OVARIAN PATHOLOGY

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Learning outcomes

1. **Classify epithelial surface tumours of the ovary.**
2. Describe the embryological link of the surface epithelial tumours [good to know]
3. **Recognise the features and the differences of gross and histological morphology of mucinous, and serous tumours [must know]**
4. **Classify, described gross and histological morphology germ cell tumours of the ovary. [must know]**
5. Classify the sex cord stromal tumours of the ovary [good to know]
6. **Recognize the gross and histology of endometriosis [must know]**
7. Describe the hypothesis of endometriosis and its clinical features [good to know]

OUTLINES

Neoplastic Ovarian Tumours

- Surface epithelial tumours
- Germ cell tumours
- Sex cord stromal tumours
- Metastatic tumours

Non-Neoplastic Ovarian cysts

- Follicle cyst
- Luteal cyst
- Chocolate Cysts (endometrioma)
- Polycystic Ovaries

NEOPLASTIC OVARIAN TUMOURS

OVARIAN TUMORS

- Occur between 20-45 year-old.
- 80-90% of ovarian tumours are benign.
- Ovarian cancer 4th most common tumour in women
- **Primary ovarian tumours** are classified based on their site of origin.
- Most of them derived from **surface epithelium**
- CA-125 is the tumor marker for surface epithelial tumors of the ovary.
- Known risk factors are nulliparity, family history, and specific inherited mutations (*BRCAI & BRCAII*).

Do you know the symptoms of ovarian cancer?

NEOPLASTIC OVARIAN TUMOURS

SURFACE EPITHELIAL TUMORS

- **Serous Tumors**
- **Mucinous Tumors**
- **Endometrioid Ovarian Tumors**
- Clear Cell Carcinoma
- Brenner Tumors

GERM CELL TUMORS

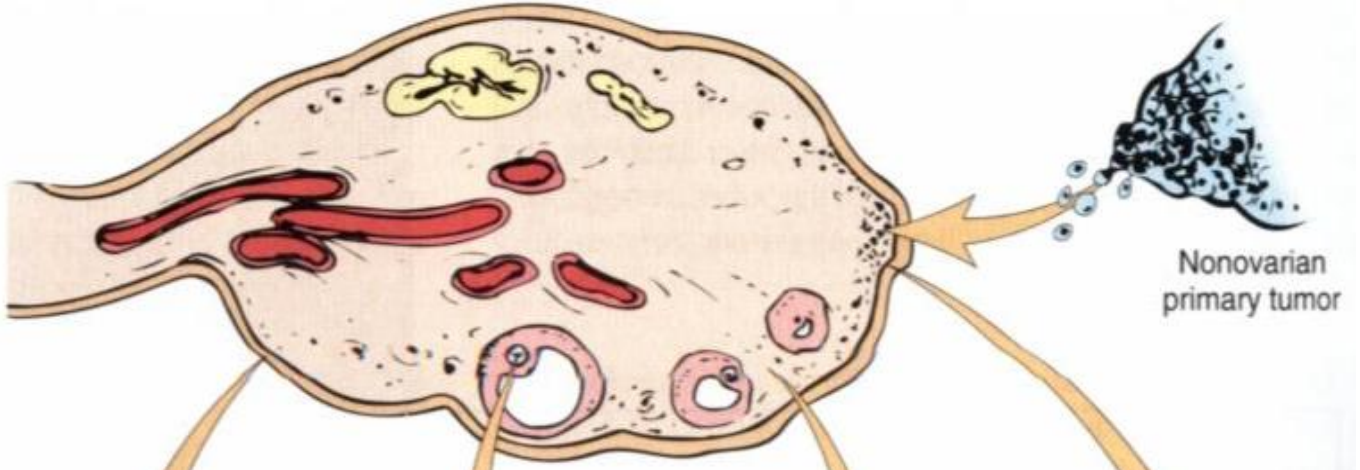
- **Teratoma**
- **Dysgerminoma**
- **Choriocarcinoma**
- **Yolk sac carcinoma**
- Embryonal carcinoma

SEX CORD - STROMAL TUMORS

- **Granulosa Cell Tumors**
- Fibromas, Thecomas, Fibrothecomas
- Sertoli-Leydig Cell Tumors

METASTATIC TUMOUR

Classification based on both differentiation and extent of proliferation of the epithelial cells



Germinal epithelium
- Simple cuboidal mesothelium on the surface of the ovary

Follicles
-contain oocytes.

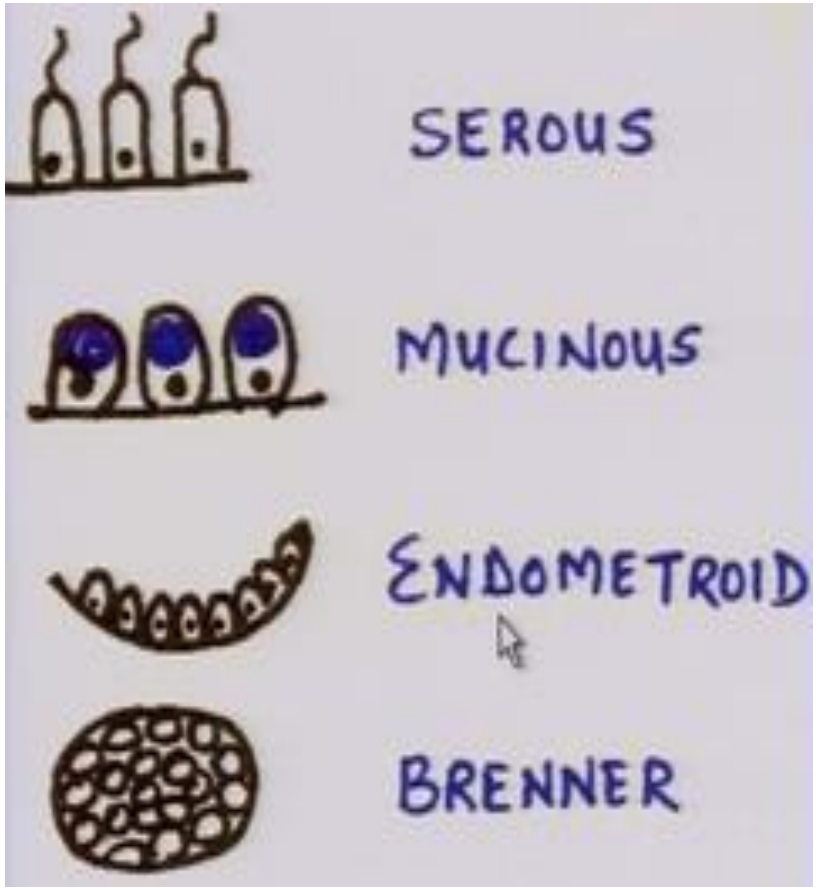
Ovarian stroma
- spindle-shaped cells, fine collagen fibers

ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial–stromal cell tumors)	GERM CELL	SEX CORD–STROMA	METASTASIS TO OVARIES
Overall frequency	65%–70%	15%–20%	5%–10%	5%
Proportion of malignant ovarian tumors	90%	3%–5%	2%–3%	5%
Age group affected	20+ years	0–25+ years	All ages	Variable
Types	• Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma	• Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma	• Fibroma • Granulosa-theca cell tumor • Sertoli-Leydig cell tumor	

SURFACE MULLERIAN EPITHELIAL TUMORS

Benign, borderline and malignant

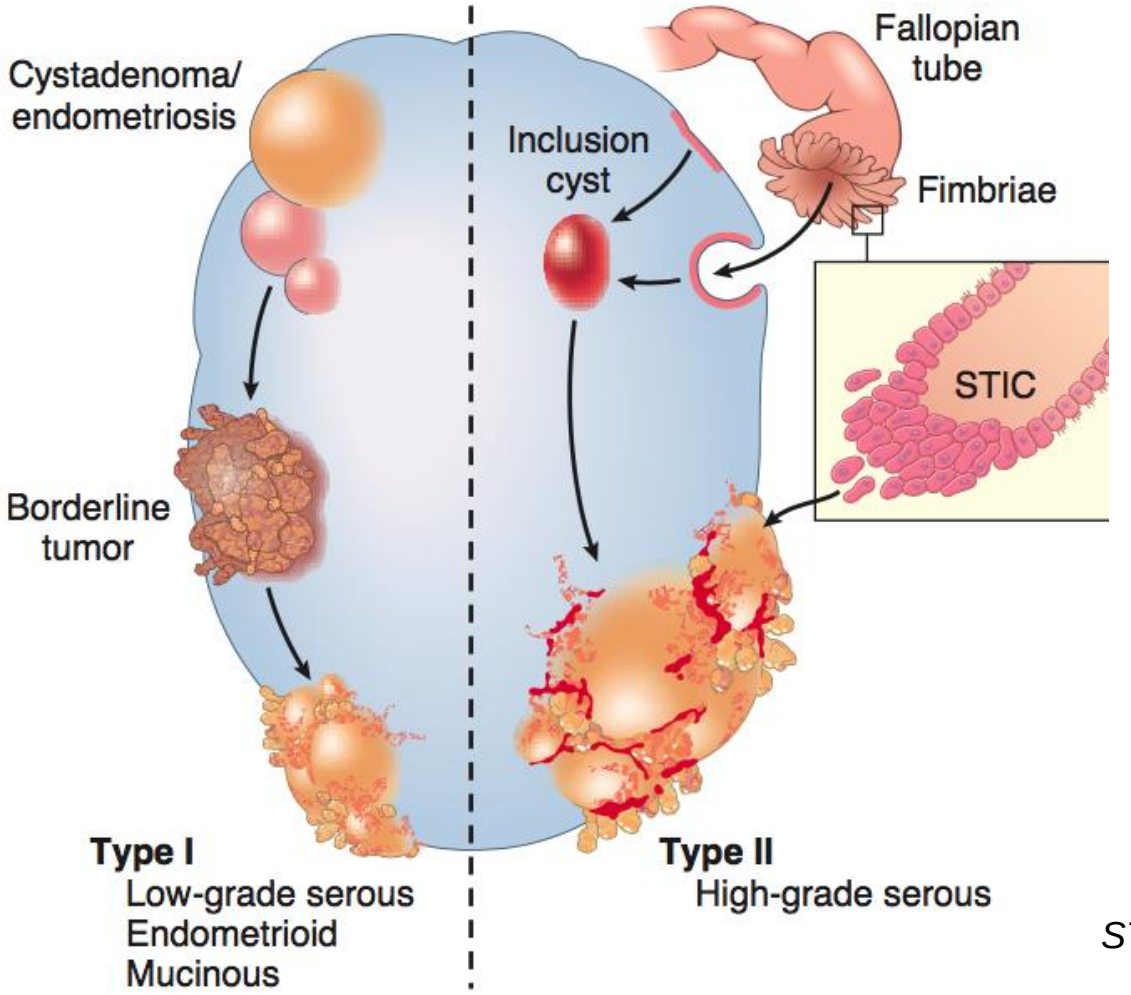
1. **Serous tumours**: composed of ciliated columnar (tubal type) epithelium-most common
2. **Mucinous tumours**: composed of mucus-secreting (cervical canal type) epithelium
3. **Endometrioid tumours**: composed of glandular (endometrium-like) epithelium.
4. **Brenner's tumours**: composed of transitional (urothelium-like) epithelium
5. **Clear cell tumours**



SURFACE EPITHELIAL TUMORS

Clinicopathologic and molecular studies have suggested that ovarian carcinoma may be categorized into 2 different types:

Type I tumors
-progress from benign tumors to borderline tumors that may give rise to a low-grade ca.



Type II tumors
-arise from inclusions cysts/ fallopian tube epithelium via <u>intraepithelial precursors</u>

-demonstrate high-grade features most commonly of serous histology.

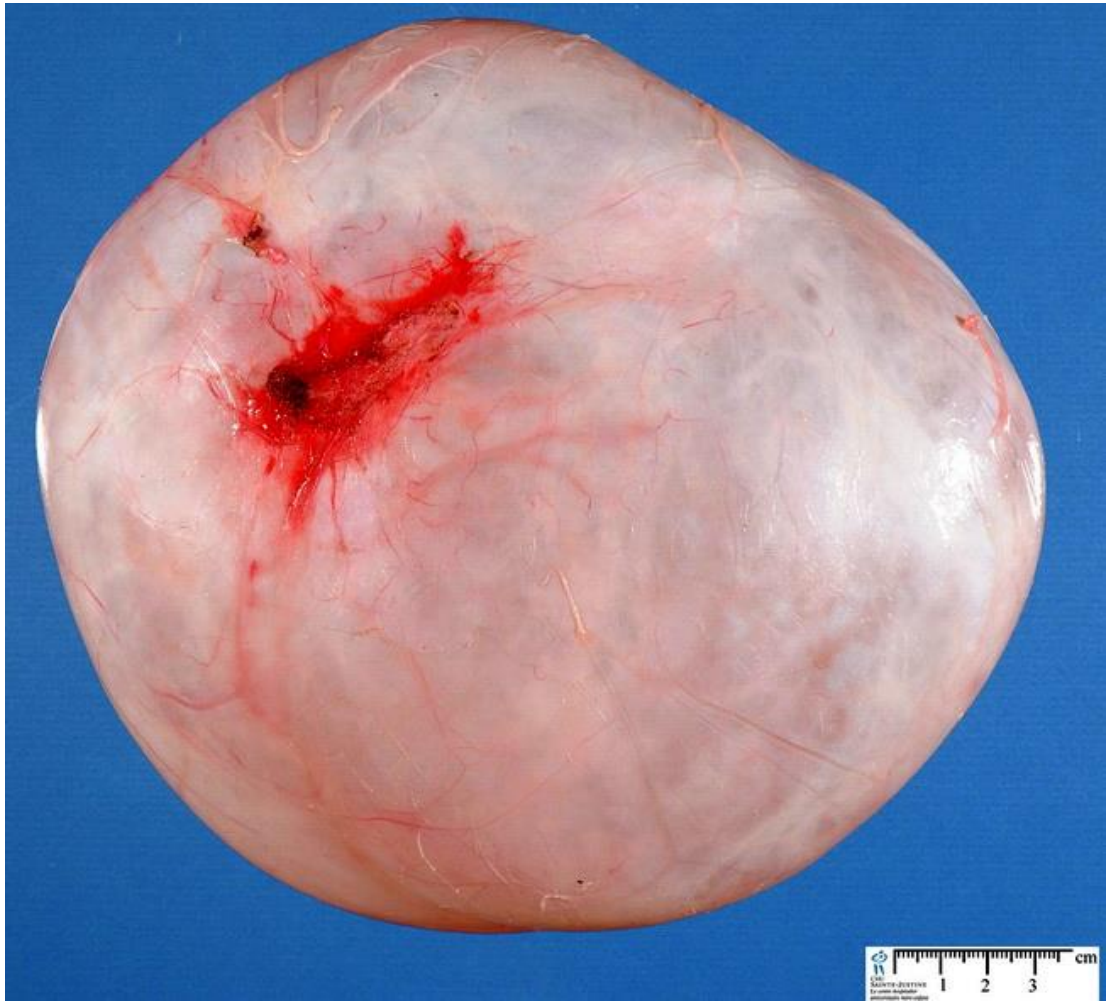
STIC, Serous tubal intraepithelial carcinoma.

1. SEROUS TUMORS

- Tumors exhibit serous differentiation / composed of cells **resembling fallopian** tube epithelium
- Account for about **30%** of all ovarian tumors
- About **70% are benign** / borderline; 30% are malignant
- Concentric calcifications (**psammoma bodies**) are common in ALL TYPES of serous tumors (not specific for neoplasia)

Benign Serous Tumors

- **<u>MACROSCOPIC APPEARANCE</u>**
- Typically have smooth glistening cyst wall with no epithelial thickening / small papillary projections
- Vary widely in size
- **Serous Cystadenoma:**
  - Cyst >1cm
  - Smooth outer and inner surfaces.
  - May be septated and filled with watery fluid
- **Other type of benign serous tumour: cystadenofibromas, serous adenofibromas, serous surface papilloma**

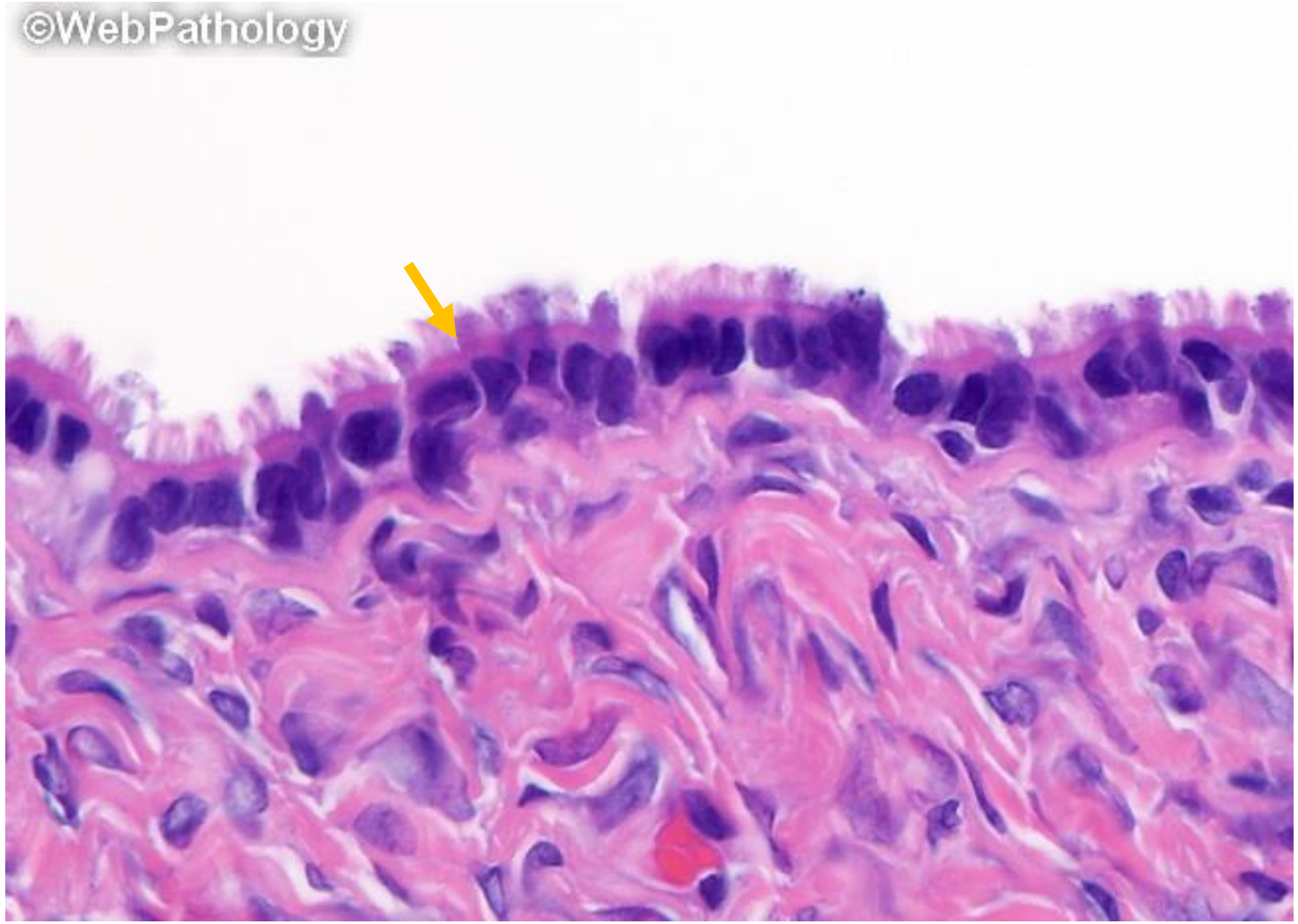


Serous Cystadenoma

Benign Serous Tumors

MICROSCOPIC APPEARANCE

- Epithelial lining consists of non-stratified cuboidal or columnar cells (resembling tubal secretory / ciliated cells)
- No nuclear atypia; +/- Psammoma bodies



Serous Cystadenoma

Serous Borderline Tumors

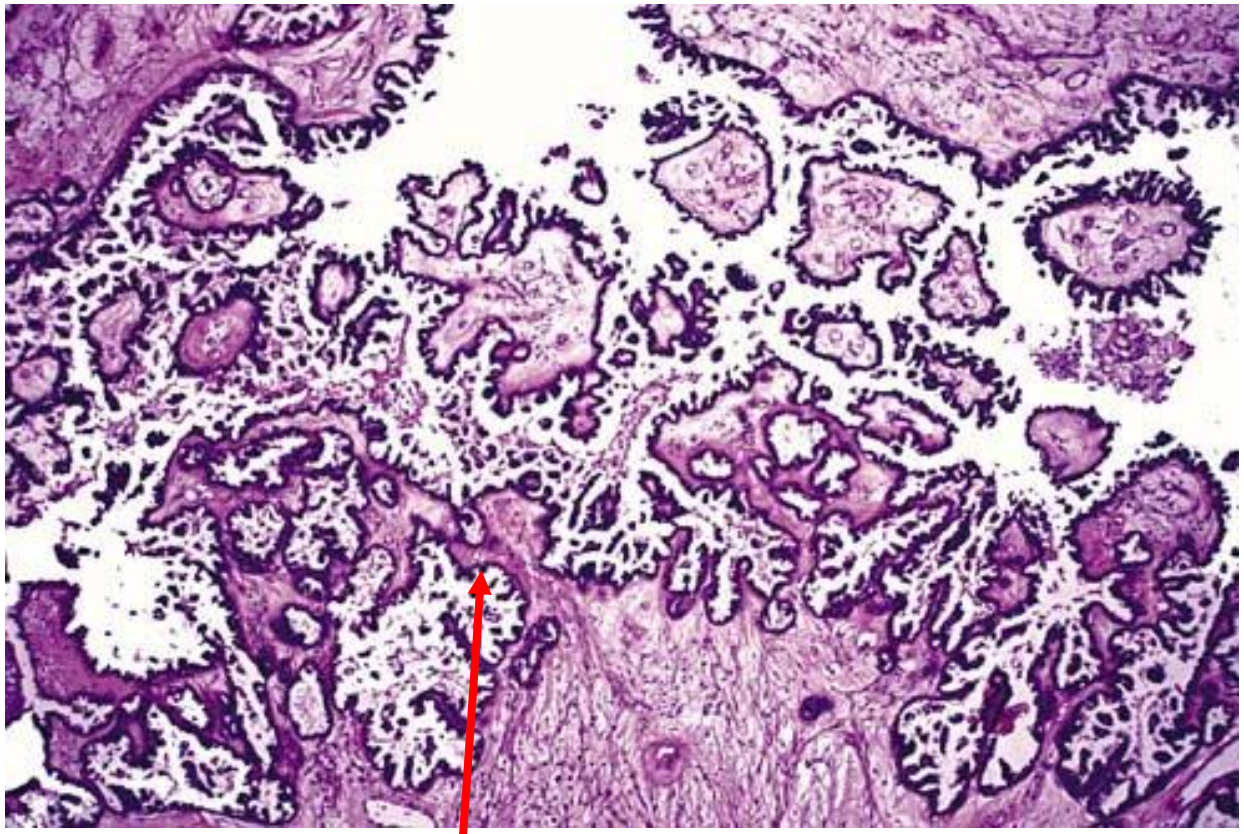
- SBT is a **non-invasive**, **low-grade**, proliferative serous epithelial neoplasm
- Precursor to low-grade serous carcinoma

MACROSCOPIC APPEARANCE

- Generally > 5cm; 1/3 are bilateral
- May be intracystic / exophytic with surface involvement
- Contain an increased numbers of papillary projections

MICROSCOPIC APPEARANCE

- Characterized by hierarchical branching papillae / micropapillary / cribriform pattern
- Epithelium is stratified with tufting and cell detachment
- Mild nuclear atypia, +/- Psammoma bodies



SBT with hierarchical branching. Fibrous papillae are covered by proliferating epithelial cells with tufting and exfoliated cell clusters. Stromal invasion is absent.

Malignant Serous Tumors

- Serous carcinoma of the ovary is divided into 2 major groups based on the degree of nuclear atypia:

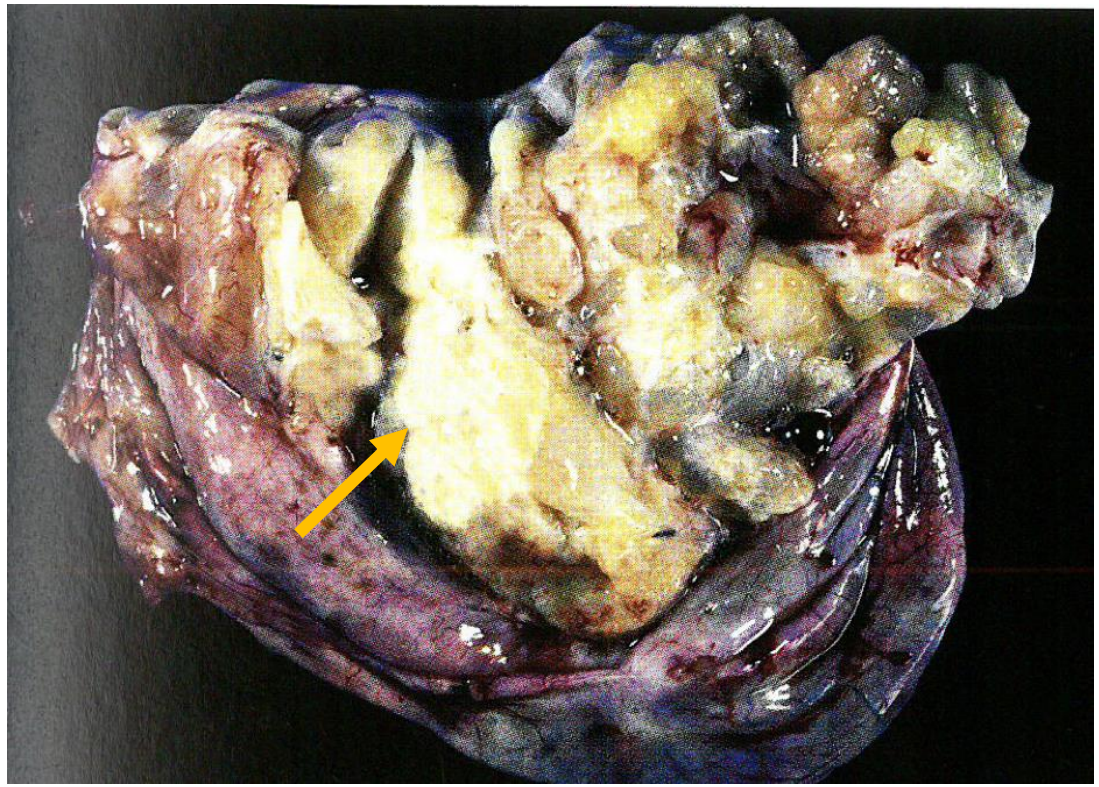
  - **Low-grade serous carcinoma**
    - May arise from serous borderline tumors
    - KRAS, BRAF, ERBB2 oncogenes, wild-type TP53 genes

  - **High-grade serous carcinoma**
    - Arise from in situ lesions in fallopian tube fimbriae (**serous tubal intraepithelial carcinoma**) / from **serous inclusion cysts** within the ovary
    - *BRCA1, BRCA2*, TP53

Low-grade Serous Carcinoma, LGSC

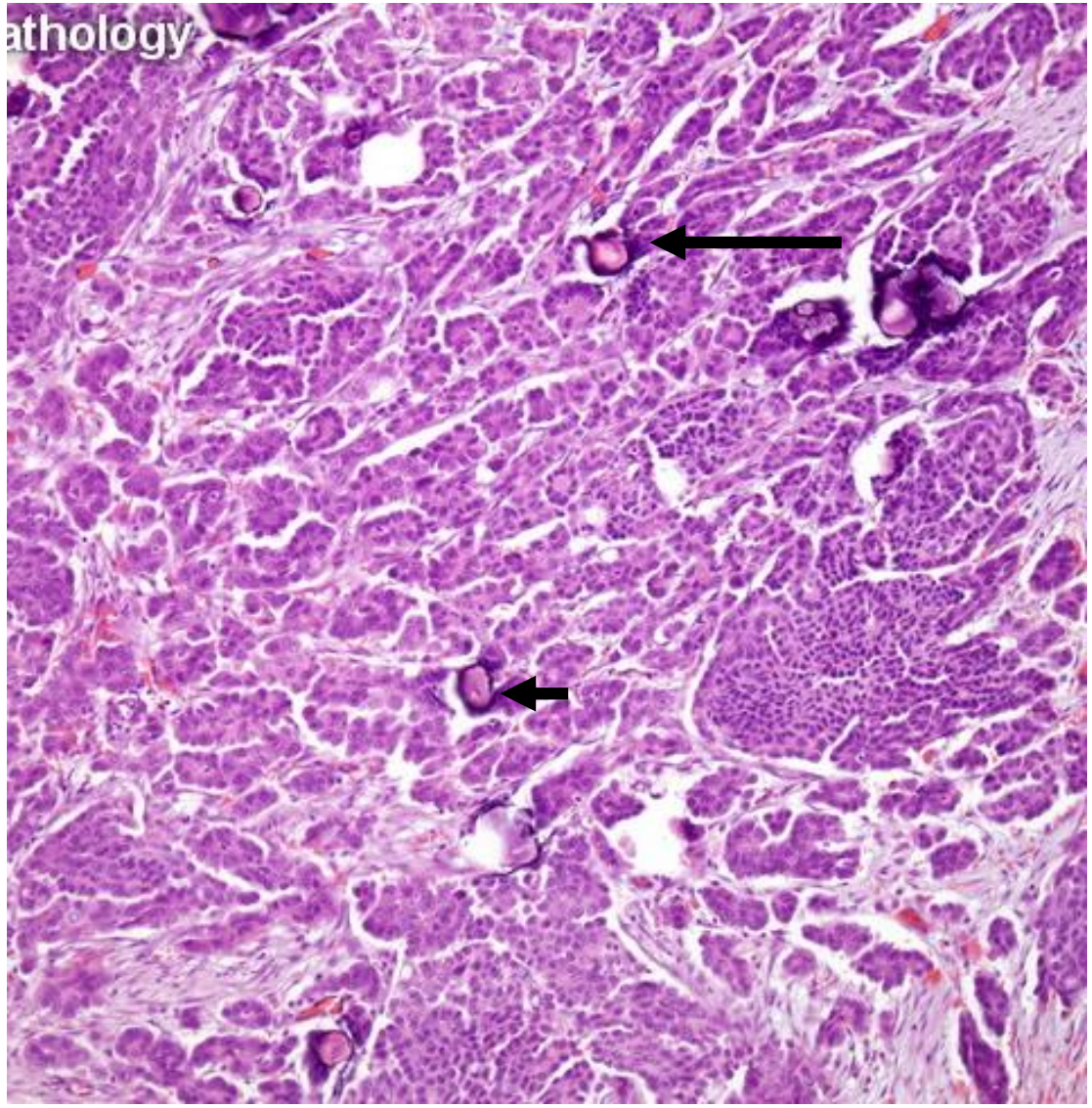
MACROSCOPIC APPEARANCE:

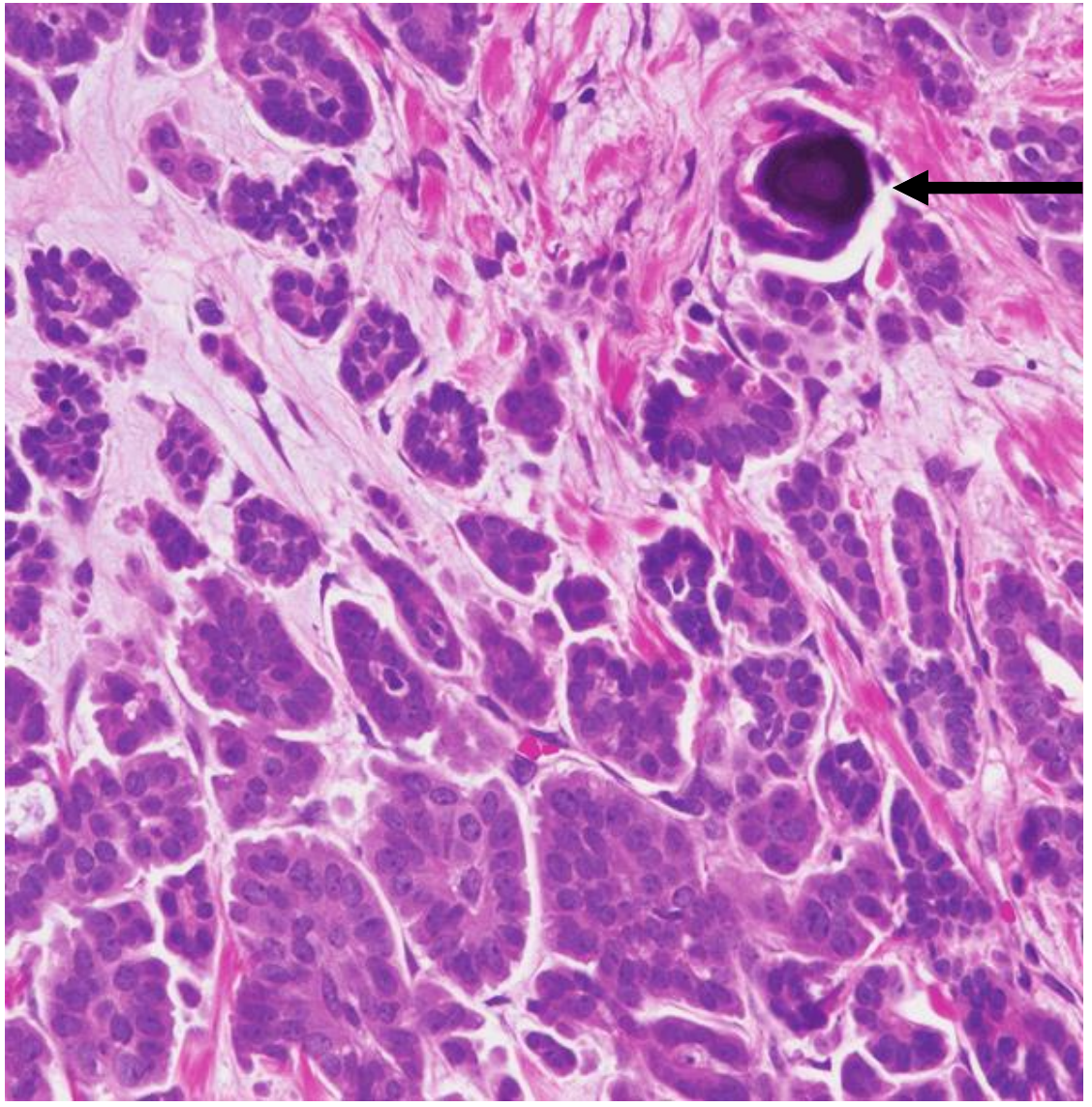
- Invasive LGSC usually shows more abundant, fleshy, soft papillary growth.
- Often bilateral. Tumors may be gritty due to calcification



MICROSCOPIC APPEARANCE:

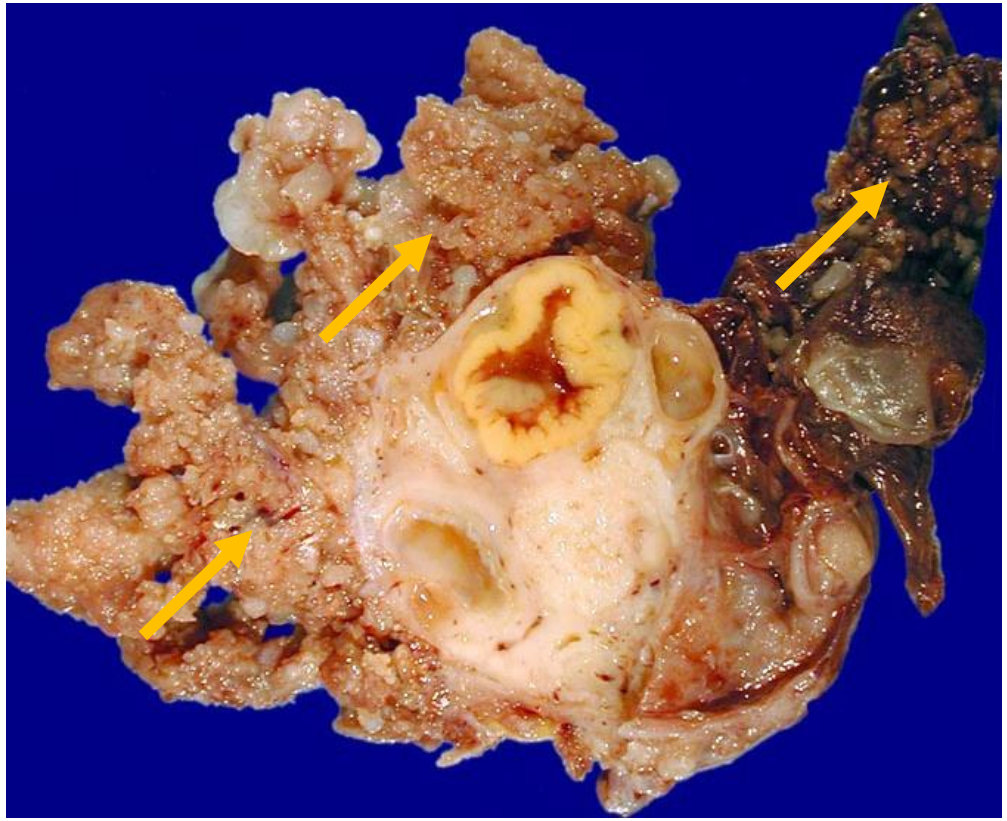
- Small nests, glands, papillae, micropapillae
- Presence of invasions
- Nuclei exhibit mild to moderate atypia
  - < 3x variation in nuclear size
  - Occasionally with central nucleolus
- Presence of mitotic figures
- Psammoma bodies are often present
- Necrosis is rare
- Frequently associated with co-existing SBT

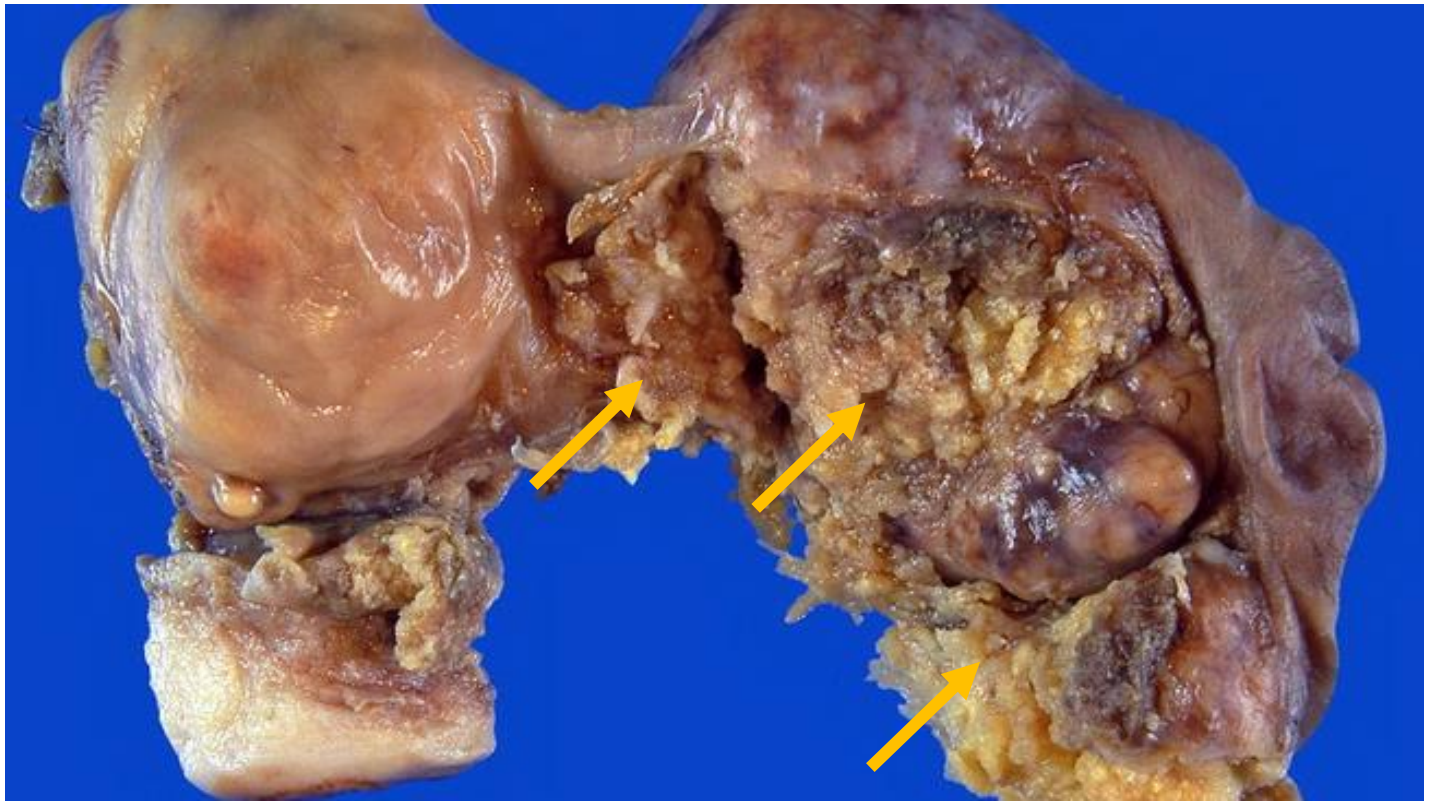




LOW-GRADE SEROUS CARCINOMA: consists of isolated tumor cells, small glands and irregular nests infiltrating desmoplastic stroma. Psammoma bodies are a frequent finding (black arrow.

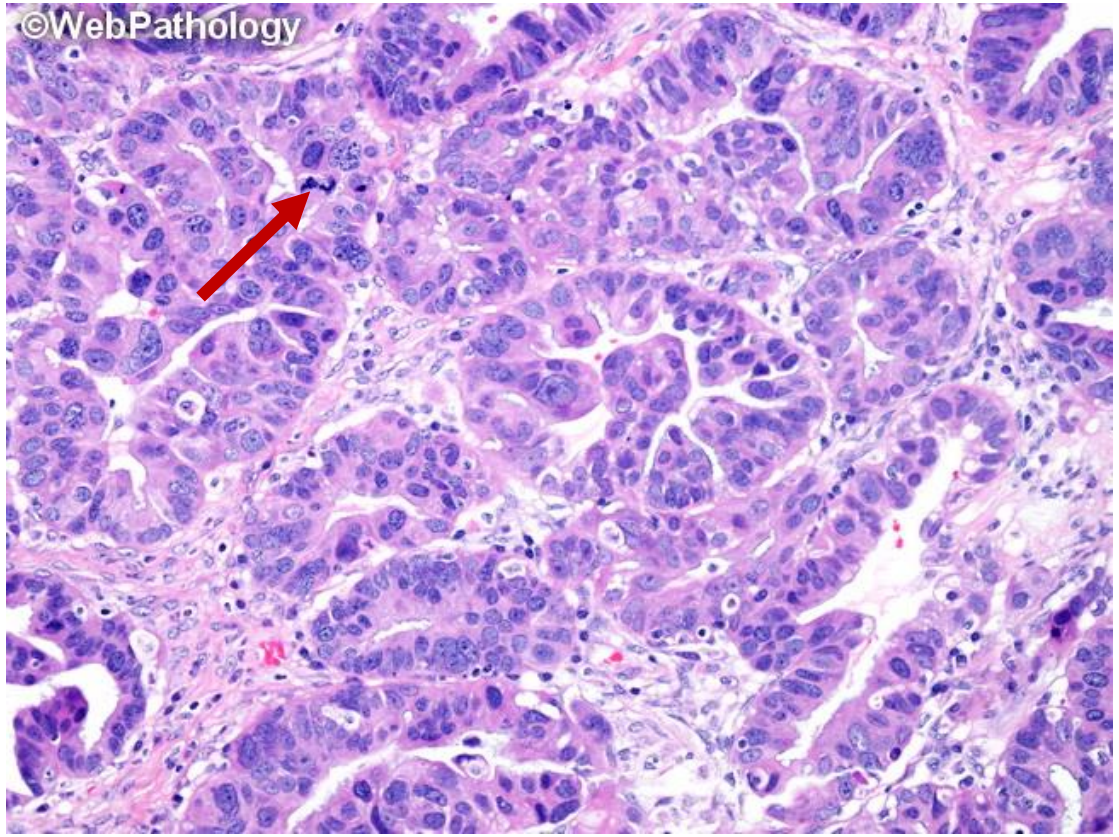
High-grade Serous Carcinoma: Gross

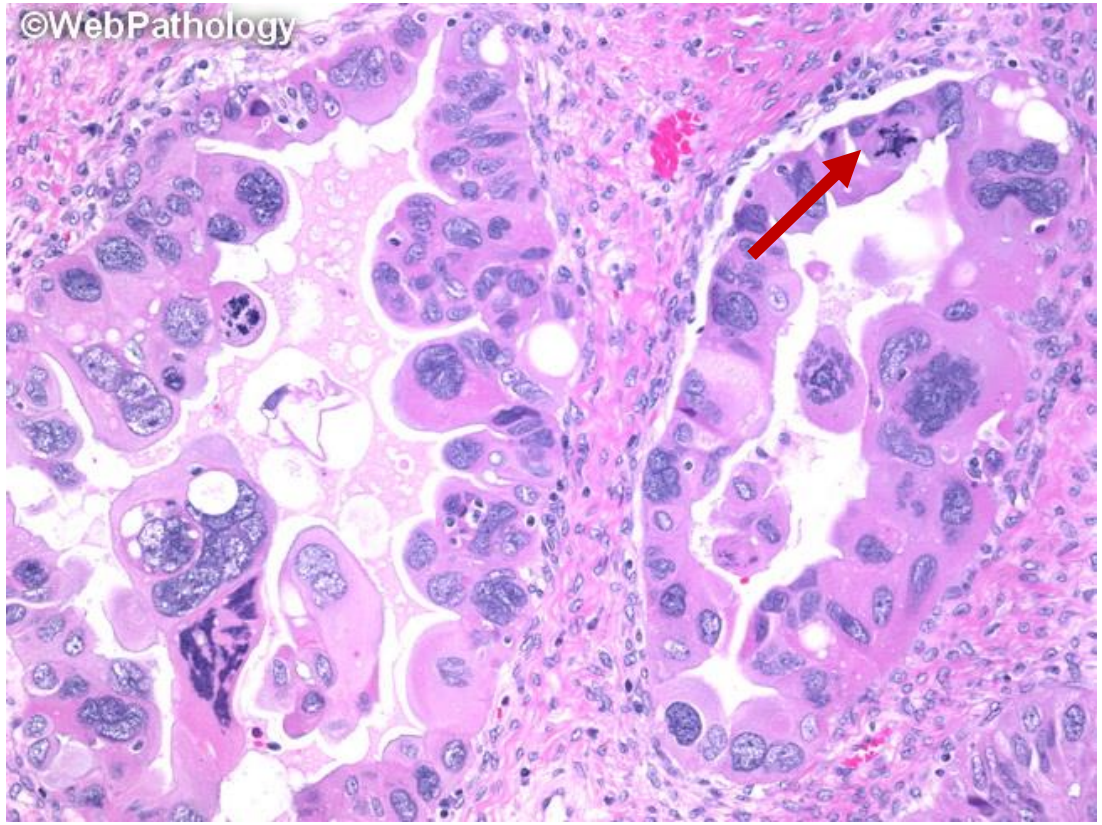




- Usually bilateral, large and exophytic
- Demonstrate solid and papillary growth, with fluid-filled cysts
- Solid areas are tan to white, frequently display necrosis
- Fallopian tube is commonly embedded within the ovarian tumor
- Extensive extraovarian involvement

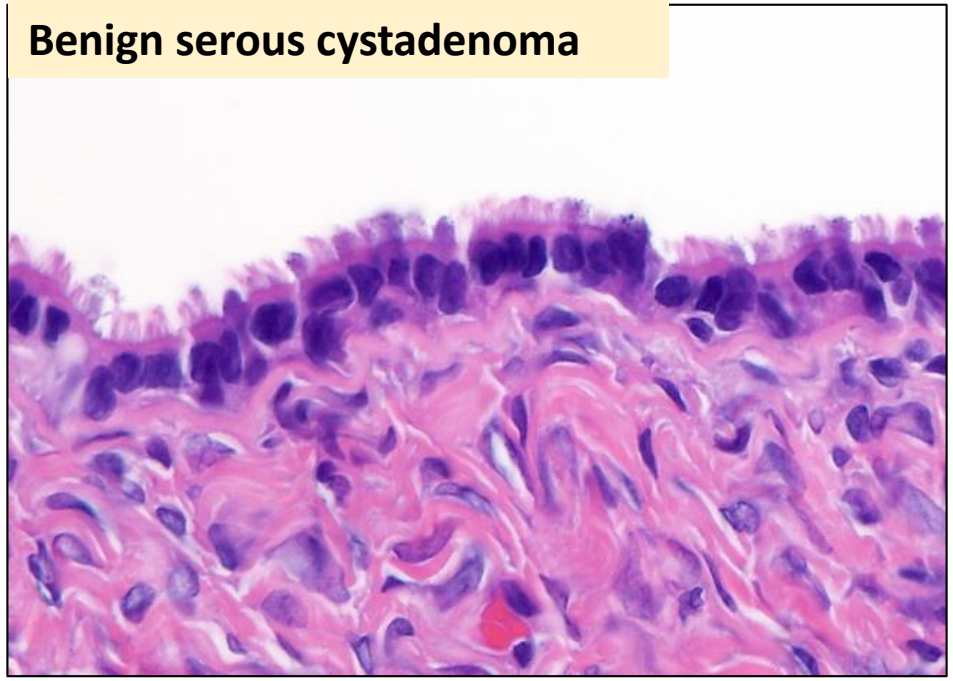
High-grade Serous Carcinoma: Microscopic



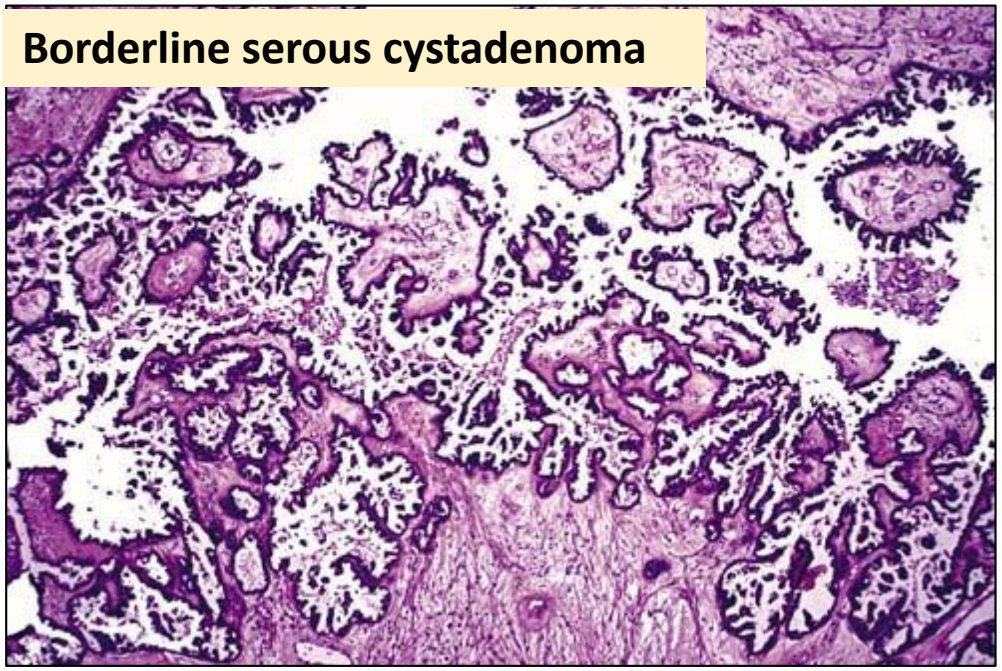


- Solid, papillary, slit-like spaces, glandular or cribriform architecture. Necroses are common
- Nuclei are large and markedly atypia
  - Nuclear size variability of > 3 folds. Multinucleation
  - High mitotic activity with atypical mitoses (red arrow)

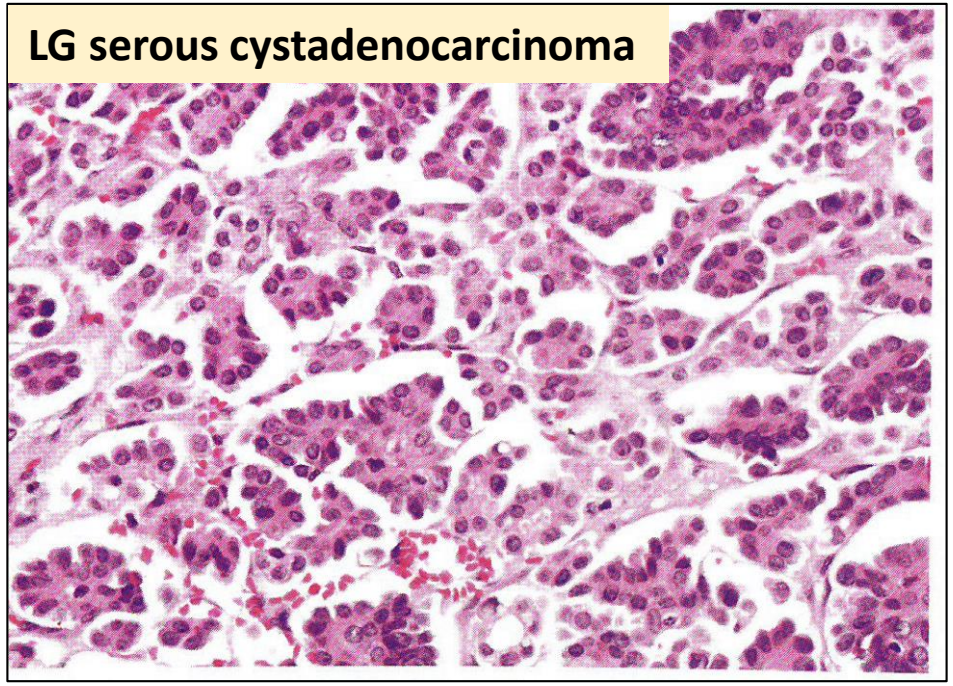
Benign serous cystadenoma



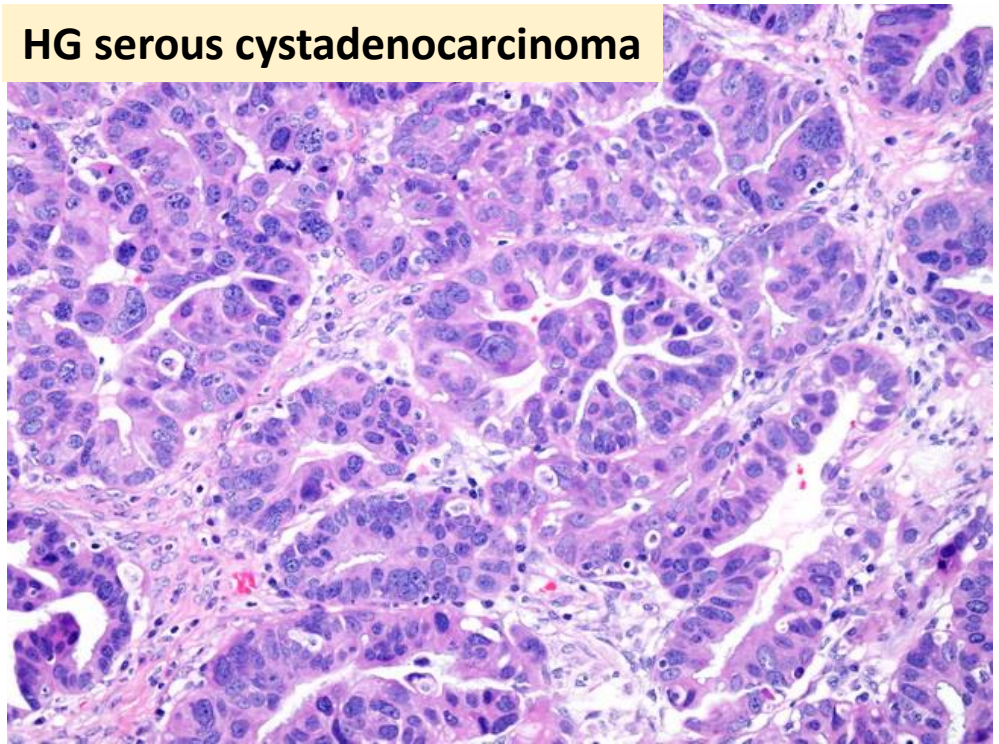
Borderline serous cystadenoma



LG serous cystadenocarcinoma



HG serous cystadenocarcinoma



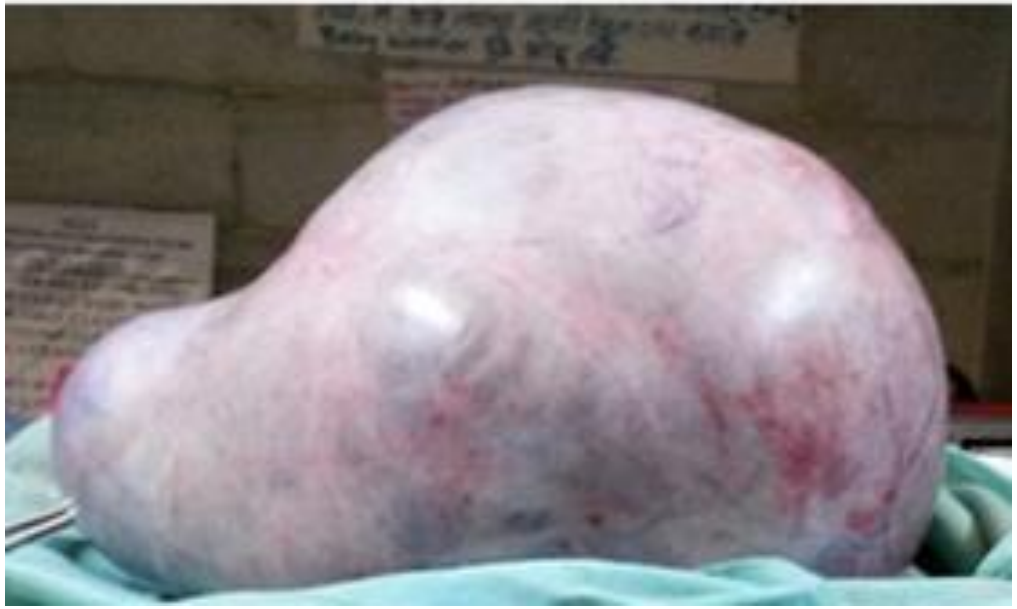
2. MUCINOUS TUMORS

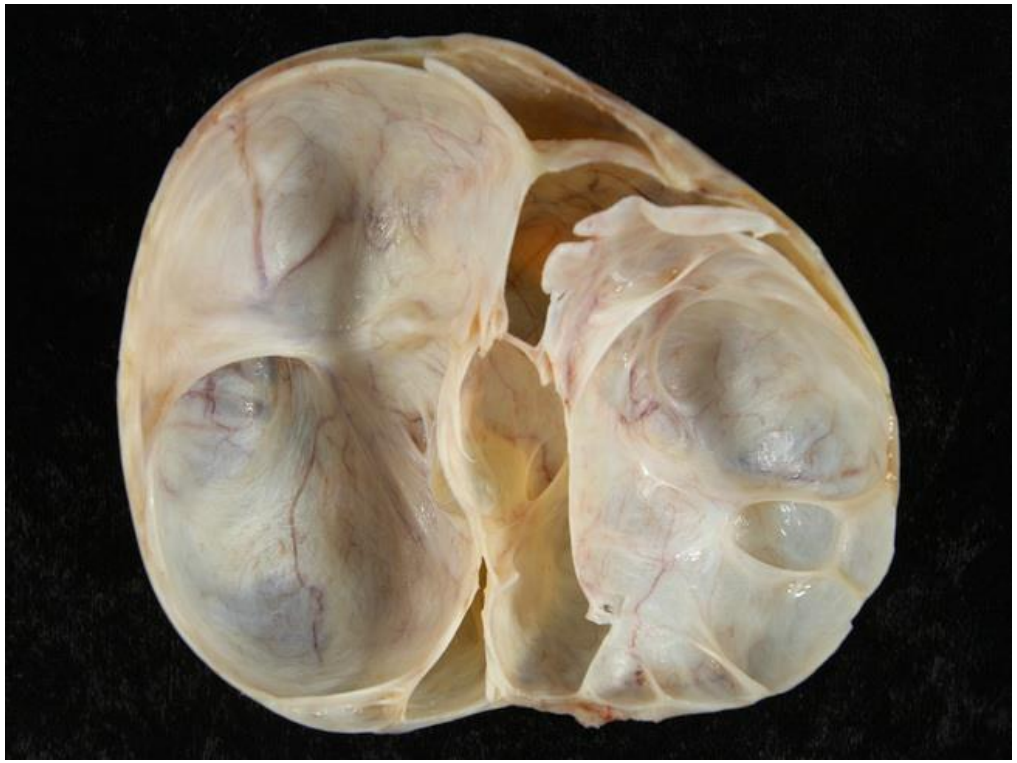
- Accounts for about **20-25%** of all ovarian neoplasms
- Divide into
  - Benign mucinous tumour/mucinous cystadenoma (majority)
  - Borderline mucinous tumors
  - Mucinous carcinomas (~ 3%)
- Occur principally in middle adult life
  - Rare before puberty / after menopause
- Mutations of **KRAS proto-oncogenes** is consistent genetic alteration in all mucinous tumors of the ovary

Mucinous cystadenoma

MACROSCOPIC APPEARANCE:

- Mostly unilateral; rarely bilateral (5%)
- Tends to produce **larger** cystic masses
- Surface of the ovary is rarely involved
- Multiloculated tumors filled with **sticky, gelatinous fluid rich in glycoproteins**
- Some tumours may rupture and can be associated with adhesions

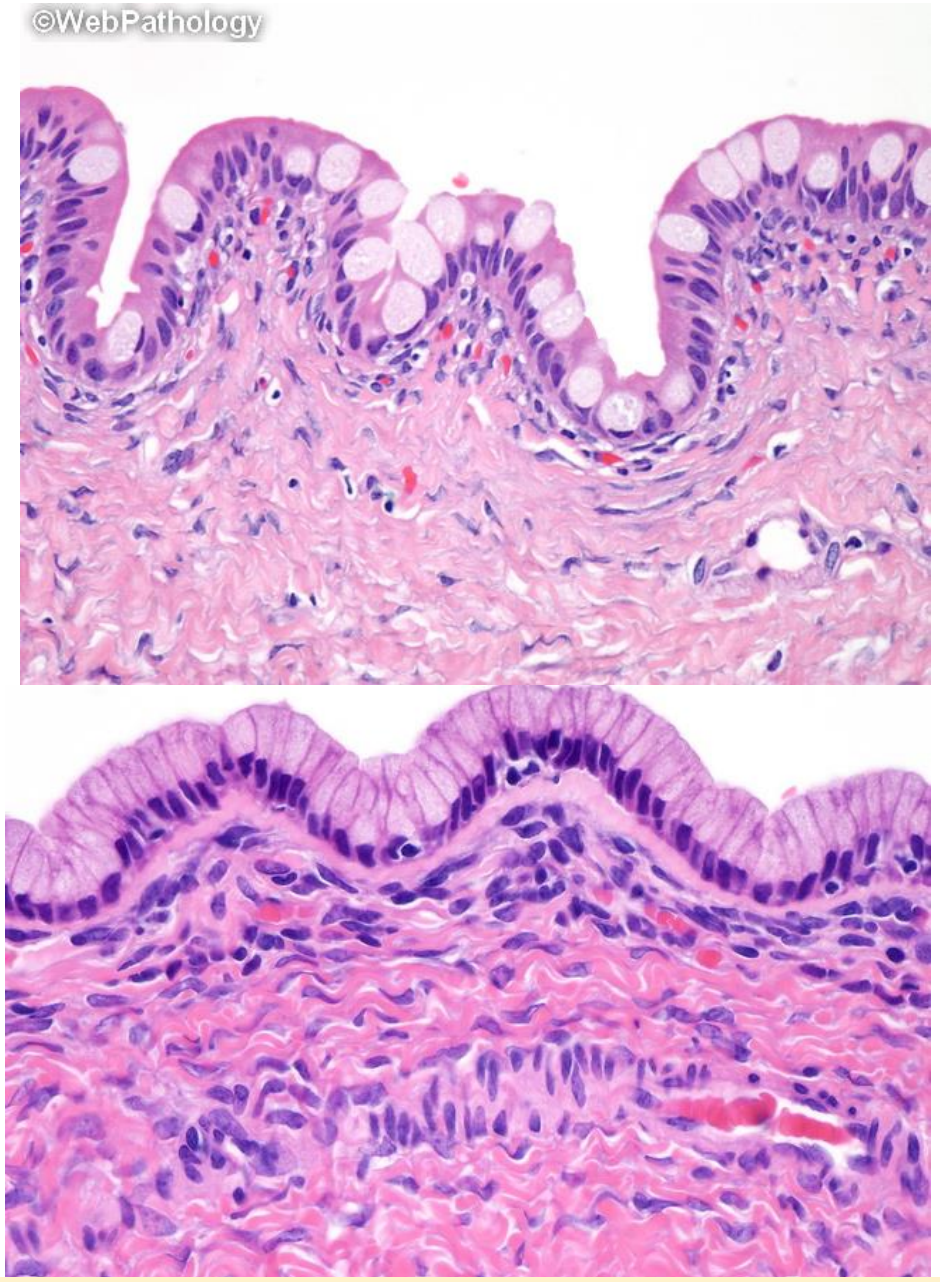




Mucinous cystadenoma

MICROSCOPIC APPEARANCE:

- Composed of multiple cysts and glands lined by simple non-stratified mucinous epithelium resembling Mullerian, gastric folveolar-type, or intestinal epithelium containing goblet cells.
- Nuclei are small and basally located.
- Absence of cytological atypia
- Absent / minimal mitotic activity and apoptotic body



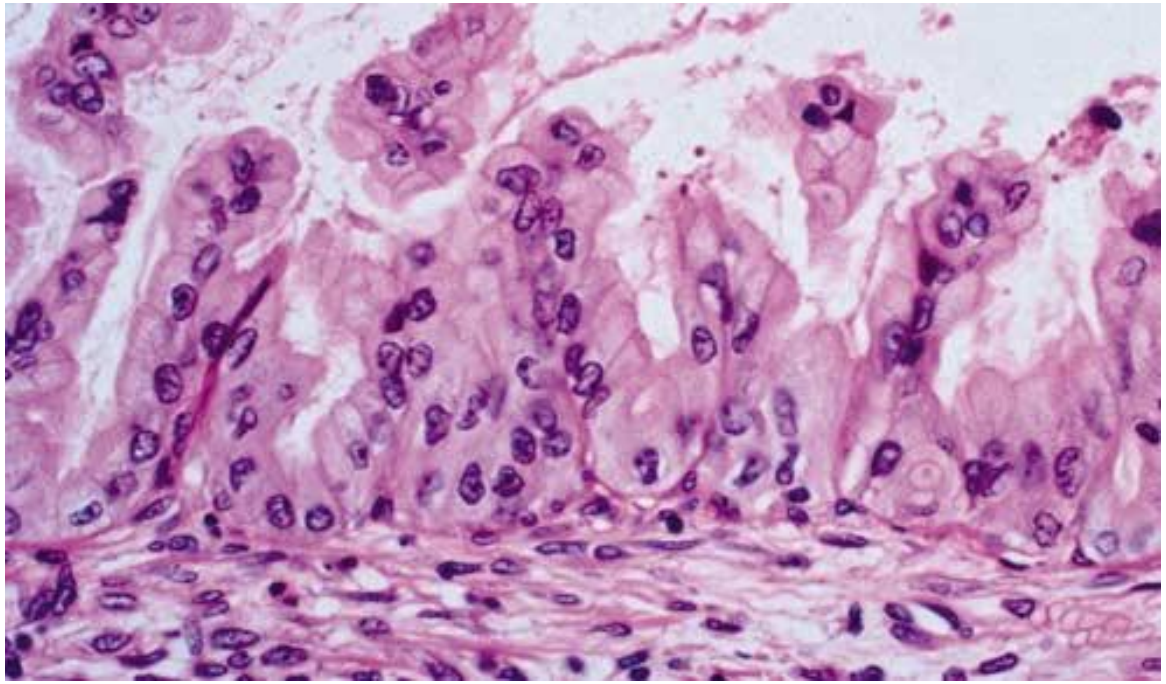
Cyst wall is lined by simple, non-stratified columnar epithelium with basally-located hyperchromatic nuclei and resembles **gastric foveolar epithelium**

Self study

Mucinous Borderline Tumor

MICROSCOPIC APPEARANCE:

- Multiple cysts lined by gastrointestinal type mucinous epithelium showing variable degree of stratification, tufting or villous papillae
- **Epithelial proliferation must be > 10%** of the epithelial volume for a tumor
- Mitotic activity can be present predominantly in crypts, less prominent on luminal surfaces
- Might have microinvasion
  - Small foci of stromal invasion, measuring < 5mm



Proliferating epithelial cells in a mucinous borderline tumor of intestinal type have slight-to-moderate nuclear atypia.

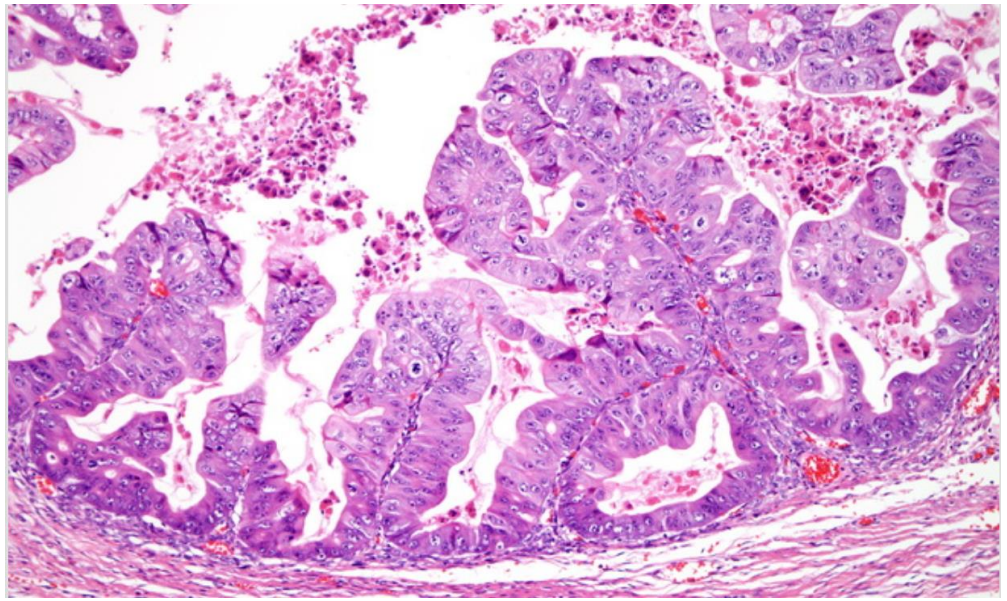
Mucinous Carcinoma

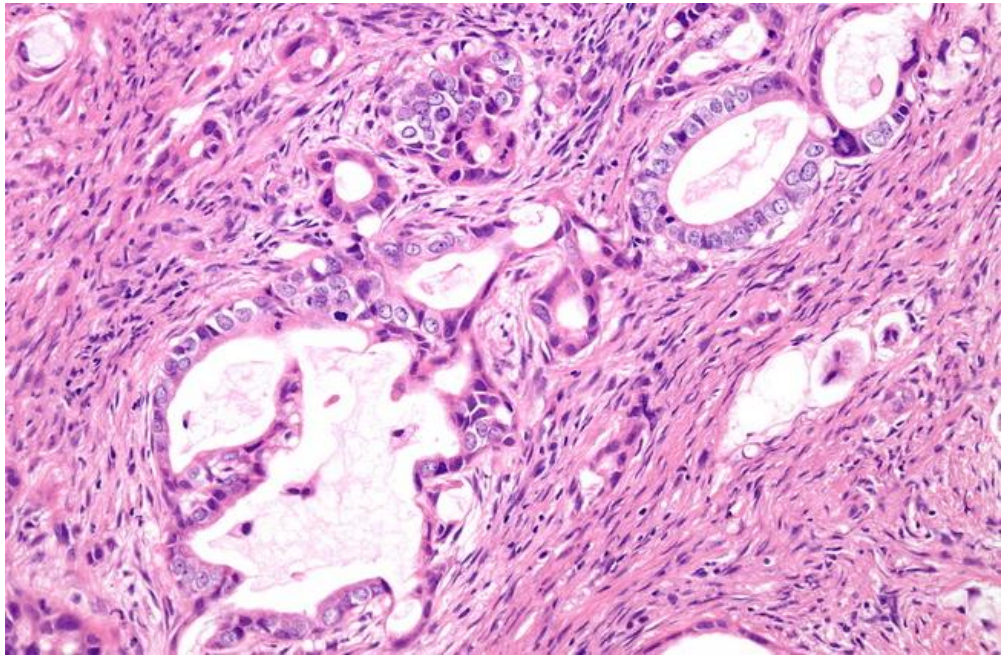
- Invasive mucinous neoplasm composed of gastrointestinal-type epithelium

MICROSCOPIC APPEARANCE:

2 patterns of invasion:

- **Expansile / confluent pattern**
  - Confluent glandular growth with “expansile” invasion
  - Marked glandular crowding with little / absent intervening stroma
- **Infiltrative / destructive pattern**
  - Irregular gland, nests and single cells with malignant cytological features, often in desmoplastic stroma

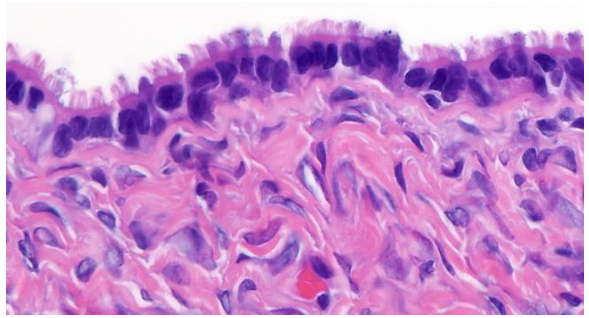


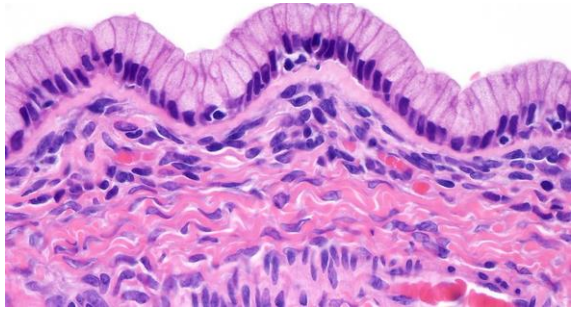


Mucinous carcinoma with **destructive stromal invasion**

Serous tumors vs Mucinous tumors

	Serous Tumors	Mucinous Tumors
Frequency	Benign varieties about equal Malignant types predominantly serous	
Bilateral involvement	50%	5%-benign,20%-malignant
Size	Moderate	Often huge
Character of fluid	Transudate	Slimy, viscid
Malignant potential	High %	Low %
Tendency to metastasize	High %	Low %
Mircoscopic features	Cuboidal	High columnar, basally situated nucleus
Cilia	Often present	Never present
Psammoma bodies	Frequent in well-differentiated types	Never present





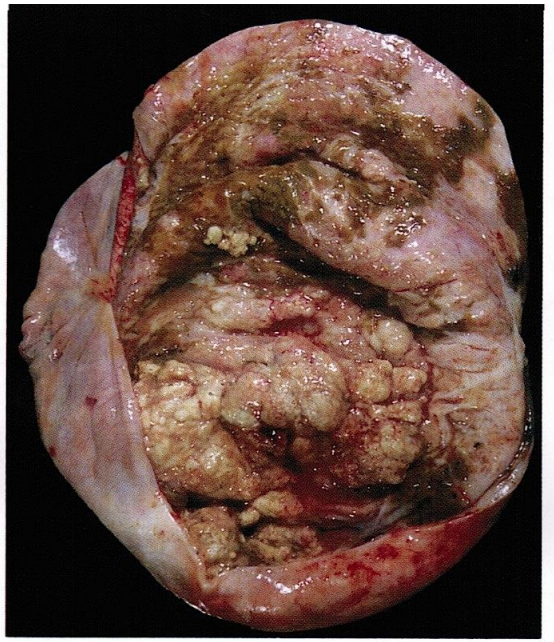
3. ENDOMETRIOID OVARIAN TUMORS

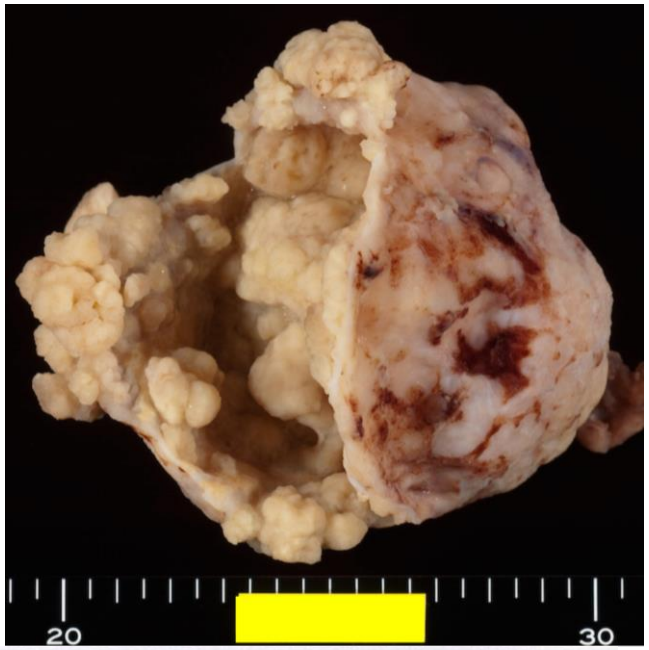
- Ovarian endometrioid carcinoma accounts for ~ 10 to 15% of all ovarian cancers.
  - 15 – 30% are accompanied by carcinoma of the endometrium
  - 15 – 20% coexists with endometriosis

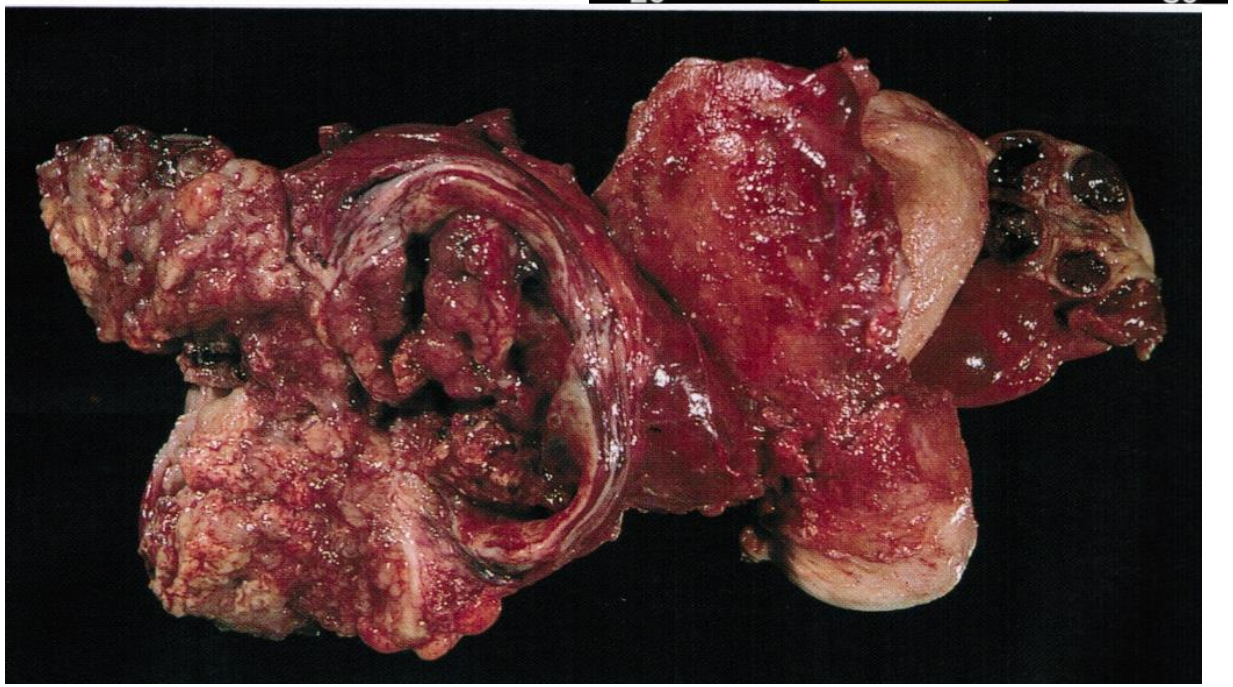
- Both endometriosis and endometroid carcinoma shared similar mutations:
  - Alterations that increase **PI3K / AKT** pathway signaling → Mutations in PTEN, PIK3CA, ARID1A, and KRAS
  - Mutations in mismatch DNA repair genes
  - TP53 mutations are common in poorly differentiated tumors

Endometrioid Carcinoma

- **<u>MACROSCOPIC APPEARANCE</u>:**
- Usually unilateral and large (mean size: 11cm)
- Smooth outer surface
- Solid and cystic cut surface
- Haemorrhage or necrosis may be extensive
- If arising in an endometriotic cyst, the tumors form a polypoid nodule projecting into the lumen of blood-filled cyst.







Endometrioid Carcinoma

MICROSCOPIC:

- Resembles endometrial cavity endometrioid adenocarcinoma
  - **Back-to-back glands** with confluent or cribriform growth
  - Complex villoglandular, papillary, or Labyrinthine glands
- The glands are lined by endometrioid epithelium and have smooth luminal borders.
- Nuclei are round to oval, with open chromatin and low to moderate cytological atypia.
- Squamous metaplasia (morules), can be seen
- Components of benign / borderline endometrioid adenofibroma is sometimes present.

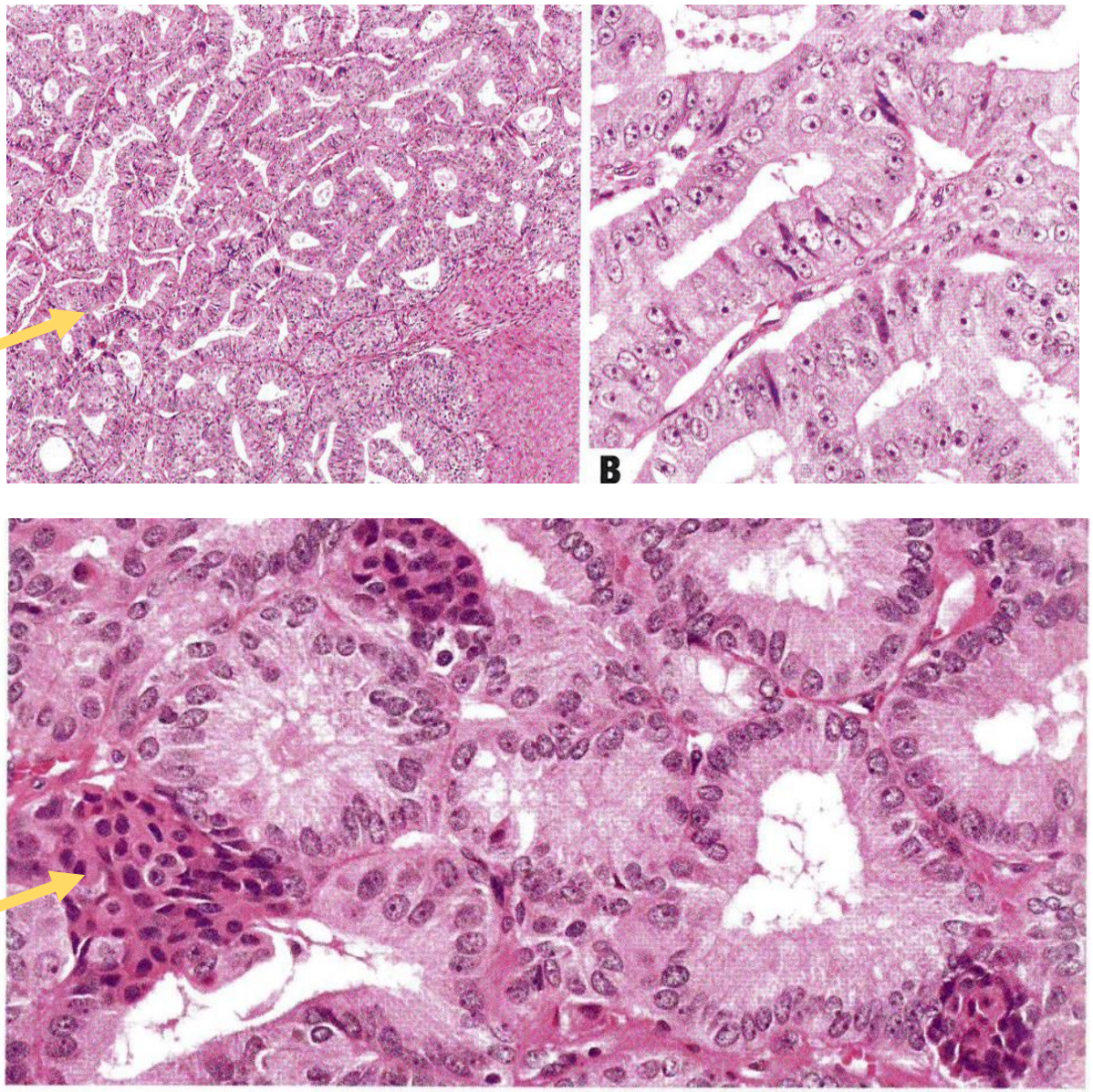
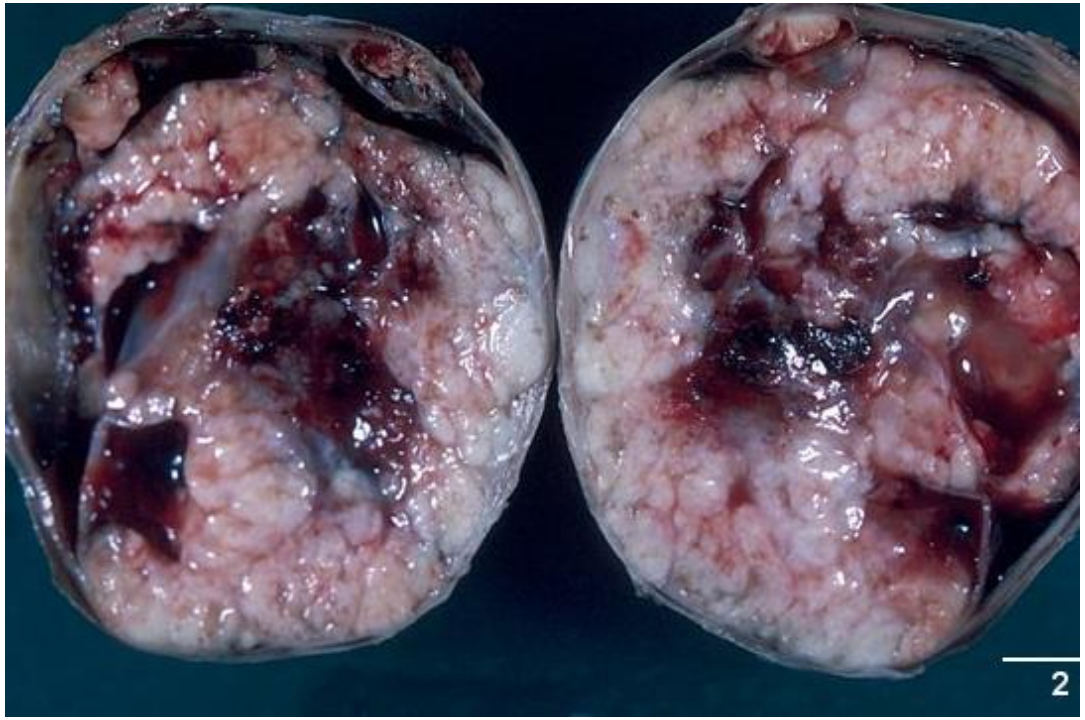


Fig. 1.41 Endometrioid carcinoma. The lining cells exhibit abundant cytoplasm and

4. CLEAR CELL CARCINOMA

- Composed of large epithelial cells with abundant clear cytoplasm.
- Sometimes occur in a/w endometriosis
- a/w paraneoplastic hypercalcemia and venous thromboembolism



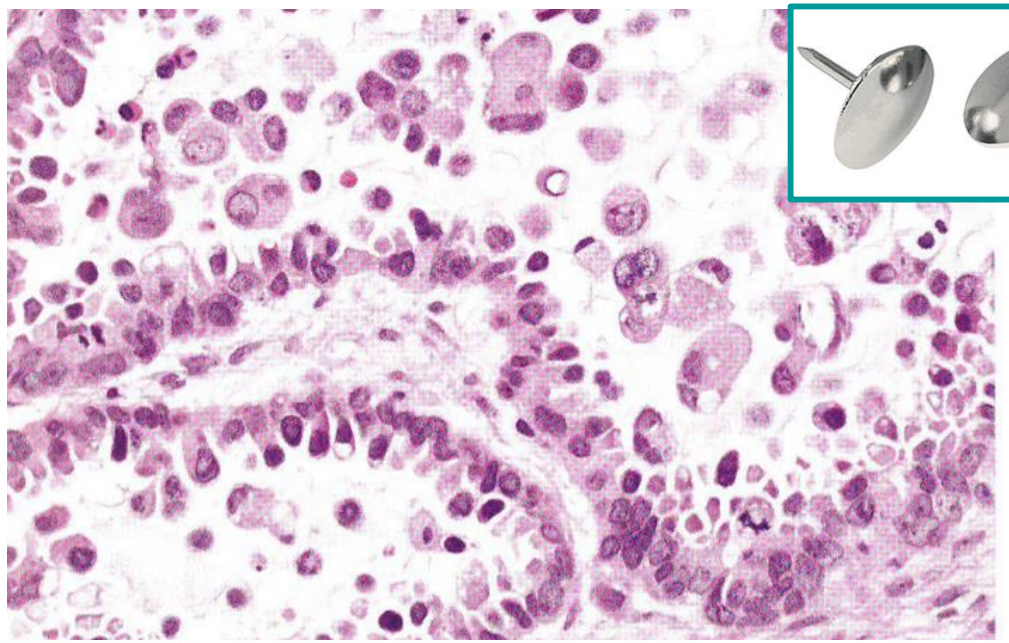
MACROSCOPIC:

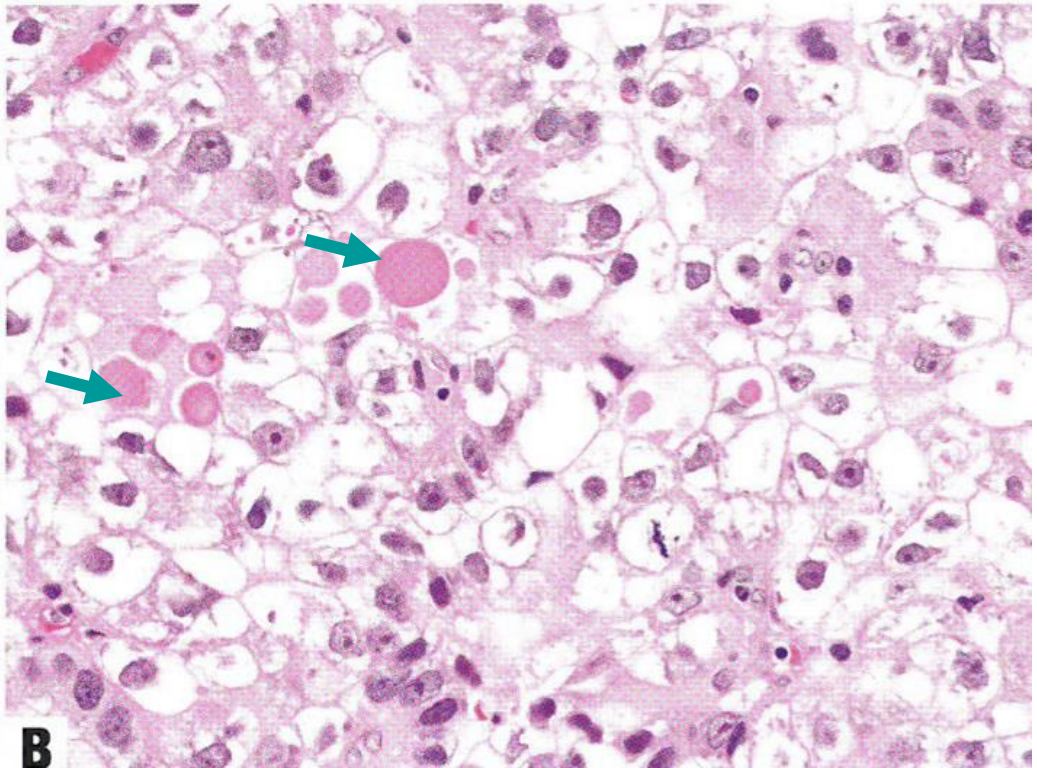
- Typically unilateral
- Mean size: 13cm
- Cut surface varies from solid, solid-cystic, to mainly cystic with fleshy, pale-yellow.
- The cyst lumen contains serous or mucinous fluid or chocolate-coloured material

Clear Cell Carcinoma

MICROSCOPIC APPEARANCE:

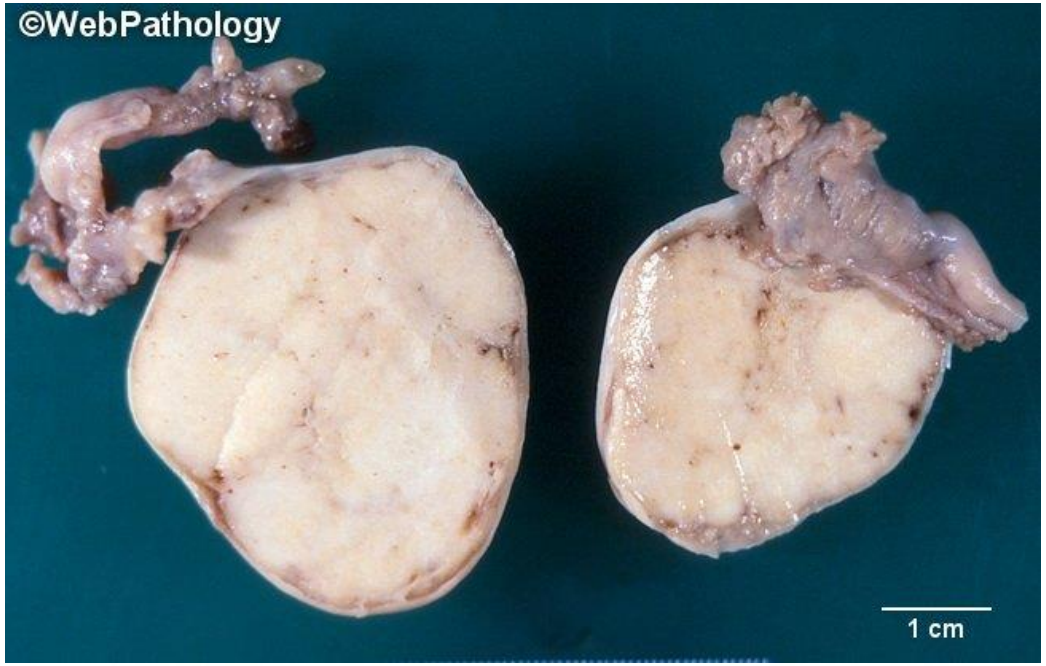
- Clear cell morphology:
  - Clear or eosinophilic granular cytoplasm
  - Angulated, pleomorphic, hyperchromatic nuclei, with prominent nucleoli
  - Hobnail cells
- Varied architecture: Papillary, tubulocystic, glandular, or solid sheets
- Eosinophilic hyaline globules may be seen (arrow)
- Low mitotic index

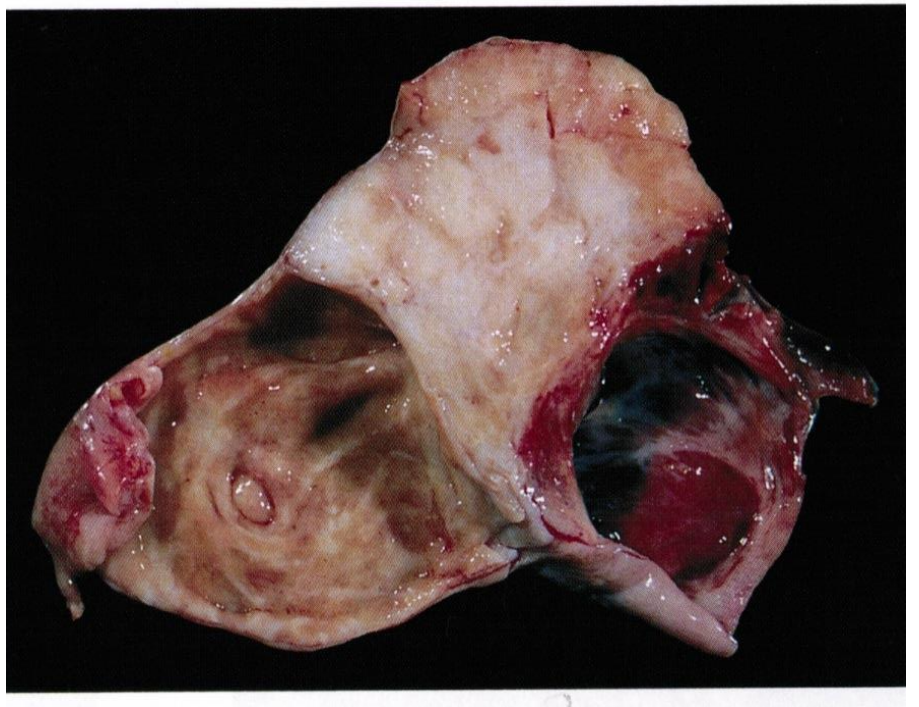




5. BRENNER TUMORS / TRANSITIONAL CELL TUMORS

- Benign
  - Neoplastic epithelial cells resembling urothelium
  - ~ 10% of ovarian epithelial tumors
  - Majority arise in adults in the 5th to 6th decade of life
- Borderline Brenner tumors
- Malignant Brenner tumors





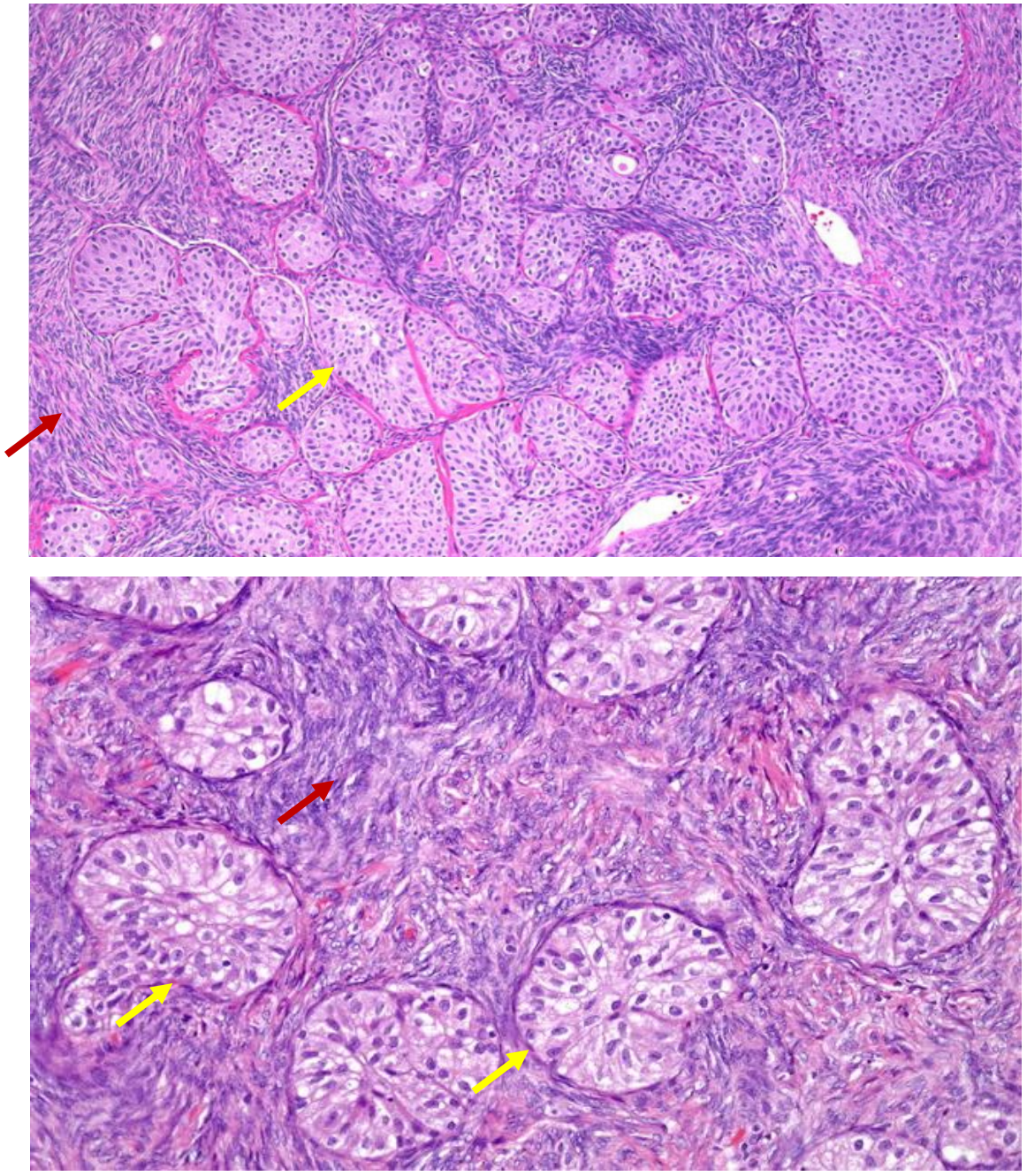
<u>MACROSCOPIC APPEARANCE</u>:

- Typically unilateral (90%), solid or cystic
- size from < 1cm-20-30cm
- Well-circumscribed, firm rubbery consistency.
- Greyish-white / yellow cut surface.

Brenner Tumor

MICROSCOPIC APPEARANCE:

- Composed of small oval to irregular nests of bland transitional / urothelial epithelium (yellow arrow) in dense fibromatous stroma (red arrow).
- Cytological features: uniform oval cells with pale cytoplasm, nuclei with occasional grooves, fine chromatin and small nucleoli.
- Mucinous differentiation can be common
- Calcifications common



NEOPLASTIC OVARIAN TUMOURS

SURFACE EPITHELIAL TUMORS

- Serous Tumors
- Mucinous Tumors
- Endometrioid Ovarian Tumors
- Clear Cell Carcinoma
- Brenner Tumors

GERM CELL TUMORS

- Teratoma
- Dysgerminoma
- Choriocarcinoma
- Yolk sac carcinoma
- Embryonal carcinoma

SEX CORD - STROMAL TUMORS

- Granulosa Cell Tumors
- Fibromas, Thecomas, Fibrothecomas
- Sertoli-Leydig Cell Tumors

METASTATIC TUMOUR

GERM CELL TUMORS

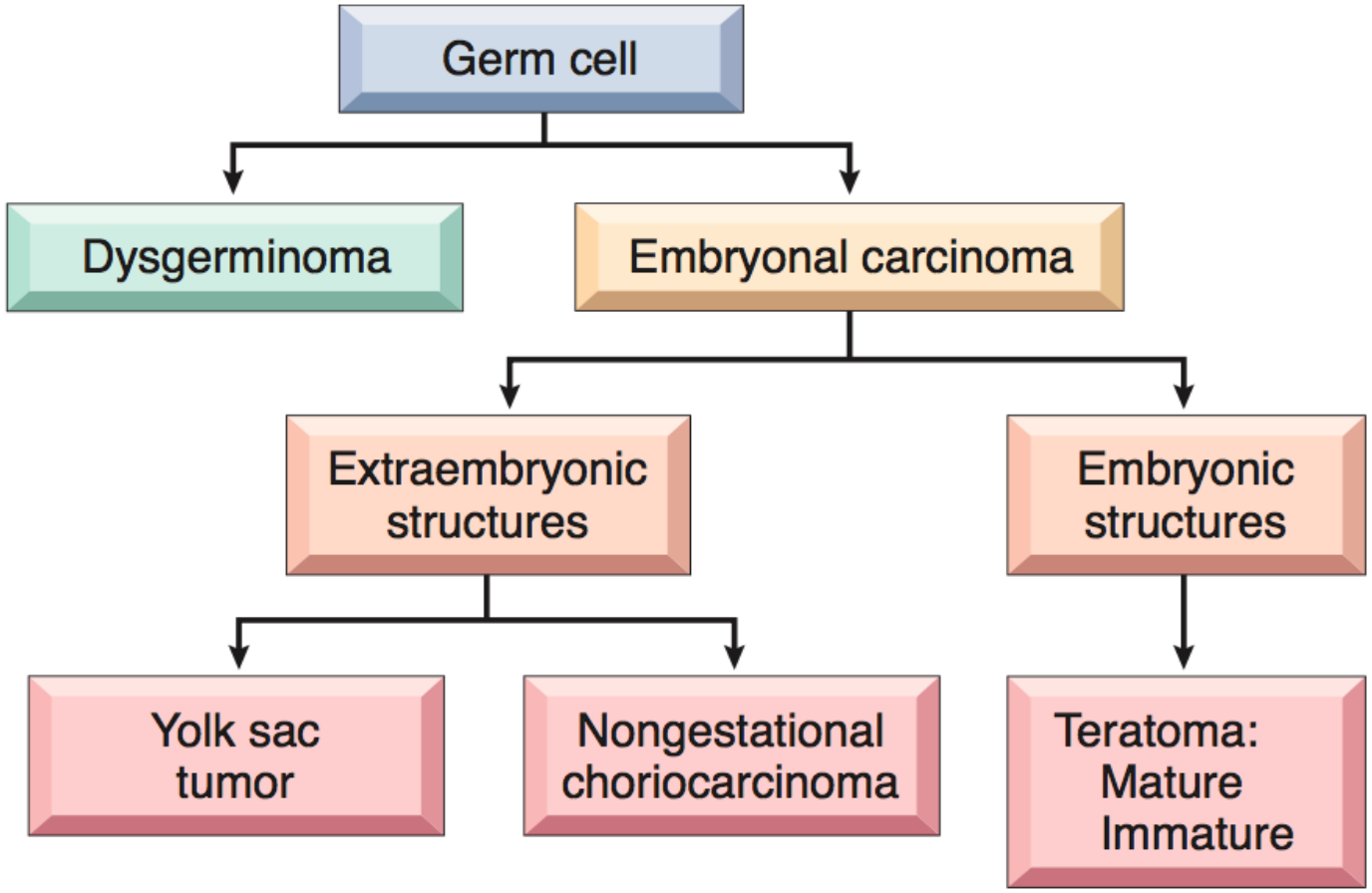


Figure 22.37 Histogenesis and interrelationships of ovarian tumors of germ cell origin.

- Accounts for 15-20% of all ovarian tumors
- Most are **benign cystic teratomas**

1. TERATOMA

Teratomas are divided into 3 categories:

1. Mature (benign) teratoma
2. Immature (malignant) teratoma
3. Monodermal / highly specialized teratoma

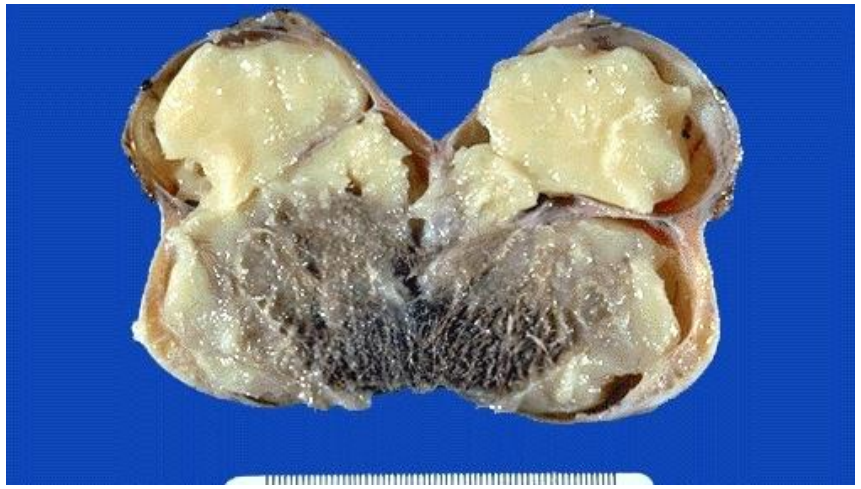
Mature (Benign) Teratomas

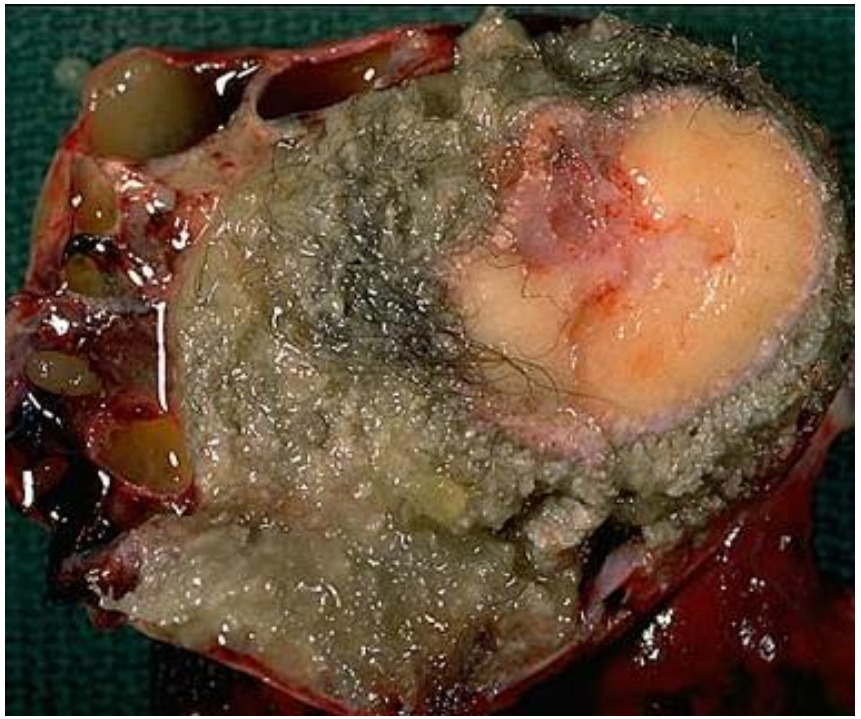
- A tumor composed exclusively of mature tissues from **2 or 3 germ layers** (ectoderm, mesoderm, and / or endoderm)
- Account for 20% of all ovarian neoplasms
- Often referred as **dermoid cyst** – almost always lined by skin-like structures
- Most cases occur in women of reproductive age
- 1% undergo malignant transformation, most commonly to squamous cell carcinoma and rarely thyroid carcinoma, melanoma.

Mature (Benign) Teratomas

MACROSCOPIC APPEARANCE:

- Bilateral in 10-15%
- Usually 5-10cm
- Most are cystic, unilocular, containing sebaceous materials, hair and sometimes teeth or cartilage.
- Some can be solid, with interspersed cysts.

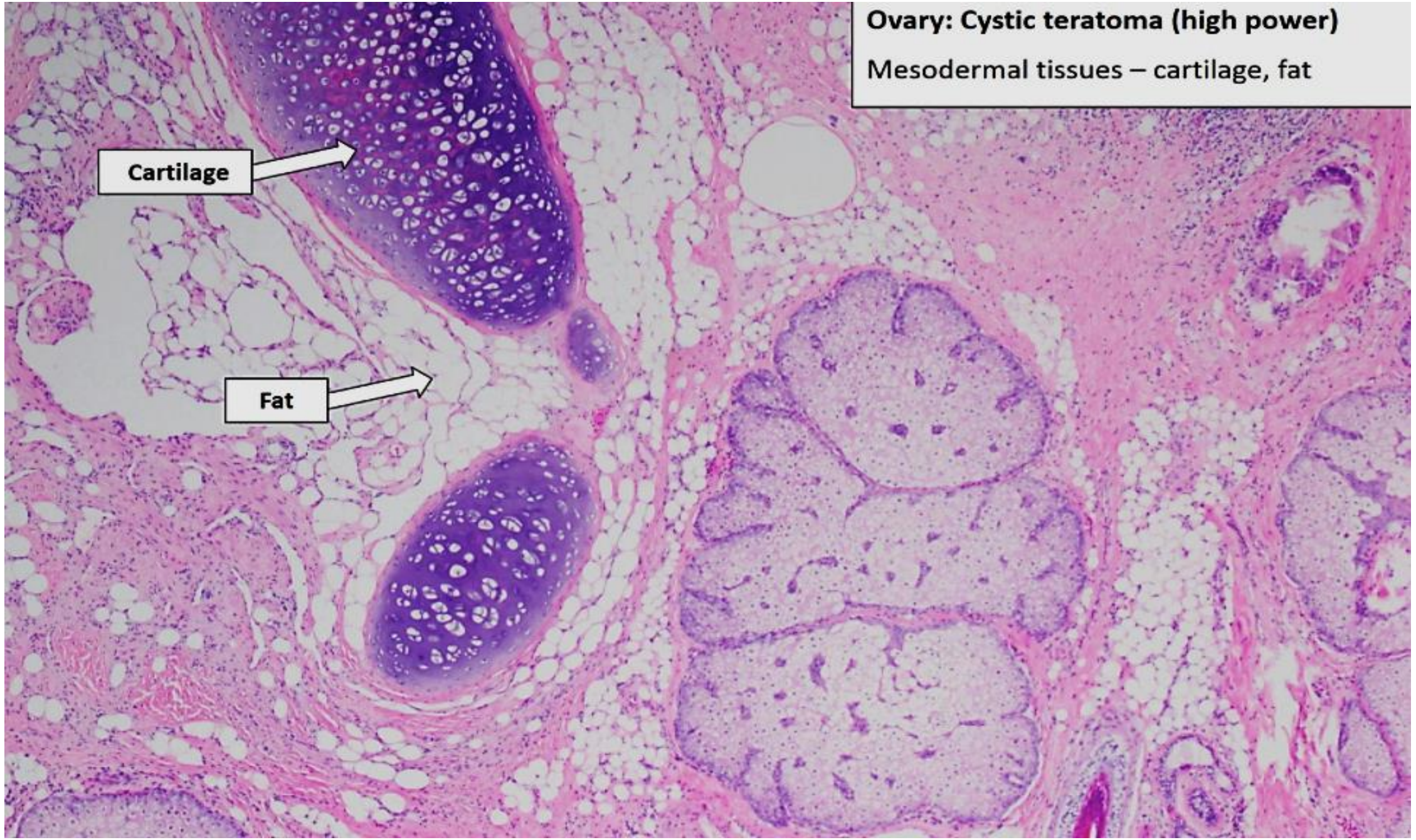


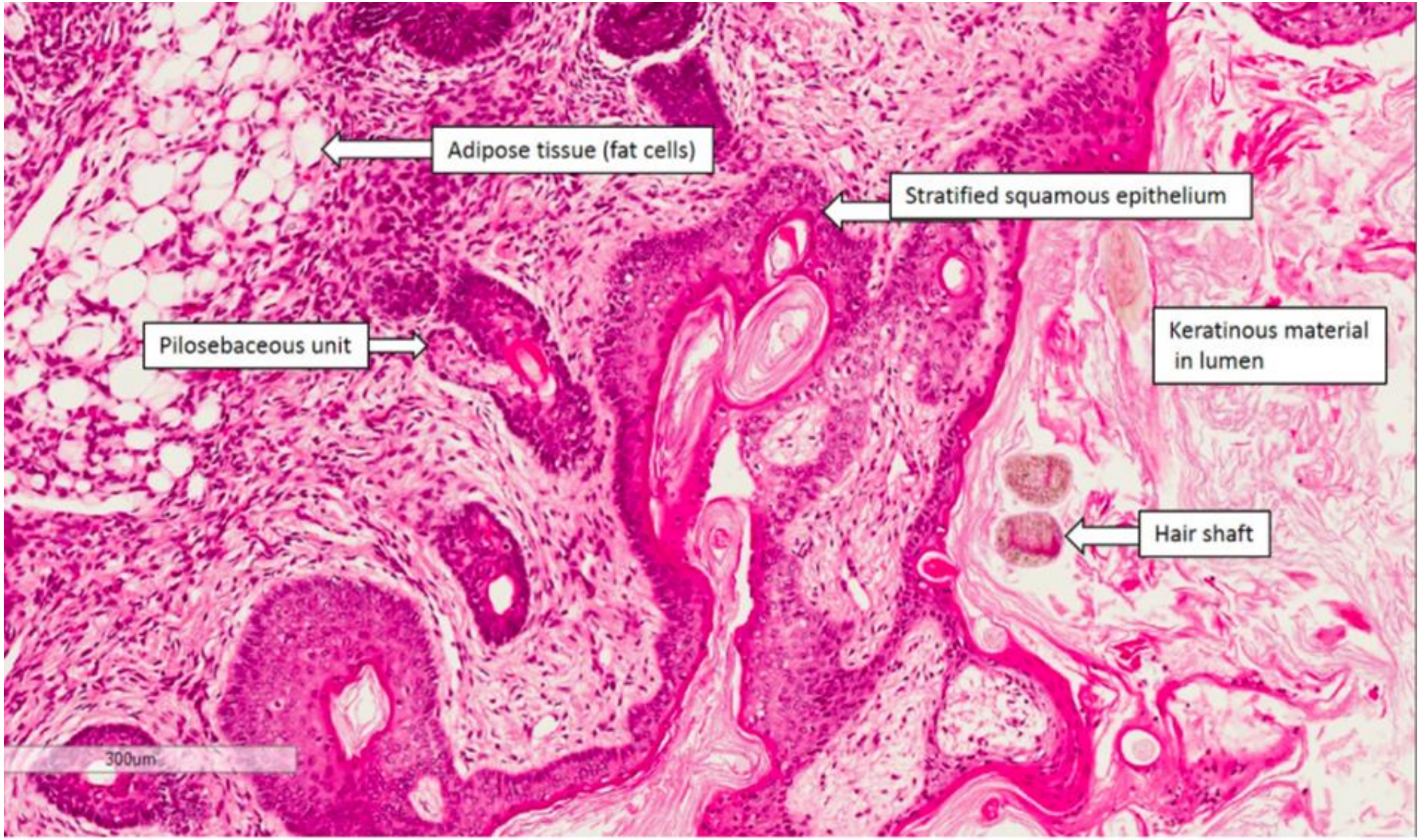


Mature (Benign) Teratomas

MICROSCOPIC APPEARANCE:

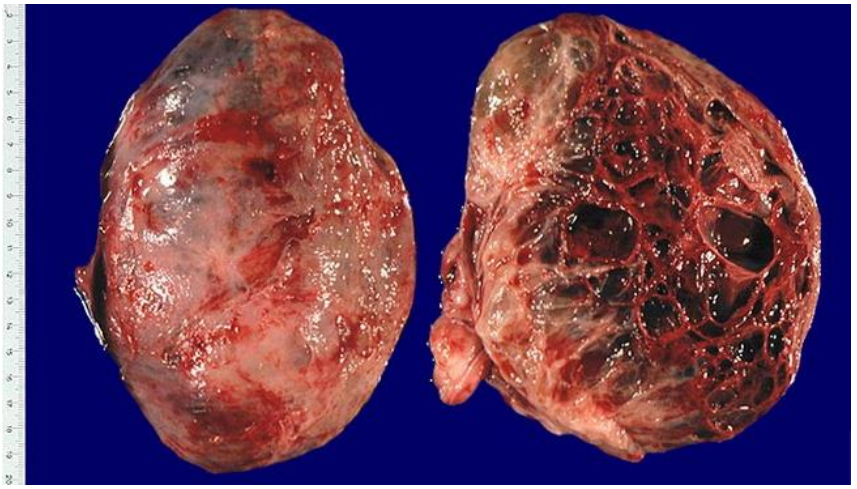
- Cyst wall is composed of stratified squamous epithelium with underlying sebaceous glands, hair shafts, and other adnexal structures (**ectodermal derivatives**)
- Tissues from other germ layers can be identified:
  - **Neuroectoderm** (glia, ependyma and cerebellum)
  - **Mesodermal derivatives** (adipose, bone, cartilage, and smooth muscle)
  - **Endodermal derivatives** (gastrointestinal and respiratory / bronchial epithelium, thyroid, salivary glands)
- No immature element


Ovary: Cystic teratoma (high power)
Mesodermal tissues – cartilage, fat
Cartilage
Fat


Adipose tissue (fat cells)
Stratified squamous epithelium
Pilosebaceous unit
Keratinous material in lumen
Hair shaft
300um

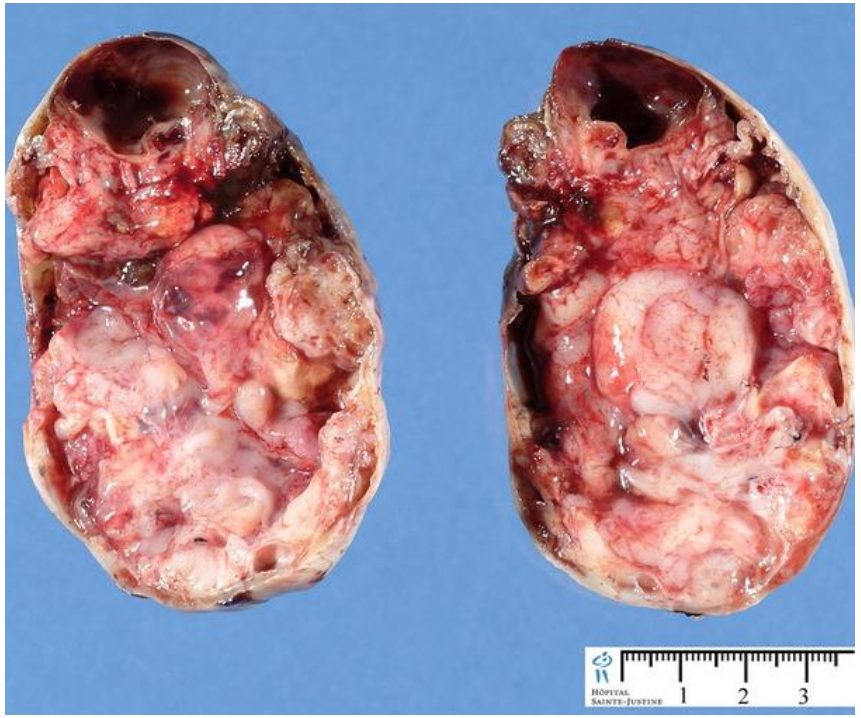
Immature (Malignant) Teratomas

- containing **immature** (resemble embryonal and immature fetal tissues) and variable amounts of mature tissues
- prepubertal adolescents and young women
- Grow rapidly, frequently penetrate the capsule and spread either locally / distantly.



MACROSCOPIC APPEARANCE:

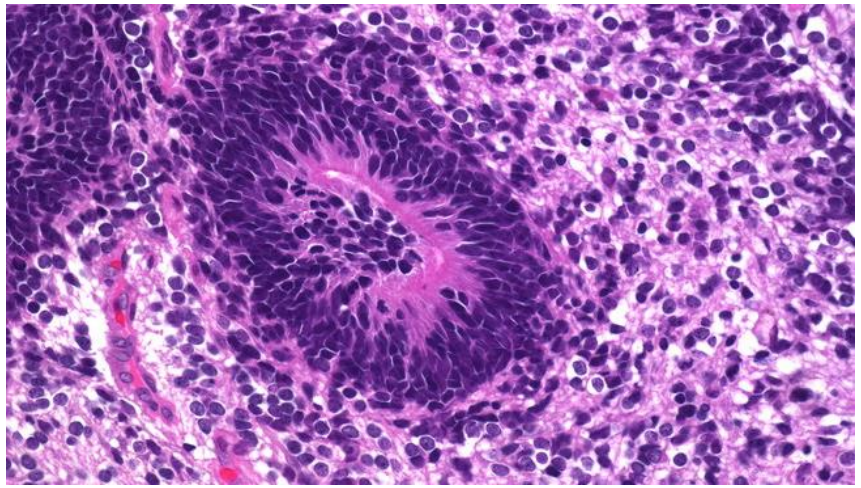
- Bulky, predominantly solid with few small fluid-filled cysts
- Solid components show variegated cut surfaces with areas of hemorrhage and necrosis (if present)
- Hair, sebaceous material, cartilage, bone and calcification may be present.

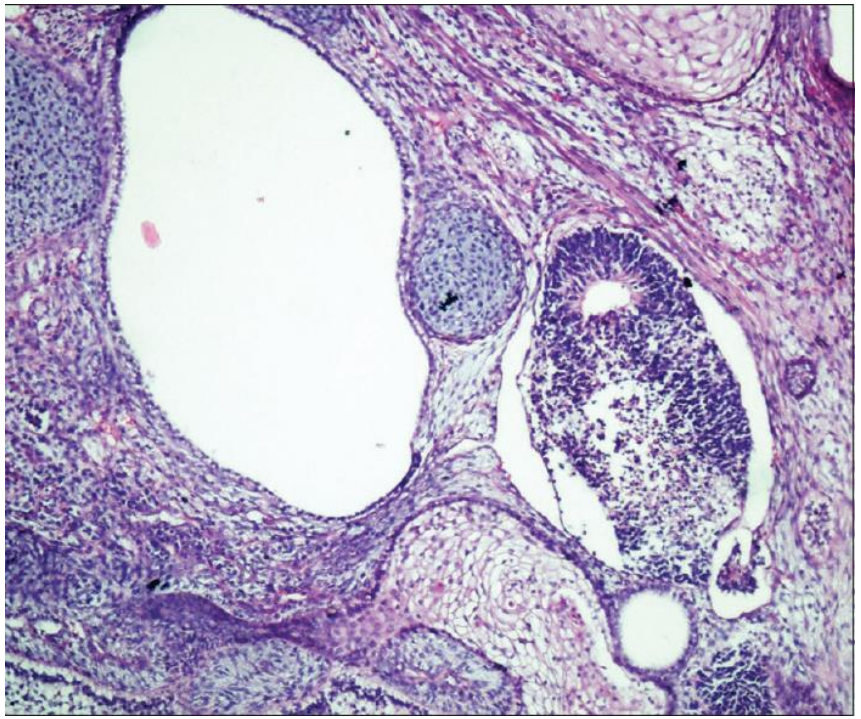


Immature (Malignant) Teratomas

MICROSCOPIC APPEARANCE:

- Haphazardly arranged immature tissues derived from ectoderm, mesoderm and endoderm mixed with mature elements
- **Ectoderm**: neuroectodermal tubules and rosettes, composed of mitotically active hyperchromatic cells.
- **Mesoderm**: Immature cartilage, muscles
- **Endoderm**: Tubules lined by columnar epithelium





Immature cartilage, immature neuroepithelial tissue with rosettes

Monodermal Teratoma

STRUMA OVARII:

- Most commonly occurs as part of a teratoma but may occasionally be encountered with serous or mucinous cystadenomas.
- May be functional and cause hyperthyroidism
- Presence of **mature thyroid tissues** (variably sized macro and microfollicles often containing colloid) comprising more than 50% of the overall mass.

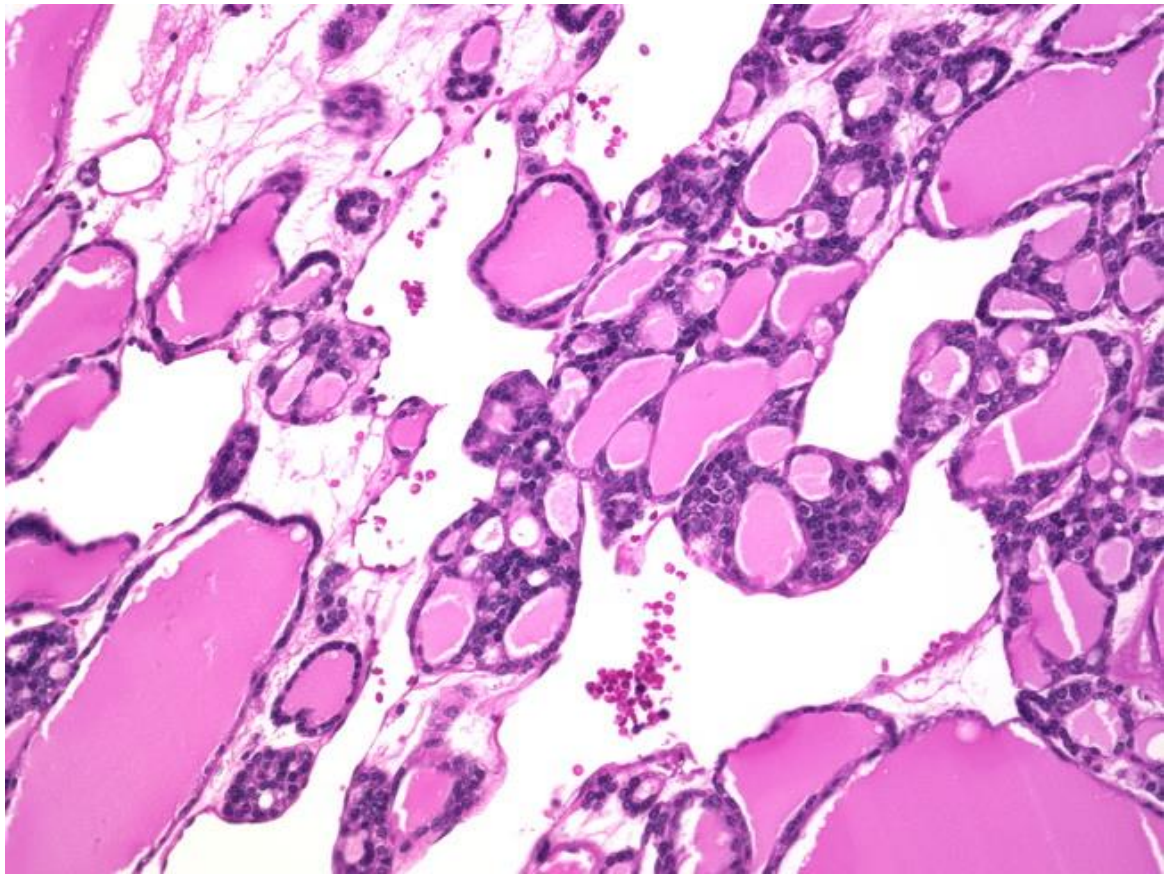


TABLE 18.3. Differences between mature and immature teratoma

Features	Mature teratoma	Immature teratoma
Component tissue	Mature	Immature
Age affected	Young women (reproductive age group)	Adolescents and young adults (before age 20)
Bilateralism	Bilateral in 10–15% cases	Mostly unilateral
Type	Mostly cystic (dermoid cyst)	Usually solid
Gross appearance	Unilocular cyst lined by the epidermis. Cyst may have areas of calcification, teeth, matted hair and sebaceous material	Predominantly solid with areas of necrosis and haemorrhage
Microscopy	• Cyst wall lined by mature stratified squamous epithelium with appendageal structures. • No immature elements/neuroepithelium seen	• Immature structures differentiating towards cartilage, glands, muscles, bones, neuroepithelium, etc., seen. Tissue resembles fetal or embryonic tissue rather than adult tissue. • Proportion of immature neuroepithelium in tumour determines the prognosis

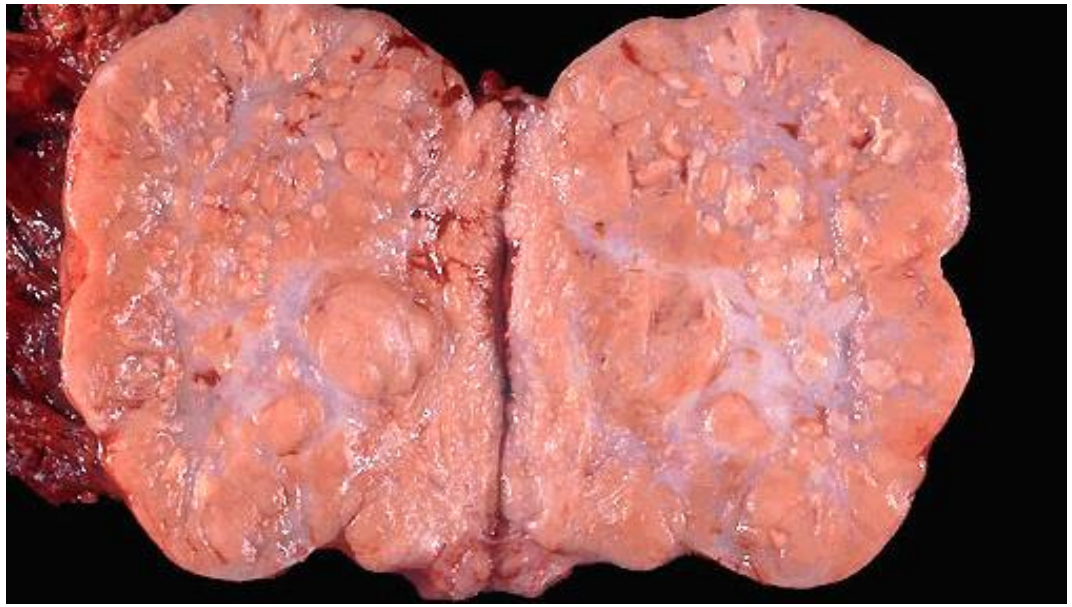
2. DYSGERMINOMA

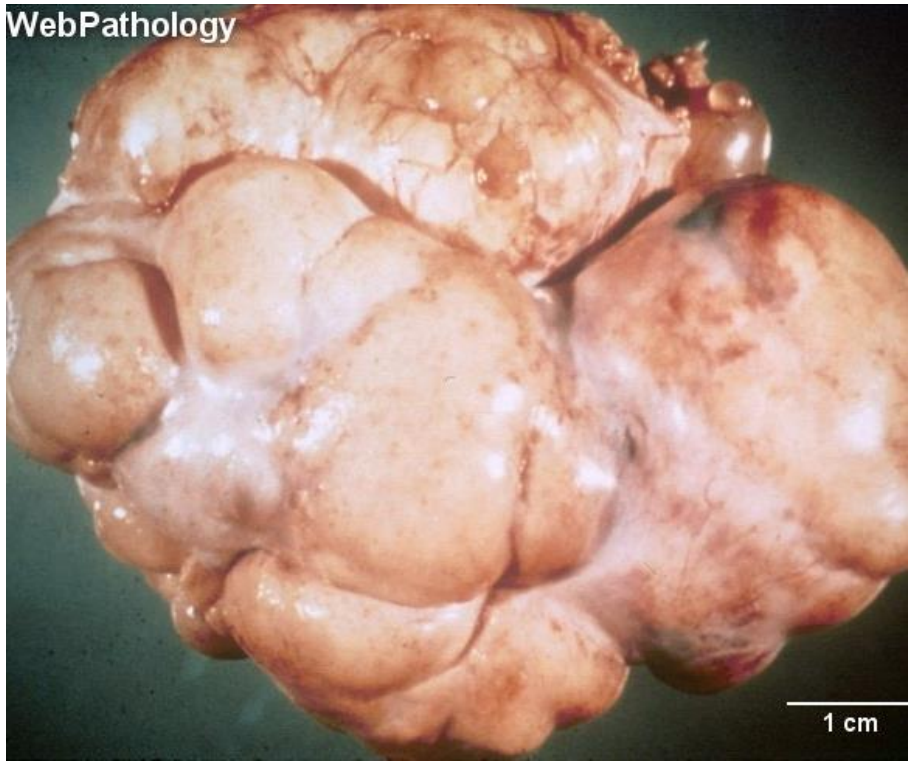
- **Primitive germ cell tumor** composed of cells showing no specific differentiation (the ovarian counterpart of testicular seminoma)
- Accounts of 2% of ovarian ca, roughly 50% of malignant ovarian GCTs
- 75% occur in 2nd and 3rd decades of life, childhood
- Genetic alterations:
  - Isochromosome 12p (80%)
  - KIT mutations (30-50%), KIT amplification (30%)
- All dysgerminoma are malignant
- Responsive to chemotherapy
- Overall survival > 80%

Dysgerminoma

MACROSCOPIC APPEARANCE:

- Most are unilateral tumors (80-90%)
- Size range from barely visible nodules to masses that virtually fill the abdomen
- Cut section shows solid yellow-white to gray-pink appearance, often soft and fleshy / lobulated
- Cystic degeneration, hemorrhage and necrosis may be present.

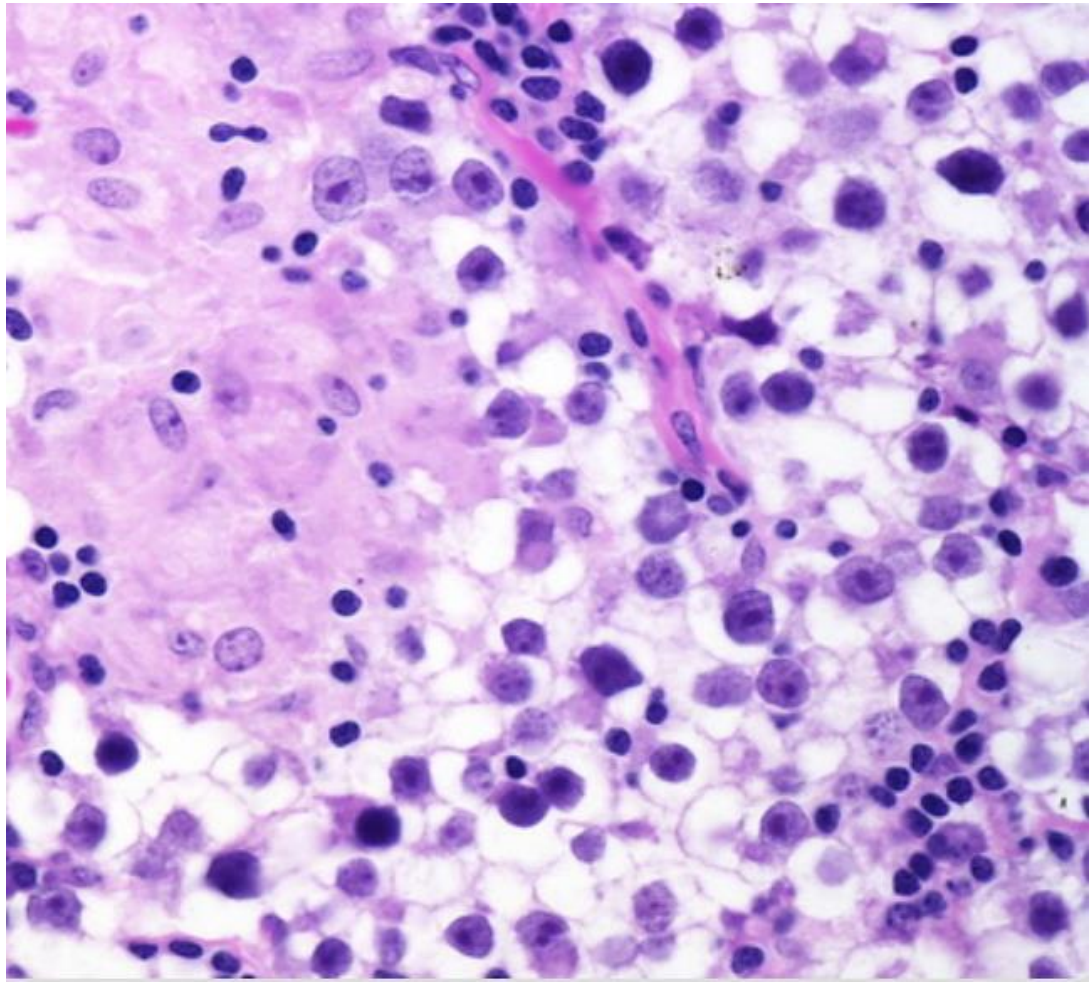


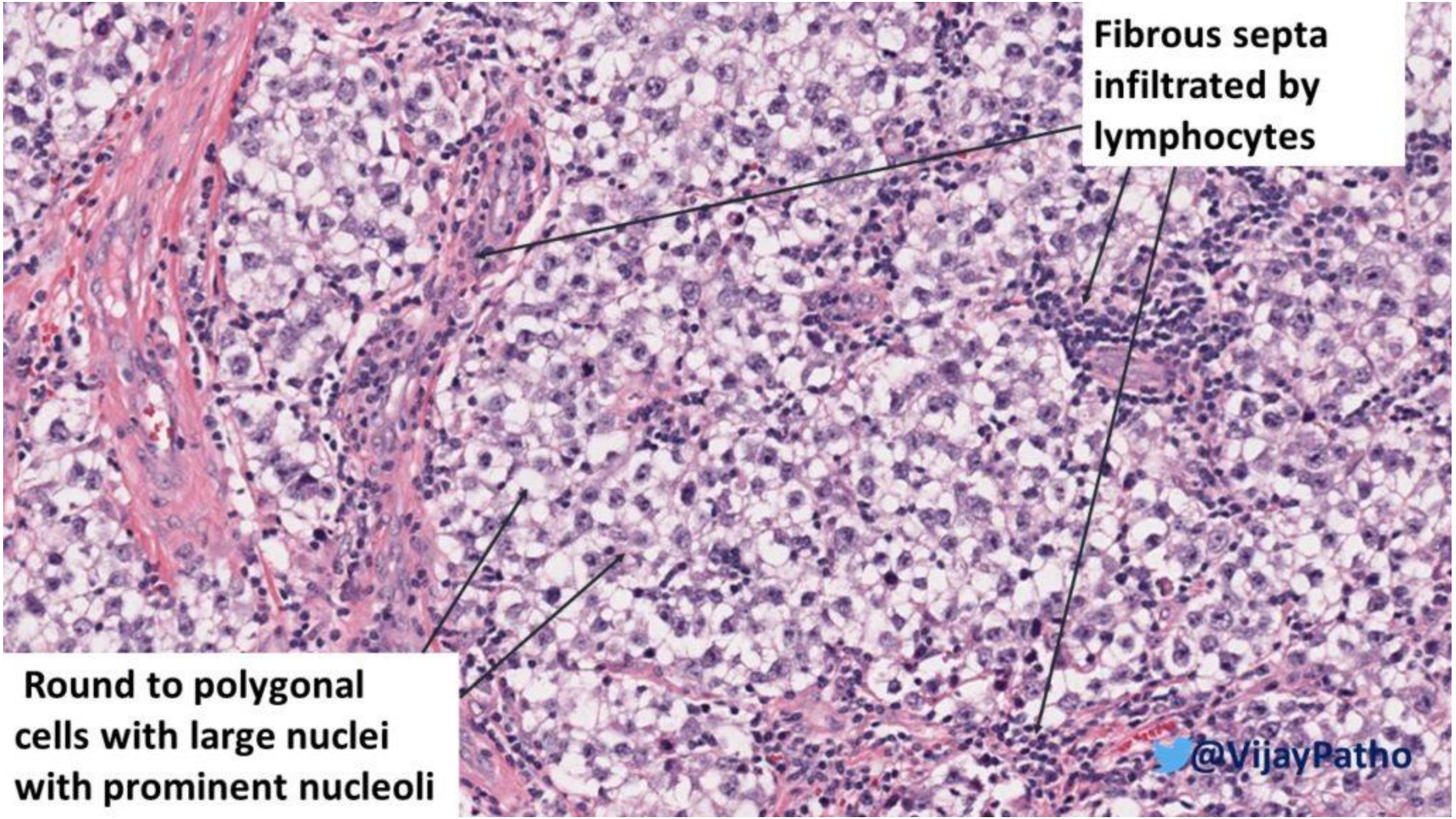


Dysgerminoma

MICROSCOPIC APPEARANCE:

- Sheets and nests of monotonous tumor cells, separated by thin fibrous septa containing lymphocytic infiltrations.
- Tumor cells are polygonal, with well-defined cell borders, abundant clear or eosinophilic cytoplasm
- Nuclei are centrally located, large, round and vesicular, with one or two prominent nucleoli
- Mitoses are common





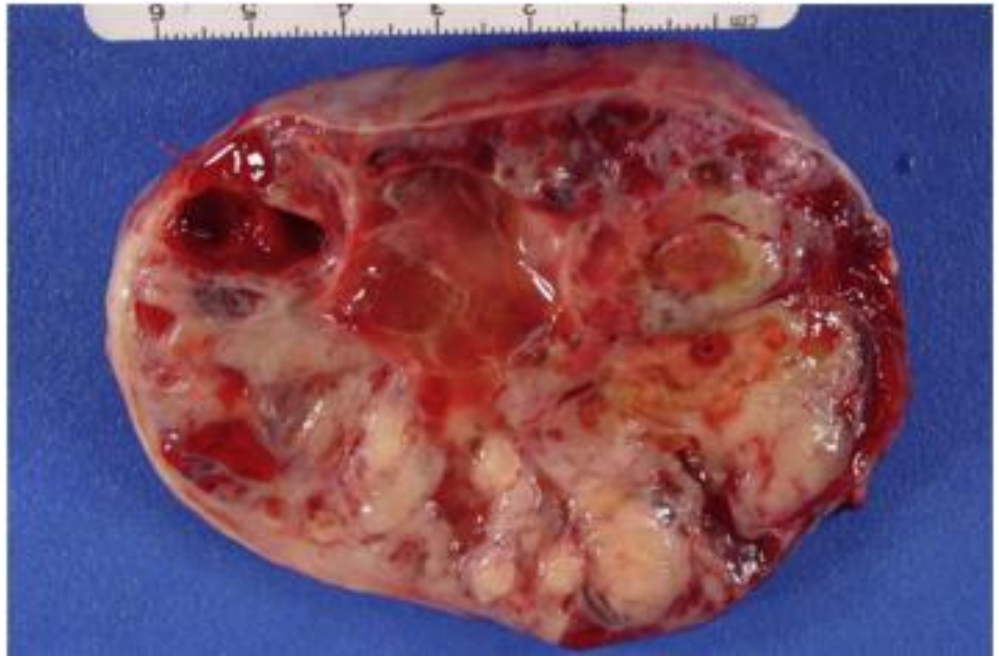
Dysgerminoma

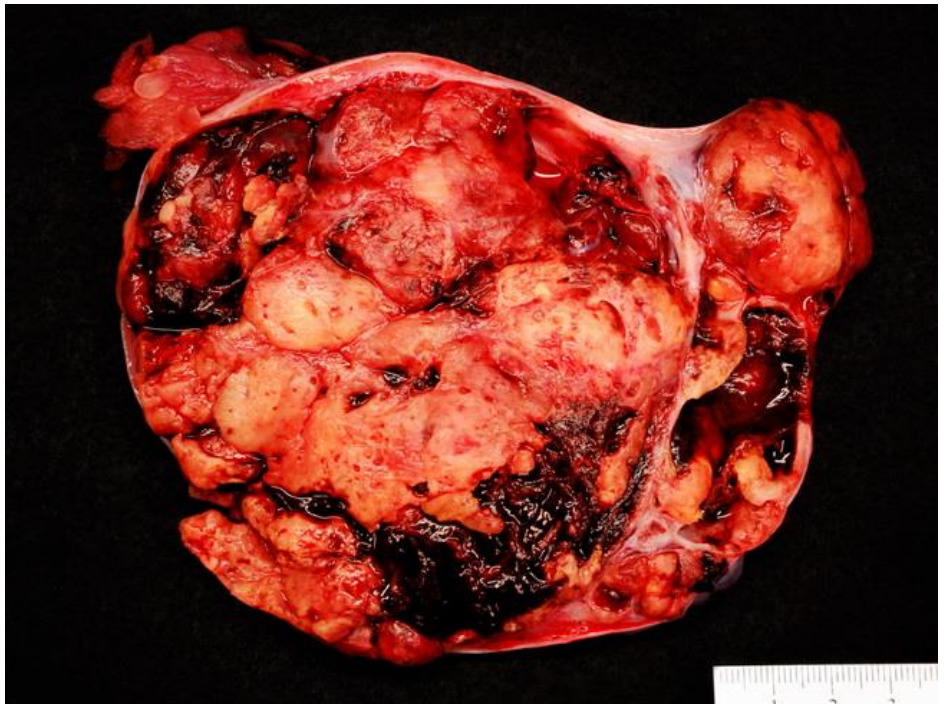
3. YOLK SAC TUMORS

- **Endodermal sinus tumor**
- Primitive germ cell tumor
- 2nd most common malignant ovarian GCTs
- 2nd and 3rd decades of life
- High level of **serum alpha-fetoprotein**
- Survival > 80% with chemotherapy

MACROSCOPIC APPEARANCE:

- Unilateral, large (average: 15cm)
- Solid-cystic lesions
- Extensive haemorrhage, necrosis & cystic degeneration

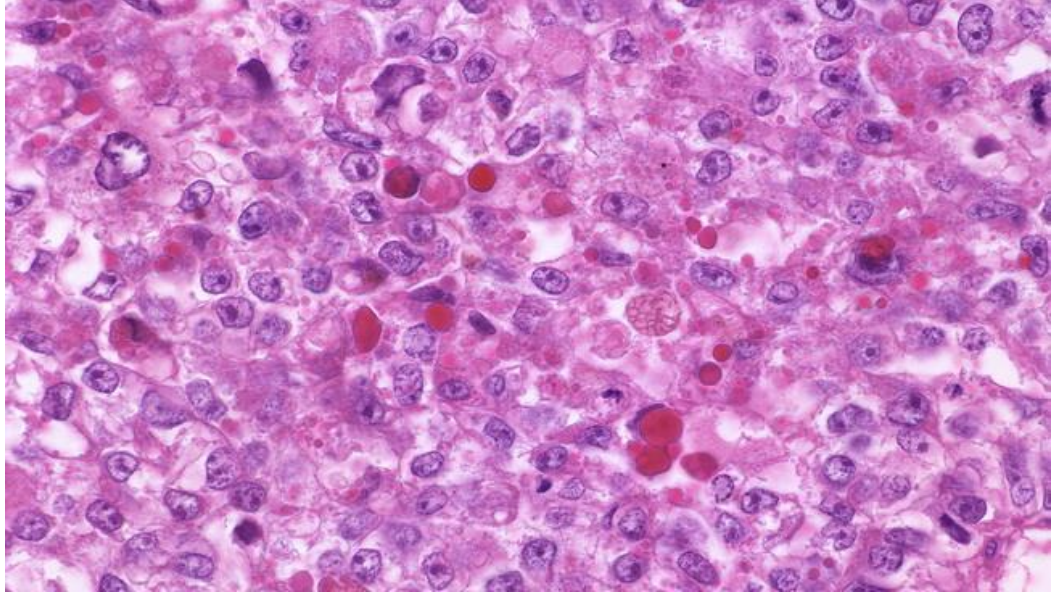


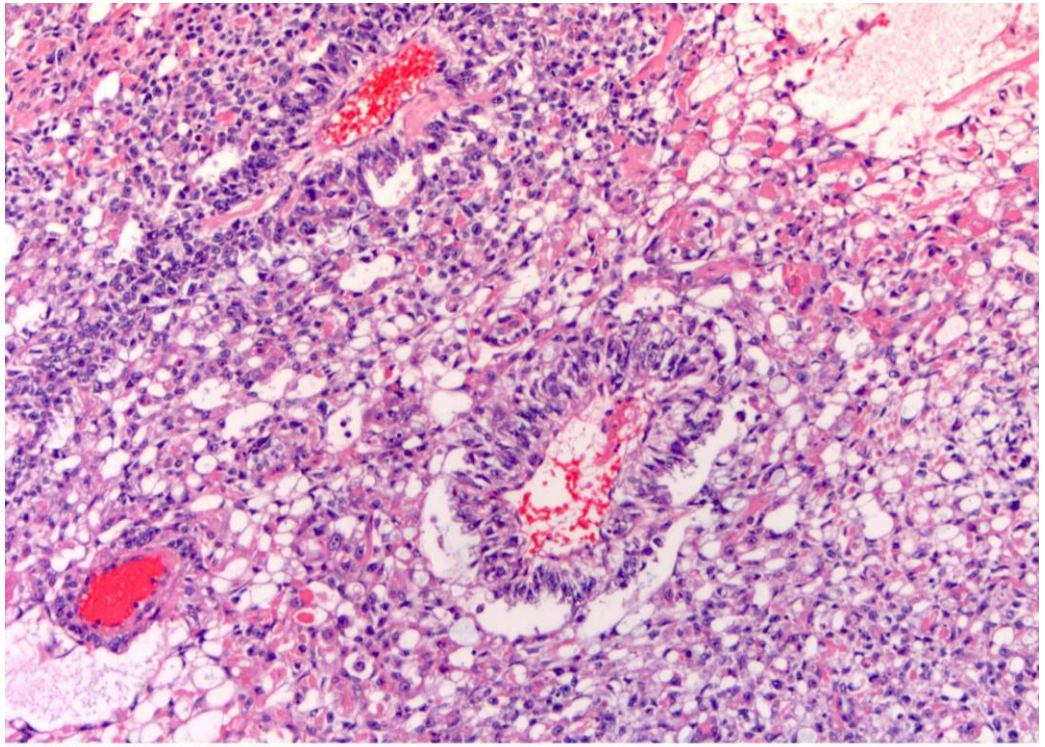


Yolk Sac Tumors

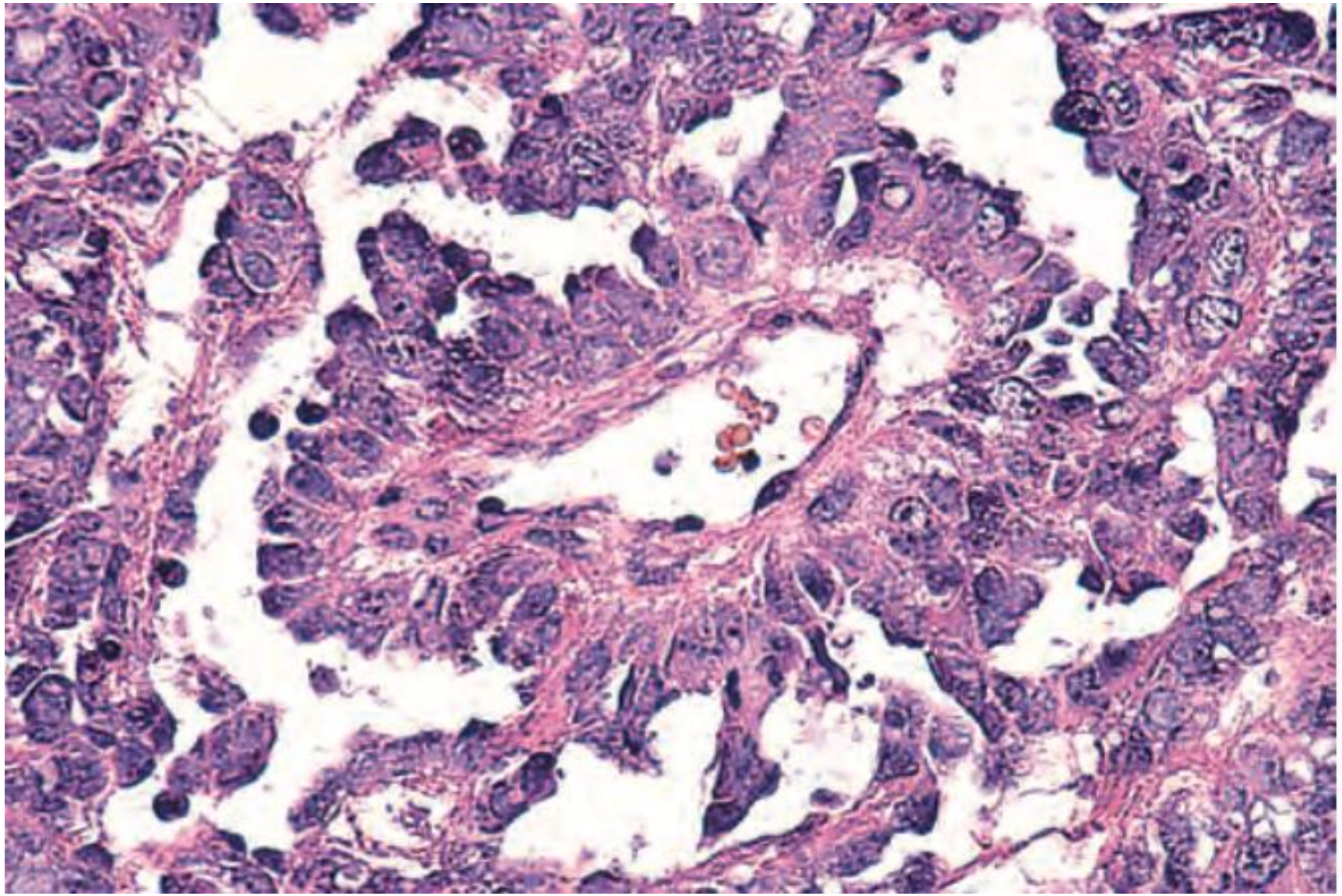
MICROSCOPIC APPEARANCE:

- Most common pattern: **reticular / microcystic**
- Tumor cells contain clear cytoplasm (glycogen / lipid), nuclei are large, pleomorphic, hyperchromatic with prominent nucleoli
- Frequent mitoses
- **Schiller-Duval bodies**
  - Glomerulus-like structure composed of a central blood vessel enveloped by tumor cells
- Intracellular & extracellular **hyaline globules**





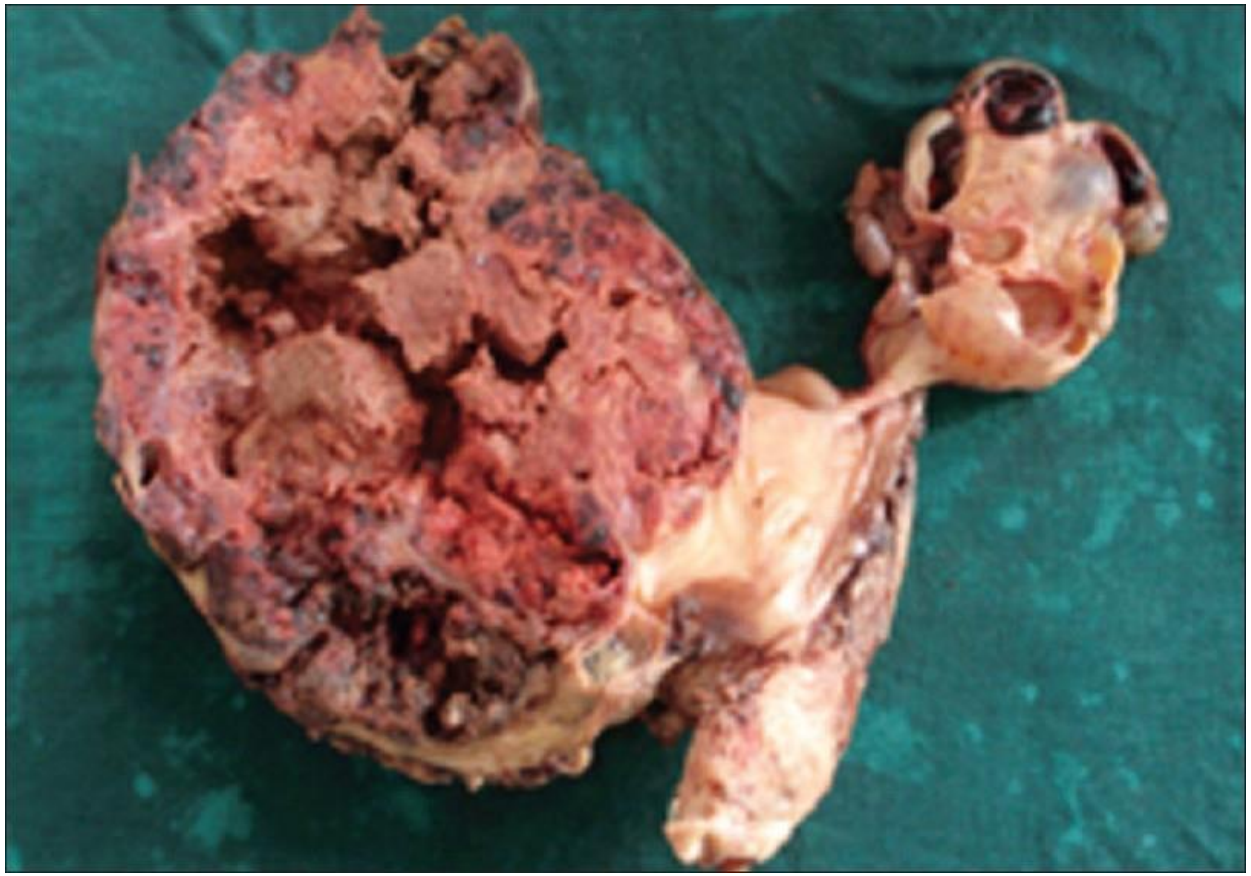
Schiller-Duval body



Schiller-Duval bodies
Glomerulus-like structure composed of a central blood vessel enveloped by tumor cells

4. CHORIOCARCINOMA

- Composed of cytotrophoblast and syncitiotrophoblast
- Affects children and young adults
- Aggressive, usually have metastasized hematogenously to lungs, liver, bone and other sites by the time of diagnosis
- Serum β-hCG is typically elevated



MACROSCOPIC APPEARANCE:

- Large solid mass
- Extensive areas of necrosis and haemorrhage

Choriocarcinoma

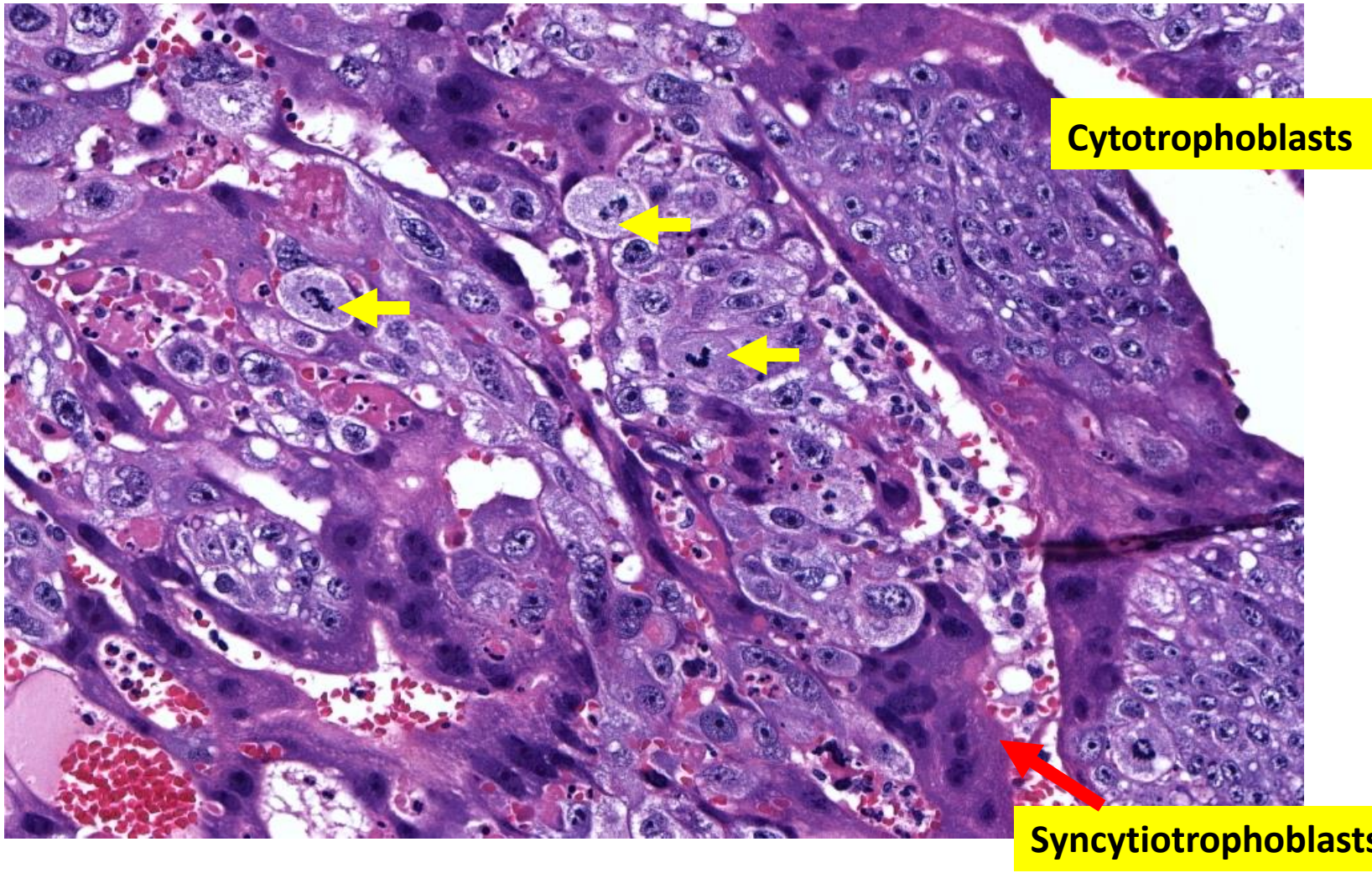
MICROSCOPIC APPEARANCE:

Two cells populations:

- **Mononuclear Cytotrophoblast**: Distinct cell borders, clear cytoplasm, small centrally located, round, vesicular nuclei with prominent nucleoli

- **Multinucleated Synsytiotrophoblasts**: Larger cells with basophilic, vacuolated cytoplasm

Abundant haemorrhage



Self study

OTHER GERM CELL TUMORS

Embryonal carcinoma

- A highly malignant tumor of primitive embryonal elements
- Histologically similar to embryonal carcinoma arising in the testes

Mixed germ cell tumors

- Contain various combinations of dysgerminoma, teratoma, yolk sac tumor and choriocarcinoma

NEOPLASTIC OVARIAN TUMOURS

SURFACE EPITHELIAL TUMORS

- Serous Tumors
- Mucinous Tumors
- Endometrioid Ovarian Tumors
- Clear Cell Carcinoma
- Brenner Tumors

GERM CELL TUMORS

- Teratoma
- Dysgerminoma
- Choriocarcinoma
- Yolk sac carcinoma
- Embryonal carcinoma

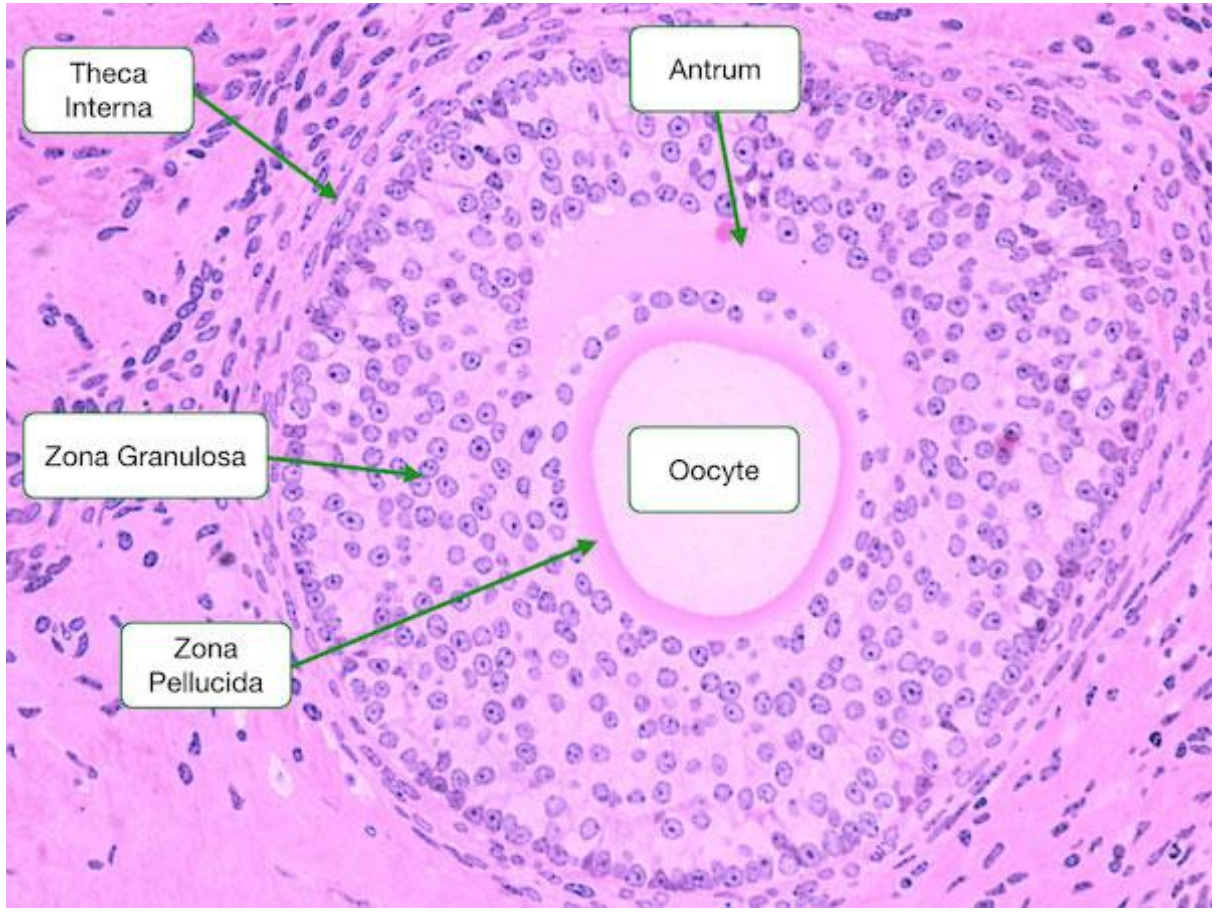
SEX CORD - STROMAL TUMORS

- Granulosa Cell Tumors
- Fibromas, Thecomas, Fibrothecomas
- Sertoli-Leydig Cell Tumors

METASTATIC TUMOUR

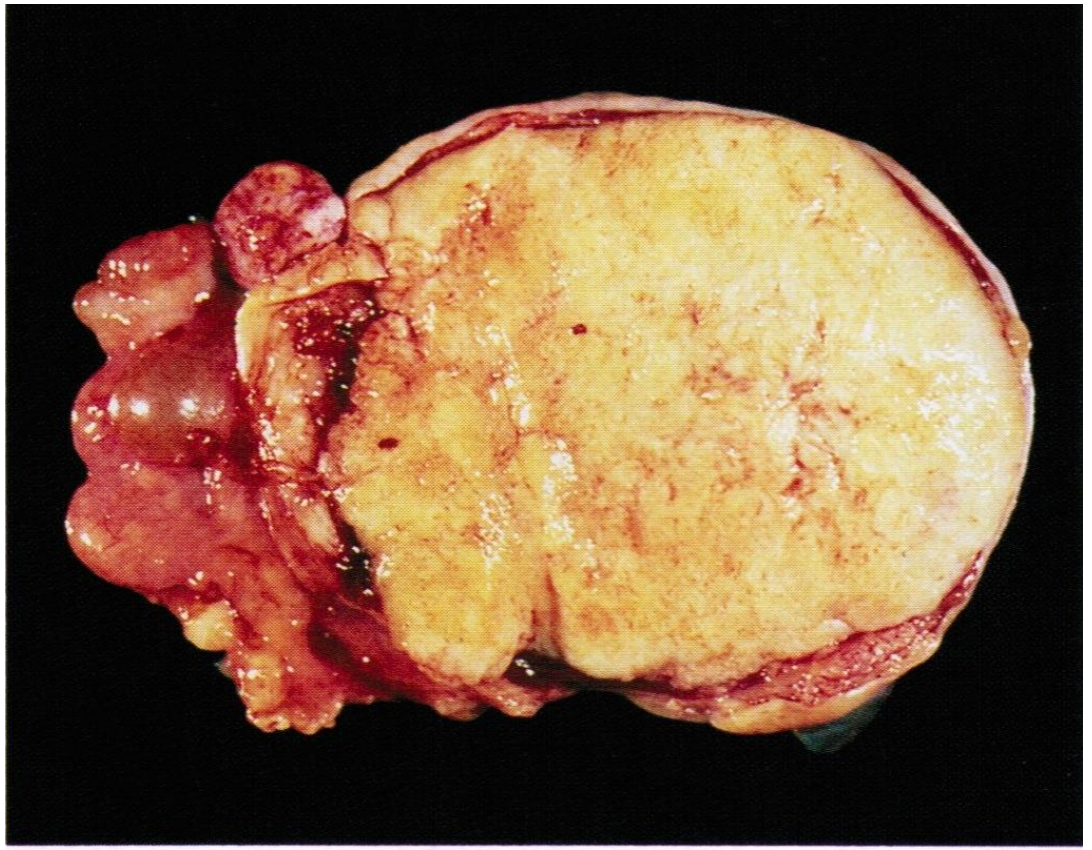
SEX CORD – STROMAL TUMORS

- Arise from **ovarian stroma**, derived from the **sex cords** of the embryonic gonad.
- These cells normally secrete hormones:
  - **Granulosa / Theca cells** – estrogen
    - Corresponding tumors may be feminizing
  - **Leydig cells** – androgens
    - Corresponding tumors may be musculinizing



Granulosa Cell Tumors

- Composed of cells that resemble **granulosa cells** of a developing ovarian follicle.
- Account for ~ 5% of all ovarian tumors.
- Divided into 2 categories based on the age of patients:
    1. **Adult granulosa cell tumors** (95%) – 2/3 occur in postmenopausal women
    2. **Juvenile granulosa cell tumor**
- Elevated tissue & serum levels of **inhibin** (product of granulosa cells)
- 97% of adult GCT have mutations in the FOXL2 gene.



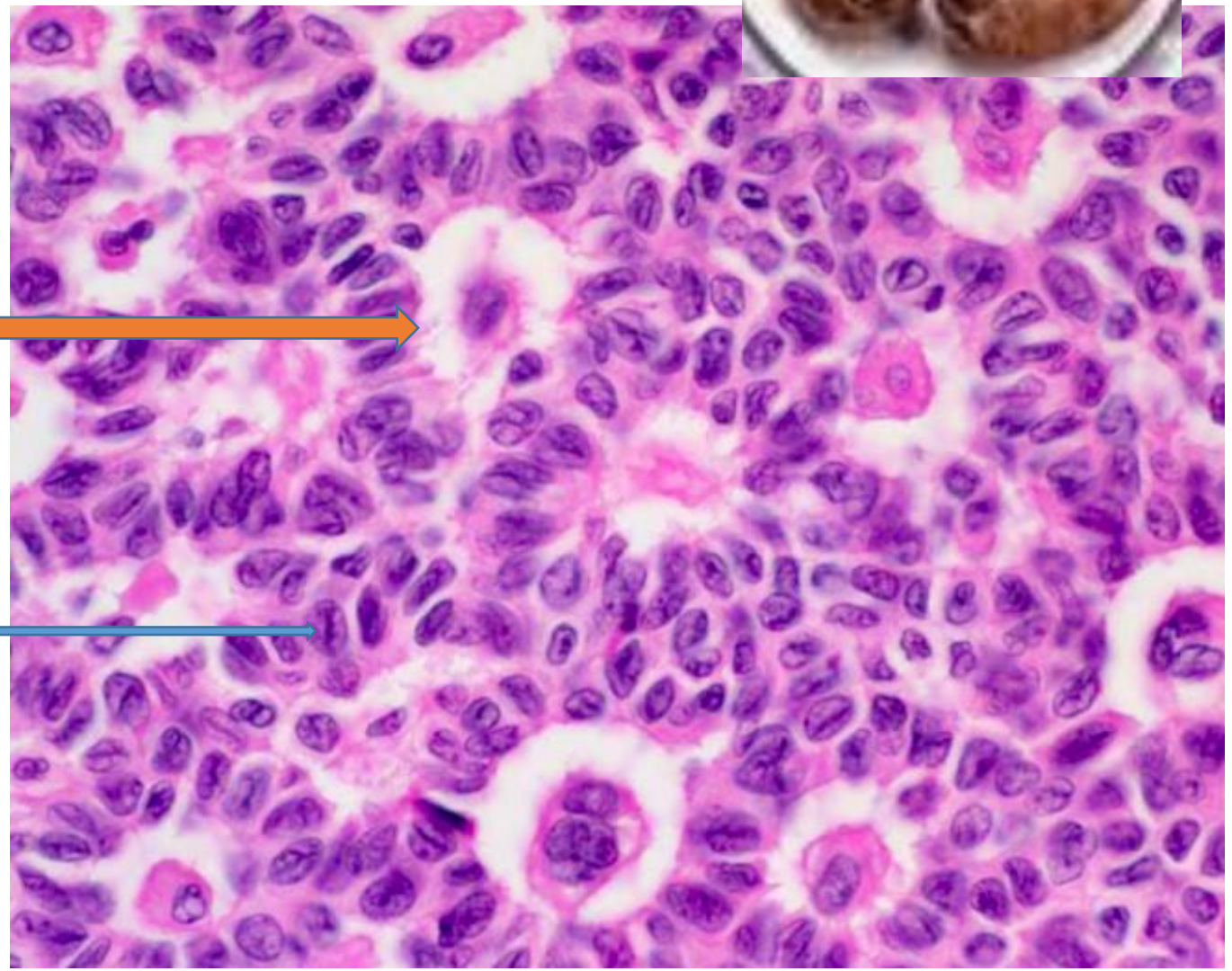
MACROSCOPIC APPEARANCE:

- Usually unilateral.
- Varied in size, solid-cystic encapsulated masses.
- Solid areas are soft, tan to yellow cut surface.
- Haemorrhage is common

Granulosa Cell Tumors

MICROSCOPIC APPEARANCE:

- Anastomosing cords, sheets or strands patterns
- Gland like structures filled with an eosinophilic hyaline materials **(Call-Exner bodies)**
- Tumor cells have uniform, pale, round to oval nuclei with irregular nuclear membrane and **nuclear grooves (coffee bean nuclei),** and scant cytoplasm.

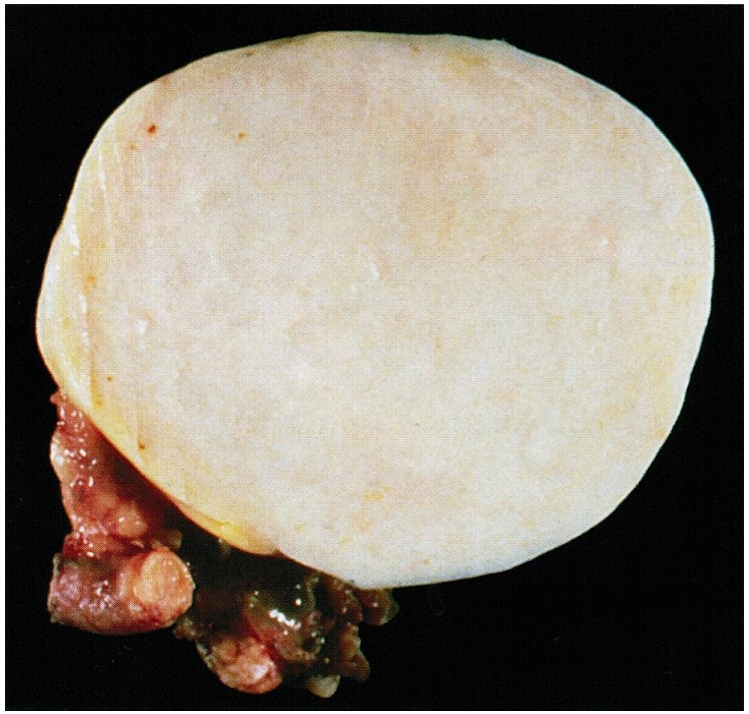


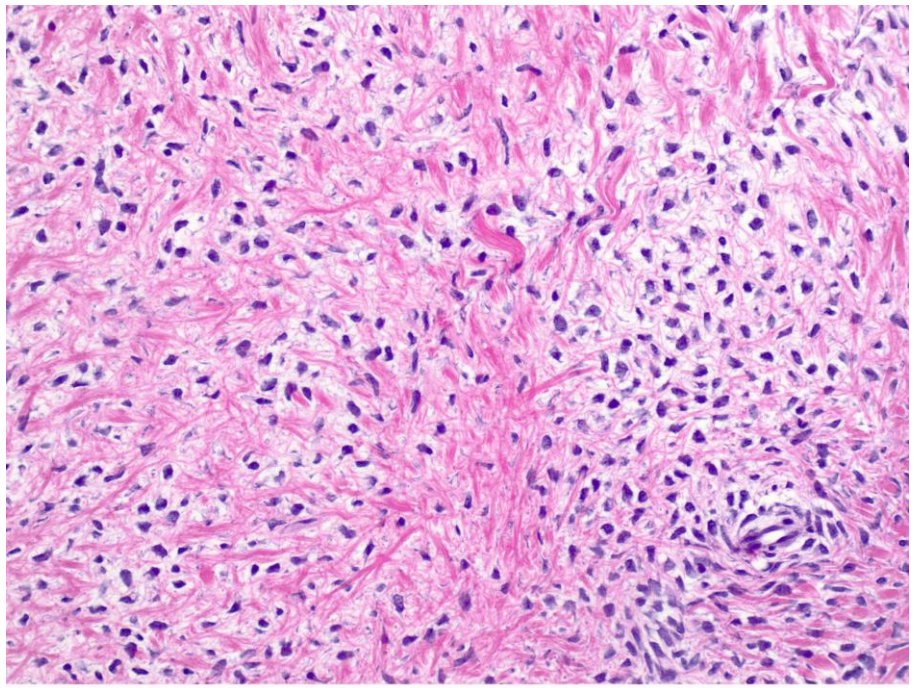
Self study

Fibroma

- Benign ovarian stromal tumor composed of **fibroblastic cells** within a variably collagenous stroma
- Associated with:
  - Meigs syndrome (Ovarian tumor – most commonly a fibroma + ascites + right-sided hydrothorax)
  - Basal cell nevus syndrome

solid, lobulated, encapsulated, hard, gray-white masses





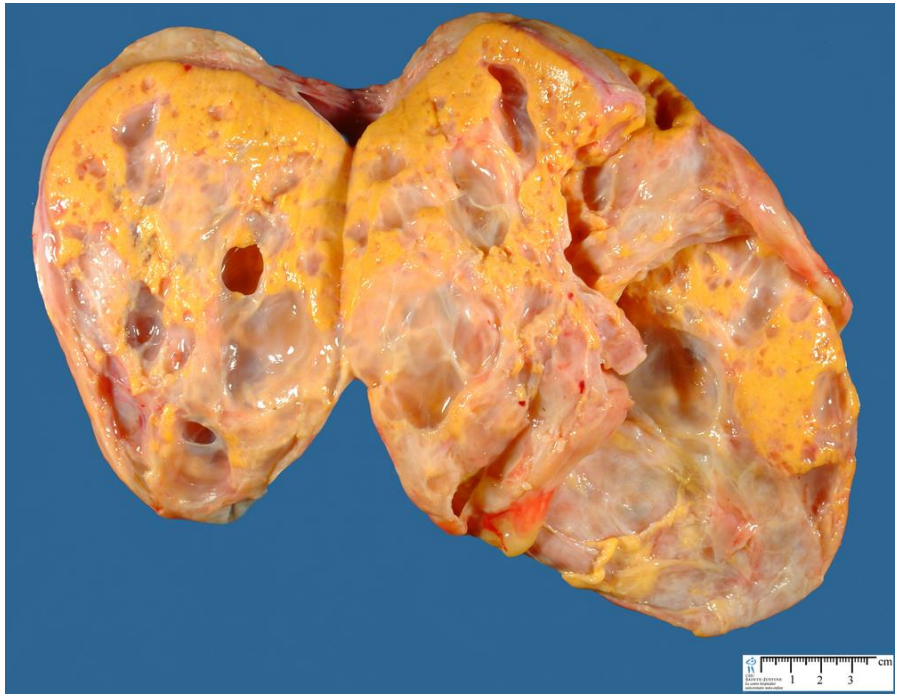
Typical fibroma

Intersecting fascicles of cells with bland, spindled to ovoid nuclei and scant cytoplasm

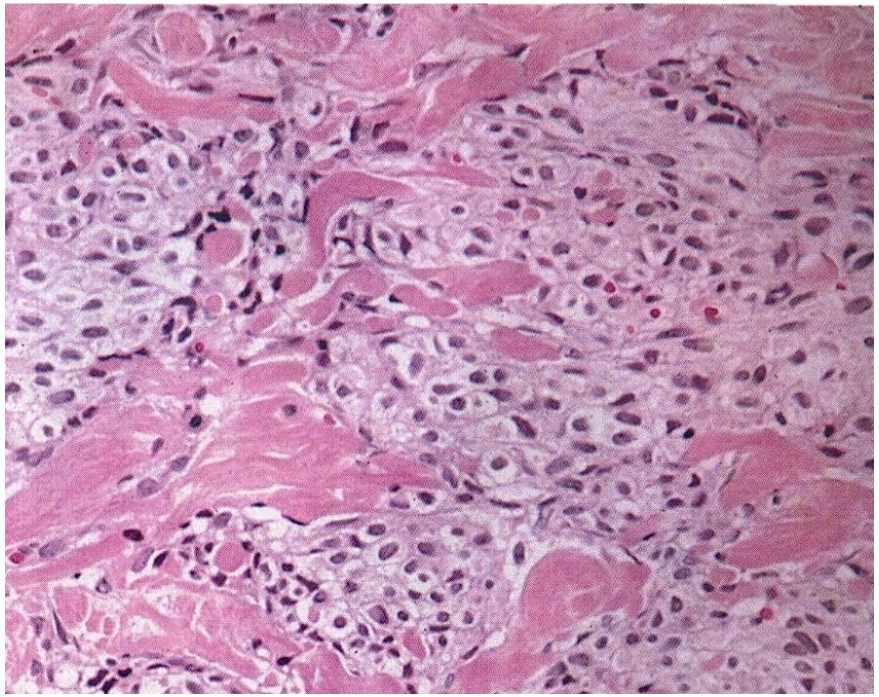
Self study

Thecoma

- Ovarian stroma tumor composed predominantly of cells **resembling theca cells**.
- Uncommon
- Typically occur in postmenopausal women (mean age: 59 years)
- May present with hormonal manifestations (estrogenic / less commonly androgenic)



Solid, occasionally lobulated, yellowish-tan cut surfaces

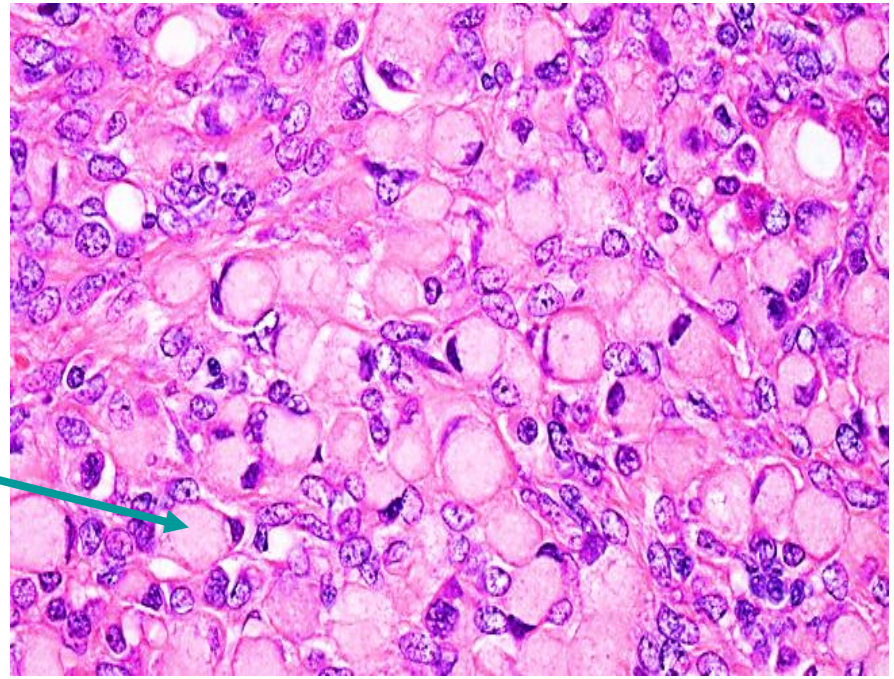


Tumor cell nuclei are ovoid to round. Intervening stroma has collagen deposition

Metastatic Tumors

The metastatic tumors of the ovary are derived:

- Müllerian origin: uterus, fallopian tube, contralateral ovary, or pelvic peritoneum.
- Extra-müllerian: breast ca, stomach, biliary tract, and pancreas, pseudomyxoma peritonei (derived from appendiceal tumors).
    - **Krukenberg tumor***:* bilateral metastases composed of mucin- producing cancer cells with a “signet-ring” appearance, most often of gastric origin.

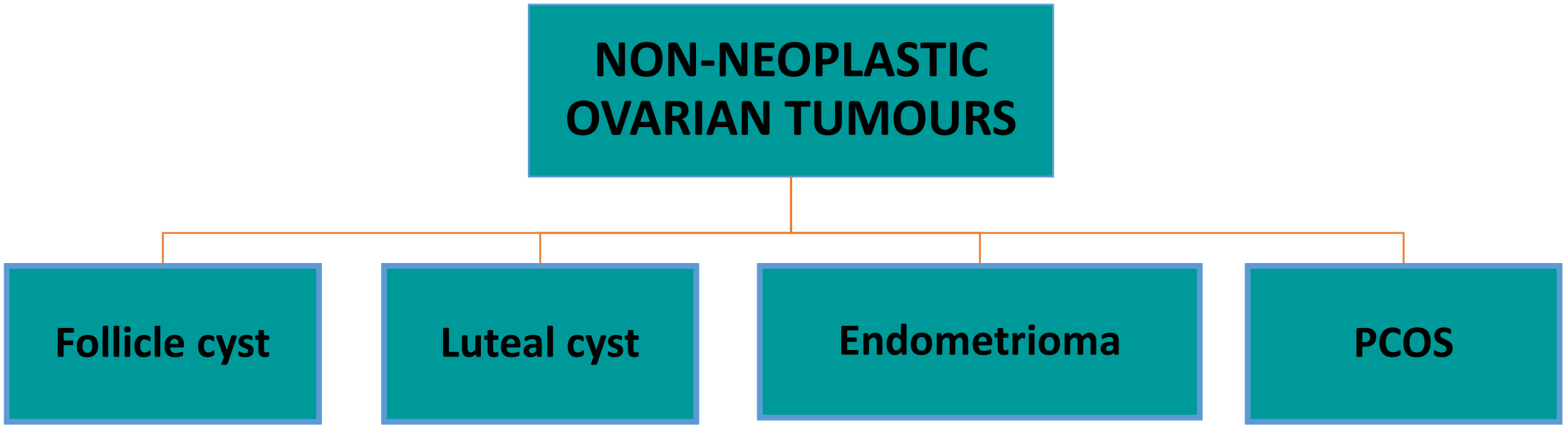


Clinical correlation

- Management is a challenge.
- Symptoms & signs usually appear only when tumors are well advanced.
- About 30% of all ovarian neoplasms are discovered incidentally on routine gynaecological examination.
- Large masses may cause an increase in abdominal girth.
- Smaller masses such as dermoid cysts may produce acute pain due to torsion.
- Metastatic seeding causes ascites.
- Functioning ovarian tumors may present with endocrinopathies.
- Staging: FIGO

Role of tumor markers- CA -125

- CA -125 measurements are of greatest value in **monitoring response to therapy.**
- Its usefulness as a **screening test** in asymptomatic postmenopausal women *is limited*.
- Its specificity & sensitivity are not sufficient to be utilized as a screening test currently.
- Hence screening tests that detect early tumors are very much needed.


NON-NEOPLASTIC OVARIAN TUMOURS
Follicle cyst
Luteal cyst
Endometrioma
PCOS

ENDOMETRIOMA (CHOCOLATE CYST)

- Endometriosis: presence of endometrial glands & stroma outside the uterus.
- Most common site of involvement is ovary.
- Deep ovarian endometriosis → repeated bouts of haemorrhage → convert ovary into a cyst with filled with brown materials which can vary in size known as **endometriomas / endometriotic cyst / "chocolate cysts"**
- The patients are usually of child-bearing age
- Present with infertility and **cyclical pain associated with menstruation.**

Pathogenesis – Current hypothesis

REGURGITATION THEORY

- Menstrual backflow through the fallopian tubes predisposes to endometrial implants.
- The endometriotic tissue is not just misplaced but is also abnormal.
- As compared to normal endometrium, endometriotic tissue increased levels of prostaglandin E2 by endometrial stromal cells.
- Stromal cells also make aromatase, leading to local production of estrogen. These factors enhance the survival and persistence of the endometriotic tissue within a foreign location.

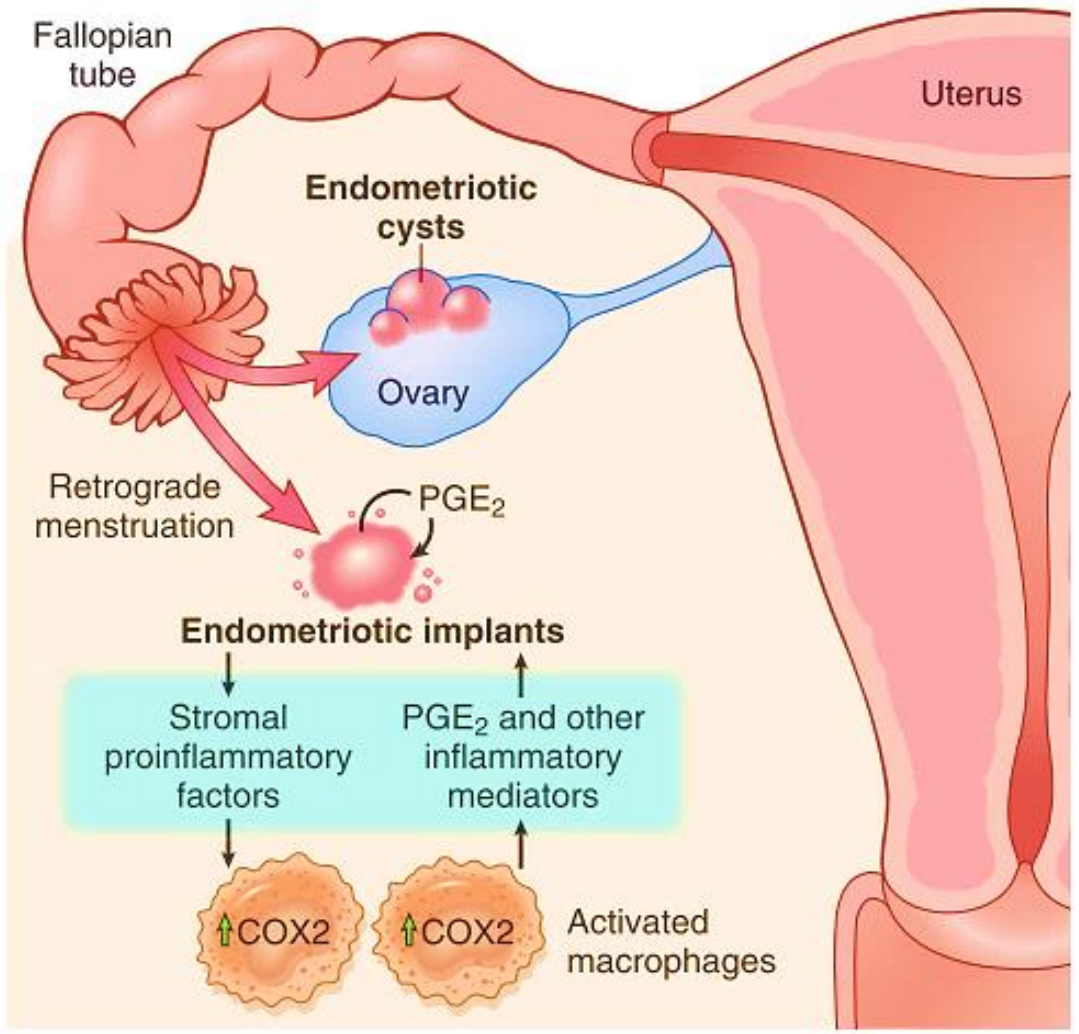
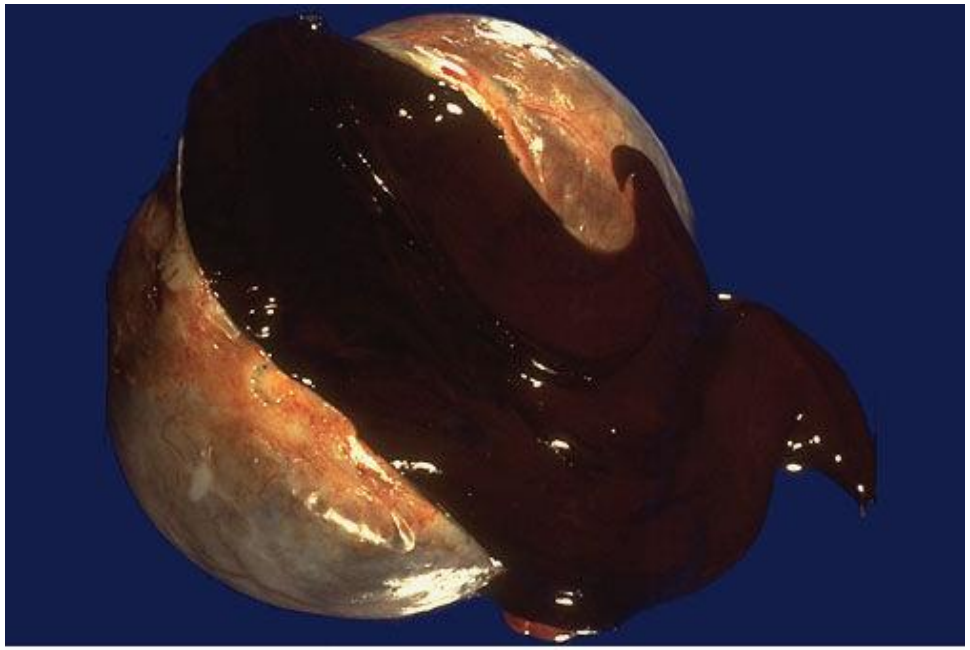


Fig. 19.9 Proposed origins of endometriosis.

ENDOMETRIOMA (CHOCOLATE CYST)

MACROSCOPIC APPEARANCE:

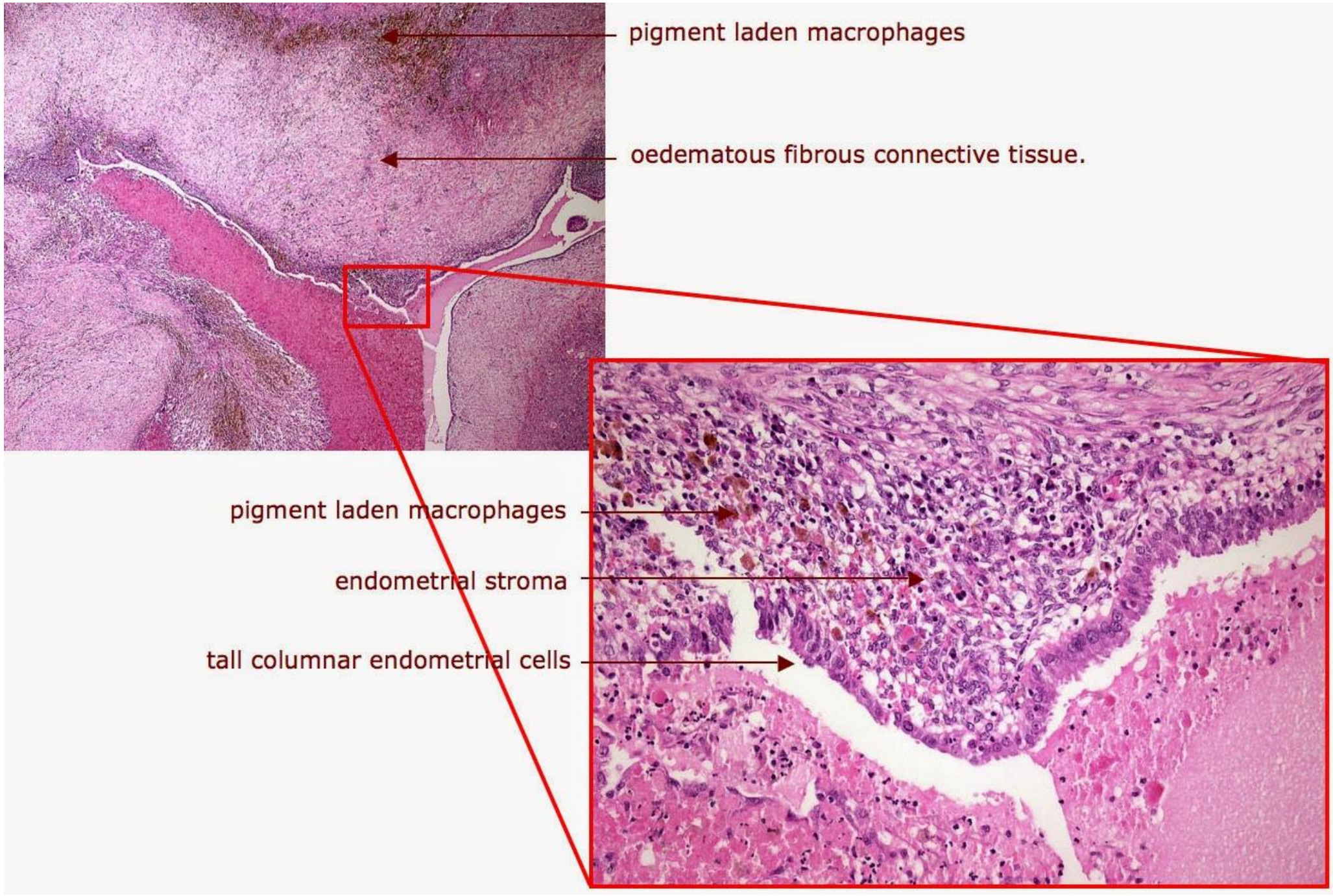
- Cyst with fibrotic walls
- A smooth lining and dark brown cyst contents (chocolate cyst)
- Often adherent to adjacent organs



Ovarian endometriotic (chocolate) cyst

MICROSCOPIC:

- An intact **endometrial lining and stroma**, scattered foci of fresh **haemorrhage** and occasional hemosiderin-laden macrophages near the surface.
- In long-standing cases, repeated cycles of hemorrhage efface the endometrial tissue making it difficult to find endometrial glands and stroma in the cyst wall.


pigment laden macrophages
oedematous fibrous connective tissue.
pigment laden macrophages
endometrial stroma
tall columnar endometrial cells

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