Dani Srpske Medicinske Dijaspore- Beograd

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Days of Serbian Medical Diaspora- Belgrade

5th October 2012

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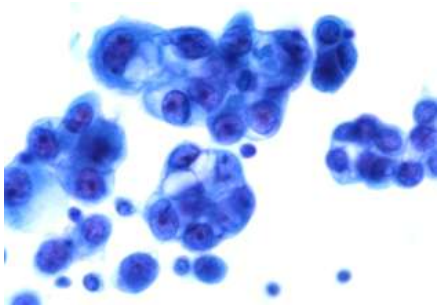
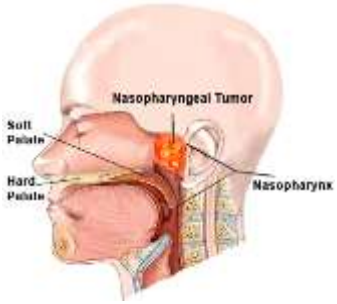
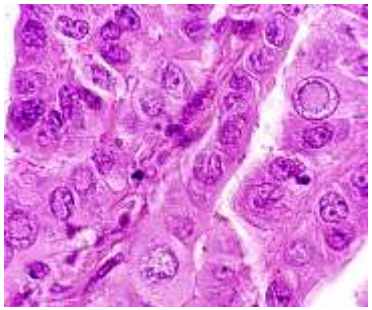
Preoperativana i intraoperativna dijagnostika u hiruskoj patologiji glave i vrata, pljuvacnih zlezda i tiroide.







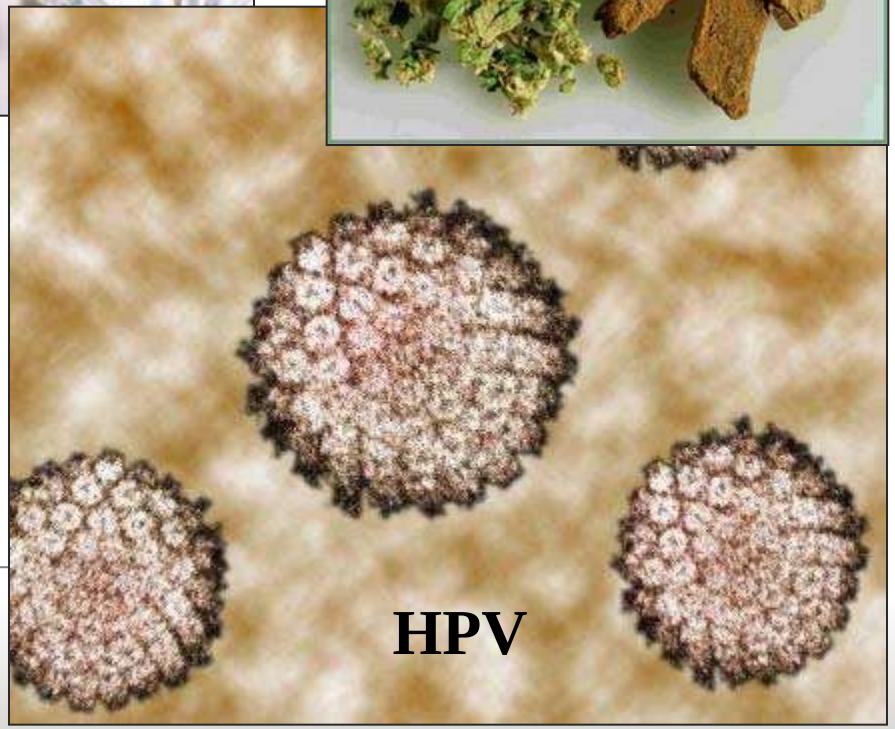
Preoperative and intraoperative diagnostic in surgical pathology of the head & neck, salivary glands and thyroid.

Head and neck squamous cell carcinoma (SCC) (oral cavity, pharynx & larynx)

- ranks as 6th most common malignancy,
- 500,000 new cases/year *(up to 40% of the Indian subcontinent)*
- males at 6th and 7th decades of life,
- increase in incidence: younger males (30%) and females (18%)
- HPV group of patients at risk and cancer biological behavior seem to be different, presenting an increasing public health issue.
- the five-year survival rate of patients is about 40-50%.

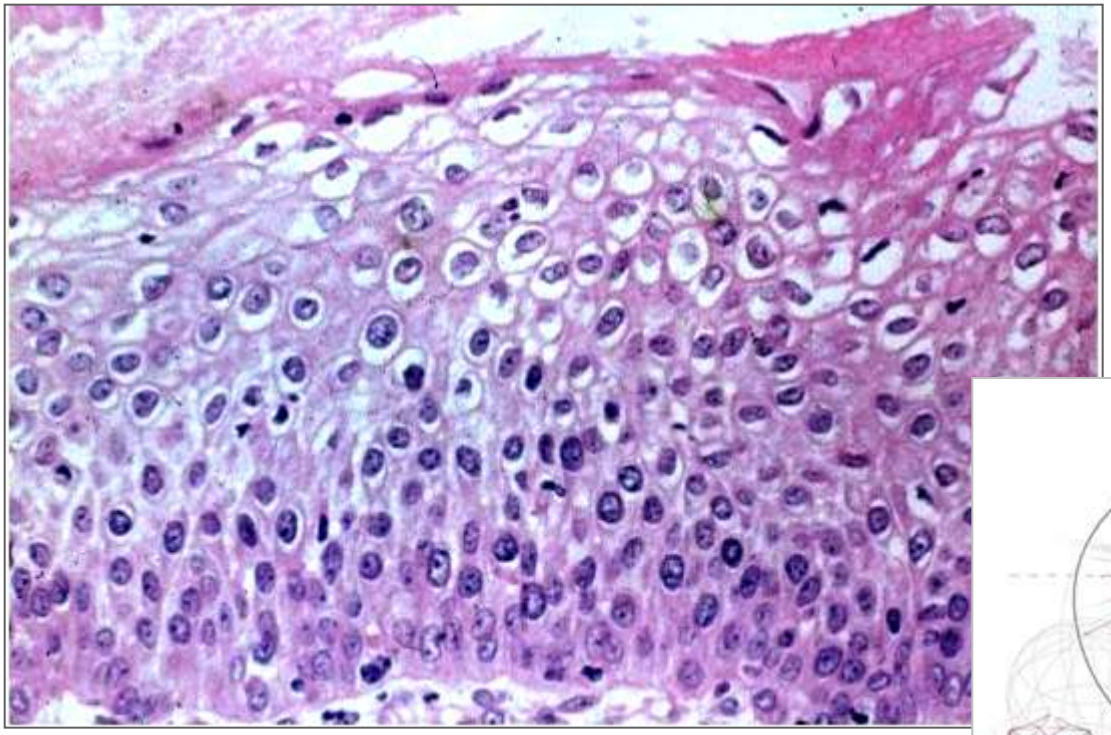
Risk factors….

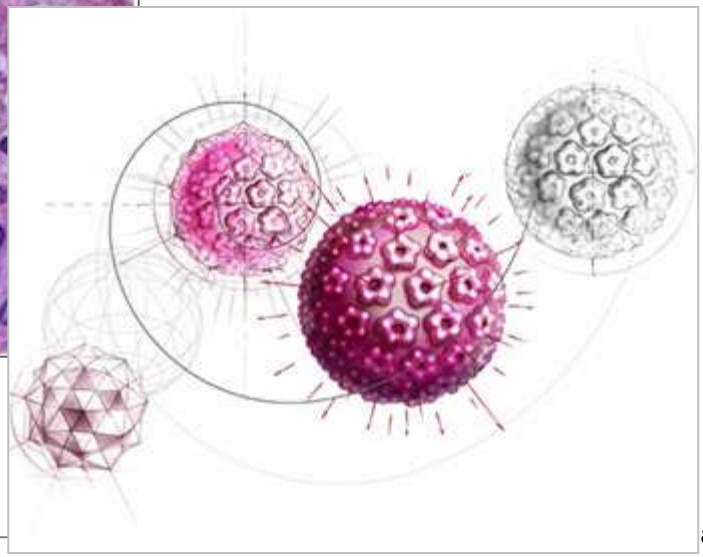
…alcohol consumption & tobacco



HPV infection (16 & 18)

HPV status is an important prognostic factor (associated with a favourable outcome in HN SCC.)





HPV 16, 18, 30, 33

al

Content:

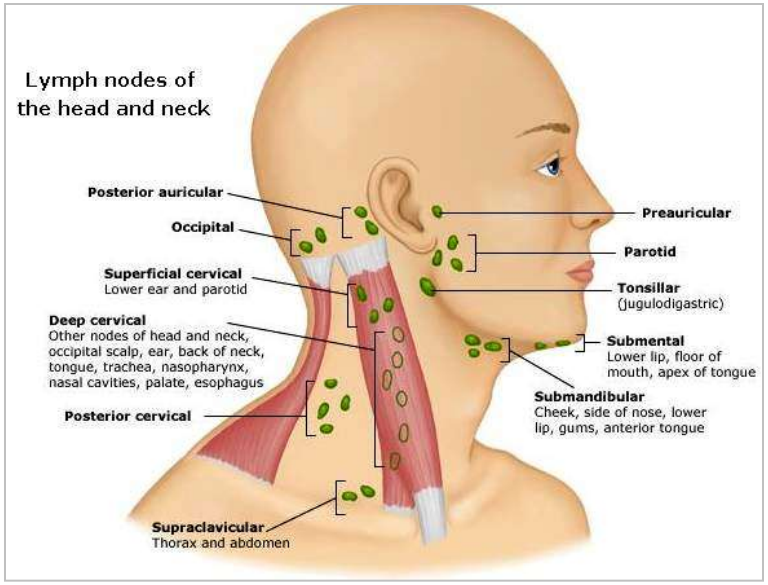
1) Diagnostic approach and management of carcinoma of unknown primary (CUP) in the head and neck

2) A thyroid nodule: Diagnostic challenge en cytology & histology

3) Pitfalls and unusual cases of « squamous proliferation » in head & neck, thyroid and salivary gland pathology

4) Teaching cases

1.Diagnostic approach and management of carcinoma of unknown primary (CUP) in the head and neck



… among **500** lymph nodes in the body, **200** are in the head and neck….

…60% of the neck masses in patients older than 40 years are caused by **malignant tumors**,

and **85%** of them are from primary tumors in the **head and neck area** (SCC)…..

CUP: History & Controversy…..

1882 Volkmann: described **three cases** of latero-cervical lymph node metastasis in **level II** w/o a primary tumor, «typical» for lateral cysts of the neck, defined as "***deep branchiogenic carcinoma of the neck***"

Until the **1940s** several authors reported cervical lymph node metastasis of unknown primary being caused by ***branchiogenic carcinomas*** of the neck.

1950 Martin: Histologic and clinical criteria of so-called **branchiogenic carcinoma**:

*1) Location of a **cystic lesion** in the area of the carotid triangle.*

*2) Remains of **branchiogenic structures**.*

*3) No appearance of primary tumor in the **five** years after initial diagnosis.*

4) Histological detection of neoplastic cells in the wall of the cyst…..

DD with cervical cystic LN metastasis of CUP has create a great deal of skepticism regarding the existence of branchiogenic carcinoma…

1957 Commes et al. described a cervical lymph node metastasis without diagnosis of a primary tumor and defined the malignant disease as **CUP**

Today many author consider branchiogenic carcinoma as misinterpreted cervical cystic LN metastasis of occult primary (in the area of the Waldeyer's tonsilar ring.)

The most used system of nodal mapping anatomically classifies lymph nodes into levels (Sakorafas et al., 2010).

Lymph nodes (Level I-VI)

Unilabs

Level I: Oral cavity, lip, gingival mucosa, vocal cords

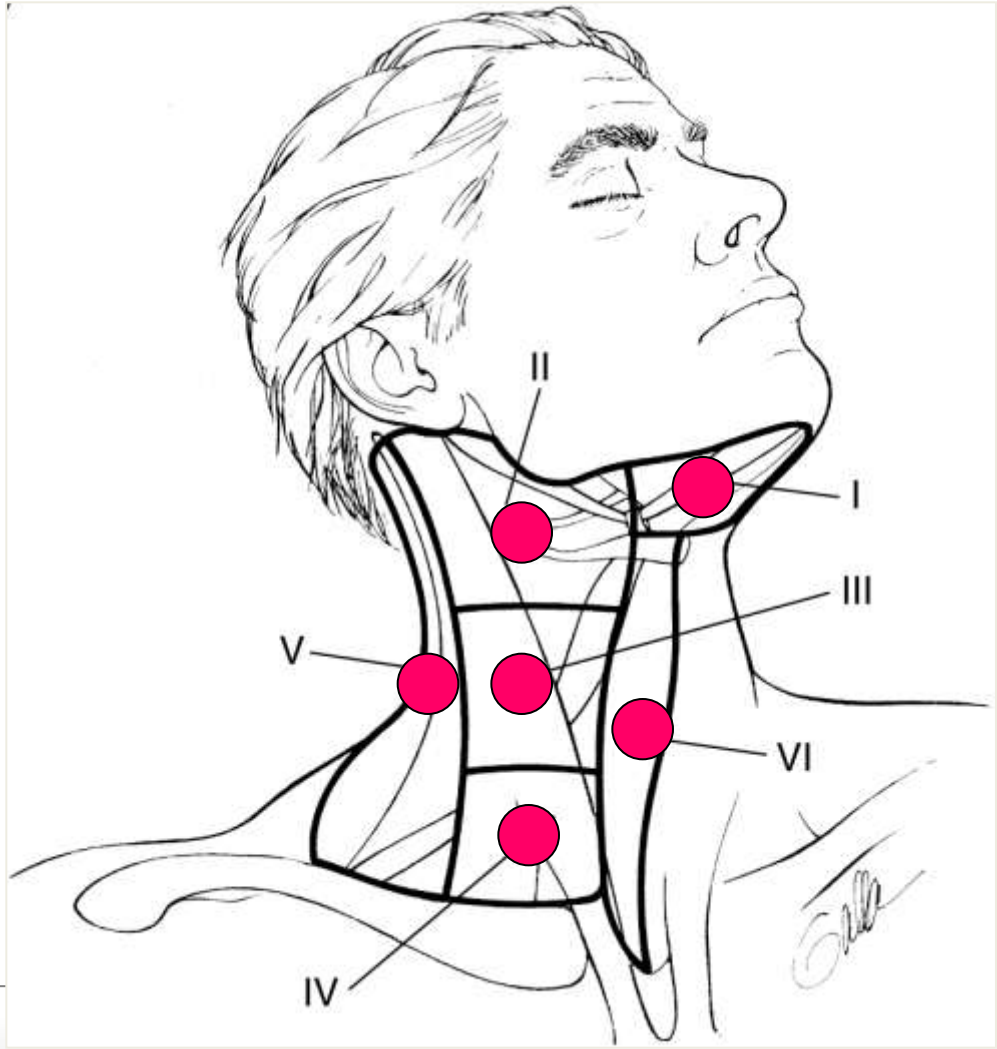
Level II: Oral cavity, retro-molar space, oro- naso- hypopharynx, base of the tongue, larynx (supra-glottis).

Level III: Base of the tongue, hypopharynx, larynx, thyroid.

Level IV: Hypopharynx, larynx, thyroid, esophagus.

Level V: Nasopharynx, thyroid, esophagus, lung.

Level VI: Thyroid, trachea.



CUP: Definition & Epidemiology

The **CUP** is defined as the **histological diagnosis** of metastasis without the emergence of a primary tumor (tumor presented **initially with metastases**).

The **source** of the primary cancer **remains unknown** after complete investigation.

It constitutes **5–15%** of all human malignancies (***7th most common malignancy***).

40-60%of **CUP** includes **cervical lymph node metastases.**

Median **age 55- 65 years**, slight **male** predominance.

No primary site of origin can be identified in **3 to 5**% of patients.

Overall 5-year survival rate 15-20%.

CUP (Lymph node level I-VI)

Level I: Oral cavity, lip, gingival mucosa, vocal cords

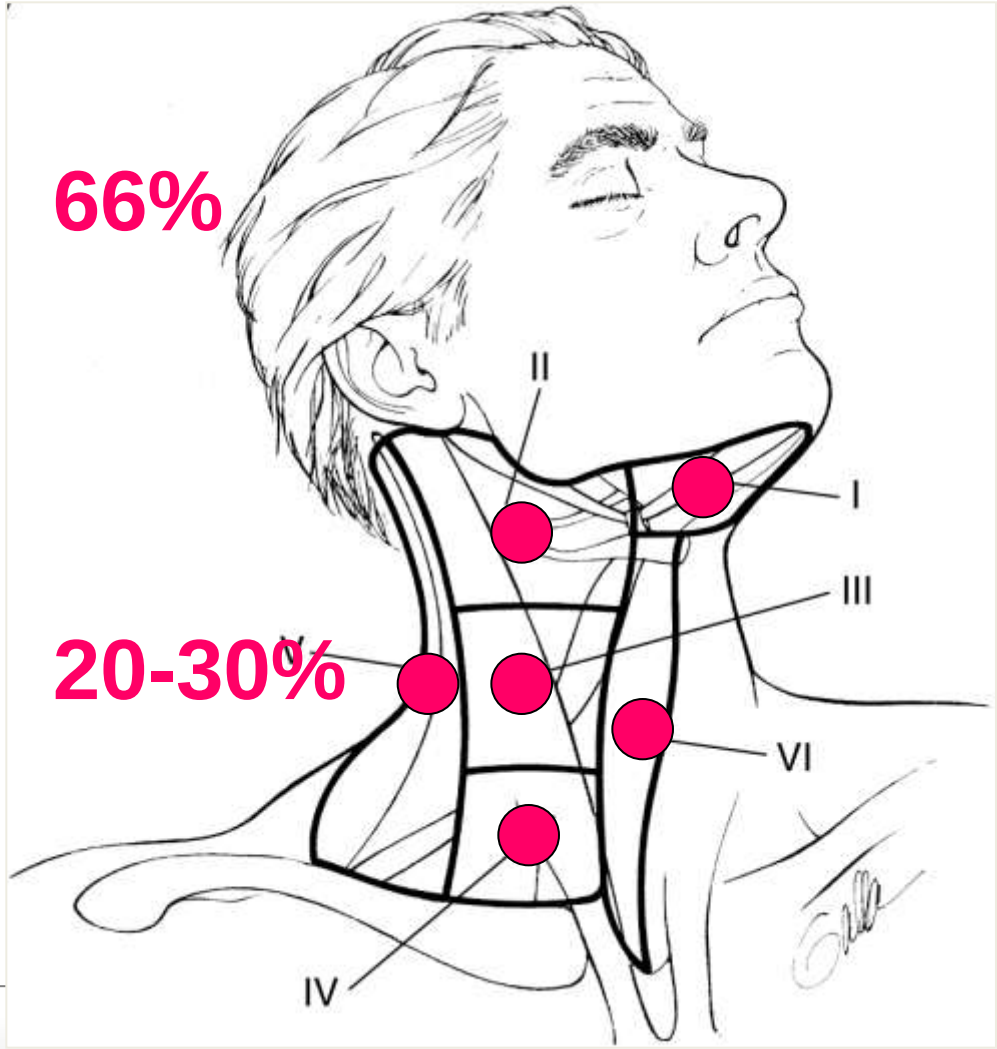
Level II: Oral cavity, retro-molar space, oro- naso- hypopharynx, base of the tongue, larynx (supra-glottis).

Level III: Base of the tongue, **tonsil,** hypopharynx, larynx, thyroid

Level IV: Hypopharynx, larynx, thyroid, esophagus.

Level V: Nasopharynx, thyroid, esophagus, lung.

Level VI: Thyroid, trachea.



4%= unknown….

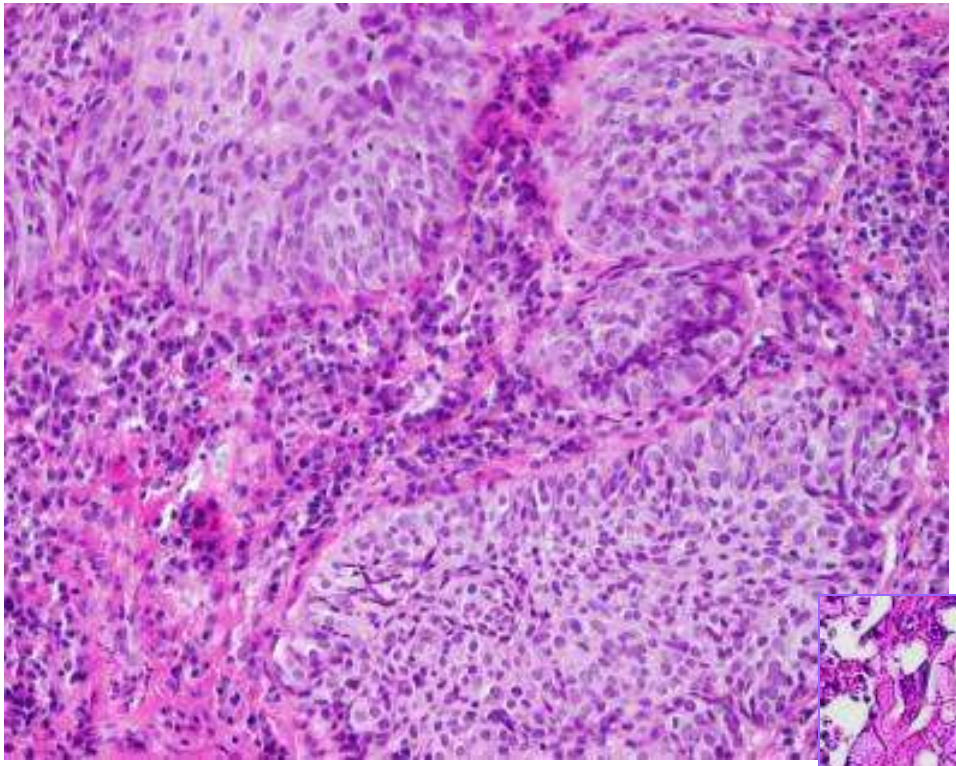
CUP: Incidence & localization

Lymph node metastasis in Groups I-II-III:

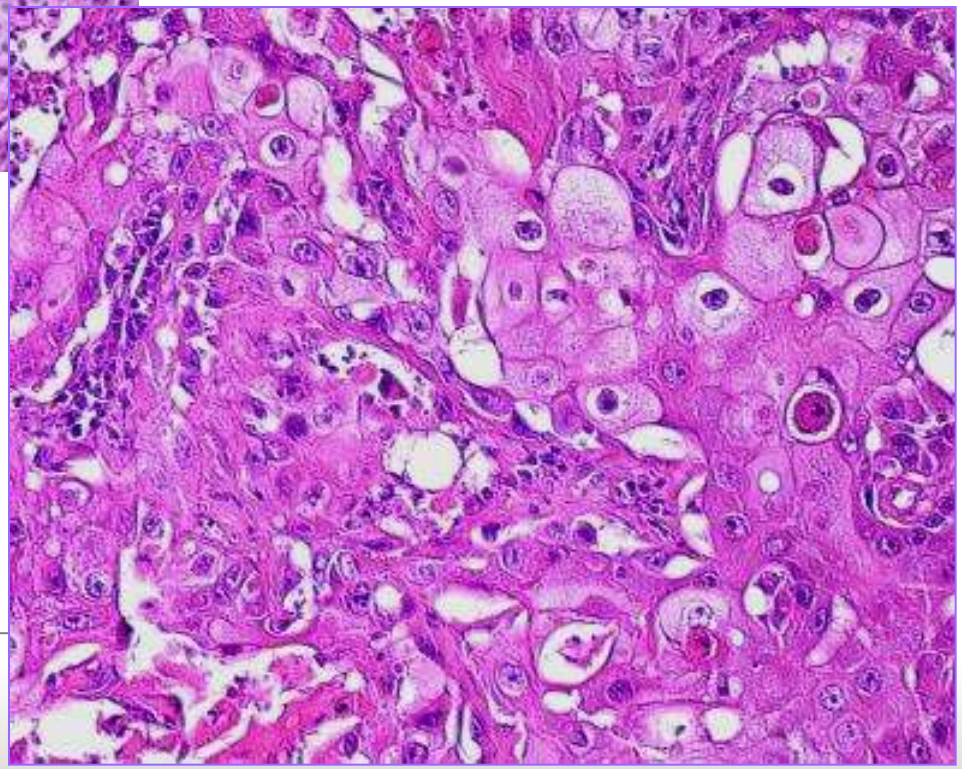
- **66%** SCC of the upper aero-digestive tract (UAT).

Lymph node metastasis in Groups IV-V-VI:

- **30%** **adenocarcinomas**, (*lung, stomach, breast, kidney, prostate*).
- **25%** **poorly differentiated or undifferentiated carcinomas** of rhynopharynx (*eliminate lymphoma!*).
- **20%** **thyroid carcinomas**.
- less than **15%** SCCs of the UAP.

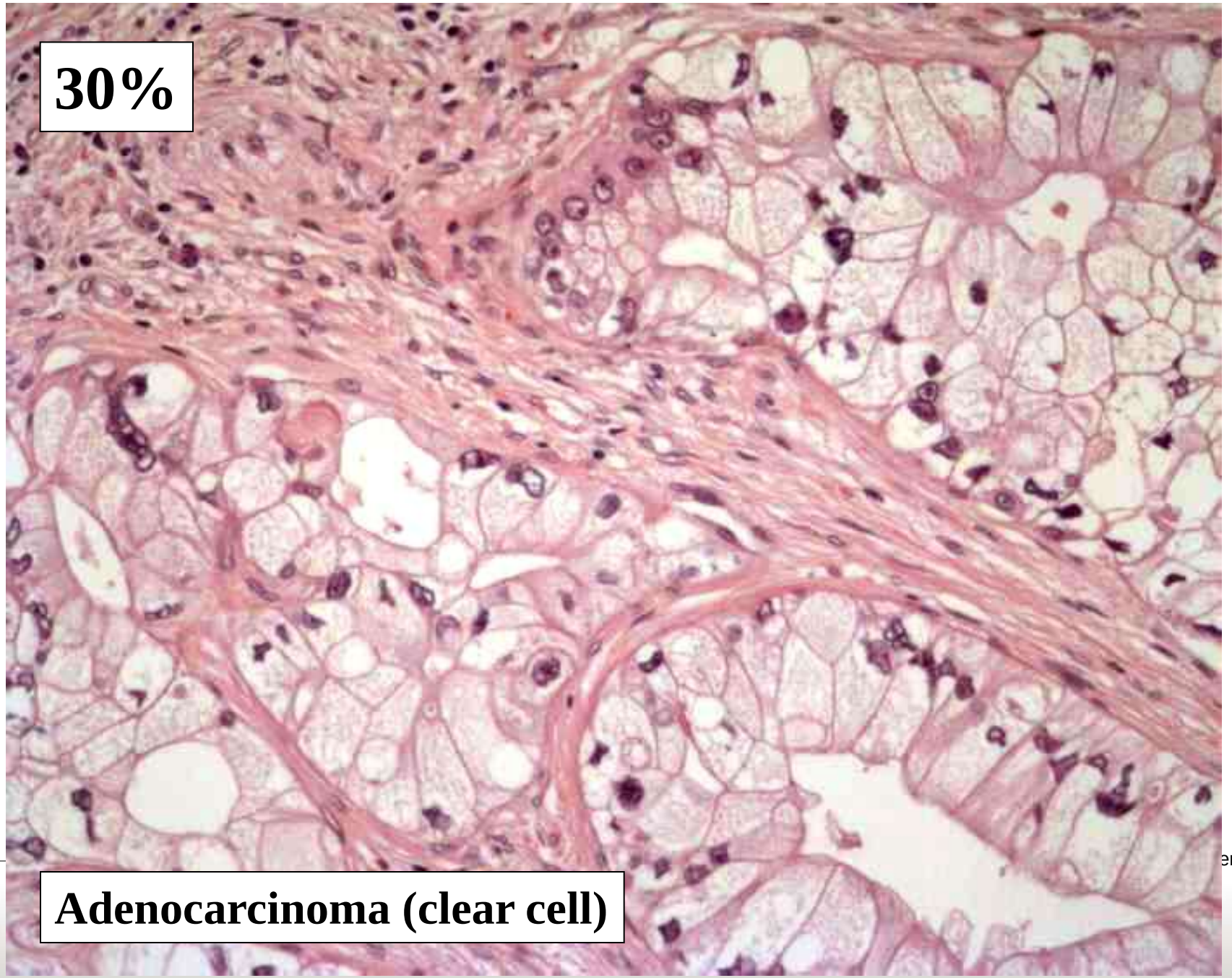


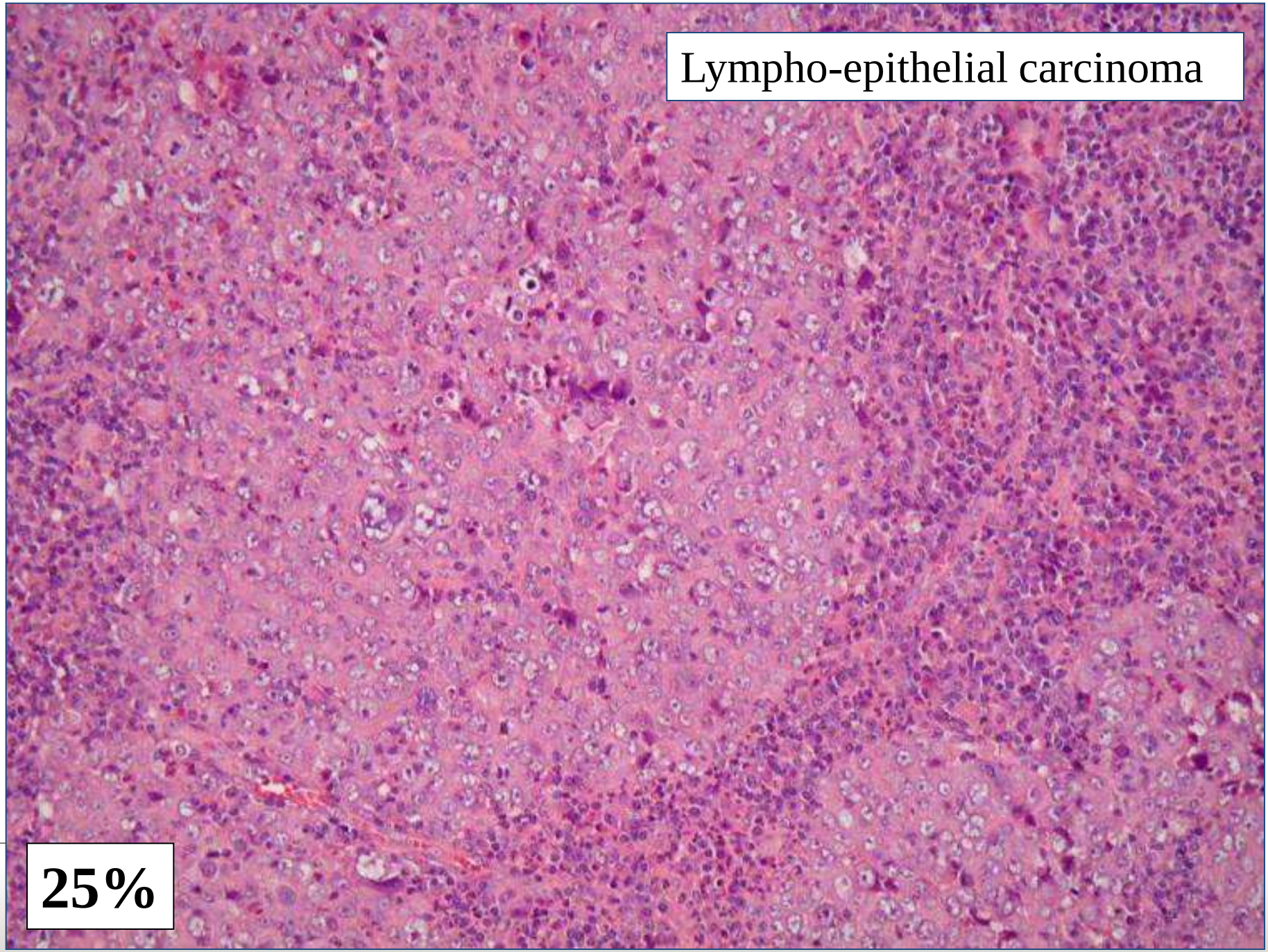
Unilabs



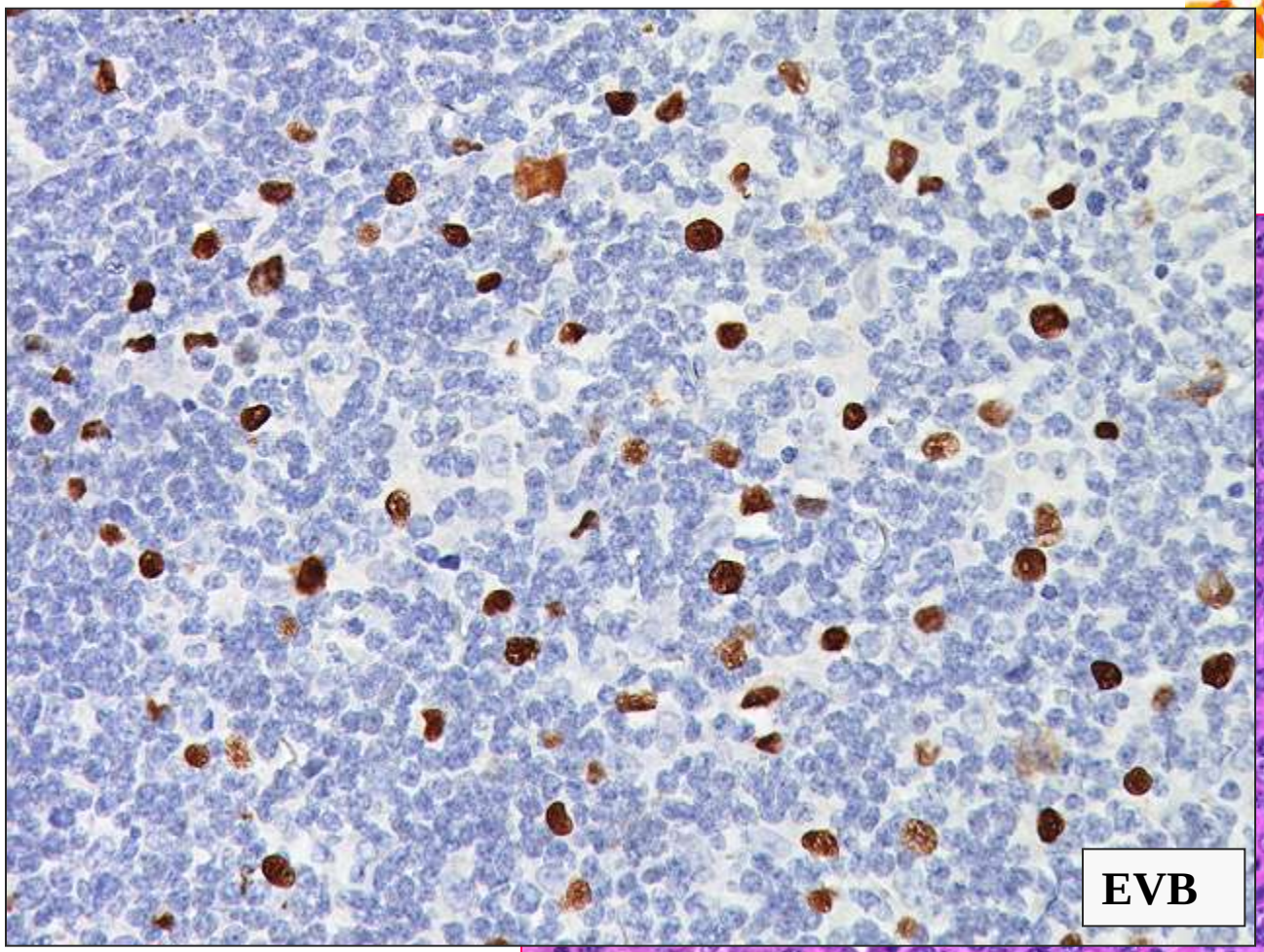
66%

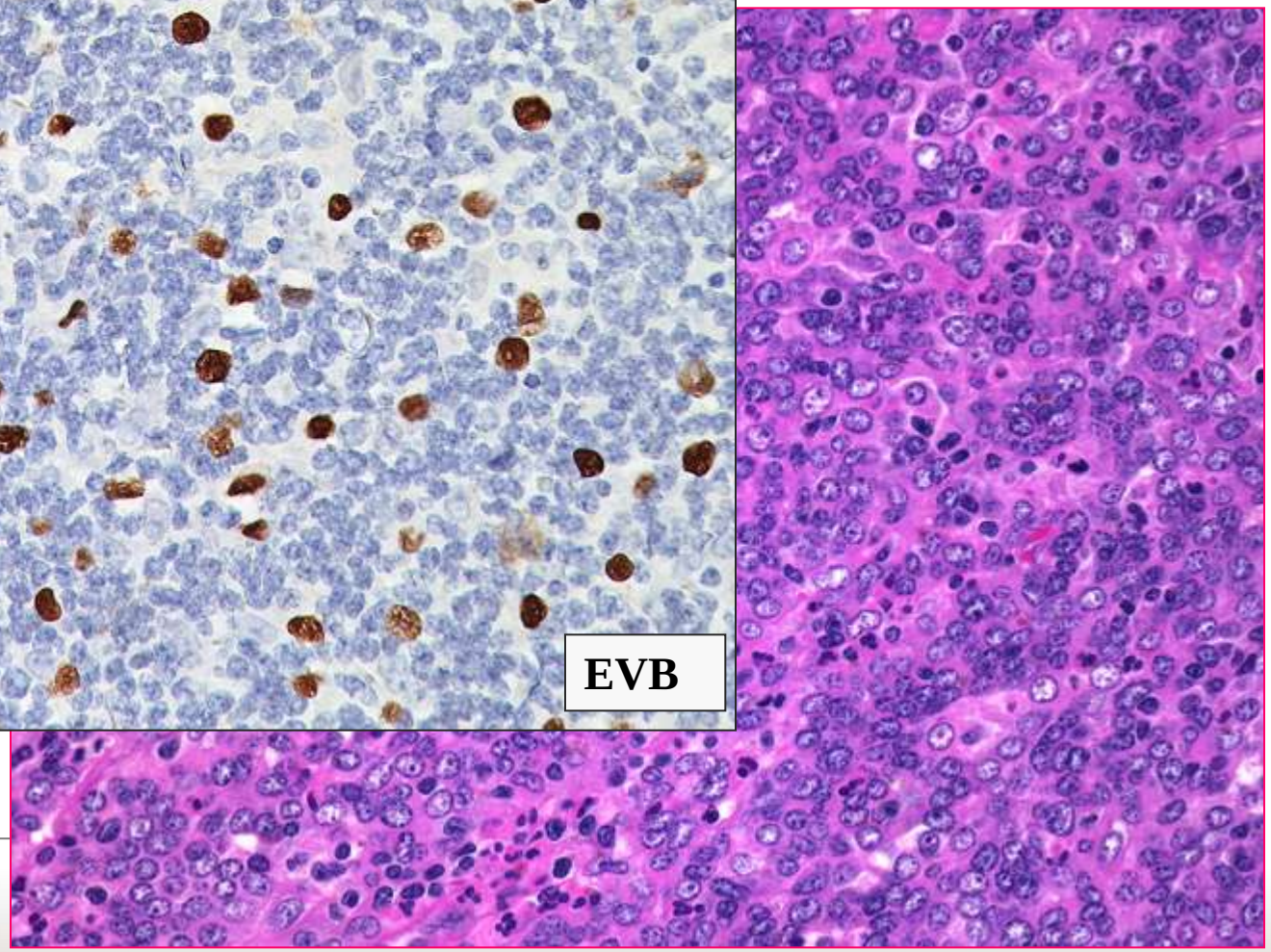
HNSCC → **HPV status**



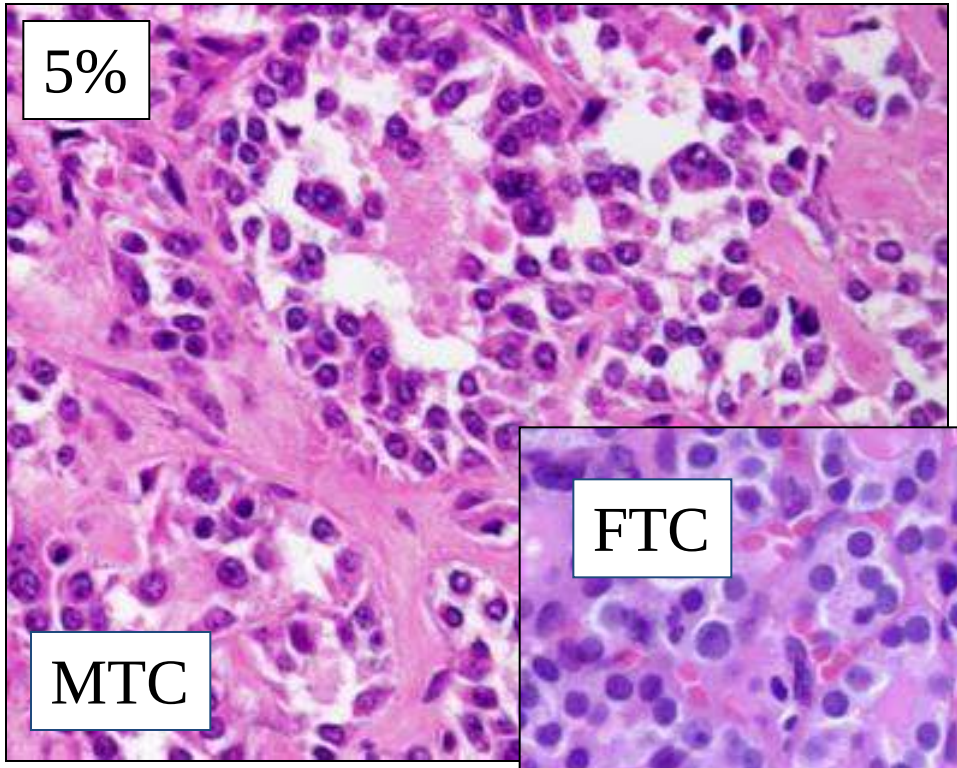

Lympho-epithelial carcinoma
25%

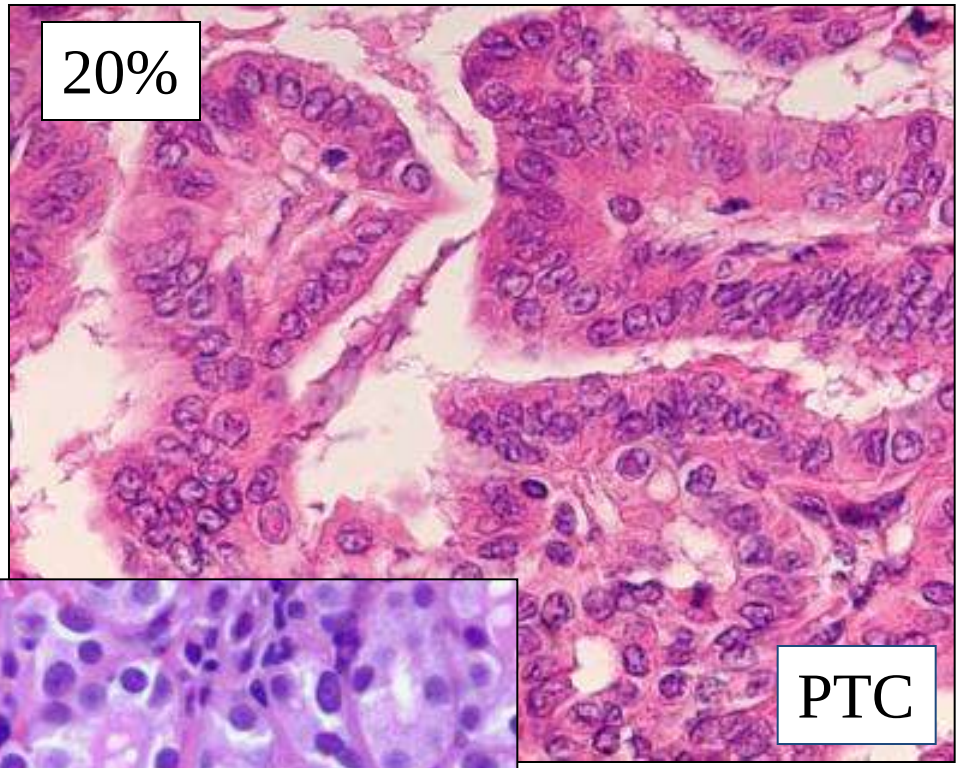
SCC (lympho-epithelial type)

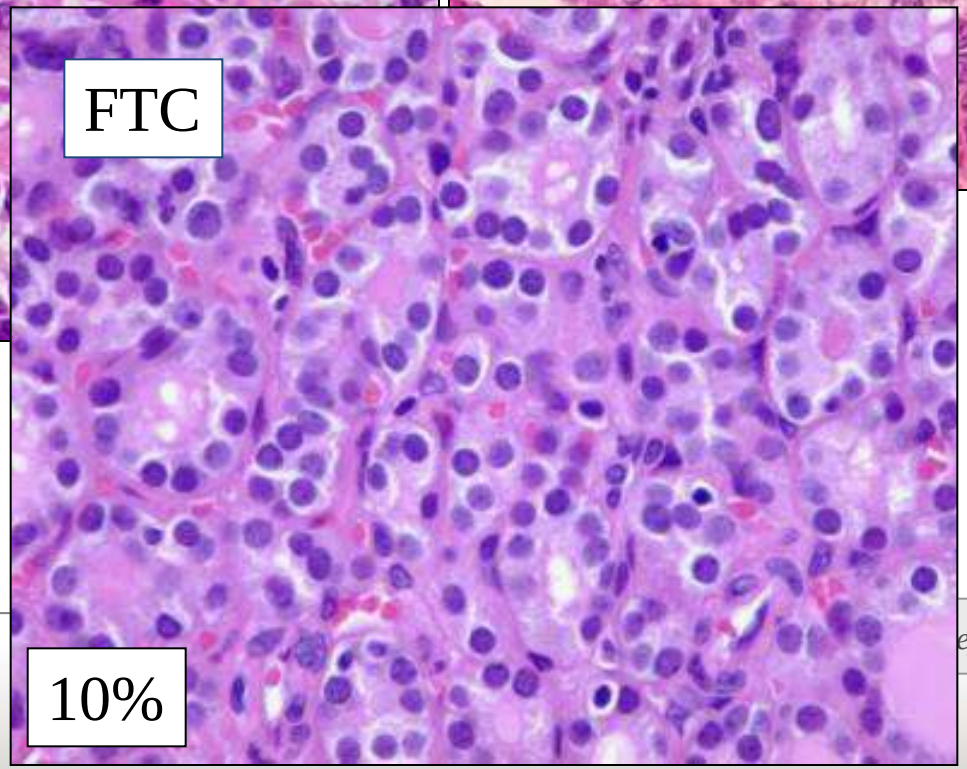




Thyroid carcinomas







CUP/SCC: Incidence & localization

- **4-5%** of all head and neck and UAT SCC,
- **up to 30%** of occult **tonsil SCC**
- **60 %** of cases unique adenopathy
- **30%** multiples homo-lateral adenopathy
- **10 %** multiples bilateral adenopathy.
- **90%** of cases, primary tumor of UAT is detected

Non invasive diagnostic tools: FNA & Radiology

- **FNA** in **98%** of cases lymph node ***metastasis of SCC***
- If poorly or undifferentiated carcinoma consider **rhinopharynx** as primary site.
- detection of **EBV** genome by *in situ* hybridization,
- **HPV status in younger patients***
- **Rx thorax**
- **CT-Scan/US**: capsular effraction in lymph node and distant metastasis
- **MRI**: w/o contrast
- **PET-CT**: occult lesion.

****Cystic cervical LN metastasis associated with HPV-related tonsillar SCC (D. Goldenberg 2008)***

Invasive diagnostic tools:

Panendoscopy, Tonsillectomy, Adenectomy

Panendoscopy with multiples sites biopsies:

- UAT (bronchi & esophagus)
- rhinopharynx, hypopharynx,
- base of the tongue

Diagnostic routine tonsillectomy (uni/bilat)

The most common sites of primary lesion

Diagnostic adenectomy: allow IHC study (typisation)

CAVE: Never BX of lymph node, high risk of dissemination!!!

No intraoperative frozen section!!!(take your time…)

Invasive diagnostic tools: Routine tonsillectomy

Enlarged, bilateral (also on site after previous tonsillectomy)

Inclusion and analysis in 5 μm paraffin serial sections (whole tonsil)

Small cryptic SCC found in up to 30% of cases

Complementary study: IHC, HPV status

IMPORTANT:
Impact on therapeutic approach: *RTH = primary site + LN « boost »*

Prof. Dr Med S. Andrejevic-Blant, Oct 2012

Invasive diagnostic tools: Diagnostic Adenectomy

After several non conclusive/ non contributive FNA

Diagnostic intent

Allows…

- **to study morphology,**
- **other prognostic criteria (**ex extracapsular extension, vascular invasion)
- **extensive IHC analysis,**
- **complementary** molecular assays (FISH, PCR)

  EBV genome: nasopharyngeal SCC

  HPV high risk phenotype: oropharyngeal cancer

  Microsatellite mutation analysis of metastatic nodal tissue and « normal» mucosa *(J. Califano et al 1999)*

Diagnostic of CUP….

*…It is mandatory and strongly recommended that clinicians, radiologists and expert ENT pathologists (Tumor Board) confront their opinions **before** and **after** final diagnosis (according to institutional SOP)…*

Diagnostic algorithme of **TUMOR** of the unknown primary

Anatomopathological analysis

- Adenocarcinoma
- **Undifferentiated malignant tumor**
- Squamous cell carcinoma

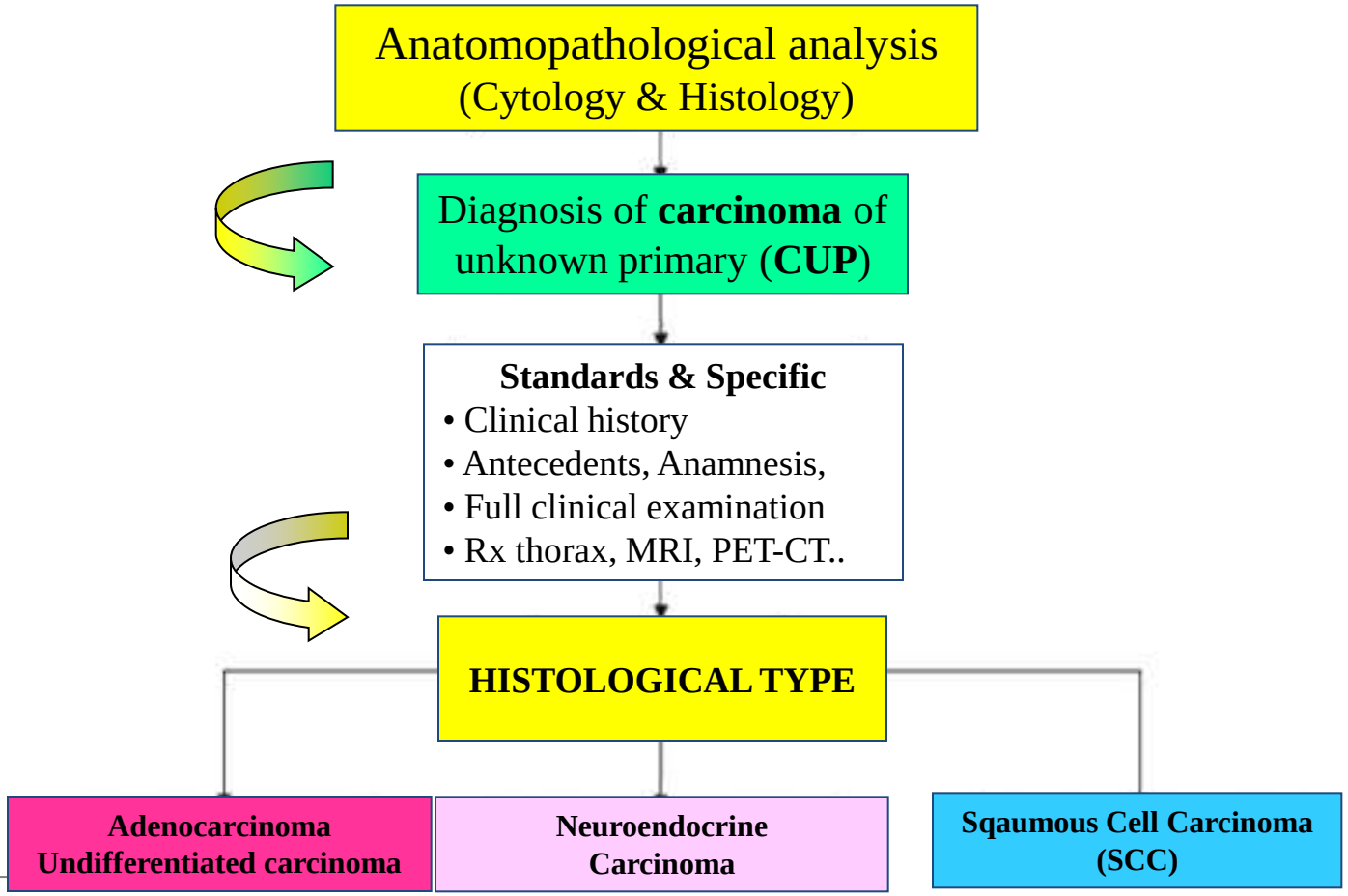
Undifferentiated malignant tumor

CK +	**CK** +	CK -	CK -	CK -
CD45 +	CD45 -	**CD45** +	CD45 -	CD45 -
S-100 +	S-100 -	S-100 -	**S-100** +	S-100 -
Problem!! **Artifacts?** **Repeat IHC!!**		**Lymphoma** B & T phenotype EMA, CD30, ALK (large cell)	**Melanoma** *(Melan-A, HMB-45)* **Liposarcoma** **PMNST**	**Sarcoma** *(SML, DES, CD31, CD34, CD99, CD117)*

- **Germinal tumor** *(PLAP, βHCG, αAFP)* Embyonal-CA Chorio-CA, Yolk sac tumor
- Malignant **mesothelioma** *(CK5/6, WT-1, Calret)* Synovial **sarcoma** Epitheliod **sarcoma**
- **Undifferentiated carcinoma**

Prof. Dr Med S. Andrejevic-Blant, Oct 2012

Diagnostic algorithme of carcinoma of unknown primary (CUP)….



CUP: Therapeutic approach

The main goal of treatment is to offer the local control of:

- **metastatic LN cervical disease,**
- **occult contralateral LN cervical disease,**
- **occult primary lesion.**

Therapeutic options:

1) Surgery alone:

unilateral or bilateral neck dissection (levels I-V)

2) RTH therapy alone :

unilateral or bilateral neck irradiation (levels I-V-III & pharynx)

3) Surgery + RTH (unilat and/or bilat & pharynx)

4) RTH/CTH follow by salvage surgery

CUP: Therapeutic approach

Clinical stage **cN1** or **cN2a**, w/o extra capsular extension, or ≤ **3** LNs	**Surgery alone**
Clinical stage **cN1** or **cN2a** with extra capsular extension, **cN2b, cN2c** or > 3 LNs	**RTH uni/ bilateral ± Surgery (?)**
Clinical stage **cN3**	**Radical neck dissection + RTH ± CTH** **Neo-adjuvant CTH + Surgery + RTH** **RTH/CTH ± Surgery**

Neck dissection (Level I -V)
Pathology rapport

Unilabs

Inclusion and serial section analysis of all LNs

- precise …

  total number, and **topography** of LN **(by level)**

  mean size

  size of **biggest** LN (if more than **3cm**, additional section 1/cm)

  consistence, and mobility,

  (relation with skin, muscle, jugular vein, carotid artery)

- looking for extra-capsular extension, LVI, Pn1….

N stage: ….. Tx, **pN2a**, Mx…. and level…

CUP: tumor biology

Chromosomal Abnormalities

Aneuploidy in **70%–90%**

(without any relationship to patterns of metastatic involvement or survival).

Tumor Suppressor Genes and Proteins

p53 overexpression

KiSS-1 metastasis-suppressor gene was correlated with poor prognosis

Angiogenesis

no prognostic value of a microvessel density marker (**CD34 and VEGF-A**)

Microarray technology should be used to compare expression profiles between CUP and known primary tumors, as well as for assigning CUP cases to sites of origin leading to elucidate **what is really missing in CUP: the primary or the biology?**

CUP: Prognosis

• The **nodal status** is considered as the **most important** prognostic factor *(prognosis equivalent to that observed in patients with known primary and similar nodal stage)*

• For patients **treated with neck dissection**, prognostic factors include (*N-stage, number of nodes, grading, extracapsular extension*)

• EBV genome: nasopharyngeal SCC (worst prognosis)

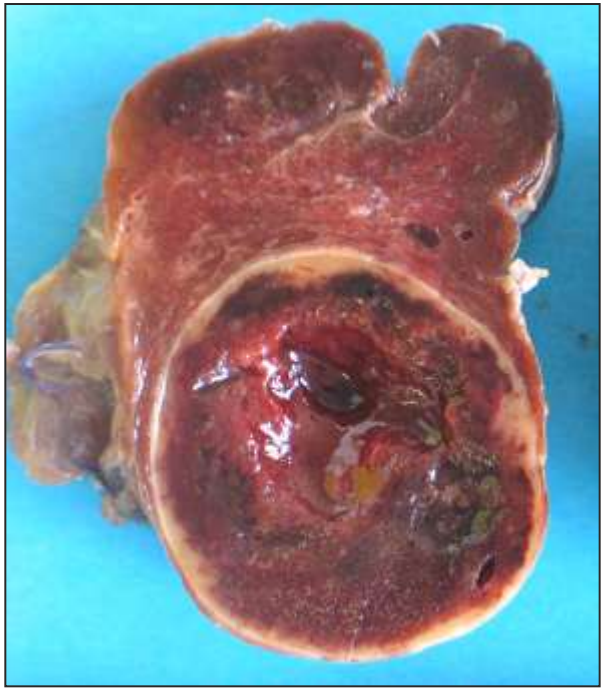
The overall 5-year survival rate 15-20%.

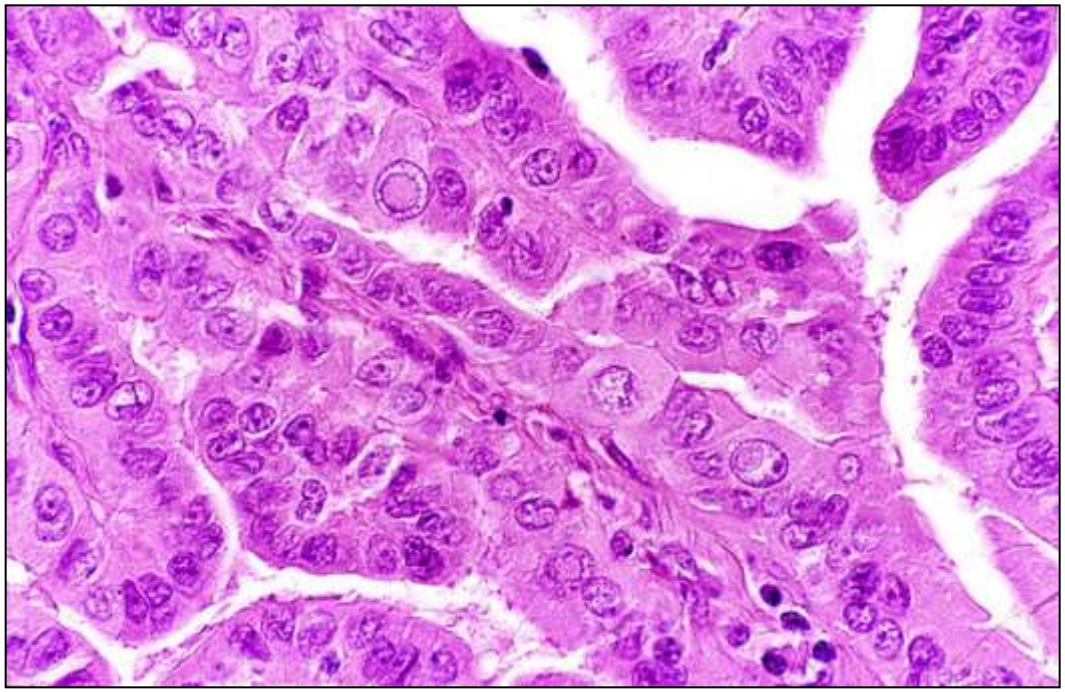
Head & Neck CUP: *Take home message….*

- **Thinking at the beginning…(cystic metastasis, tonsil, HVP…)**
- Anatomo-clinical confrontation **BEFORE** & **AFTER** diagnostic is mandatory (*expert team agreement*).
- Multicentric approach
  (biopsies, tonsillectomy, lymph node adenectomy)
- Particular technical approach during FNA or histological analysis.
- Extensive complementary analysis:
  IHC according to histological type,
  Topography of LN (levels I-VI),
  Molecular biology (EBV, HPV).

Pre-therapeutic assessment & TTT Approach

2. A thyroid nodule:
Diagnostic challenge in cytology & histology





FNA- Cytology

Benignant **50-75%**

Nodule

Cyst

Thyroiditis:

Lymphocytic

Subacute granulomatous (*de Quervain*)

Malignant **5-10%**

Carcinomas:

papillary

medullary

undifferentiated

Insufficient **2-15%**

(< 5-6 groups of thyreocytes)

Suspect **15-30%**

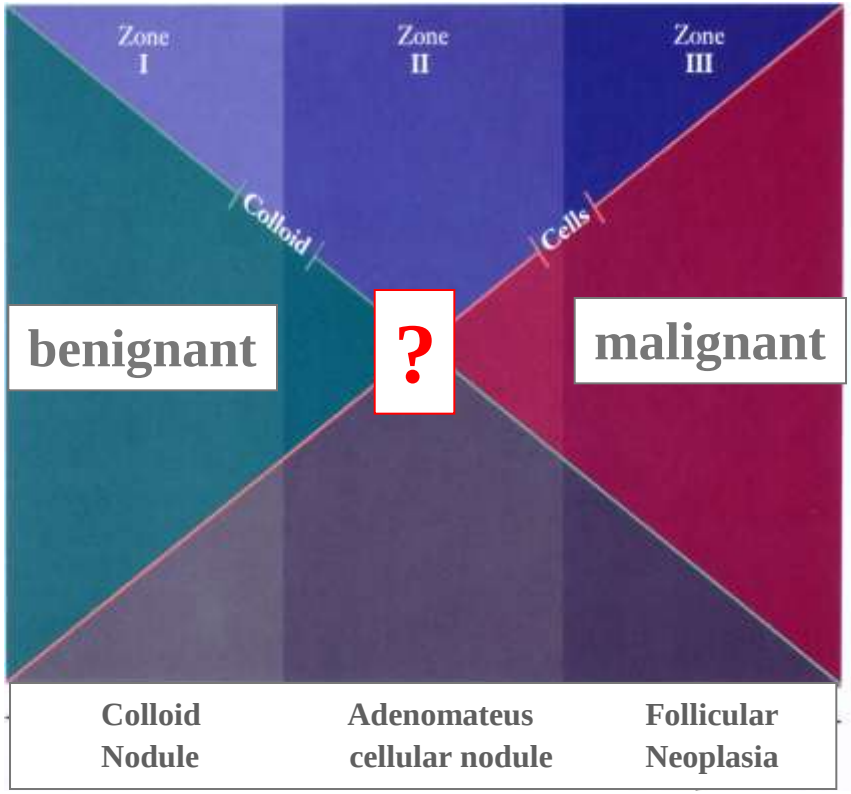
Proliferations:

– follicular

– oncocytic

Cytology: suspect/indeterminate

15-30% of follicular/oncocytic proliferation

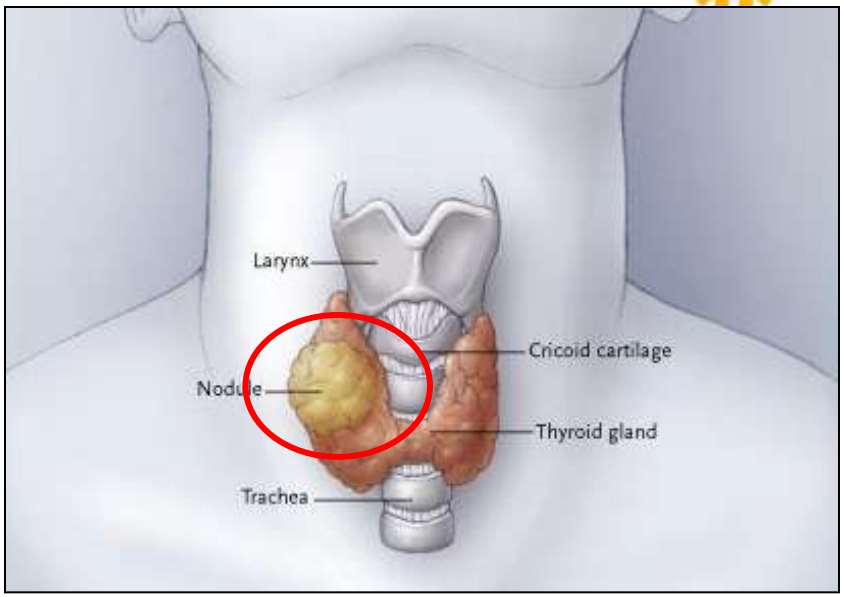


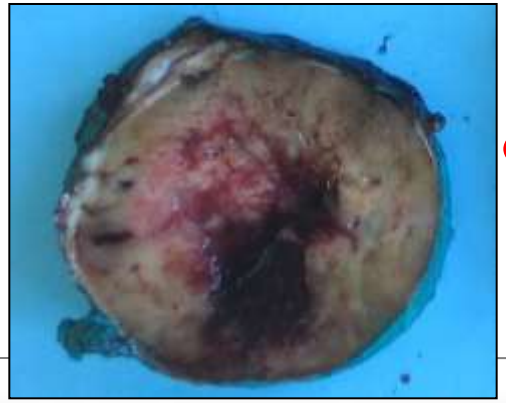
increasing of cellularity

decreasing of colloid

Blant, Oct 2012

Thyroid nodule-histology





Benignant (95%)

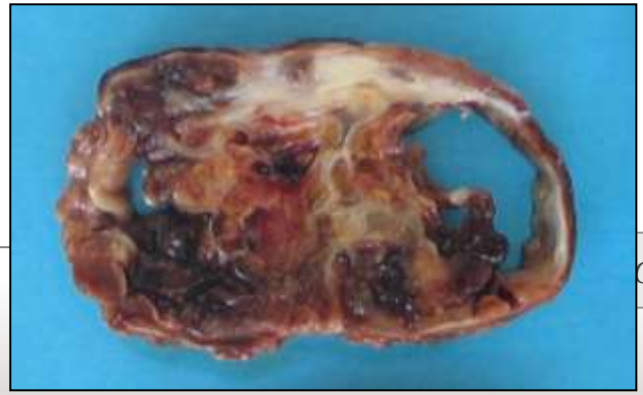
Hyperplasia (85%)

Adenoma (14%)

Cyst (1%)

Malignant (5%)

……



Thyroid nodule-histology

Follicular adenoma

Carcinomas

Derivates from follicular cells

Papillary	**(75-85%)**
Follicular	**(10-20%)**
Poorly differentiated	**(> 5%)**
Undifferentiated	**(> 5%)**

Derivates from C cells cellules (parafollicular)

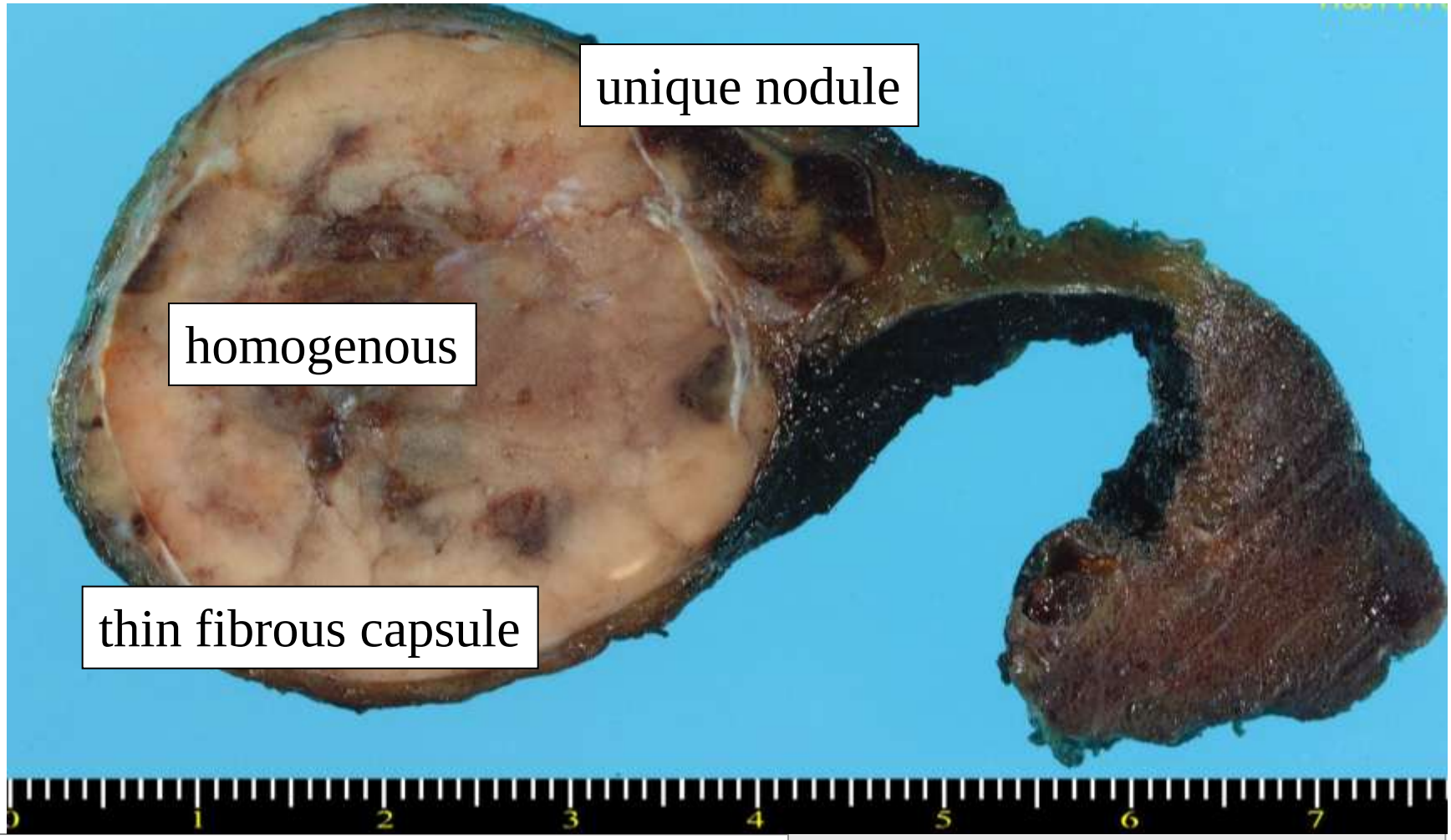
Medullary	**(> 5%)**

Well differentiated tumor of uncertain malignant potential

Spindle cell tumor with « thymus-like » differentiation

Other (rare): Lymphomas, metastasis (*kidney, breast, melanoma, lung…)*

Follicular adenoma



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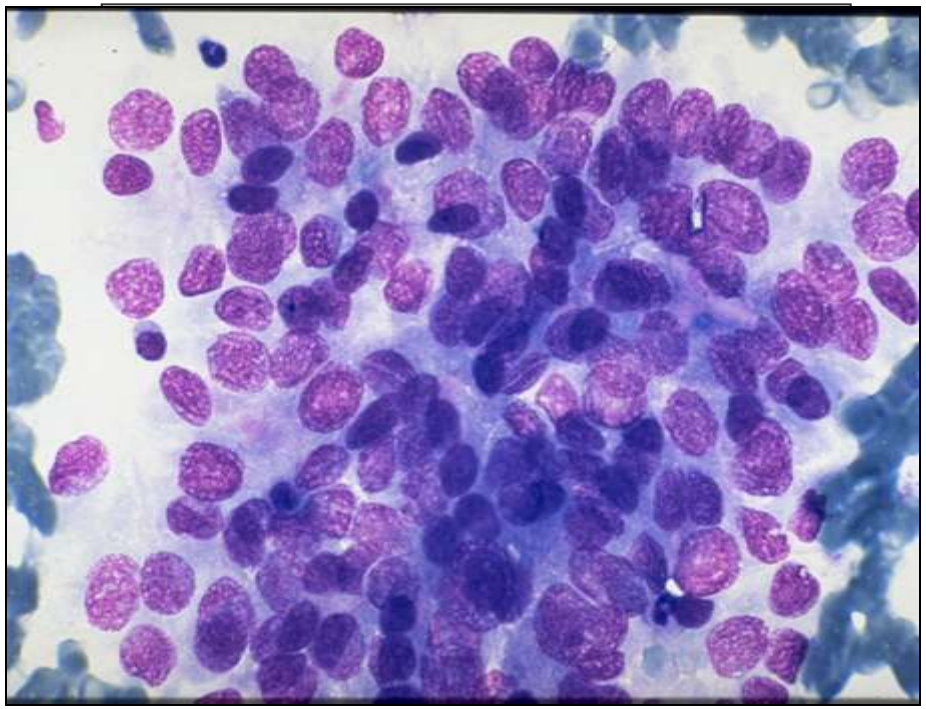
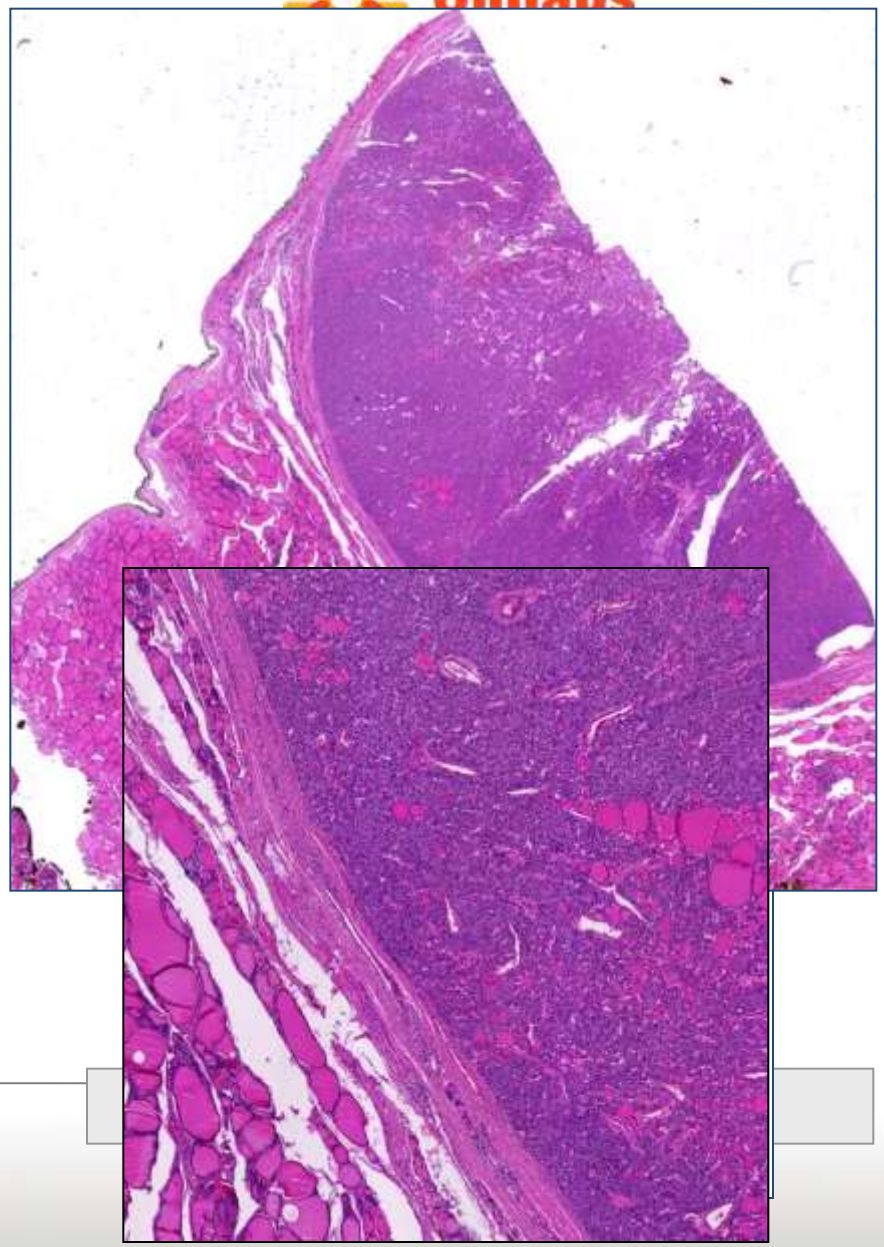
FNA diagnosis NOT possible (no information about capsule…)

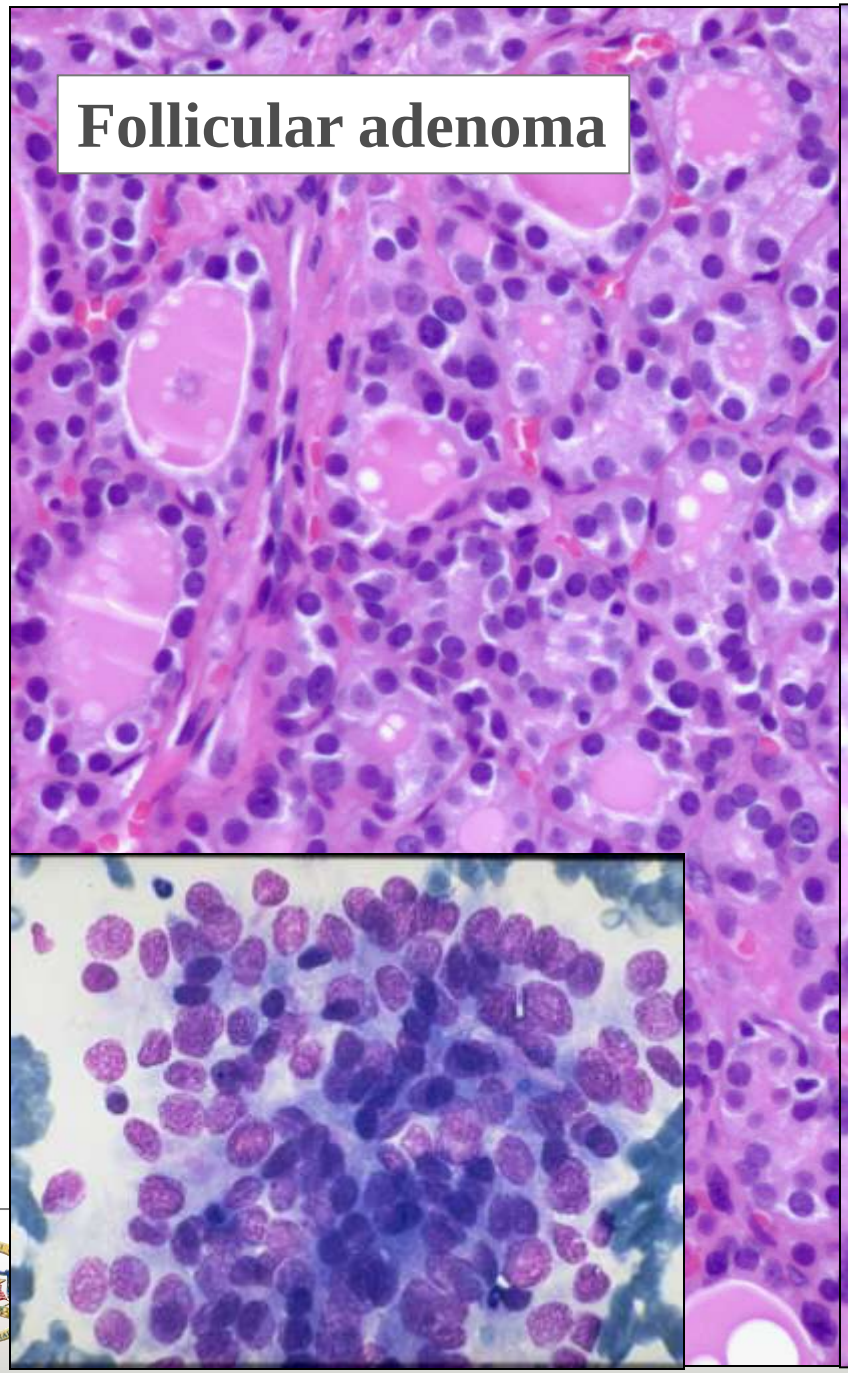
Follicular adenoma

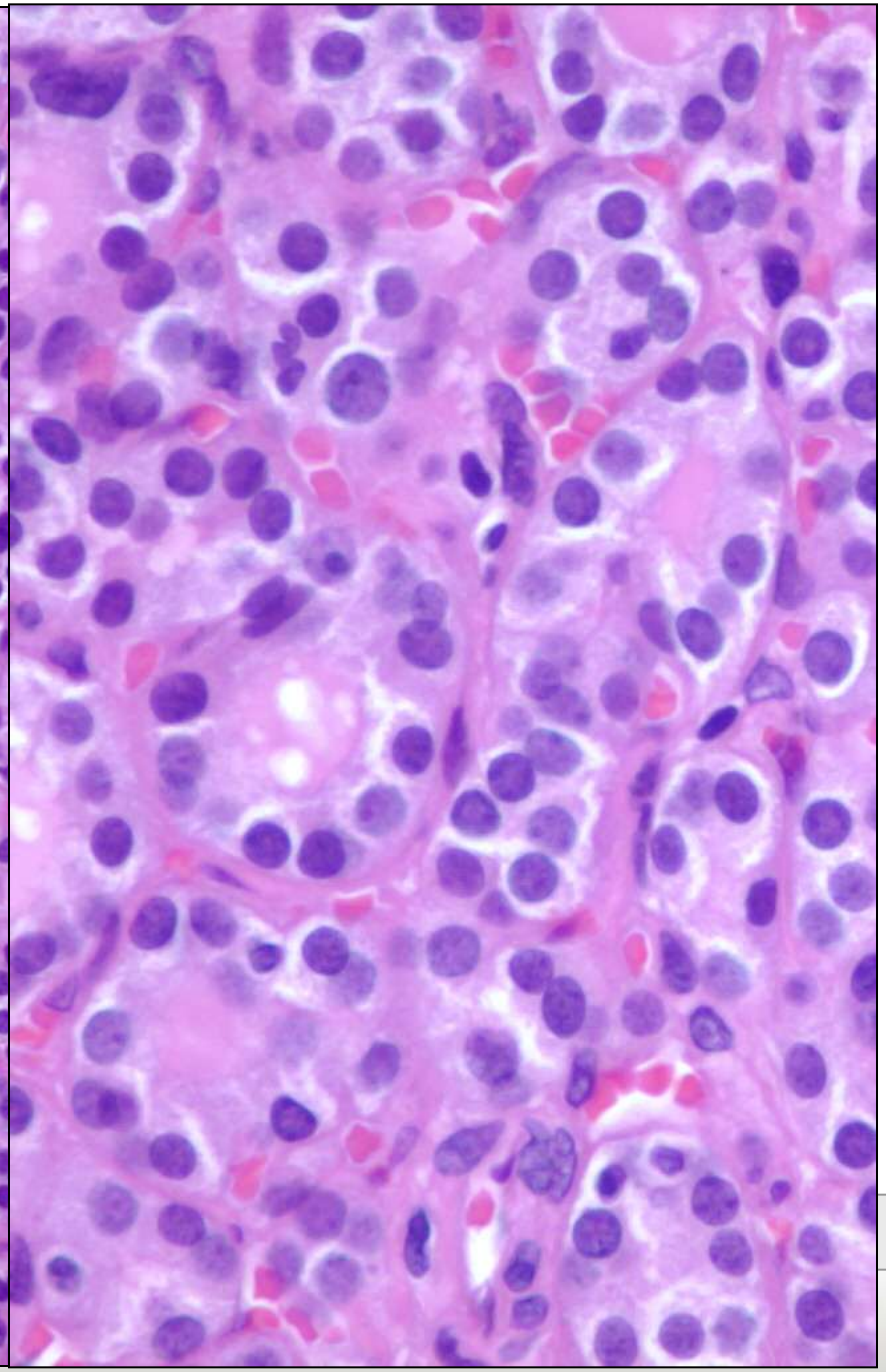




Follicular proliferation …

Follicular adenoma

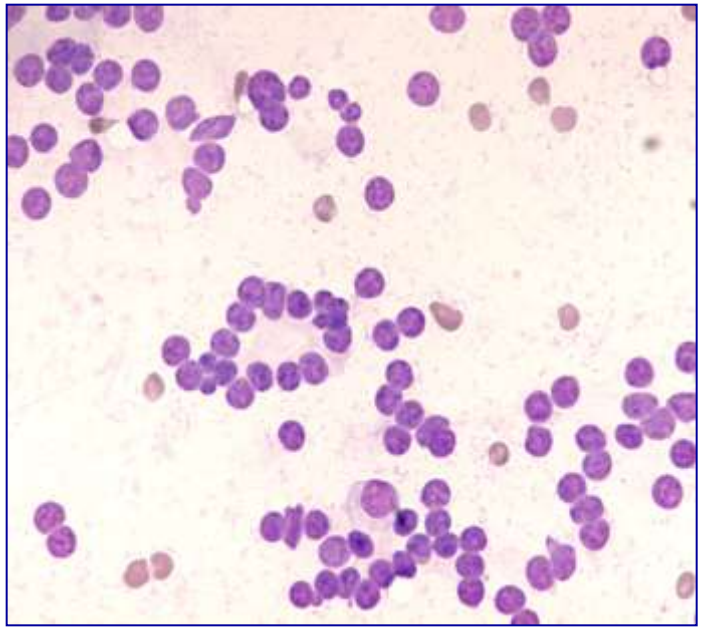


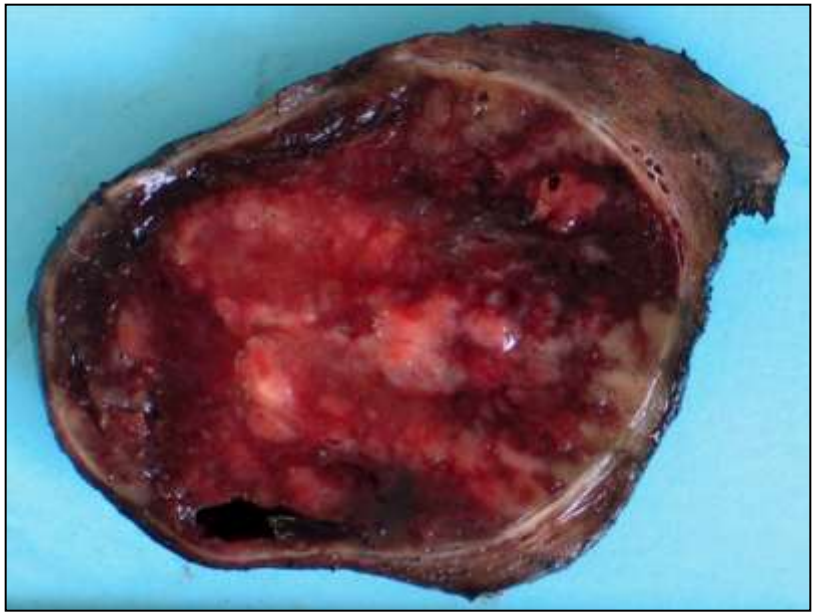


FNA diagnosis NOT possible (no information about capsule…)

Unilabs

Follicular carcinoma



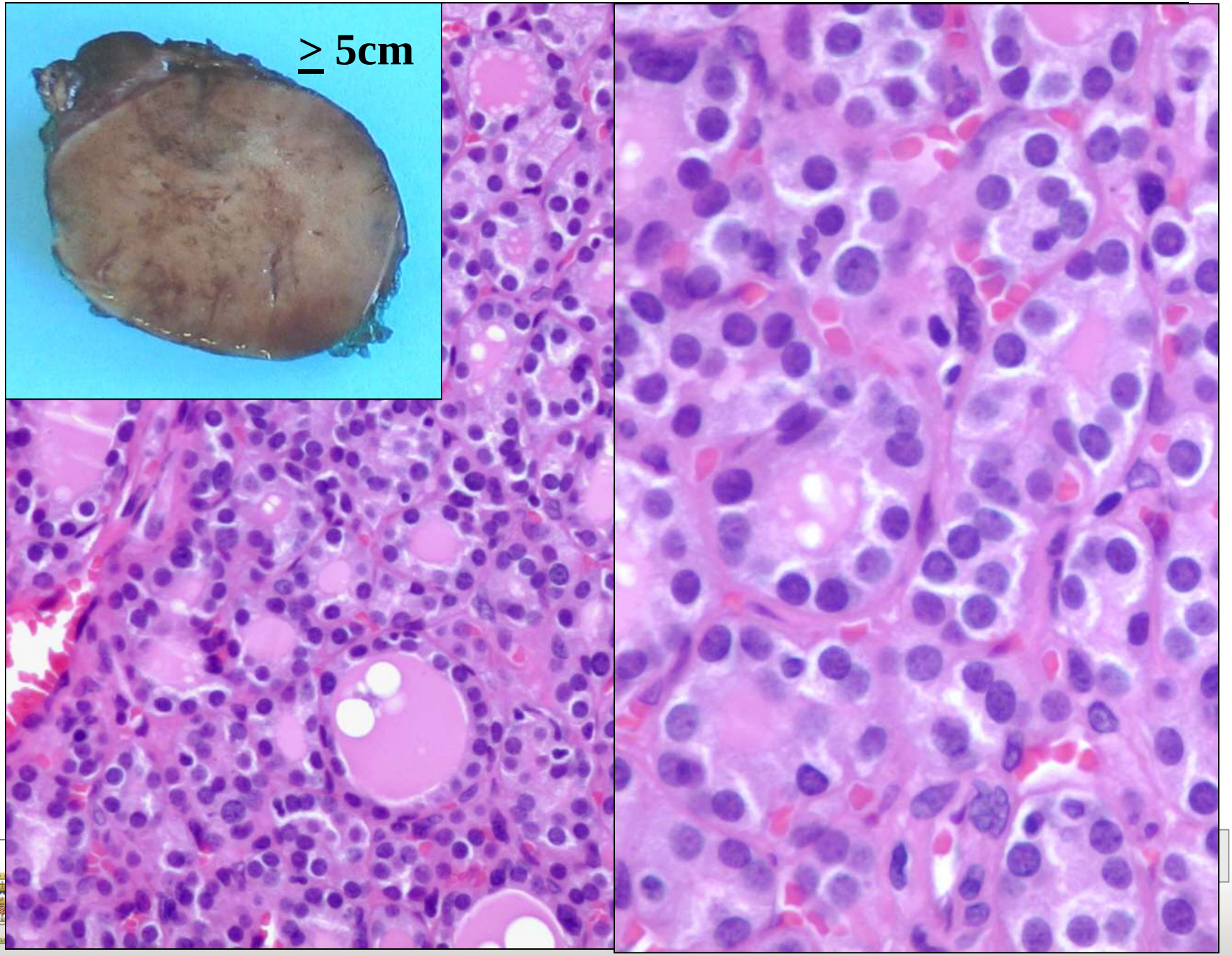


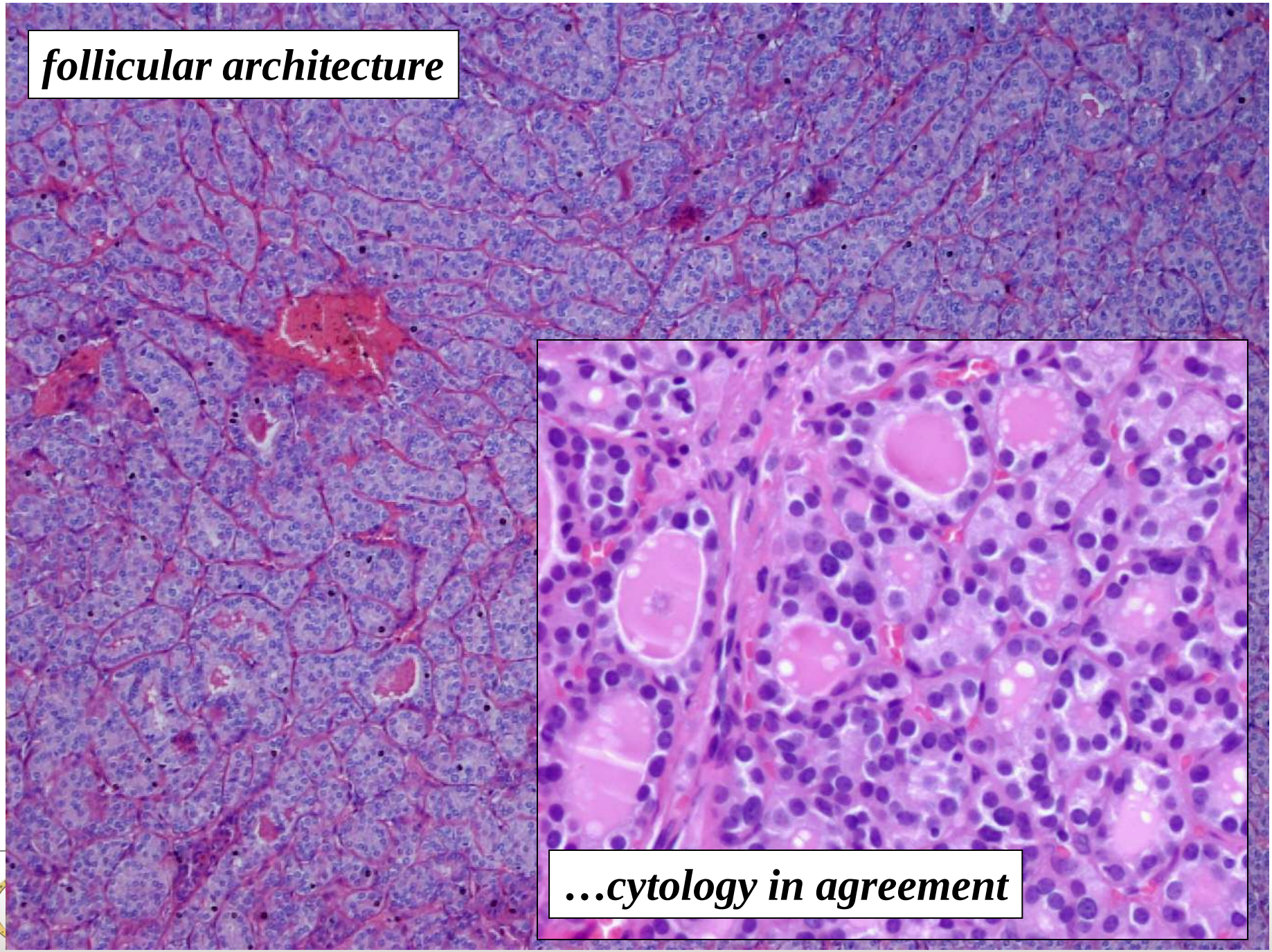
Follicular proliferation …

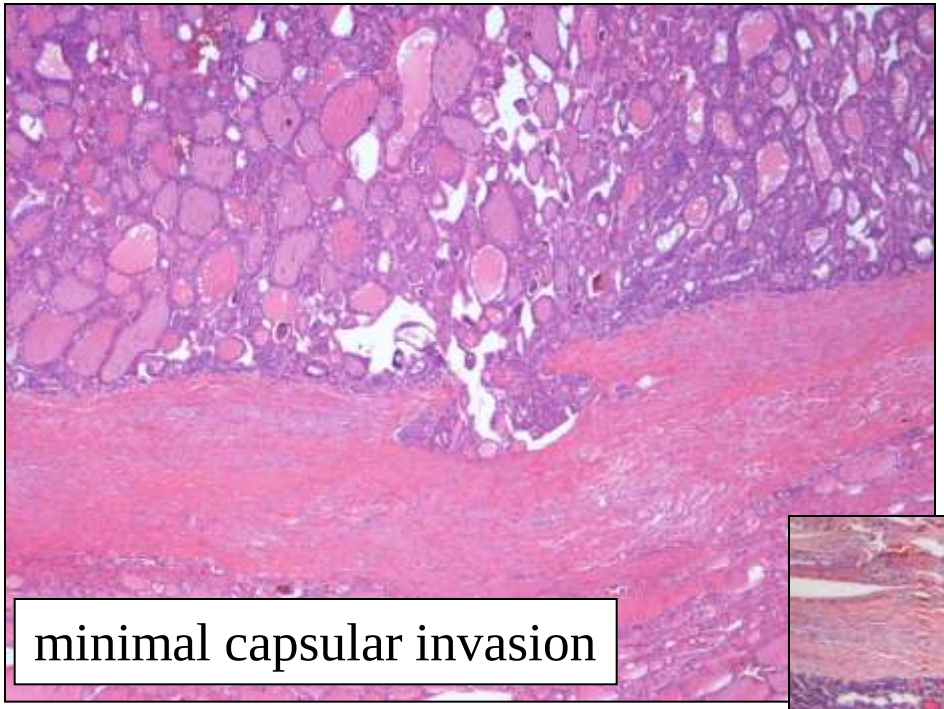
Two variants:

Minimally invasive (capsular/vascular)

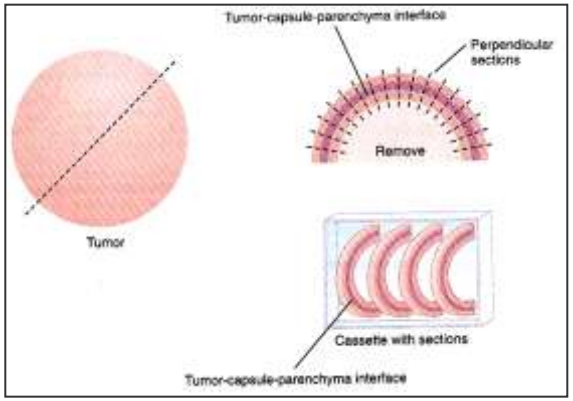
Invasive (extra-capsular extension)


≥ 5cm


follicular architecture
…cytology in agreement

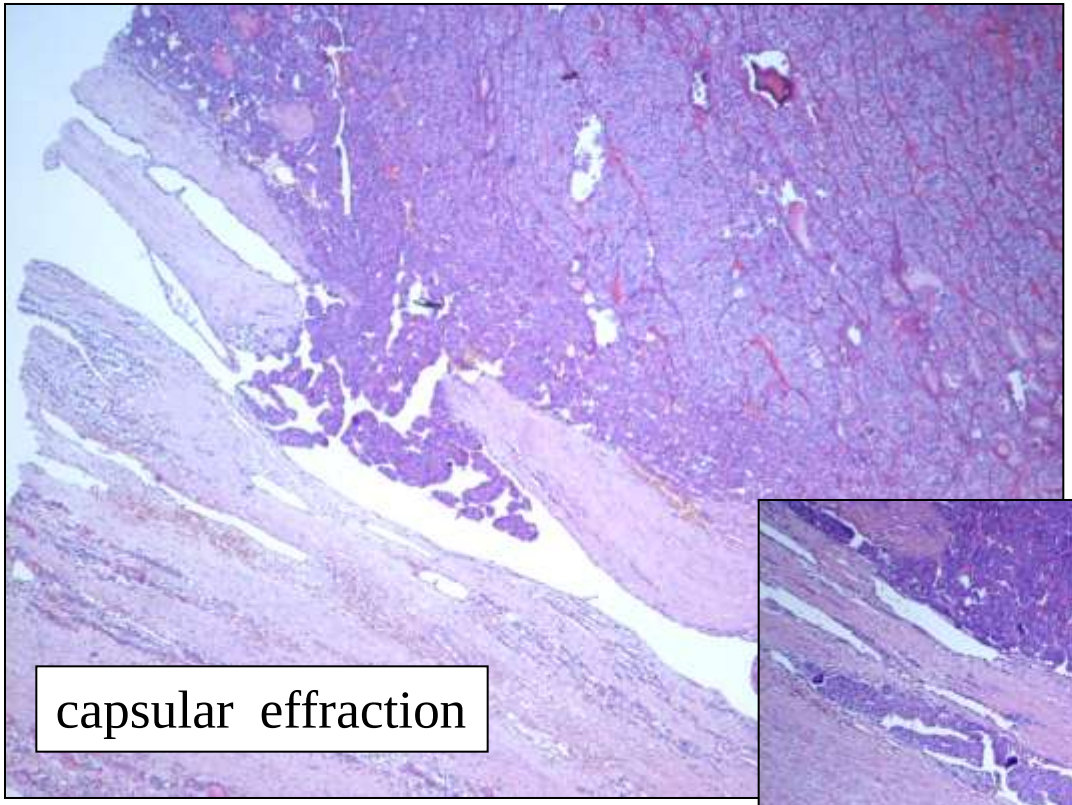


minimal capsular invasion

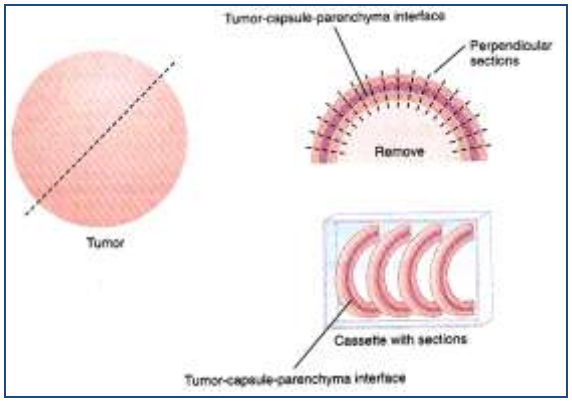


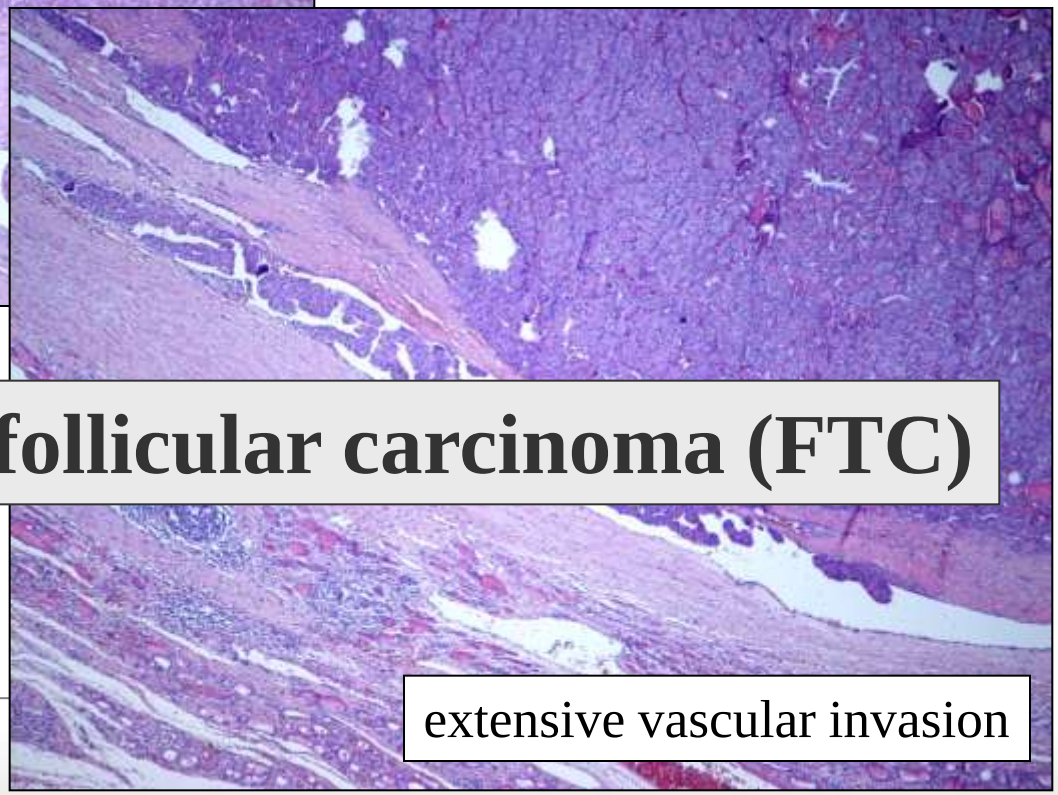
vascular invasion

Follicular carcinoma *minimally invasive*



capsular effraction

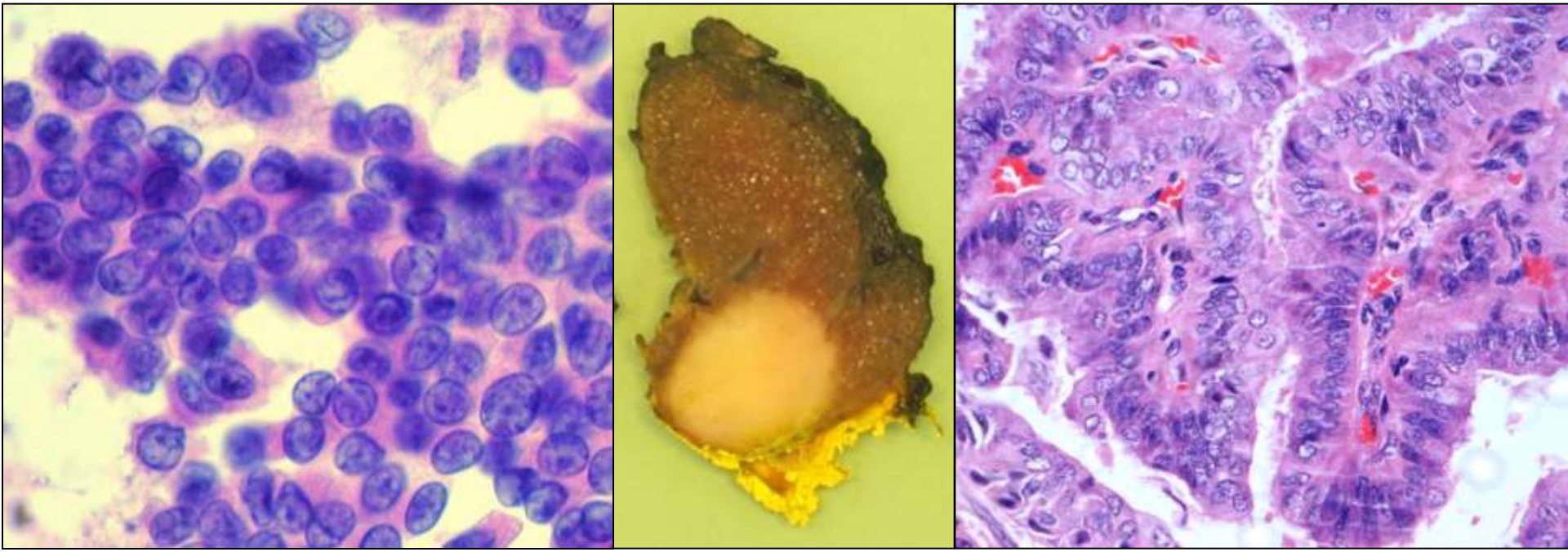




extensive vascular invasion

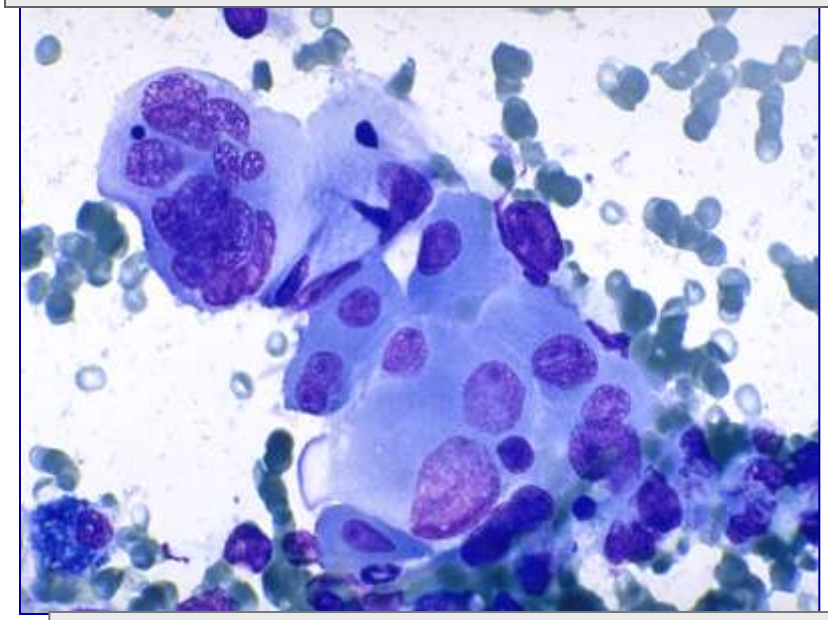
Widely invasive follicular carcinoma (FTC)

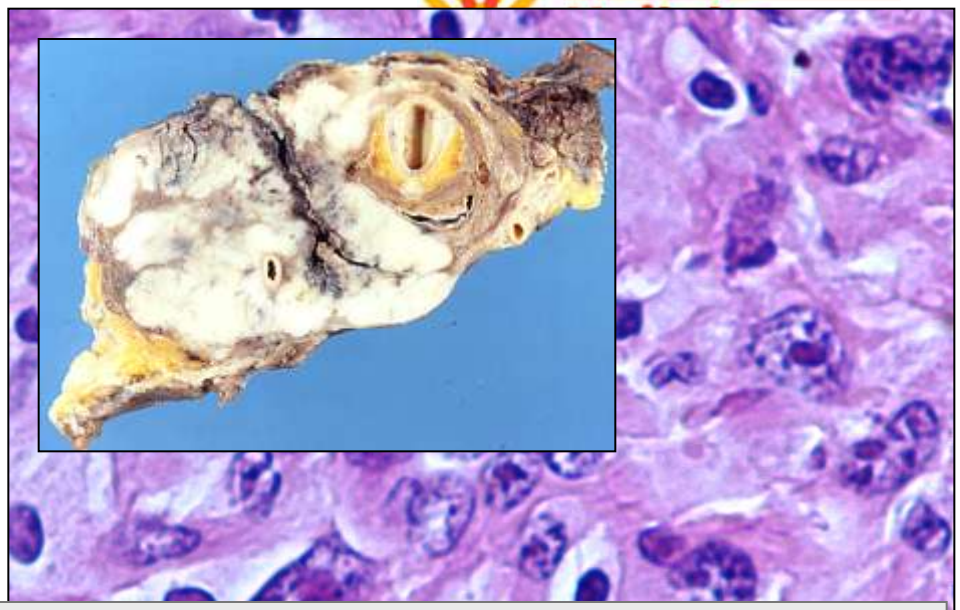
FNA diagnostic possible & reliable…



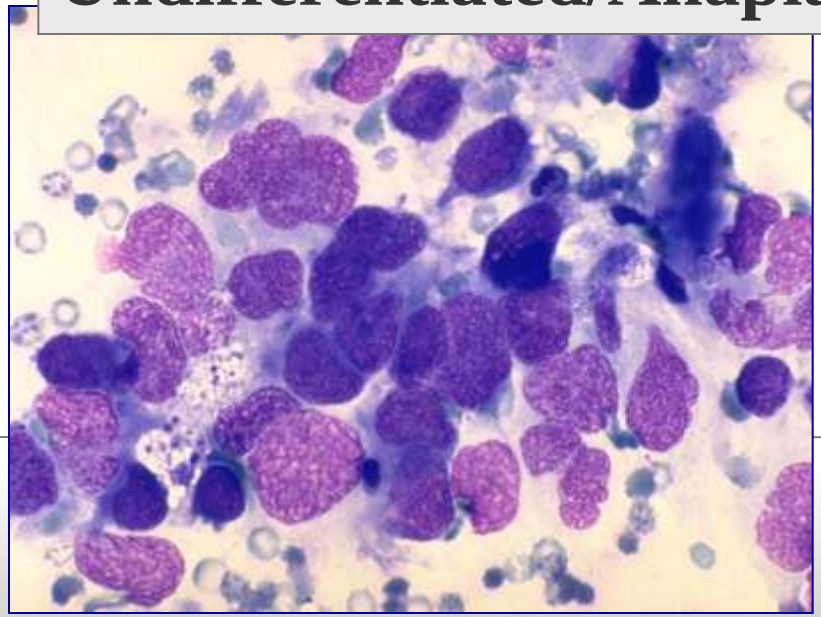
Papillary carcinoma, conventional type (PTC)

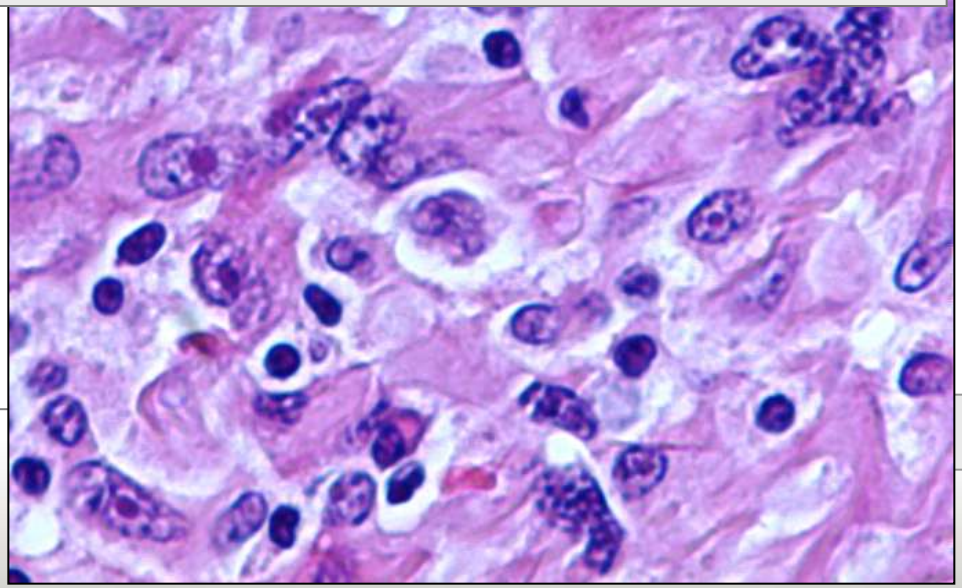
FNA diagnostic possible & reliable…..





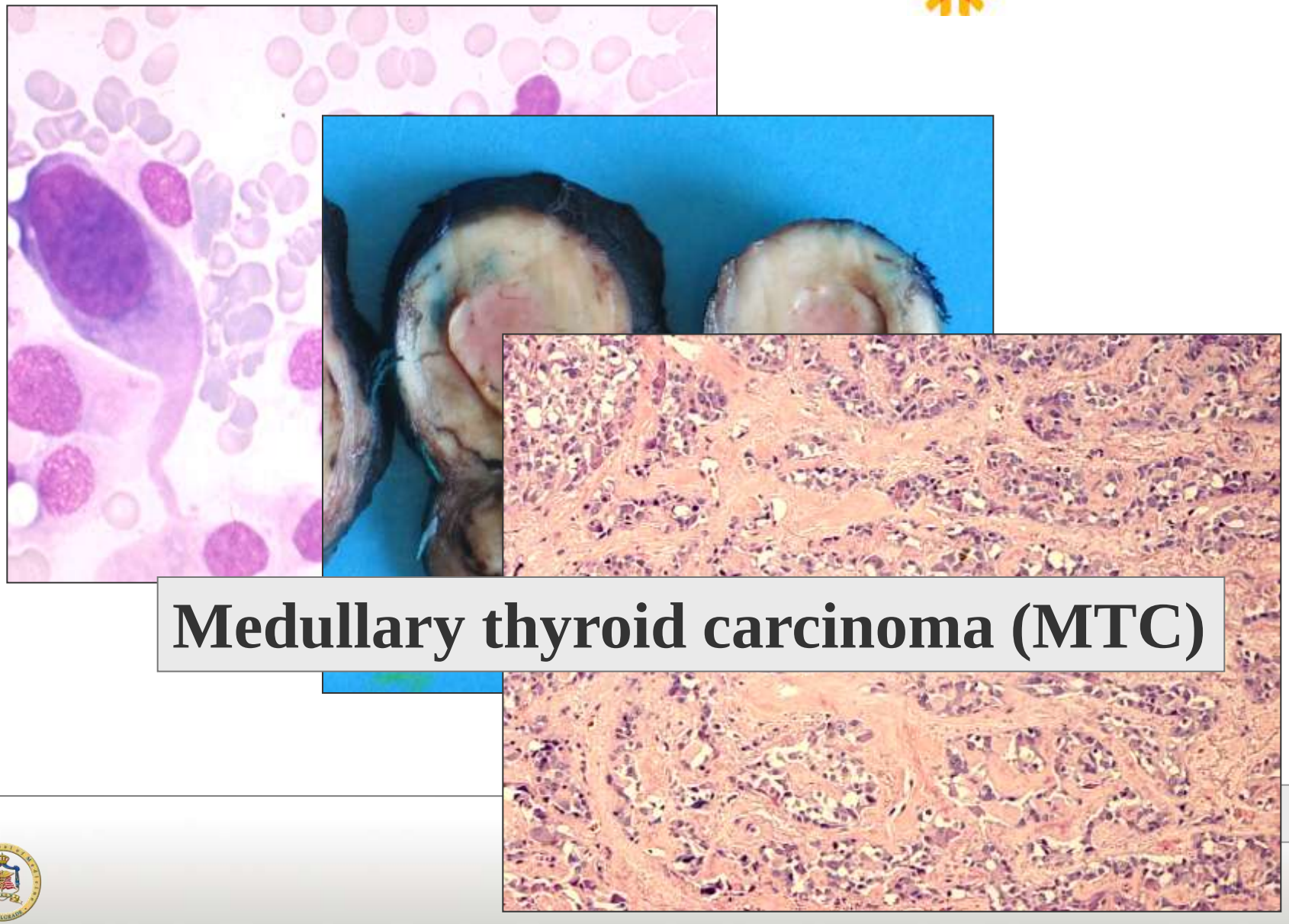
Undifferentiated/Anaplasic thyroid carcinoma (ATC)





FNA diagnostic possible & reliable…

Unilabs



Medullary thyroid carcinoma (MTC)

FNA diagnosis difficult … uncertain… impossible...

Papillary carcinoma (variants)
- **Follicular variant of papillary carcinoma (FVPTC)**
- **Oncocytic variant (*Hurthle cell carcinoma*)**
- **Tall cell variant**
- **Diffuse sclerosing variant**

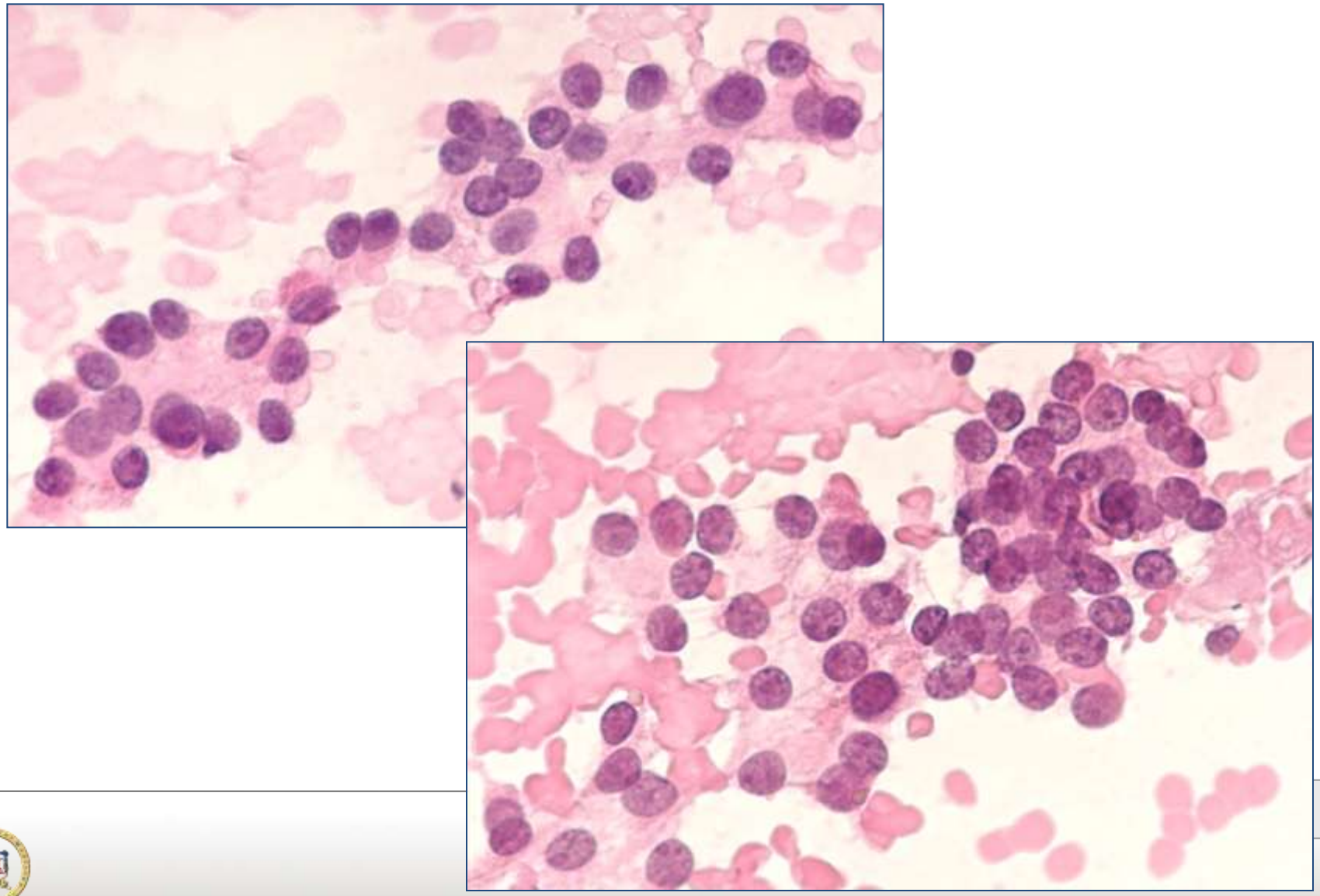
Poorly differentiated carcinoma

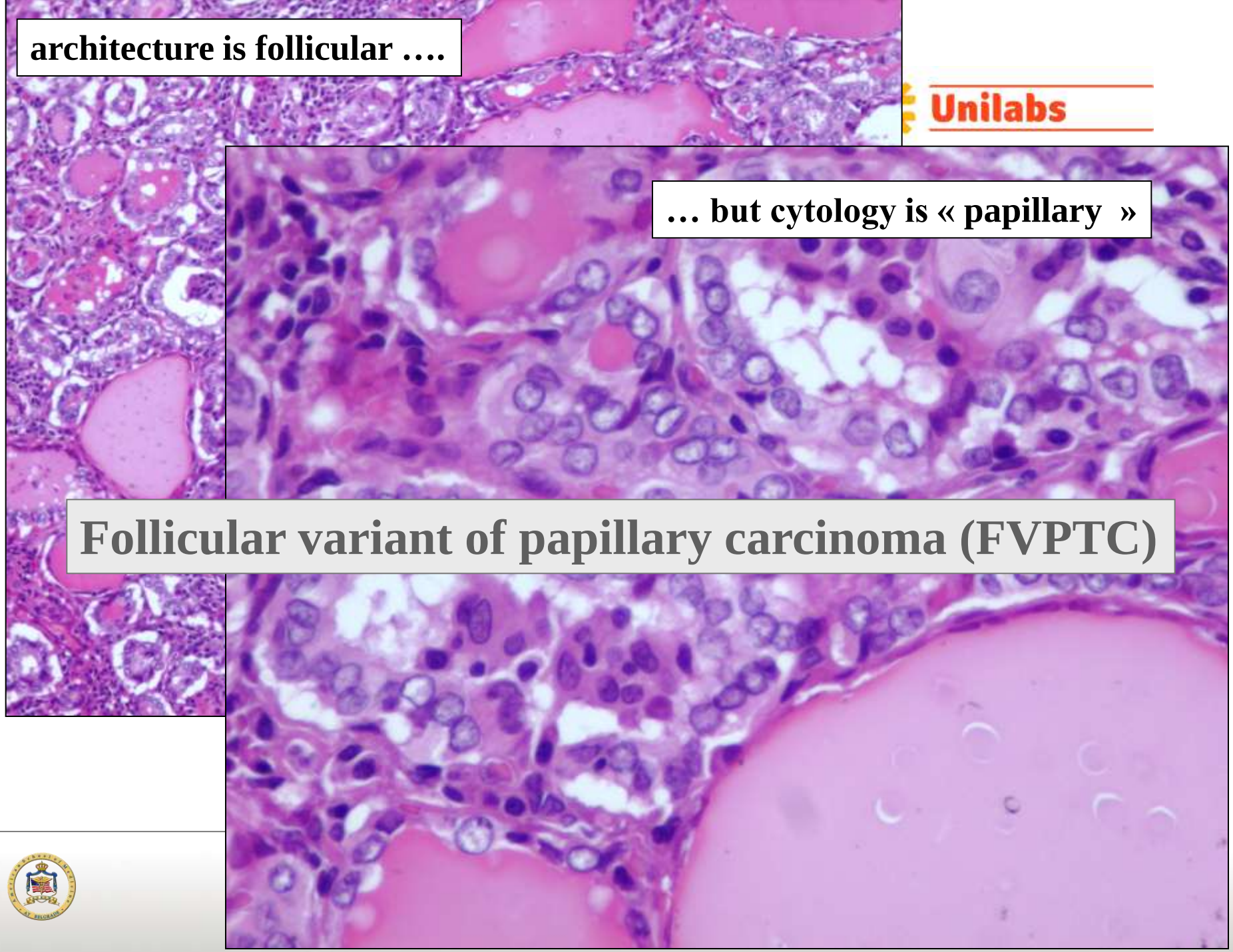
Well differentiated tumor of uncertain malignant potential

Spindle cell tumor with « thymus-like » differentiation

*(**SETTLE**- spinde cell tumor with thymus like differentiation & **CASTLE** - Carcinoma showing « thymus like » differentiation)*

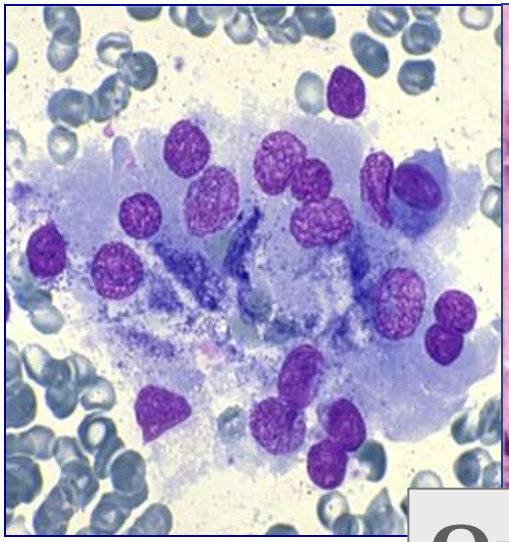
FNA: follicular proliferation …

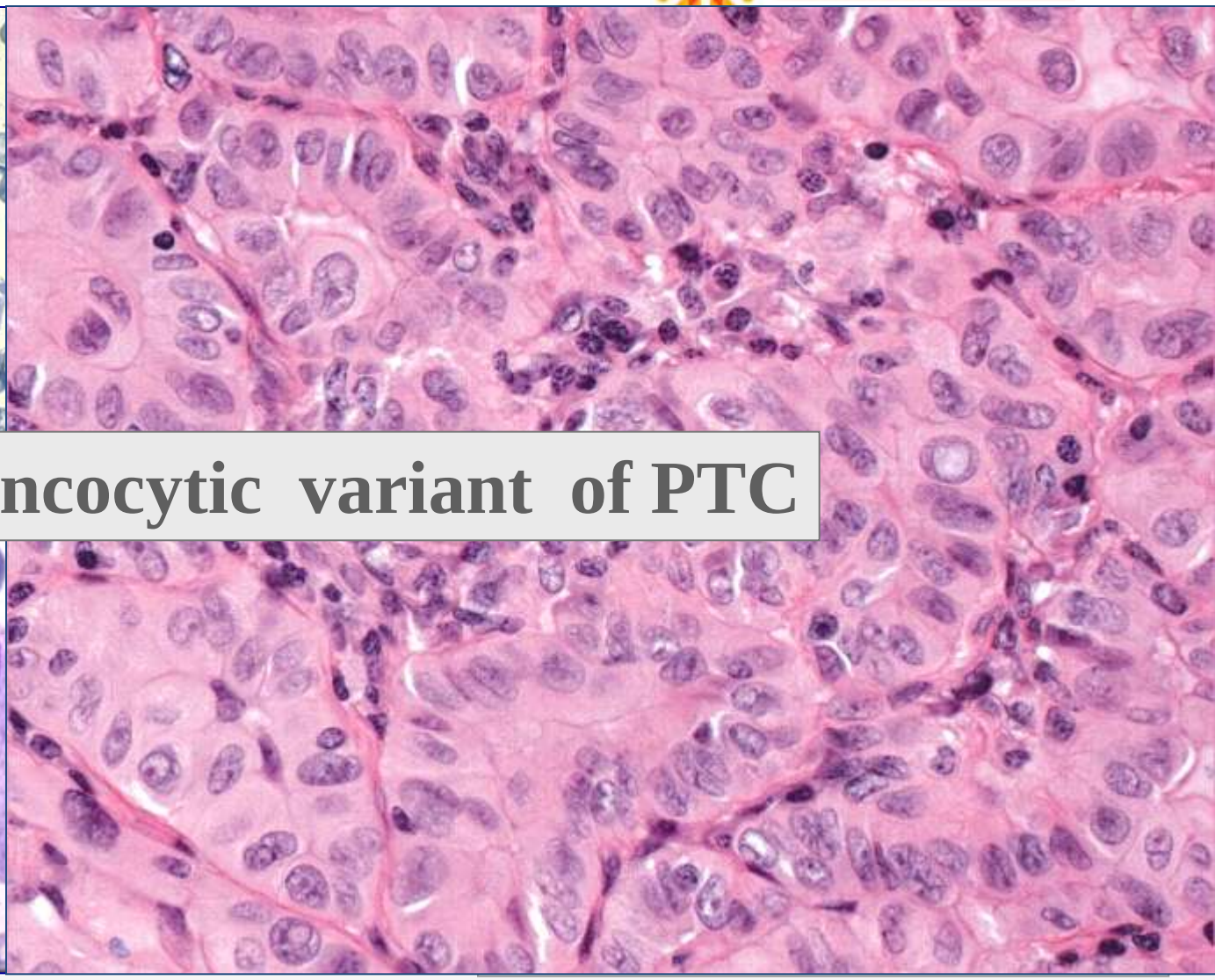



architecture is follicular ….
Unilabs
… but cytology is « papillary »
Follicular variant of papillary carcinoma (FVPTC)

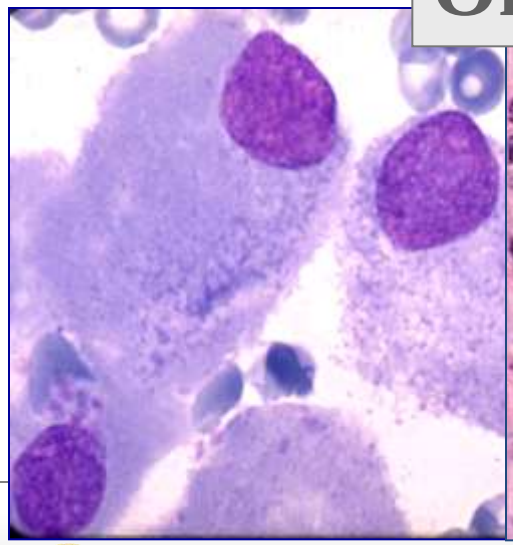
Oncocytic cells proliferation …

Unilabs

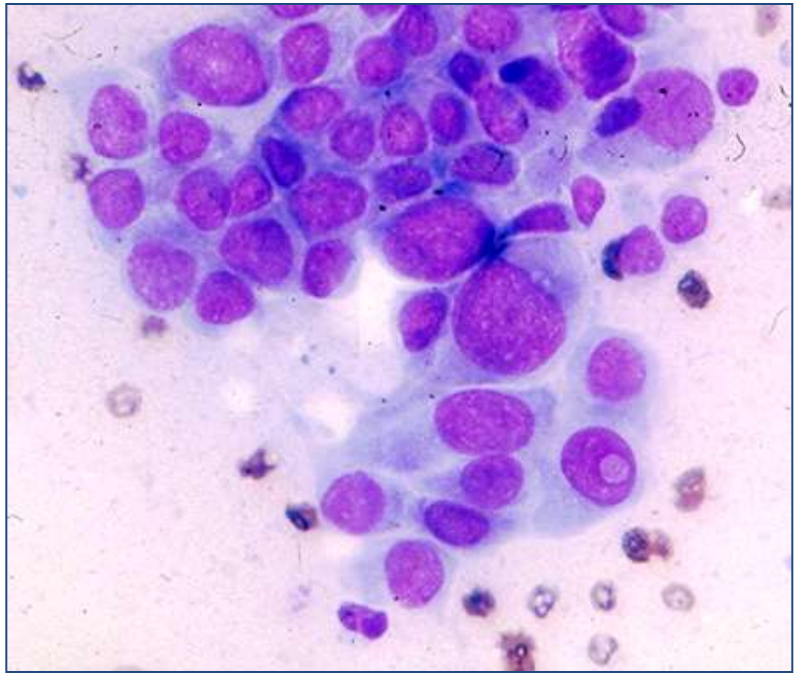


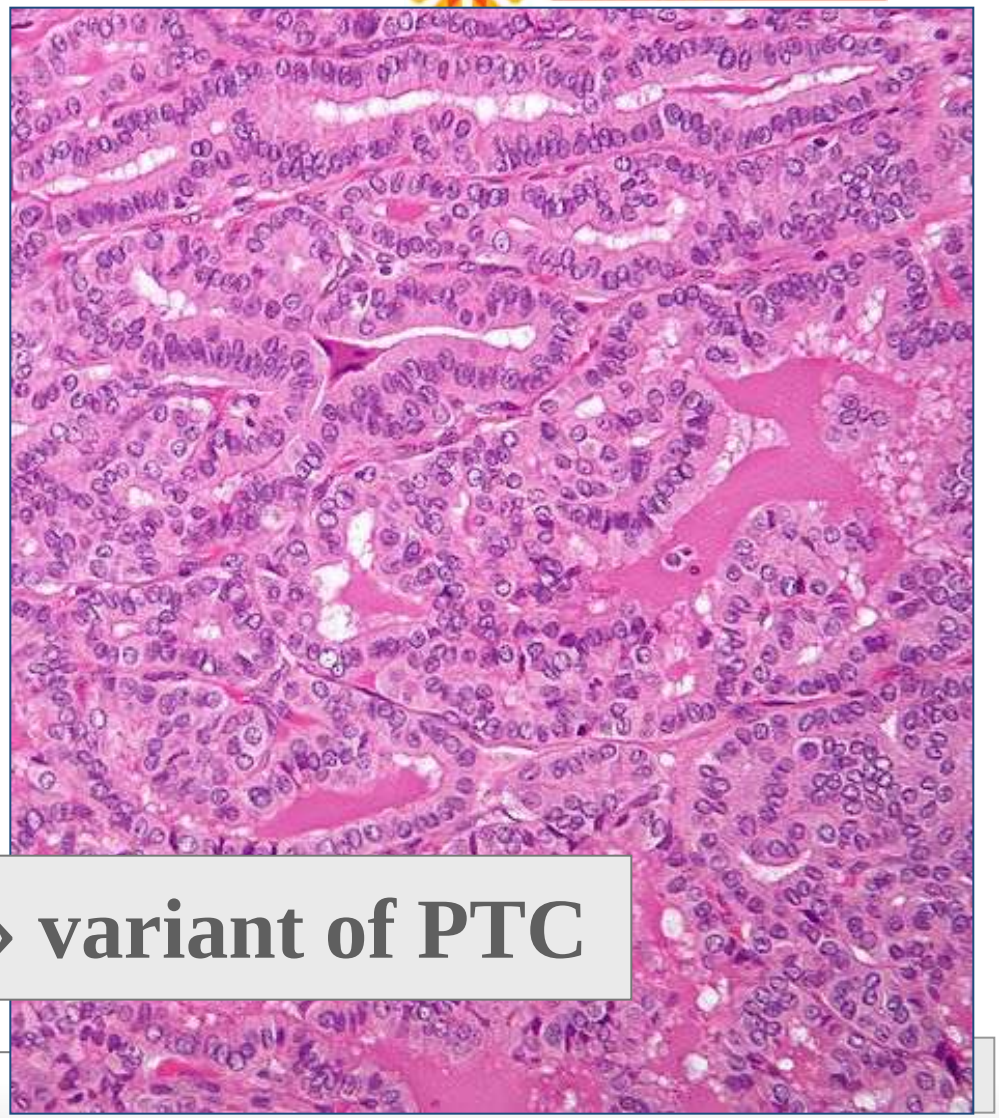


Oncocytic variant of PTC



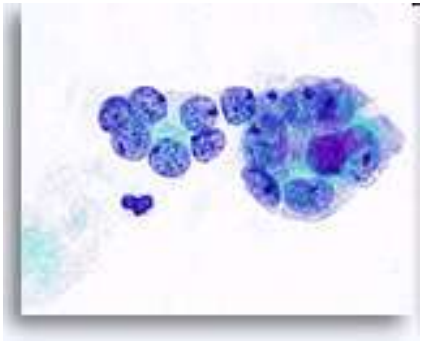
Oncocytic cells proliferation …

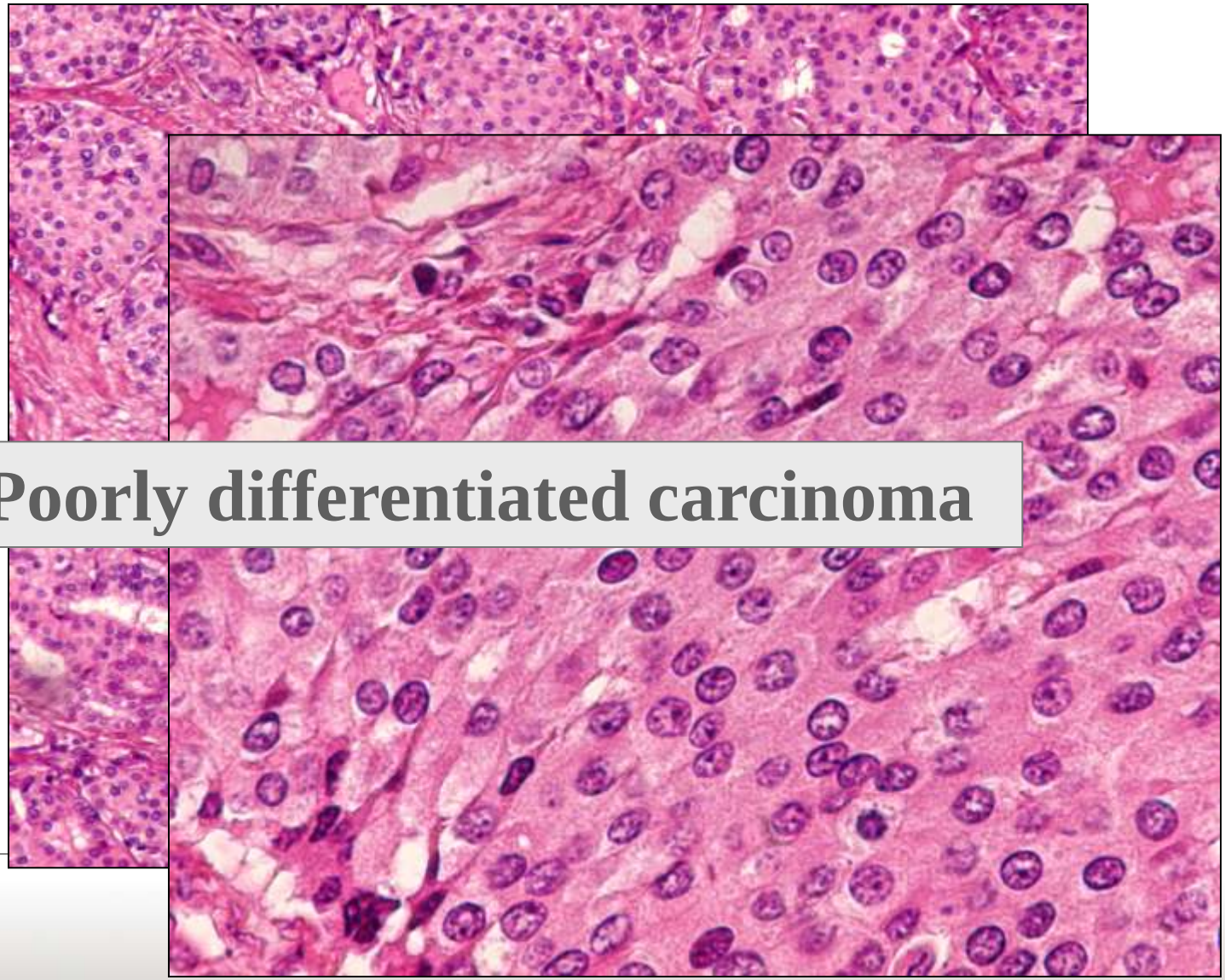




« Tall cell » variant of PTC

« Atypical» proliferation



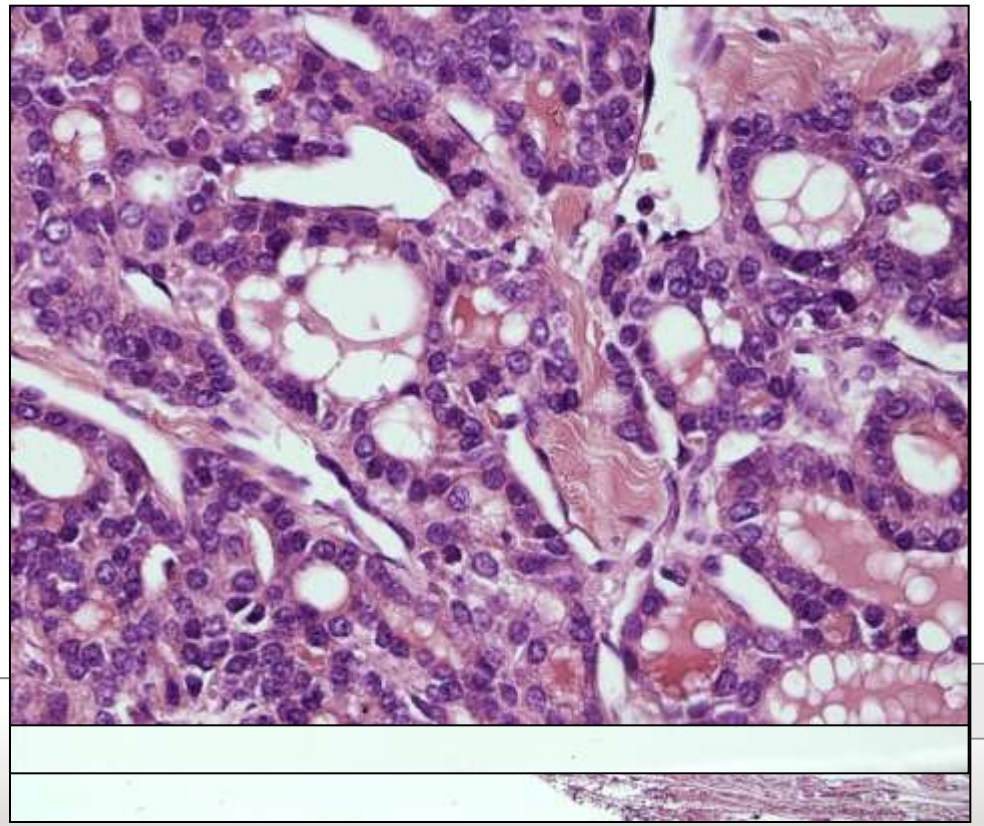


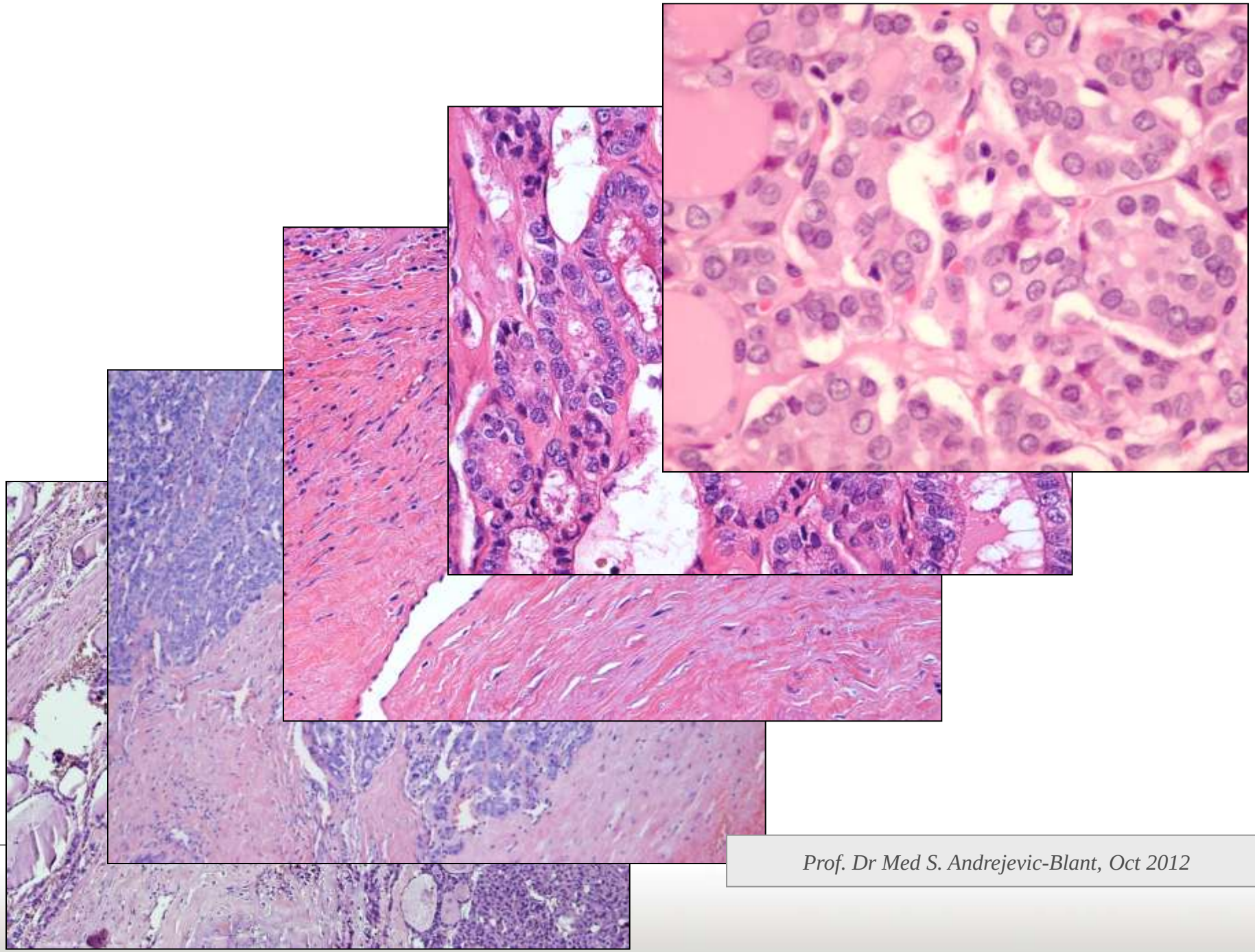
Poorly differentiated carcinoma

Well differentiated tumor of uncertain malignant potential (WHO 2004)

Difficult interpretation...of **encapsulated thyroid tumor with follicular pattern**…..

DD: **Follicular adenoma**
Minimally invasive follicular carcinoma
Follicular variant of PTC





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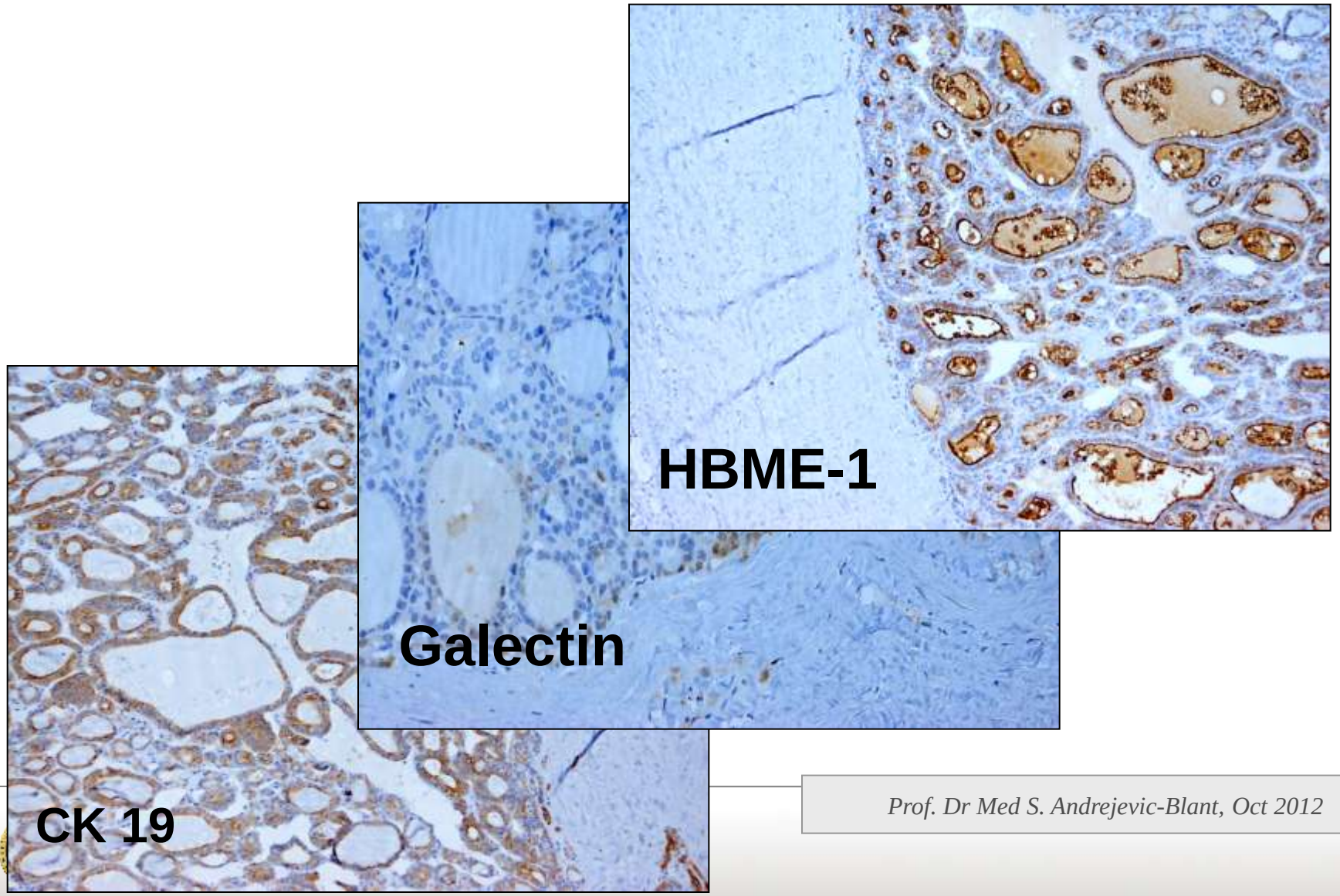
Well differentiated tumor of uncertain malignant potential



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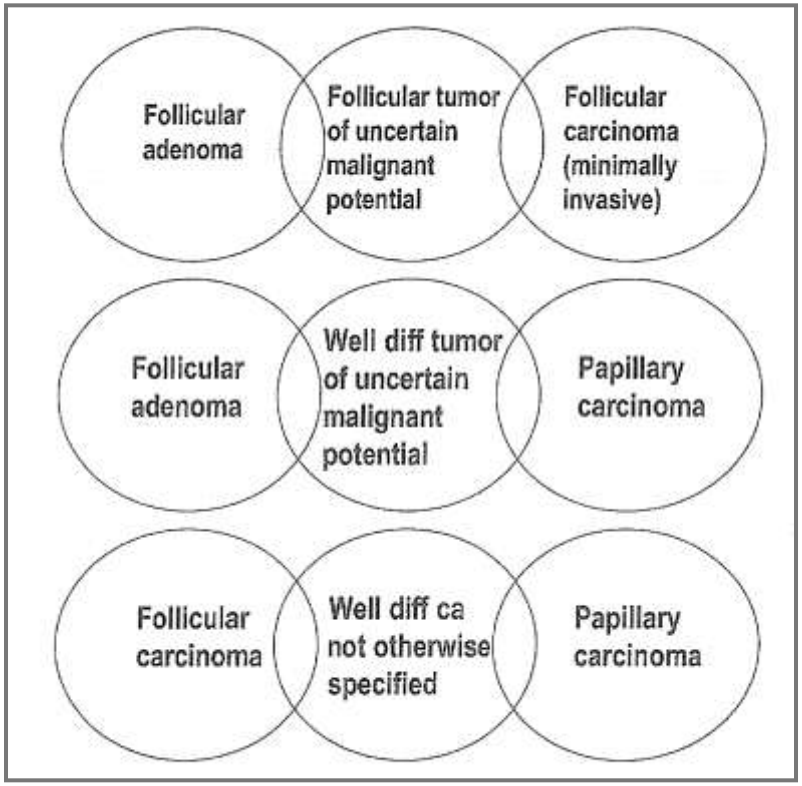
Well differentiated tumor of uncertain malignant potential:

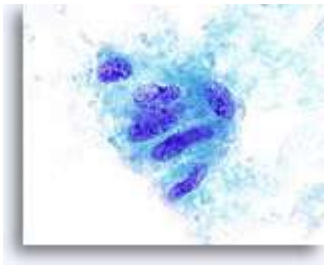
differential diagnosis of encapsulated follicular-patterned tumors according to the **nuclear characteristics** and the **presence/absence of the capsular invasion**

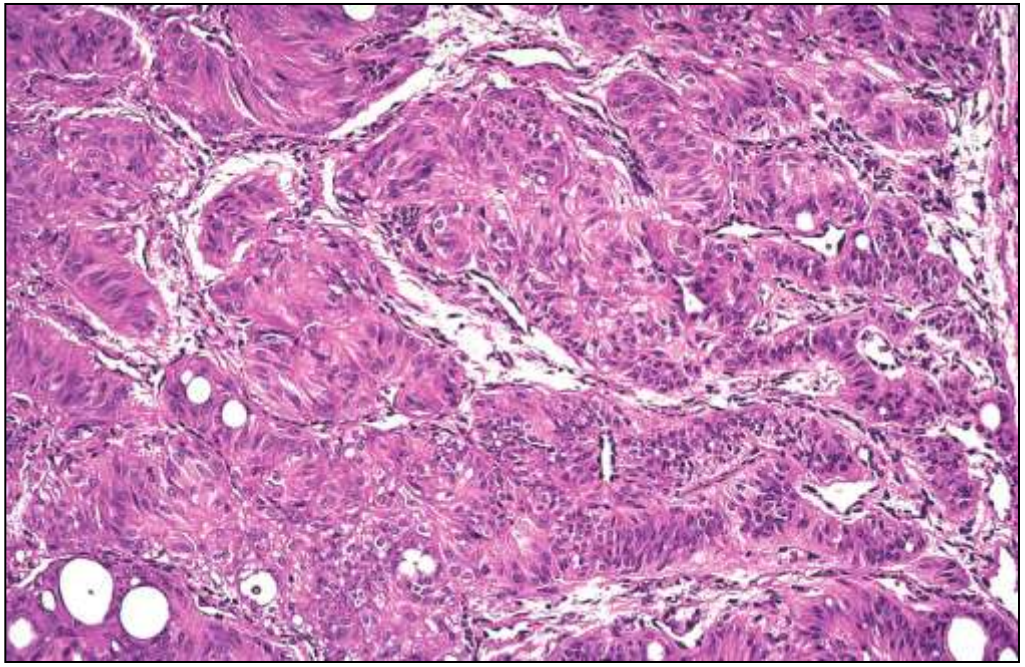


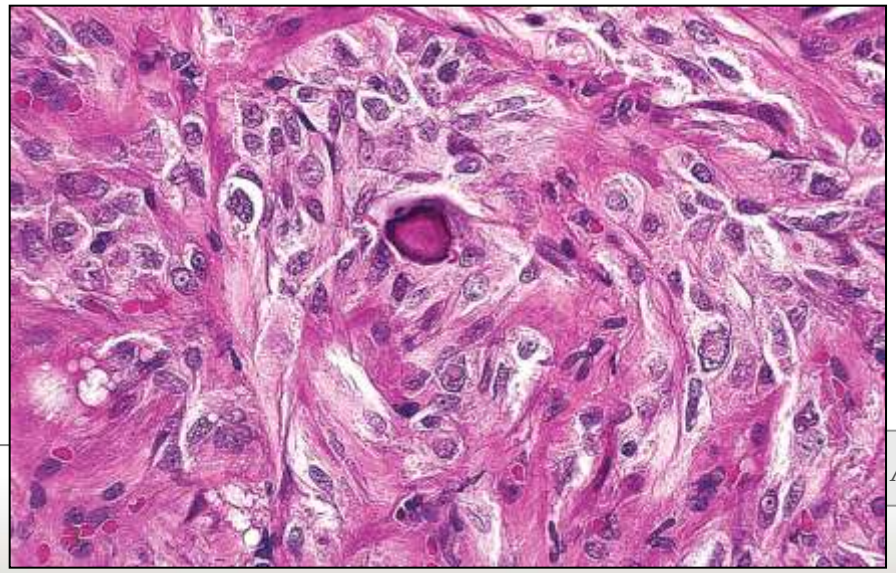
Prof. M. Sobrinho-Simoes
Endocrine Pathology Vol 17, 2006

Prof. Dr Med S. Andrejevic-Blant, Oct 2012

Spindle cell proliferation …







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Disease fact sheet:

Asymptomatic

solitary encapsulated tumor, incidentally found

Female (50-60 years)

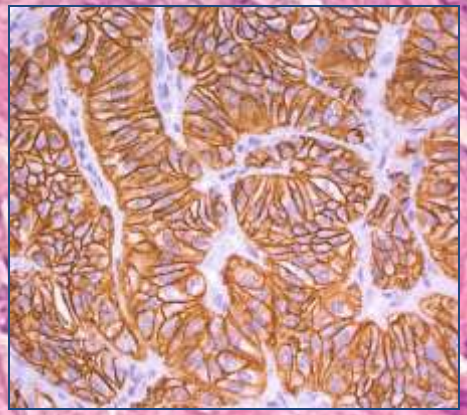
Surgical treatment

Excellent prognosis

Rare metastatic disease (*relationship with PTC*)

Trabecular hyalinizing tumor

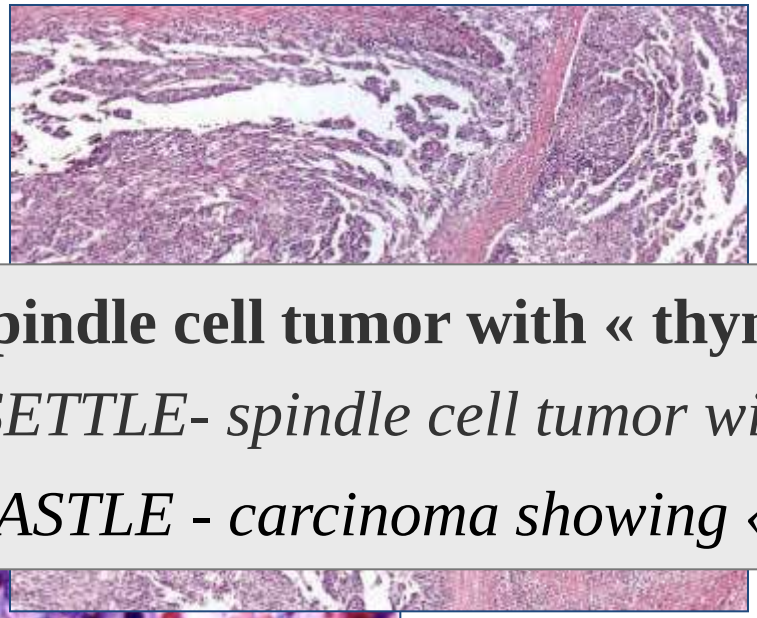
(paraganglioma-like adenoma)

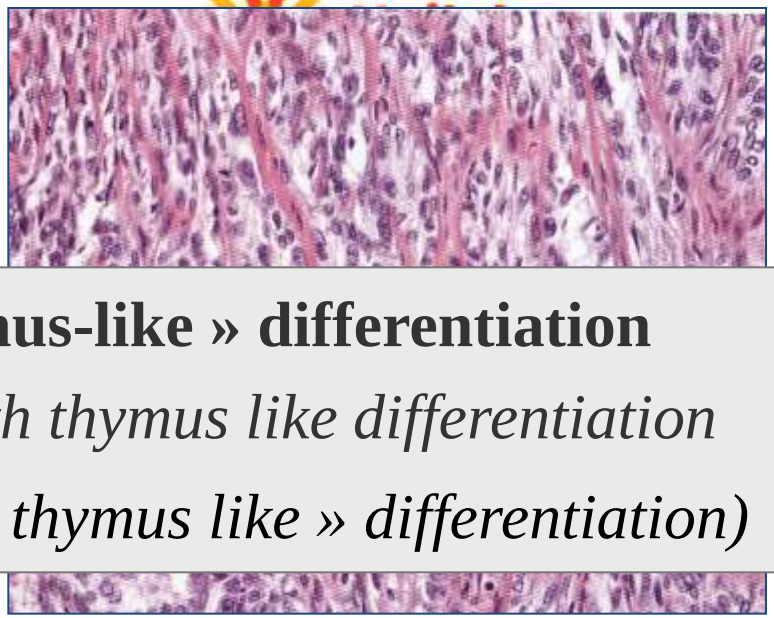


TG	**+**
TTF1	**+**
CK19	**+**
MIB-1*	**+**

***cytoplasmic**

Spindle cell proliferation …

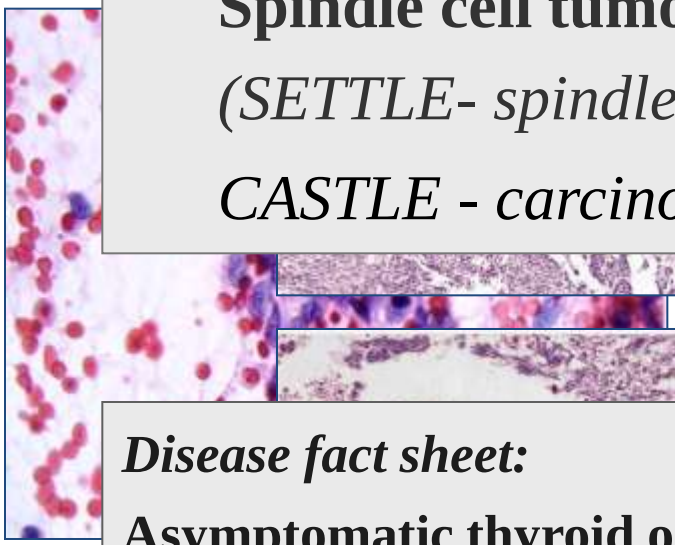


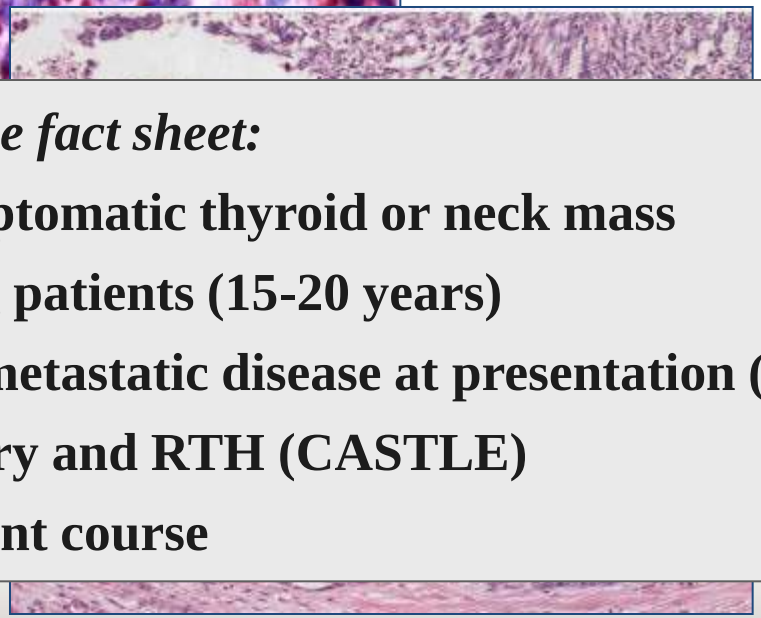


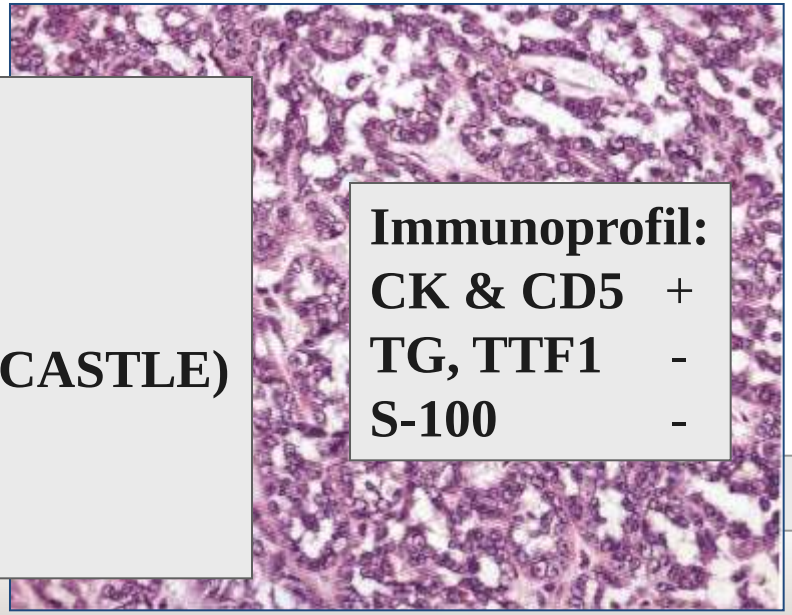
Spindle cell tumor with « thymus-like » differentiation

(SETTLE- spindle cell tumor with thymus like differentiation

CASTLE - carcinoma showing « thymus like » differentiation)







Disease fact sheet:

Asymptomatic thyroid or neck mass

Young patients (15-20 years)

30% metastatic disease at presentation (CASTLE)

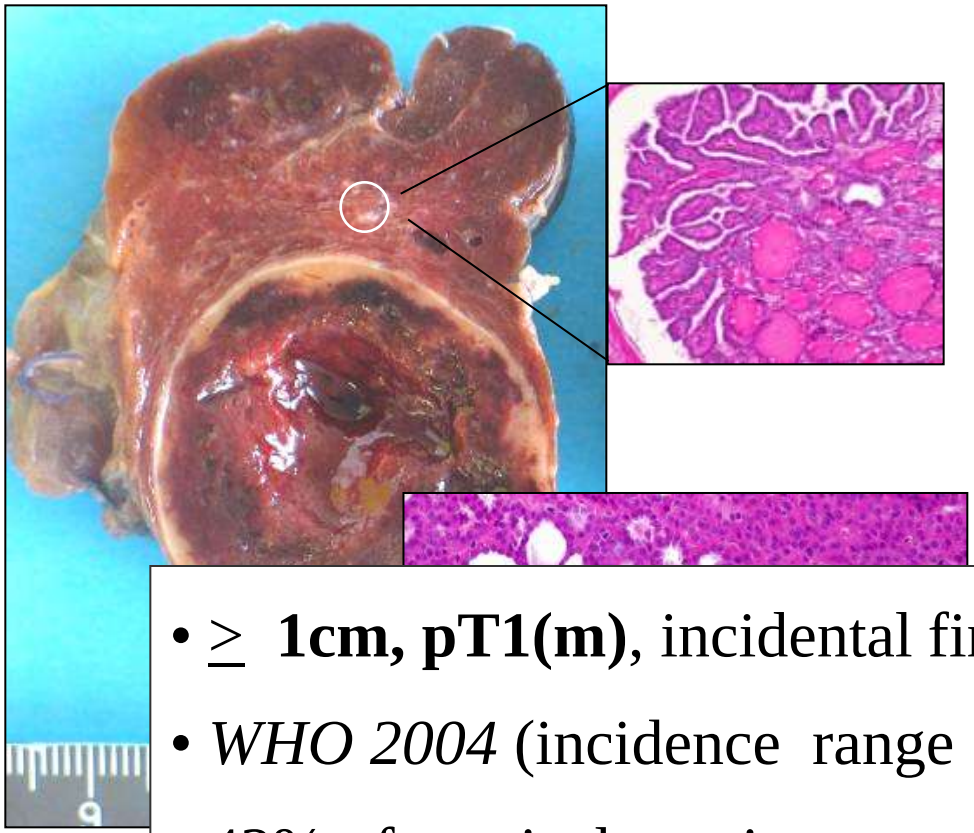
Surgery and RTH (CASTLE)

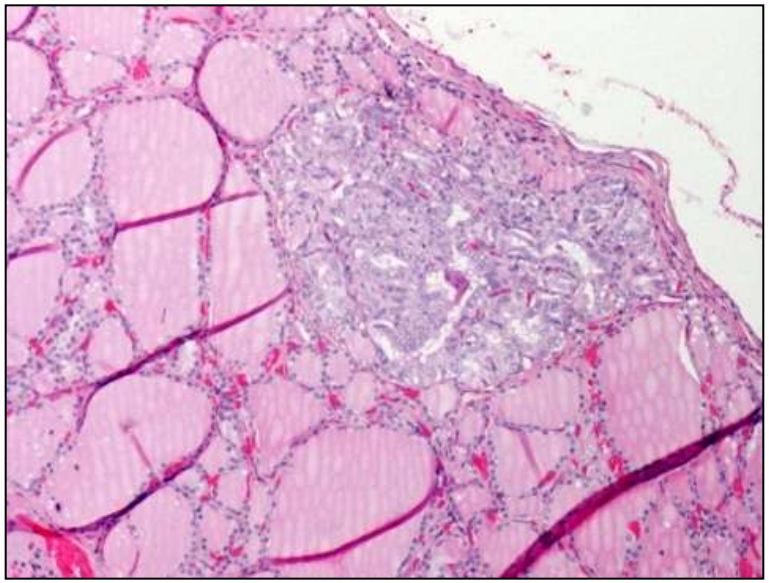
Indolent course

Immunoprofil:

CK & CD5	**+**
TG, TTF1	**-**
S-100	**-**

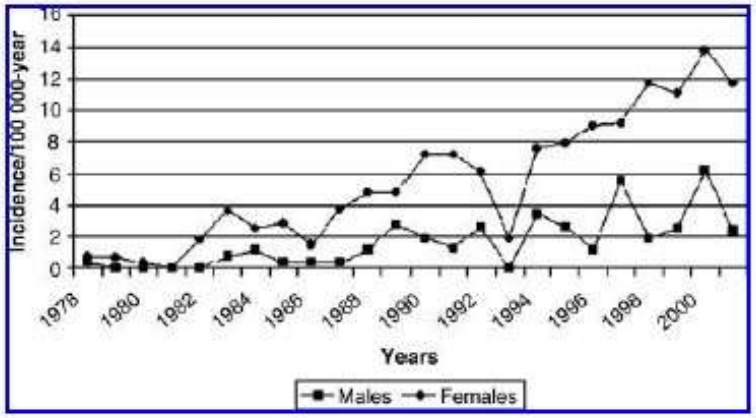
Papillary micro-carcinoma (mPTC)





- ≥ **1cm, pT1(m)**, incidental finding, often multiple
- *WHO 2004* (incidence range 15-30% to 45-50%)
- 43% of surgical specimens (*Rego-Ireata et al. 2009*)
- incidence 100-1000 in autopsy (*Kovac et al 2005*)
- BRAF gene mutation 30-50% (*Frasca et al 2008*)

Papillary micro-carcinoma (mPTC)



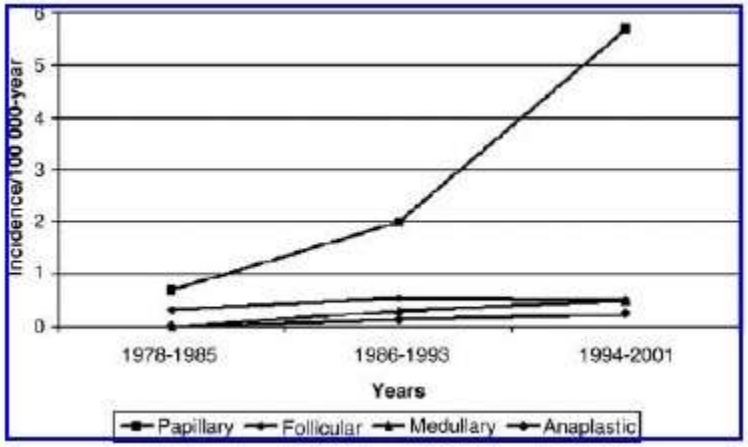


TABLE 3. TIME TREND OF PAPILLARY THYROID CARCINOMA CRUDE INCIDENCE RATES, BY SEX

	Females				*Males*			
Period	*PTC non-MPTC incidence*	*95% CI*	*MPTC incidence*	*95% CI*	*PTC non-MPTC incidence*	*95% CI*	*MPTC incidence*	*95% CI*
1978–1985	0.87	0.48–1.27	0.14	0.03–0.43	0.15	–0.02 to 0.32	0.10	–0.04 to 0.24
1986–1993	2.19	1.49–2.88	0.81	0.34–1.16	0.62	0.24–1.01	0.25	0.00–0.49
1994–2001	4.52	3.40–5.65	3.94	3.14–5.32	1.42	0.77–2.08	0.95	0.41–1.49

Molecular alterations

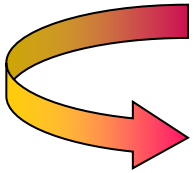
Follicular adenoma:

- mutations RAS **(20%)**
- fusion transcript PAX8-PPARy1 **(10%)**

Follicular carcinoma:

- oncogenes mutations RAS family (HRAS, NRAS, KRAS)
- fusion transcript PAX8-PPARy1
- translocation PAX8

Molecular alterations



Papillary Carcinoma (PTC & MPTC) :

BRAF mutation	(45-50%)
fusion RET/PTC	(20%)

Trabecular hyalinizing tumor

fusion RET/PTC	(60%)

Poorly differentiated Carcinoma

RAS oncogenes mutations	(35%)
BRAF mutation	(20%)
p53 mutation	(20%)

Anaplastic Carcinoma

p53 mutation	(70%)

Medullary Carcinoma

germ-line RET mutation	(95%)
sporadic RET mutation	(5%)

BRAF gene mutation

(« molecular predictor » of tumor aggressivity)

PTC with more aggressive behavior and worst outcome…

extra thyroid extension
advanced stage
lymph node metastases

Rapid progression of mPTC

Intraoperative Consultation in thyroid pathology: Current practices in performing frozen sections…

In recent years, the number of **frozen sections** in thyroid surgery has been **steadily decreasing worldwide**…

Attributed to **two major factors**:
- the high diagnostic accuracy of FNA for PTC
- low sensitivity of frozen section diagnosis for follicular lesions.

Many institutions have **restricted the use** of thyroid frozen sections to thyroid nodules with a preoperative cytology diagnosis of "**atypical**" or "**suspicious.**

FS absolutely not recommended…

Encapsulated nodules with follicular pattern (follicular proliferation)

- in 95% unable to diagnose follicular carcinomas (capsular and vascular invasion),
- post-FNA alterations in the tumor capsule can be mistaken for capsular and/or vascular invasion,
- impossible to recognize the follicular variant of PTC (*freezing artifact*).

Small lesions (≤1 cm)

- absolutely to **avoid freezing** of entire lesion,
- the tissue alterations make a diagnosis on permanent sections nearly impossible.

Multinodular goiter

- should not be performed unless one nodule is worrisome or suspicious based on the gross appearance.
- time consuming

Prof. Dr Med S. Andrejevic-Blant, Oct 2012

References

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3. Pitfalls and unusual cases of « squamous proliferation » in head & neck, thyroid and salivary gland pathology

Case 1

Dentist Story: Lichen & papilloma

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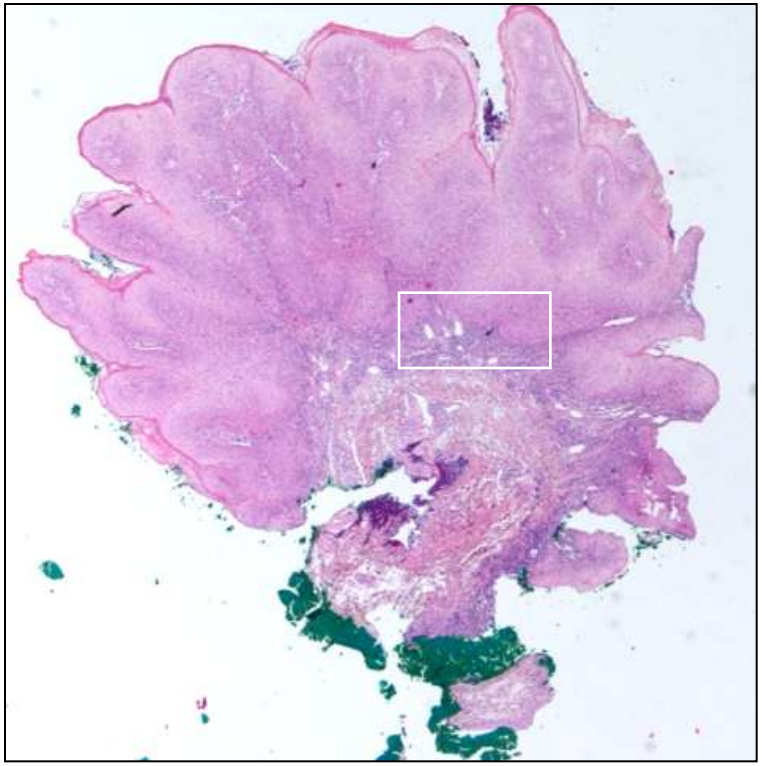
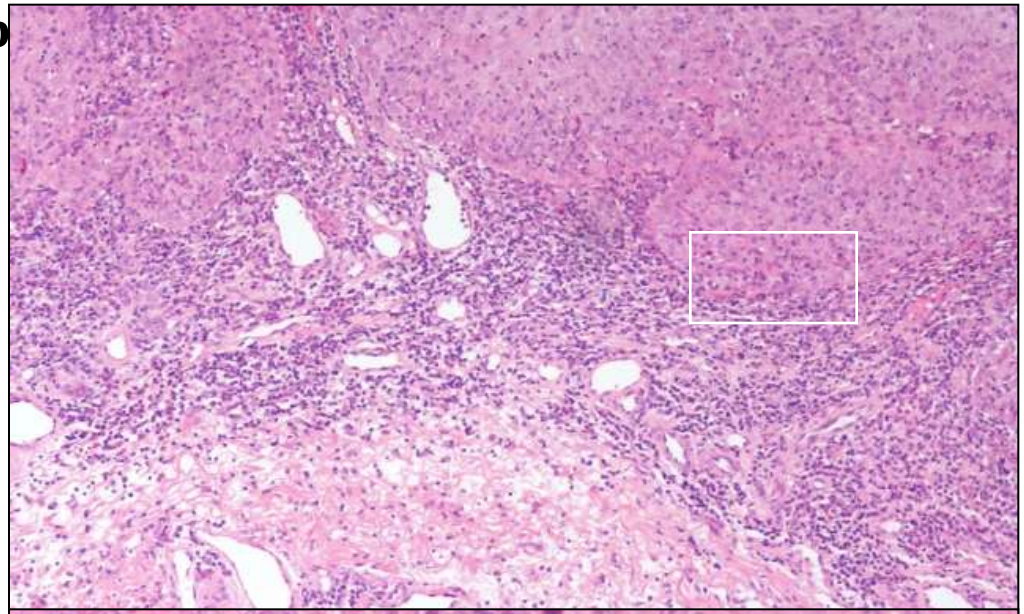
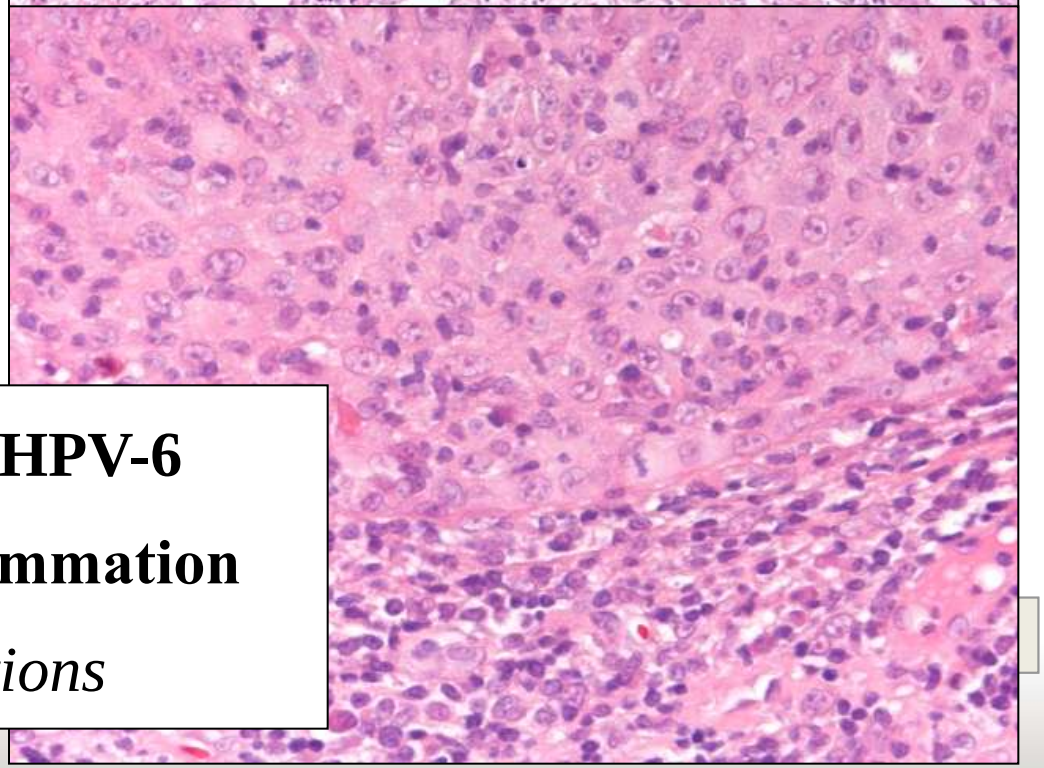
May 2008: **49-year old female p**

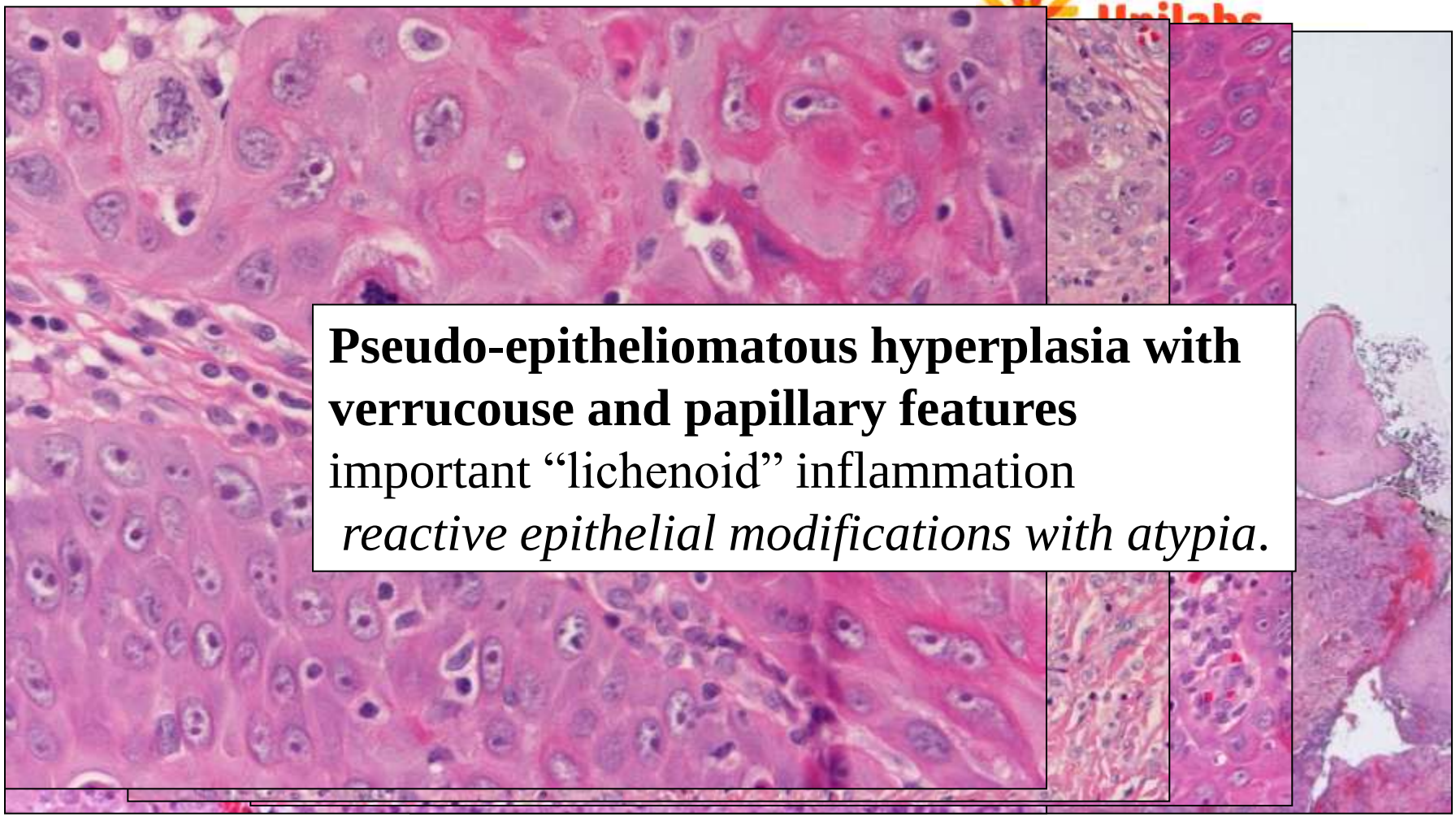






- **oral squamous papilloma, HPV-6**
- important "**lichenoid" inflammation**
- *reactive epithelial modifications*

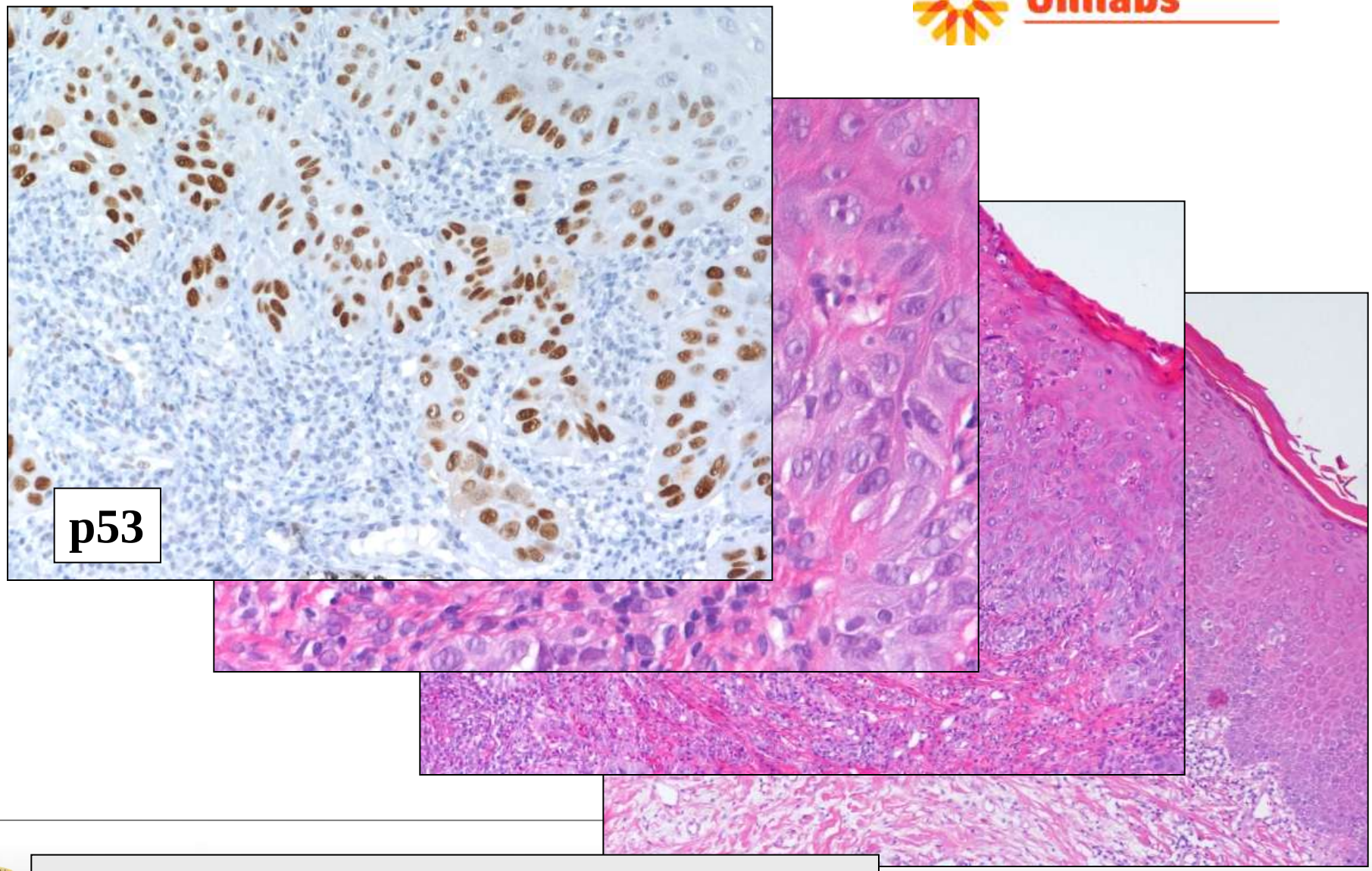
Decembre 2008: Re-excision



Pseudo-epitheliomatous hyperplasia with verrucouse and papillary features
important “lichenoid” inflammation
reactive epithelial modifications with atypia.

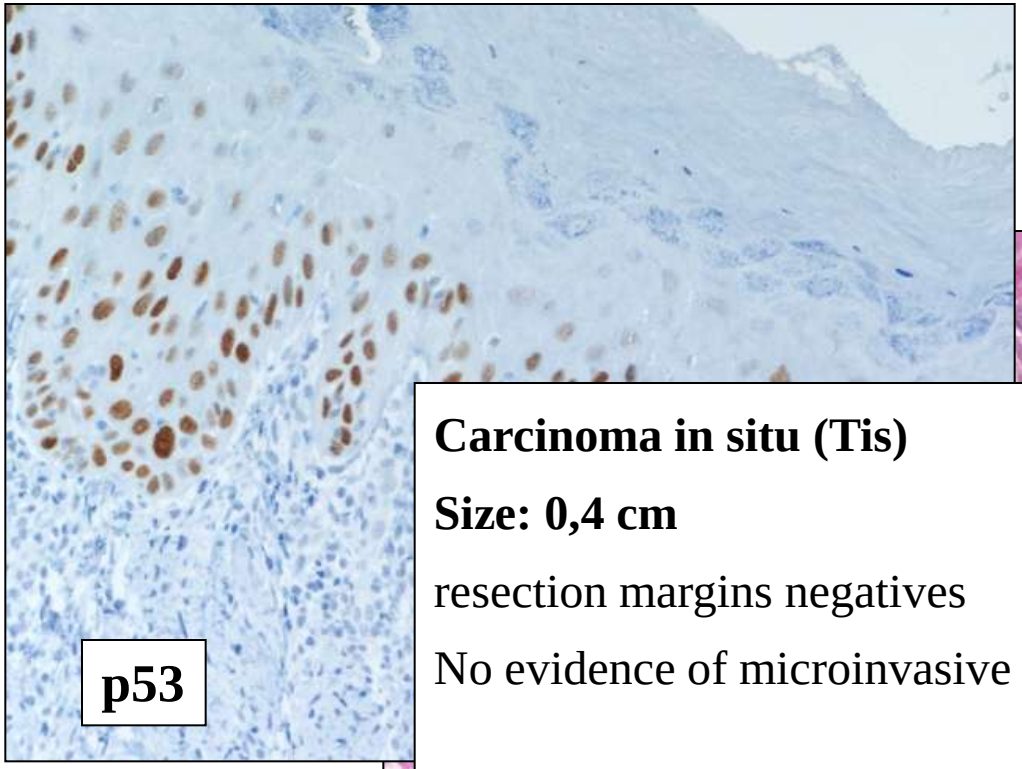
Comment:
Differential diagnosis: **benignant vs. Tis . Observation!!**

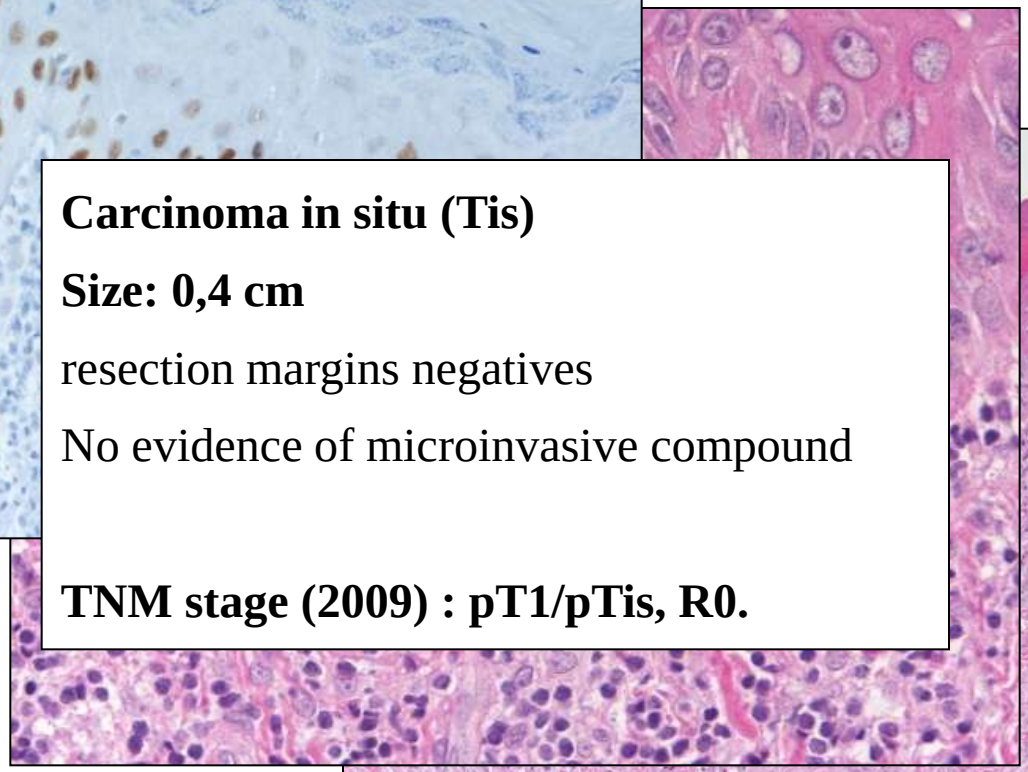
December 2010: Excision retromolar trigone



Micro-invasive SCC (size 0,2 cm), marginas +

January 2011: Re-excision retromolar trigone





Carcinoma in situ (Tis)

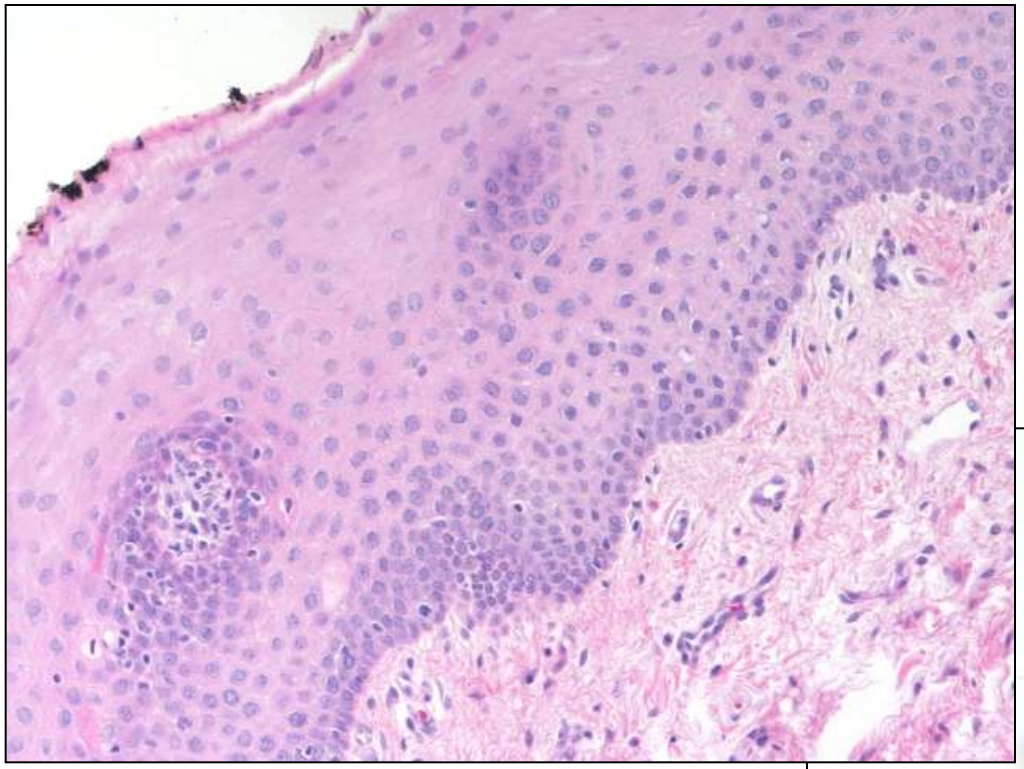
Size: 0,4 cm

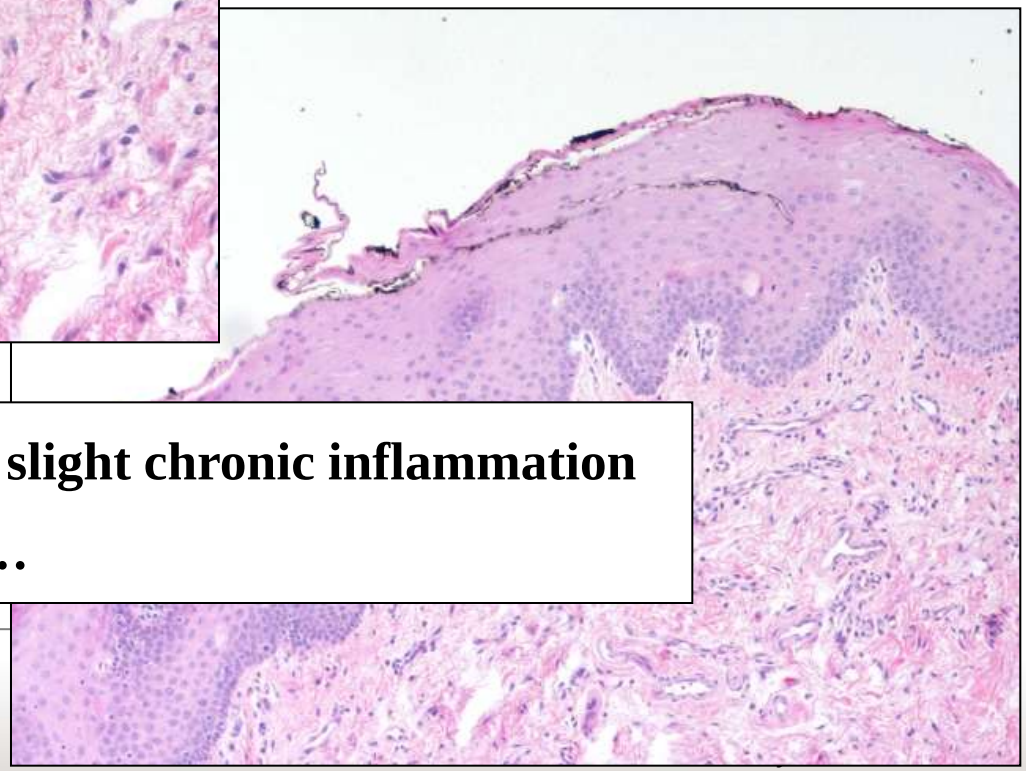
resection margins negatives

No evidence of microinvasive compound

TNM stage (2009) : pT1/pTis, R0.

2011, 2012 (3,6,9,12 months): follow up control bx





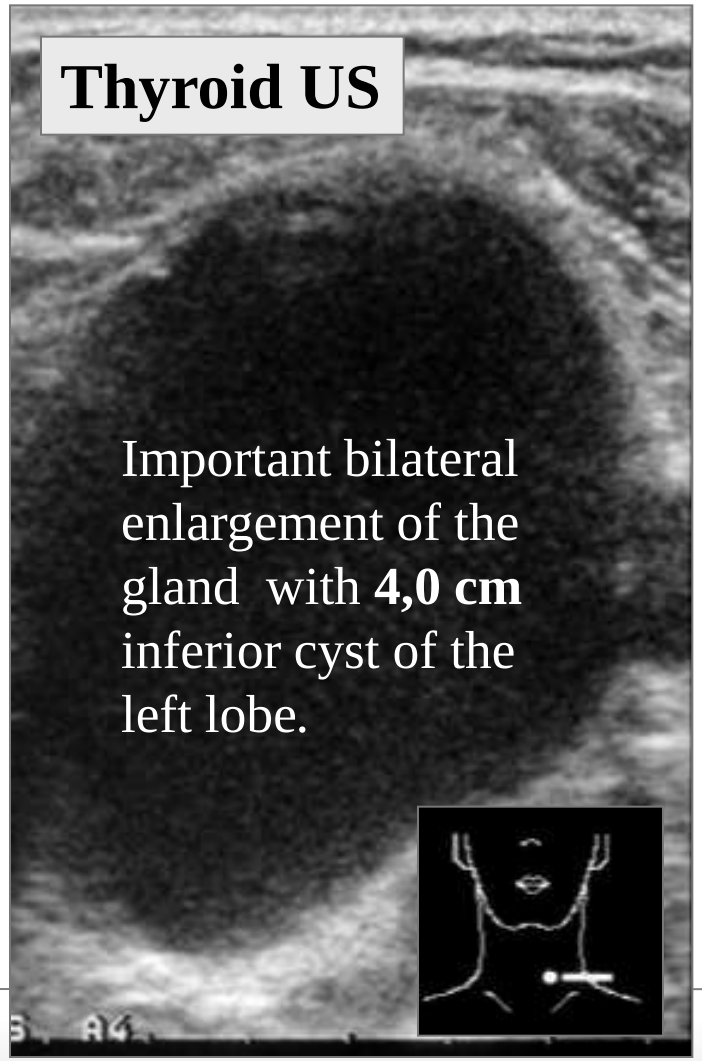
Hyperplasia, hyperkeratosis slight chronic inflammation

No dysplasia, no carcinoma…

Case 2

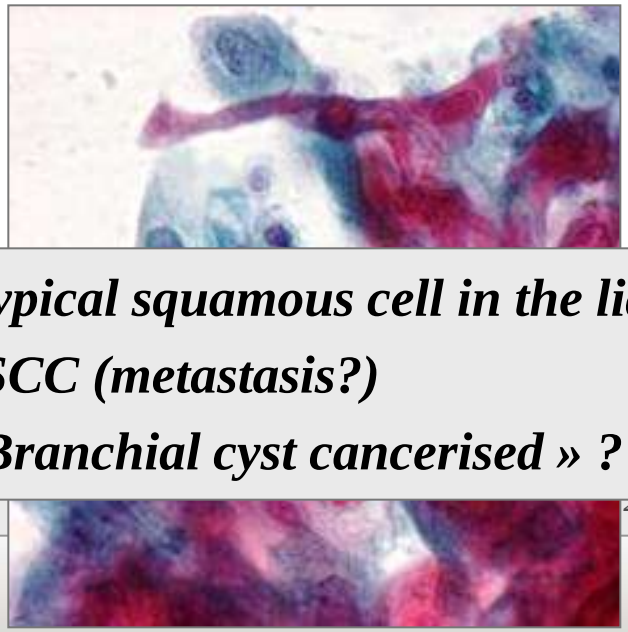
Cystic tumor with squamous differentiation in the thyroid gland

Clinical history…



- **82**-year old female
- Left lateral neck swelling rapidly growing in 6 months
- **Clinical examination:**
  - 8,0 cm painless mass
  - Palpable adenopathies (size: 2 cm)
  - Compressing trachea and esophagus
  - Severe dyspnea
- **Panendoscopy** (**OGD):** normal

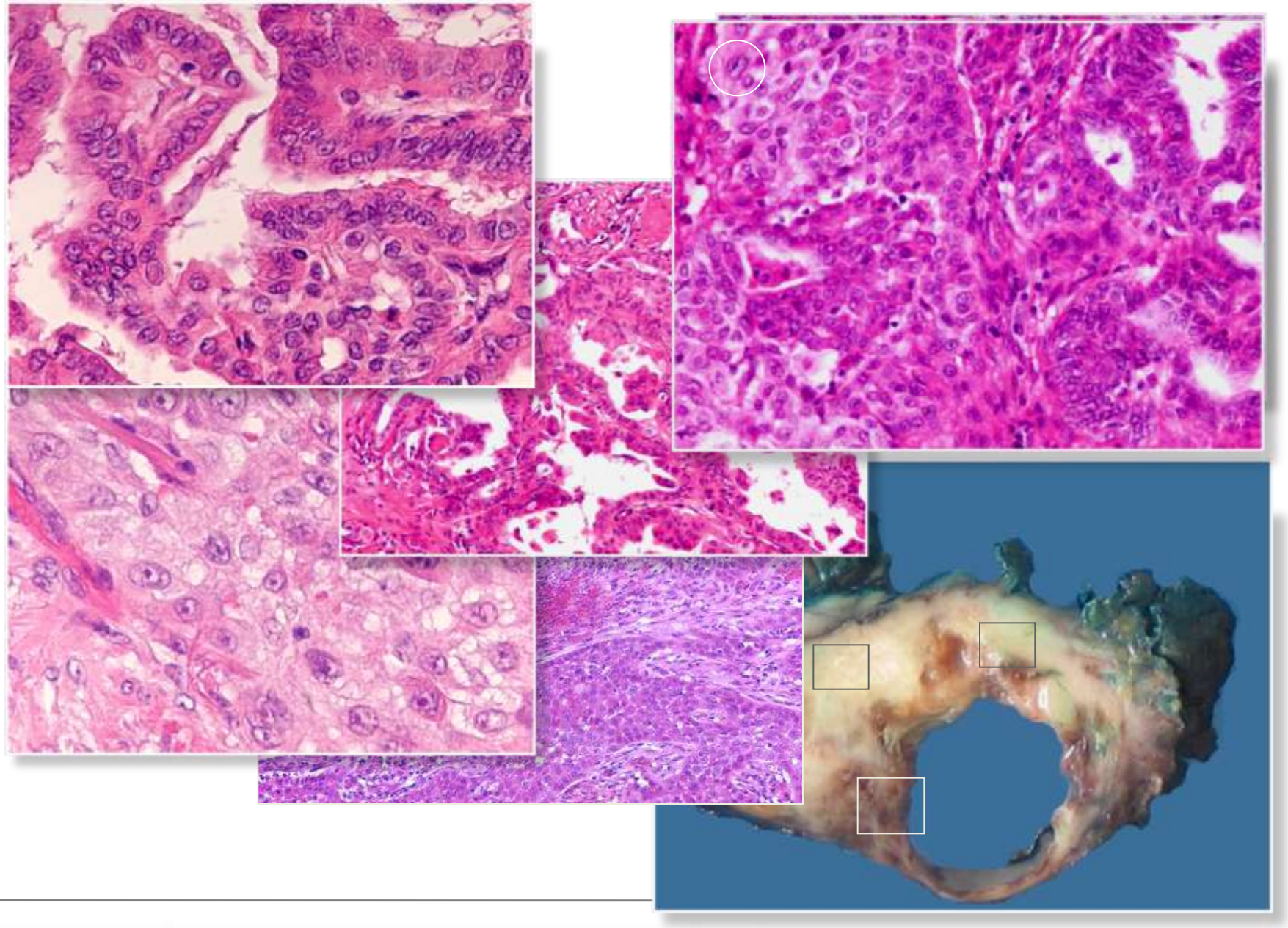
FNA



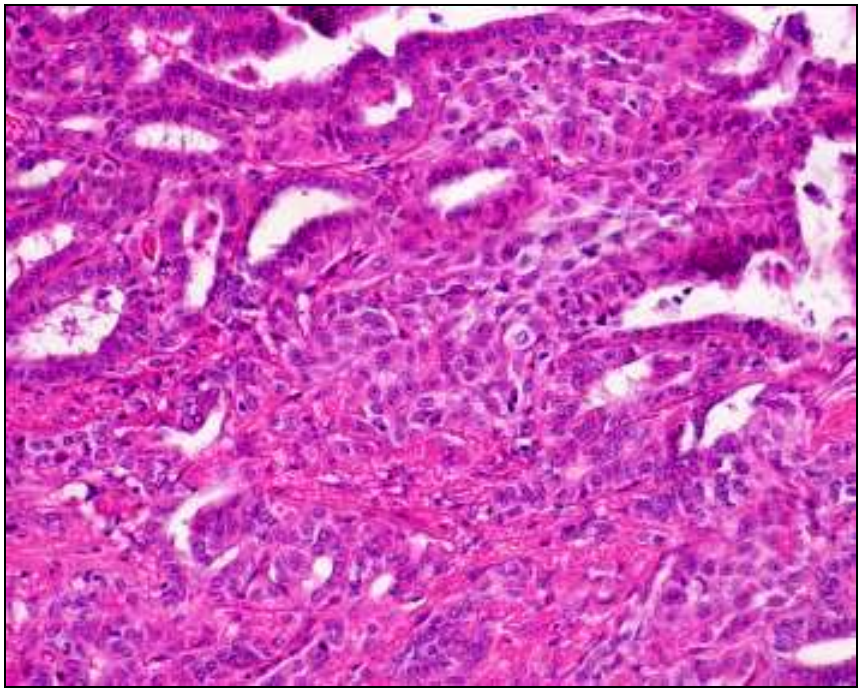
Atypical squamous cell in the liquid

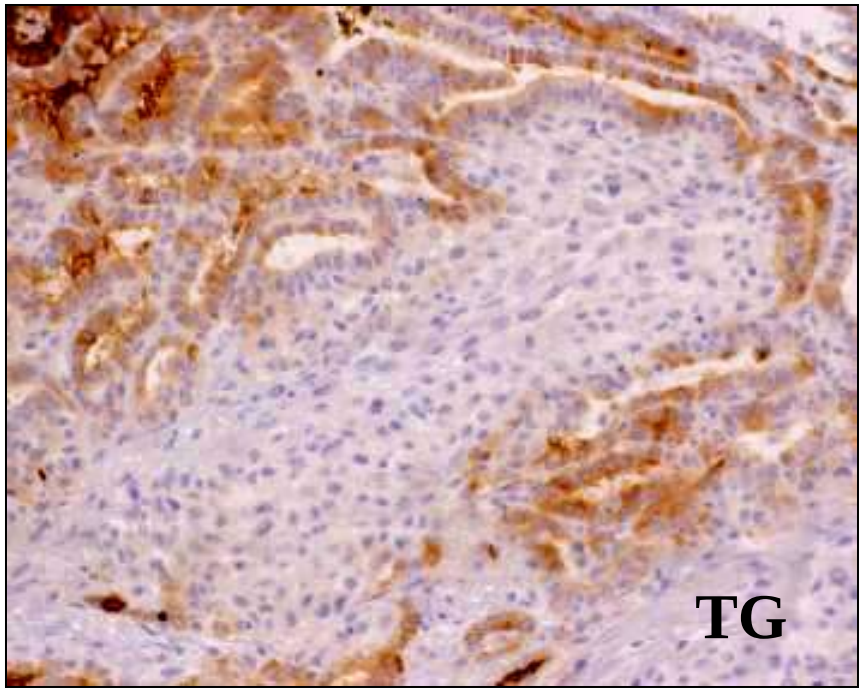
SCC (metastasis?)

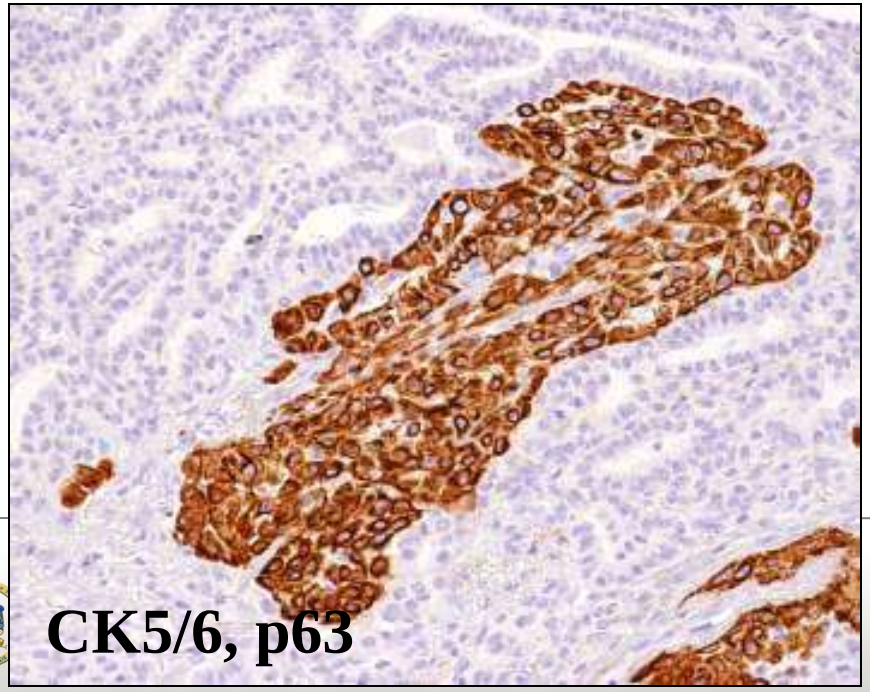
« Branchial cyst cancerised » ?

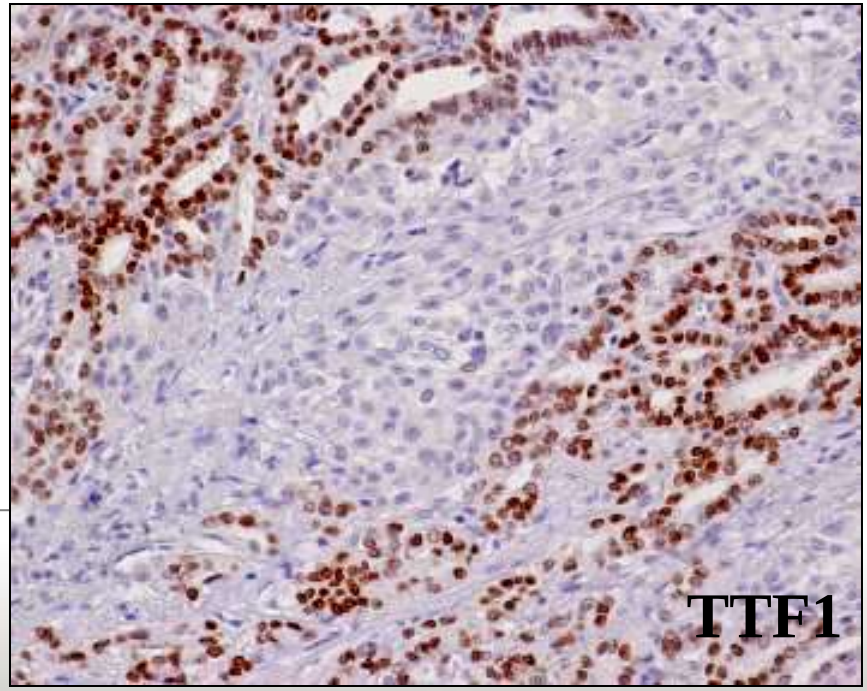


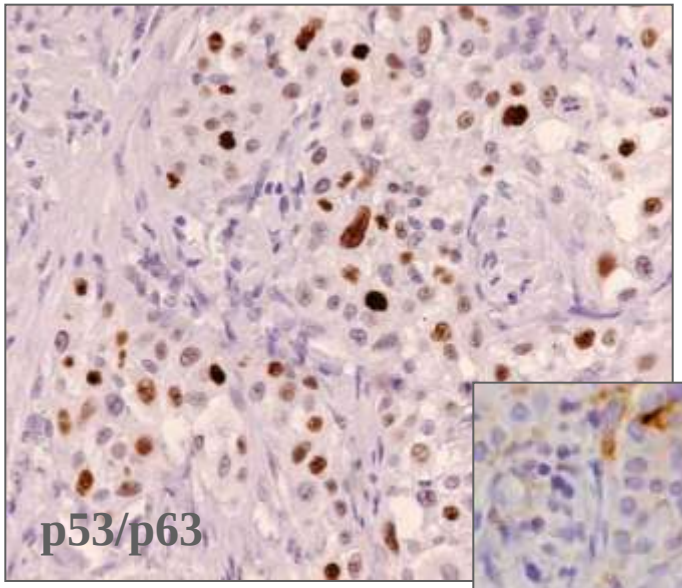
Cervical monobloc resection involving trachea, left lobe of the thyroid & radical ipsilateral cervical dissection

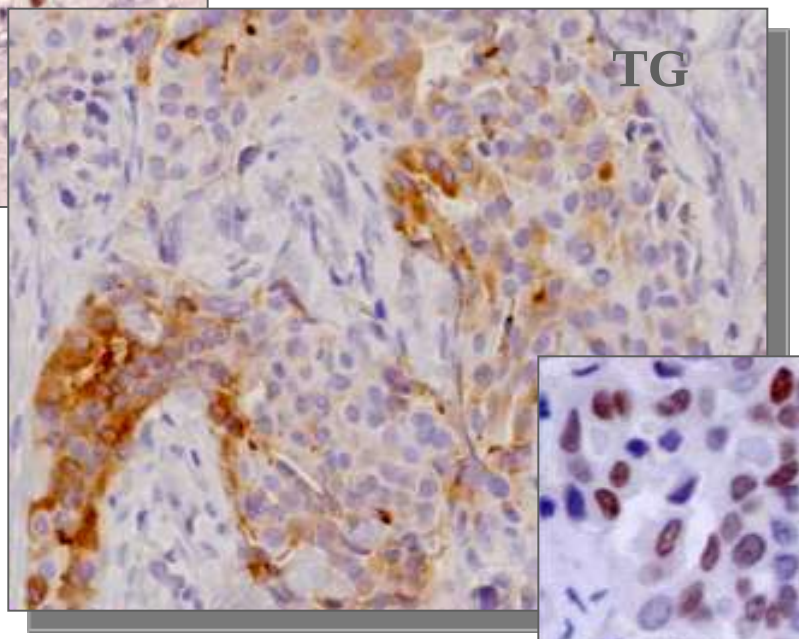


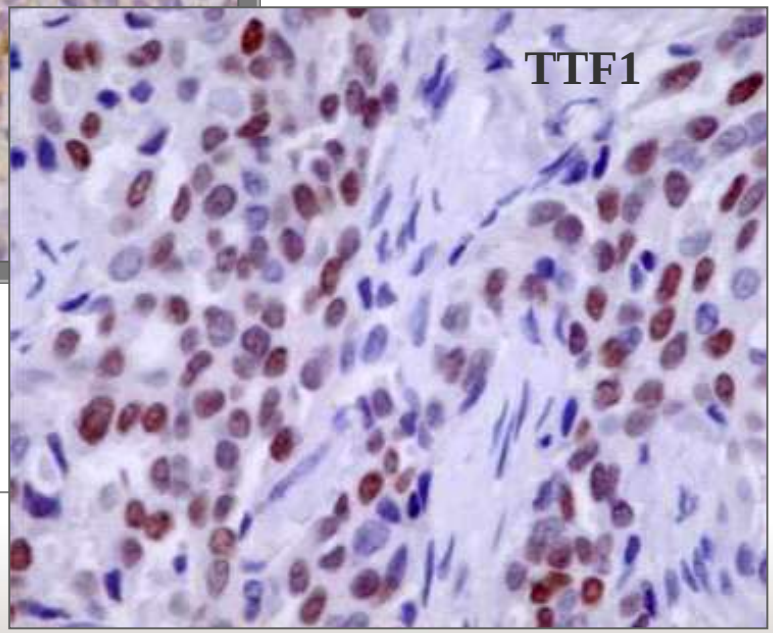

TG


CK5/6, p63


TTF1



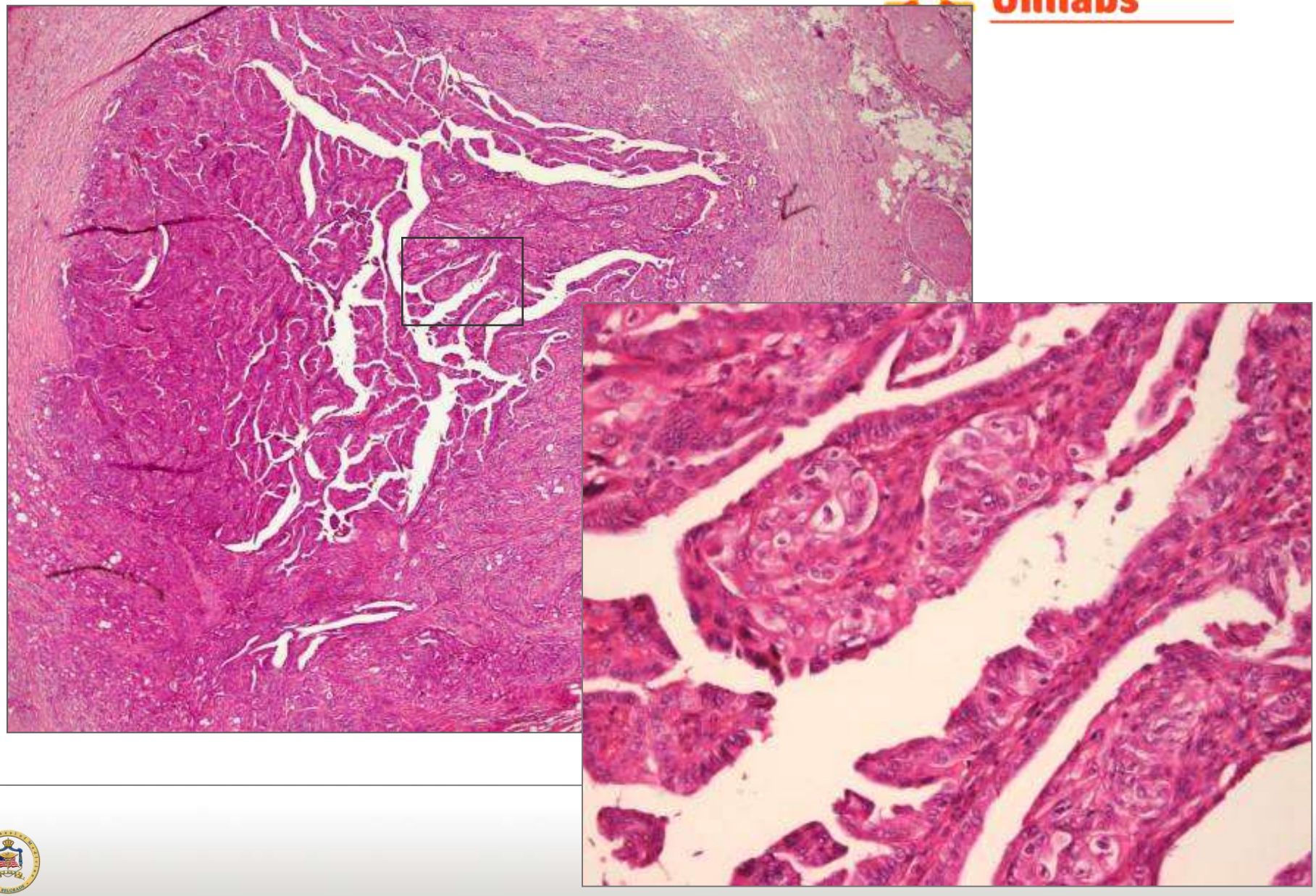




Focal co-expression p53/p63 & TG, TTF1 in the solid squamous counterpart of tumor

Lymphnode metastasis

Unilabs



Working hypothesis

1) Collision tumors phenomenon: PTC & metastasis of a SCC (?)

2) Branchial cleft cyst cancerisation (*branchiogenic carcinoma*) associated with papillary carcinoma in ectopic thyroid tissue

3) Papillary thyroid carcinoma with squamous differentiation

Collision tumors phenomenon

Histologically distinct tumors in adjacent anatomic sites

Origin :

- same or adjacent organ infiltration (tongue-larynx)
- Metastases (2% in the thyroid)

Etiology: accidental / micro-environnement event

Diagnostic was not retained:

Metastasis and or malignant extension in the thyroid was excluded by exhaustive clinical examination (panendoscopy & RX)

Branchial cleft cyst cancerisation (*branchiogenic carcinoma*)

Martin et al. criteria (*Ann Surg 1950;132(5):867-87.)*:

- arise in the wall of a branchial cyst,
- occur along the anterior border of the sternomastoid
- histology compatible with the branchial apparatus
- no other primary tumor within a 5-year follow-up
- premalignant changes found in the epithelium of the cyst

Diagnostic was not retained in the absence of the appropriate diagnostic criteria.

Most cases described in literature were found to be metastasized lesions from occult primary SCC Lin YC Int J Oral Maxillofac Surg 2004;33(2):209-12

Squamous differentiation in PTC

*1) Squamous **metaplasia** (found in 20% of PTC)*

2) Solid cell nests ultimobranchial body

- remnants of the ultimobranchial body
- from the inferior part of the fourth pharyngeal pouch
- incidentally finding in 60% of adult % 89% of neonatal thyroid
- reservoir of cells from which PTC/SCC may arise in the thyroid
- **Stem cell phenotype**

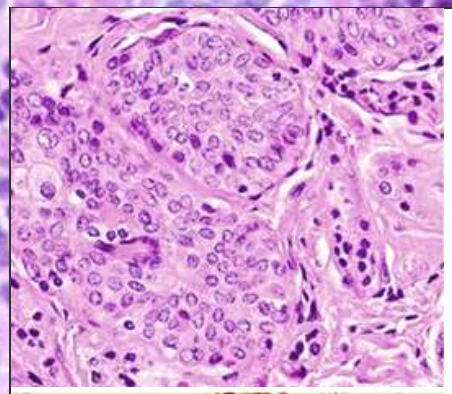
  self renewal (telomerase activity)
  expression stem cell markers (**OCT4, GATA4, HNFα4**)
  differentiation (expression of **p63, Bcl2**)

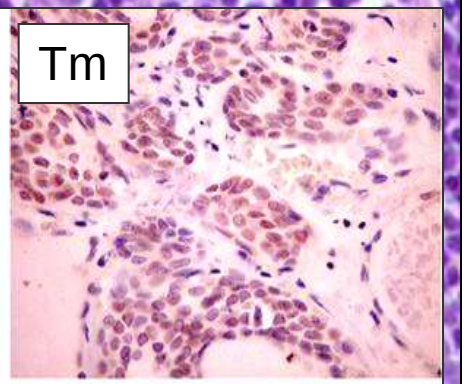
3) Other:

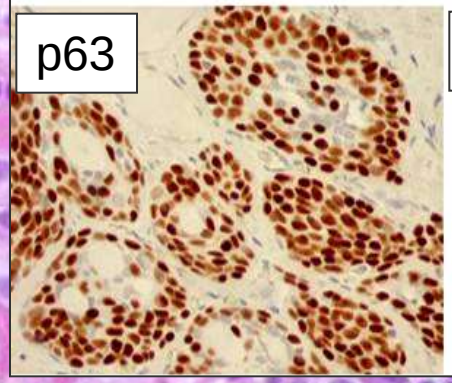
- primary/secondary SCC metastasis,
- thyroglossal cysts,
- MTC or PTC microcarcinoma.

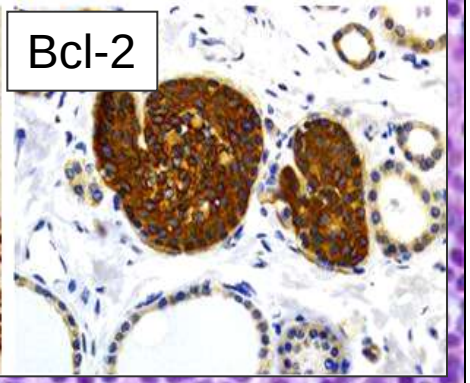
Refs: A. Preto, Modern Pathol, 2004, T. Thomas, Thyroid 2006;
T. Hunt JL, Human Pathol. 2004; Reimann JD. Am J Surg Pathol 2006.

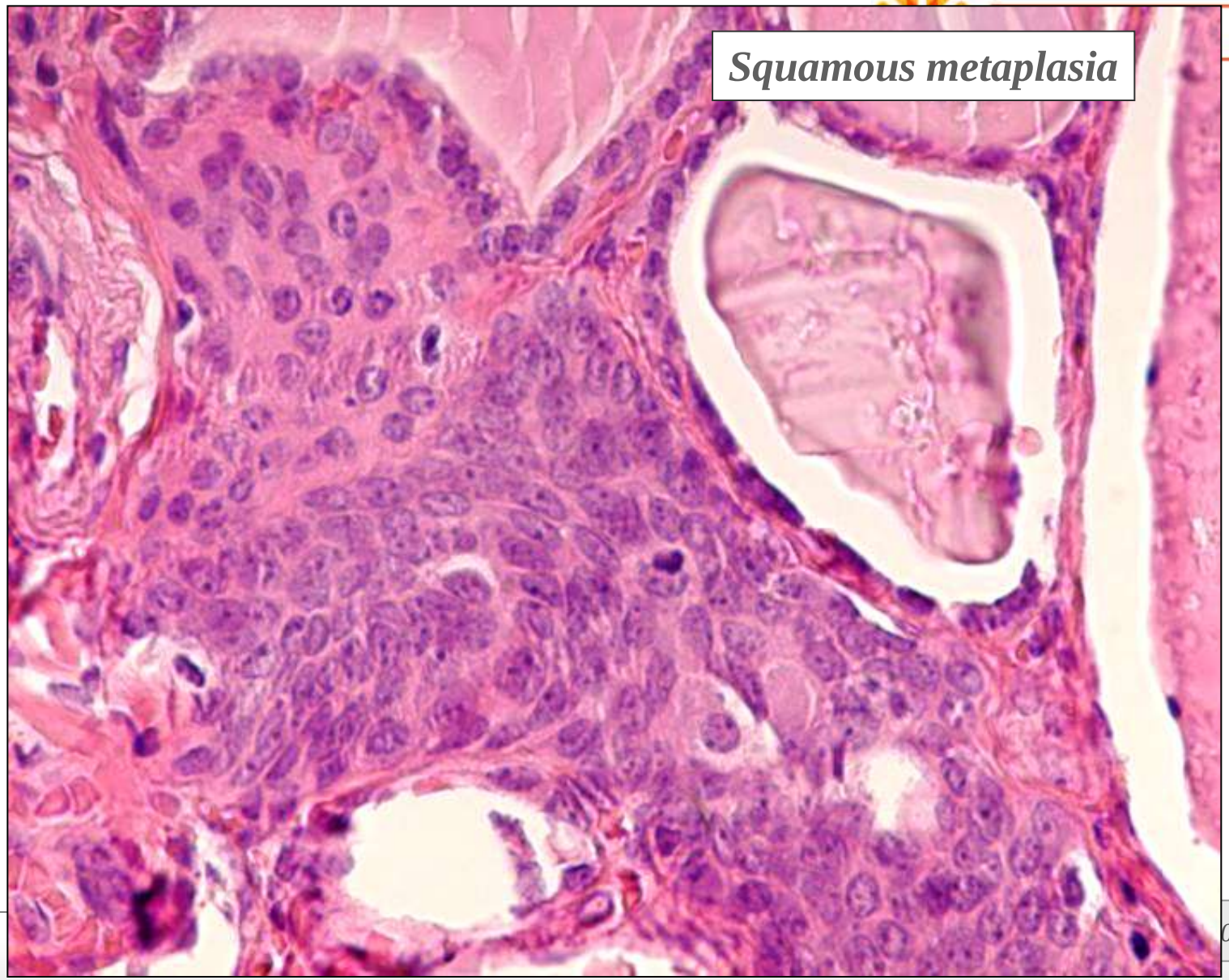
Solid cell nests ultimobranchial body





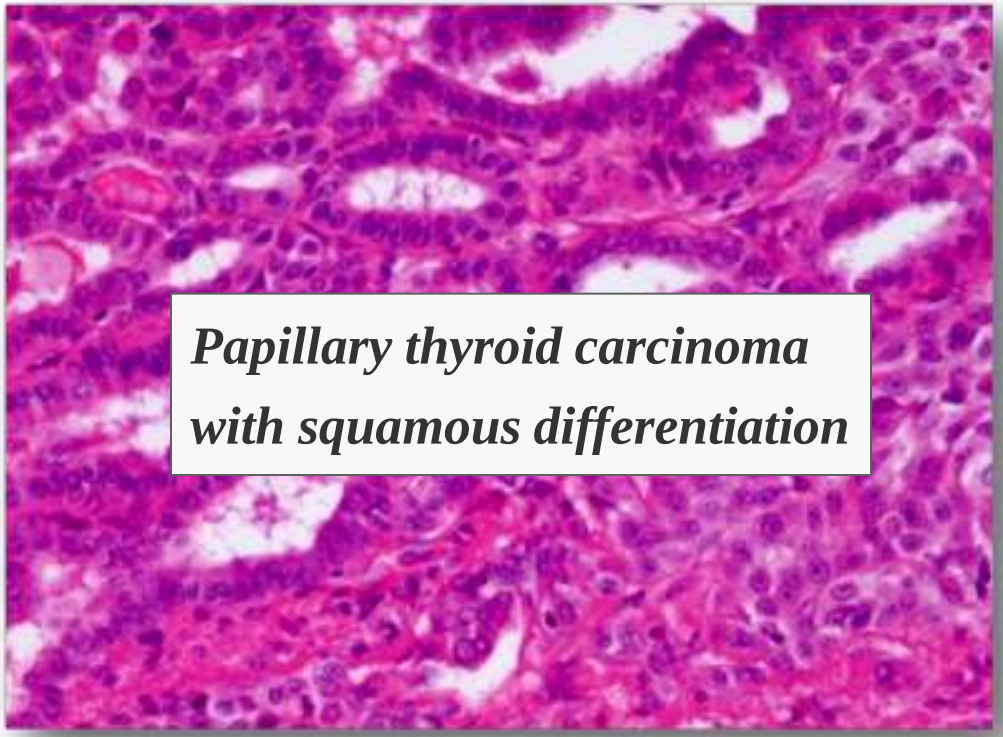





Squamous metaplasia

Final diagnosis according to…

clinical presentation, morphology, IHC phenotype, metastasis pattern



Thyroid carcinoma with papillary and squamous features: Report of a case with histogenetic considerations
Th. Rausch, J.Benhattar, M.Sutter and S.Andrejevic-Blant
TEACHING CASE Pathology Research and Practice 2009

Case 3

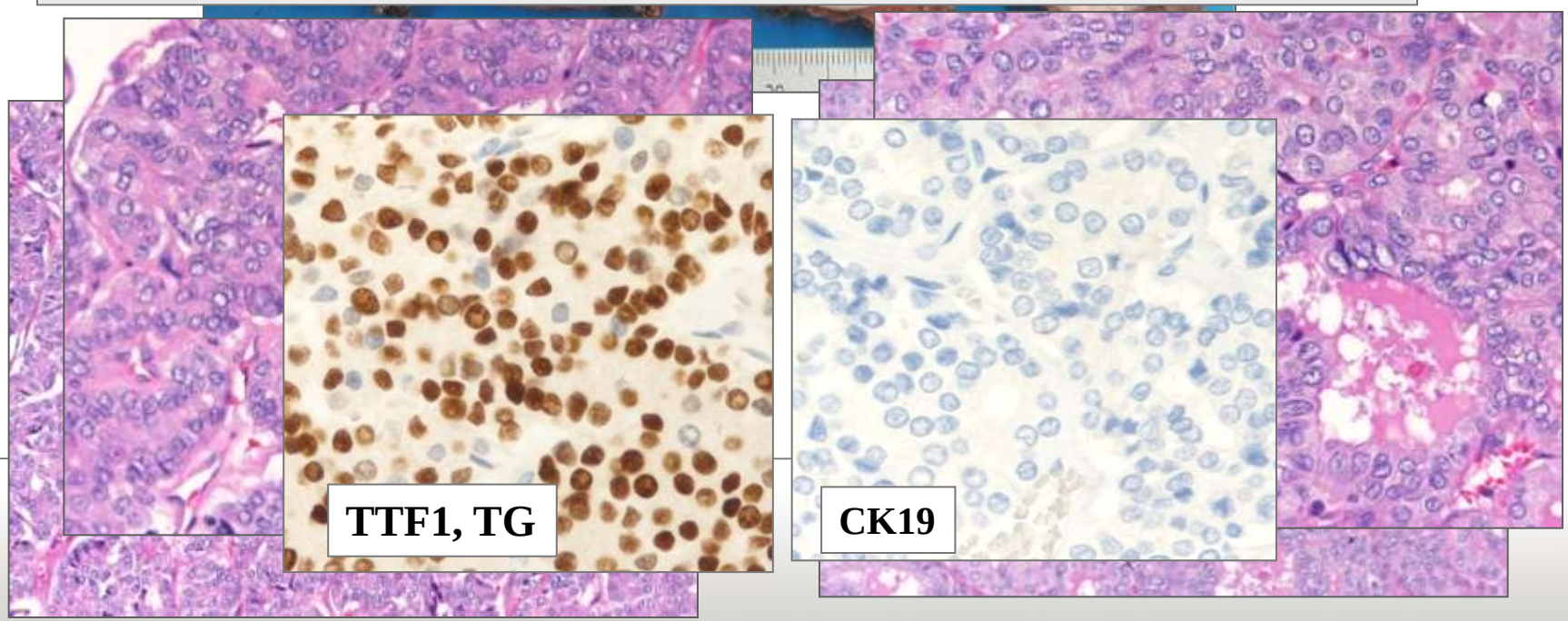
….Second look: intraoperative lymph node analysis in patient with thyroid carcinoma….

Clinical history & 1st diagnosis

Unilabs

- 73-year old male, goiter
- Right thyroid nodule, increasing in size (5,0 cm)
- FNA: follicular proliferation
- **April 2012: Righ-thyroidectomy**

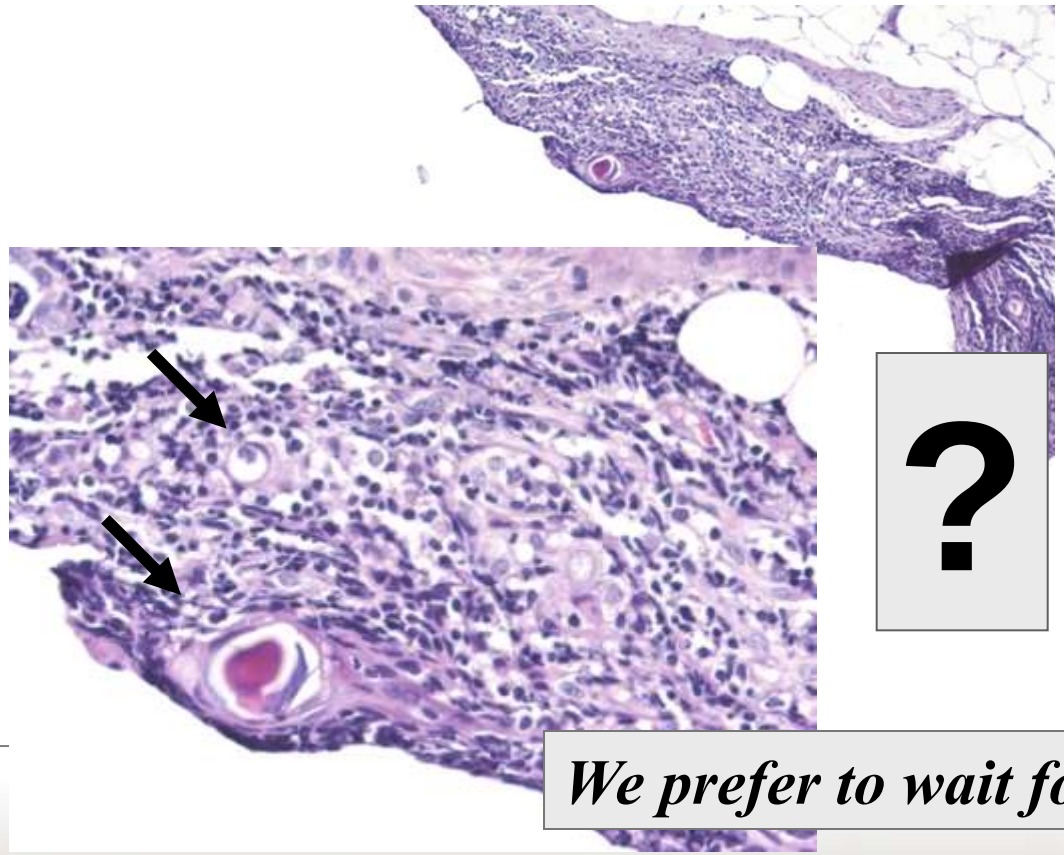
Poorly differentiated thyroid carcinoma with FVPTC component (pT3, R0)



Clinical history…

May 2012: second look & complementary surgery

- Contralateral LN sampling level VI (FS)
- Left-thyroidectomy
- Homolateral radical neck dissection (III-VI)



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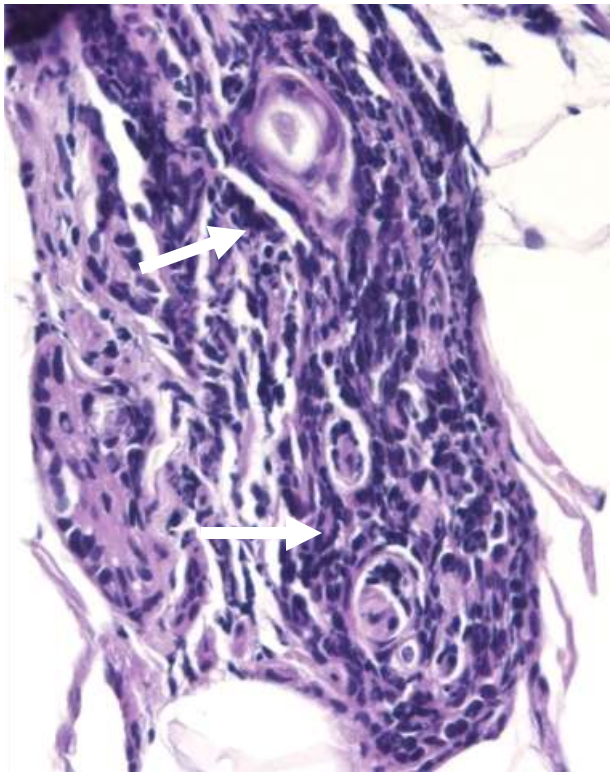
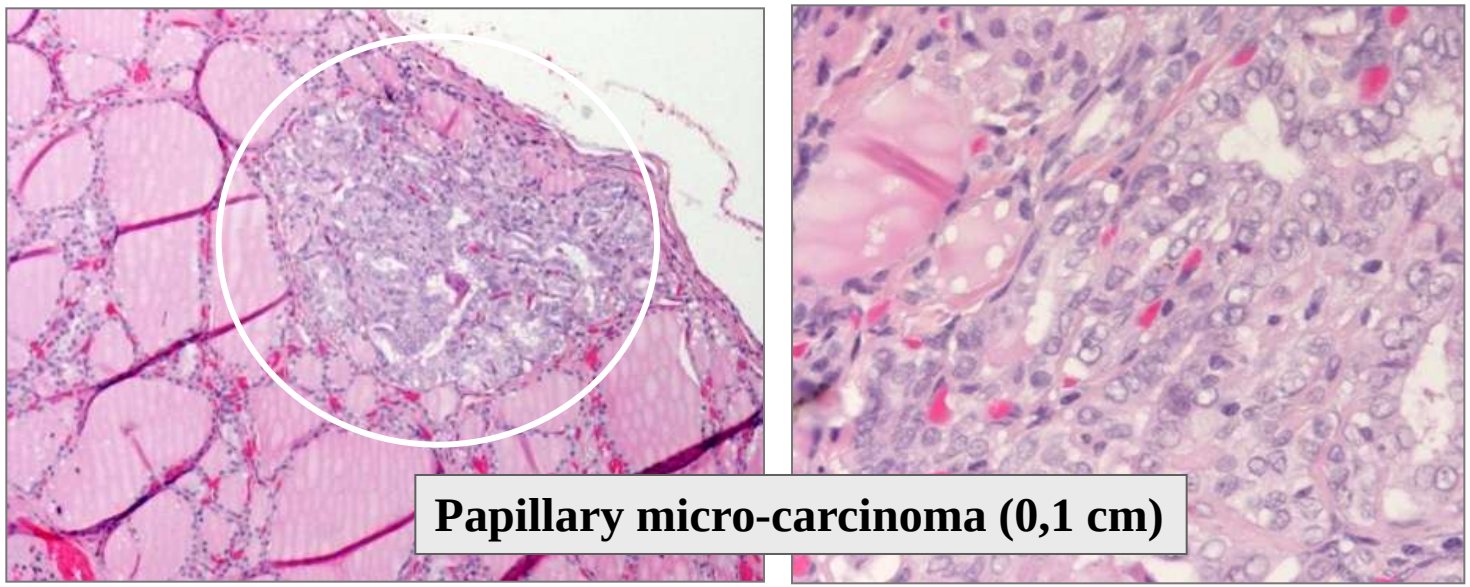


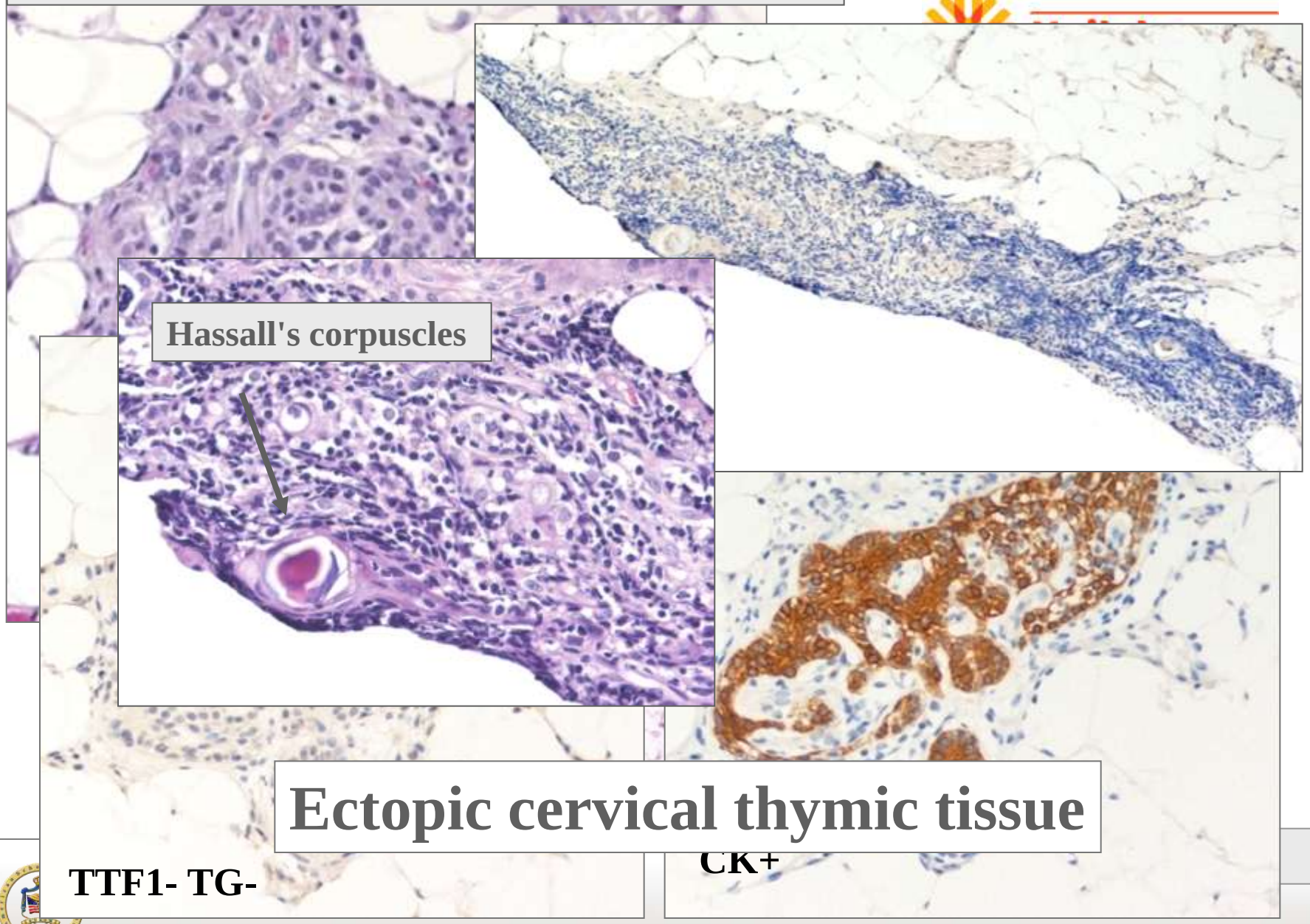
We prefer to wait for permanent section…

Left-thyroidectomy:



Homolateral radical neck dissection (III-VI): 15 LN w/o metastasis (**0/15**)

Contralateral LN sampling level VI: permanent section



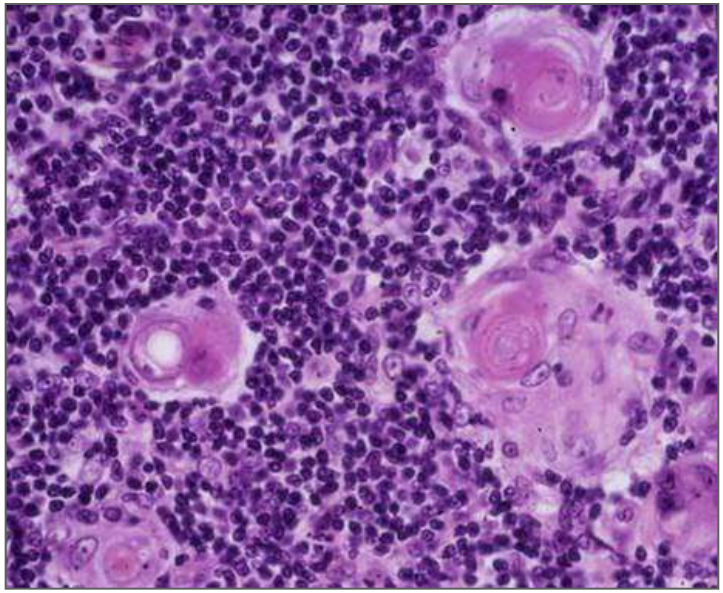
Ectopic cervical thymic tissue

TTF1- TG-

CK+

Ectopic cervical thymic tissue

- Consequence of migrational defects during thymic embryogenesis.
- From 1900 only 90 cases have been reported in the literature
- 2/3 of all reported cases were identified in children younger than 10 years
- Rare in patients older than 20 years

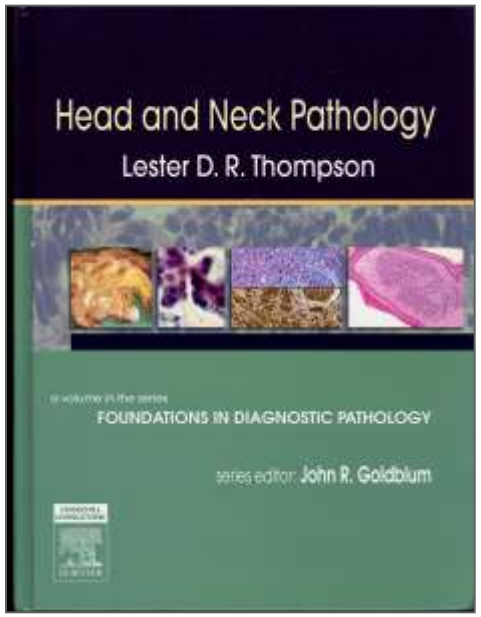


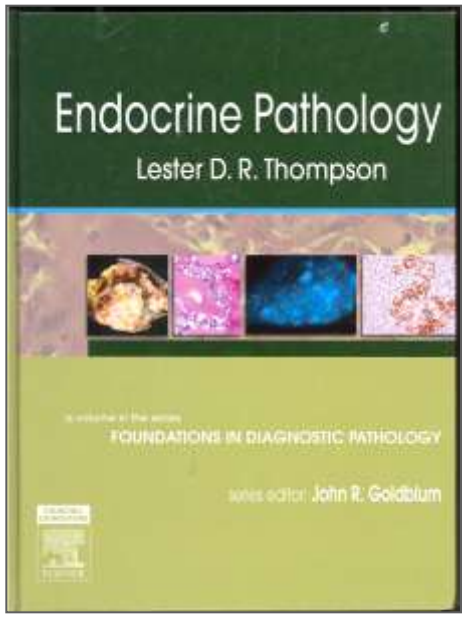
Prof. Dr Med S. Andrejevic-Blant, Oct 2012

Nguyen Q et al. Laryngoscope,1996. Loney DA et al. Arch Pathol Lab Med, 2001.
Tunkel et al. Int J Pediatr Otorhinolaryngology,1998. Millman B et al Int J Pediatr Otorhinolaryngology,1999.

Take home message….

…..A cervical **ectopic thymus** should be included in the **differential diagnosis** of a **neck mass in adults**, and should **not be misdiagnosed** as a **metastatic carcinoma** by frozen section….


Head and Neck Pathology
Lester D. R. Thompson
FOUNDATIONS IN DIAGNOSTIC PATHOLOGY
series editor: John R. Goldblum


Endocrine Pathology
Lester D. R. Thompson
FOUNDATIONS IN DIAGNOSTIC PATHOLOGY
series editor: John R. Goldblum


Le Mont Cervin (4478 m)
Thank you very much for your attention!