

Thyroid

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Thyroid

Anatomy

- **Thyroid gland forms 2 lobes in the neck and begins to develop at 24 days after conception**
- **The adult thyroid gland weighs 15-25 gm**
- **Thyroid follicular cells produce, store and release thyroxine (T4) and tri-iodothyronine (T3)**
- **Parafollicular cells, or C-cells, secrete calcitonin**

Thyroid

Follicular Cells

- **Follicular cells capture iodine from circulation which is then organified and incorporated into thyroglobulin.**
- **Thyroglobulin is stored in follicles which are surrounded by the follicular cells.**
- **When thyroid releases active hormone, iodinated thyroglobulin is hydrolysed in the follicular cell to T3 and T4, which are released into circulation.**

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Follicular Cells II

- **Follicular cell function is controlled by thyroid stimulating hormone (TSH).**
- **TSH stimulates the cell to increase thyroid hormone release, thyroglobulin synthesis, and growth of thyroid tissue.**

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Parafollicular Cells

- C-cells are derived from neural crest cells of the ultimobranchial body
- Calcitonin release is stimulated by high serum levels of calcium.
- Calcitonin does not play a major role in calcium metabolism in the normal state, however it may have a more significant role during growth, pregnancy, or lactation

Thyroid

Biochemical Thyroid Function Testing

- Introduction of sensitive thyrotropin assays
- Measurement of TSH and free T4 is most efficient battery to order in patients with suspected thyroid disorders
- Resin T3 uptake: measures unoccupied thyroid hormone binding sites on TBG by allowing radiolabeled T3 to compete for binding between TBG and a resin
- Free T4 index (total T4 x RT3 U)
- Antithyroid microsomal antibodies

Thyroid

Thyroid Imaging

- Thyroid scan (technetium 99m)
 - Cold nodules: 15-20% malignant
 - Hot nodules: almost never malignant
- Thyroid scan (iodine-131): useful to identify metastatic differentiated thyroid tumors, diagnose Graves', predict response to radioablation
- Ultrasonography
- CT scanning/ MRI

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Evaluation of Thyroid Disorders

Hyperthyroidism results from excess secretion of thyroid hormone

- Clinical manifestations of hyperthyroidism reflect increased catabolism and excessive sympathetic activity
- Symptoms: weight loss, heat intolerance, excessive perspiration, anxiety, irritability, palpitations, fatigue, muscle weakness, oligomenorrhea
- Signs: goiter, sinus tachycardia or atrial fibrillation, tremor, hyper-reflexia, thinning hair, thyroid bruit
- Young patients present with hypermetabolism
- Older patients may present with tachyarrhythmias or cardiac failure

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Evaluation of Thyroid Disorders

Hypothyroidism

- Clinical features include cold intolerance, weight gain, constipation, edema (especially of eyelids, hands and feet), dry skin, weakness, somnolence, menorrhagia

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Specific Thyroid Disorders

Graves' Disease

- Most common cause of hyperthyroidism
- Caused by circulating immunoglobulins against TSH receptor

Thyroid

Specific Thyroid Disorders

Hyperthyroidism: Lifetime Risk

- **Women - 5%**
- **Men - 1%**

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Specific Thyroid Disorders

Graves' Disease

- **Diffuse goiter**
- **Hyperthyroidism**
- **Exophthalmos**

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Specific Thyroid Disorders

Graves' Disease Laboratory Evaluation

- **TSH** ↓
- **T3, T4** ↑
- **Thyroid stimulation antibody (TSAb)** ↑

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Specific Thyroid Disorders

Graves' Disease

- **Treatment:**
 - **Medical:** Thionamide drugs such as PTU long term remission achieved in less than 20-30% patients
 - **Radioactive iodine:** Ablation with RAI is *treatment of choice* for most patients with Graves' disease (exceptions are pregnant women, newborns, pts who refuse RAI)
 - **Surgery:** Thyroidectomy

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Specific Thyroid Disorders

Graves' Disease-Medical Treatment

- **Blockade of the hormone and its effects:**
 - Thionamide drugs such as propylthiouracil (PTU) 100-300 mg PO tid are most frequently used
 - Rare serious adverse events such as agranulocytosis (0.5%)
 - About 1/3 of patients who tolerate thionamide therapy for 6 months will remain in remission following discontinuation of medicine
 - Young patients with mild hyperthyroidism of recent onset most likely to achieve remission

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Specific Thyroid Disorders

Graves' Disease-Radioactive Iodine Treatment

- **Radioiodine ablation of thyroid tissue:**
 - I-131 is the isotope of choice for radioablation
 - 80 mCi per gram of estimated thyroid tissue is effective for most patients
 - A second dose may be necessary if the patient remains hyperthyroid after 6 months
 - RAI is effective, safe, and does not appear to increase risk of secondary thyroid cancer or other malignancies

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Specific Thyroid Disorders

Graves' Disease-Surgery

- **Surgical resection of thyroid tissue:**
 - Subtotal or total thyroidectomy is effective in treating Graves' hyperthyroidism
 - Surgical treatment appropriate in selected situations

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Specific Thyroid Disorders

Indications for Operation in Graves' Disease

- Synchronous suspicious thyroid nodule
- Pregnancy or the wish to conceive within one year
- Inability to comply with medications or follow-up

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Complications of Graves' Therapy

	Thyroidectomy	RAI	Thionamides
Hypothyroidism	>90%	>95%	
Hyperthyroidism	>5%	5%	60-70%
Hypoparathyroidism	2%		
Nerve injury	1%		
Granulocytopenia			0.02-0.5%
Intolerance of medicine			5-10%

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Specific Thyroid Disorders

Other Causes of Hyperthyroidism

- **Multinodular goiter**
- **Toxic adenoma**
- **Rare causes:**
 - **factitious hyperthyroidism**
 - **pituitary TSH-secreting adenoma**
 - **iodine-induced hyperthyroidism**
 - **trophoblastic tumors and struma ovarii**
 - **thyroiditis**

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Specific Thyroid Disorders

Toxic Adenoma

- **5-10% of hyperthyroidism**
- **Benign tumor of thyroid producing excessive thyroid hormone**
- **No associated exophthalmopathy**
- **“Hot” nodules rarely cancer**
- **Best treated by thyroid lobectomy, although radioiodine also may be used**

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Specific Thyroid Disorders

Hypothyroidism

- **Non-goiterous (primary atrophy)**
- **Goiterous hypothyroidism-Hashimoto's**
- **Post-ablative**
 - **thyroidectomy**
 - **post RAI**

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Specific Thyroid Disorders

Thyroiditis

- Hashimoto's thyroiditis - chronic autoimmune disorder characterized by lymphocytic infiltration of gland
- Acute suppurative thyroiditis - rare, caused by infection with *Streptococcus* or *Staphylococcus* species
- Subacute (de Quervain's) thyroiditis - rare condition, young women, often following viral URI
- Reidel's thyroiditis - progressive inflammatory condition, fibrosis

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Specific Thyroid Disorders

Solitary Thyroid Nodule

- Occurs commonly (4-7% of adults)
- Approximately half of thyroid nodules are solitary and half occur in association with multinodular goiter
- Thyroid nodules are common, thyroid cancer is rare

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Specific Thyroid Disorders

Solitary Thyroid Nodule

- History and physical examination
 - Family history, exposure to ionizing radiation
 - Rapid nodule growth, fixed, compressive symptoms, hoarseness, pain suggest malignancy
- Laboratory evaluation
 - Sensitive TSH, T4

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Specific Thyroid Disorders

Solitary Thyroid Nodule

- FNA
 - Safe, inexpensive, best selection of patients for operation (*Ann Int Med* 118:282, 1993)
 - Benign, malignant, indeterminate, insufficient material
 - False-negative rate <6%

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Specific Thyroid Disorders

Solitary Thyroid Nodule

- FNA
 - Basis for evaluation of most thyroid nodules
 - Approx. 3-6% of patients with benign FNA will have cancer
 - About 85% of nodules that are malignant on FNA will have cancer
 - FNA has decreased by half the number of operations performed, and increased the incidence of cancer in thyroidectomy specimens

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Specific Thyroid Disorders

FNA

- Thyroid malignancies commonly diagnosed
 - Papillary thyroid carcinoma: nuclear features
 - Medullary thyroid carcinoma
- Follicular adenomas cannot be distinguished from follicular carcinomas by cytology
 - Capsular invasion is necessary for diagnosis

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Specific Thyroid Disorders

FNA

- Patients with benign nodules by FNA should be followed at 6 mo intervals by physical exam and US
- If a nodule enlarges during follow-up, repeat FNA or surgery indicated
- The minimal operation for a suspicious nodule is lobectomy and isthmusectomy

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Specific Thyroid Disorders

Solitary Thyroid Nodule-Radiographic evaluation

- Ultrasonography
- CT
- Radionuclide scans
 - Most useful in patients with hyperthyroidism to distinguish diffuse goiter from toxic adenoma

Thyroid

Thyroid Neoplasms

Differentiated Thyroid Cancer

- Female to male ratio 2.5:1.0
- Rare in children and increase in frequency with age
- Risk factors:
 - Childhood exposure to ionizing radiation
 - Family history

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Thyroid Neoplasms

Prognosis

- **AGES**
- **AMES**
- **MACIS**
 - **Metastasis**
 - **Age**
 - **Completeness of resection**
 - **Invasion**
 - **Size**

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Thyroid Neoplasms

Factors that Correlate with Poor Prognosis-
Differentiated Thyroid Neoplasms

- **Male gender**
- **Age > 50 years**
- **Primary tumor larger than 4 cm**
- **Poorly differentiated tumor**
- **Local invasion outside thyroid capsule**
- **Distant metastatic disease**

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Thyroid Neoplasms

Papillary Thyroid Carcinoma (85%)

- **Can occur in any age group, more common in children and women <40 years of age**
- **Often multifocal and metastasizes early to cervical LNs**
- **Occult, clinically insignificant PTCs are found in 4-28% of autopsies or thyroidectomy for benign conditions**
- **Young age at diagnosis is favorable**
- **Even presence of cervical LN metastases does not adversely affect prognosis**

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Thyroid Neoplasms

Follicular Thyroid Carcinoma (10%)

- **Rare before age 30 years**
- **Slightly worse prognosis than PTC**
- **Spreads hematogenously to bone, lung, liver**
- **Small, unilateral FTCs with limited capsular invasion may be treated by thyroid lobectomy**
- **Total thyroidectomy for larger FTCs**
- **Radioablation indicated following thyroidectomy**

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Thyroid Neoplasms

Medullary Thyroid Carcinoma (8-10%)

- **Arises from thyroid C-cells of neural crest origin**
- **May occur sporadically or as a component of multiple endocrine neoplasia type 2A or 2B**

Thyroid

Thyroid Neoplasms

Medullary Thyroid Carcinoma (8-10%)

- **Sporadic MTC - firm palpable unilateral nodule**
- **Hereditary MTC - bilateral, multifocal MTCs; often diagnosed on basis of family screening**
- **Metastases to cervical LNs and then liver, lung, bone**
- **Total thyroidectomy and central LN dissection**
- **Exclude pheochromocytoma prior to surgery**

Thyroid

Thyroid Neoplasms

Undifferentiated or Anaplastic Thyroid Carcinoma (1-2%)

- **Presents as hard, fixed, rapidly enlarging mass**
- **Invasion of local structures**
 - Dysphagia
 - Respiratory compromise
 - Hoarseness
- **Role of thyroidectomy controversial**
- **Chemotherapy (low-dose Doxorubicin) and external irradiation**
- **Extremely poor prognosis**

Thyroid

Summary: Surgical Treatment of PTC and FTC

- **Total thyroidectomy advocated by most surgeons for lesions greater than 2 cm, but operative morbidity must be low**
- **Ipsilateral lobectomy is appropriate for small tumors**
- **Total thyroidectomy allows the use of RAI for post-operative ablation, detection of recurrence or metastases, and use of thyroglobulin levels as marker of tumor recurrence**
- **TSH suppressive therapy with thyroid hormone is begun after radioiodine ablation**