

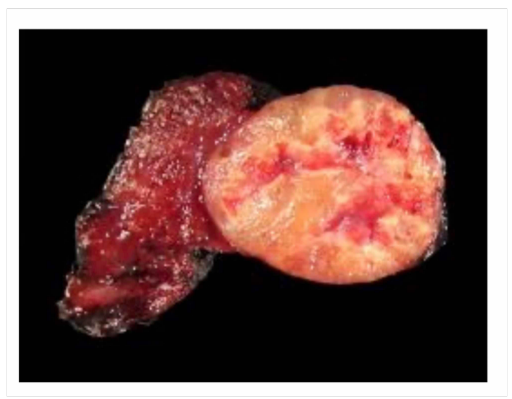
Thyroid tumors

- Thyroid neoplasms present as single nodules

- Tumors of the thyroid gland can be **benign or malignant**.

- They are usually **solitary** (single not multiple)

- Benign lesions in the thyroid are commoner than malignant ones.



Solitary thyroid nodules

- In clinical practice, if you see a patient with solitary nodule, your differential diagnosis will include neoplastic and non- neoplastic lesions such as:

- a. Follicular adenomas

- b. A dominant nodule in multinodular goiter

- c. Simple cysts

- d. foci of thyroiditis

So: neoplasms usually present as single (solitary) nodules, but not every single nodule is neoplastic.

* Neoplastic thyroid lesions

Benign: follicular adenoma and its variants (example: Hurthle cell adenoma, atypical adenoma)

Malignant:

- 1.papillary carcinoma

2. Follicular carcinoma

3. medullary carcinoma

4. Anaplastic carcinoma.

Follicular adenomas

- Are benign neoplasms derived from follicular epithelium.

- Usually **solitary**.

- The tumor is demarcated and compresses the adjacent thyroid parenchyma by a well-defined, intact **capsule**

Microscopic examination of follicular adenoma,

- The cells are arranged in follicles and its **variants**

- a. **Hurthle** cell adenoma:

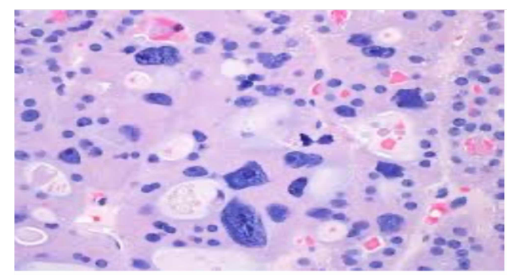
- The neoplastic cells show oxyphil or Hürthle cell change) and its **behavior is not different** from those of a conventional adenoma.

- b.**Atypical** adenoma:

- The neoplastic cells exhibit focal nuclear atypia, (**endocrine atypia**);and these features do not constitute evidence of malignancy

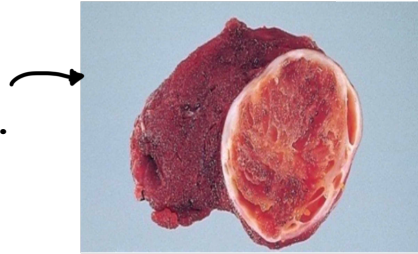
Endocrine atypia

- Note the large, hyperchromatic, pleomorphic cells. These are atypical and this atypia in endocrine glands doesn't necessarily mean malignancy.

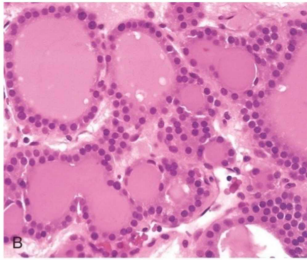


Follicular adenoma

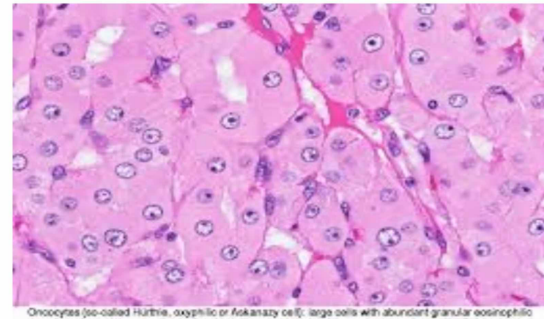
- Well demarcated, encapsulated nodules.



Micro: composed of follicles similar to the normal thyroid follicles.



Hurthle cell adenoma, cells are large with abundant eosinophilic cytoplasm.



Oncocytes (so-called Hurthle, oxophilic or Askanazy cells): large cells with abundant granular eosinophilic cytoplasm (oncocyte = saffron in Greek) and round nucleus with prominent nucleolus (H&E, high power)

- Behavior of thyroid adenomas:

- a. Carry an **excellent prognosis**
- b. **Do not recur or metastasize**
- c. **Not forerunners to carcinomas, i:e they are not premalignant.**

Thyroid carcinoma

- Account for about 1.5% of all cancers

- A **female** predominance has been noted among patients who develop thyroid carcinoma in the **early and middle adult years**

- cases manifesting in childhood and late adult life are distributed equally between men and women

Main types

1. **Papillary carcinoma** (for more than **85%** of cases)
2. Follicular carcinoma (5% to 15% of cases)
3. Anaplastic carcinoma (less than 5% of cases)
4. Medullary carcinoma (5% of cases)

Papillary Carcinoma :

Is the most common form

- accounts for the majority of thyroid carcinomas associated with previous exposure to **ionizing radiation**.
- May occur at any age.

Gross: Either solitary or multifocal lesions

- **note: papillary carcinoma can be multifocal.**

Microscopic features of papillary carcinoma

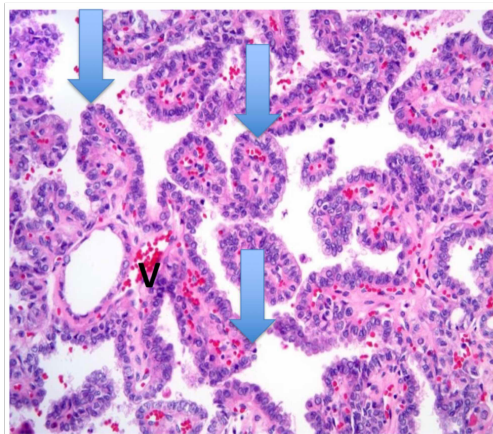
- 1. the presence of papillae.
- 2. nuclear features
- 3. Concentrically calcified structures (psammoma bodies)

Papillae

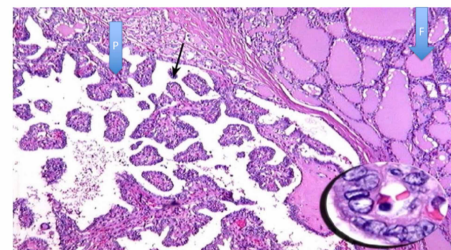
-Papillae (arrows) are finger-like projections covered by epithelial cells (the blue dots around the papillae).

-The papillae have fibro-vascular cores (central region which is fibrous and contains blood vessels (V))

Note: all the red dots in the pic are red blood cells within the vessels.



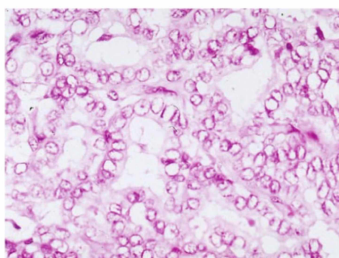
Papillae (P). Note the difference from the normal follicles (F)



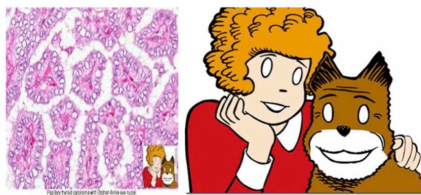
Nuclear features

1. **optically clear** nuclei, or "Orphan Annie eye" nuclei , seen on histological but not cytological preparations (**formalin artefact**)
2. Have invaginations of the cytoplasm to the nucleus (**pseudoinclusions**)
3. **Grooves** within nuclei: so the nucleus looks like a coffee bean.

Clear nuclei: note the nuclei are white.



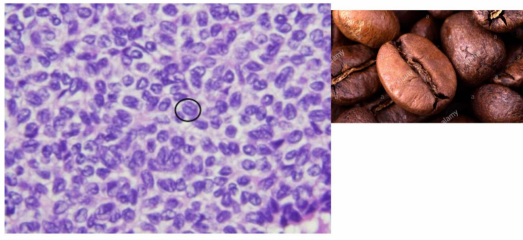
Orphan Annie eye! Because the nuclei are white and empty like Annie's character eyes!!



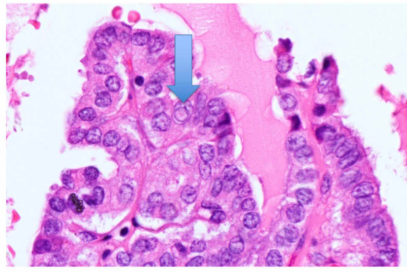
I know what you're thinking: pathological terms are funny.. You're right



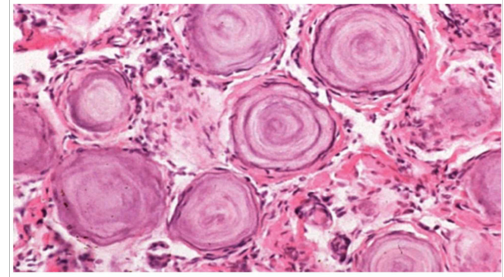
Nuclear grooves= coffee bean nuclei



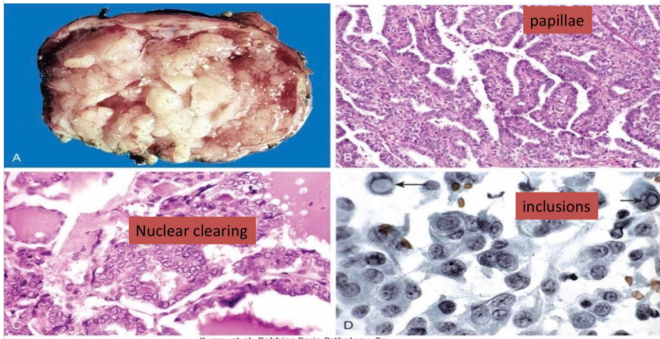
Nuclear inclusions



Psammoma bodies



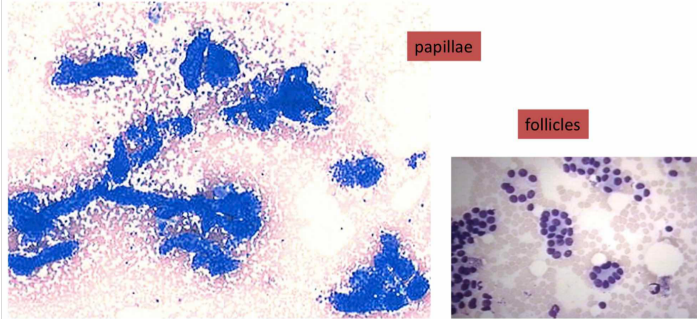
Papillary carcinoma



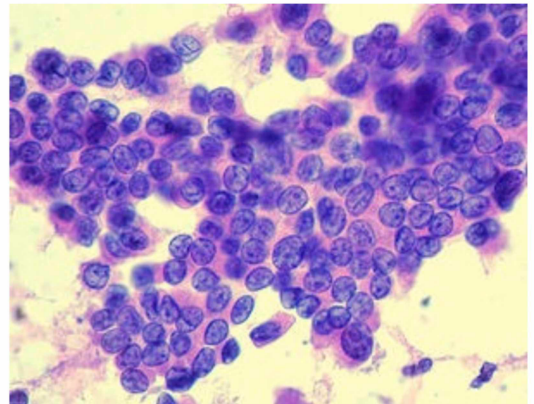
Papillary carcinoma can be diagnosed on FNA



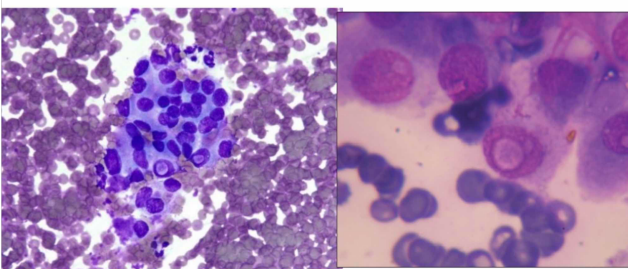
Papillae on FNA: compare to how rounded follicles are seen on the bottom pic



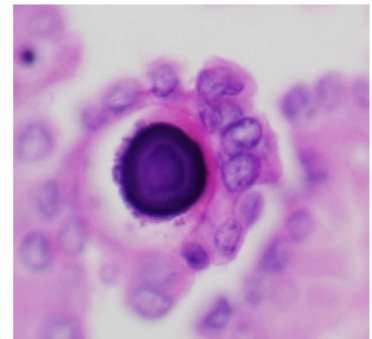
Grooves seen on FNA



Inclusions seen on FNA



Psammoma bodies can be seen on GNA



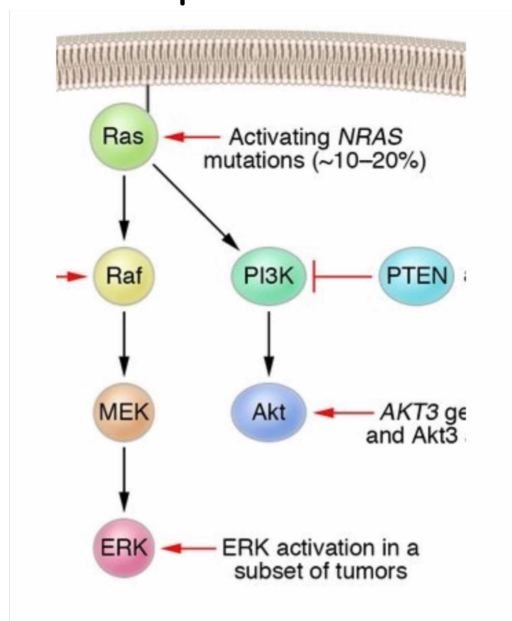
Clinical Features of papillary carcinomas

- a. Are nonfunctional tumors that manifest as painless masses in the neck, either within the thyroid or as metastasis in a cervical lymph node
- b. Are indolent lesions, with 10-year survival rates of 95%.
- c. The presence of isolated cervical nodal metastases does not have influence on good prognosis of these lesions.
- d. In a minority of patients, hematogenous metastases are present at the time of diagnosis, most commonly to lung

Genetic factors related to papillary carcinoma

- Mainly 2 oncogenes are involved:
 - 1. BRAF amplification. (protein in the ras pathway)
 - 2. RET gene rearrangement resulting in a novel protein kinase.

Remember that RAS is the most commonly mutated oncogene.
RAS acts via second messengers ..
RAF is one of them
BRAF (of the RAF family genes) is an oncogene in the RAS pathway.



RET rearrangement= translocation

- The RET gene is not normally expressed in follicular cells but in papillary cancers, chromosomal **rearrangements** place the tyrosine kinase domain of RET resulting in a novel kinase .
- RET rearrangement is present in 20% to 40% of papillary thyroid cancers.

Note: RET rearrangements and BRAF point mutations are not observed in follicular adenomas or carcinomas.

Follicular Carcinoma :

- More common in women and in areas with dietary **iodine deficiency** .
- The peak incidence between the ages of 40 and 60 years

On microscopic examination,

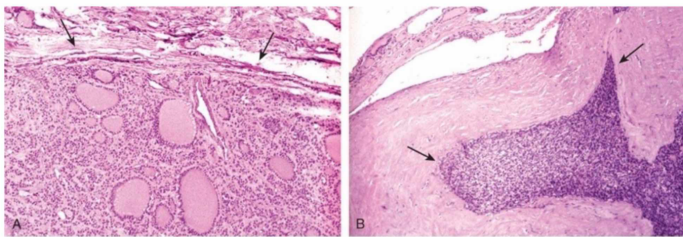
- Are composed of fairly uniform cells forming small follicles,
- In other cases, follicular differentiation is less apparent

- It may be
 - widely invasive, infiltrating the thyroid parenchyma and extrathyroidal soft tissues, or
 - Minimally invasive that may be impossible to distinguish from follicular adenomas on gross examination and the .
- requires extensive histologic sampling to exclude capsular and/or vascular invasion

Clinical Features

- Manifest most frequently as solitary cold thyroid nodules.
- Tend to metastasize through the **bloodstream** (hematogenous dissemination) to lungs, bone, and liver.
- Regional nodal metastases are uncommon .
- As many as half of patients with widely invasive carcinomas die from their disease within 10 years, while less than 10% of patients with minimally invasive follicular carcinomas die within the same time span.

Follicular carcinoma



Kumar et al: Robbins Basic Pathology, 9e.
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GENETIC FACTORS

Follicular thyroid carcinomas:

- activation of **RAS**
- Loss-of-function mutations of PTEN**, a suppressor gene
- (2;3) translocation**,

3. Anaplastic Carcinoma

- Are **undifferentiated** tumors of the thyroid epithelium,
- The mean age of **65 years**.
- They are **aggressive**, with a mortality rate of 100%.
- Approximately a quarter of patients have a past history a well-differentiated carcinoma, and a 1/4th harbor a well-differentiated tumor in the resected specimen.
- **Metastases to distant sites are common**, but death occurs in less than 1 year as a result of aggressive local growth which compromise of vital structures in the neck.

GENETIC FACTORS

Anaplastic carcinomas:

Inactivation of **TP53**, restricted to anaplastic carcinomas and may also relate to their aggressive behavior

4. Medullary Carcinoma

- Arises from **C cells**.

- **neuroendocrine** neoplasms.

- Secrete **calcitonin**, the measurement of which plays an important role in the diagnosis and postoperative follow-up evaluation of patients.

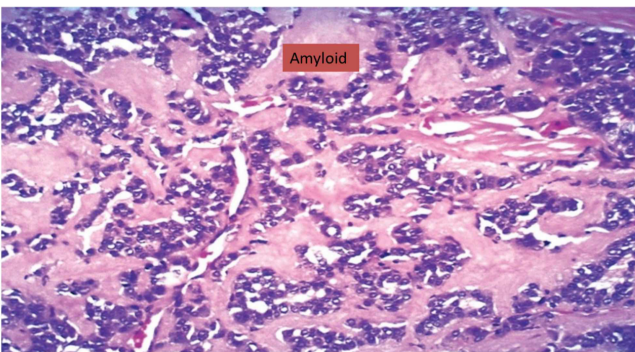
- Are sporadic in about 70% of cases and the remaining 30% are familial cases

Note: Both familial and sporadic forms demonstrate activating RET mutations.

• Because medullary carcinoma secrete calcitonin; this calcitonin can accumulate and form amyloid protein.

• Amyloid: is several, chemically different proteins that share similar physical characteristics.. They can accumulate and form pink material called amyloid.. See next pic.

Medullary carcinoma



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Amyloid stains with Congo red stain



With polarized light, amyloid gives this apple green color when stained with congo red

