Pathology
GUS

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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

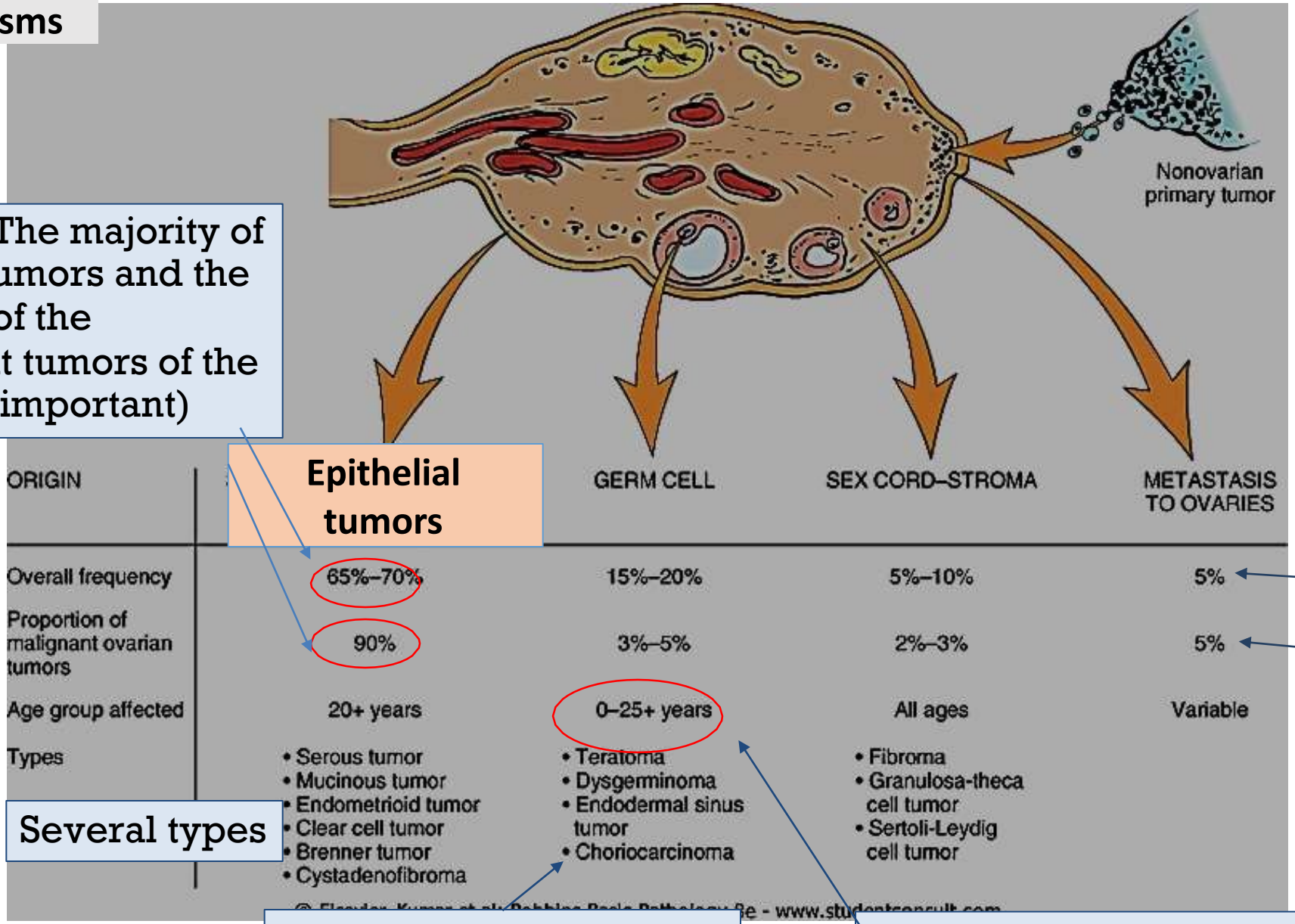
- Account for the majority of ovarian tumors
- in their malignant forms, account for 90% of ovarian cancers
- Previously were thought to arise from coelomic epithelium that covers the ovarian surface so they were called surface epithelial tumors
- Recent studies have shown that they actually arise from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

Account The majority of ovarian tumors and the majority of the malignant tumors of the ovaries (important)

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 pf them are benign)

Ovarian Neoplasms



Account The majority of ovarian tumors and the majority of the malignant tumors of the ovaries (important)

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	

All of them are malignant

Several types

We are familial with them from the male testicular neoplasms lec

In Young adults and children , ovarian tumors most frequently originate from the germ cells (important)

Ovarian neoplasms - Pathogenesis:

- Risk factors:
- **Nulliparity**

Null = zero Parity = birth
= Not having children
Not 100% as infertility

- **family history** (Only 10%)
- Note: OCPs + pregnancy may **reduce** risk.

Oral contraceptive pills = hormonal drugs contain estrogen and progesterone

So we can conclude that estrogen is implicated in the pathogenesis of the tumors while progesterone seems to be protective somehow from the ovarian neoplasms

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) Protoncogene

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

BRCA = tumor suppressor gene related to breast cancer but also seen in ovarian tumors especially serous ovarian tumors

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.

In some people it's benign and in other it's malignant or borderline and this differs according to some characteristics of the tumor and the spread of it

- **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

So that means that serous tumors are the most frequent epithelial tumors and the most frequent ovarian tumors & the most common malignant ovarian tumors (triple)

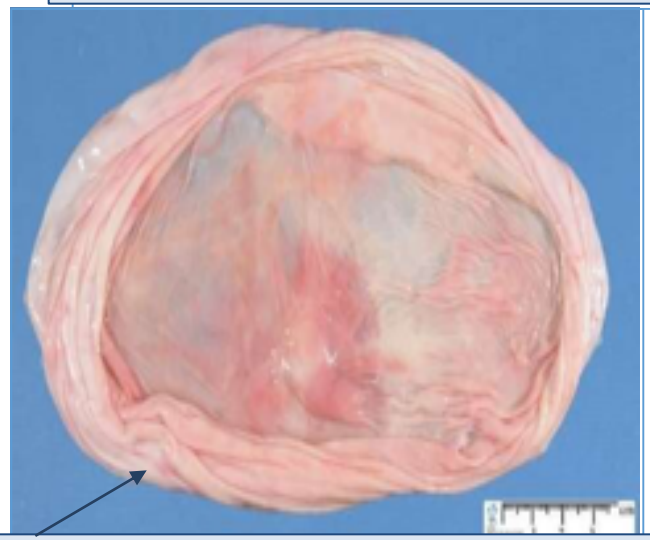
Benign serous tumors: Morphology

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

The tumor could be resected as it's benign

SEROUS CYSTADENOMA

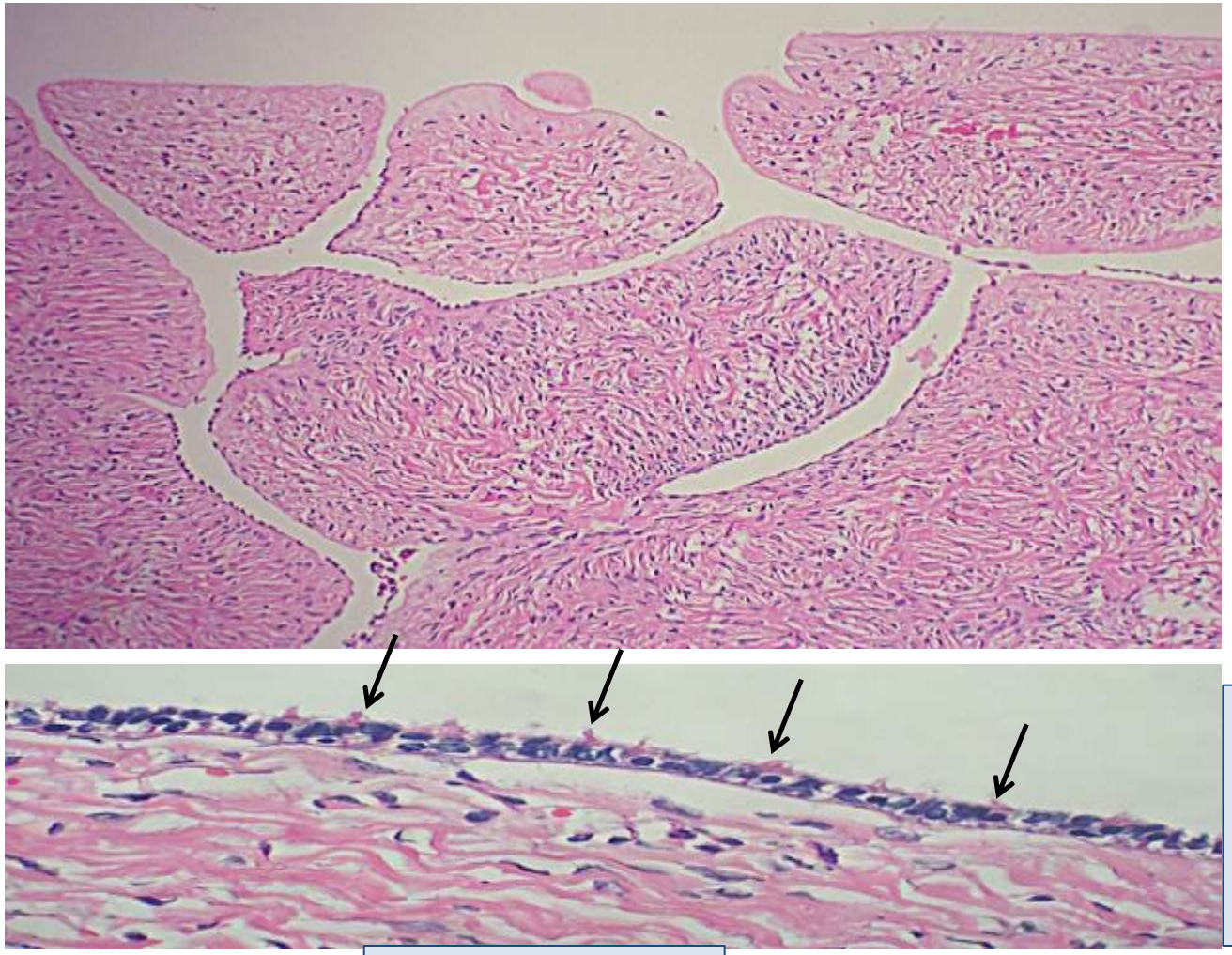
The outer surface of the cyst



The cyst is removed and opened, we are looking at the interior aspect of the cyst, the cyst wall from inside is smooth (no nodules) and described as being unilocular (one lumen) —>> benign serous tumor

A Female patient complains from abdominal pain , abnormalities in the menstrual cycle & increased abdominal girth, when examined, a large abdominal or pelvic mass found , an ultrasound is done for evaluation, they found a large mass in the ovary which looks like a cyst containing fluid so suspecting ovarian tumor

Benign serous tumors:



Single epithelial cell layer , and some of the cells are ciliated

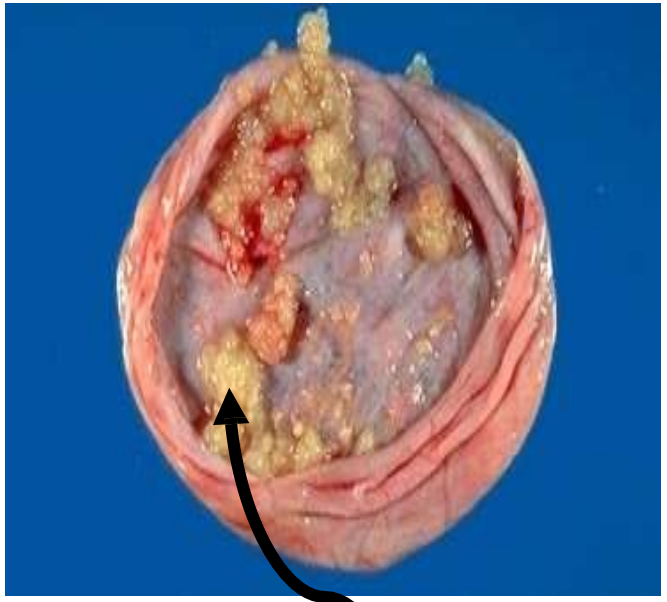
Arrows = cilia

Borderline Serous Tumors

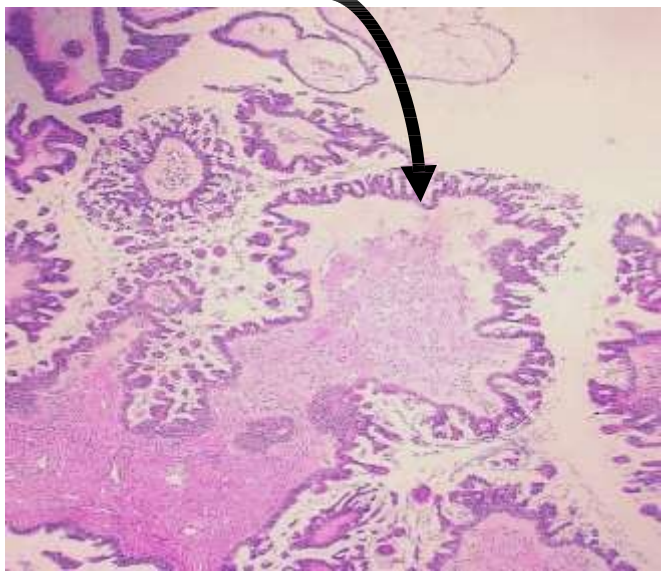
Borderline—>> Don't have enough characteristics to be considered as malignant and also can't be considered benign (the prognosis is different and there's risk of recurrence & progression)

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

We are looking inside the tumor, solid papillae are seen



Under microscope, small papillae covering the single layer , more complex architecture and cytologic atypia at higher magnification is seen



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

  Looks like serous tumors

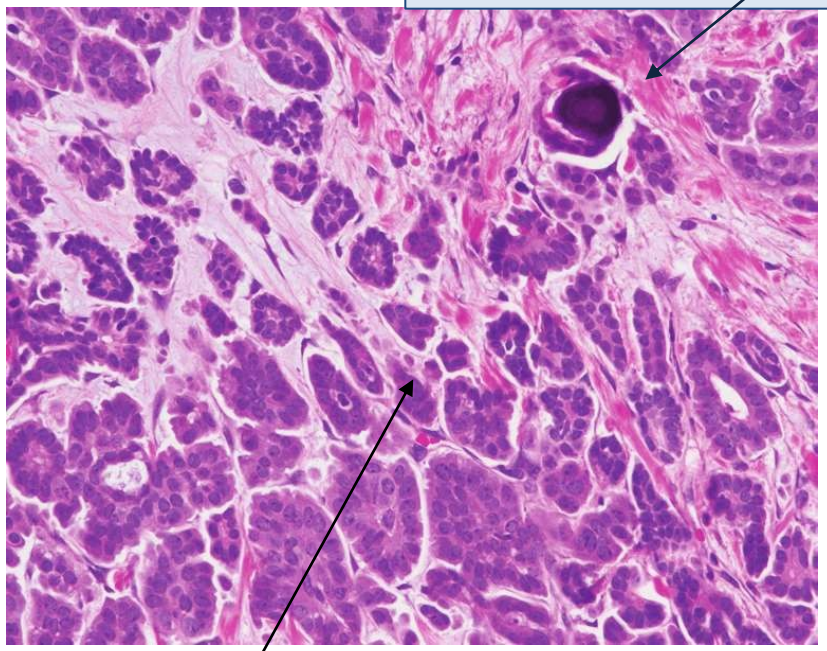
- mutations in KRAS

- **high-grade serous carcinoma:**

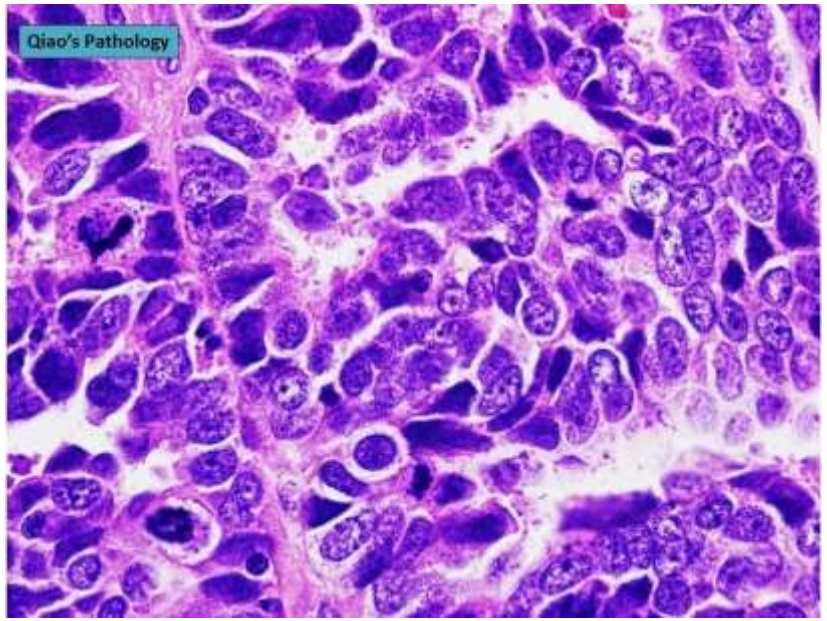
- develop rapidly
- many arise form fallopian tube via serous tubal intraepithelial carcinoma, rather than ovarian coelomic epithelium.
- mutations in TP53

- 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

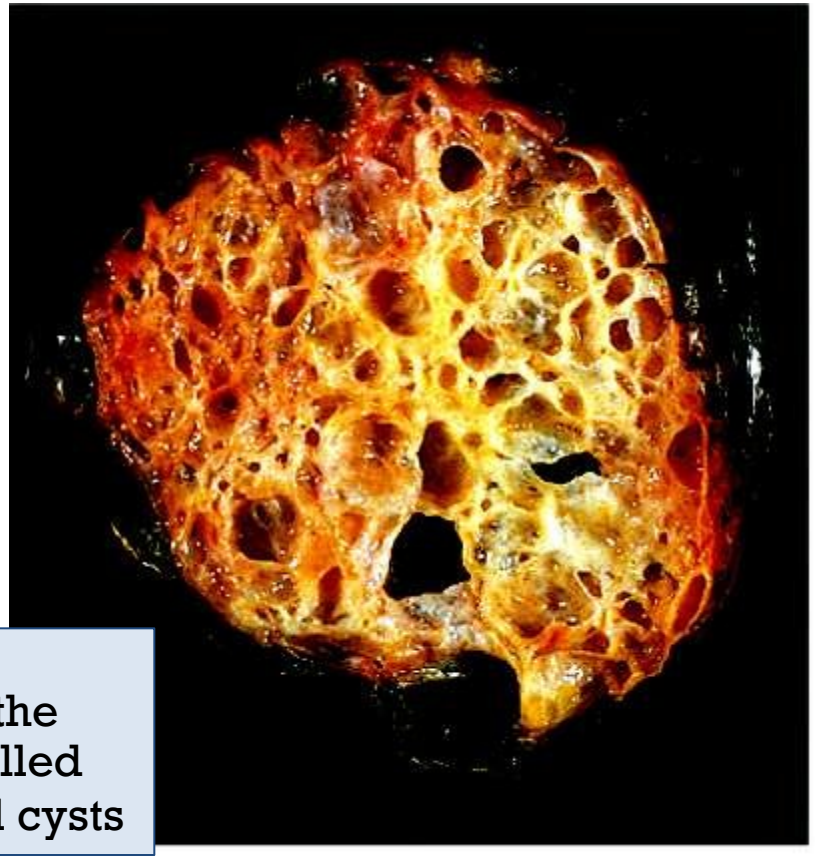


Cells are undifferentiated, high degree of anaplasia, large nuclei, a lot of mitotic figures

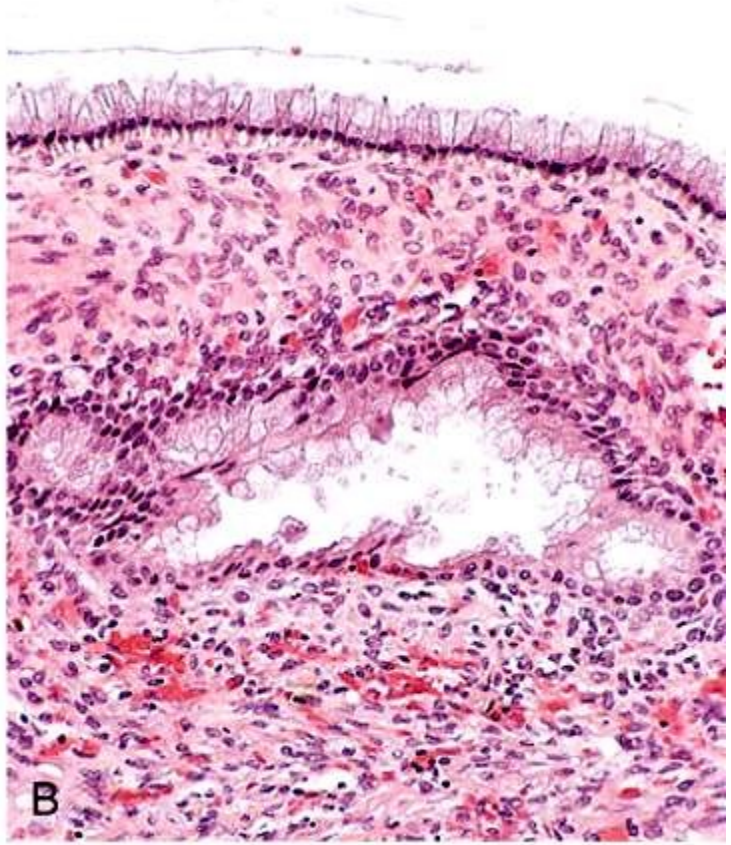
2- Mucinous ovarian tumors

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

Mucinous ovarian tumors



The inner aspect of the tumor is filled with small cysts



Germ Cell Tumors

- Types according to differentiation:
- dysgerminoma (differentiation to oogonia) (instead of seminoma)
- 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

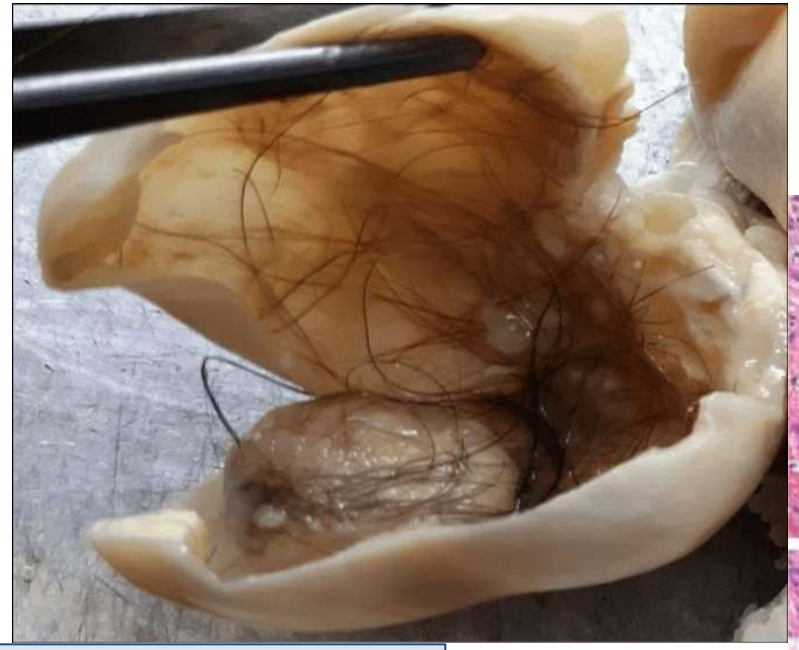
But they are among the most common germ cell tumors in the ovaries

- Many discovered incidentally

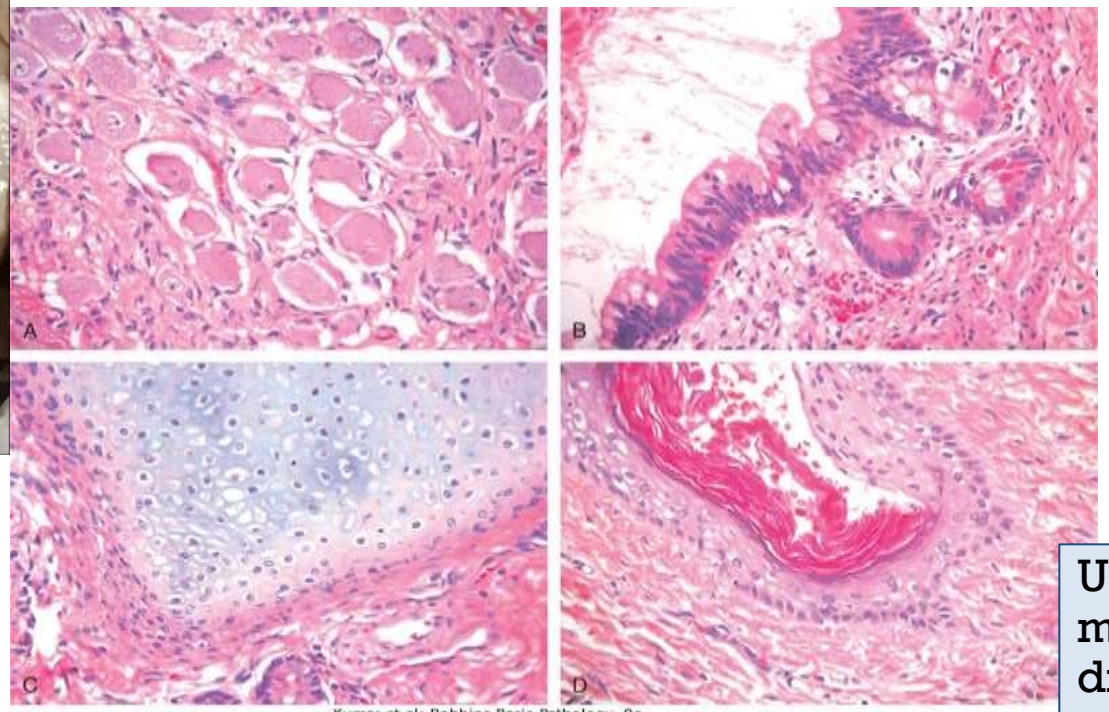
Or from non-specific symptoms like abdominal or pelvic pain , menstrual abnormalities or torsion

- 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



Teeth , cartilage, hair



Under microscope, different types of mature cells

Clinical Correlations for All Ovarian Tumors

- Clinical presentation of all is similar:

Non- specific symptoms —>> disadvantage

-Abd. pain, gastrointestinal complaints, urinary frequency; rarely torsion (of the pedicles or the hilar structures of the ovaries producing ischemia) producing severe abdominal pain mimicking an "acute abdomen."

Acute abdomen is a severe acute abdominal pain maybe results from a problem inside the pelvis or the abdomen that should be treated immediately, because if left untreated could lead to morbidity and mortality

- Ascites (accumulation of Excess fluid in the peritoneal cavity) (in Fibromas and malignant serous tumors).

- Functioning ovarian tumors (secreting) : Estrogens or androgens.

- Treatment: surgery (benign) + chemotherapy + radiotherapy (borderline and malignant)

Staging or debulking surgery : major surgery is done to remove the ovaries, uterus , Fallopian tubes, pelvic lymph nodes and pelvic fluid and peritoneal & omental samples +- chemotherapy depending on the case

- Outcome of ovarian **cancers** remains unsatisfactory (unlike testicular and cervical cancers)
- **Malignant** tumors are usually discovered in advanced stages
- survival minimally improved since 1970s.
- No early Screening methods are yet available

The prognosis is poor and the management is not very successful and still it's critical cause of cancer related death

Pathology of the Fallopian tubes

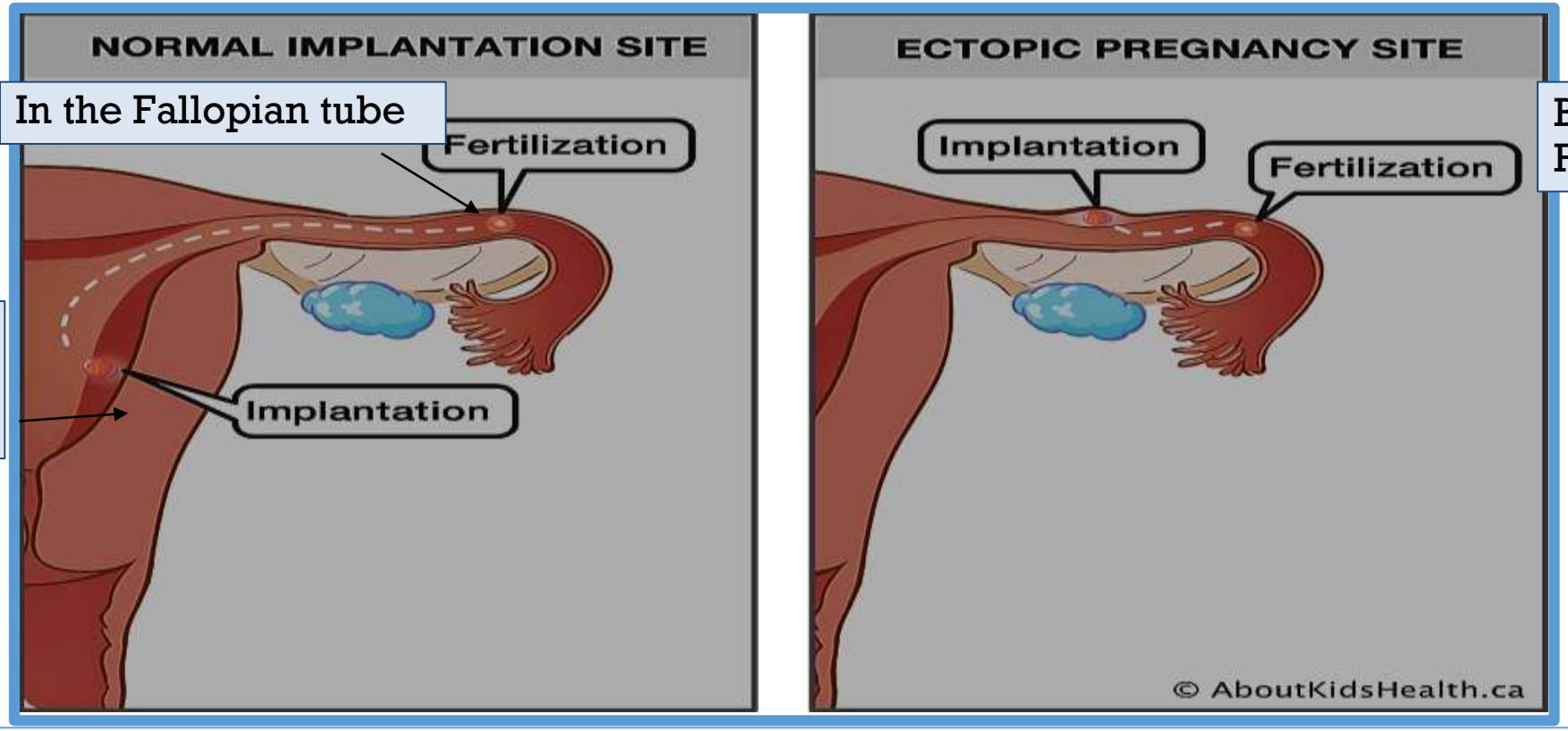
ECTOPIC PREGNANCY

- implantation of the fertilized ovum outside uterus
- Incidence: 1%
- 90% of cases ocurr in fallopian tubes
- other sites: ovaries, abdominal cavity
- Predisposing factors: tubal obstruction (50%) PID; tumors; endometriosis; **IUCD**..

Intrauterine contraceptive device

- In 50% : no anatomic cause can be demonstrated.

Normal versus ectopic pregnancy



In the Fallopian tube

In the endometrium of the uterus

Both inside the Fallopian tube

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.

Removal of the infected or the whole Fallopian tube

The Fallopian tube is not formatted to support the growth of the embryo

Ectopic pregnancy- Management

Treatment: salpingectomy

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). Aggressive