Female genital Tract (2)
Two lectures

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Urogenital Tract Pathology Module

Endometrial Carcinoma

- It is **The most common cancer in female genital tract.**
- Common in 50s and 60s and is **distinctly uncommon** in women younger than 40 years of age
- Arise in one of two clinical settings:

1)Perimenopausal women with estrogen excess

2)older women with endometrial atrophy.

- These scenarios are correlated with differences in histology:
- 1-***endometrioid***
- 2-***serous carcinoma***, respectively.

Endometrioid carcinoma:

•Termed because similar to normal endometrium.

•Risk factors point to increase estrogen stimulation include:
: **Obesity;** (mostly an association and not a true risk factor);
Infertility(nulliparous, often with nonovulatory cycles);

Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors.

Other risk factors **Diabetes and Hypertension**

- **Precancerous** lesion is atypical endometrial hyperplasia.
- **Breast ca occurs in women with E ca (& vice versa) more frequently than by chance alone.**

Pathogenesis

- Endometrial ca is the 2nd most common cancer associated with hereditary nonpolyposis colon cancer syndrome ,an inherited genetic defect in a DNA mismatch repair gene, resulting in (microsatellite instability).

- Mutations in DNA **mismatch repair genes** and **PTEN.**

- **Both mismatch repair gene &** PTEN **mutations** are **early events** in endometrial carcinogenesis, occurring in the progression from abnormal proliferation to atypical hyperplasia.

Serous carcinoma

- **No relation with endometrial hyperplasia.**
- **Not hormone-dependent.**

- (1) it typically arises in a background of **atrophy**, sometimes in the setting of an **endometrial polyp**
- (2) Mutations in DNA mismatch repair genes & PTEN are **rare** in serous ca; however,
- (3) **all cases have mutations in the** p53 **tumor suppressor gene.**

- **Grossly, Endometrioid ca** may be **fungating or infiltrative**, infiltrating the myometrium.
- H, T closely resemble normal **E,** ranging from mucinous to tubal (ciliated) to squamous or adenosquamous differentiation.

For **Endometrioid ca**, the grading (grades I-III) & the staging closely parallel outcome:
stage I, confined to the **corpus**; stage II, involvement of the **cervix**; stage III, beyond the uterus but **within the true pelvis**; stage IV, distant **metastases** or involvement of other viscera.

Serous carcinoma forms small papillae (rather than the glands seen in endometrioid ca) & has much greater cytological atypia. They behave as poorly differentiated cancers **are not graded**, & are particularly **aggressive.**

Clinically, **irregular bleeding is** the first clinical indication of all E ca, caused by erosion & ulceration of the T surface.

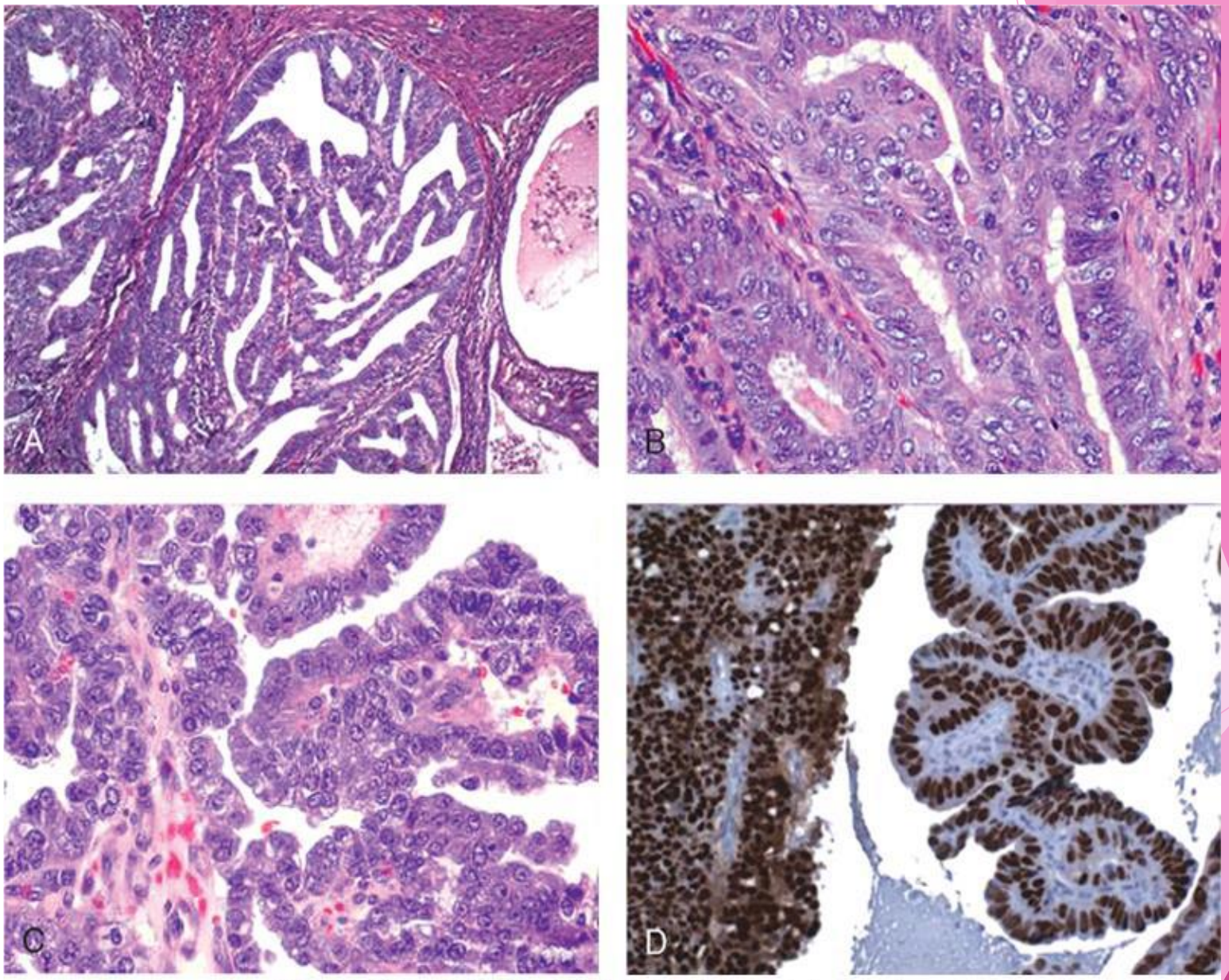
- With progression, the uterus may be palpably **enlarged**, &in time, extension of the E ca beyond the uterus **fixed** it to surrounding structures.

- Fortunately, E ca is usually **late-metastasizing cancer**, but dissemination eventually occurs, with involvement of ovary ,LN & distant sites.
- **Papillary serous ca** prognosis is strongly dependent on the extent of tumor, as determined by operative staging with peritoneal cytology; since even very small or superficial serous T may spread via the fallopian tube to the peritoneal cavity.

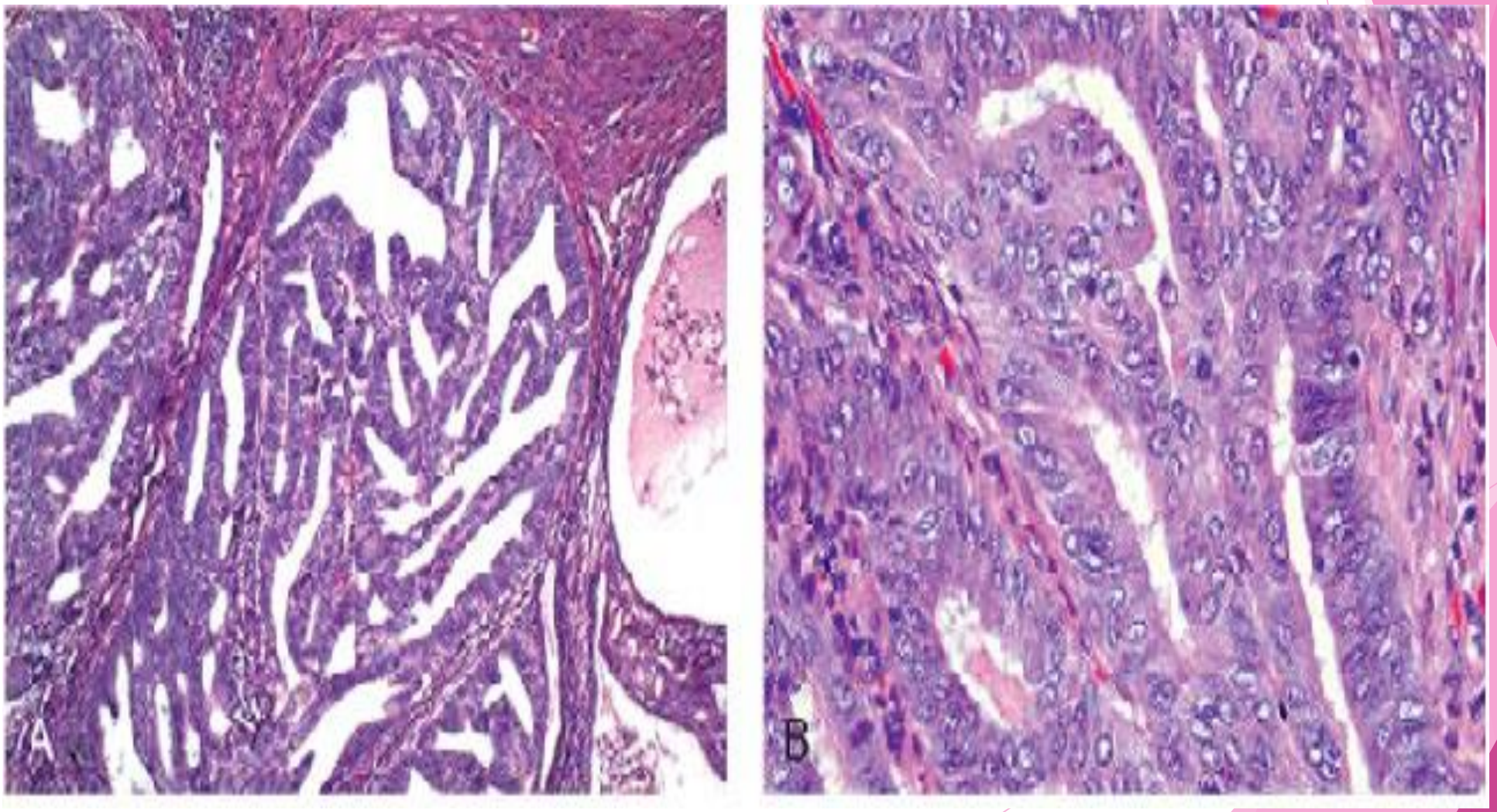
- **Prognosis: depends on stage.** 5-year survival in stage I= 90%; drops to 20% in stages III and IV.

Endometrioid carcinoma

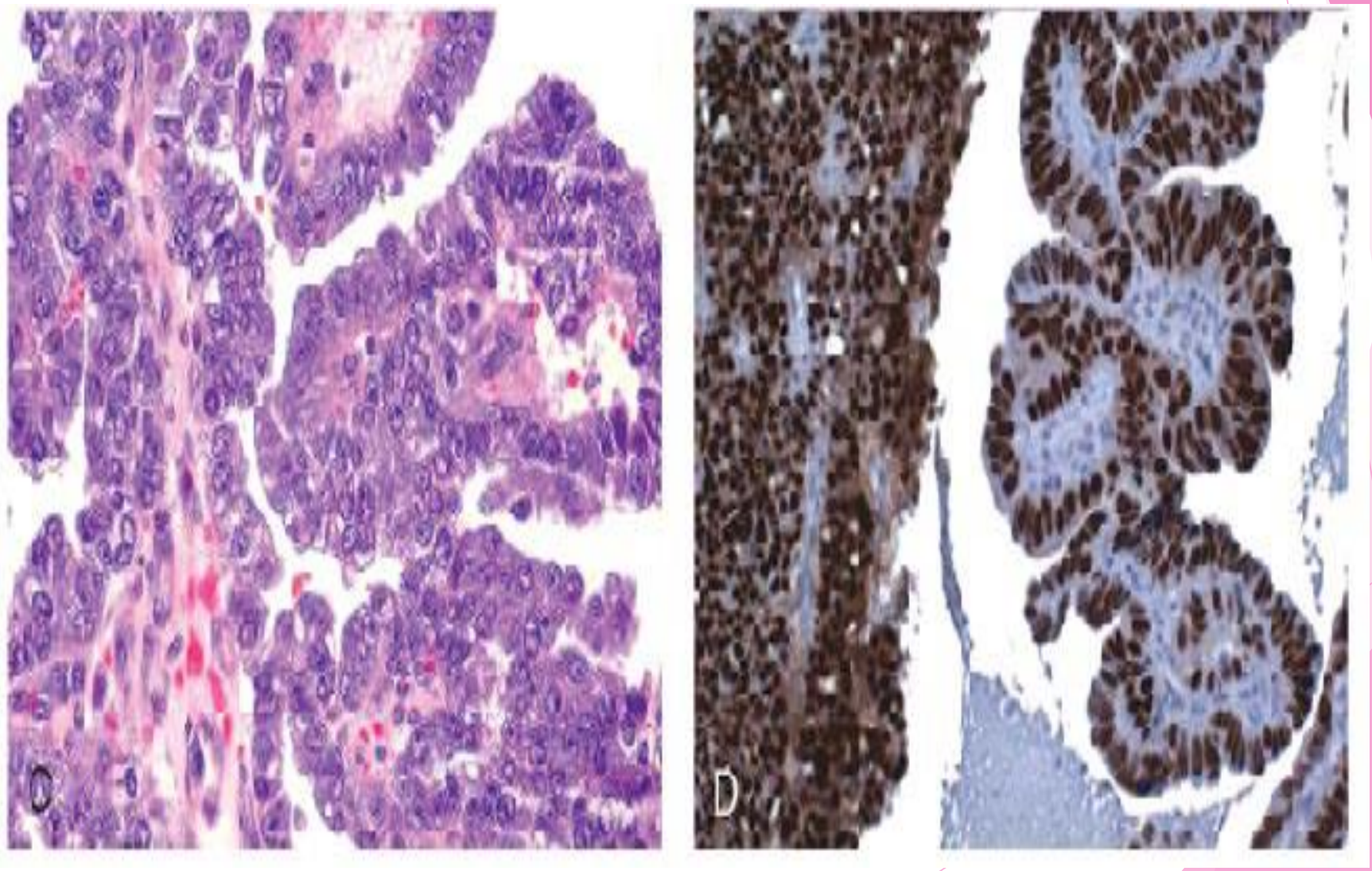
Serous carcinoma



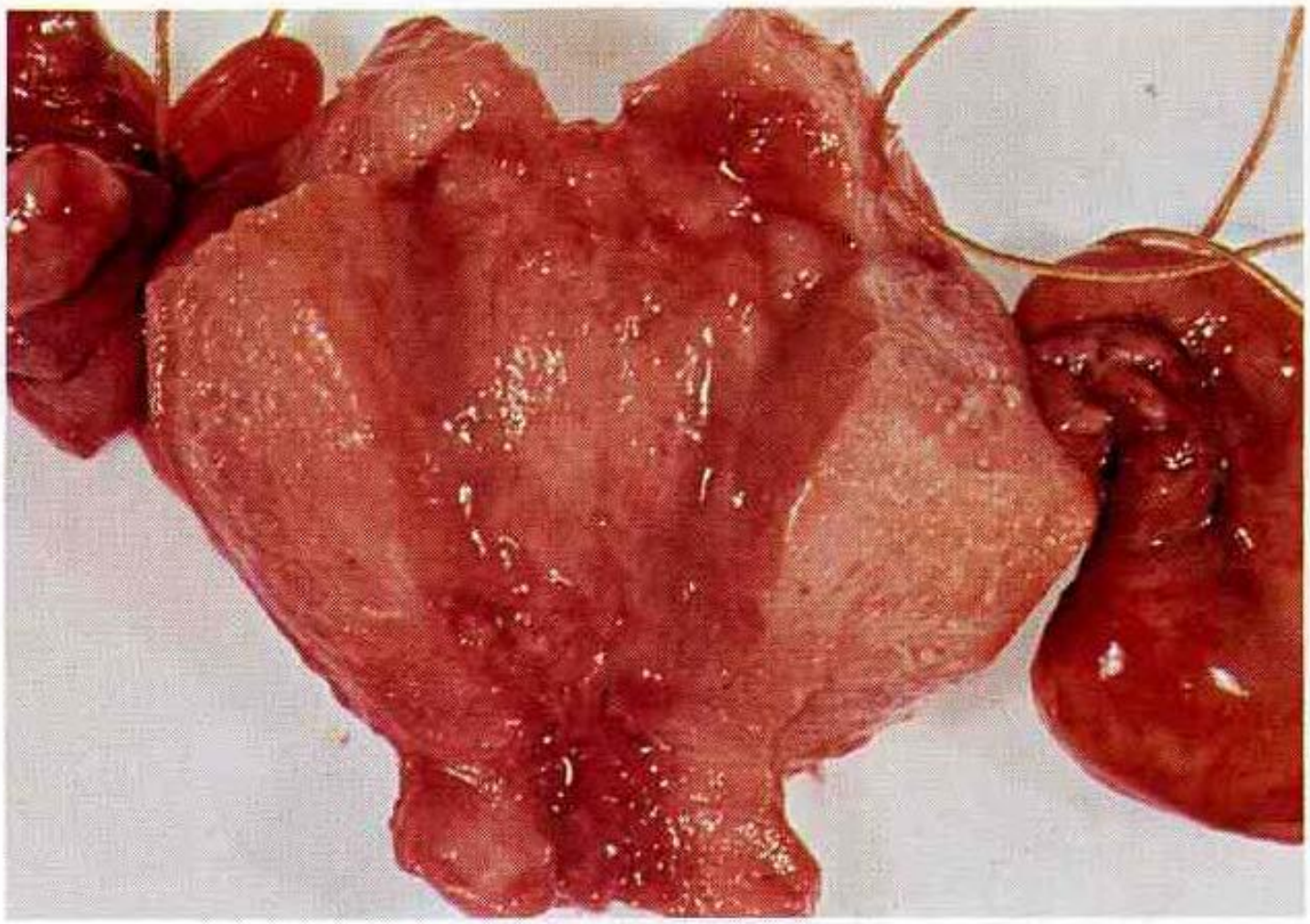
Endometrioid type of endometrial carcinoma:A,Displaying cribriform architecture & infiltrating the myometrium . **B,**Reveals back to back glands, loss of polarity & nuclear atypia.



Serous type of endometrial carcinoma C, Showing formation of papillae & marked cytoplasmic atypia. **D,** Immunohistochemical stain for p53 reveals accumulation of mutant p53 in the serous carcinoma



Endometrium adenocarcinoma: 3 irregular fundal pale cancer nodules in the opened uterus.



12.42 Adenocarcinoma: endometrium

Tumors of the myometrium

- **Lieomyoma= fibroids**
- Benign tumor of smooth muscle cells
- Most common benign tumor in females (30% -50% in reproductive life).
- Estrogen-dependent; shrink after menopause.

Grossly, are firm, white, **not encapsulated, sharply** circumscribed masses, with a characteristic

firm gray-white masses with whorled cut surface.

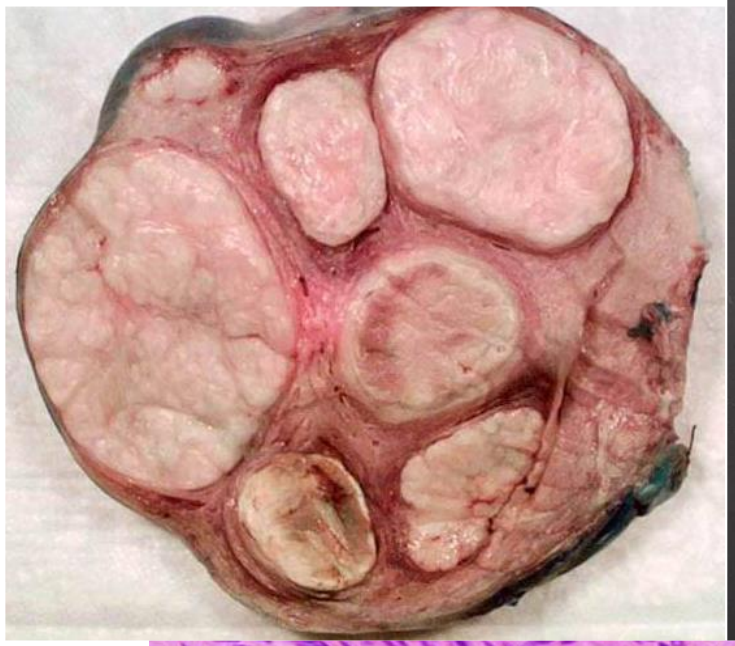
Tumor may be **single**, but **most** often they are **multiple.**

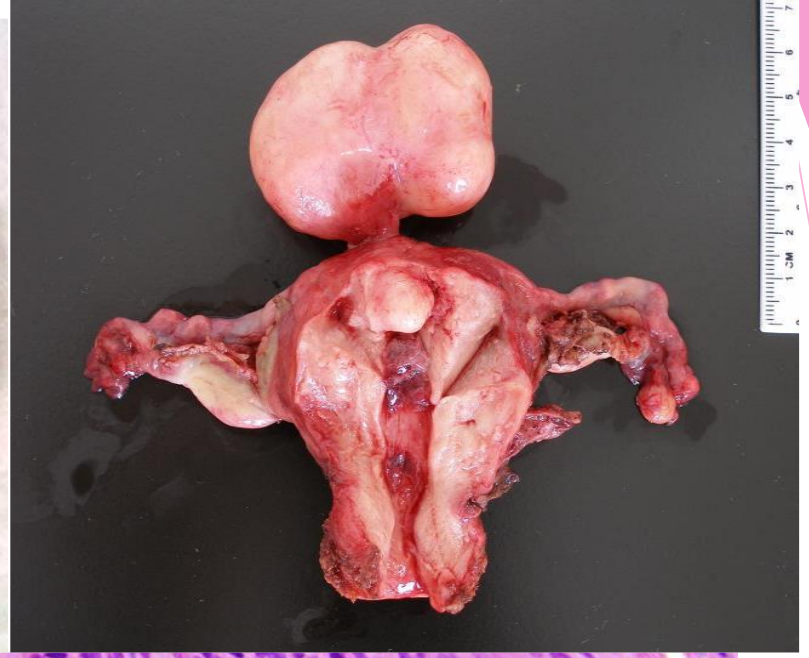
Size rang from **small (1 gram)** to **massive** T.

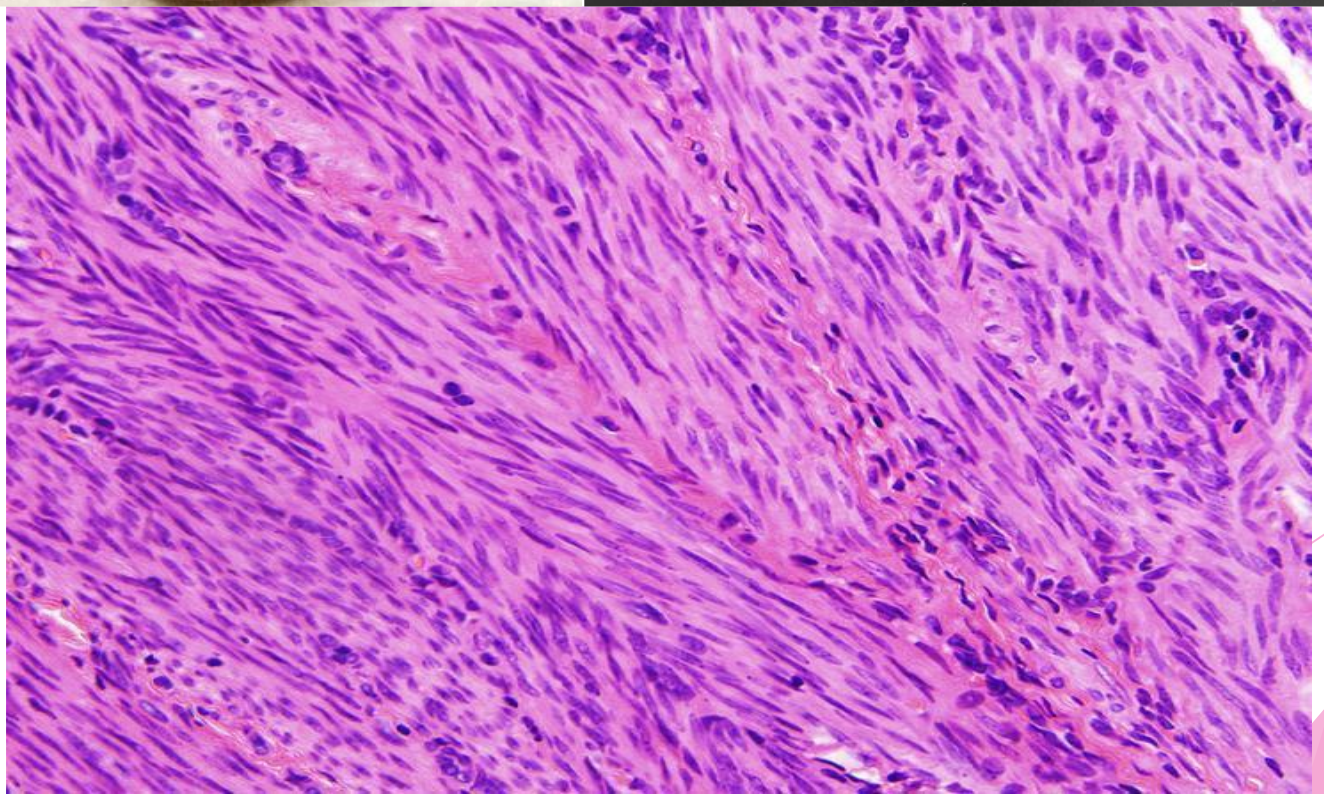
Lieomyomas

- Location: (intramural), (submucosal), or(subserosal).
- Changes include May develop hemorrhage, cystic changes or calcification.
- Larger L may develop ischemic necrosis (if extensive, called Red degeneration, causing **severe pain,** which requires it's removal), areas of hemorrhage& cystic softening,& after menopause, they may become densely collagenous& calcified.

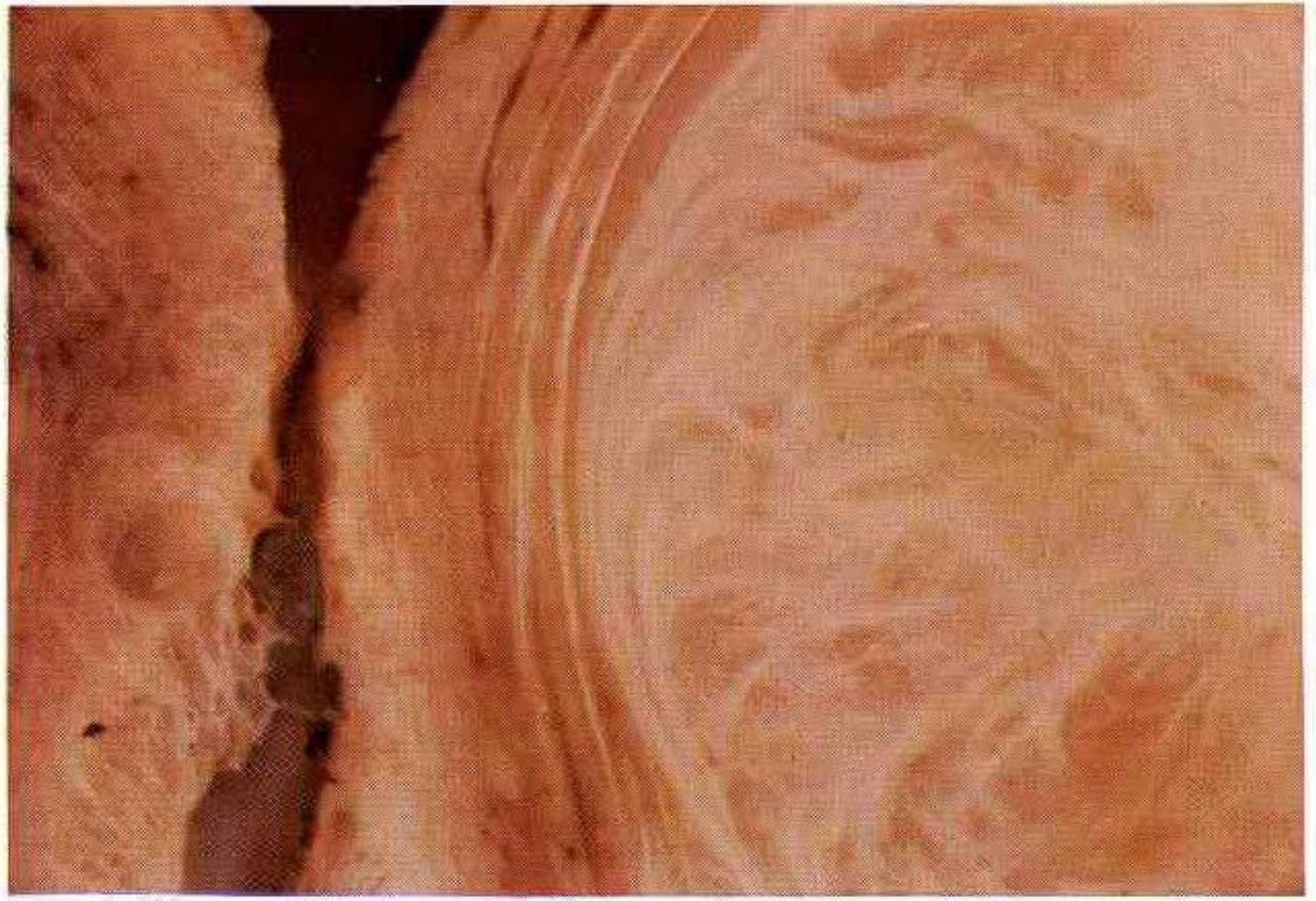
- **•Clinically**: asymptomatic or symptomatic; menorrhagia; a dragging sensation, anemia, etc...
- Leiomyomas almost **never** transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.





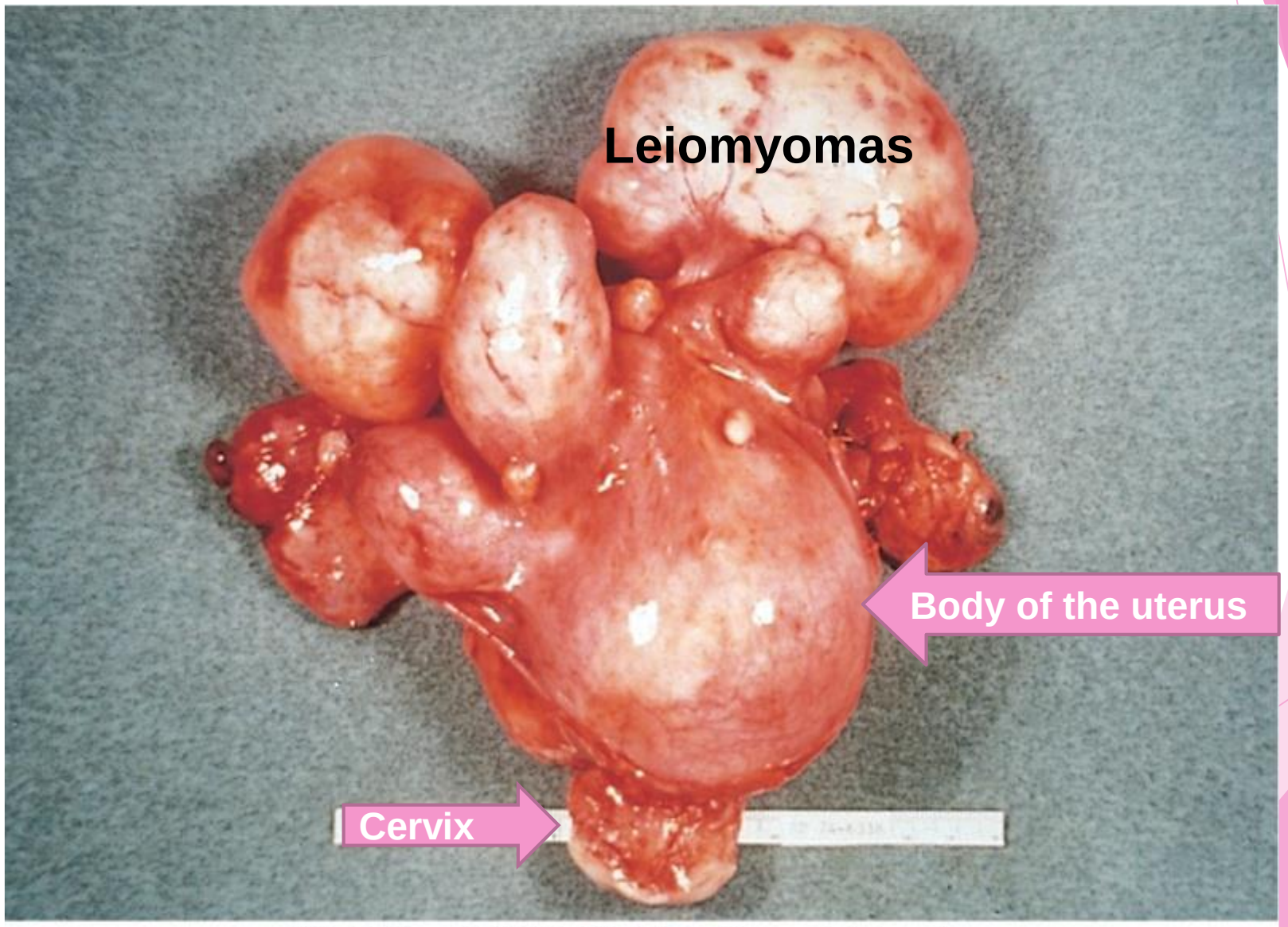


Leiomyoma: uterus. C/S of leiomyoma, showing the characteristic (1) shiny, pinkish-white whorled appearance of the tumor, & (2) the well-developed **false**capsule of compressed muscle & fibrous tissue around the it.

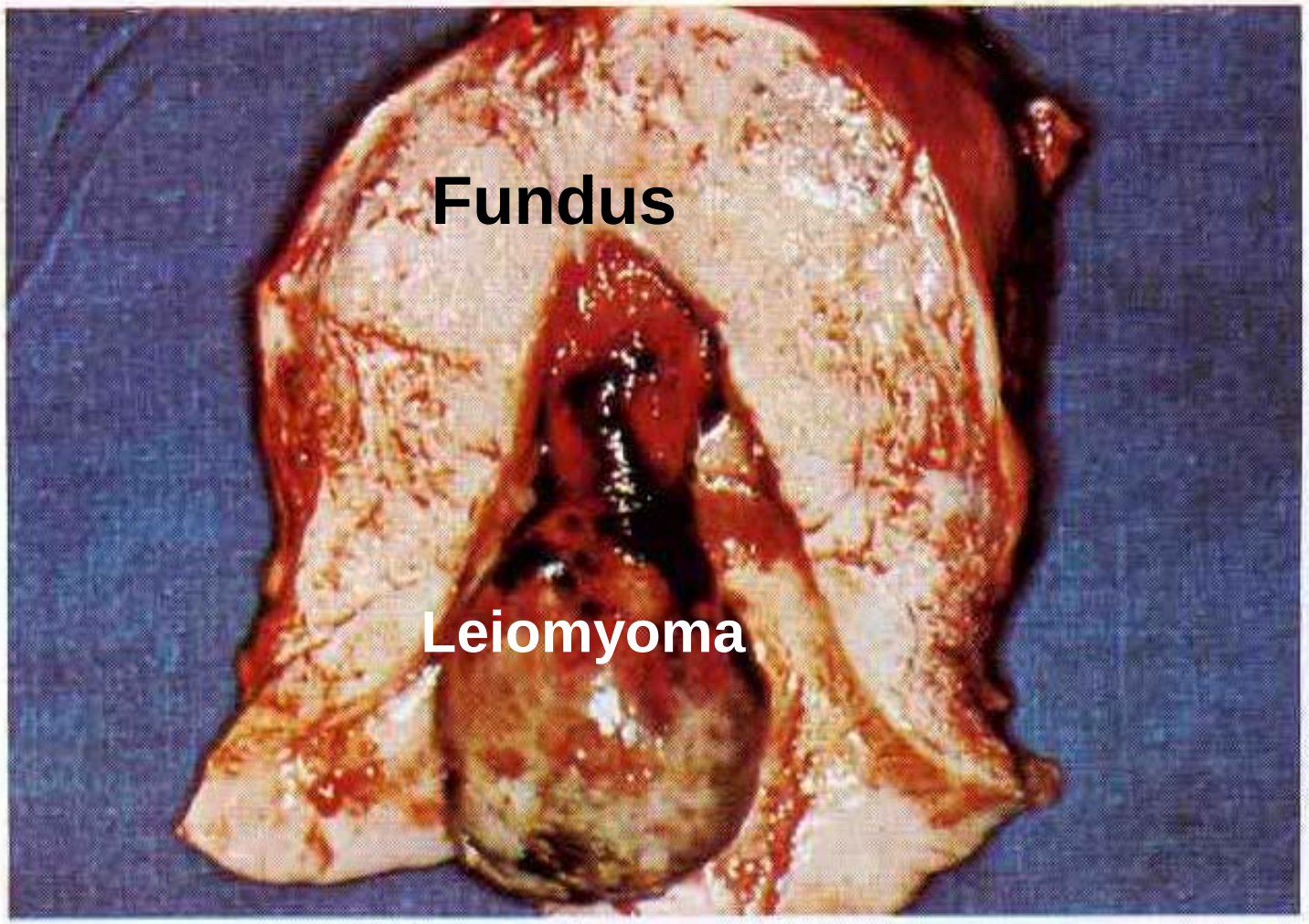


12.32 Leiomyoma: uterus

Uterus: Multiple large pedunculated subserosal **leiomyomas**, protruding from the dome of the fundus



Leiomyoma; uterus. Pedunculated submucosal leiomyoma, arising from the fundus & protruding through the cervical os. **Torsion** of the pedicle results in impairment of the tumor blood supply with its subsequent necrosis & gangrene.



12.35 Leiomyoma: uterus

Lieomyosarcoma

- Malignant counterpart of leiomyoma.
- Typically **arise de novo** from the mesenchymal cells of the myometrium, not from preexisting leiomyomas.
- Almost always solitary tumors, in contrast to the frequently multiple benign leiomyomas.

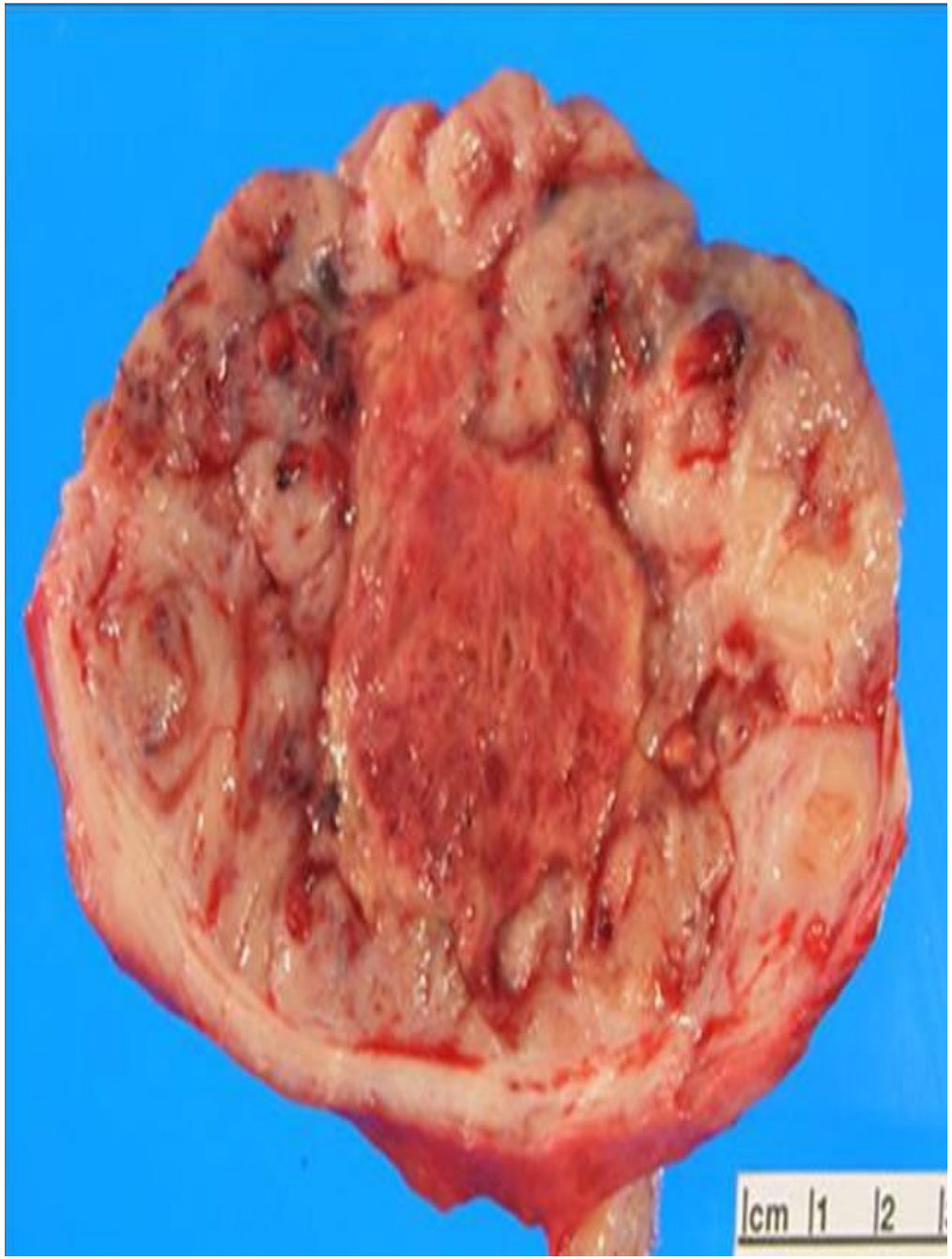
❑ **Grossly,** leiomyosarcomas may develop as:

(a) bulky masses **infiltrating** the uterine wall.

(b) **polypoid** lesions.

•They are frequently Soft ,Hemorrhagic, necrotic, infiltrative borders.

- Diagnosis: coagulative necrosis, cytological atypia, and mitotic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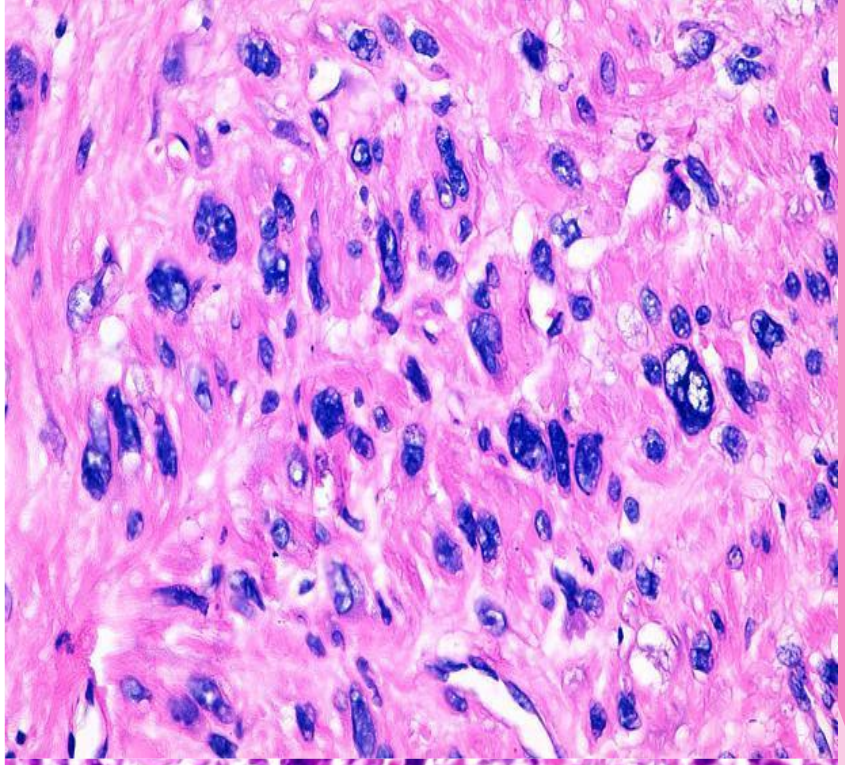
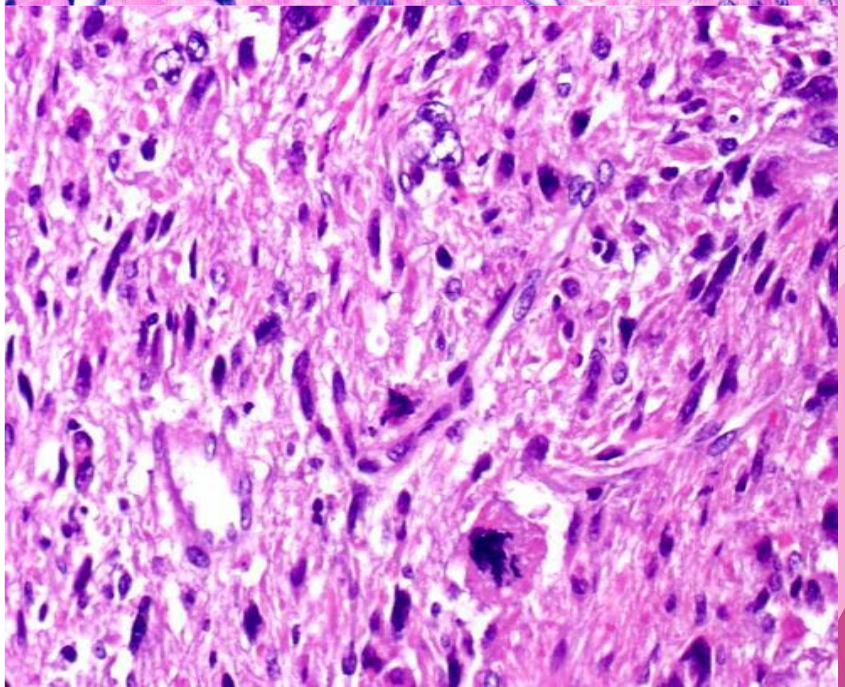




Ovarian Neoplastic Tumor

5th most common cancer in women.

- 5^{th} leading cause of cancer death in women.
- 3 Origins of primary ovarian tumors:

I-The multipotential **surface (coelomic) epithelium,**Tumor of which account for the great majority (75%) of primary ovarian T, & their malignant forms account for **90% of ovarian cancers.**

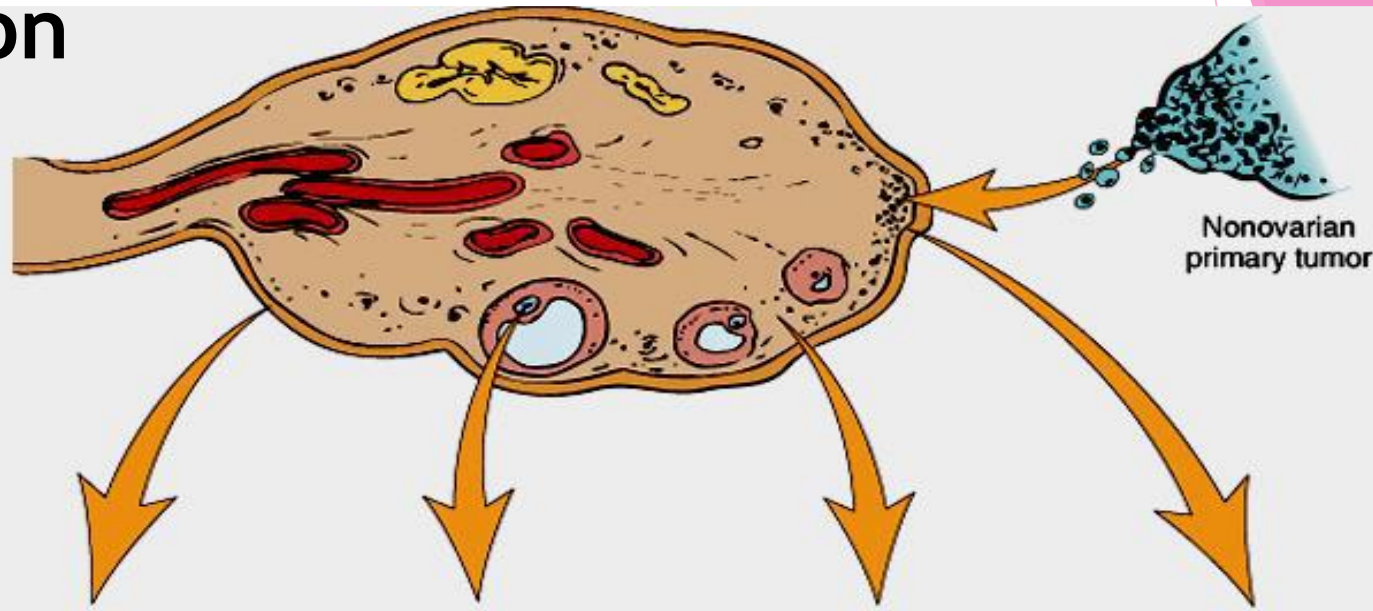
II- The totipotential **germ cells**

III- The multipotential **sex cord/stromal** cells **.**

- Each of these cell types gives rise to a variety of tumors

Both II & III T collectively are less frequent &, although they constitute 25% of all ovarian T, they account for **10% of ovarian cancers.**

Derivation of various ovarian tumors & some data on their frequency & age distribution



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	

Pathogenesis -familial cases

Risk factors: **nulliparity** and **family history**.

- use of OCPs may **reduce** risk.
- Only 5%-10% are familial

molecular pathogenesis: mutations in **BRCA1**and **BRCA2 genes.**

- There is **5% to 10%** only of ovarian ca **are familial (like Breast Ca)**. The majority of **hereditary** ovarian & breast cancers seem to be caused by **mutations in the** BRCA1**&** BRCA2 **genes. Indeed**, with mutations in these genes, there is increase **risk for both ovarian & breast cancers.**

Pathogenesis-Sporadic cases

- BRCA mutations: 10% of sporadic cases

- other important molecular pathways:

- **p53** is mutated in **50%** of all ovarian cancers.
- **HER2/NEU** over-expression (35%)
- **K-RAS** protein over-expression (30%) mostly mucinous cystadenocarcinomas.

Surface epithelial Tumor -Types

- **1-Serous**
- **2-Mucinous**
- **3-Endometrioid**
- **4-Clear cell**
- **5-Brenner**
- **All types include benign, borderline, and malignant tumors**

(I) Benign lesions usually cystic (cystadenoma), or with an **accompanying stromal component (cystadenofibroma);**

(II) Malignant tumors may be cystic (cystadenocarcinoma), solid (carcinoma), or combine.

(III) Intermediate = **borderline**= tumors of low malignant potential=low-grade cancers with limited invasive potential, which have a better prognosis than the fully malignant ovarian carcinomas.

Serous tumor

- **the most frequent ovarian tumors.**
  - Include: 60% benign, 15% borderline, and 25% malignant.
- **the most common malignant ovarian tumors (60%).**
- **Genetics:**
  - **BRAF** and **K-RAS** mutations → borderline & low grade cancers
  - **p53** and **BRCA1** mutations → High-grade serous carcinomas
  - Grossly ;most serous T are large(10-40 cm inØ)spherical or ovoid cysts.
- 25% of the benign forms are bilateral .
- The serosal covering of benign is smooth& glistening, while that of the carcinoma is irregularly nodular from tumor penetration of serosa.
- O/S,smaller cystic T are unilocular, {with single cavity}; but larger ones are usually divided by multiple septa into a multiloculated cyst.
- The cystic spaces are usually filled with a clear serous fluid, but mucus may also be present.
- Papillary projections into the cystic cavities are usually seen, more marked in malignant T.

Morphology :

- The benign tumor are: (a) lined by a single layer of tall, ciliated or dome-shaped secretory columnar epithelium cells.

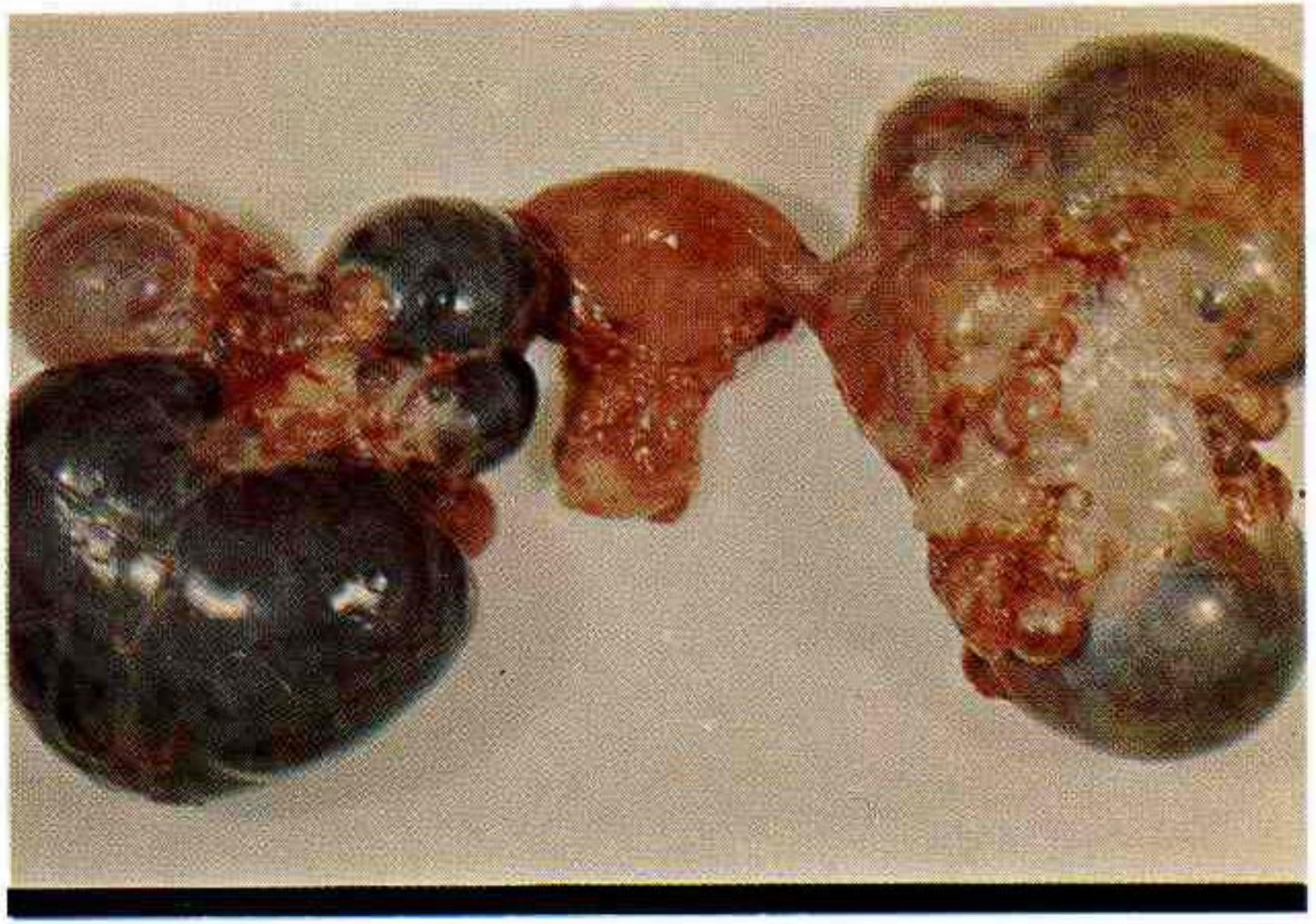
- (b) Psammoma bodies(concentrically laminated calcified concretions) are commonly seen in the tips of papillae.

- When frank carcinoma develops: (a) anaplasiao f the lining cells appears, as does (b) invasion of the stroma, & capsule.
- Papillary formations are complex & multilayered, with invasion of the axial fibrous tissue by nests or totally undifferentiated sheets of malignant cells.

❑ Between these benign & malignant serous tumors are tumors of low malignant potential,with milder cytologic atypia & typically, little or no stromal invasion.

❑ Malignant serous T spread through (a) metastatic seeding of the peritoneal cavity, & (b) through lymphatics to regional LN, including periaortic LNs, but distant lymphatic & hematogenous metastases are rare

Bilateral benign serous cystadenomas of the ovary. An irregular, lobulated masses replacing both ovaries. The bluish discoloration is due to hemorrhage into the cyst.



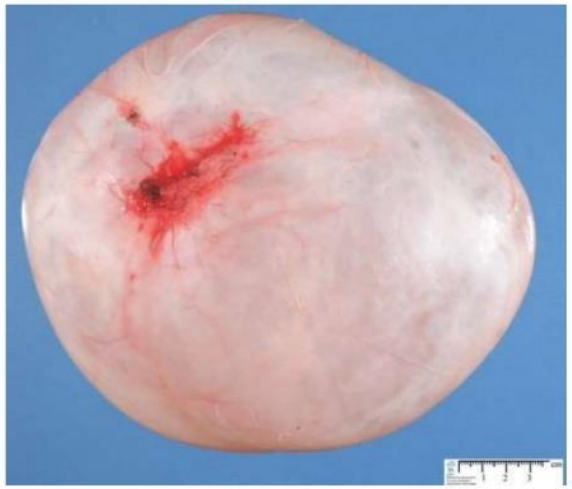
12.60 Serous cystadenomas: ovaries

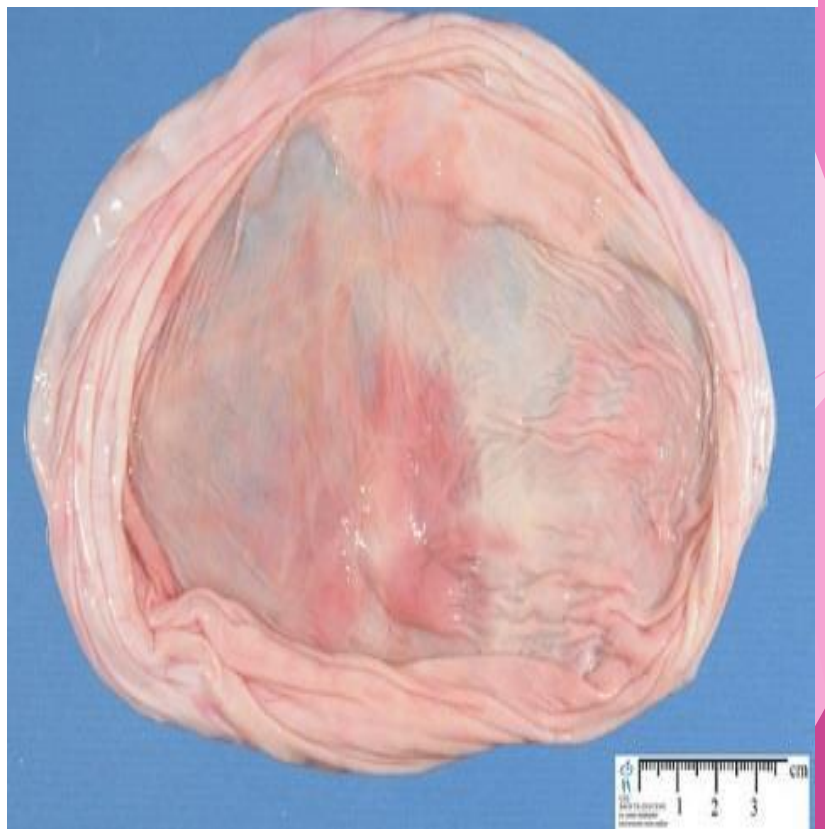
Morphology

Benign serous tumors:

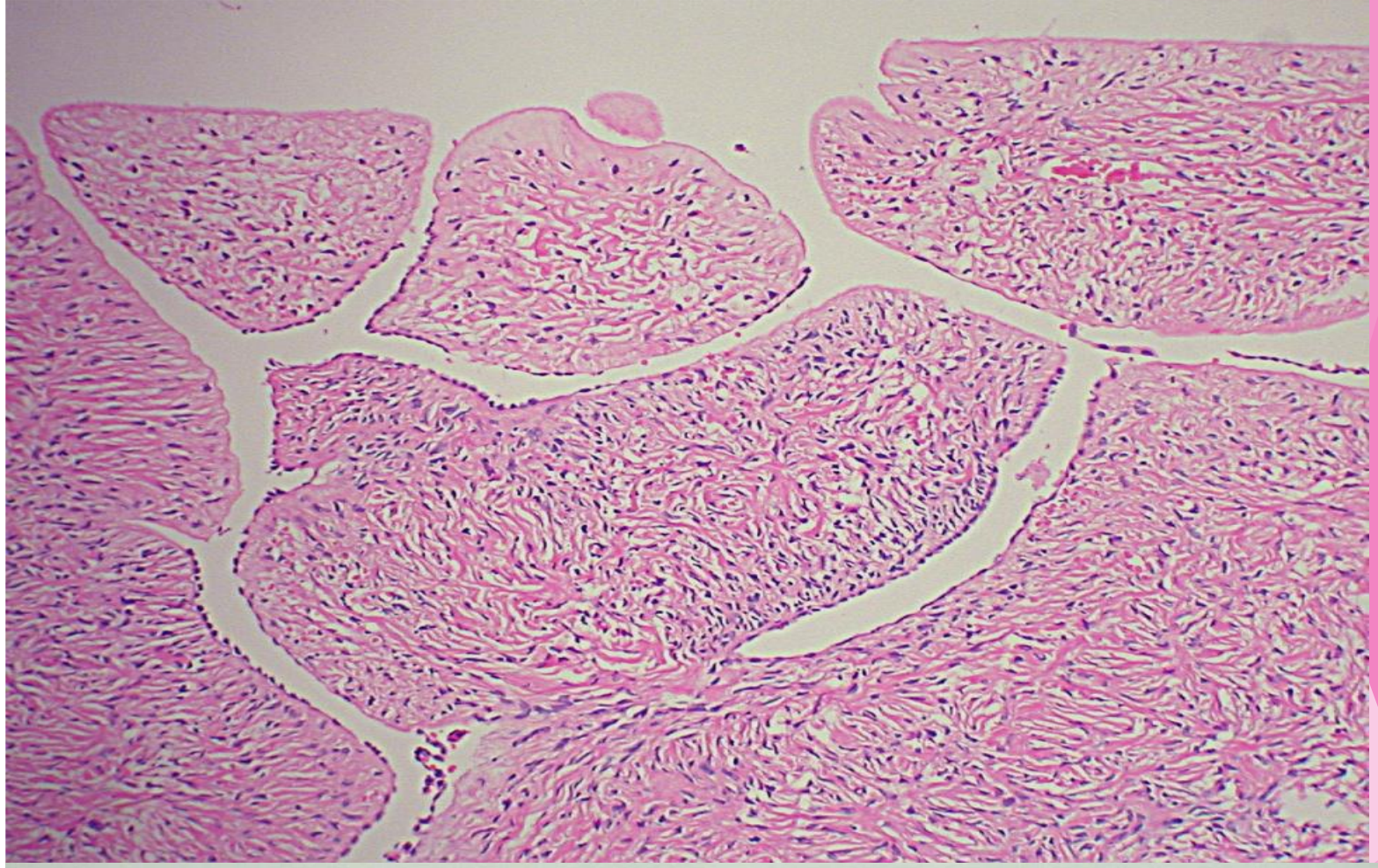
- large cystic, (30 cm).
- May be bilateral.
- filled with a clear serous fluid
- **single layer** of columnar epithelium. Some cells are ciliated.
- **Psammoma bodies**(laminated calcified concretions) are common in tips of papillae of **all** serous tumors

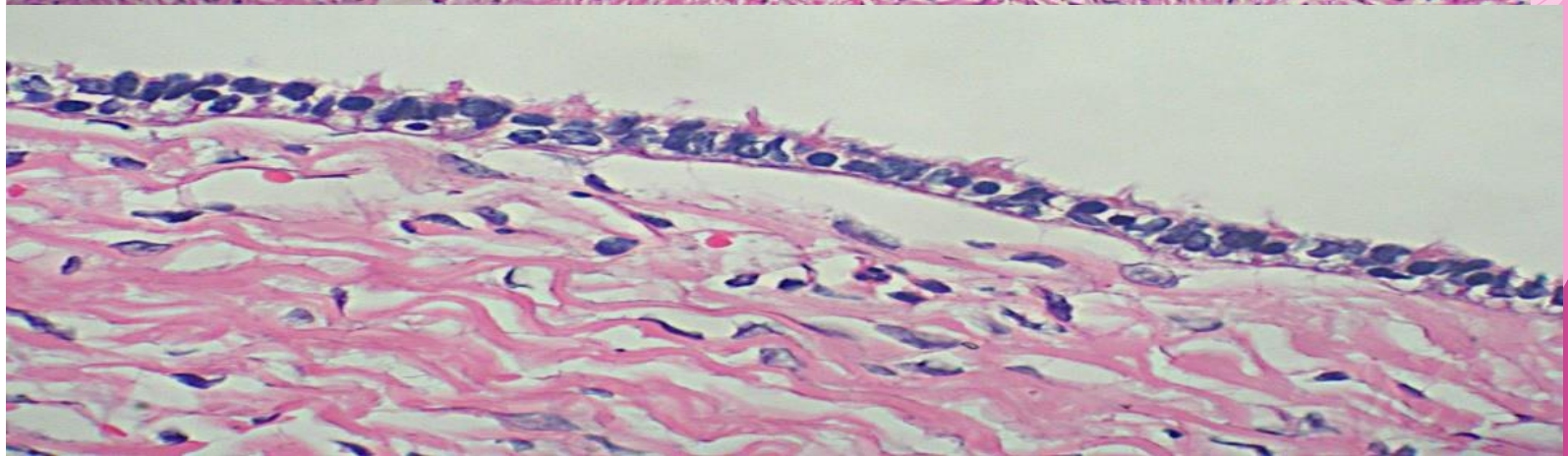
SEROUS CYSTADENOMA





Benign Serous Tumor



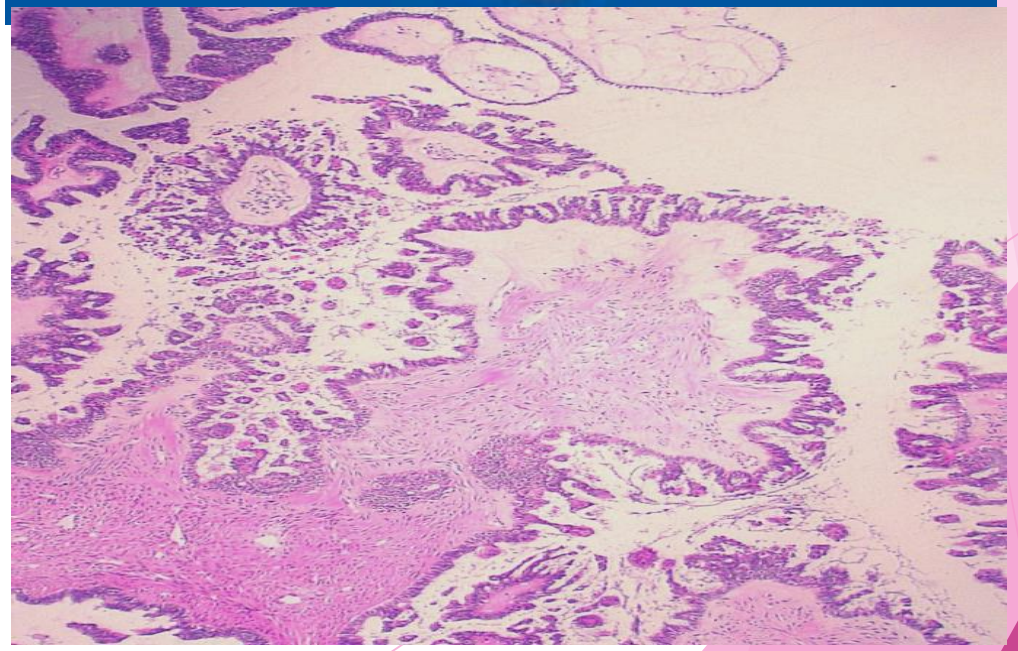


Borderline Serous tumor

More complex architecture

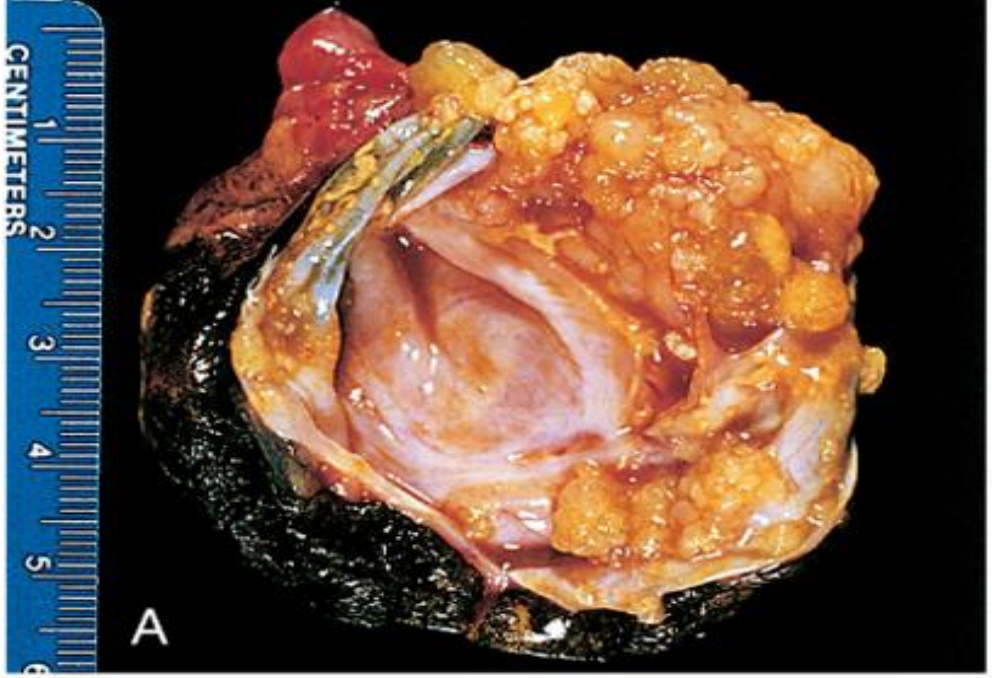
- **mild cytological atypia**
- **but no stromal invasion.**
- **might be associated with peritoneal implants**

- **Prognosis intermediate between benign and malignant types (survival with peritoneal metastases 75%)**



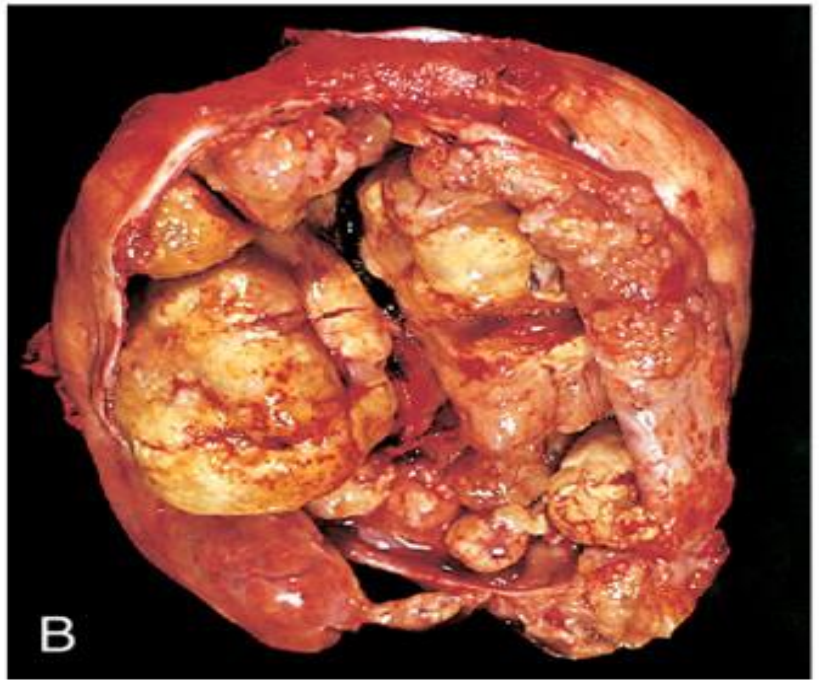
A, Borderline serous cystadenoma.

Opened cyst cavity lined by delicate papillary tumor growths



B,**Cystadenocarcinoma:**

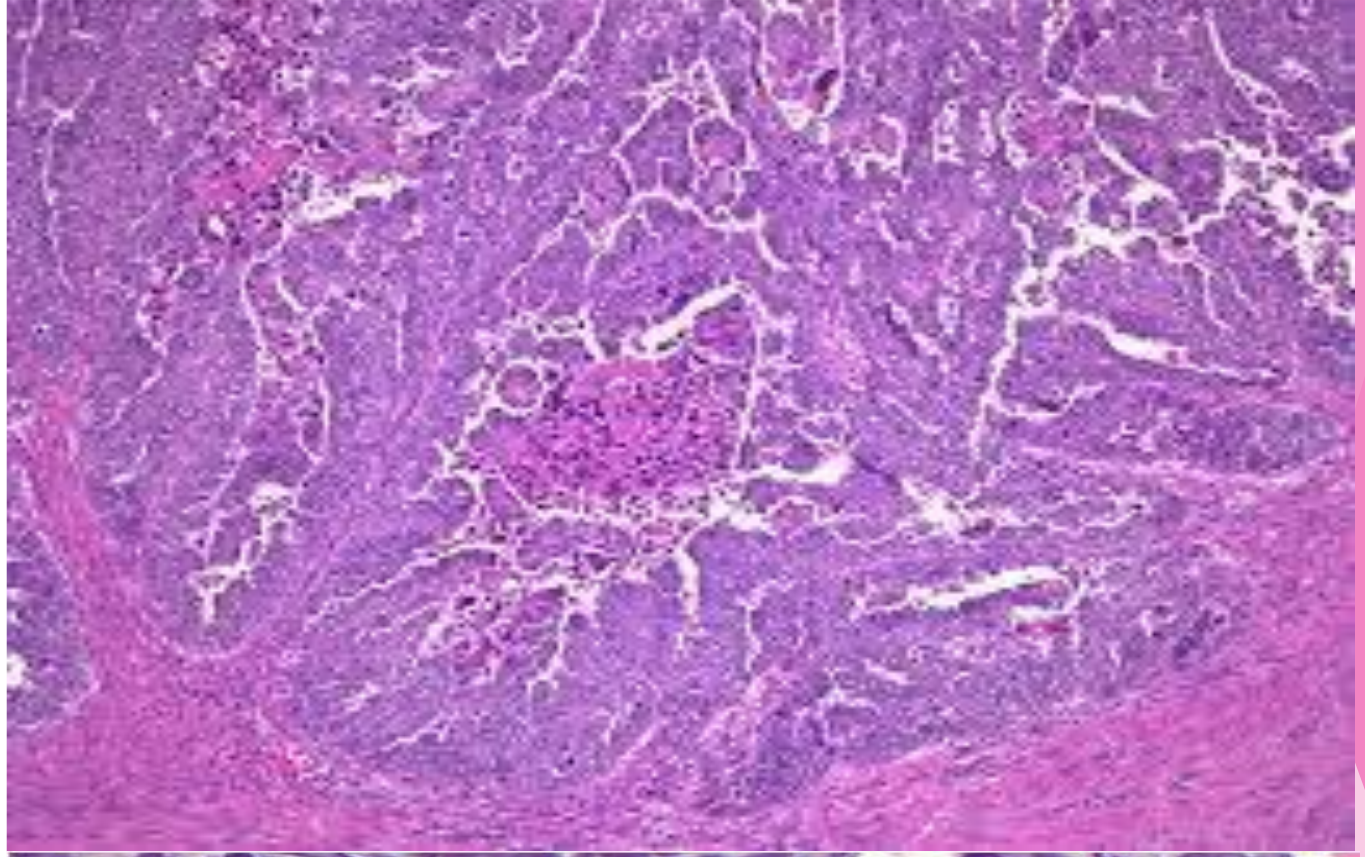
Opened cyst reveal a large, bulky tumor mass

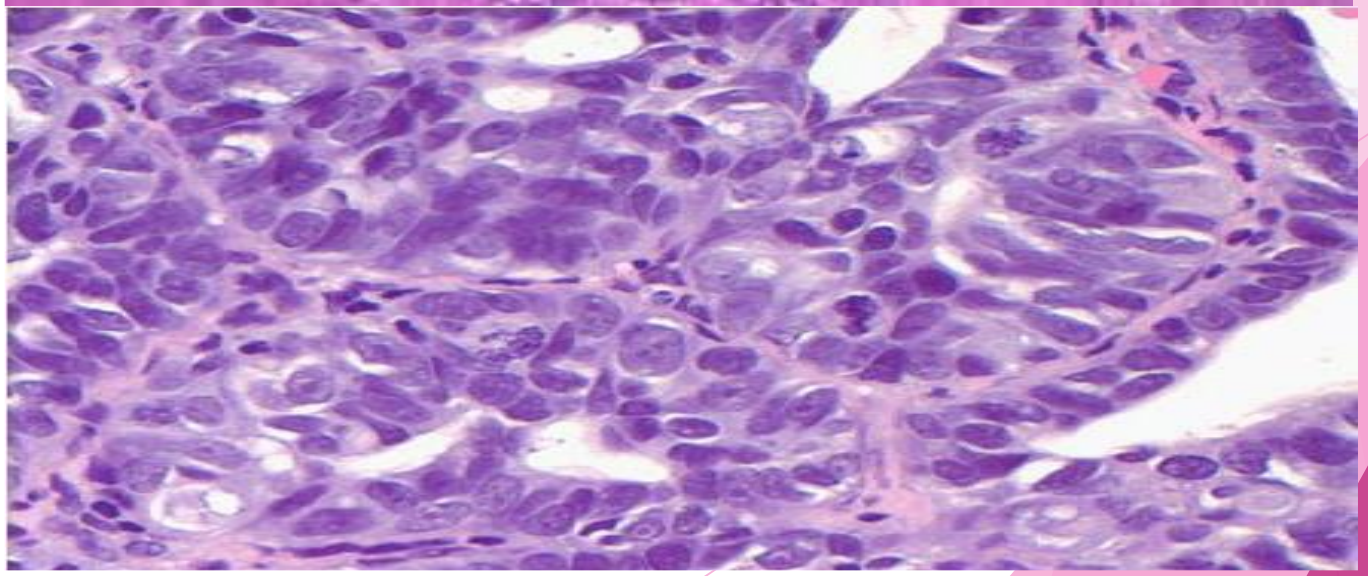


Malignant Serous Carcinoma

- Anaplasia of cells and invasion of the stroma.

- Prognosis poor, depends on stage at the time of diagnosis.





Mucinous Ovarian Tumor

- **Mucin-secreting** cells. their mucin-secreting epithelium cell lining, similar to that of the endocervical mucosa,
- are less likely to be malignant than the serous T (80% are benign mucinous cystadenomas),
- Depending on the architectural complexity:

❖ 80% benign; 10% borderline; **10% malignant** (cystadenocarcinoma)

- **Usually large** and **multilocular**.
- Psammoma bodies **not** found.
- Stage is major determinant of prognosis

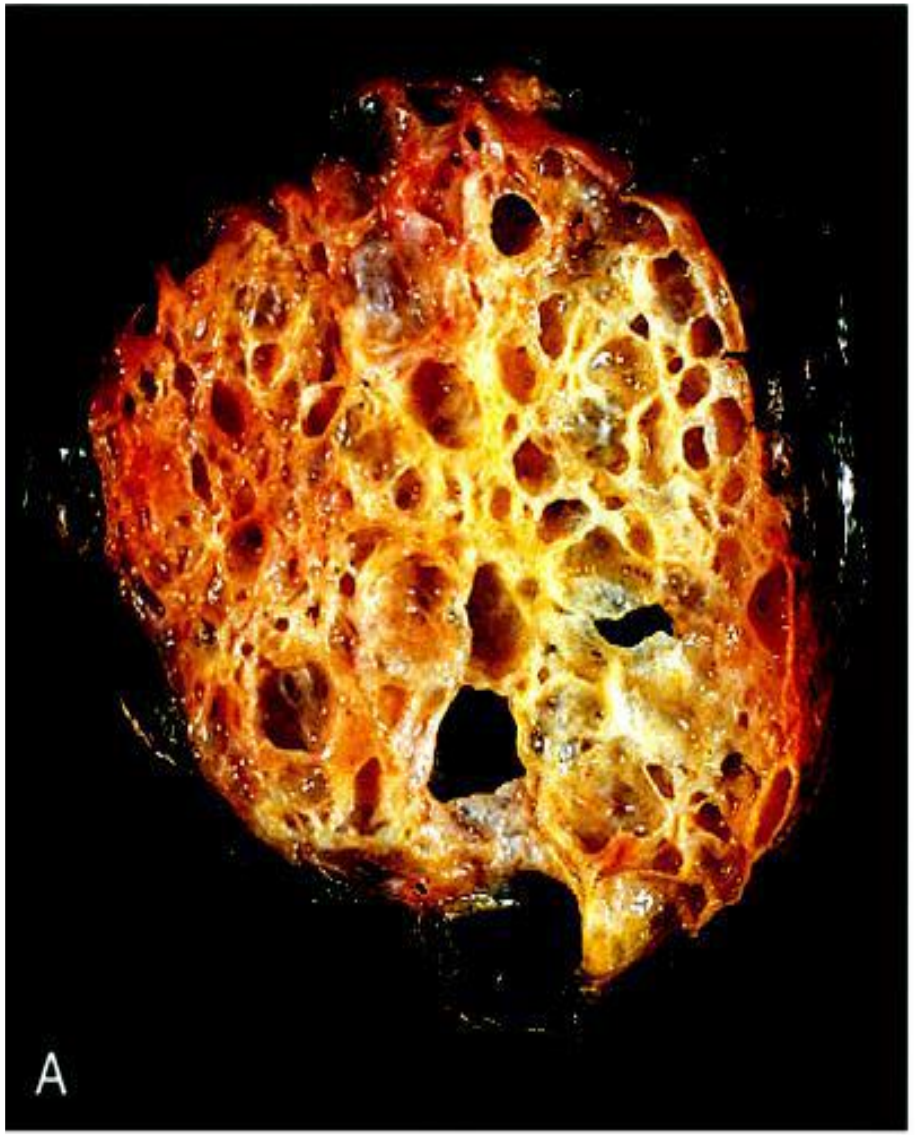
- Much **less likely to be bilateral,** with only 5% of benign & 20% of malignant mucinous tumors been **bilateral.**

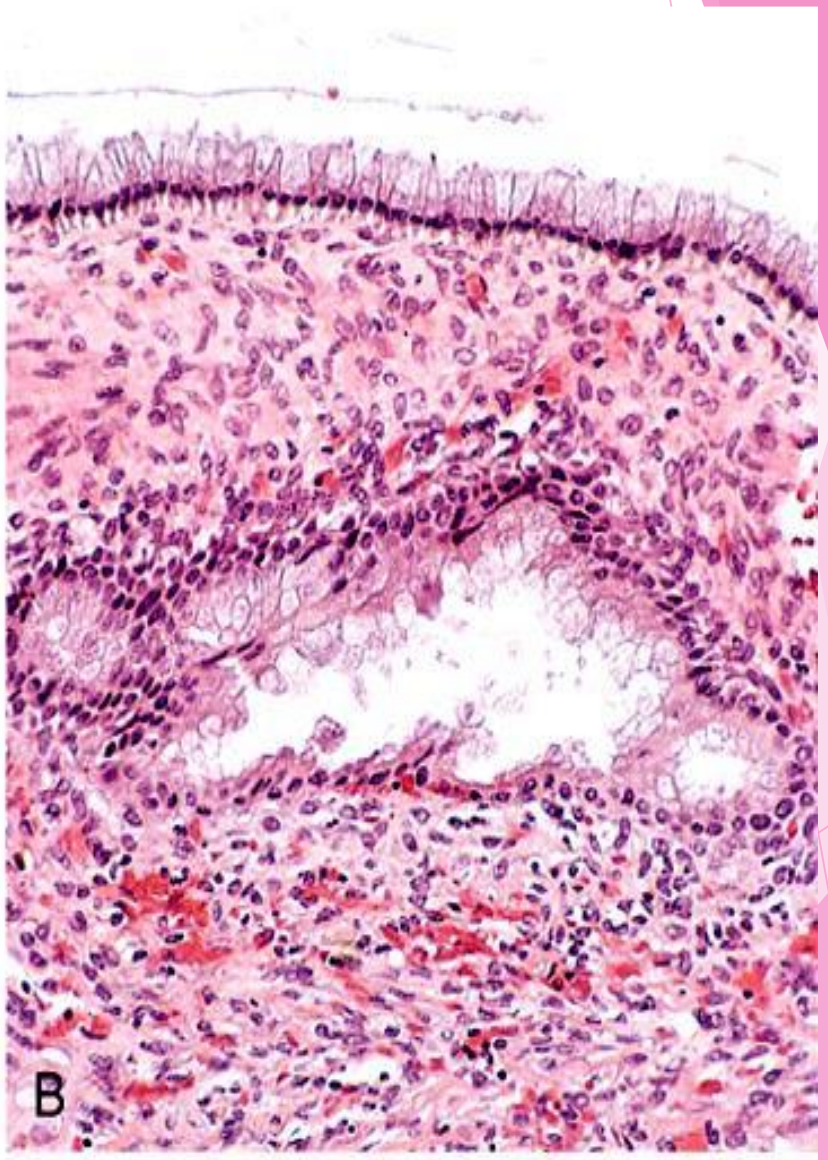
- bilateral mucinous ca of the ovary must be differentiated from metastatic adenocarcinoma in the ovaries (Krukenberg tumor), which may present as ovarian masses.
- **Grossly** , mucinous T are similar to serous T, except that filled by mucin.The presence of prominent papillation, serosal penetration, & solid areas, point to malignancy.

- Implantation of mucinous T cells in the peritoneum with production of copious amounts of mucin is called **pseudomyxoma peritonei**; the vast majority of these cases are caused by metastasis from the GIT tumors, primarily the appendix.

- Metastasis of mucinous ca of the GIT to the ovaries (**Krukenberg tumor**) may also mimic an ovarian primary,

Mucinous ovarian tumors





Endometrioid Tumors

Grossly:

- these T may be solid or cystic, but some develop as a mass projecting from the wall of an endometriotic ovarian cyst filled with chocolate-colored fluid.
- they are distinguished by the formation of tubular glands, similar to those of the endometrium, within the linings of cystic spaces.
- Are usually malignant, although benign & borderline forms exist,and bilateral in 30% of cases.
- 15% to 30%of women with these ovarian T have a concomitant endometrial carcinoma of the endometrium.
- Similar to endometrial endometrioid cancer, ovarian endometrioid carcinomas have mutations in the PTEN suppressor gene.

Germ cell tumor

- **testicular epithelial tumors are very rare.**
- **benign cystic teratomas are never seen in the testis, while testicular malignant germ-cell tumors are the most common**
- **Teratomas constitute 20% of ovarian T.**
- **Majority of teratomas are Benign in ovaries.**
- **The immature malignant variant is rare (5-10%).**

Benign (Mature) Cystic Teratomas :

- All are marked by full **differentiation** from totipotential germ cells into mature tissues, representing all three germ cell layers: ectoderm, endoderm, & mesoderm.

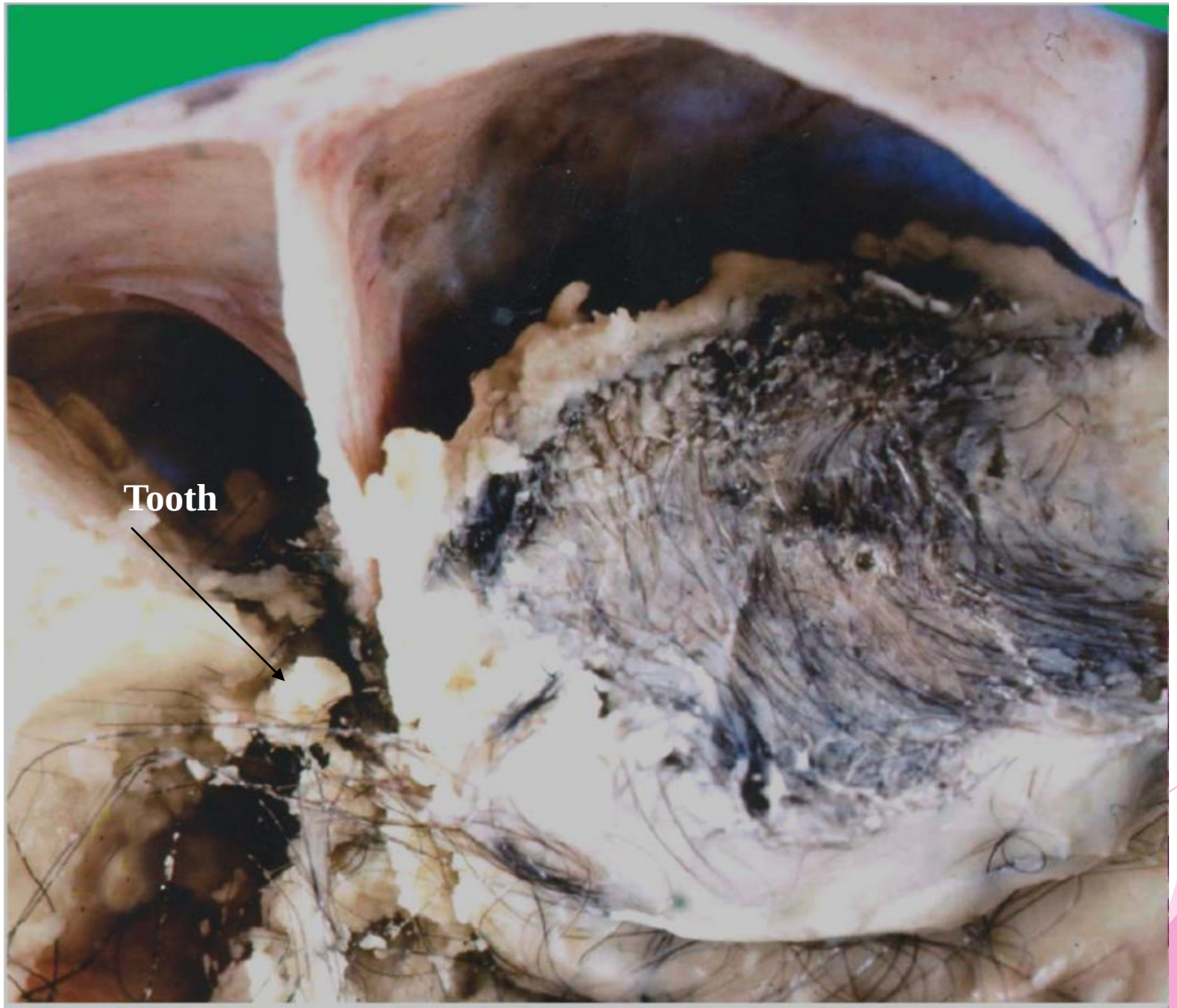
- Most are discovered in young women (**1-20 years)** as an ovarian **masses** or incidentally found by X-ray

- Grossly: cyst filled with sebaceous secretion and hair; bone and cartilage; epithelium, or teeth.

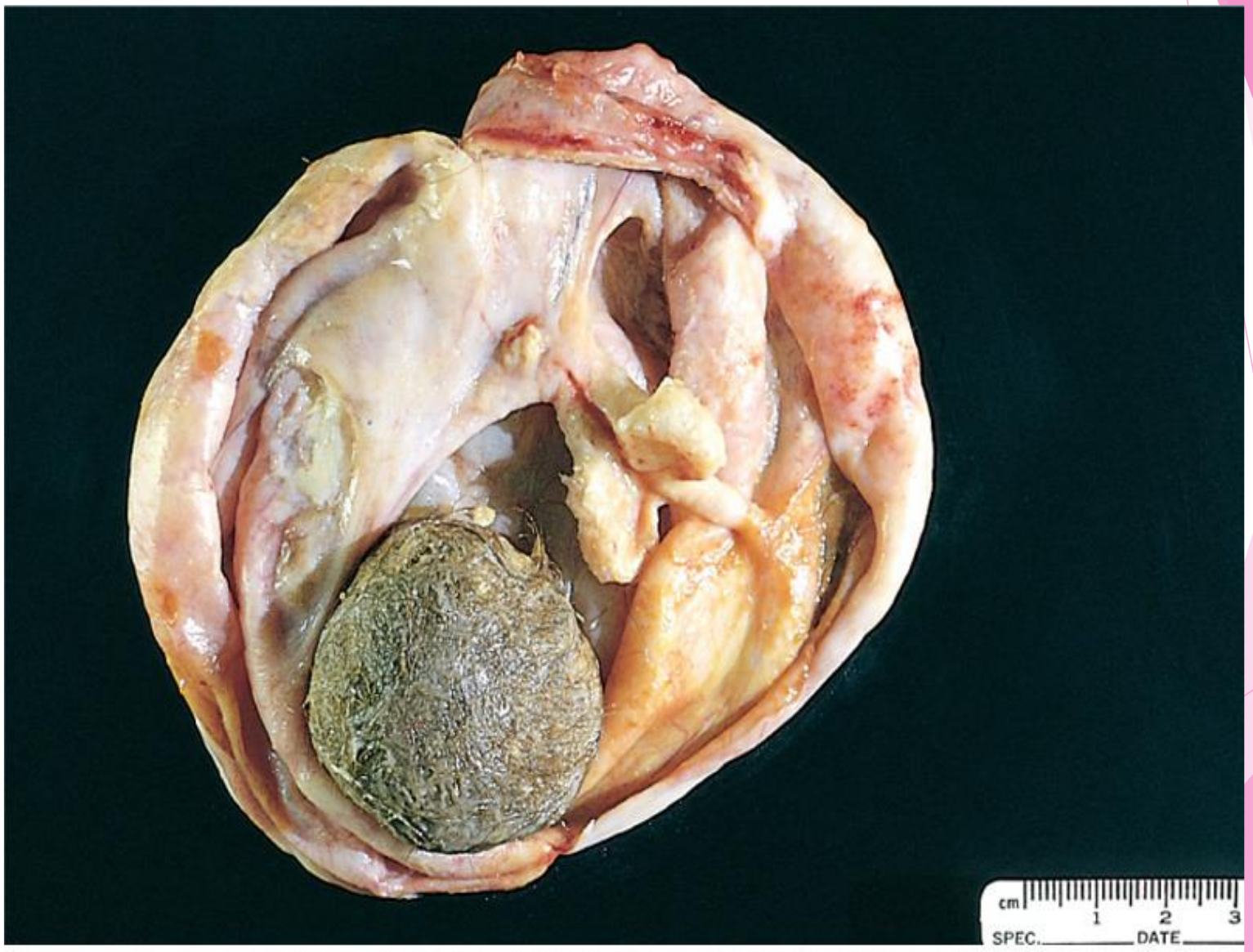
- 1% →malignant transformation.
- torsion (10% to 15% of cases).
- Most discovered incidentally.
- 90% unilateral.

- **Struma ovarii** composed entirely of **mature thyroid tissue** appearing as small or large solid, unilateral brown ovarian masses. Interestingly may hyper function & produce thyrotoxicosis.

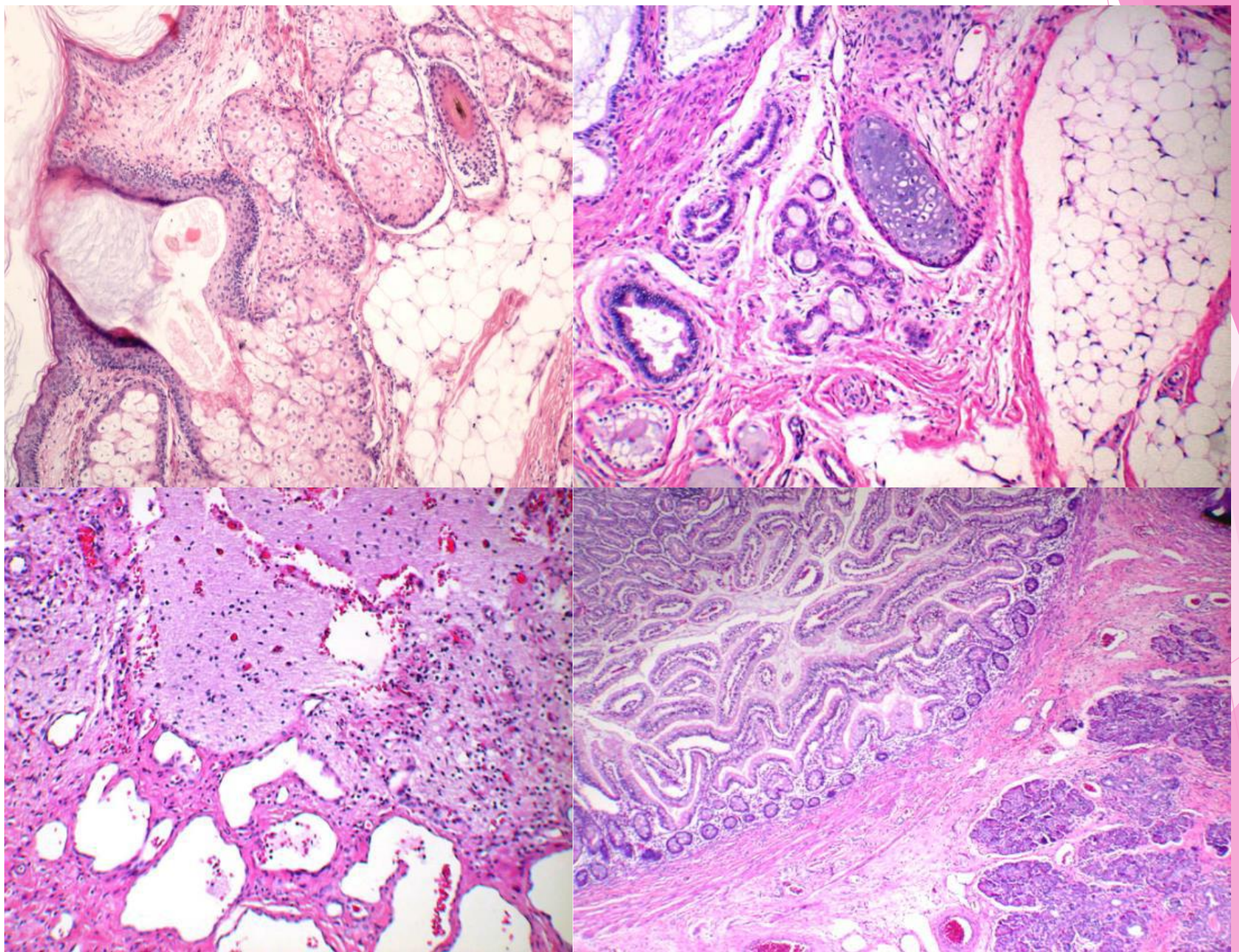
Benign (Mature) Cystic Teratomas



Opened mature cystic teratoma (dermoid cyst) of the ovary with a ball of hair.



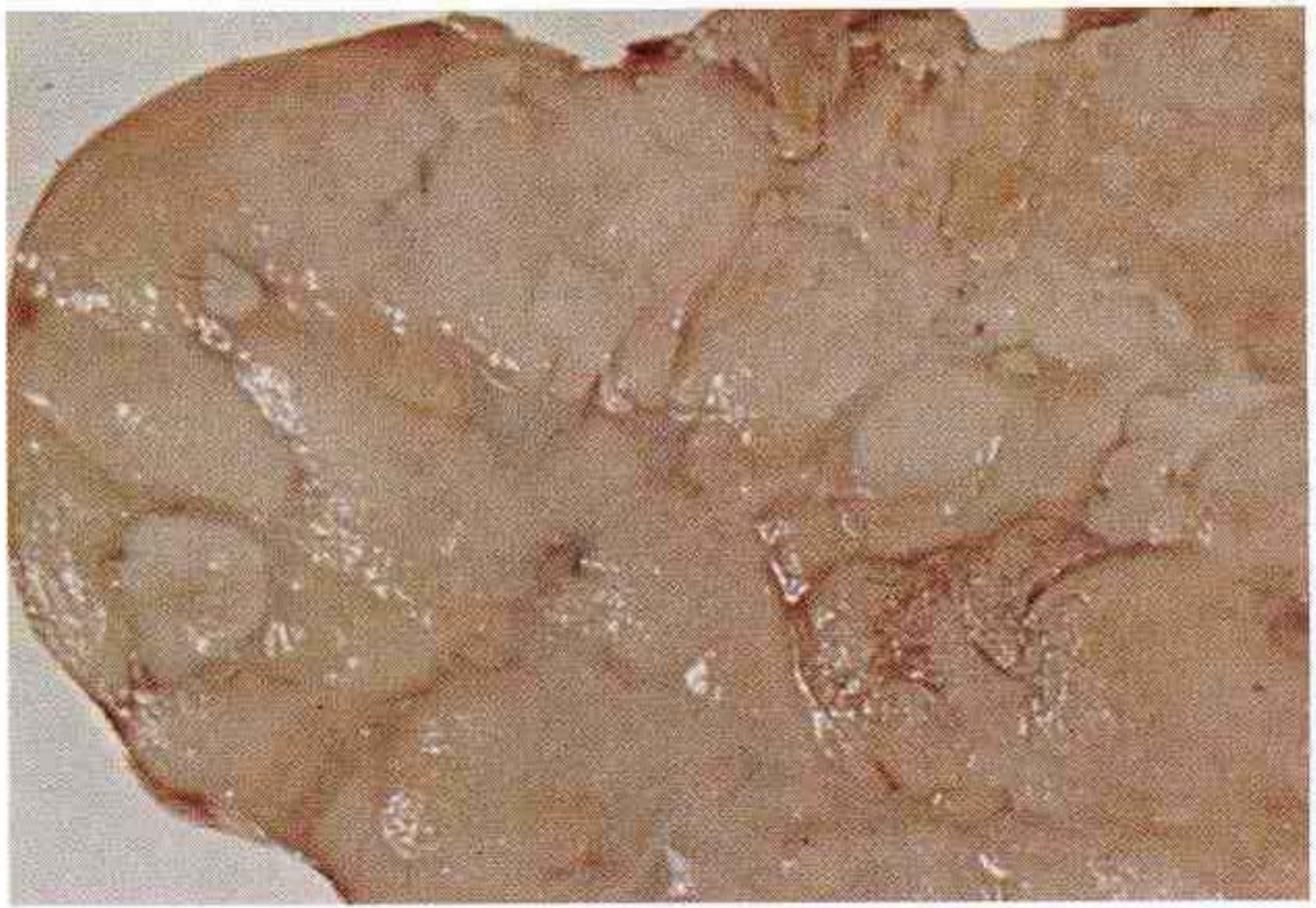
Benign (Mature) Cystic Teratomas



Dysgerminoma

- Counterpart of testicular seminoma
- 2nd to 3rd decades.
- occur with gonadal dysgenesis.
- All are malignant, but only one-third aggressive & spread; All radiosensitive with 80% cure.
- Mostly unilateral, solid, small to large potato-like gray masses

Dysgerminoma: ovary =counterpart of testicular **seminoma**. The C/S is **potato**-like, solid, lobulated, pinkish-grey with foci of whitish necrosis.



12.63 Dysgerminoma: ovary

Sex Cord Tumors;

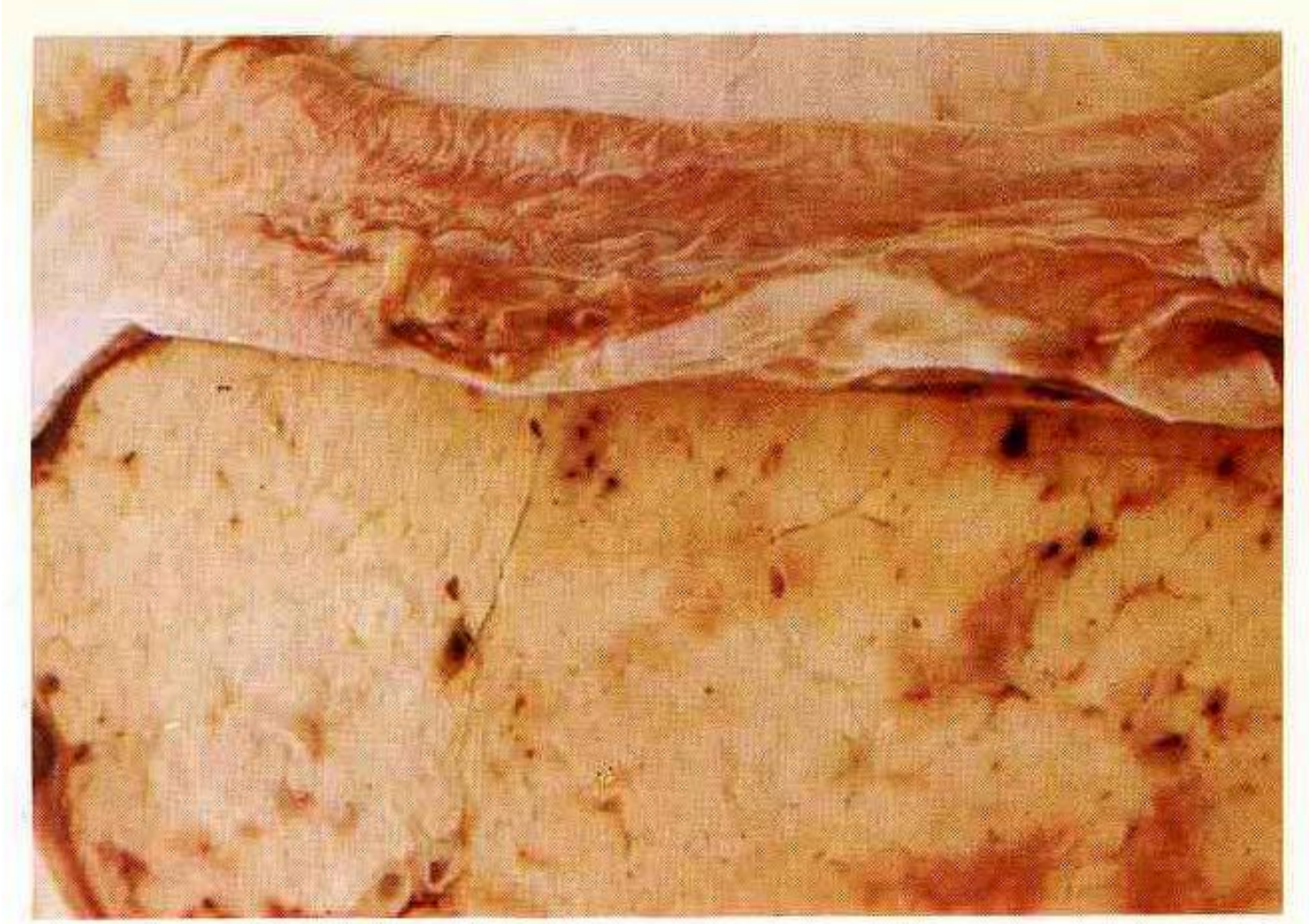
(I) Granulosa-thecal cell:

- (5-10% of all ovarian T).
- Mostly postmenopausal, but may occur at any age.
- Unilateral, small to large, gray to yellow with cystic spaces.
- Morphology :composed of mixture of: (1) cuboidal granulosa cells (may recapitulate ovarian follicle as Call-Exner bodies, arrange in cords, sheets, or strands, Mostly benign, but malignant granulosa cell T are seen in 5% to 25% of cases, & (2) spindled/plump lipid-laden thecal cells which elaborate large amounts of estrogen promoting endometrial or breast ca.

(II) Thecoma-fibroma:

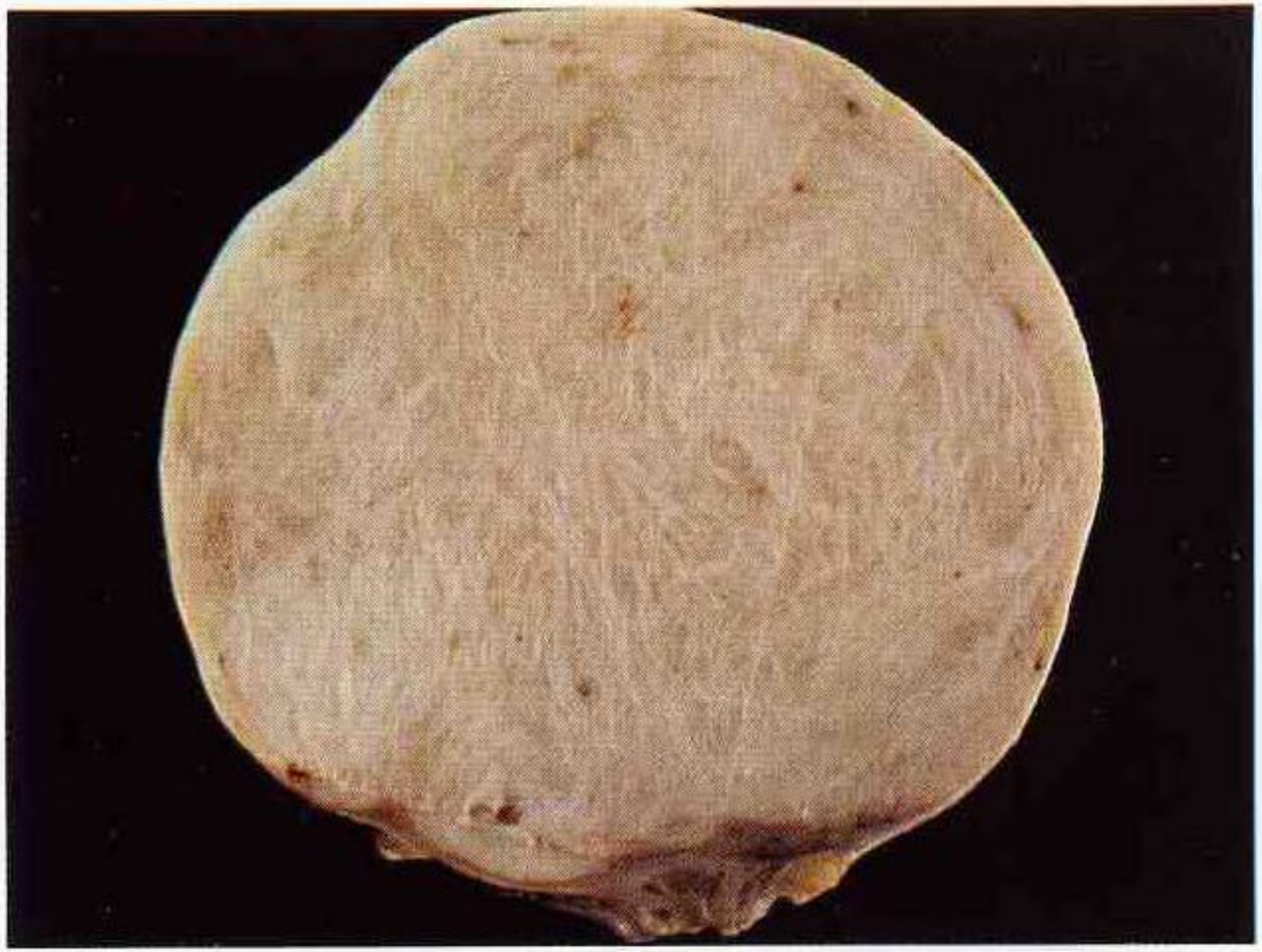
- Any age, Benign, unilateral, Solid, & gray
- Morphology: fibrocytes, to yellow (lipid-laden) plump thecal cells.
- Most are hormonally inactive; few elaborate estrogens.
- **For obscure reasons, about 40% produce ascites + hydrothorax = (Meig's syndrome).**

Granulosa cell tumor: ovary. Unilateral, solid encapsulated, C/S is yellow with foci of hemorrhage.



12.67 Granulosa cell tumour: ovary

Fibroma: ovary. Spherical, firm & smooth-surfaced, O/S whorled with fibrous trabeculae.



12.66 Fibroma: ovary

(III) Sertoli-Leydig cell: All ages, Unilateral,
★Usually small, gray to yellow-brown, & solid. ★Recaps (simulate) testis development, with tubules or cords & plump pink Sertoli cells;
★Many masculinizing or defeminizing.
★ Rarely malignant.

➔**Metastases to Ovary = Krukenberg tumors**

- ★Older ages, Mostly **bilateral**
- ★Solid gray-white masses up to 20 cm in Ø(1 Kg)
- Anaplastic T cells in cords, glands, dispersed through fibrous background.
- Cells may be "signet-ring" mucin-secreting. ★Primaries are GIT, breast, & lung.

Clinical Correlation of all Ovarian Tumors

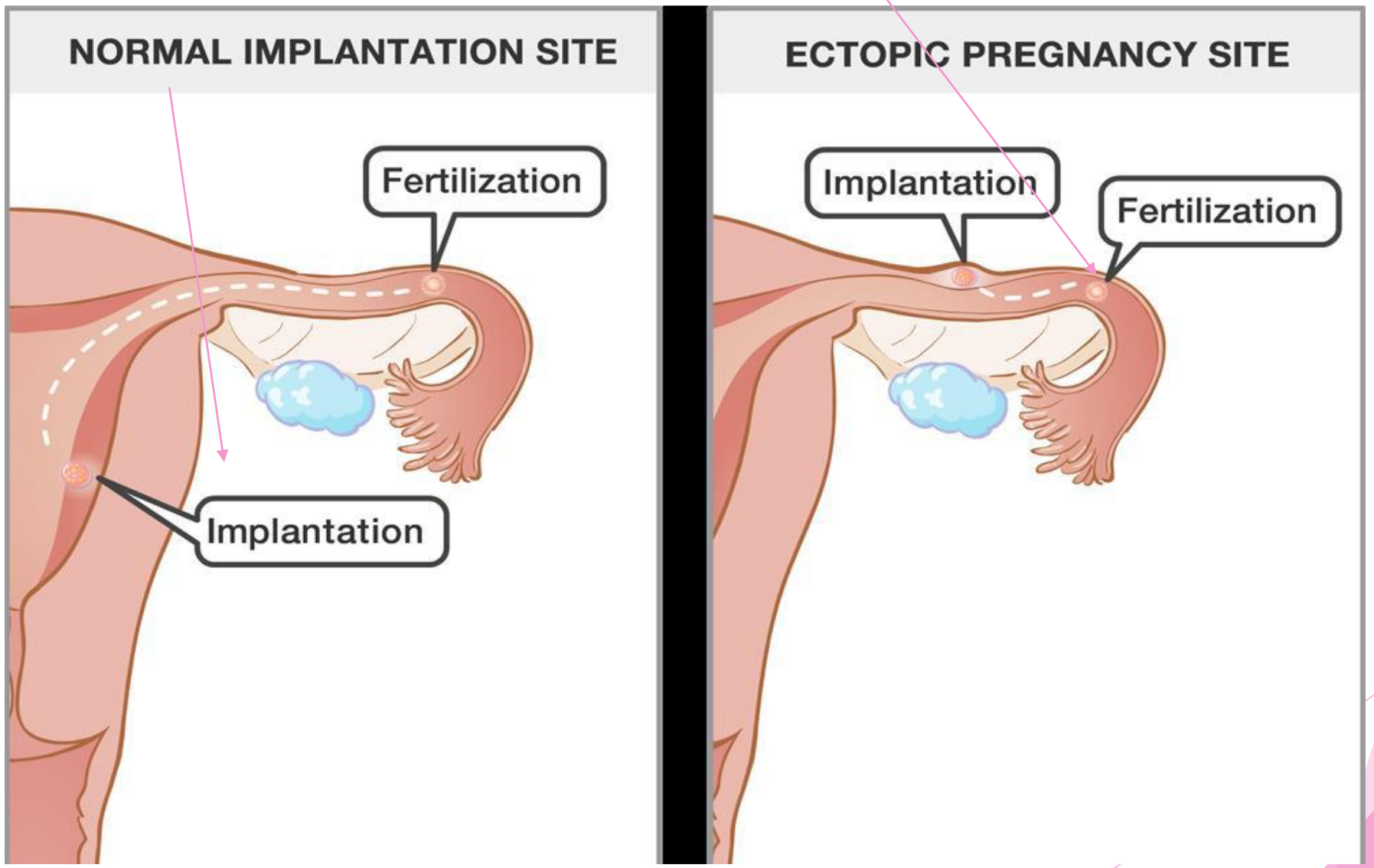
- clinical presentation of all is similar:
  - pain, gastrointestinal complaints, urinary frequency; rarely torsion producing severe abdominal pain mimicking an "acute abdomen."
  - Ascites (in Fibromas and malignant serous tumors).
  - Functioning ovarian tumors often come to attention because of hormonal production (Estrogens or androgens).
- **Most** ovarian T are asymptomatic until they are well advanced.
- **30%** of all ovarian T are discovered incidentally on routine gynecologic examination!

Pathology of Fallopian Tube

Ectopic pregnancy

- implantation of the fertilized ovum outside uterus
- Incidence: 1%
- 90% of cases →in fallopian tubes
- other sites: ovaries, abdominal cavity
- Predisposing factors: tubal obstruction (50%) PID; tumors; endometriosis; **IUCD**..
- In 50% : no anatomic cause can be demonstrated.

Normal Versus ectopic pregnancy.



Ectopic Pregnancy

- Early: Grossly, EP in all sites is characterized by fairly normal early development of the embryo, with the formation of placental tissue, decidual changes & the amniotic sac.

- Later: the placenta burrows through tubal wall causing intratubal **hematoma (hematosalpinx) and intraperitoneal hemorrhage.**
- Rupture of an ectopic pregnancy: intense abdominal pain (**acute abdomen)**, often followed by shock.

- **Prompt surgical intervention is necessary.**
- **Histological diagnosis & confirmation** depends on the visualization of the ® **placental villi or, rarely, of the embryo.**

- **Until rupture occurs**, **EP** may be indistinguishable from a normal pregnancy, with amenorrhea & elevation of serum & urinary hCG (Positive pregnancy test).

- Under the influence of hCG, the **endometrium** undergoes characteristic hypersecretory & decidual changes called ® **Arias Stella Reaction** (in 50% of cases), But, as expected, there are **NO chorionic villi in the uterus**.
- However, the **absence** of elevated hCG levels & positive pregnancy test **does not exclude** the diagnosis of EP because poor attachment with necrosis of the placenta is common.

- **Rupture of an EP may be catastrophic, with** sudden onset of intense abdominal pain & signs of an **acute abdomen**, often followed by sever hemorrhage & hypovolemic shock. Prompt surgical intervention is **life-saving**

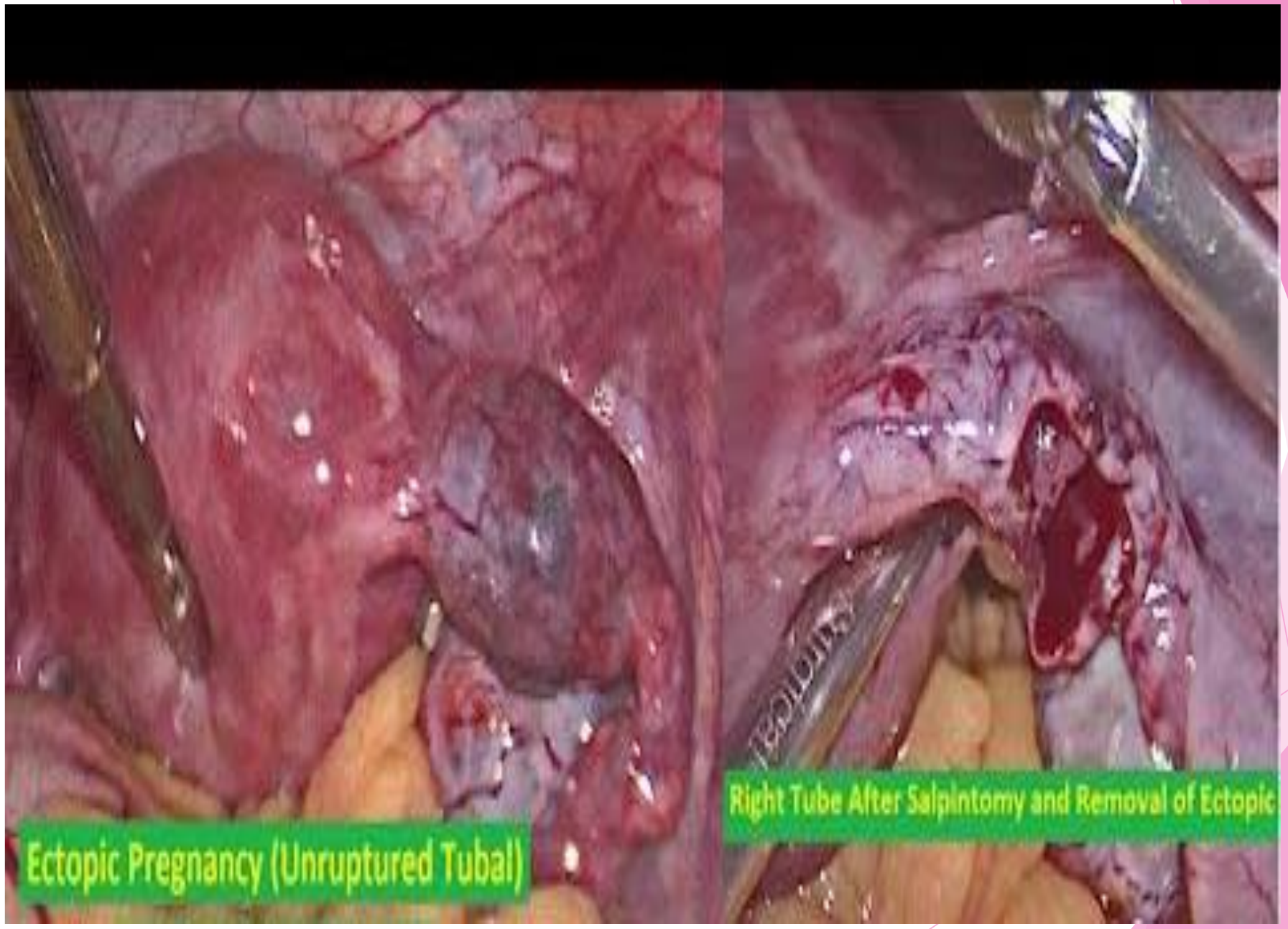
Tubal malignancy

- considered rare.

most common histo. type is serous carcinoma.

increased in women with **BRCA mutations (**In studies of prophylactic oophorectomies:10% →occult foci of malignancy in fimbria).

Because **of access to peritoneal cavity**, fallopian tube carcinomas frequently spread to omentum and peritoneal cavity at time of presentation (advanced).


Ectopic Pregnancy (Unruptured Tubal)
Right Tube After Salpintomy and Removal of Ectopic

GESTATIONAL TROPHOBLASTIC DISEASE

- Gestational trophoblastic T are divided into 3 categories, ranging in their aggressiveness from the:
- (I) Benign, Complete & Partial Hydatidiform moles (HM),
- To (II) Invasive mole.
- to the (III) highly malignant Choriocarcinomas (Chorio ca).

- All trophoblastic T elaborate human chorionic gonadotropin (hCG), which can be detected in the circulating blood & urine (used for the diagnosis of pregnancy) at titers considerably higher than those found during normal pregnancy ;the titers progressively rising from HM, to invasive mole, to Chorioca.

- The fall or the rise in the hCG level in the blood or urine can be used also to monitor the effectiveness of treatment.

- Clinicians therefore prefer the term gestational trophoblastic disease, because the response to therapy as judged by the hCG titers is significantly more important than the anatomic segregation of one lesion from another.

Hydatidiform Mole (HM): Complete & Partial

- Typical HM appears grossly as grape like structure, is a voluminous mass of swollen, cystically dilated chorionic villi.
- The swollen villi are covered by varying amounts of normal to highly atypical chorionic epithelium.
- HM is due to an abnormal contribution of paternal chromosomes in gestation.

- Two distinctives subtypes of HM, complete& partial have been characterized & the 2 patterns result from abnormal fertilization, in which a:

- Complete HM, an empty egg is fertilized by 2 spermatozoa(or a diploid sperm),yielding a diploid karyotype (46, XX or, uncommonly, 46, XY) composed entirely paternal genes.

- The complete HM does not permit embryogenesis & therefore never contains fetal parts. All of the chorionic villi are abnormal, & the chorionic epithelial cells are diploid & all chromosomes are paternal.

- While Partial HM, a normal egg is fertilized by 2 spermatozoa (or a diploid sperm), resulting in a triploid karyotype (69, XXY) with a preponderance of paternal genes.

- The partial HM is compatible with early embryo formation & therefore contains fetal parts, has some normal chorionic villi, & is always triploid & having 2 sets of paternal chromosomes.

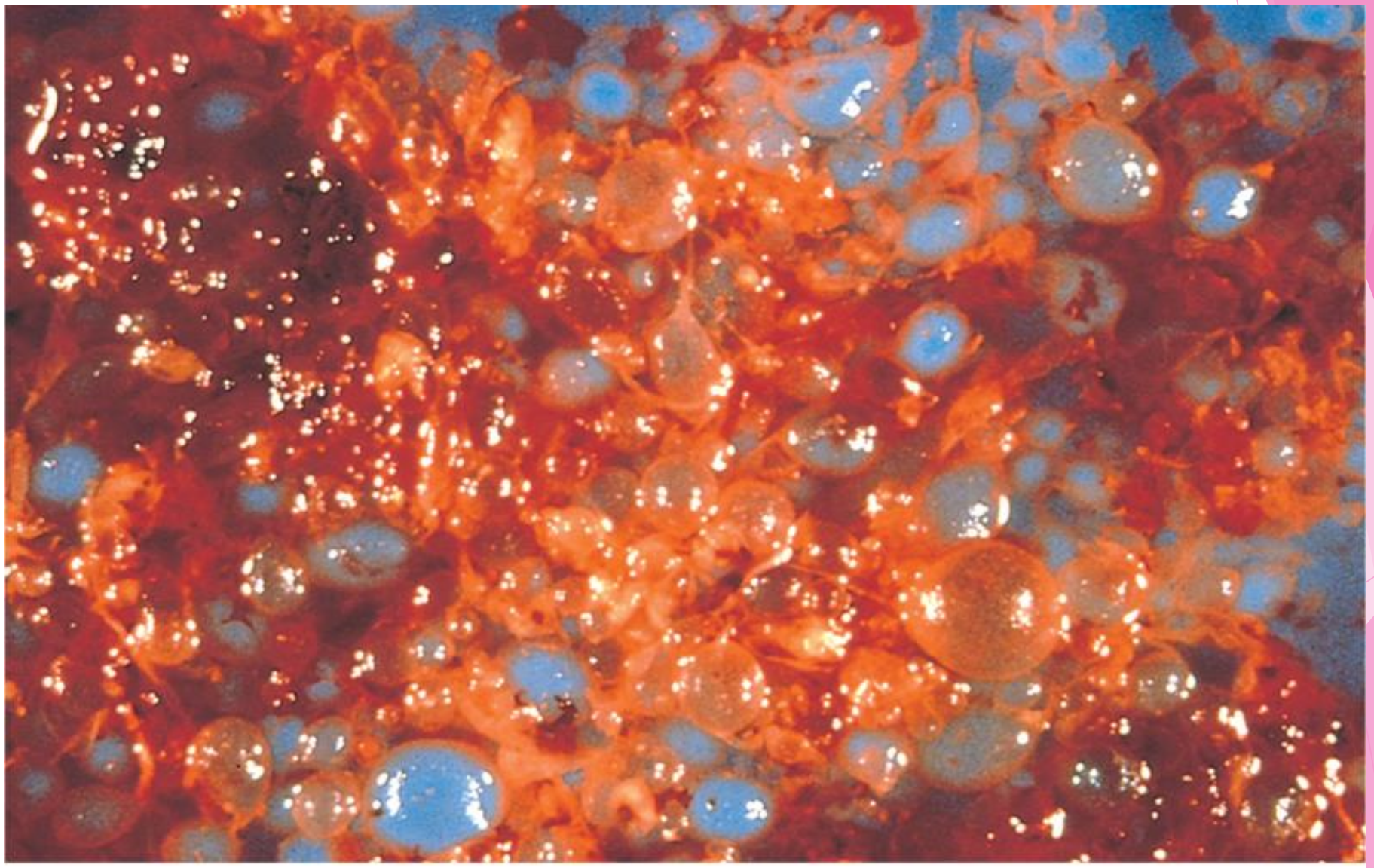
Table showing Features of Complete	&	Partial HM:
Karyotype: 46, XX (46, XY)		Triploid (69, XXY)
Villous edema: All villi		All villi
Trophoblast Proliferation: Diffuse & circumferential		Focal & slight
Atypia: Often present		Absent
Serum hCG: Elevated		Less elevated
hCG in tissue: ++++		+
Progress to choriocarcinoma: 2%		Rare

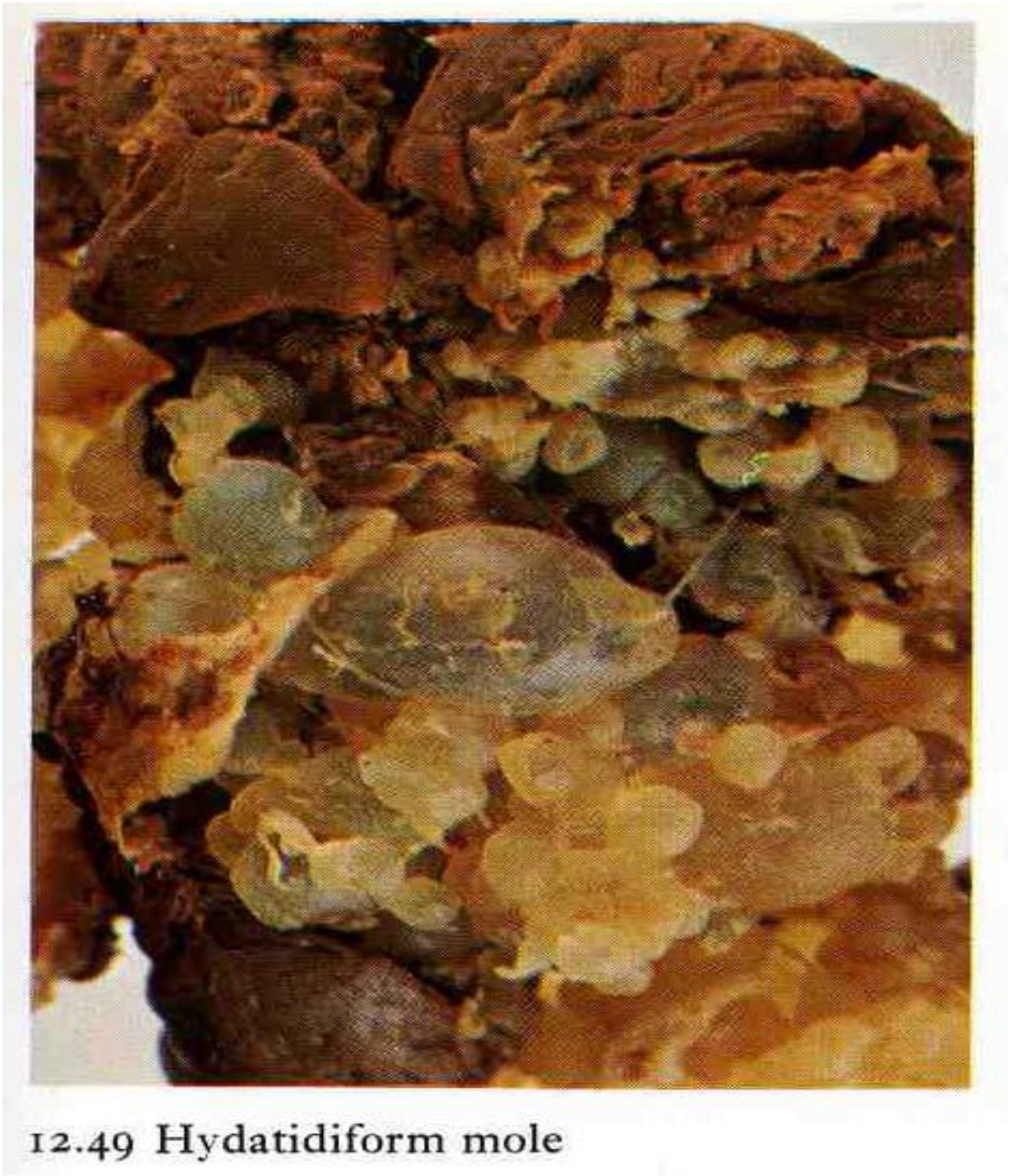
- Complete HM incidence is about 1/1000 pregnancies in the US & other Western countries. For unknown reasons there is a much higher incidence in Asian countries.
- HM are most common before age 20 years & after age 40 years, & a history of HM increase the risk in subsequent pregnancies.
- HM is traditionally discovered at 12 to 14 weeks of pregnancy because of a gestation that was "too large for dates," however;…

- An **early diagnosis** of HM can be done by
  - (1) early monitoring of pregnancies by ultrasound **(U/S)** which reveal **typical absence of fetal parts, or fetal heart sounds,**
  - **(2) by detecting elevations of hCG** in the maternal blood .

- **Grossly**, in early HM, the uterus may be normal in size; but in fully developed HM the uterine cavity is **larger** than the expected date, **filled** with a delicate, friable mass of thin-walled, translucent cystic structures **.**Fetal parts are not seen in complete HM but are common in partial HM.
- H, the **complete mole** shows:
- (I) **Hydropic swelling** of chorionic villi, with loose, edematous & myxomatous stroma.
- (II) Virtual **absence of vascularization** of villi.
- (III) **Proliferation** of both cytotrophoblast & syncytiotrophoblast of the chorionic epithelium which may be mild, or striking circumferential hyperplasia.

Complete hydatidiform mole suspended in saline showing numerous swollen (hydropic) villi.



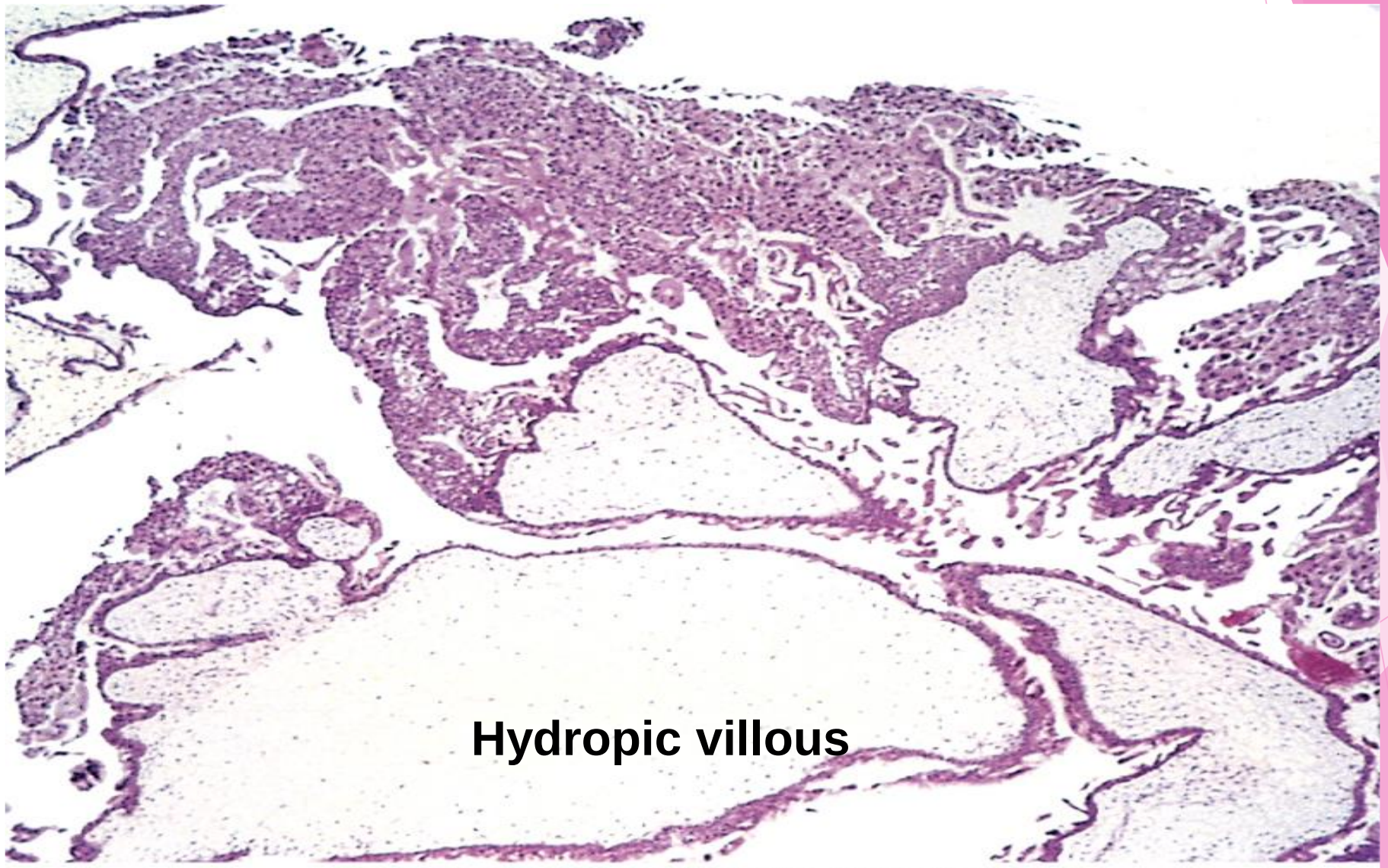


12.49 Hydatidiform mole

Hydatidiform mole.

Mass of grape-like, discrete, rounded translucent vesicles which consist of hydropic & cystic chorionic villi.

Complete HM showing (1) distended hydropic villi, (2)absence of BV & (2) proliferation of the chorionic epithelium (above).



- **Microscopically** : in **partial moles** the
- (1) villous edema involves only **some** of the villi &
- (2) the trophoblastic proliferation is **focal & slight**.
- (3) the villi have a characteristic irregular **scalloped** margin,
- (4) in most cases of partial HM there is evidence of an **embryo** or fetus, which may be in the form of fetal RBCs in placental villi or, in some cases, a fully formed fetus that, despite a triploid karyotype, is morphologically nearly normal in appearance.
- **Prognosis**: Overall, 80% to 90% of HM do not recur after thorough curettage; **10%**of complete HMs are invasive, & **2% to 3% give rise to chorio ca**.
- Partial HM rarely give rise to choriocarcinomas.
- With complete HM, monitoring the post-curettage blood & urinary β-subunit of hCG concentrations, permits detection of incomplete removal or a more ominous complication which can be treated by **chemotherapy, which is almost always curative.**

Invasive Mole

- **Invasive moles are complete HM that are more invasive locally but do not metastasize.**
- An invasive mole retains hydropic villi (which are absent in choriocarcinoma),
- Microscopically : the villi epithelium shows
- (1) **atypical** hyperplastic cytotrophoblast & syncytiotrophoblasts proliferation &
- (2) **penetration of the uterine wall deeply, possibly causing rupture**& sometimes serous **hemorrhage**.
- Local spread to the broad ligament & vagina may also occur.
- **Although they are invasive, metastases do not occur.**

- Hydropic villi may embolize to distant organs, such as lungs or brain, but these emboli do not constitute true metastases & may actually regress spontaneously. Invasive mole is **difficult to remove completely by curettage**, because of the greater depth of myometrium invasion.

- So, serum hCG may remain elevated & required further treatment by **chemotherapy** which is fortunately **curative** in most cases.

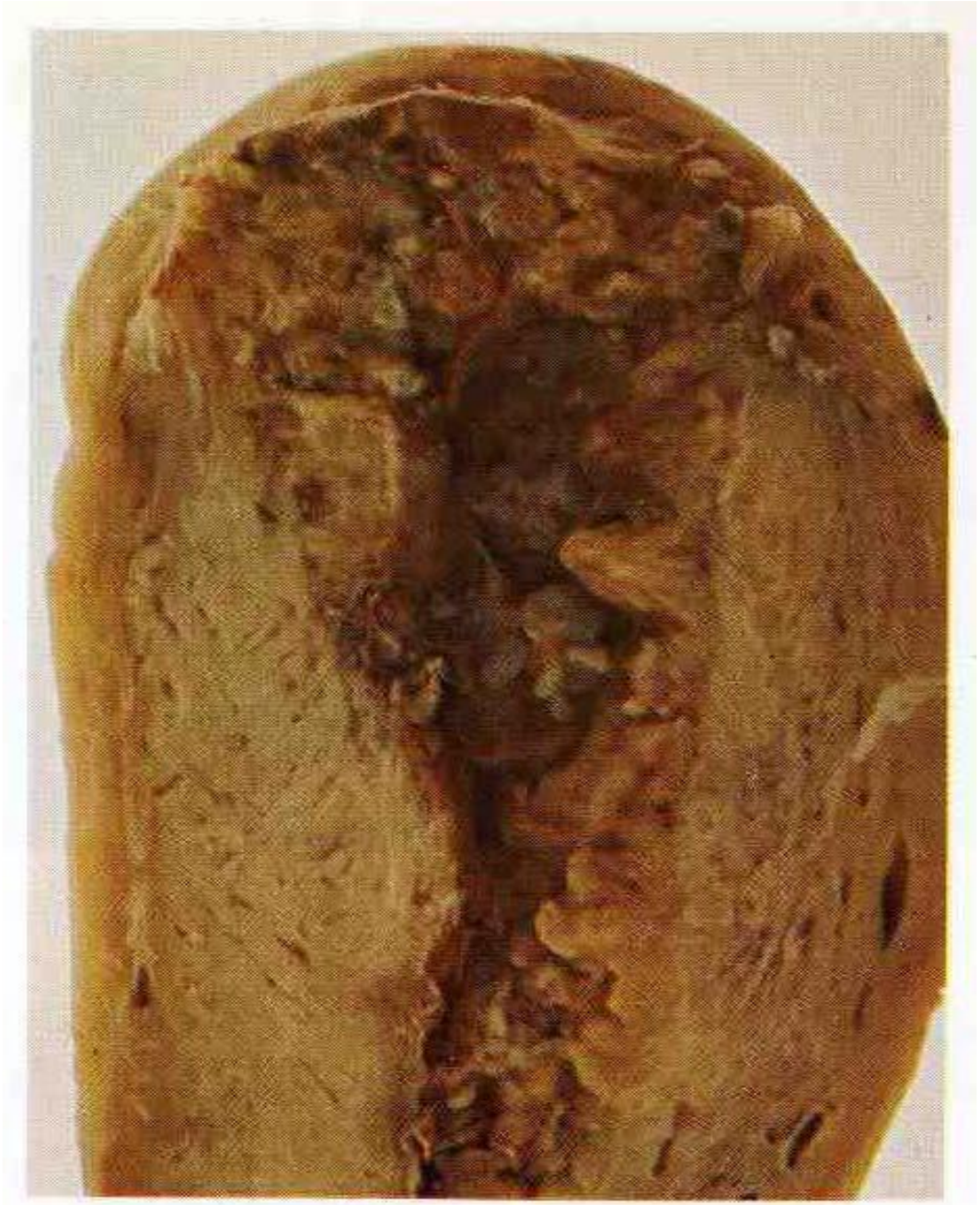
Choriocarcinoma (Chorio ca)

- Very aggressive malignant T, **arises either from gestational chorionic epithelium** or, less frequently, from **totipotential cells within the gonads (testis or ovary) or elsewhere.**

- Chorio ca are **rare** in the West, & in the US but are much more common (X15 fold) in Asian & African countries.
- The risk is more before age 20 & is significantly elevated after age 40.
- **50%**of chorio ca arise in complete HM;
- **25%**arise after an abortion,
- **25%** occurs during what had been a normal pregnancy.

Most chorio ca are discovered by the appearance of

- (1) **bloody uterine discharge** accompanied by
- (2) a **rising titer of β-hCG** in blood & urine (much higher than those associated with a HM),
- (3) the **absence of marked uterine enlargement**, such as would be anticipated with a HM.



12.50 Hydatidiform mole: uterus

Invasive hydatidifrom mole.

★Uterus sagittal section, showing grape-like vesicles in the cavity, extensively invading the myometrial muscular wall locally (as a result of proliferating trophoblastic activity). The lesion sometimes may **cause (1) hemorrhage, (2) uterine wall perforation**.

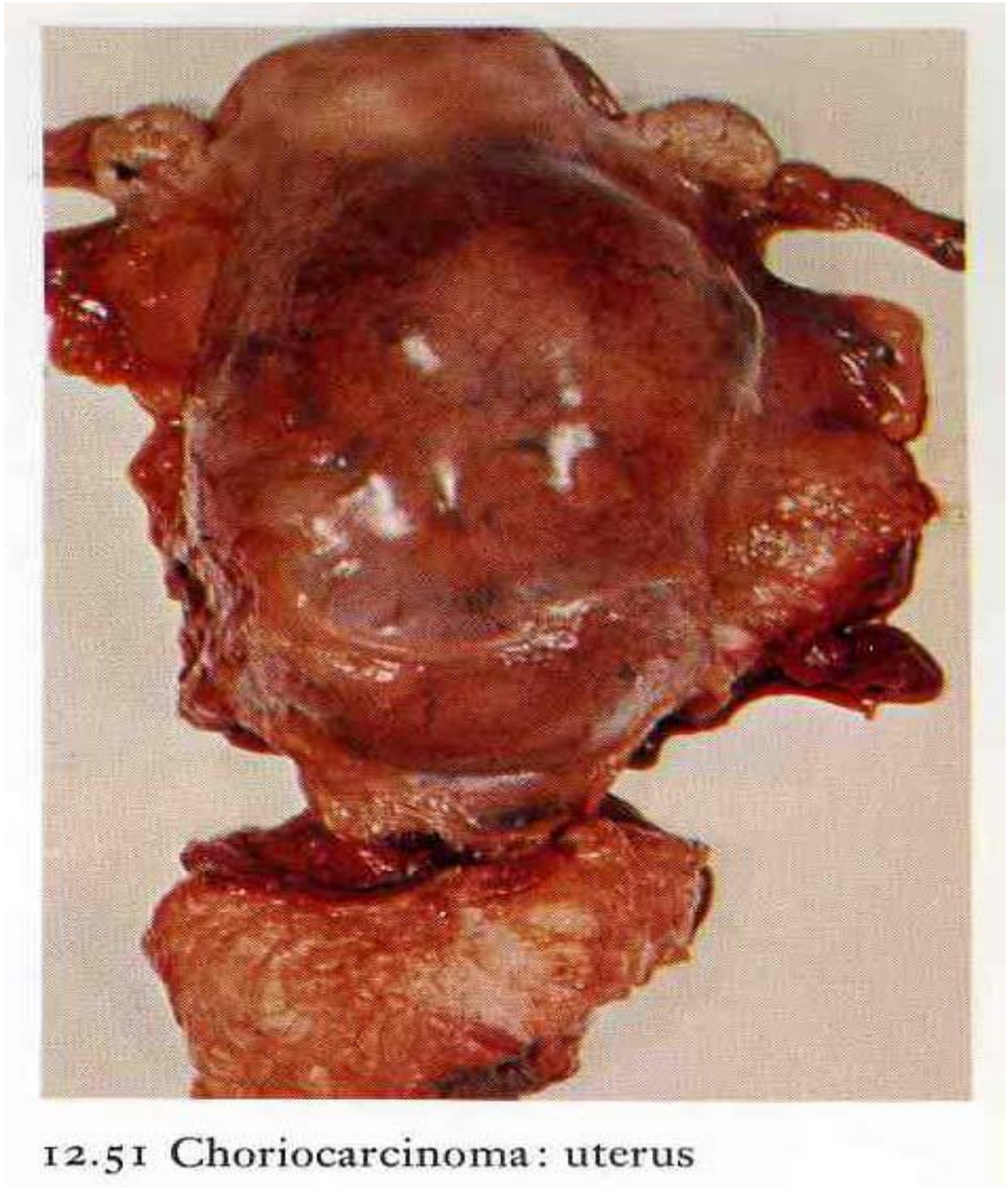
❖**Grossly,** chorio ca is very hemorrhagic, necrotic T mass within the uterus, so much so that, sometimes, the histologic diagnosis is difficult. Indeed, the primary lesion may self-destruct, & only the metastases “mets” tell the story.

❖Very early, the T invades into the myometrium & into BV.

❖**Microscopically:,** in contrast to HM & invasive moles, the chorionic villi are not formed & are never seen; instead, the T is purely epithelial, composed of anaplastic cytotrophoblast & syncytiotrophoblast .

❖When discovered, most chorioca are widely disseminated via the blood, most often to the lungs (50%), vagina (30% to 40%), brain, liver, & kidneys.

❖ Lymphatic invasion is uncommon

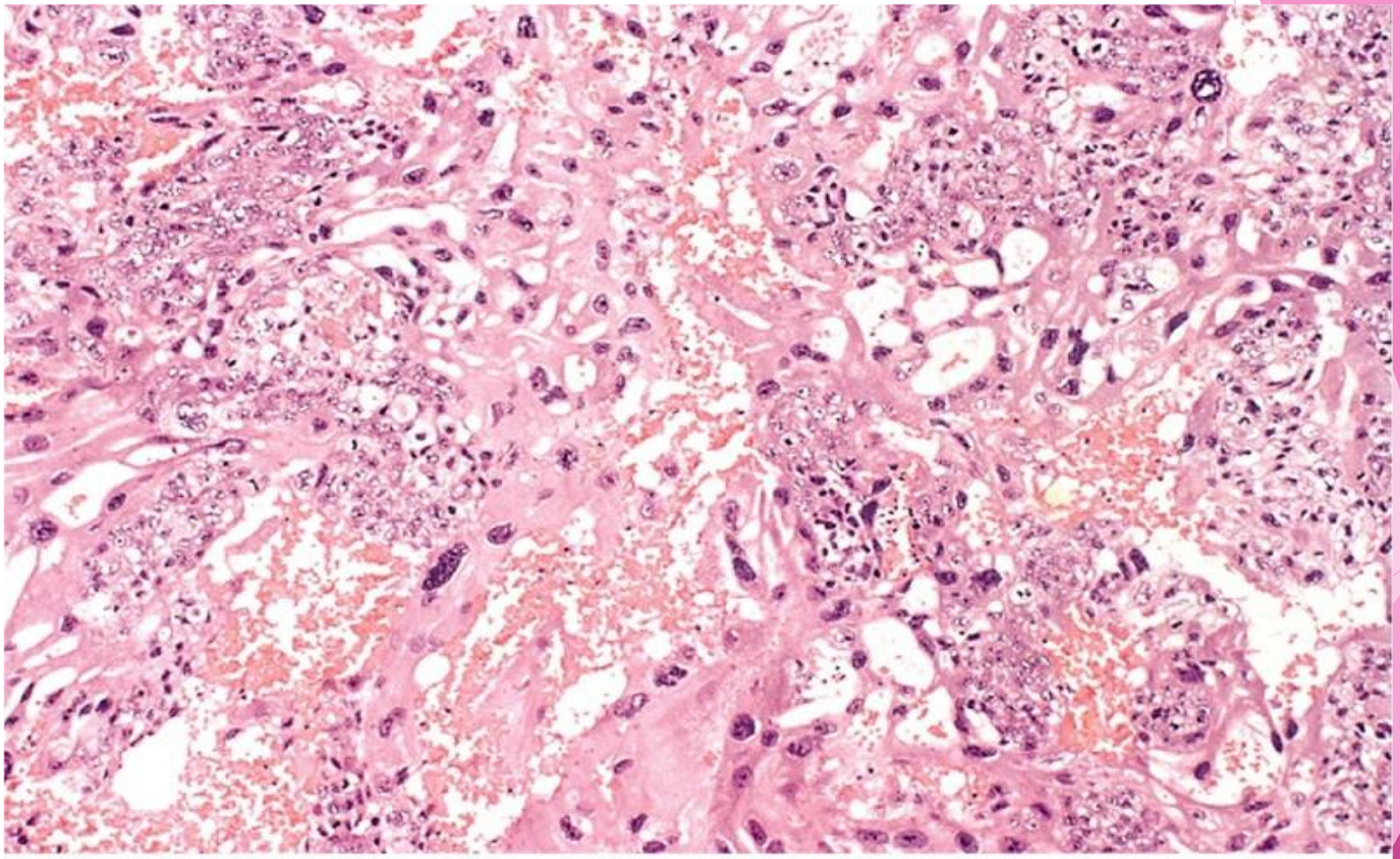


12.51 Choriocarcinoma: uterus

Choriocarcinoma: uterus.

The tumor forms a large mass which has expanded the lower part of the body of the uterus & invaded the cervix & the upper vagina

Choriocarcinoma showing: both (1) Neoplastic cytotrophoblasts & syncytiotrophoblasts; & (2) Complete **absence** of chorionic villi.



- Despite the extreme aggressiveness of chorio ca, which made them uniformly fatal in the past, **chemotherapy** has achieved remarkable results with nearly 100% cure, even with T that have spread beyond the pelvis & vagina & into the lungs.

- Equally remarkable are reports of healthy infants born later to these survivors!
- By contrast, there is poor response to chemotherapy in chorio ca that arise in the gonads (ovary or testis).
- This striking difference in prognosis may be related to the presence of paternal antigens on placental chorioca but not on gonadal lesions. Conceivably, a maternal immune response against the foreign (paternal) antigens helps by acting as an adjunct to chemotherapy.