Hypothyroidism and Thyrotoxicosis

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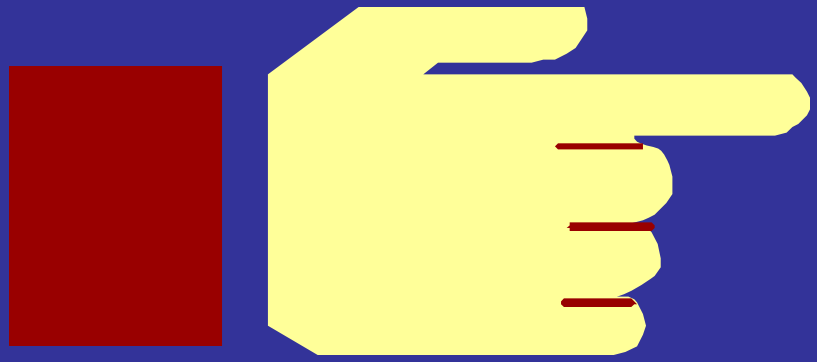
Examination of the thyroid



- Have patient sit on chair
- *Look* at neck before and after swallowing
- Remember the rule of thumbs
- Examine patient in relaxed position
- Palpate firmly down to trachea

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Definition of goiter

- Lateral lobes > terminal phalanges of thumbs

- Grade 0: no goiter
- Grade 1: detectable only by palpation
- Grade 2: visibly enlarged + palpable

- Pemberton's sign in retrosternal goiters

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Thyroid nodules

- Palpable nodules are generally > 1 cm
- Single nodules should generally be aspirated to exclude malignancy
- Multiple nodules suggest benign multinodular goiter
  - Exclude hypo- and hyperthyroidism

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Hypothyroidism: definition

Biochemical and physiologic complex when inadequate serum levels of thyroid hormone are present.

Hypothyroidism and thyrotoxicosis: epidemiology

- both much more common in women
- prevalence of hypothyroidism ↑ with age
  - 0.5-2% of women between 18-60
  - 4-5% of European and American women over 60 years
- Lifetime prevalence of thyrotoxicosis is less common than hypothyroidism
  - ~0.5-2% European women over 60 years

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Symptoms of hypothyroidism

- **Common: cold intolerance, fatigue, mild weight gain, constipation, weakness, muscle cramps, menorrhagia, alopecia, dry skin, brittle nail**

- **Rare: carpal tunnel syndrome, non-pitting edema, yellow skin, hoarseness, arthralgia, mental impairment, tinnitus**

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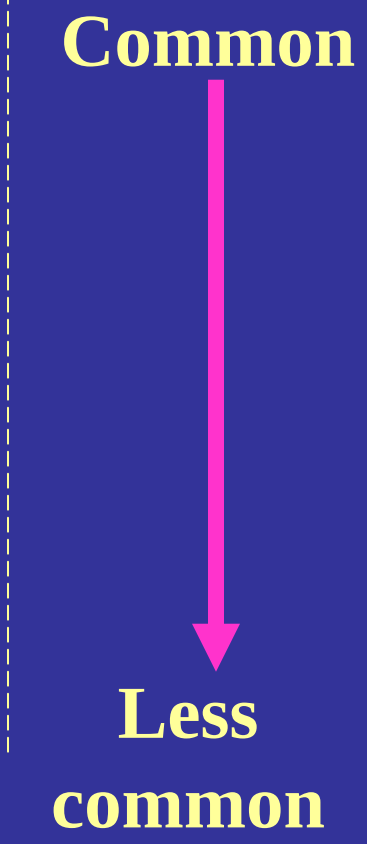
Signs of hypothyroidism

- Delayed relaxation of reflexes
- Dry skin
- Diffuse non-pitting (doughy) edema
- Bradycardia
- Slow speech
- Periorbital edema
- Confusion, altered mental status



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Differential diagnosis of hypothyroidism

- Iodine deficiency
- Autoimmune (Hashimoto's)
- Congenital
- Drugs (e.g., lithium)
- Radioactive iodine
- Thyroidectomy
- Pituitary tumor
  - Suggested by headache, visual impairment, loss of LH/FSH secretion

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Iodine (I_2) deficiency

- Daily requirement
  - 90 micrograms daily for infants < 1 year
  - 200 micrograms daily for adults
- Causes cretinism in children
  - Severe mental retardation, microcephaly
  - Cerebellar ataxia
  - Spasticity
  - Deaf-mutism
- Goiter and hypothyroidism in adults

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I_2 deficiency: epidemiology

- ~35% of population in southeast Asia at risk
- ~15% has goiter (>200 million)
- Selenium ↓ and ↑ cassava exacerbates

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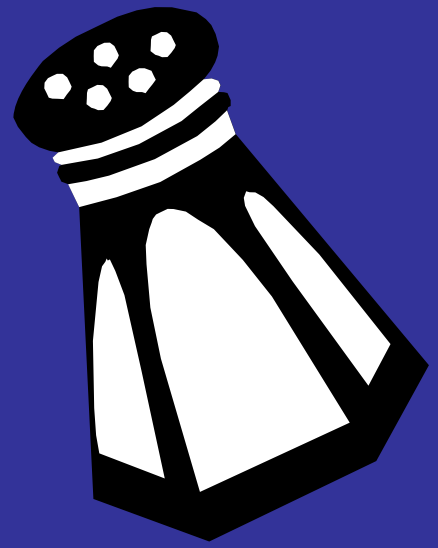
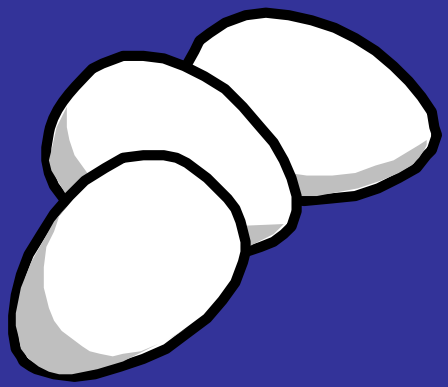
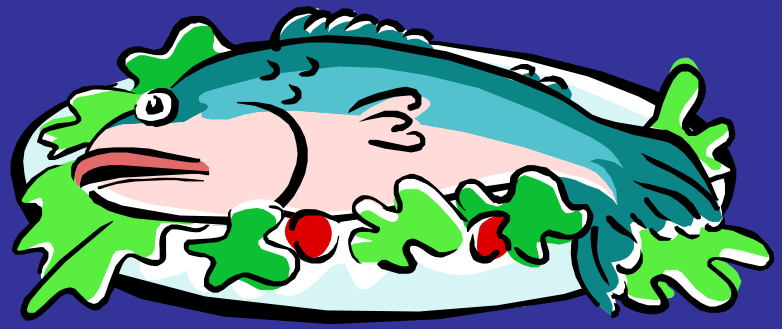
I_2 deficiency: treatment and prevention

- iodinized salt
- Fish, meat, milk, eggs
- NO formula milk
- Thyroid replacement if necessary







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Etiology of hypothyroidism

- **Not important to determine etiology except for I_2 deficiency and pituitary disease**

- **I_2 deficiency**
  - **treat with I_2 +/- thyroxine**
- **All other forms of primary hypothyroidism**
  - **Treat with thyroxine**
- **Secondary hypothyroidism (pituitary disease)**
  - **Treat with thyroxine and exclude pituitary tumor**

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Diagnosis of hypothyroidism

- **Serum TSH is most sensitive indicator of thyroid function *except* when pituitary disease is suspected**
- **Serum total T4 level is also a reasonable test to order if serum TSH cannot be determined**
- **Serum T4 must be measured if pituitary disease is suspected**
- **Primary hypothyroidism: ↓ or normal T4 + ↑ TSH**
- **Secondary hypothyroidism: ↓ T4 + ↓ or normal TSH**

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Treatment of hypothyroidism

- **Treat with levothyroxine**
  - **Typical replacement dosage**
    - **~100 to 125 micrograms daily for women**
    - **~125-150 micrograms daily for men**
    - **~1.5-2.0 microgram per kilogram of body weight daily**

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Treatment of hypothyroidism

- **Initial therapy**
  - **Start at low dosage (25-50 micrograms daily) with frail, elderly patients or in patients with heart disease**
  - **Start at the estimated full dosage for younger, healthier patients**
  - **Check TSH in 4-6 weeks**
- **Adjustment of dosage**
  - **Wait 6 weeks after change of dosage before rechecking TSH and adjusting dosage**

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Thyrotoxicosis: definitions

Thyrotoxicosis:

Biochemical and physiologic complex when excessive serum levels of thyroid hormone are present.

Hyperthyroidism

Thyrotoxicosis that results when thyroid gland overproduces thyroid hormone

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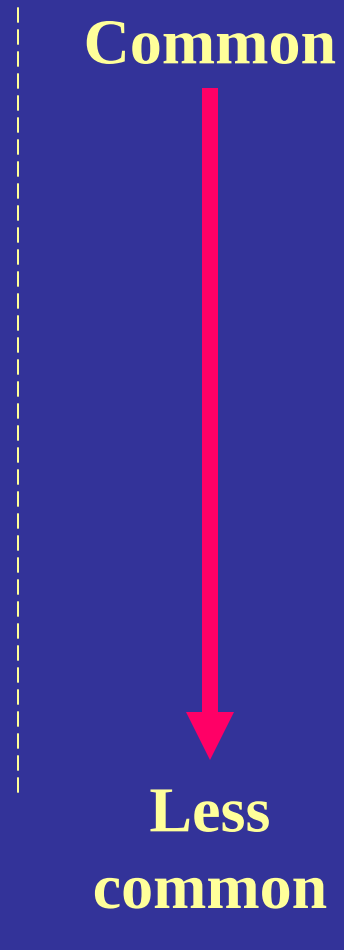
Symptoms of thyrotoxicosis

- **Common primary complaints:**
  - **nervousness, irritability, hand tremor, weight loss, fatigue, palpitations, heat intolerance, amenorrhea/menometrorrhagia**
- **Less common (as primary complaint):**
  - **dyspnea, gynecomastia, proptosis or "burning sensation in eyes", weight *gain*, muscle weakness, diarrhea, osteoporosis**

Signs of hyperthyroidism

- Warm, moist skin
- Tachycardia (heart rate > 85)
- Tremor
- Extraocular tissue inflammation*
- Irregular heart beat (atrial fibrillation)
- Muscle weakness
- Proptosis*
- Pretibial myxedema*



*Graves' disease only

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Differential diagnosis of thyrotoxicosis (common)

Hyperthyroidism

- **TSH receptor antibodies (Graves' disease)**
- **Multinodular goiter**
- **Toxic adenoma**

Thyrotoxicosis not associated with hyperthyroidism

- **Silent thyroiditis**
- **Subacute thyroiditis**
- **Exogenous hormone (medication or food)**

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Differential diagnosis of thyrotoxicosis (rare)

Hyperthyroidism

- **TSH adenoma in pituitary**
- **hCG-mediated: trophoblastic tumor, hyperemesis gravidarum**
- **Thyroid cancer**
- **Struma ovarii**
- **Iodine-induced hyperthyroidism**
- **Drugs: amiodarone, interferon**

Thyrotoxicosis not associated with hyperthyroidism

- **Drugs, radiation thyroiditis, infarction**

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Evaluation of hyperthyroidism: exam

- Look for a goiter (double normal size)
  - Smooth diffusely enlarged goiter (with bruit) suggests Graves' disease
  - Lumpy, bumpy goiter suggests multinodular goiter
  - Tender goiter suggests subacute thyroiditis
- Examine eyes for inflammation
  - Proptosis, extraocular muscle inflammation and chemosis suggests Graves' disease
- Nonspecific findings
  - Warm, moist, smooth skin, fine hair, onycholysis, lid lag, infrequent blinking, irregularly irregular heart beat

Diagnosis of hyperthyroidism

- **Serum TSH is most sensitive indicator of thyroid function**
- **Serum total T4 level is also a reasonable test to order if serum TSH cannot be determined**
- **Serum T4 must be measured if TSH-dependent hyperthyroidism is suspected**
- **Hyperthyroidism (common):**
  - **↑ (or high-normal) T4 + ↓ TSH**
- **Hyperthyroidism (rare!):**
  - **↑ (or high-normal) T4 + ↑ TSH**

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Clinical diagnosis of etiology of common causes of thyrotoxicosis

	Graves' disease	Multi-nodular goiter	Single "hot" adenoma	Subacute thyroiditis	Silent thyroiditis
Goiter	Diffuse +/- bruit	Yes	No	*Painful* goiter	Goiter in 50%
Nodules	No	Multiple	Single	No	No
Eye disease	Proptosis Chemosis	No	No	No	No
Pretibial edema	~5-10%	No	No	No	No

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Radioiodine uptake in thyrotoxicosis

Graves' disease	↑ ↑
Multinodular goiter	↑
Single functional adenoma	↔
Subacute thyroiditis	↓ ↓
Silent thyroiditis	↓ ↓
Acute iodine excess	↓
Exogenous thyroid	↓

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Treatment of thyrotoxicosis

- **Nonspecific treatment of hyperadrenergic state**
  - **Beta blockers for any form of thyrotoxicosis**
  - **Does not reverse hyperthyroxinemia**
  - **Corticosteroids are used only in severe hyperthyroidism**
    - **Block conversion of T4 to more active T3**
- **Specific therapy**
  - **Graves' disease: radioactive iodine, PTU or methimazole, surgery**
  - **Multinodular goiter: radioactive iodine, surgery**
  - **Autonomous nodules: surgery**
  - **Thyroiditis: specific therapy not needed because of eventual spontaneous remission**

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Treatment of Graves' disease

- **Nonspecific treatment of hyperadrenergic state**
  - **Beta blockers**
  - **Corticosteroids are used only in severe hyperthyroidism**
    - **Block conversion of T4 to T3**
- **Specific therapy**
  - **radioiodine: preferred treatment in US**
  - **Medical therapy: PTU, methimazole**
  - **Surgery: seldom indicated**

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Radioiodine for Graves' disease

- **Preferred therapy in United States**
- **Resolution of hyperthyroidism occurs in ~85% with first dose of radioactive iodine; another 10% with second dose**
  - **Safe! Only side effect is occasional salivary gland pain**
  - **Most patients become hypothyroid eventually**
  - **No other longterm risk: no association with malignancy**
- **Pre-medication with anti-thyroid drugs generally not recommended (unless patient is very hyperthyroid)**
  - **Pre-medication with PTU ↓ effectiveness of radioiodine**
  - **Antithyroid drugs should be stopped one week prior to radioiodine**

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Anti-thyroid drugs for treatment of Graves' disease

- **Only ~30-50% chance of "cure"**
- **Most patients will be euthyroid within 6 weeks**
  - **Recurrent hyperthyroidism when drug is stopped**
- **Requires 1-3 years of treatment before "cure"**
- **Highest cure rates seen in patients with small goiters, lower T4 levels at time of diagnosis and small requirements for anti-thyroid drugs to achieve euthyroidism**
- **Methimazole is preferred over PTU**
  - **10 mg once a day dosing *vs* 150-300 mg three times daily**
  - **Dose does not usually need to be adjusted**
  - **Lower incidence of granulocytopenia**

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Summary of treatment of Graves' disease

- **Beta blocker (eg, atenolol)**
- **Proceed directly to radioiodine therapy (6-8 milliCuries)**

  Except...

  - **For very hyperthyroid patients (serum T4 > 30 mcg/dl) or frail patients (eg, elderly patients with coronary disease)**
    - **Methimazole 10 mg daily for 6-8 weeks**
    - **Dose does not usually need to be adjusted**
    - **Lower incidence of granulocytopenia**
  - **Patients who refuse to have radioiodine may opt to take anti-thyroid medication for at least 1-2 years**

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Summary of treatment of multinodular goiter

- **Treatment of hypothyroidism**
  - **Occasional patients with multinodular goiter is hypothyroid**
- **Treatment of hyperthyroidism**
  - **Radioiodine may used but hyperthyroidism may recur years later**
  - **Anti-thyroid drugs will *not* offer any chance of cure**
  - **Surgical extirpation is the definitive therapy**
- **Treatment of anatomic effects**
  - **Radioiodine may shrink goiter 20-60%**
  - **Surgical extirpation is the definitive therapy**

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Summary of treatment of thyrotoxicosis

- **Nonspecific treatment of hyperadrenergic state**
  - **Beta blockers for any form of thyrotoxicosis**
  - **Corticosteroids are used only in severe hyperthyroidism**

- **Specific therapy**
  - **Graves' disease: radioactive iodine, methimazole,**
  - **Multinodular goiter: radioactive iodine, surgery**
  - **Autonomous nodules: surgery**
  - **Thyroiditis: specific therapy not needed because of eventual spontaneous remission**

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Summary of hypothyroidism and thyrotoxicosis

- **Hypothyroidism**
  - **Signs and symptoms are nonspecific**
  - **Iodine deficiency is important to prevent**
  - **Do not check TSH more frequently than every 4-6 weeks**

- **Hyperthyroidism**
  - **Determination of the etiology is important**
    - **Etiology can usually be determined clinically**
    - **Therapy is determined by etiology**

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Case #1

A patient complains of "sandy" sensation in his eyes, weight loss, and a tremor. His extraocular muscles are inflammed. His thyroid is diffusely enlarged and nontender.

The most likely diagnosis is

a. Iodine deficiency

b. Subacute thyroiditis

c. Multinodular goiter

d. Graves' disease

e. Silent thyroiditis

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Case #1

A patient complains of "sandy" sensation in his eyes, weight loss, and a tremor. His extraocular muscles are inflammed. His thyroid is diffusely enlarged and nontender.

The most likely diagnosis is Graves' disease (d).

- **Symptoms of hyperthyroidism**
- **Diffuse enlarged goiter with eye inflammation**
- **No tenderness**

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Case #2

A 60 year patient from Nguyen Binh complains of constipation. He has a heart rate of 60, dry thick skin, and a tongue that has scalloped edges from teeth indentation. He has a goiter.

The most likely diagnosis is

a. Iodine deficiency

b. Subacute thyroiditis

c. Graves' disease

d. Silent thyroiditis

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Case #2

A 60 year patient from Nguyen Binh complains of constipation. He has a heart rate of 60, dry thick skin, and a tongue that has scalloped edges from teeth indentation. He has a goiter.

The most likely diagnosis is iodine deficiency (a).

Signs and symptoms of hypothyroidism

Region of endemic iodine deficiency

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Case #3

A 25 year old woman is three months pregnant. She has a large goiter. Her exam is otherwise normal. Her thyroid tests are normal.

You recommend

a. Cassava five times weekly

b. Fish three times weekly

c. Formula milk for the baby when it is born

d. A very low salt diet

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Case #3

A 25 year old woman is three months pregnant. She has a large goiter. Her exam is otherwise normal. Her thyroid tests are normal.

You recommend fish (b). It is critical to avoid iodine deficiency for mother and child. Cassava exacerbates effects of iodine deficiency. Formula milk provides less iodine to the baby. Iodinated salt is an important source of iodine for many people.

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Case #4

A 72 year old man complains of tremor and inability to concentrate. On exam, he has a heart rate of 100 beats per minute. He has a large goiter with many nodules. He has a fine tremor. His serum T4 is very high and TSH is very low.

Treatments that are likely to improve his symptoms are

a. Iodine therapy

b. ethanol injection of his thyroid

c. 6 weeks of methimazole

d. Radioiodine therapy

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Case #4

A 72 year old man complains of tremor and inability to concentrate. On exam, he has a heart rate of 100 beats per minute. He has a large goiter with many nodules. He has a fine tremor. His serum T4 is very high and TSH is very low.

Hyperthyroidism from a multinodular goiter can be treated with radioiodine (d) or surgical extirpation. Iodine could cause worsening hyperthyroidism in a multinodular goiter. Antithyroid drugs are only a temporizing measure for hyperthyroidism due to a multinodular goiter; hyperthyroidism will recur with discontinuation of the drug.

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Case #5

Radioiodine uptake is high in the thyroid of patients with

a. Silent thyroiditis
b. Single functional adenoma
c. Subacute thyroiditis
d. Acute ingestion of animal thyroid
e. Graves' disease

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Case #5

Radioiodine uptake is high in the thyroid of patients with Graves' disease. Low uptake is seen in thyroiditis and exogenous thyroid ingestion. A single "hot" adenoma usually results in normal iodine uptake.

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