

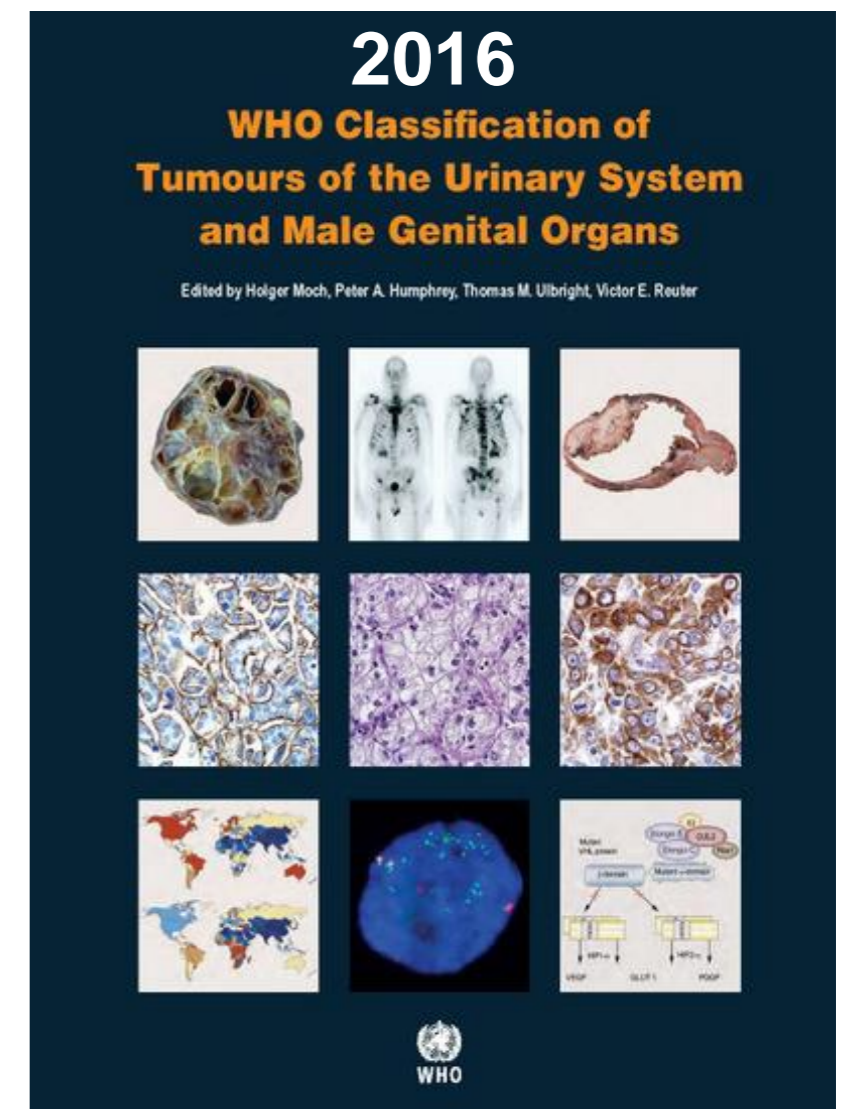
Pathology of Testicular Testicular Tumors: Relevant Issues in the WHO 2016 Classification

Dr. Carlos E. Bacchi
Lab Bacchi



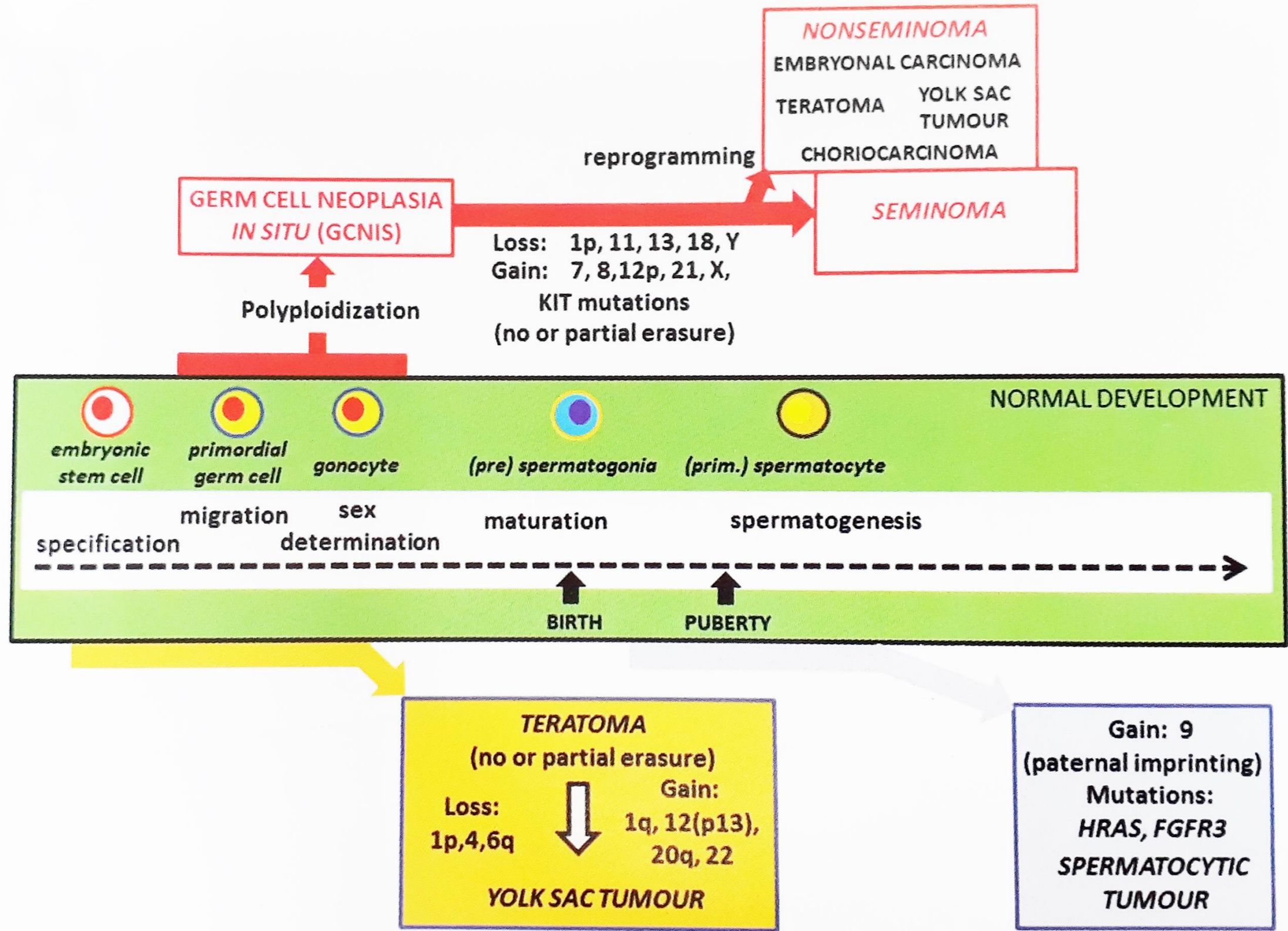
Relevant Issues in the WHO 2016 Classification

- Last WHO classification, 2004
- Current WHO classification, 2016
- Germ cell neoplasia in situ (GCNIS)
- Restructuring the classification
 - seminoma
 - trophoblastic tumors
 - teratoma, postpubertal type
 - prepubertal type tumors
 - spermatocytic tumors

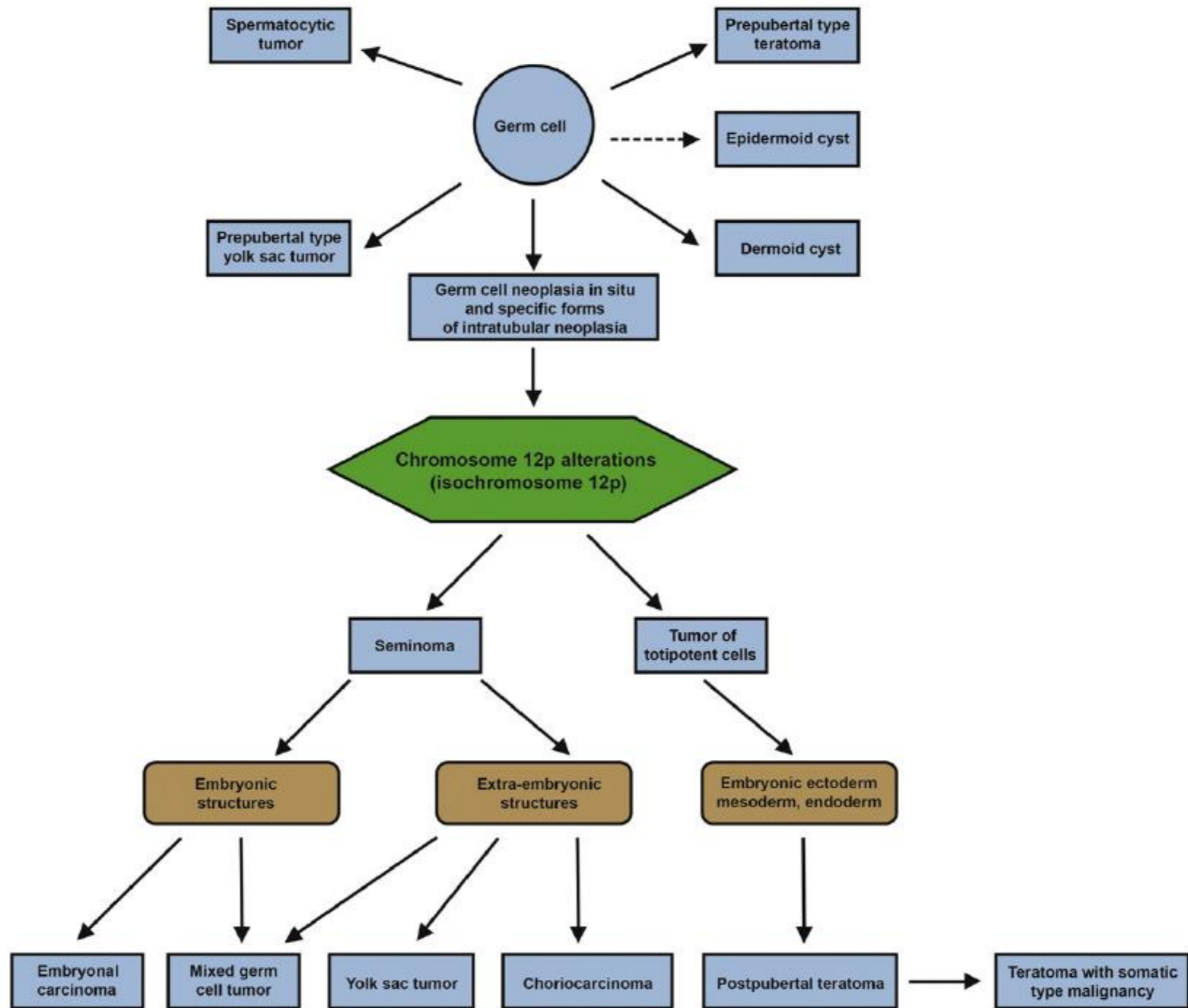


Pathogenic Model of Variou Types of Testicular Tumors

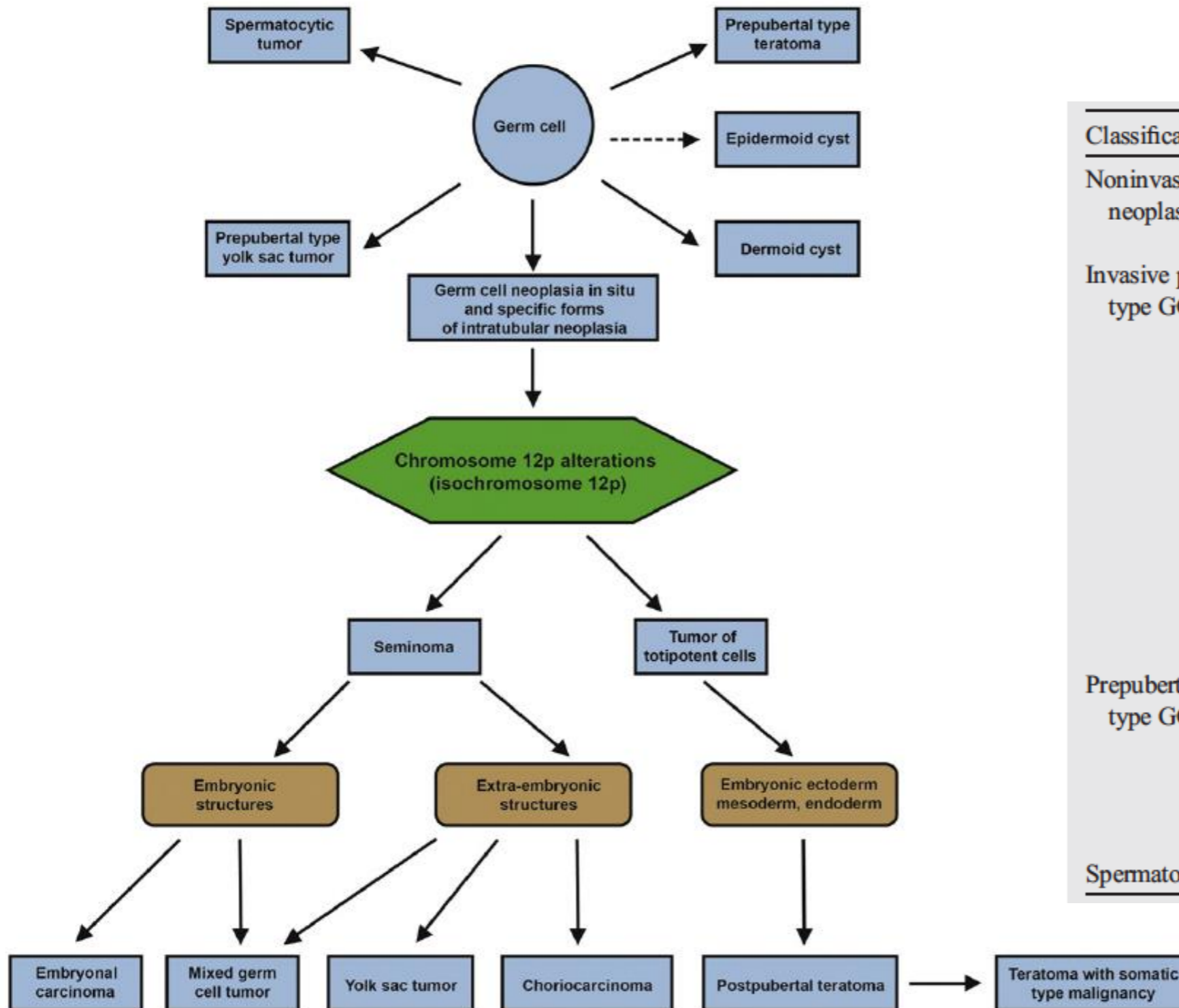
GCNIS RELATED



Pathways for the development of testicular germ cell tumors



Pathways for the development of testicular germ cell tumors

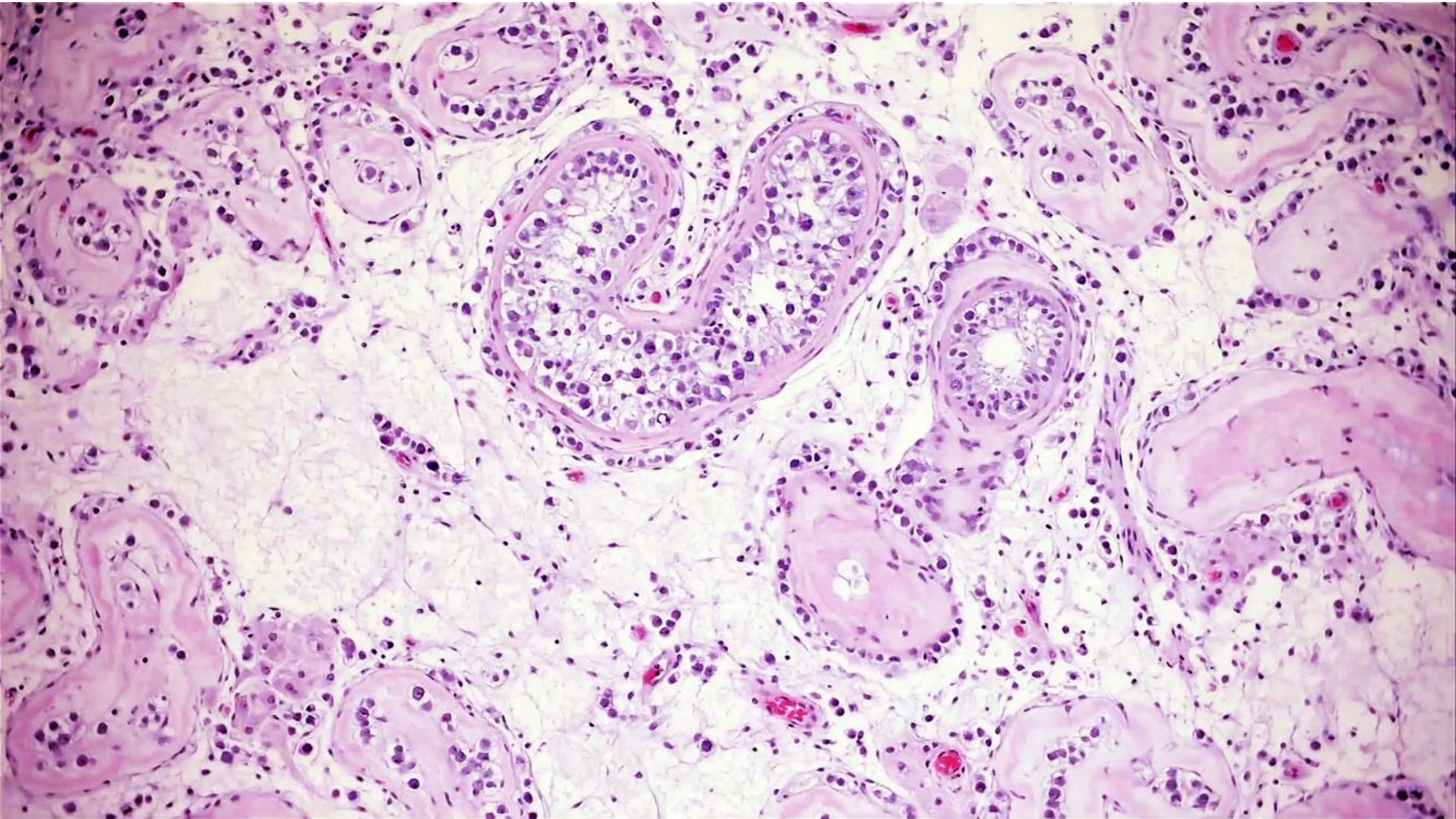


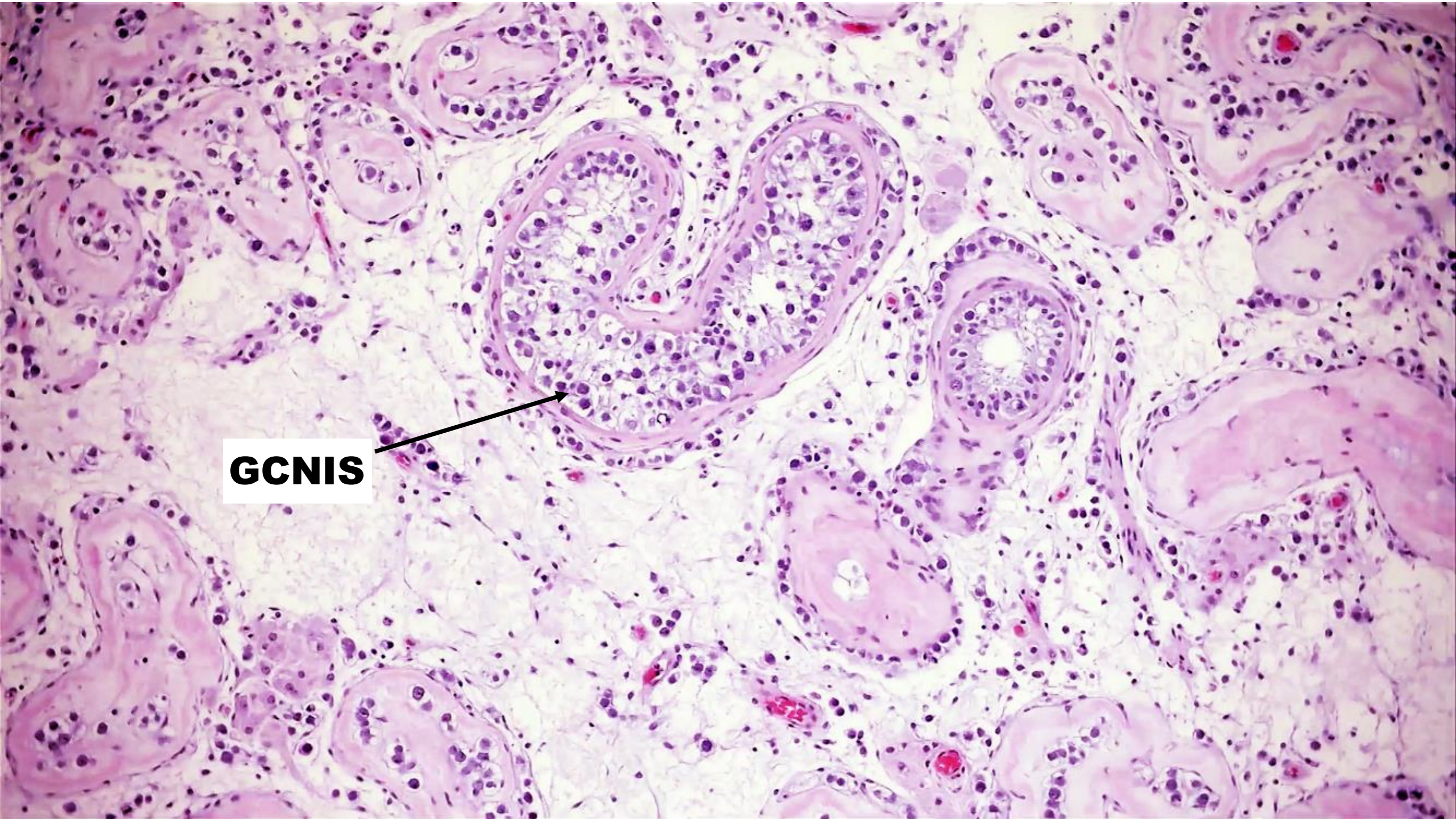
Classification of germ cell tumours of the testis

Classification	Tumor types
Noninvasive germ cell neoplasia	GCNIS Specific forms of intratubular germ cell neoplasia (specify type)
Invasive postpubertal-type GCTs	Seminoma Embryonal carcinoma Yolk sac tumor Teratoma Teratoma with somatic-type malignancy Choriocarcinoma Nonchoriocarcinomatous trophoblastic tumor Placental site trophoblastic tumor Epithelioid trophoblastic tumor Cystic trophoblastic tumor Mixed GCT
Prepubertal-type GCTs	Prepubertal-type yolk sac tumor Prepubertal-type teratoma Dermoid cyst Epidermoid cyst Combined prepubertal-type teratoma and yolk sac tumor
Spermatocytic tumor	

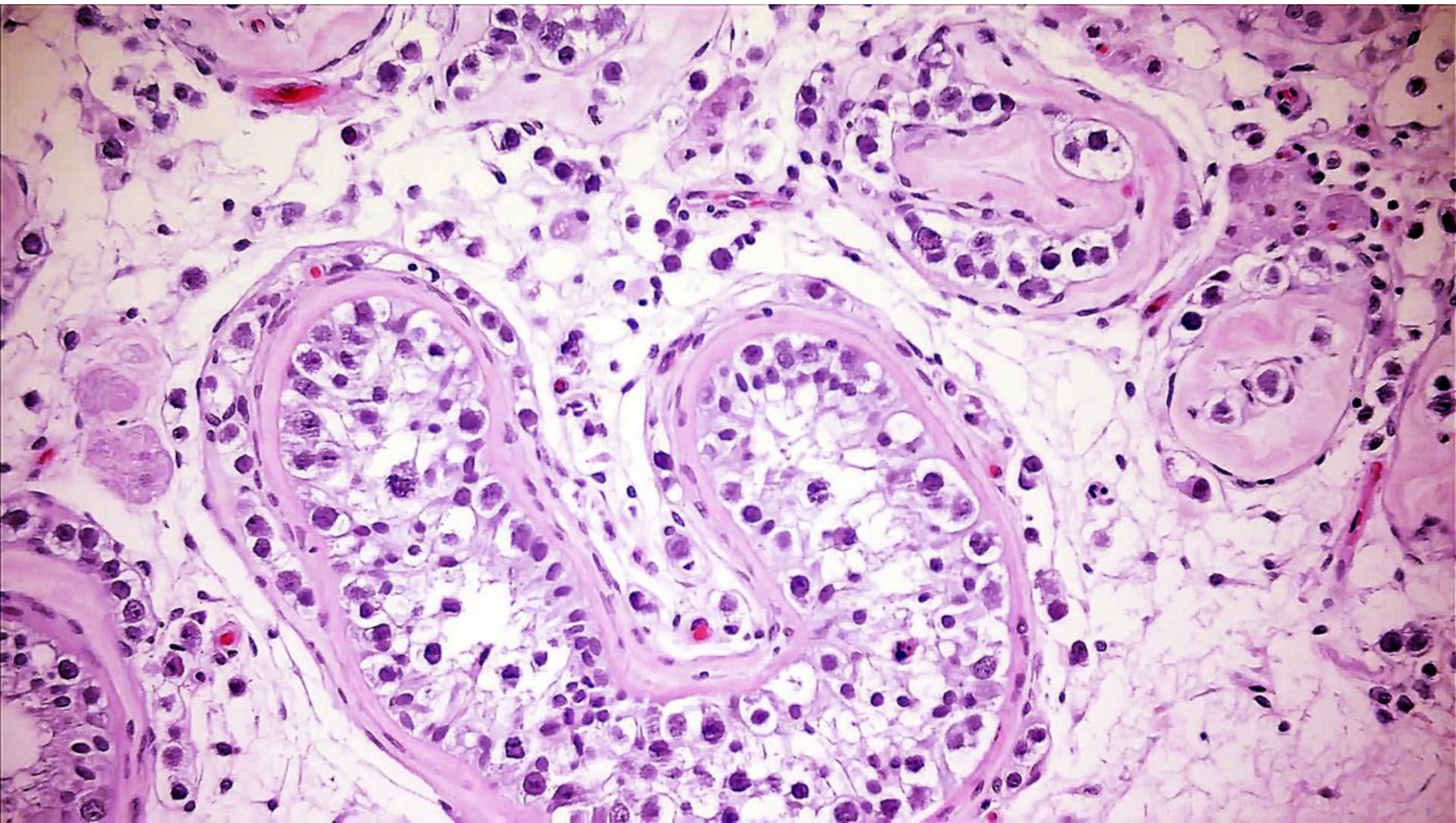
Clinical Case:

- Clinical History:
40-year-old male with a right inguinal mass and history of cryptorchidism.
Resection showed a testis measuring 2.5 x 1.5 cm.



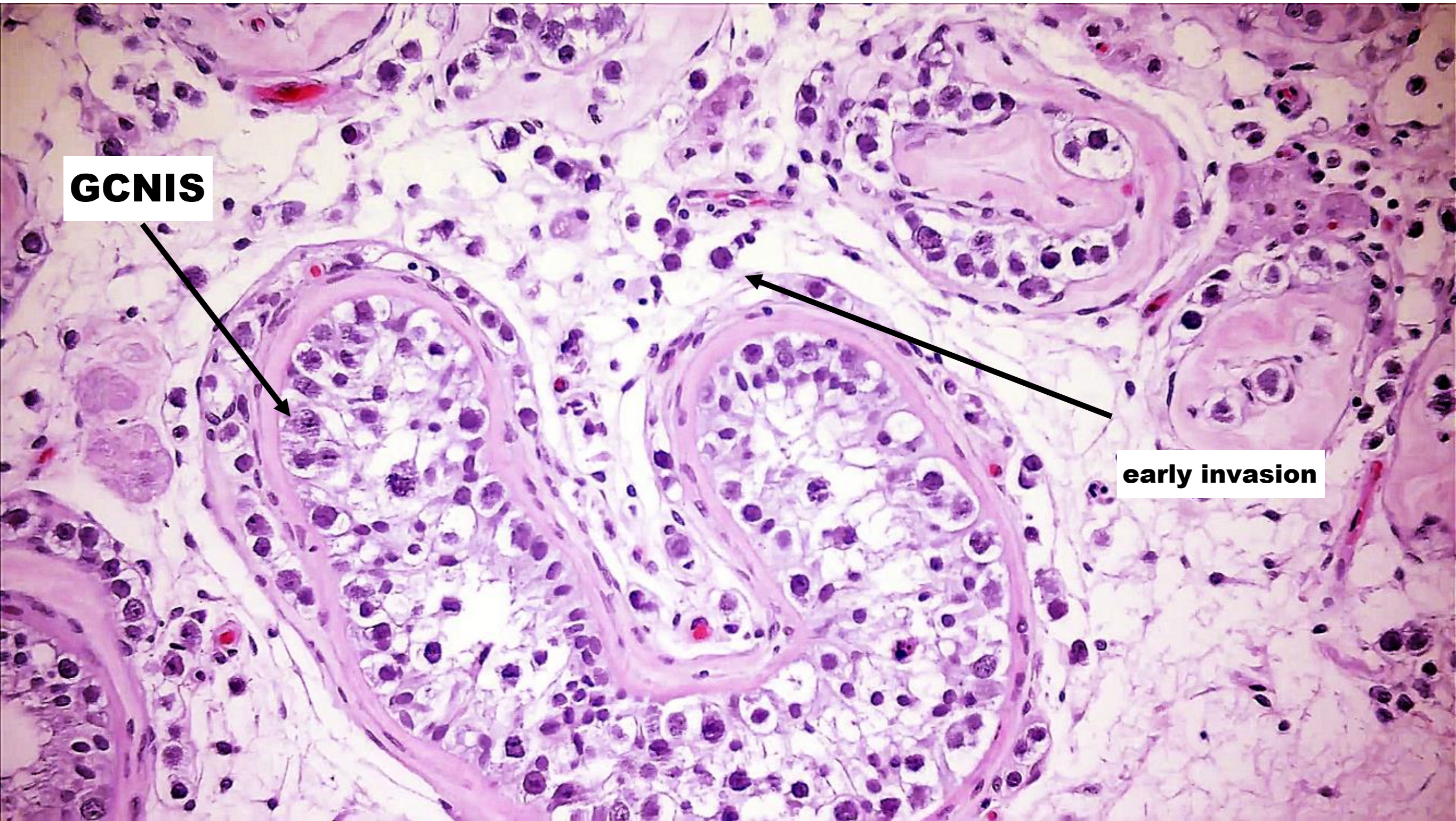


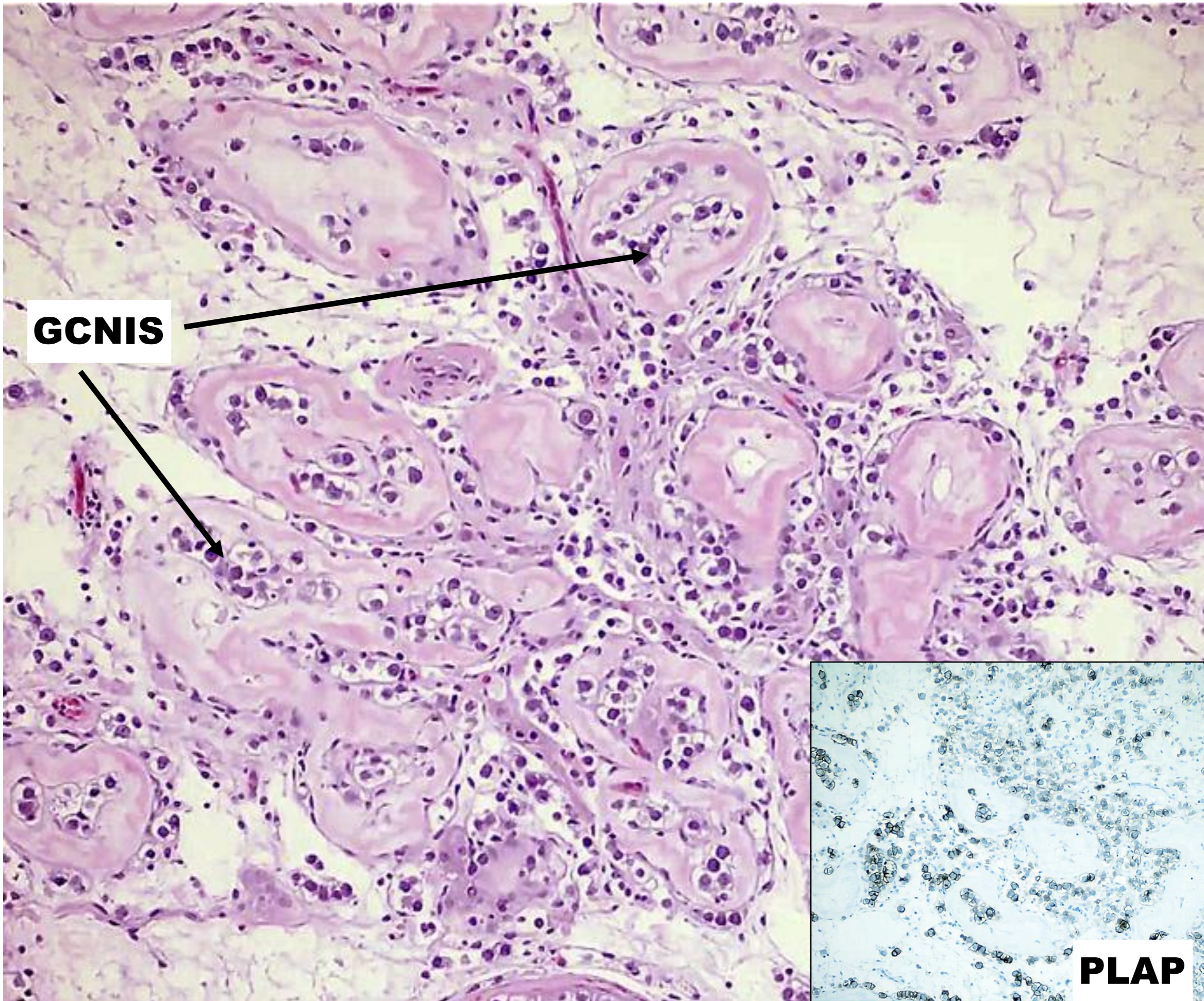
GCNIS



GCNIS

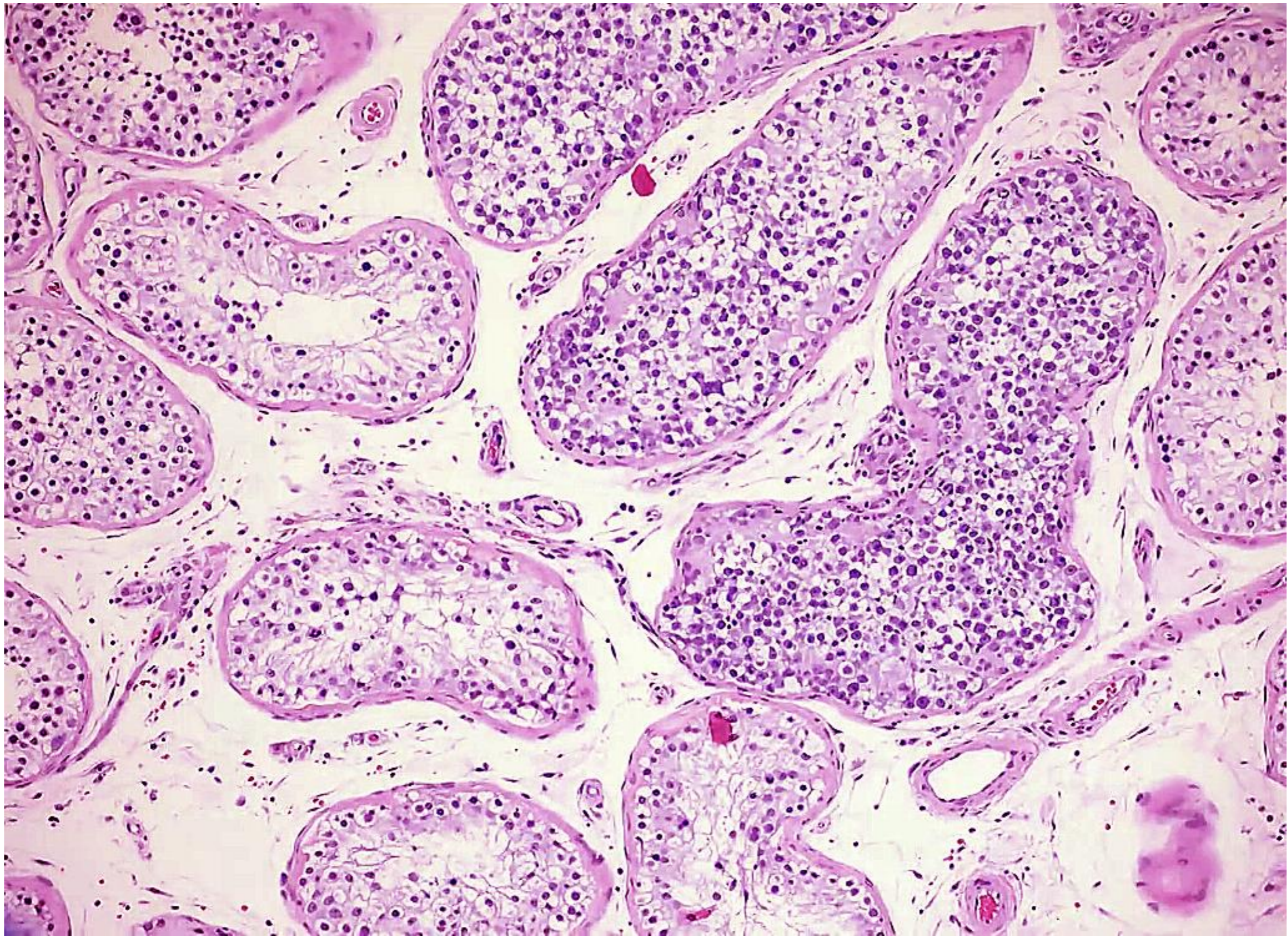
early invasion

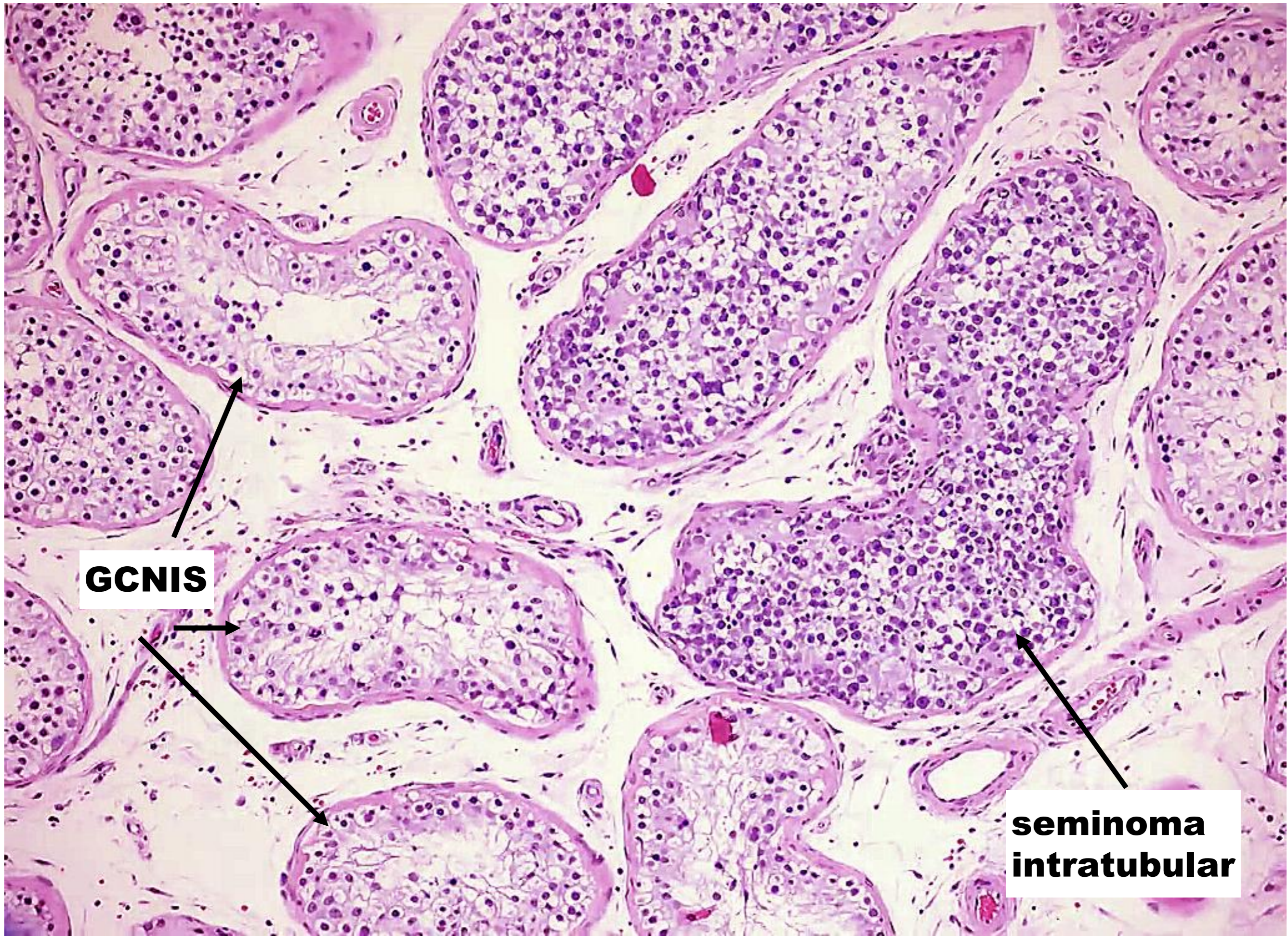




GCNIS

PLAP





GCNIS

seminoma intratubular

Clinical Case:

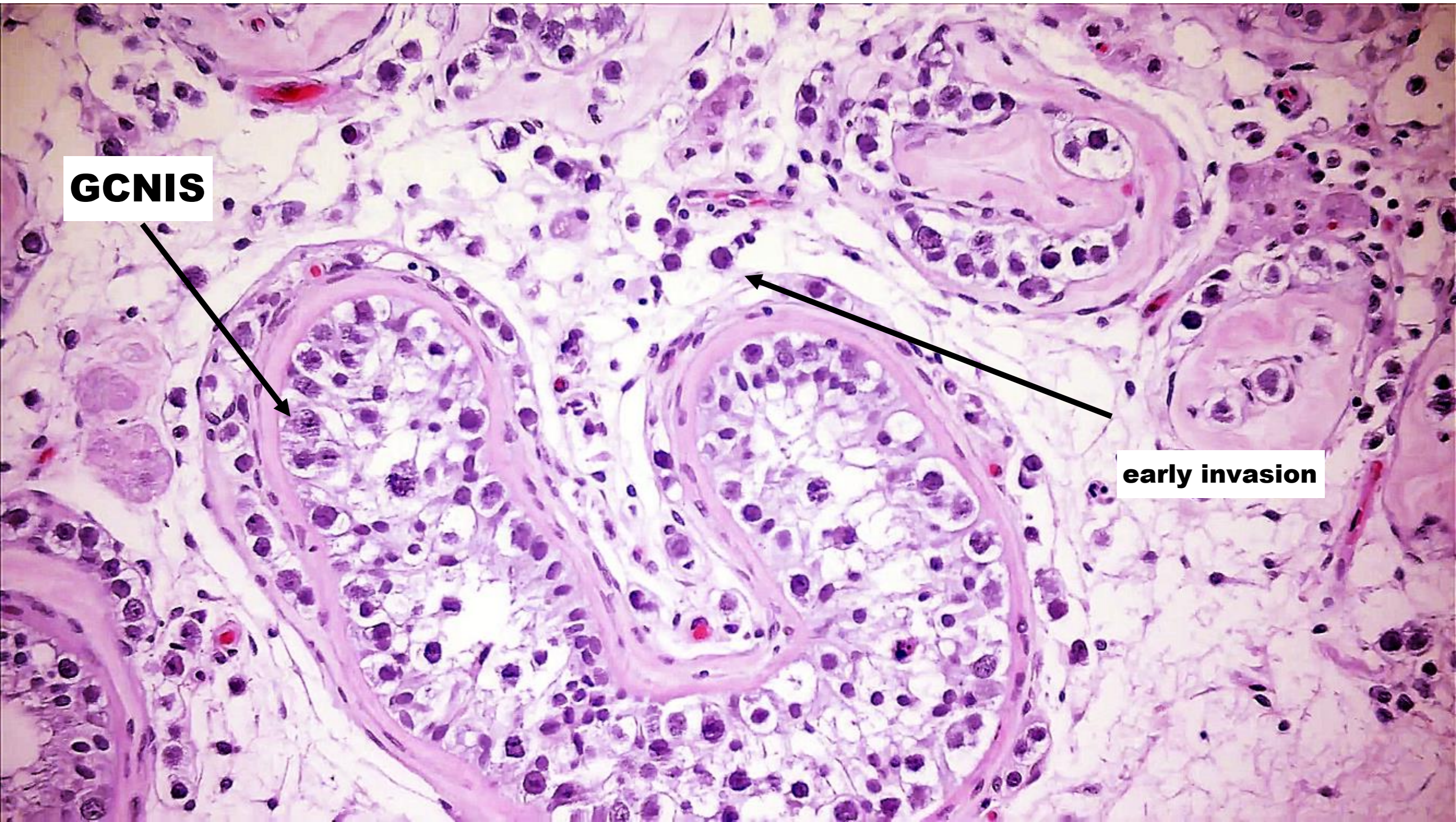
- Final Diagnosis:
- **GERM CELL NEOPLASIA IN SITU
AND INTRATUBULAR SEMINOMA IN
CRYPTORCHID TESTIS**

Precursor Lesion for Testicular Germ Cell Tumors (TGCT)

- Terms used in the past for TGCT: carcinoma in situ and intratubular germ cell neoplasia, unclassified
- WHO, 2016: **GCNIS (germ cell neoplasia in situ)**
- Definition: neoplastic embryonic-type germ cells confined to the spermatogonial stem cell niche
- GCNIS cells are derived from primordial germ cells/gonocytes that failed to differentiate into spermatogonia

GCNIS

early invasion



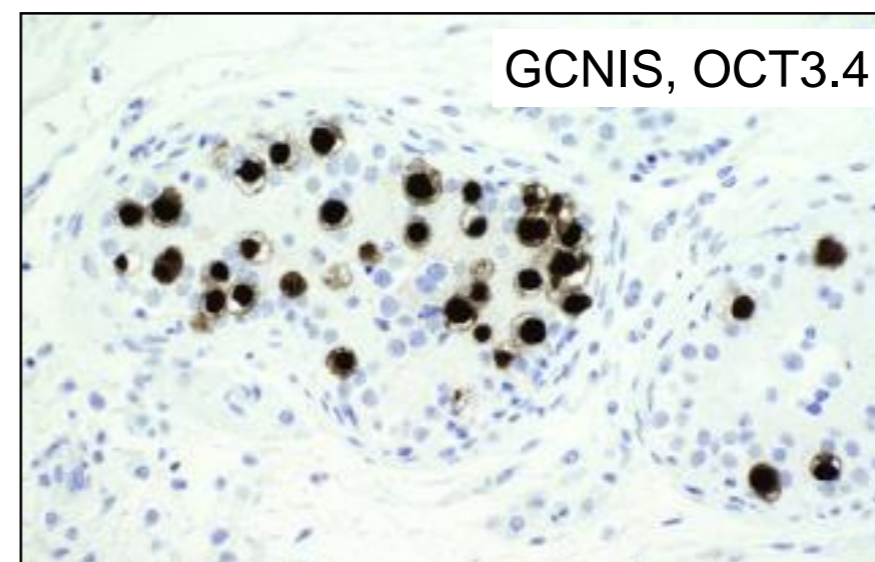
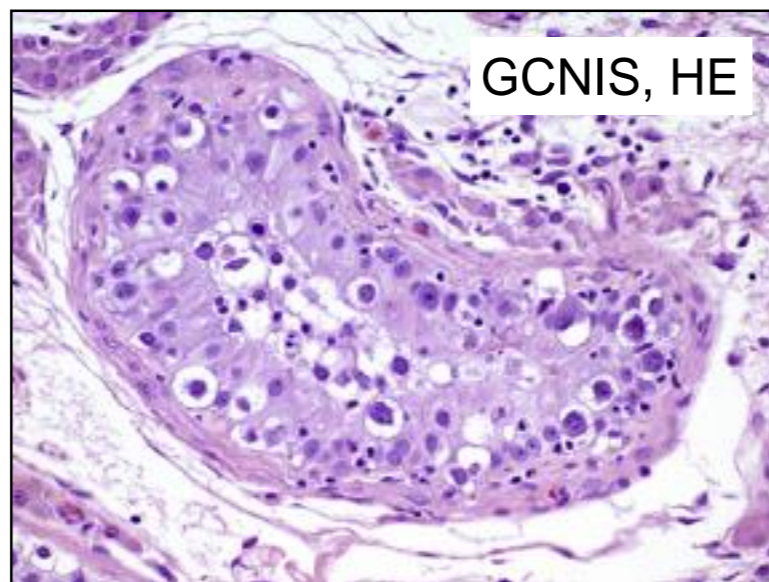
GCNIS (germ cell neoplasia in situ)

early progression

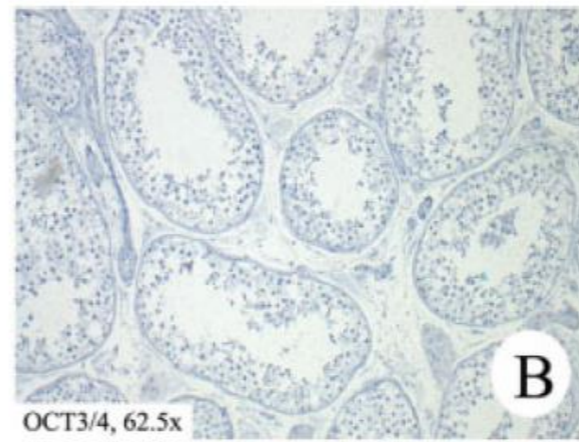
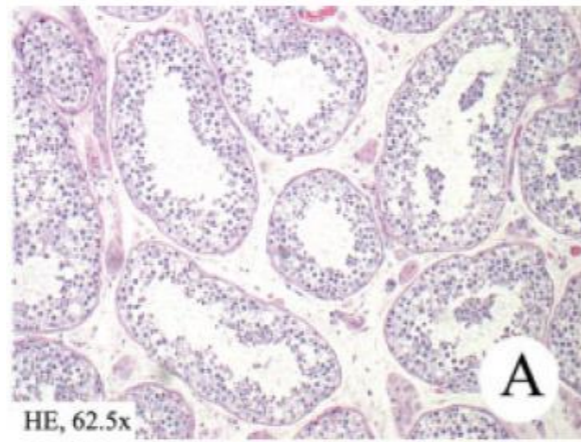
- Delayed maturation of gonocytes (expression of OCT3.4 in centrally located gonocytes)
- pre-GCNIS lesion: gonocytes located all the basement membrane, OCT3.4+/TSPY and focal KIT ligand expression in the tubules by Sertoli cells.
- GCNIS: atypical gonocytes located at basement membrane with OCT3+ and accompanied by KIT ligand expression in the tubules by Sertoli cells and, in autocrine fashion, by the atypical gonocytes, usually with coexpression of TSPY

GCNIS (germ cell neoplasia in situ)

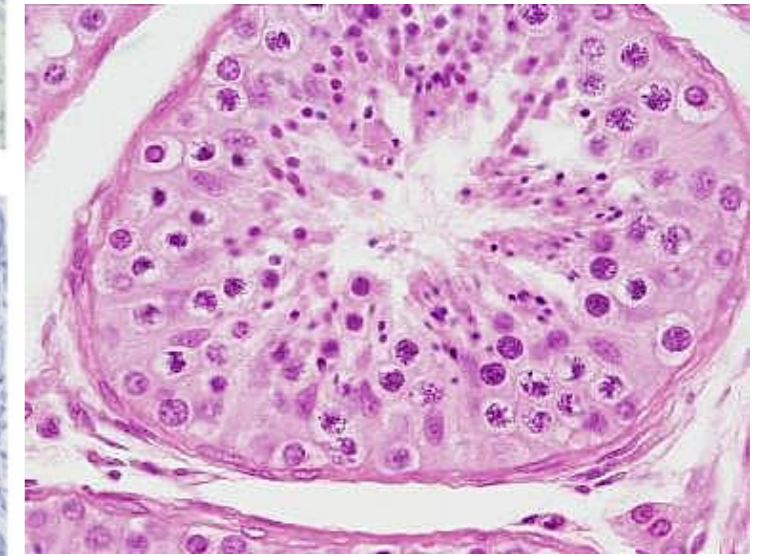
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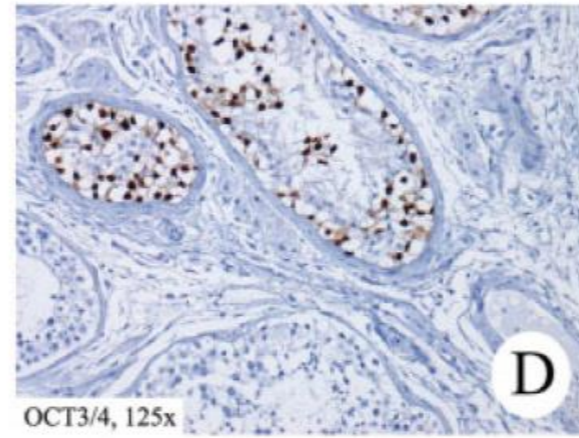
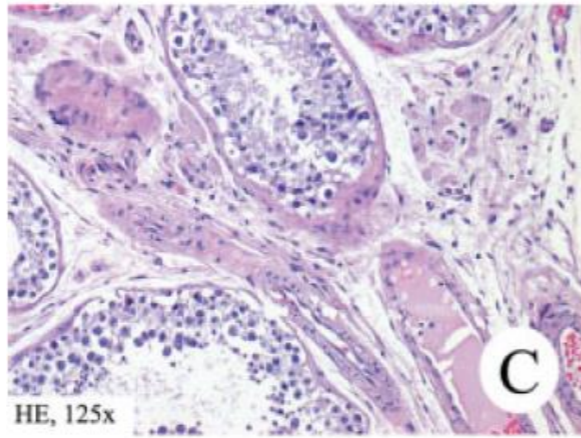
Testis with normal spermatogenesis →



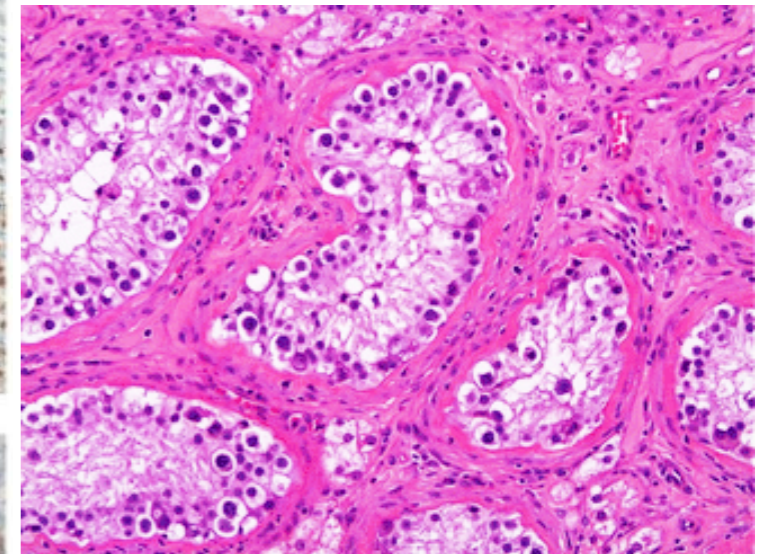
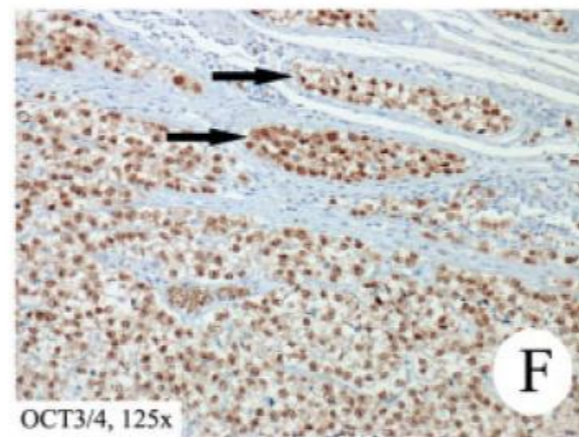
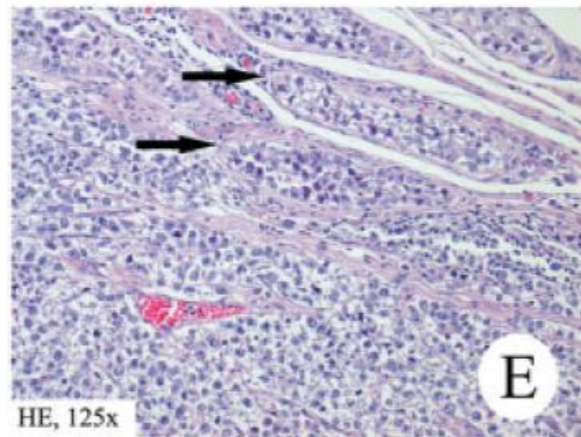
Testis with normal spermatogenesis



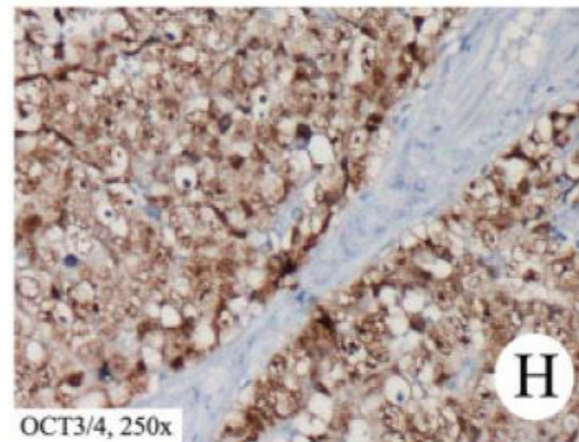
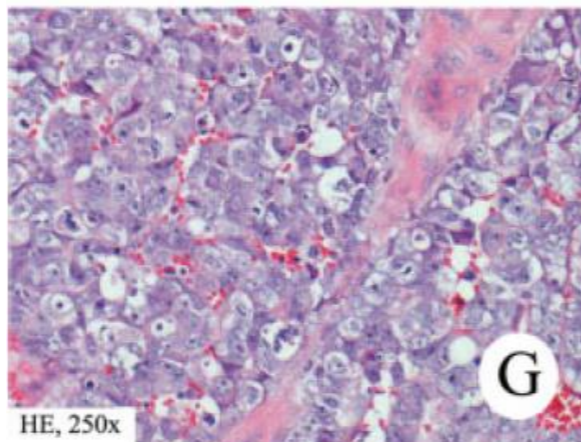
GCNIS →



Intratubular Seminoma →



Embryonal Carcinoma →



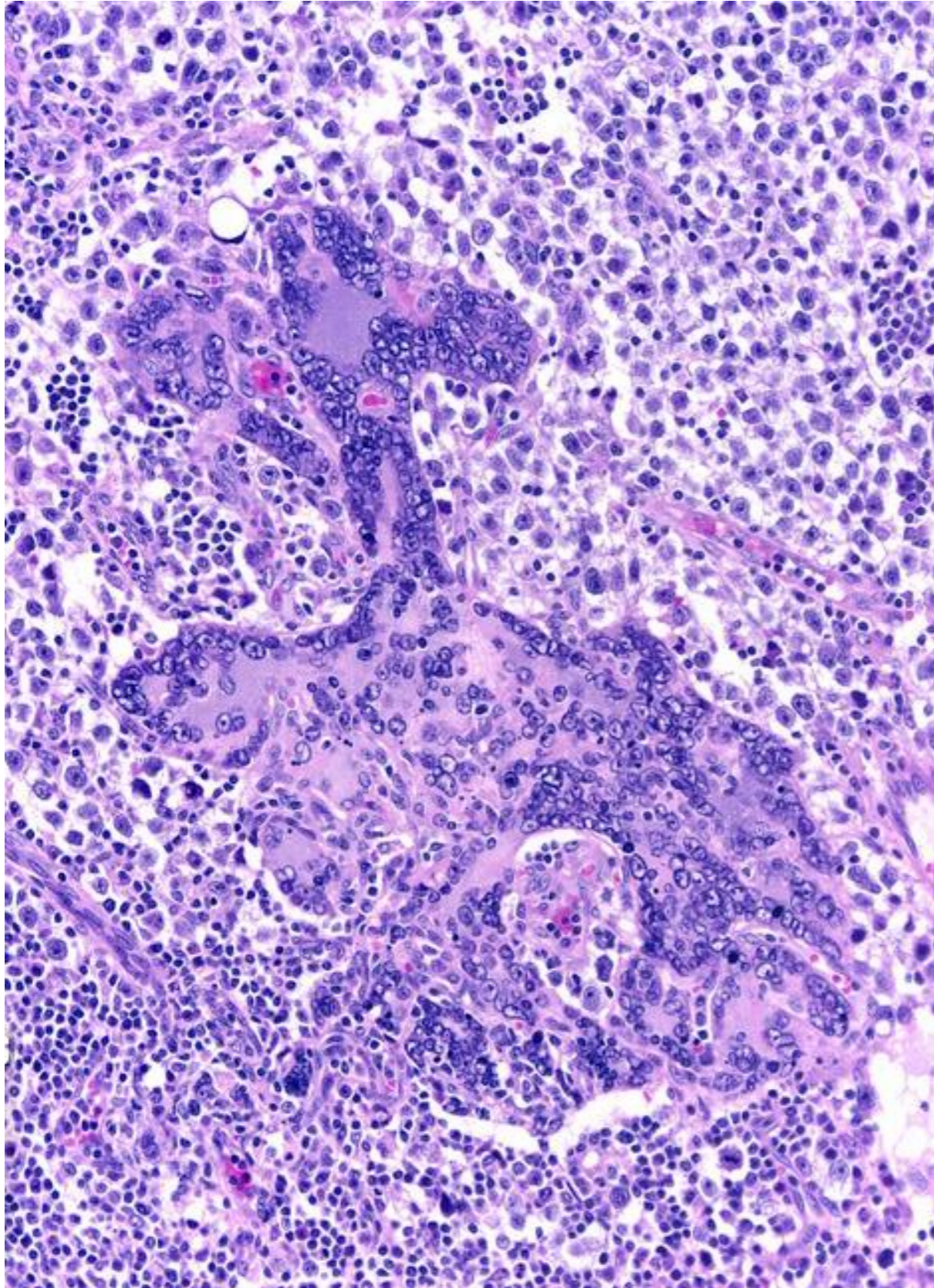
GCNIS

Seminoma, WHO, 2016

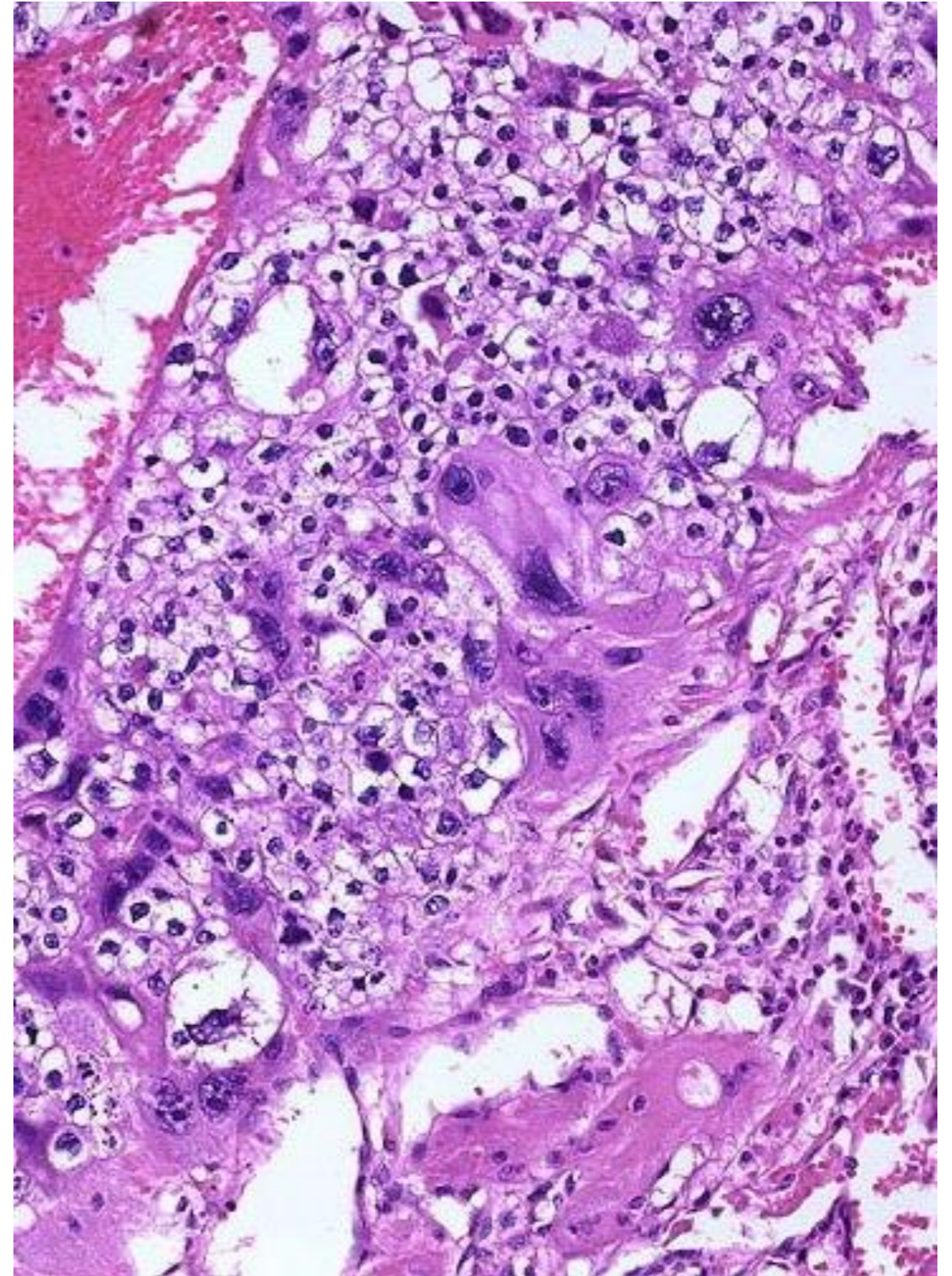
- ~~Classic~~ Seminoma

- No clinical significance in cases of seminoma with variety of histological patterns (microcystic, granulomatous component etc) or anaplasia
- Seminoma with syncytiotrophoblast cells
 - 10-20% of tumors
 - May be widely scattered to prominent aggregates, including haemorrhage
 - β -hCG positive by IHC
 - Modest elevation of β -hCG; if high levels (>500 IU/mL) primary or metastatic choriocarcinoma should be considered
 - Differential diagnosis with choriocarcinoma (lack of cytotrophoblast)

Seminoma with
syncytiotrophoblast



Choriocarcinoma

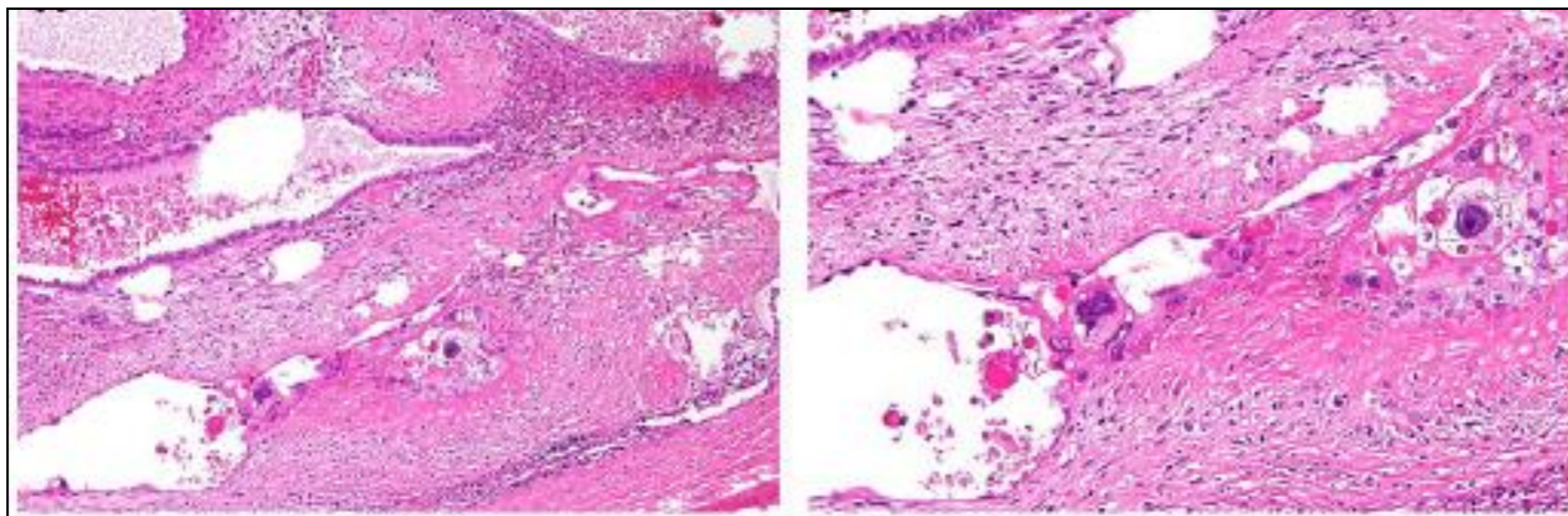
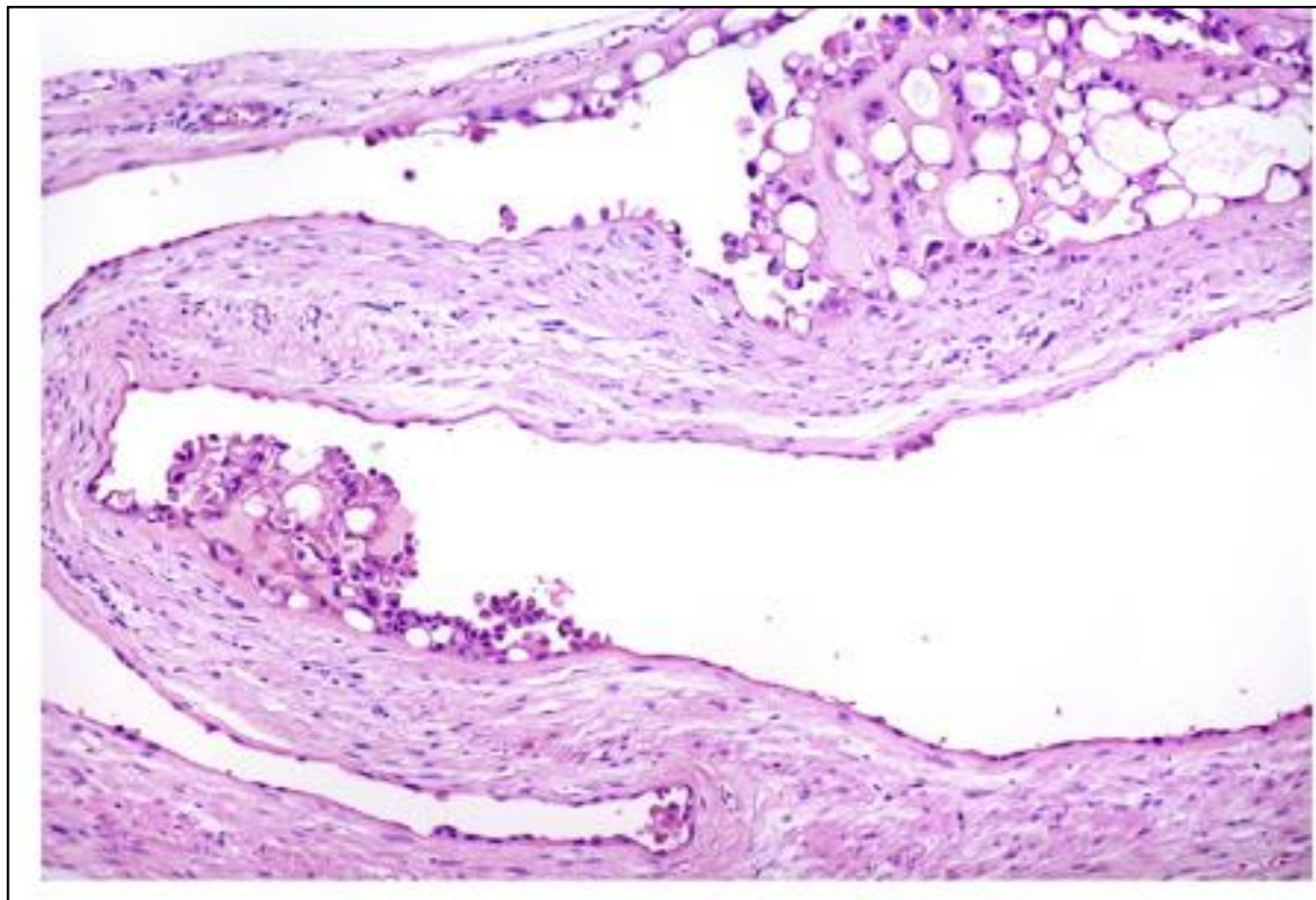
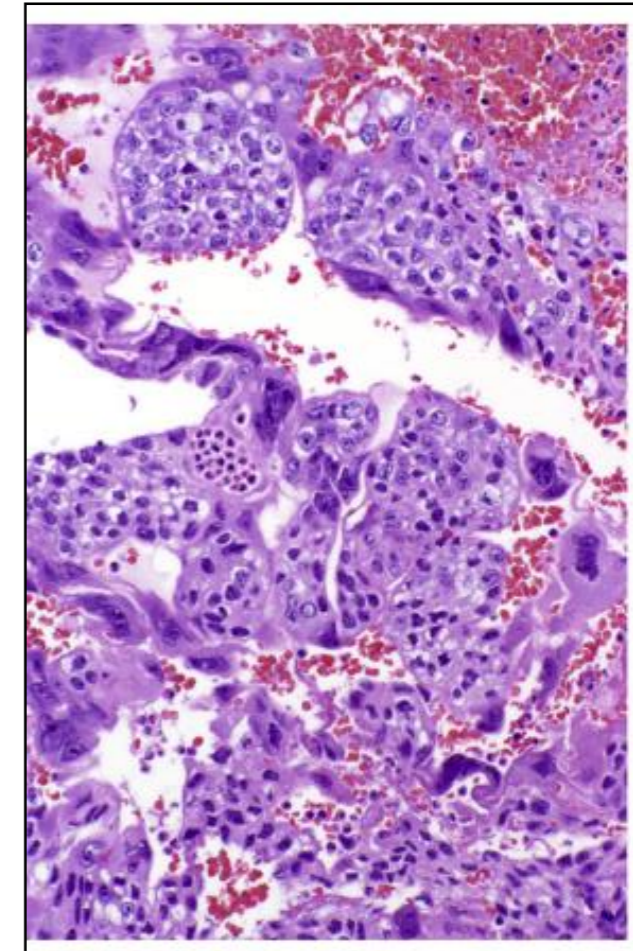


Trophoblastic Tumor, WHO, 2016

- The spectrum of trophoblastic tumors arising in the setting of testicular germ cell tumor is expanding, beyond choriocarcinoma
- Placental site trophoblastic tumor
- Epithelioid trophoblastic tumor
- **Cystic trophoblastic tumor**
 - non-aggressive behaviour
 - often associated with teratomas
 - cystic spaces lined by trophoblasts
 - occasional reactivity for β -hCG (patients with modest elevation of β -hCG, may be negative)
 - not infiltrative, biphasic growth pattern not present
 - should be managed as similarly to residual teratoma (no germ cell tumor-direct chemo, only surgical resection of persistent disease)

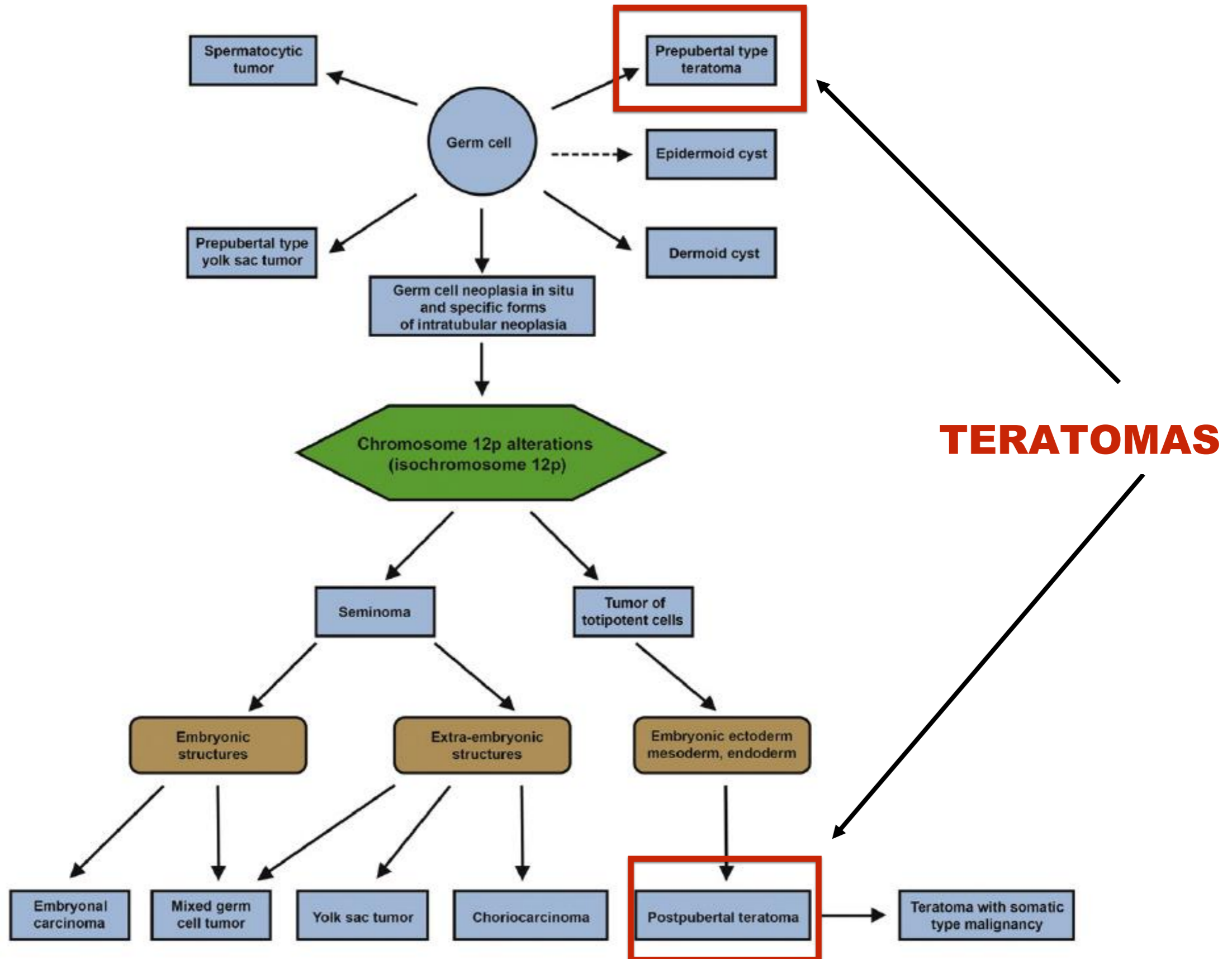
Cystic Trophoblastic Tumor, WHO, 2016

choriocarcinoma



cystic trophoblastic tumor

WHO, 2016: Two Types of Teratomas



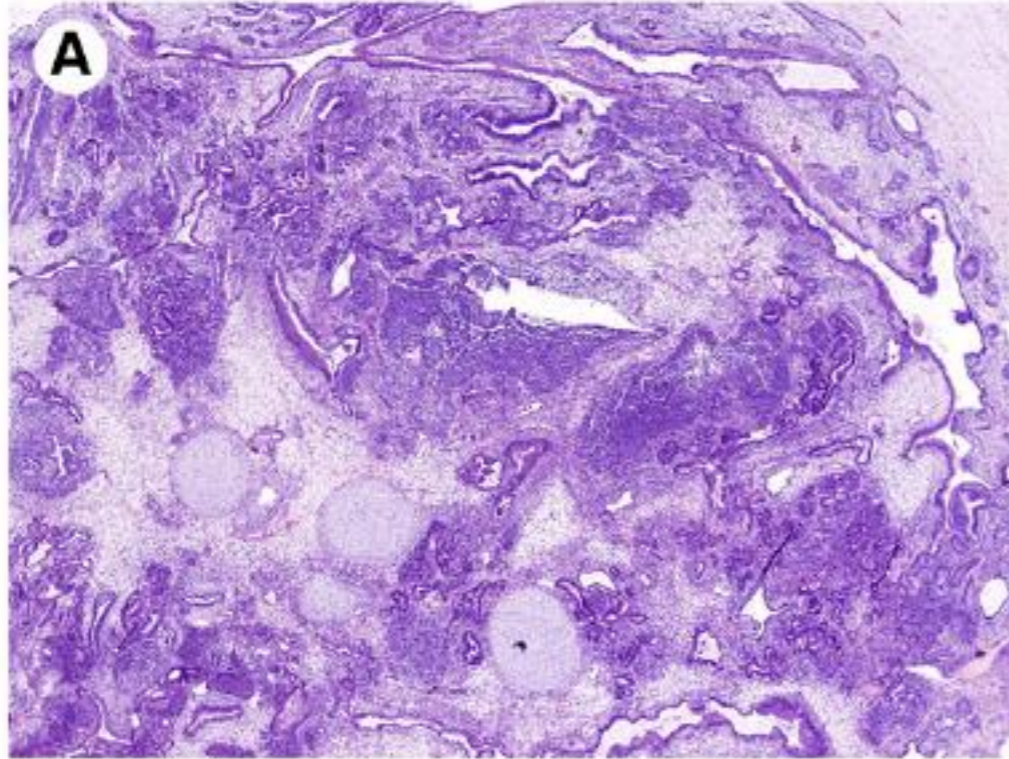
Teratoma, Postpubertal Type, WHO, 2016

- Previous known as mature teratoma and immature teratoma
- **Malignant** germ cell tumor composed of several types of tissues
- May be formed exclusively of well-different, mature tissues or have immature embryonic tissues
- Association with GCNIS and other tumors (yolk sac tumor, embryonal carcinoma) with subsequent differentiation to teratoma
- Often has GCNIS in the testis and may develop metastases consisting of teratoma or other germ cell tumors
- Different entity from prepubertal teratoma (**benign**)

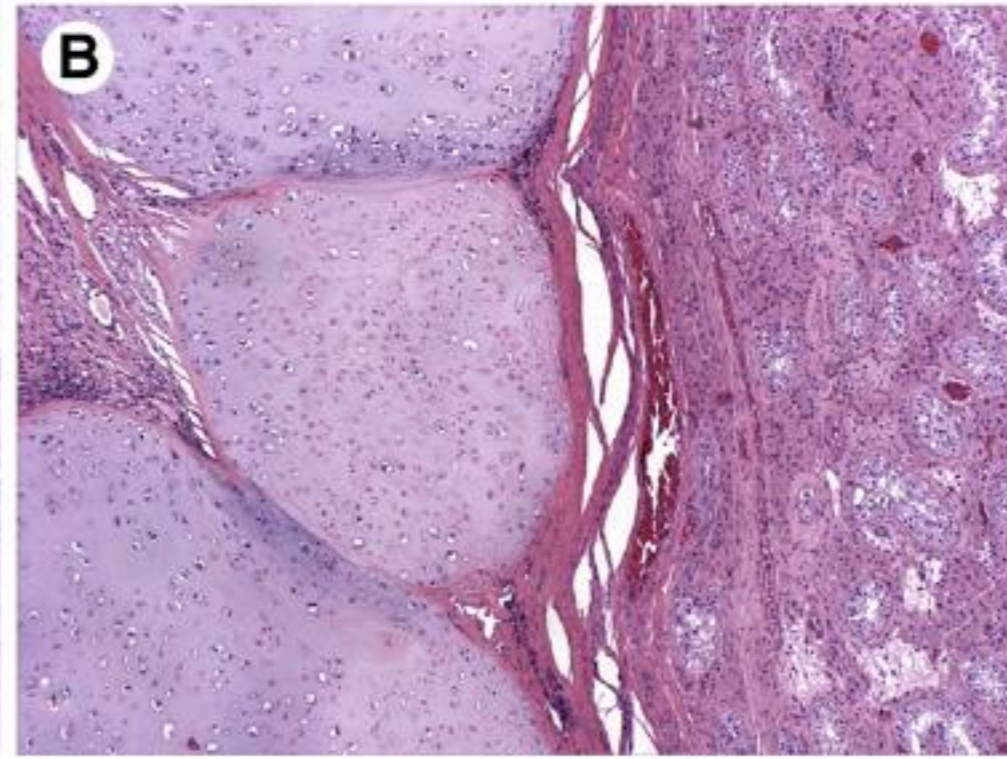
Teratoma, Postpubertal Type, WHO, 2016

- Immature vs mature
 - no prognostic value
 - pathologists should NOT comment about these elements
- Somatic-type malignancy arising from teratoma
 - sarcoma, PNET, carcinoma, gliomas, lymphomas, etc
- Young adults; presence of metastatic disease in 22-37% of the cases
- Presence of teratoma in metastases has good prognosis in treated GCT with chemo
- Epidermoid cyst is one type of teratoma (potentially malignant)

Teratoma, Postpubertal Type, WHO, 2016



↑
**postpubertal teratoma:
various somatic-type
tissue elements**



↑
**postpubertal teratoma:
cartilage only**

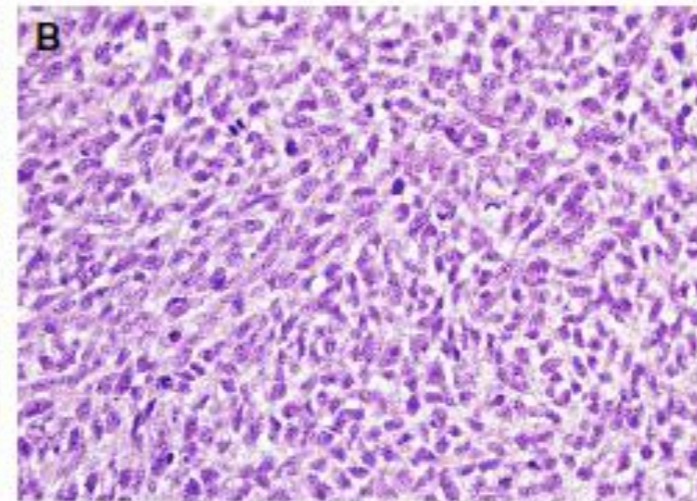
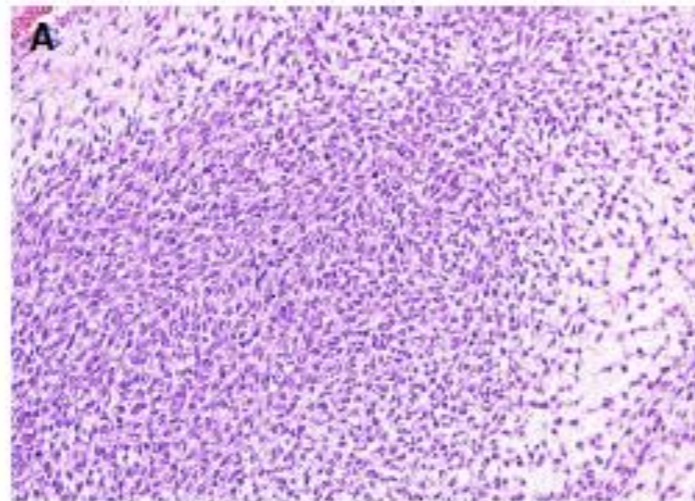
All testicular postpubertal-type teratomas are potentially malignant regardless of the presence or absence of an immature component or somatic-type malignancy

Teratoma, Postpubertal Type, WHO, 2016

Somatic-Type of Malignancy

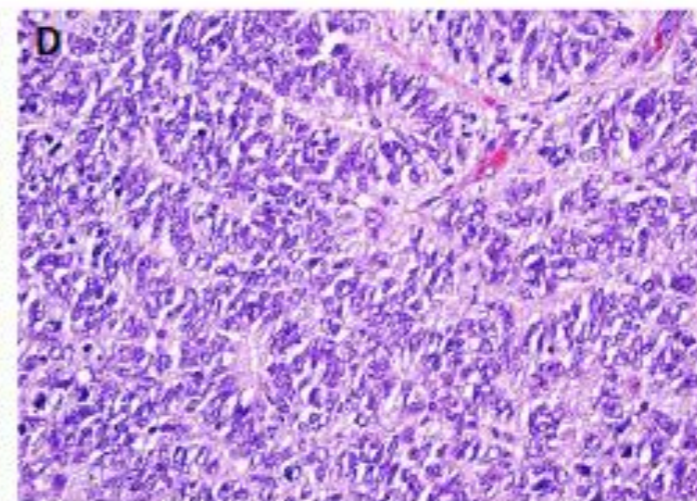
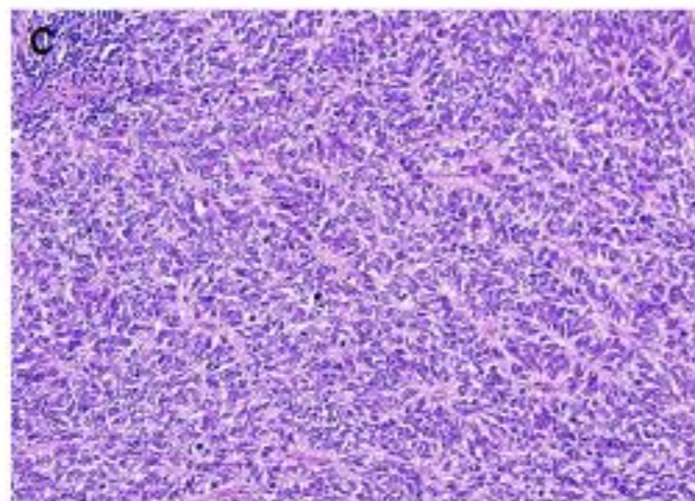
- Overgrowth of a particular component of teratoma
- Secondary malignancy, teratoma with “malignant transformation” (no recommended)

**Rhabdo-
myosarcoma**



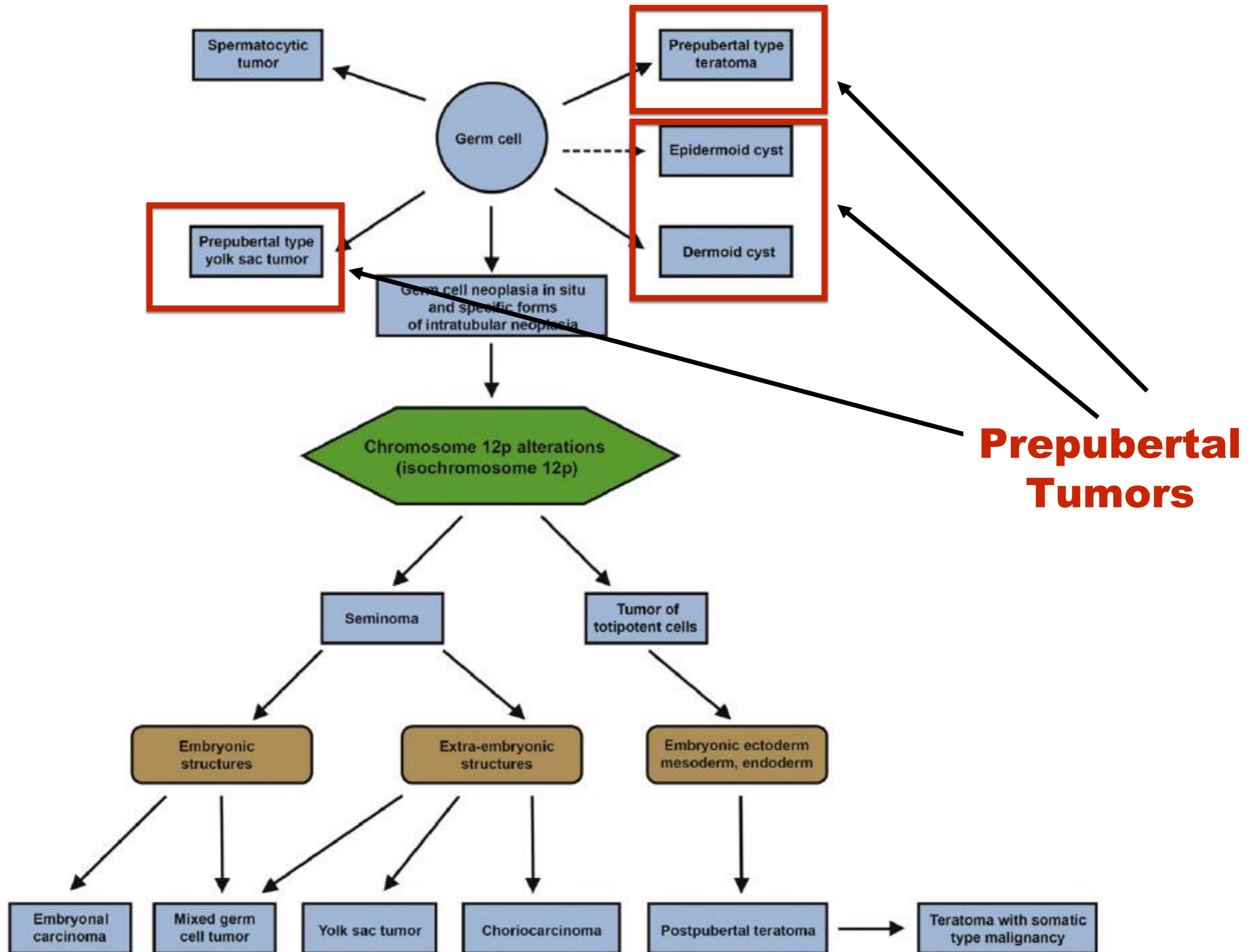
**Rhabdo-
myosarcoma**

PNET



PNET

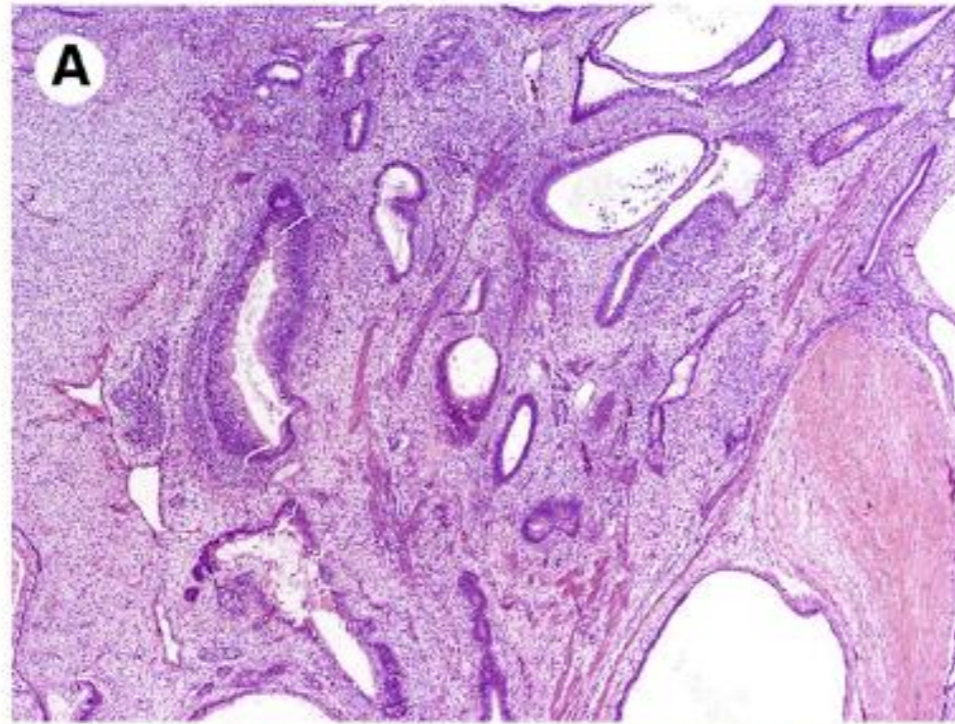
WHO, 2016: Prepubertal Tumors



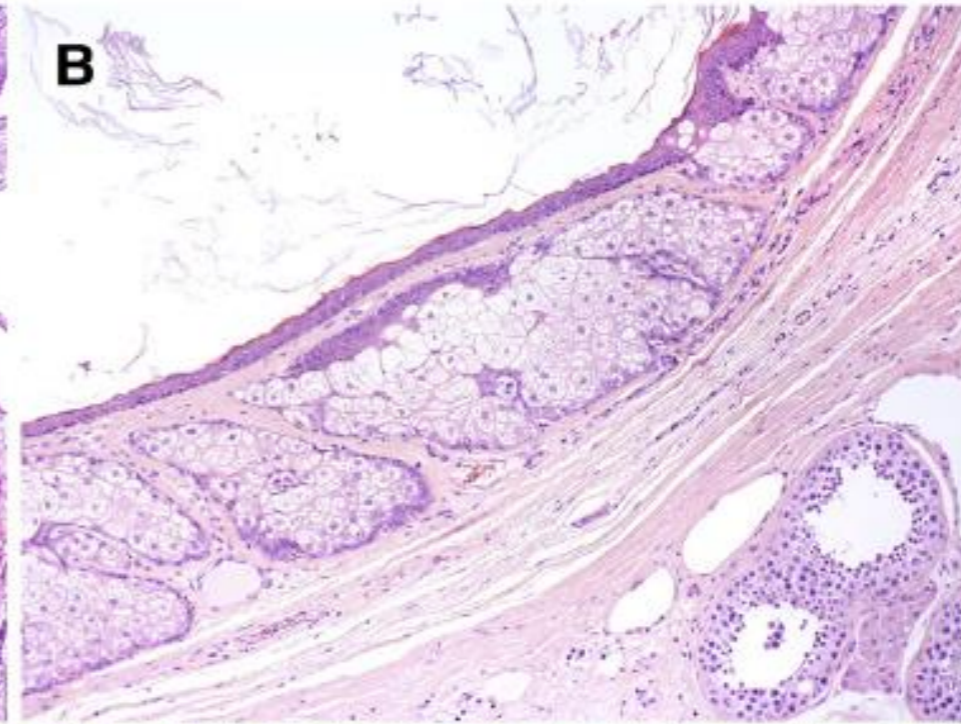
Teratoma, Prepubertal Type, WHO, 2016

- NO association with GCNIS
- Pathologic findings
 - organoide architecture
 - lack of significant atypia
 - 12q amplification, not present
- Benign (no metastases reported)
- Prepubertal type can be found in postpubertal patients!
- Dermoid and epidermoid cysts: now prepubertal type of teratoma

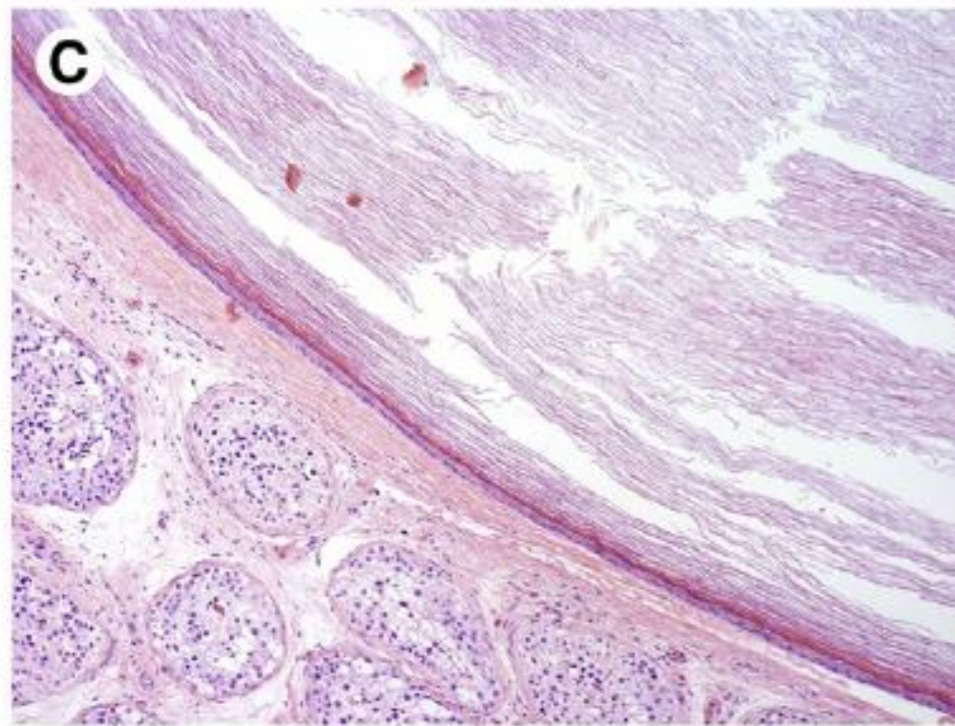
Teratoma, Prepubertal Type, WHO, 2016



**Prepubertal
teratoma**



**Dermoid
cyst**



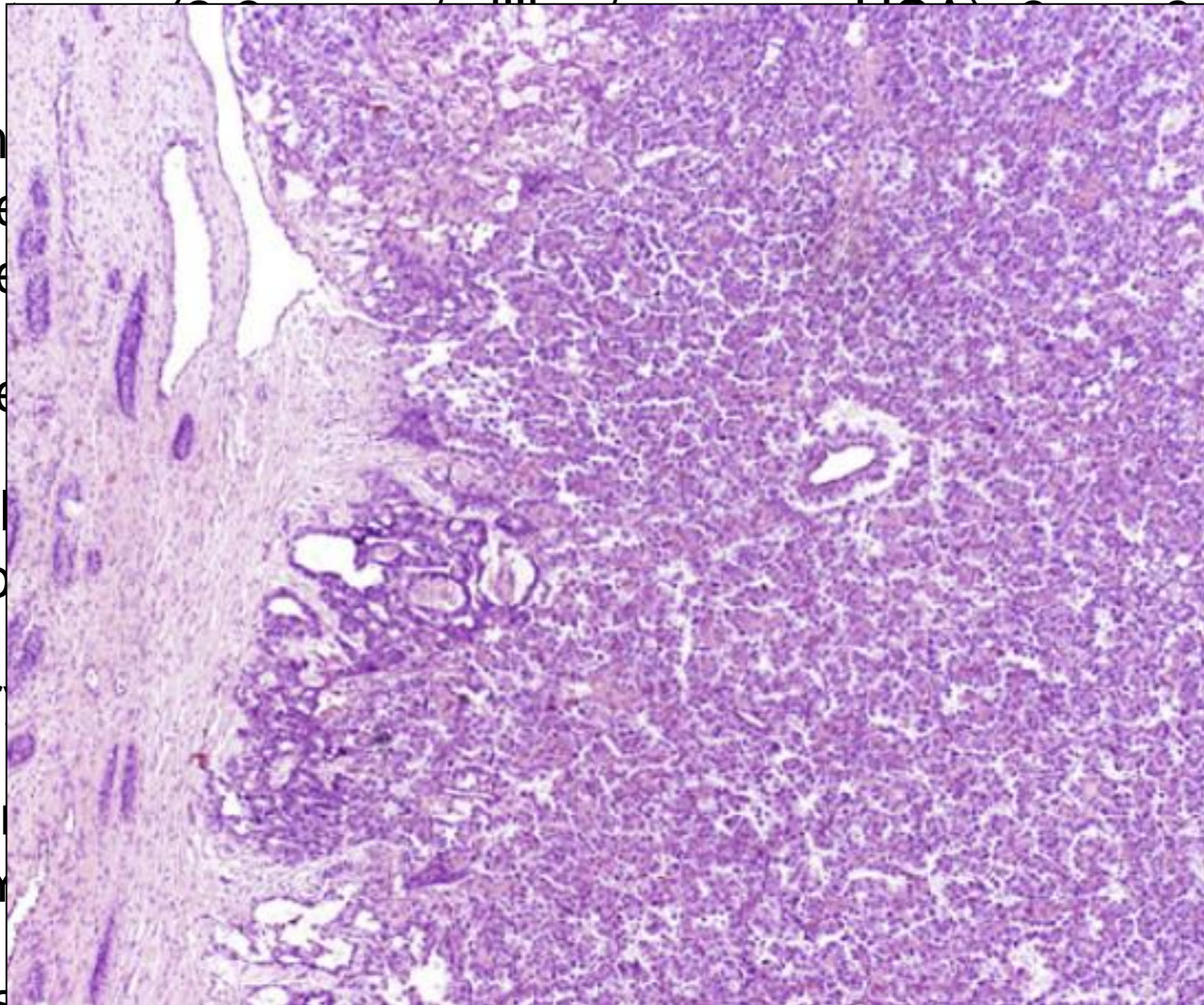
**Epidermoid
cyst**

Yolk Sac Tumor, Prepubertal Type, WHO, 2016

- Rare tumor (2-3 cases/million/per year, USA); 3 mo-8 yo
- Germ cell tumor that differentiate to resemble extraembryonic structures including yolk sac, allantois and extraembryonic mesenchyme.
- Unlike YST, postpubertal is NOT associated with GCNIS
- Usually occurs in pure form rather than mixed form (only associated with teratoma)
- No cryptorchidism, no GCNIS
- Low incidence of extratesticular involvement as compared with YST postpubertal
- In case of advanced disease, chemo is very efficient

Yolk Sac Tumor, Prepubertal Type, WHO, 2016

- Rare
- Germ cell tumor of the ovary and testis
- extraembryonic
- extraembryonic
- Unlike
- Usual
- teratoma
- No cr
- Low in
- with Y
- In case of advanced disease, chemo is very efficient

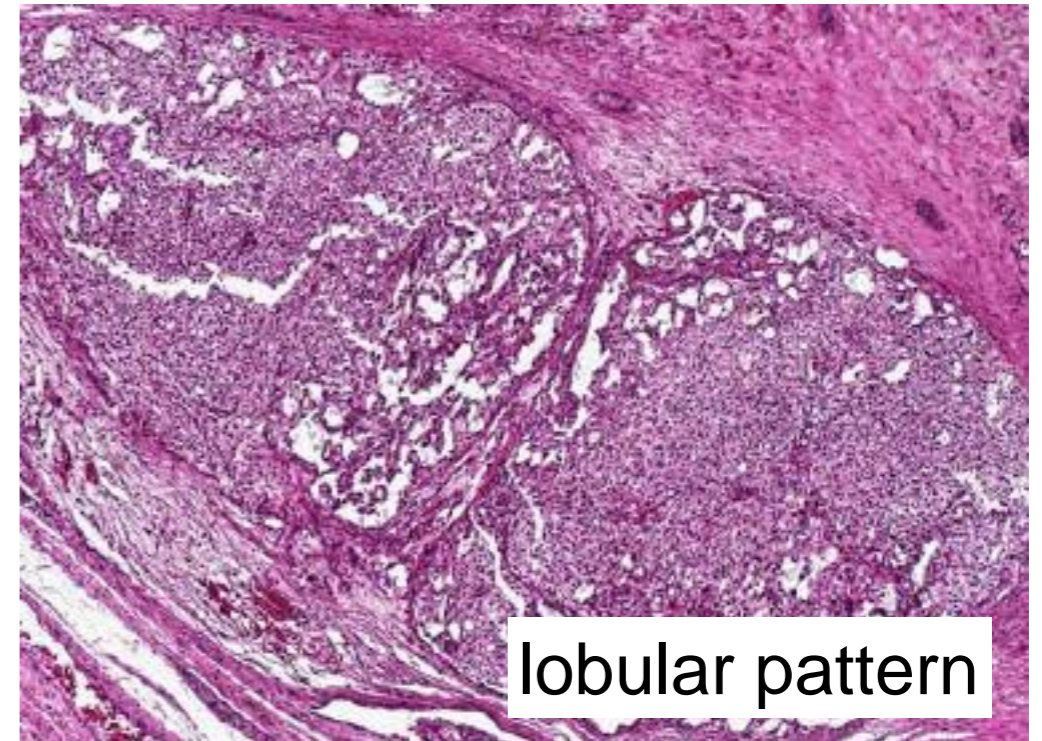
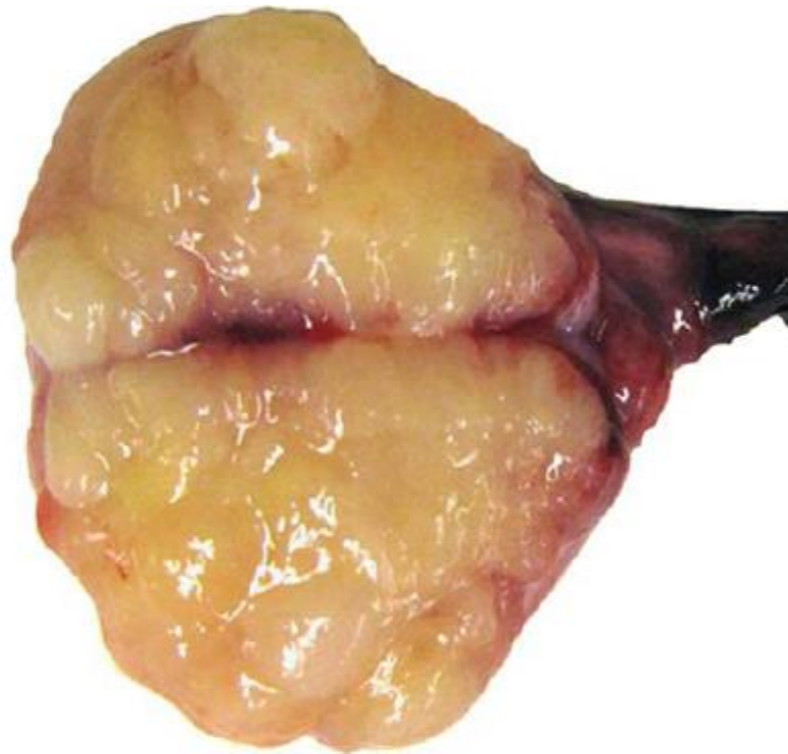


Yolk Sac Tumor of the Testis in Infants and Children

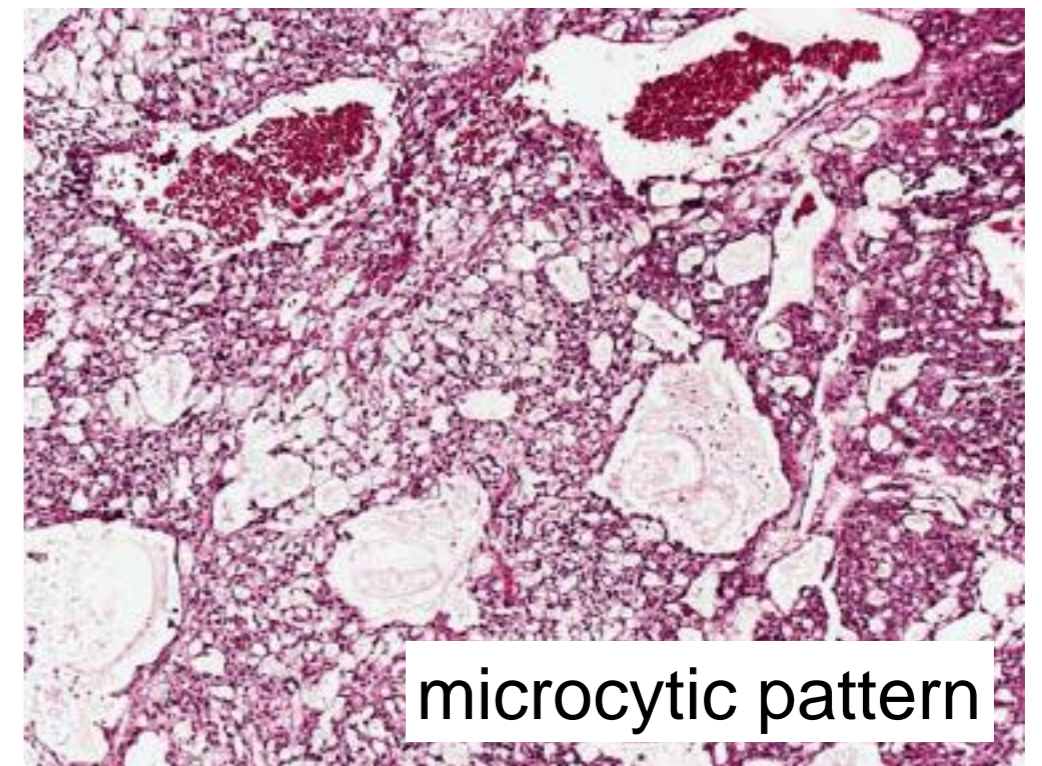
A Clinicopathologic Analysis of 33 Cases

Kristine M. Cornejo, MD,† Lindsay Frazier, MD, ScM,‡ Richard S. Lee, MD,§||
Harry P.W. Kozakewich, MD,†¶ and Robert H. Young, MD*†*

The **survival** of young boys with testicular yolk sac tumor **is very good** because of both effective chemotherapy and likely, the inherent characteristics of the tumor in this age group.



lobular pattern

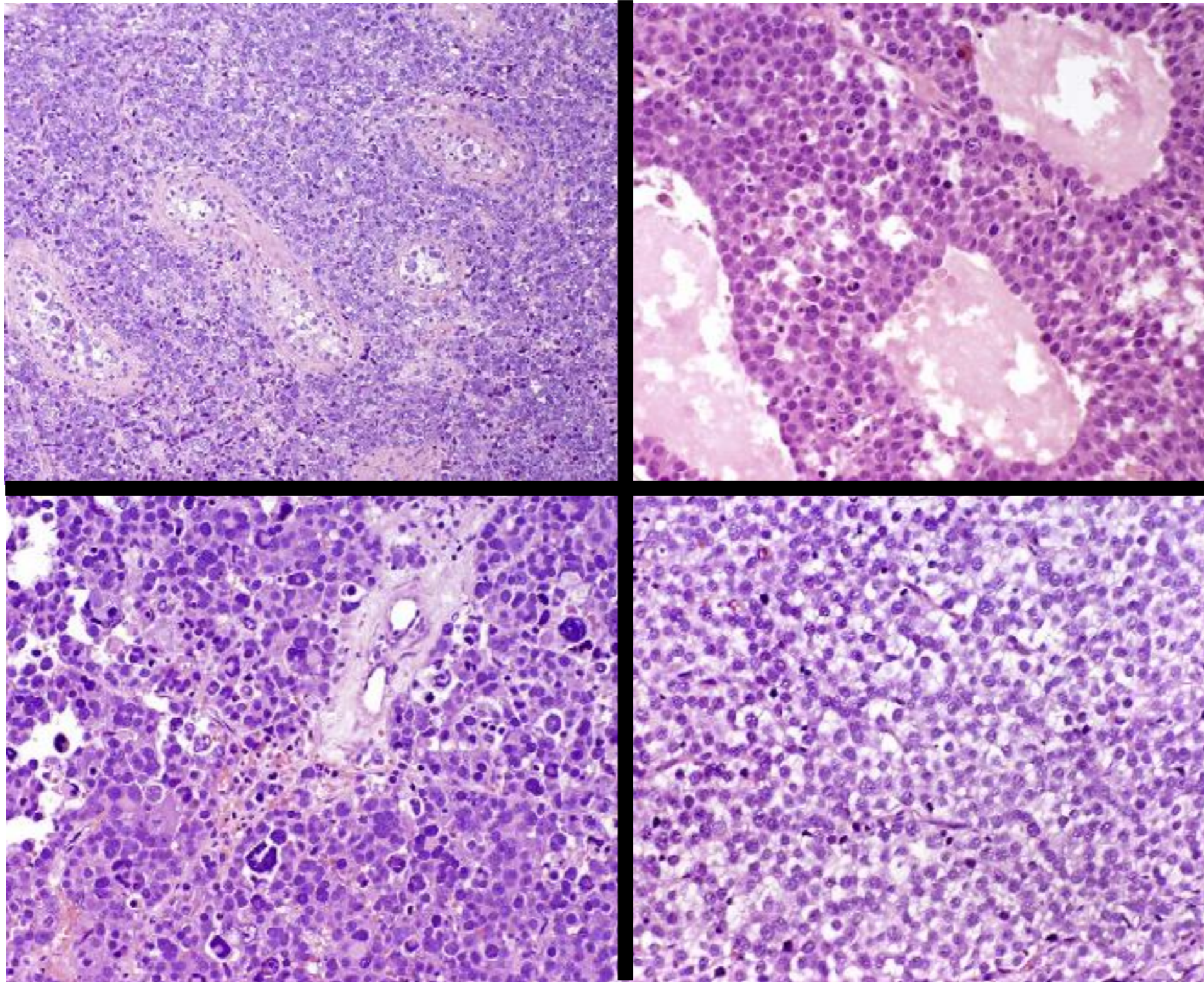


microcytic pattern

Spermatocytic tumor, WHO, 2016

- No more spermatocytic seminoma; changed to **spermatocytic tumor**
- Non-aggressive tumor with only very rare examples of metastases
- No true relationship to usual seminoma
- Germ cell tumor derived from postpubertal-type germ cells
- Resemble spermatogenic cells, mostly common spermatogonia or early spermatocytes
- Older individuals (sixth decade); no extragonadal counterpart
- Treatment with orchiectomy is curative; rare cases with progression or dedifferentiation into sarcoma

Spermatocytic tumor, WHO, 2016



Take Home Message

- The 2016 update to the WHO classification of tumors of urinary tract and male organs brings a number of changes and refinements to the classification of germ cell tumors
- GCNIS replaces IGCNU
- GCNIS-derived and non-GCNIS-derived tumors, largely, but not exclusively, related to postpubertal and prepubertal, respectively
- Reclassification of spermatocytic seminoma
- Category of non-choriocarcinoma trophoblastic tumors has been expanded to analogous entities to gynecologic tract counterpart
- Existence of benign teratoma of the postpubertal testis (termed prepubertal teratomas)
- Presence of immaturity in teratomas has no prognostic importance