone level abnormalities is suspected (to check bound thyroid)

Patients with thyroid disease

Introduction





- Thyroid enlargement (goiter): diffuse or nodular
- Symptoms of hypothyroidism or hyperthyroidism
- Complications of a specific form of hyperthyroidism- Graves' disease-which may present with:
  - Striking prominence of the eyes (exophthalmos)
  - Thickening of the skin over the lower leg (thyroid dermopathy)
- Thyroid diseases are amongst the most prevalent antibody mediated autoimmune diseases and are associated with other organ-specific autoimmunity .
- Autoantibodies may produce inflammation and destruction of thyroid tissue, resulting in hypothyroidism, goitre (in Hashimoto's thyroiditis) or sometimes even transient thyrotoxicosis ('Hashitoxicosis'), or they may stimulate the TSH receptor to cause thyrotoxicosis (in Graves' disease).
- There is overlap between these conditions, since some patients have multiple autoantibodies.

History

1. **Exposure** to ionizing radiation
2. Iodide **ingestion**:
   - - Kelp
   - - Iodide-containing cough preparation
   - - IV Iodide-containing contrast media
3. **Lithium** carbonate
4. Residence in an area of **low dietary iodide**
5. **Family history**
   - Thyroid disease
   - Immunologic disorders:
     - Diabetes, Rheumatoid disease
     - Pernicious anemia
     - Alopecia, Vitiligo
     - Myasthenia gravis, MEN 2A

Physical Exam[1]

Helpful video

Observe the neck, especially as the patient swallows

Examine from the front, rotating the gland slightly with one thumb while palpating the other lobe with the other thumb

Examine from behind, using three fingers and the same technique

Determine the size of the thyroid lobes, consistency, presence of nodules

1. Also check for any bruit, lymph nodes or extension of the goiter behind the clavicle which might cause obstruction (Eg. Pemberton's sign for thoracic outlet obstruction).

Hypothyroidism

◀ Primary Causes:

Hashimoto's thyroiditis	Iatrogenic

• Chronic autoimmune thyroiditis, Could be with goiter.
• Could present as **"Idiopathic" thyroid atrophy:** presumably end-stage autoimmune thyroid disease, following either:
  ○ Hashimoto's thyroiditis or Graves' disease
• Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies
	• Results from prior treatments of hyperthyroidism:
	  ○ Radioiodine therapy or External irradiation
	  ○ thyroidectomy
	  ○ Excessive iodine intake (radiocontrast dyes)
	Drugs: thionamides, lithium, amiodarone, interferon-alfa, interleukin-2, perchlorate.

Transient hypothyroidism	**Other**
• Painless (silent, lymphocytic) thyroiditis • Subacute granulomatous thyroiditis • Postpartum thyroiditis • Subtotal thyroidectomy for Graves' disease or nodular goiter • following radioiodine therapy for Graves' hyperthyroidism • following withdrawal of suppressive doses of thyroid hormone in euthyroid patients	• Iodine deficiency or excess • Infiltrative diseases (hemochromatosis, sarcoidosis and fibrous thyroiditis) • Inborn errors of thyroid hormone synthesis, Transient hypothyroidism, congenital hypothyroidism, dysgenesis or defect in hormone synthesis.

◀ Secondary, Tertiary & other causes:

Secondary	Tertiary	Other
Hypopituitarism (TSH deficiency) due to • Pituitary adenoma • Pituitary ablative therapy • Pituitary destruction	Hypothalamic dysfunction (TRH deficiency) (rare)	**Peripheral resistance of the action of thyroid hormone**

An area for your notes

Hypothyroidism

◀ Pathogenesis:

- Thyroid hormone deficiency affects every tissue in the body, so that the symptoms are multiple
- **Accumulation of glycosaminoglycans** (mostly hyaluronic acid) in interstitial tissues
  - due to reduced breakdown (not elevated synthesis)
- **Increase capillary permeability to albumin** causes Interstitial edema evident in the skin, heart muscles and striated muscles.

◀ Children with hypothyroidism

- May not show classic features but often have a slow growth velocity
- Poor school performance
- Sometimes arrest of pubertal development.

◀ Clinical presentations and findings (in adults):

Mechanism	Symptom	Sign
Slowing of metabolic processes	• Fatigue and weakness • Cold intolerance • Dyspnea on exertion • **Weight gain** • Cognitive dysfunction • Growth failure • **Mental retardation (infants)** • constipation • growth failure	• **Slow movement and slow speech** • delayed relaxation of tendon reflexes • bradycardia • yellowish skin discoloration caused by excess carotenemia that is metabolized by the thyroid hormone
Accumulation of matrix substances	• Dry skin • hoarse husky voice • Edema	• **coarse skin** ★ **Puffy face** and hands • loss of eyebrows • periorbital edema • enlargement of the tongue
Others	• Decreased hearing • Myalgia • **Depression** • **Menorrhagia** • Arthralgia • Pubertal delay	• diastolic hypertension • pleural and pericardial effusion • ascites • galactorrhea • cool skin

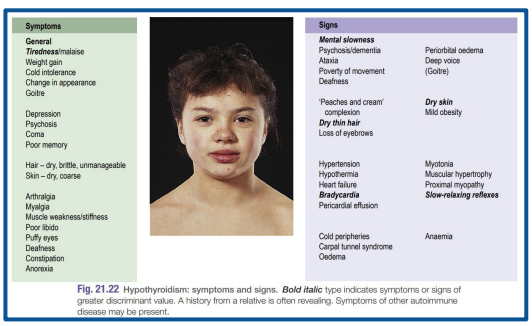


Fig. 21.22 Hypothyroidism: symptoms and signs. *Bold italic* type indicates symptoms or signs of greater discriminant value. A history from a relative is often revealing. Symptoms of other autoimmune disease may be present.

Hypothyroidism

◀ Clinical presentations and findings (in adults) Cont.

Cardiovascular

- Bradycardia
- Decreased cardiac output
- **Low voltage ECG** (due to pericardial effusion)
- Cardiomegaly
- Pericardial effusion

Anemia

- Impaired hemoglobin synthesis
- Iron deficiency
- Folate deficiency
- Pernicious anemia, with B12 deficiency megaloblastic anemia

CNS[1]

- Chronic fatigue
- Lethargy
- **Decreased concentration**
- Anovulatory cycles and infertility
- Menorrhagia
- Depression, Agitation

Renal function

- Impaired GFR
- Water intoxication

Pulmonary function

- Shallow and slow respiration
- Respiratory failure

Neuromuscular system

- Severe muscle cramps
- Paresthesias
- Muscle weakness
- Carpal tunnel syndrome

GI

- Chronic constipation
- Ileus

◀ Diagnosis:

- **Serum TSH is the investigation of choice; a High TSH, level confirms primary hypothyroidism.**
- **A low free T4** level confirms the hypothyroid state (and is also essential to exclude TSH deficiency if clinical hypothyroidism is strongly suspected and TSH is normal or low).
- **Low T3,** unhelpful since they do not discriminate reliably between euthyroidism and hypothyroidism.
- TRH stimulation test (old, not used)
- **Positive TPO antiboidies**
- **Other abnormalities include the following:**
  - **Anaemia**, which is usually normochromic and normocytic in type but may be macrocytic (sometimes this is due to associated pernicious anaemia) or microcytic (in women, due to menorrhagia or undiagnosed coeliac disease)
  - **Low Na** due to an increase in ADH and impaired free water clearance (dilutional hyponatremia due to fluid retention).
  - increased serum aspartate transferase levels, from muscle and/or liver
  - increased serum creatine kinase levels, with associated myopathy
  - **High cholesterol,** mainly hypertriglyceridemia

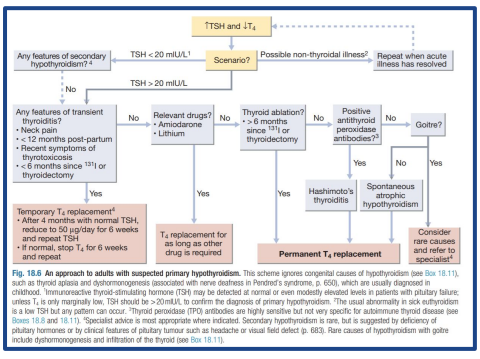


Fig. 18.6 An approach to adults with suspected primary hypothyroidism. This scheme ignores congenital causes of hypothyroidism (see Box 18.11), such as thyroid aplasia and dyshormonogenesis (associated with nerve deafness in Pendred's syndrome, p. 650), which are usually diagnosed in childhood. [1]Immunoreactive thyroid-stimulating hormone (TSH) may be detected at normal or even modestly elevated levels in patients with pituitary failure; unless T_4 is only marginally low, TSH should be >20 mIU/L to confirm the diagnosis of primary hypothyroidism. [2]The usual abnormality in sick euthyroidism is a low TSH but any pattern can occur. [3]Thyroid peroxidase (TPO) antibodies are highly sensitive but not very specific for autoimmune thyroid disease (see Boxes 18.8 and 18.11). [4]Specialist advice is most appropriate where indicated. Secondary hypothyroidism is rare, but is suggested by deficiency of pituitary hormones or by clinical features of pituitary tumour such as headache or visual field defect (p. 683). Rare causes of hypothyroidism with goitre include dyshormonogenesis and infiltration of the thyroid (see Box 18.11).

1. Confusion, loss of memory, problems in concentration are common presentations especially in the elderly.

Hypothyroidism

◀ Treatment:

Hypothyroidism

Lifelong Levothyroxine (T4).

- Follow serum Free T4 and TSH
- Take dose in AM
- Do blood test fasting before taking the daily dose
- Adults: 1.7-2 ug/kg/d, but lower in elderly (1.6 ug/kg/d)
- For TSH suppression (nodular goiters or cancer): 2.2 ug/kg/d
- Increase dose of T4 in malabsorptive states or concurrent administration of aluminum preparations, cholestyramine, calcium, or iron compounds. make sure to separate them at least 4 hours apart
- Increase dose of T4 in pregnancy and lactation
- The t1/2 of levothyroxine is 7 days

i 18.12 Situations in which an adjustment of the dose of levothyroxine may be necessary

Increased dose required

Use of other medication
- Increase T_4 clearance: phenobarbital, phenytoin, carbamazepine, rifampicin, sertraline*, chloroquine*
- Interfere with intestinal T_4 absorption: colestyramine, sucralfate, aluminium hydroxide, ferrous sulphate, dietary fibre supplements, calcium carbonate

Pregnancy or oestrogen therapy
- Increases concentration of serum thyroxine-binding globulin

After surgical or ^{131}I ablation of Graves' disease
- Reduces thyroidal secretion with time

Malabsorption

Decreased dose required

Ageing
- Decreases T_4 clearance

Graves' disease developing in patient with long-standing primary hypothyroidism
- Switch from production of blocking to stimulating TSH receptor antibodies

*Mechanism not fully established.

Toxic effects of levothyroxine therapy

- No allergy has been reported to pure levothyroxine.
- If FT4 and TSH are followed and T4 dose is adjusted, no side effects are reported
- If FT4 is higher than normal: hyperthyroidism symptoms may occur:
  - Cardiac symptoms
  - Osteopenia
  - Osteoporosis

Myxedema with heart disease

- Start treatment slowly in long standing hypothyroidism and in elderly patients particularly those with known cardiovascular disease
- 25 ug/d x 2 weeks, increase by 25 ug every 2 weeks until a daily dose of 100-125 ug is reached

◀ Hypothyroidism in pregnancy

- Women with hypothyroidism usually require an increased dose of levothyroxine in pregnancy.
- Inadequately treated hypothyroidism in pregnancy has been associated with impaired cognitive development in the fetus.

◀ Complications:

1. **Myxedema coma.**
2. **Myxedema and heart disease**
3. **Hypothyroidism and neuropsychiatric disease**

Myxedema coma

◀ Clinical features

Myxoedema coma is a medical emergency and treatment must begin before biochemical confirmation of the diagnosis. it is The end stage of untreated hypothyroidism.
Associate illnesses and precipitating factors: Pneumonia, MI, cerebral thrombosis, GI bleeding, ileus, excessive fluid administration, and administration of sedatives and narcotics.

Three main issues:

1. CO2 retention and hypoxia
2. Fluid and electrolyte imbalance
3. Hypothermia.

Clinical presentation

- **Cardinal symptoms:** impaired mental status, hypothermia, and concurrent myxedema
- Progressive Weakness, stupor hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, death.

◀ Treatment

- **IV** combination of **levothyroxine** and **liothyronine** plus IV **hydrocortisone**

1	Acute medical emergency	6	Avoid excessive hydration
2	Monitor blood gases	7	Assess adrenal function and treat if needed
3	Patient may need intubation and mechanical ventilation	8	Active rewarming of the body in contraindicated
4	Treat associated medical problems	9	Be cautious in patients with coronary artery disease
5	In pituitary myxedema, glucocorticoid replacement is essential	10	**IV levothyroxine:** loading 300-400 ug, daily maintenance 50 ug

Recommendations for the treatment of myxedema coma			
Hypothyroidism	large initial intravenous dose of 300-500 µg T4; if no response within 48 hours, add T3	**Hypocortisolemia**	intravenous hydrocortisone 200-400 mg daily
Hyponatremia	mild fluid restriction	**Hypoglycemia**	glucose administration
Hypotension	Cautious volume expansion with crystalloid or whole blood	**Hypothermia**	blankets, no active rewarming
Hypoventilation	don't delay intubation and mechanical ventilation too long	**Precipitating event**	identification and elimination by specific treatment (liberal use of antibiotics)

Hyperthyroidism & Thyrotoxicosis

Definition

- **Thyrotoxicosis:** is the clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormone
- **Hyperthyroidism:** is the hyperactivity of the thyroid gland

Conditions associated with thyrotoxicosis

Diffuse toxic goiter (Graves' disease)	Toxic adenoma (Plummer's disease)	Toxic multinodular goiter	Subacute thyroiditis	Hyperthyroid phase of Hashimoto's	Thyrotoxicosis factitia	Other rare causes:
most common cause of hyperthyroidism. Result of IgG antibodies binding to TSH receptor.	autonomous thyroid nodule overproduces thyroid hormones leading to hyperthyroidism → decrease in pituitary TSH secretion. Solitary, hot nodule	multiple hyperfunctioning (hot) nodules.	**Painful goiter.** Features of hyperthyroidism due to leakage of hormone from inflamed thyroid followed by features of hypothyroidism	transient hyperthyroidism.	The T4 :T3 ratio (typically 30 : 1 in conventional thyrotoxicosis) is increased to above 70 : 1	• ovarian struma • metastatic thyroid carcinoma (follicular), • hydatidiform mole, • TSH secreting pituitary tumor, • pituitary resistance to T3 and T4

Clinical features of hyperthyroidism

Cardio&Respa

- Dyspnoea & tachycardia
- **Atrial fibrillation**[1] in 10-20 %
- High output cardiac failure
- Wide pulse pressure
- hypertension

Thyroid function tests are mandatory in any patient with atrial fibrillation

Skin

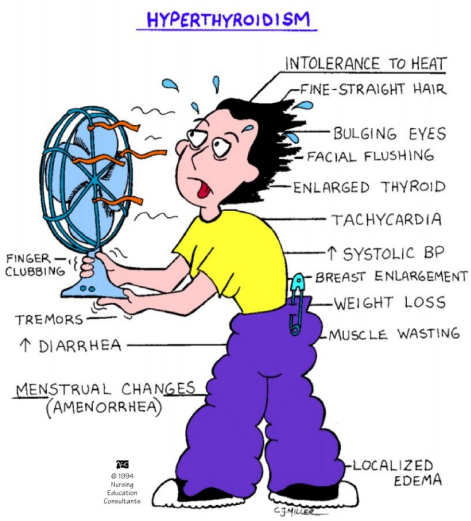
- **Warm, excessive sweating**
- Onycholysis & clubbing
- **hyperpigmentation**
- Pruritus, vitiligo, alopecia, **thinning** of the hair[2]
- **Pretibial myxedema**[3]

GI

- Weight loss
- diarrhoea
- increase liver enzyme

Eyes

- **Sympathetic overactivity**
- **Common only in graves' disease**
- **Extraocular muscles dysfunction**[4]**:** diplopia, proptosis, lid retraction, corneal ulceration[5], optic neuropathy and blindness
- **Periorbital swelling** and **conjunctival edema**



Others

Bone:
- increased turnover: osteoporosis

Neuropsychiatry:
- Behavioral and personality changes: irritability, depression, anxiety, restlessness and psychosis

1. Thromboembolic vascular complications are particularly common in thyrotoxic atrial fibrillation so that anticoagulation is required, unless contraindicated.
2. due to autoimmunity
3. Characteristically seen in graves.
4. why do these happen? the eye muscles contain TSH receptors → autoimmunity against these receptors leads to hypertrophy of the muscles
5. due to inability to close the eyes

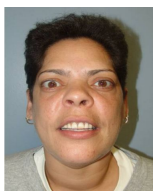
Hyperthyroidism

◄ Diffuse Toxic Goiter (Graves' disease):

Graves disease is an Autoimmune disease of unknown cause. It is the **most common form** of **thyrotoxicosis**. Affects Females more than Males. Peak incidence in the 20- to 40- year age group.

➔ There is a strong familial predisposition

➔ There is an association with HLA-88, DR3 and DR2



Features include:

- Thyrotoxicosis
- Goiter
- **Orbitopathy*** (**exophthalmos**)
- **Dermopathy*** (pretibial myxedema) (rare)

* **specific for graves**

Pathogenesis

Inflammatory reaction due to local **viral** infection[1]

↓

Production of **IFN-g** and other cytokines by **non-thyroid-specific infiltrating immune cells**

↓

Will induce the expression of **HLA class II** molecules on the surface of thyroid follicular cells.

↓

Subsequently, **thyroid specific T-cells** will recognize the antigen presented on the HLA class II molecules and will be activated

↓

The activated thyroid-specific T-cells **stimulate B cells** to produce **TSH receptor-stimulating antibodies**

↓

Hyperthyroidism

◄ Diagnosis

- **Elevated FT4**
- **Suppressed TSH**

The first-line investigations are serum T3(↑) , T4(↑) and TSH(↓)

→ **Eye signs?** (**Eg. exophthalmos**)

+Ve → **This is graves disease, No further test needed.**

-Ve → **Do Thyroid scan "Radioactive uptake"** (next slide)

• Other labs:

- **Increased Free T3:**
  - You order FT3 especially when TSH is suppressed & normal T4. To check for T3 thyrotoxicosis.
- **TSH receptor stimulating antibodies:**
  - Especially in pregnancy
  - They are **specific** for **Graves' disease**.

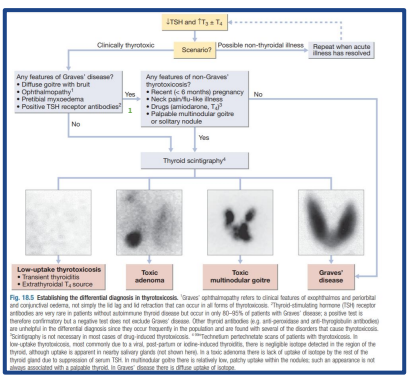
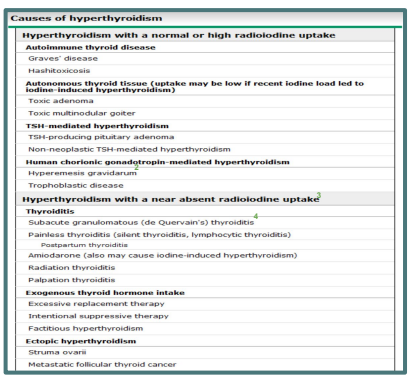


Fig. 18.5 Establishing the differential diagnosis in thyrotoxicosis. 'Graves' ophthalmopathy refers to clinical features of exophthalmos and periorbital and conjunctival oedema, not simply the lid lag and lid retraction that can occur in all forms of thyrotoxicosis. [1]Thyroid-stimulating hormone (TSH) receptor antibodies are very rare in patients without autoimmune thyroid disease but occur in only 80–95% of patients with Graves' disease; a positive test is therefore confirmatory but a negative test does not exclude Graves' disease. Other thyroid antibodies (e.g. anti-peroxidase and anti-thyroglobulin antibodies) are unhelpful in the differential diagnosis since they occur frequently in the population and are found with several of the disorders that cause thyrotoxicosis. [2]Scintigraphy is not necessary in most cases of drug-induced thyrotoxicosis. [3,4]Technetium pertechnetate scans of patients with thyrotoxicosis. In low-uptake thyrotoxicosis, most commonly due to a viral, post-partum or iodine-induced thyroiditis, there is negligible isotope detected in the region of the thyroid, although uptake is apparent in nearby salivary glands (not shown here). In a toxic adenoma there is lack of uptake of isotope by the rest of the thyroid gland due to suppression of serum TSH. In multinodular goitre there is relatively low, patchy uptake within the nodules; such an appearance is not always associated with a palpable thyroid. In Graves' disease there is diffuse uptake of isotope.



Causes of hyperthyroidism
Hyperthyroidism with a normal or high radioiodine uptake
Autoimmune thyroid disease
Graves' disease
Hashitoxicosis
Autonomous thyroid tissue (uptake may be low if recent iodine load led to iodine-induced hyperthyroidism)
Toxic adenoma
Toxic multinodular goiter
TSH-mediated hyperthyroidism
TSH-producing pituitary adenoma
Non-neoplastic TSH-mediated hyperthyroidism
Human chorionic gonadotropin-mediated hyperthyroidism
Hyperemesis gravidarum
Trophoblastic disease
Hyperthyroidism with a near absent radioiodine uptake
Thyroiditis
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
Exogenous thyroid hormone intake
Excessive replacement therapy
Intentional suppressive therapy
Factitious hyperthyroidism
Ectopic hyperthyroidism
Struma ovarii
Metastatic follicular thyroid cancer

1. Yersinia enterocolitica, Escherichia coli and other Gram-negative organisms contain TSH-binding sites. This raises the possibility that the initiating event in the pathogenesis may be an infection with possible 'molecular mimicry' in a genetically susceptible individuals
2. Happens in early pregnancy due to increased HCG, which is structurally similar to TSH, which leads to transient gestational hyperthyroidism that resolves on its own by the 3rd trimester.
3. Why? Because it is only an inflammation (excessive intake, URTI, or ectopic production)
4. Caused by upper respiratory tract infection

Diffuse Toxic Goiter (Graves' disease)

◀ Thyroid scan:

A Technetium or Radioiodine uptake scan:

- **Graves disease:** The gland is **hyperactive** → Will take more iodine → **Hot** gland on imaging (Increased uptake)
- **Thyroiditis:** The gland is **NOT** hyperactive because it is **destroyed** due to inflammation → **Cold** gland on imaging

Elevated uptake in:

1. **Graves' disease**
2. Toxic Multinodular goiter

Hyperthyroidism with a normal or high radioiodine uptake
Autoimmune thyroid disease
Graves' disease
Hashitoxicosis
Autonomous thyroid tissue (uptake may be low if recent iodine load led to iodine-induced hyperthyroidism)
Toxic adenoma
Toxic multinodular goiter
TSH-mediated hyperthyroidism
TSH-producing pituitary adenoma
Non-neoplastic TSH-mediated hyperthyroidism
Human chorionic gonadotropin-mediated hyperthyroidism
Hyperemesis gravidarum
Trophoblastic disease

Low uptake in:

1. Spontaneous resolving hyperthyroidism
2. Subacute thyroiditis
3. Thyrotoxic phase of Hashimoto's thyroiditis
4. Iodine loaded patients
5. Patients on LT4 therapy
6. Struma ovarii

Hyperthyroidism with a near absent radioiodine uptake
Thyroiditis
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
Exogenous thyroid hormone intake
Excessive replacement therapy
Intentional suppressive therapy
Factitious hyperthyroidism
Ectopic hyperthyroidism
Struma ovarii
Metastatic follicular thyroid cancer

◀ Atypical presentation:

Thyrotoxic periodic paralysis	• Because of thyrotoxicosis and hypokalemia
Thyrocardiac disease	• Try to treat cardiac pts early to prevent IHD aggravation
Apathetic hyperthyroidism	• Especially in the **elderly** they might have Hyperthyroidism without its characteristic signs and symptoms, they might present only with weight loss (or clinical picture more like that of hypothyroidism.)
Familial dysalbuminemic hyperthyroxinemia	• Rare condition.

◀ Complications:

Thyrotoxic crisis (thyroid storm)

Predisposing conditions such as stress, infection or surgery in an unprepared patient. **Clinical features:**

- Fever, agitation, Altered mental status
- Atrial fibrillation, Heart failure, liver dysfunction
- Extreme restlessness

Treatment:

- Antithyroid drugs
- **Steroids**: Prevent the conversion of T4 to T3
- BB and IV fluid
- **Ipodate sodium:** inhibits the release of thyroid hormone + reduces the conversion of T4 to T3

Orbitopathy

- First it needed to be managed medically with **steroids (best initial)** to avoid dryness.
- If the patient is cured from graves but still have exophthalmos, this could be corrected surgically.

Treatment of Graves' disease

◀ Antithyroid drug therapy:

Thionamides: Propylthiouracil, methimazole, or carbimazole

- Inhibit the production of the thyroid hormone, Good for short term treatment
  - (Duration of treatment 6 months – years)
- It is important to **start Antithyroid drugs** before Radioactive iodine or surgery in patients with severe graves, because it may precipitate **thyroid storm.**
- Spontaneous remission 20-40%. Relapse 50-60%. Reactions to antithyroid drugs are rare

Advantages	Chance of permanent remission, some patients avoid permanent hypothyroidism, lower cost
Dis-advantages	Risk of **fetal goiter and hypothyroidism if pregnant**. Requires more frequent monitoring. **Major side effects: agranulocytosis**, vasculitis (Lupus-like syndrome), hepatitis, bone marrow suppression **Minor side effects:** rash, hives, arthralgia, transient granulocytopenia, GI symptoms

◀ Radioactive iodine therapy

- Given to patients of all ages, although it is contraindicated in pregnancy and while breastfeeding.
- **^{131}Iodine** is most commonly used. **Dose**: 131I (uci/g) x thyroid weight x 100/ 24-hr RAI uptake.

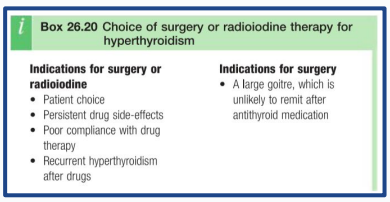
Advantages	**Permanent resolution** of hyperthyroidism. There is no increased risk of malignancy after RAI.
Dis-advantages	Permanent hypothyroidism. Patient must take radiation precautions for several days after treatment, avoiding contact with young children and pregnant women. Patient concerns about long-term effect of radiation. Rare radiation thyroiditis.

◀ Surgical treatment:

When? Either for **big goiter** or **failure** of the previous two modalities .

- Subtotal thyroidectomy
- Preparation for surgery: control HR,BP, thyroxine levels
- **Complications:**
  - Permanent Hypothyroidism/ hypoparathyroidism and hypocalcemia
  - Recurrent laryngeal nerve injury, hoarseness

When to start thyroxine therapy after removal of the gland? IMMEDIATELY!



Box 26.20 Choice of surgery or radioiodine therapy for hyperthyroidism

Indications for surgery or radioiodine
- Patient choice
- Persistent drug side-effects
- Poor compliance with drug therapy
- Recurrent hyperthyroidism after drugs

Indications for surgery
- A large goitre, which is unlikely to remit after antithyroid medication

Advantages	Rapid, permanent cure of hyperthyroidism

◀ Others:

Symptomatic treatment	• **Beta-blockers:** used to provide rapid partial symptomatic control; they also decrease peripheral conversion of T4 to T3 • Super saturated potassium Iodine (**SSKI**)
Thyrotoxicosis & Pregnancy: Males slides	• Treat with **Propylthiouracil** in **first trimester**, and then you can switch to carbimazole, it is recommended in the **second** and **third** trimesters, as liver problems are more frequently described on PTU. • Make sure to keep T4 level at the **upper** normal range (12-**20**) to prevent hypothyroidism in the fetus.

Hyperthyroidism

◀ Treatment of other forms of thyrotoxicosis:

Toxic adenoma

- Antithyroid medications
- Radioactive iodine (It will treat it, but it won't reduce the size of the nodule to zero)
- **Surgery** (Best if there are no contraindications)

toxic multinodular goiter

Same approach.

- Antithyroid medications
- Radioactive iodine
- Surgery

Amiodarone

If the patient's arrhythmia is controlled with amiodarone and they have thyroid problems. **The best is to remove the gland**, **DO NOT stop the medication.**

Subacute thyroiditis:

Symptomatic treatment

- **Thyrotoxic phase:** Give BB
- **Hypothyroid phase:** short duration of thyroxine therapy

Thyrotoxicosis factitia

thyrotoxicosis caused by the ingestion of exogenous thyroid hormone

- To diagnose and treat this condition; you need to take a good and detailed history.

Strauma ovarii

Rare disease; Exogenous thyroxine production

- Treated surgically.

◀ Other thyroid disorders

- **Nontoxic goiter:** if the function is normal, no malignancy, no compression symptoms? Just observe
- **Subacute thyroiditis (De Quervain's):** Symptomatic therapy
- **Chronic thyroiditis:** Usually they end up with hypothyroidism, so treat it as hypothyroidism
- **Acute thyroiditis:** VERY painful, give pain medications and BB
- **Thyroid cancer**
- **Thyroid nodules:**
  - **a.** Anybody with thyroid nodule, **do FNA**. Unless the TSH is low (so the patient might have toxic nodule) which the risk of malignancy is very low. in this case you do thyroid scan.

In ANY thyroid problem, you need to remember and assess THREE principals:

1. **Anatomy** (The size)**:**
   - **Big gland causing compression symptoms, regardless** of the **biochemistry (Hyper/Hypo)** and **pathology (Benign/Malignant)**. **The ideal is to remove the gland.**
2. **Biochemistry**
   - Normal size, No pathology, but **the function is abnormal (Hyper/Hypo)** then you treat accordingly.
3. **Pathology**
   - Normal size, the function is completely normal. **But has one nodule**, you did FNA and came to be **malignant**; so the gland **need to be removed**

Hyperthyroidism & Hypothyroidism

◄ Case from the doctor

A 29 year old female came to the clinic complaining of fatigue, increased sleepiness, not feeling well . Nothing significant on examination. Her TSH is 1 mU/L (normal 0.4 and 4.0mU/L), FT4 is normal, high antithyroglobulin antibodies and high antithyroperoxidase antibodies. What should you do?

- **Apply the three principles**;
  1. **Size?** normal
  2. **Function?** Normal
  3. **Pathology?** No nodules

➔ **So just follow up the patient.**

◄ Patterns of thyroid function test during assessment of thyroid function

Serum TSH	Serum T4	Serum T3	Assessment
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
	Normal of high	Normal or high	Euthyroid or hyperthyroxinema
	Normal or low	Normal or low	Euthyroid or hyporthyroxinema
	Low	Normal or high	Euthyroid : triiodothyronine therapy
	Low normal or low	Normal or high	Euthyroid : thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
	Normal	Normal	Subclinical hypothyroidism
Low	High or Normal	High	Hyperthyroidism
	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic-pituitary function			
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.

◄ Goiter:

Common Thyroid disorders			
Goiter	**Goiter:** Chronic Enlargement of thyroid gland not due to neoplasm **Endemic Goiter:** common in china and central africa **Sporadic Goiter:** multinodular goiter **Familial:**	**Others**	• Chronic iodine excess • Medication: lithium in 6% • neoplasm • Diet: cabbage, Cauliflower
Hashimoto's thyroiditis	in early stage due to inflammation	**Thyroid function assessment**	**By:** • Free T4, T3 • TSH • Ultrasound neck
Graves' disease:	Due to chronic stimulation of TSH receptor	**Non-toxic goiter** (normal thyroid function)	**Treatment options:** • **Thyroxine suppression therapy:** not useful • **Surgery:** – If pressure symptoms – Malignancy – Lymphadenopathy • **Radioactive iodine therapy**

◄ Unique features of thyroid diseases

Diagnosis	Unique feature
Graves disease	Eye (proptosis) (20%–40%) and skin (5%) findings
Subacute thyroiditis	Tender thyroid
Painless "silent" thyroiditis	Nontender, normal exam results
Exogenous thyroid hormone use	Involuted gland is not palpable
Pituitary adenoma	High TSH level

◄ Significance of thyroid antibodies

Antibody	Significance
Thyroglobulin	Detects recurrence of thyroid cancer
Thyroid-stimulating immunoglobulin (TSI)	- **Confirms Graves disease** - **Not positive** in toxic multinodular goiter
Thyroperoxidase antibody (TPO)	Confirms presence of Hashimoto thyroiditis

Drugs affecting thyroid function

◀ Drugs causing Hypothyroidism

Inhibition of thyroid hormone synthesis and\or release

Thionamides , lithium , perchlorate , aminoglutethimide , thalidomide , and iodine and iodine containig drugs including amiodarone , radiographic agents , expectorants (organidin , combid) , kelp tablets , potassium idoine solutions (sski) , betadine douches , topical antiseptics

Decreased absorption of T4

Cholestyramine , colestipol , colesevelam , aluminum hydroxide , calcium carbonate , surcraflate , iron sulfate , raloxifene , omeprazole , lansoprazole , and possibly other medications that impair acid secretion , sevelemer , lanthanum carbonate , and chromium , malabsorption syndrome 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

◀ Drugs causing Hyperthyroidism

Stimulation of thyroid hormone synthesis and\or release:

- Iodine
- Amiodarone

Immunedysregulation:

- Interferon-alfa
- Interleukin-2
- Denileukin diftitox

◀ Drugs affecting Thyroid function or Tests without thyroid dysfunction:

Low serum TBG	Androgens - danazol , glucocorticoids , slow release niacin (nicotinic acid) , I,aspraginase
High serum TBG	High serum TBG , estrogen , tamoxifen , raloxifene , methadone , 5-fluouracil , clofibrate, heroin, mitotane
Decreased T4 binding to TBG	Decreased T4 binding to TBG - salicylate , salsalate , furosemide, heparin , (via free fatty acids) , certain NSAIDs
Increased T4 clearance	Increased T4 clearance - phenytoin , carbamazepine , rifampicin , phenobarbital
Suppression of TSH secretion	Suppression of TSH secretion - dobutamine , glucocorticoids ,octeoride
Impaired conversion of T4 to T3	Impaired conversion of T4 to T3 - amiodarone , glucocorticoids , contrast agents for oral cholecystography (iopanoic acid) , propylthiouracil , propranolol , Nadol

Summary

	Hyperthyroidism	Hypothyroidism

Causes	Diffuse toxic goiter (Graves' disease)
	Toxic adenoma (Plummer's disease)
	Toxic multinodular goiter
	Subacute thyroiditis
	Hyperthyroid phase of Hashimoto's thyroiditis
	Iodine-induced hyperthyroidism
	Thyrotoxicosis factitia
	ovarian struma
		1-primary:
		• Hashimoto disease (chronic thyroiditis)
		  ○ most common cause of primary hypothyroidism.
		• Iatrogenic—second most common cause of primary hypothyroidism; results from prior treatments of hyperthyroidism, including:
		  ○ Radioiodine therapy
		  ○ Thyroidectomy
		  ○ Medications (e.g., lithium)
		2-secondary: due to pituitary disease(low TSH)
		3-tertiary: (due to hypothalamic disease (low TRH)

Clinical manifestations:	• Tachycardia, palpitations, arrhythmia (atrial fibrillation) • Diarrhea (hyperdefecation) • Weight loss • Anxiety, nervousness, restlessness • Hyperreflexia • Heat intolerance • Fever	• Bradycardia • Constipation • Weight gain • Fatigue, lethargy, coma • Decreased reflexes • Cold intolerance • Hypothermia (hair loss, edema)
Diagnosis:	All thyroid disorders are **best tested first with a TSH**. If the TSH level is suppressed, measure **free T4** levels. TSH levels are markedly elevated if the gland has failed.	
	Biochemical: • Clinical Hyperthyroidism: FT4 high, FT3 high, TSH low • Subclinical Hyperthyroidism: FT4 normal, FT3 normal, TSH low. • TSH Mediated Hyperthyroidism : FT4 high, FT3 high, TSH high. **Radiological**: Thyroid Scan **Serology**: Thyroid antibodies, TSH Receptor antibodies.	**-Biochemical**: • Primary Hypothyroidism : High TSH, Low T4 • Secondary Hypothyroidism : Low TSH, Low T4 **-Serology**: Thyroid antibodies **-ECG**

Treatment	• Radioactive iodine therapy
	• Anti-thyroid medications:
	  ○ Propylthiouracil
	  ○ methimazole
	• Beta Blockers
	• Thyroidectomy
		Replacing thyroid hormone with Levothyroxine (T4) is sufficient

Complications:	Thyrotoxic crisis (thyroid storm): • Fever / Agitation • Altered mental status • Atrial fibrillation / Heart failure	• Myxedema coma • heart disease • neuropsychiatric disease

Lecture Quiz

Q1:A 33-year-old obese woman complains of tiredness. She has recently given birth to a healthy baby boy and is enjoying being a mother. However, she is becoming more reliant on her partner for support as she always feels exhausted and often becomes depressed. The patient has a poor appetite and often does not finish her meals, despite this she has gained 5 kg in the last 2 weeks. The most likely diagnosis is:

A- Oral glucose tolerance test
B- Eating disorder
C- Hyperthyroidism
D- Hypothyroidism

Q2:A 16-year-old girl presents to her GP complaining of a swelling in her neck which she has noticed in the last 2 weeks. She has felt more irritable although this is often transient. On examination, a diffuse swelling is palpated with no bruit on auscultation. The most likely diagnosis is:

A- Hyperthyroidism
B- Simple goitre
C-Thyroid carcinoma
D- Riedel's thyroiditis

Q3:A 47-year-old woman is referred to the endocrine clinic complaining of a twomonth history of tiredness. Despite wearing several items of clothing, the patient appears intolerant to the room temperature. She has noticed an increase in weight, particularly around her waist. The most appropriate investigation is:

A- Radioiodine scan
B- Thyroid stimulating hormone (TSH)
C- Total tetraiodothyronine level (T4)
D- Tri-iodothyronine level (T3)

Q4: A 58-year-old woman presents with an acutely painful neck, the patient has a fever, blood pressure is 135/85 mmHg and heart rate 102 bpm. The patient explains the pain started 2 weeks ago and has gradually become worse. She also notes palpitations particularly and believes she has lost weight. The symptoms subside and the patient presents again complaining of intolerance to the cold temperatures. The most likely diagnosis is:

A- Thyroid papillary carcinoma
B- Plummer's disease
C- De Quervain's thyroiditis
D- Hyperthyroidism

Q5: A 60-year-old woman comes to the emergency room in a coma. The patient's temperature is 32.2°C (90°F). She is bradycardic. Her thyroid gland is enlarged. There is diffuse hyporeflexia. BP is 100/60. Which of the following is the best next step in management?

A- Await results of T4 and TSH.
B-Obtain T4 and TSH; begin intravenous thyroid hormone and glucocorticoid.
C- Begin rapid rewarming.
D- Obtain CT scan of the head.
E- Begin intravenous fluid resuscitation.

Answers: Q1:D | Q2:B | Q3:B | Q4:C | Q5:B |

Answers Explanation File!

THANKS!!

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Send us your feedback:
We are all ears!