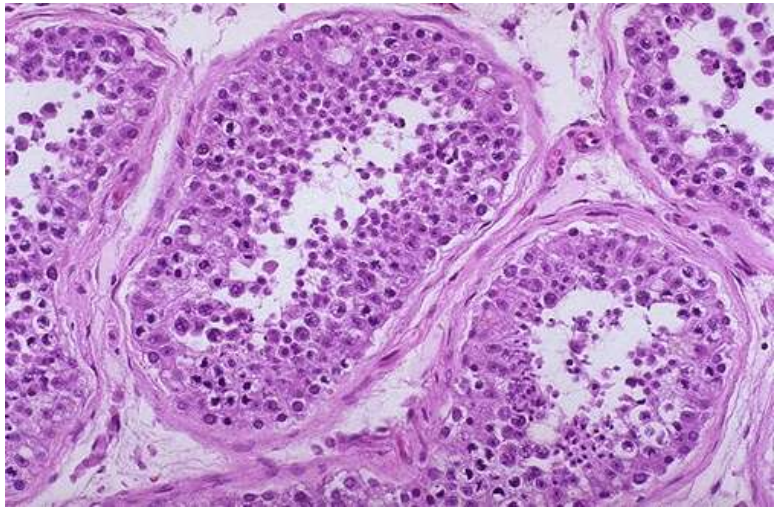
PATOLOGIA DEL TESTICOLO

Testicolo

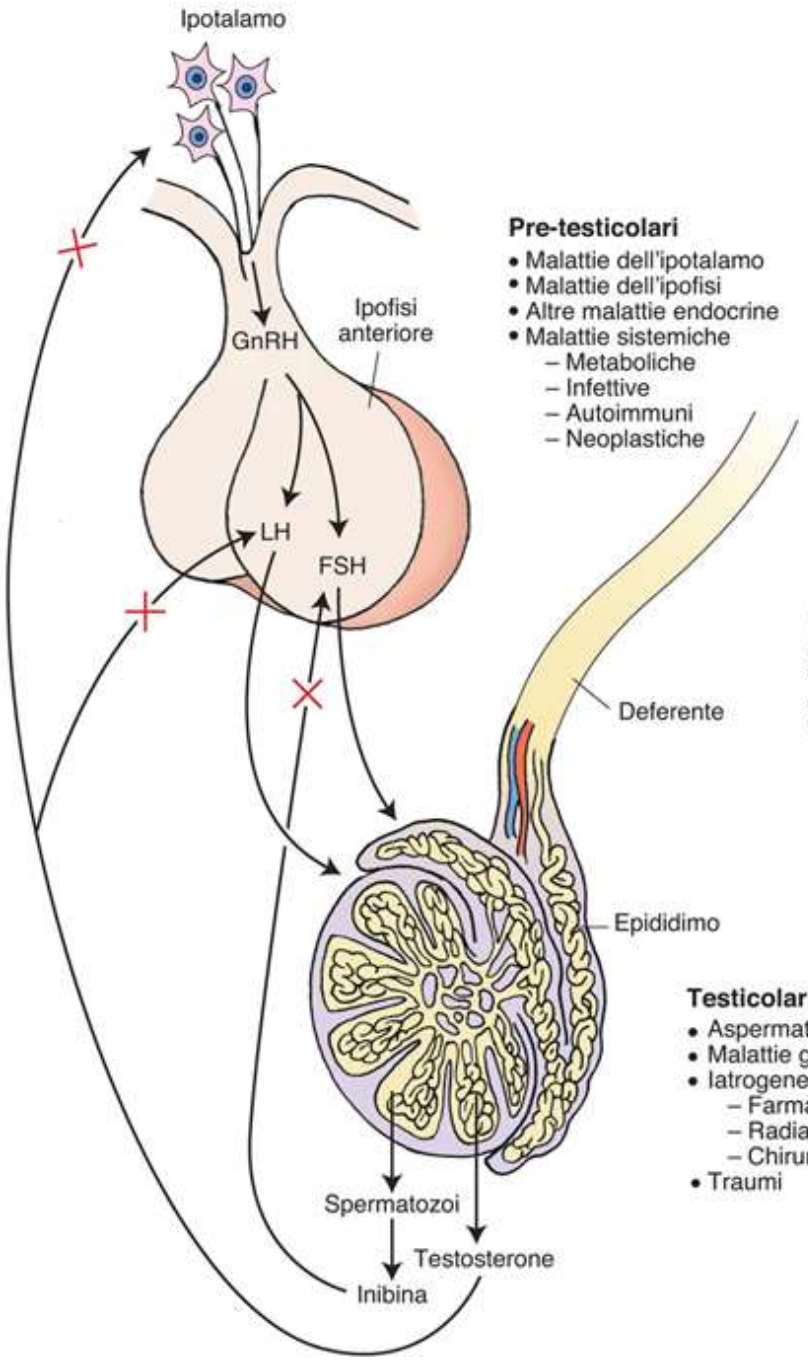


- Anomalie della differenziazione sessuale: possono essere legate ad alterazioni cromosomiche, o a difetti della produzione di ormoni o insensibilità tissutale alla loro azione.
  - Sesso genetico
    - Presenza o assenza dei cromosomi X e Y
  - Sesso gonadico
    - Presenza o assenza dei testicoli e delle ovaie
  - Sesso genitale
    - Comparsa degli organi genitali esterni
  - Orientamento sessuale o psicosociale
    - Percezione del sè

ANOMALIE DELLA DIFFERENZIAZIONE SESSUALE

- Anomalie dei cromosomi sessuali
  - S. di Klinefelter, Turner,…
- Deficit di singoli geni
  - Sindromi adrenogenitali
  - Ipersensibilità all'androgeno
  - Deficit di sostanza inibitoria mulleriana
- Effetti ormonali prenatali: ormoni, tumori
- Patologie idiopatiche: ermafroditismo disgenesia gonadica

Sterilità maschile: incapacità al concepimento



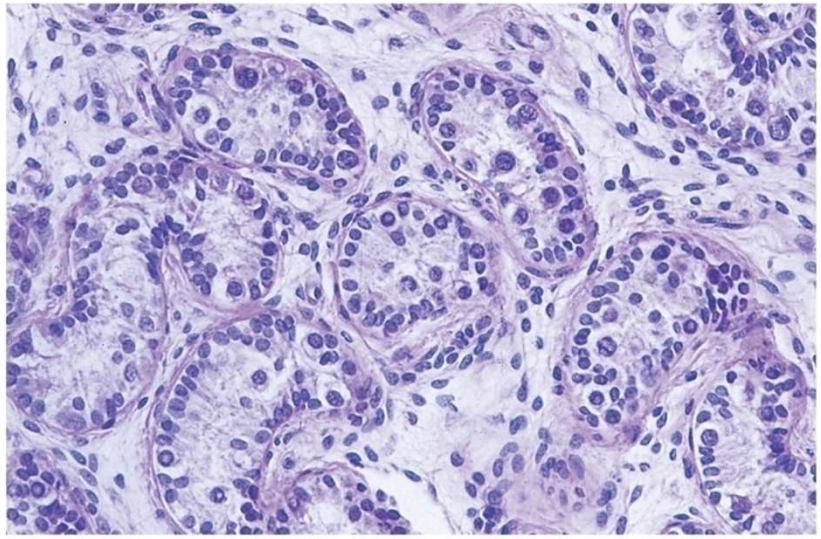
Pre-testicolari
- Malattie dell'ipotalamo
- Malattie dell'ipofisi
- Altre malattie endocrine
- Malattie sistemiche
  - Metaboliche
  - Infettive
  - Autoimmuni
  - Neoplastiche

Post-testicolari
- Anomalie congenite dello sviluppo
- Infezioni
- Traumi
- Chirurgia (vasectomia)

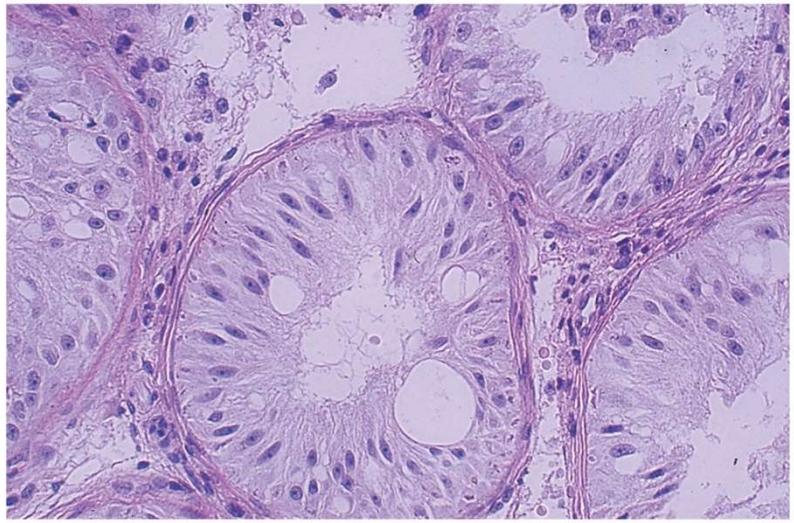
Testicolari
- Aspermatogenesi idiopatica
- Malattie genetiche cromosomiche
- Iatrogene
  - Farmaci
  - Radiazioni
  - Chirurgia
- Traumi

Biopsia testicolare

- Immaturità dei tubuli seminiferi
- Ipospermatogenesi
- Arresto maturativo
- Aplasia delle cc. Germinali
- Orchite
- Fibrosi tubulare e peritubulare



Ipogonadismo ipogonadotropico
•aspetto prepuberale in adulto da immaturità dei tubuli seminiferi

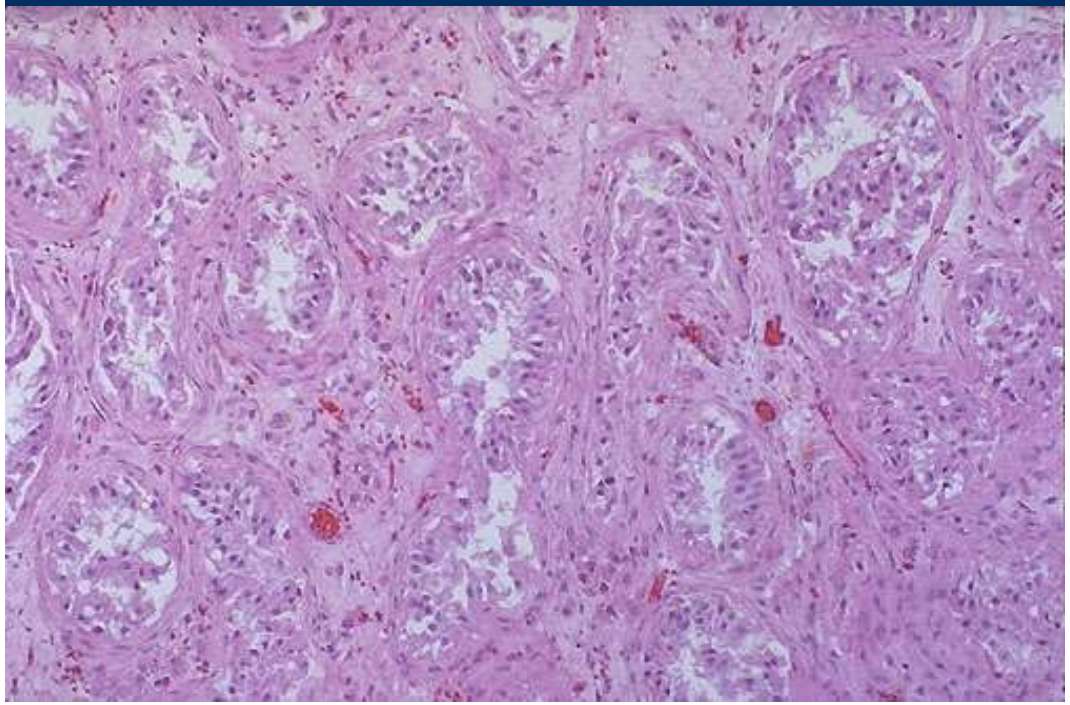


Sindrome delle sole cc di Sertoli
•Aplasia delle cc germinali

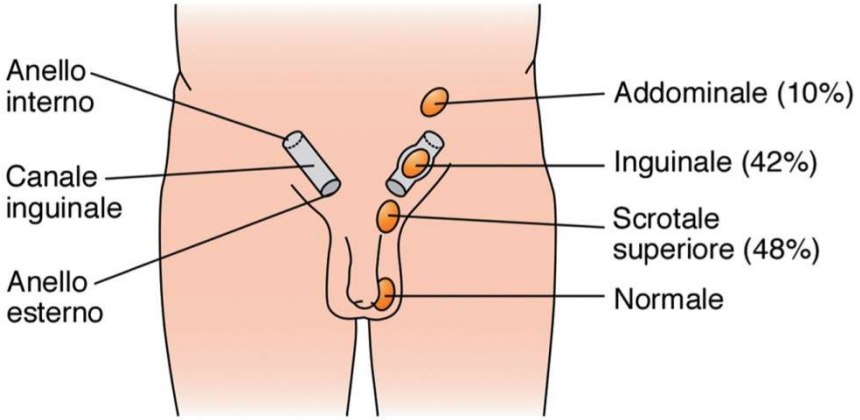
Atrofia testicolare

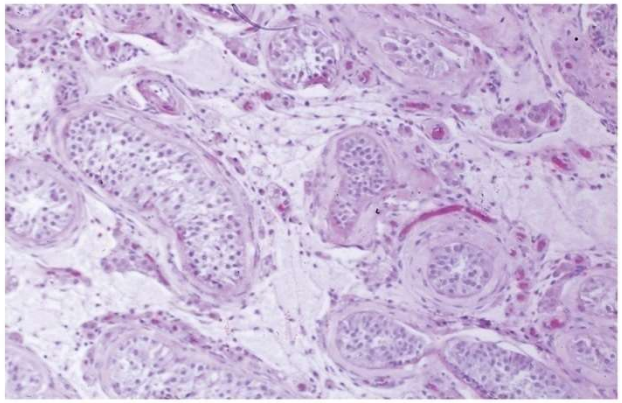
- On the left is a normal testis.
- On the right is a testis that has undergone atrophy.
- Bilateral atrophy may occur with a variety of conditions including chronic alcoholism, hypopituitarism, atherosclerosis, chemotherapy or radiation, and severe prolonged illness.
- A cryptorchid testis will also be atrophic. Inflammation may lead to atrophy.
- Mumps, the most common cause for orchitis, usually has a patchy pattern of involvement that does not lead to sterility.

- Note the marked loss of germ cells with remaining tall pink Sertoli cells, peritubular fibrosis, and interstitial fibrosis.



Criptorchidismo: discesa del testis incompleta nel sacco scrotale





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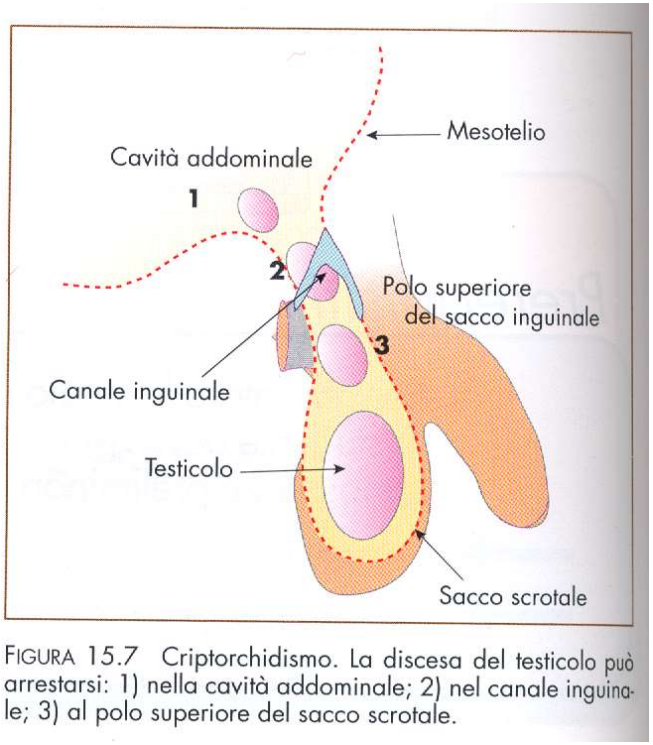


FIGURA 15.7 Criptorchidismo. La discesa del testicolo può arrestarsi: 1) nella cavità addominale; 2) nel canale inguinale; 3) al polo superiore del sacco scrotale.

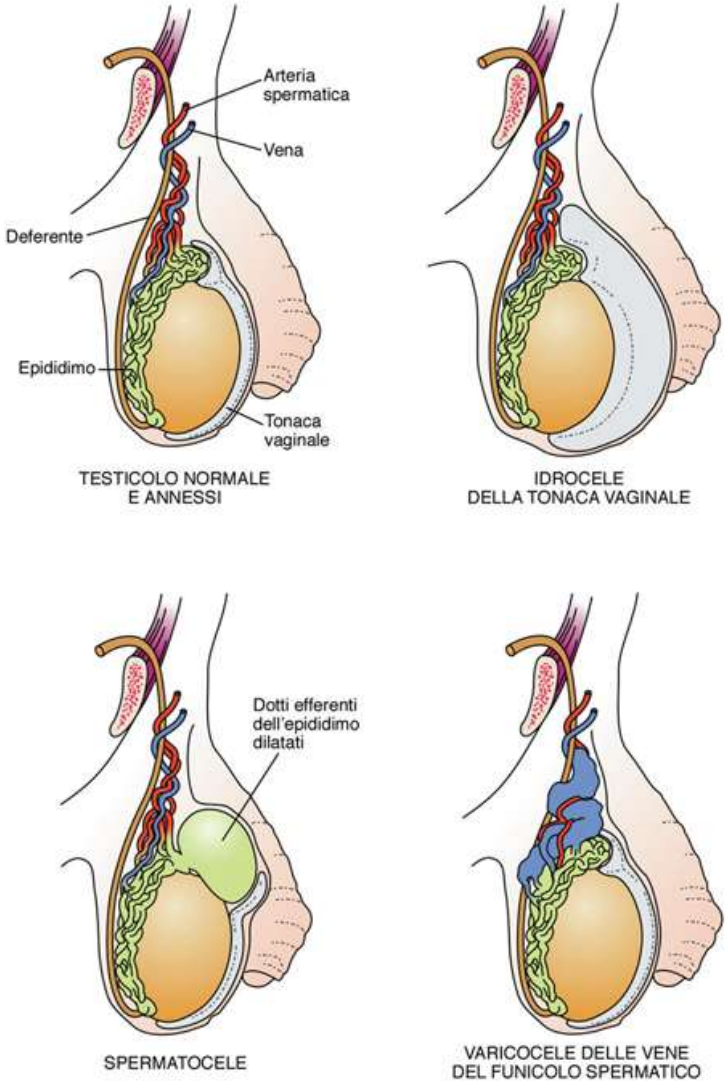
Criptorchidismo postpuberta'
- Focale ialinizzazione dei tubuli
- Fibrosi interstiziale
- Assenza spermatozoi

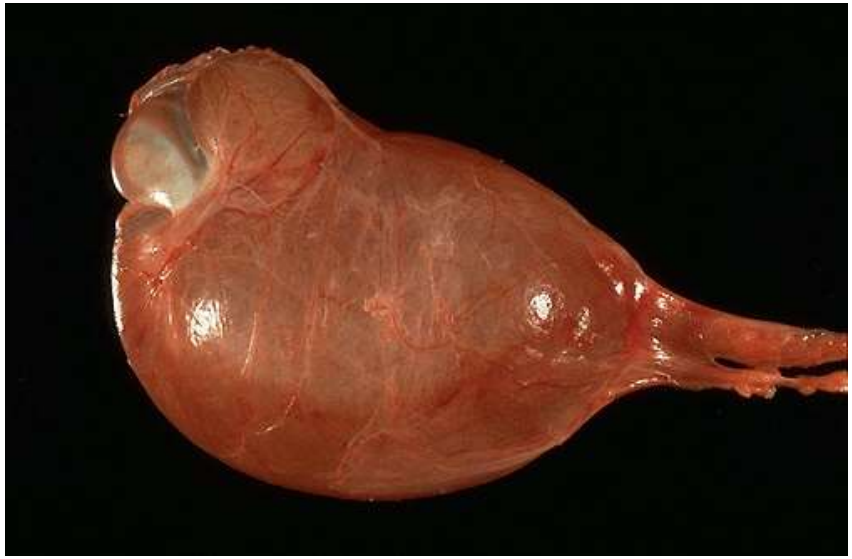
1% dei neonati

Frequente discesa spontanea nel 1° anno

t.del testicolo 20-40 volte + frequente

Masse scrotali non tumorali





Here is a large hydrocele of the testis.
•Such hydroceles are fairly common.
•Clear fluid accumulates in a sac of tunica vaginalis lined by a serosa with a variety of inflammatory and neoplastic conditions.
•A hydrocele must be distinguished from a true testicular mass, and transillumination may help, because the hydrocele will transilluminate but a testicular mass will be opaque.

Macroscopic mimickers (pseudotumors) of testicular and paratesticular neoplasia

Vascular lesions

Intratesticular hemorrhage
Segmental testicular infarction
Organizad testicular hematocele
Cholesterol granuloma of the tunica vaginalis

Inflammatory lesions

Nonspecific infectious inflammatory lesions
Specific infectious inflammatory lesions
Non-infectious inflammatory lesions
Idiopathic inflammatory lesions
Idiopathic granulomatous orchitis
Testicular malakoplakia
Testicular sarcoidosis
Meconium periorchitis
Sperm granuloma

Cysts

Testicular cysts
Albuginea cysts
Parenchymal cysts
(Epidermoid cysts)
Rete-testis cysts- Cystic displasia of the rete testis
Epididymal cysts and Spermatoceles
Spermatic cord cysts

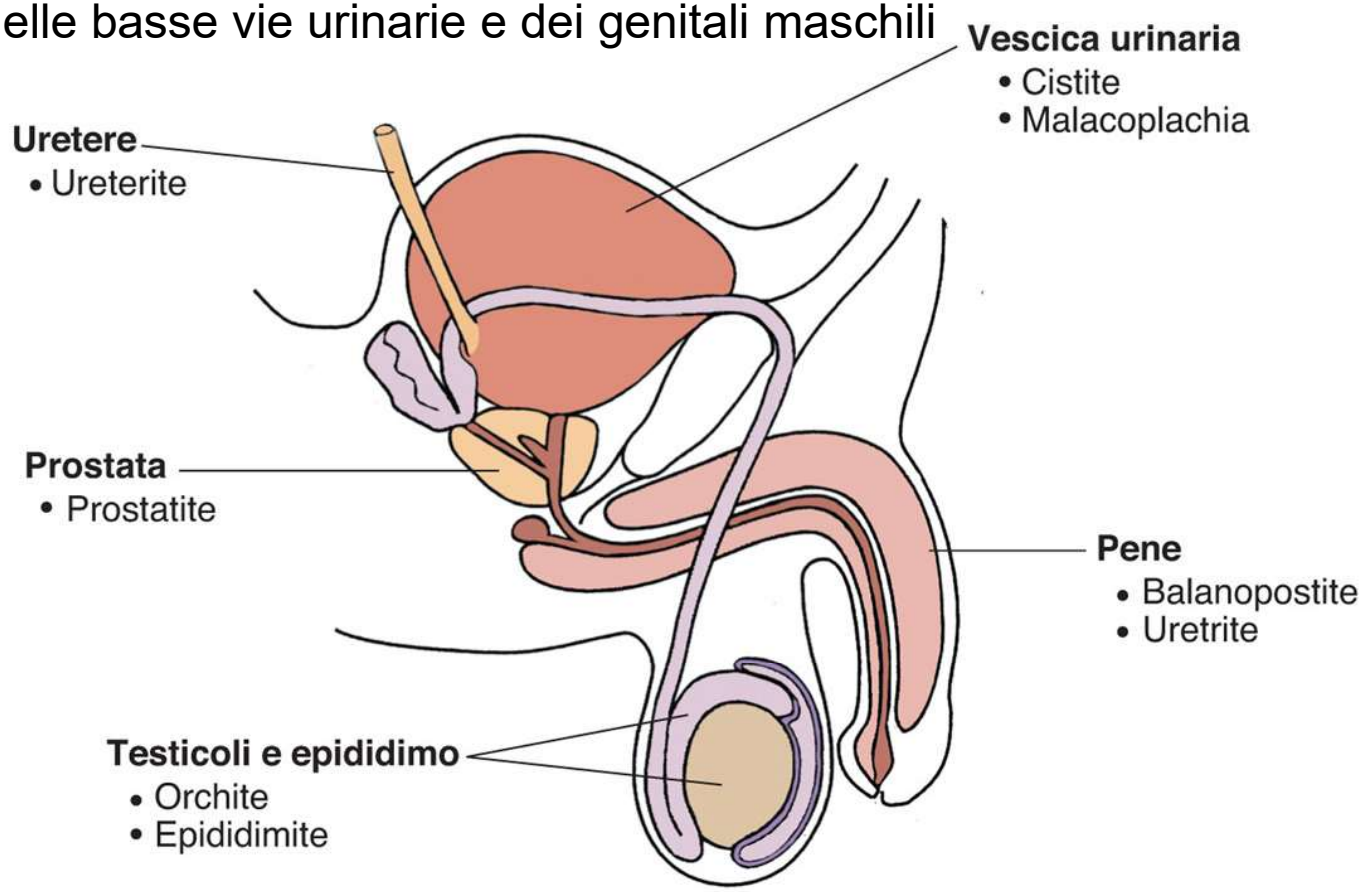
Ectopic tissues

Adrenal cortical rests
Spleno-gonadal fusion
Testicular appendages

Miscellaneous other lesions

Fibrous pseudotumors;
(Fibromatous periorchitis-Nodular periorchitis)
Amyloidosis
Polyorchididm
Sclerosing lipogranuloma

Infezioni delle basse vie urinarie e dei genitali maschili



Infezioni sessualmente trasmesse

- Herpes simplex virus
- *Chlamydia*
- *Mycoplasma*
- *Treponema pallidum*
- *Neisseria gonorrhoeae*
- HIV

Infezioni ascendenti delle vie urinarie

- *Escherichia coli*
- *Klebsiella*
- *Proteus*

Infezioni ematogene

- Virus della parotite
- *Streptococcus*
- *Staphylococcus*

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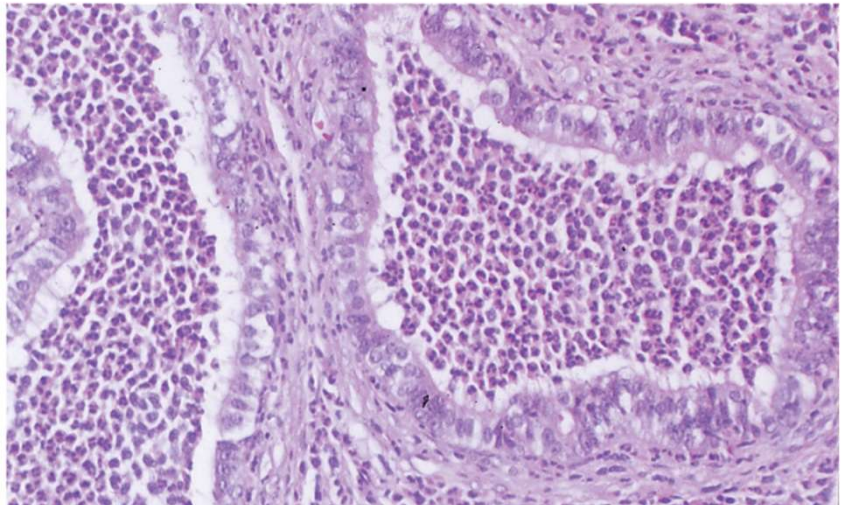
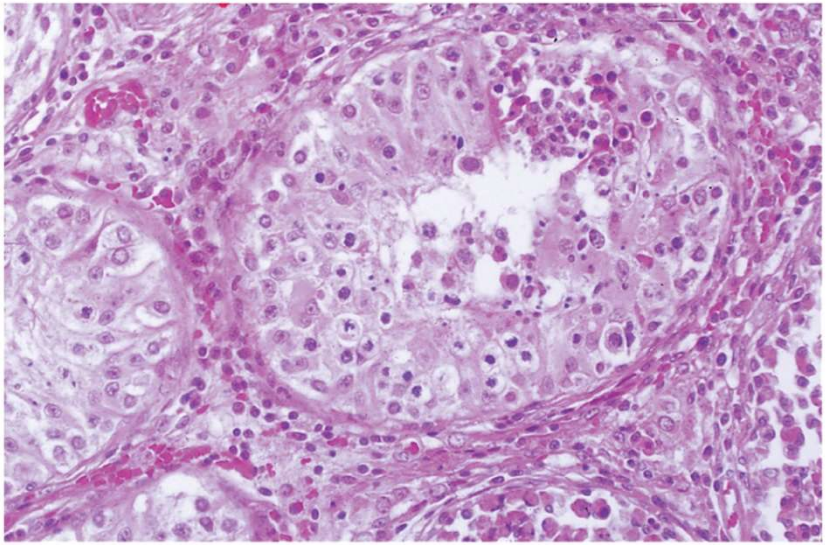
Flogosi

- Orchiti – epididimiti – orchiepididimiti
- Acute
- Croniche
  - Aspecifiche
  - Granulomatose
    - Specifiche
    - Non specifiche (orchite granulomatosa, granuloma spermatico)

Infarto testis: torsione del funicolo spermatico (dolore!)



Epididimite batterica



Orchite virale

- Flogosi interstiziale
- Interruzione temporanea della normale spermatogenesi
- Spesso da virus della parotite

Neoplasie

- Epidemiologia
  - Tra 25 e 45 anni
  - Meno dell'1% di tutte le neoplasie
  - Comportamento maligno
  - Curabilità con chirurgia e radio-chemioterapia
  - Metastasi ai linfonodi periaortici
- Etiopatogenesi:
  - Criptorchidismo, disgenesia gonadica
  - Familiarità (isocromosoma p12): frammento aggiuntivo nel cr
  - Fattori acquisiti?
  - ITGCN (neoplasia testicolare germinale intratubulare o in situ)
  - Secrezione di marcatori sierici nel 65% dei casi

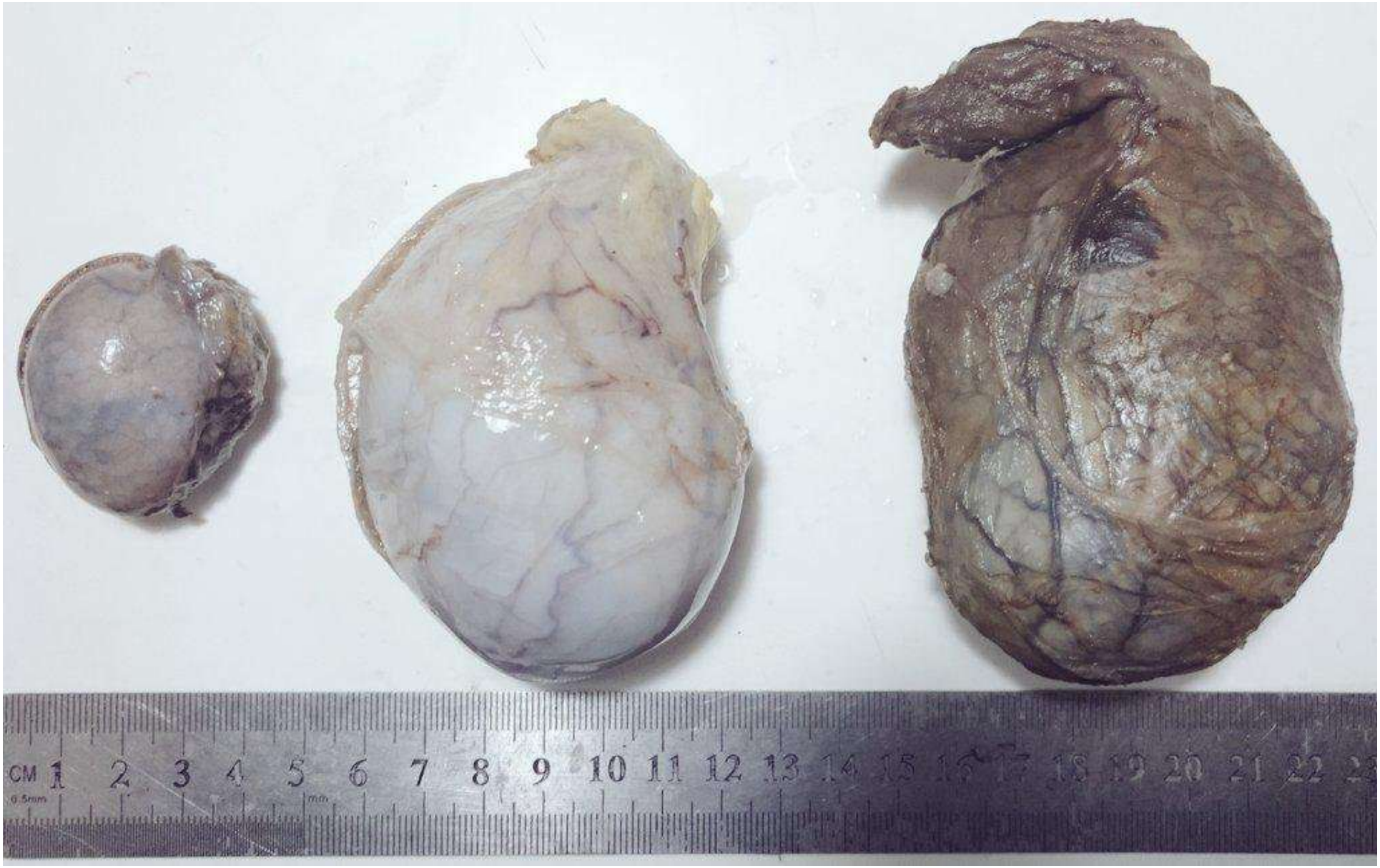

CM 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

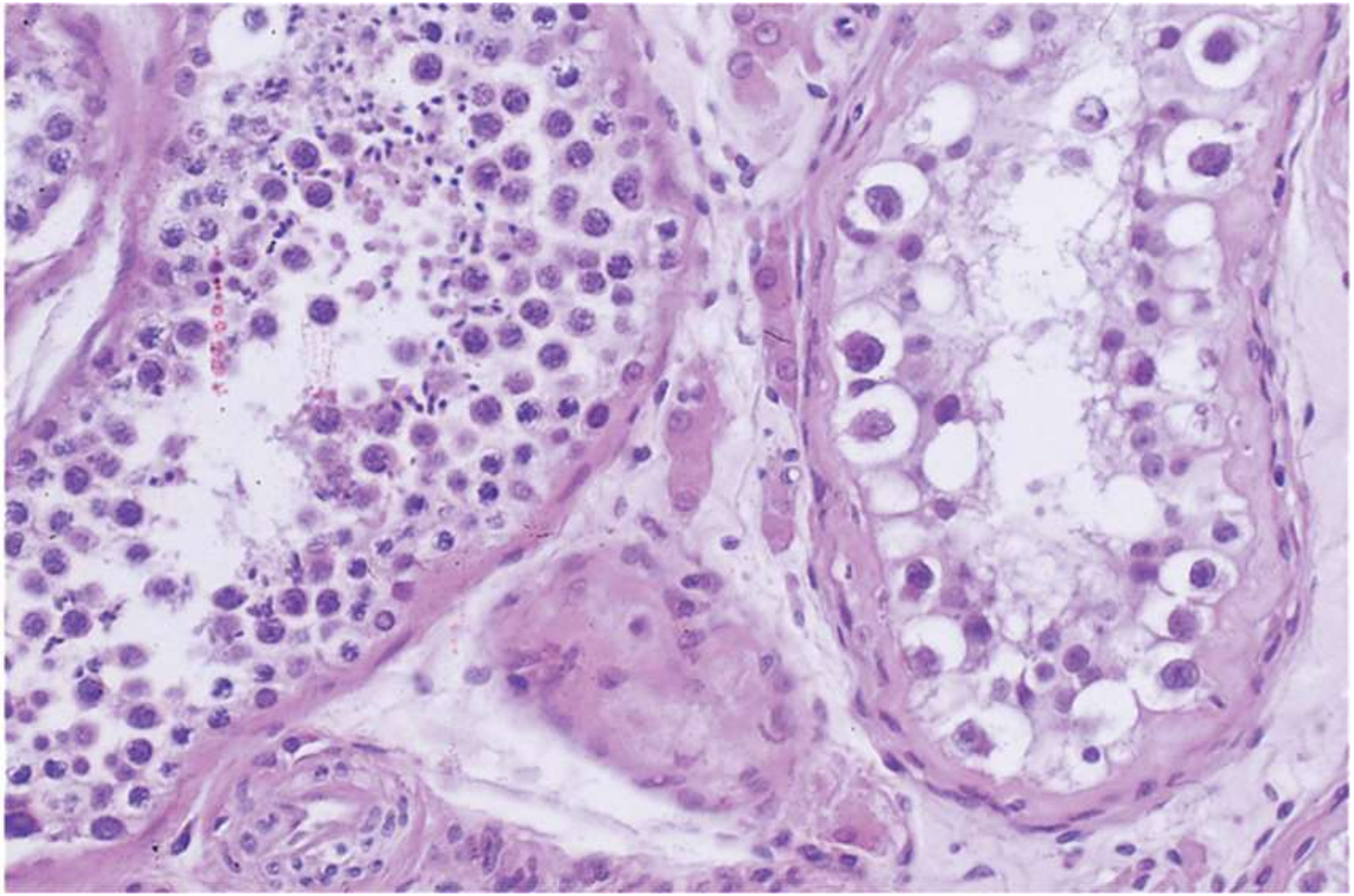
TABELLA 15.3 Classificazione istogenetica e frequenza dei tumori del testicolo.

Tumori delle cellule germinali (95%)
• Lesione *in situ* (IGCNU)
Tumori seminomatosi
• Seminoma (40%)
• Seminoma spermatocitico
Tumori non seminomatosi
• Carcinoma embrionale (5%)
• Tumore del sacco vitellino (<1%)
• Corioncarcinoma (<1%)
• Teratoma (35%)
Tumori di più tipi istologici
• Tumore misto a cellule germinali (15%)
• Poliembrioma (<1%)
• Embrioma diffuso (<1%)
Tumori stromali dei cordoni sessuali
• Tumori delle cellule di Leydig
• Tumori delle cellule del Sertoli
Tumori misti germinali e dei cordoni sessuali
Linfomi primitivi
Metastasi

IGNCU (intratubular germ cell neoplasia, unclassified type): cc simili a spermatogoni o cc embrionali fetali

- **Seminoma**: spermatogoni maligni
- **Non seminomatosi** (tendono a ricapitolare l'embriogenesi)
- Forme miste

ITGCN precursore di cr invasivo 50-70%

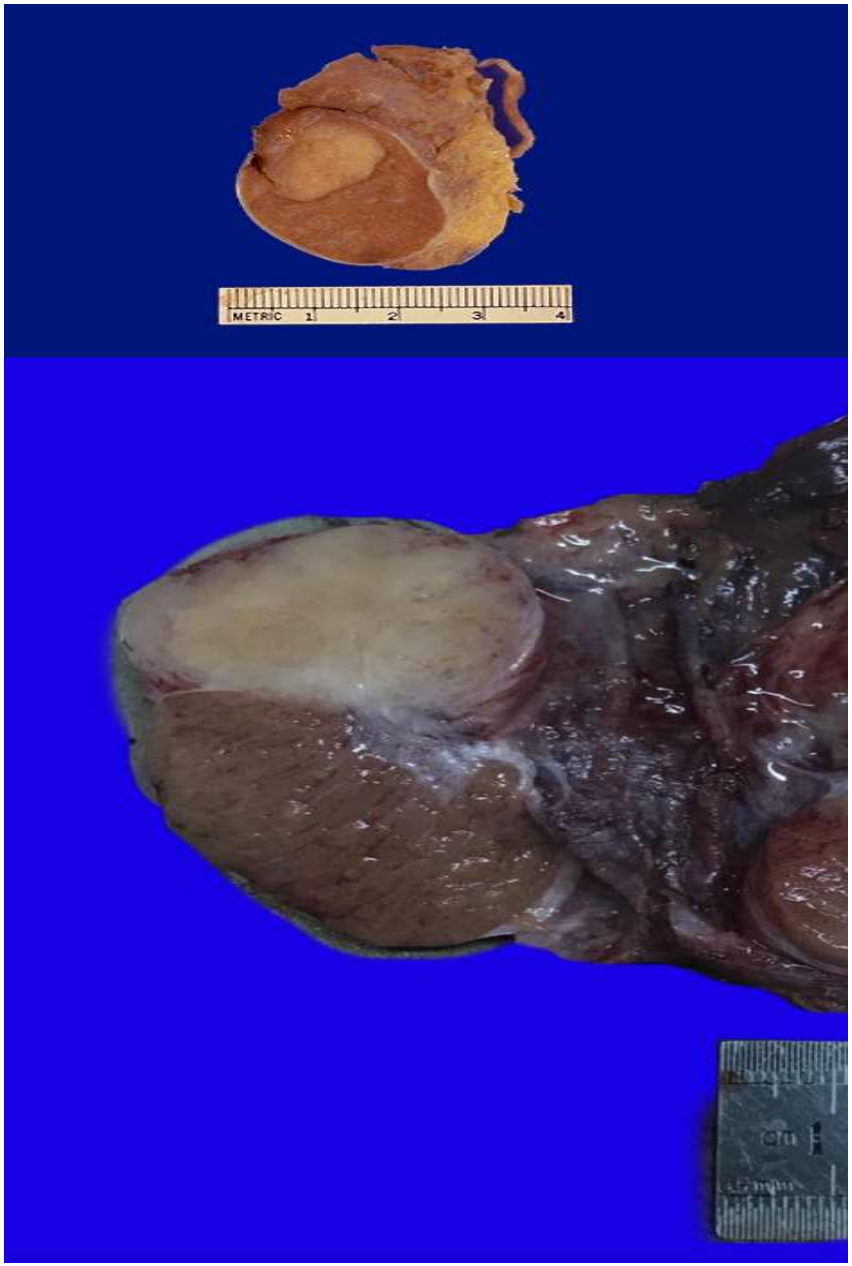


Tubuli seminiferi normali

Neoplasia germinale intratubulare

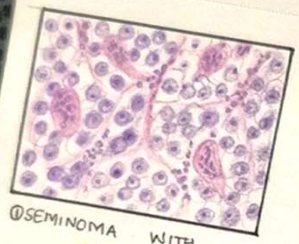
Seminoma

- 20-40 aa
- 30-40% dei germinali
- Morfologia del classico:
  - Macro
    - Noduli a contorni policiclici
  - Micro
    - Popolazione uniforme di cc poligonali
    - Setti fibrosi infiltrati da linfociti, plasmacc e macrofagi
- Marcatori: PLAP, c-Kit, OCT4, CD133
- Forme particolari:
  - s. spermatocitico (anziani, bilaterale, buona prognosi),
  - s. anaplastico,
  - con cellule sinciziotrofoblastiche

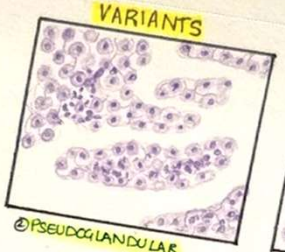


SEMINOMA

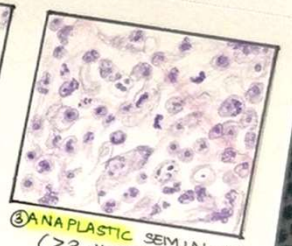
VARIANTS



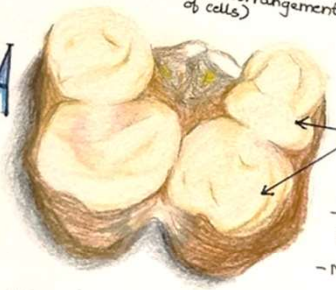
① SEMINOMA WITH SYNCYTIOTROPHOBLAST



② PSEUDOGLANDULAR SEMINOMA (alveolar arrangement of cells)



③ ANAPLASTIC SEMINOMA (>3 mitosis/HPF) and nuclear pleomorphism

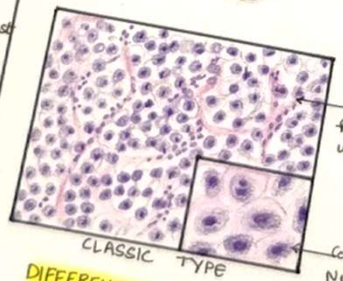


GROSS

- Well demarcated Homogenous / coarsely lobulated, bulging form mass – grey white
- Haemorrhage and necrosis is uncommon
- Measures – 2 to 6 cm

IMMUNOHISTOCHEMISTRY

1. PLAP – strongly positive
2. CD117 – positive
3. PAS – positive
4. HCG – syncitiotrophoblast cells positive
5. PODOPLANIN (D2-40) – Diffuse membranous positivity
6. EMA, AFP, CD30 – Negative



MICROSCOPY

Delicate fibrovascular septae with lymphocytes

CLASSIC TYPE

cells with clear cytoplasm Nuclei have distinct cell membrane and prominent nucleoli

DIFFERENTIAL DIAGNOSIS

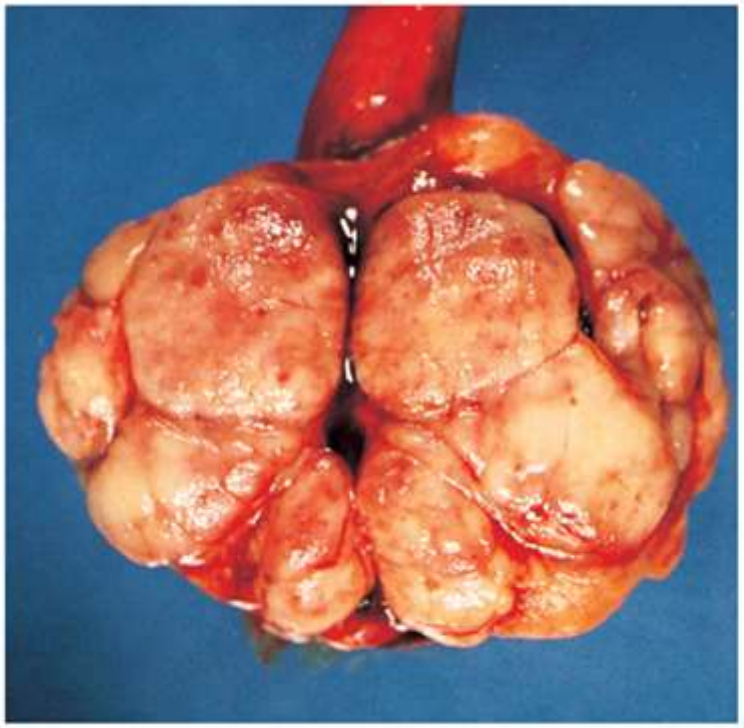
EMBRYONAL CARCINOMA

- CD 30 positive
- STRONGER positivity for CYTOKERATIN
- WEAK positivity for PLAP

LACK LYMPHOCYTIC INFILTRATE ABSENCE OF FIBROUS SEPTAE

YOLK SAC TUMOUR

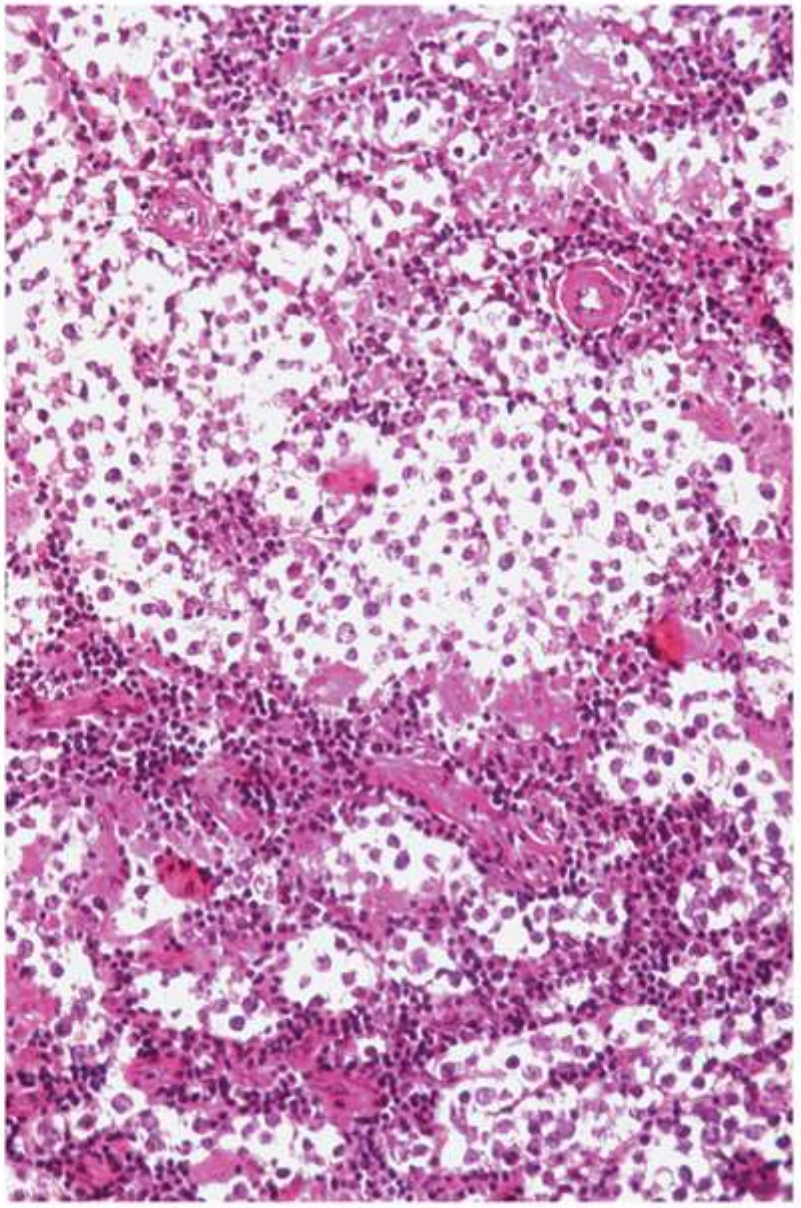
- Hyaline globules & extracellular basement membrane material present
- AFP and glypican 3 – positive



A

seminoma

Setti fibrosi infiltrati da linfociti



B

- Normal testis appears at the left, and seminoma is present at the right. Note the difference in size and staining quality of the neoplastic nests of cells compared to normal germ cells. Note the lymphoid stroma between the nests of seminoma.

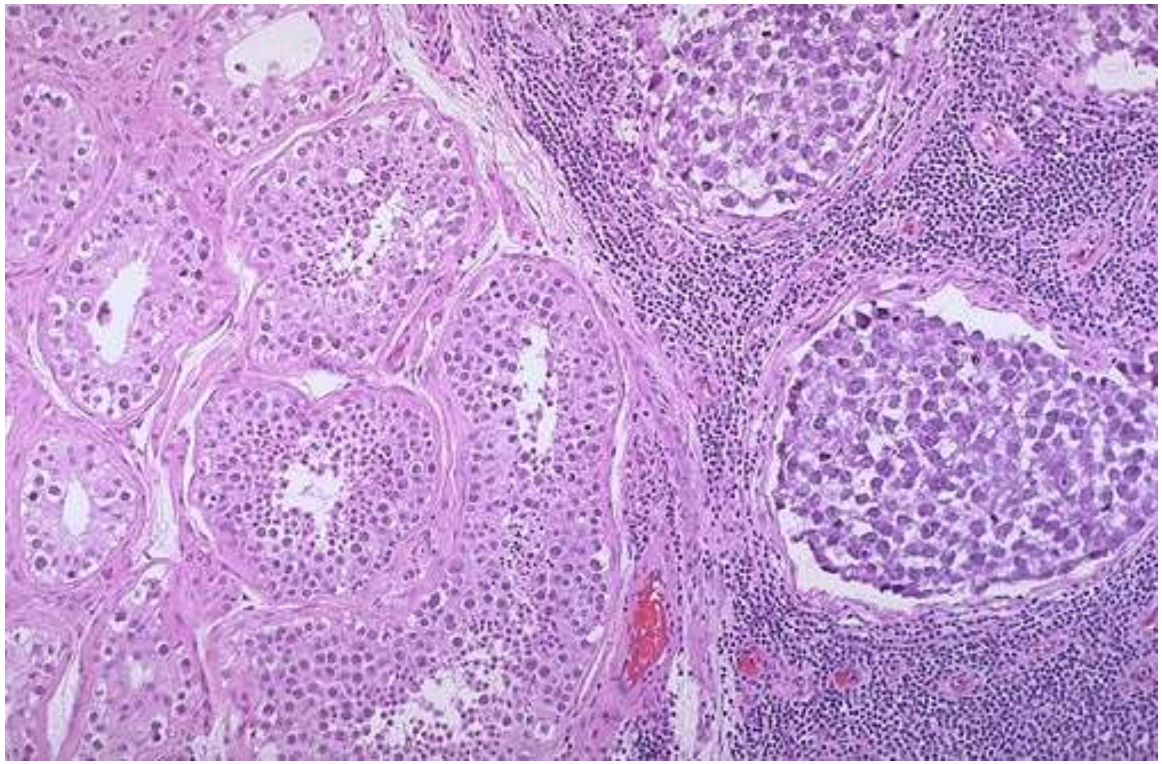


Table 4.05 Comparison of the clinical and pathological features of spermatocytic tumour (formerly called spermatocytic seminoma) with typical seminoma, modified and updated from Scully {2461A}

	Spermatocytic tumour	Typical seminoma
Proportion of germ cell tumours	1–2%	40–50%
Site(s)	Testis only	Testis, ovary (dysgerminoma), mediastinum, pineal gland, retroperitoneum
Associated with cryptorchidism	No	Yes
Bilaterality	9%	2%
Median patient age at diagnosis	52–59 years	40 years
Associated with other forms of germ cell tumour	No	Yes
Associated with germ cell neoplasia in situ	No	Yes
Intercellular oedema	Common	Uncommon
Composition	3 cell types, with denser cytoplasm, round nuclei	1 cell type, often clear cytoplasm, less-regular nuclei
Stroma	Scanty	Prominent
Lymphoid reaction	Rare to absent	Prominent
Granulomas	Extremely rare	Often prominent
Sarcomatous transformation	Occasional	Absent
Glycogen	Absent to scant	Abundant

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Testicular tumour in elderly- Spermatocytic tumour or Lymphoma?

Spermatocytic tumour

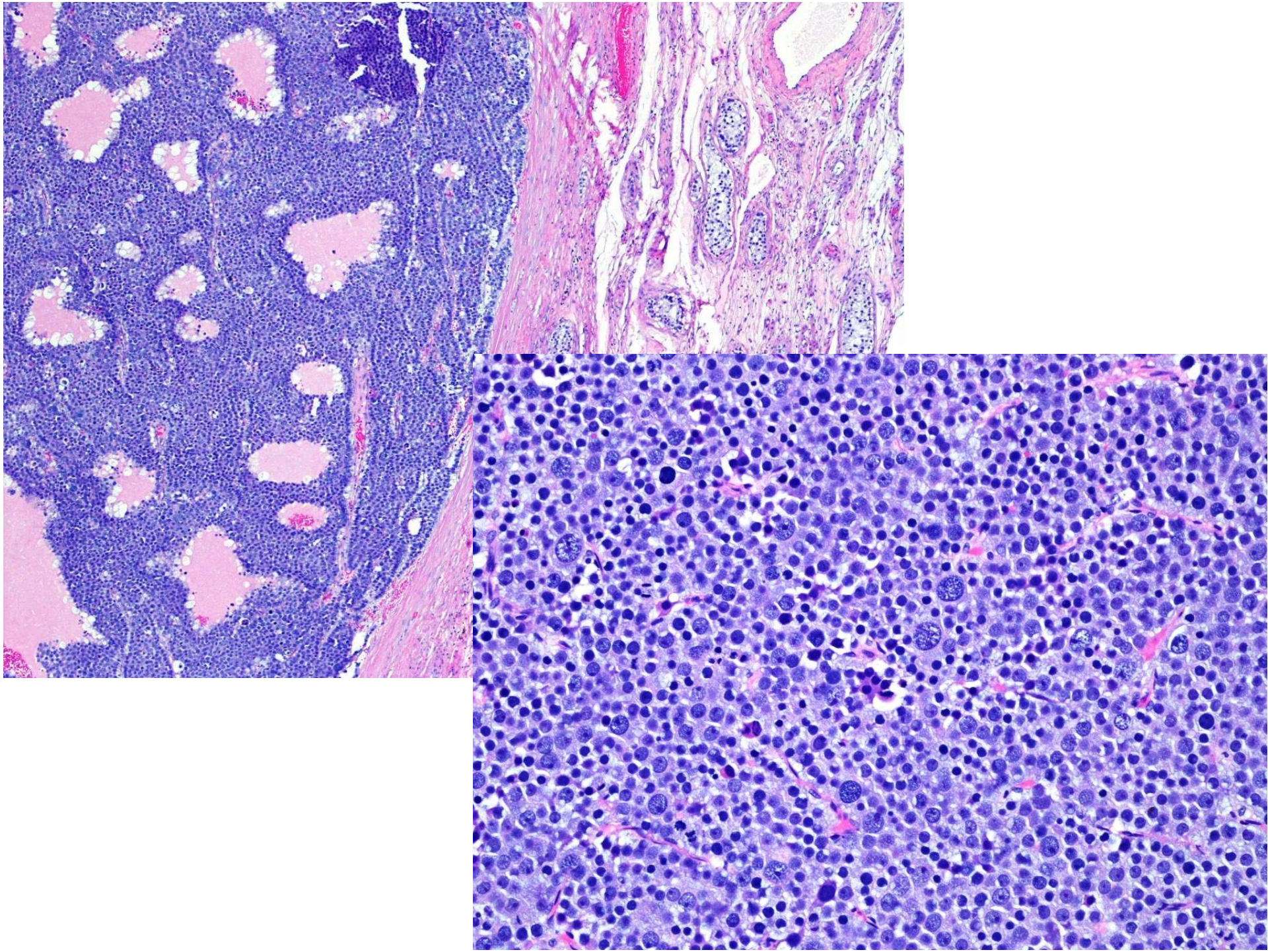
- Usually unilateral
- Polymorphic population of cells, usually consisting of 3 population of cells
- Less likely to produce extra testicular extension
- CD 45 -
- Spireme chromatin
- No hepatosplenomegaly/ lymphaenopathy of clinical exam
- No a/w isochromosome 12p, ITGCN (c/ w seminomas)

Lymphoma

- Usually bilateral
- Monomorphic population of cells
- More likely show extratesticular extension
- CD 45+
- Pleomorphic nuclei, variable mitosis, gross may show hemorrhagic or necrotic areas
- Associated with hepatosplenomegaly and lymphadenopathy on clinical exam

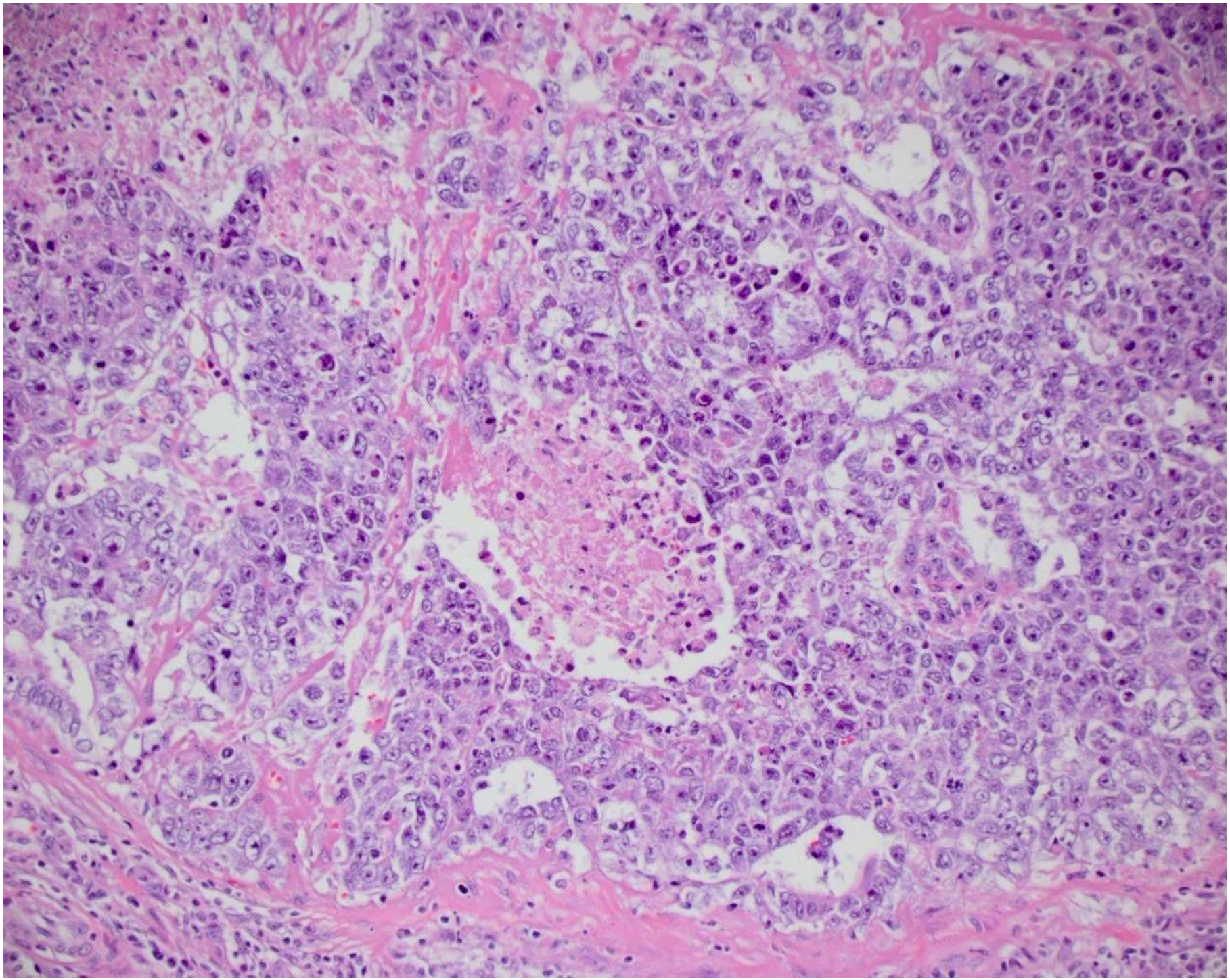
LINFOMA

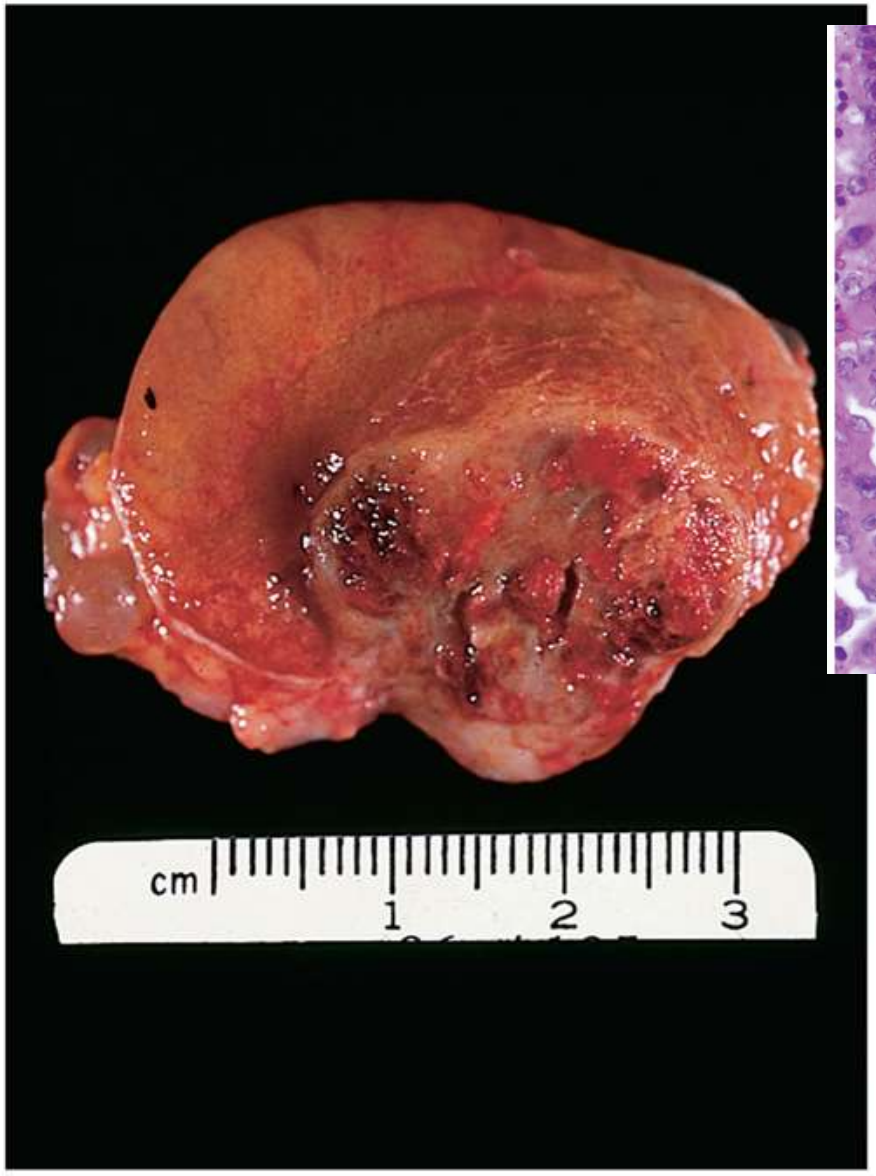
La + frequente neoplasia testicolare dopo i 60 anni



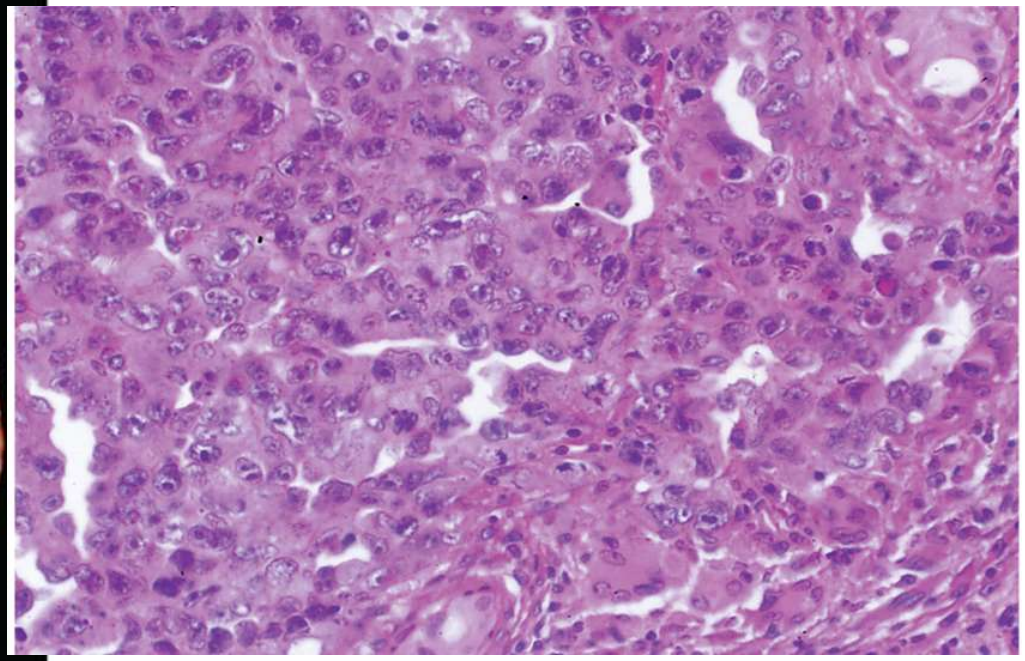
Carcinoma embrionale

- Tra 20 e 40 anni
- Morfologia
  - Macro
    - Aspetto solido o cistico
  - Micro
    - Grande variabilità
- Marcatori: CD30, CK (negative nel seminoma),
- Forme particolari: spesso misto





Tumore germinale non seminomatoso del testicolo



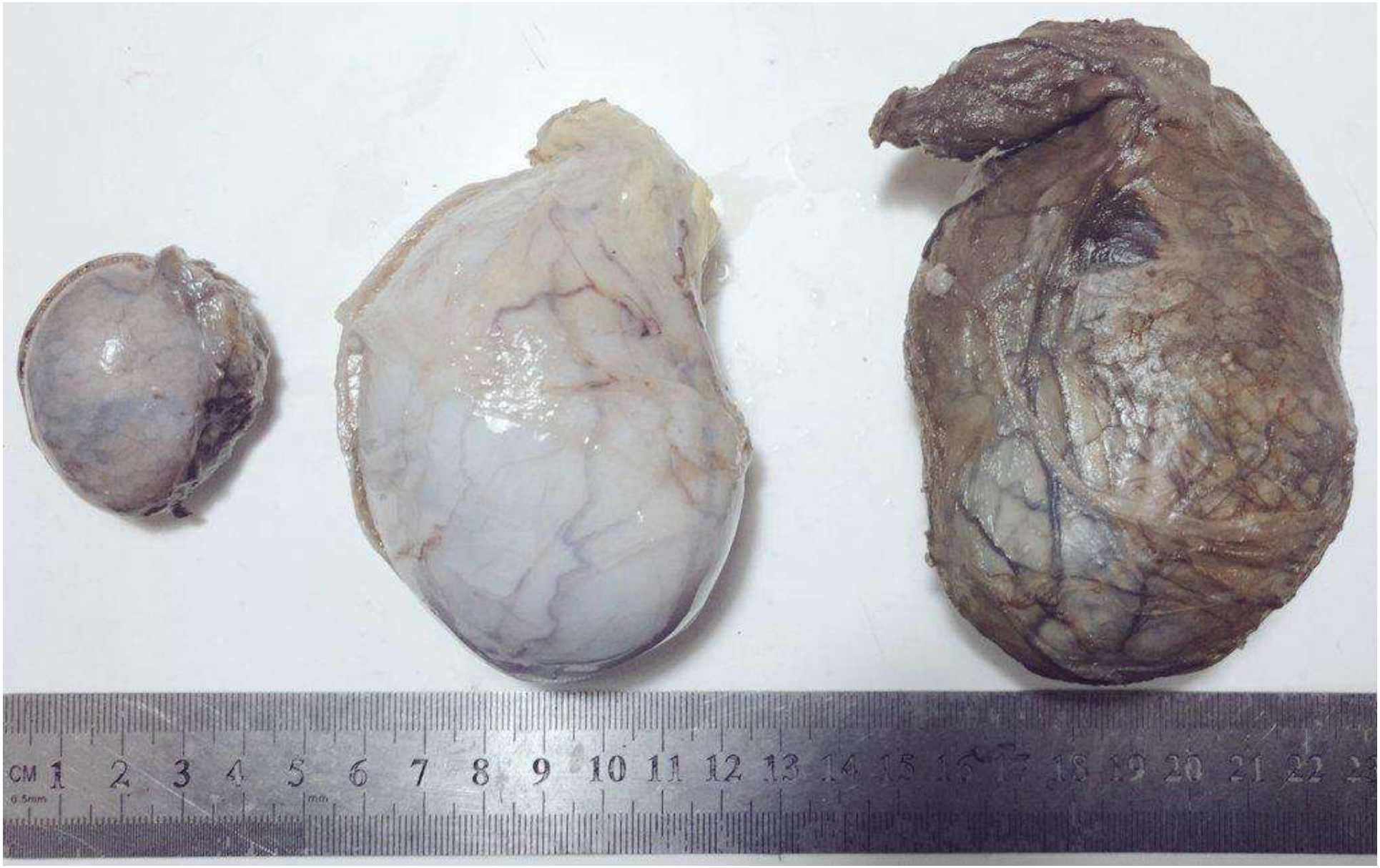
Componente di cr embrionario in NSGCT

ALTRE FORME

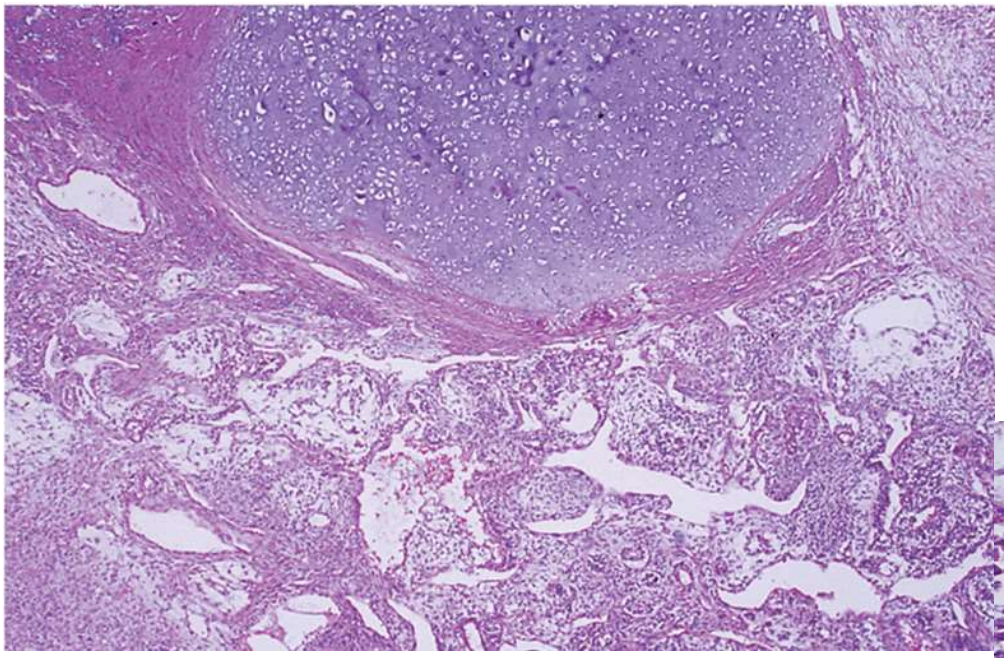
- Teratoma
- T. del sacco vitellino
- Corion carcinoma <1%
- T. germinali misti

There is a mixture of bluish cartilage with red and white tumor tissue. This neoplasm microscopically contained mainly teratoma, but areas of embryonal carcinoma were also present.

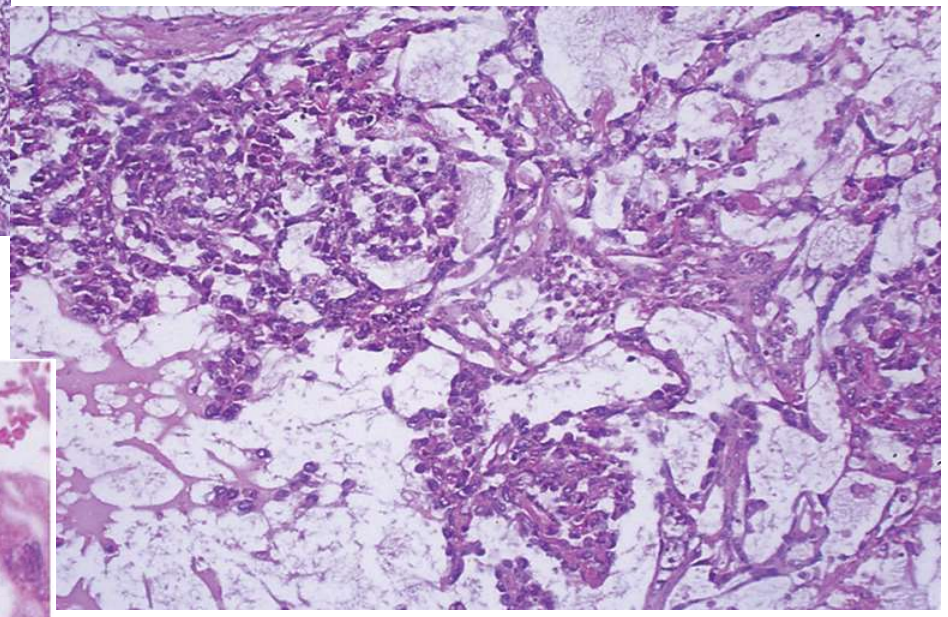
NORMALE – YOLK SAC TUMOR – SEMINOMA+CARCINOMA EMBRIONALE



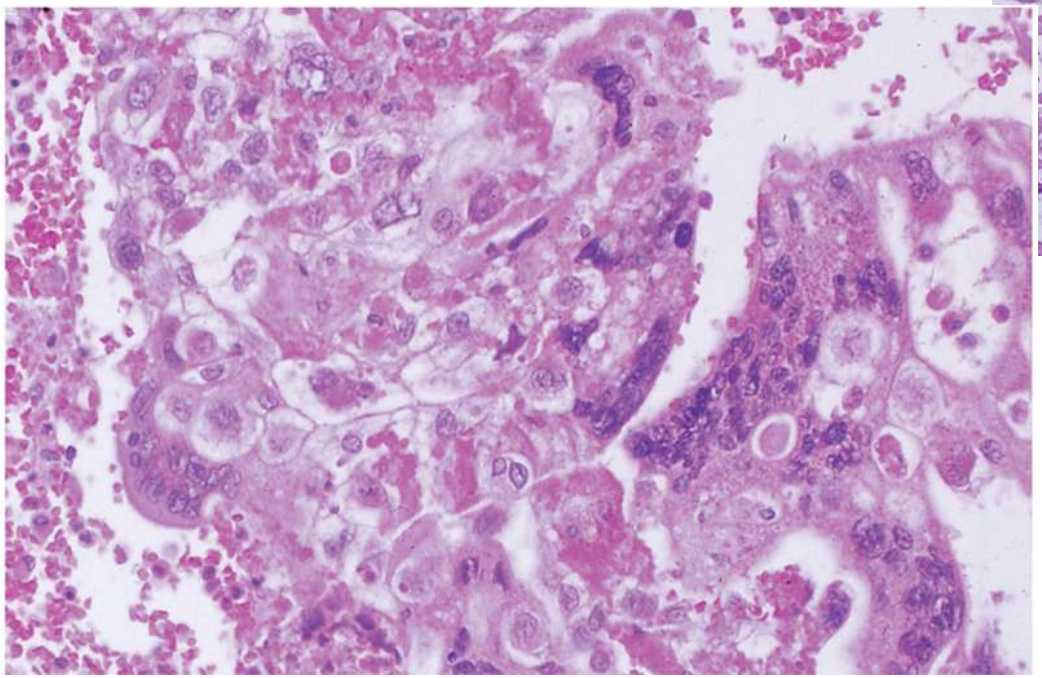
Tumore germinale non seminomatoso



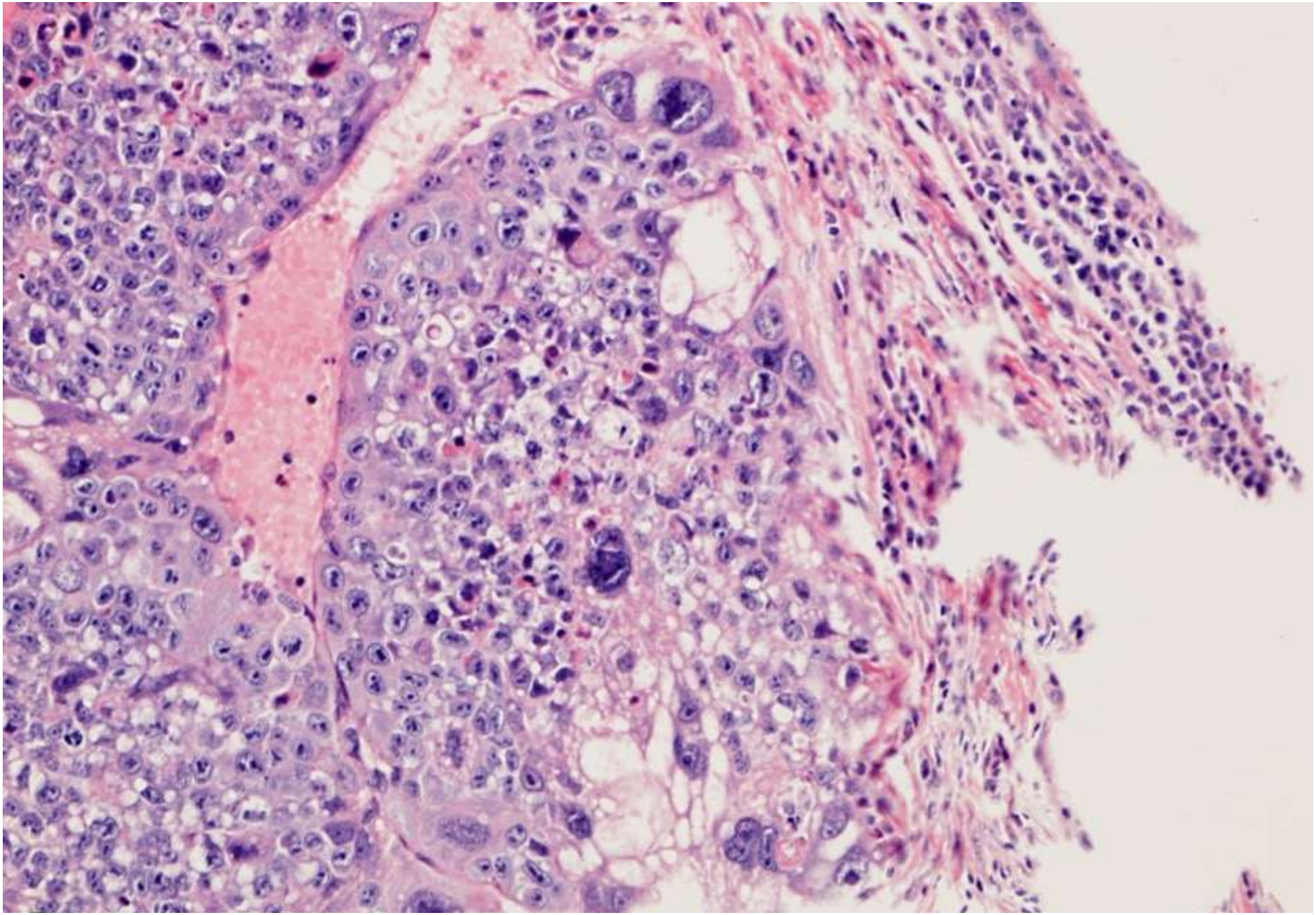
Componente di tt connettivi ben differenziati



Componente del sacco vitellino

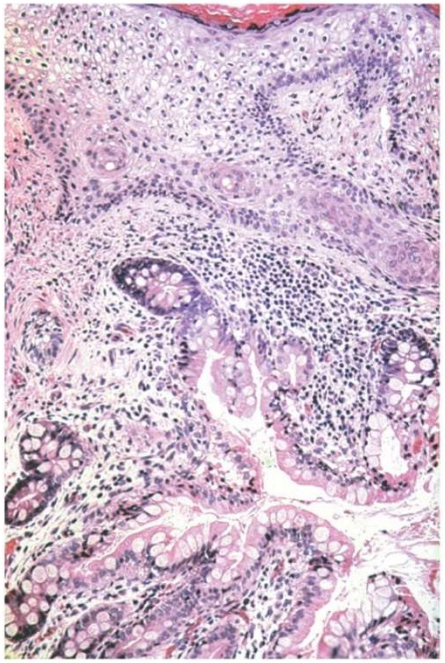


Componente di coriocarcinoma



COMPONENETE TROFOBLASTICA DI UN CORIOCARCINOMA

teratoma



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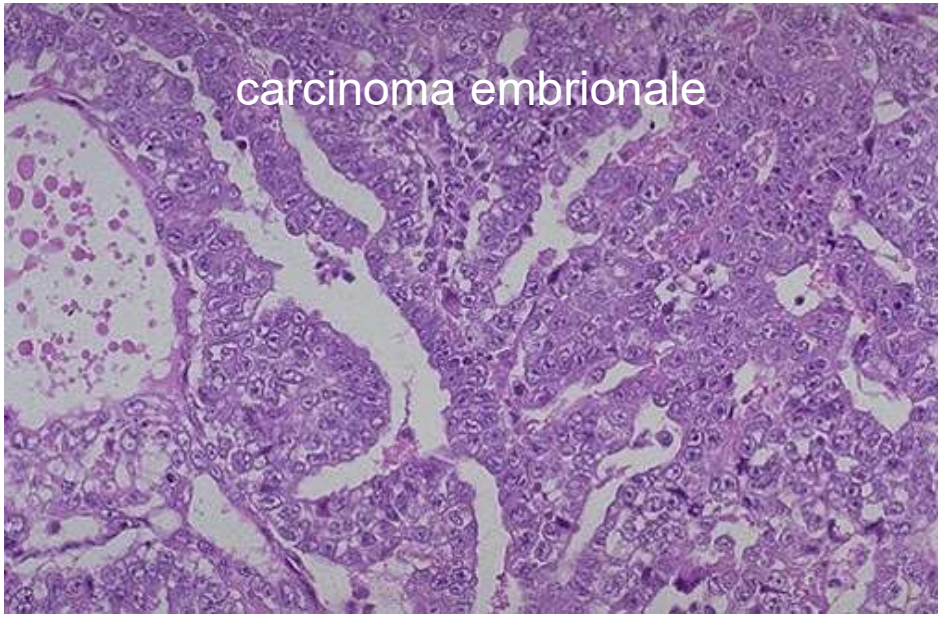

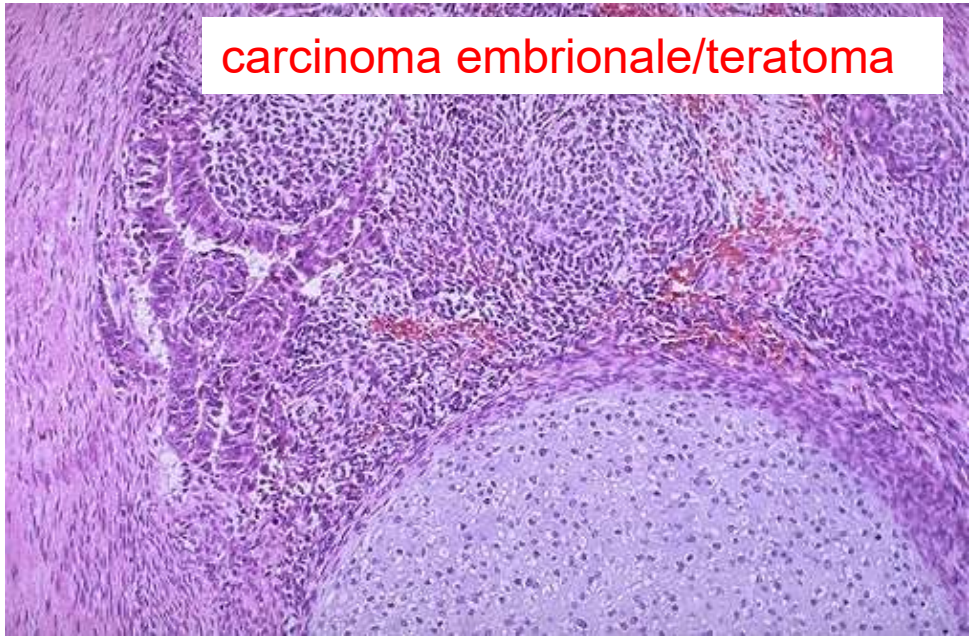

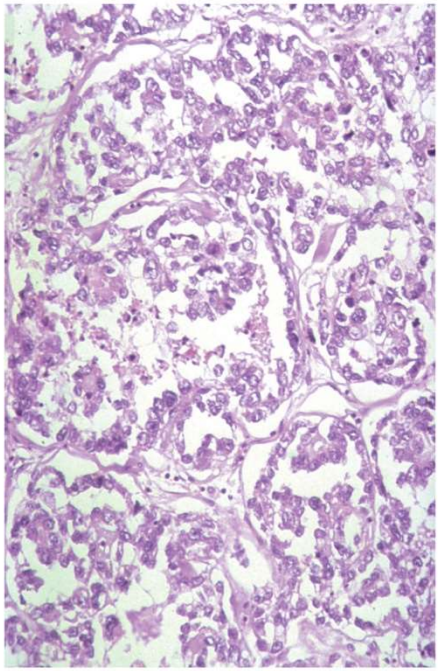

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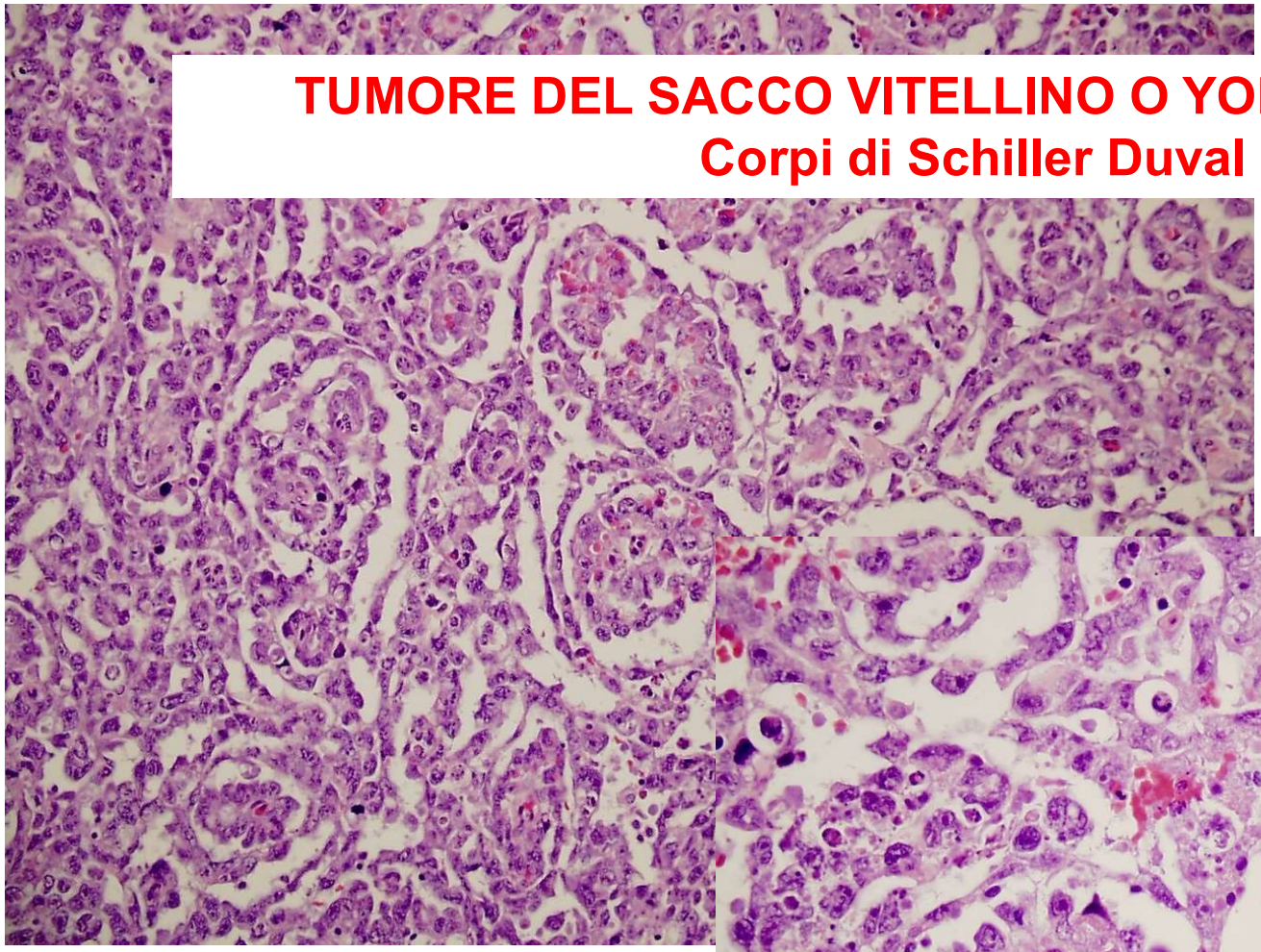
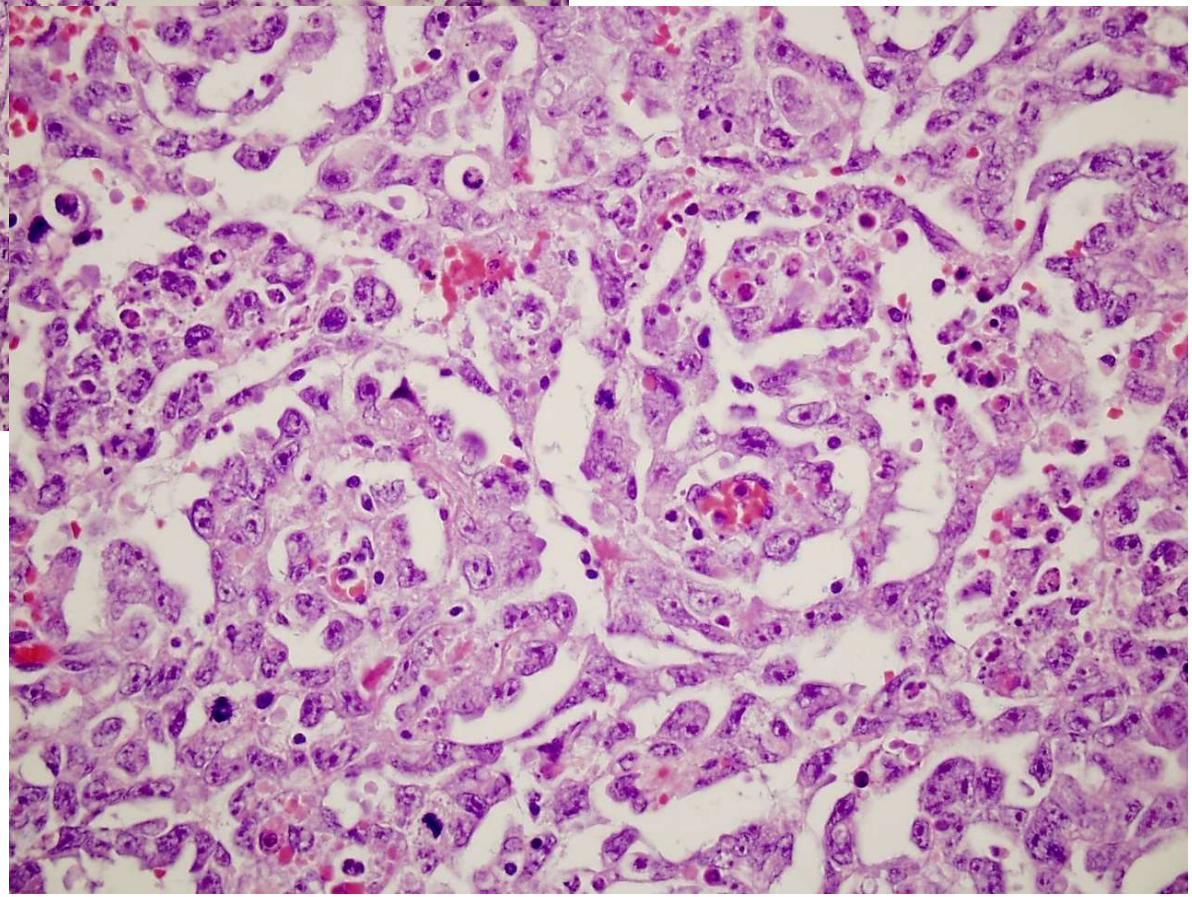
Tumore del sacco vitellino: + freq. nei bambini

TUMORE DEL SACCO VITELLINO O YOLK SAC TUMOR
Corpi di Schiller Duval





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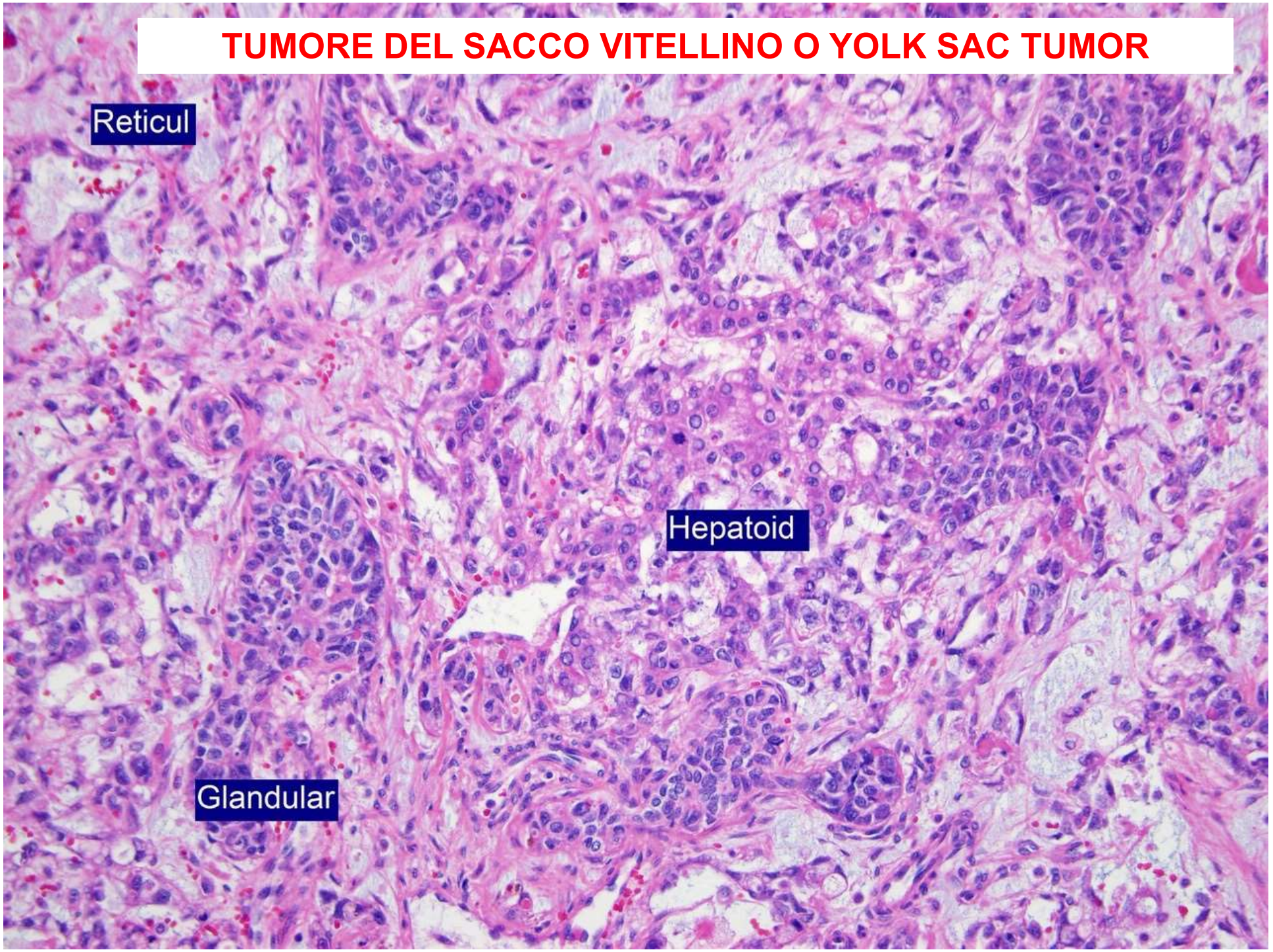

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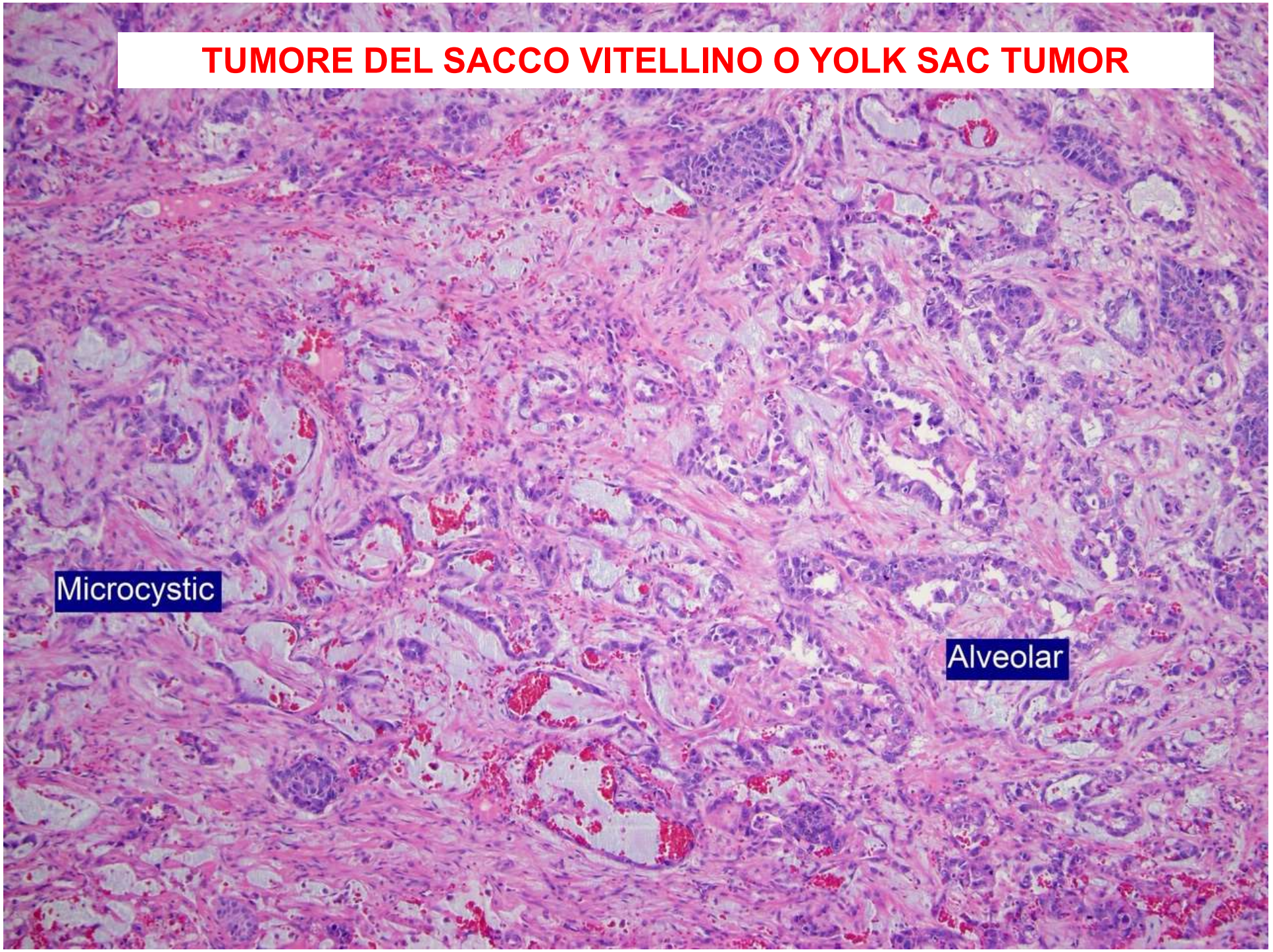
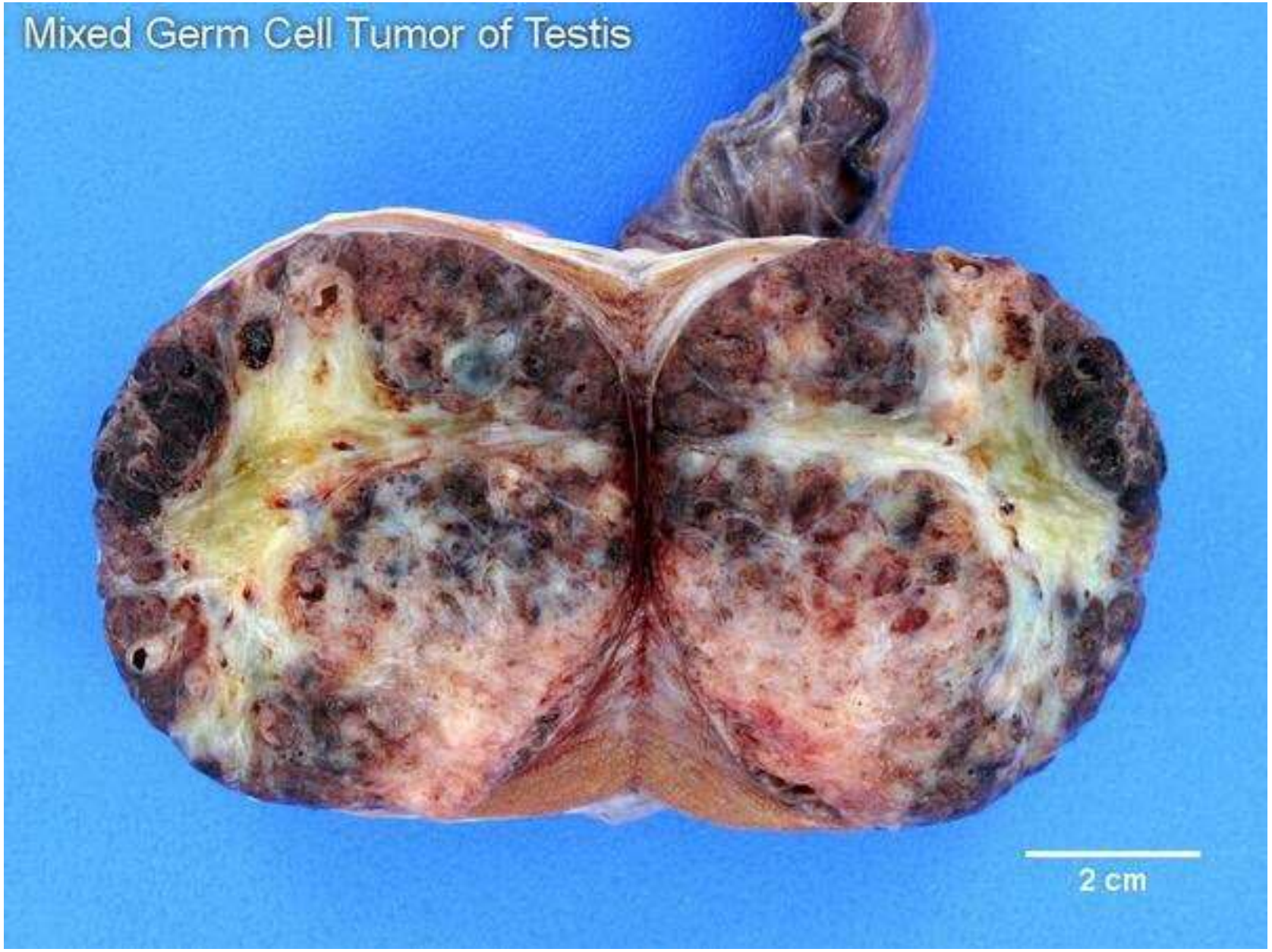
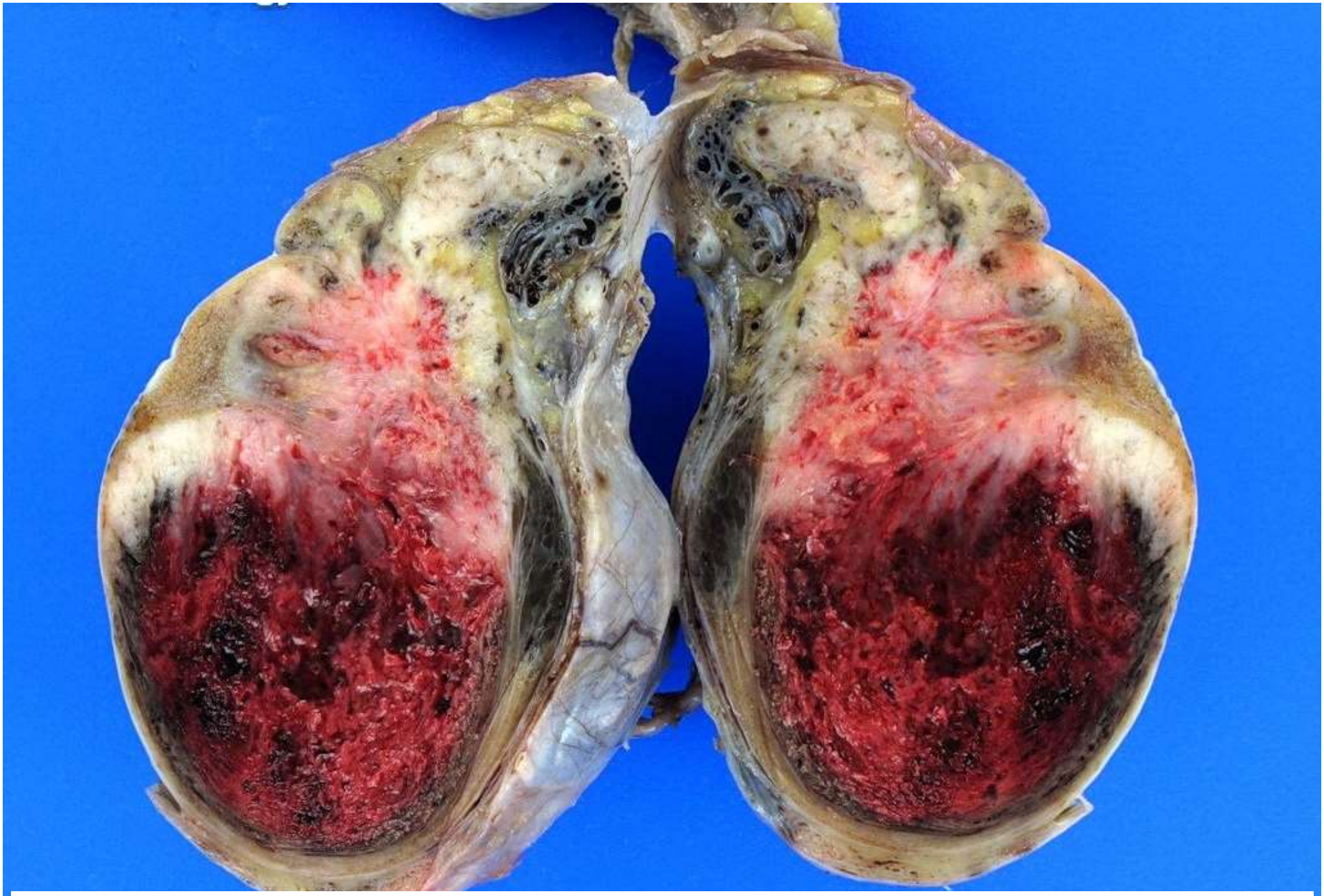


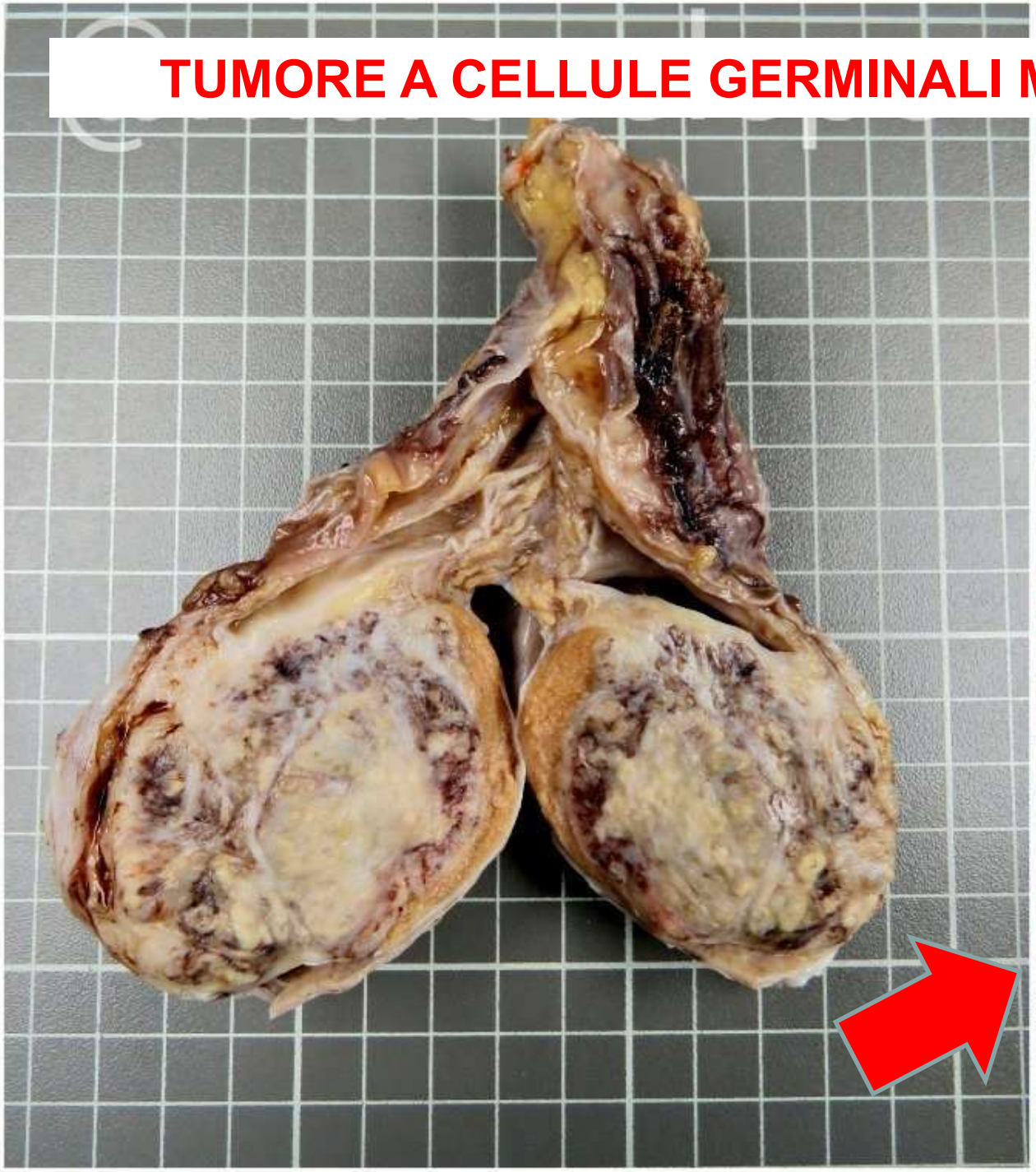


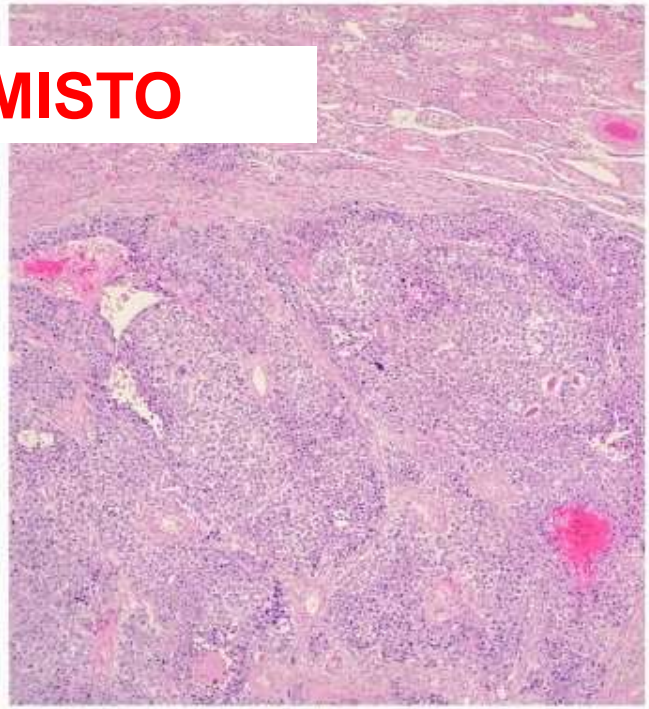
SEMINOMA + TERATOMA+ CARCINOMA EMBRIONALE

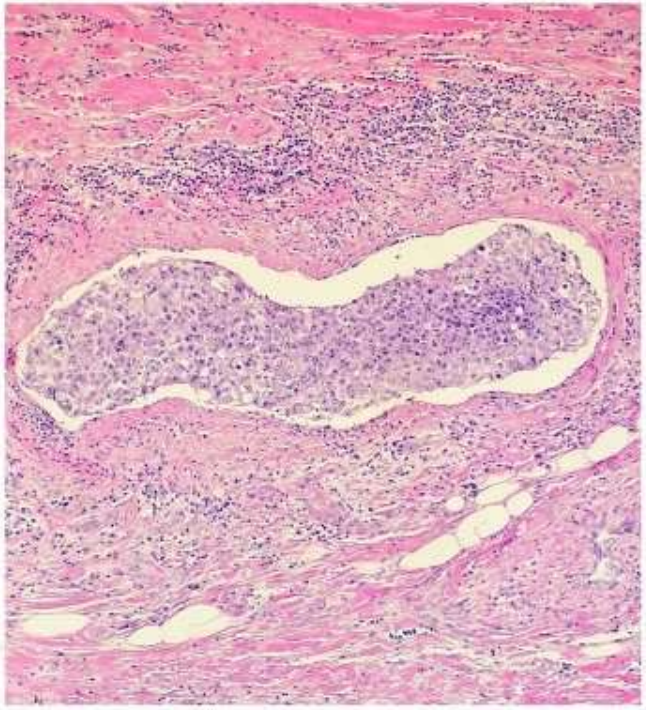


CORIOCARCINOMA + YOLK SAC TUMOR + CARCINOMA EMBRIONALE
Beta-hCG >3000; AFP > 2000

TUMORE A CELLULE GERMINALI MISTO







Tumors of the Testis
Morphologic Features and Molecular Alterations

Brooke E. Howitt, MD[a], Daniel M. Berney, FRCPath[b,*]

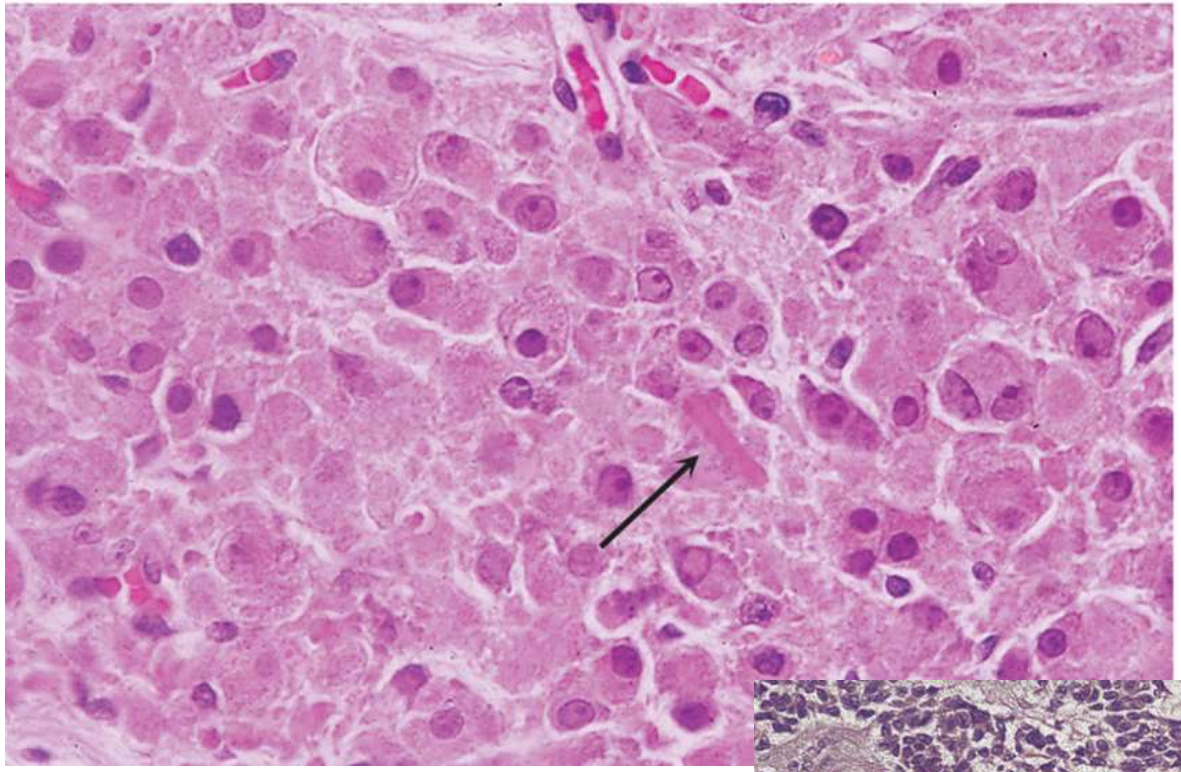
Table 2
Immunohistochemistry in testicular germ cell tumors

Tumor Type	SALL4	OCT4	CD30	GPC3	AFP	Keratin	c-kit	D2-40	Sox2	hCG	GATA3
Classic/typical seminoma	+	+	–	–[c]	–	–	+	+	–	–[c]	–[c]
Spermatocytic tumor[a]	+	–	–	–	–	–	–/+	–	–	–	–
Embryonal carcinoma	+	+	+	–/+[c]	–	–/+	–	–	+	–[c]	–[c]
Yolk-sac tumor	+	–	–	+	+	+	–/+	–	–	–	+/–
Teratoma[b]	+/–	–/+	–	–	–	+	–	–	+/–	–	–/+
Choriocarcinoma	+/–	–	–	+	–/+	+	–	–/+	–	+	+

–, negative; +, positive.
[a] Previously called "spermatocytic seminoma."
[b] Staining patterns depend on the teratomatous elements present.
[c] Individual syncytiotrophoblast present in GCTs may be positive for Beta-hCG, GPC3, and GATA3.

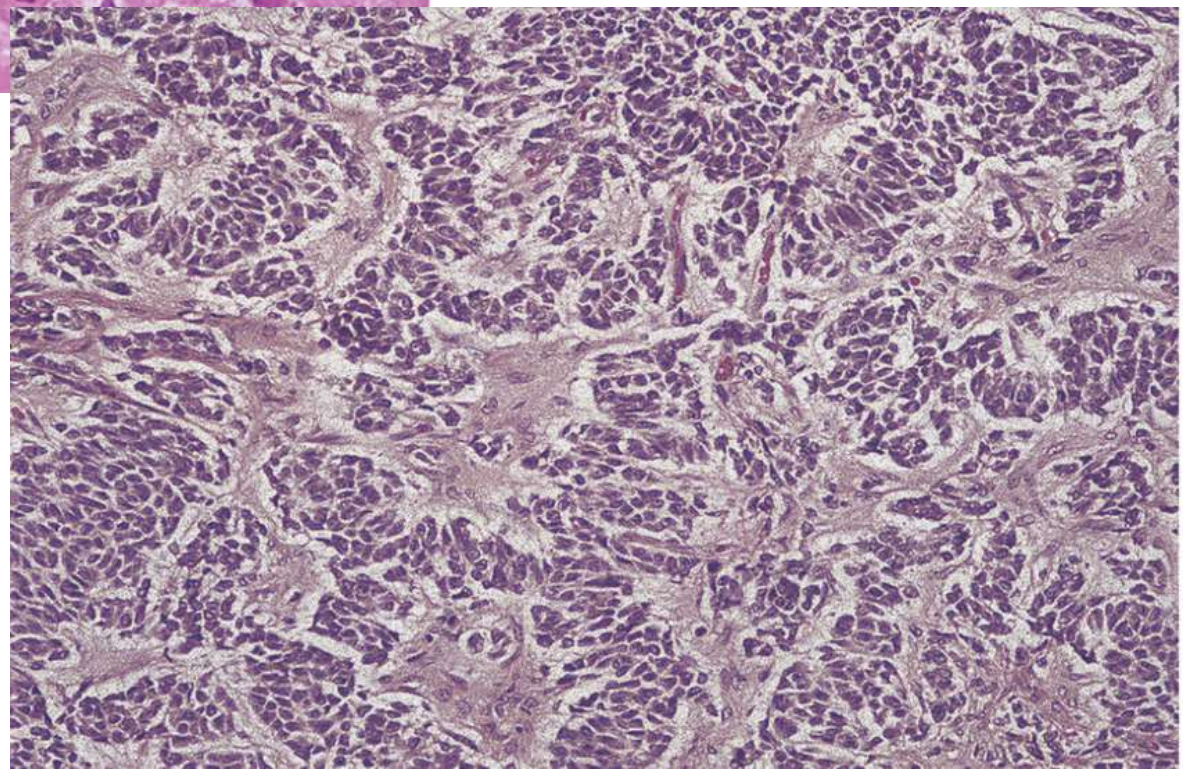
ALTRE NEOPLASIE

- Tumori dei cordoni sessuali (2%; per lo più t. benigni)
  - T. a cellule del Leydig
    - Possono secernere androgeni e estrogeni
      - Pubertà precoce
      - Nell'adulto ginecomastia e femminilizzazione
  - T. a cellule del Sertoli
  - T. a cellule della granulosa giovanile (<6 mesi; anche a sede intra-addominale; benigno; mitosi++)



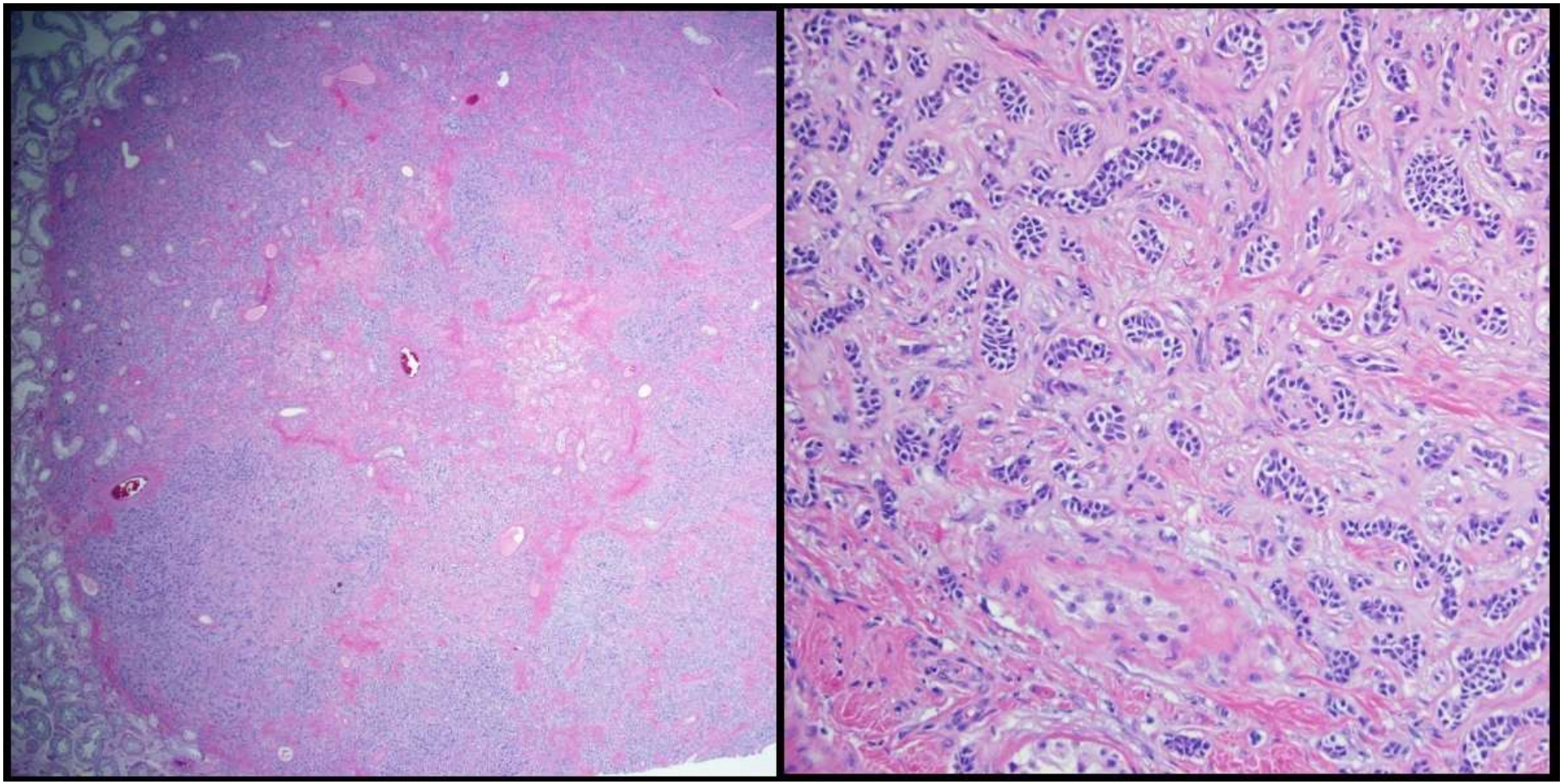
Tumore a cc di Leydig

Cristalli di Reinke

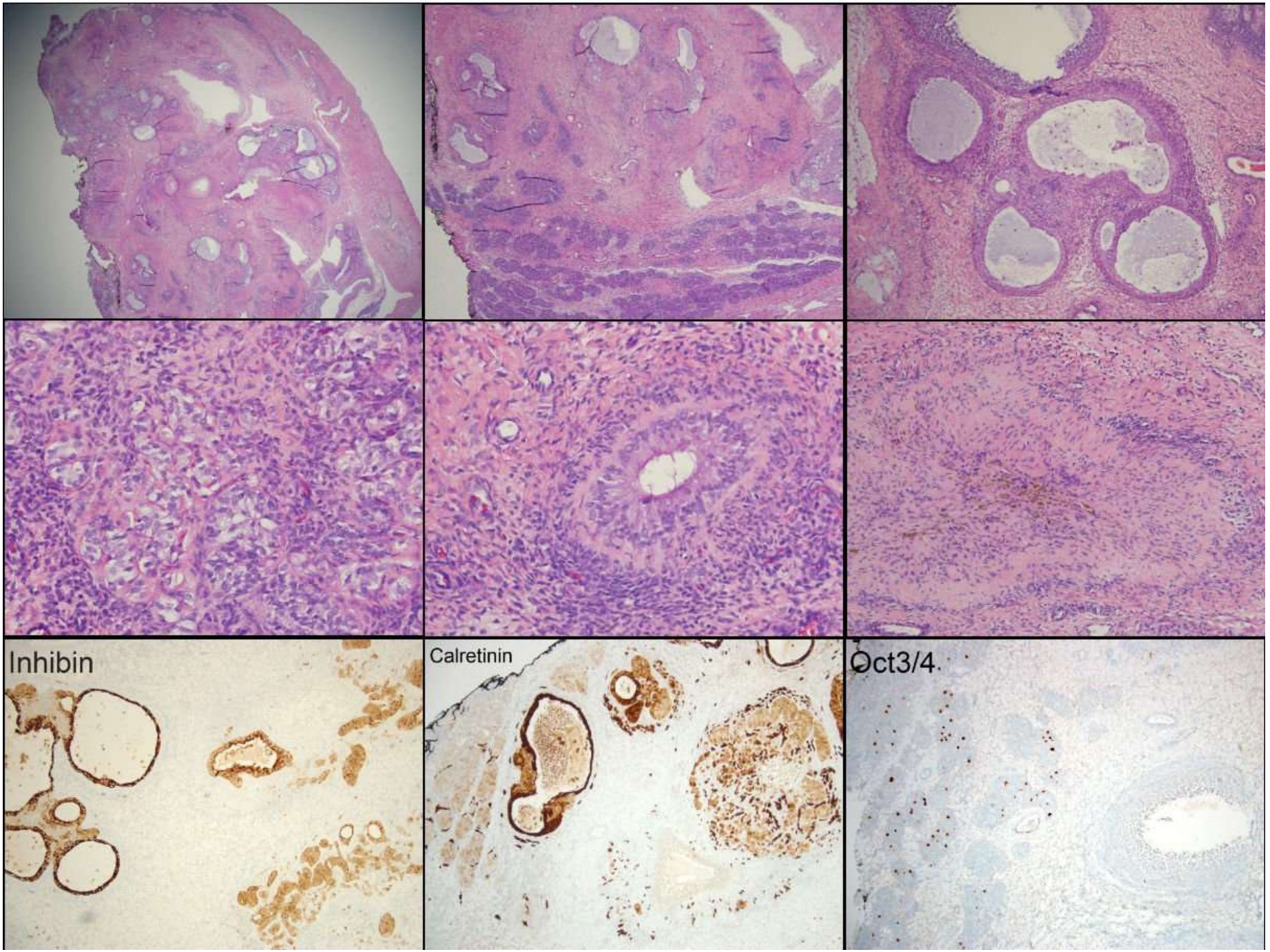


Tumore a cc di Sertoli

Tumore a cc di Sertoli



JUVENILE GRANULOSA CELL TUMOR OF THE TESTIS



REGRESSIONE TUMORALE: «BURN OUT»

GCT should also be [illegible] ing of the components.

Genetic profile and genetic susceptibility

See *Germ cell tumours derived from germ cell neoplasia in situ* (pp. 189,197).

Prognosis and predictive factors

The presence and proportion of EC, vascular invasion, and rete testis invasion correlate with higher risk of metastasis in clinical stage I tumours [636,910,928,2477], whereas the presence of YST and teratoma components is associated with a lower incidence of metastasis [910,2974]. Rete testis and hilar soft tissue invasion have also been shown to correlate with clinical stage II or III (compared with stage I) disease at presentation [3022]. A teratomatous component in the testis is also associated with higher probability of teratoma in post-chemotherapy retroperitoneal lymph nodes in higher-stage tumours [409]. Like in pure tumours, the predominance of a

Germ cell tumours of unknown type

Regressed germ cell tumours

Definition

Regressed germ cell tumours (GCTs) are GCTs that have undergone either partial or complete regression, leaving behind a generally well-delineated nodular focus of scar/fibrosis in the testis.

ICD-O code 9080/1

Synonym

Burnt-out germ cell tumours

Epidemiology

Less than 5% of testicular GCTs undergo complete or partial spontaneous regression, and their clinical demographics parallel those of non-regressed GCTs [104,182,1511].

Clinical features

Spontaneous regression of GCTs often first presents as metastases, most commonly manifesting as back pain secondary to retroperitoneal mass effect, often with elevated germ cell tumour markers. Less common, in order of decreasing prevalence, are testicular enlargement, elevated serum markers, and testicular pain. Historically, many regressed testicular GCTs with retroperitoneal metastases were thought to be extratesticular primary GCTs, but subsequent studies have found evidence of a regressed (so-called burnt-out) testicular primary in most cases. The diagnosis of a regressed GCT therefore requires a high degree of clinical suspicion. It is quite critical to determine whether the testis is the site of origin, because chemotherapy administered for metastatic GCTs is less effective in the testis, and testicular relapse may occur if orchiectomy is not performed. If the primary tumour is

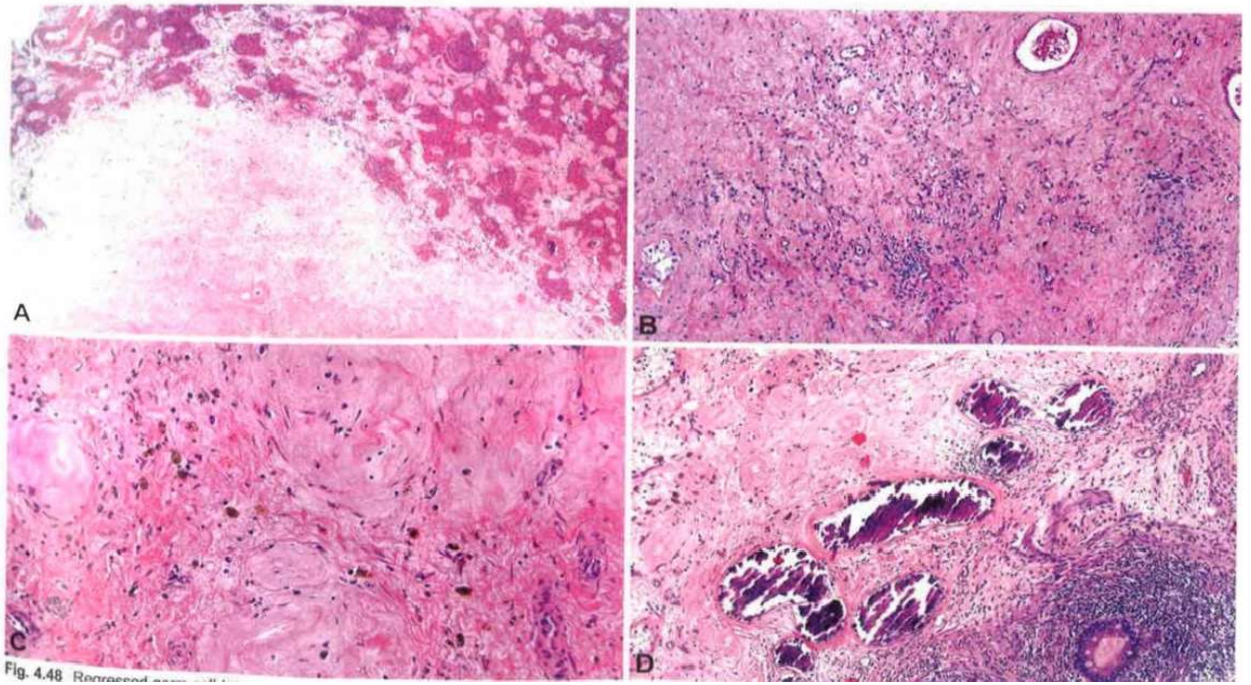


Fig. 4.48 Regressed germ cell [illegible]

Ovaio

- I tumori a cellule germinali sono il 30%.
- Nel 95% dei casi si tratta di tumori benigni (teratomi maturi).
- I tumori germinali maligni sono le + comuni neoplasie ovariche in età pediatrica e giovanile.

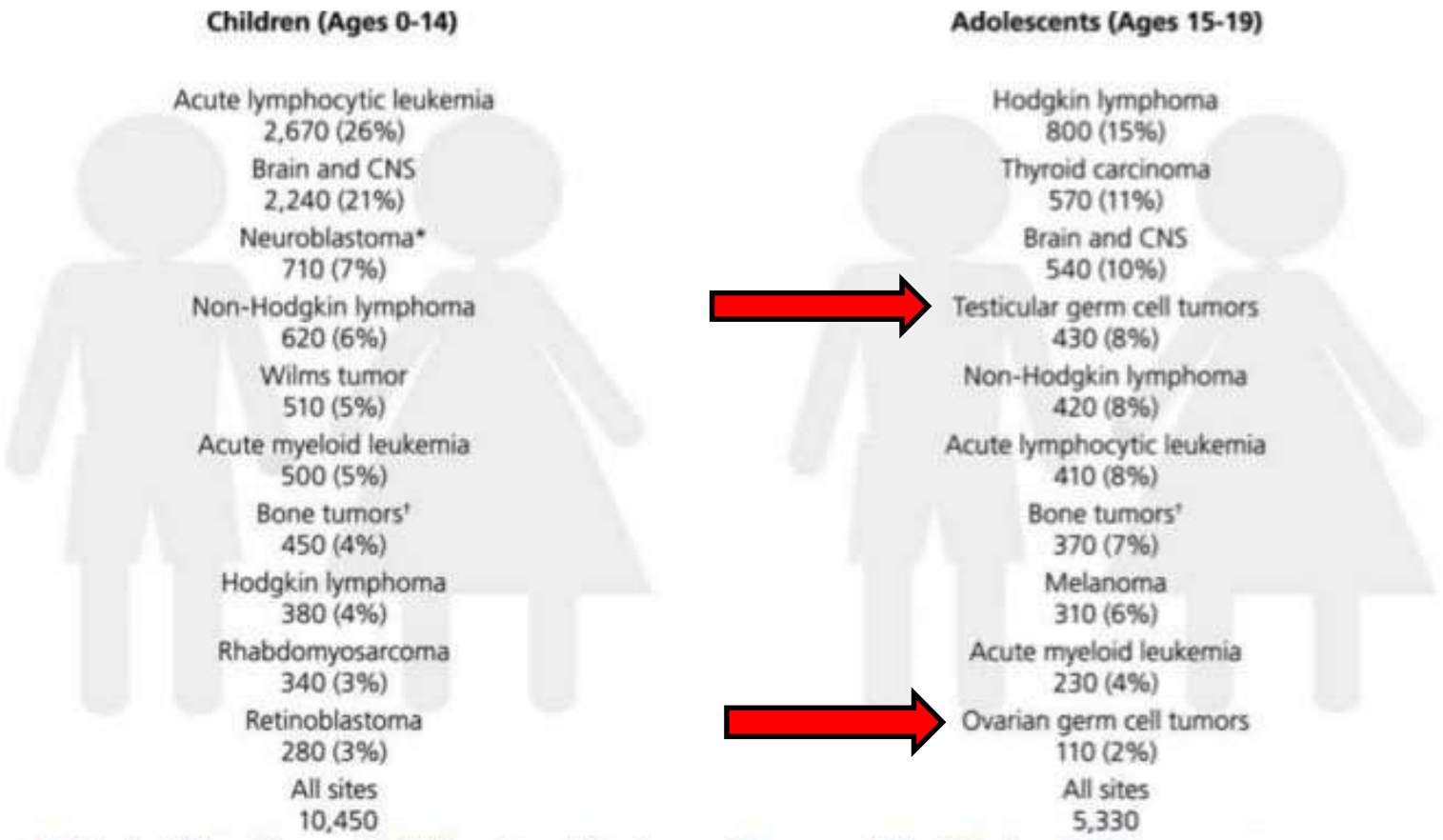


FIGURE 1. Estimated New Cases of Childhood and Adolescent Cancers, United States, 2014.

Estimates are for malignant cancers only and are rounded to the nearest 10. In addition, 730 children and 630 adolescents will be diagnosed with benign and borderline brain tumors in 2014. *Includes ganglioneuroblastoma. †Bone tumors include osteosarcoma and Ewing sarcoma.

Presentation of malignant disease in children

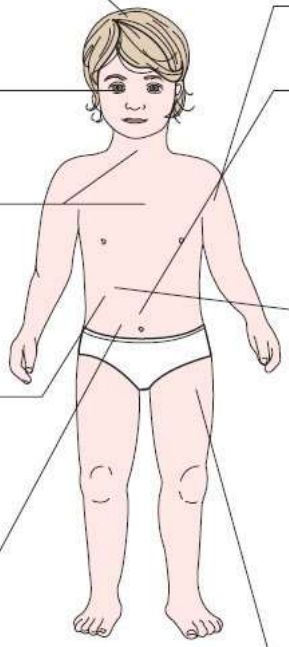
Brain tumours:
- Raised intracranial pressure
- Neurological signs – depends on anatomical position

Retinoblastoma:
- Screening if positive family history
- White pupillary reflex or squint

Lymphomas:
- Enlarged lymph nodes in the head and neck or abdomen
- Mediastinal mass – may cause superior vena caval obstruction.

Wilms tumour:
- Large abdominal mass in a well child
- Occasionally anorexia, abdominal pain, haematuria

Langerhans cell histiocytosis:
- Seborrhoeic rash
- Widespread soft tissue infiltration
- Bone pain, swelling or fracture
- Diabetes insipidus



Soft tissue sarcomas:
- Mass any site

Neuroblastoma:
- Abdominal mass, crosses the midline
- Spinal cord compression
- Weight loss and malaise
- Pallor, bruising
- Bone pain

Acute lymphoblastic leukaemia (ALL):
- Malaise, anorexia
- Pallor, lethargy
- Infections
- Bruising, petichiae, nose bleeds
- Lymphadenopathy
- Hepatosplenomegaly
- Bone pain

Malignant bone tumours:
- Localised bone pain

Pre-school (<5 years old)	School-aged	Adolescence
Acute lymphoblastic leukaemia (ALL) – peak incidence Non-Hodgkin lymphoma	Acute lymphoblastic leukaemia (ALL)	Acute lymphoblastic leukaemia (ALL) Hodgkin lymphoma
Neuroblastoma	Brain tumours	Malignant bone tumours
Wilm tumour		Soft tissue sarcomas
Retinoblastoma		

Source : Illustrated Textbook of Paediatrics Fourth Edition