Thyroid Nodules and Neoplasms

Objectives

- Know the definition of a solitary nodule in the thyroid.
- Recognize the differential diagnosis of a solitary thyroid nodule.
- Understand the classification, pathology and behavior of thyroid carcinoma.

Thyroid nodules

- **Several clinical criteria provide a clue to the nature of a given thyroid nodule:**
- *Solitary nodules, in general, are more likely to be neoplastic than are multiple nodules.*
- *Nodules in males are more likely to be neoplastic than are those in females.*
- *Nodules in younger patients* are more likely to be neoplastic than are those in older patients.
- *A history of radiation treatment to the head and neck region is associated with an increased incidence of thyroid malignancy.*
- *Nodules that take up radioactive iodine in imaging studies (hot nodules) are more likely to be benign than malignant.*

- Ultimately, it is the morphologic evaluation of a given thyroid nodule by fine needle aspiration, combined with histologic study of surgically resected thyroid parenchyma, that provides the most definitive information about its nature.

Thyroid Nodules

- **Non-neoplastic:**

  e.g., a dominant nodule in multinodular goiter, simple cysts, or foci of thyroiditis

- **Neoplastic:**

  *Adenoma

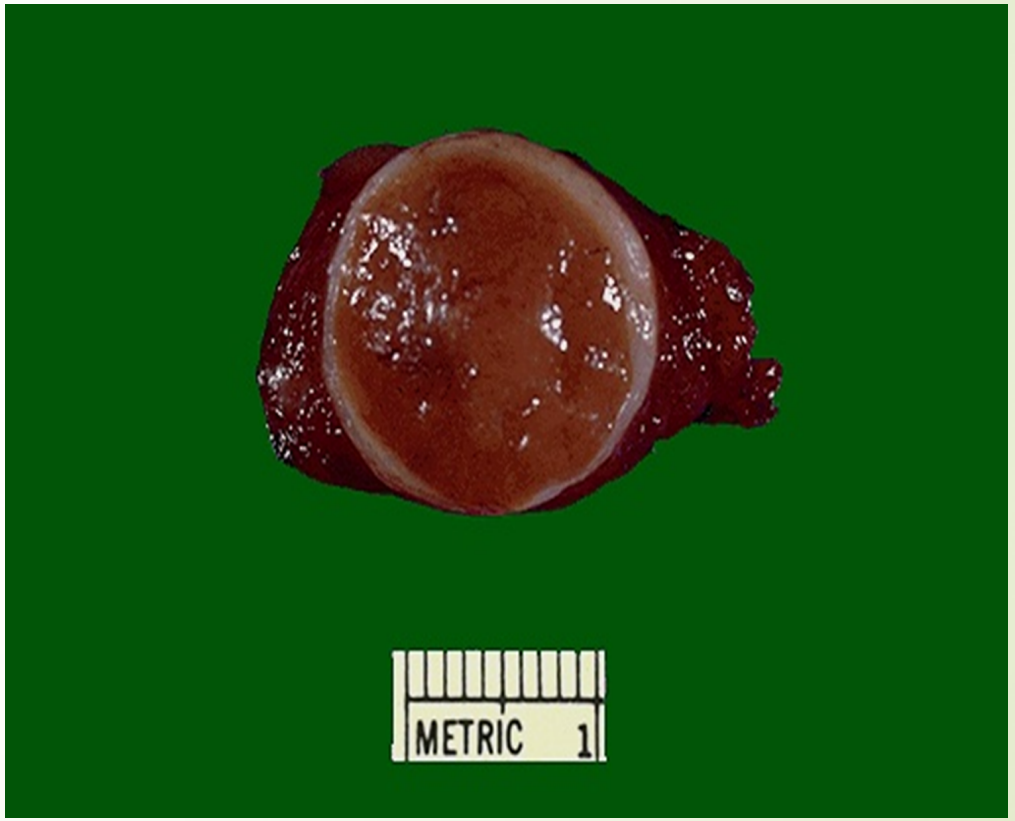
  * Carcinoma

Adenoma

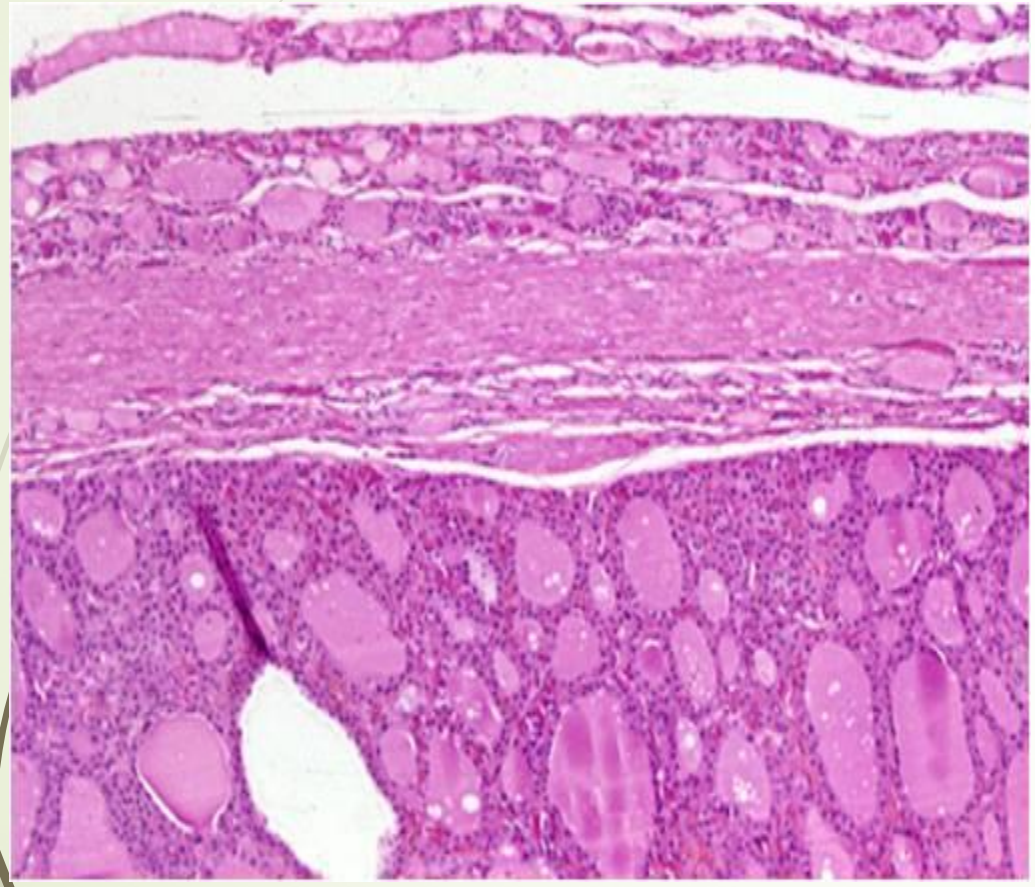
- Adenomas of the thyroid are benign neoplasms derived from follicular epithelium. Follicular adenomas usually are solitary.
- On clinical and morphologic grounds, they may be difficult to distinguish from a dominant nodule in multinodular goiter, or from follicular carcinomas
- In general, follicular adenomas are *not* forerunners to carcinomas

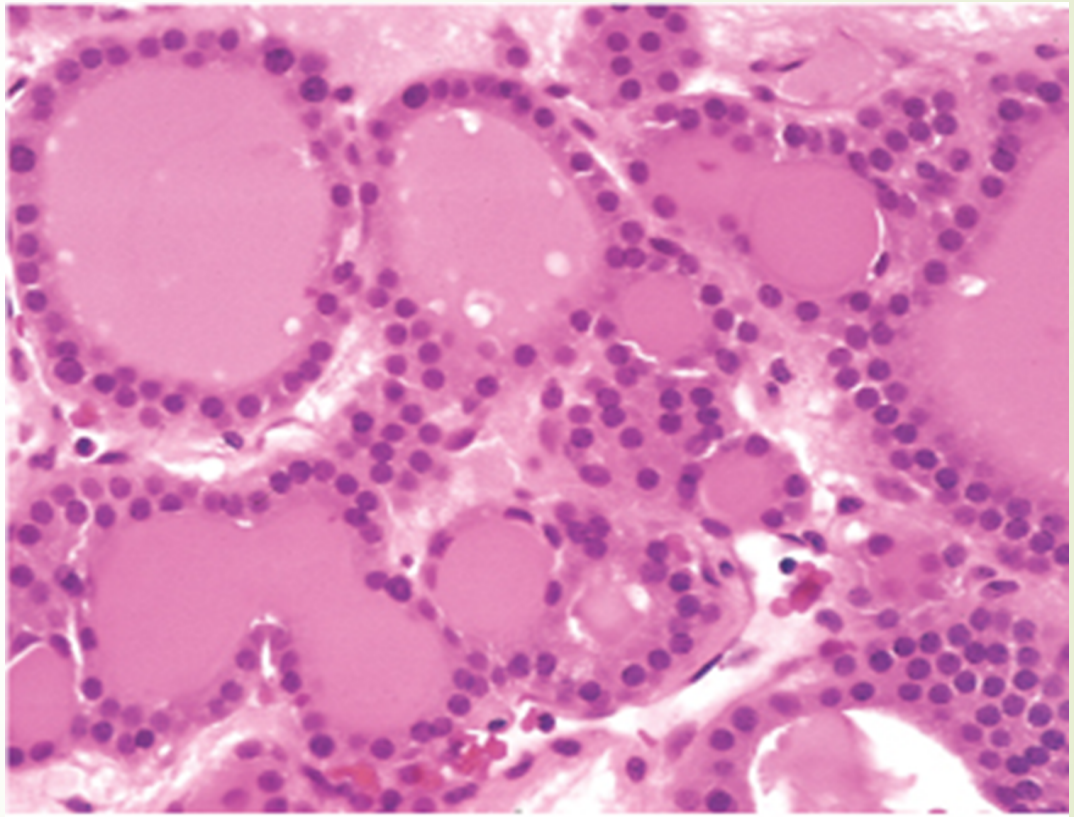
Adenoma

- The typical thyroid adenoma is a **solitary,** spherical lesion that compresses the adjacent non-neoplastic thyroid.
- The neoplastic cells are demarcated from the adjacent parenchyma by a **well-defined, intact capsule** . **These features are important in making the distinction from multinodular goiters,** which contain multiple nodules on their cut surface , do not demonstrate compression of the adjacent thyroid parenchyma, and lack a well-formed capsule.
- On microscopic examination, the constituent cells are arranged in uniform follicles that contain colloid .



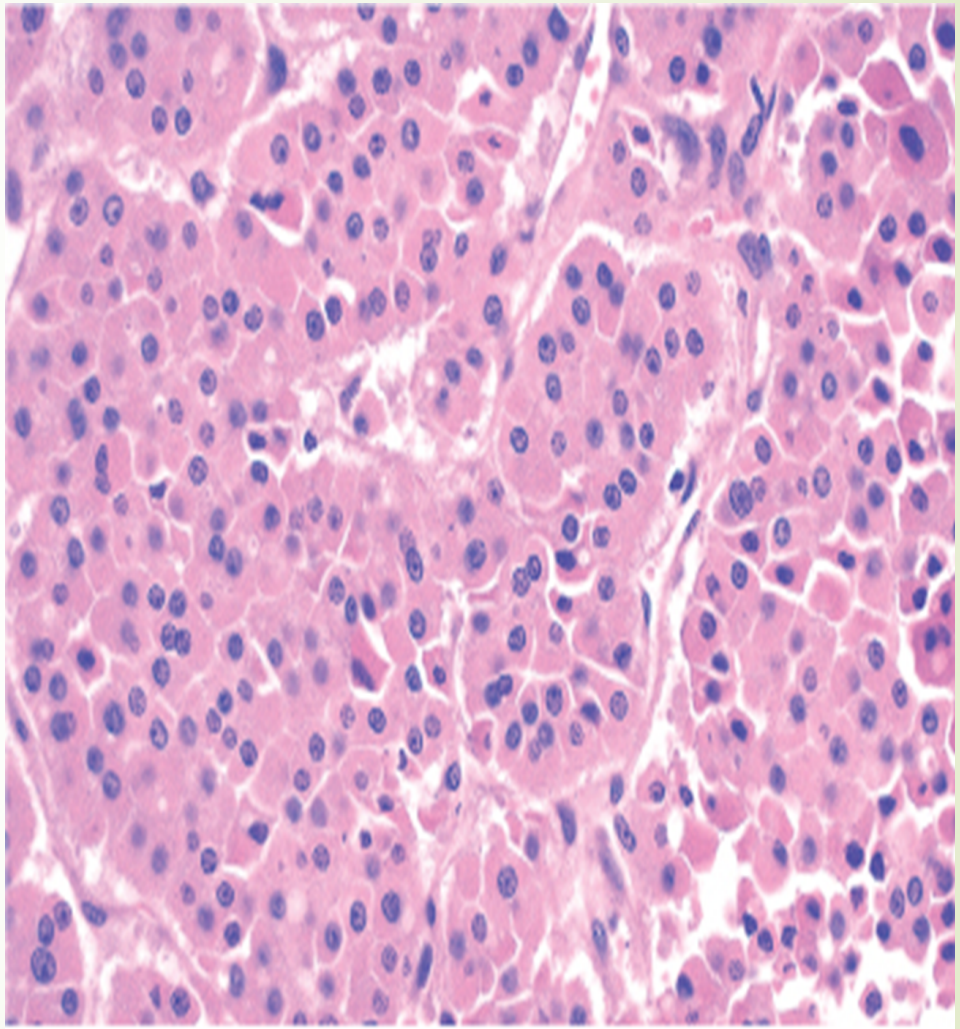
Adenoma





Adenoma

- Occasionally, the neoplastic cells acquire brightly eosinophilic granular cytoplasm (oxyphil or Hürthle cell change)
- the clinical presentation and behavior of a **Hürthle cell adenoma** are no different from those of a conventional adenoma.
- Careful evaluation of the integrity of the capsule is critical in distinguishing follicular adenomas from follicular carcinomas, which demonstrate capsular and/or vascular invasion



- On radionuclide scanning, adenomas appear as *cold* nodules relative to the adjacent normal thyroid gland.
- Essential techniques used in the preoperative evaluation of suspected adenomas are ultrasonography and fine needle aspiration biopsy.
- Suspected adenomas of the thyroid are removed surgically to exclude malignancy.
- Thyroid adenomas carry an excellent prognosis and do not recur or metastasize.

Carcinomas

- **Carcinomas of the thyroid : 1.5% of all cancers**
- Papillary carcinoma (> 85% of cases)
- Follicular carcinoma (05% to 15% of cases)
- Medullary carcinoma (5% of cases)
- Anaplastic carcinoma (<5% of cases)

Pathogenesis

- Follicular Thyroid Carcinomas: mutations in the RAS family of oncogenes
- Papillary Thyroid Carcinomas. rearrangements of the tyrosine kinase receptors RET or NTRK1 or activating point mutations in BRAF
- Medullary Thyroid Carcinomas: Familial medullary thyroid carcinomas occur in multiple endocrine neoplasia type 2 (MEN-2) RET protooncogene mutation
- Anaplastic Carcinomas: Inactivating point mutations in the p53 tumor suppressor gene are rare in well-differentiated thyroid carcinomas but common in anaplastic tumors.

Pathogenesis

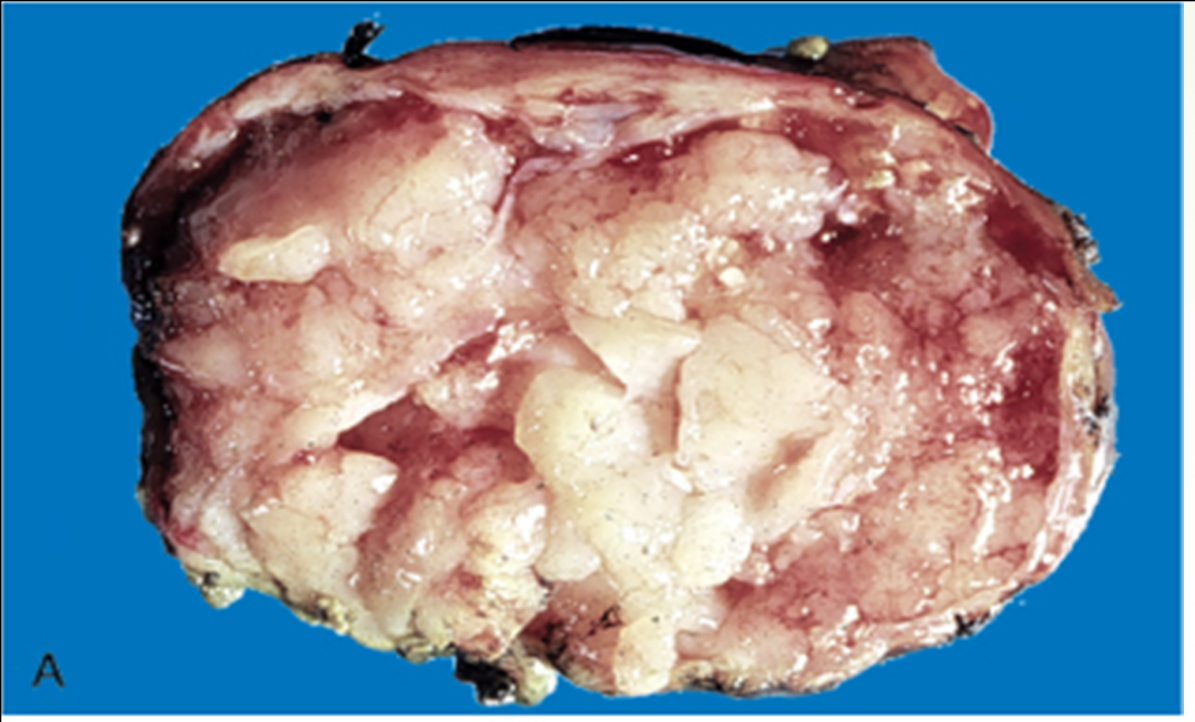
- Environmental Factors. The major risk factor predisposing to thyroid cancer is exposure to *ionizing radiation*
- Most often between the ages of 25 and 50
- Majority of thyroid carcinomas associated with previous exposure to ionizing radiation.
- The incidence of papillary carcinoma has increased markedly in the last 30 years
- Solitary or multifocal lesions

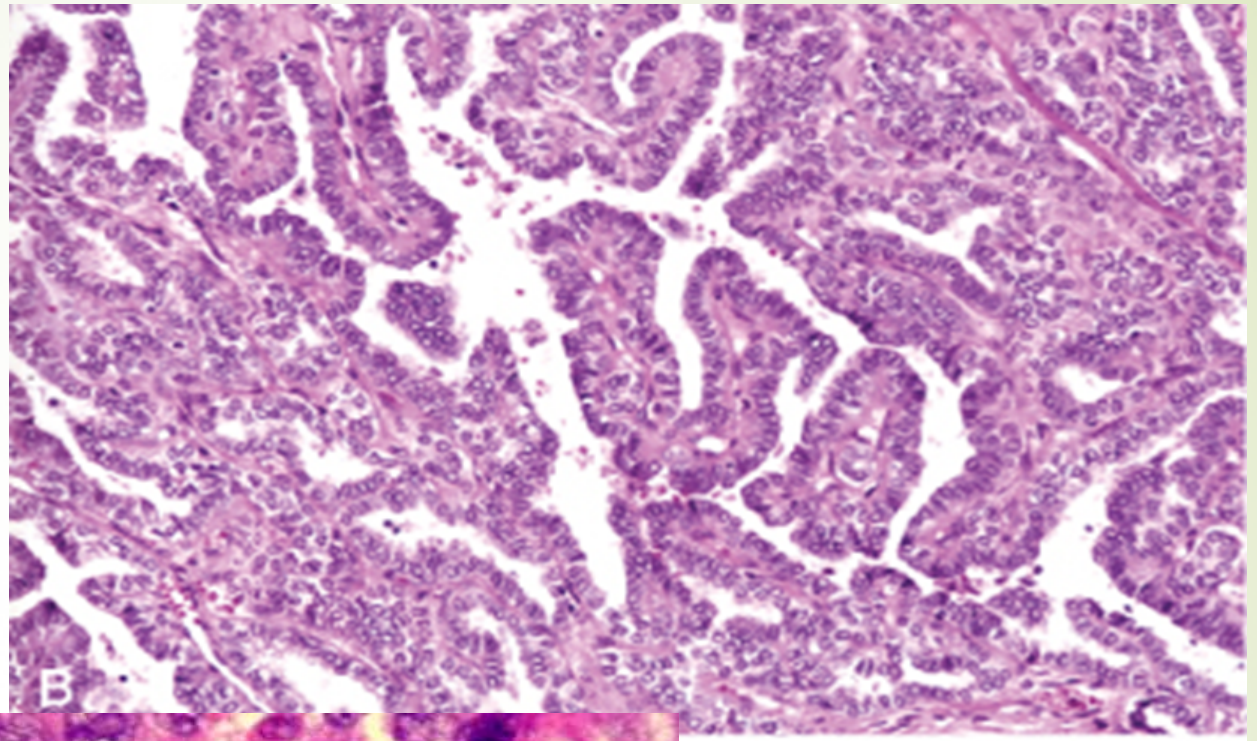
Papillary carcinoma(PTC)

- **papillary carcinomas represent the most common form of thyroid cancer. These tumors may occur at any age, and they account for the vast majority of thyroid carcinomas associated with previous exposure to ionizing radiation.**
- Papillary carcinomas are nonfunctional tumors, so they manifest most often as a painless mass in the neck, either within the thyroid or as metastasis in a cervical lymph node.
- A preoperative diagnosis usually can be established by fine-needle
- Papillary carcinomas are indolent lesions, with 10-year survival rates in excess of 95%.
- Prognosis of PTC is dependent on several factors including age (in general, the prognosis is less favorable among patients older than 40 years), the presence of extra-thyroidal extension, and presence of distant metastases (stage).

PTC

- **the diagnosis of papillary carcinoma is based on nuclear features** even in the absence of a papillary architecture.
- The nuclei of papillary carcinoma cells:
- very finely dispersed chromatin, with an **optically clear** appearance, giving rise to the designation **ground glass** or “Orphan Annie eye” nuclei .
- Grooves.
- invaginations of the cytoplasm may give the appearance of intranuclear inclusions (**pseudoinclusions**)
- **papillary architecture**
- Concentrically calcified structures termed **psammoma bodies** often are present
- There are over a dozen variants of papillary thyroid carcinoma, but the most common is one composed predominantly or exclusively of follicles (**follicular variant** of papillary thyroid carcinoma).





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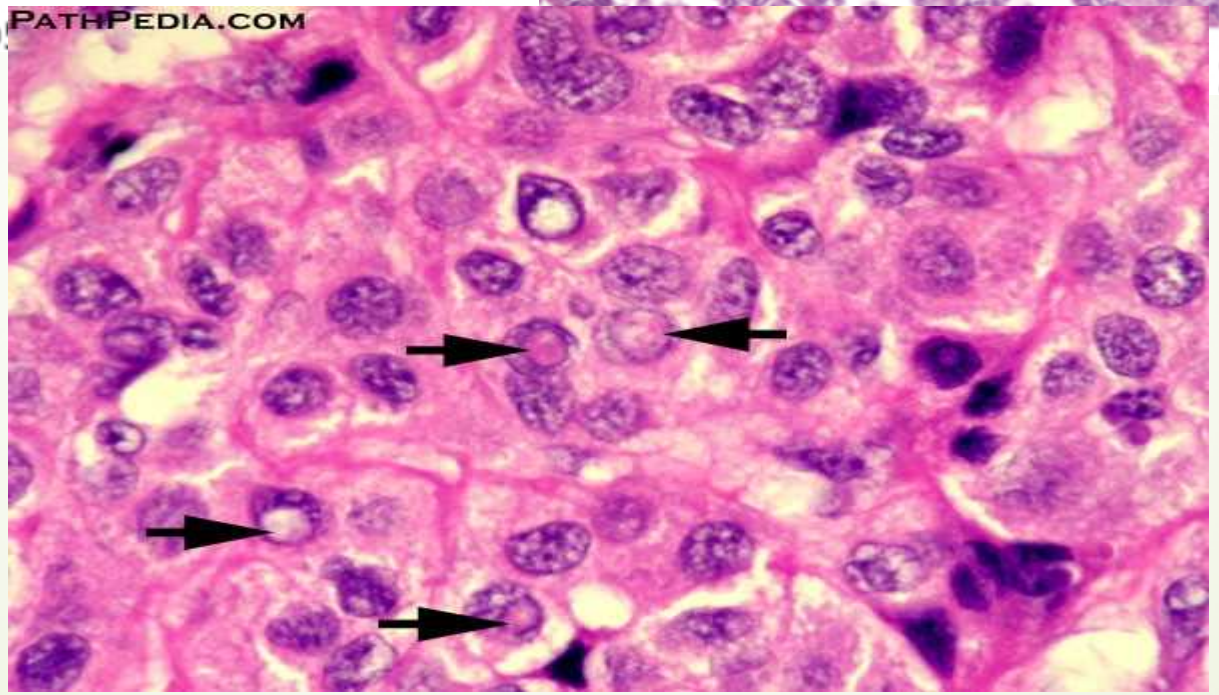


Follicular carcinoma

- 5% to 15% of primary thyroid cancers.
- More common in women (3 : 1)
- Peak incidence between 40 and 60 years.
- More frequent in areas with dietary iodine deficiency

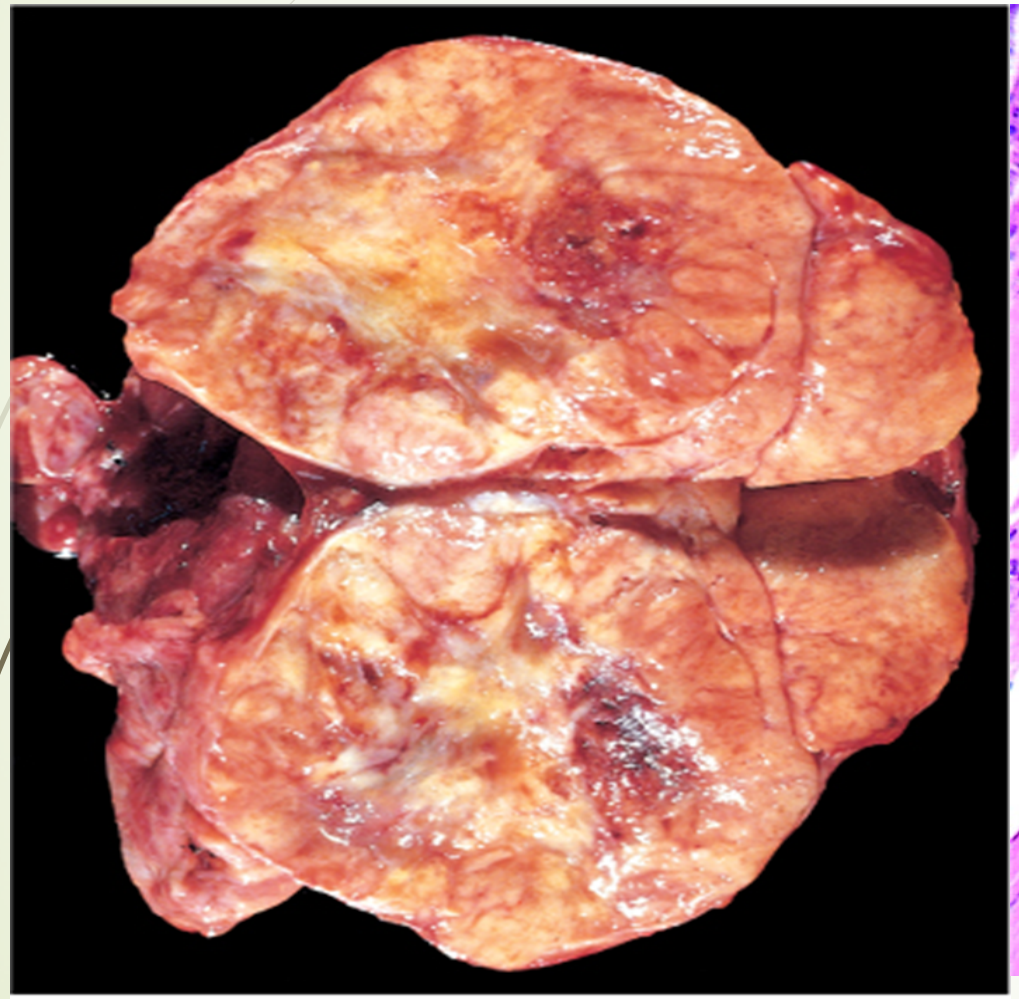
Follicular carcinoma

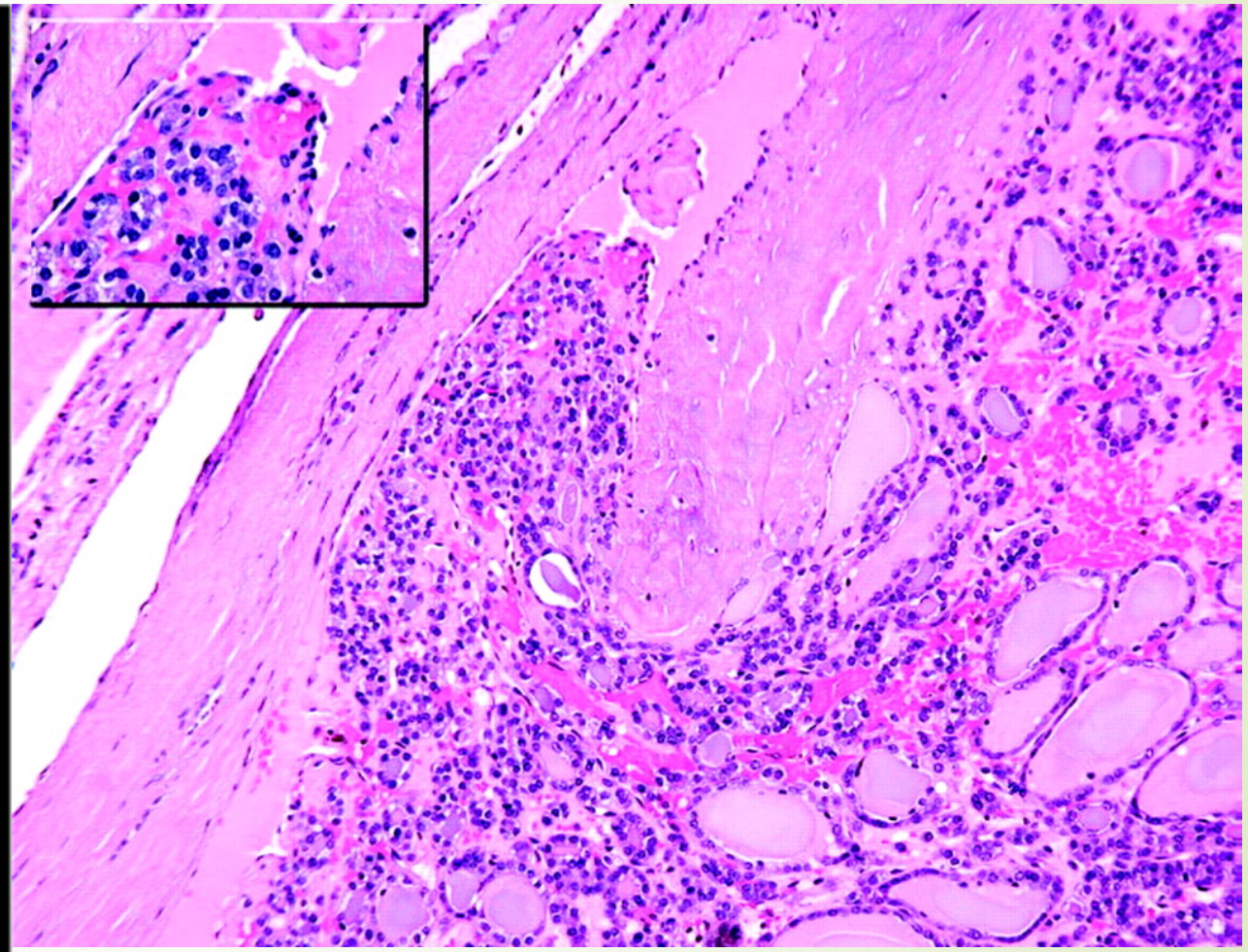
- Follicular carcinomas manifest most frequently as solitary *cold thyroid nodules*.
- These neoplasms tend to metastasize through the bloodstream to the lungs, bone, and liver.
- Minimally invasive(well encapsulated), 10 year survival rate 90%.
- Widely invasive carcinoma, 10 year survival rate less than 50%.

Morphology

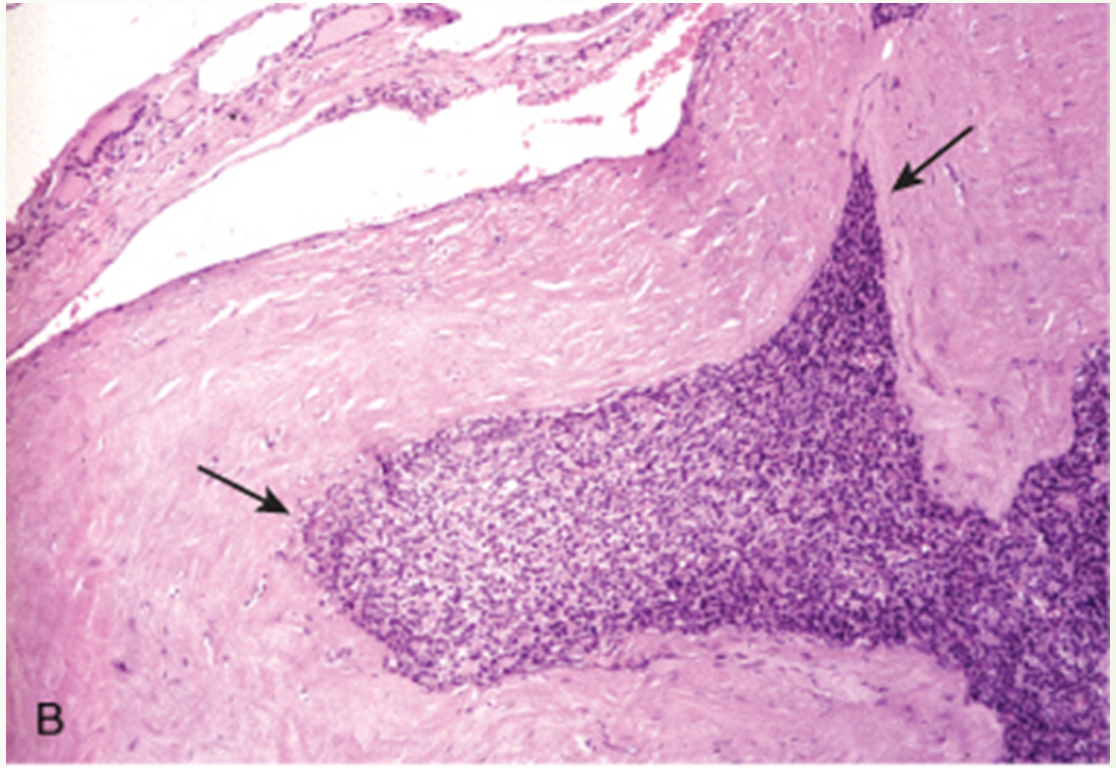
- On microscopic examination, most follicular carcinomas are composed of fairly uniform cells forming small follicles, reminiscent of normal thyroid
- Follicular carcinomas may be
- **widely invasive,** infiltrating the thyroid parenchyma and extrathyroidal soft tissues, or
- **minimally invasive.** are sharply demarcated lesions that may be impossible to distinguish from follicular adenomas on gross examination.**This distinction requires extensive histologic sampling of the tumor capsule–thyroid interface, to exclude capsular and/or vascular invasion**

Follicular carcinoma





Follicular carcinoma



Medullary carcinoma

- Medullary carcinomas of the thyroid are *neuroendocrine neoplasms derived from the parafollicular cells, or C cells, of the thyroid.*

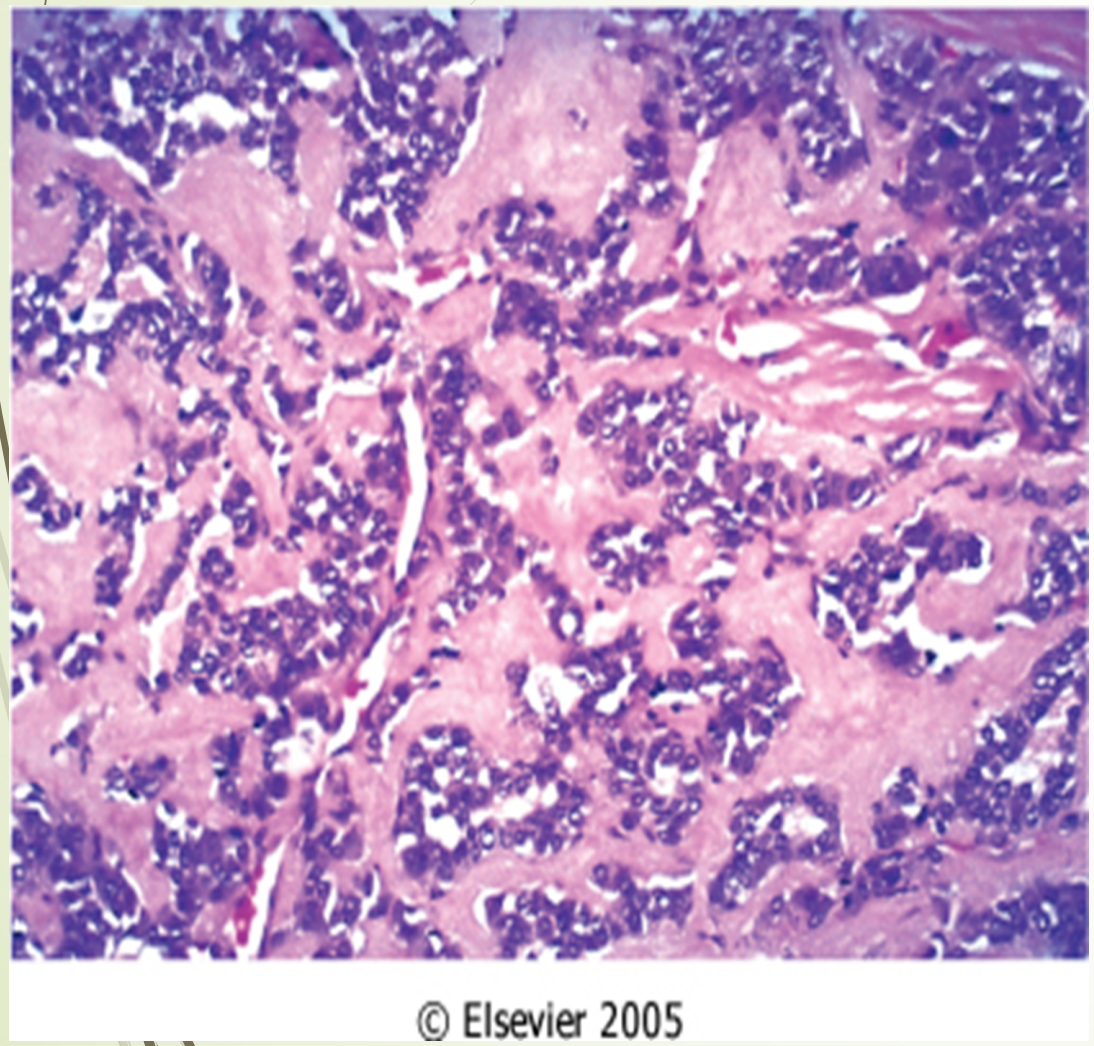
Medullary carcinoma

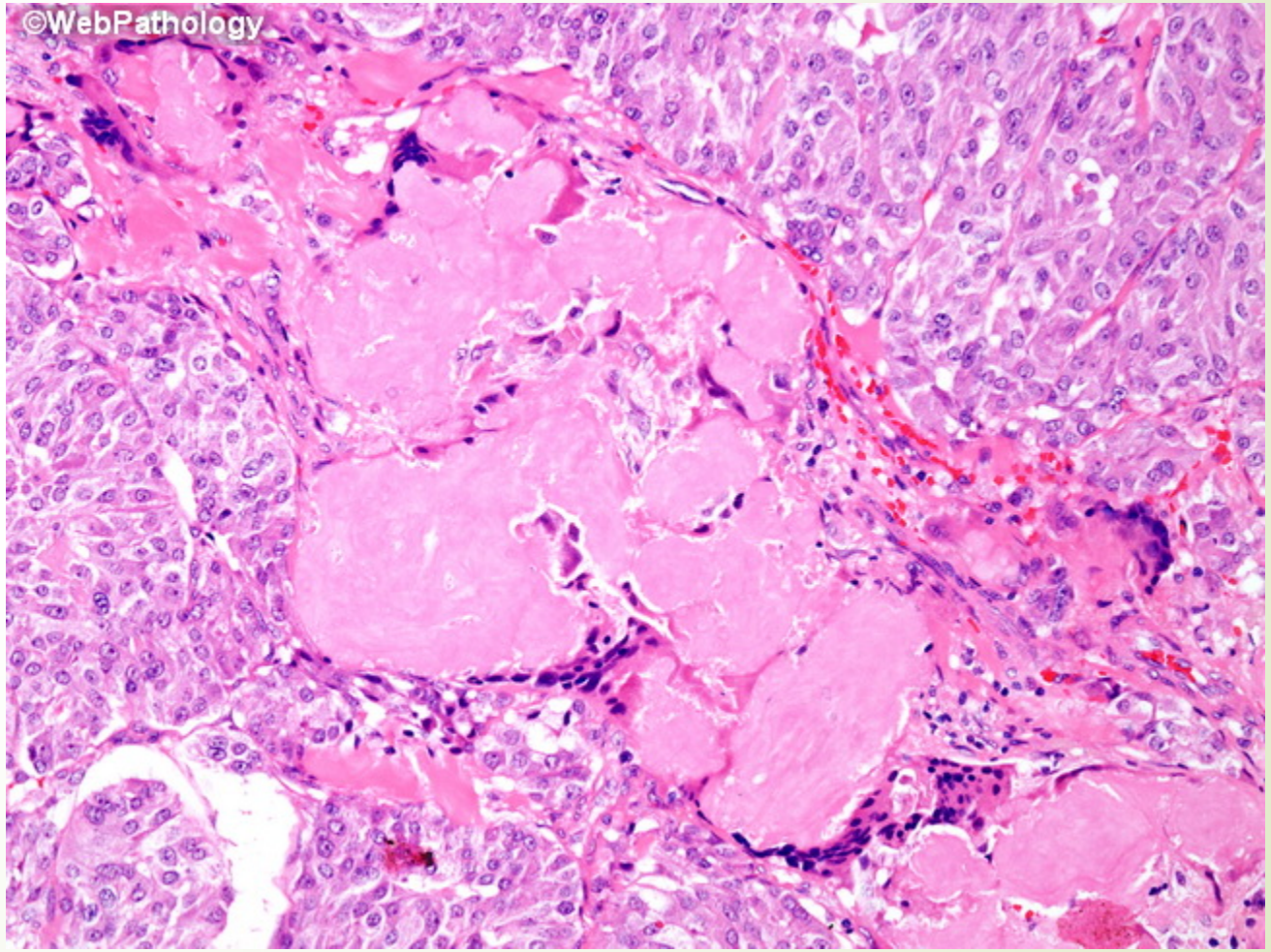
- Medullary carcinomas, similar to normal C cells, secrete *calcitonin*, the measurement of which plays an important role in the diagnosis and postoperative follow-up of patients.
- About 70% of tumors arise sporadically.
- The remainder occurs in the setting of MEN syndrome 2A or 2B or as
- Familial tumors without an associated MEN syndrome (familial medullary thyroid carcinoma, or FMTC)

Medullary carcinoma

- Polygonal to spindle cells
- Amyloid deposition
- Bilaterality
- Multicentricity
- Necrosis
- Hemorrhage

Medullary carcinoma





Anaplastic Carcinomas

- Anaplastic carcinomas of the thyroid are undifferentiated tumors of the thyroid follicular epithelium.
- Can be arising from a more differentiated carcinoma (papillary)
- Lethal (100%)
- Older age group > 65 year

Anaplastic Carcinomas

Highly anaplastic cells:

(1) large, pleomorphicgiant cells, including occasional osteoclast-like multinucleate giant cells

(2) spindle cells with a sarcomatous appearance

(3) mixed spindle and giant cells

(4) small cells

Anaplastic Carcinomas