CLASSIFICATION OF

TUMORS

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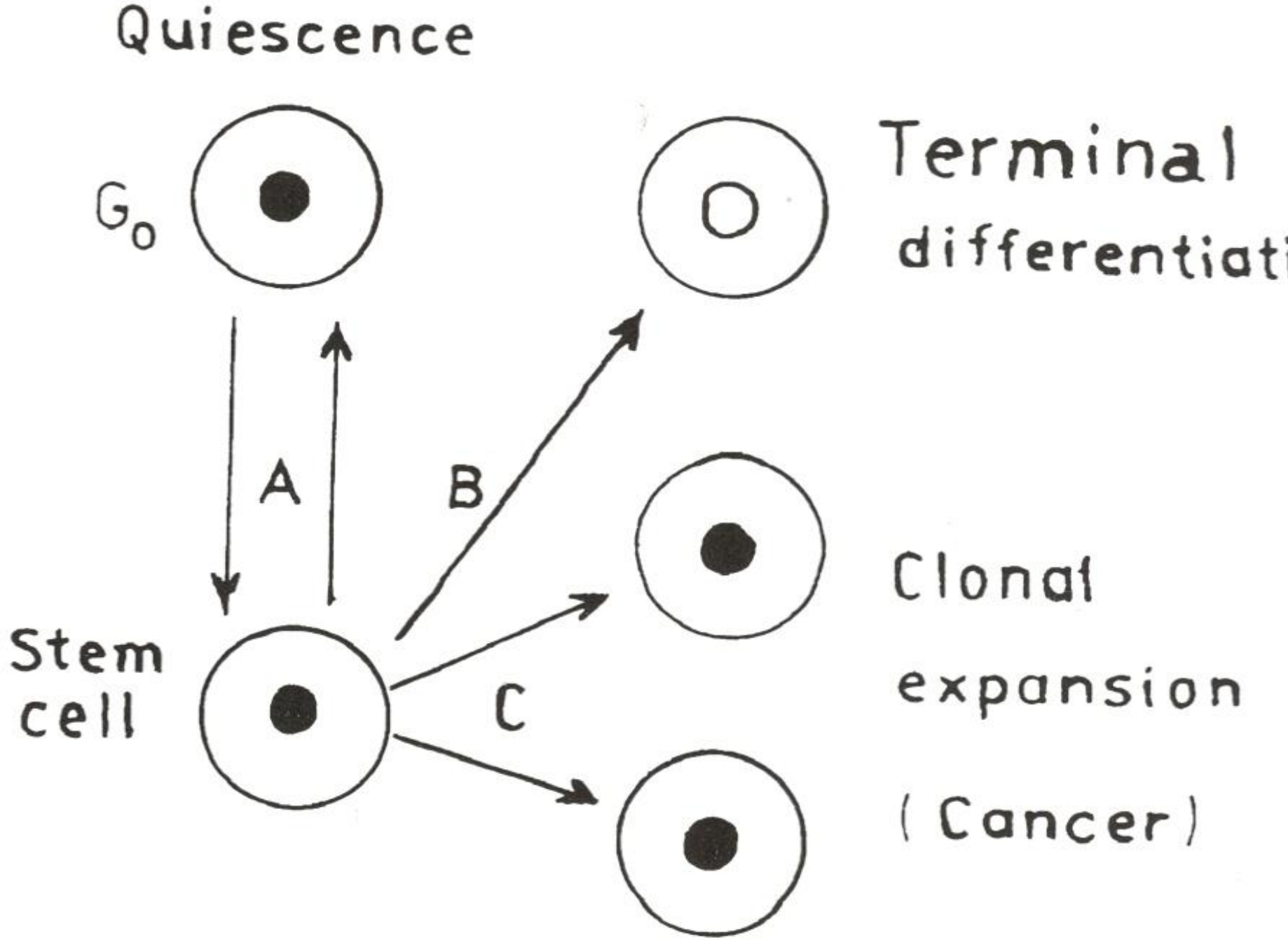
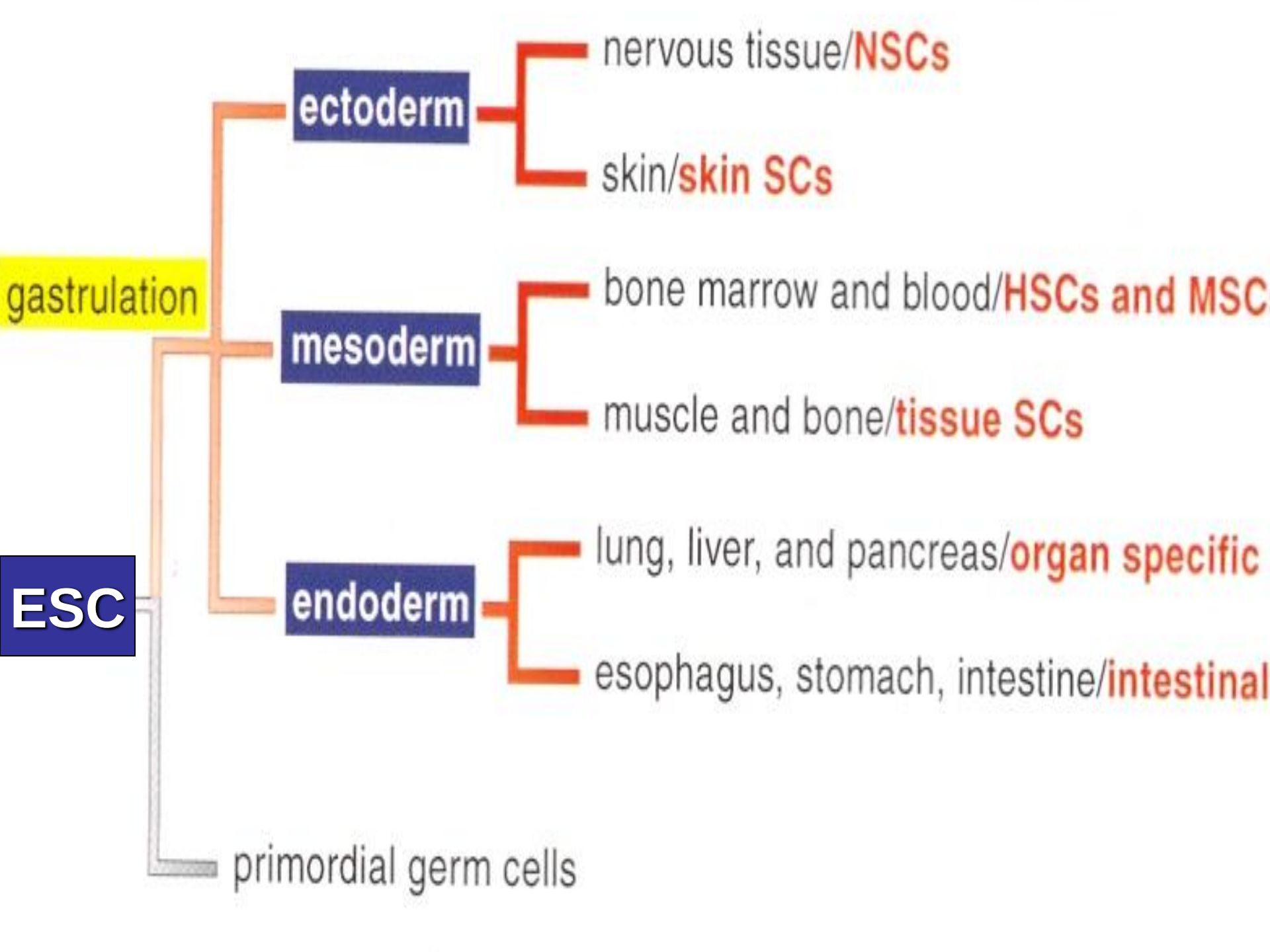
2010

BASIC CONCEPTS

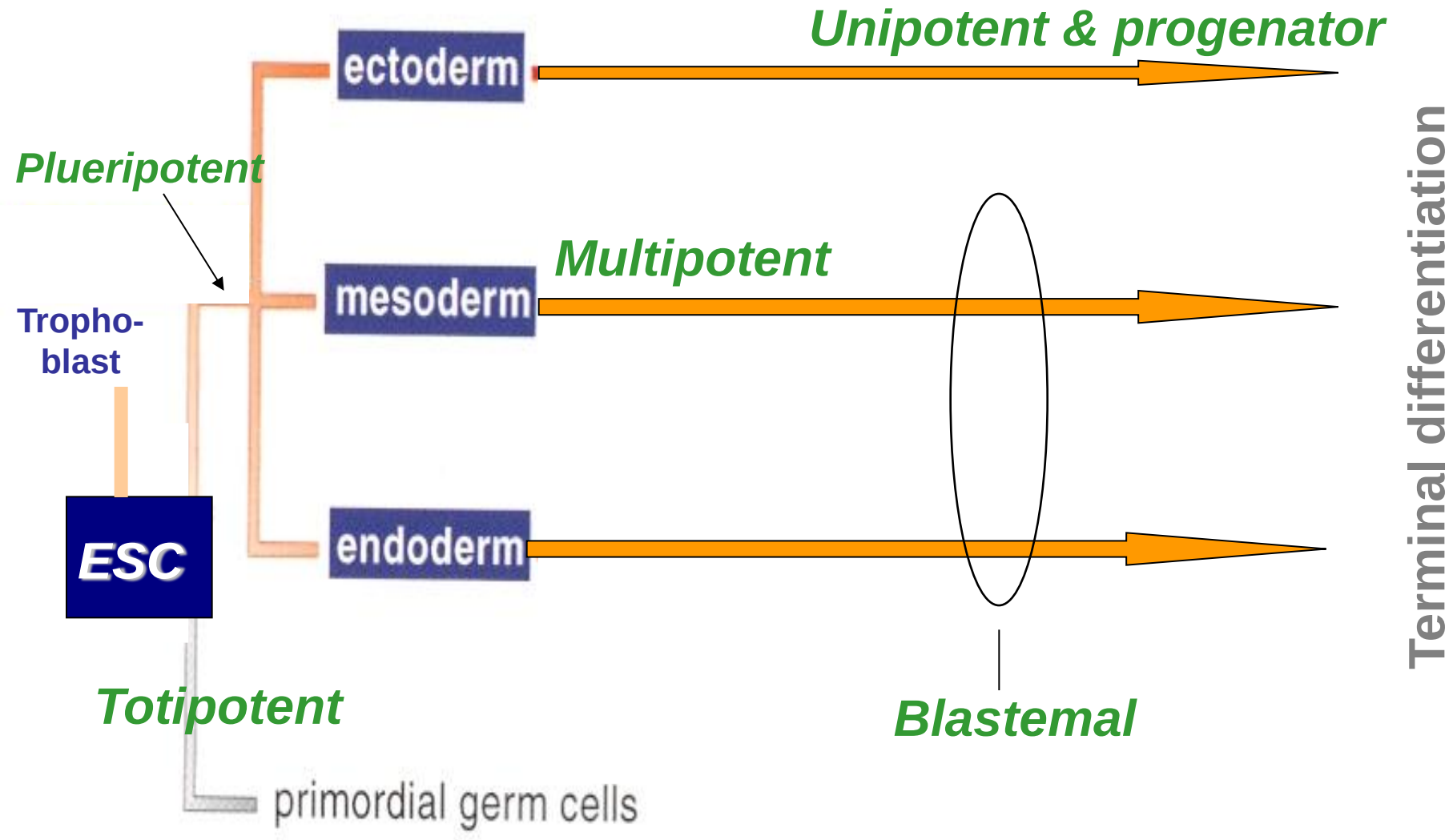
- Tumors arise from stem cells, which are normally present (2%) among normal cells , and are immortal hence are more liable to accumulate multiple mutations

- Stem cells are capable of both proliferation and differentiation of various degrees, hence explaining the extreme diversity of tumors


Quiescence
G_0
A
B
C
Stem cell
Terminal differentiati
Clonal expansion
(Cancer)


ESC
gastrulation
ectoderm
nervous tissue/NSCs
skin/skin SCs
mesoderm
bone marrow and blood/HSCs and MSC
muscle and bone/tissue SCs
endoderm
lung, liver, and pancreas/organ specific
esophagus, stomach, intestine/intestinal
primordial germ cells

CELL POTENCY



SOME IMPORTANT TERMS

- Differentiated: to have a definite phenotype, both structure and function
- Undifferentiated: absence of any definite phenotype
- Transdifferentiation (metaplasia): change of one phenotype into another phenotype
- Dedifferentiation: change of a differentiated cell to an undifferentiated cell

METAPLASIA
"TRANSDIFFERENTIATION"

1. Unidirection:

   Columnar ← Transitional → Squamous

2. Bidirection:

   Histiocyte ↔ Fibroblast ↔ Myofibroblast

   Columnar ↔ Squamous

   Barrett

   Bronchus, endometrial & gall bladder

BASIS OF CLASSIFICATION

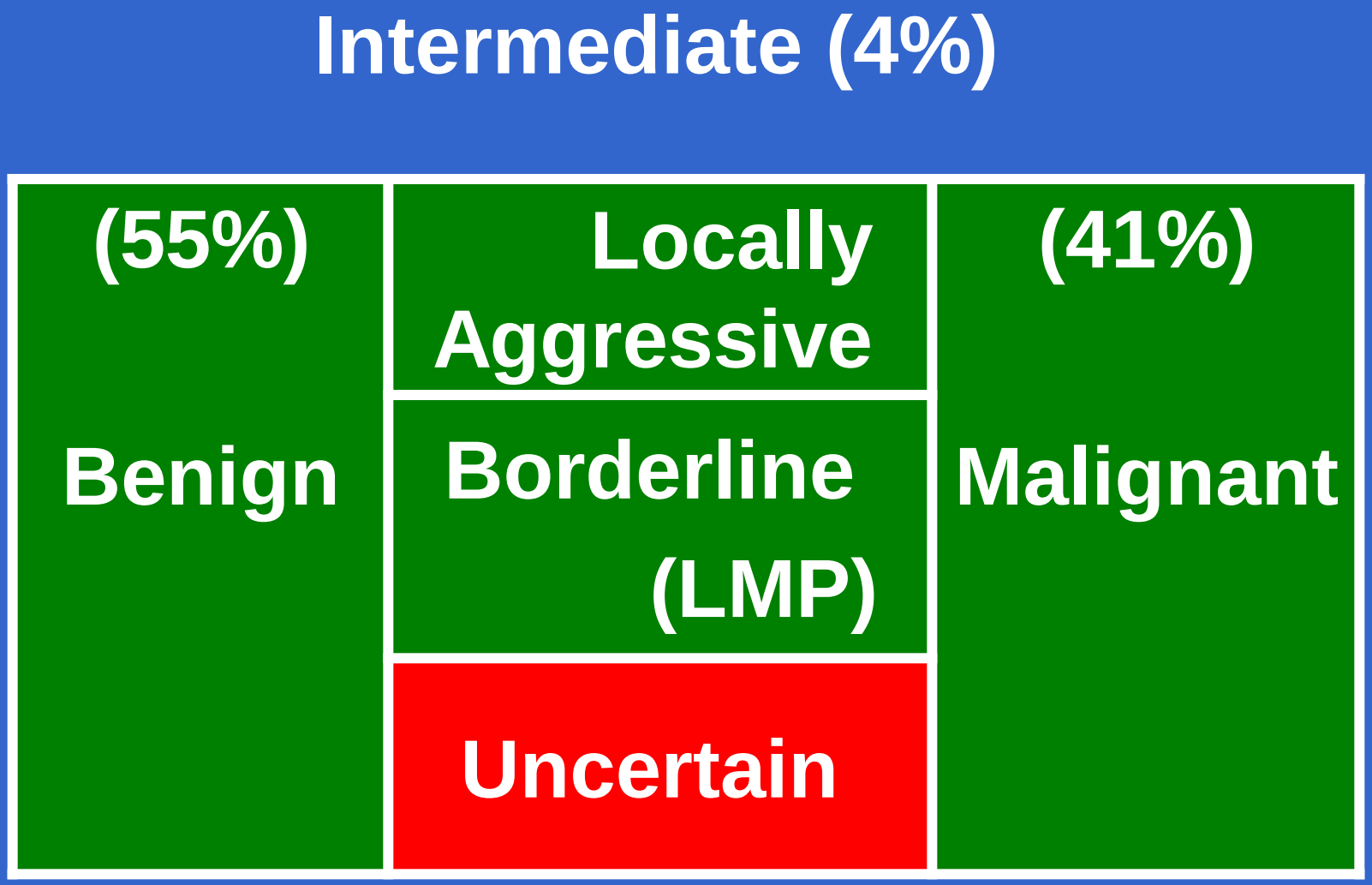
Differentiation Cell type

- Adult or embryonic cell
- Sarcoma or carcinoma
- Mono or multiphasic

CLINICAL Behavior

- Benign
- Intermediate
- Malignant

BEHAVIOR CATEGORIES OF NEOPLASMS



BEHAVIOR CATEGORIES OF NEOPLASMS

Category	Invasion	Recurrence	Metastasis
Benign	No	No	No
Locally aggressive	Yes	Yes	No
Borderline*	No	Yes	Rare
Malignant	Yes	Yes	Yes
Uncertain	(Indeterminate from histology)		

*** Low malignant potential (LMP), metastatic < 5%**

BENIGN NEOPLASMS

Epithelial	Mesenchymal
Adenoma	Fibroma
Papilloma	Lipoma
Epithelioma	Myoma
	Osteoma

LOCALLY AGGRESSIVE NEOPLASMS

Epithelial	Mesenchymal
Verrucous sq.ca	Fibromatosis
Ameloblastoma	Giant cell tumor
Inverted papilloma	Myxoma

BORDERLINE NEOPLASMS

Epithelial	Mesenchymal
Ovarian borderline	Inflammatory myo-fibroblastic tumor
Basal cell carcinoma	Solitary fibrous tumor
	Phyllodes tumor

NEOPLASMS OF UNCERTAIN BEHAVIOR

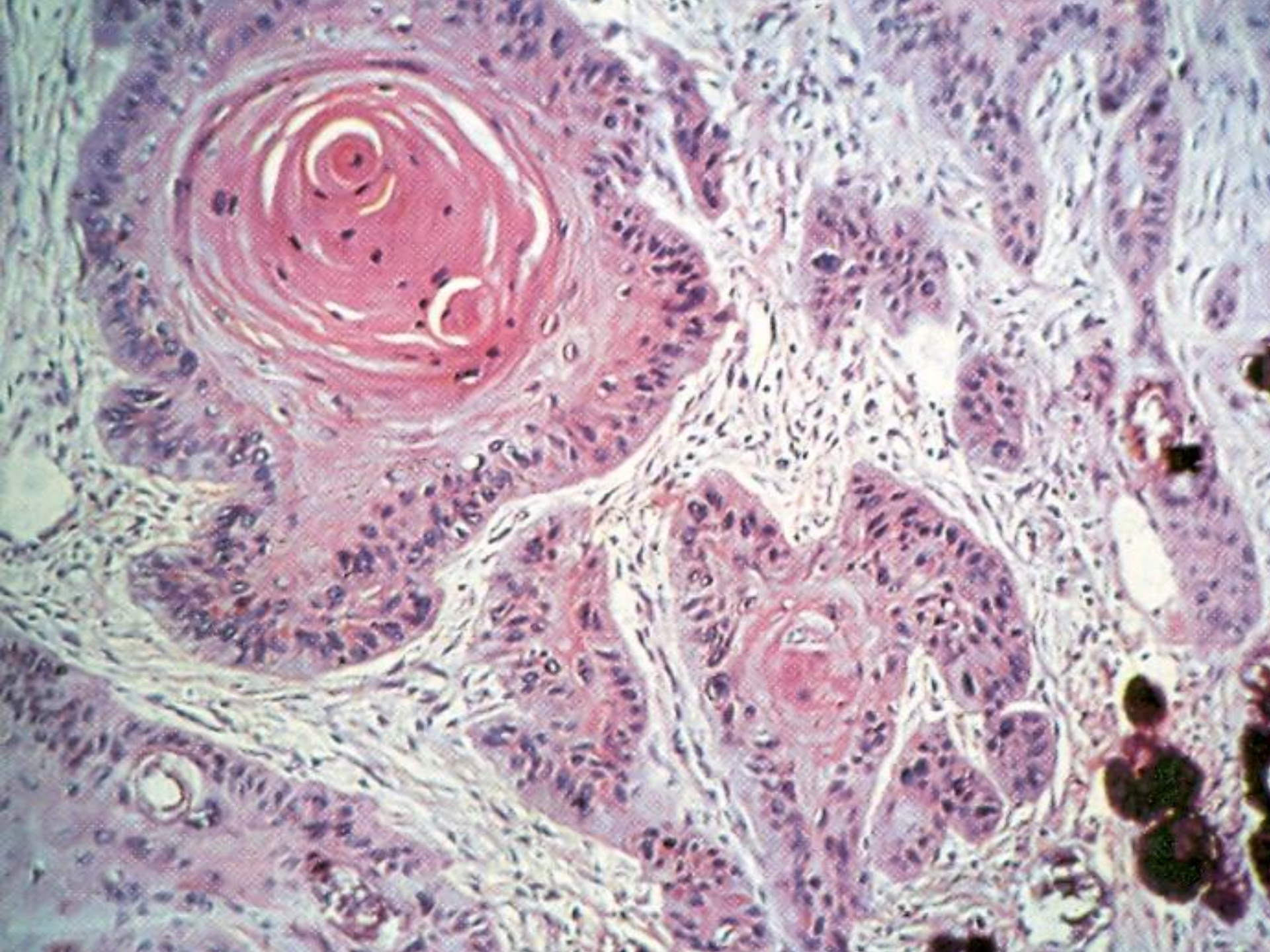
1. Paragangliomas
2. Neuroendocrine tumors
   (e.g. Carcinoid)
3. Gastrointestinal stromal tumor
   (GIST)
4. Granulase cell tumor
5. Adrenal cortical tumors

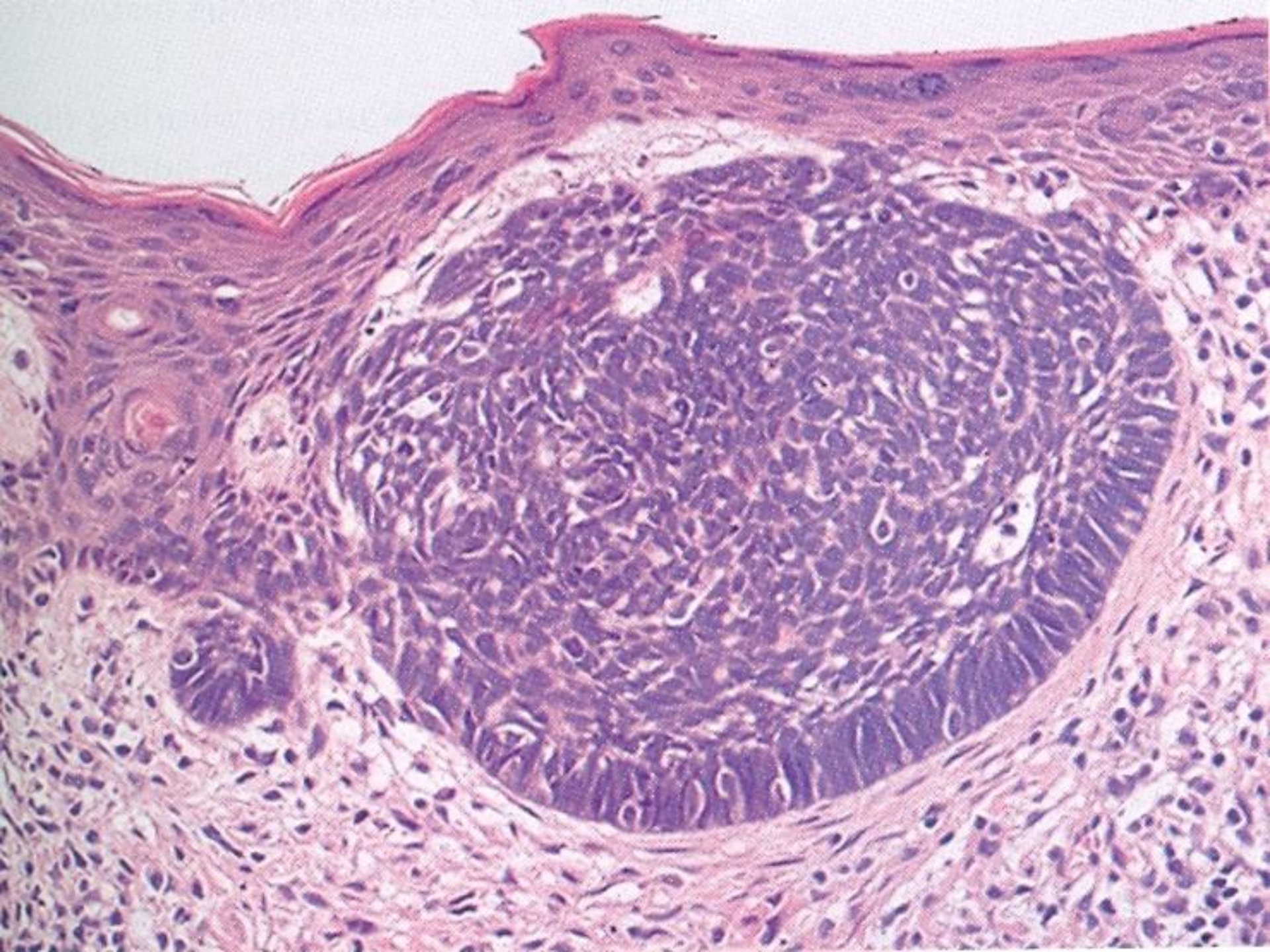
THE CLASSES OF CANCER

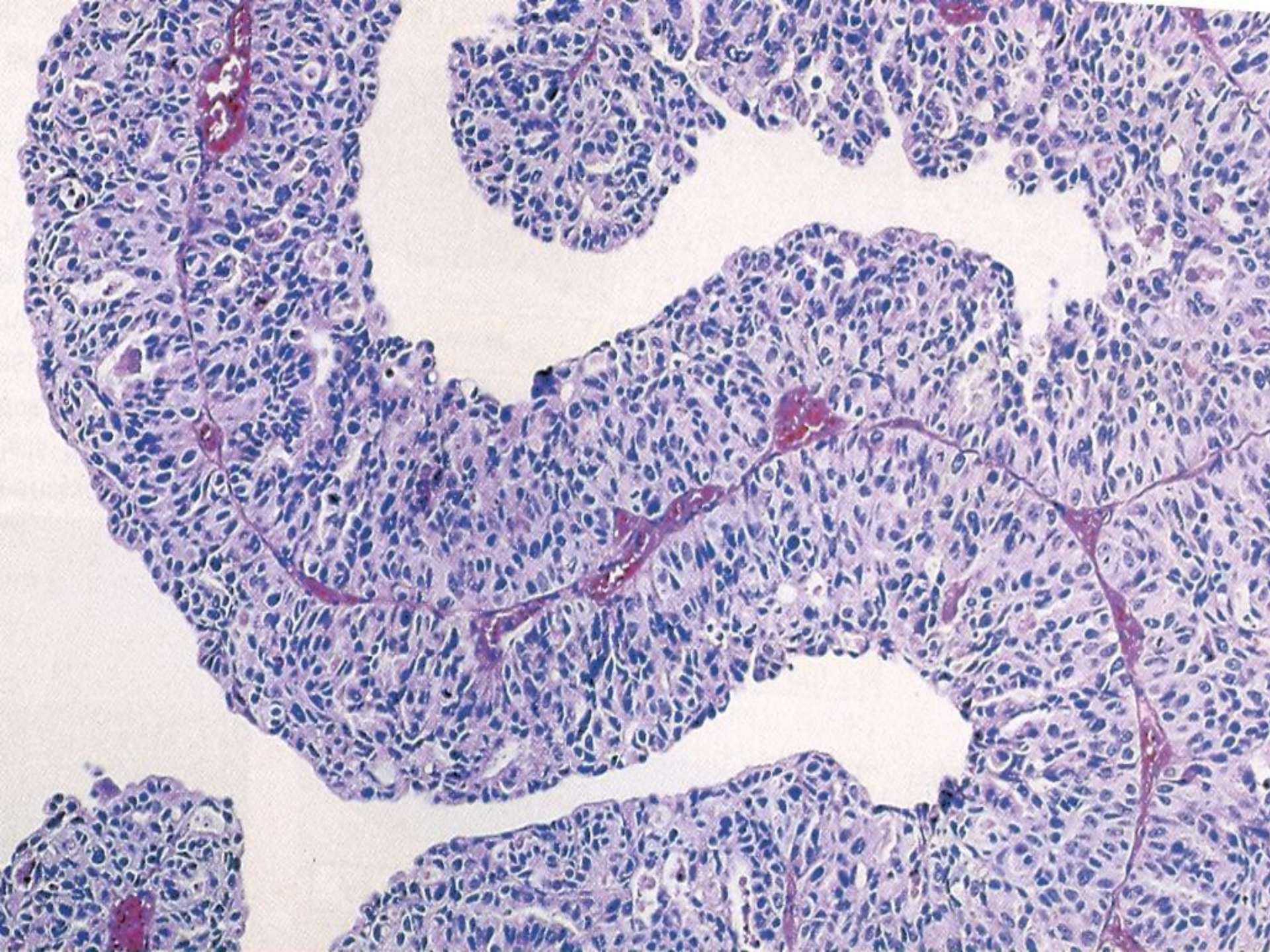
1. Carcinomas
2. Neuroectodermal
3. Sarcomas
4. Hemolymphoid
5. Germ cell tumors
6. Blastemal tumors
7. Vestigeal remnants
8. Uncertain origin
9. Undifferentiated.

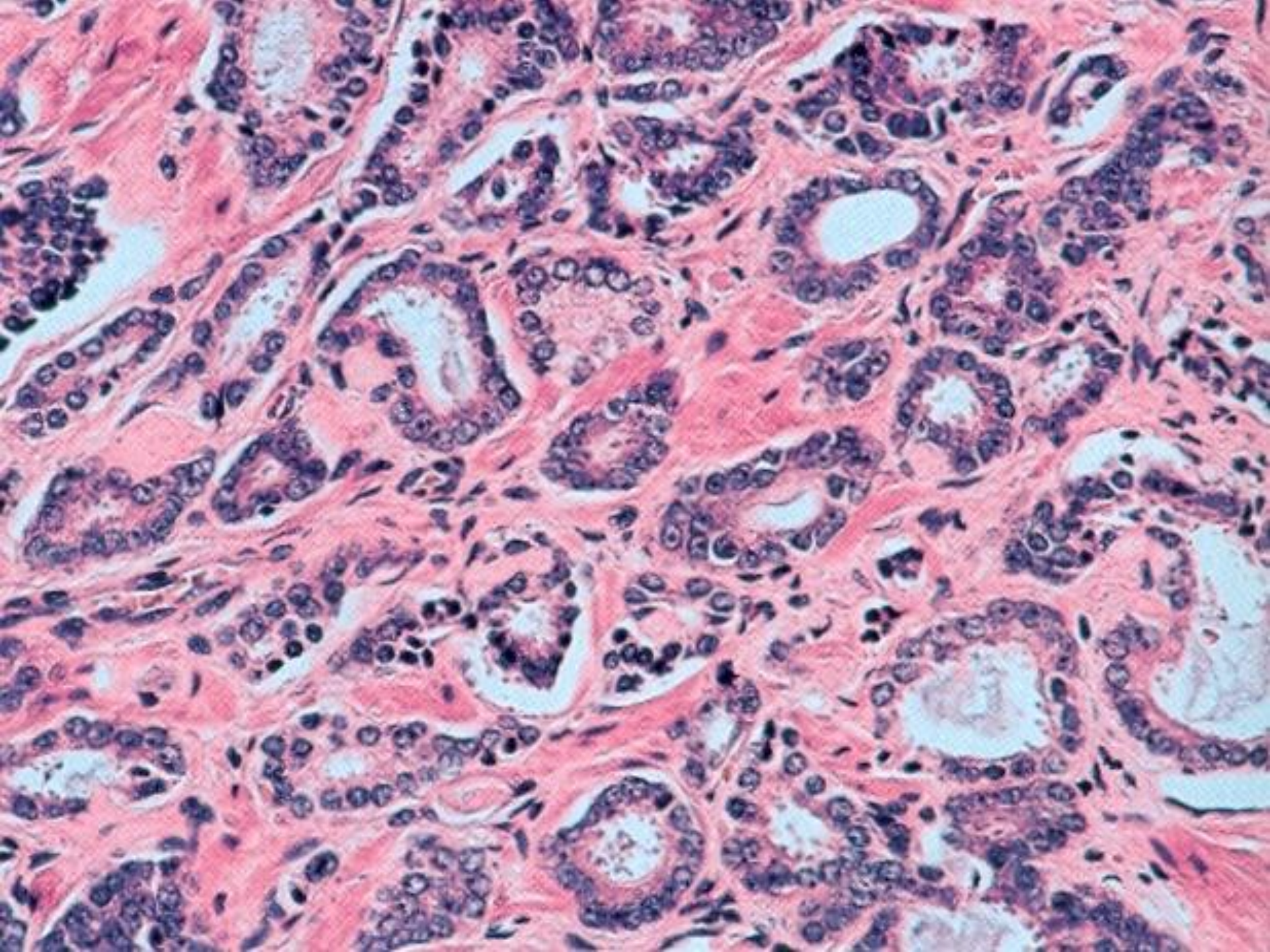
HISTOLOGIC TYPES OF CARCINOMAS

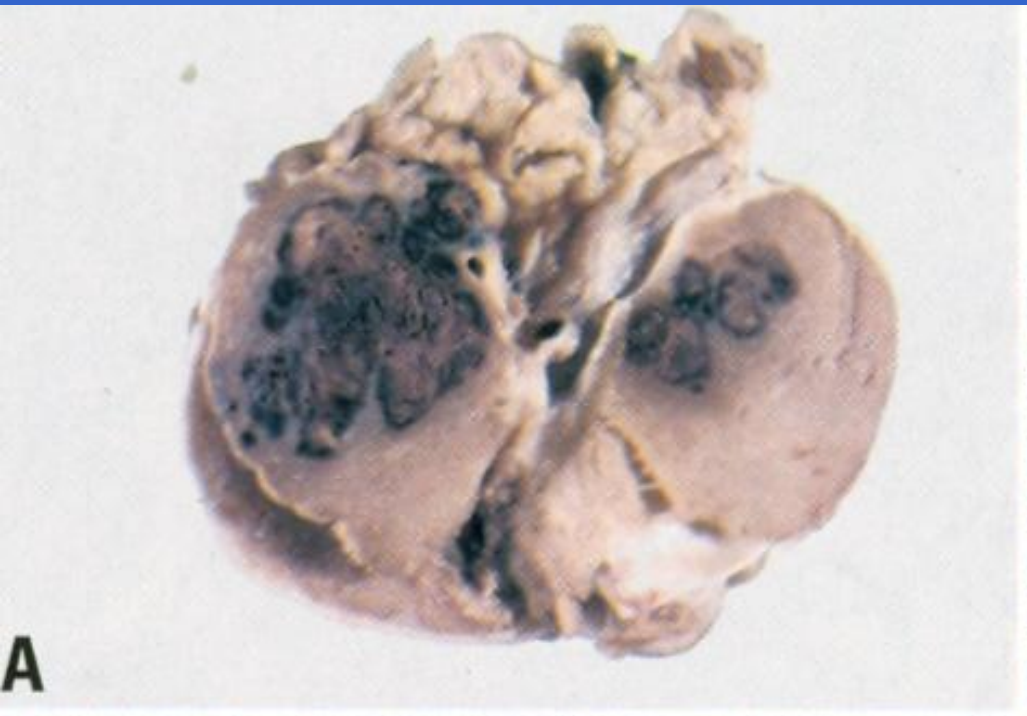
1. Squamous cell carcinoma.
2. Basal cell carcinoma.
3. Transitional cell carcinoma.
4. Adenocarcinoma.
5. Choriocarcinoma.







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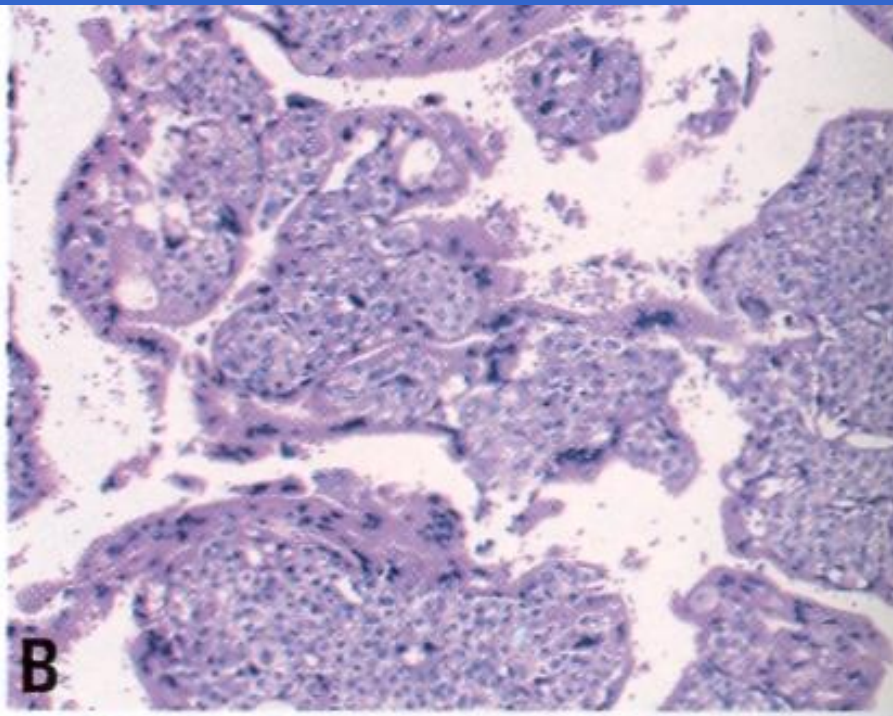
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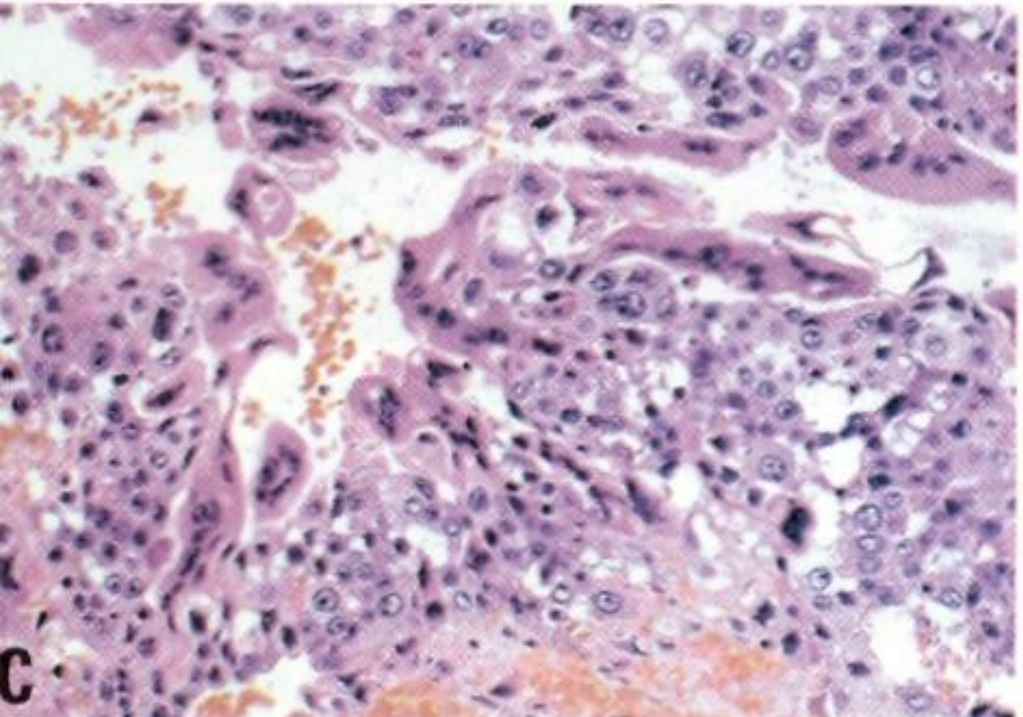
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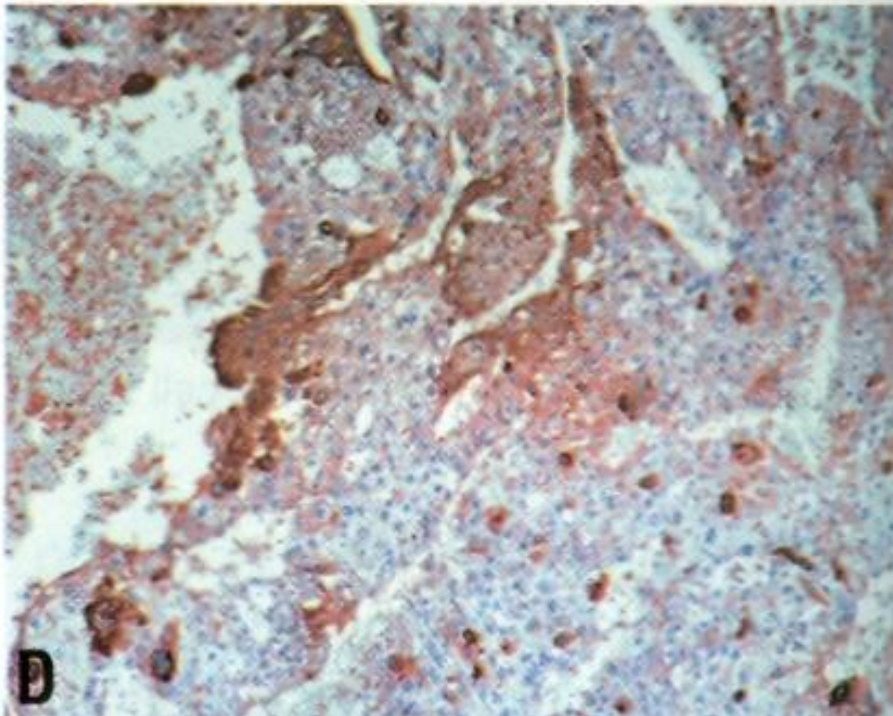
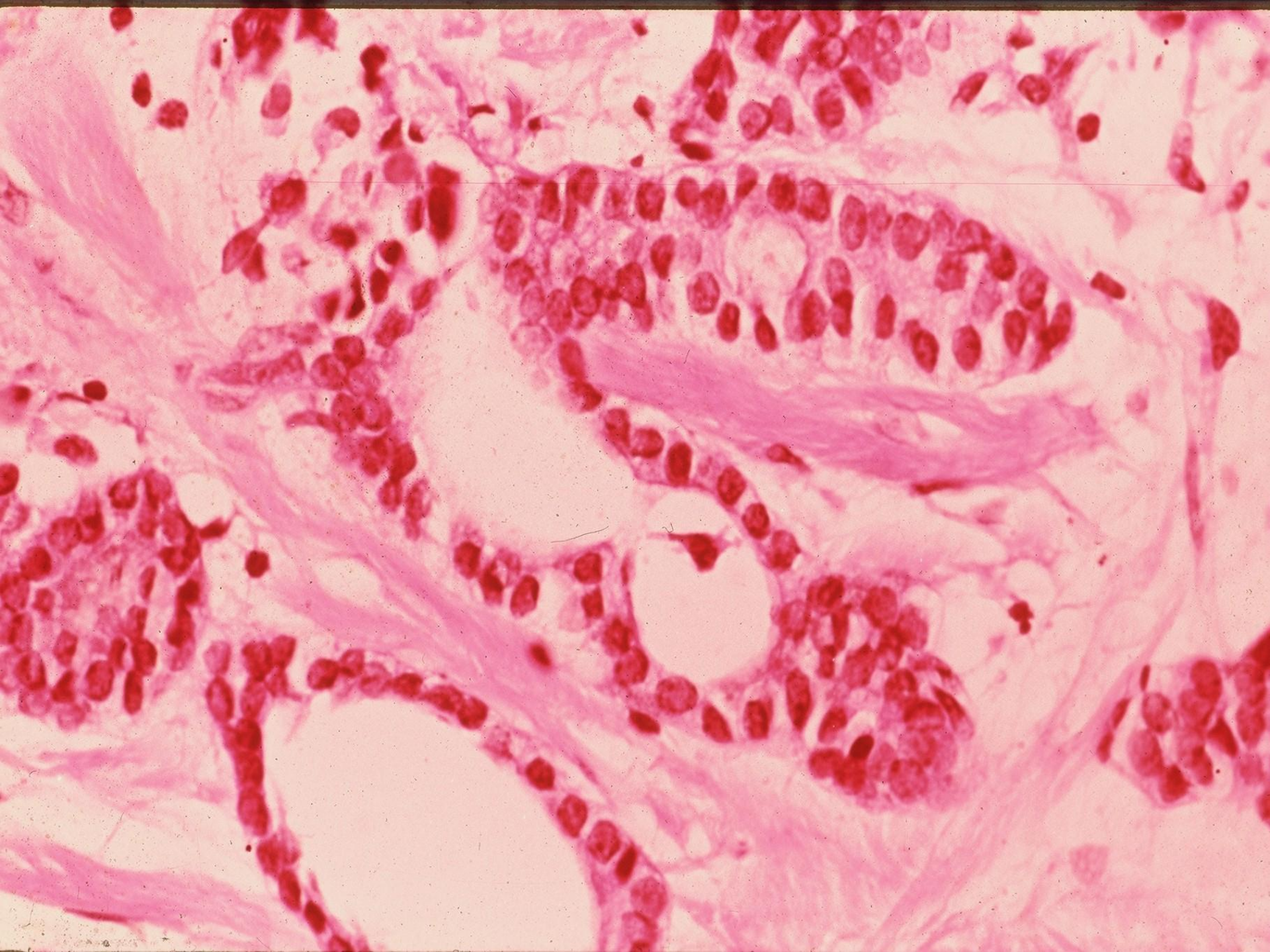

D

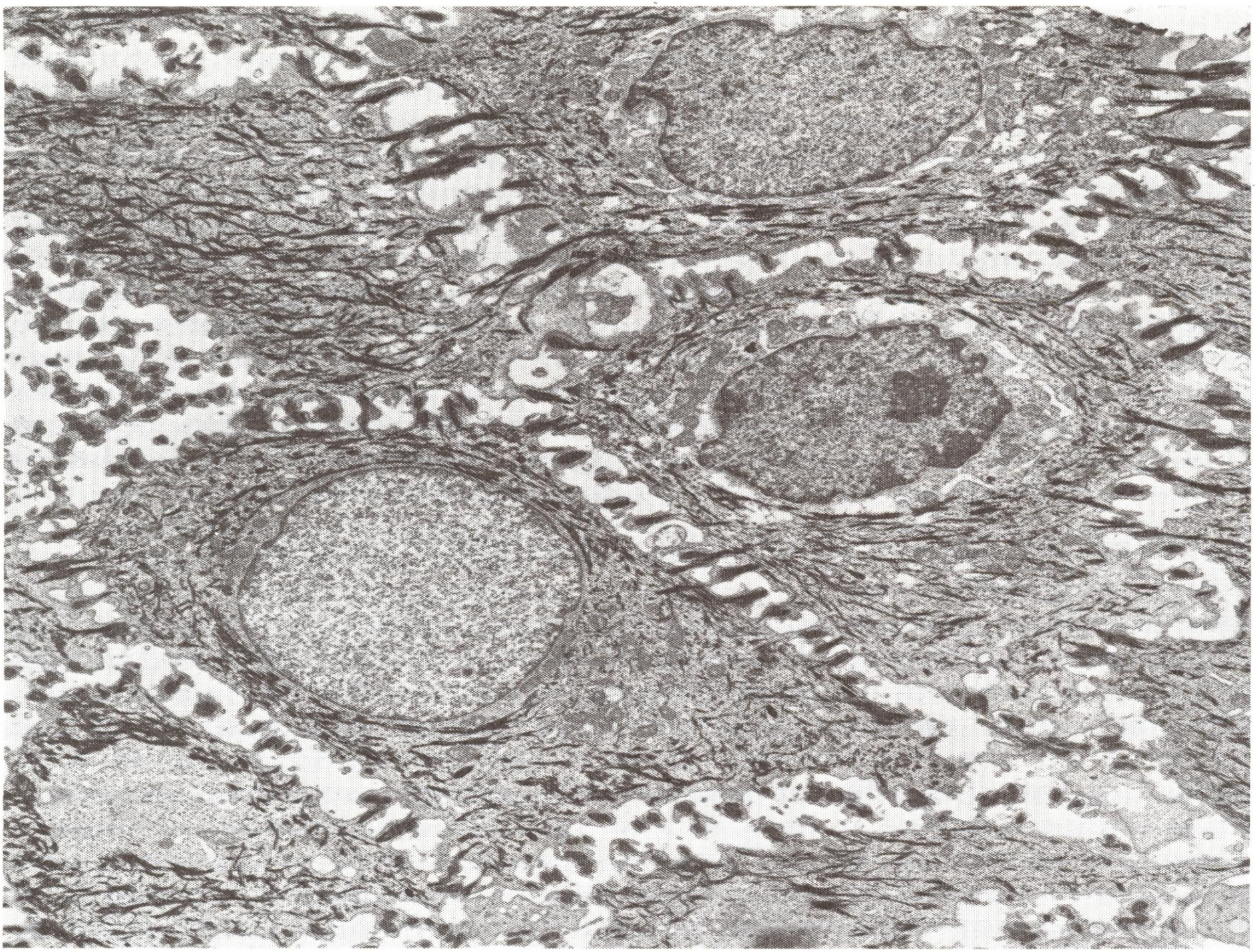
CARCINOMAS OF MESENCHYMAL ORIGIN

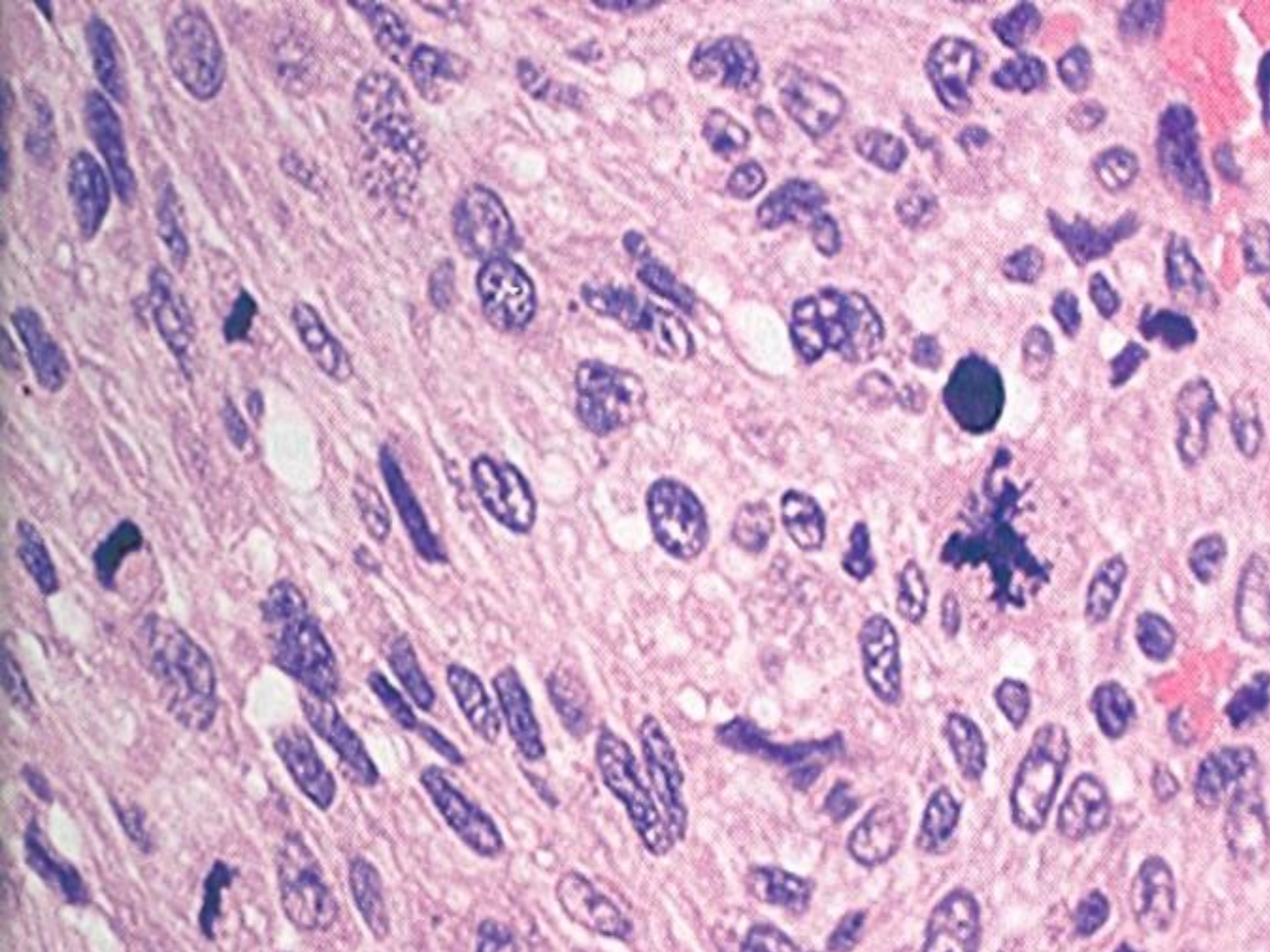
1. Adrenal cortical ca.
2. Renal cell ca.
3. Epithelioid mesothelioma
4. Ovarian carcinomas
5. Mullerian & mesonephric ca.
6. Bladder trigone carcinoma
7. Central prostate carcinoma

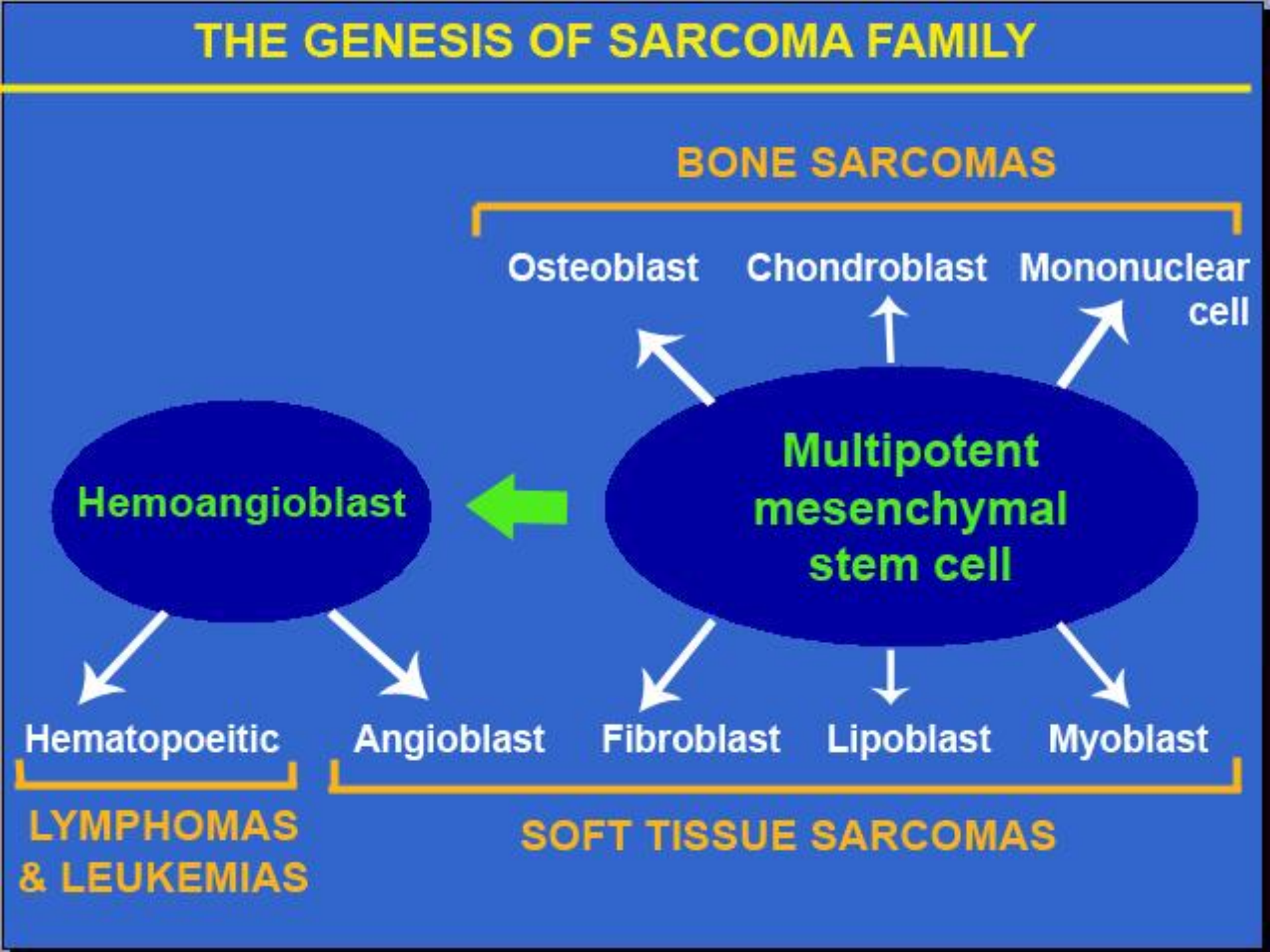
MAJOR CLASSES OF CANCER

Feature	Carcinoma	Sarcoma
Frequency	80%	20%
Size	Small (<5 cm)	Large (>5 cm)
Pattern	Groups	Diffuse
Desmosomes	Present	Absent
Markers	Cytokeratin	Vimentin
Growth rat	Slow	Rapid
Main spread	Lymphatic	Hematogenous

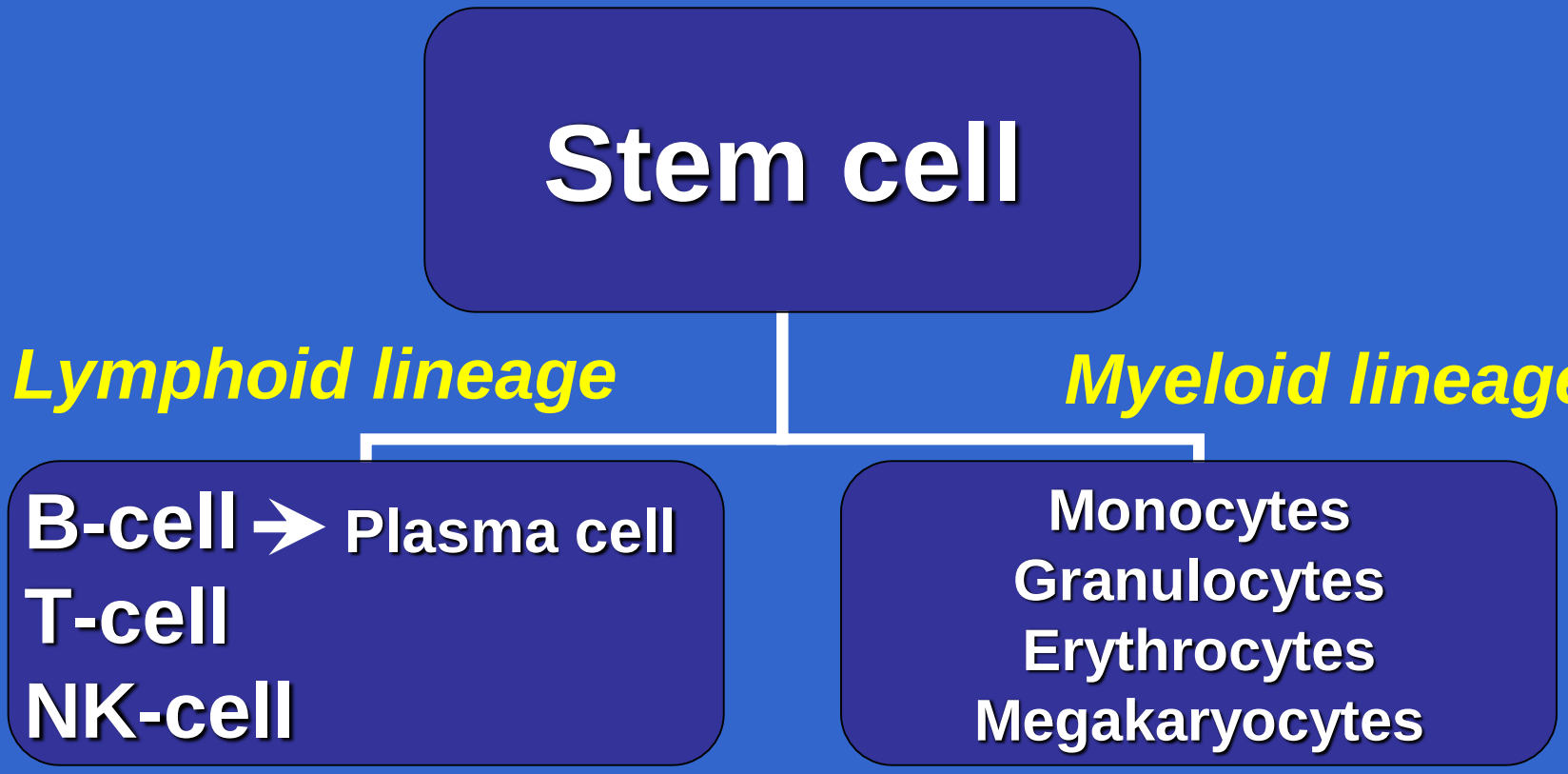







THE GENESIS OF SARCOMA FAMILY
BONE SARCOMAS
Osteoblast
Chondroblast
Mononuclear cell
Multipotent mesenchymal stem cell
Hemoangioblast
Hematopoeitic
Angioblast
Fibroblast
Lipoblast
Myoblast
LYMPHOMAS & LEUKEMIAS
SOFT TISSUE SARCOMAS

HEMATOLYMPHOID MALIGNANCES



- NHL/L.Leukemias
- Plasma cell myeloma
- Hodgkin Lymphoma

- Histiocytic tumors
- Mastocytoma
- Leukemias
- Myeloid dysplasia

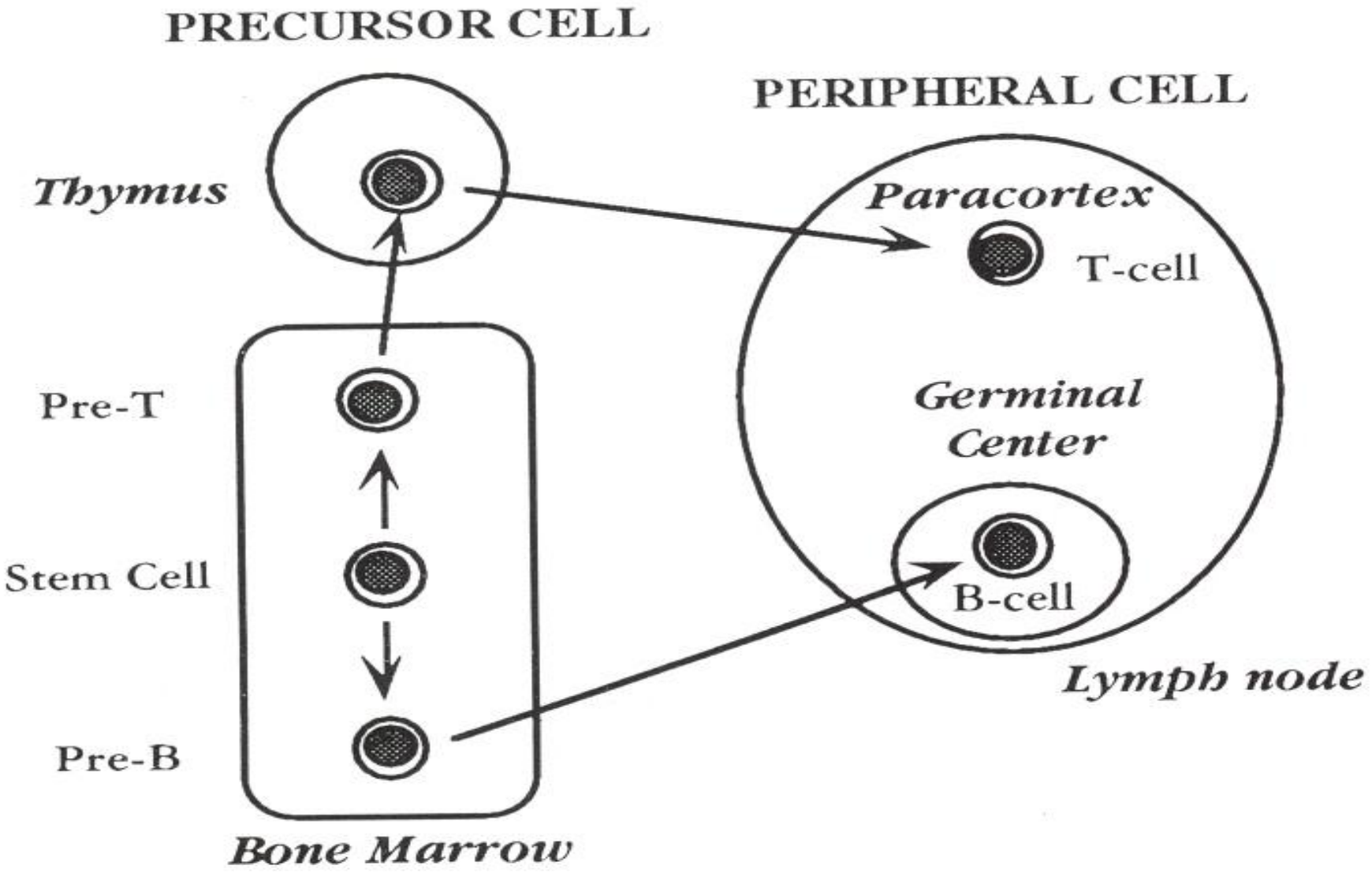
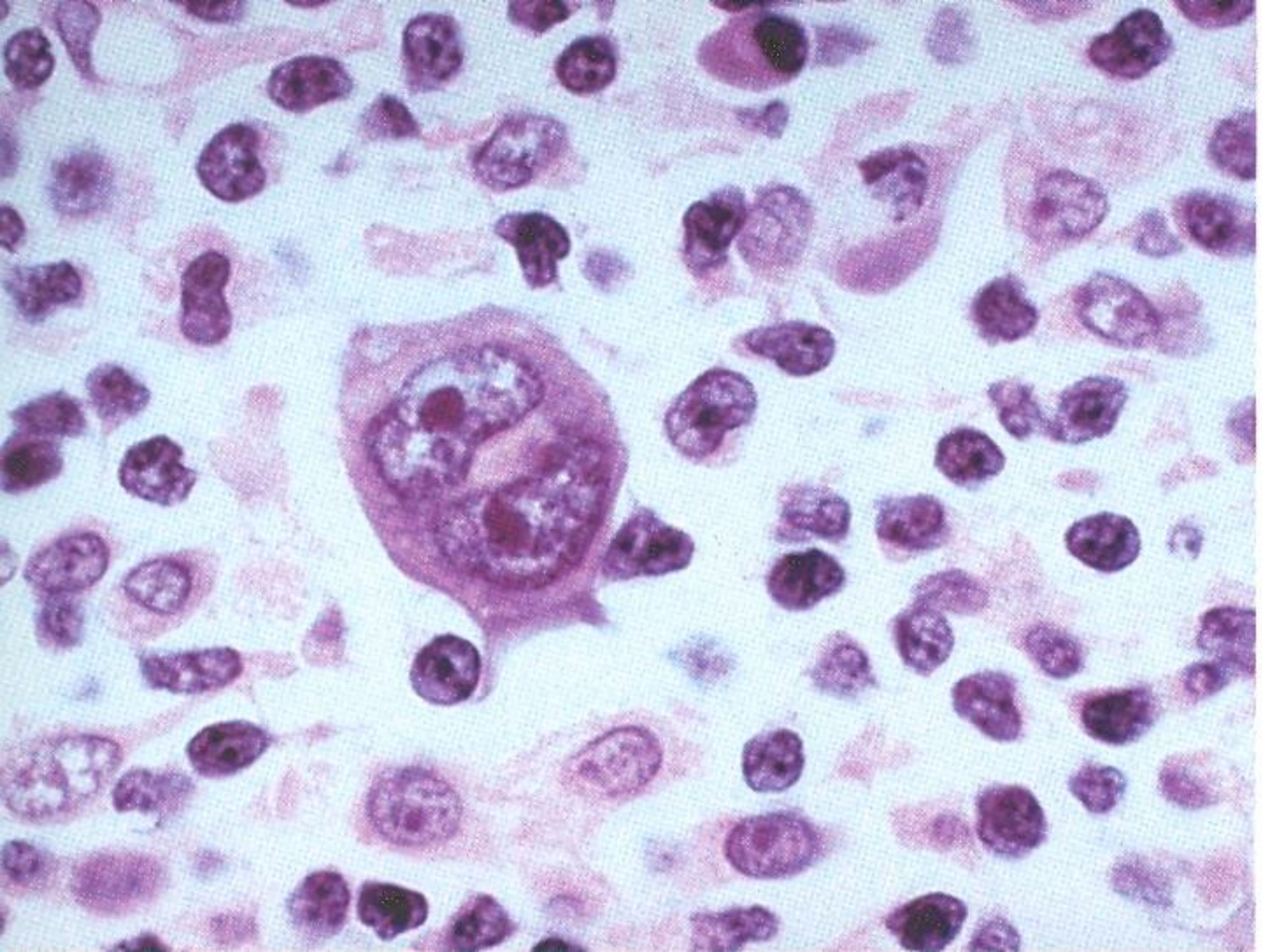
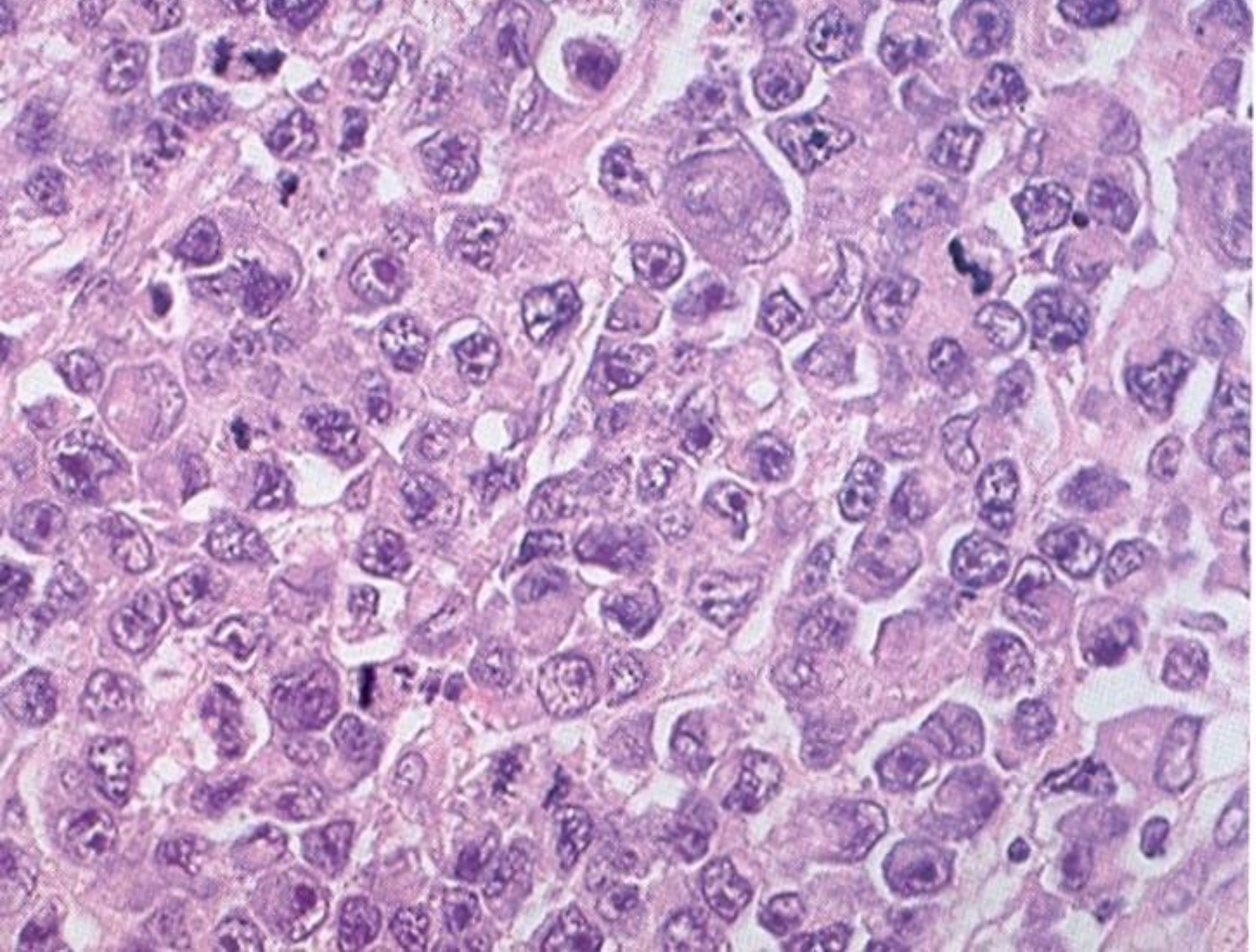


Fig. 2.4. Differentiation pathways of B and T lymphocytes.

HODGKIN & NHL COMPARED

Feature	Hodgkin	NHL
Entity	Single	Multiple
Histogenesis	B (crippled)	B or T
Malignant cells	Reed-Sternbeg	All cells
Spread	Contiguous LN	Noncontiguous
Nodal pattern	Central	Periferal
Extranodal	None	May occur
Leukemia	None	May occur
Treatment	Standard	Variable
Prognosis	Favorable	Less favorable





CLASSIFICATION OF HISTIOCYTOSIS

Cell Origin/Type	Diagnostic Markers
I. Hematopoietic stem cell:	
1. Langerhans	S-100,CD1a, CD207
2. Non-Langerhans	CD68, CD163
II. Mesenchymal stem cell:	
3. Follicular dendritic	CD21, CD23

CLASSIFICATION OF HISTIOCYTOSIS

Cell Oregin/Type		
Frequency	80%	20%
Size	Small (<5 cm)	Large (>5 cm)
Pattern	Groups	Diffuse
Desmosomes	Present	Absent
Markers	Cytokeratin	Vimentin
Growth rat	Slow	Rapid
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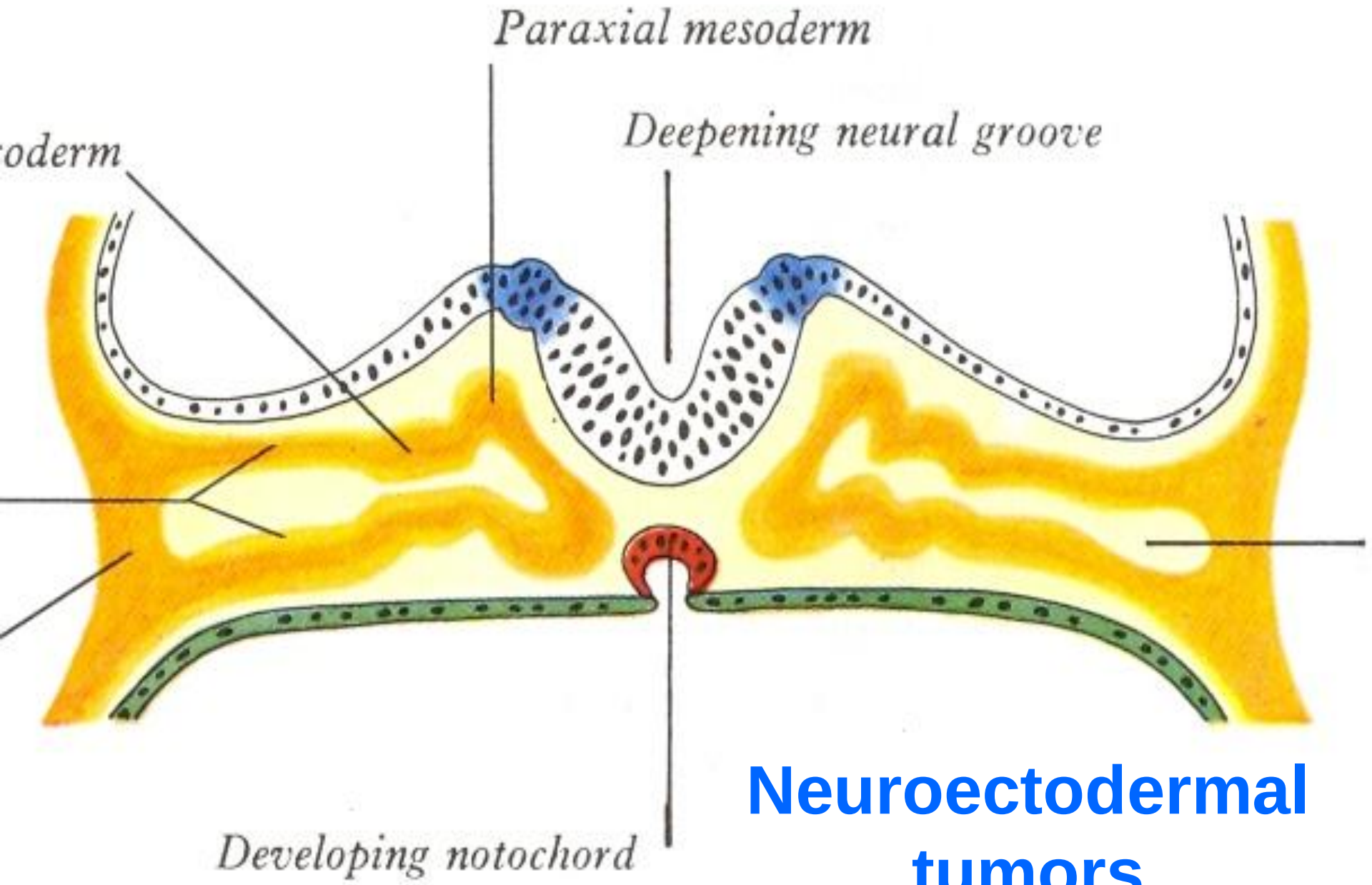
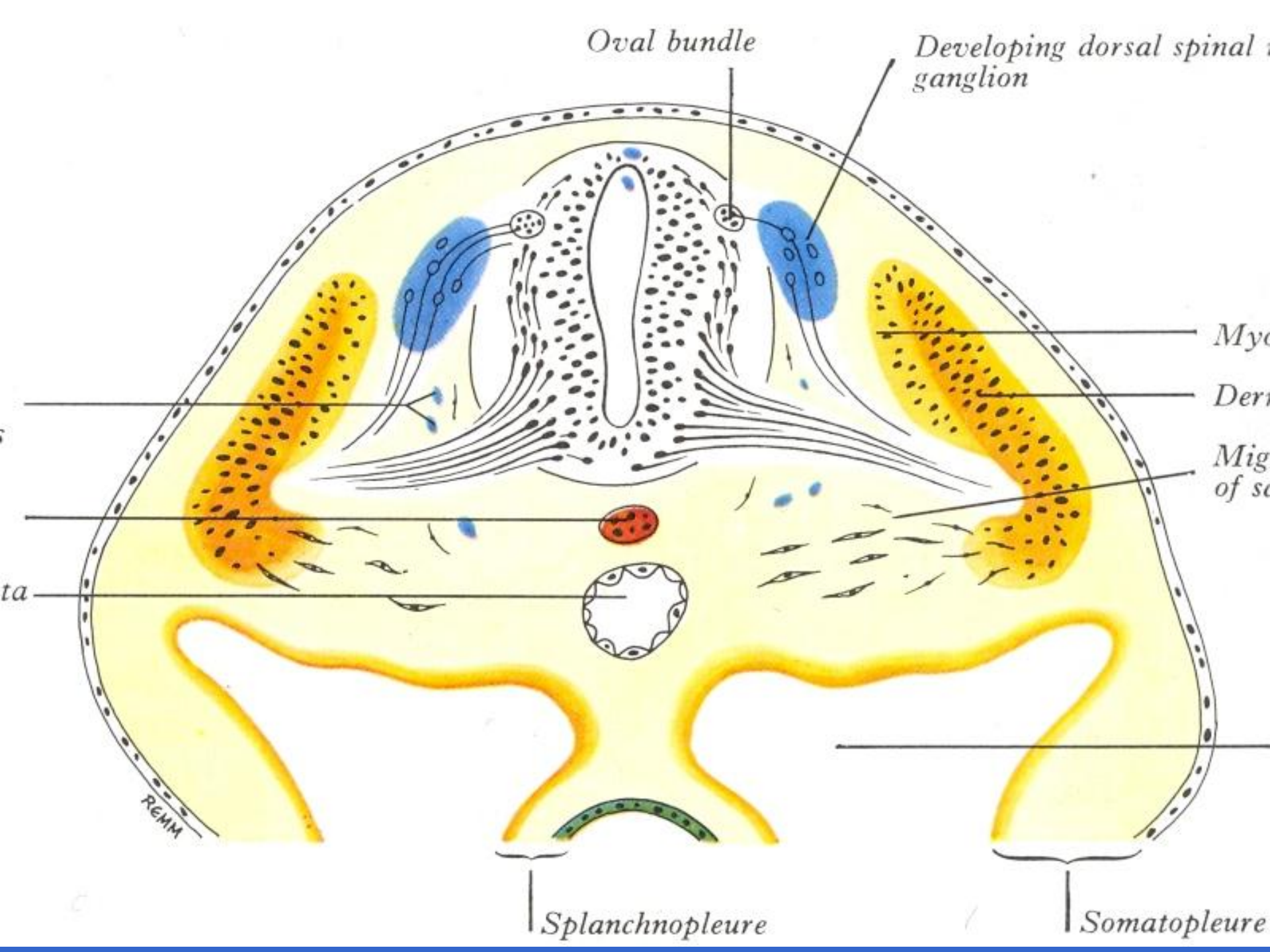


Neuroectodermal tumors


Oval bundle
Developing dorsal spinal
ganglion
Myo
Der
Mig
of so
ta
REMM
Splanchnopleure
Somatopleure

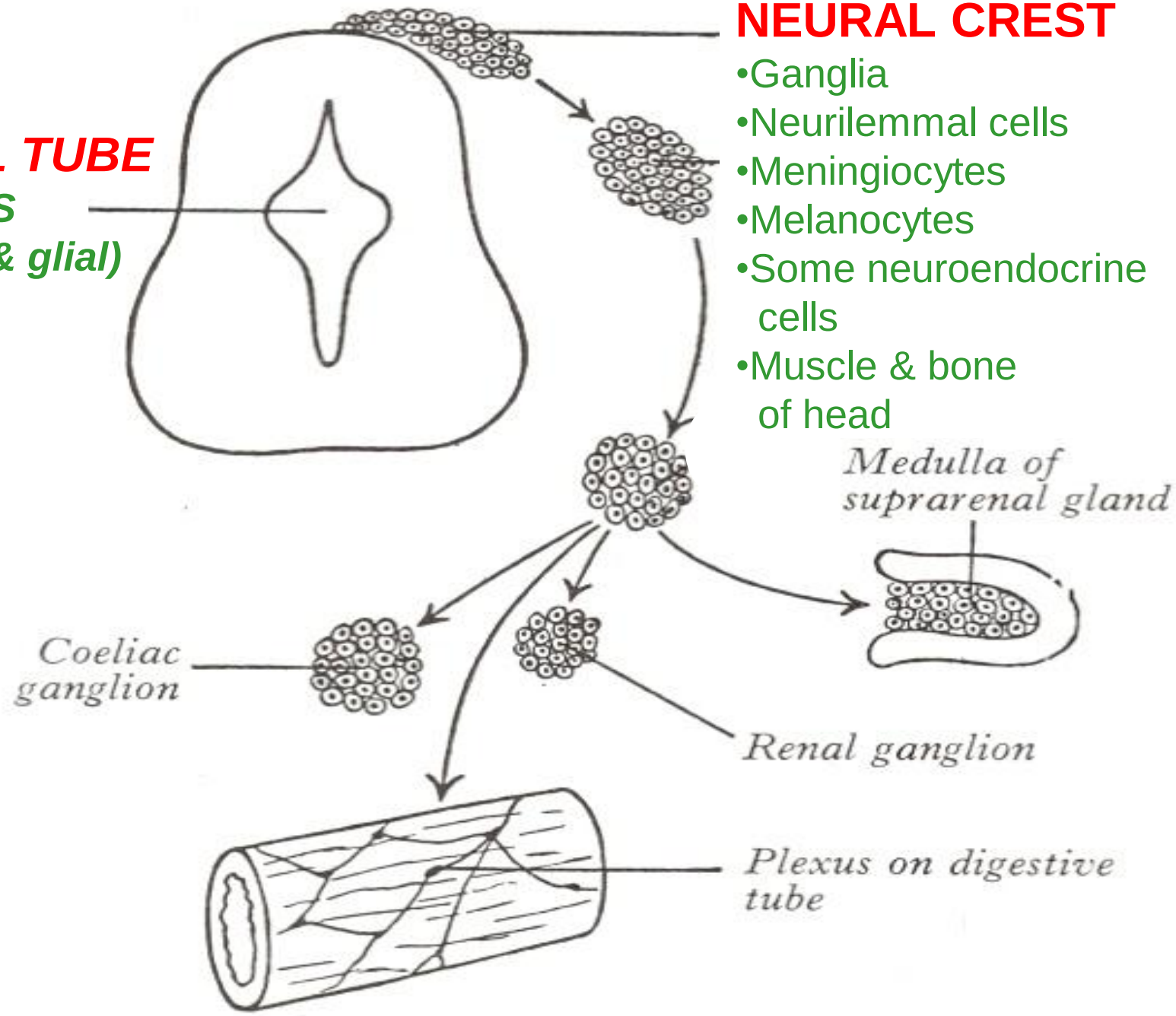
NEURAL TUBE

CNS

(Neural & glial)

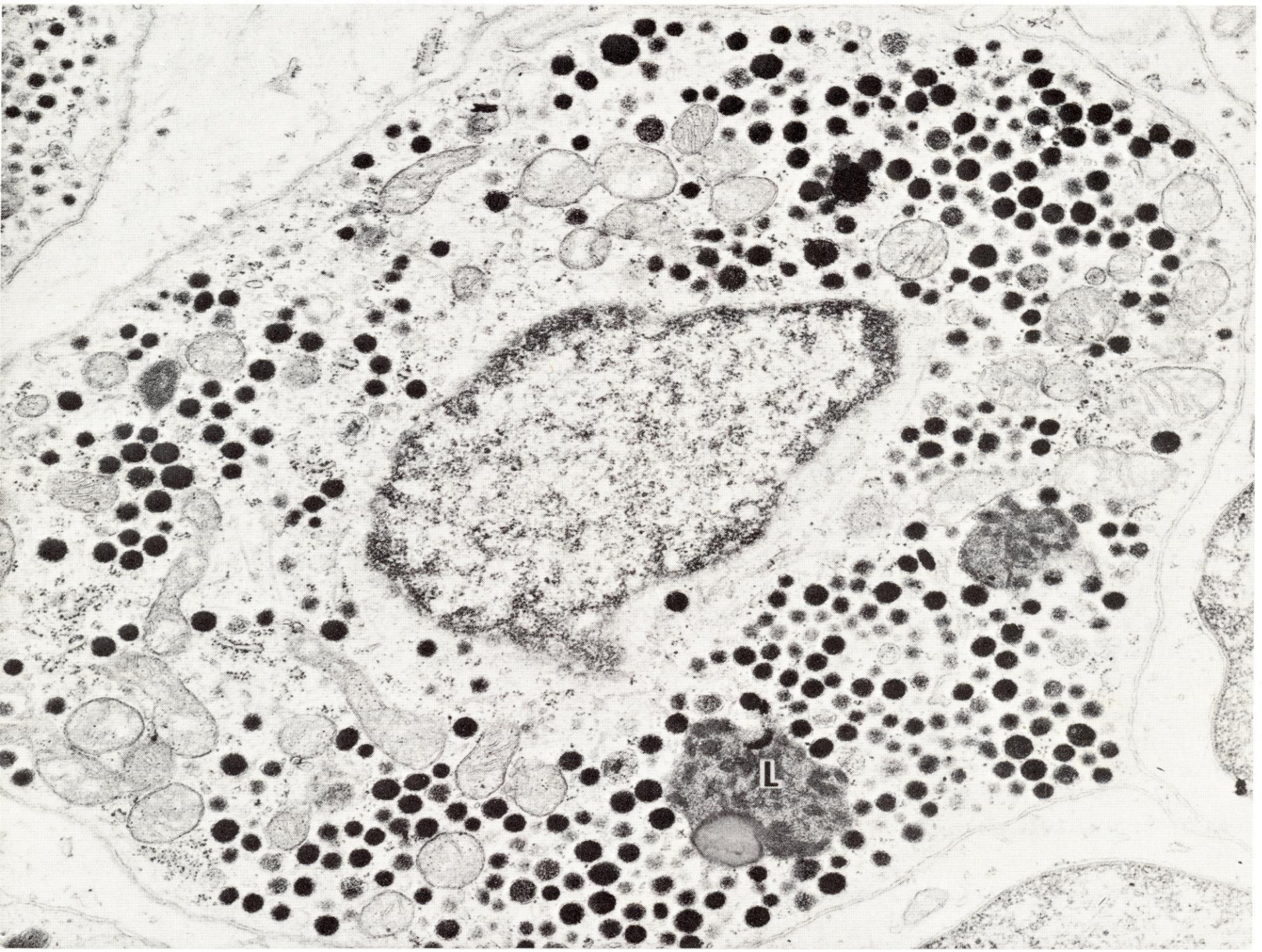
NEURAL CREST

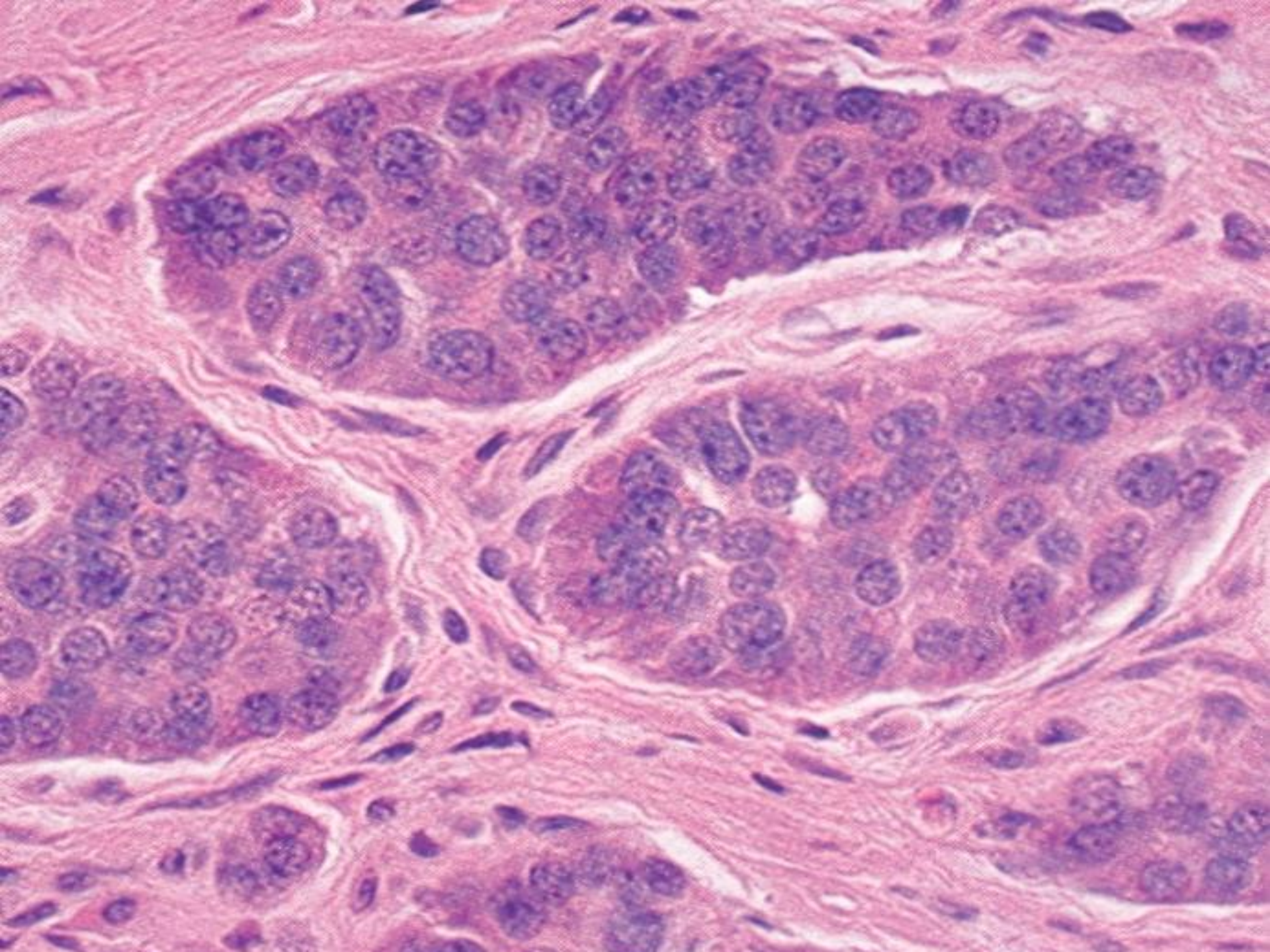
- Ganglia
- Neurilemmal cells
- Meningiocytes
- Melanocytes
- Some neuroendocrine cells
- Muscle & bone of head



COMMON FEATURES OF NET

1. Contain decarboxylase(amine precursor uptake & decarboxylation: APUD), may secrete peptide hormones.
2. EM: Dense core membrane-bound neurosecretory granules.
3. Markers: NSE and chromogranin.
4. Pattern: Carcinoma, sarcoma or rosette, with vascular stroma.
5. Nuclei: Uniform, fine dispersed chromatin.


L



NEUROECTODERMAL TUMORS (NET)

Differentiated

- Gliomas
- Meningioma
- Melanocytic tumors
- Pigmented NET infancy
- Nerve sheath tumors
- Granular cell tumors

Neuroendocrine

NET:

1. Medullary ca, TR
2. Paragangliomas
3. Neuroblastoma

Ectodermal:

1. Ant. pituitary
2. Pineal

Endodermal:

1. Endocrine pancreas
2. Carcinoids (lung & GIT)
3. Small cell ca.

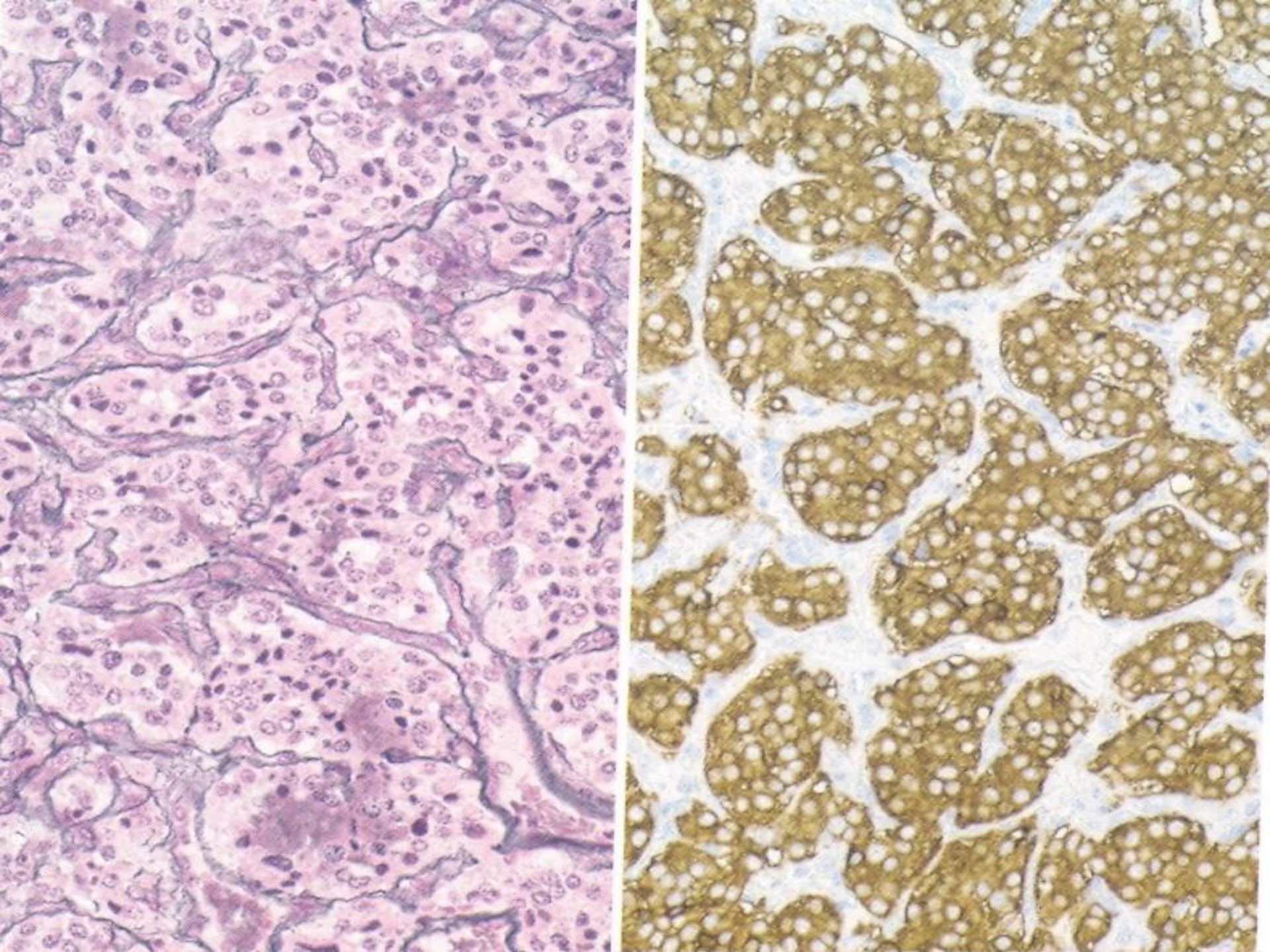
Undiff. (PNET)

Central:

1. Medulloblastoma
2. Neuroblastoma
3. Olfactory NB

Peripheral:

1. Ewings (BN)
2. Askin (ST)
3. Merkel (SK)



PARAGANGLIOMA

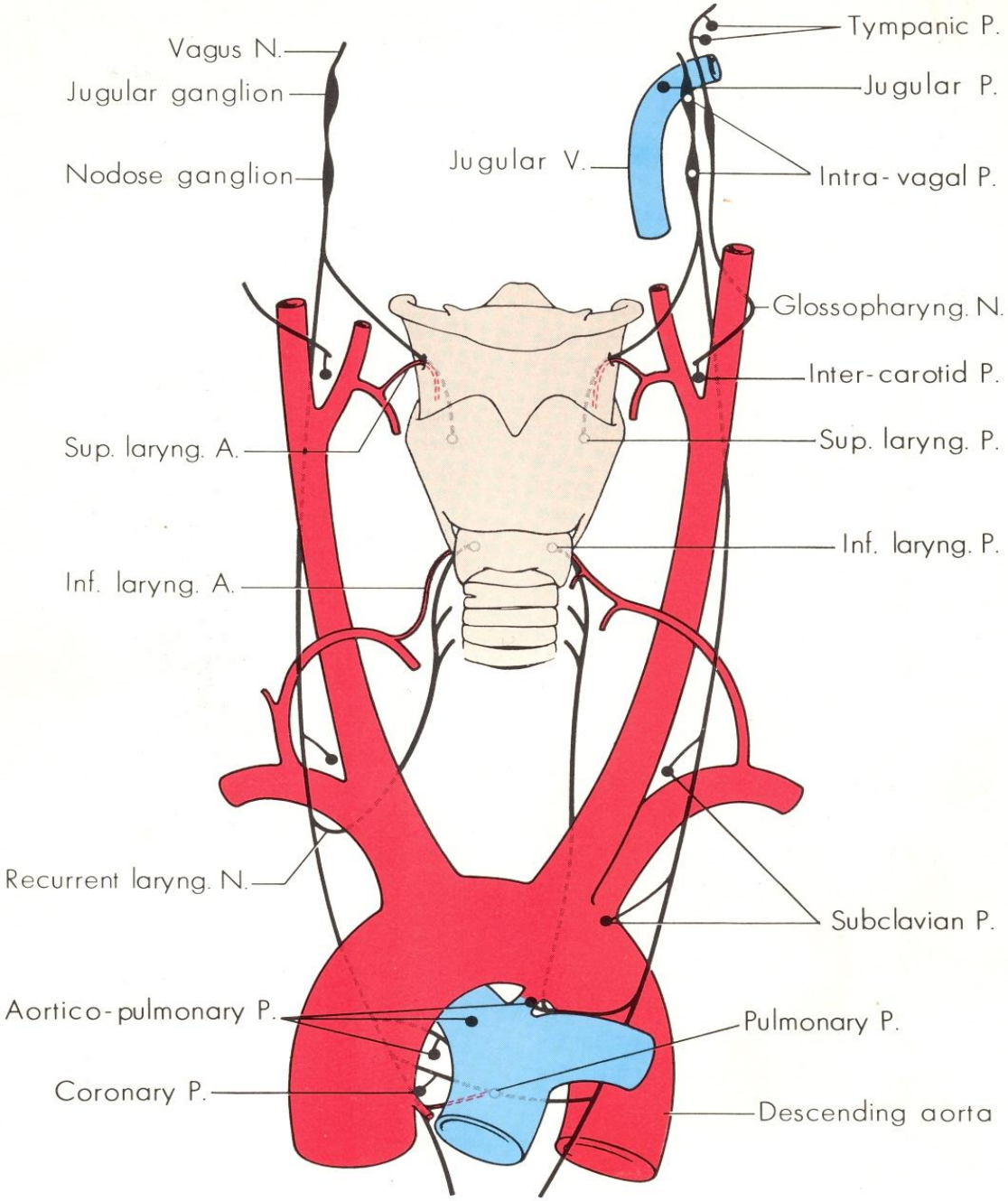
Tumors of autonomic nervous system

PARASYMPATHETIC

- ***Cervical & aortic ganglia***

SYMPATHETIC

- ***Thoracoabdominal ganglia***


Vagus N.
Jugular ganglion
Nodose ganglion
Tympanic P.
Jugular P.
Jugular V.
Intra-vagal P.
Glossopharyng. N.
Inter-carotid P.
Sup. laryng. A.
Sup. laryng. P.
Inf. laryng. P.
Inf. laryng. A.
Recurrent laryng. N.
Subclavian P.
Aortico-pulmonary P.
Pulmonary P.
Coronary P.
Descending aorta

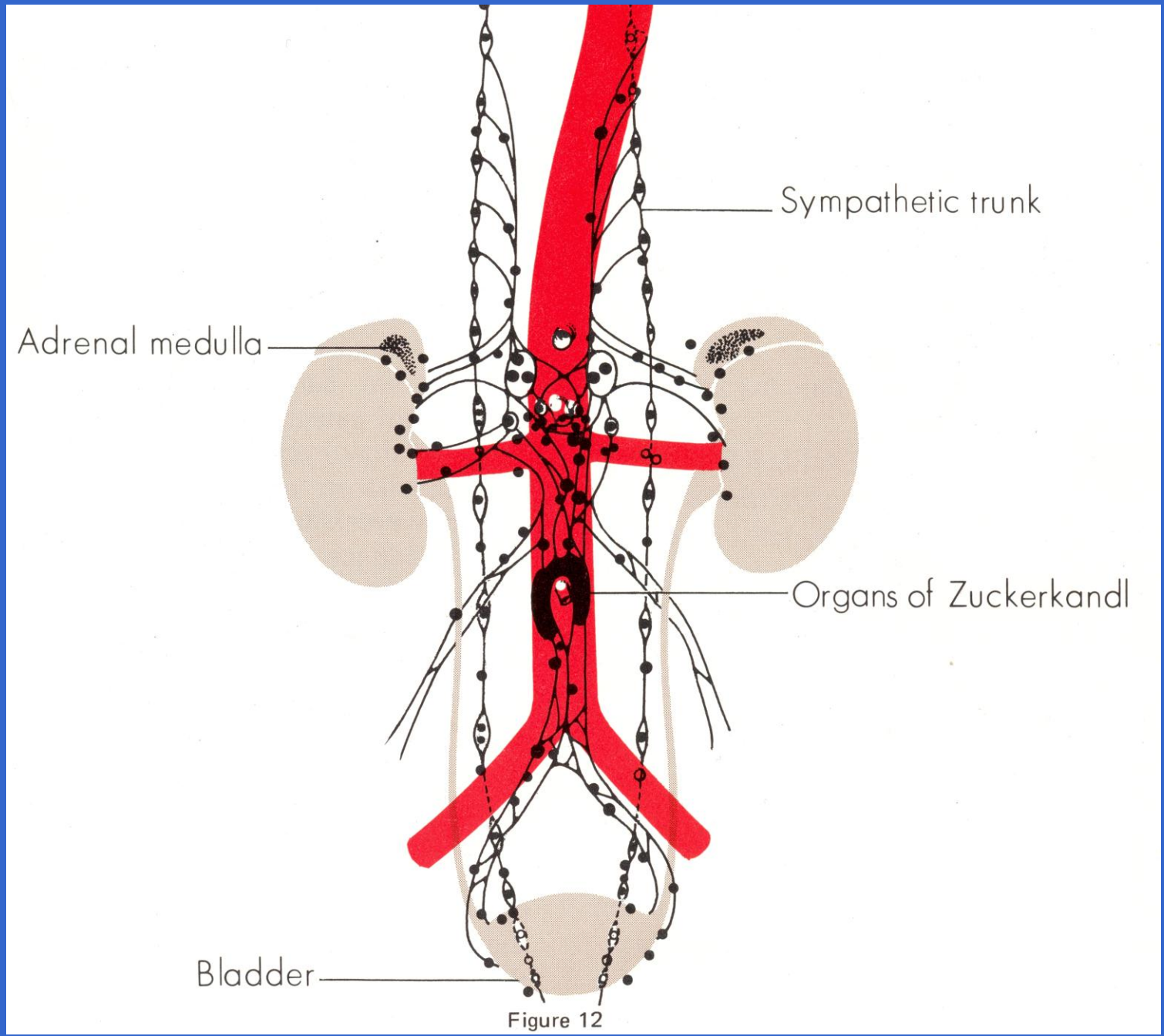
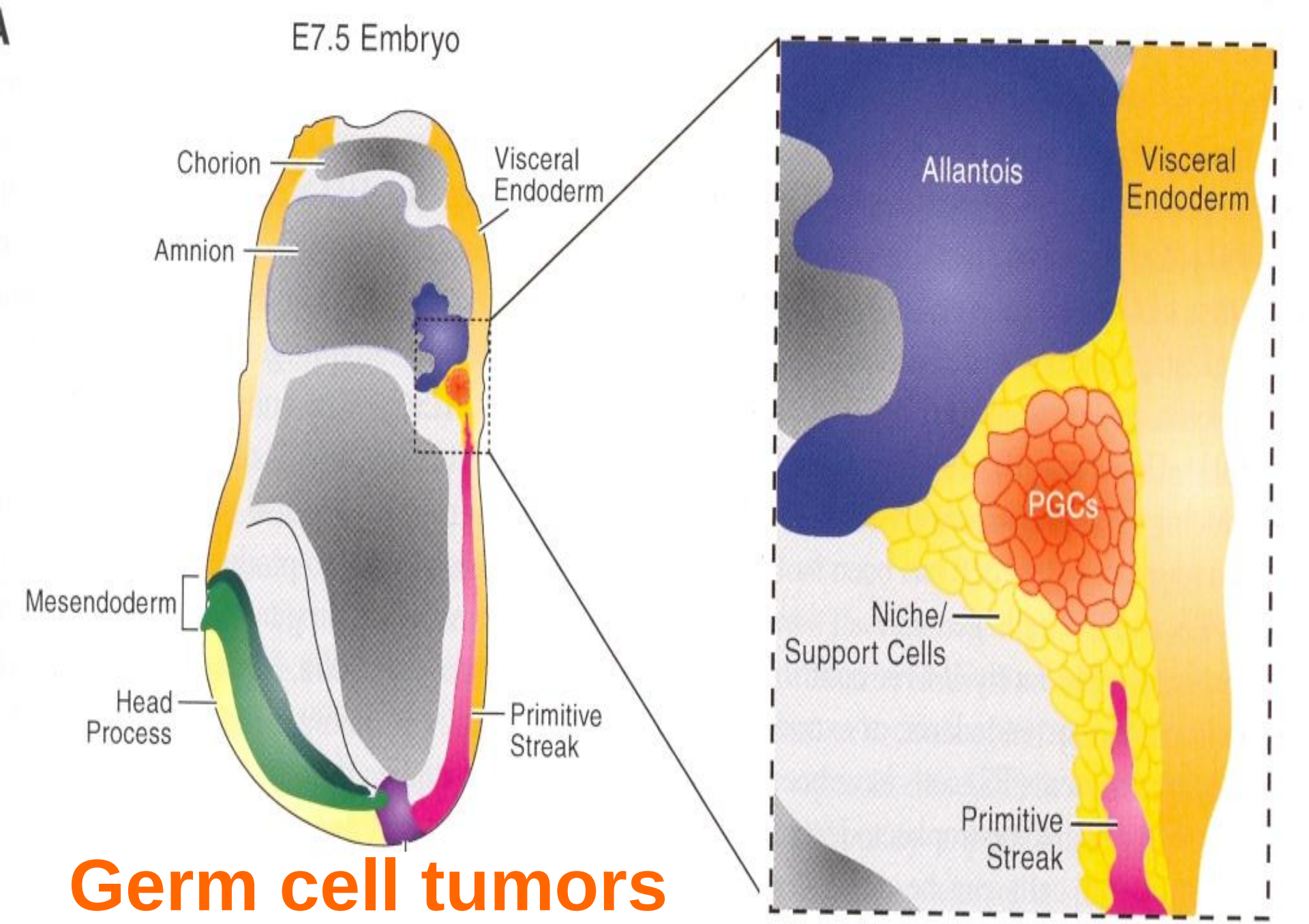
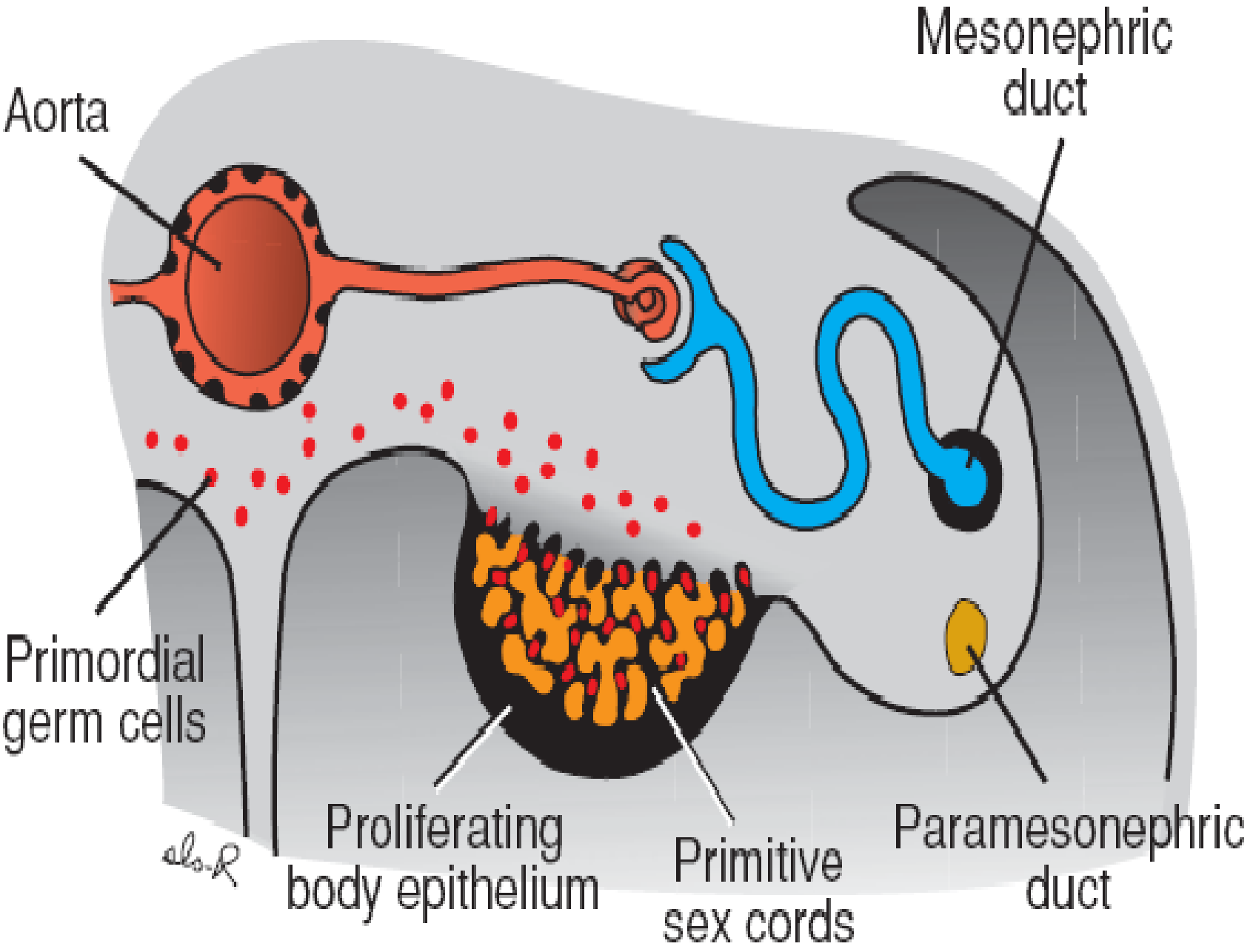
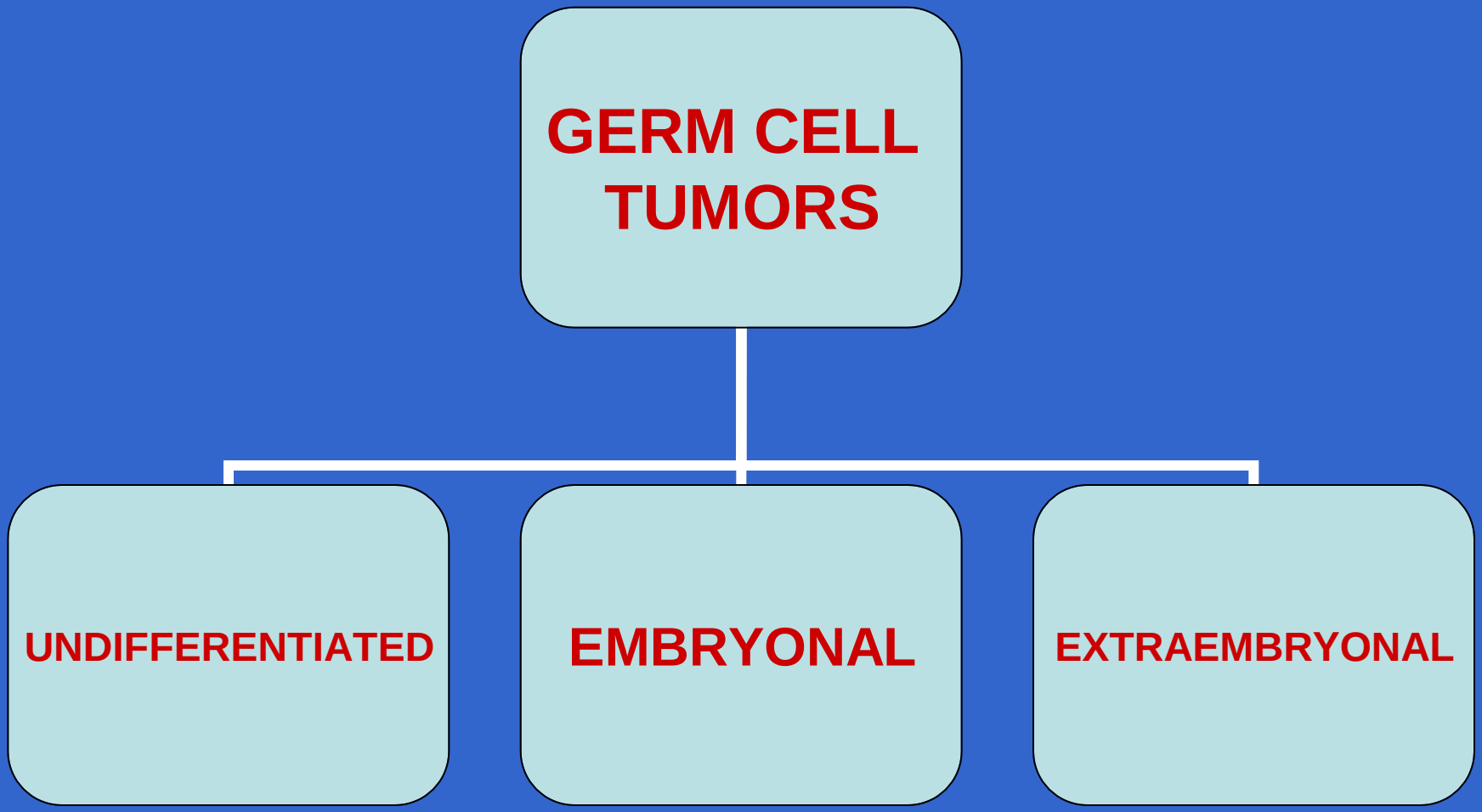

Sympathetic trunk
Adrenal medulla
Organs of Zuckerkandl
Bladder

Figure 12



Germ cell tumors


Aorta
Mesonephric duct
Primordial germ cells
Proliferating body epithelium
Primitive sex cords
Paramesonephric duct



- *Germinoma*

- *Embryonal carcinoma*
- *Teratomas*

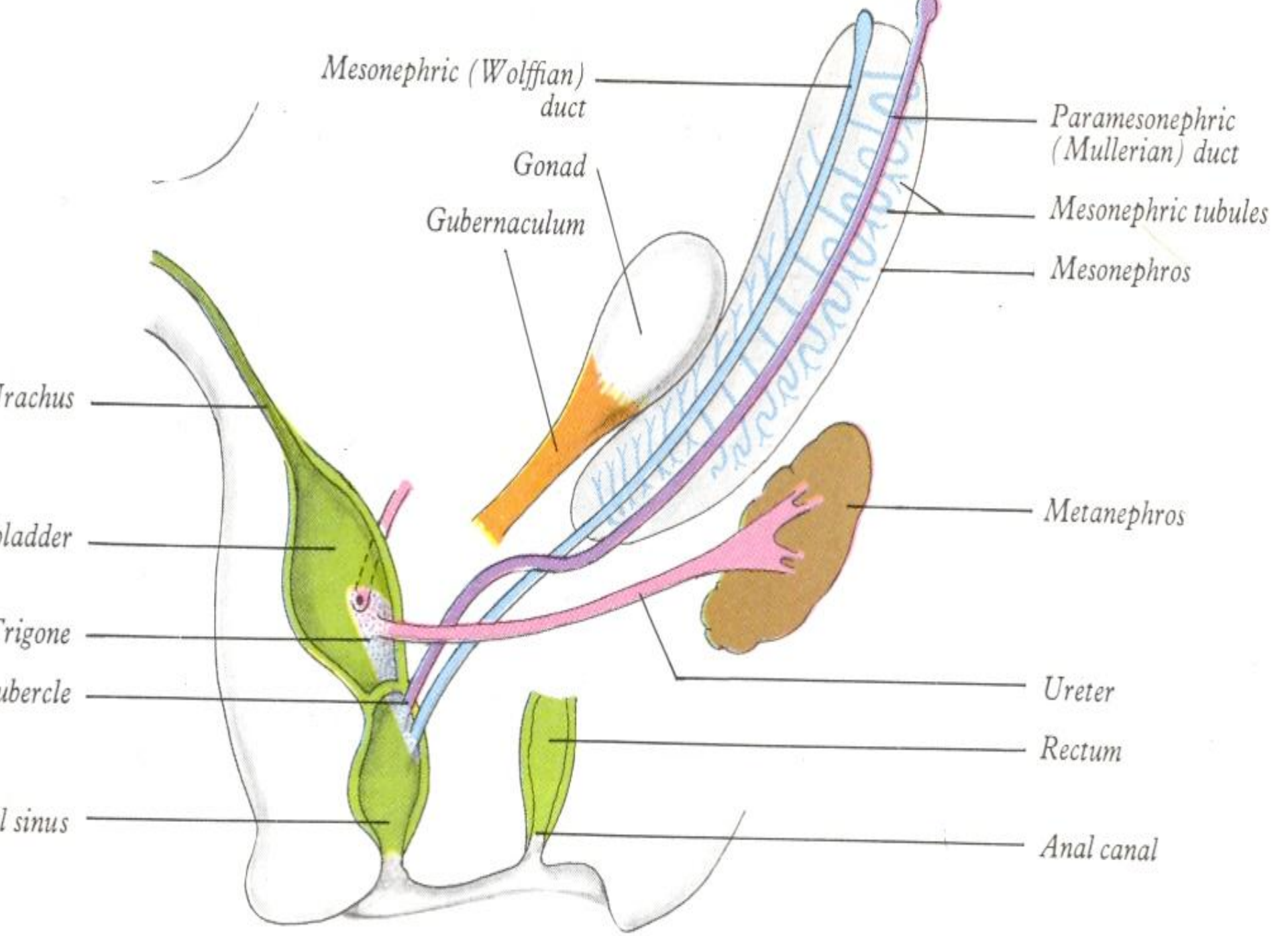
- *Choriocarcinoma*
- *Yolk sac tumor*

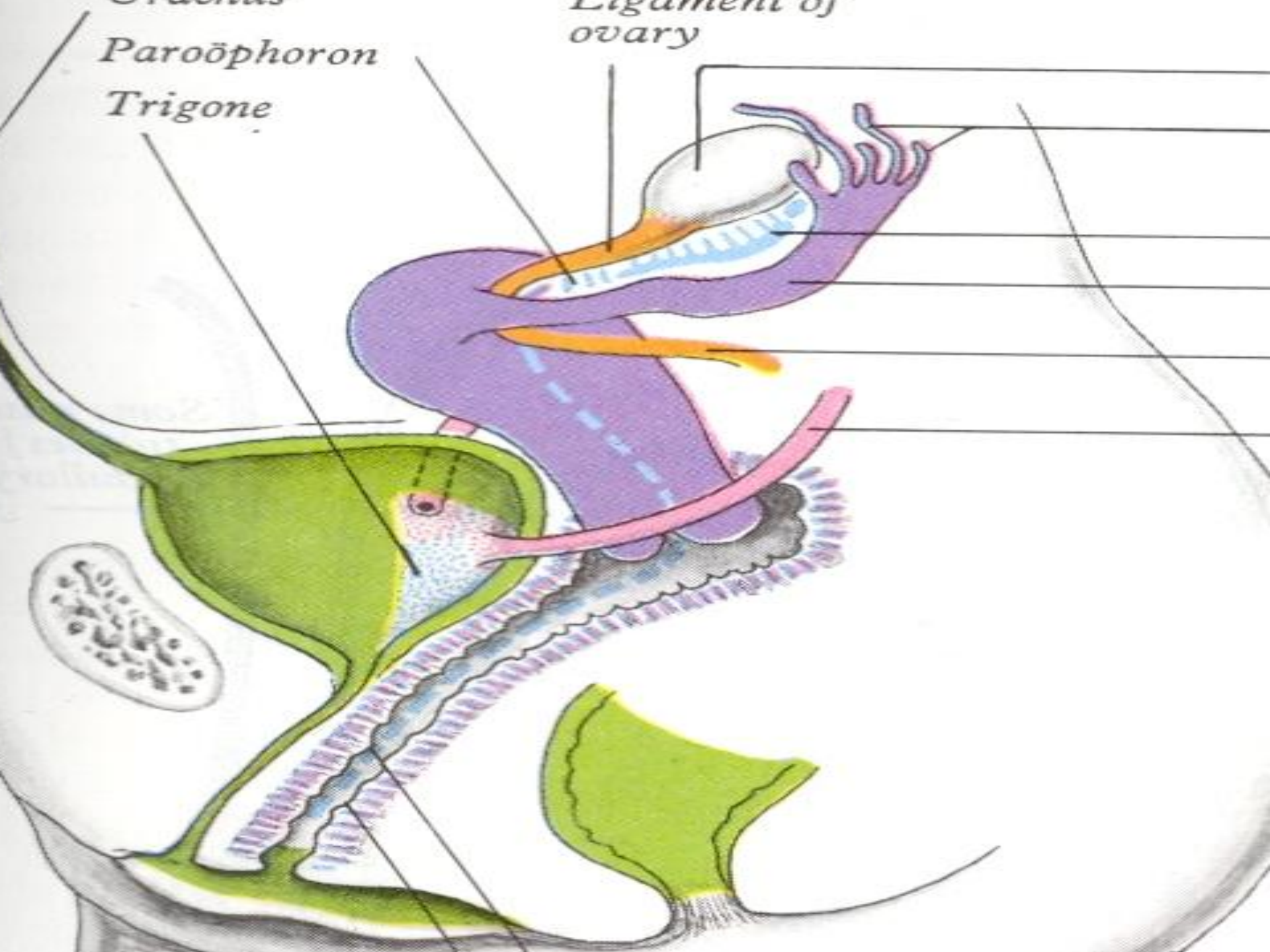
BLASTEMAL TUMORS

- Affects infants
- Arise from blastemal remnants
- Composed of primitive embryonal cells
- Complex structure of epithelial and stromal elements, native or foreign to the part
- Examples: *Nephroblastoma, hepatoblastoma, pancreatoblastoma & pulmonary blastoma*

TUMORS OF VESTIGEAL REMNANTS

1. Chordoma
2. Odontogenic tumors
3. Branchial carcinoma
4. Urachal carcinoma
5. Mesonephroma
6. Mullerian carcinosarcoma


Mesonephric (Wolffian) duct
Paramesonephric (Mullerian) duct
Gonad
Gubernaculum
Mesonephric tubules
Mesonephros
Urachus
Bladder
Trigone
Tubercle
Metanephros
Ureter
Rectum
Anal sinus
Anal canal


Ligament of ovary
Paroöphoron
Trigone

TUMORS OF UNCERTAIN ORIGIN

1. Synovial sarcoma
2. Alveolar soft part sarcoma
3. Epithelioid sarcoma
4. Desmoplastic small round cell tumor
5. Myxoma
6. Inflammatory myxohyaline tumor
7. Malignant rhabdoid tumor
8. Giant cell tumor
9. Parachordoma

UNDIFFERENTIATED CANCER

1. Undifferentiated carcinoma
2. Undifferentiated sarcoma
3. Undifferentiated malignant tumor

MIXED TUMORS

- Synonems:

  Multiphasic, Multimorphic

- Definition:

  A tumor composed of more than one cell type regardless of histogenesis or biologic behavior of cellular elements

MECHANISM OF MIXED TUMORS

1. Multipotent stem cell
2. Multihit carcinogenesis
3. Tumor cell metaplasia
4. Tumor dedifferentiation
5. Somatic malignancy in teratoma
6. Cancer metastatic into another tumor

CLASSIFICATION OF MIXED TUMORS

1. Mixed epithelial
2. Mixed mesenchymal
3. Mixed epithelial & mesenchymal
4. Mixed neuroectodermal tumors

"Each group is subclassified into benign and malignant"

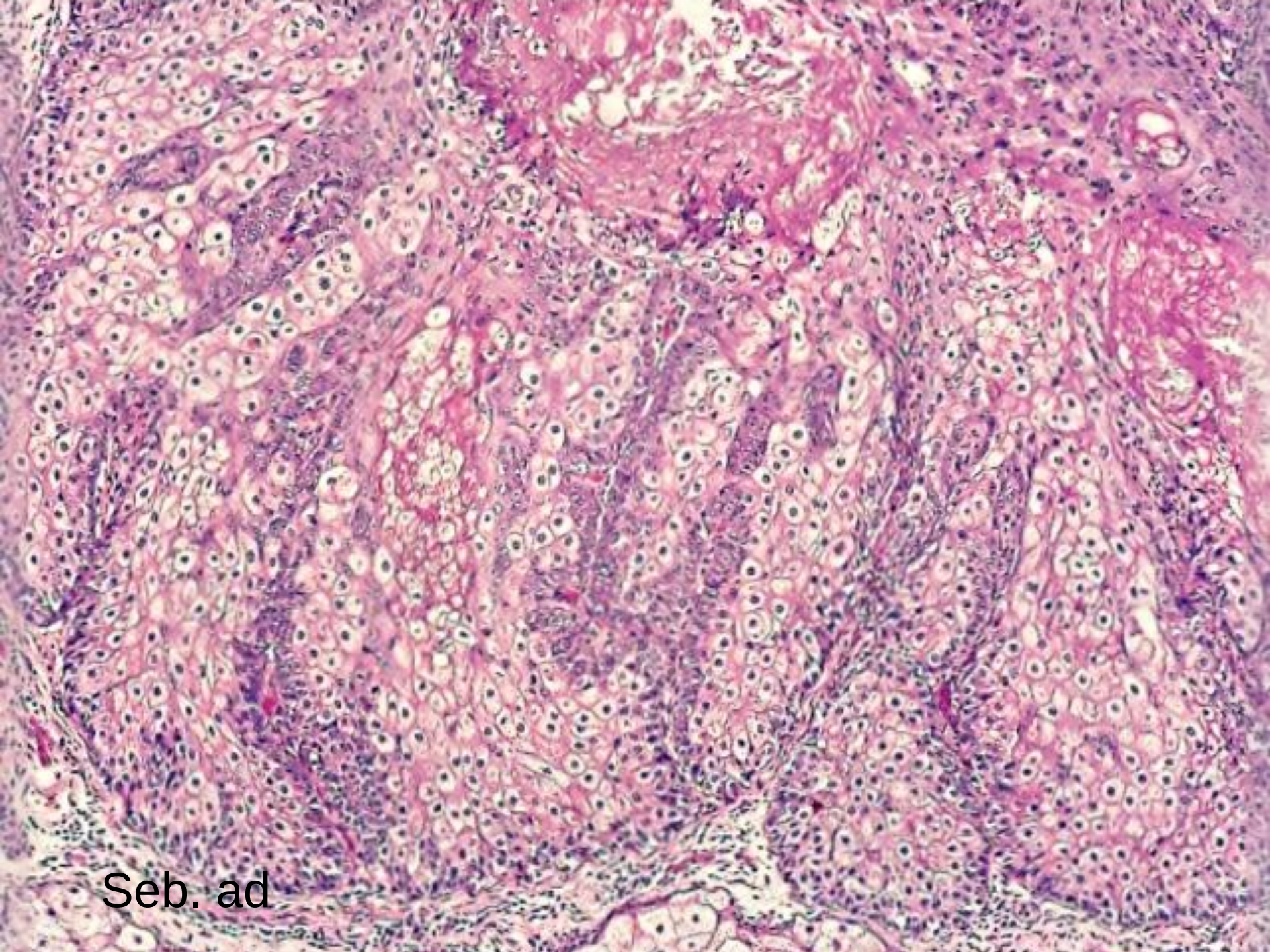
MIXED EPITHELIAL TUMORS

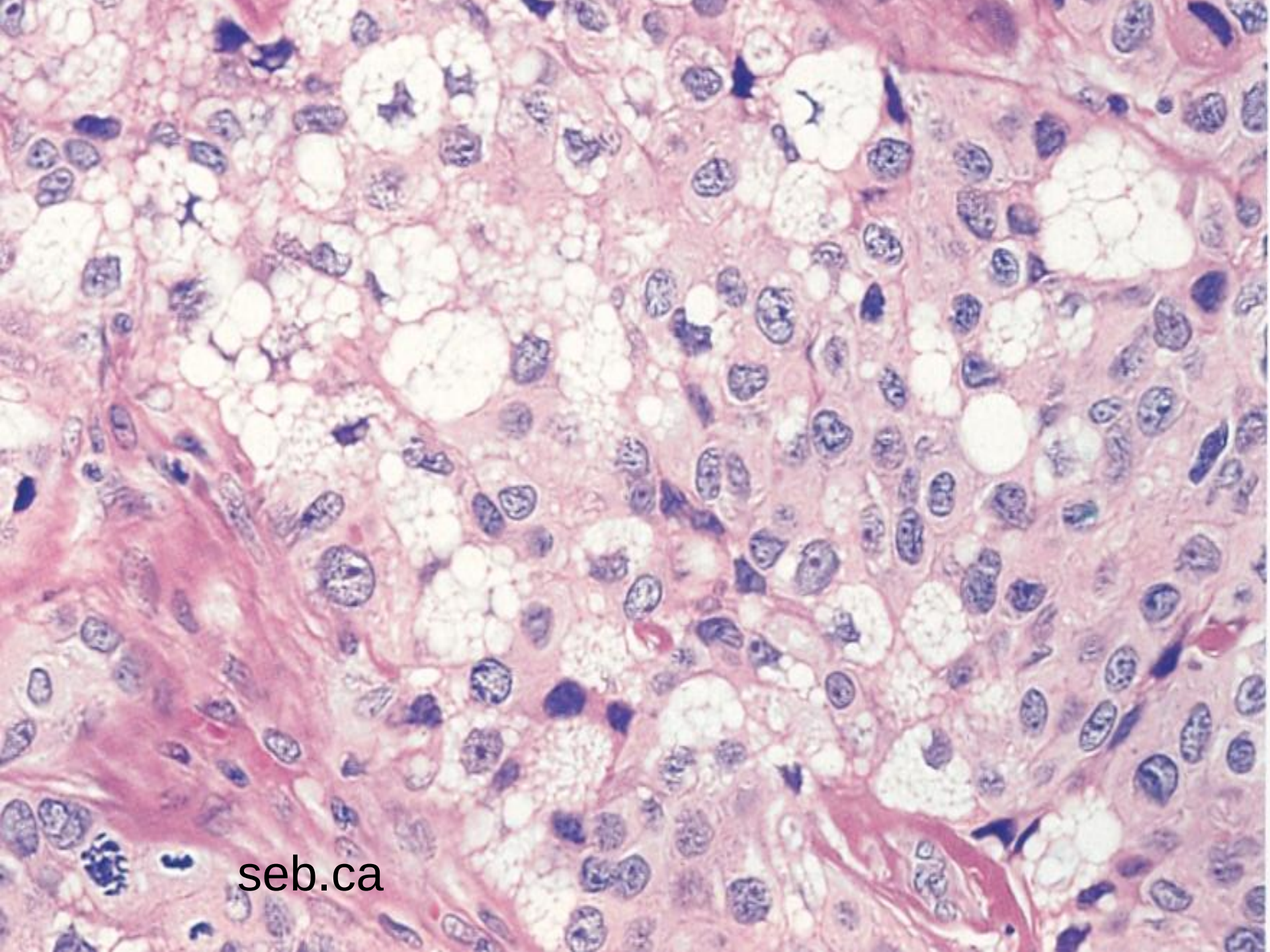
BENIGN

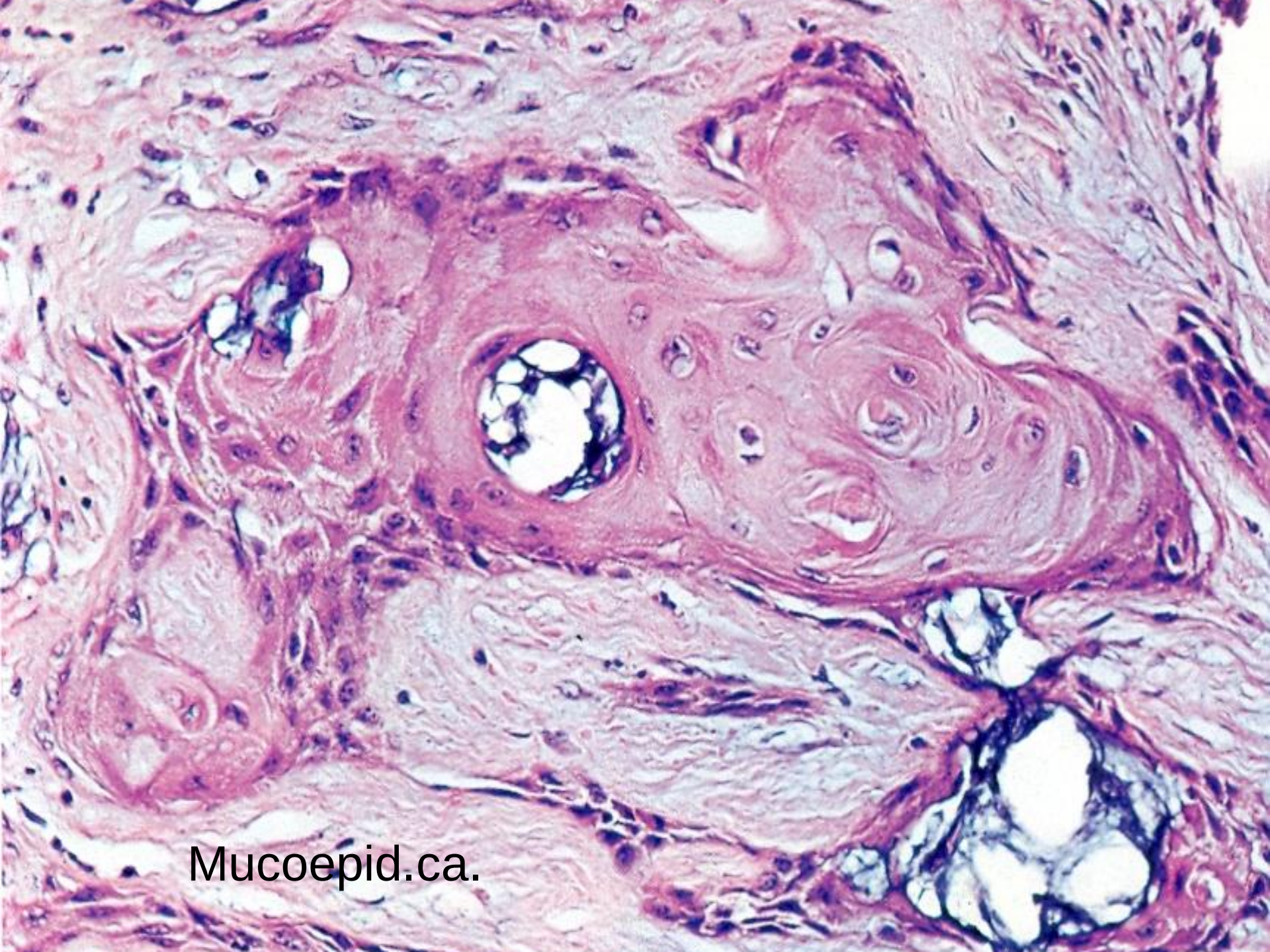
1. Trophoblastic mole
2. Sebaceous adeoma

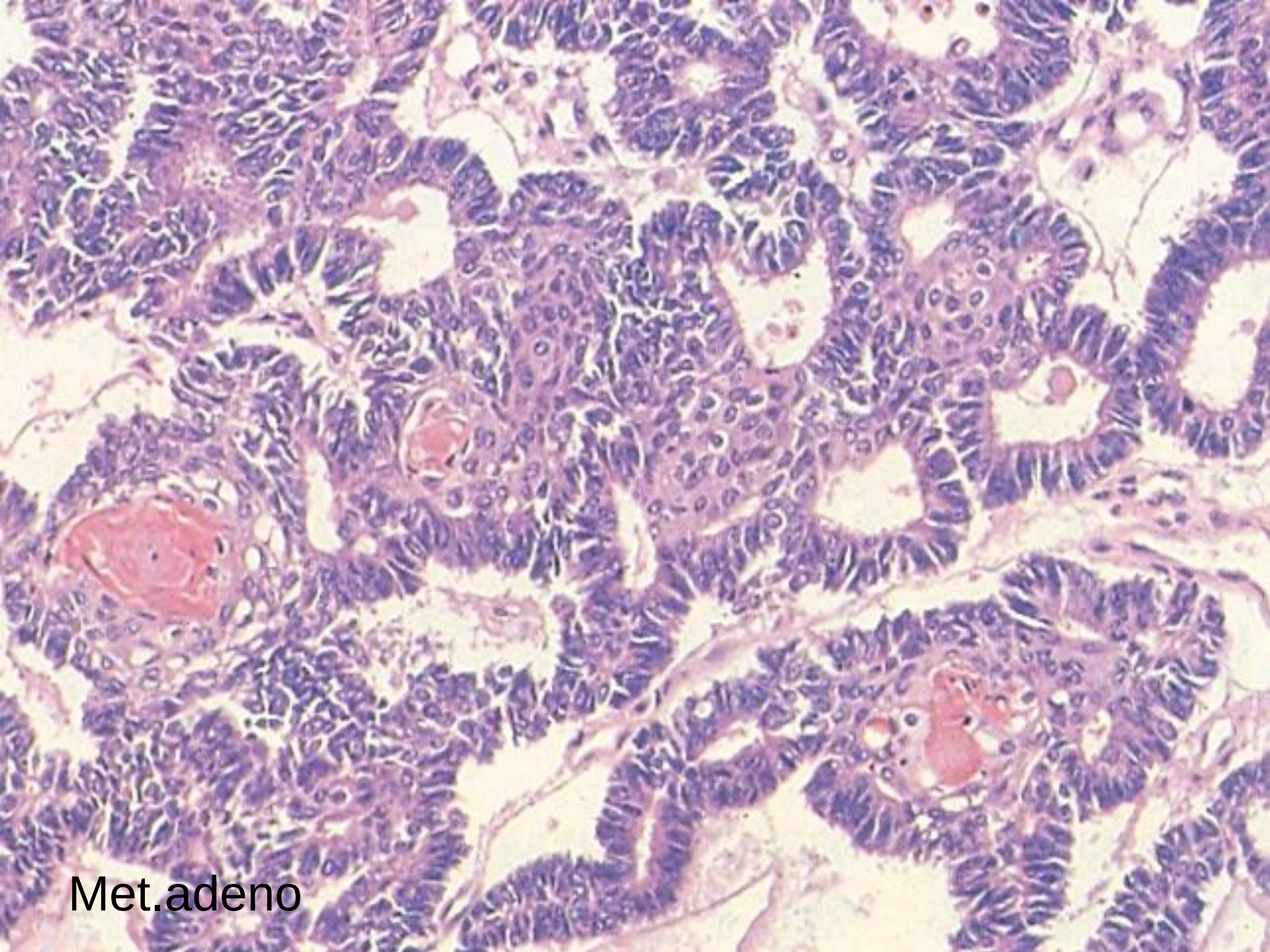
MALIGNANT

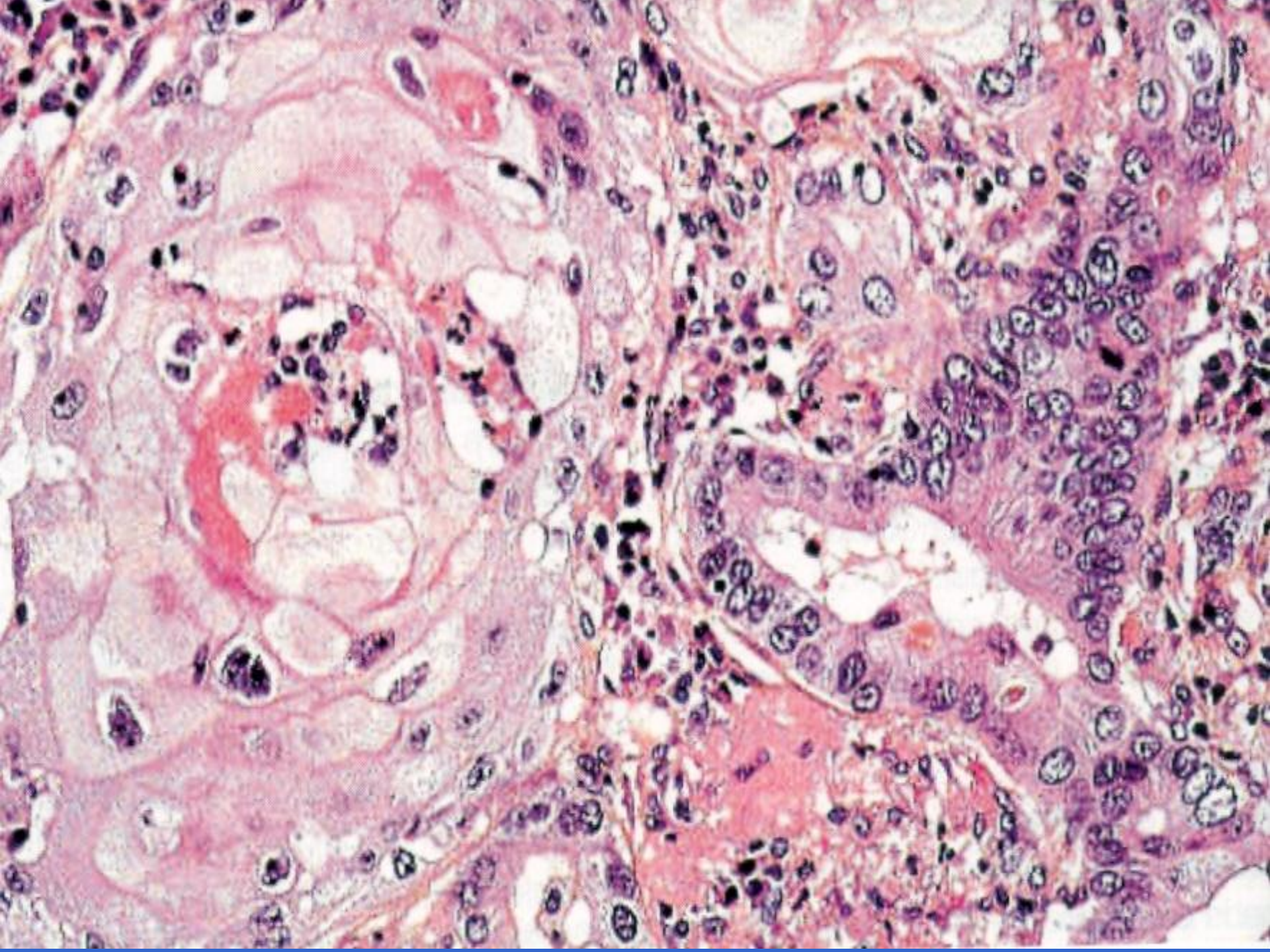
1. Sebaceous ca.
2. Choriocarcinoma
3. Mucoepidermoid ca.
4. Adenosquamous ca.
5. Metaplastic ca.
6. Cholangiohepatoma
7. Ameloblastoma

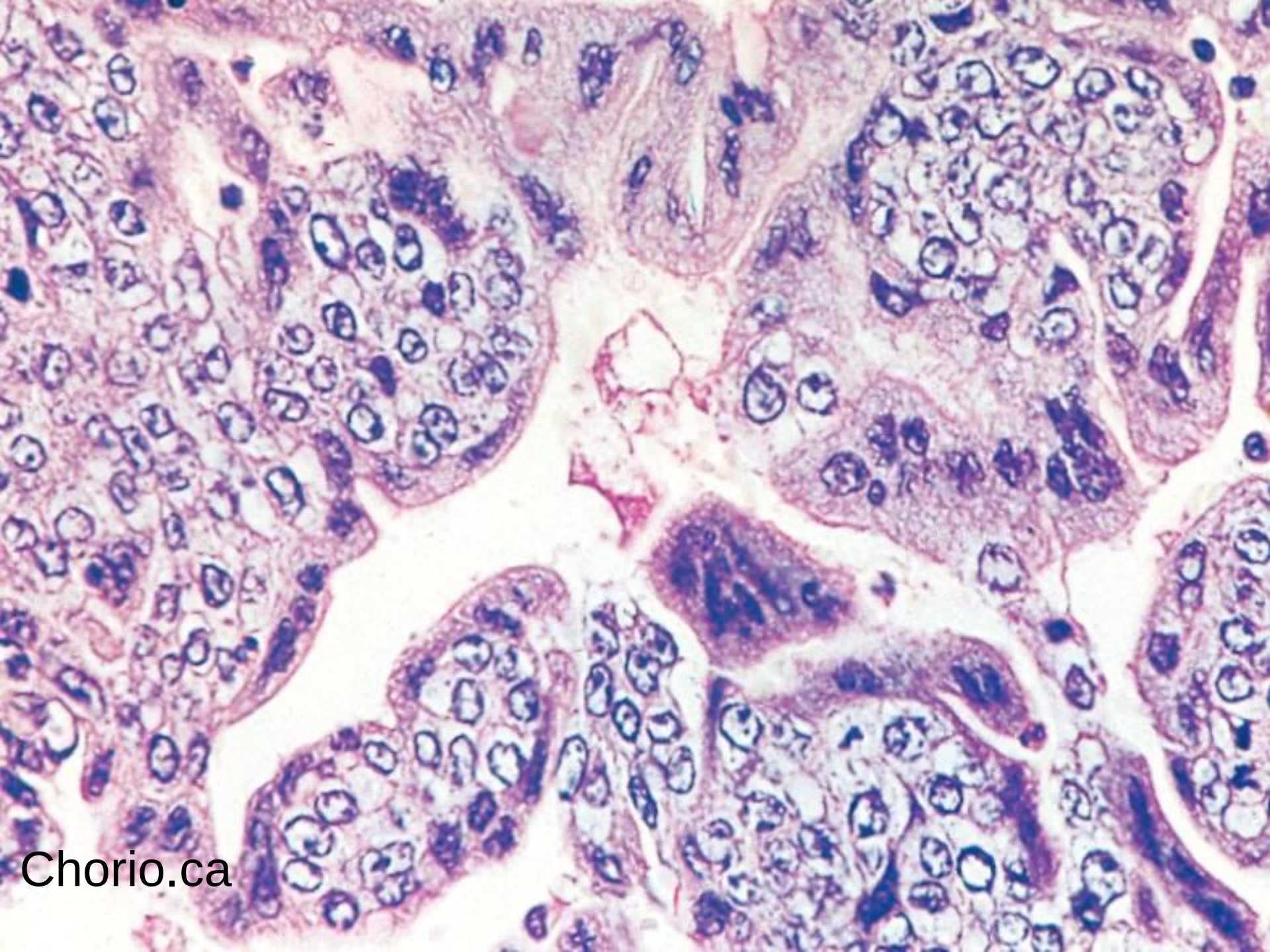

Seb. ad

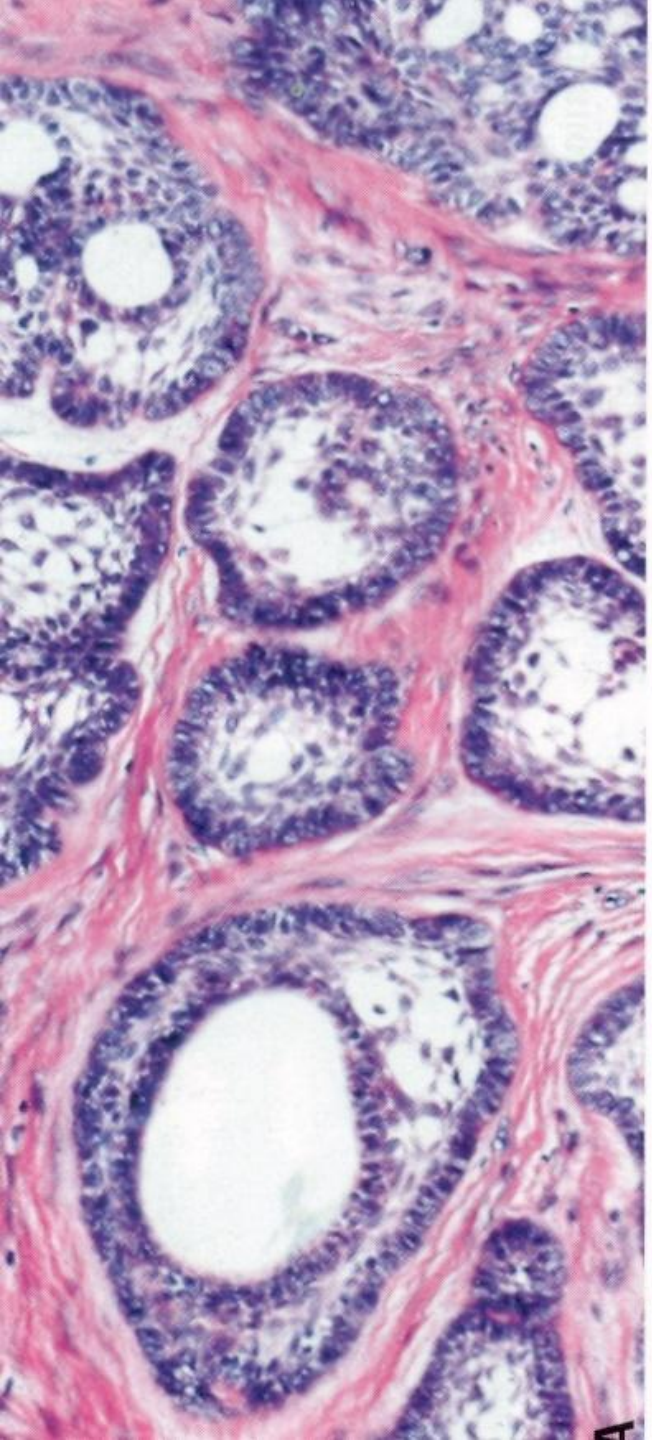

seb.ca

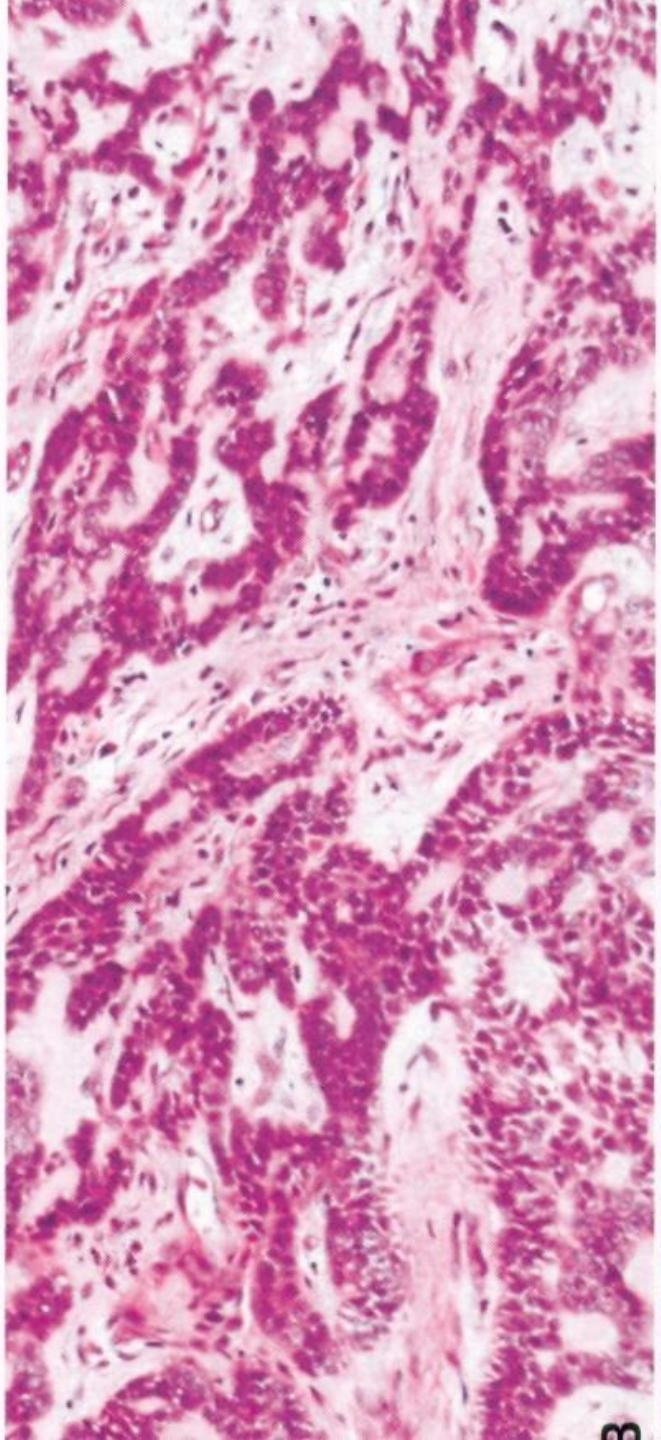

Mucoepid.ca.

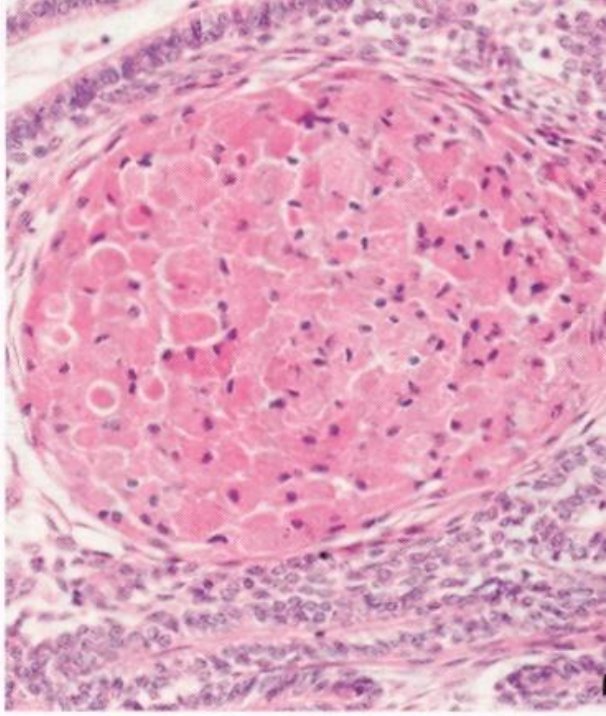

Met.adeno

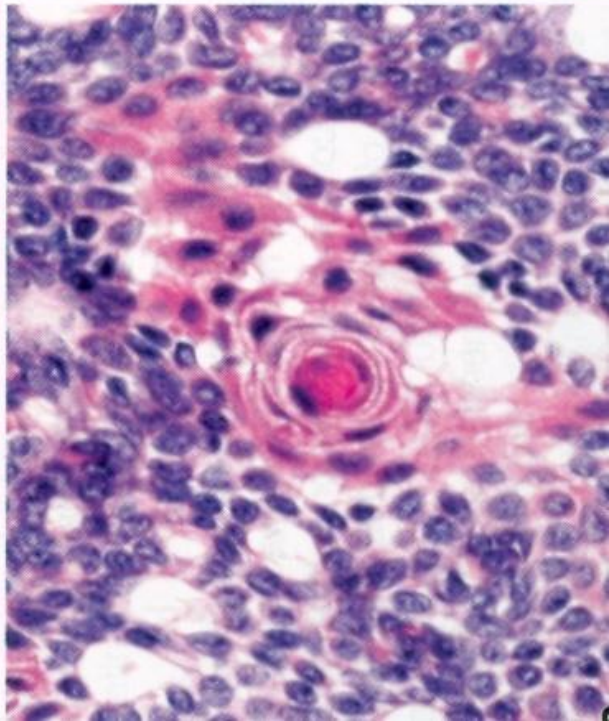


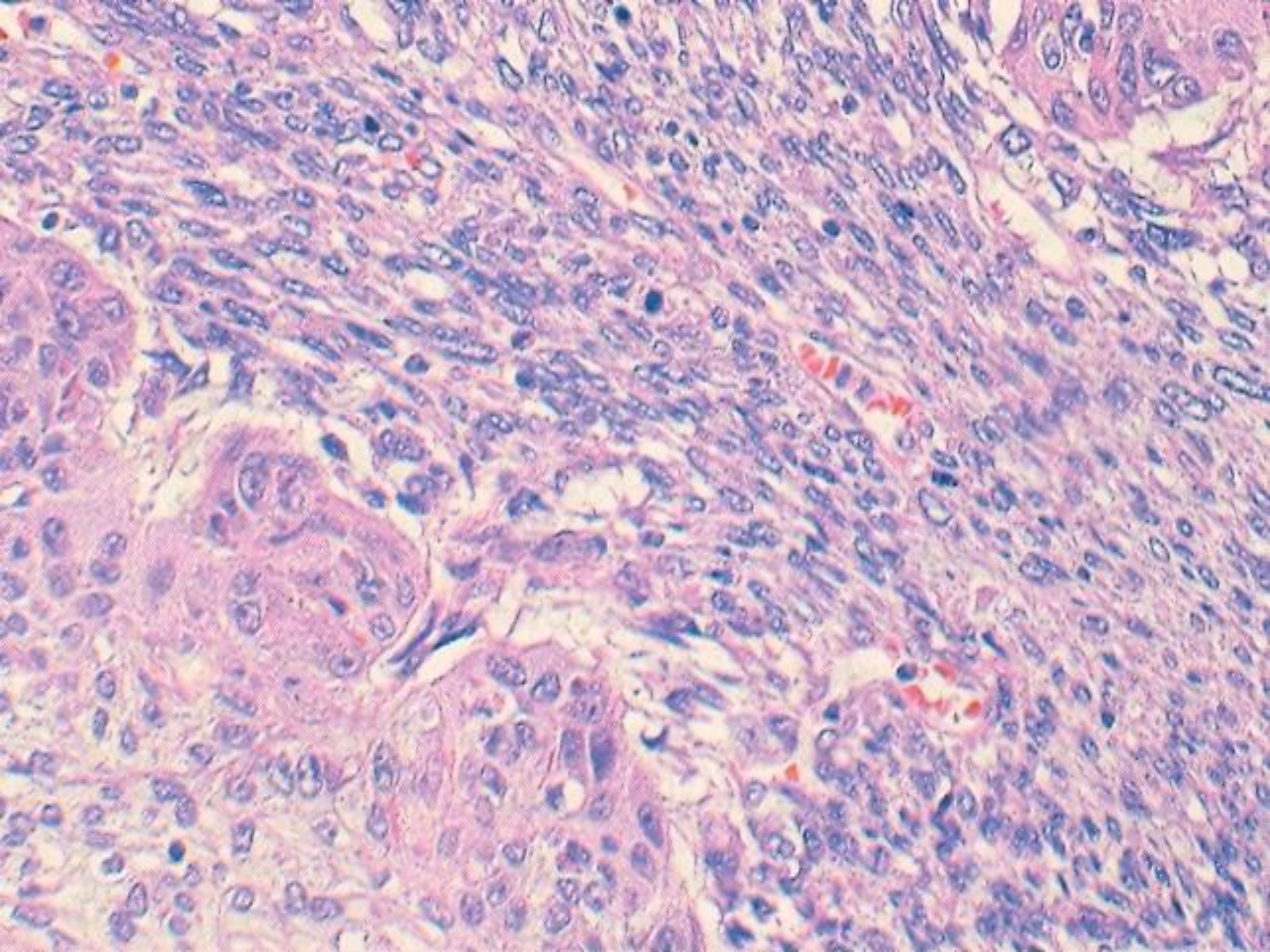

Chorio.ca











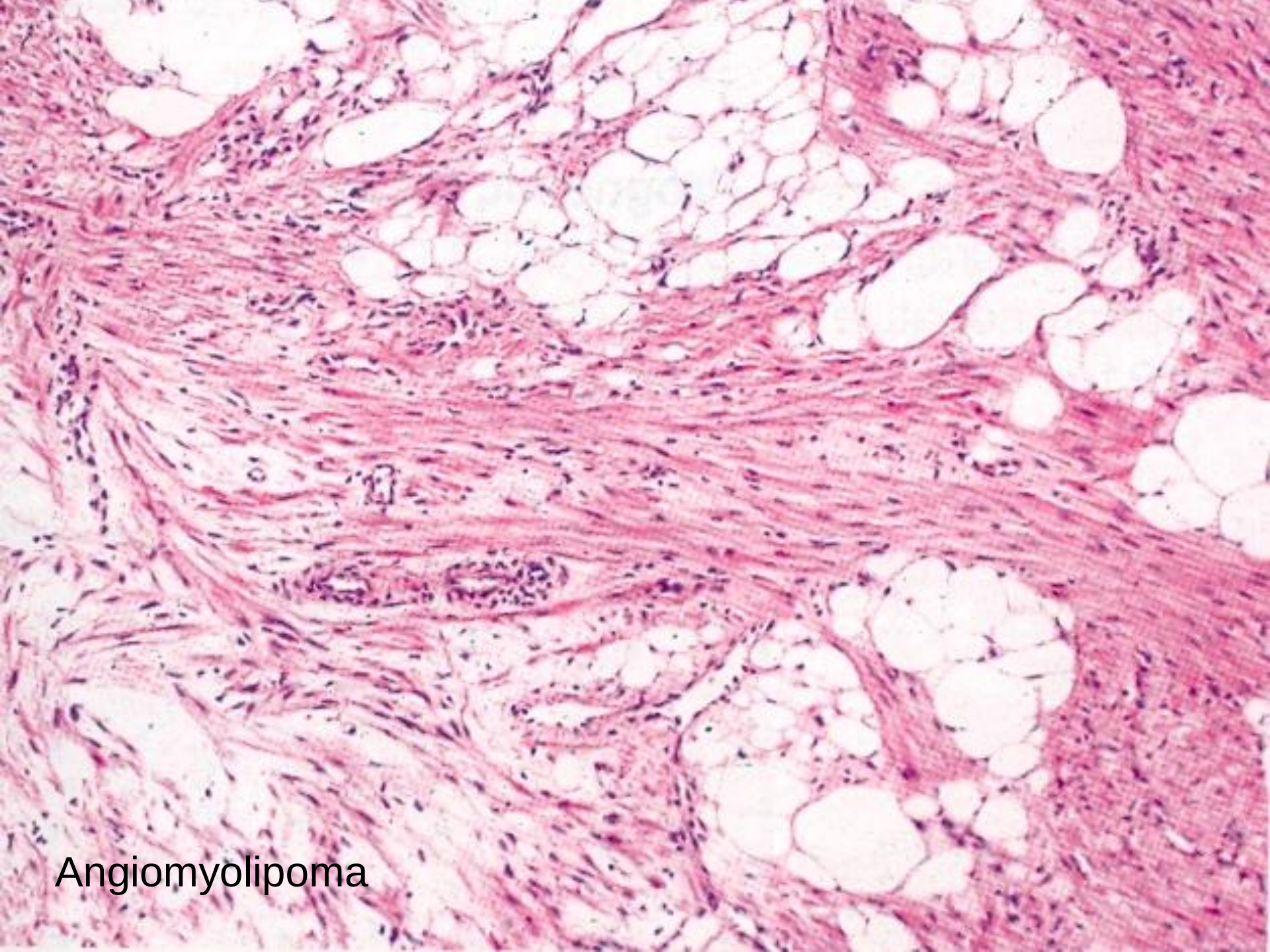
MIXED MESENCHYMAL TUMORS

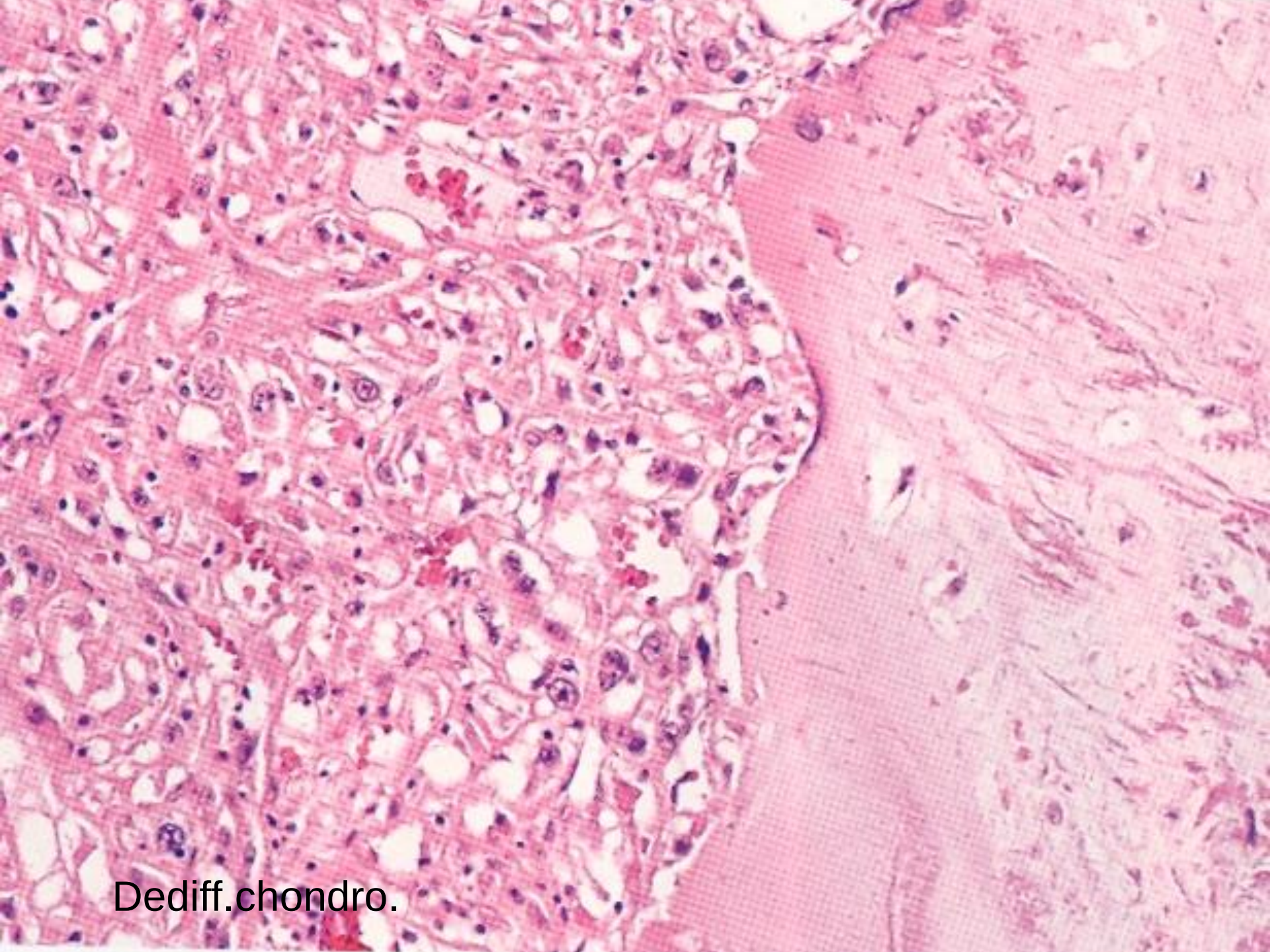
BENIGN

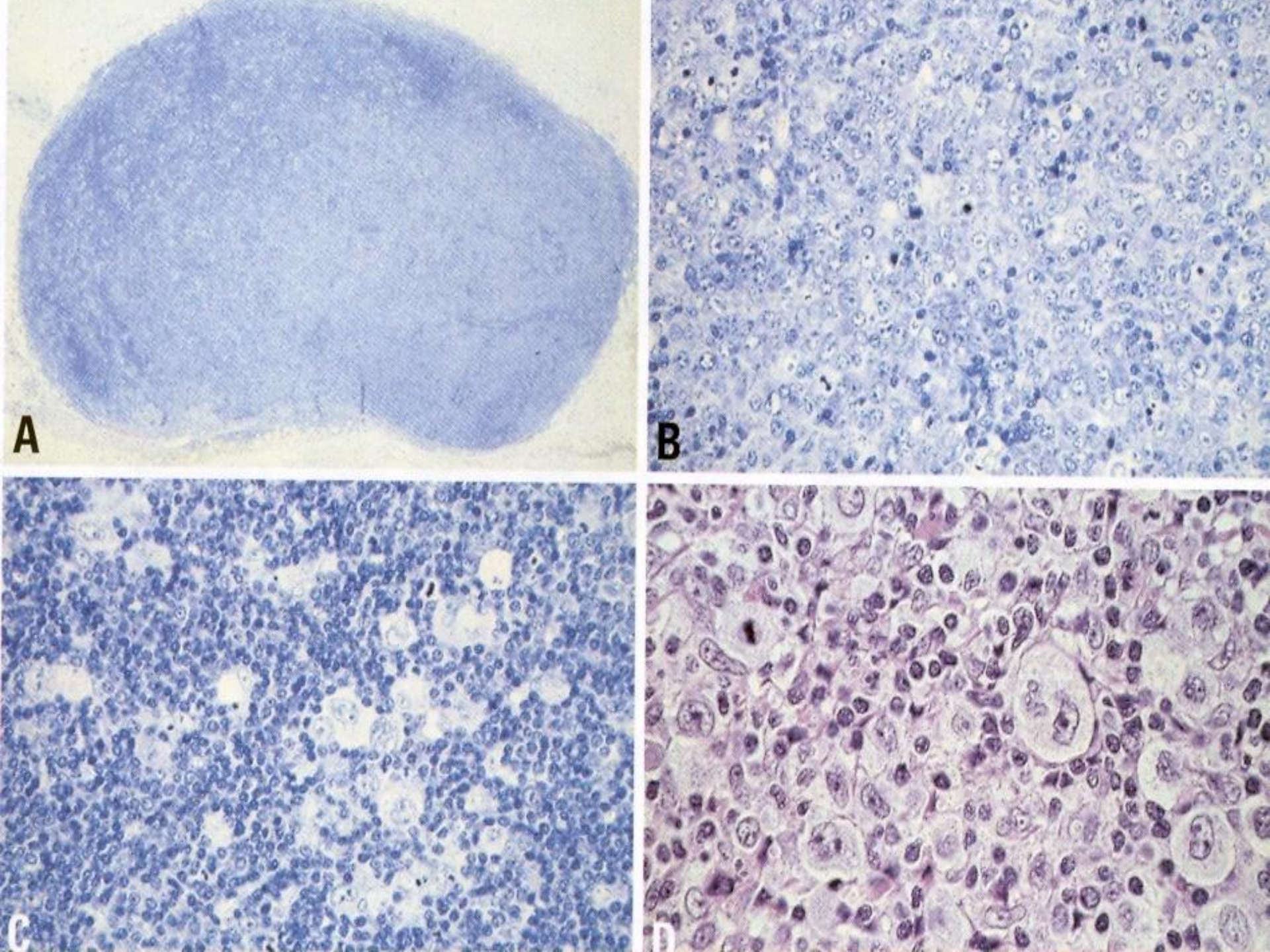
1. Angiomyolipoma
2. Spindle cell lipoma
3. Osteochondroma

MALIGNANT

1. Mesenchymoma
2. Dedifferentiated chondrosaroma
3. Composite lymphoma


Angiomyolipoma


Dediff.chondro.


A
B
C
D

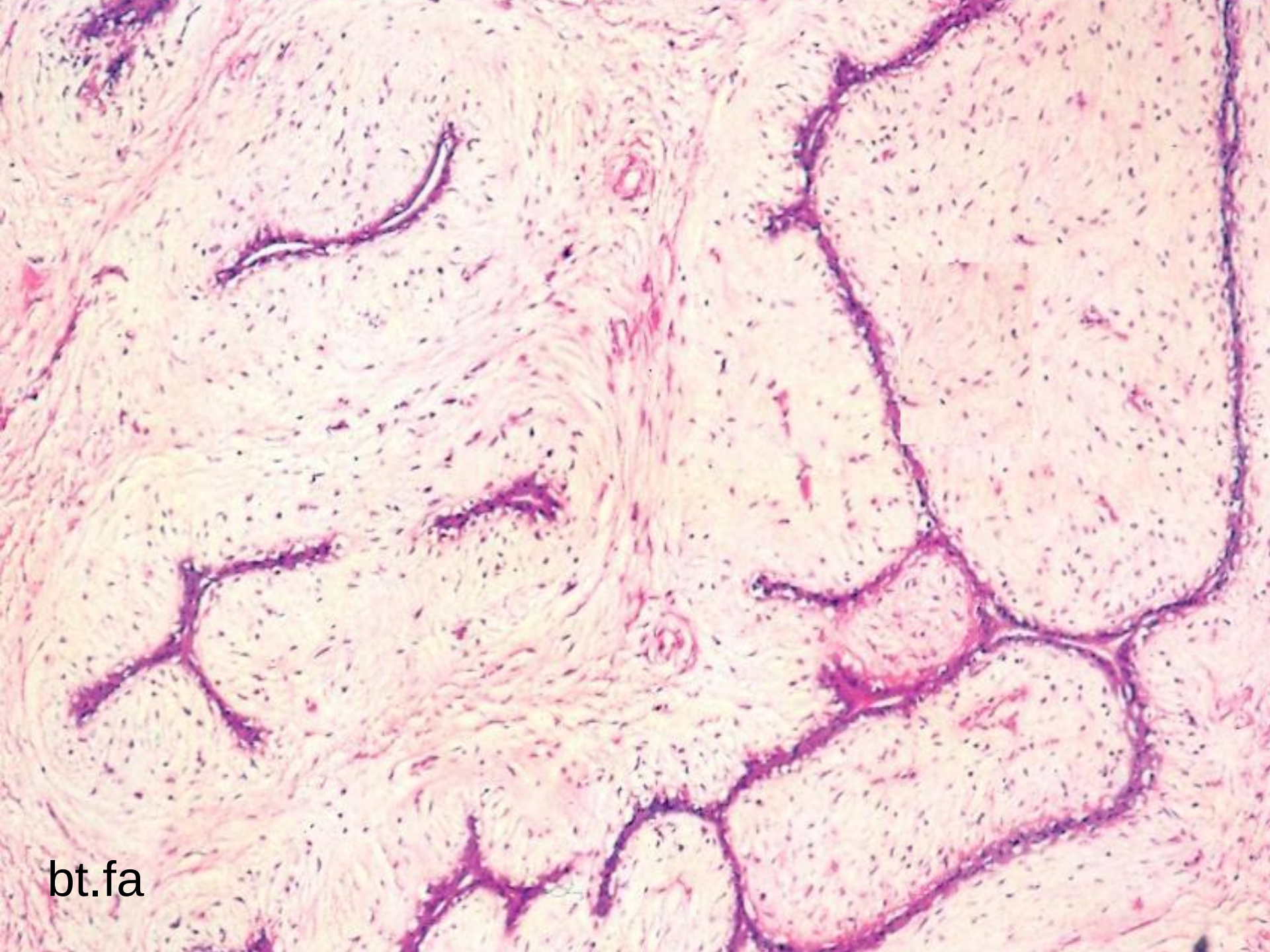
MIXED EPITHELIAL & MESENCHYMAL

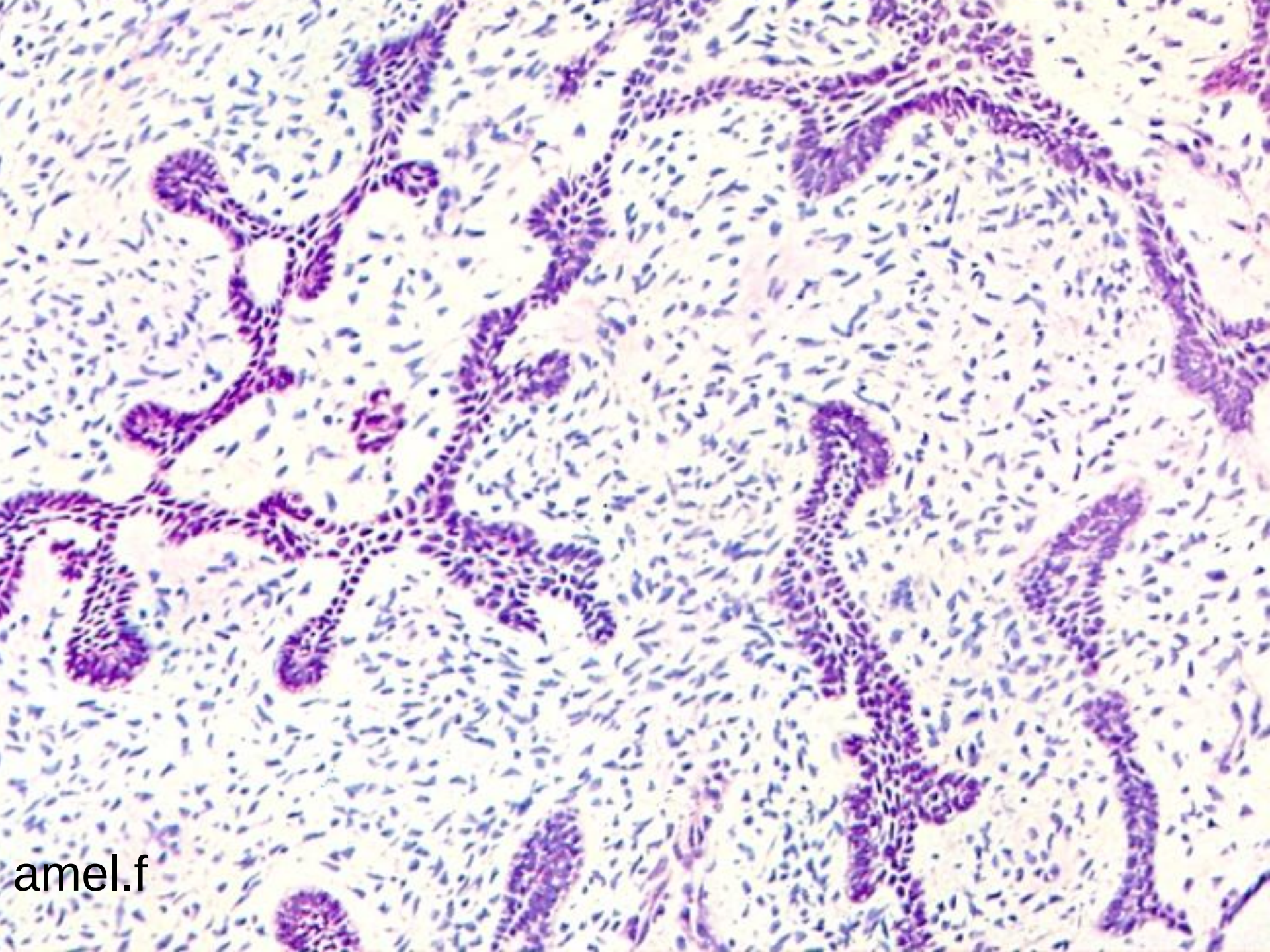
BENIGN

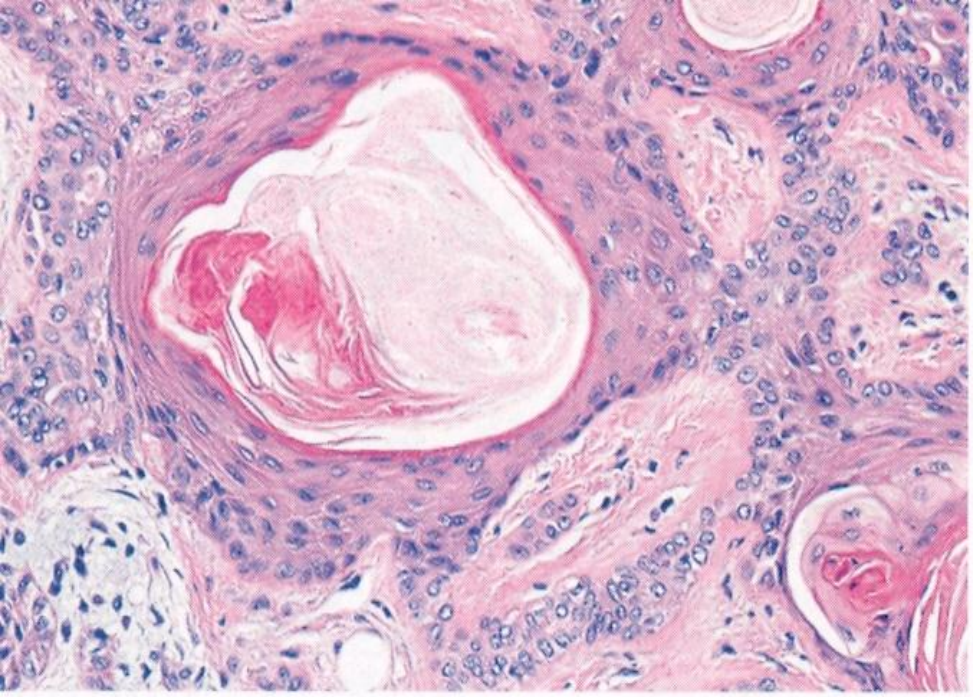
1. Pleomorphic adenoma
2. Myoepithelioma
3. Fibroadenoma
4. Adenofibroma
5. Odontogenic fibroma
6. Benign teratoma

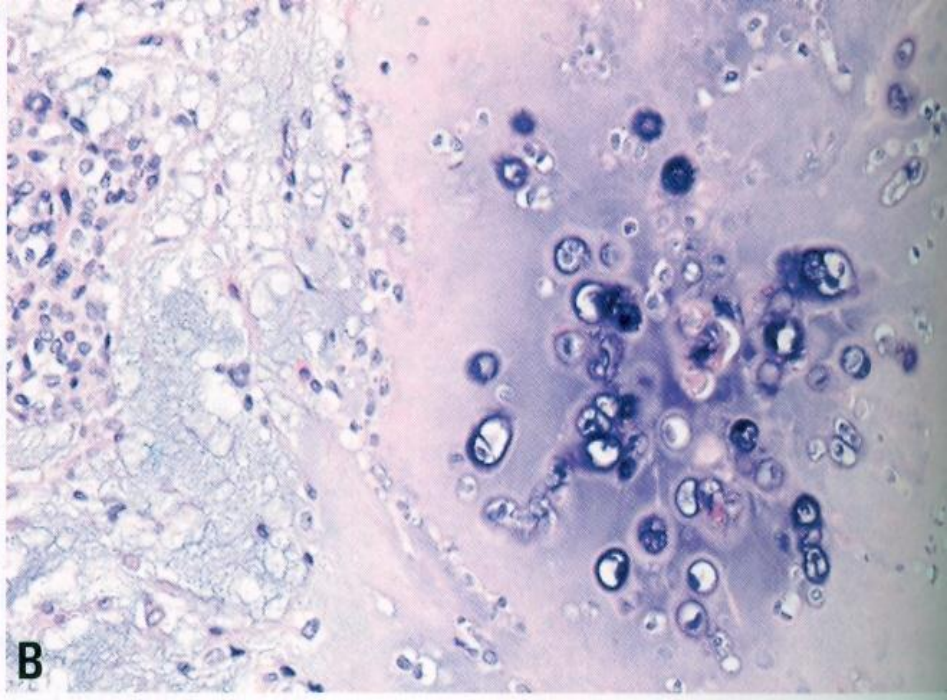
MALIGNANT

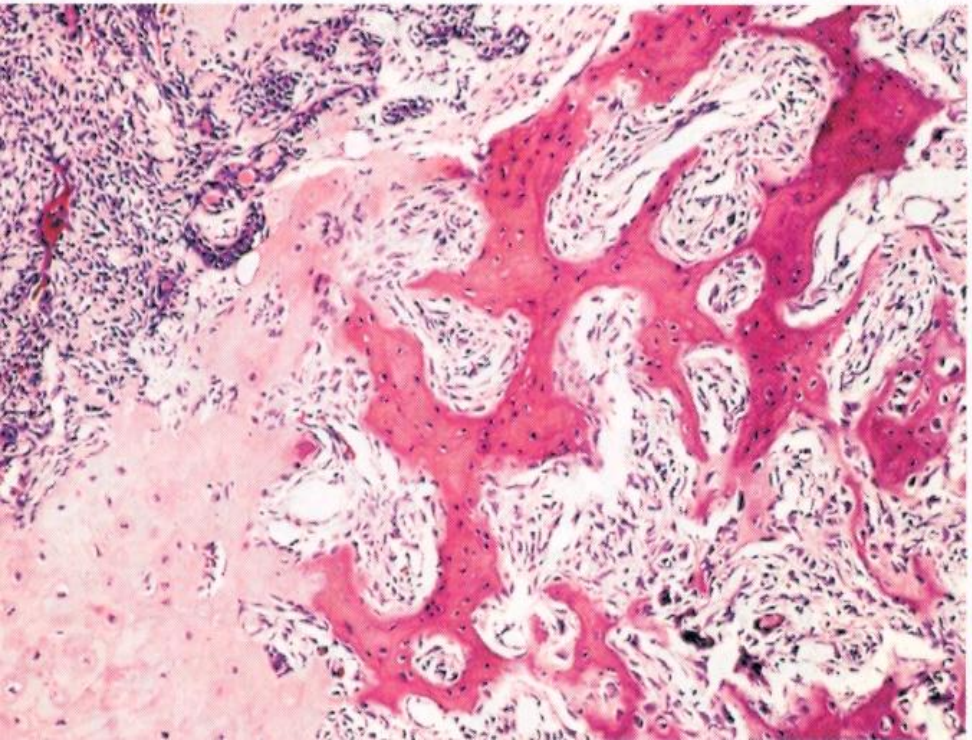
1. Mesothelioma
2. Synovial sarcoma
3. Mixed mullerian
4. Malignant phyllodes
5. Epith. Myoepith. Ca.
6. Blastemal tumors
7. Malignant teratoma
8. Somatic malignancy in germ cell tumor (sarc., ca. or NET)

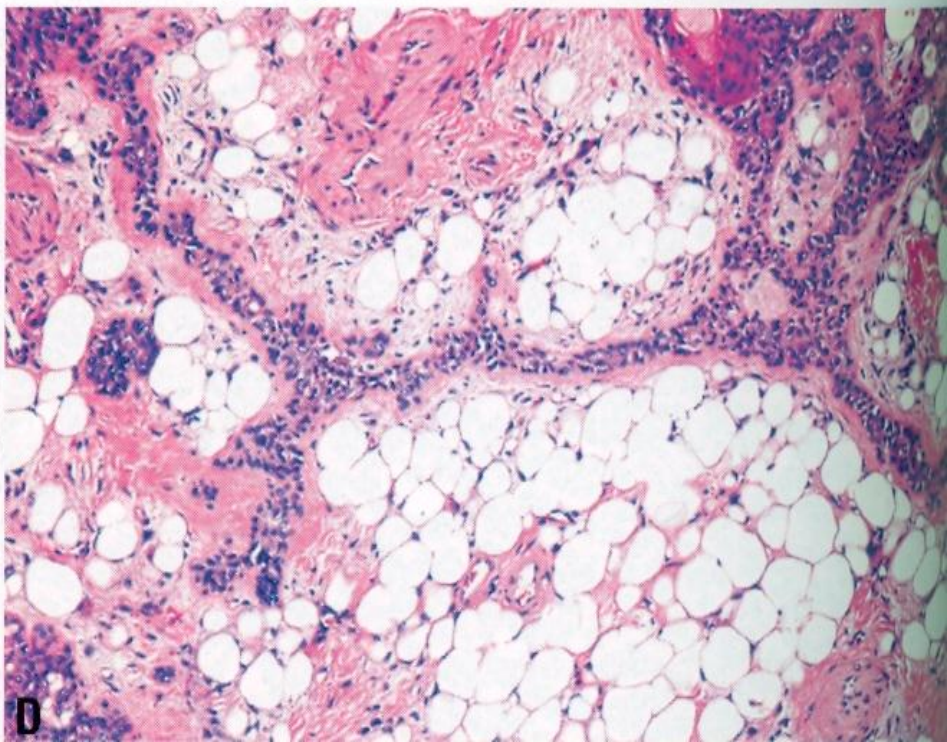

bt.fa

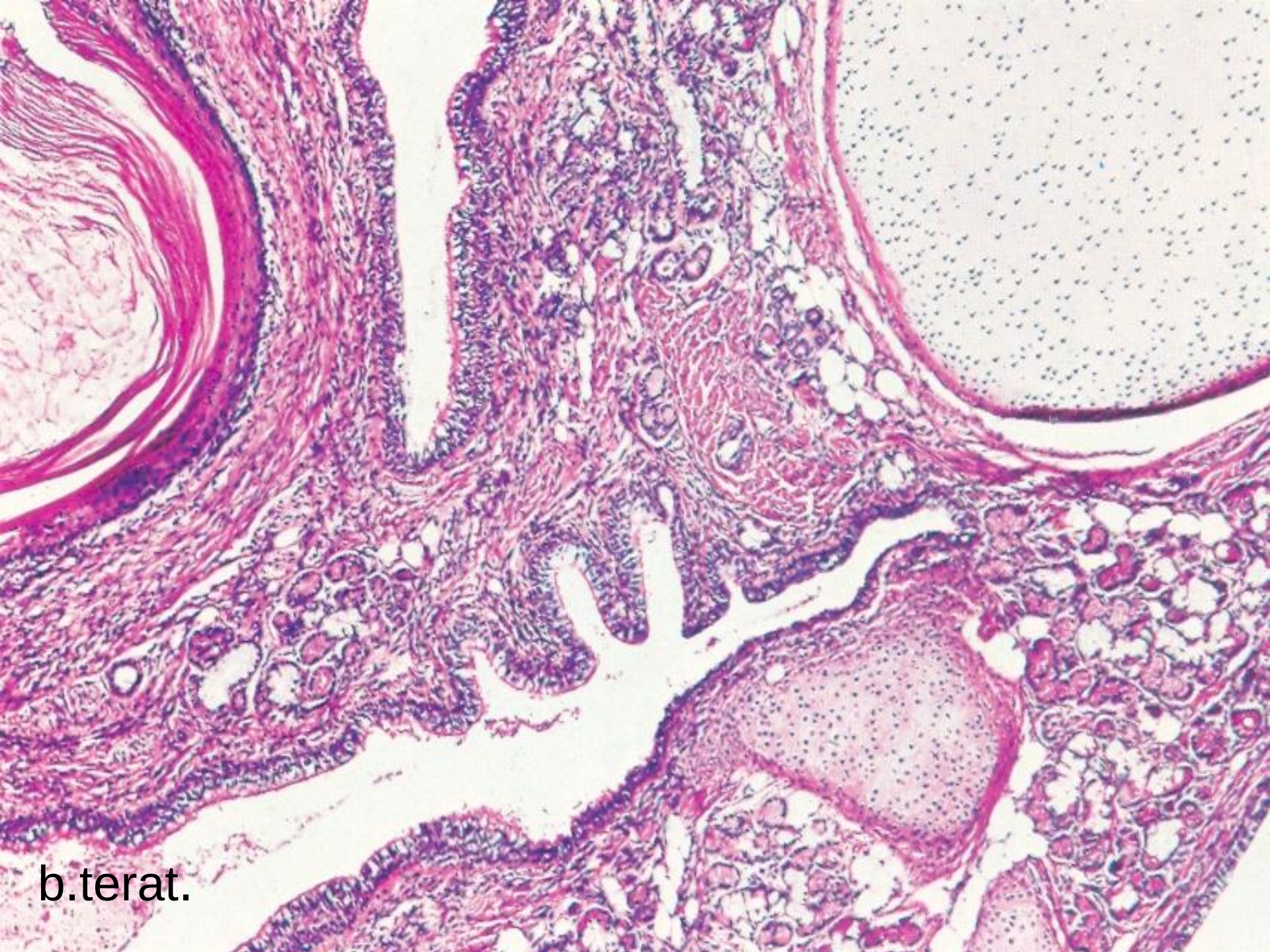

amel.f

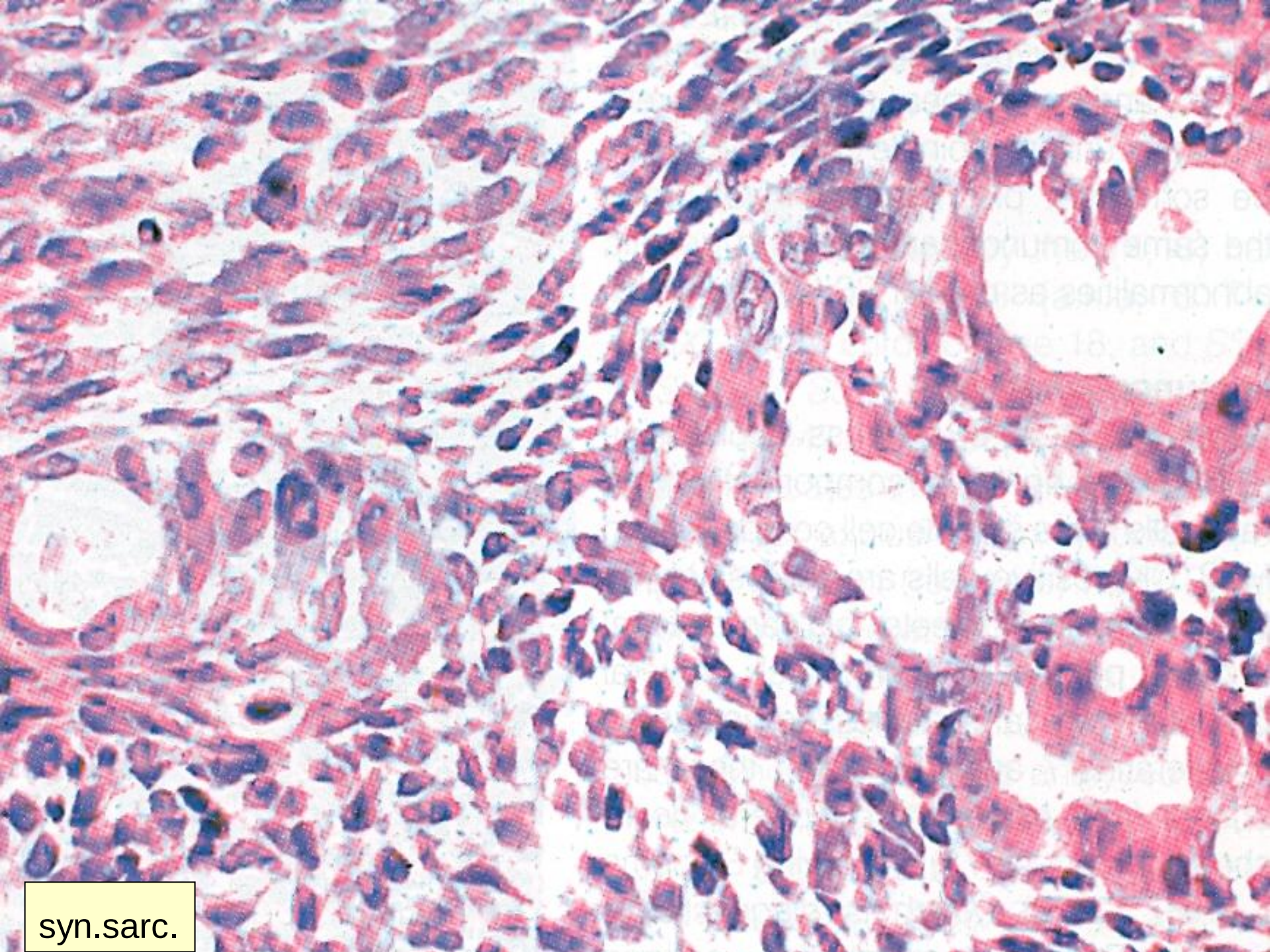


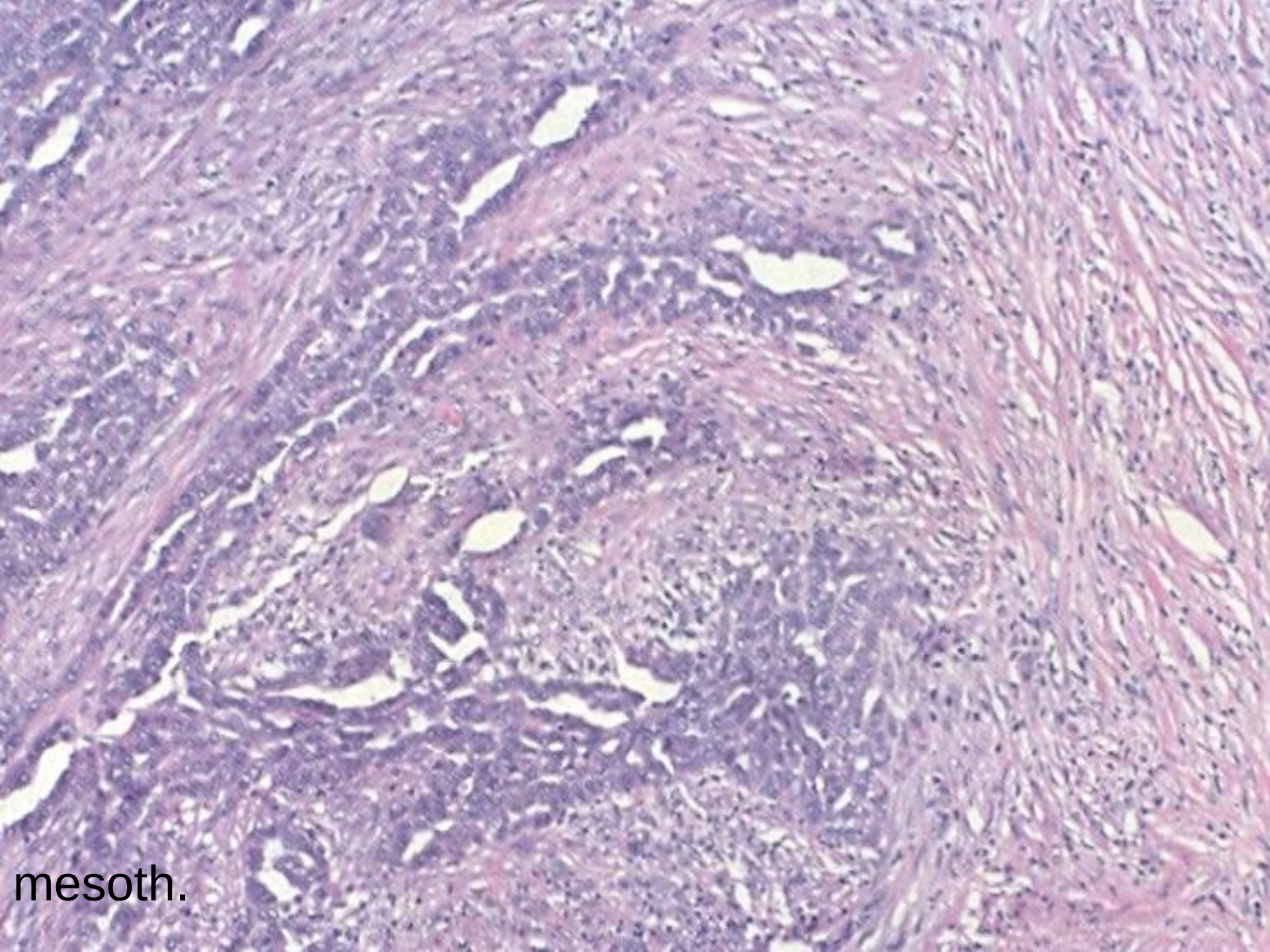

B

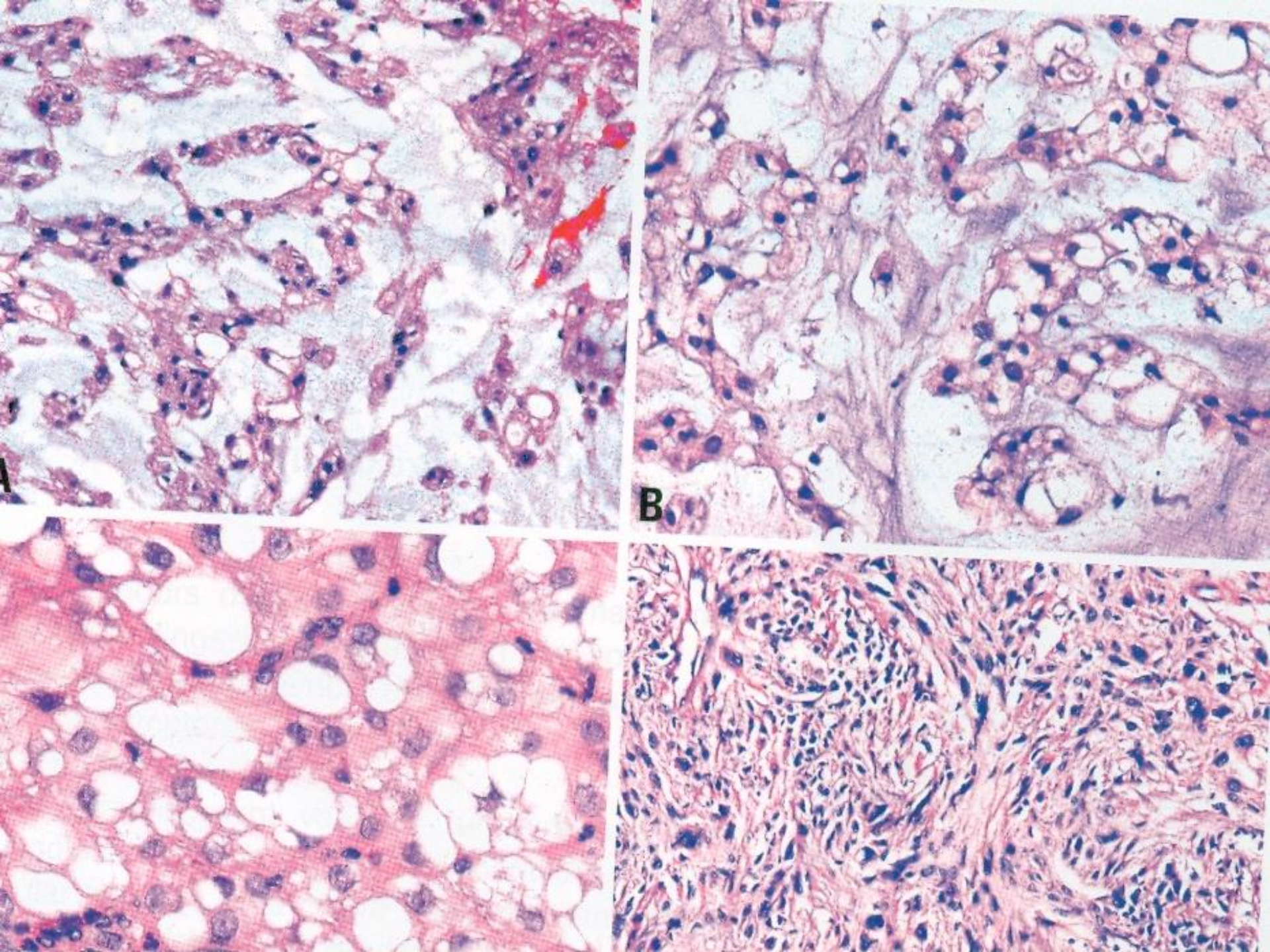


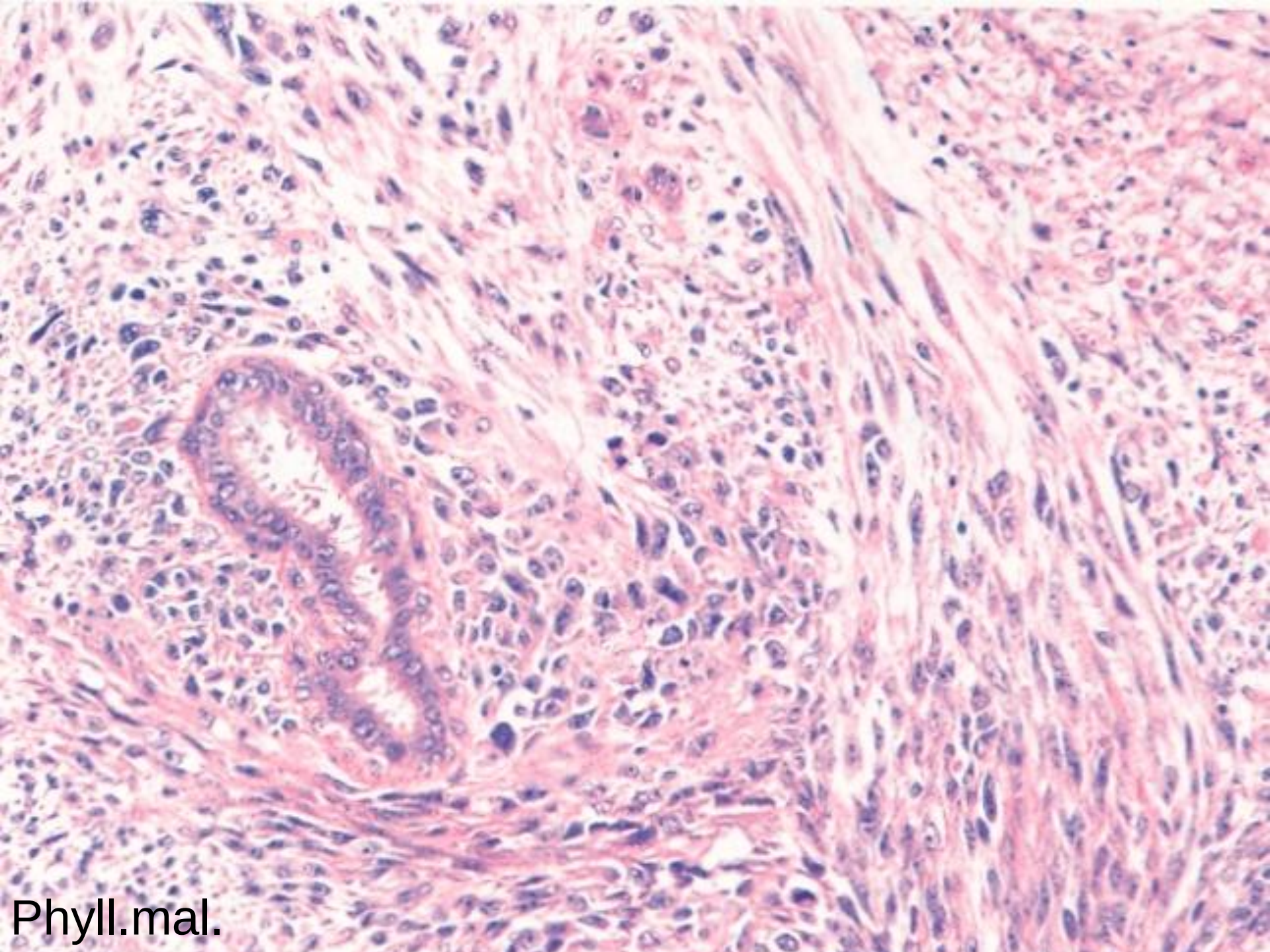

D

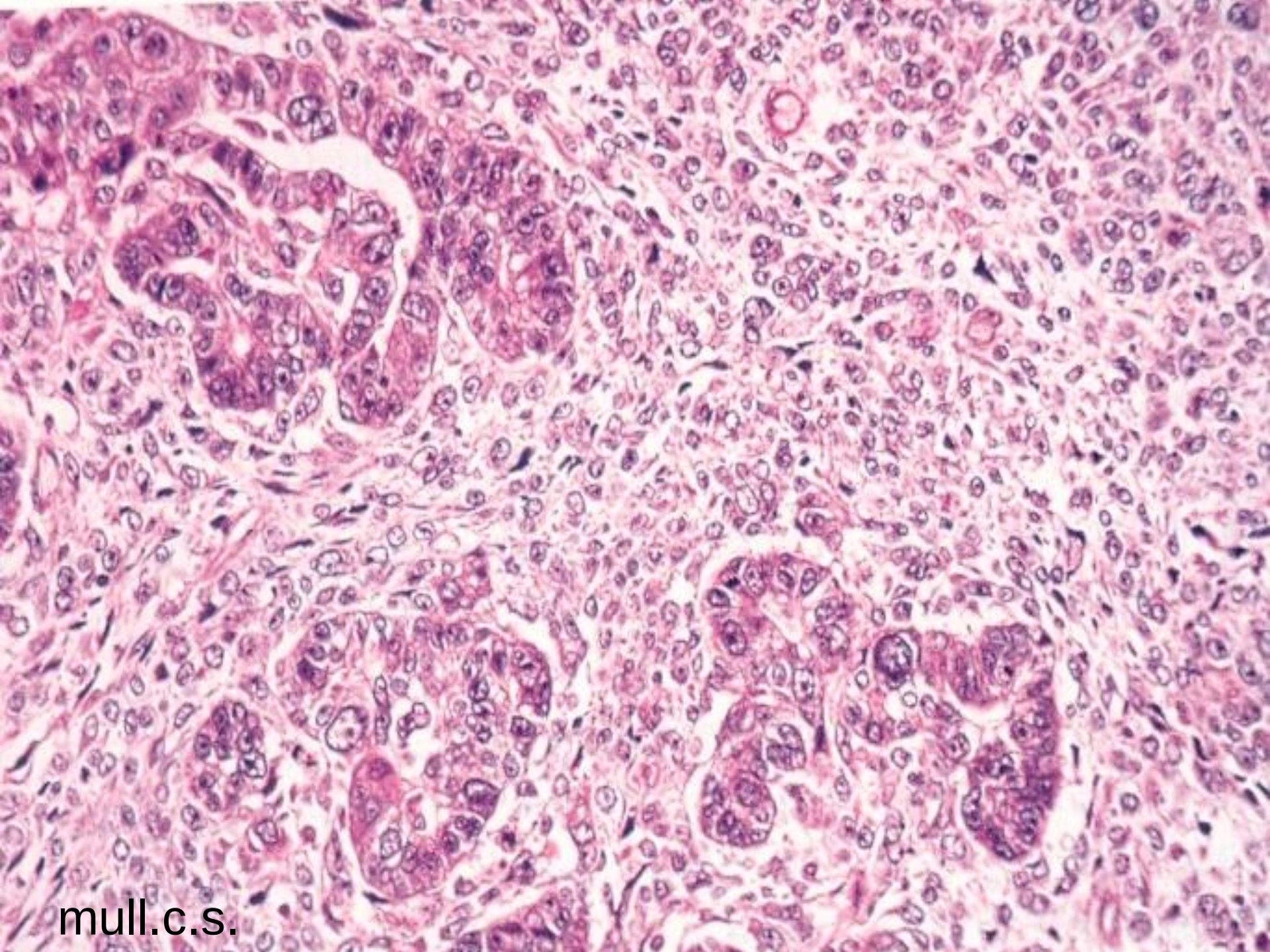

b.terat.

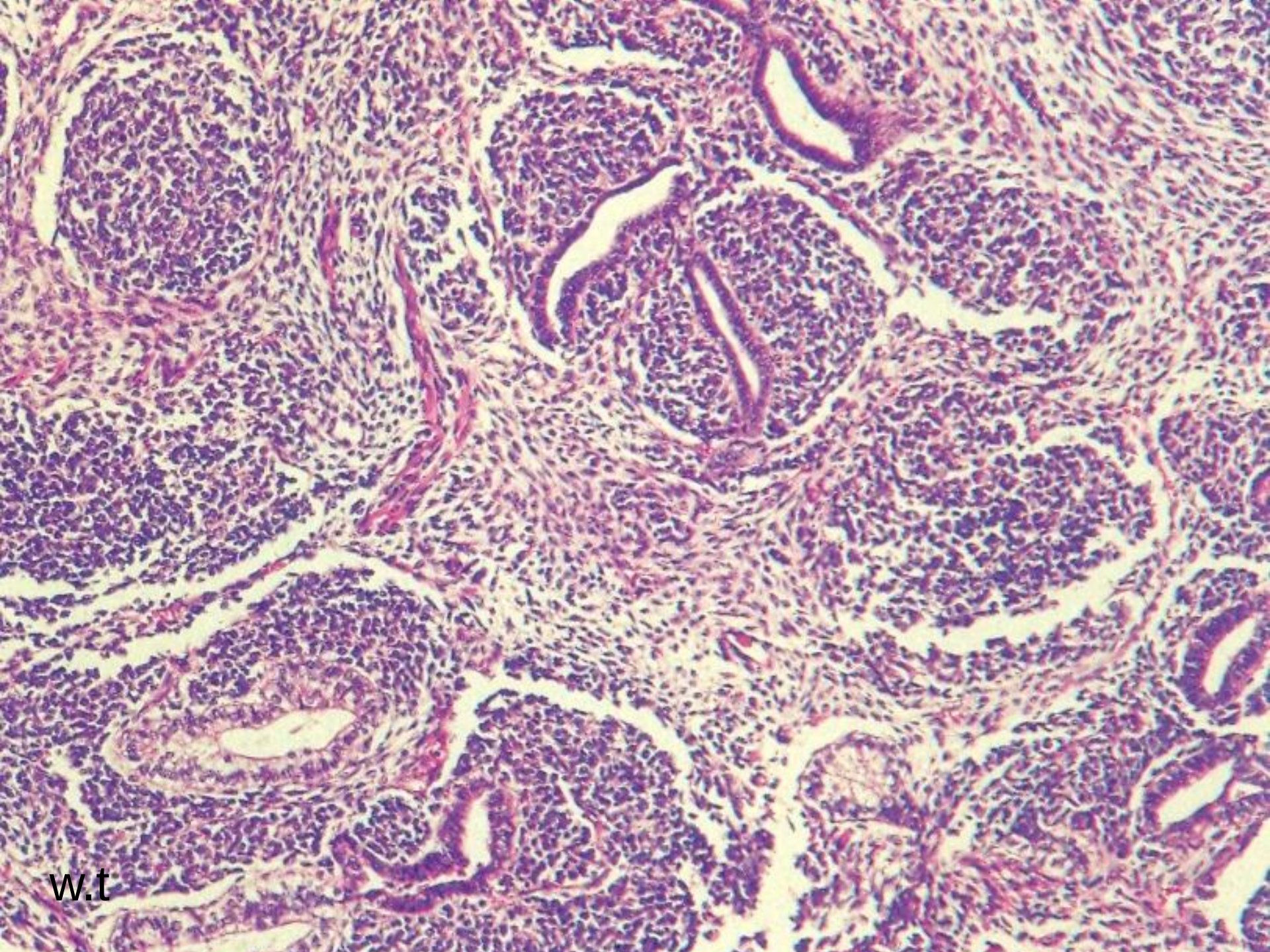

syn.sarc.

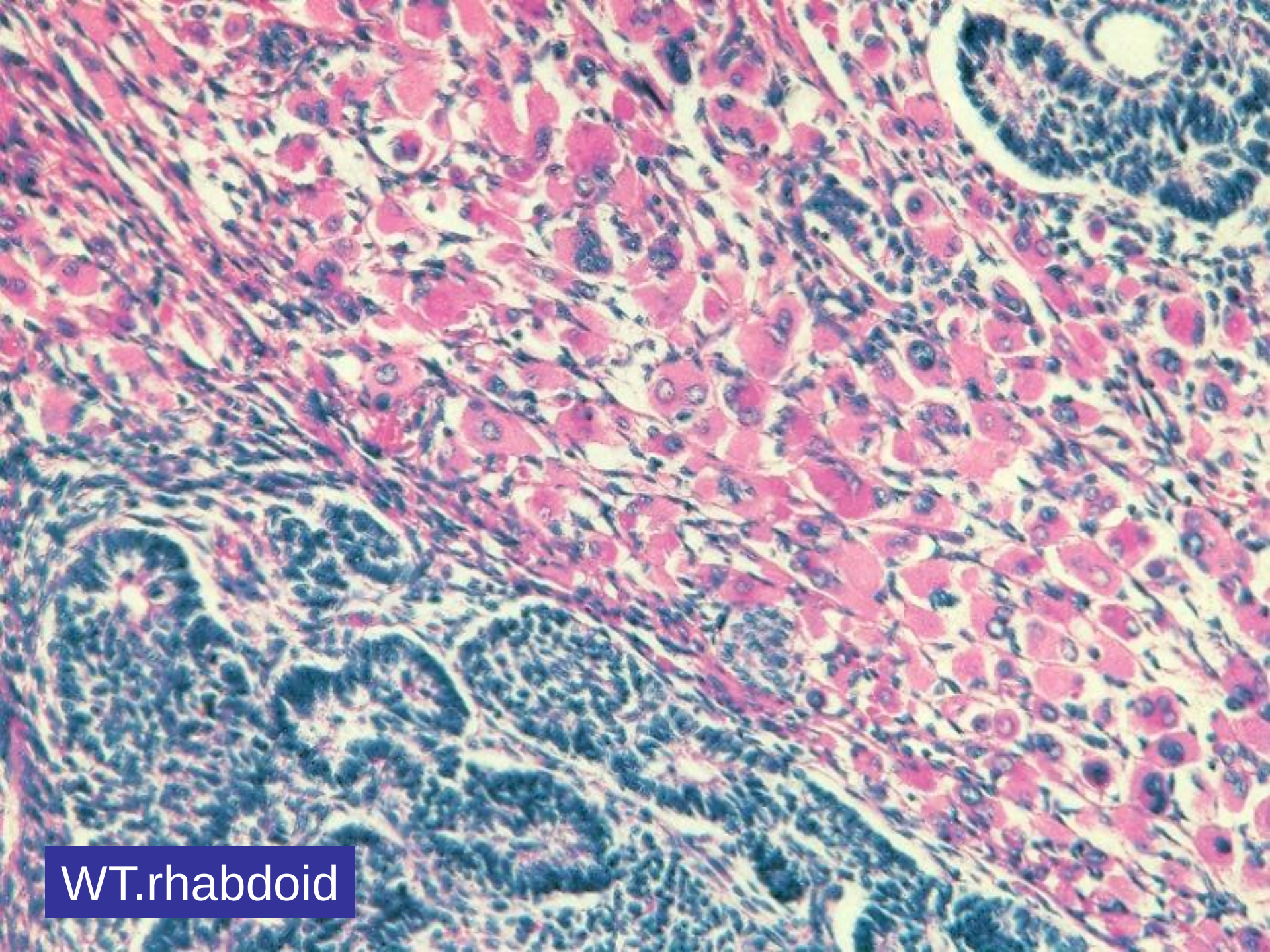

mesoth.

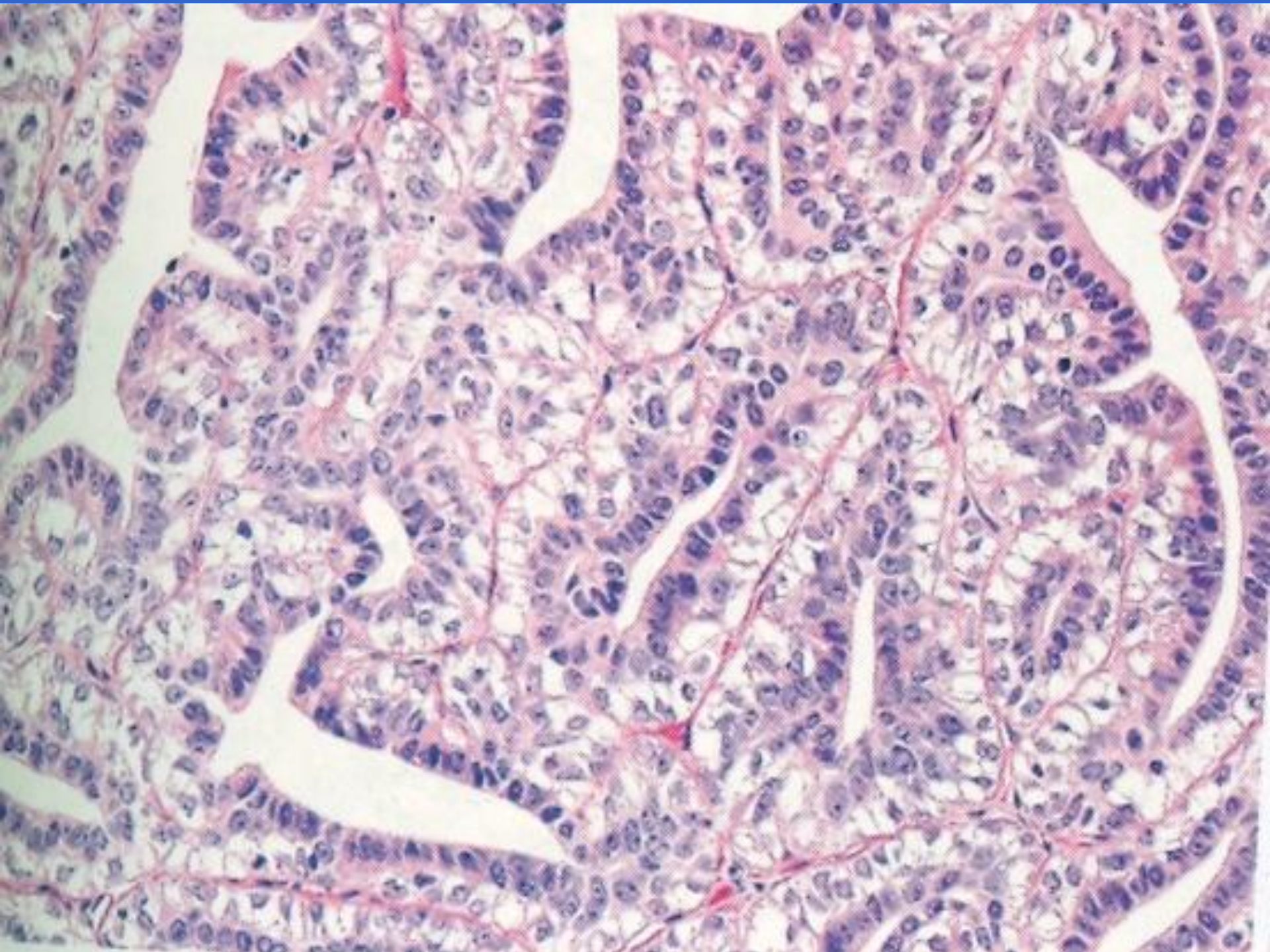

A
B


Phyll.mal.


mull.c.s.


w.t


WT.rhabdoid



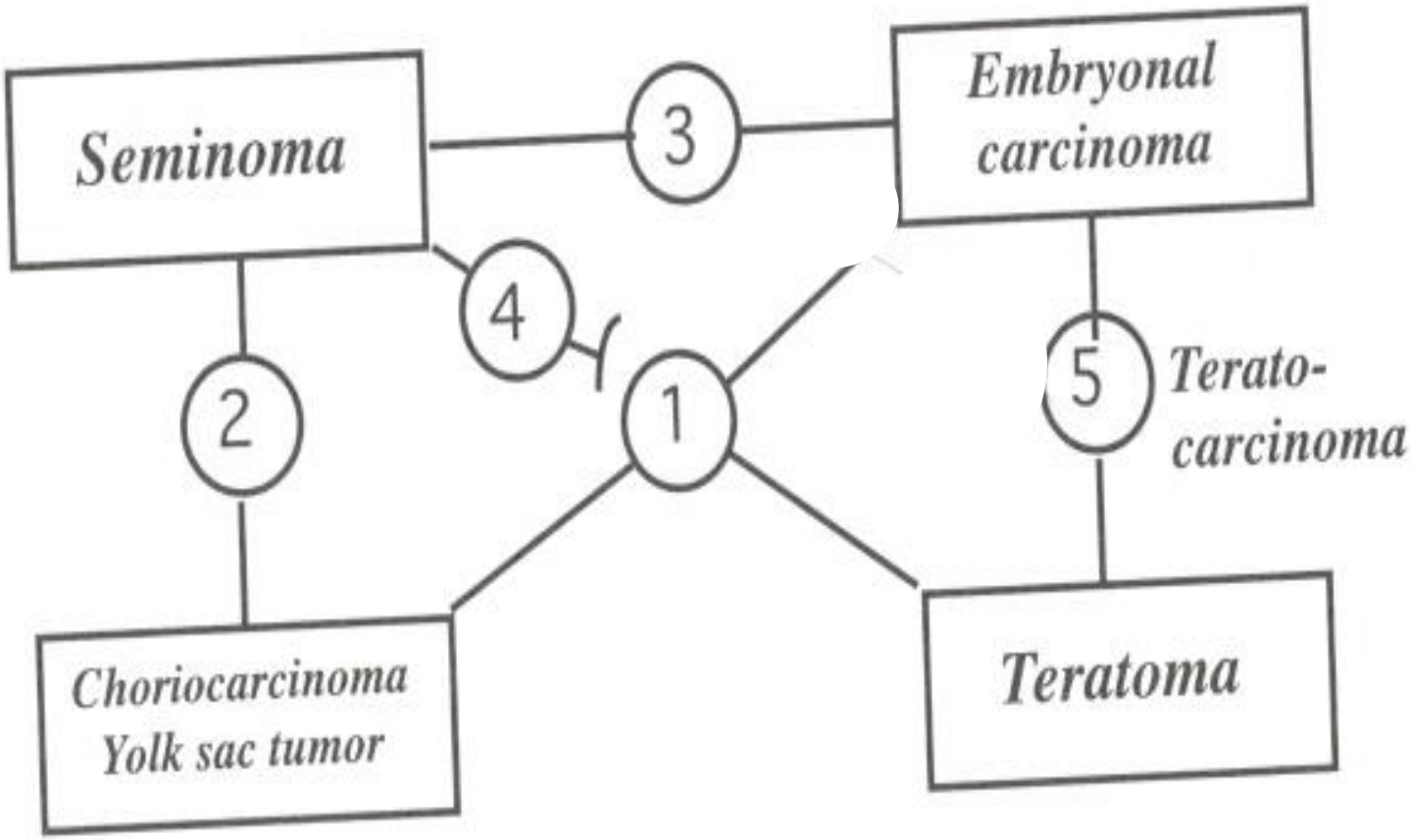
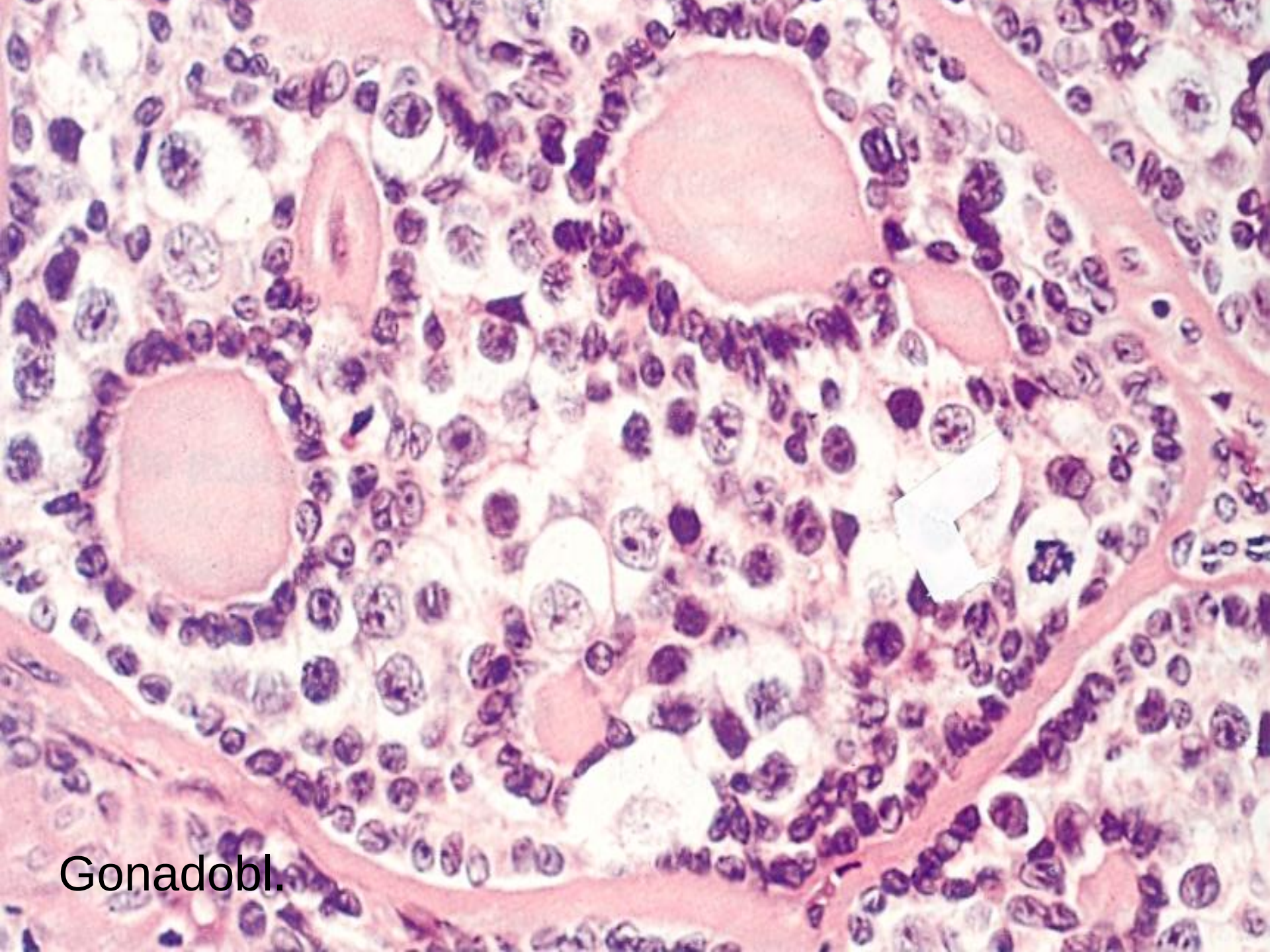
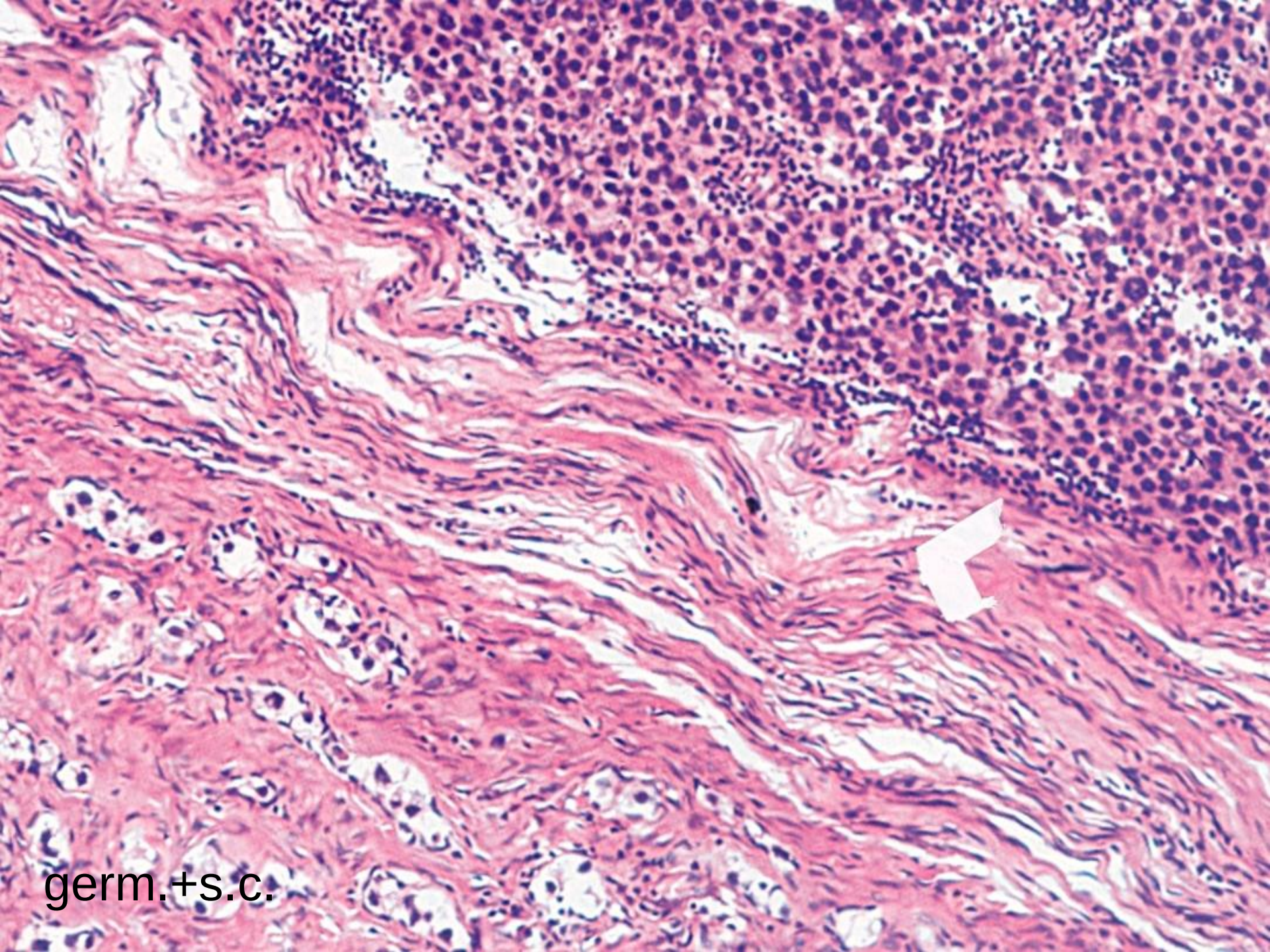


Fig. 8.8. Mixed NSGCT.


Gonadobl.


germ.+s.c.

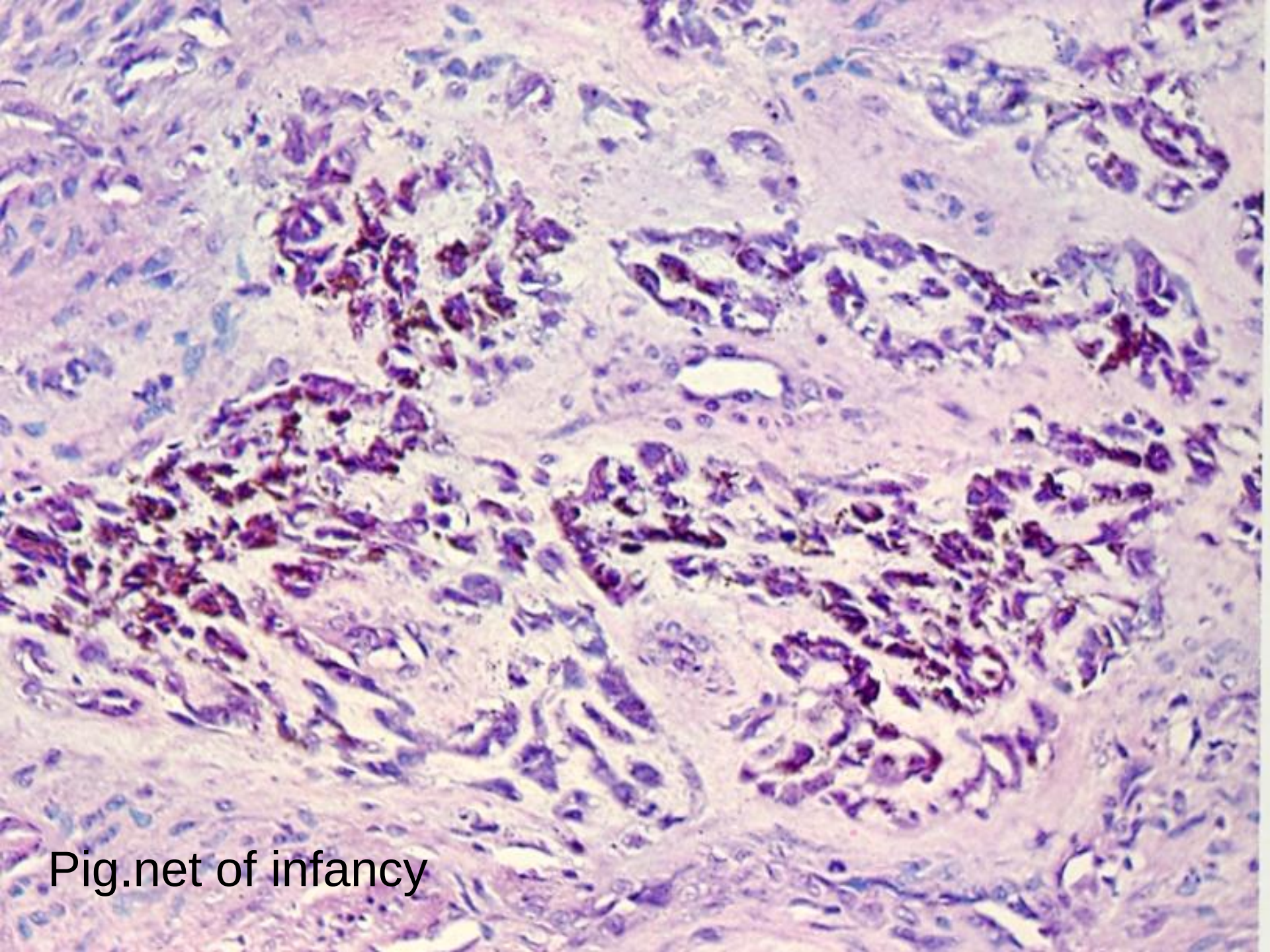
MIXED NEUROECTODERMAL TUMORS

BENIGN

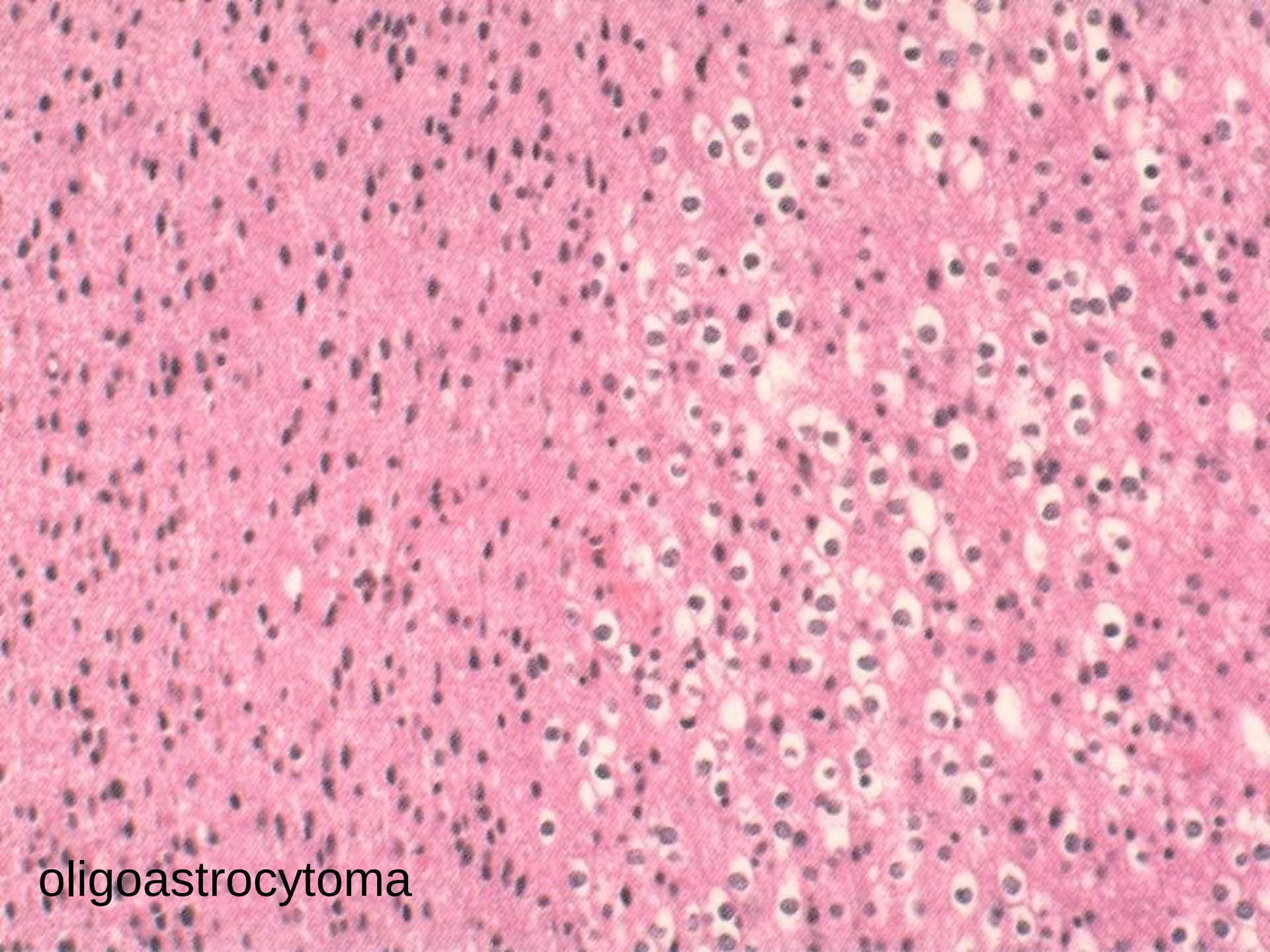
1. Pigmented neuroectodermal tumor of infancy
2. Ganglioneuroma
3. Melanotic neurofibroma

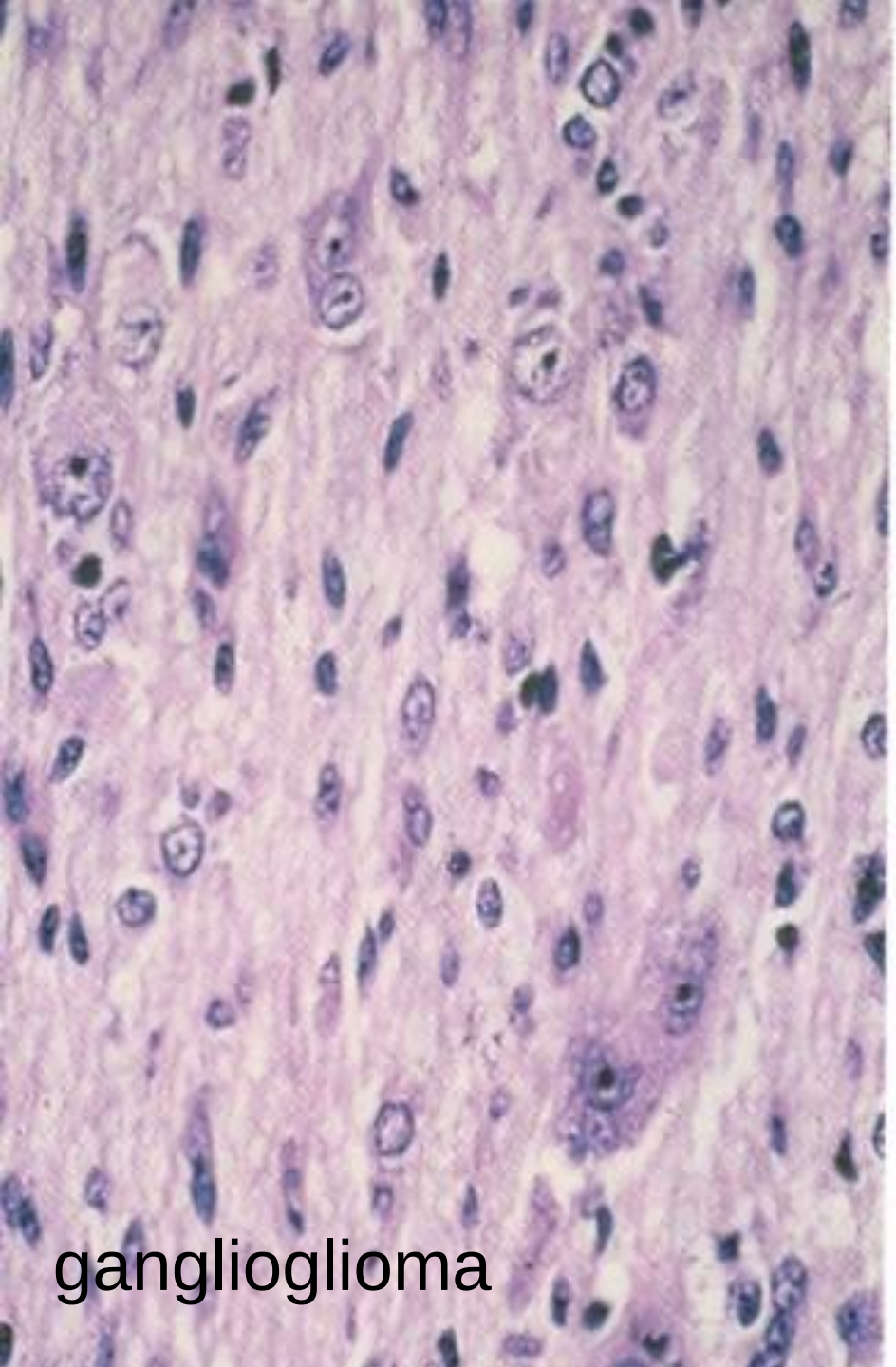
MALIGNANT

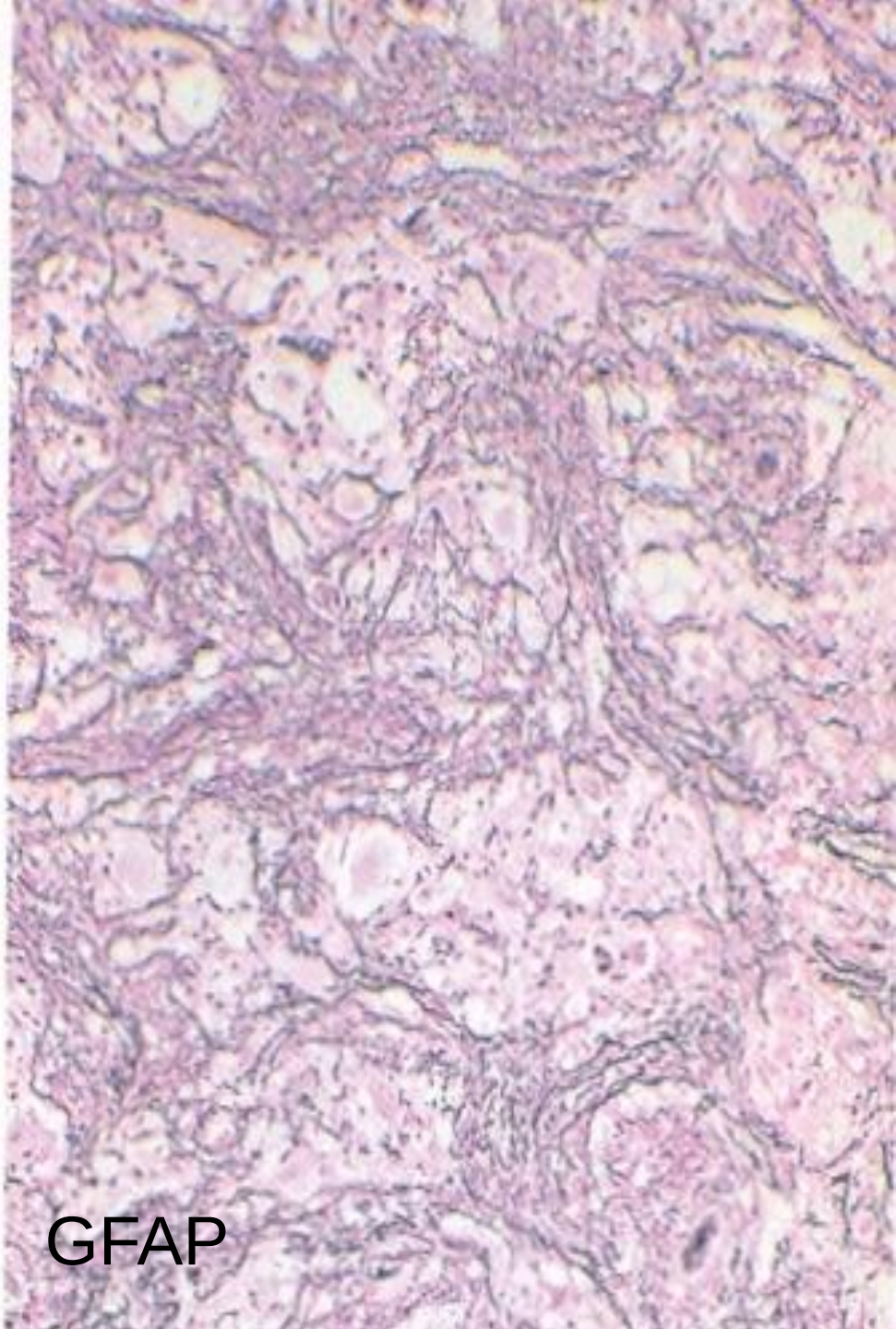
1. Oligoastrocytoma
2. Ganglioglioma
3. Gliosarcoma
4. Melanotic medulloblastoma
5. Melanotic DFSP
6. Adenocarcinoid (cl)
7. Combined SCLC & ca. (lg)
8. NET in teratoma (carcinoid or PNET)
9. Triton (RMS + MPNST)
10. Medullomyoblastoma (RMS + PNET)

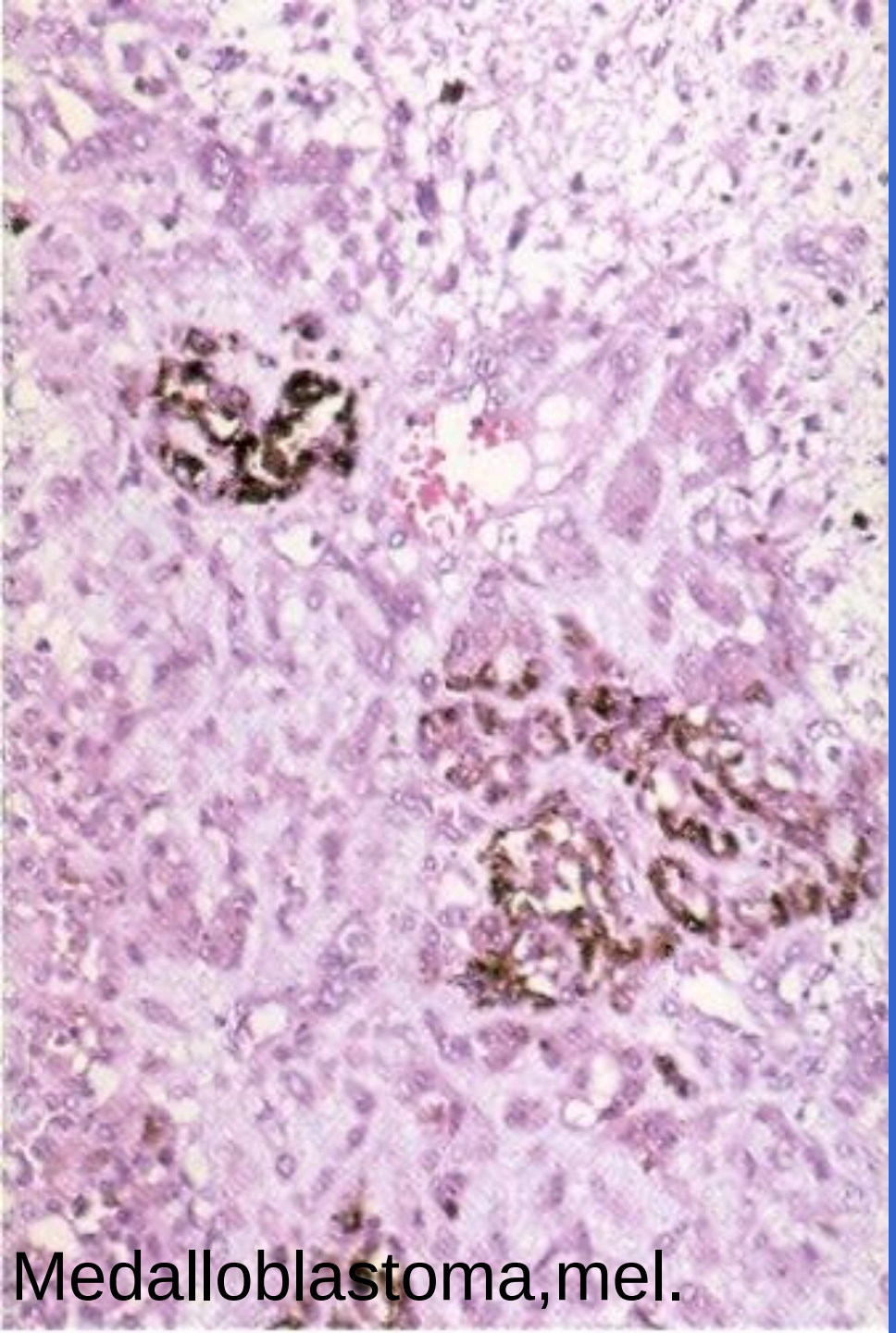


Pig.net of infancy

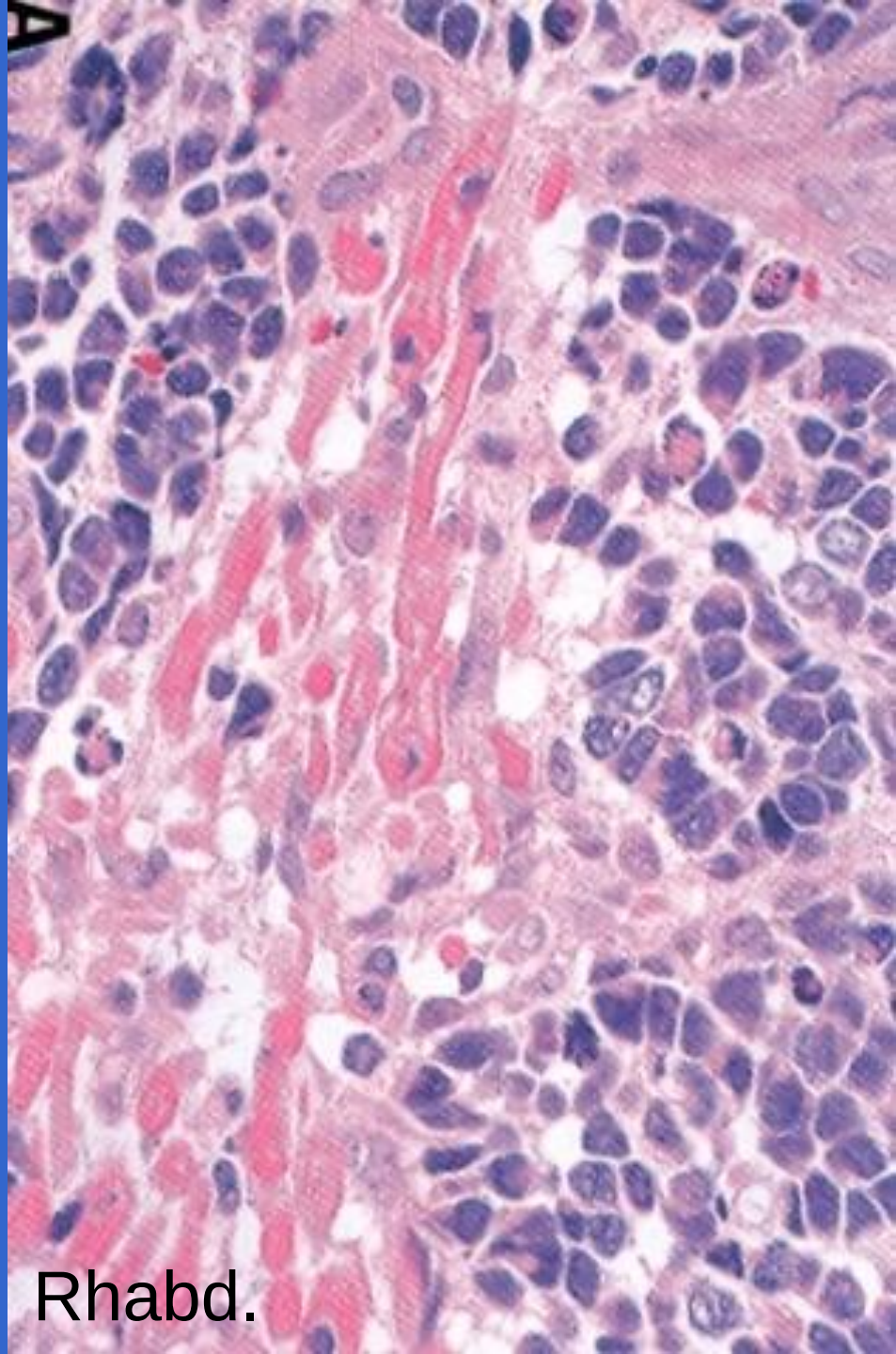

oligoastrocytoma


ganglioglioma

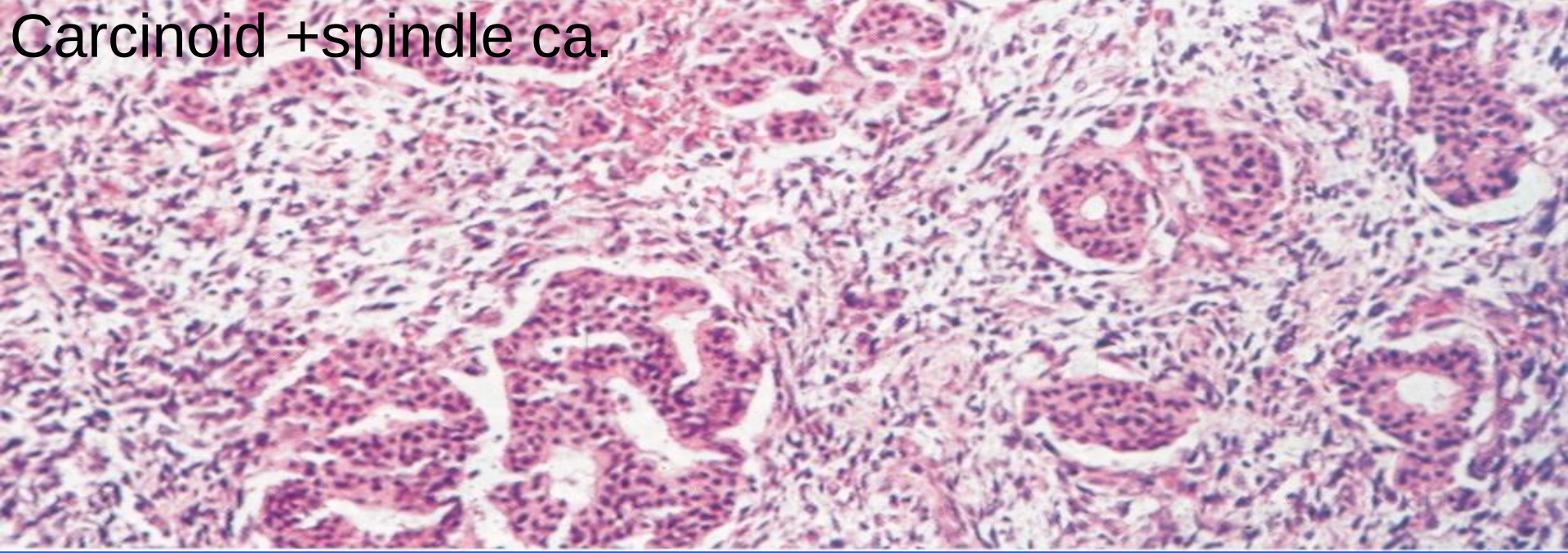

GFAP

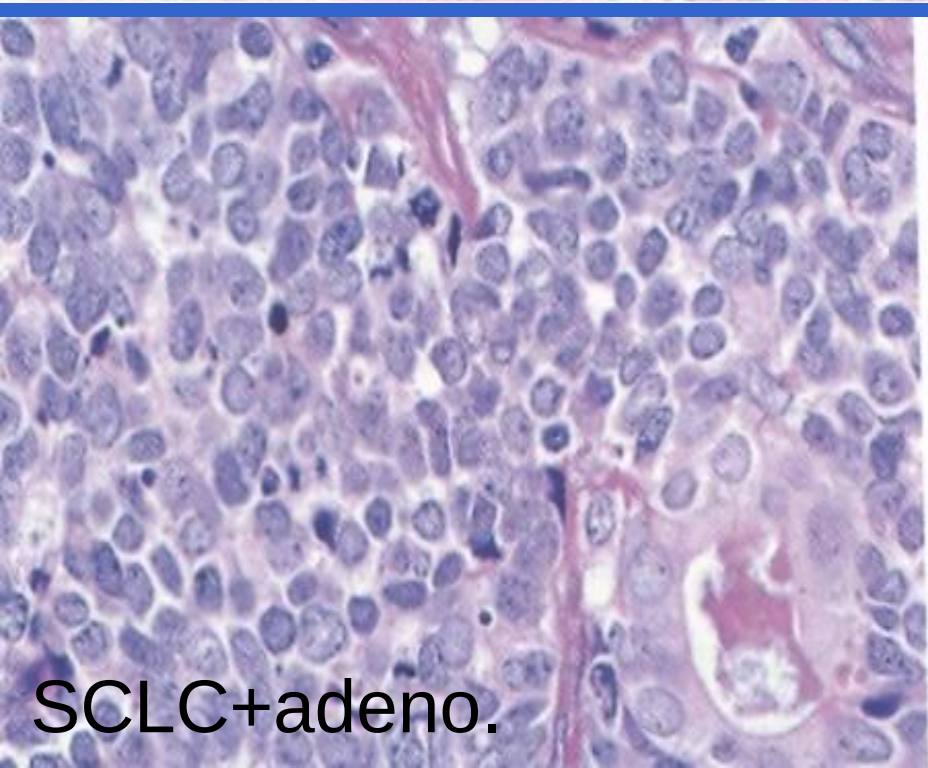


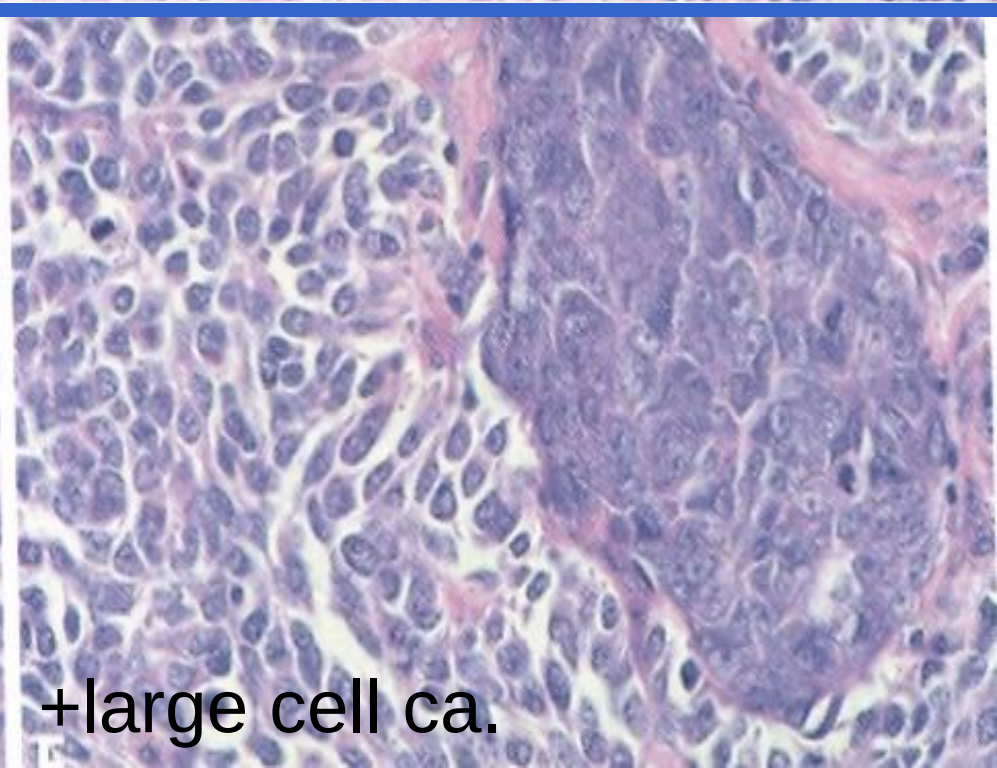
Medalloblastoma,mel.



Rhabd.


Carcinoid +spindle ca.


SCLC+adeno.


+large cell ca.

ECTOPIC TUMORS

1. Extragonadal germ cell tumors
2. Extraosseous bone tumors
3. Extracranial brain tumors
4. Extranodal lymphomas
5. Ectopic endocrime glands tumors
6. Ectopic tissue tumors (e.g. pancreas and thymus)