Ovarian and Fallopian Tube Pathology

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Topics covered in this lecture:

- **Ovarian neoplasms:**
  - Classification
  - Serous tumors
  - Mucinous tumors
  - Teratomas
  - Clinical aspects
- **Fallopian tube diseases:**
  - Ectopic pregnancy
  - Tubal malignancies

Ovarian Neoplastic Diseases

- 5th most common cancer in women.
- 5th leading cause of cancer death in women.
- 3 Origins of primary ovarian tumors:

  1- epithelium

  2- germ cells

  3- sex cord/stromal cells.

  - Each of these cell types gives rise to a variety of tumors
- Secondary tumors of the ovary are metastatic malignancies that spread to the ovaries.

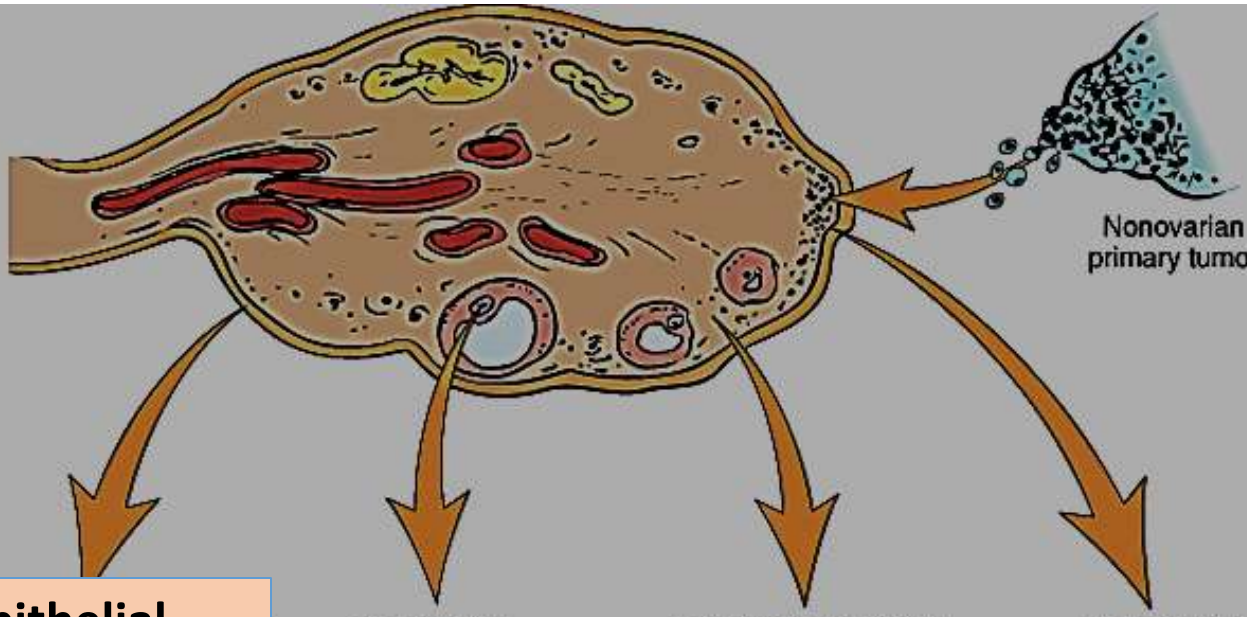
Epithelial Ovarian Neoplasms

- Account for the majority of ovarian tumors
- in their malignant forms, account for 90% of ovarian cancers
- Previously were thought to arise from coelomic epithelium that covers the ovarian surface
- Recent studies have shown that they actually arise from the fimbriated end of fallopian tube or epithelial cysts in the cortex of ovary.

Germ cell and sex cord–stromal cell tumors

- less frequent
- constitute 20% to 30% of ovarian tumors
- collectively responsible for less than 10% of malignant tumors of the ovary (so many of them are benign)

Ovarian Neoplasms



Epithelial tumors

ORIGIN		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	

Ovarian neoplasms - Pathogenesis:

- Risk factors:
- **nulliparity**
- **family history** (Only 10%)

- Note: OCPs may **reduce** risk.

Ovarian Epithelial Neoplasms- Pathogenesis:

- Sporadic cases
- ***BRCA*** 1 and 2 mutations: 10% of sporadic cases
- ***p53*** (50%)
- **HER2/NEU** over-expression (35%)
- **K-RAS** protein over-expression (30%) (mucinous)

- Familial cases
- **BRCA1** and **2**

EPITHELIAL TUMORS - types:

- **1- Serous**
- **2- Mucinous**
- **3- Endometrioid**
- **4- Clear cell**
- **5- Brenner**

- **All types include benign, borderline, and malignant tumors**

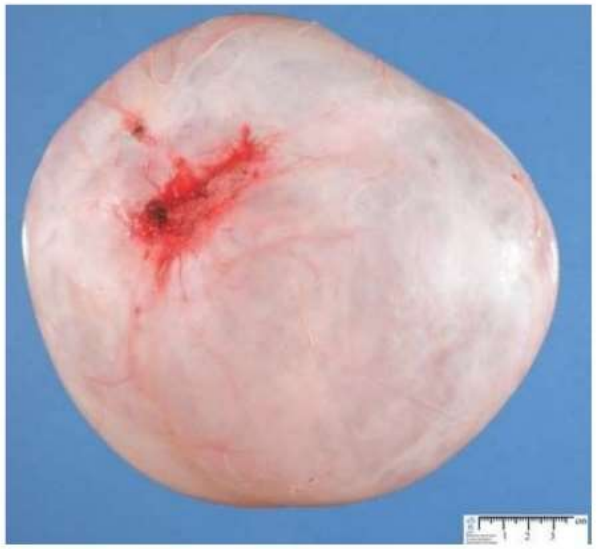
1- Serous Tumors

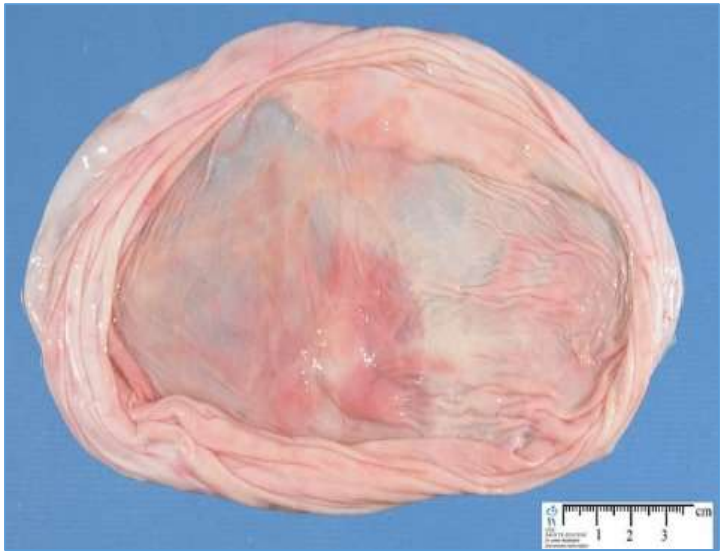
- **the most frequent ovarian tumors.**
- Include: 60% benign, 15% borderline, and 25% malignant.
- **the most common malignant ovarian tumors (60%)**
- Genetics:
- ***BRAF*** and ***K-RAS*** mutations→ borderline & low grade serous carcinomas
- ***p53*** and ***BRCA1*** mutations →High-grade serous carcinomas

Benign serous tumors: Morphology

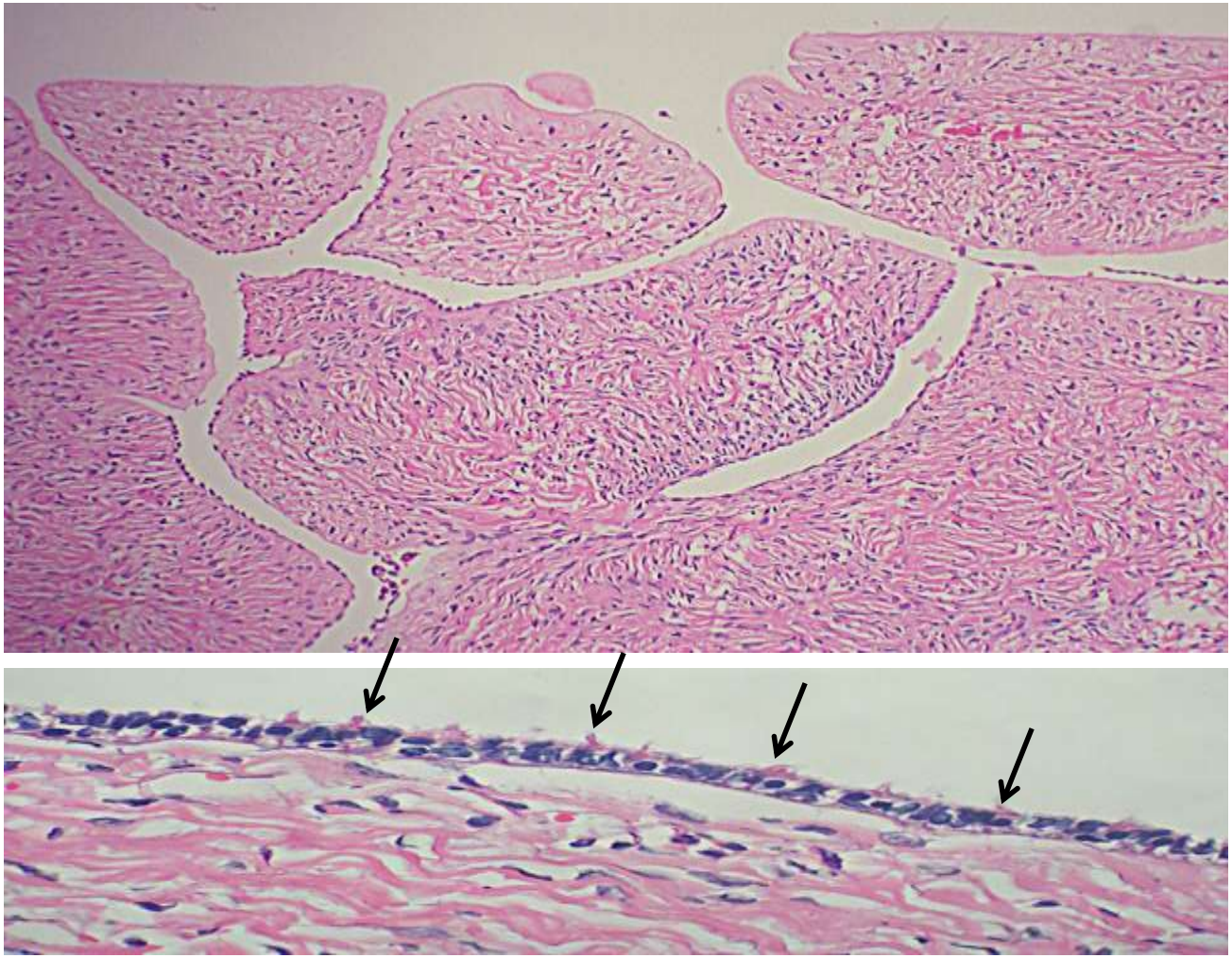
- **Benign serous tumors**:
- cystic ; large; (30 cm).
- May be bilateral.
- filled with a clear serous fluid
- **single layer** of columnar epithelium. Some cells are ciliated.
- **Psammoma bodies** (laminated calcified concretions) are common in tips of papillae of **all** serous tumors

SEROUS CYSTADENOMA



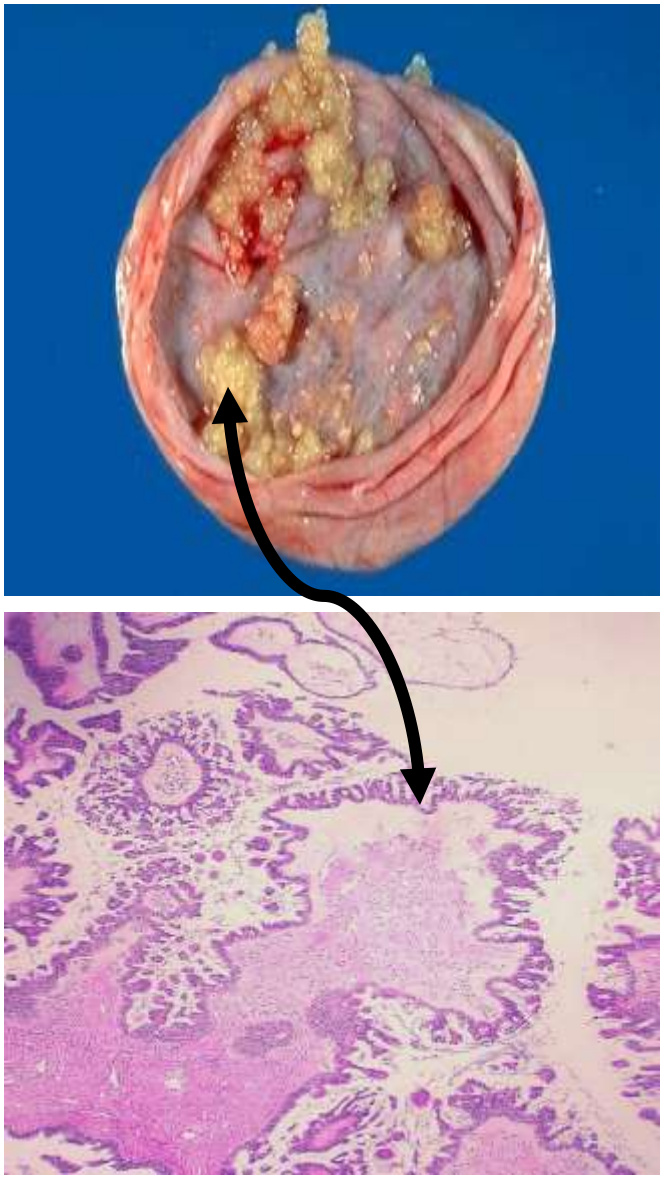


Benign serous tumors



Borderline Serous Tumors

- **Complex architecture**
- Mild cytologic atypia
- **No** stromal invasion
- May have peritoneal implants
- can recur and some can progress to carcinoma
- Prognosis: intermediate between benign and malignant types
- (survival with peritoneal metastases 75%)



Malignant Serous Tumors-There are two types of ovarian serous carcinomas:

- **low-grade serous carcinoma:**

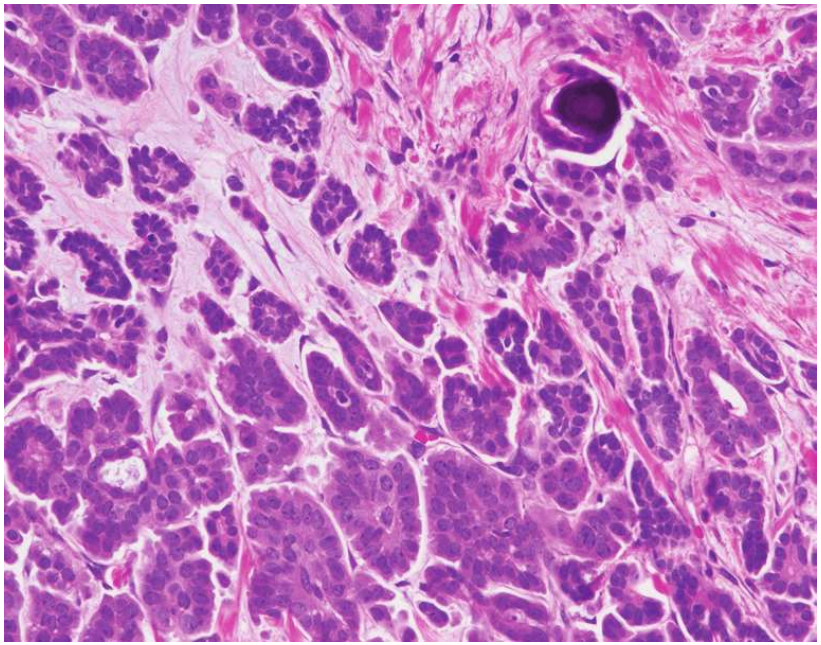
- arise from borderline lesions
- progress slowly to become invasive carcinoma
- Differentiated morphology
- mutations in KRAS

- **high-grade serous carcinoma:**

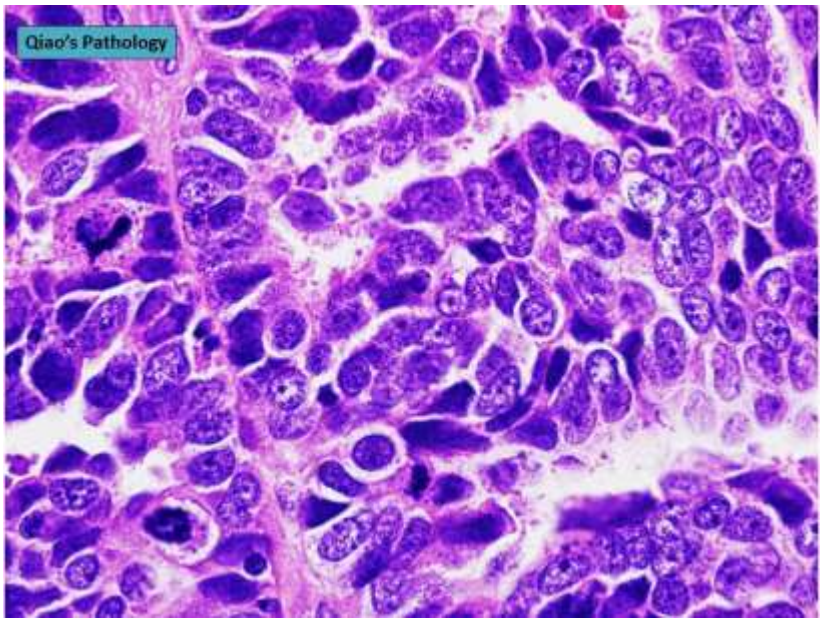
- develop rapidly
- many arise form fallopian tube via serous tubal intraepithelial carcinoma, rather than ovarian coelomic epithelium.
- mutations in TP53

- Anaplasia of cells and invasion of the stroma.
- prognosis poor, depends on stage at the time of diagnosis.

Low grade serous carcinoma



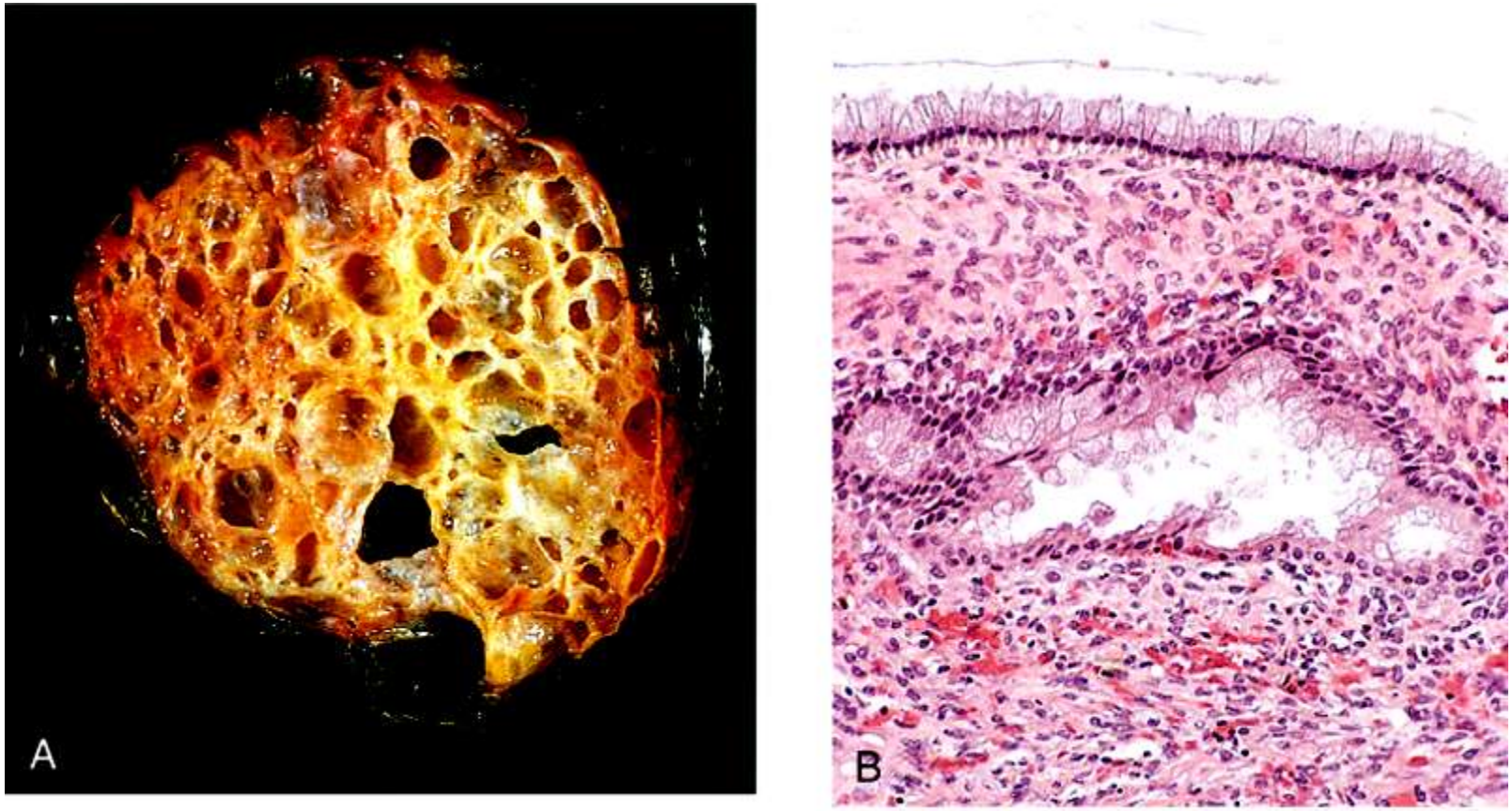
High grade serous carcinoma



2- Mucinous ovarian tumors

- **mucin-secreting** cells.
- 80% benign; 10% borderline; **10**% **malignant** *(cystadenocarcinoma)*
- **Usually large** and **multilocular**.
- psammoma bodies **not** found
- stage is major determinant of prognosis

Mucinous ovarian tumors



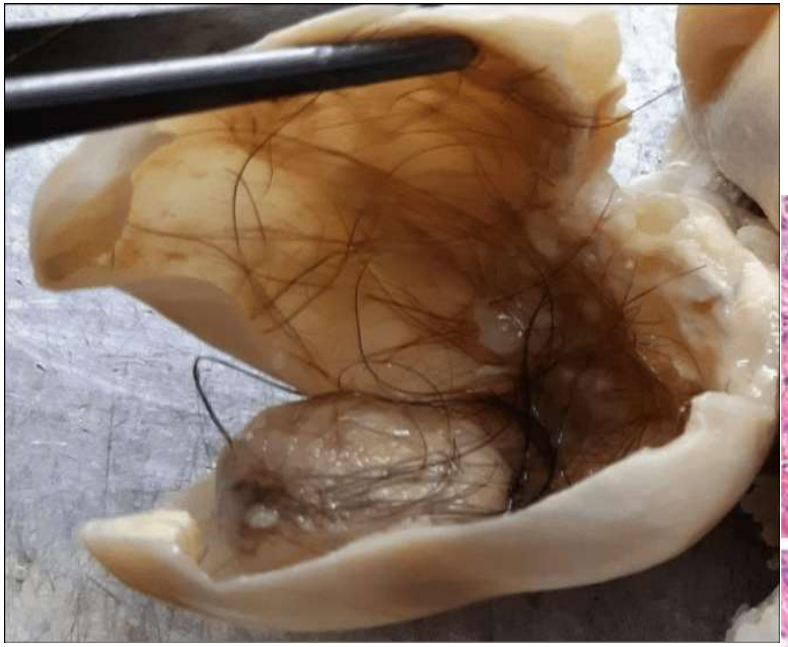
Germ Cell Tumors

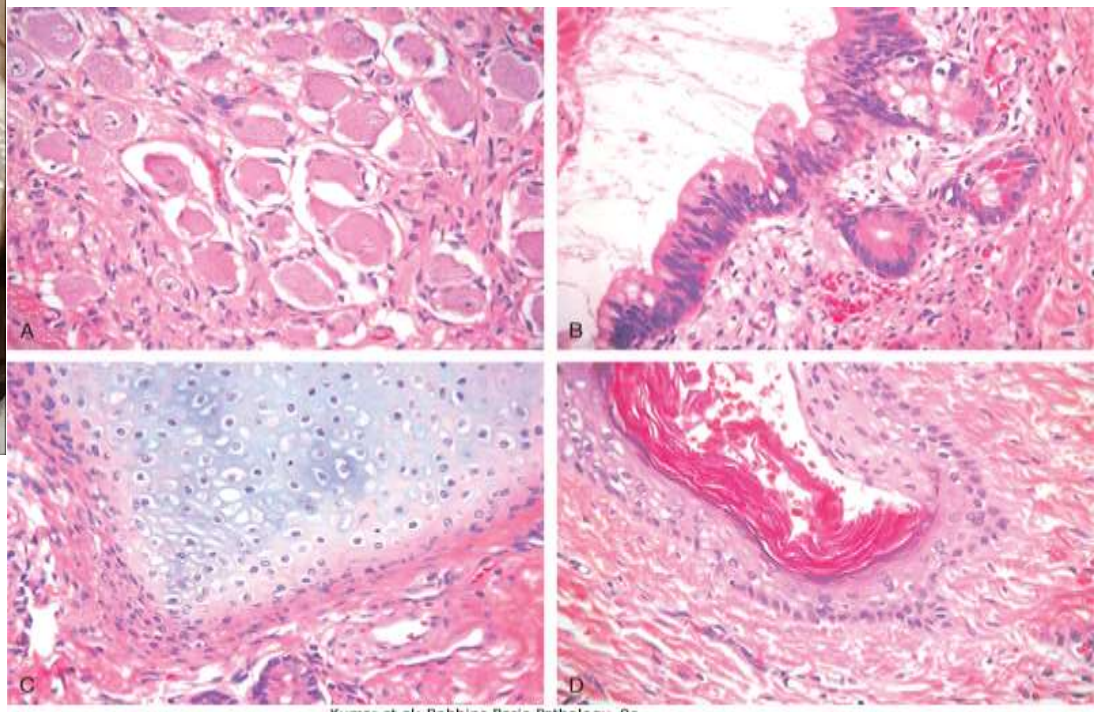
- Types according to differentiation:
- dysgerminoma (differentiation to oogonia)
- Embryonal carcinoma (differentiation to primitive embryonal tissue)
- yolk sac tumor(differentiation to endodermal sinus)
- choriocarcinoma (differentiation to placental tissue)
- Teratoma (differentiation to multiple tissue types).

Benign (Mature) Cystic Teratoma

- totipotential germ cells form mature tissues of all three germ cell layers
- 15% -20% of ovarian tumors
- Many discovered incidentally
- 90% unilateral
- cyst filled with sebaceous secretion and hair; bone and cartilage; epithelium, or teeth.
- > 90% are benign mature cystic teratomas
- immature (malignant variant) is rare.
- torsion (10% to 15% of cases)

Benign (Mature) Cystic Teratoma





Kumar et al: Robbins Basic Pathology, 9e.

Clinical Correlations for All Ovarian Tumors

- Clinical presentation of all is similar:

- Abd. 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 : Estrogens or androgens.

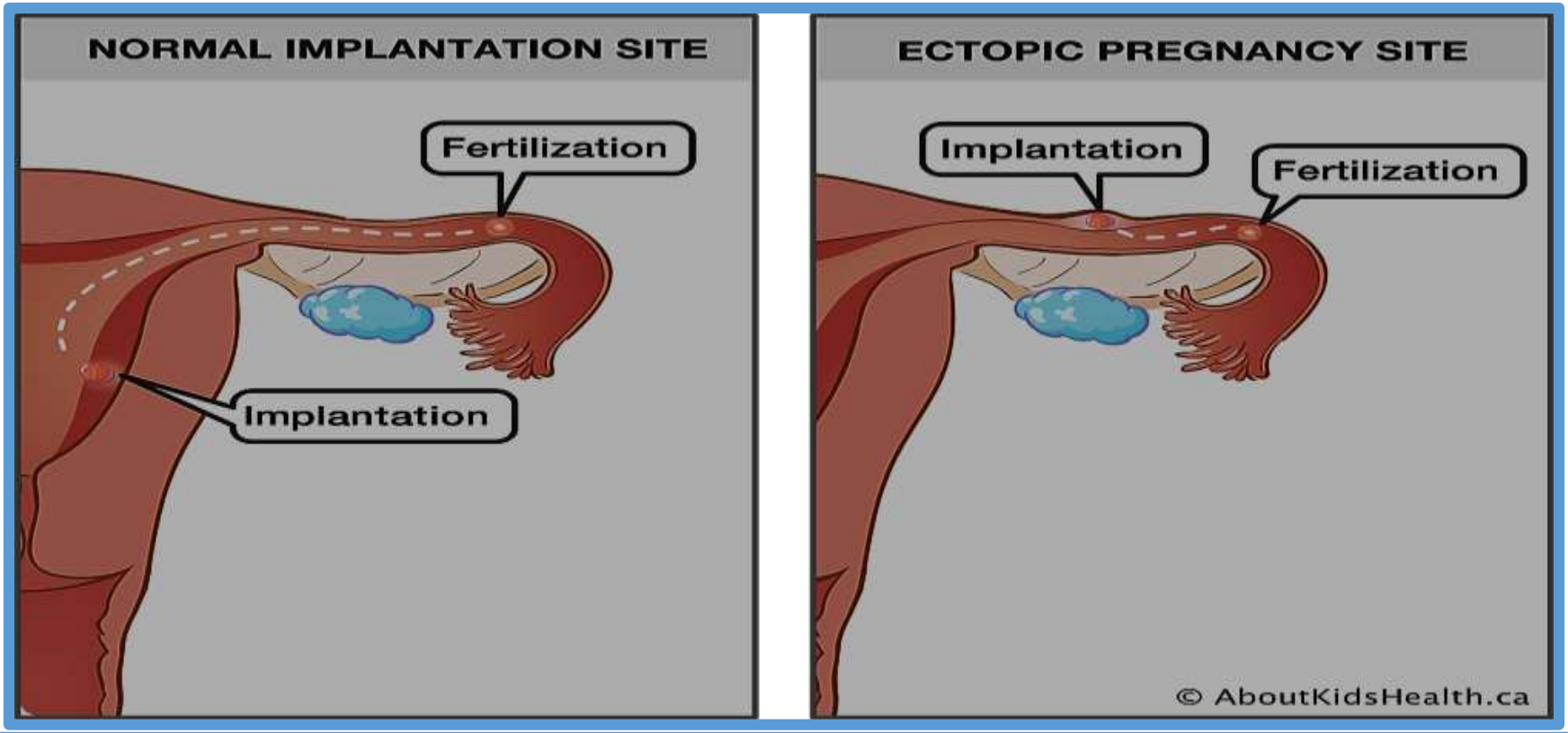
- Treatment: surgery + chemotherapy + radiotherapy
- Outcome of ovarian **cancers** remains unsatisfactory
- **Malignant** tumors are usually discovered in advanced stages
- survival minimally improved since 1970s.
- No early Screening methods are yet available

Pathology of the Fallopian tubes

ECTOPIC PREGNANCY

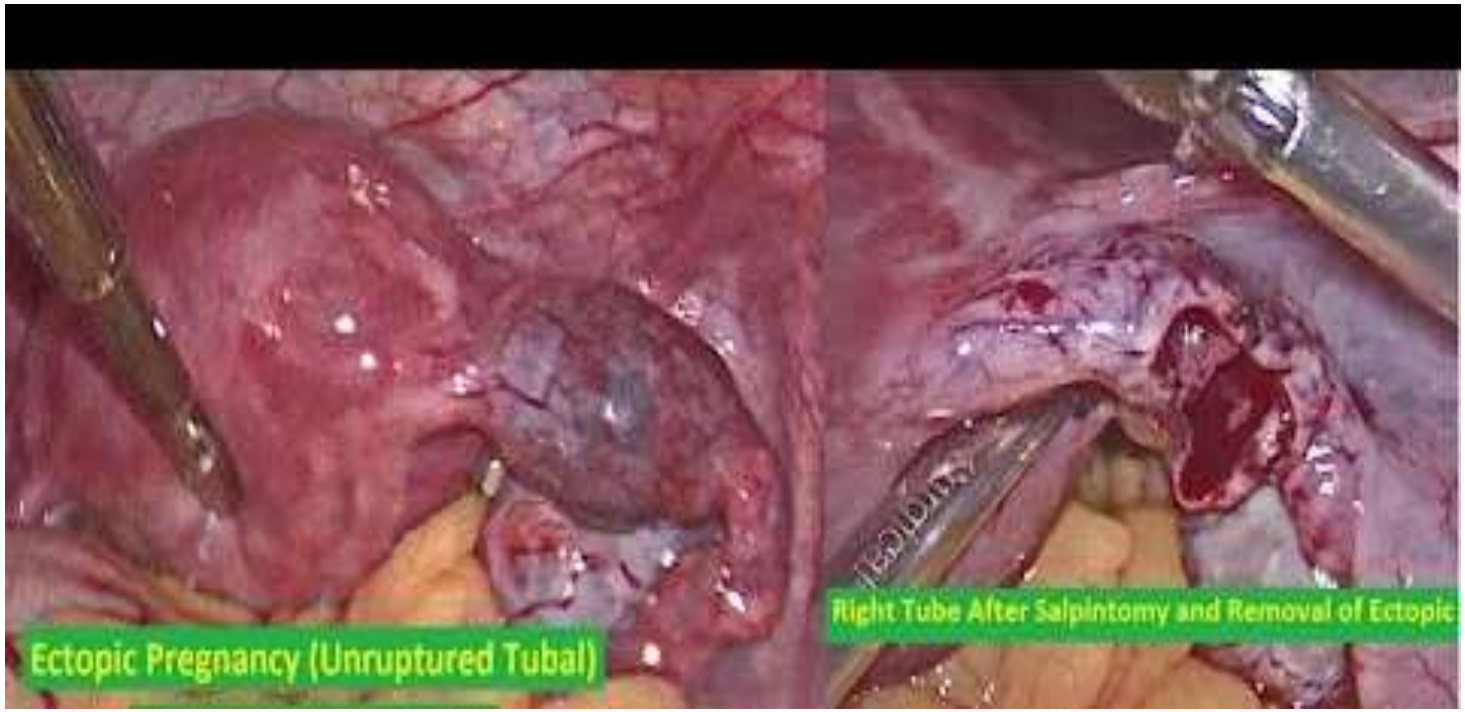
- implantation of the fertilized ovum outside uterus
- Incidence: 1%
- 90% of cases occur in fallopian tubes
- other sites: ovaries, abdominal cavity
- Predisposing factors: tubal obstruction (50%) PID; tumors; endometriosis; **IUCD**..
- In 50% : no anatomic cause can be demonstrated.

Normal versus ectopic pregnancy



Early: development of embryo and placental tissue
Later: placenta burrows through tubal wall causing intratubal hematoma (hematosalpinx) and intraperitoneal hemorrhage.
Rupture: intense abdominal pain (acute abdomen), often followed by shock.
Prompt surgical intervention is necessary.

Ectopic pregnancy- Management



Tubal malignancies

- **most common histologic type is serous carcinoma.**
- may be the **origin** for many ovarian high-grade serous carcinomas
- **serous tubal intraepithelial carcinoma (STIC**) in fimbriated ends of fallopian tubes.
- STICs have mutations in TP53 in 90% of cases
- increased in women with ***BRCA* mutations**
- Because **of their access to peritoneal cavity**, fallopian tube carcinomas frequently spread to omentum and peritoneal cavity at time of presentation (advanced).