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

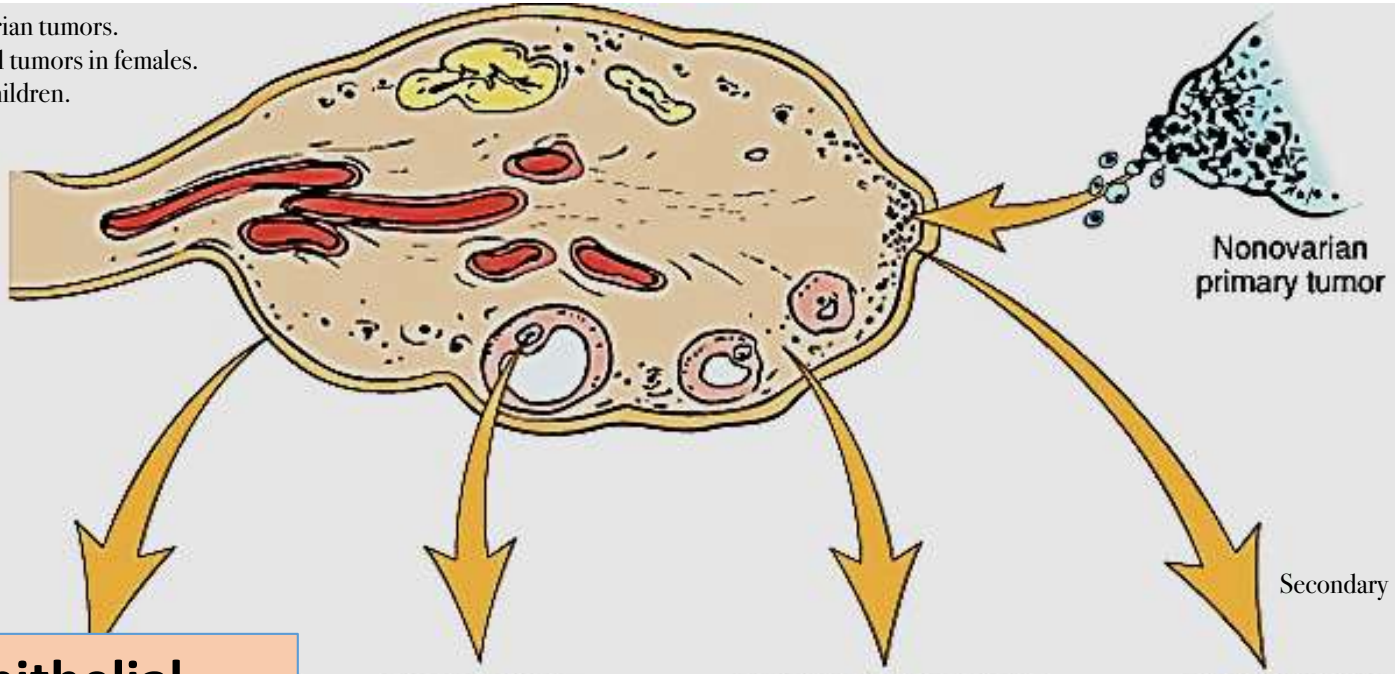
- Account for the majority of ovarian tumors
- in their malignant forms, account for 90% of ovarian cancers
- Previously were thought to arise from coelomic epithelium that covers the ovarian surface
- Recent studies have shown that they actually arise from the fimbriated end of fallopian tube or epithelial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

- Serous tumors are the most frequent ovarian tumors.
- Teratoma are the most common germ cell tumors in females.
- Germ cell ovarian tumors mainly affect children.



ORIGIN	Epithelial 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	

Ovarian neoplasms - Pathogenesis:

- Positive family history of ovarian neoplasms is considered a risk factor for ovarian neoplasms.
- Therefore ovarian, as well as fallopian tube neoplasms may be familial.

- 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*** (serous)
- **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**

Borderline tumors are intermediate:
- They have distinct histological features.
- They have distinct behavioral and prognostic features, where their behavior is intermediate, between benign and malignant.

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

Serous = watery, thin, colorless fluid.

1- Serous Tumors

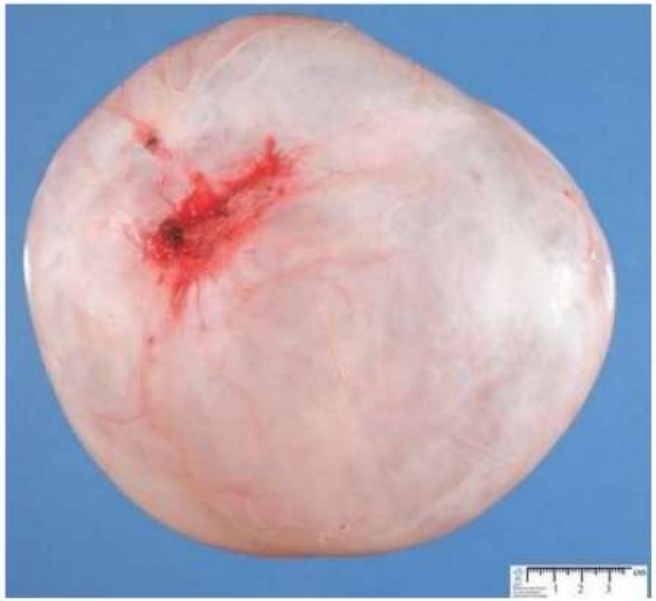
- The epithelial cells that form this tumor have the capacity to secrete serous fluid.
- This fluid collects inside the ovary forming a cyst.
- So these tumors are cystic in nature.

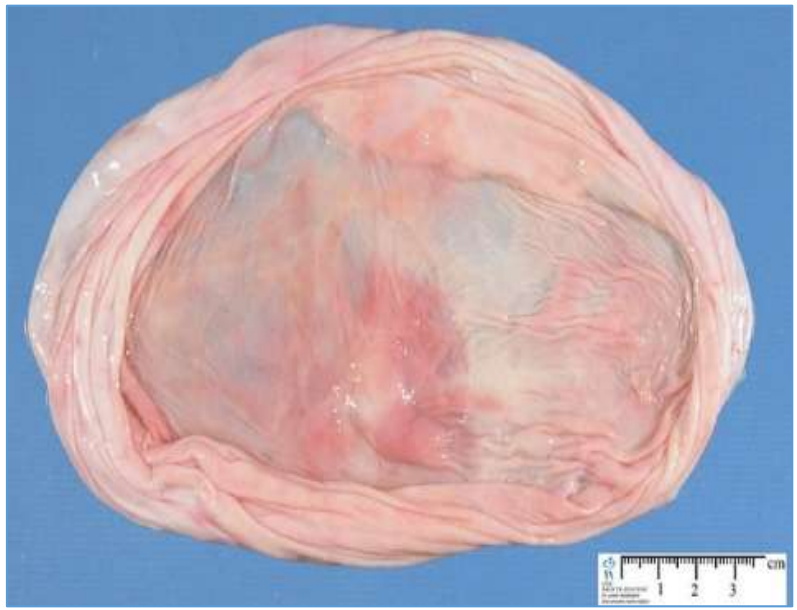
- **the most frequent ovarian tumors.**
- Include: 60% benign, 15% borderline, and 25% malignant. Depending on the behavior, features and growth patterns of the cells.
- **the most common <u>malignant</u> ovarian tumors (60%)**
- <u>Genetics:</u>
- ***BRAF*** and ***K-RAS*** mutations→ borderline & low grade serous carcinomas
- ***p53*** and ***BRCA1*** mutations →High-grade serous carcinomas

Benign serous tumors: Morphology

- **Benign serous tumors**:
- cystic ; large; (30 cm). May produce a pelvic mass.
- May be bilateral. But keep in mind both are primary tumors, the tumor didn't spread from one ovary to the other.
- 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
- Behavior is excellent, 5-year survival is 100%, it's benign, does not spread or metastasize.

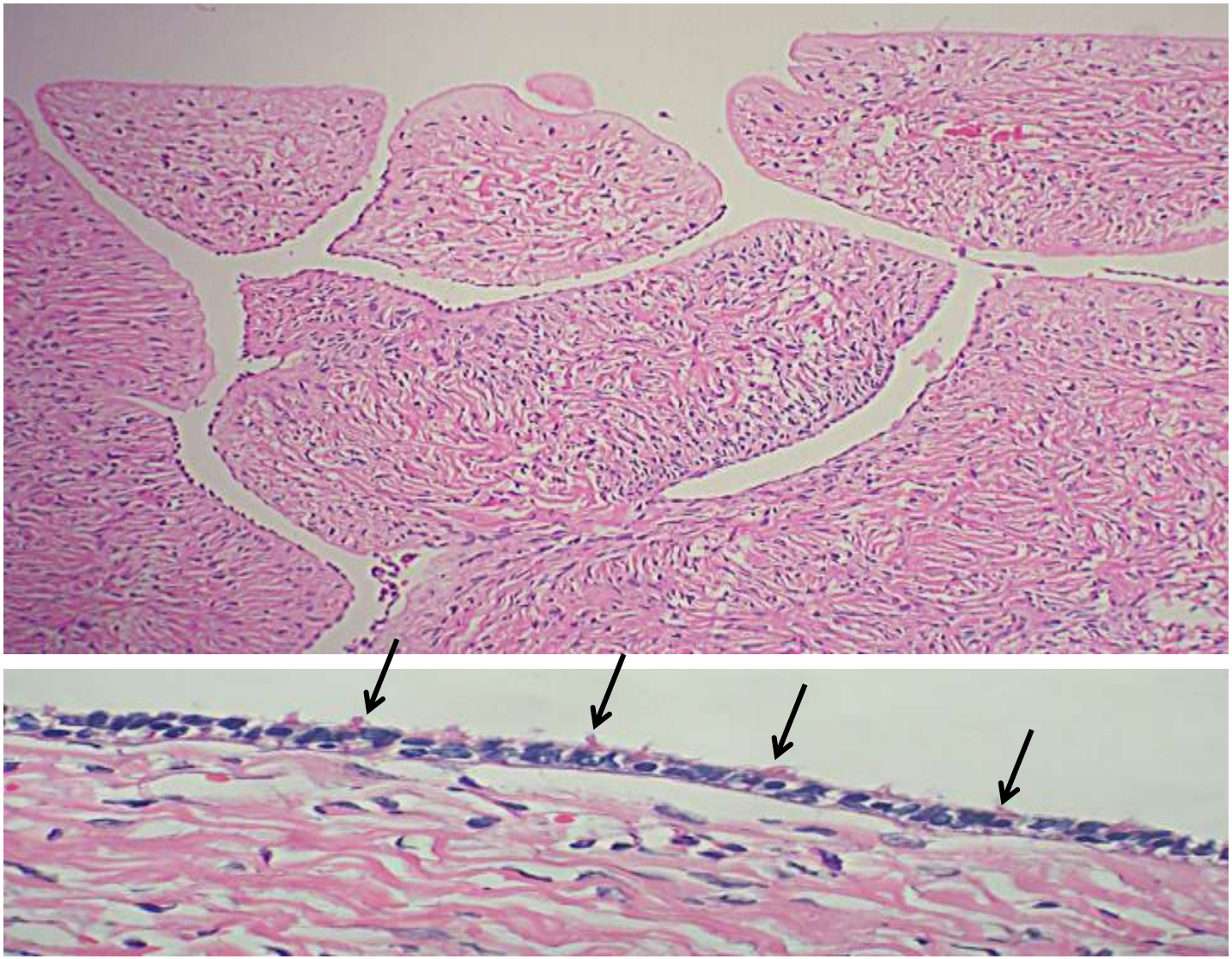
SEROUS CYSTADENOMA





Inside aspect of the cyst:
- Thin
- Smooth

Benign serous tumors



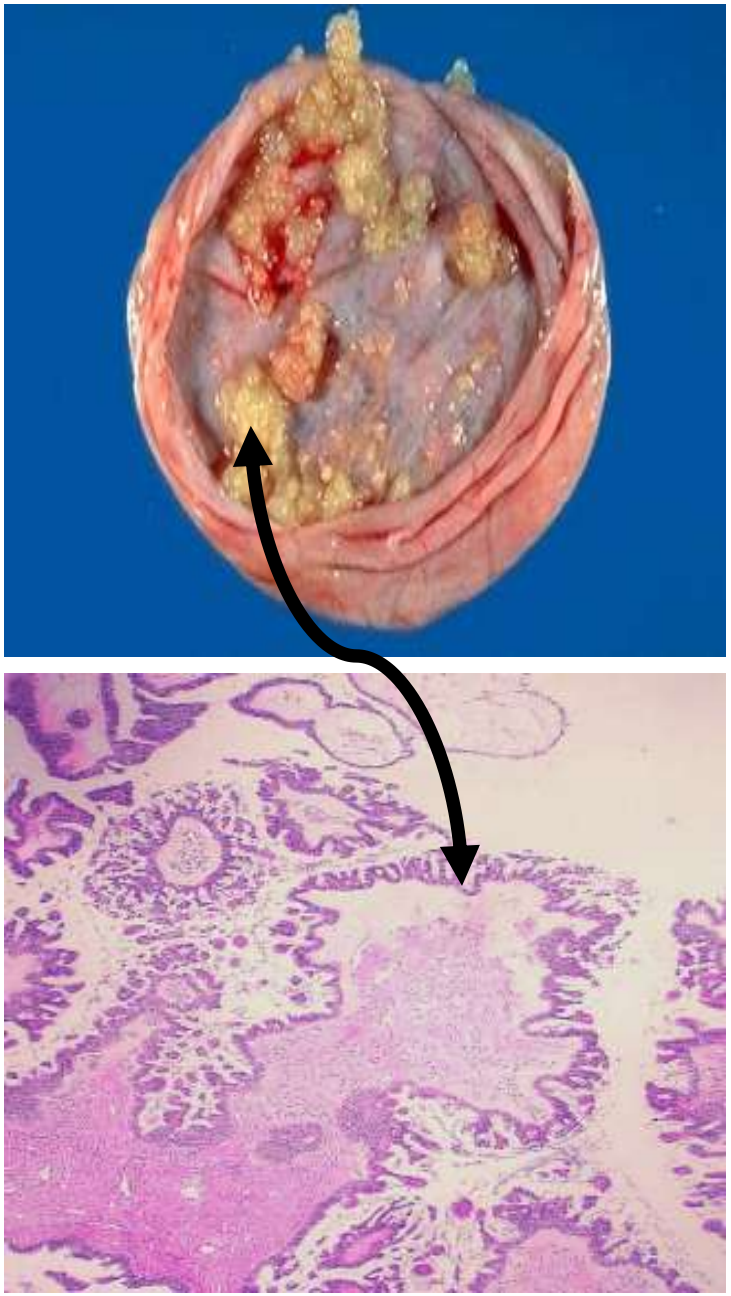
Thin layer of neoplastic columnar epithelial cells, some of which have cilia, just like the fallopian tubes.

Borderline Serous Tumors

- Spherical tumor.
- Cystic in nature.
- When incised, serous fluid is see, but the inside aspect is what's different.
  - It is not smooth.
  - There is solid growths forming nodules, plaques, papillae, therefore, the architecture is more complex.
- These patients require excision and follow up after further evaluation.

- **Complex architecture**
- Mild cytologic atypia
- **No** stromal invasion
- May have peritoneal implants (Metastasis), this is why it's classified as borderline, its behavior isn't fully benign neither is it fully malignant.
- can recur and some can progress to carcinoma
- Prognosis: intermediate between benign and malignant types
- (survival with peritoneal metastases 75%)

But



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

- Two types of malignant serous carcinomas according to their pathogenetic mechanism of formation and their behavior.
- Low grade malignant arise from borderline serous tumors.
- So in summary, benign serous tumors may progress into borderline tumors, some of the borderline tumors that are left untreated may progress to low grade serous carcinoma.

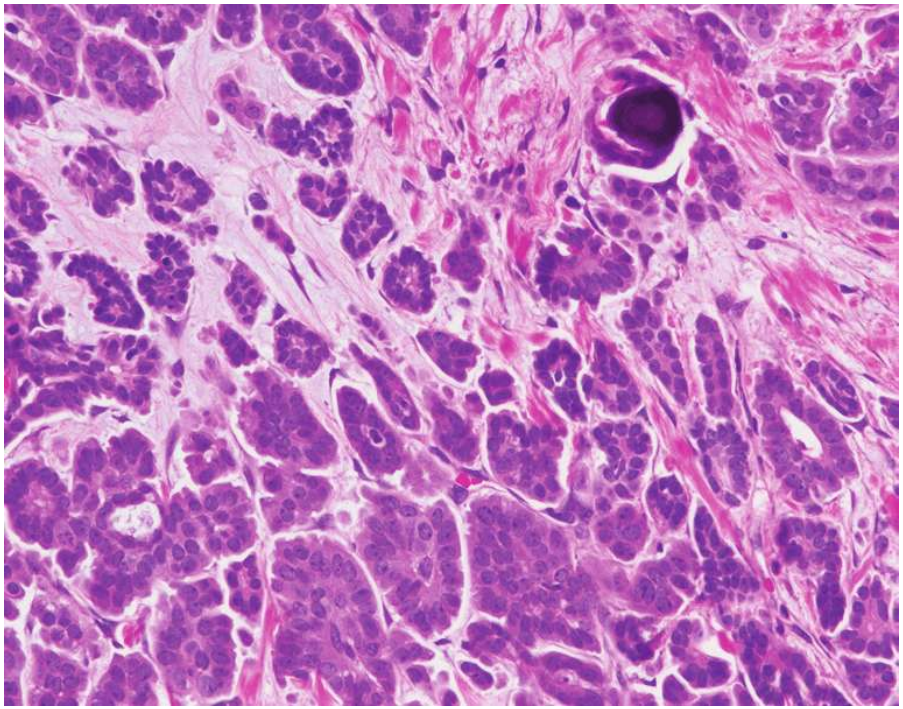
- High grade serous carcinomas are very aggressive tumors.
- They may have a different kind of origin from outside the ovary.
- As mentioned earlier, serous tumors are the most frequent ovarian neoplasms, and in their malignant form, they also represent the most frequent ovarian malignant neoplasms.

- **high-grade serous carcinoma:**

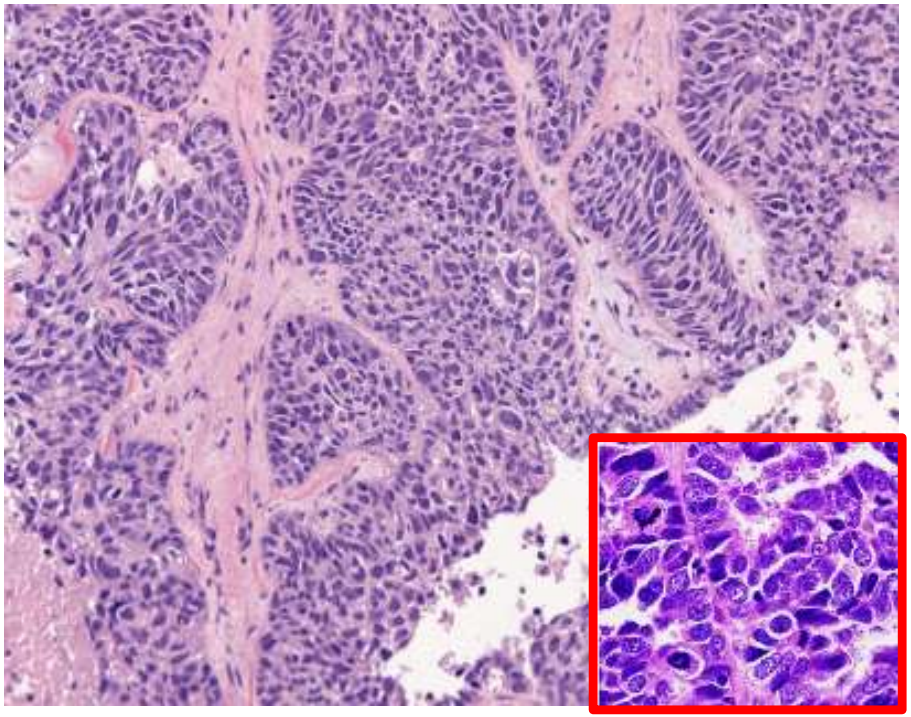
- develop rapidly
- many arise form fallopian tube via serous tubal intraepithelial carcinoma, rather than ovarian coelomic epithelium.
- mutations in TP53

- 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

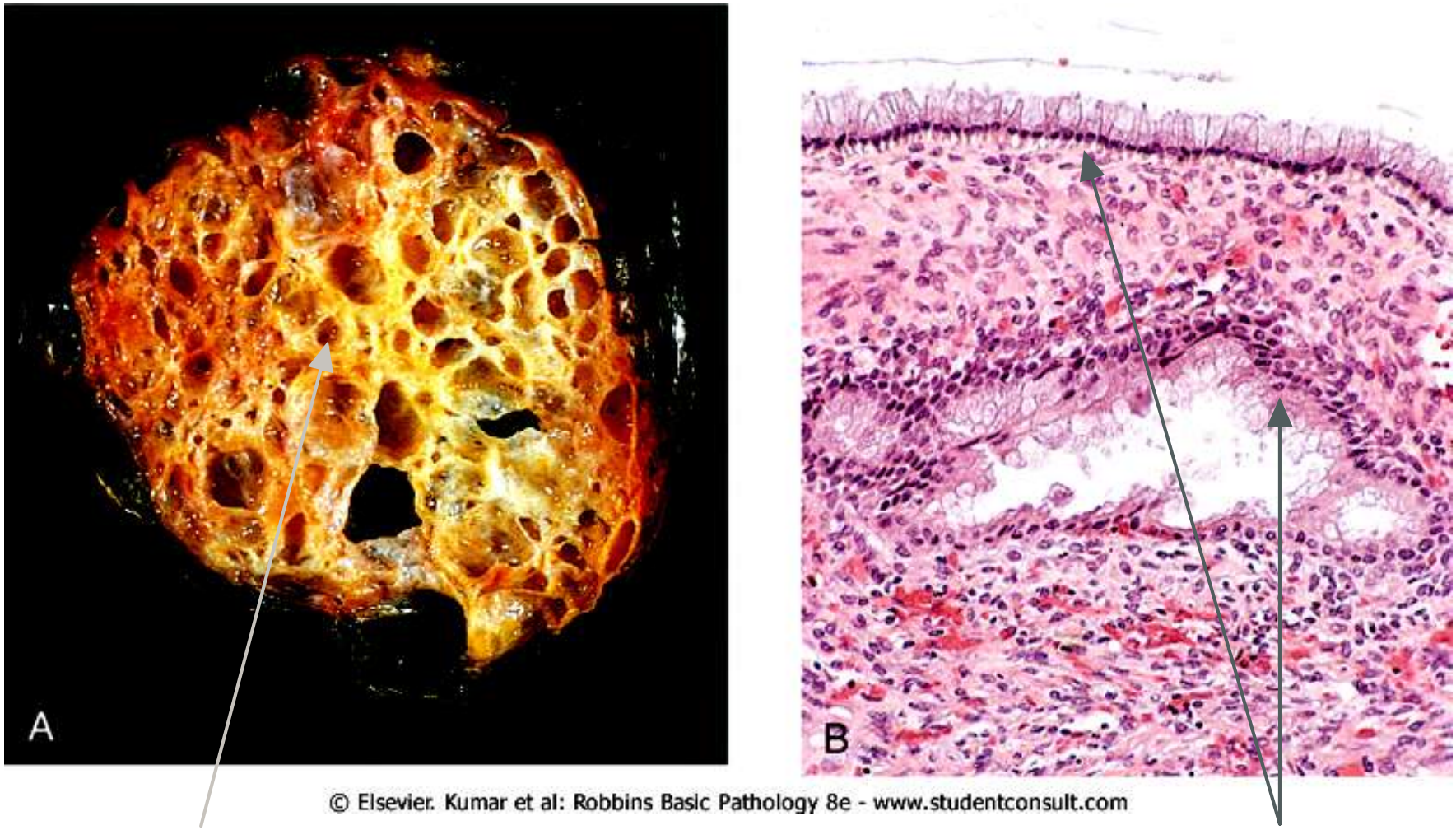


Thick, gelatinous, gel-like mucoid.

2- Mucinous ovarian tumors

- **mucin-secreting** cells. And this mucin will collect inside the ovary, so with time, the patient will develop a cyst.
- 80% benign; 10% borderline; **10% malignant** *(cystadenocarcinoma)*
- **Usually large** and **multilocular** cystic tumors Forming a large ovarian or pelvic mass. Multilocular = multiple cysts within the cyst.
- psammoma bodies **not** found
- stage is major determinant of prognosis

Mucinous ovarian tumors



Multilocular

Mucin-secreting cells.

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

Which means it *could* be asymptomatic, but it may lead to dull pelvic/abdominal pain.

- 90% unilateral
- cyst filled with sebaceous secretion and hair; bone and cartilage; epithelium, or teeth.

A female patient presents with ovarian mass, the mass is evaluated and the patient undergoes surgery to remove this mass, upon examining the cyst, the surgeon will notice unusual material within the cyst.

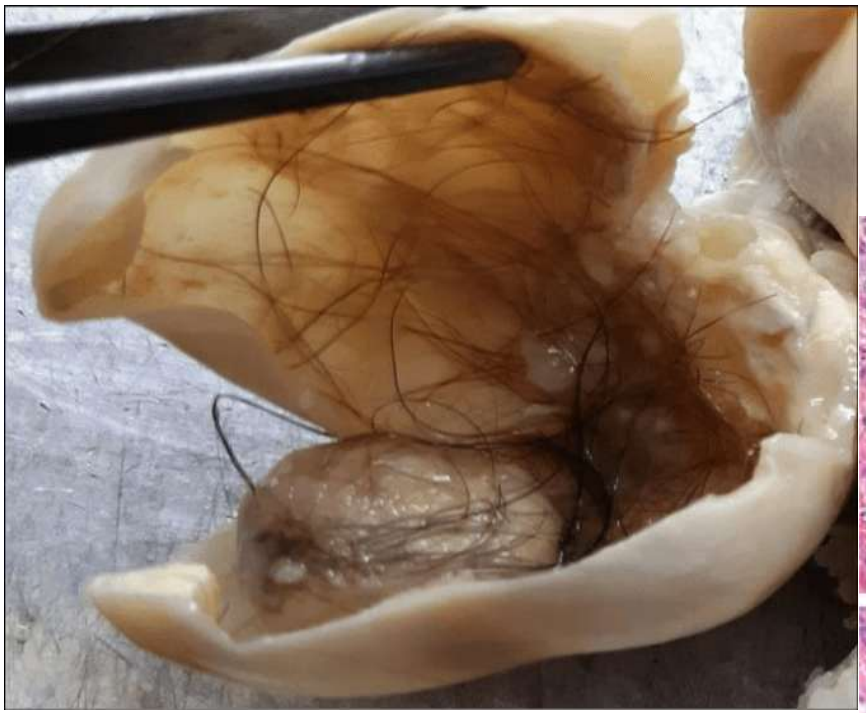
- > 90% are benign mature cystic teratomas
- immature (malignant variant) is rare.

Since the tumor originates from germ cells, some cells may be immature, and these immature cells may what cause malignancy.
In ovarian cystic teratomas, presence of immature embryonic-like cells indicates malignancy.

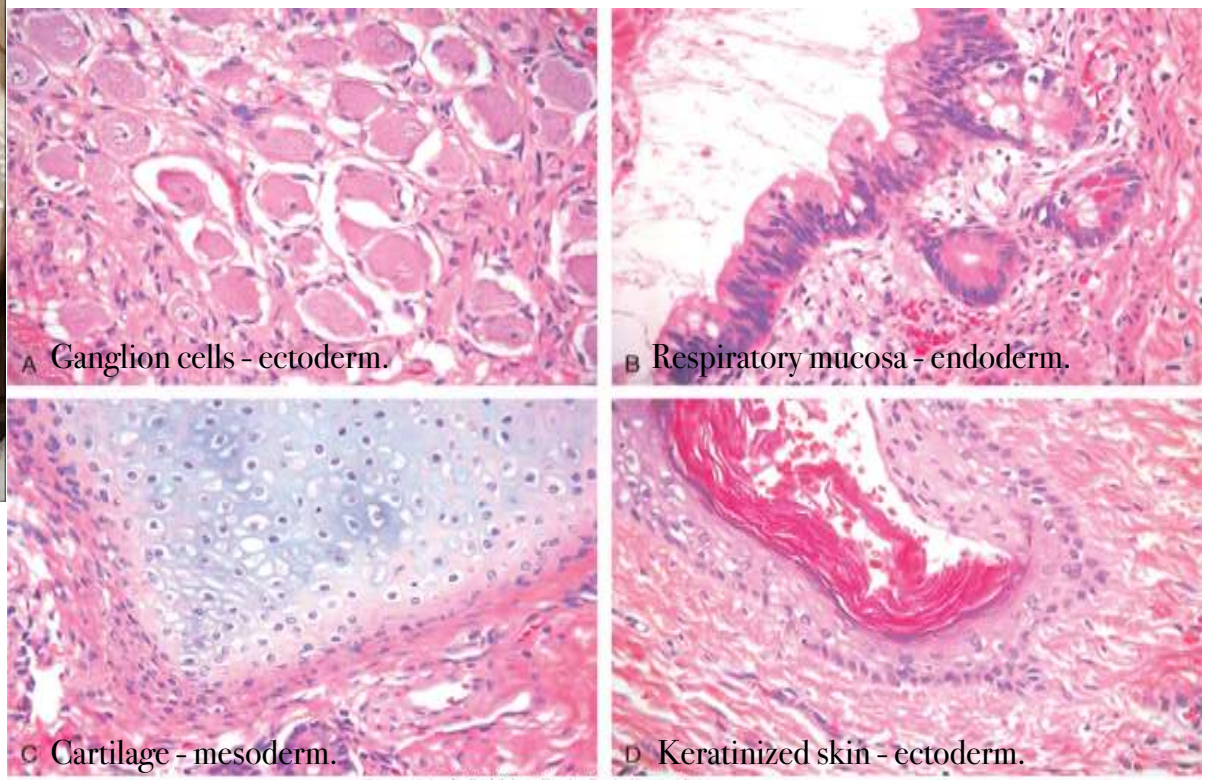
- torsion (10% to 15% of cases)

Some patients present with "acute abdomen," because of torsion, meaning the tumor itself isn't the one causing pain, but the tumor leads to ovarian torsion (twisting along the vascular axis), which leads to sudden obstruction of blood supply and thus ischemia and necrosis/infarction.

Benign (Mature) Cystic Teratoma



Under the microscope, any type of mature somatic tissue may be seen.



Clinical Correlations for All Ovarian Tumors

- Clinical presentation of all is similar: But may be subtle, give rise to non-specific symptoms

- Abd. pain, gastrointestinal complaints, urinary frequency; rarely torsion producing severe abdominal pain mimicking an "acute abdomen." + increased abdominal girth due to a large mass.

- Ascites (in Fibromas and malignant serous tumors).

- Functioning ovarian tumors : Estrogens or androgens. → And those may present to medical attention because of those, e.g. a patient with hirsutism, or a patient with endometrial hyperplasia due to the estrogen.

- Treatment: surgery + chemotherapy + radiotherapy → For malignant tumors, meanwhile benign ovarian tumors have excellent prognosis and are usually dealt with surgical excision.
- 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

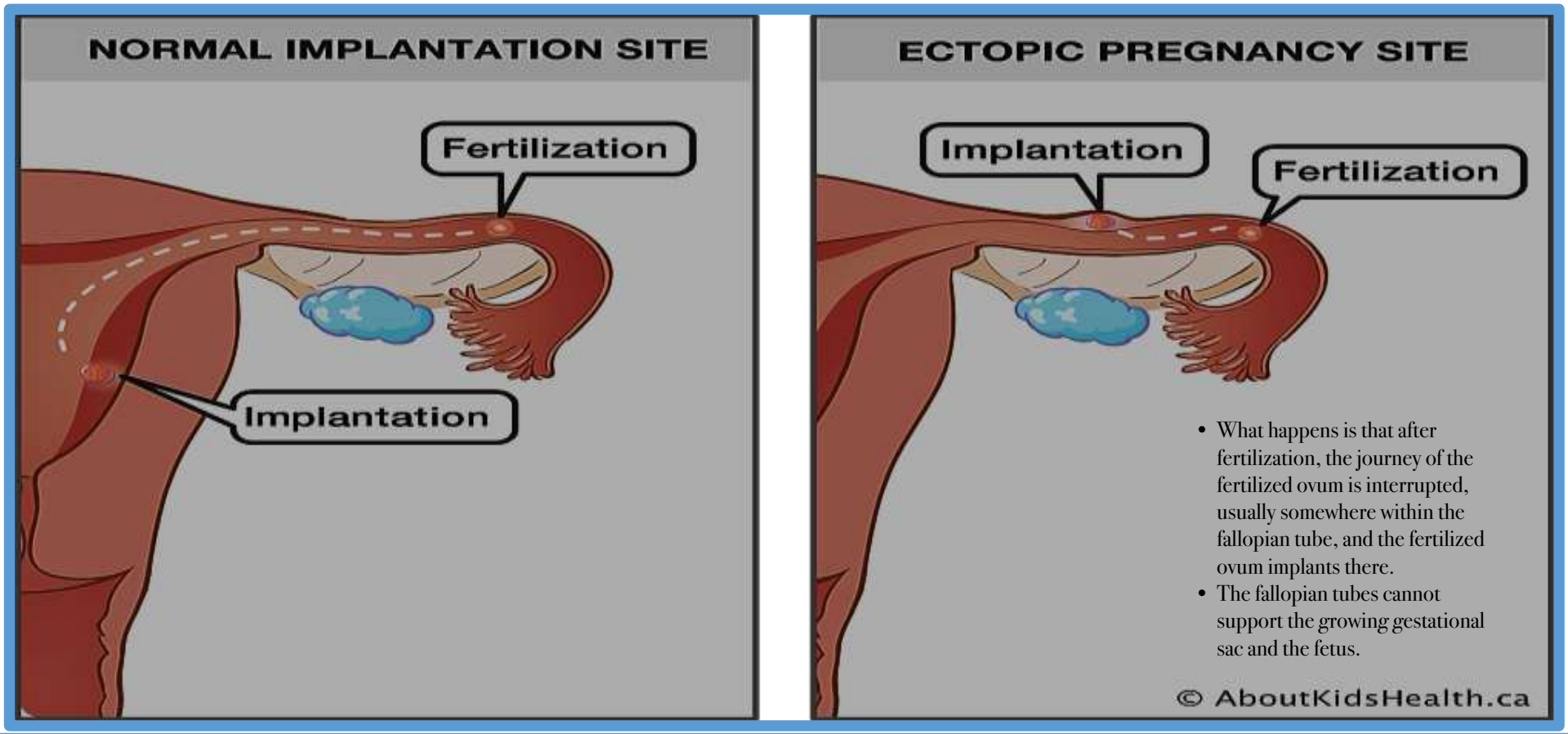
Pathology of the Fallopian tubes

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.

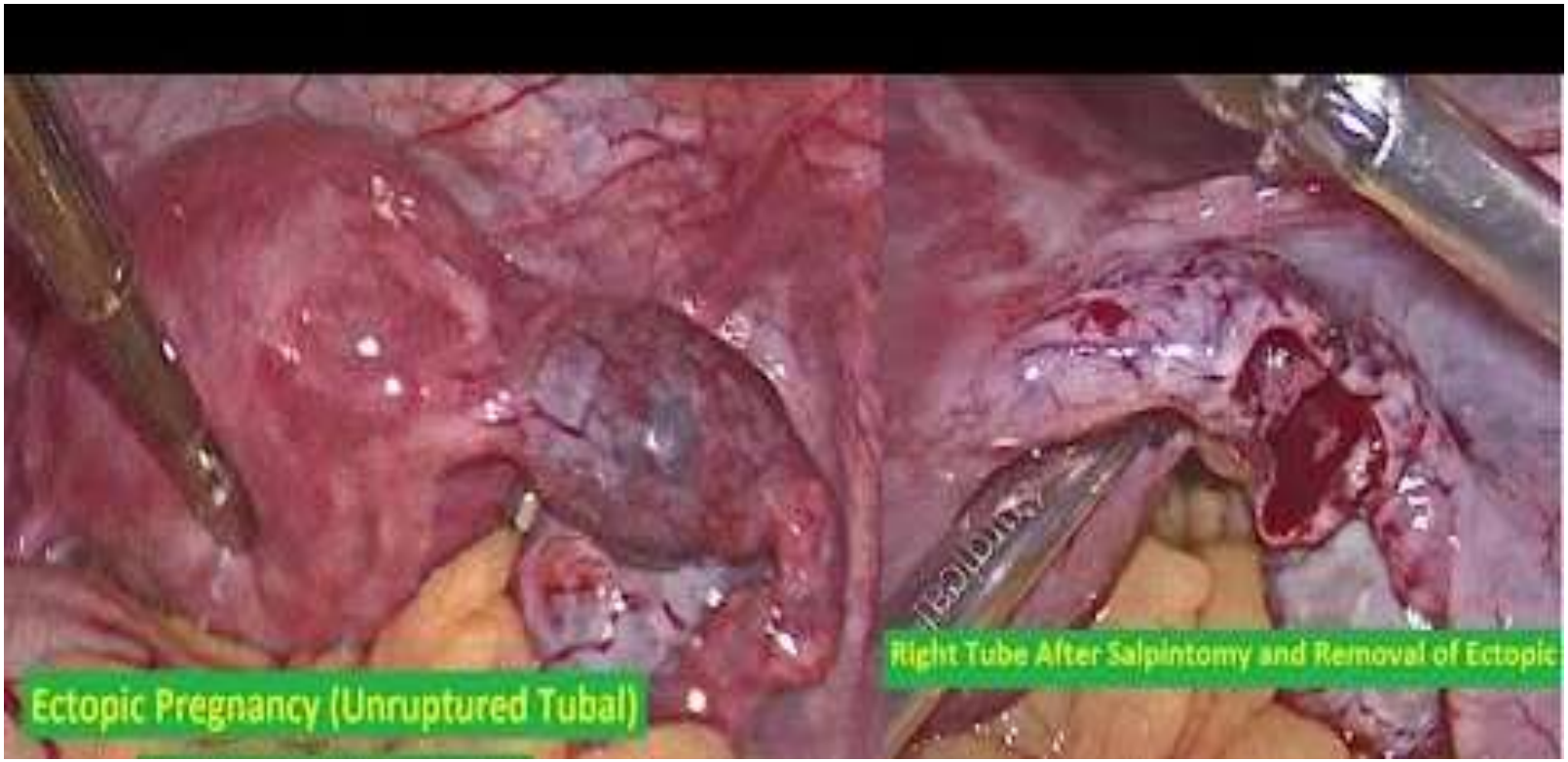
Half of patients have a mechanical predisposing factor, like tubal obstruction, PID, tumors inside or outside and compressing the fallopian tubes, endometriosis, IUCD.

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 ↓ Via
- **serous tubal intraepithelial carcinoma (STIC**) in fimbriated ends of fallopian tubes. It is CIS.
- STICs have mutations in TP53 in 90% of cases
- increased in women with ***BRCA* mutations** 1 and 2
- Because **of their access to peritoneal cavity**, fallopian tube carcinomas frequently spread to omentum and peritoneal cavity at time of presentation (advanced).

Can develop into invasive tumors in the fallopian tube, they can also send malignant tumors into the ovary, which are high grade malignant serous tumors.

- It's location is very critical, especially in the fimbriated ends, where they have access to the peritoneal cavity.
- These usually spread and metastasize early, thus advanced at time of presentation.