

The Thyroid Gland

Chaitan K. Narsule, M.D.

The Thyroid Gland

- *Thyreoides* = “shield shaped”
- Goiter well-described in literature in 19th century
- Seaweed was medical treatment (iodine rich)

The Thyroid Gland

- Physiology of, and surgical treatment for, thyroid developed and elucidated by:
 - Theodor Biliroth
 - Emil Theodor Kocher (Nobel Prize, 1909)

Embryology

- Derived from endoderm, as midline diverticulum from floor of pharynx
- Descends into neck, forms a bilobar structure
- Point of attachment in pharynx: *foramen cecum*

Embryology

- Thyroglossal duct
 - from foramen cecum to pyramidal lobe
 - often reabsorbed at 6 weeks of age
- Calcitonin-producing C-cells
 - arise from fourth pharyngeal pouch
 - migrate from neural crest cells to lateral lobes

Embryology

- Thyroglossal duct cysts and fistulas can develop from retained tissue along the duct
 - can be chronically infected or draining
 - treated surgically
 - because thyroglossal duct passes through the middle of the hyoid bone, the central portion of it is also resected

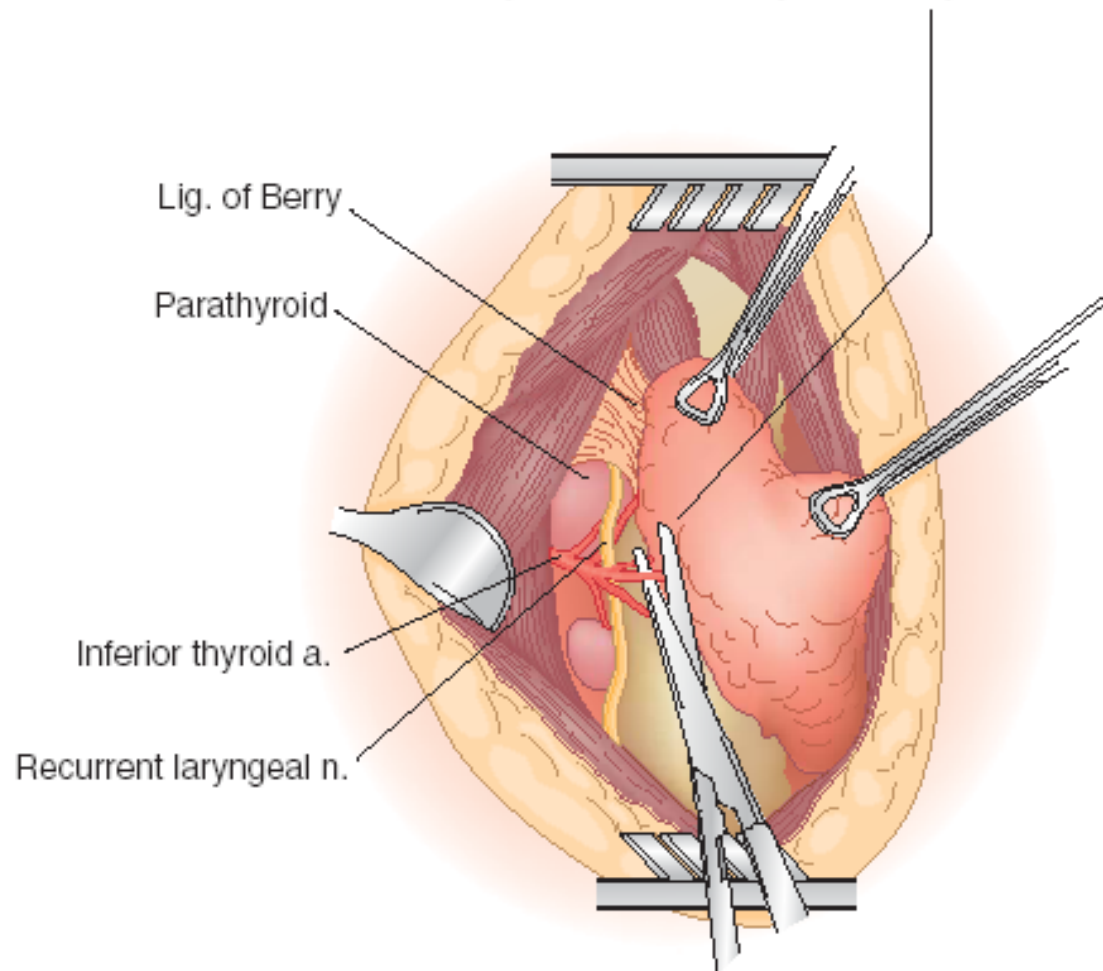
Anatomy

- Encircles 75% of the junction of the trachea and pharynx anteriorly and laterally
- Bilateral lobes joined at center by isthmus, either directly anterior to, or just below, the cricoid cartilage

Anatomy

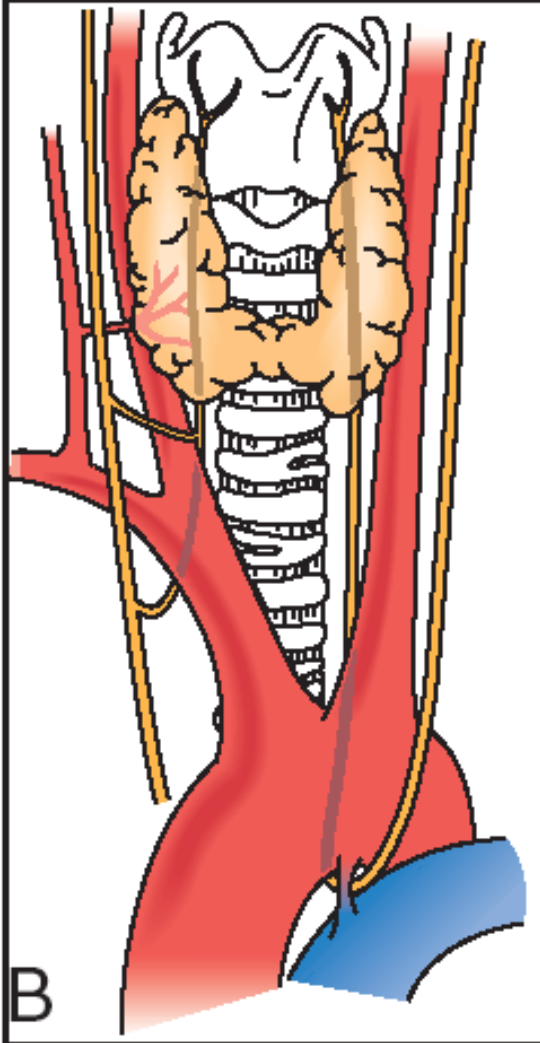
- Fascia surrounds the thyroid and invests the trachea
- Fascia coalesces laterally and posteriorly with thyroid capsule, and forms the ligament of Berry; closely attached to cricoid cartilage

Ligation and division of distal branches
of inferior thyroid a. for total thyroidectomy



Anatomy

- Recurrent laryngeal nerve
 - motor function: abduction of the vocal cords from the midline
 - damage = paralysis of vocal cord on affected side
 - if cords remain abducted: no closure
 - ineffective cough & severely affected voice
 - if cords remain adducted: closure
 - complete loss of voice & AIRWAY OBSTRUCTION (intubation or tracheostomy may be necessary)



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Anatomy

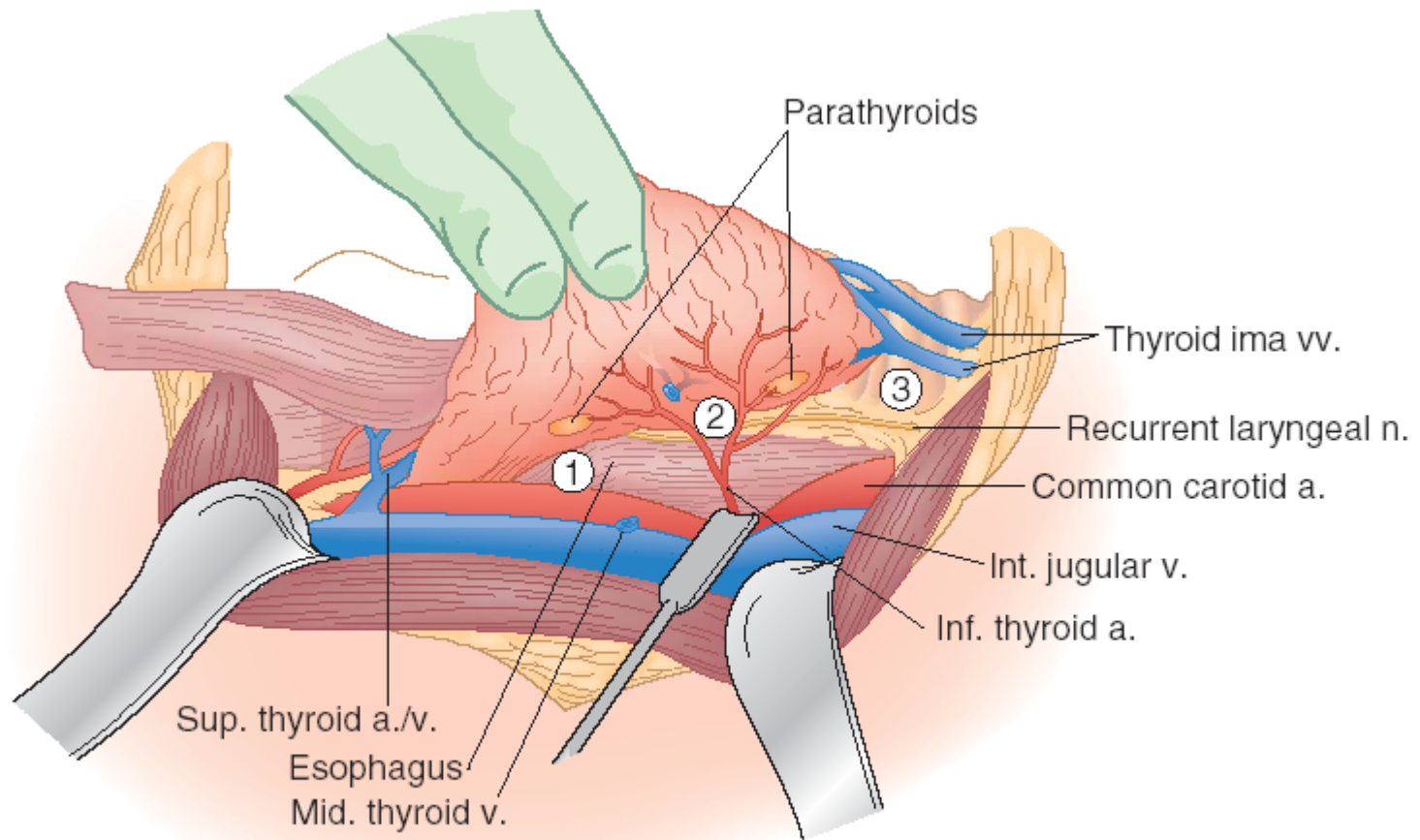
- Superior laryngeal nerve
 - separates from vagus n. as it exits base of skull
 - internal branch = sensory function to larynx
 - enters thyrohyoid membrane
 - external branch = motor to cricothyroid m.
 - damage leads to severe loss in quality of voice or voice strength

Anatomy

- Superior thyroid arteries
 - first branch of external carotid artery
 - separates immediately after carotid bifurcation
- Inferior thyroid arteries
 - origin from the thyrocervical trunk
- Thyroidea ima artery (<5% of all patients)
 - origin from the innominate artery or the aorta

Anatomy

- Inferior thyroid artery almost always supplies superior and inferior parathyroids
 - end arteries with no collateral arterial supply
 - glands almost always invested in fatty islands on posterior surface of thyroid gland



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Anatomy

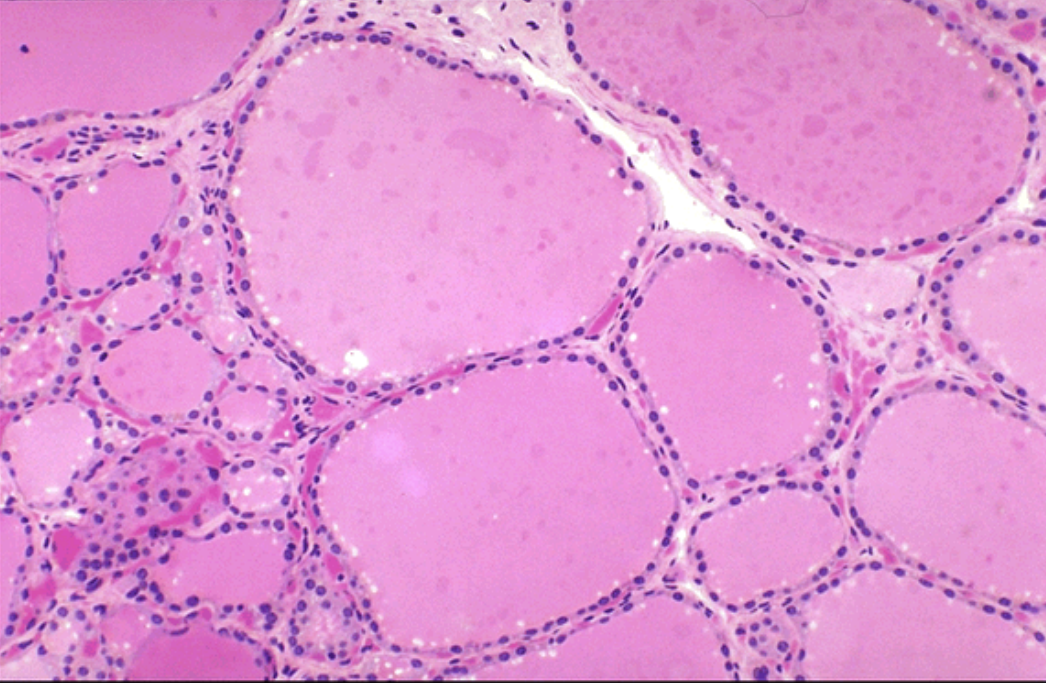
- Thyroid venous drainage:
 - superior thyroid vein: to internal jugular vein
 - middle thyroid vein: to internal jugular vein
 - inferior thyroid vein: to innominate and brachiocephalic veins

Anatomy

- Lymphatic system
 - lymph channels of each lobe connect to contralateral lobe via isthmus
 - drainage to regional lymph nodes
 - pretracheal, paratracheal, tracheoesophageal groove, mediastinal, jugular, retropharyngeal, esophageal

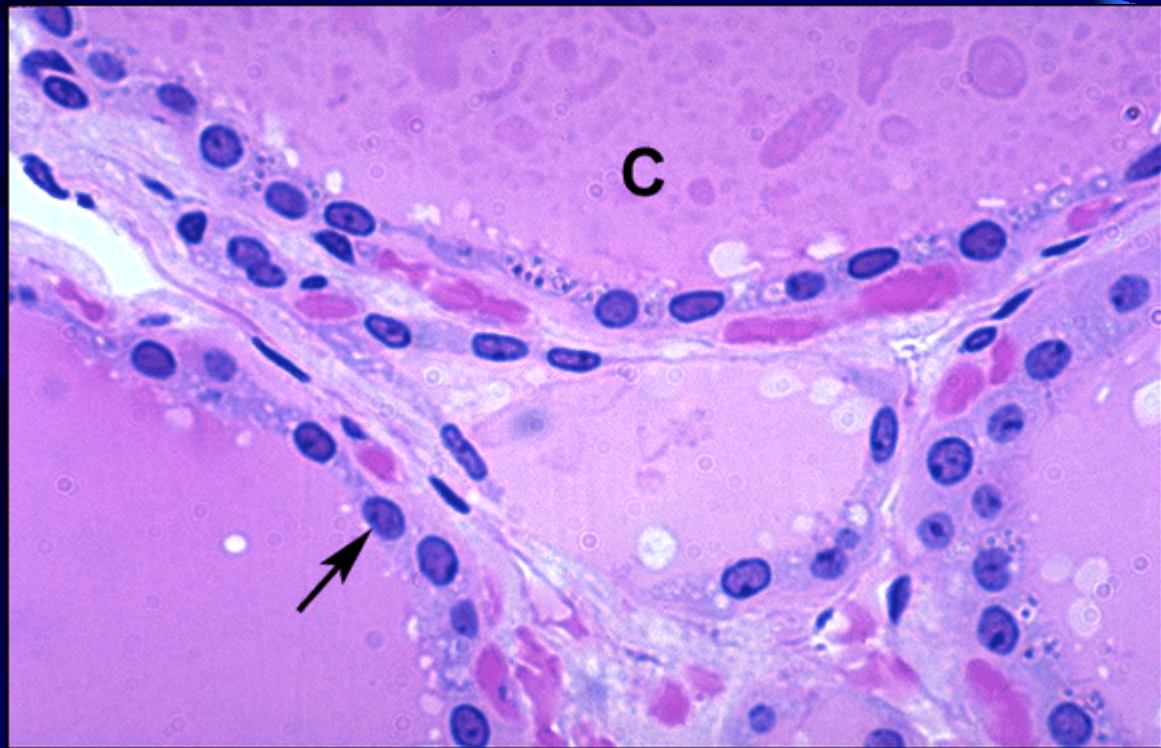
Physiology (Crash-Course)

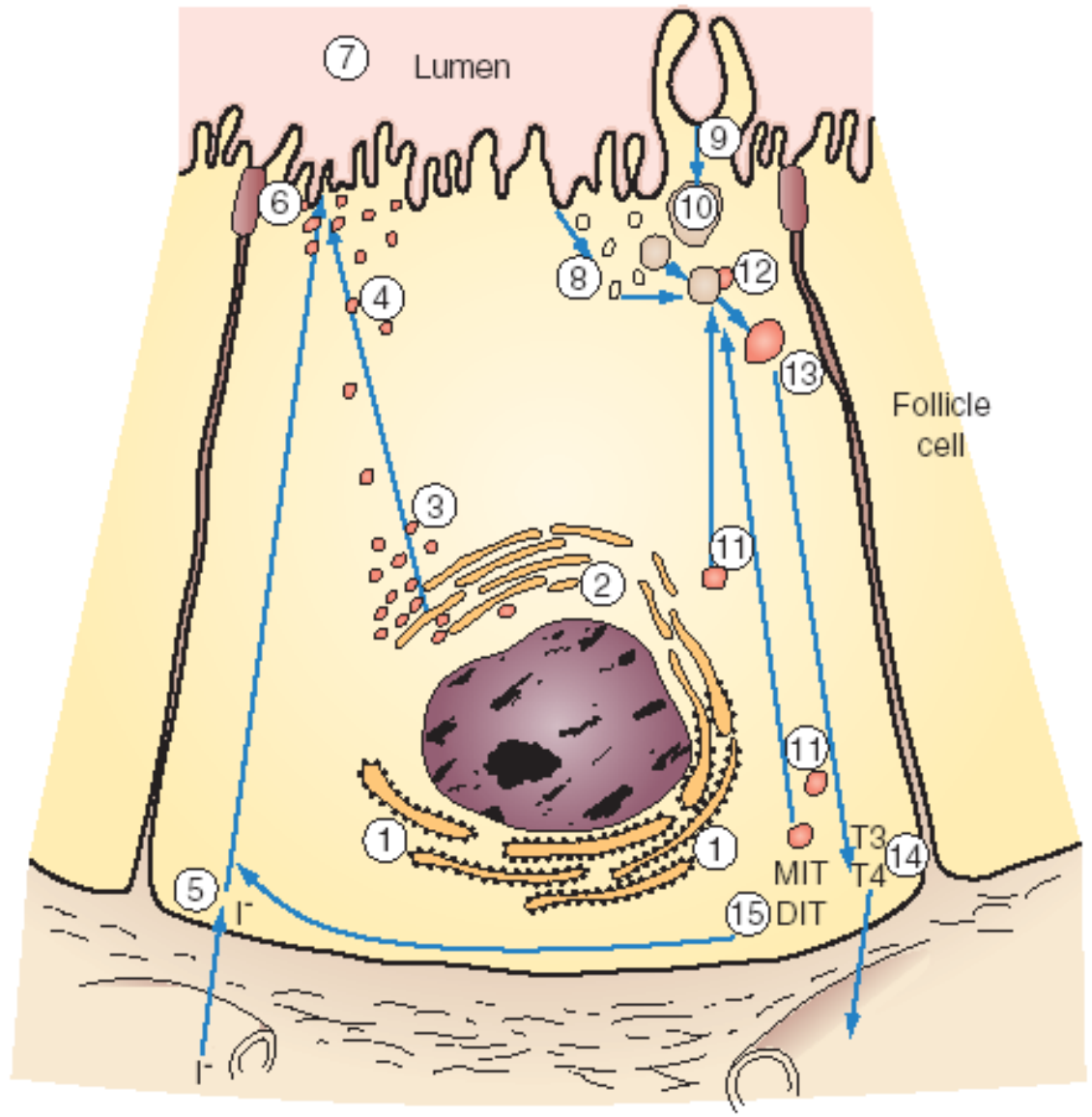
- Hormone production
 - T4 (2 x DiIodoTyrosine)
 - T3 (1 DiIodoTyrosine + 1 MonoIodoTyrosine)
 - Calcitonin



Histological section
through normal thyroid
gland

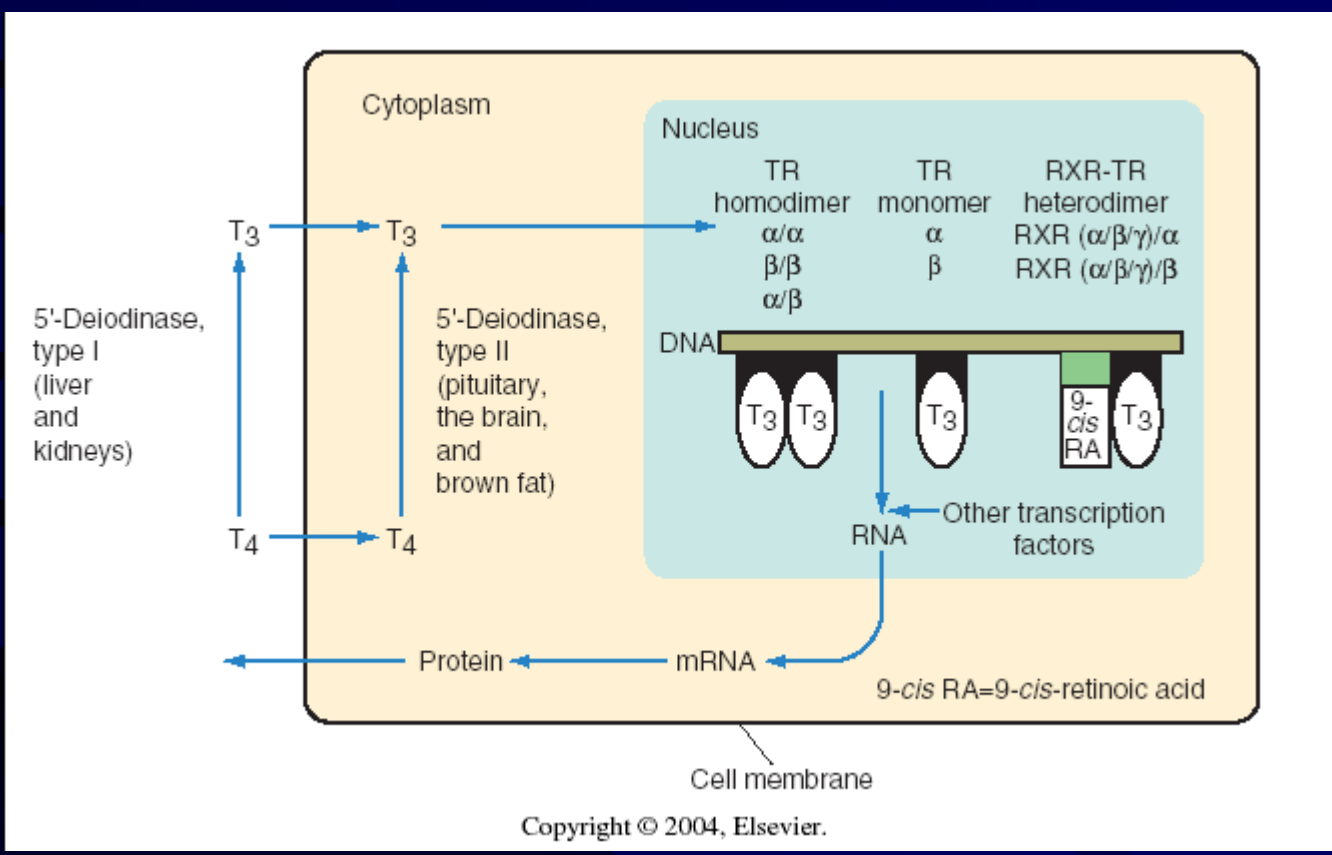
Magnification,
showing cuboidal
cells surrounding
colloid, of a normal
thyroid gland





Physiology

- T4 and T3
 - Regulated by TSH from ant. pituitary gland
 - T3 half-life is 8-12 hours, T4 is 7 days
 - T3 more active than T4
 - T4 is peripherally converted to T3
 - T3 binds to nuclear thyroid hormone receptors (TRs)
 - Bound TRs act on various genes, resulting in polypeptide production



Physiology

- T4 and T3 (cont'd)
 - bound to thyroxine binding globulin, prealbumin thyroxine binding protein, and albumin
 - free thyroxine is less than 1% of peripheral hormone
 - thyroid hormone must be in free form to be biologically active
 - T4 is peripherally converted to T3

Physiology

- Calcitonin
 - synthesized and secreted by C cells
 - secretion stimulated by elevated $[Ca^{2+}]$
 - acts on osteoclasts
 - may or may not decrease serum calcium levels
 - medullary carcinoma of the thyroid

Inhibiting Thyroid Synthesis

- Propylthiouracil (PTU) & Methimazole (Tapazole)
 - inhibits organification and oxidation of inorganic iodine
 - inhibits linking of MIT and DIT
 - PTU: inhibits peripheral conversion of T4 to T3
 - MTX: single day dosing, but crosses placenta

Inhibiting Thyroid Synthesis

- Iodine
 - large doses can inhibit thyroid hormone release
 - alters organic binding process
- Wolff-Chaikoff effect: Increase in iodine supplementation initially promotes iodine uptake by thyroid, but then suppresses it

Inhibiting Thyroid Synthesis

- Steroids
 - suppress the pituitary-thyroid axis
 - inhibit peripheral conversion of T4 to T3
 - decreases serum TSH
 - used as a rapid inhibitory agent in hyperthyroid conditions

Inhibiting Thyroid Synthesis

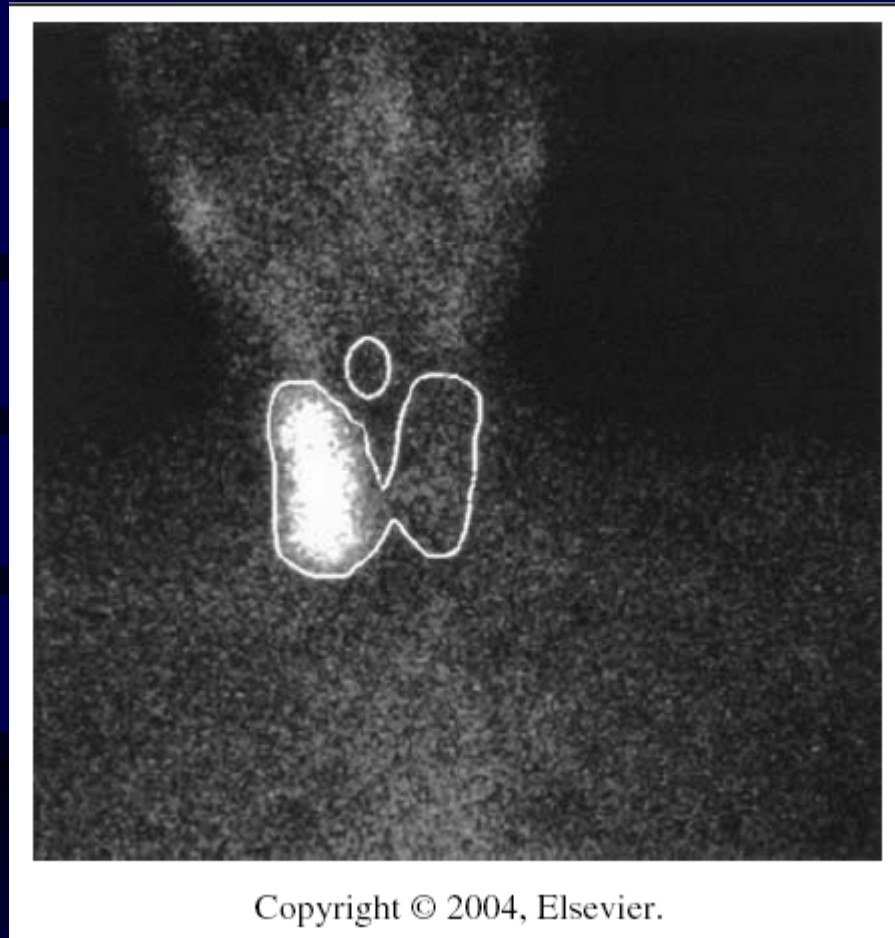
- Beta blockers
 - don't inhibit thyroid synthesis
 - control peripheral sensitivity to catecholamines in a thyrotoxic state
 - improves cardiovascular symptoms of pulse rate, tremor, and anxiousness

Tests of Thyroid Function

- TSH
- TRH stimulation test (elevates TSH in 15-35 min)
- T₃ suppression test
- Total T₄
- Free T₄
- T₃ resin uptake
- Calcitonin
- Radioactive iodine uptake (¹²³I vs ¹³¹I)
- Thyroid autoantibody levels
 - Graves: Ab to TSH receptor
 - Hashimoto's and Graves: antimicrosomal Ab's

Radiographic Evaluation

- Thyroid Scintigraphy (^{123}I)
 - Used to determine presence, size, and function of nodules
 - Technetium pertechnetate ($^{99\text{m}}\text{Tc}$) also used; trapped by thyroid but not organified (short $t_{1/2}$, low radiation dose)
- Thyroid Ultrasound
 - Delineates solid vs. cystic characteristics, diameter, and multicentricity of nodules



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Scintigraph of hot right thyroid lobe

Benign Disease: *Hypothyroidism*

- Hypothyroidism
- Endemic goiter
- Postirradiation hypothyroidism
- Postsurgical hypothyroidism
- Pharmacologic hypothyroidism
 - Cytokines (interferon-alfa, IL-2)
 - Lithium (inhibits thyroid hormone formation)
 - Amiodarone (contains significant amt of iodine)
 - Antithyroid medications: PTU, methimazole

Benign Disease: *Thyroiditis*

- Acute Suppurative Thyroiditis
 - Rare, due to severe pyogenic infection of upper airway
- Hashimoto's Thyroiditis
 - Formation of immune complex and complement on basement membrane of follicular cells
 - Leads to fibrosis and infiltration of lymphocytes, and decreased number of follicles

Benign Disease: *Thyroiditis*

- Subacute Thyroiditis
 - Females (2:1), mean age is 40's
 - Fever, weight loss, severe fatigue
 - FNA → giant cells
 - Tx → steroids & adrenocorticotrophic hormone

Benign Disease: *Thyroiditis*

- Riedel's Thyroiditis
 - Chronic inflammatory process involving entire thyroid
 - Can extend into trachea and esophagus with obliteration of anatomic landmarks and planes
 - May present with impending airway obstruction or dysphagia
 - Tx → thyroid hormone replacement (& surgery if needed)

Benign Disease: *Hyperthyroidism*

- Graves' Disease
 - high incidence in women 20-40 years
 - antibodies agonize the TSH receptor of thyroid
 - unknown etiology
 - enlarged nodular gland, diffuse or asymmetrical
 - triad of disease: goiter, clinical thyrotoxicosis, exophthalmos
 - also, hair loss, myxedema, gynecomastia, and splenomegaly, sweating, heat intolerance, thirst, weight loss

Benign Disease: *Hyperthyroidism*

- Graves' Disease (cont'd)

- Findings:

- elevated T3 & T4, suppressed TSH, diffuse uptake of ^{123}I , elevated amount of thyroid antibodies

- Treatment:

- ^{131}I radioablation (90% cure rate with ingestion of 10-15 mCi, but 10% possibility of hypothyroidism)
 - Antithyroid medications: PTX, methimazole
 - Thyroid resection

Work-Up and Diagnosis of the Thyroid Nodule

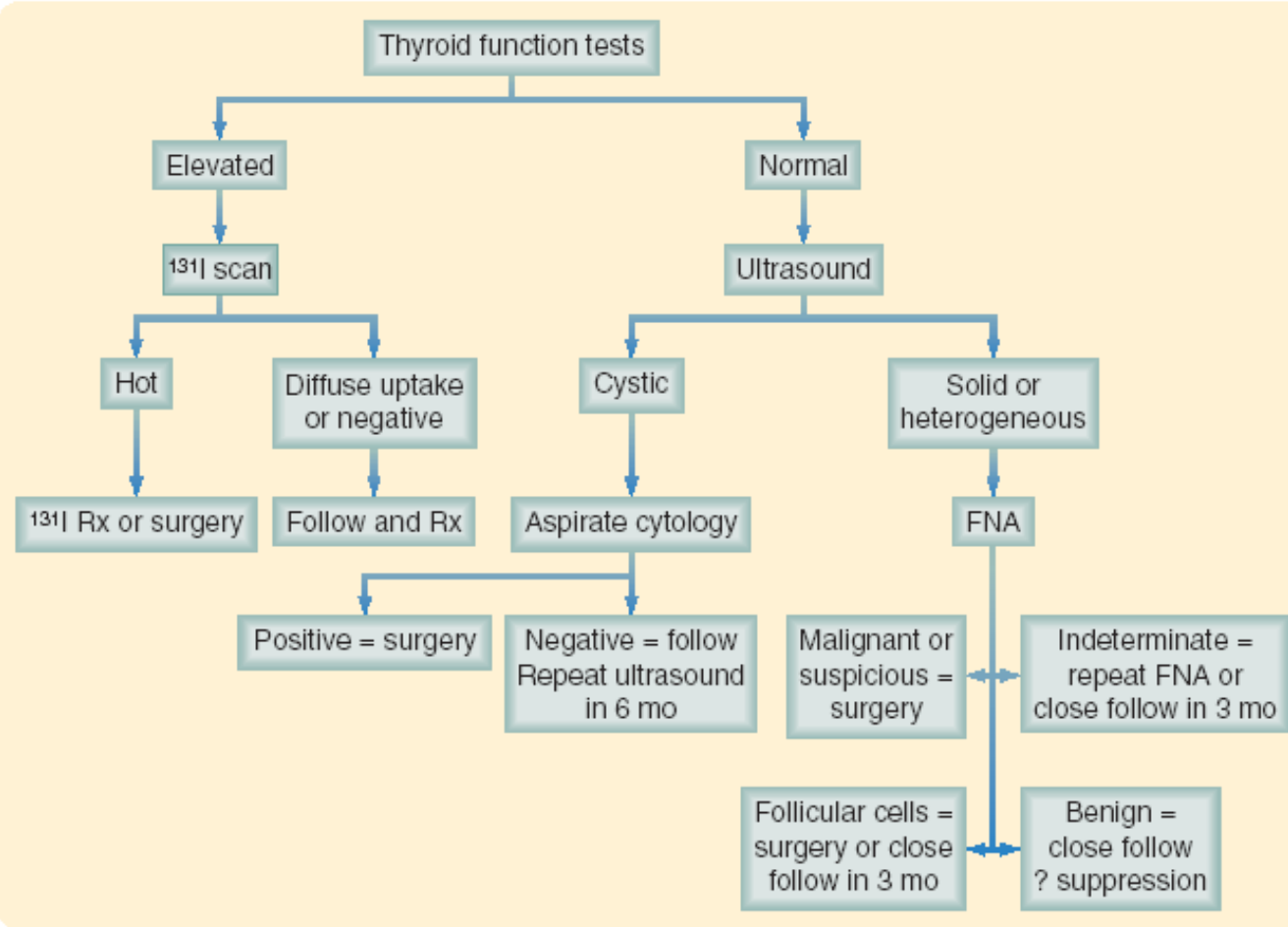
- Most solitary nodules are benign
- Frequency of presentation proportional to age
- Women > men
- Exposure to radiation (major risk factor)
- Rapid recent growth and signs of invasion suggest malignancy

Work-Up and Diagnosis of the Thyroid Nodule

- History
 - exposure to radiation
 - endocrine disorders
 - medullary carcinoma
 - MEN type 2
 - papillary thyroid cancer
 - familial polyposis and Gardner's syndromes

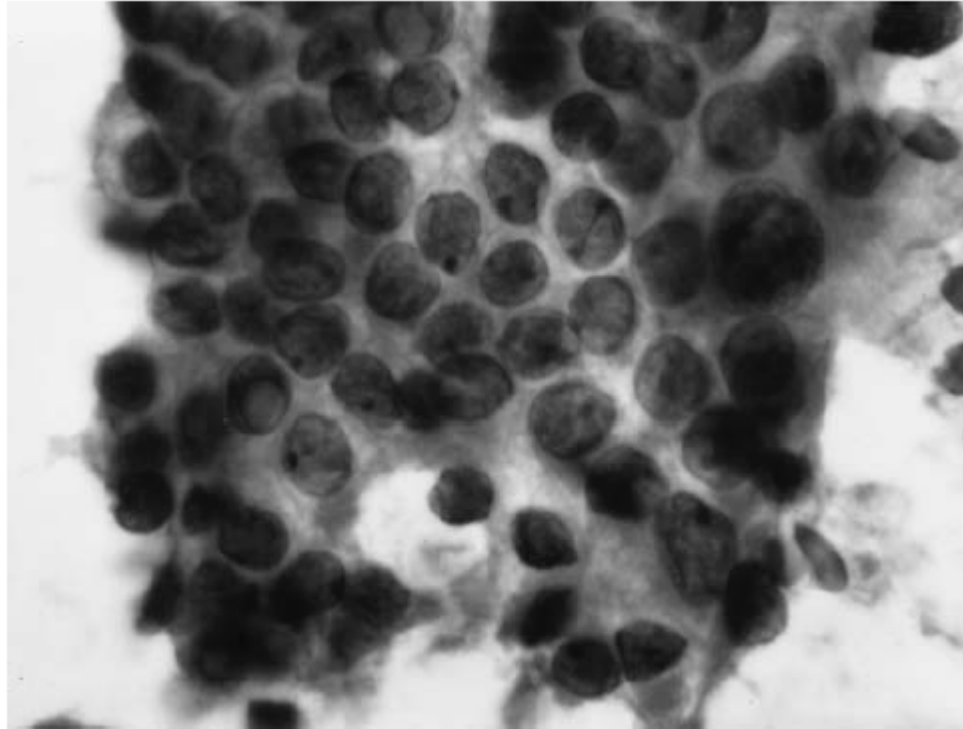
Work-Up and Diagnosis of the Thyroid Nodule

- Physical exam
 - Palpation
 - single nodule vs. multiple; lymph nodes?
 - Ultrasound (office)
 - cystic nodule vs. solid; lymph nodes?
 - Exceptions: cystic papillary carcinoma, calcified cyst
- Laboratory tests
 - T4 & T3 resin uptake, TSH
 - calcitonin (medullary carcinoma), electrolytes



Work-Up and Diagnosis of the Thyroid Nodule

- Fine Needle Aspiration
 - insertion of small gauge needle into nodule for aspiration biopsy
 - up to 86% sensitivity and 91% specificity
 - can be 20-25% nondiagnostic
 - false negative rate: 1-6%
 - CAVEAT: cannot diagnose follicular carcinoma (requires evidence of cellular invasion of thyroid capsule or of vasc/lymph channels)



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Aspirate of FNA of a thyroid nodule, showing cells with ground-glass nuclei (called “orphan-Annie” eyes), definitive for papillary carcinoma of the thyroid

Work-Up and Diagnosis of the Thyroid Nodule

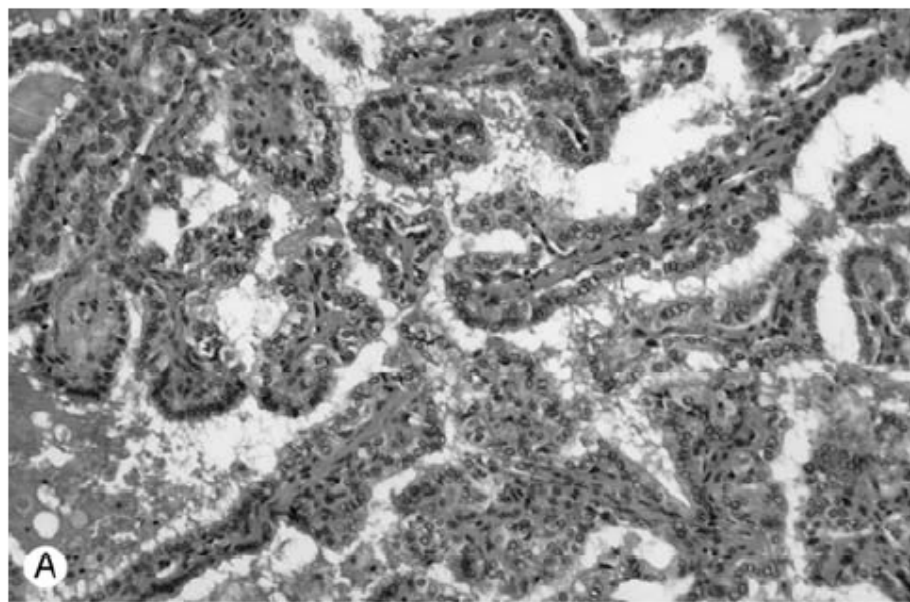
- FNA can diagnose:
 - papillary carcinoma
 - medullary carcinoma
 - anaplastic carcinoma
 - colloid nodule (colloid and macrophages)
- FNA cannot:
 - diagnose follicular carcinoma
 - confirm benign disease

Review of Thyroid Nodules: *BENIGN*

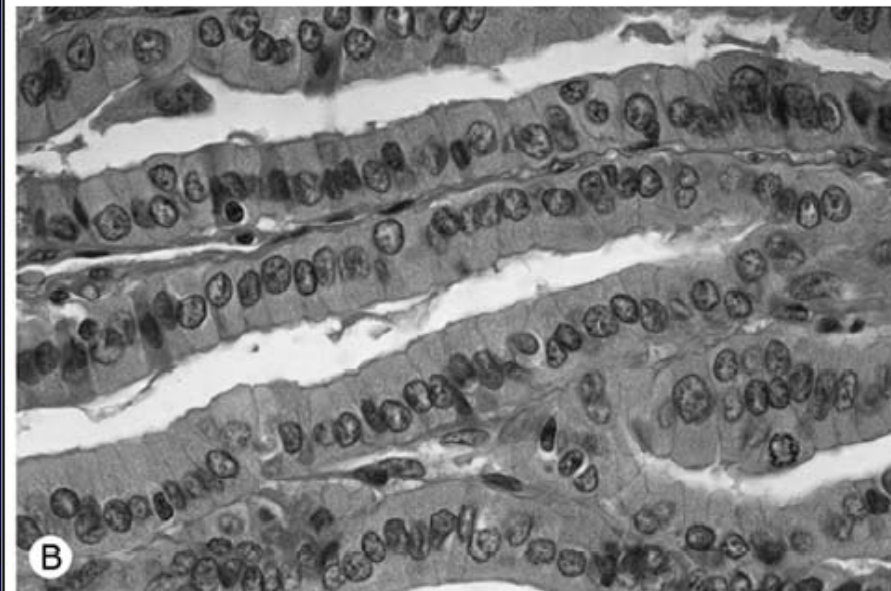
- Colloid
 - Associated with:
 - multinodular goiter
 - FNA showing colloid and macrophages
 - Confirmed by Surgery
- Hyperfunctioning nodule
 - Associated with hyperthyroidism
 - Confirmed by ^{123}I or ^{131}I scan

Review of Thyroid Nodules: *MALIGNANT*

- Papillary carcinoma (70-80% of carcinomas)
 - Associated with:
 - Radiation exposure
 - Previous surgery for papillary carcinoma
 - Confirmed by
 - FNA (psammoma bodies, “Orphan Annie eyes”)
 - Surgery

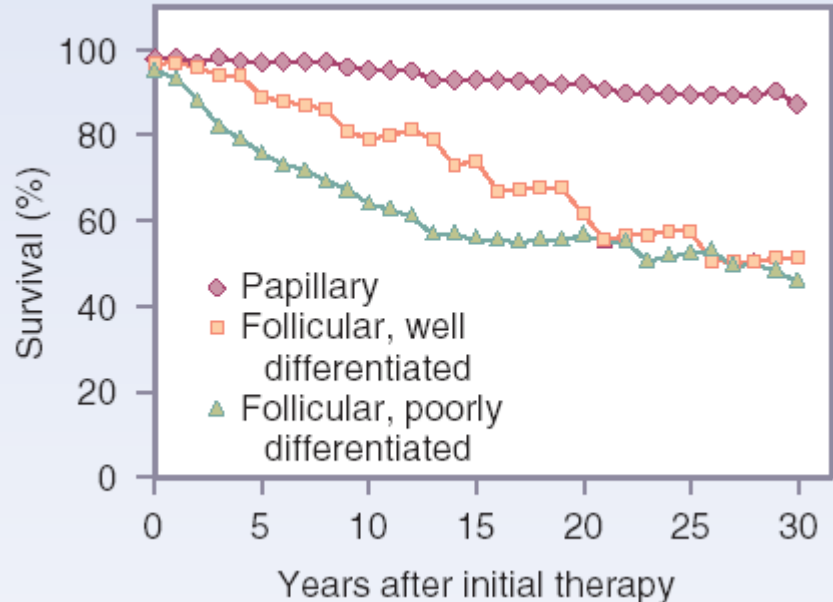


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A. Histology of papillary carcinoma; B. Tall cell variant of papillary carcinoma



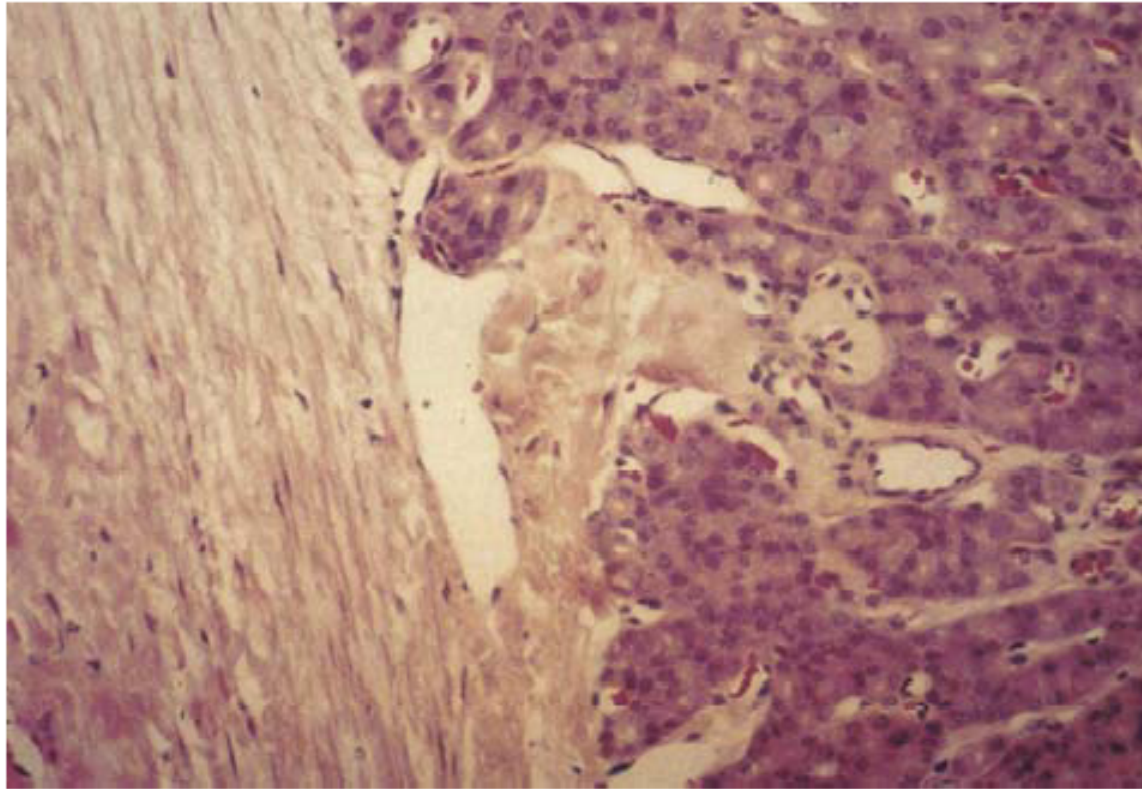
Overall survival (no distant mets at time of diagnosis)

Review of Thyroid Nodules: *MALIGNANT*

- Papillary carcinoma (cont'd)
 - Worse prognosis:
 - male gender, age > 40 years, size > 3cm, tall cell variant
 - Treatment: surgery
 - <1cm: lobectomy plus isthmectomy
 - 1-2cm: above or total thyroidectomy
 - >2cm: total thyroidectomy

Review of Thyroid Nodules: *MALIGNANT*

- Follicular carcinoma (10% of all carcinomas)
 - Associated with “follicular cells” by FNA
 - Confirmed by permanent section pathology from surgery
 - Worse prognosis:
 - Male gender, age > 40 years, size > 3 cm, poorly differentiated histology
 - Treatment: surgery
 - <2cm: lobectomy and isthmectomy
 - >2cm: total thyroidectomy



B

Histology of follicular carcinoma of the thyroid; follicular cells invading thyroid (stromal) capsule, definitive for the diagnosis. This finding must be seen in order to document follicular carcinoma of the thyroid. Therefore, FNA cannot diagnose this carcinoma.

Review of Thyroid Nodules: *MALIGNANT*

- Medullary carcinoma (5-10%)
 - Involves C cell (parafollicular cell) which secretes calcitonin
 - Associated with MEN 2a and 2b, elevated calcitonin
 - Confirmed by surgery, FNA, calcitonin levels, *ret oncogene*
 - Worse prognosis: MEN type 2b and sporadic

Review of Thyroid Nodules: *MALIGNANT*

- Medullary carcinoma
 - Treatment: surgery
 - total thyroidectomy
 - postoperative radioablation for residual thyroid tissue (detected by increasing calcitonin)

Review of Thyroid Nodules: *MALIGNANT*

- Anaplastic carcinoma
 - Poor histologic differentiation
 - Associated with rapid progression of tumor mass, pain, and hoarseness
 - Confirmed by FNA and surgery
 - Worse prognosis associated with diagnosis
 - 50% mortality within 6 months
 - 11% 3 year survival rate
 - Surgery for resectable mass or palliation (tracheostomy)