Female Genital System, Lecture 4

FALLOPIAN TUBES & OVARIES

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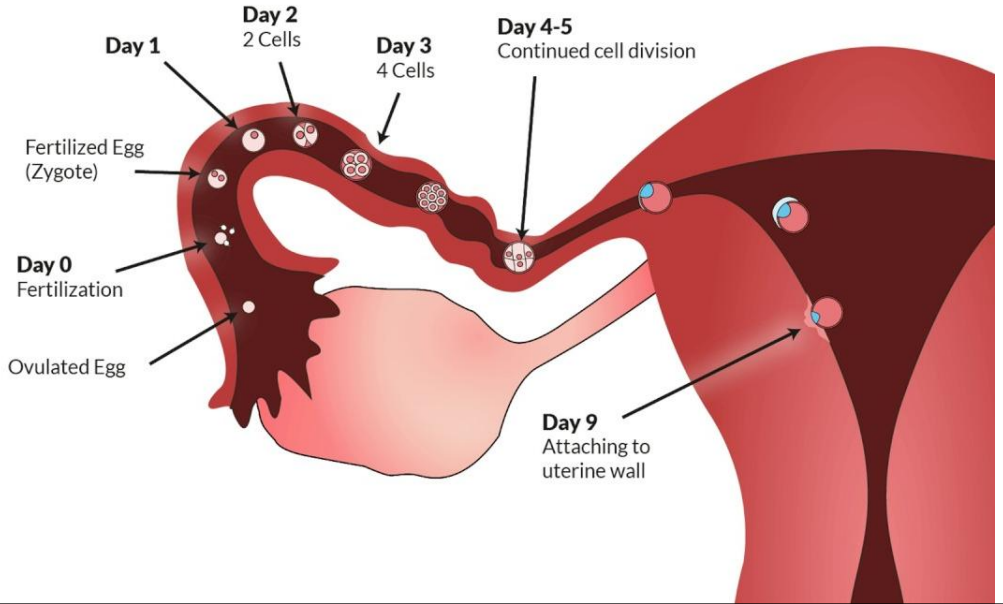
Fallopian Tubes Pathology



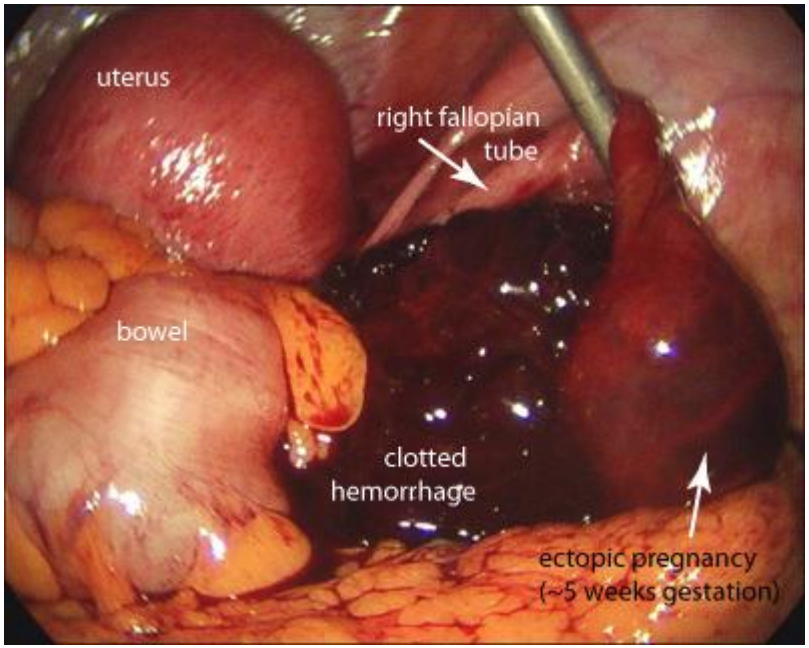
Fallopian Tubes - Ectopic Pregnancy

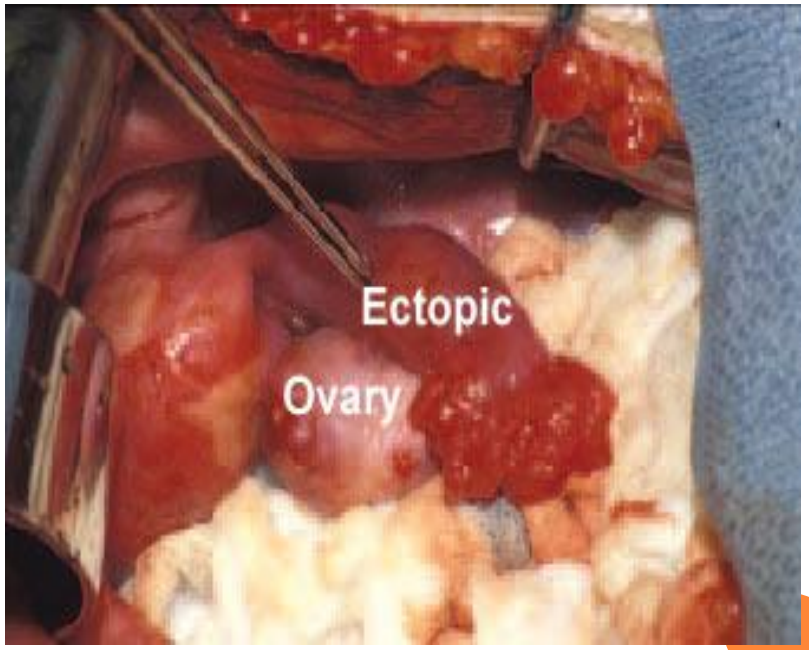
- **Implantation of a fertilized ovum in any site other than the uterus.**
- 1% of all pregnancy & 90% of cases in fallopian tubes.
- Other sites: ovaries, abdominal cavity.
- Predisposing factors: tubal obstruction (intraluminal: PID or peritubal: endometriosis or surgery); IUD
- 50% no anatomic cause can be identified.

Fallopian Tubes - Ectopic Pregnancy

- Early: ectopic pregnancies proceeds normally, later the invading placenta eventually burrows through the wall of the fallopian tube, causing **intratubal hematoma (hematosalpinx), intraperitoneal hemorrhage**, or both.
- Rupture of an ectopic pregnancy may be catastrophic → sudden onset of intense abdominal pain and signs of an acute abdomen & followed by shock.
- Prompt surgical intervention is necessary.

Fallopian Tubes - Ectopic pregnancy

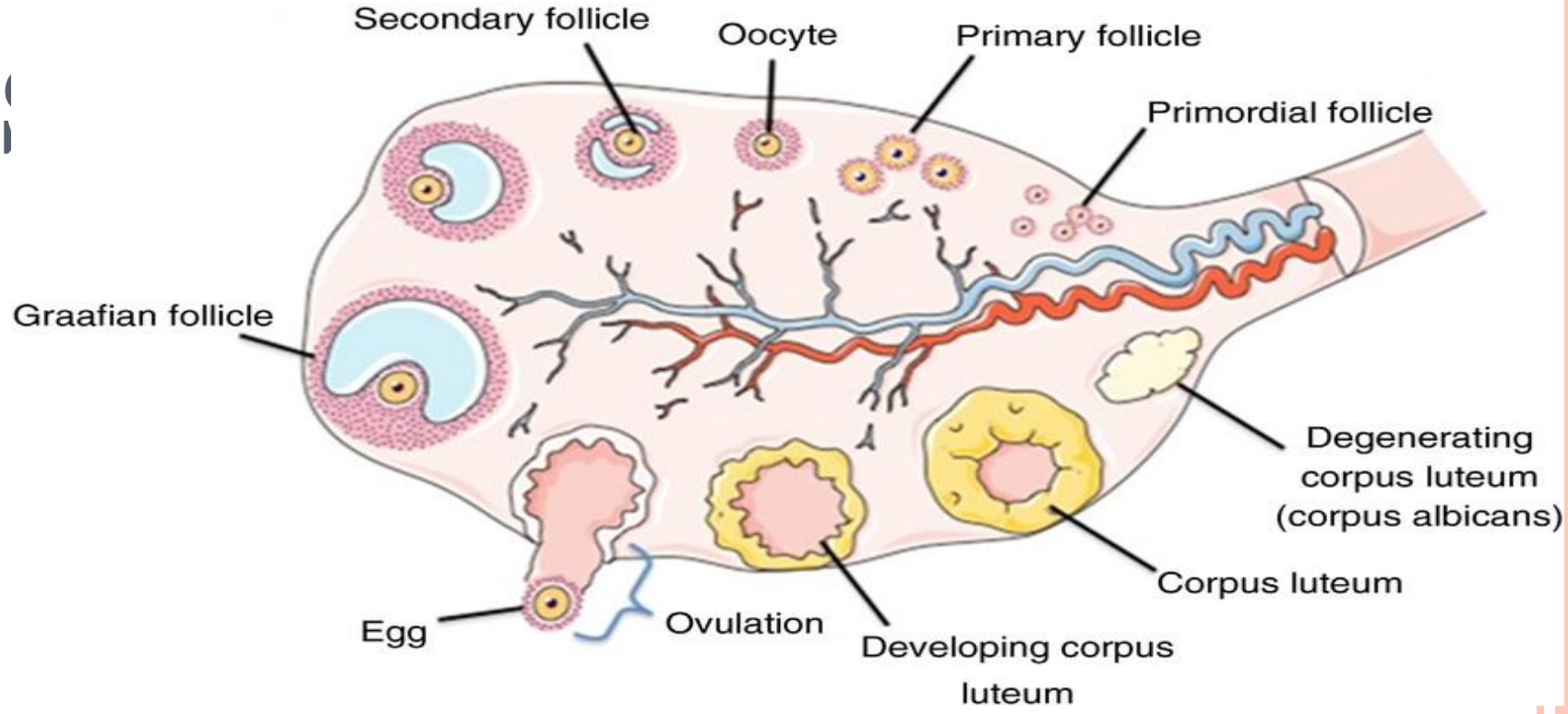




FALLOPIAN TUBES - TUMORS

- **Primary adenocarcinomas of fallopian tube maybe the site of origin for many of high-grade serous carcinomas long thought to arise in the ovary.**
- Serous tubal intraepithelial carcinoma (STIC) in the fimbriated ends of tubes have been identified. (intimately ass with the ovary)
- STICs have mutations in *TP53*
- Frequently found in fallopian tubes removed prophylactically from women with *BRCA1* & *BRCA2* mutations.

OVARIE

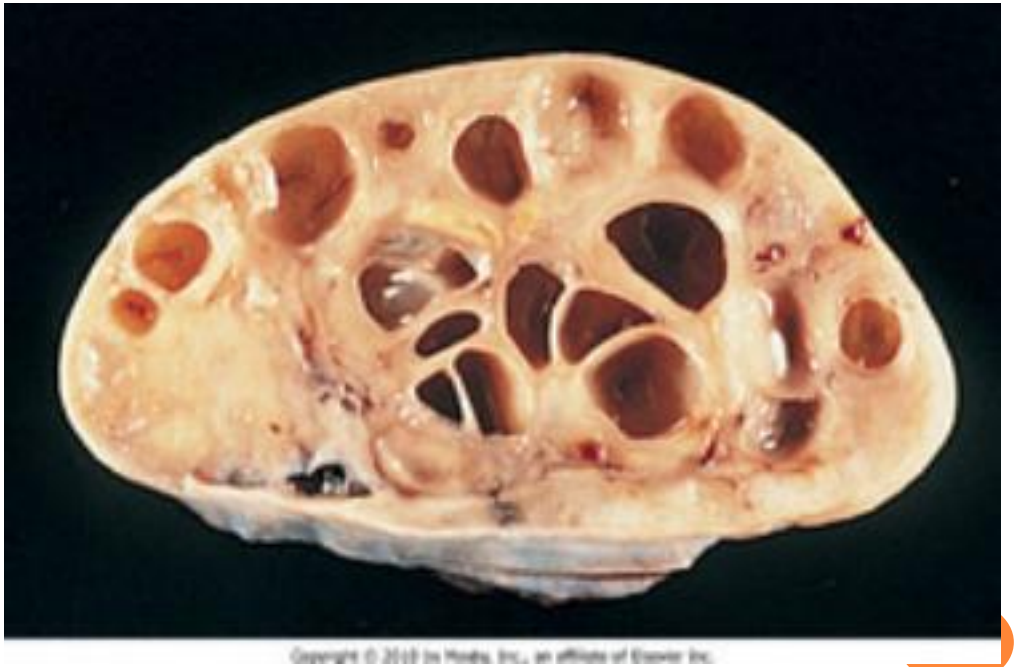

Secondary follicle
Oocyte
Primary follicle
Primordial follicle
Graafian follicle
Degenerating corpus luteum (corpus albicans)
Corpus luteum
Egg
Ovulation
Developing corpus luteum

Ovaries - Polycystic ovarian syndrome

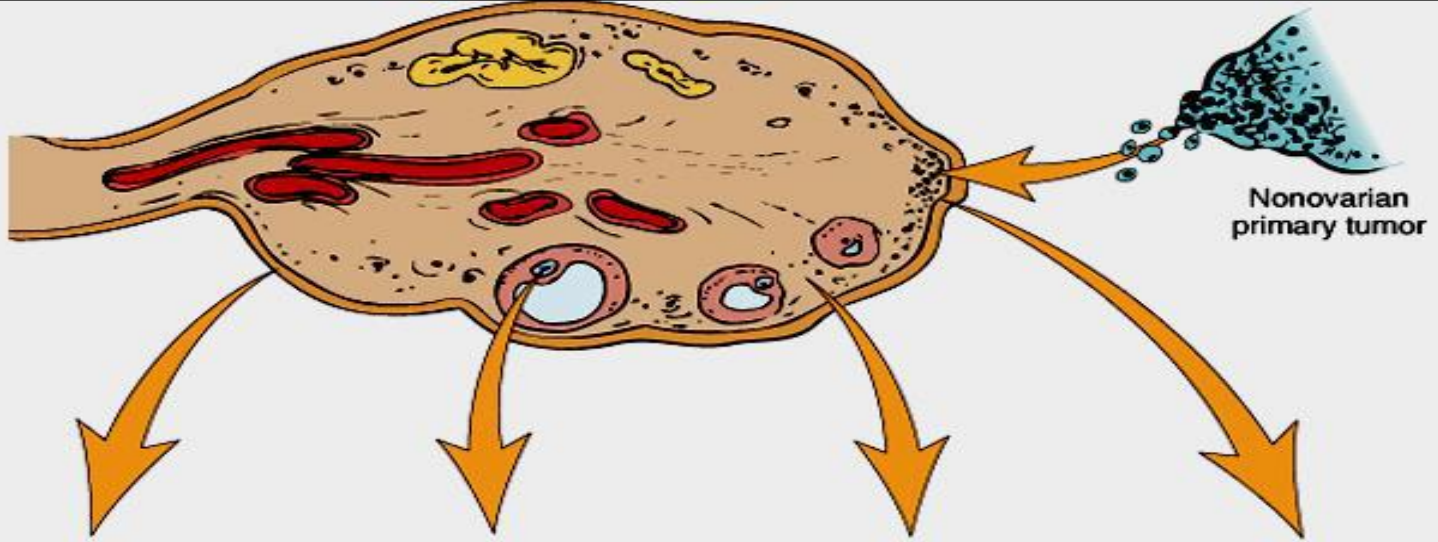
- Formerly Stein-Leventhal syndrome.
- A complex endocrine disorder; hyperandrogenism, menstrual abnormalities, polycystic ovaries, chronic anovulation, and decreased fertility, 10%
- Present after menarche in teenage - young adults
- Symptoms: oligomenorrhea, hirsutism, infertility, & sometimes obesity.

Ovaries - Polycystic ovarian syndrome

- Ovaries twice the normal size, a smooth outer cortex, and studded with subcortical cysts 0.5 to 1.5 cm in diameter.



Tumors of the ovaries



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	

Ovaries - Surface Epithelial Tumors

- Five major types: Serous, Mucinous, Endometrioid, Clear cell, or Brenner.
- Each type has benign, borderline and malignant tumors.
- Major determinant of outcome is stage rather than histologic type.
- Important risk factors:

1. nulliparity.
2. family history
3. Germline mutations in certain tumor suppressor genes;

OVARIES - BRCA1 OR BRCA2

- 5-10% of ovarian cancers are familial.
- most of them ass with mutations in the *BRCA1* or *BRCA2* tumor suppressor genes.
- Genes also ass with hereditary breast cancer.
- Present only in only 8-10% of sporadic cases.
- .. So sporadic tumor arise through alternative molecular mechanisms.

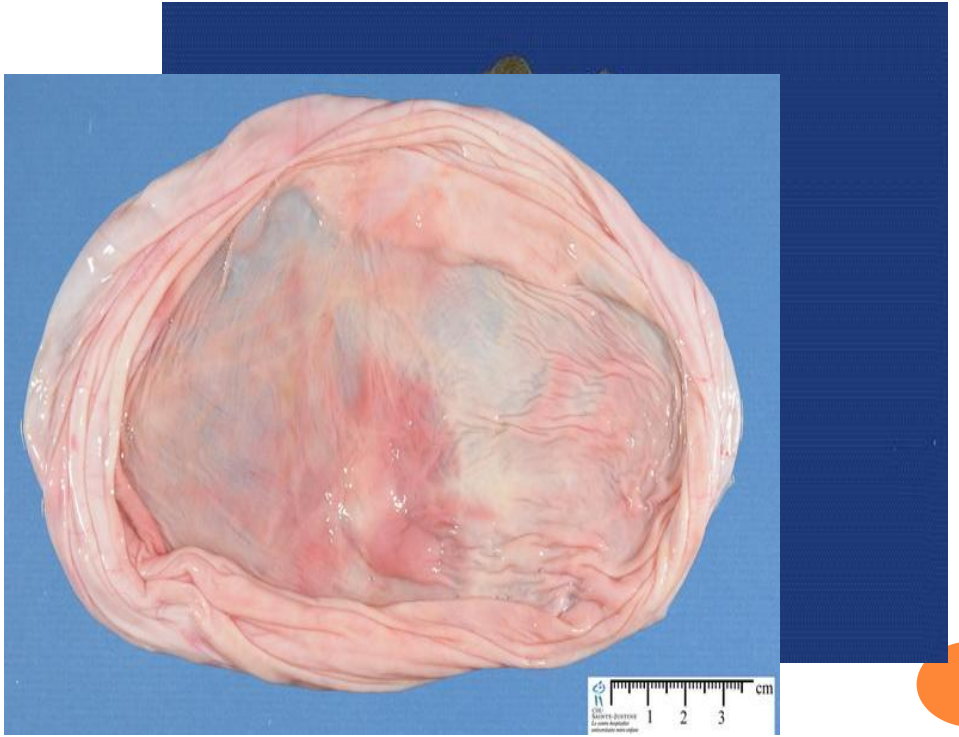
OVARIES - SEROUS TUMORS

- The most common of the ovarian tumors overall.
- The most common malignant ovarian tumors 60%.
- Two genetic pathways:

1. K-RAS mutations → borderline & low grade cancers.
2. p53 and BRCA1 mutations → High-grade serous carcinomas.

Serous Tumors - Benign serous tumors

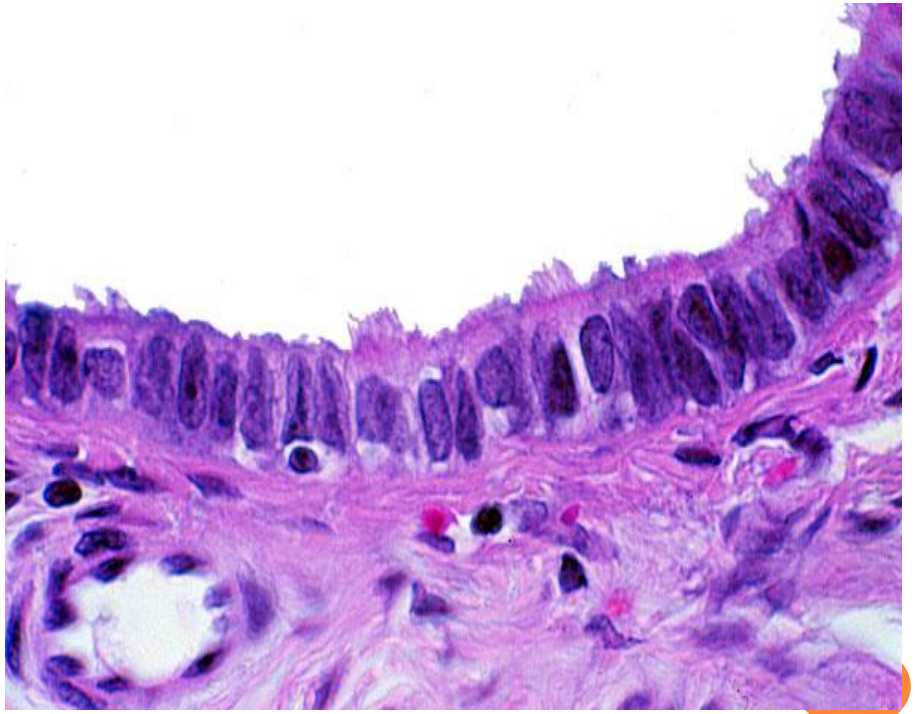
- Gross: Large & cystic (up to 30 cm), filled with a clear serous fluid
- May be bilateral.
- Called serous cystadenoma



Serous Tumors - Benign

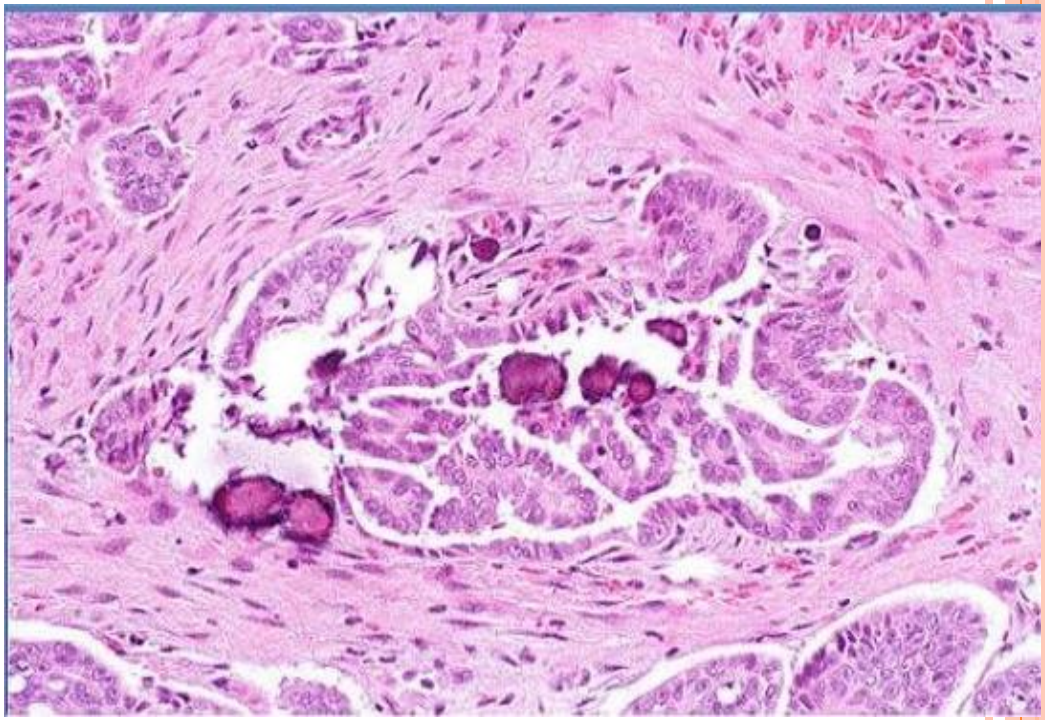
Serous tumors

Microscopy: Single layer of columnar epithelium. Some cells are ciliated.



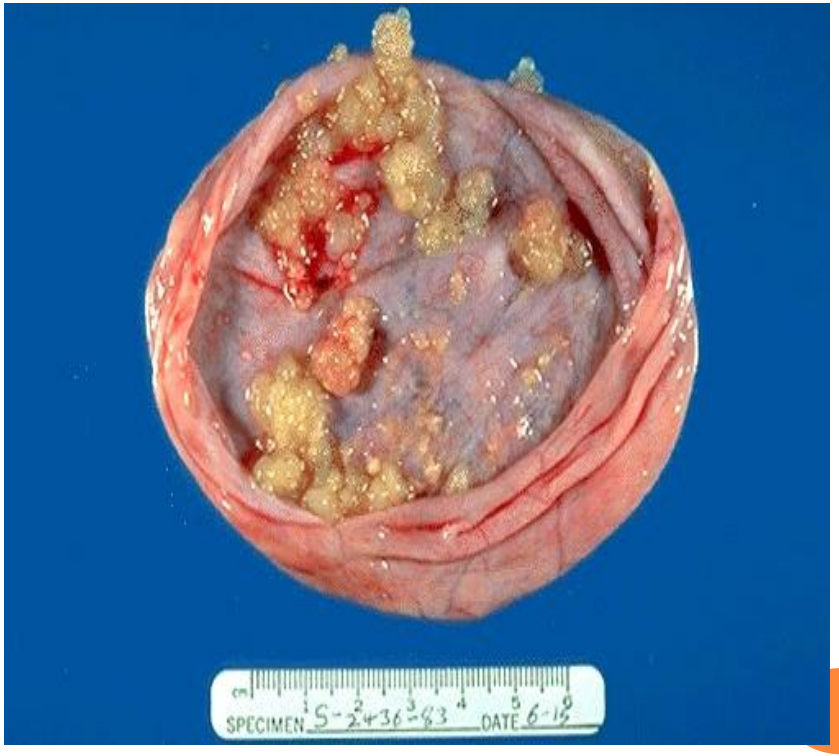
Serous Tumors - Serous tumors

Psammoma bodies (laminated calcified concretions) are common in tips of papillae of **all serous tumors**



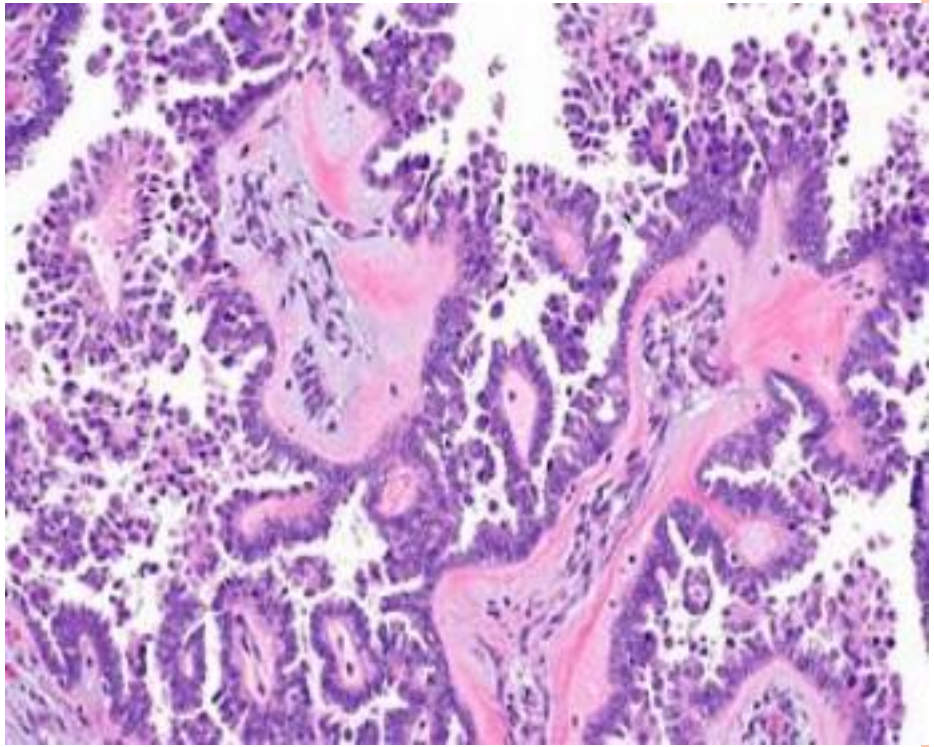
Serous Tumors - Borderline Serous Tumors

- complex architecture. (Protruding papillary projections)
- might be associated with peritoneal implants.



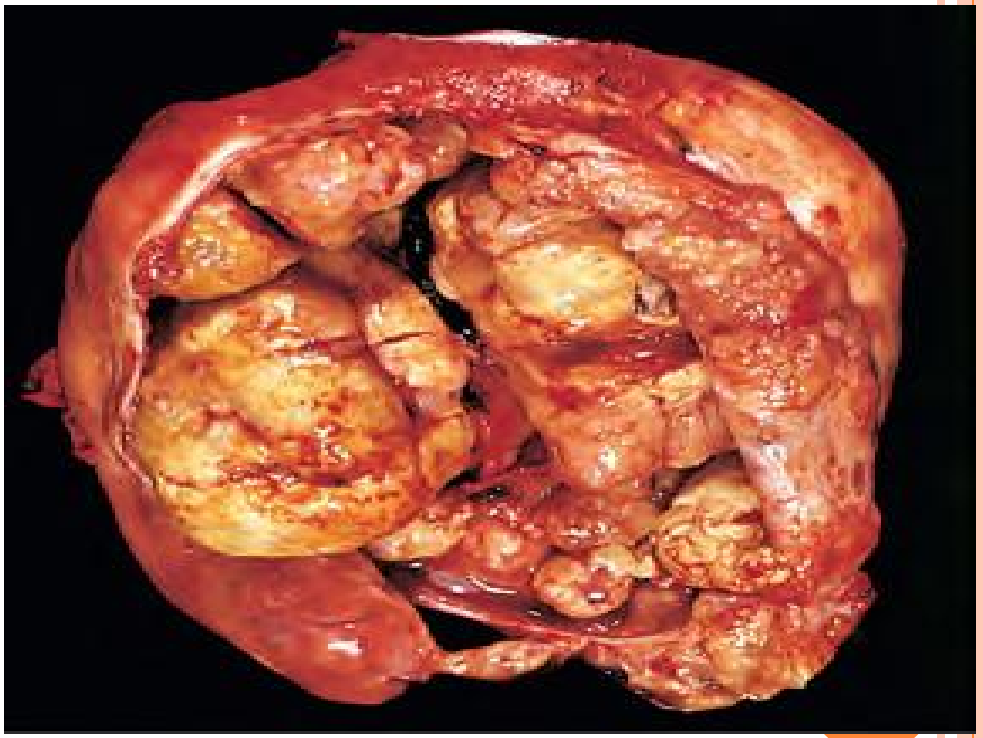
SEROUS TUMORS - BORDERLINE SEROUS TUMORS

- complex architecture.
- mild cytologic atypia, but no stromal invasion.
- Prognosis intermediate between benign & malignant.



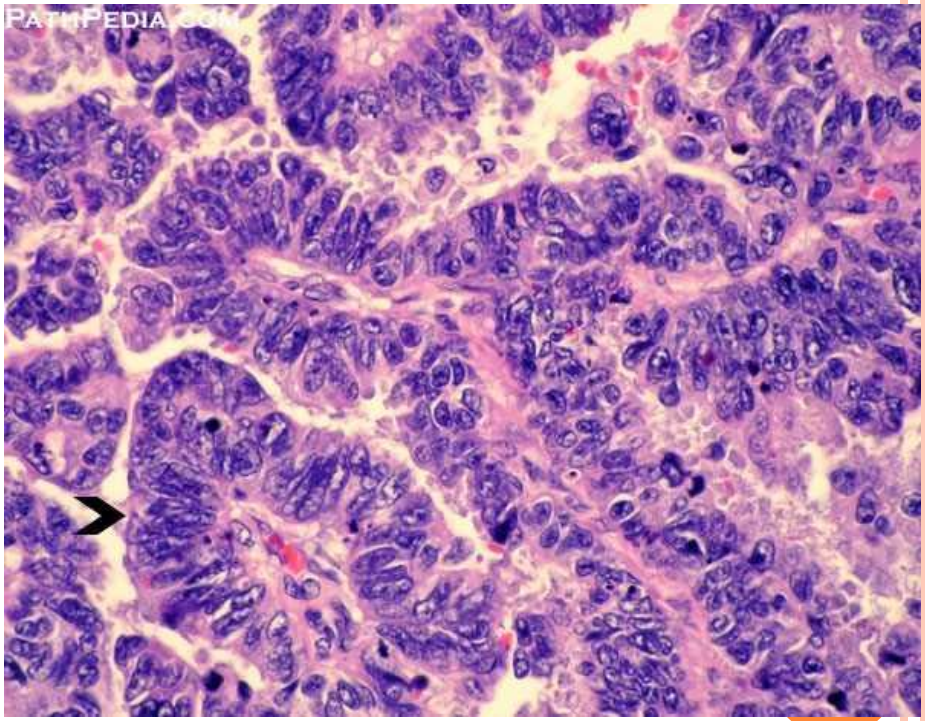
Serous Tumors - serous carcinoma

- papillary formations are usually more complex
- tumor has invaded the serosal surface.
- prognosis poor, depends on stage at the time of diagnosis.



Serous Tumors - Serous Carcinoma

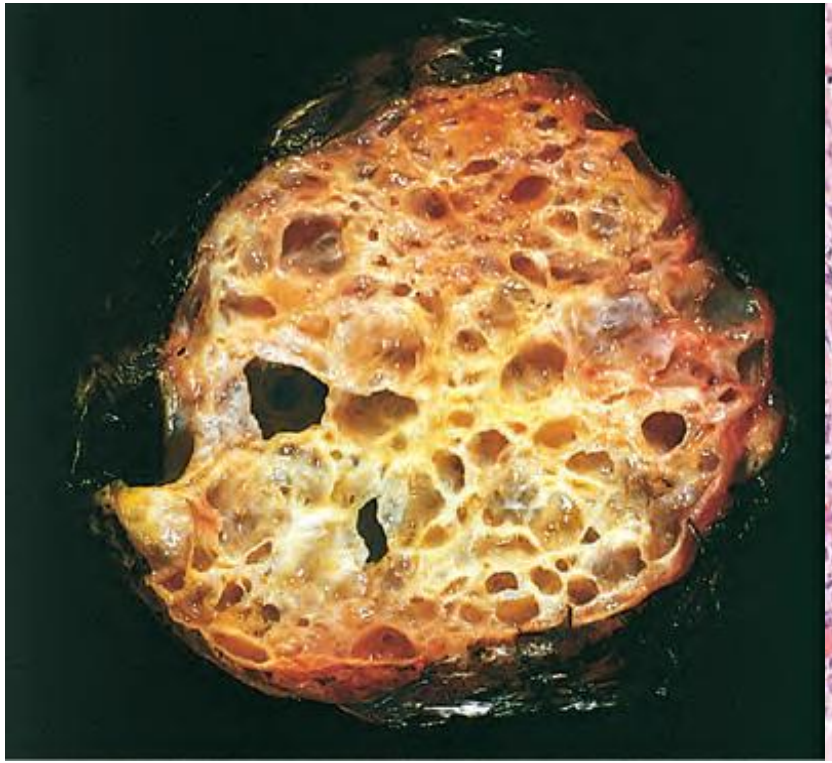
- complex papillary formations (multilayered)
- markedly cytological atypia
- By definition nests of malignant cells invade the stroma.

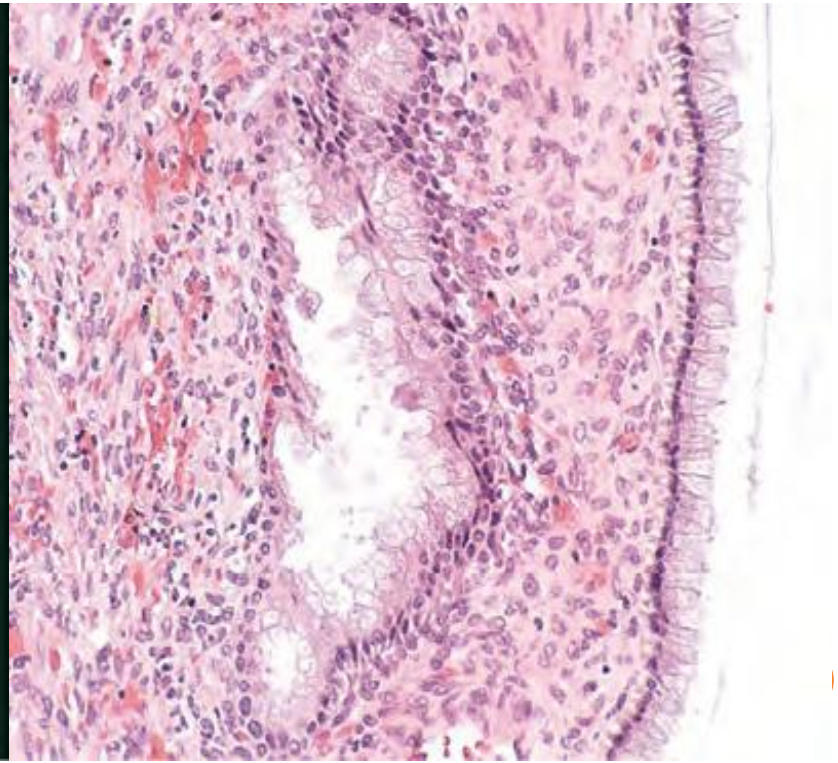


Ovaries - Mucinous Tumors

- Neoplastic epithelium consists of mucin-secreting cells.
- Mucinous tumors are less likely to be malignant; 80% benign; 10% borderline; 10% malignant.
- Compared to serous tumors → larger & multicystic grossly, filled with mucinous fluid, & less likely to be bilateral.
- Genetics: Mutations in KRAS proto-oncogene (carcinomas)
- Malignant features: solid areas of growth,

OVARIES- MUCINOUS CYSTADENOMA





Ovaries - Surface Epithelial Tumors

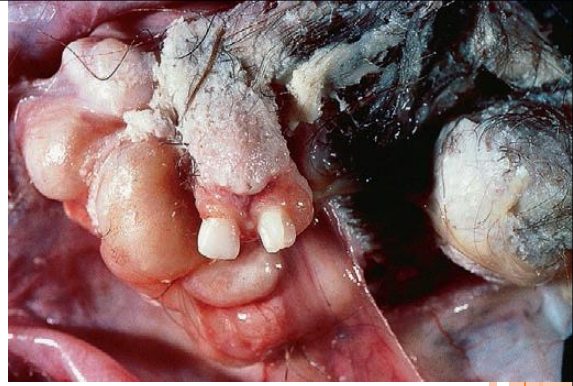
- **Endometrioid**: develop in ass with endometriosis, similar to uterine counterpart, tumors usually are malignant.
- 15-30% of ovarian tumors have a concomitant endometrial carcinoma.
- **Brenner** nests of transitional-type epithelium resembling that of the urinary tract, most are benign.

OVARIES - GERM CELL TUMORS

Germ cell tumors may differentiate toward :

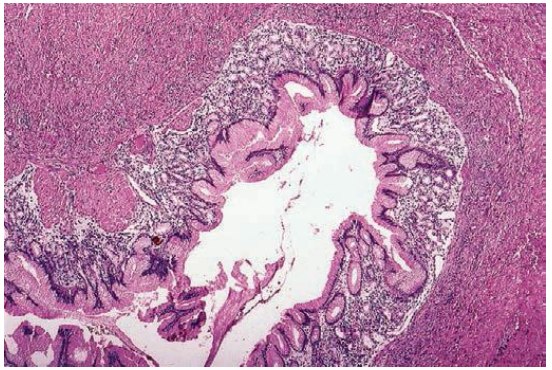
- Oogonia (dysgerminoma)
- Primitive embryonal tissue (embryonal)
- Yolk sac (endodermal sinus tumor)
- Placental tissue (choriocarcinoma)
- Multiple fetal tissues (teratoma).

Ovaries - Germ cell Tumors

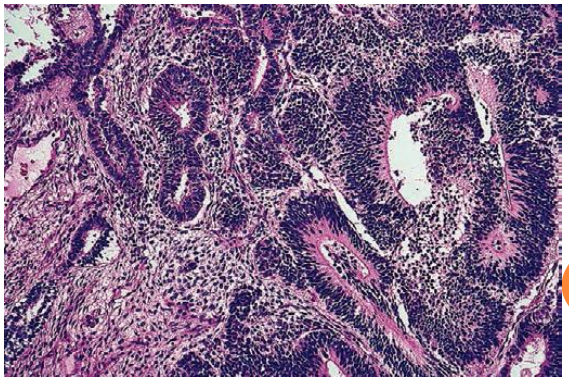


- **The most common → teratoma**
- **(90% unilateral).**
- Either: (1) benign mature cystic teratomas or (2) the immature malignant teratomas (rare)
- Mature tissues derived from all three germ cell layers: ectoderm, endoderm, and mesoderm.
- Immature: minimally differentiated **nerve** cartilage, bone, or muscle tissue.
- Gross: cyst filled with sebaceous secretion and hair; bone

BENIGN MATURE CYSTIC TERATOMAS



IMMATURE MALIGNANT TERATOMA

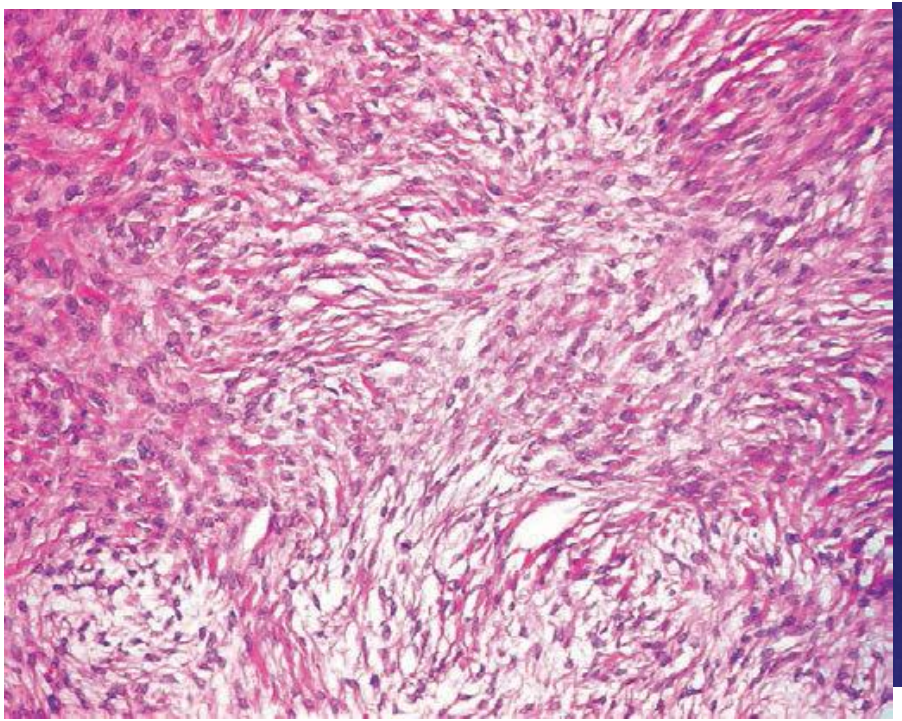


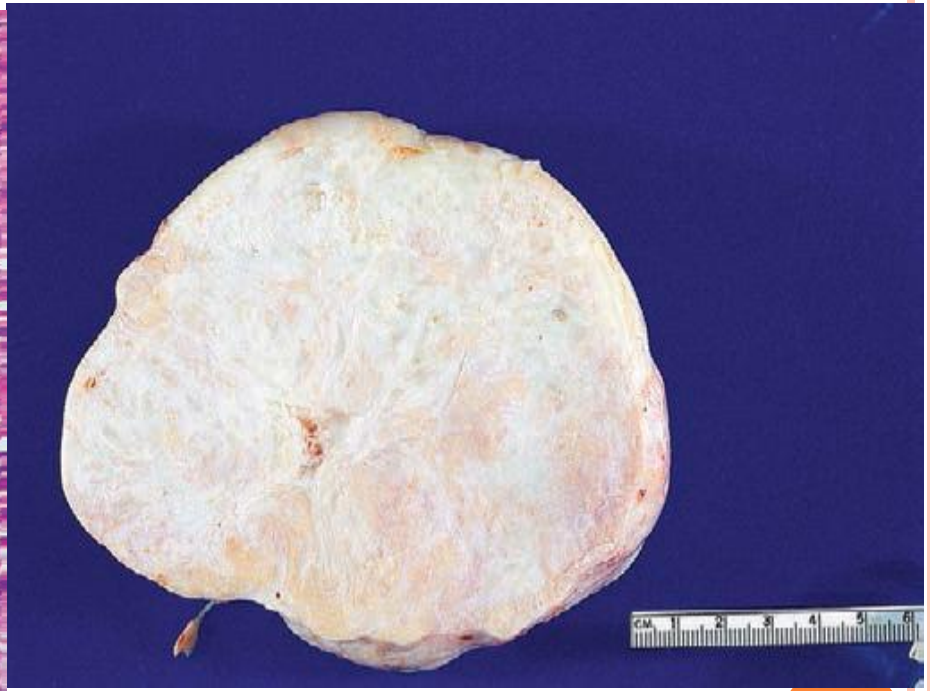
- Tumors contain cysts lined by epidermis replete with adnexal appendages—hence the common designation *dermoid cysts*
- A rare subtype of teratoma is composed entirely of specialized tissue.
- The most common example is struma ovarii, which is composed entirely of mature thyroid tissue that may actually produce hyperthyroidism.
- Other specialized teratomas may take the form of ovarian carcinoid, which in rare instances produces carcinoid syndrome.

Ovaries – Sex cord Tumors

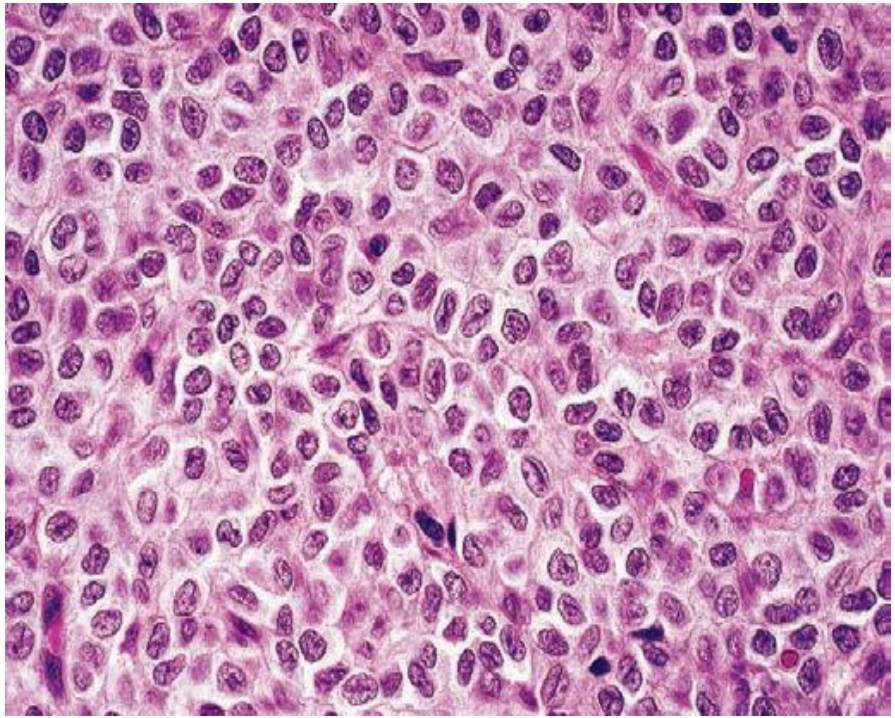
Neoplasm	Peak Incidence	Usual Location	Morphologic Features	Behavior
Sex Cord Tumors				
Granulosa-theca cell	Most postmenopausal, but may occur at any age	Unilateral	May be tiny or large, gray to yellow (with cystic spaces) Composed of mixture of cuboidal granulosa cells in cords, sheets, or strands and spindled or plump lipid-laden theca cells Granulosa elements may recapitulate ovarian follicle as Call-Exner bodies	May elaborate large amounts of estrogen (from thecal elements) and so may promote endometrial or breast carcinoma Granulosa element may be malignant (5% to 25%)
Thecoma-fibroma	Any age	Unilateral	Solid gray fibrous cells to yellow (lipid-laden) plump thecal cells	Most hormonally inactive A few elaborate estrogens About 40%, for obscure reasons, produce ascites and hydrothorax (Meigs syndrome) Rarely malignant
Sertoli-Leydig cell	All ages	Unilateral	Usually small, gray to yellow-brown, and solid Recapitulates development of testis with tubules or cords and plump pink Sertoli cells	Many masculinizing or defeminizing Rarely malignant

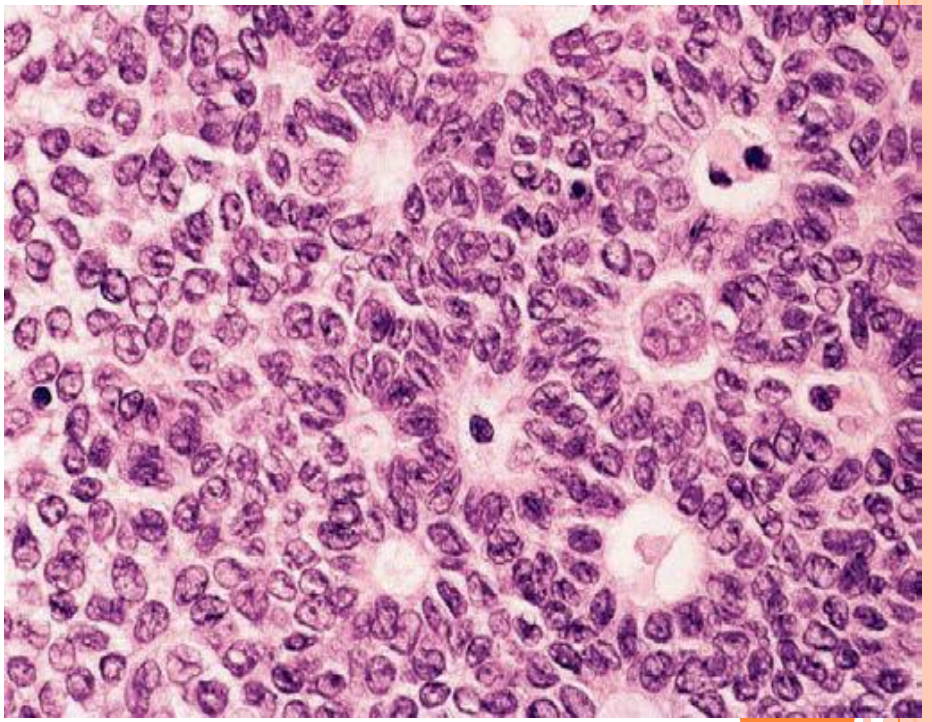
Ovarian fibroma





OVARIES-GRANULOSA CELL TUMOR.





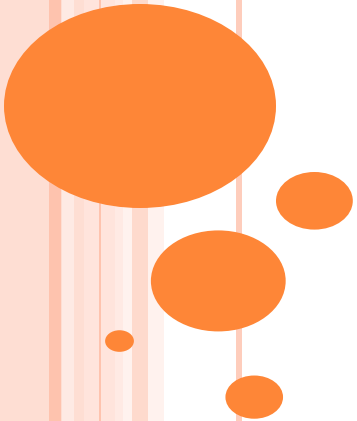
OVARIES - TUMORS OF THE OVARY - CLINICAL

- Symptoms & signs appear only when tumors are well advanced.
- Sx: pain, gastrointestinal complaints, urinary frequency.
- Smaller masses, sometimes twist on their pedicles(torsion) producing severe abdominal pain that mimics an acute abdomen.
- Sex cord–stromal tumors may display differentiation toward granulosa, Sertoli, Leydig, or ovarian stromal cell type. Depending on differentiation, they may produce estrogens or androgens, Functioning ovarian tumors (sex –cord stromal) come to attention because of the endocrinopathies they produce.
- One such marker, the protein CA-125, is elevated in the sera of 75% to 90% of women with epithelial ovarian cancer.

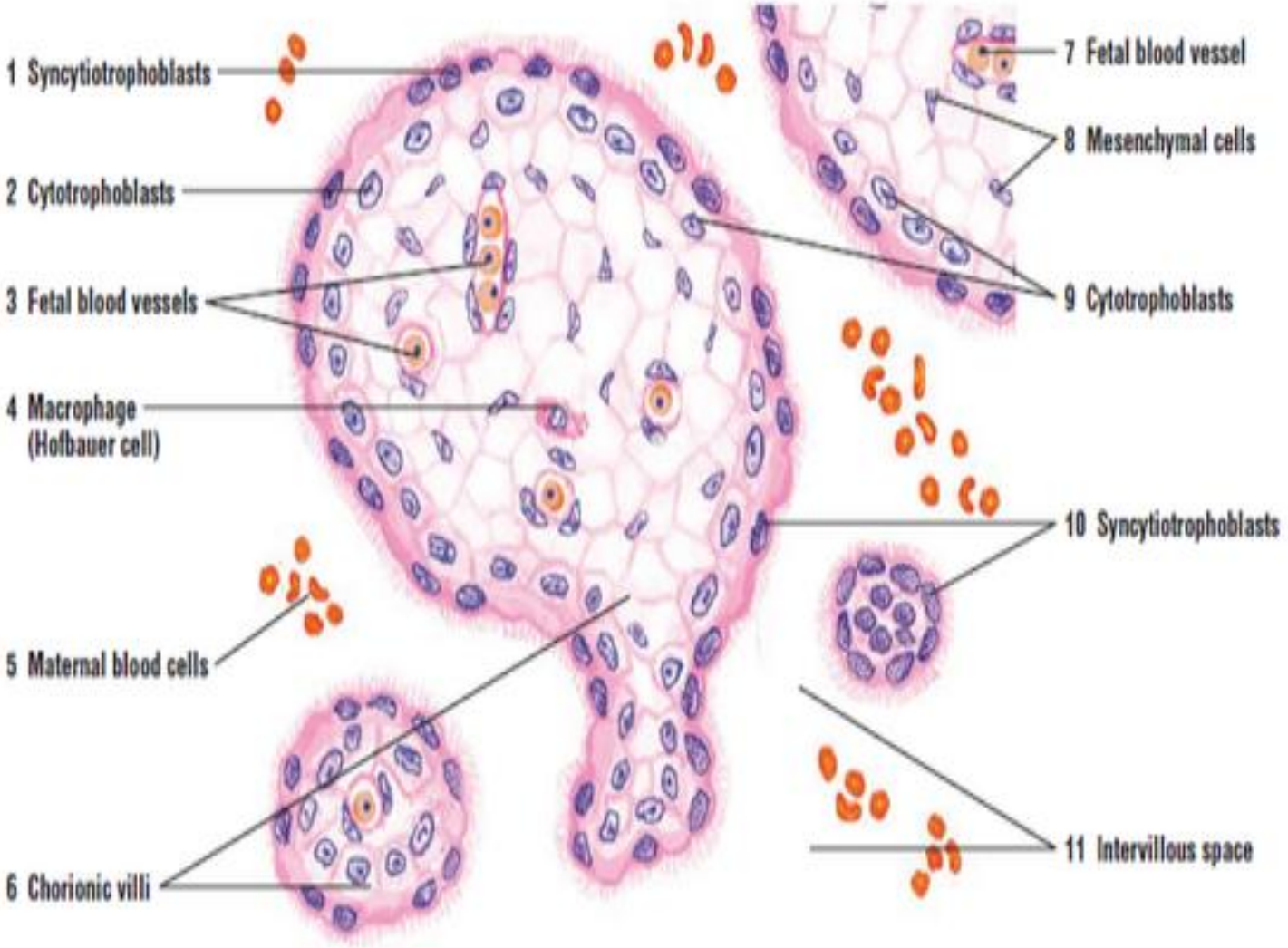
Metastases to Ovary

- Older ages.
- Laterality: mostly bilateral
- Size: mostly < 10cm
- Surface involvement: mostly multiple small nodules on surface
- Extensive intraabdominal spread: mostly true for metastatic mucinous tumor
- Hilar involvement common in hematogenous spread
- Microscpocally: Similar to primary tumor
- Primaries are gastrointestinal tract (Krukenberg tumors), breast, and lung.

Gestational trophoblastic disease



PLACENTAL DISC HISTOLOGY



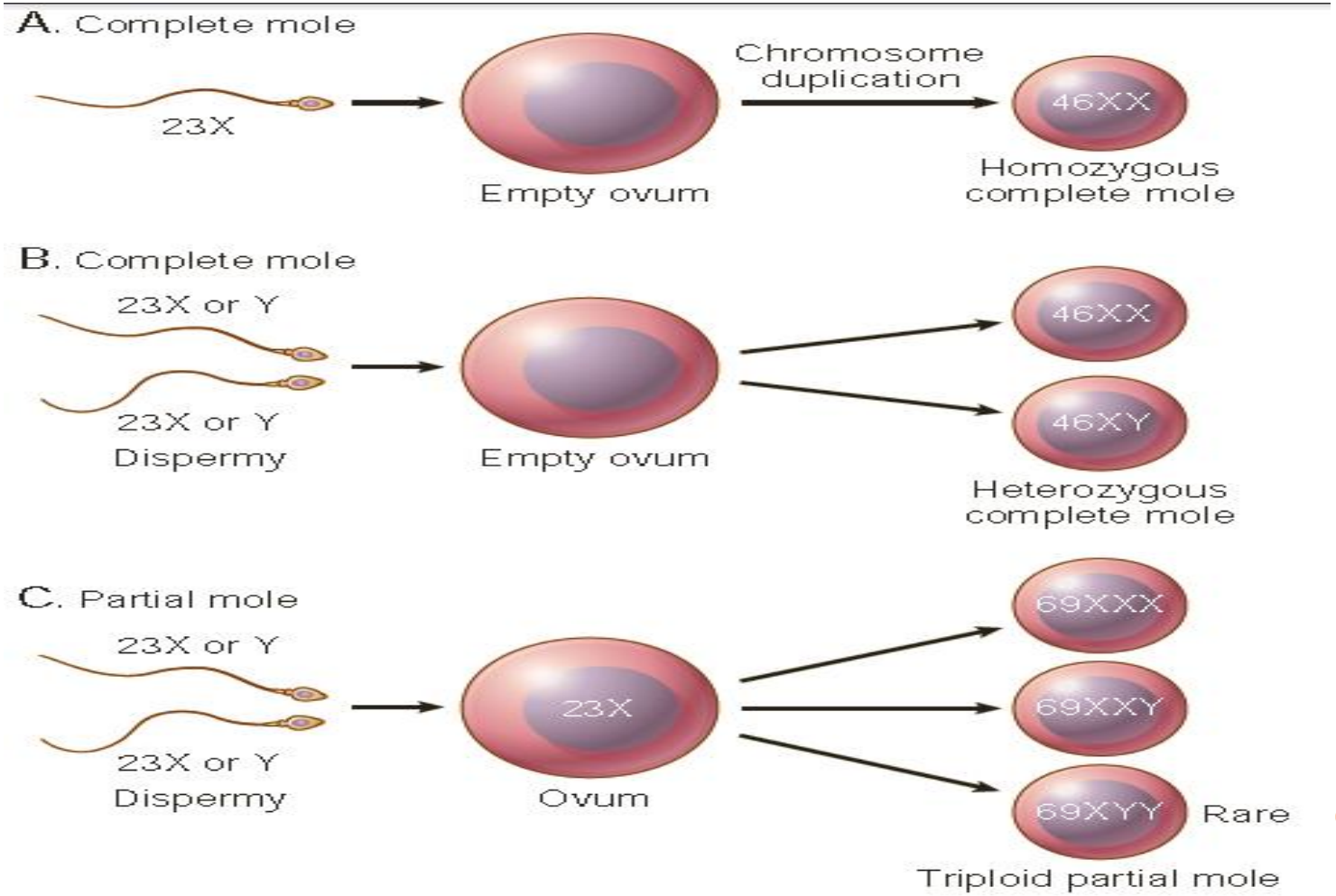
GESTATIONAL TROPHOBLASTIC DISEASE

- An abnormal proliferation of fetal trophoblast cells. (normal cells of placenta in pregnancy)
- In early embryo trophoblast cells form chorionic villi → in time they make the placenta (provide a large contact area between fetal & maternal circulations to allow gas & nutrient exchange).
- All elaborate human chorionic gonadotropins (hCG) → detected in the blood & urine at levels higher than those found during normal pregnancy. (diagnosis, follow up).

Hydatidiform Mole - Pathogenesis

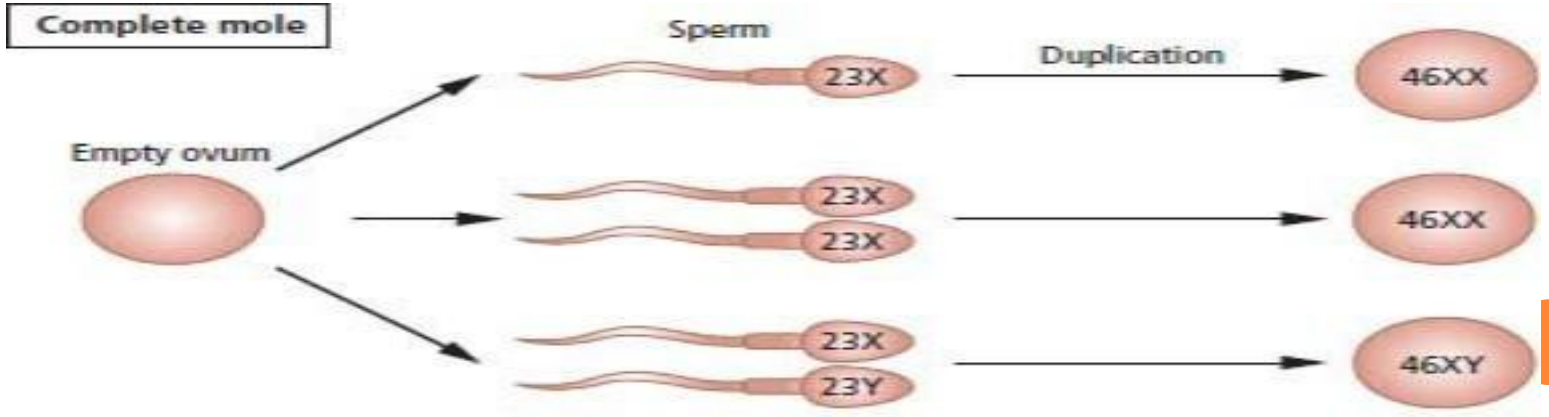
- An abnormal gestational process due to abnormal fertilization with an excess of paternal genetic material, two forms:

1. Complete mole: an empty egg fertilized by two spermatozoa (or a diploid sperm) → diploid karyotype containing only paternal chromosomes.
2. Partial mole: a normal egg is fertilized by two spermatozoa (or a diploid sperm) → triploid karyotype with a dominance of paternal genes.


A. Complete mole
23X
Empty ovum
Chromosome duplication
46XX
Homozygous complete mole
B. Complete mole
23X or Y
23X or Y
Dispermy
Empty ovum
46XX
46XY
Heterozygous complete mole
C. Partial mole
23X or Y
23X or Y
Dispermy
23X
Ovum
69XXX
69XXY
69XYY
Rare
Triploid partial mole

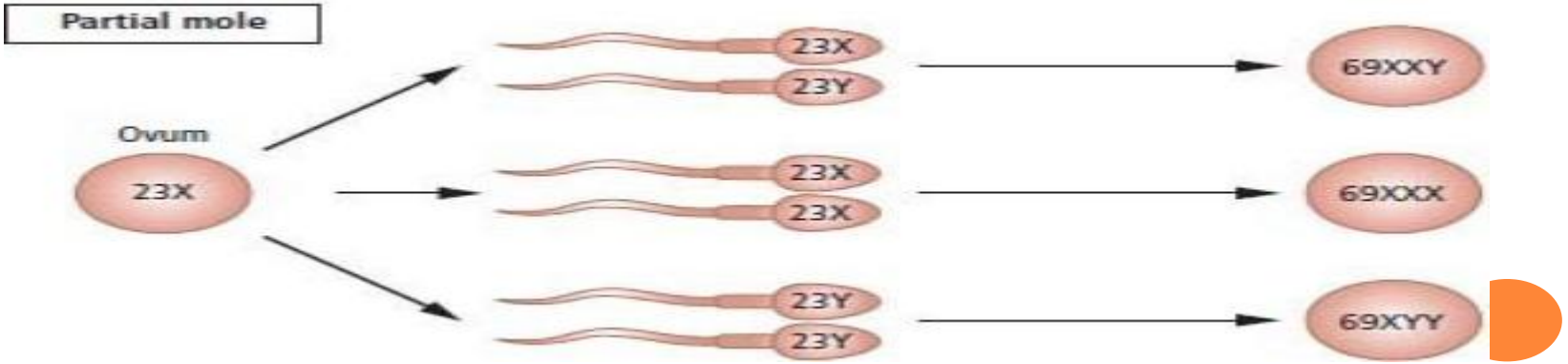
Hydatidiform Mole - Complete

- Complete mole are not compatible with embryogenesis & **does not contain fetal parts.** The chorionic epithelial cells are diploid (46,XX or, uncommonly, 46,XY)



Hydatidiform Mole - Partial

- Partial mole is compatible with early embryo formation → **may contain fetal parts & some normal chorionic villi.** Chorionic epithelial cellsalmost always triploid (e.g., 69,XXY)

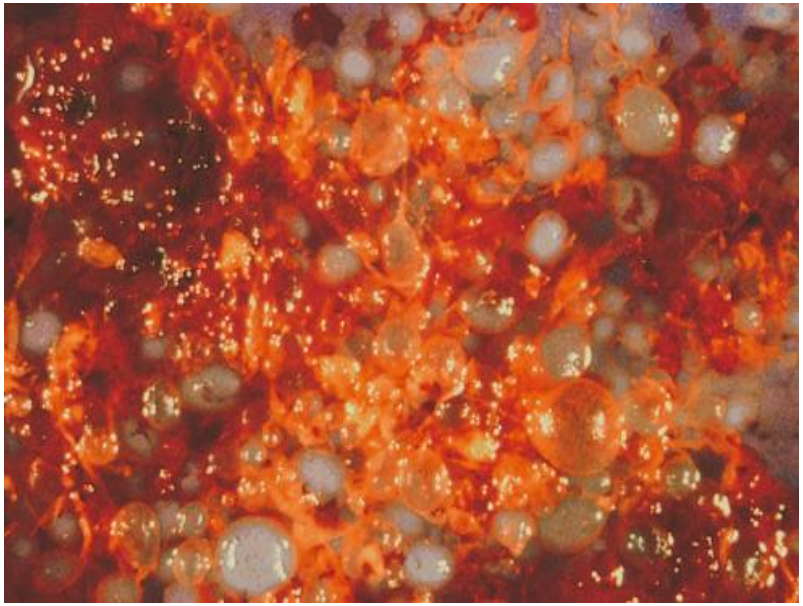


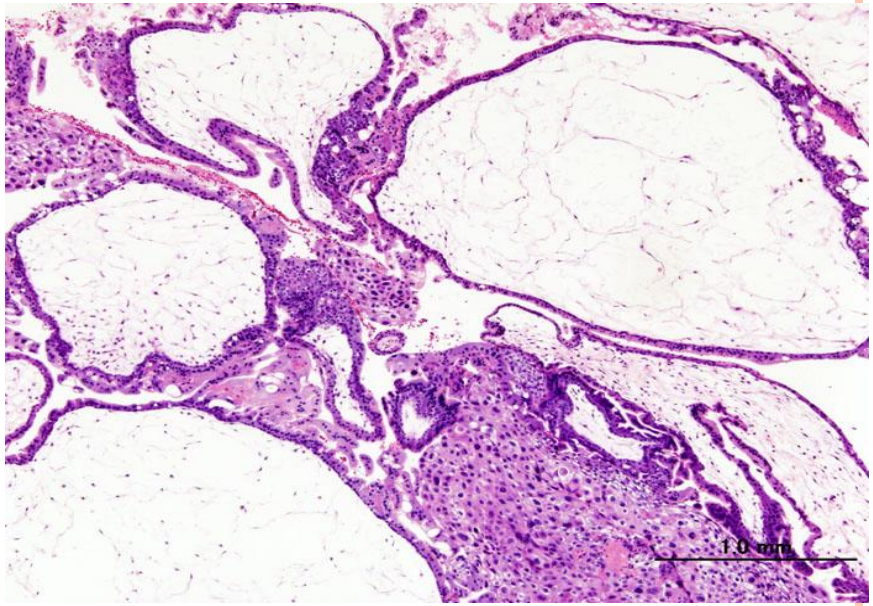
Hydatidiform Mole – Epidemiology & Clinical

- Incidence complete hydatidiform mole is about 1 to 1.5 per 2000 pregnancies(higher in Asian)
- Most common before 20 & after 40 years (maternal age)
- **History of Mole increases the risk for molar disease in subsequent pregnancies**.
- **Presentation**: At 12-14 weeks of pregnancy during investigation for a gestation "too large for dates,".
  +both moles → Hyperemesis, elevation of hCG in maternal blood & no fetal heart sounds.

Hydatidiform Mole – Morphology

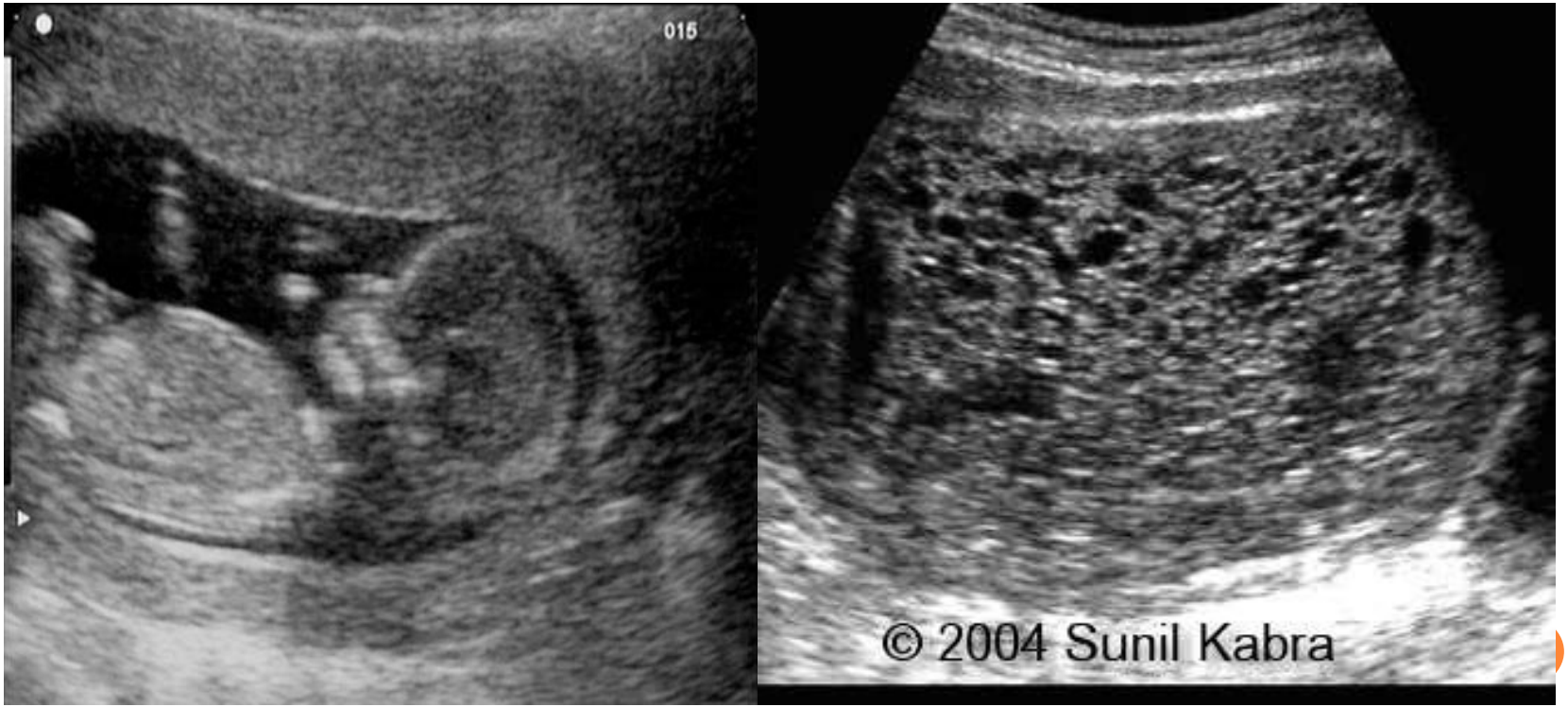
Uterine cavity is expanded by friable mass (**Grape-like villi**) composed of thin-walled, cystically dilated chorionic villli covered by varying amount of atypical chronic epithelium.





Hydatidiform Mole – Ultrasound

SNOW STORM



HYDATIDIFORM MOLE – TREATMENT & PROGNOSIS

- Tx: surgical evacuation of the uterine cavity & close follow up with serum hCG.
- The majority of moles do not recur after thorough curettage, 10% of complete moles are invasive
- No more than 2-3% give rise to choriocarcinoma **(usually complete, rarely partial).**
- **So partial mole has much better prognosis**

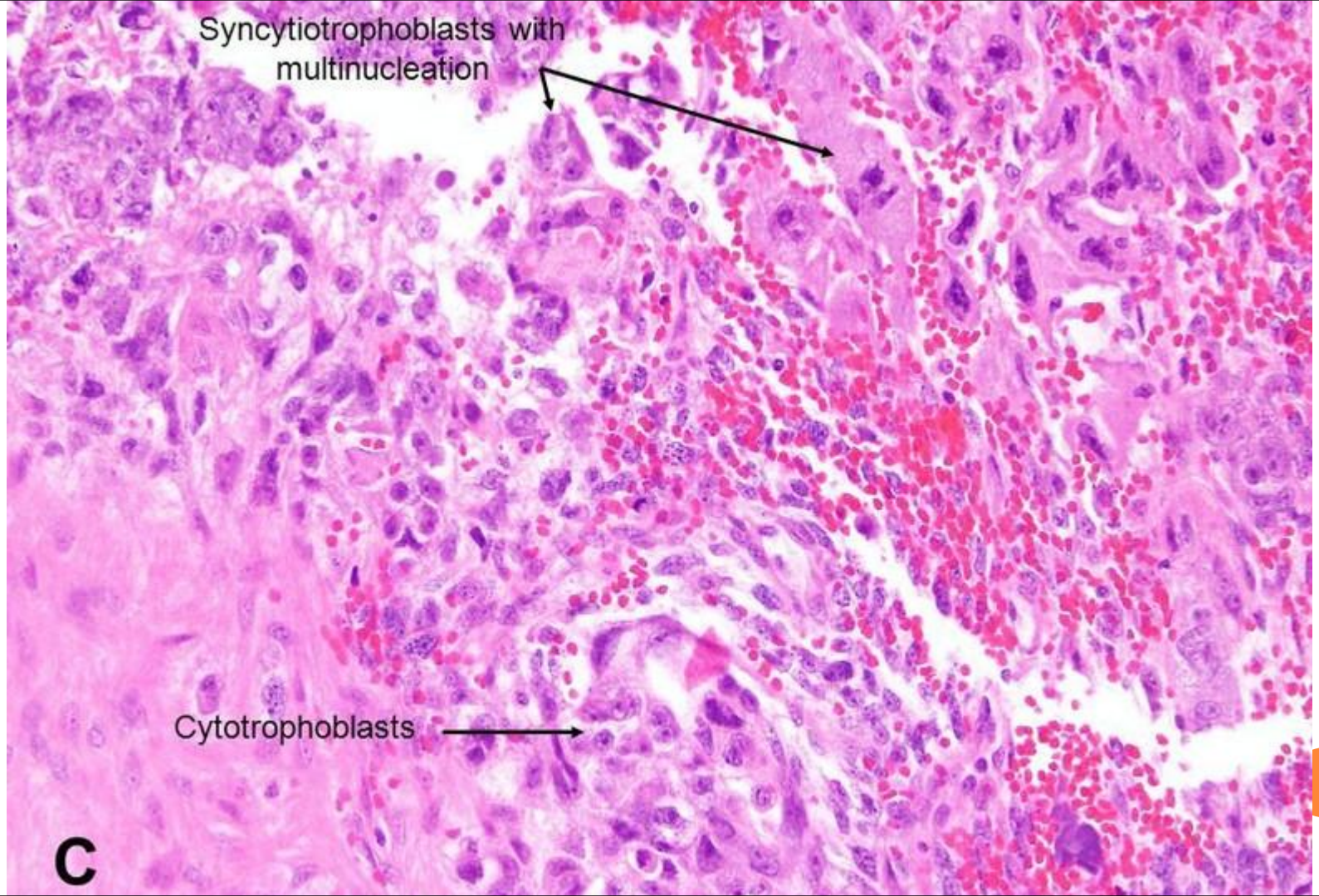
Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid (69,XXY)
Villous edema	All villi	Some villi
Trophoblast proliferation	Diffuse; circumferential	Focal; slight
Atypia	Often present	Absent
Serum hCG	Elevated	Less elevated
hCG in tissue	++++	+
Behavior	2% choriocarcinoma	Rare choriocarcinoma

Gestational Choriocarcinoma

- A very aggressive malignant tumor, arises from gestational chorionic epithelium or, less frequently, from totipotential cells within the gonads (as a germ cell tumor).
- Rare tumor (higher in Asian)
- Most common before 20 & after 40 years (maternal age)
- 50% from complete moles; 25% after an abortion, 25% after an apparently normal pregnancy

Gestational Choriocarcinoma - Morphology

- **Presentation**: a bloody, brownish discharge, very high hCG absence of marked uterine enlargement (not like mole)
- **Gross**: hemorrhagic, necrotic uterine masses.
- **Microscopic:** In contrast with hydatidiform moles chorionic villi are not formed; the tumor is composed of anaplastic cuboidal cytotrophoblasts & syncytiotrophoblasts


Syncytiotrophoblasts with multinucleation
Cytotrophoblasts
C

GESTATIONAL CHORIOCARCINOMA – PROGNOSIS

- **Very aggressive disease.**
- At diagnosis widespread vascular (hematogenous) spread usually the lungs & brain.
- Lymphatic invasion is uncommon.
- Despite the extremely aggressive of placental choriocarcinoma → sensitive to chemotherapy.
- By contrast, response to chemotherapy in gonads choriocarcinomas is poor.

GOOD LUCK IN YOUR EXAMS