

# A PRACTICAL APPROACH TO THE MORPHOLOGIC EVALUATION OF GERM CELL TUMORS OF THE TESTIS



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# Testicular mass; what should I be thinking about?

- Neoplastic or not?
  - Infection, infarct
- If neoplastic, primary or not?
- If primary, what type?
  - Are there ancillary studies I can depend on?
  - After I classify it, what factors must I evaluate to predict prognosis and how do I stage the tumor?
- If metastatic, what are the more likely sources?
  - Clinical history

# WHO 2016

## **Germ cell tumors derived from germ cell neoplasia in situ (GCNIS)**

*Tumors of one histological type (pure forms)*

Seminoma

Non-seminomatous germ cell tumors

Embryonal carcinoma

Yolk sac tumor, post-pubertal type

Trophoblastic tumors

Choriocarcinoma

Non-choriocarcinomatous trophoblastic tumors

Placental site trophoblastic tumor

Epithelioid trophoblastic tumor

Teratoma, post-pubertal type

Teratoma with somatic-type malignancies

*Non-seminomatous germ cell tumors of more than one histological type*

Mixed germ cell tumors

Regressed germ cell tumors

## **Germ cell tumors unrelated to germ cell neoplasia in situ**

Spermatocytic tumor

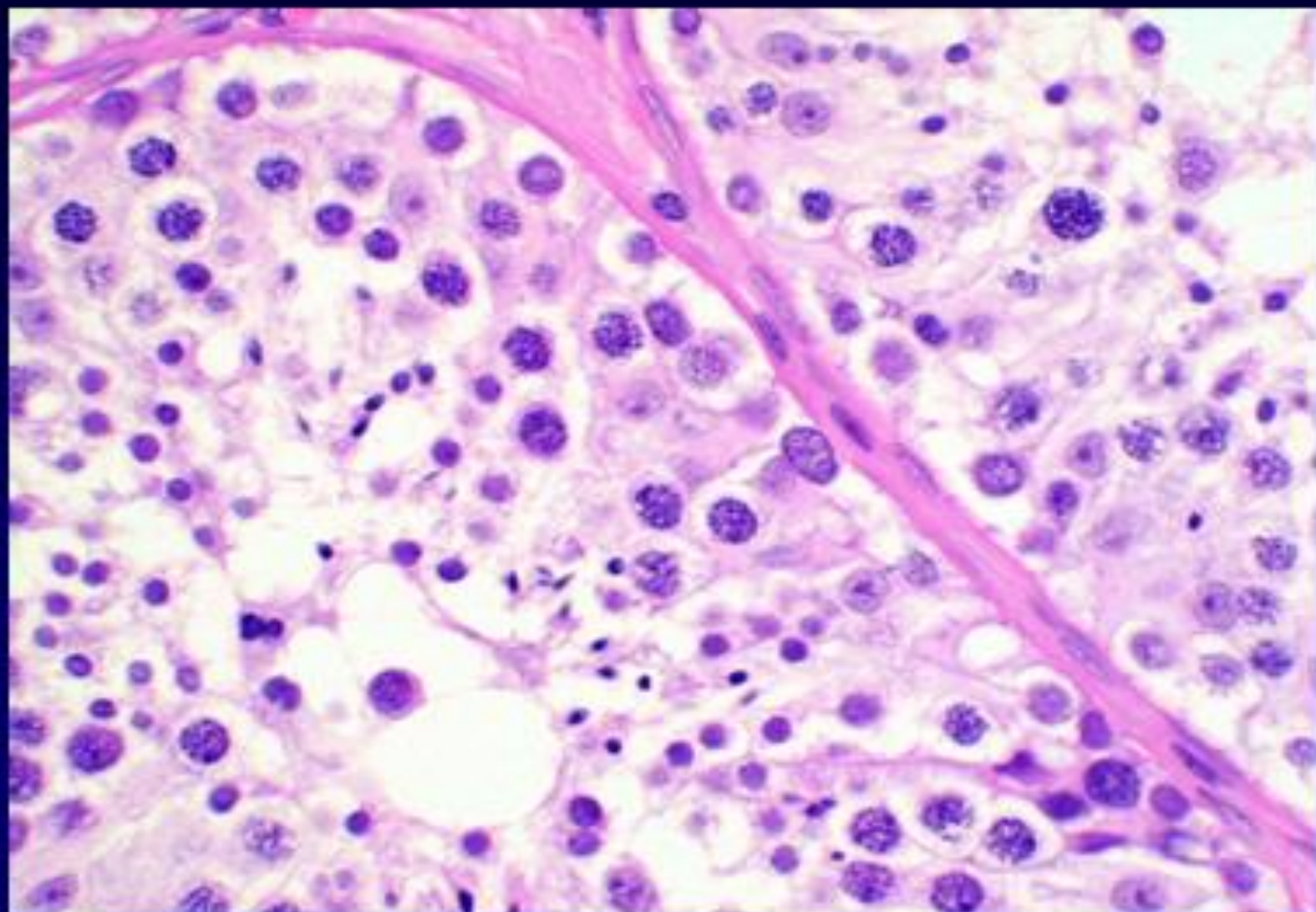
Teratoma, prepubertal type

Dermoid cyst

Epidermoid cyst

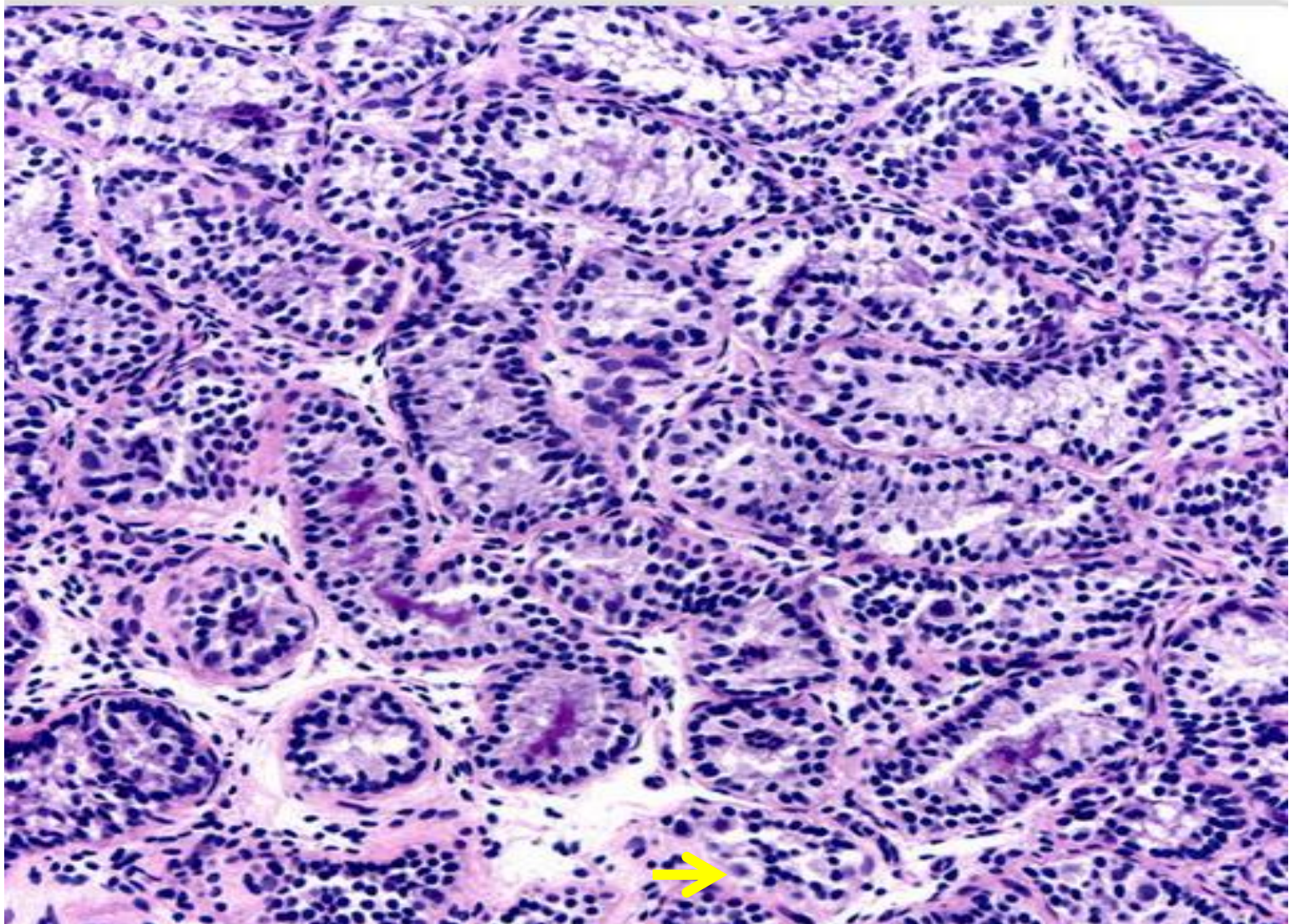
Yolk sac tumor, pre-pubertal type

## Post-pubertal testis





# Pre-pubertal testis



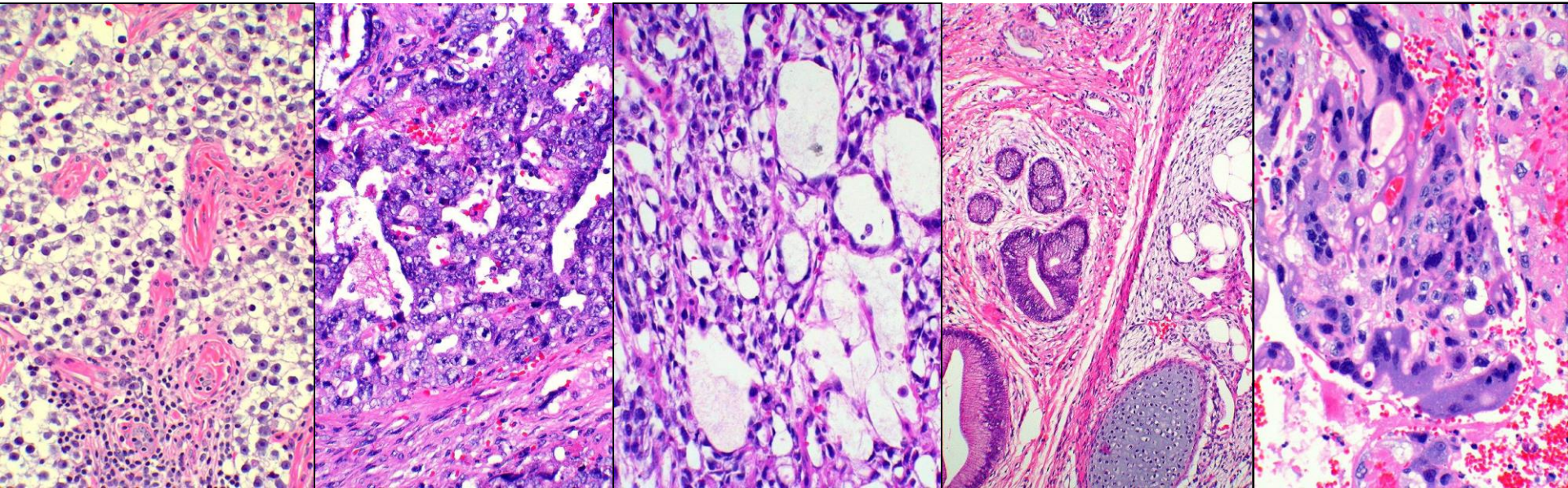


How do I make sure it's a germ cell tumor?

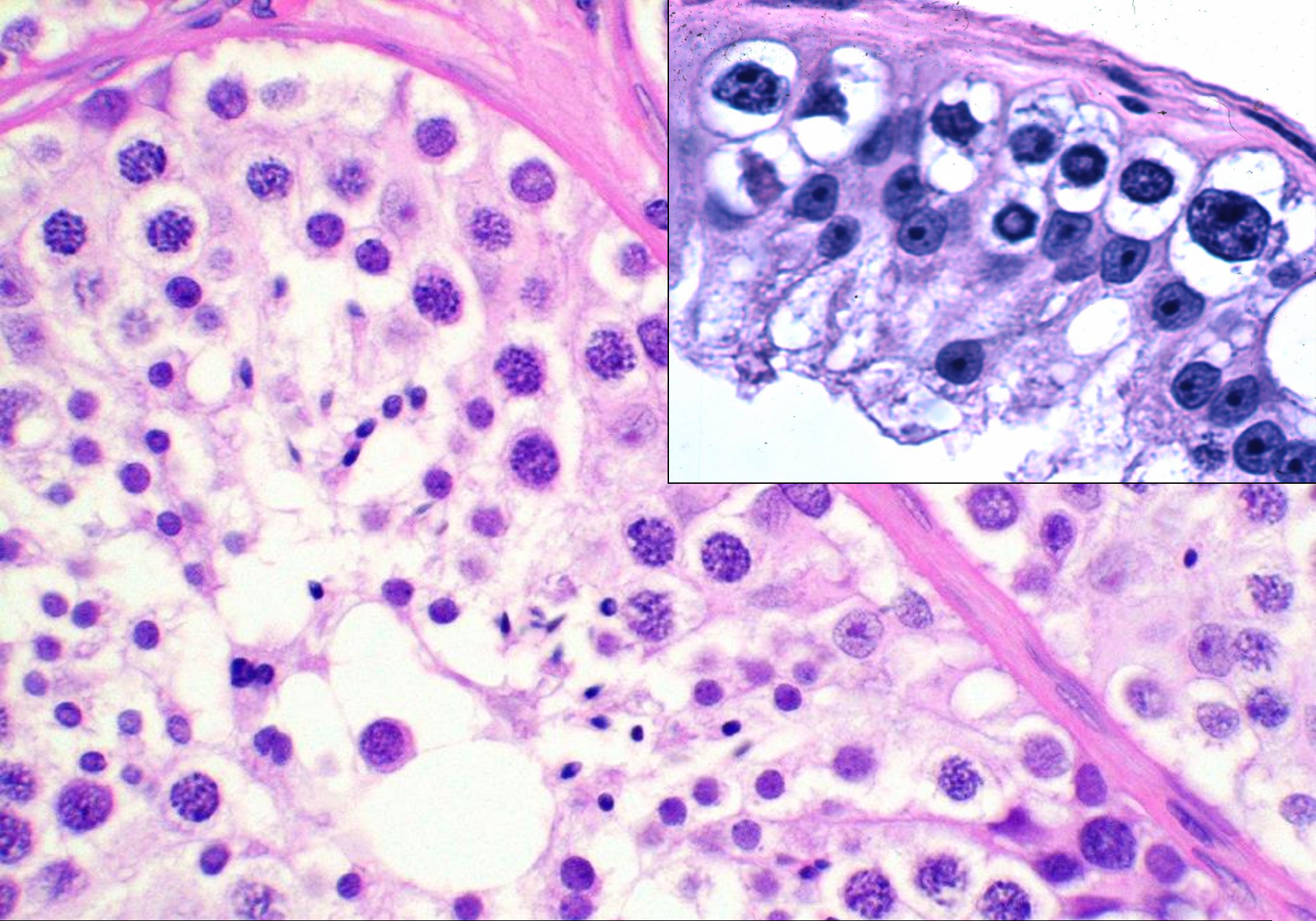
Morphology

Germ cell neoplasia in situ (GCNIS)

Immunohistochemistry



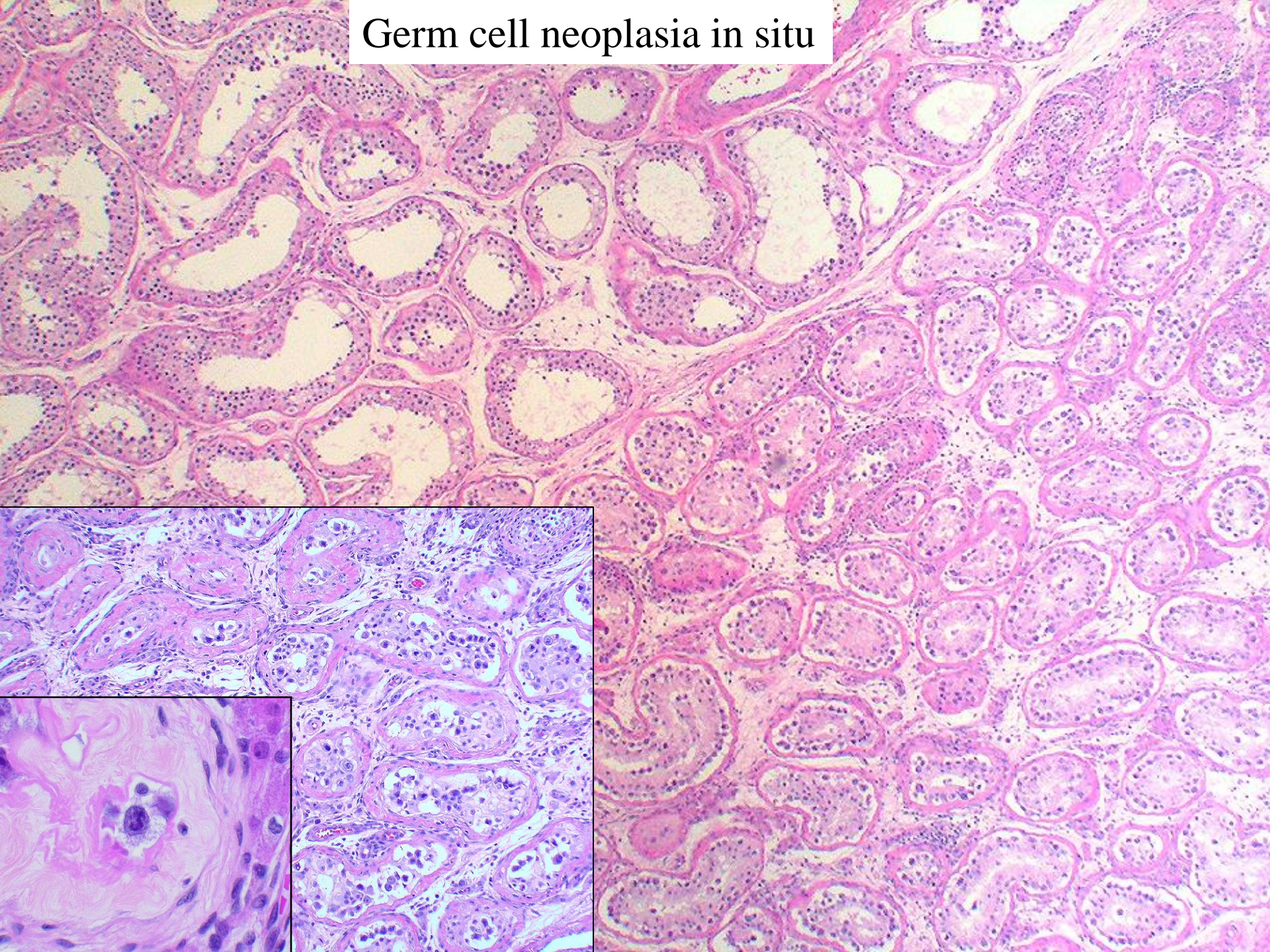




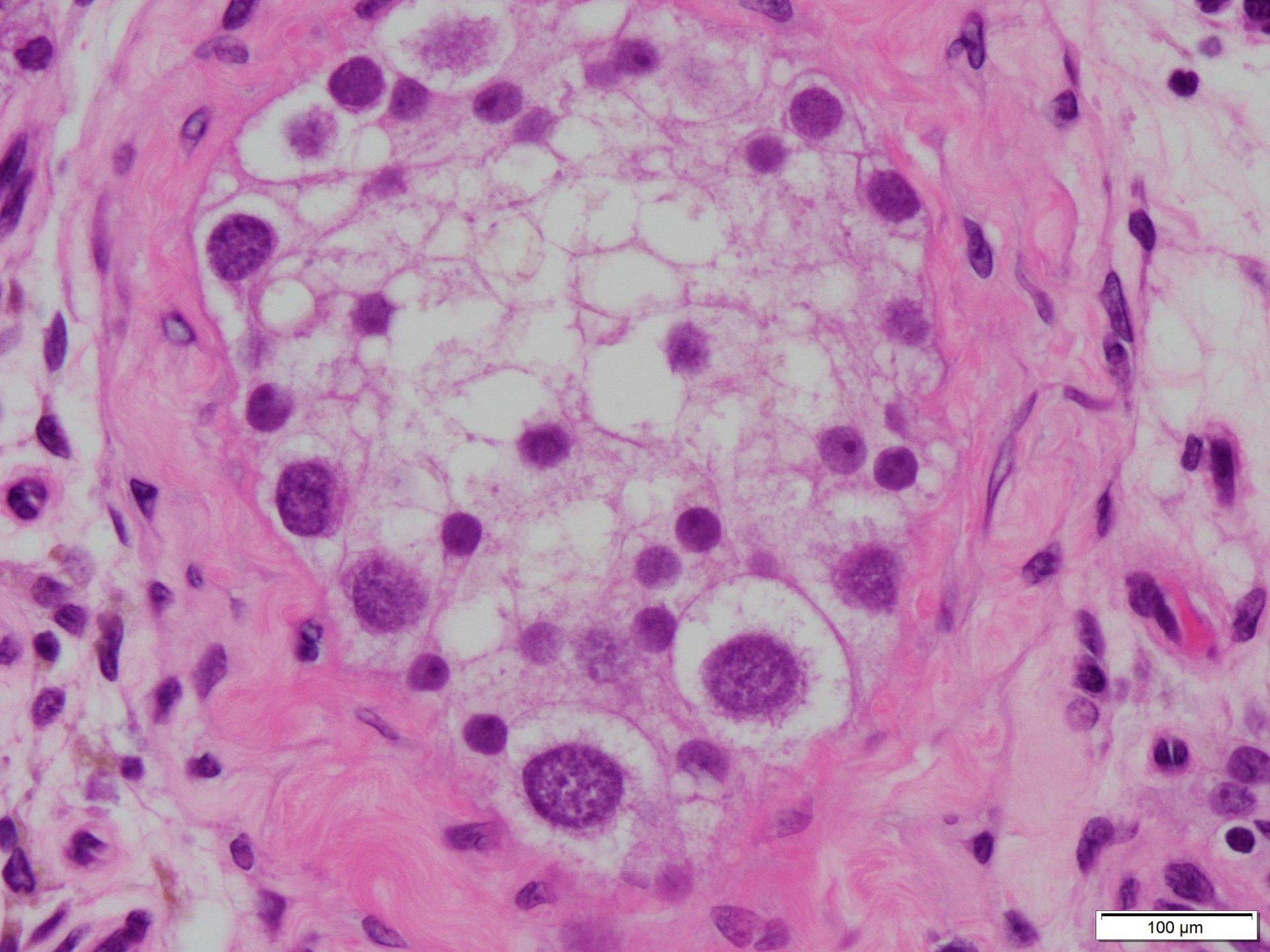
Germ cell neoplasia in situ (GCNIS); the prototypical precursor lesion



# Germ cell neoplasia in situ



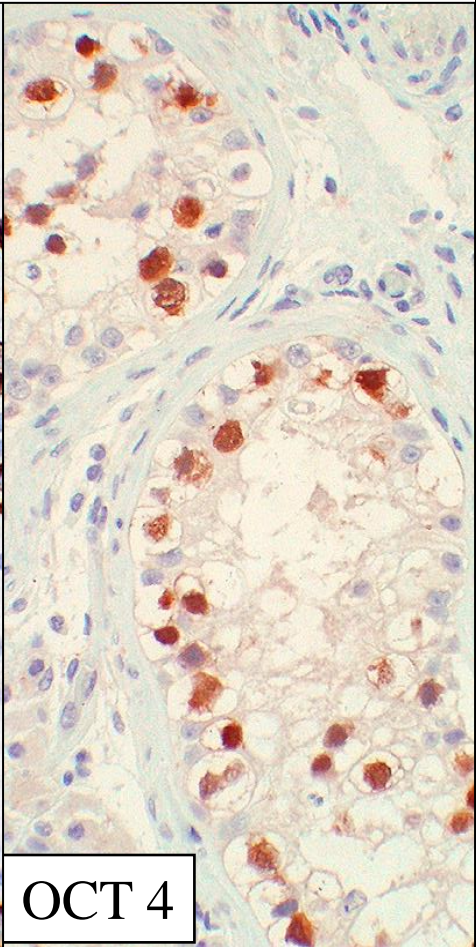
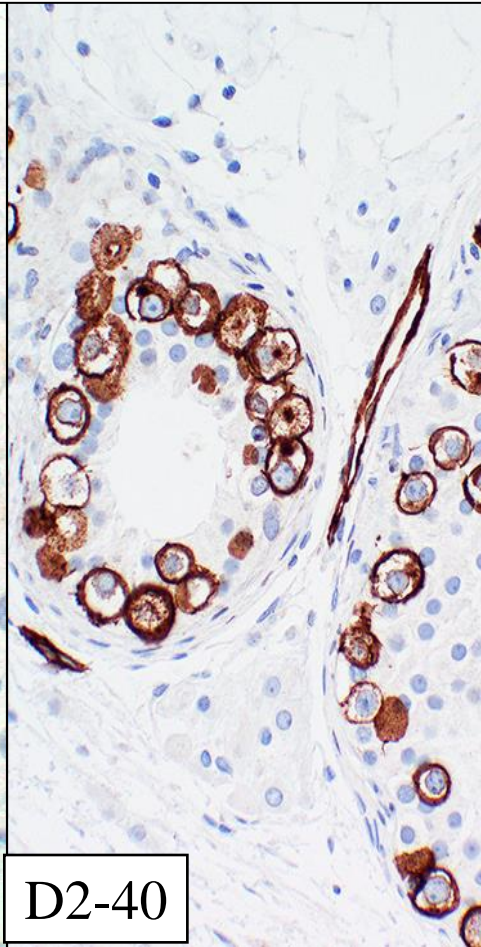
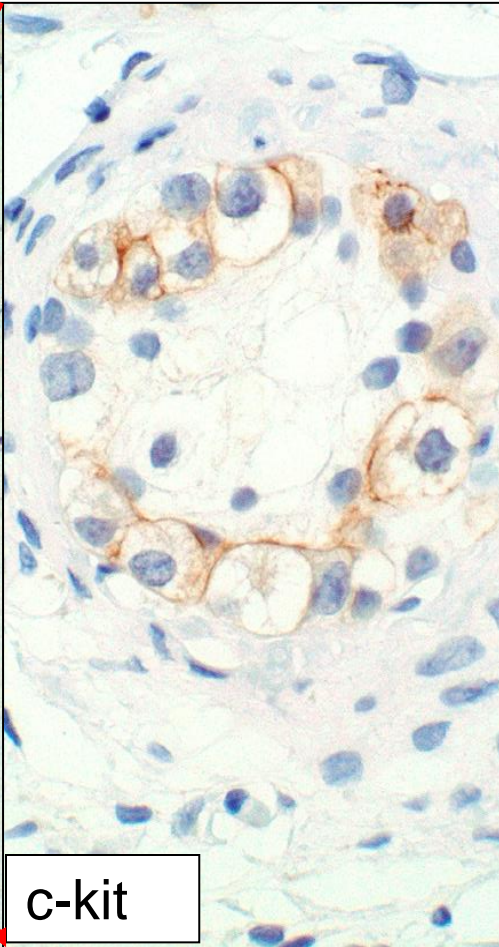
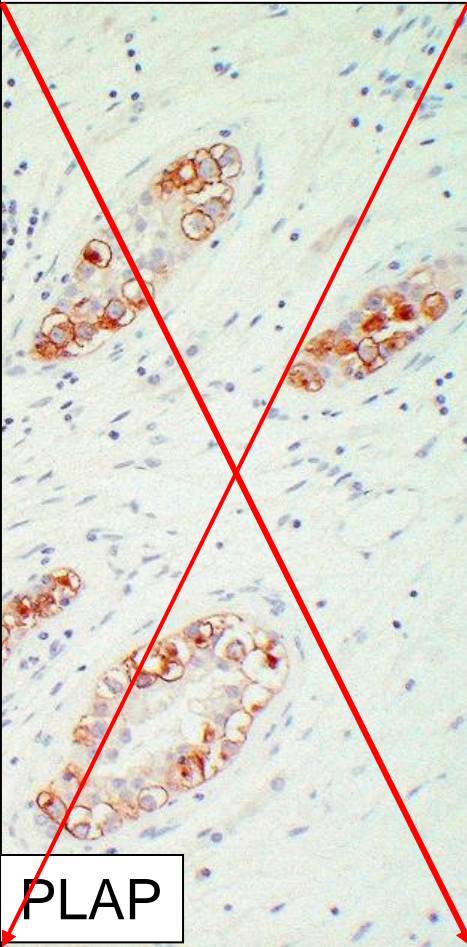




100  $\mu$ m

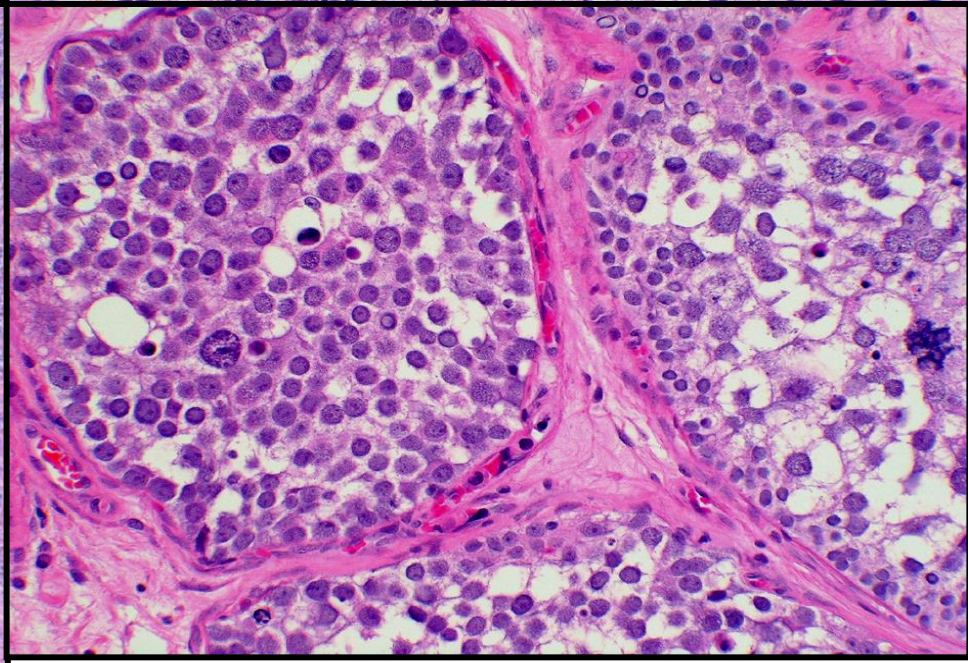
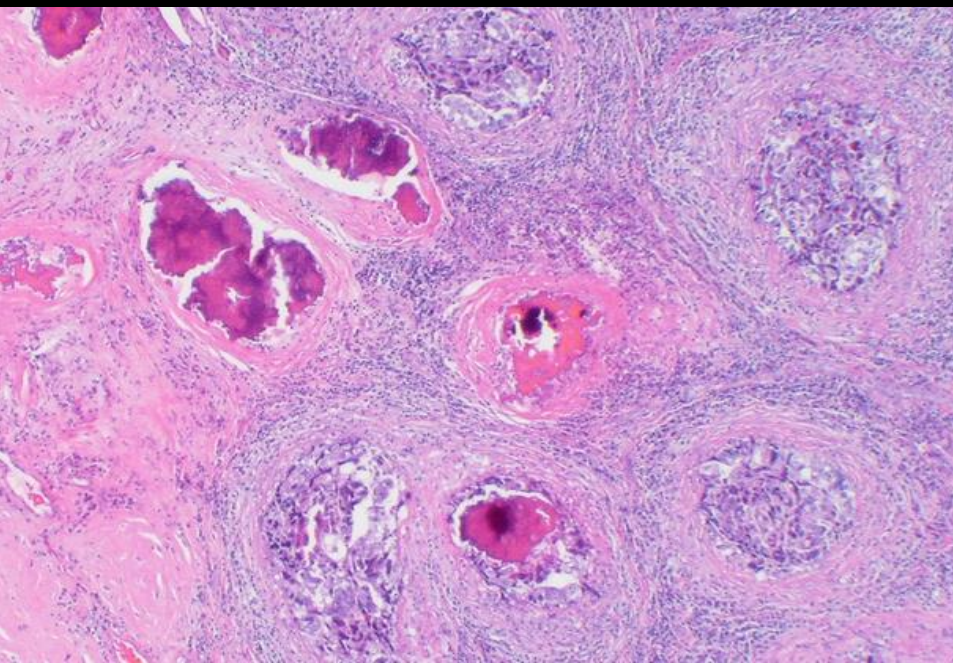
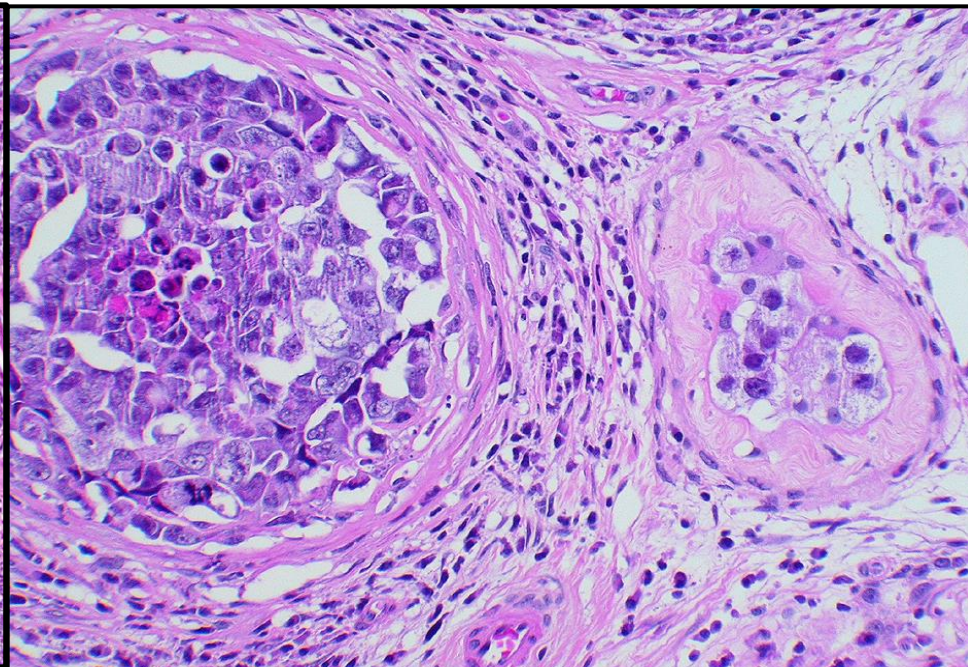
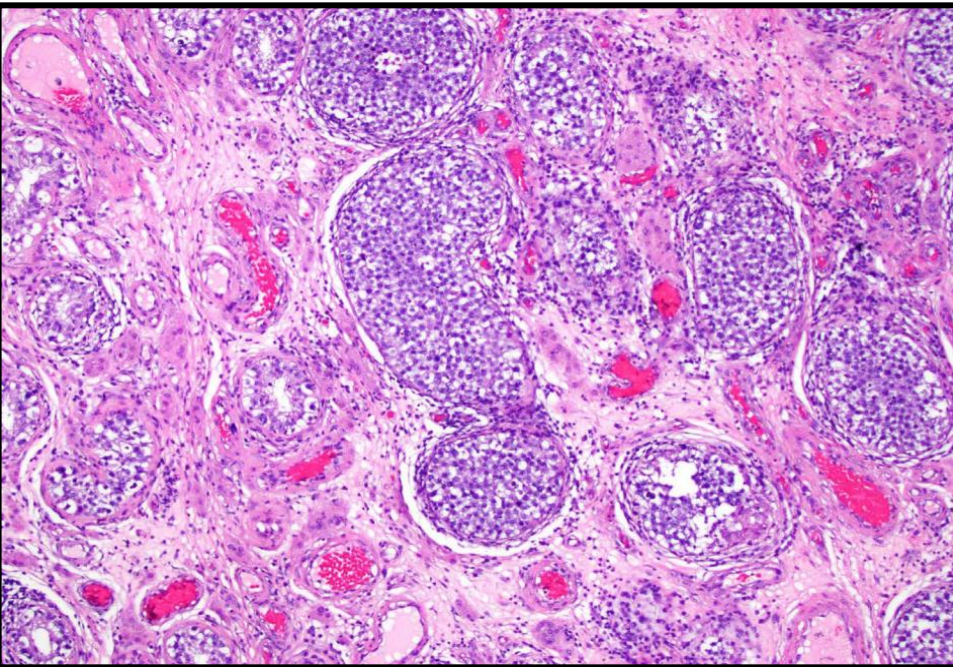


Germ cell neoplasia in situ  
immunohistochemistry

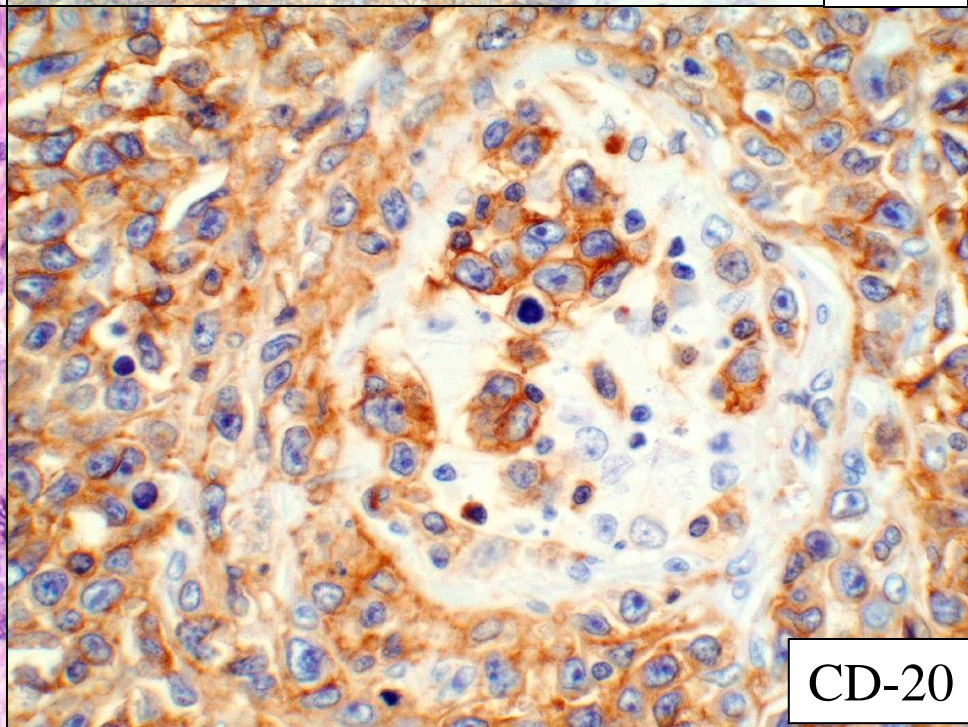
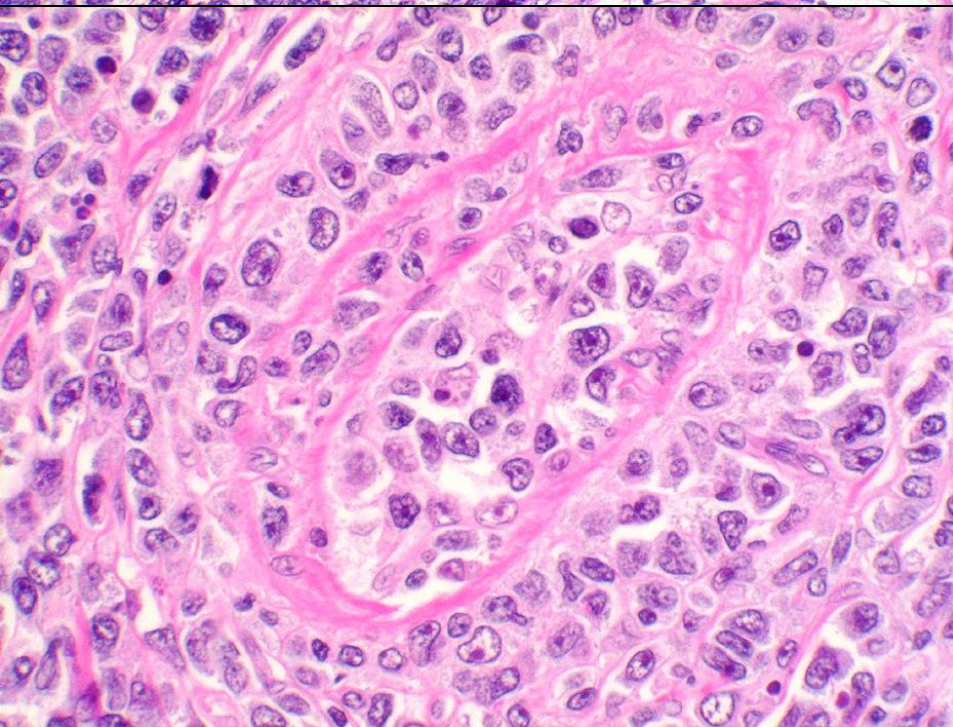
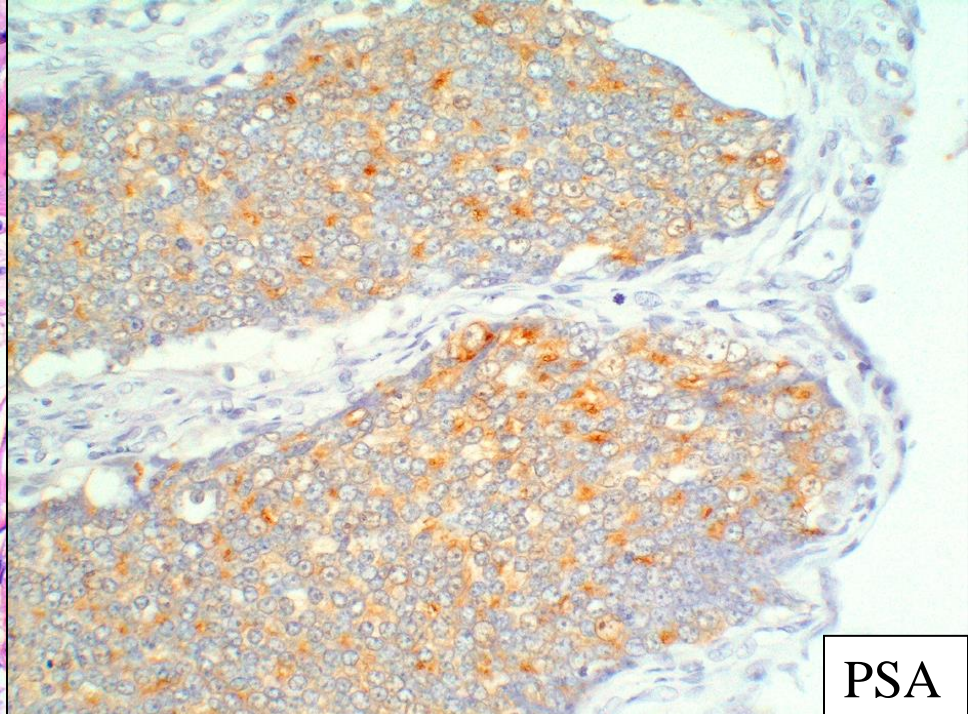
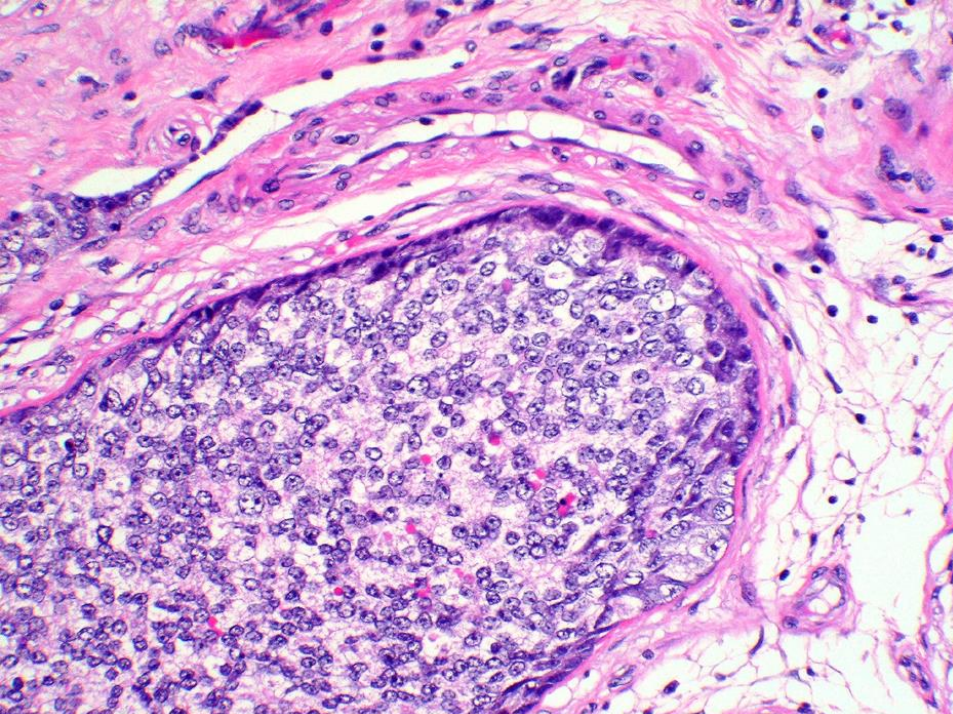




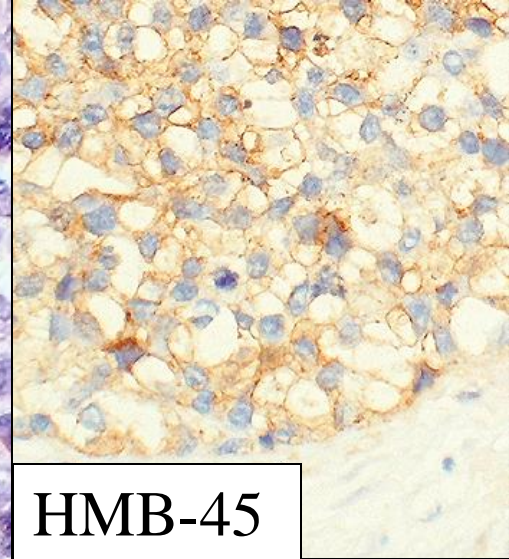
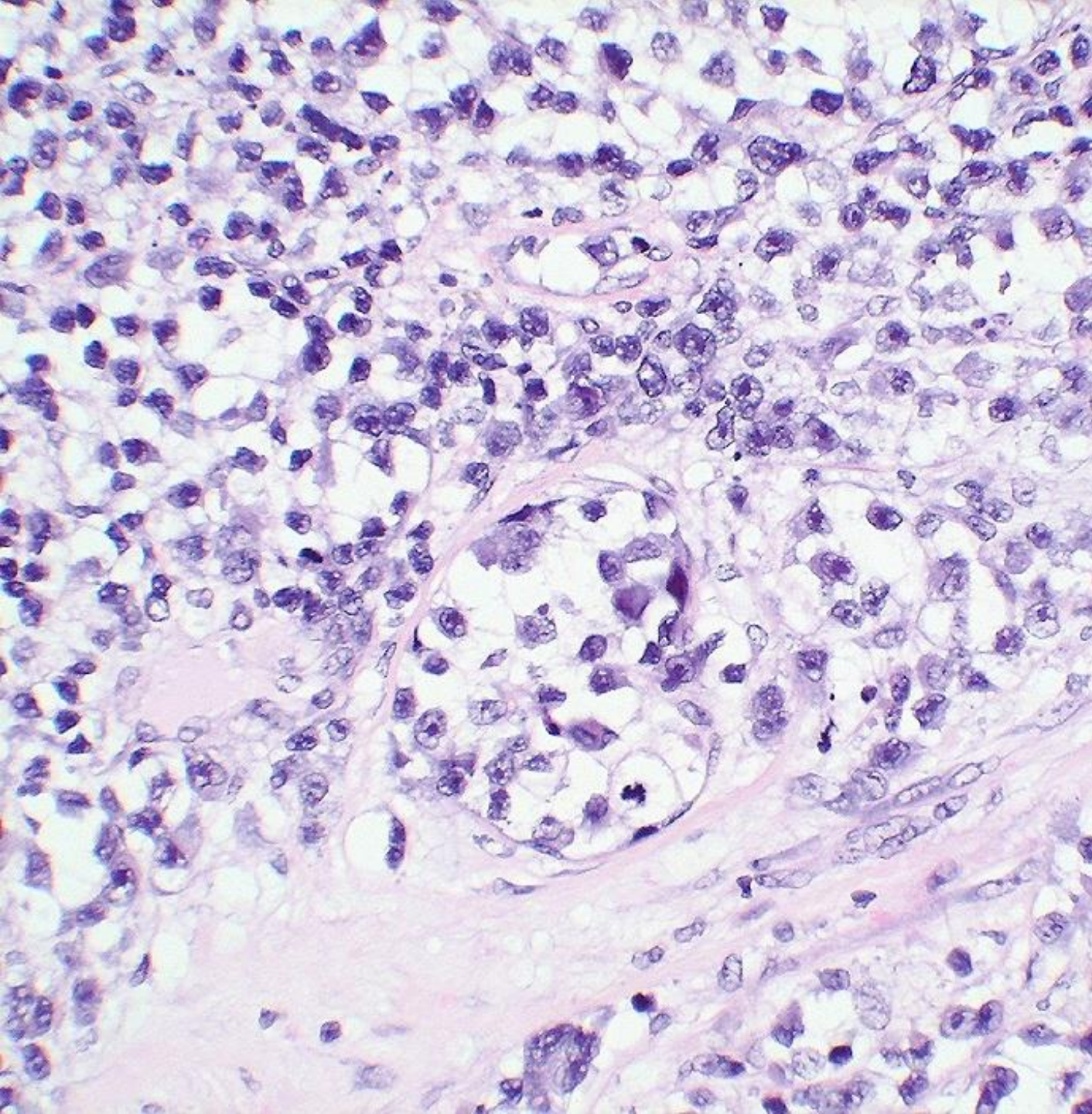
Not everything within a tubule is GCNIS



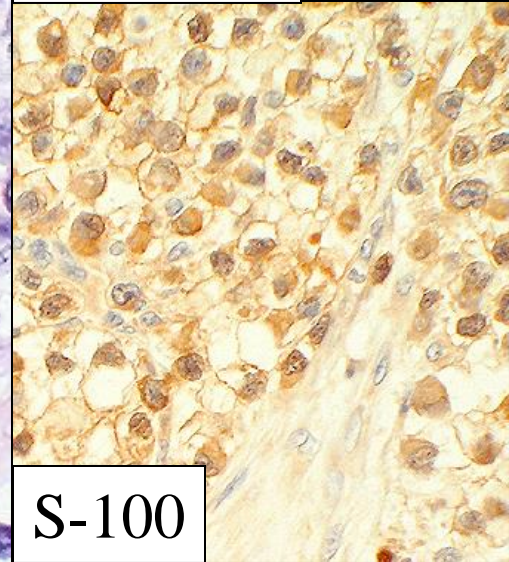








HMB-45

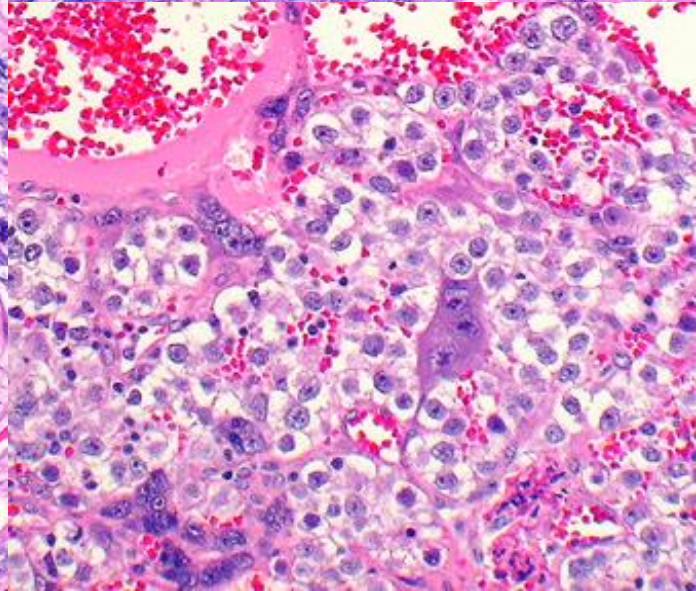
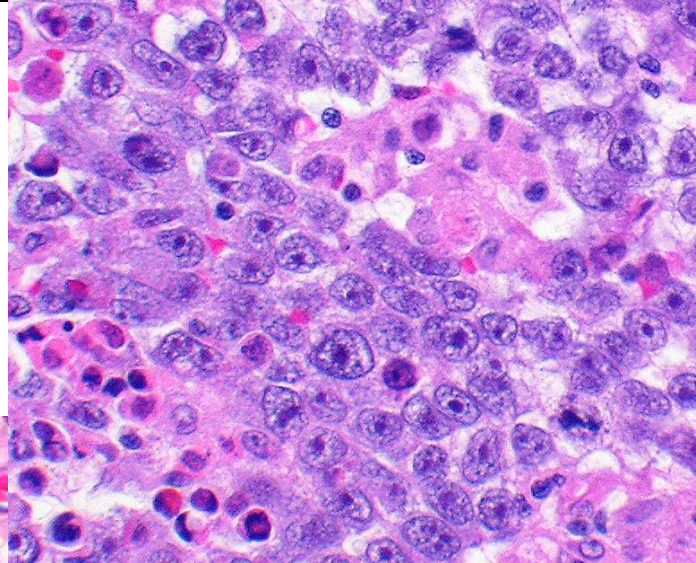
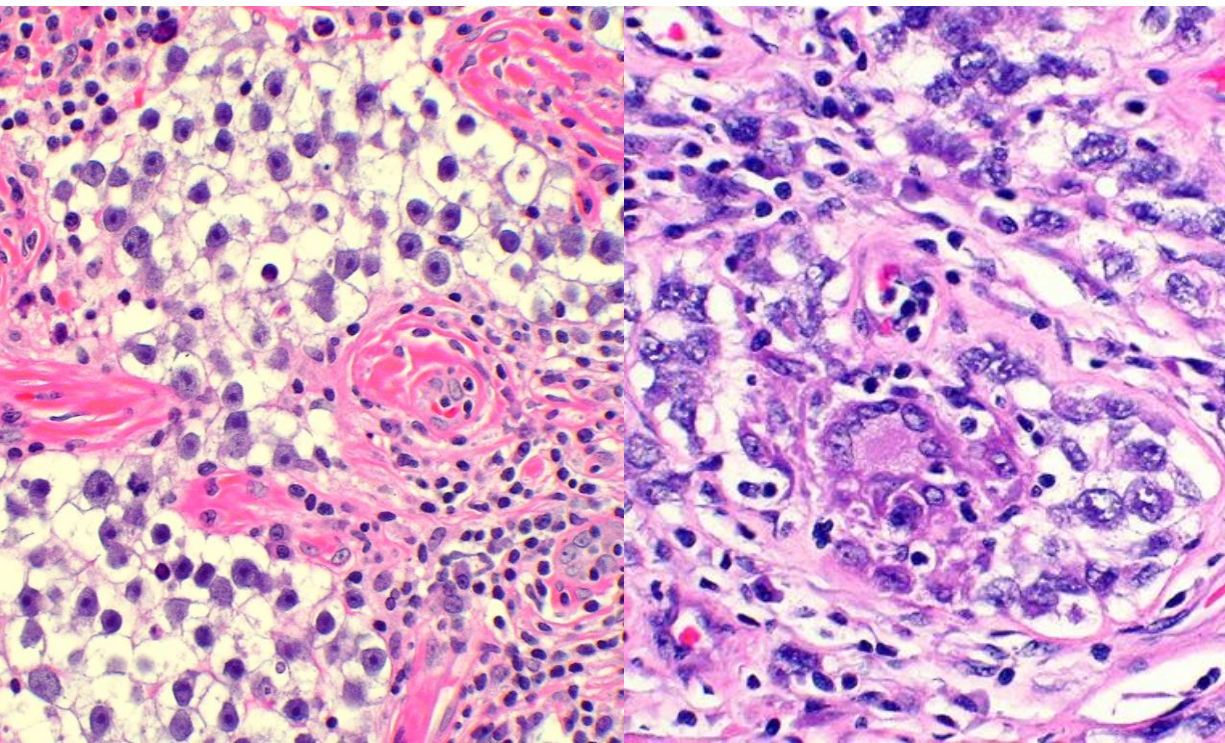


S-100

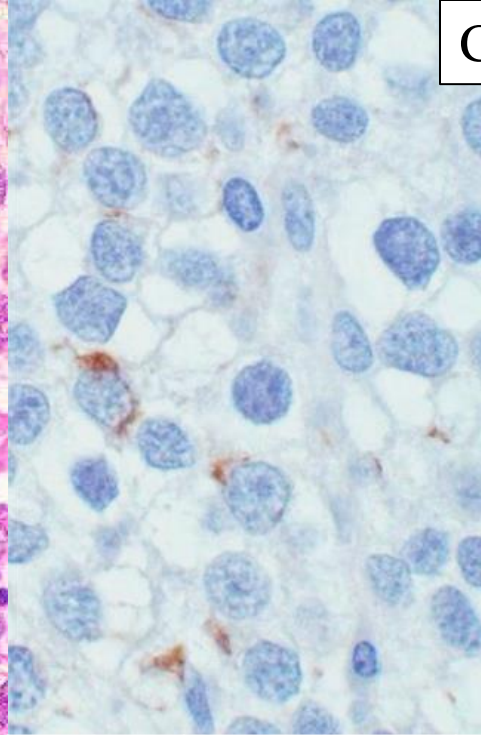
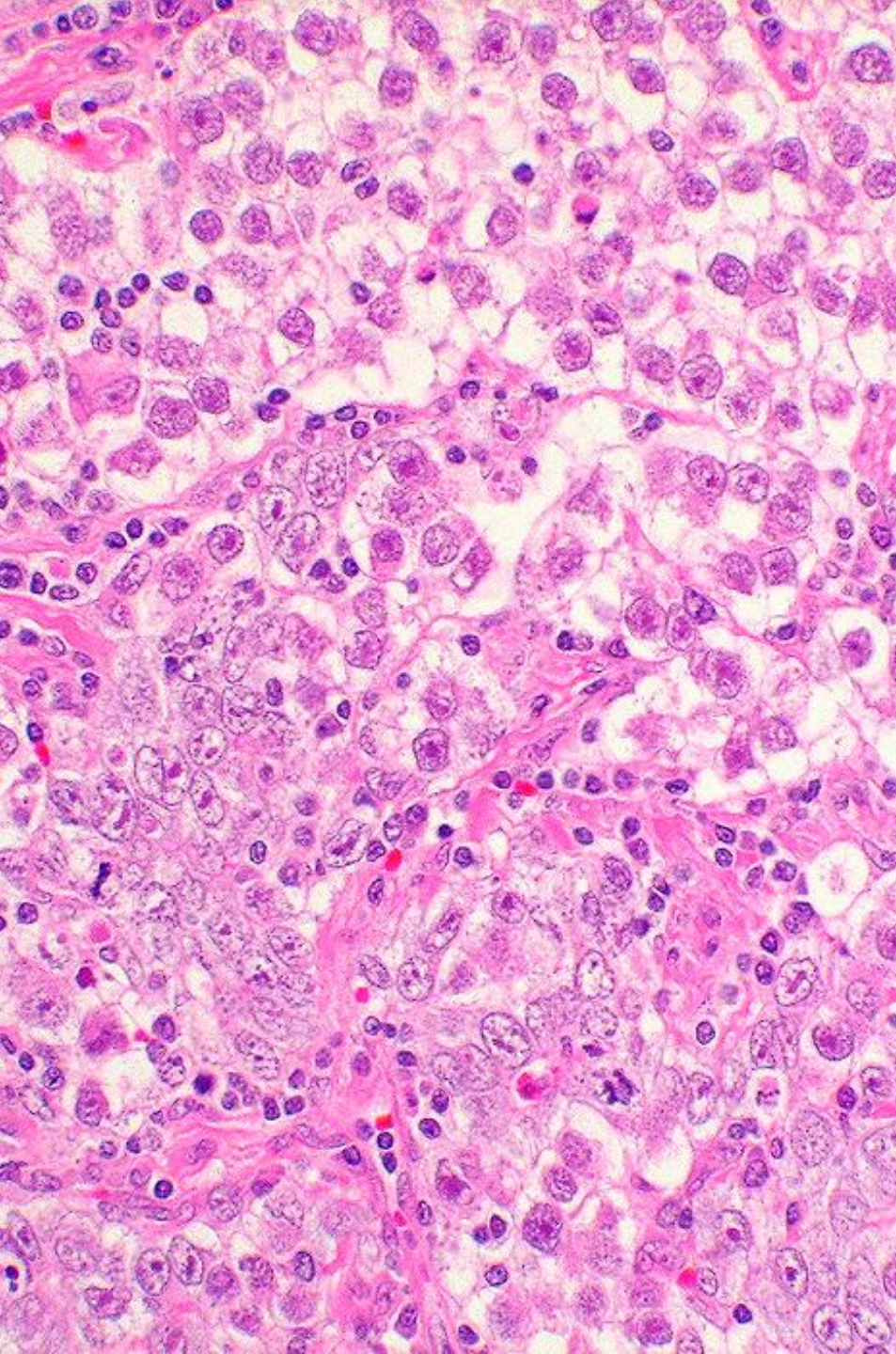


# When is a seminoma-looking germ cell tumor not a usual seminoma?

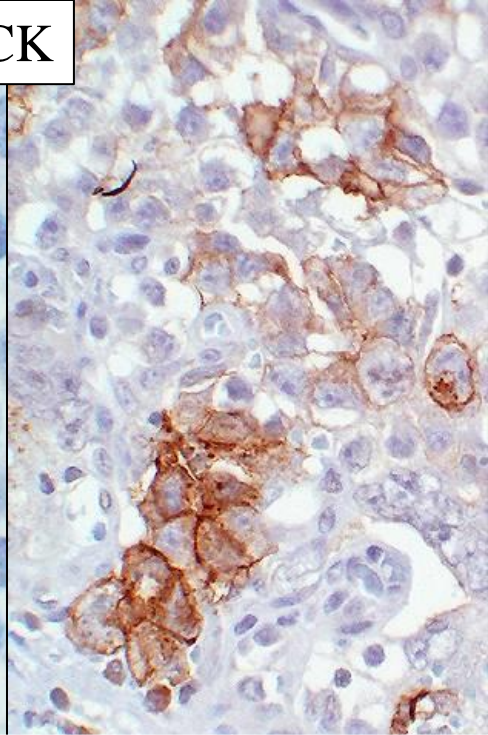
- Seminoma with atypia
  - Morphology
  - Immunohistochemistry







CK



|                     | Seminoma    | Emb Ca                     | YST         |
|---------------------|-------------|----------------------------|-------------|
| PLAP                | Cytoplasmic | Cytoplasmic                | Cytoplasmic |
| C-kit               | Membranous  | Negative                   | Negative*   |
| Oct-4               | Nuclear     | Nuclear                    | Negative*   |
| CD-30               | Negative*   | Cytoplasmic/<br>membranous | Negative*   |
| Gly-3               | Negative    | Negative                   | Cytoplasmic |
| Sall-4 <sup>^</sup> | Nuclear     | Nuclear                    | Nuclear     |

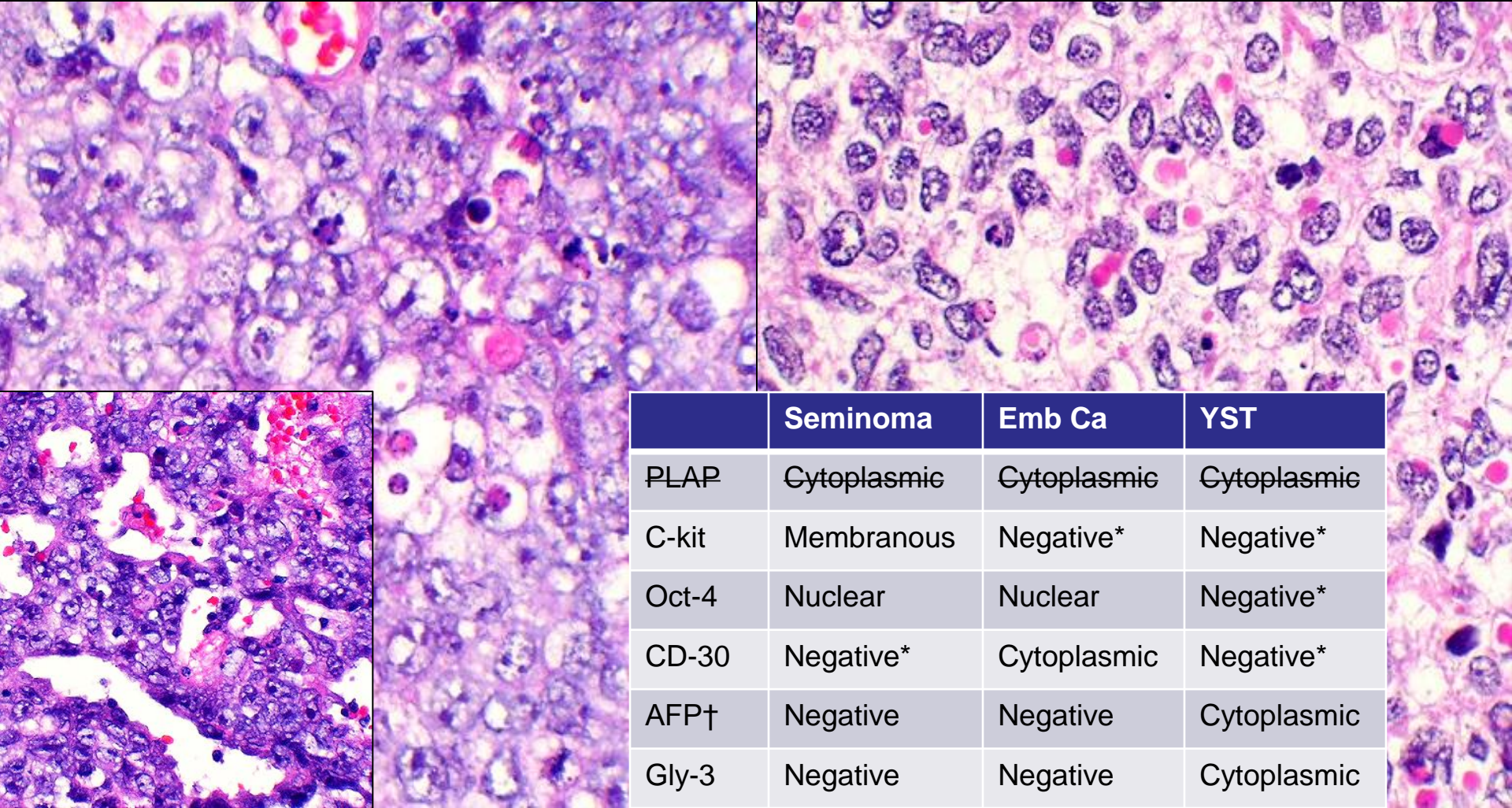
\* Could be focal and weak positive in M-GCT

<sup>^</sup> Sall-4 also in some teratoma components



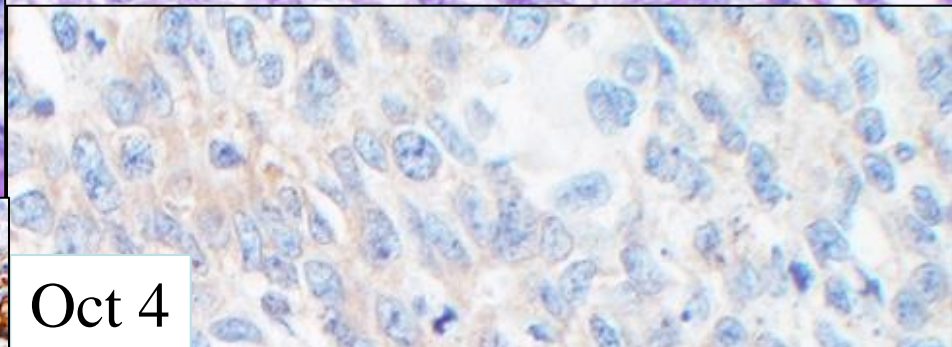
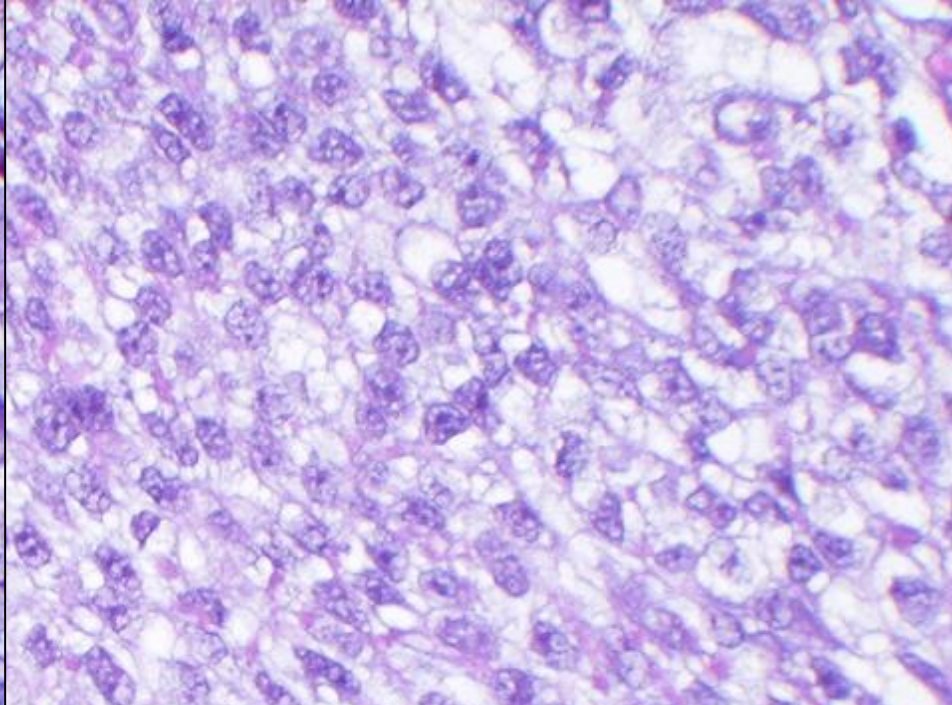
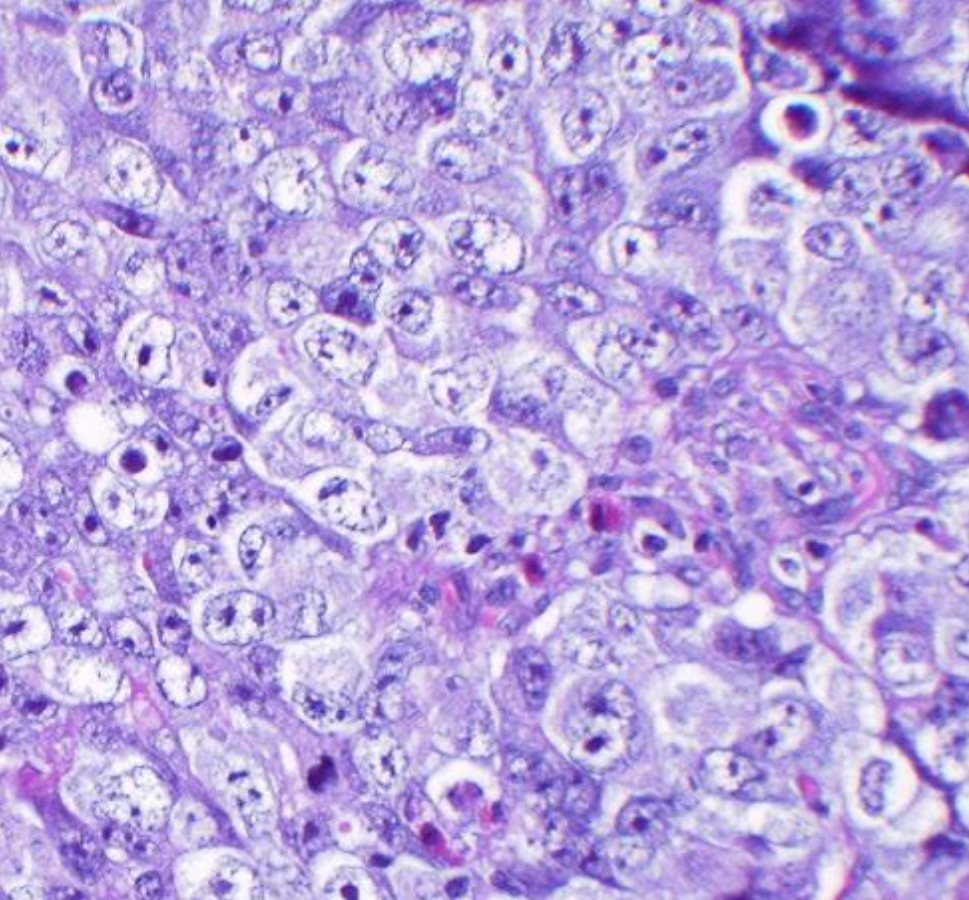
# When is an embryonal carcinoma-looking germ cell tumor not an embryonal carcinoma?

Cytology-morphology  
Immunohistochemistry

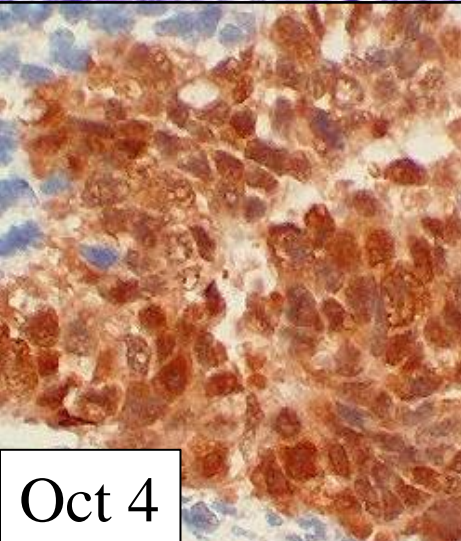


|       | Seminoma    | Emb Ca      | YST         |
|-------|-------------|-------------|-------------|
| PLAP  | Cytoplasmic | Cytoplasmic | Cytoplasmic |
| C-kit | Membranous  | Negative*   | Negative*   |
| Oct-4 | Nuclear     | Nuclear     | Negative*   |
| CD-30 | Negative*   | Cytoplasmic | Negative*   |
| AFP†  | Negative    | Negative    | Cytoplasmic |
| Gly-3 | Negative    | Negative    | Cytoplasmic |

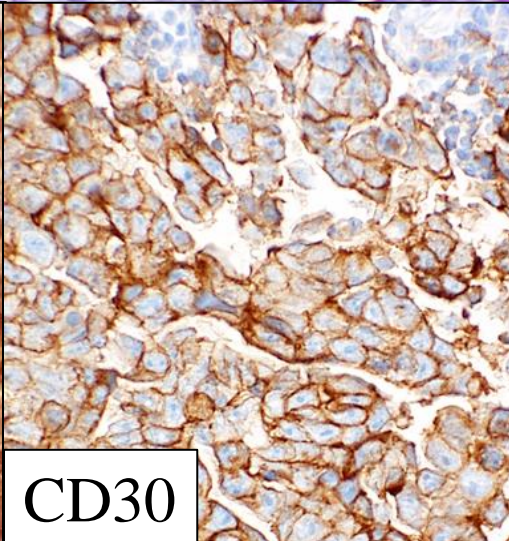




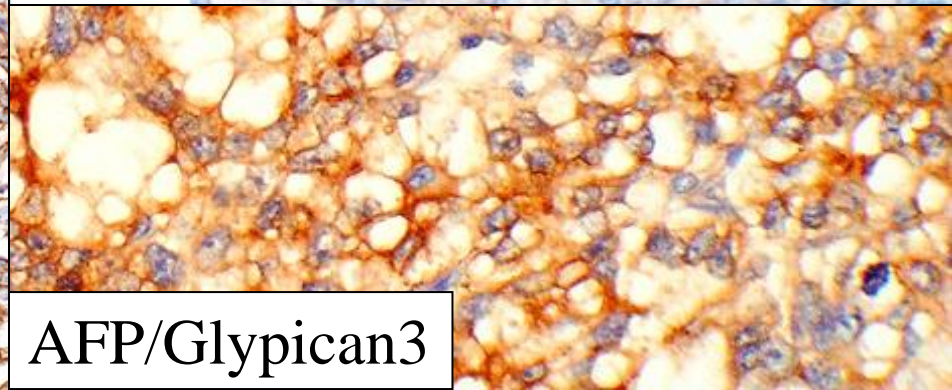
Oct 4



Oct 4

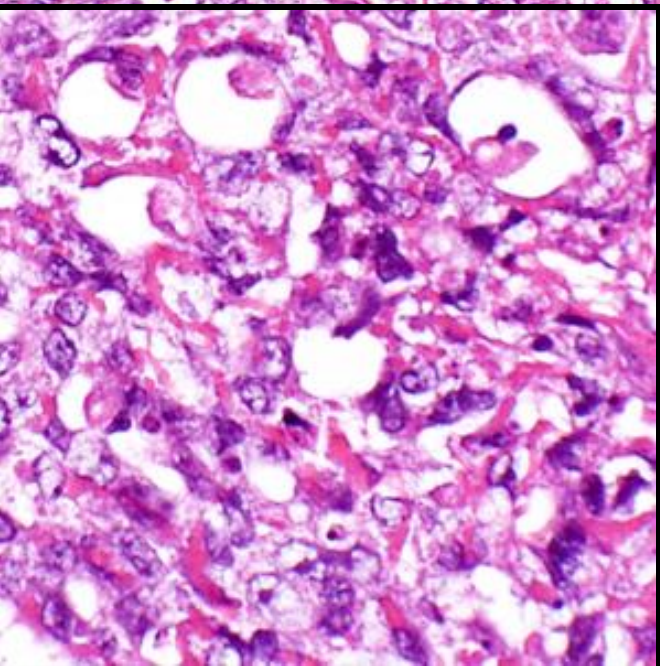
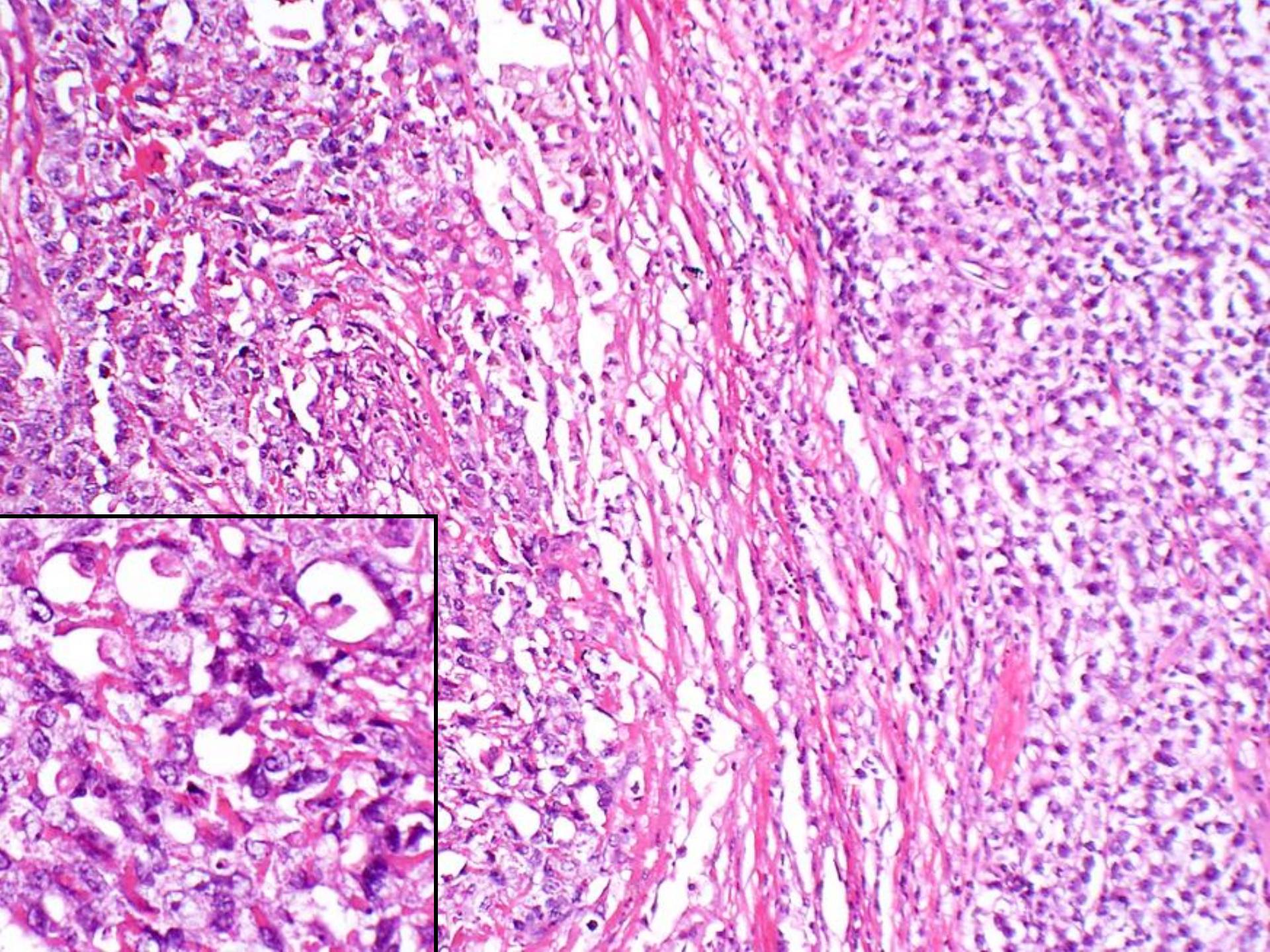


CD30

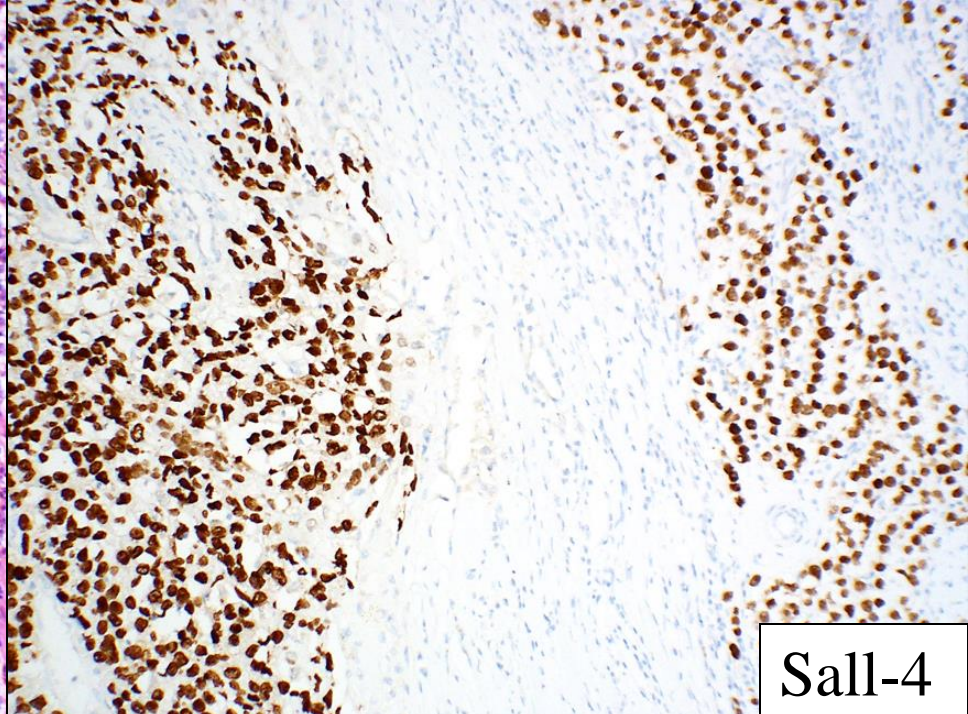
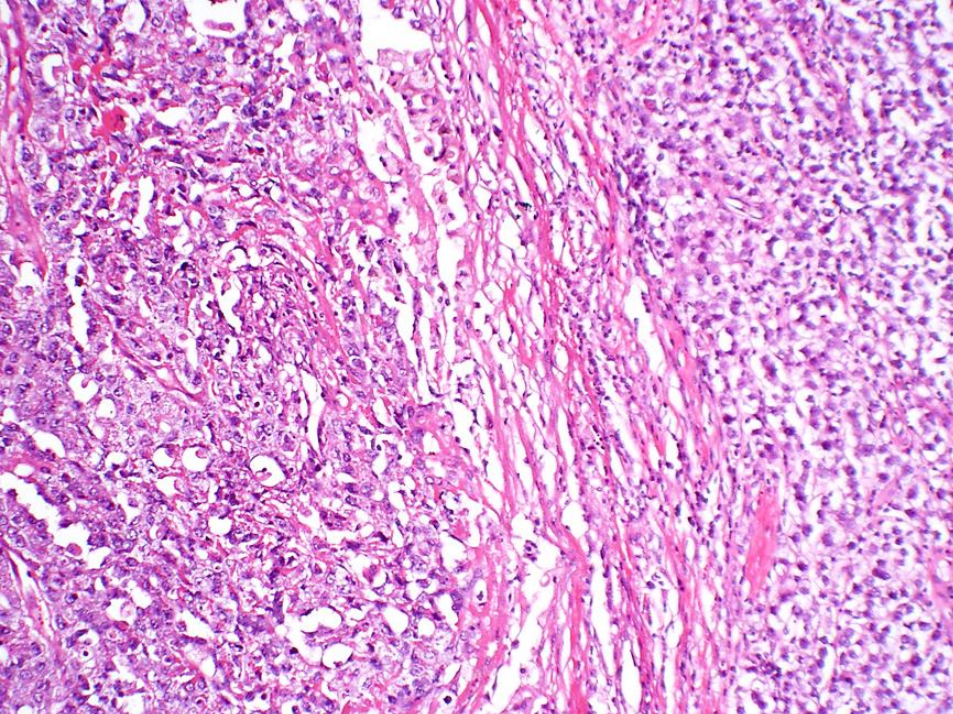


AFP/Glypican3

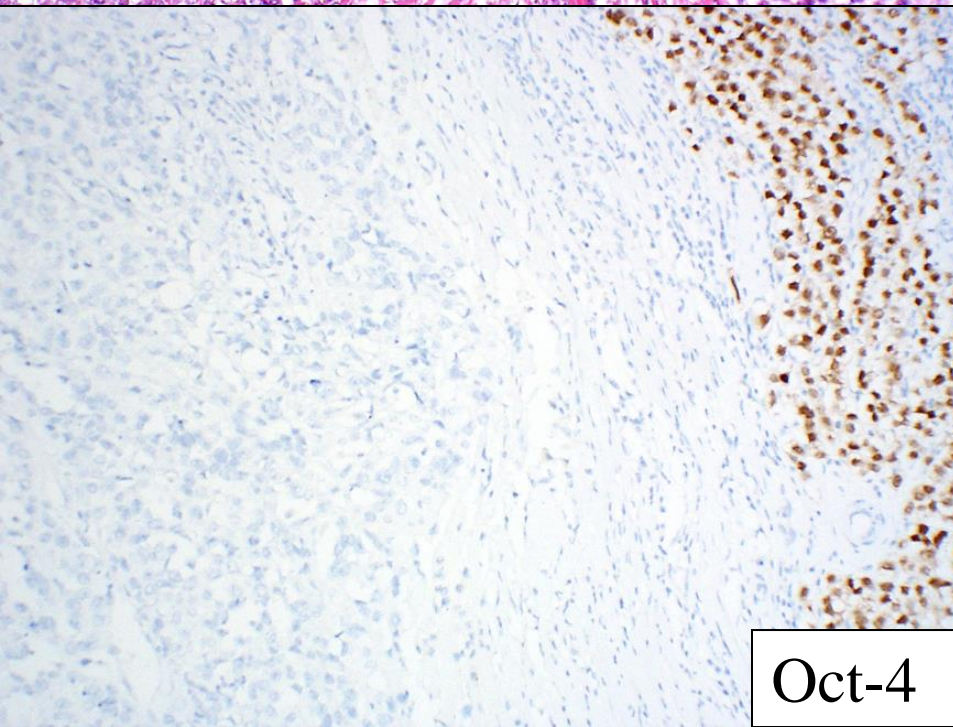




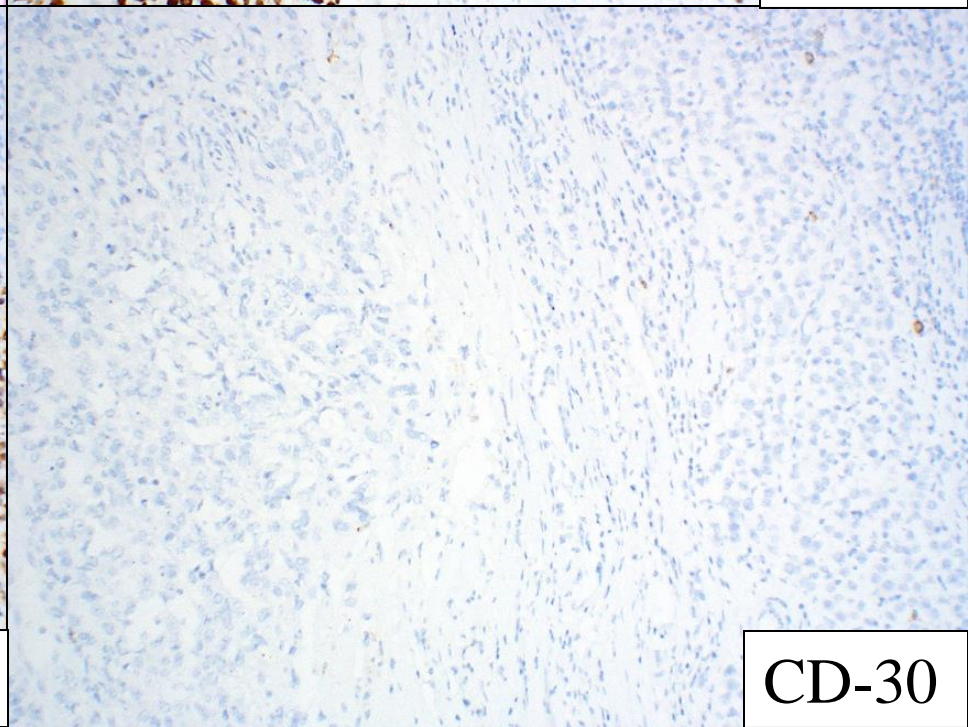




Sall-4



Oct-4

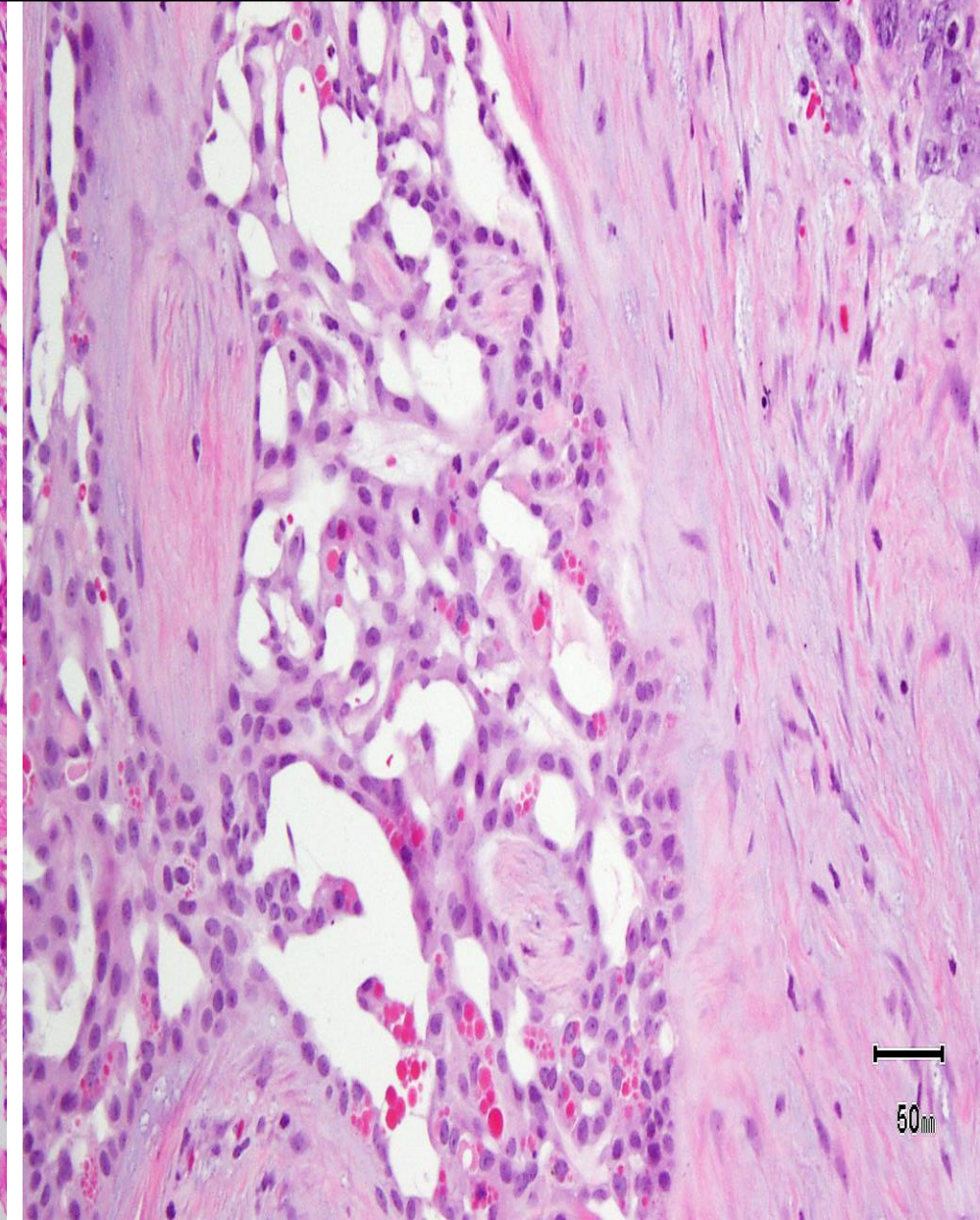
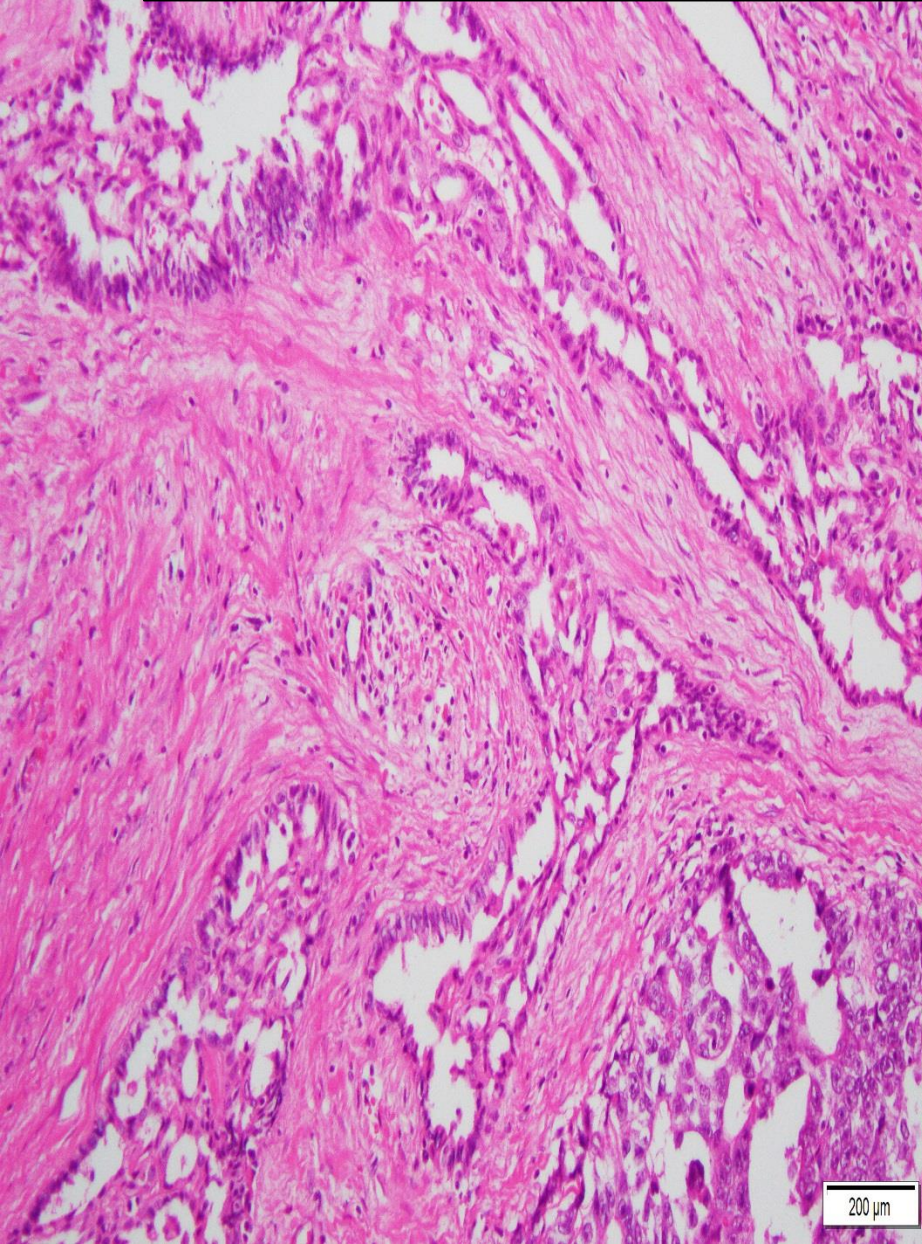


CD-30



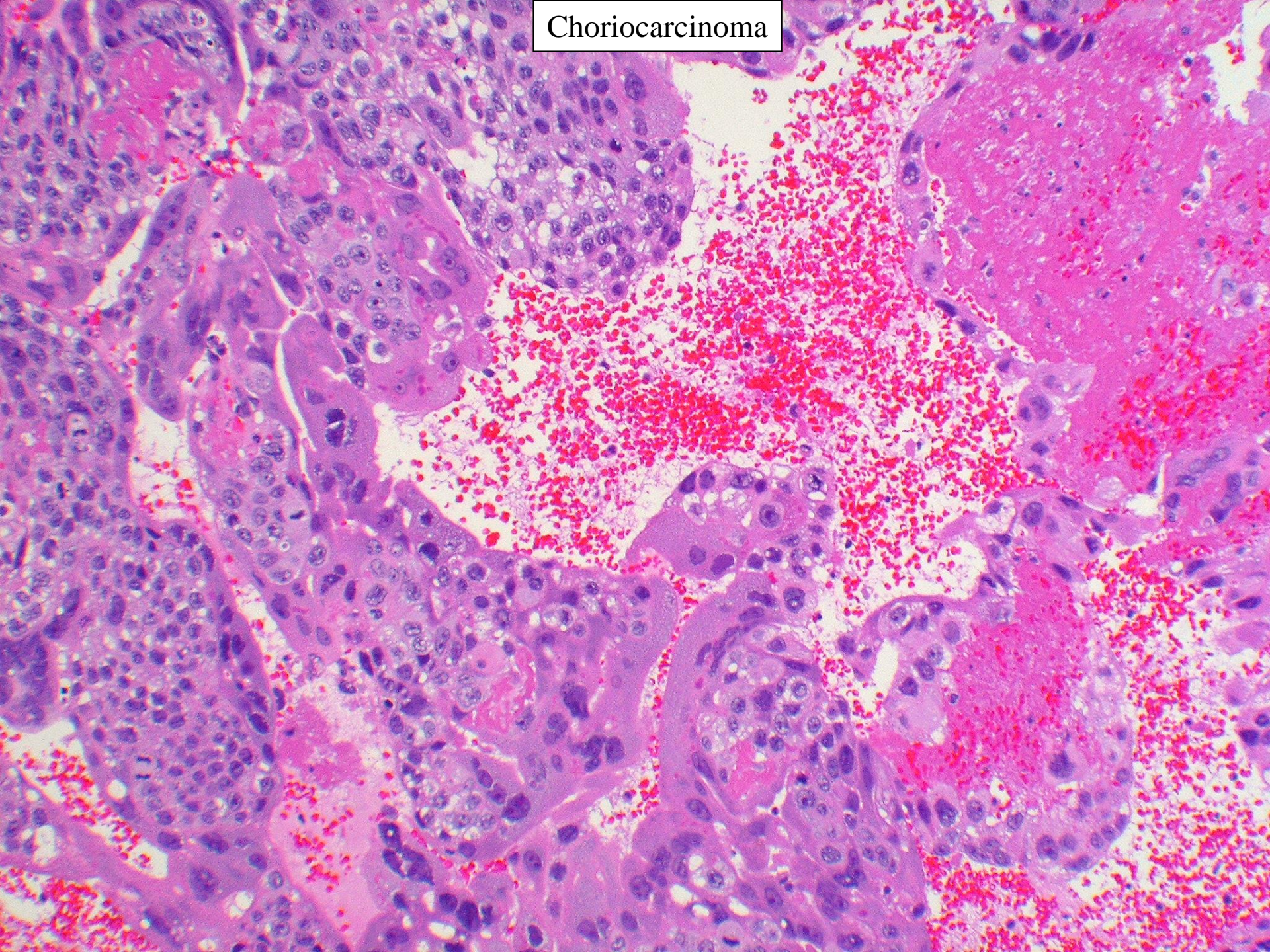


# When is a Yolk Sac Tumor-looking lesion not a Yolk Sac Tumor?



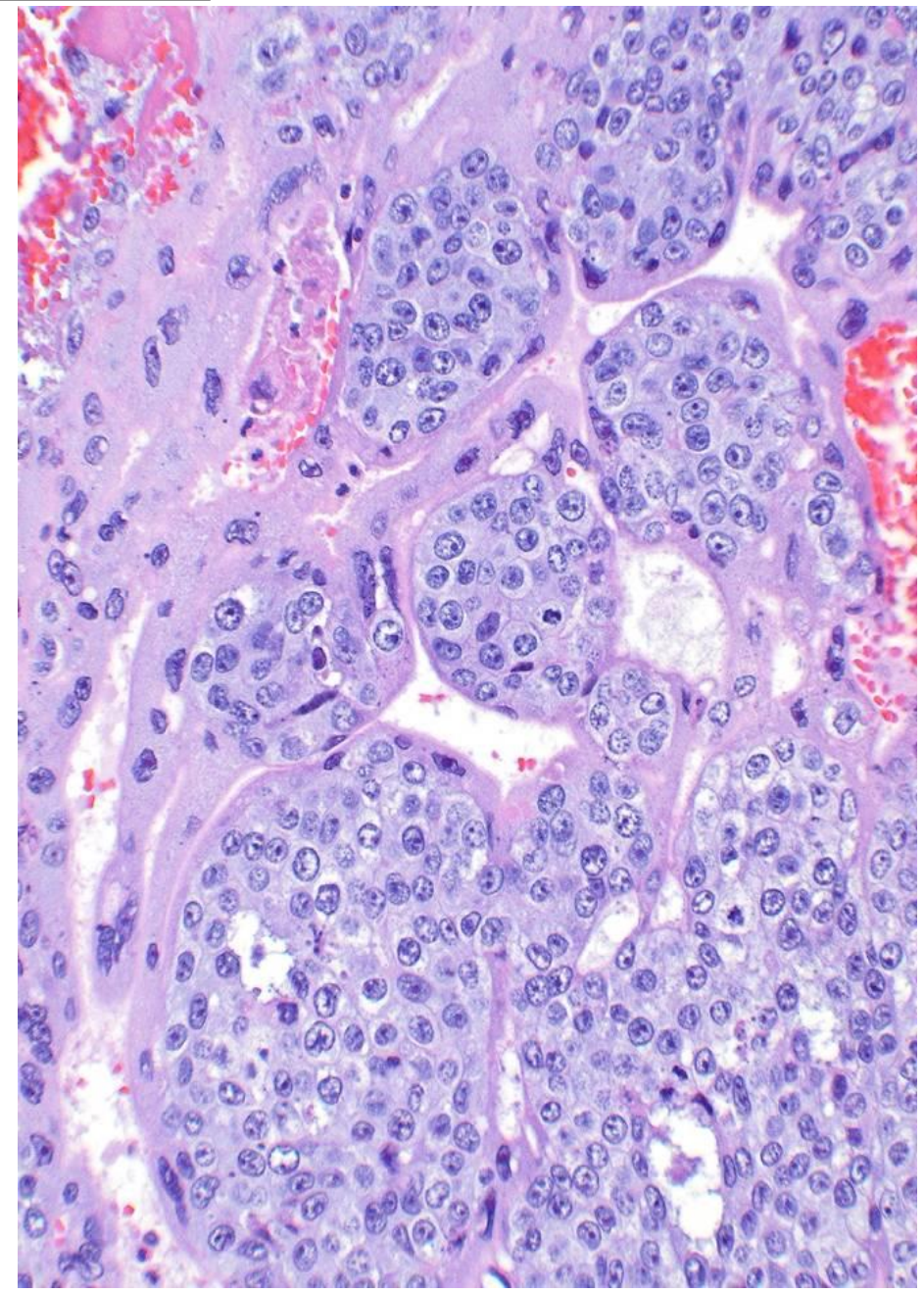
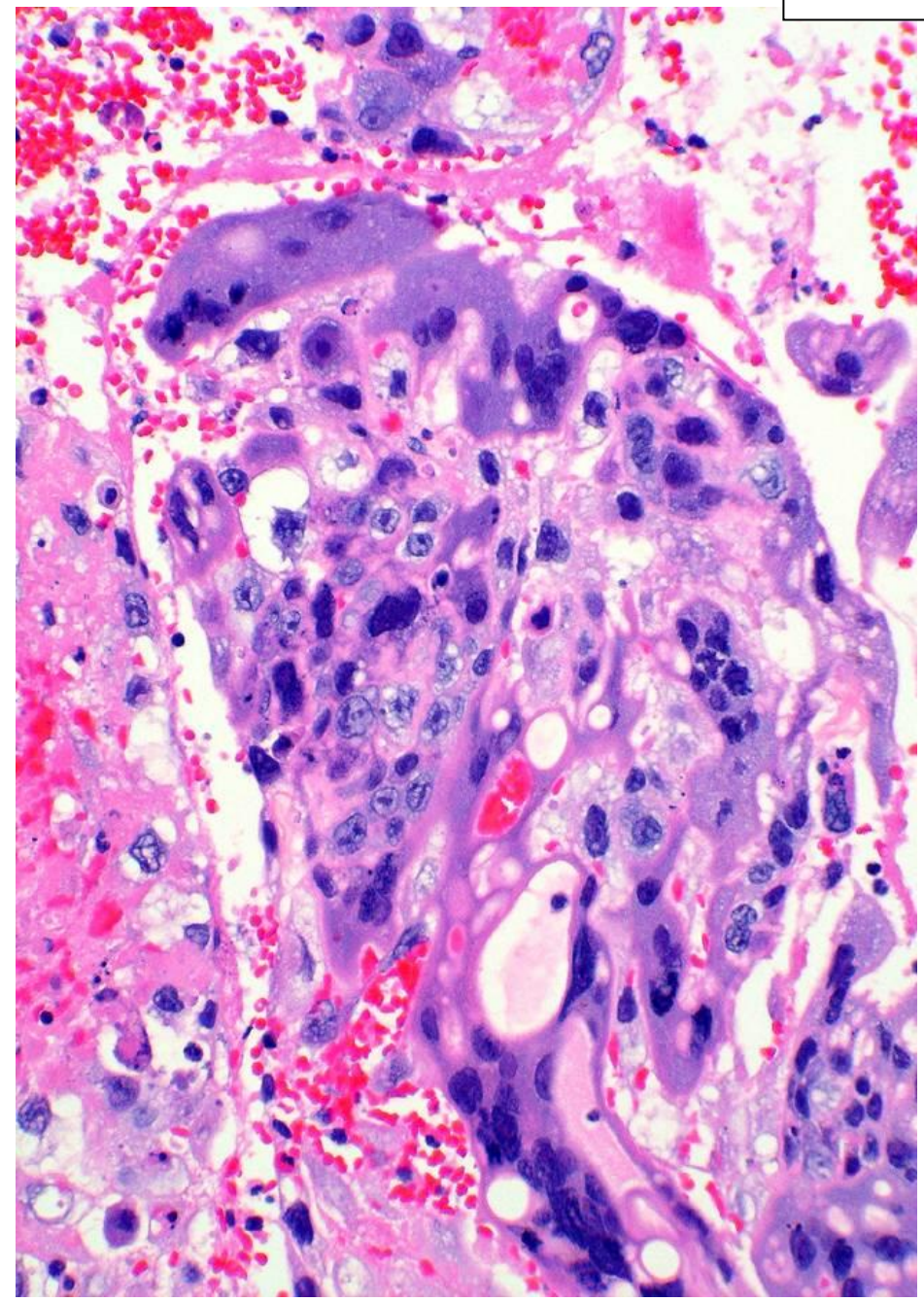


Choriocarcinoma

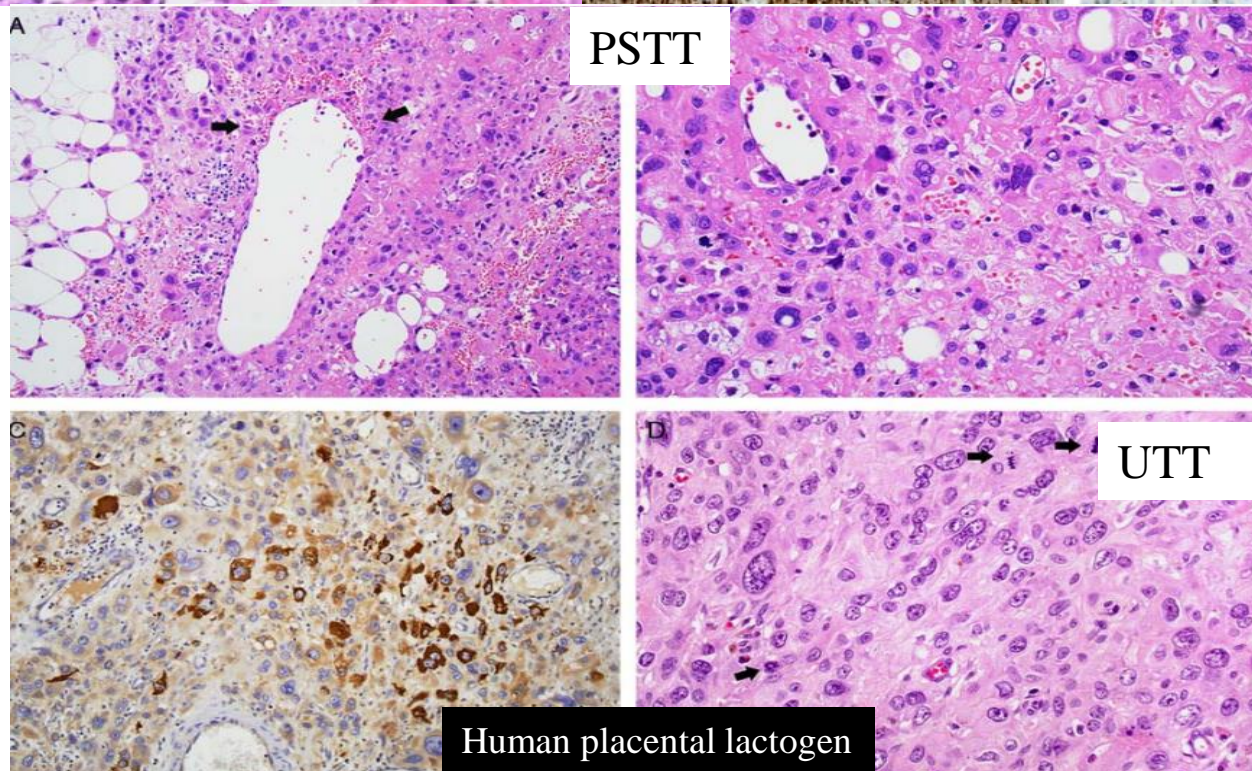
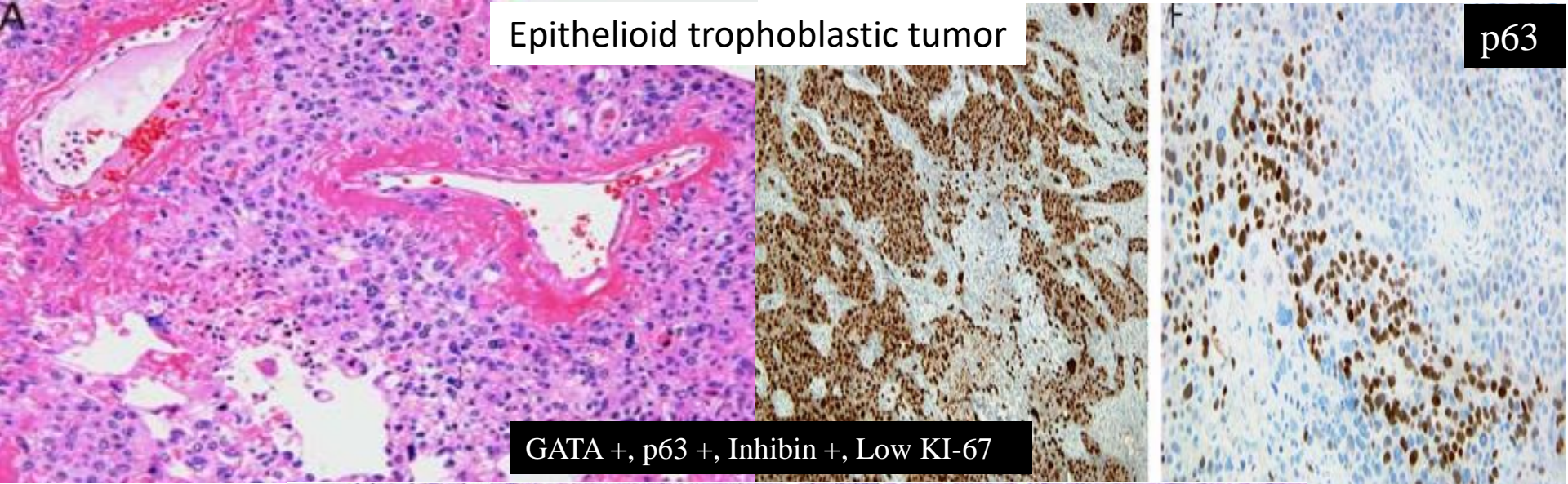




# Choriocarcinoma

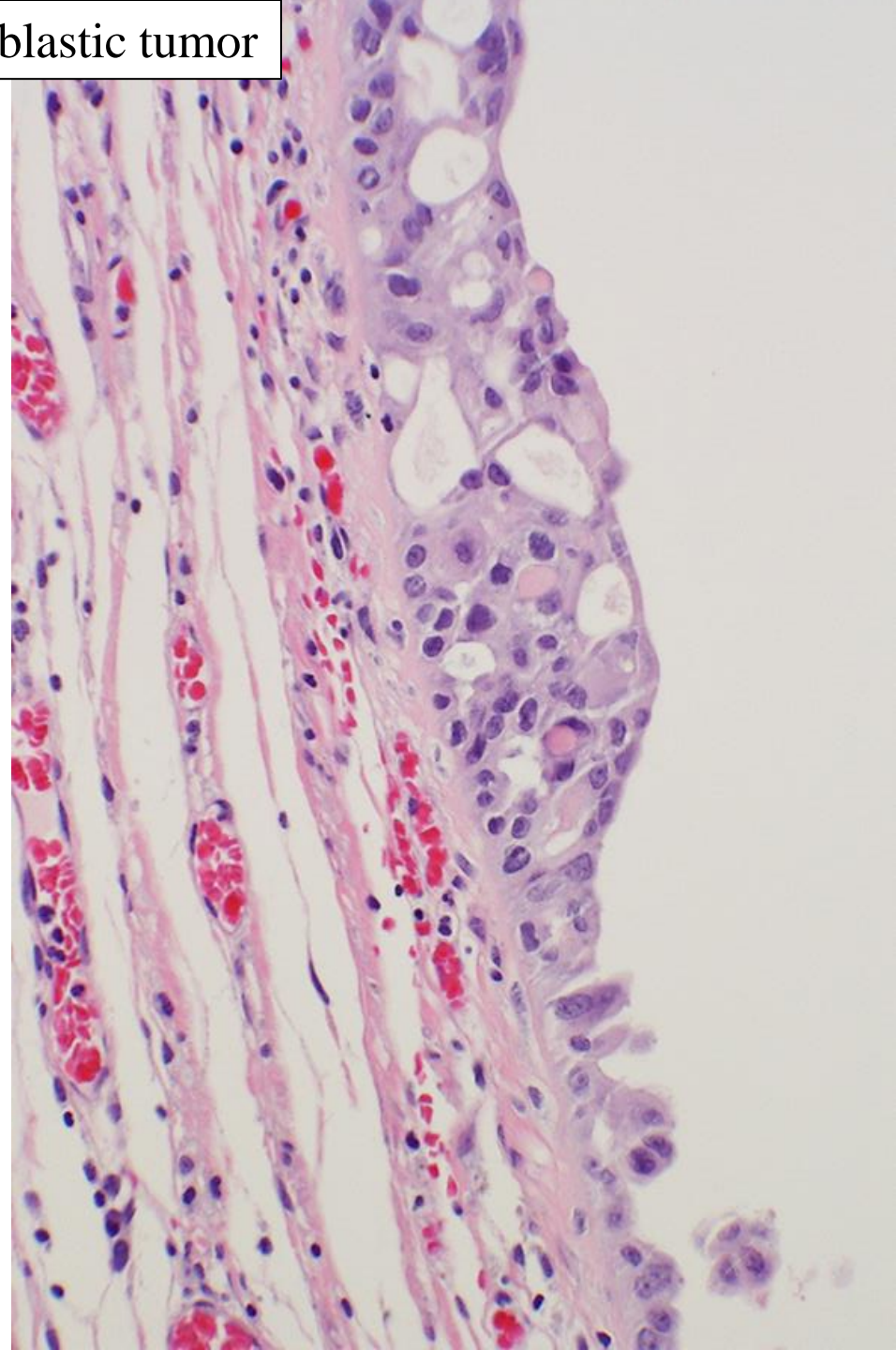
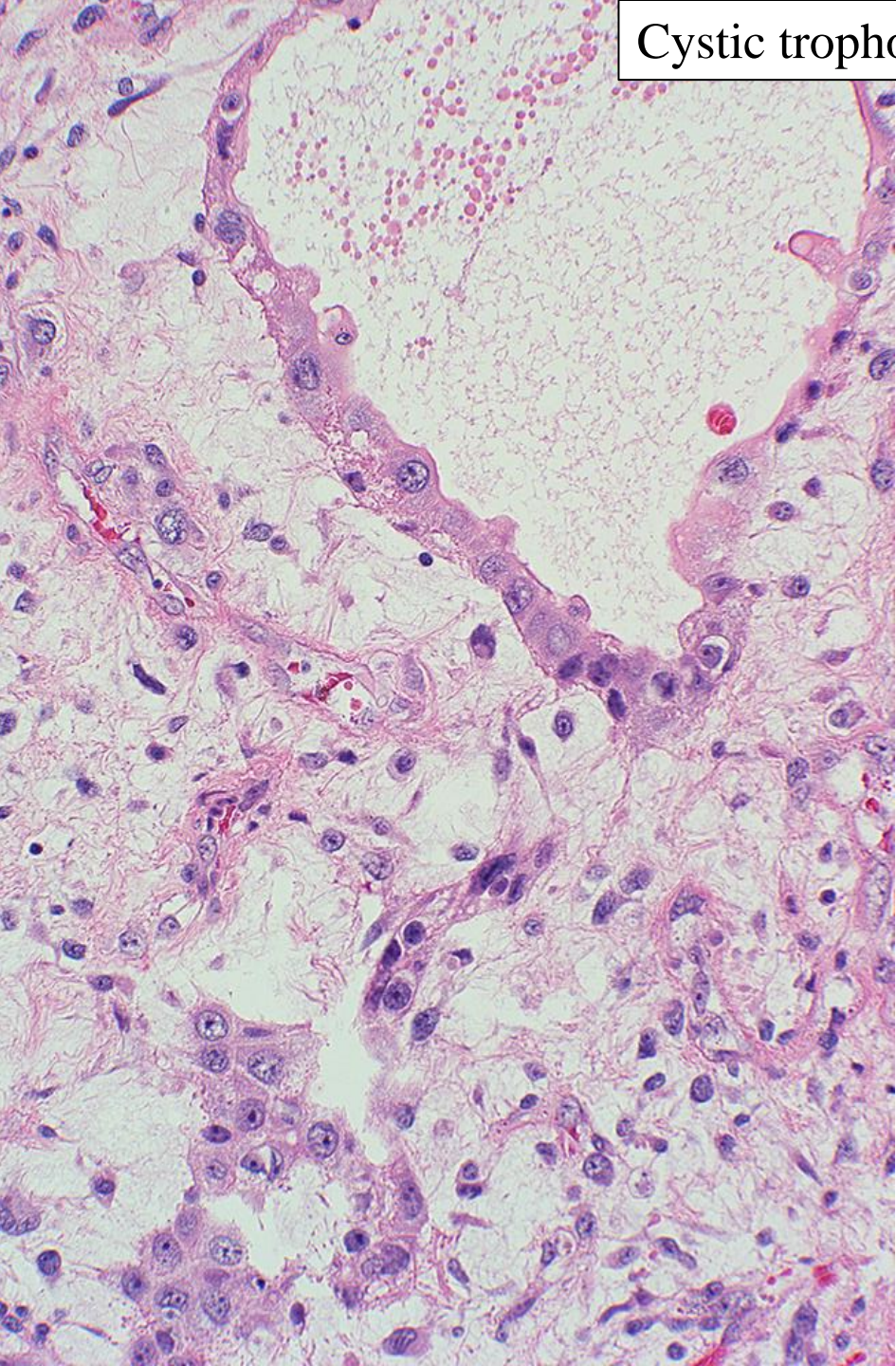








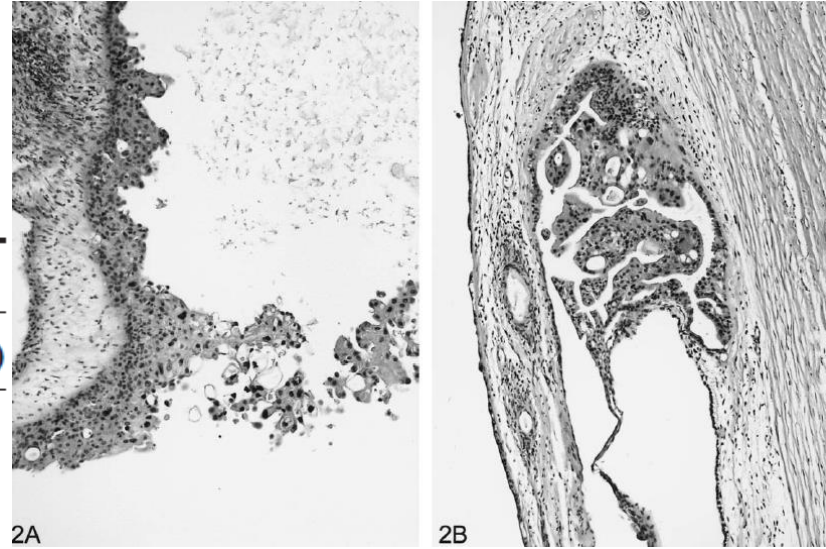
Cystic trophoblastic tumor





**TABLE 1.** Characteristics of Cystic Trophoblastic Tumor

| Characteristic            | No. of Cases (%) |
|---------------------------|------------------|
| Cystic                    | 17/17 (100)      |
| Association with teratoma | 17/17 (100)      |
| Well-circumscribed growth | 16/17 (94)       |
| hCG immunoreactivity      | 10/12 (83)       |
| Multifocality             | 13/17 (76)       |
| Fibrinoid changes         | 7/17 (41)        |
| Mitotic figures           | 3/17 (18)        |
| Hemorrhagic background    | 0/17 (0)         |



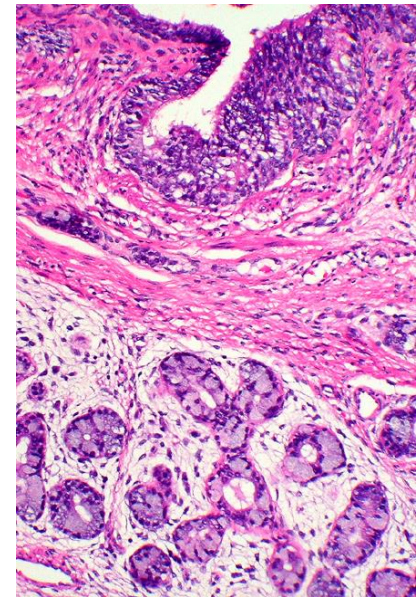
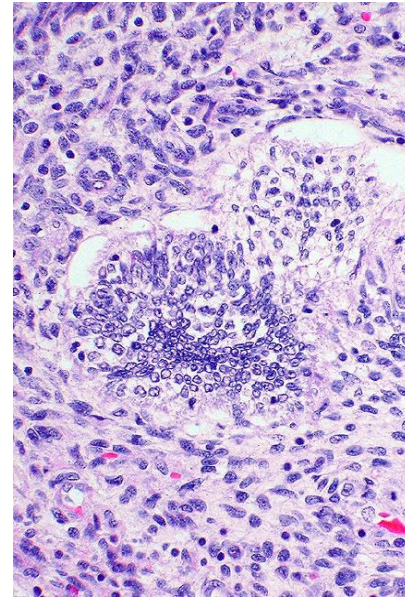
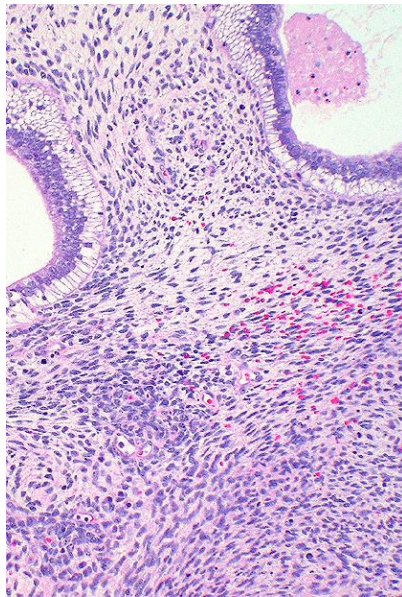
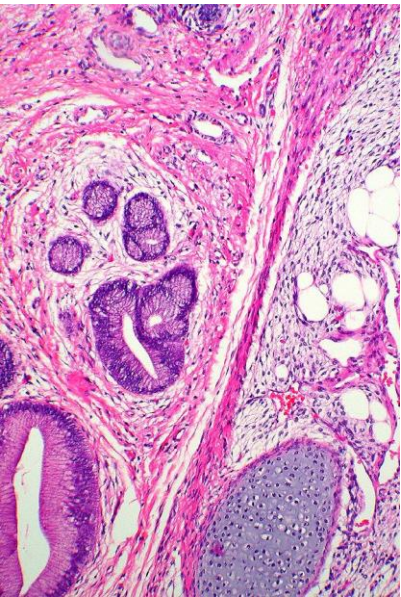
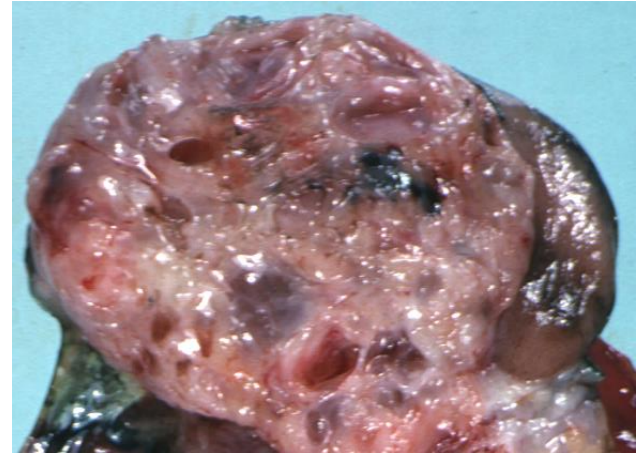
**Cystic Trophoblastic Tumor**

*A Nonaggressive Lesion in Postchemotherapy Resections of Patients With Testicular Germ Cell Tumors*

*Thomas M. Ulbright, MD,\* John D. Henley, MD,\* Oscar W. Cummings, MD,\* Richard S. Foster, MD,† and Liang Cheng, MD\**

# How do I subclassify the teratomatous component?

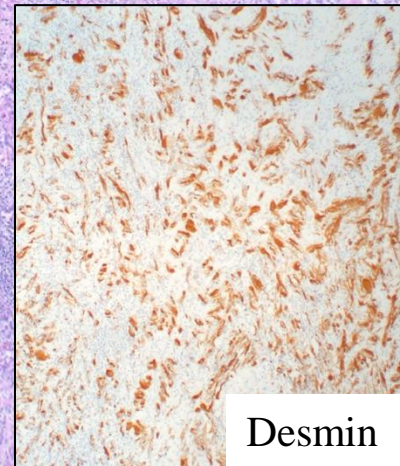
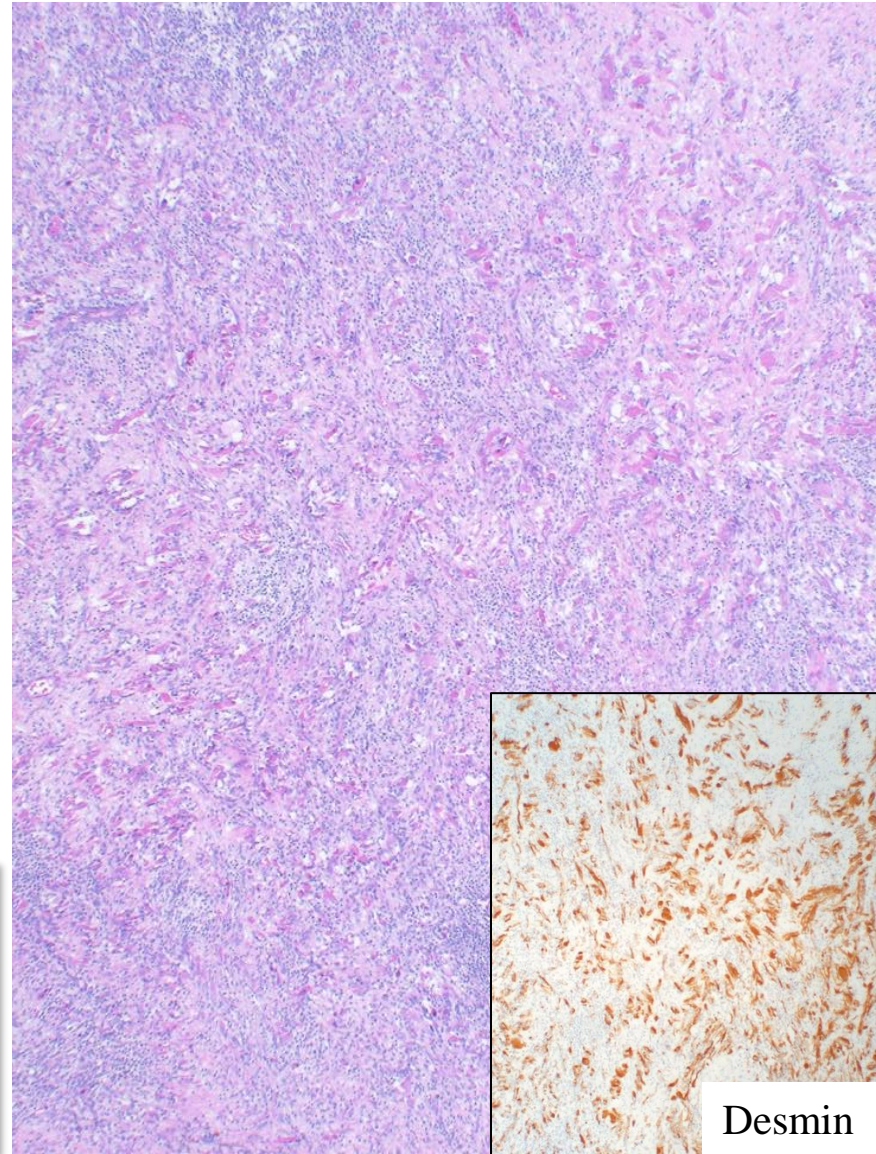
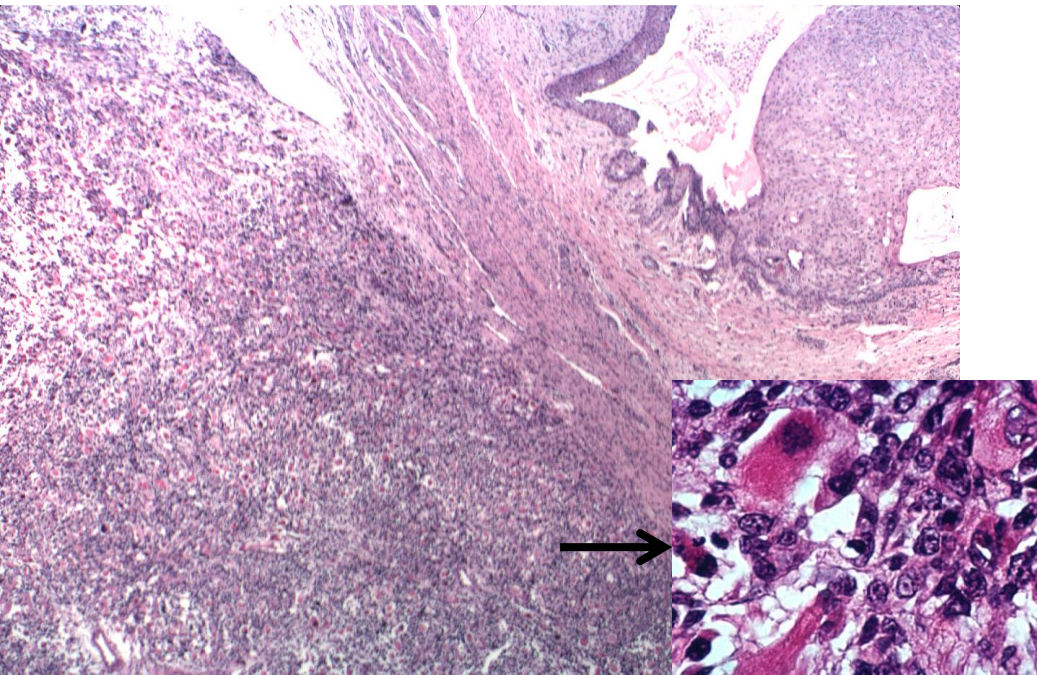
- ~~• Mature versus immature~~
- ~~• Neuroepithelial component~~
- Careful about “expansile” growth of any element





# What do you mean by “expansile growth” of any teratomatous element?

- Mostly, teratomatous elements grow in harmony
- Overgrowth of a single teratomatous component
  - 4X field (5mm)



Desmin

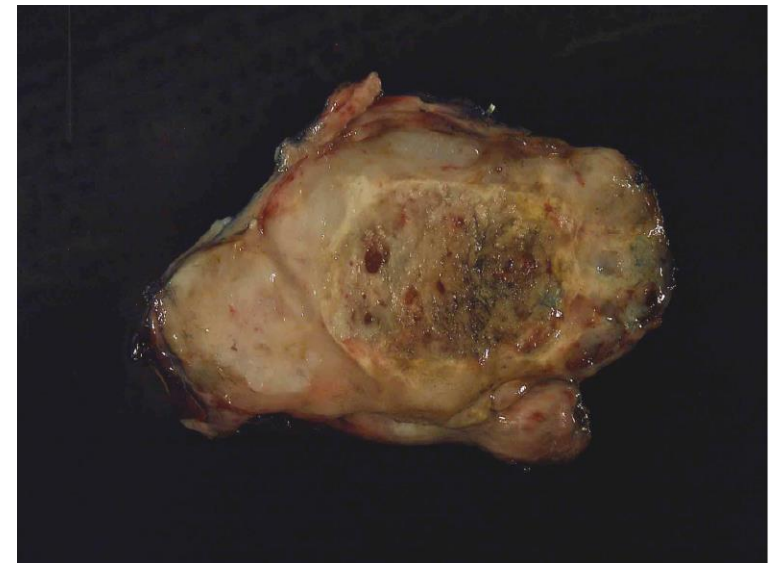
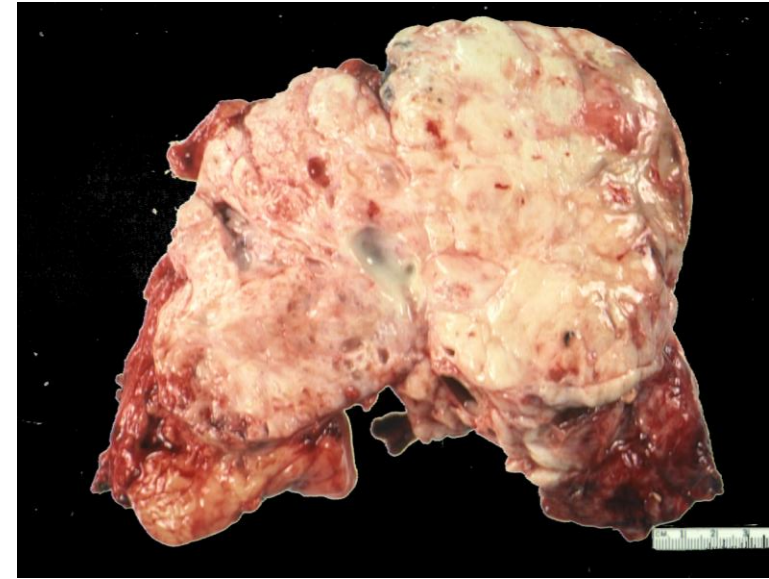


# What do you mean by “expansile growth” of any teratomatous element”

- How do I classify these lesions?

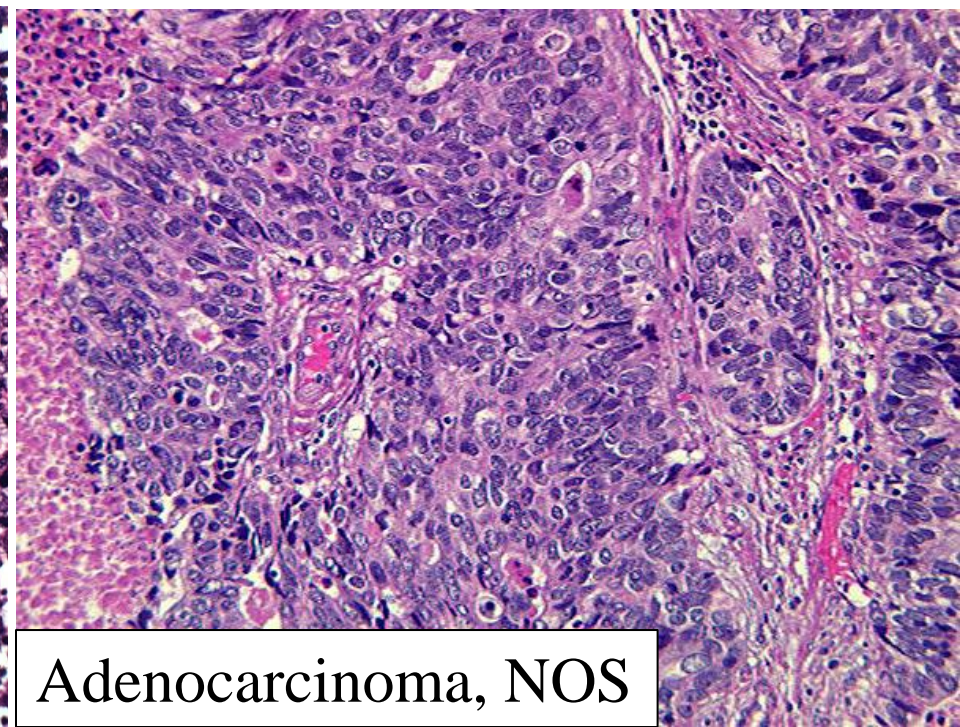
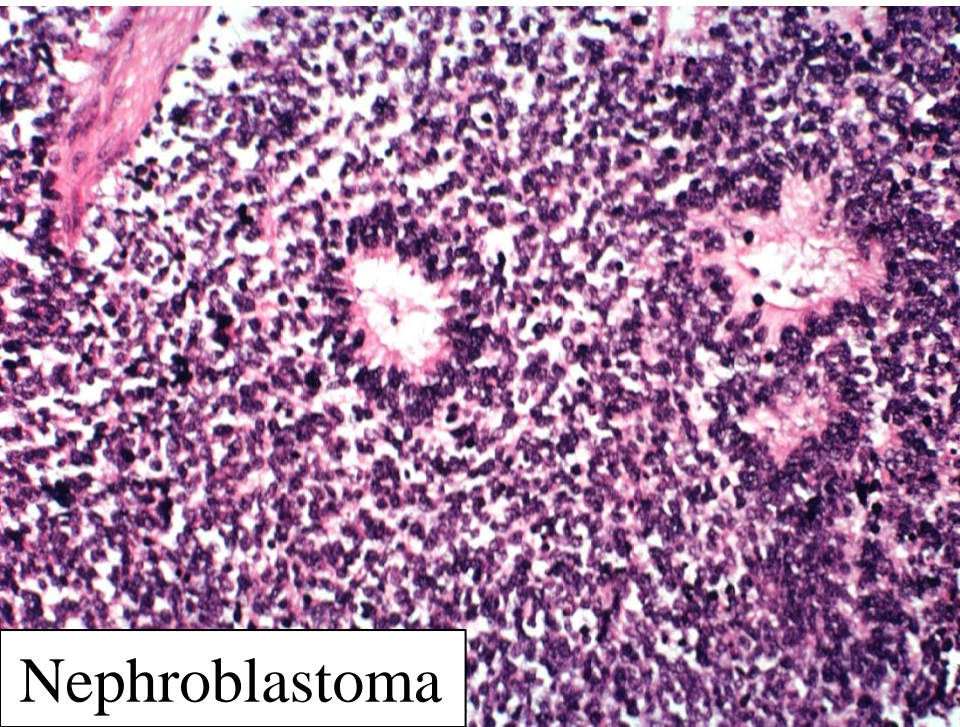
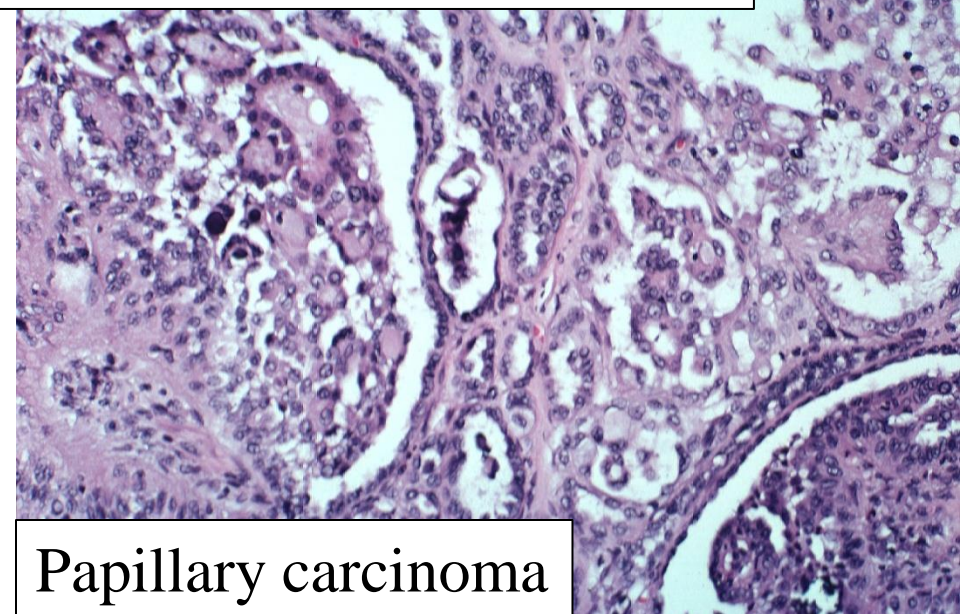
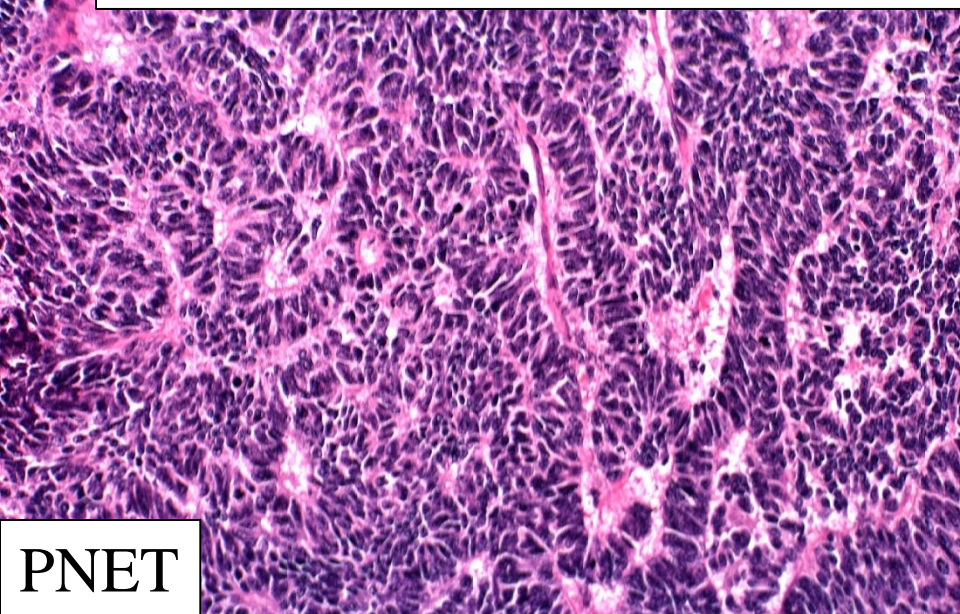
Secondary somatic-type malignancy (type) arising in association with teratoma/GCT

- When am I likely to encounter this?
  - In primary tumor
  - Residual mass post-chemo with a growing mass and negative markers
  - Late recurrence
- What does it mean clinically?
  - Testis vs. mediastinum
  - In primary vs. metastatic site





Examples of secondary somatic malignancies arising in GCT





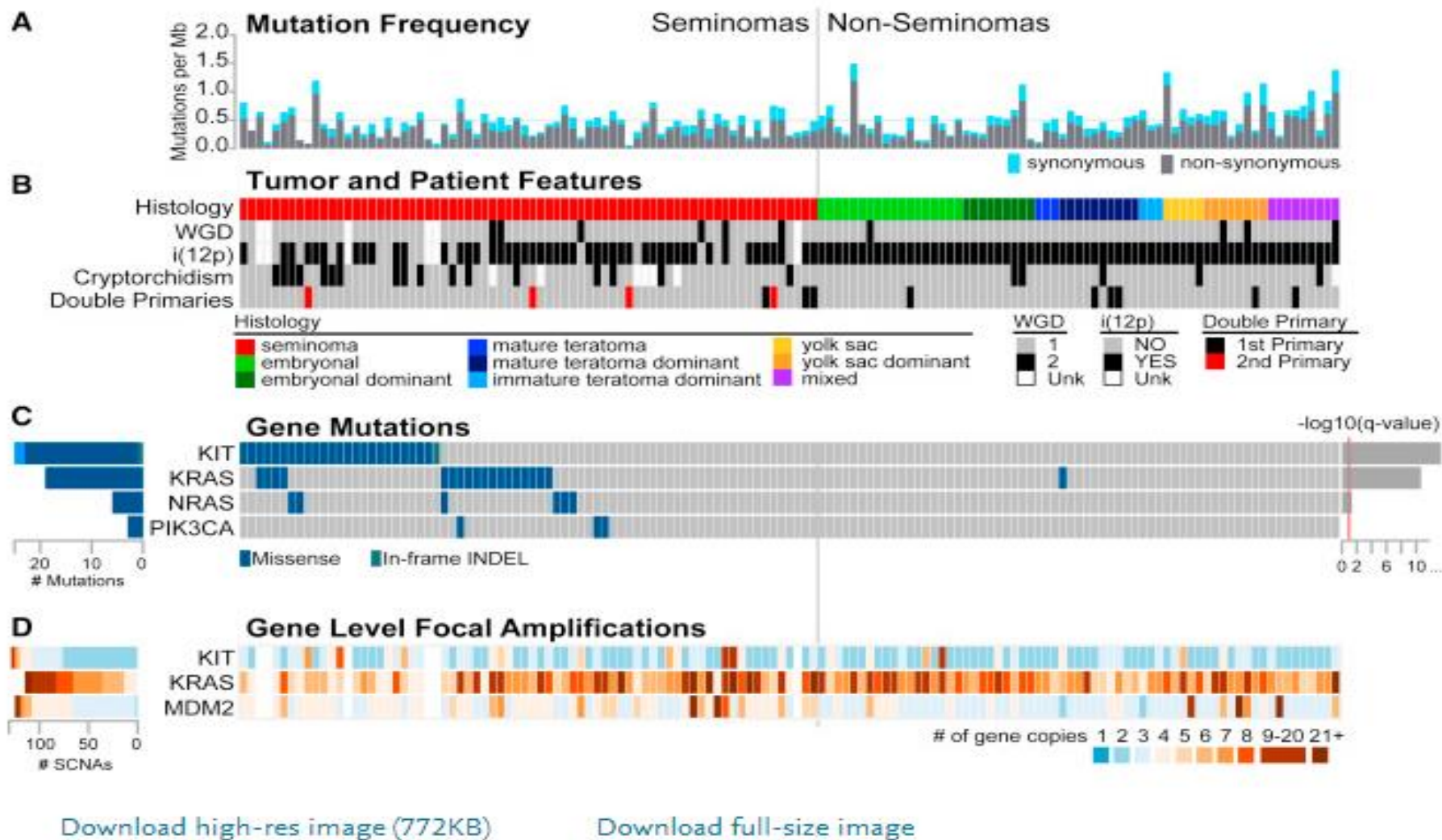


Figure 2. Molecular Alterations and Features across 137 TGCT Samples

i(12p) in 114 of 131 (87%) tumors. All 17 tumors inferred lacking the i(12p) event were seminomas and retained at least 4 copies of 12p



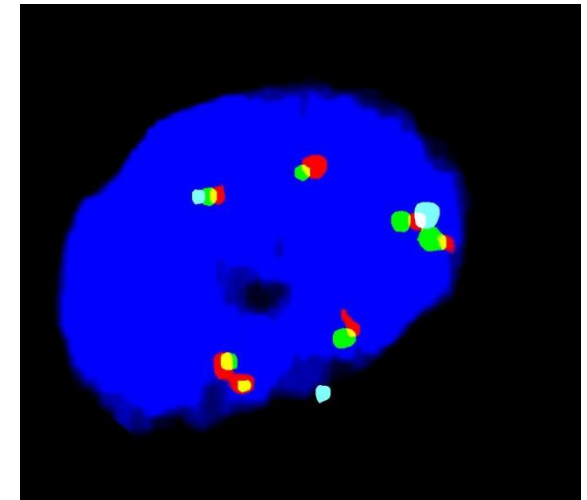
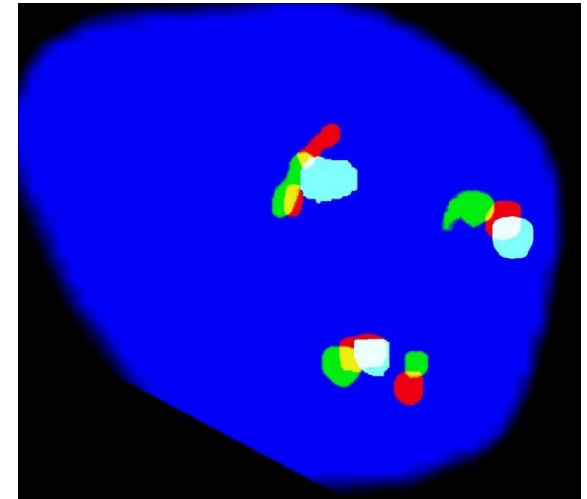
# FISH in the Diagnosis of Germ Cell Tumor in Adult Males




**Table 1. FISH Results for Germ Cell Tumors (GCT)**

| Case | FISH Result | Diagnosis   | Concordant |
|------|-------------|---|------------|
| 1    | +           | Classic Seminoma  | Yes        |
| 2    | -           | Immature Teratoma   | <b>No</b>  |
| 3    | +           | Secondary Somatic Malignancy  | Yes        |
| 4    | -           | Classic Seminoma  | <b>No</b>  |
| 5    | -           | Immature Teratoma   | <b>No</b>  |
| 6    | +           | Mixed GCT (Yolk Sac and Teratoma)                                   | Yes        |
| 7    | +           | Classic Seminoma  | Yes        |
| 8    | +           | Mixed GCT(Embryonal Carcinoma, Yolk Sac Tumor, Teratoma)            | Yes        |
| 9    | +           | Mixed GCT(Embryonal Carcinoma, Teratoma, Yolk Sac Tumor, Seminoma)  | Yes        |
| 10   | +           | Mixed GCT (Embryonal Carcinoma, Teratoma, Yolk Sac Tumor, Seminoma) | Yes        |

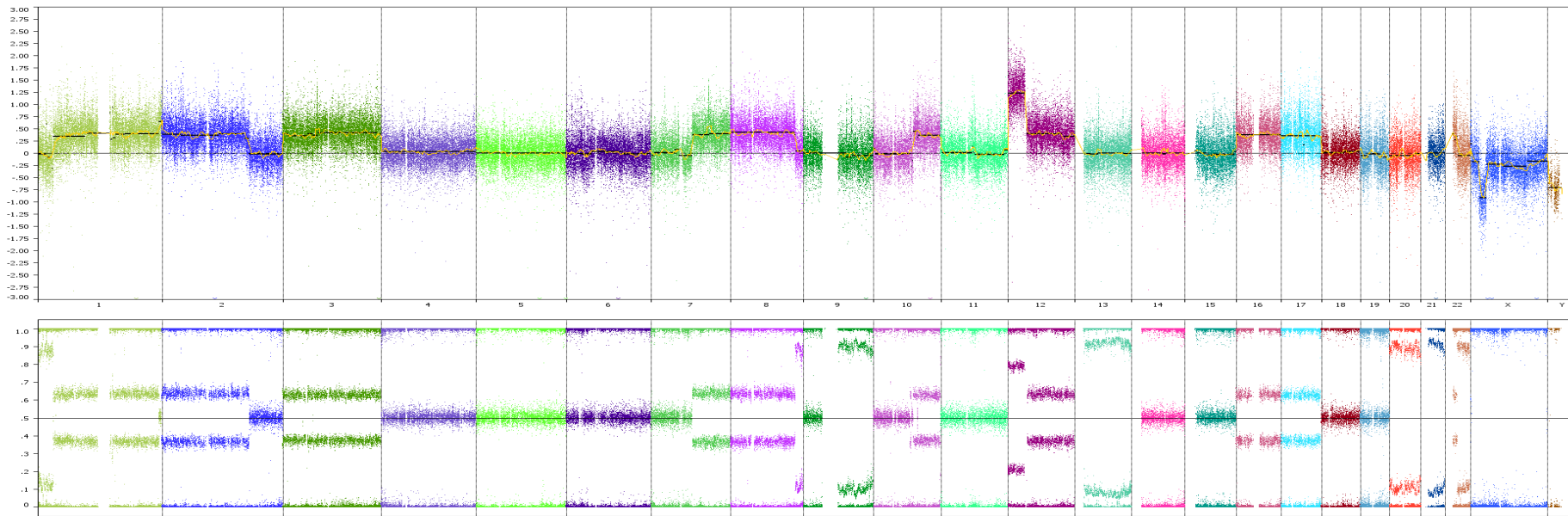
**Table 2. FISH Results for Somatic Carcinomas**

| Case | FISH Result | Diagnosis   | Concordant |
|------|-------------|---|------------|
| 11   | -           | Renal Cell Carcinoma, Clear Cell Type, with Sarcomatoid Differentiation   | Yes        |
| 12   | +           | Colonic Adenocarcinoma  | <b>No</b>  |
| 13   | +           | Pulmonary Squamous Cell Carcinoma   | <b>No</b>  |
| 14   | -           | Urothelial Carcinoma with Sarcomatoid Features                            | Yes        |
| 15   | -           | Urothelial Carcinoma  | Yes        |
| 16   | -           | Pulmonary Adenocarcinoma  | Yes        |
| 17   | +           | Colonic Adenocarcinoma  | <b>No</b>  |
| 18   | -           | Urothelial Carcinoma  | Yes        |
| 19   | -           | Pulmonary Combined Adenocarcinoma and Large Cell Neuroendocrine Carcinoma | Yes        |
| 20   | -           | Colonic Adenocarcinoma  | Yes        |



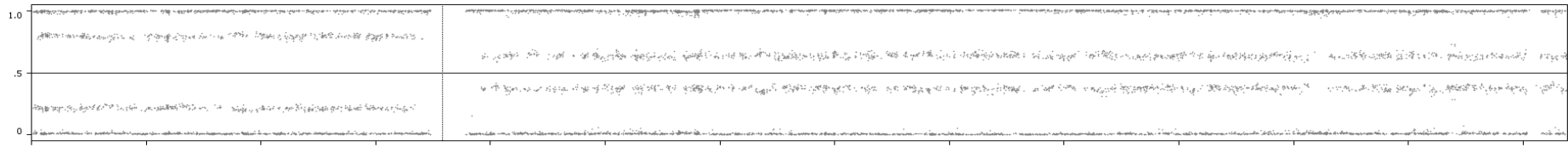
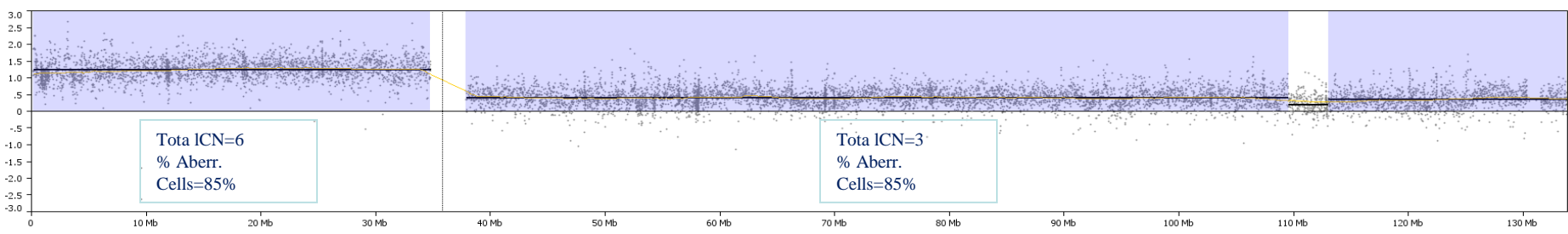
-  ETV6, 12p13
-  CEP, 12p11-12q11
-  MDM2, 12 q13





Sample: S12-26575

Chromosome 12



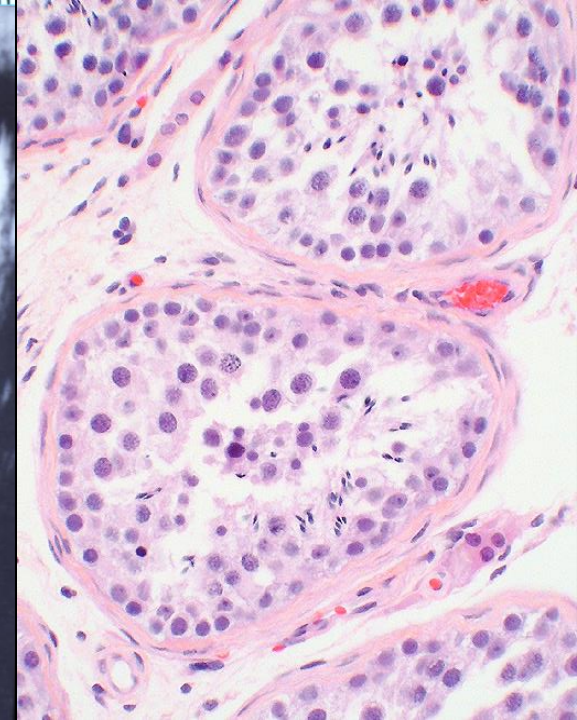
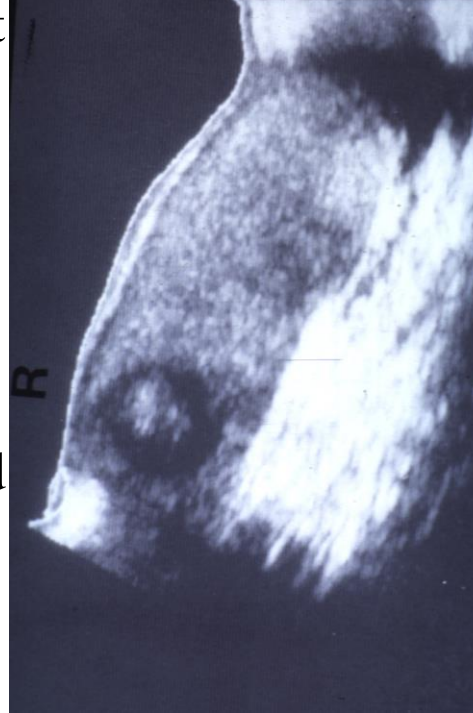
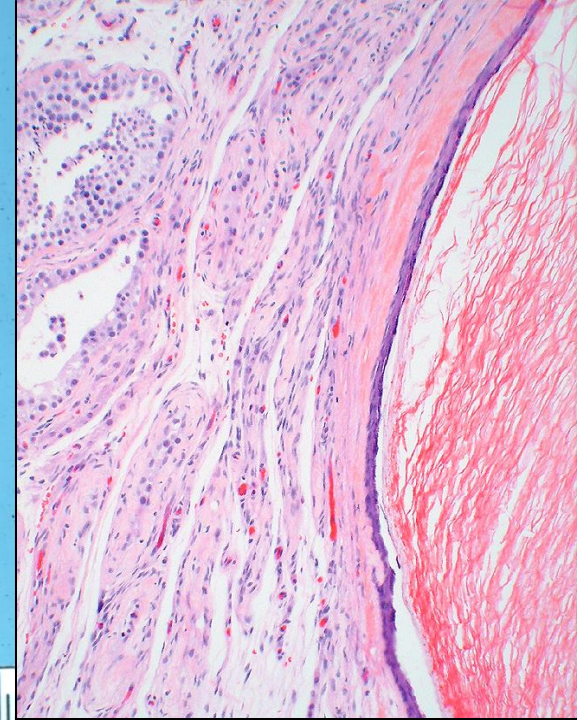


When are teratomatous-looking elements not called teratoma, post-pubertal type in adults?

## EPIDERMOID CYST

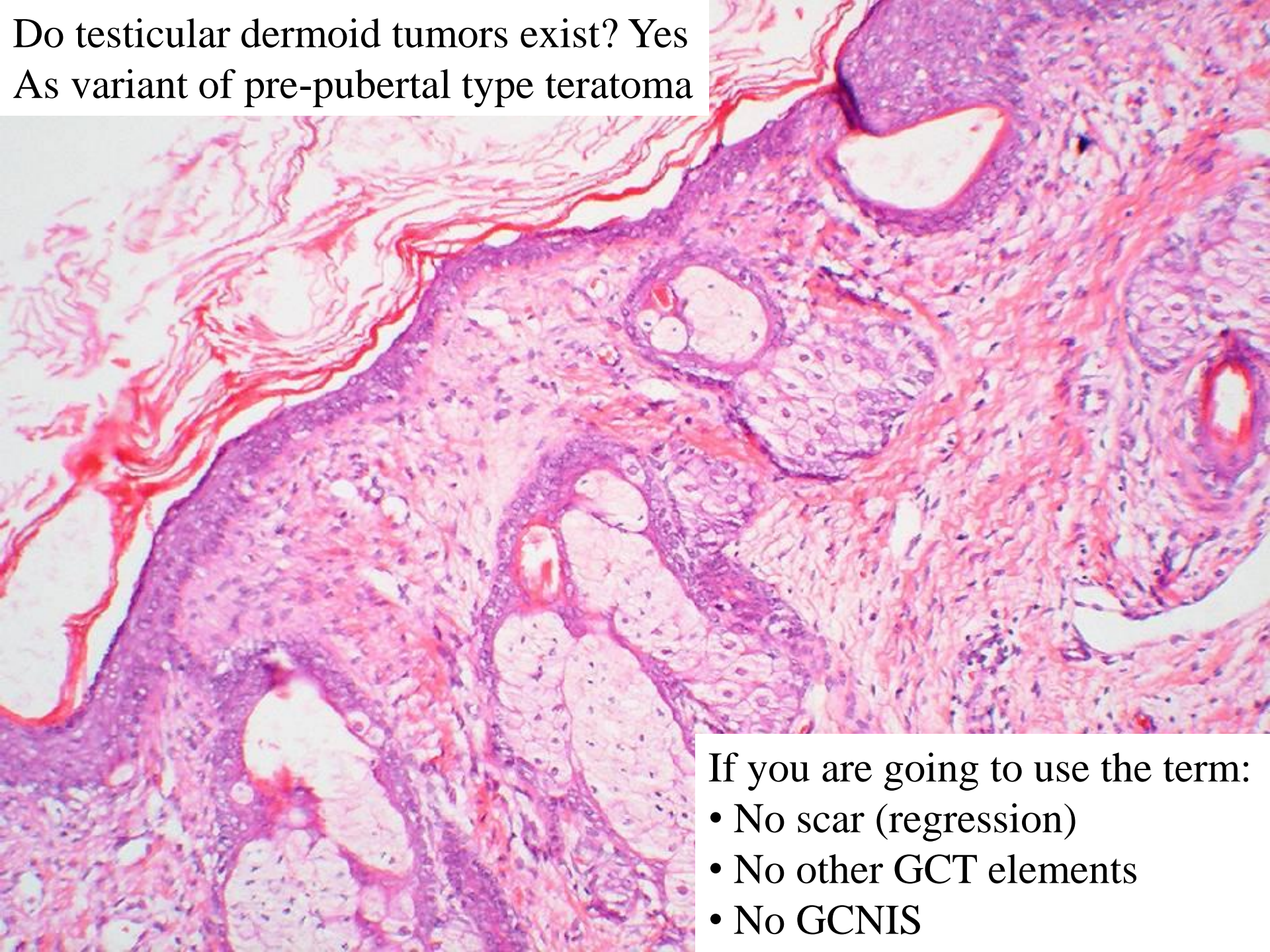
### Definition

- Intraparenchymal squamous-lined cyst containing intraluminal keratin debris
- Cyst is separated from the adjacent testicular parenchyma by a thin fibrous capsule
- No dermal adnexal elements
- No germ cell neoplasia in situ
- No distinct parenchymal scar (“burned out” lesion)
- Variant of pre-pubertal type teratoma





Do testicular dermoid tumors exist? Yes  
As variant of pre-pubertal type teratoma



If you are going to use the term:

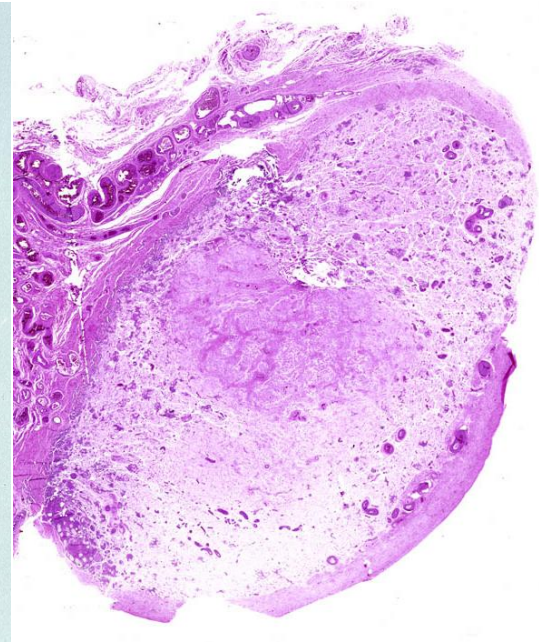
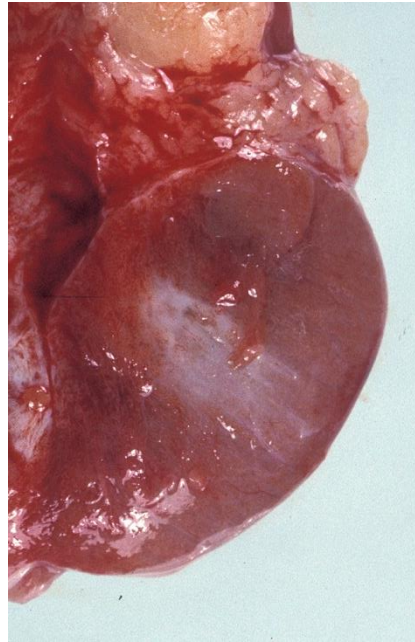
- No scar (regression)
- No other GCT elements
- No GCNIS



# What about testicular scars?

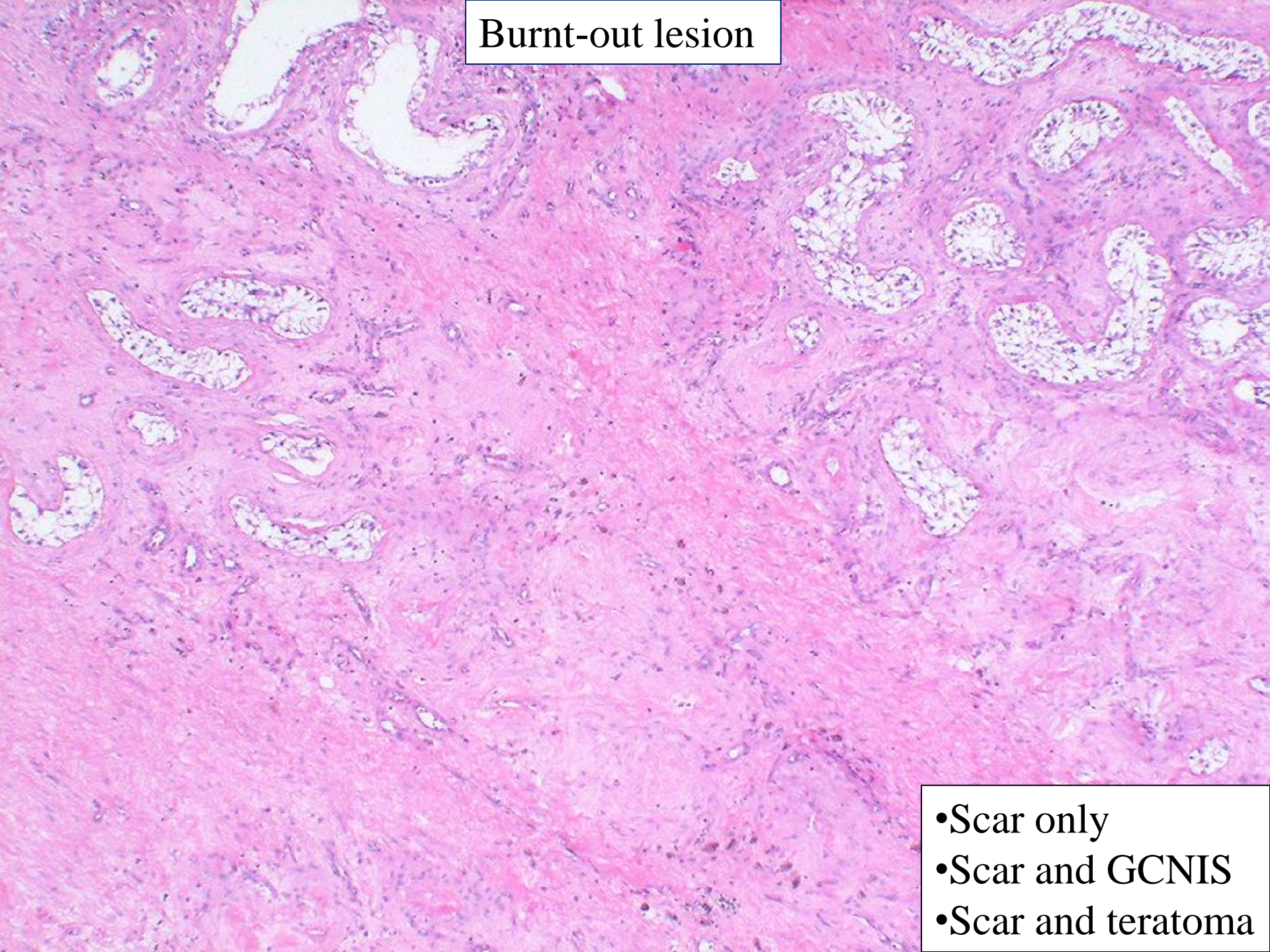
Possible etiology:

- Trauma
- Infection/inflammation
- Infarct
- Tumor regression (“burnt-out lesion”)
  - Fibrosis
  - Calcification
  - Inflammation



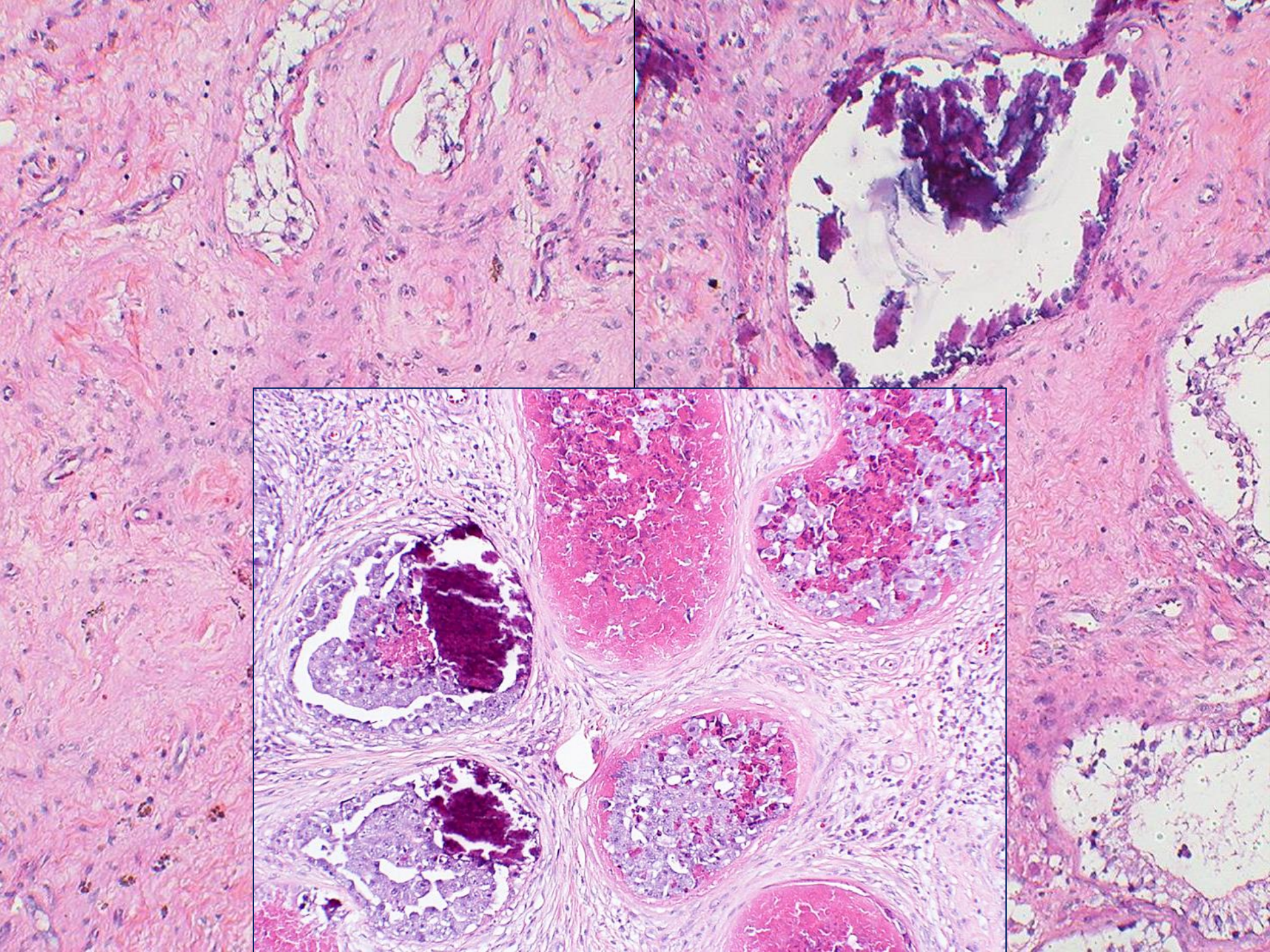


## Burnt-out lesion



- Scar only
- Scar and GCNIS
- Scar and teratoma







# AJCC/UICC TNM staging (8<sup>th</sup> Ed)

- pT0 No evidence of tumor (including scar)
- pTis Intratubular, no invasion
- pT1 Testis only, without LVI
  - pT1a <3 cm (seminoma)
  - pT1b ≥3 cm (seminoma)
- pT2 Vascular invasion or tunica vaginalis perforation  
Hilar structure invasion/epididymis
- pT3 Spermatic cord
- pT4 Scrotum



# Prognostic factors in primary clinical stage 1 testicular tumors

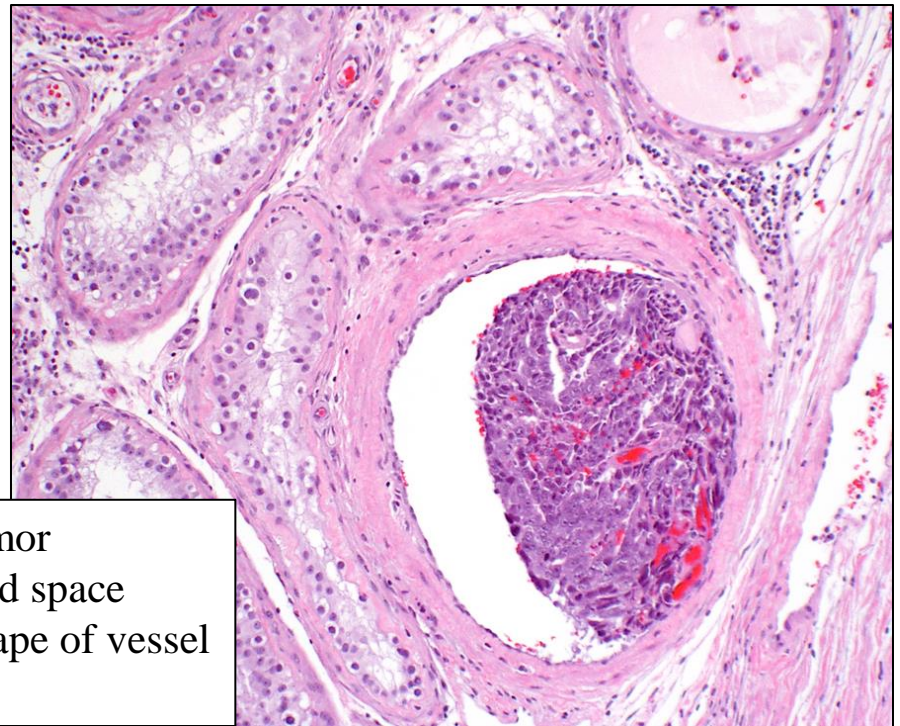
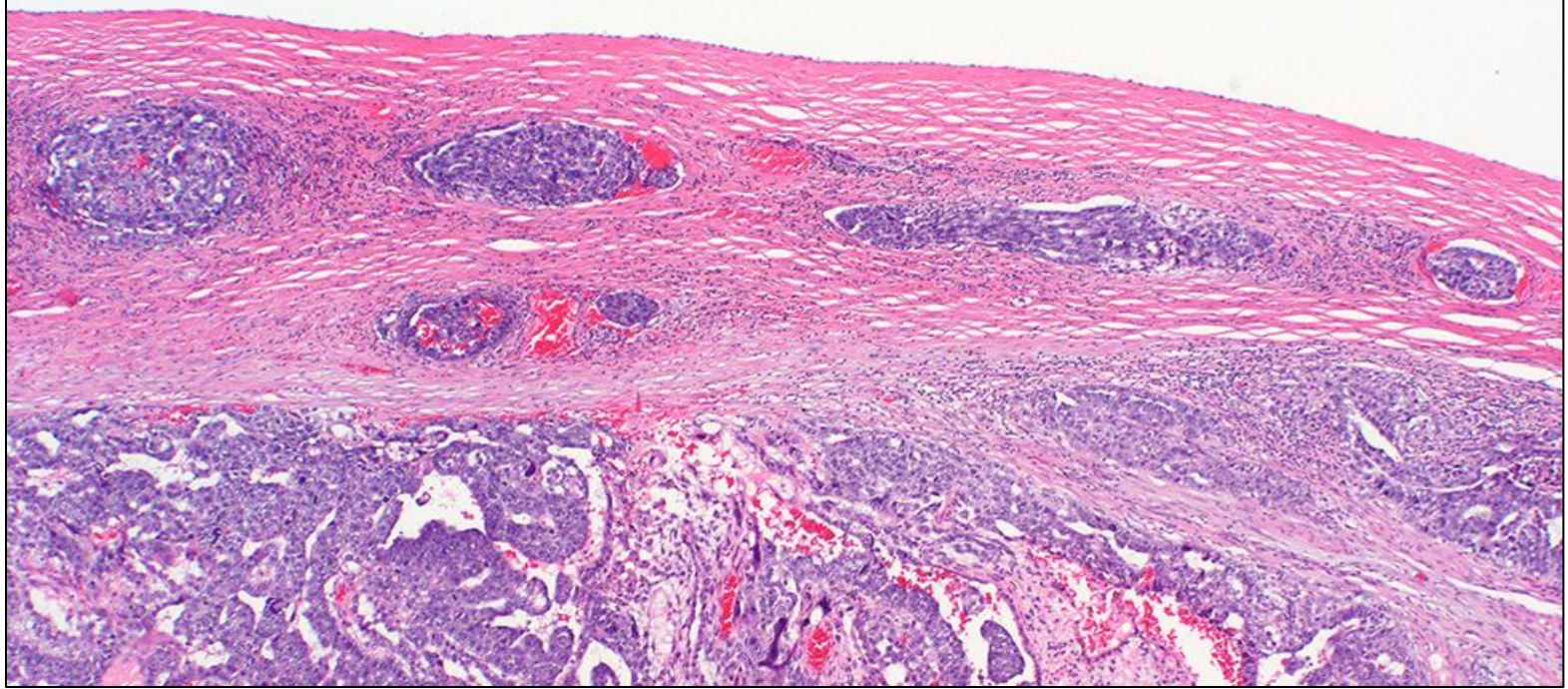
|                             | Seminoma | Mixed Germ Cell Tumor | Gonadal Stromal Tumor† |
|-----------------------------|----------|-----------------------|------------------------|
| Size                        | +        | -                     | + (>5cm)               |
| Vascular invasion           | -^       | +^                    | +                      |
| Rete testis invasion        | -*       | -                     |                        |
| Adnexa                      | -        | -                     |                        |
| Hilar soft tissue           | -        | -                     |                        |
| Infiltrative margins        | -        | -                     | +                      |
| Percentage of Emb Ca        |          | +                     | na                     |
| Necrosis                    | -        | -                     | +                      |
| Mitotic activity            | -        | -                     | ≥ 4 /10 hpf            |
| Age                         | -        | -                     | + (>60y)               |
| No endocrine manifestations | na       | na                    | +                      |

\*: controversial and not used to select therapy

^ upstage to pT2

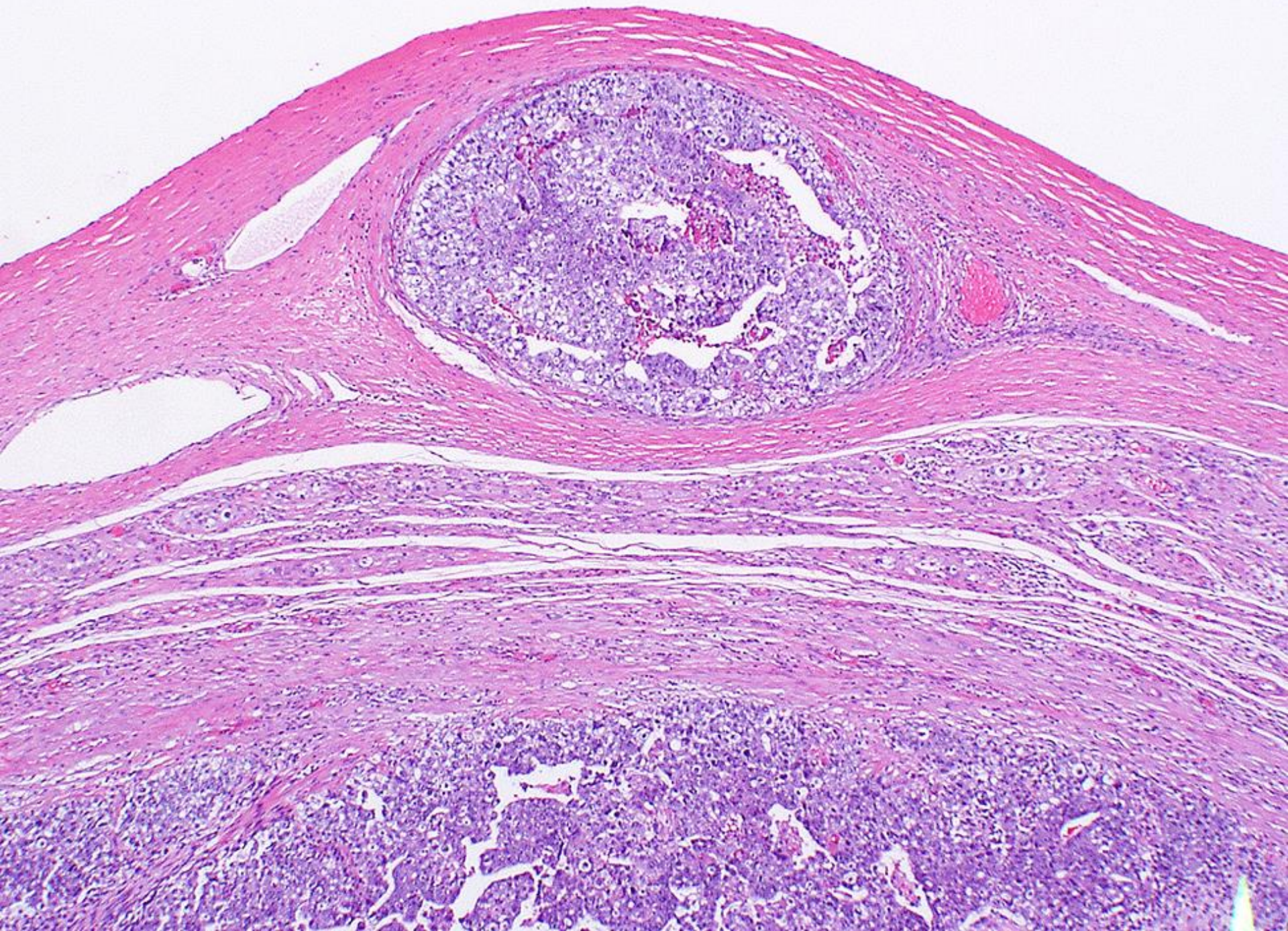
† more than 3 criteria



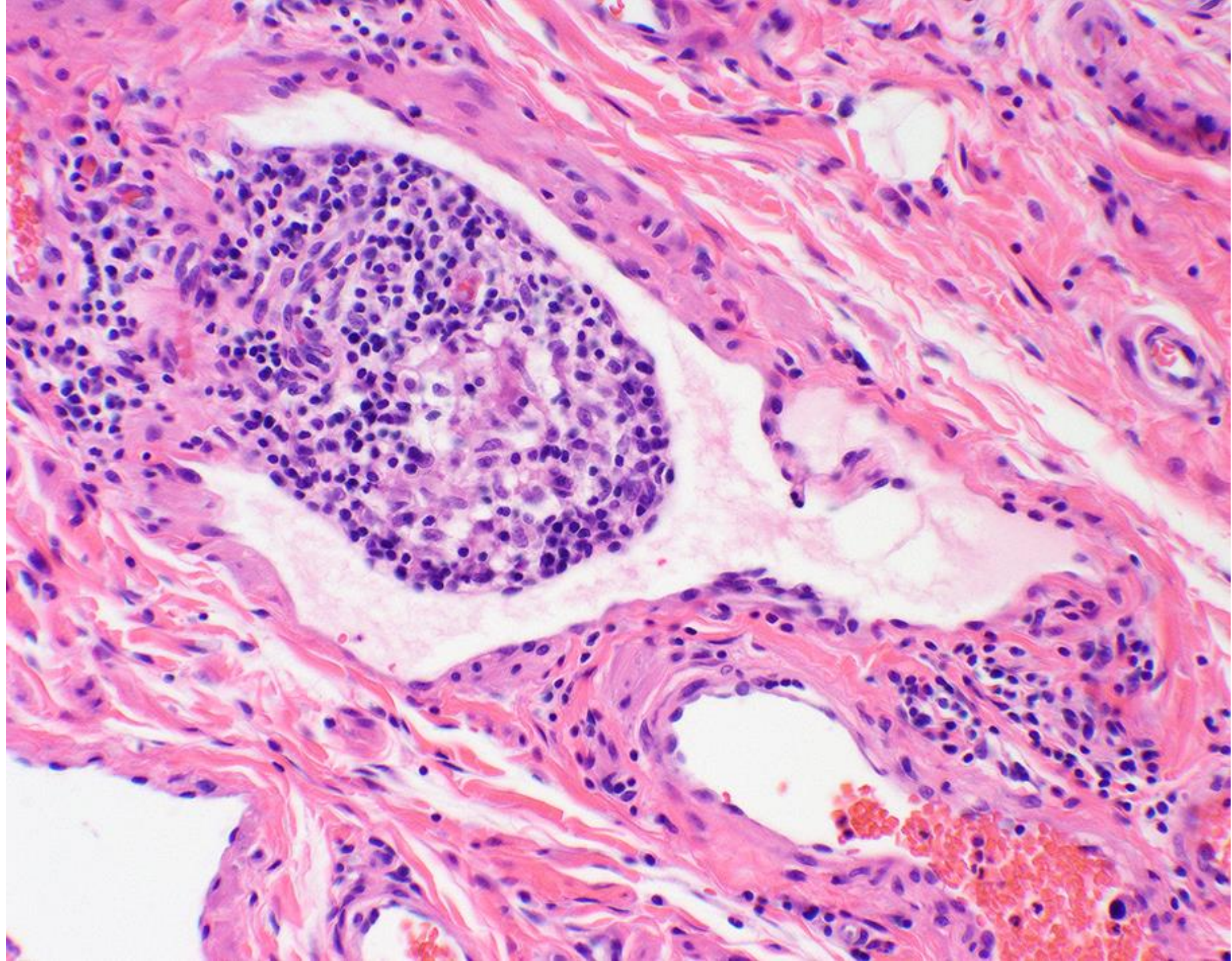


- Periphery of tumor
- Endothelial lined space
- Conforms to shape of vessel
- Fibrin/RBCs











*Thank you*