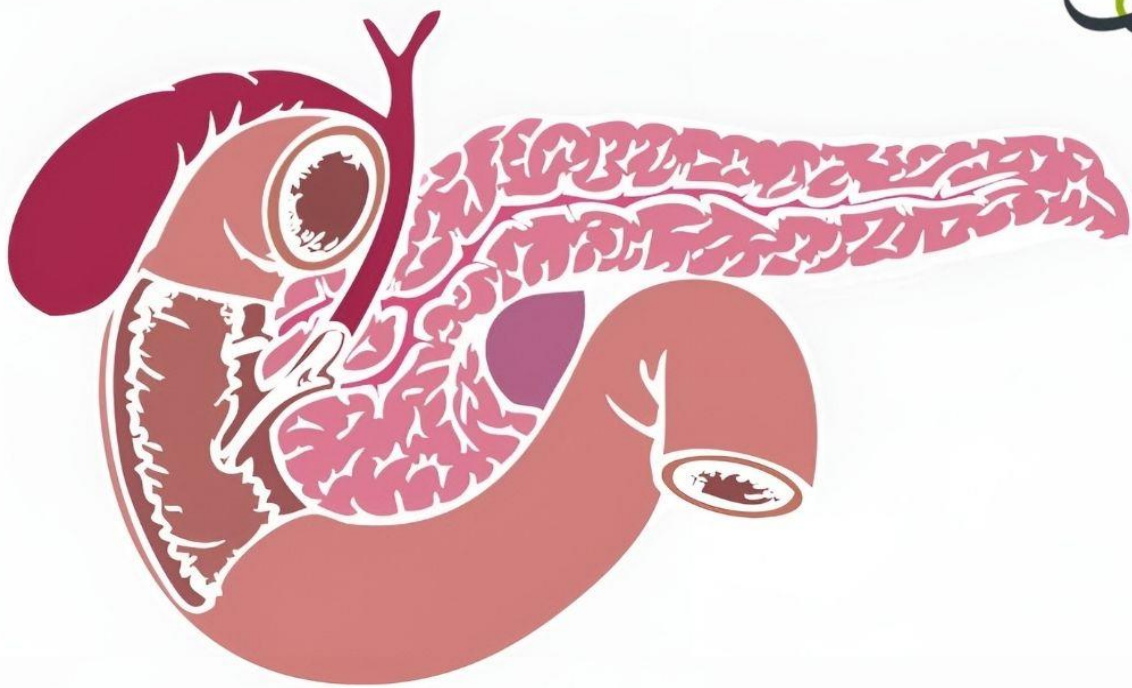


Endocrine system

Sheet

3

Pathology



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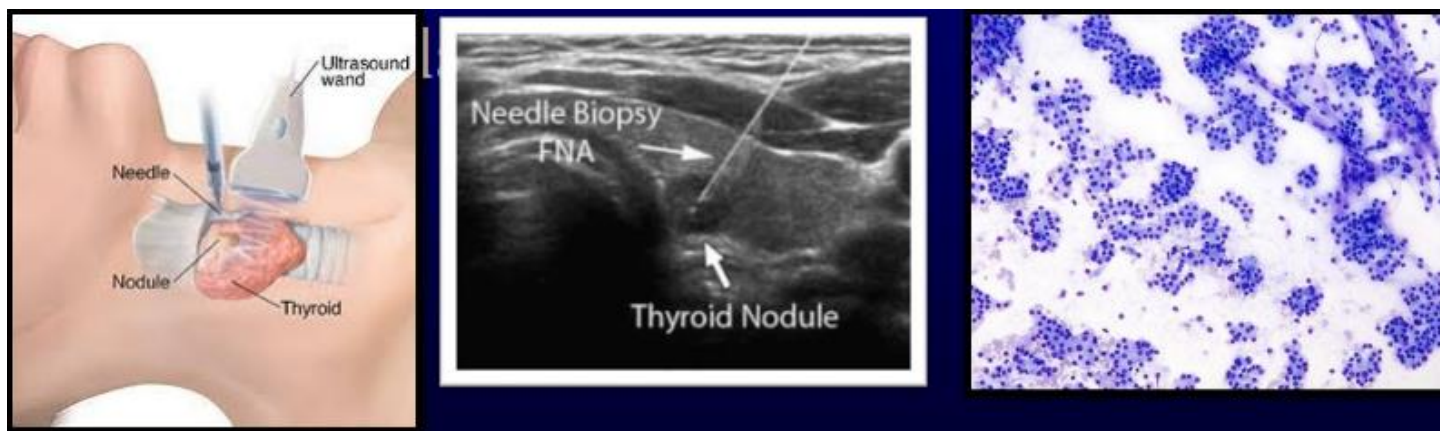
Thyroid Neoplasms

First, there are general features about Thyroid neoplasms we will mention:

- **Benign neoplasms are much more common than malignant ones.**
- **Mostly These are adenomas**
- **The Risk of malignancy increases when:**
 - 1- Solitary nodules (Cold nodules) have a higher risk than multiple ones (MNG).
 - 2- Male Nodules more than female ones
 - 3- Age less than 20 years or more than 70 years.
 - 4- The presence of Family history and history of radiation (Highly associated with Papillary carcinoma).
- ✚ Again, keep in mind that cold nodules have a higher chance of developing Malignancy (12.5%) than hot (secretory) nodules (almost 0%, these usually cause hyperthyroidism).
- ✚ Also, the term **Papillary neoplasm** only indicates Papillary carcinoma, whereas **Follicular neoplasm** may indicate either an adenoma or a carcinoma.

• Fine Needle Aspiration (FNA):

- Considered as a simple, quick and cost-effective diagnostic approach. Nowadays, considered the standard for evaluation of thyroid nodules.
- **Papillary carcinomas** are easily diagnosed by FNA in contrast to **Follicular adenocarcinoma** (In case of Follicular, the pathologist should only report Follicular neoplasm because FNA doesn't differentiate between Follicular adenoma/carcinoma).
- Nonetheless, the accuracy is very good and is currently used a lot in evaluating thyroid nodules.

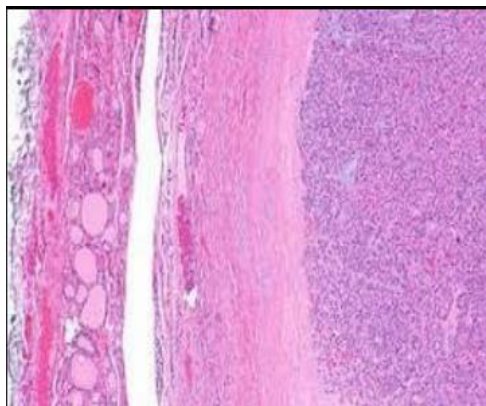
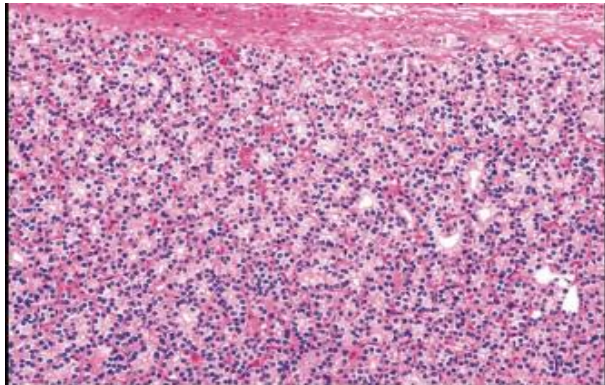


• Follicular adenomas:

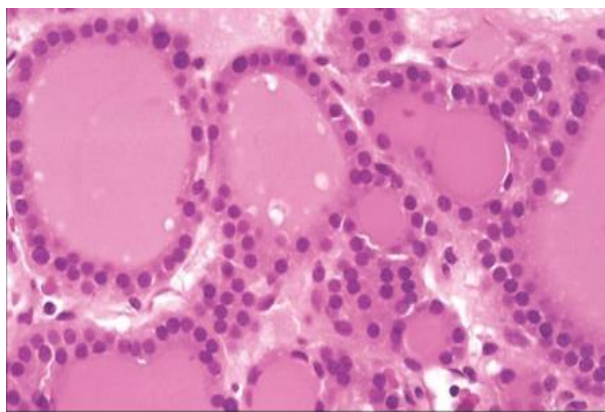
- **Almost all thyroid adenomas are follicular.**
- Considered as **Autonomous adenomas** (Independent, unresponsive to feedback mechanisms), **Driver mutations in TSH stimulation, Rarely RAS mutations.**
- Appear as **Solitary, well-circumscribed** with **intact thick capsule** (This point is important to differentiate them from hyperplastic nodules which show no thickening of the capsule and from carcinomas which show invasion to the capsule. **Occasional Atypia can be seen**
- We refer to it as **Hurthle cell adenoma** when there is a presence of Bland or Hurthle cells.
- Again, **Intact capsule** → differentiates them from Follicular carcinomas that show invasion. **Thickened capsule** → differentiates them from hyperplastic nodules which show no thickening.

Pathological features of Follicular adenomas (FA):

Notice: A well circumscribed solitary nodule with thickening of the capsule. Also, Compressing the surrounding normal thyroid tissue

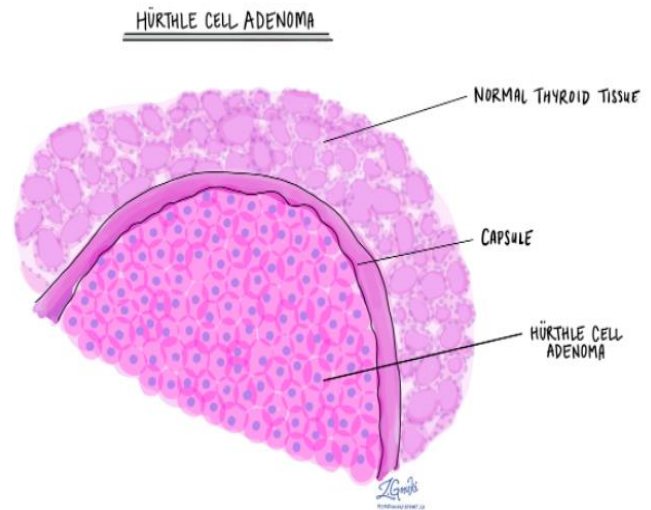
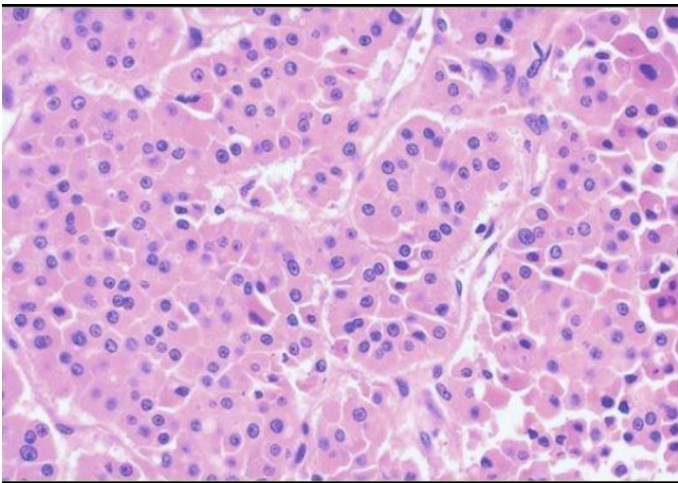


Intact thickened capsule



Small follicles, there are no nuclear features (Nuclear features are associated with Papillary carcinoma)

Finally, this figure shows **Hurthle cell adenoma** which shows all previous feature + **The presence of Hurthle cells** (FYI: Hurthle cells are characterized by having eosinophilic cytoplasm and round nucleus with prominent nucleolus).



• Thyroid Malignancies

- Relatively common but not aggressive (hence showing good prognosis sometimes).
- More common in females.
- Risk factors are: **Ionizing radiation** (Chernobyl accident 1986) and **Iodine deficiency**.

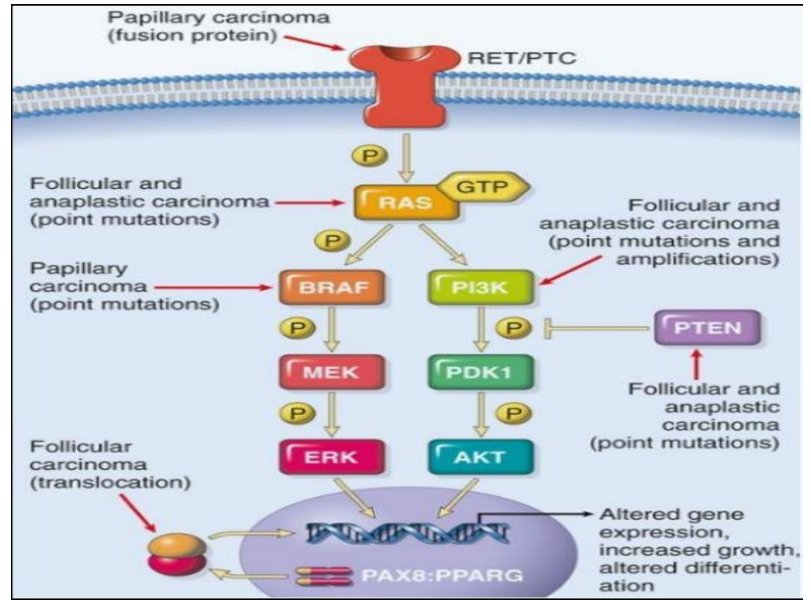
PAPILLARY CARCINOMA	85% LYMPH NODE METASTASIS
FOLLICULAR CARCINOMA	5-15% HEMATOGENOUS SPREAD
ANAPLASTIC CARCINOMA	< 5%; VERY AGGRESSIVE
MEDULLARY CARCINOMA (C-CELLS)	5%, MAYBE PART OF MEN2 SYNDROMES
LYMPHOMA	1% B CELL NON HODGKIN

- About the previous table: **Papillary CA** metastasize to neck lymph nodes and are therefore associated with high rates of recurrence. **Follicular CA** hematogenous spreads to the bone (termed bonophillic) and lungs. **Anaplastic CA** is quickly aggressive and can kill the patient quickly within 6 months via local infiltration of the surrounding structure and therefore pressuring the trachea (Patients die from suffocation thus a bad prognosis).

- Certain molecular assays can be used to detect the underlying mutations that induce these malignancies as shown here in this figure: (Expensive and therefore not used a lot).

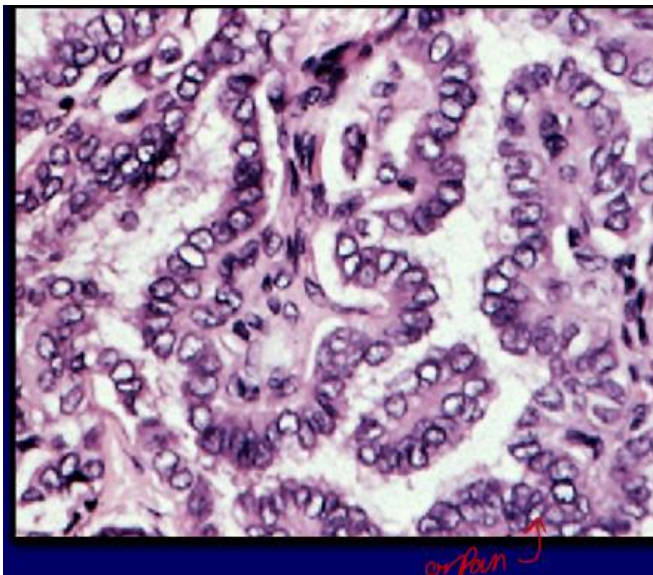
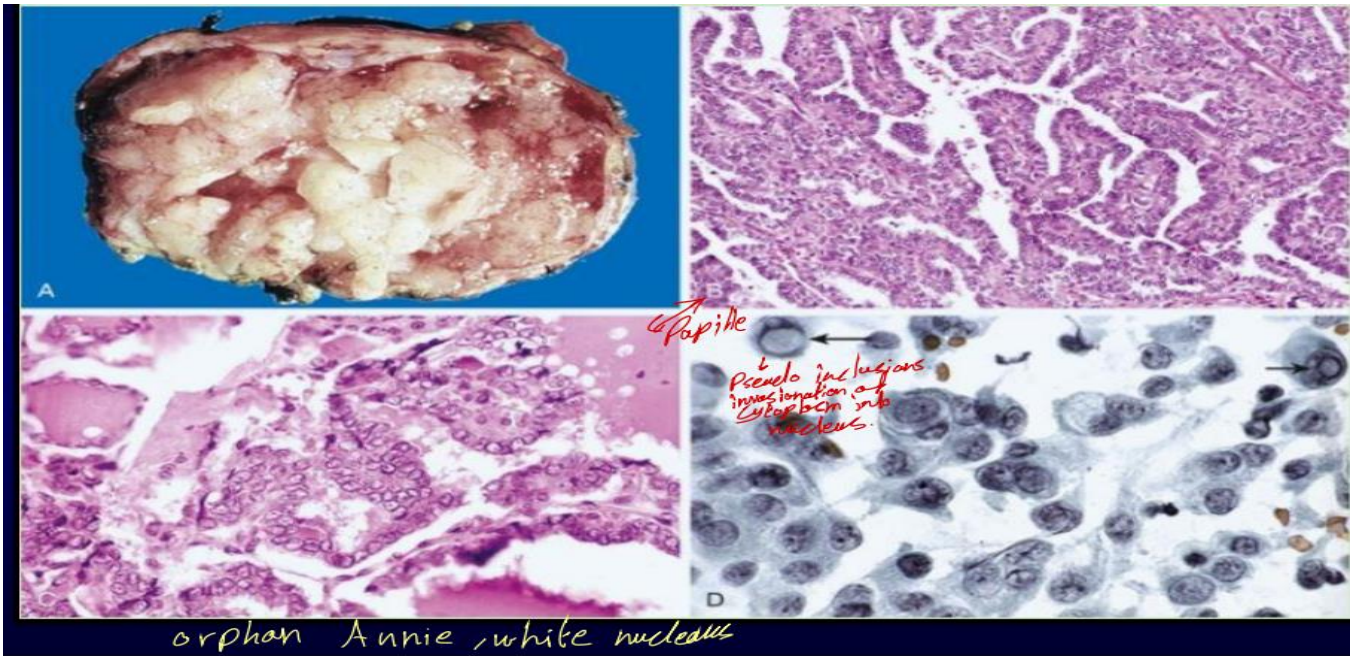
- **Papillary carcinoma** is associated with RET/PTC gene mutations leading to Papillary carcinoma fusion protein that induces excessive cellular proliferation.
- **Follicular and Anaplastic carcinoma** are associated with point mutations in the RAS-gene.

(Those are the only ones that the doctor mentioned).

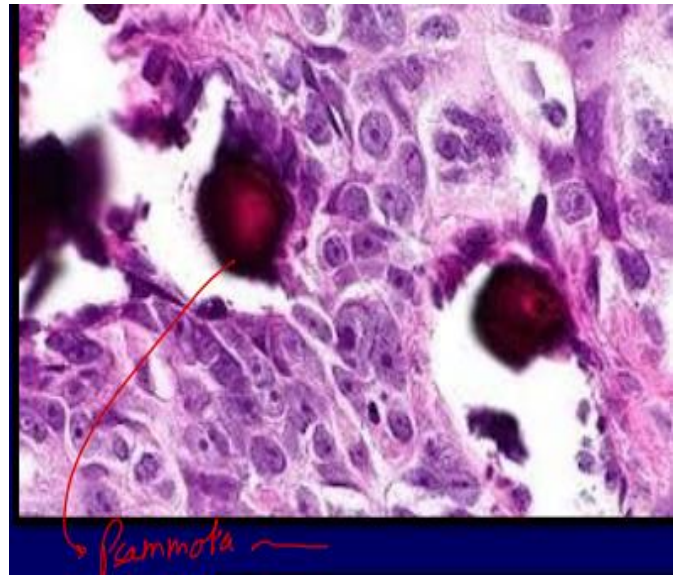


• Papillary Thyroid Carcinoma

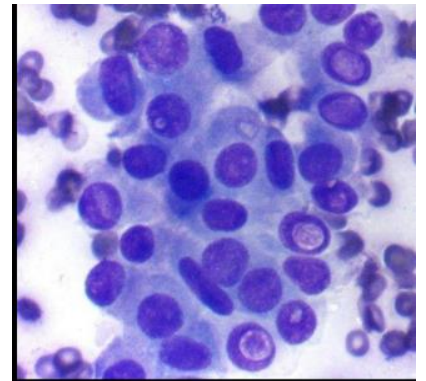
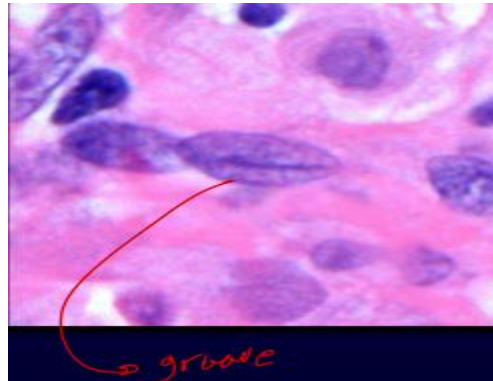
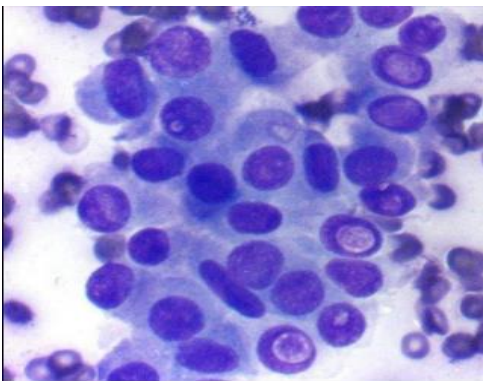
- **Most common**
- **Relatively indolent** (not aggressive, behaving like benign despite showing mets), 10 year survival more than 95% even with lymph node metastasis (Good prognosis).
- Could be uni and multifocal.
- **Can be diagnosed preoperatively by FNA (Accurate).**
- Nuclear features here are most important which are : **Papillae, Nuclear grooves, Psuendonuclear inclusions** (results from the cytoplasm impinging the nucleus giving this Psuedo (fake) appearance), **Psammoma bodies** (A special type of calcification), **Orphan Annie eye nuclei** (White, clear nucleus).
- Therefore, in order to rule out Papillary CA, we look for presence/absence of these features.



This figure shows clear white nuclei
aka **Orphan Annie eye nucleus**



This figure shows a rippling form of
calcification aka **Psammoma bodies**



Practice problems

- 1- A 62-year-old gentleman presents to the clinic with a 5cm painless neck mass as well as diarrhea for the past 3 months. A biopsy is taken, and he is subsequently diagnosed with medullary carcinoma. One of the following is consistent with his diagnosis?
A- Spreads by hematogenous spread
B- Grossly soft and tender mass
C- Diagnosis of MEN-1 syndrome
D- Associated with MEN-2 syndrome.
E- Localized amyloid deposits
- 2- A FNA-cytology sample was sent to the pathologist for evaluation. Upon histological examination, the pathologist reports (inconclusive) and demands a proper biopsy of the mass, which one of the following is most likely the case?
A- Papillary CA
B- Hashimoto thyroiditis
C- Follicular CA
D- Medullary CA
- 3- A 28-year-old man presents to his GP with a 4cm mobile anterior neck mass. A fine needle aspirate is performed which reveals cells with pseudo nuclear inclusions and some type of calcification, which one of the following is most probably the diagnosis?
A- Follicular adenocarcinoma
B- Thyroglossal duct
C- Follicular adenoma
D- Papillary adenocarcinoma
E- Medullary carcinoma
- 4- A 55-year-old man notices a small nodule near his thyroid; he has not experienced any symptoms and has no significant medical history. Ultrasound Imaging reveals a 2-cm solitary nodule located in the left superior pole. Fine-needle aspiration reveals finely dispersed and optically clear nuclei with grooves. In addition to these findings what other findings the pathologist might find:
A- Acellular, amyloid deposits
B- Granular, eosinophilic cytoplasm
C- Extracellular, calcified, spherical bodies
D- Uniform follicles containing colloid
E- Granular, eosinophilic cytoplasm

Answers: 1: D, 2: C, 3: D, 4: C