

Reproductive

Team *of* Pathology

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Ovarian cysts and ovarian tumors



4th Lecture

Introduction to ovarian cyst and tumors:

Ovarian mass Can be **either** :

- Physiological
- or Neoplastic: Benign or Malignant
- **The most important medical problems in ovaries are the neoplasms.**
- Death from ovarian cancers is more than that of cervix and uterus together.
- **Silent growth** of ovarian tumors is the rule ,which make them so dangerous.

-
- Non neoplastic cysts (**physiological**) are common but they are not serious problems
 - Primary inflammation of ovaries is rare

Salpingitis of fallopian tubes frequently causes
periovarian reaction (Salpingo-Oophoritis)

- Salpingitis is inflammation of fallopian tube.
- Oophoritis is an inflammation of the ovaries

NoN-neoplastic and functional Cysts of the ovary:(1)corpus luteum, 2)follicular 3)endometriotic)

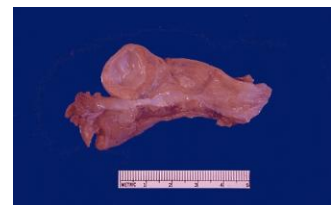
- Non Neoplastic Cyst are more common than the neoplastic .
- **Corpus Luteum and Follicular cysts**→**physiological cysts.**

Corpus luteum cyst:

- results from delayed resolution of a corpus luteum's central cavity and hemorrhage into this persistent mature corpus luteum.
- This condition is self-limited.

Follicular cysts: (most common type of ovarian cyst according to Wikipedia)

- Occasionally such cysts may reach several centimeters in size and, if they rupture, can cause abdominal pain.
- They arise from the ovarian follicles and are less than 5 cm
- Due to distension of **un-ruptured graafian follicle** (mature vesicular follicle).

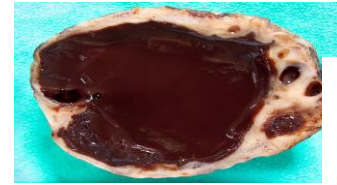


Morphology:

- Are thin walled fluid filled structures lined internally by granulosa cells and externally by theca internal cells.
- Occasionally such cysts may reach several centimeters in size and, if they rupture, can cause abdominal pain.

Chocolate/ Endometriotic cyst:

- Chocolate cyst is a **blood containing cyst resulting from endometriosis** with hemorrhage.



Endometriosis is a condition in which cells from the lining of the uterus (endometrium) appear and grow outside the uterine cavity,

Ovarian Neoplasms- Introduction:

- The fifth most common cancer in US women
- 80% are benign – young (20-45)
- 20% are Malignant - older (>40)
- 6% of all cancers in women.
- 50% deaths** due to **late detection**.

Risk Factor for ovarian neoplasm:

1. Null parity
2. Gonadal Dysgenesis
3. Family History
4. Ovarian cancer genes:

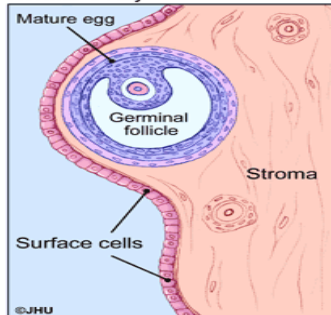
BRCA1 (17q12) & BRCA2(13q12)



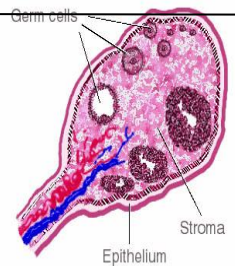
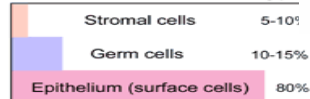
Breast carcinoma 1+2: are proteins cause a repair of the DNA damage.

(Cancer suppressor, Breast & ovary)

Normal Ovary



Origin of the ovarian cancer type



Because the three major cell types make up the normal ovary, there are > 25 types of ovarian tumors each with many variants

Ovarian Tumors classification:

There are **THREE** main types of primary ovarian tumors:

- 1) **Epithelial Surface Tumor:** are derived from the cells on the surface of the ovary. This is the most common form of ovarian cancer and occurs primarily in adults.
 - 2) **Germ Cell Tumor:** ovarian tumors are derived from the egg producing cells within the body of the ovary. This occurs primarily in children and teens and is rare by comparison to epithelial ovarian tumors.
 - 3) **Sex Cord Tumor:** ovarian tumors are also rare in comparison to epithelial tumors and this class of tumors often produces steroid hormones.
- 4) In addition cancers derived from other organs can also spread to the ovaries Secondary /Metastatic Tumors.

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	<ul style="list-style-type: none"> • Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma 	<ul style="list-style-type: none"> • Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma 	<ul style="list-style-type: none"> • Fibroma • Granulosa-theca cell tumor • Sertoli-Leydig cell tumor 	

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Surface Epithelial Tumors:

- **Most common primary neoplasms.**
- **90% of malignant tumors of ovary.(very imp)**

Types:

- Serous (Fallopian tube type; ciliated columnar cells)
- Mucinous (endocervical & intestinal mucin secreting type cells)

Both are divided into

Benign.
Malignant and
borderline.(will
come soon).

(To remember cervix and intestine secret mucin)

- Endometrioid
- Transitional cell - Brenners.

Morphology:

- Cystic – eg:Cystadenomas.
- Solid/cystic –eg: Cystadenofibromas.
- Solid – eg:adenofibromas.

All types can be benign, borderline , or malignant

Benign

- gross: mostly **cystic**
- microscopic: fine papillae, single layer covering (no stratification), no nuclear atypia, no stromal invasion.

Borderline

- gross: cystic / solid foci
- microscopic; papillary complexity, stratification, nuclear atypia, no stromal invasion.

Malignant

- gross: mostly solid & hemorrhage / necrosis.
- microscopic: papillary complexity, stratification, nuclear atypia, stromal invasion.

The difference between Malignant and Borderline is **Stromal Invasion**

Serous Tumors:

- **Frequently bilateral (30-66%).**
- 75% benign/borderline,25% malignant.
- One unilocular cysts, papillary/less solid → **benign/borderline**
- **Tall columnar ciliated epithelium(Like fallopian tube).**
- Papillary, solid, hemorrhage, necrosis or adhesions→ **malignancy**
- Extension to peritoneum – bad prognosis.

Morphology:

- **Serous cystadenoma:**

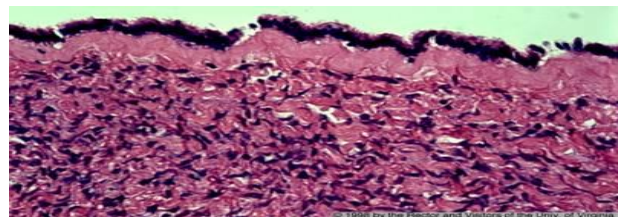


- **Bilateral cystadenoma:**



Histology of serous cystadenoma:

- Single layer of columnar ciliated.
- Fine papillae.

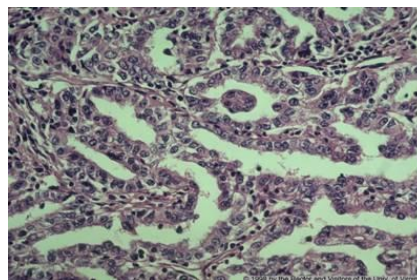


Malignant Serous Tumors:

- **Malignant serous tumors (serous cystadenocarcinoma) is the commonest malignant ovarian tumor, forming about a third of all cancers of the ovary.**
- The tumors are partly cystic and partly solid with exuberant excrescences, often with necrosis and hemorrhage.
- Ovarian surface involvement may be present.
- **These tumors usually present with ascites due to abdominal metastases.**

Morphology:

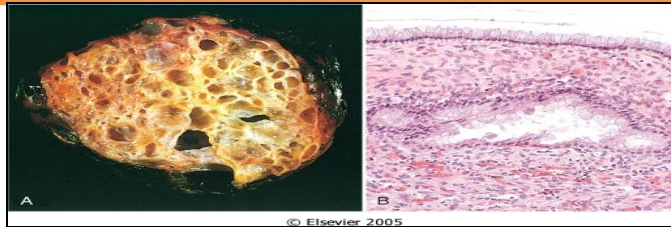
- Papillary complexity (serous cystadenoma is single layer of columnar)
- Nuclear stratification & atypia
- stromal invasion
- Psammoma bodies



Mucinous Tumors:

- Less common 25%, very large.
- Rarely malignant - 15%.
- Multiloculated, many small cysts.
- **Rarely bilateral – 5-20%.**
- Tall columnar, apical mucin.
- Pseudomyxoma peritonei.

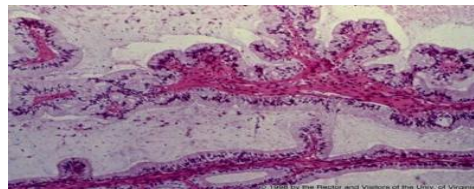
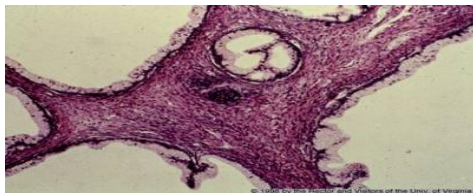
Pseudomyxoma peritonei is a condition caused by the production of abundant **mucin** by tumor cells, which fills the abdominal cavity.



Histology:

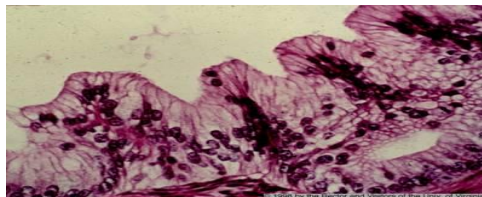
Mucinous cystadenoma:

- Multilocular cyst lined by **single layer** of columnar cells with basally placed nuclei and apical mucin.



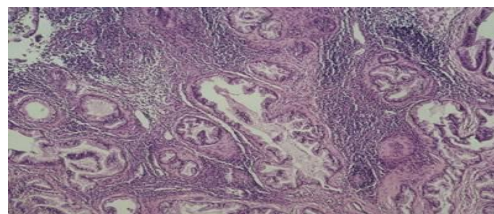
Mucinous cystadenoma-borderline (the behavior, gross appearance and morphology are in between malignant and benign) :

- Papillary complexity.
- Nuclear stratification& atypia.
- **No stromal invasion.**



Mucinous cystadenocarcinoma:

- Papillary complexity.
- Nuclear stratification& atypia.
- **Stromal invasion.**



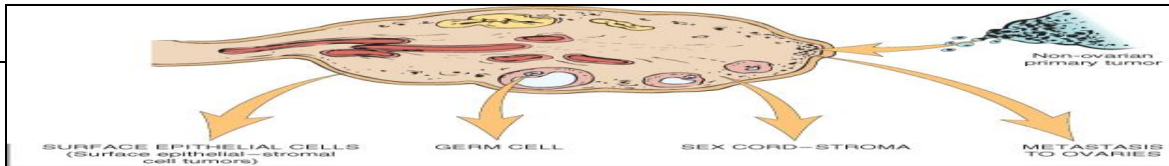
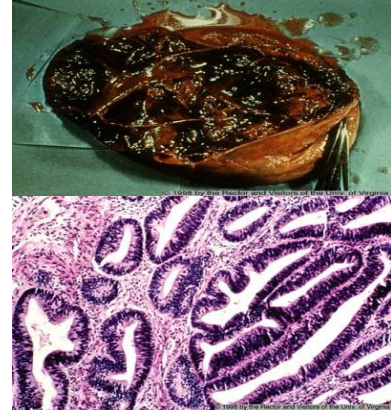
Endometrioid Tumors:

- Most are **unilateral** (40% are bilateral)
- Cells look like endometrium even though they are coming from the ovary.
- **Most of them are malignant**
- About 20% of all ovarian tumors
- **Many are associated with endometrial cancer (30%)**
- **Patient may have concurrent endometriosis.**


Morphology:


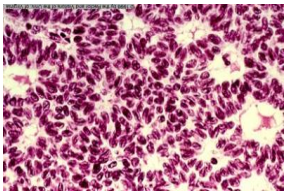
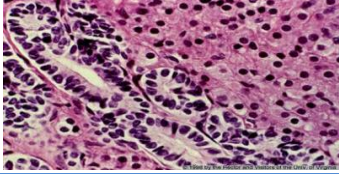
- **Gross:**
 - Solid / cyst filled by hemorrhage & necrosis.

- **Microscopic Appearance:**
 - Stromal invasion by irregular malignant endometrial glands.



Sex Cord-Stromal tumors

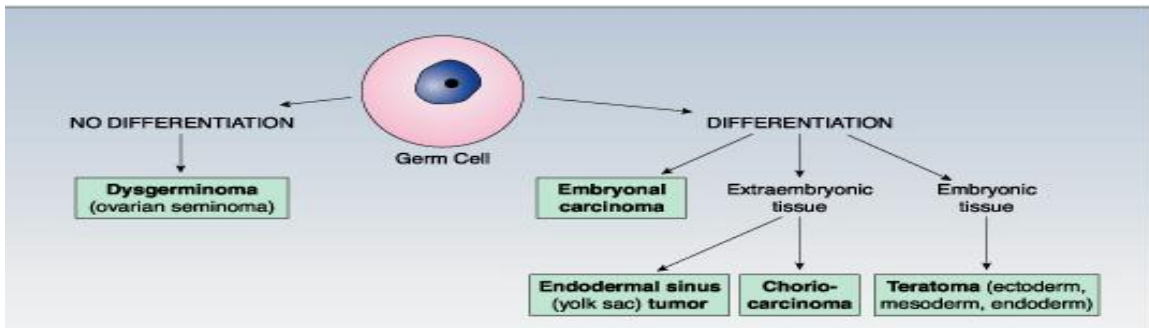
	<u>Granulosa cell tumors</u>	<u>Thecoma fibroma</u>	<u>Sertoli-leydig cell tumor</u>
<u>Features</u>	<ul style="list-style-type: none"> -Unilateral, solid and cystic -Hormonally active tumor -The most common estrogenic ovarian neoplasm. -can be associated with endometrial hyperplasia and carcinoma -The adult form occurs mainly in postmenopausal women, associated with endometrial hyperplasia and carcinoma -(The young form) The juvenile type(juvenile means young) occurs in the first two decades, cause precocious sexual development. 	<ul style="list-style-type: none"> -Functional tumors producing estrogen -It occur in postmenopausal women -Endometrial hyperplasia or carcinoma may develop 	<ul style="list-style-type: none"> -1% of ovarian neoplasms -It occur predominantly in young women. -Commonly androgenic, cause defeminization of women manifested as breast atrophy, amenorrhea, and loss of hair and hip fat , to virilization with hirsutism. -Benign with high malignant potential

<u>Gross</u>	Solid with hemorrhage 	Solid tumor with variegated yellow - orange appearance.	
<u>Microscopic</u>	Sheets of Granulosa cells, containing spaces, lined by the cells to give a follicle-like appearance (Call-Exner bodies). 	sheets of round to oval cells with pale cytoplasm containing lipid.	Tubules lined by Sertoli cells and sheet of Leydig cells 



Germ cell tumor (the same as germ cell tumors in the testis)

classification

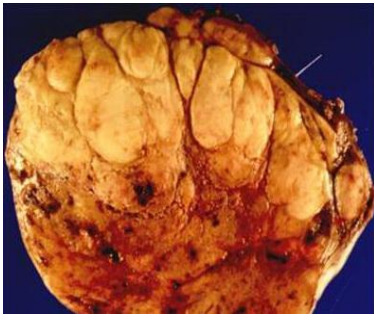


Dysgerminoma

- The ovarian counterpart of the testicular seminoma
- 2% of all ovarian malignancies
- Most common malignant germ cell tumor
- Affects primarily younger females with the majority in the second and third decades.
- **It is the most frequently encountered ovarian malignancy in pregnancy.**
- An excellent prognosis. Highly radiosensitive .
- Composed of malignant germ cells, admixed with nonneoplastic chronic inflammatory cells and fibrous septa and occasionally granulomatous inflammation.

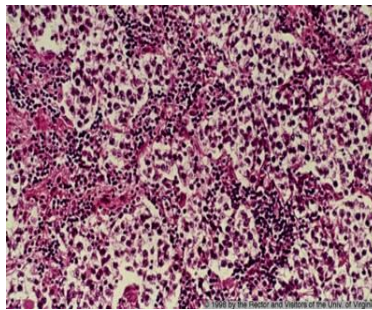
A tumor of the identical histology but not occurring in the ovary may be described by an alternate

Gross



•Solid/ lobulated mass with foci of hemorrhage

microscopic



•sheets of monotonous rounded cells with pale cytoplasm and central nuclei

GCT: Embryonal carcinoma

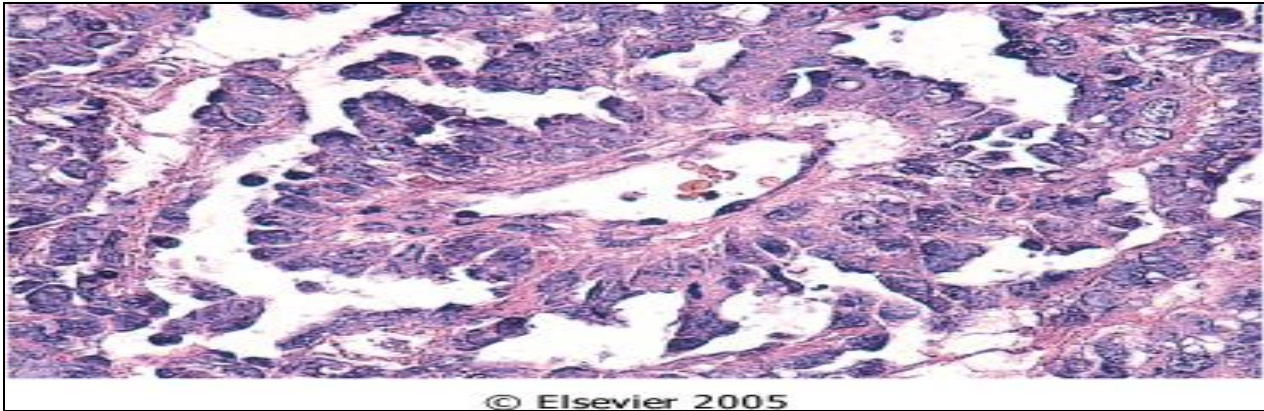
- uncommon ovarian germ cell neoplasm .
- **usually occurs in combination with yolk sac tumor .**
- occurs in children and young adults.
- Typically unilateral, solid tumor with hemorrhage and necrosis .
- Aggressive, highly malignant neoplasm that is radio-resistant but responds to combination chemotherapy.

GCT:Endodermal sinus tumor (Yolk sac carcinoma)

- Tumor is a highly malignant and clinically aggressive neoplasm
- Most frequently in children and young females
- Can be pure or a component of a mixed germ cell tumor
- Almost always a unilateral solid or solid cystic
- highly malignant neoplasm that is radio resistant but responds to combination chemotherapy
- Fatal within 2 years of diagnosis. **Associated with elevated serum AFP levels.**



Alpha feto protein= fetus- yolk sac=AFP



Its characteristic histologic feature is a glomerulus-like structure composed of a central blood vessel enveloped by germ cells within a space lined by germ cells (**Schiller-Duval body**)
 Classic pattern shows perivascular formations (Schiller-Duval bodies) and eosinophilic globules that contain AFP

GCT: Choriocarcinoma

- **Rare**
- Occurs as a pure ovarian neoplasm or as a component of a mixed germ cell tumor.
- occurs in children and young adults .
- associated with elevated serum HCG levels.
- typically a unilateral, solid, hemorrhagic tumor .
- composed of malignant cytotrophoblast and syncytiotrophoblast
- **generally have metastasized widely through the bloodstream to the lungs, liver, bone, and other viscera by the time of diagnosis.**

Choriocarcinoma:

Car is fast and it takes you places

so : it rapidly metastasizes!



GCT: Teratoma

- 15-20 % of Ovarian tumors.
- Majority in the first 2 decades.
- **The younger the patient ,the greater the likelihood of malignancy.**
- The tumors are subdivided into **mature, immature and monodermal (consist of one germ cell).**
- Unlike those in the testis, the vast majority of ovarian germ cell tumors are benign mature cystic teratomas.
- Immature teratomas are malignant and rare.

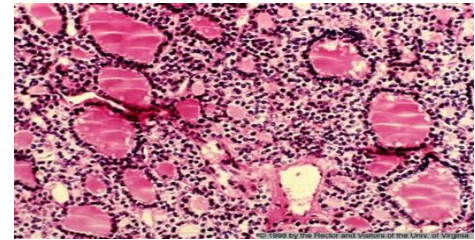
Most common germ cell tumor in ovaries

Mature cystic teratoma

- **most common ovarian teratoma and most common ovarian germ cell tumor**
- benign neoplasm that typically occurs during reproductive years
- cystic tumor with firm capsule, filled with sebaceous material and hair (occasionally teeth can be found), thickened area from which hair and teeth arise is called "Rokitansky's protuberance"
- composed of mature elements derived from all three germ layers (ectodermal elements such as skin, hair, sebaceous glands, and mature neural tissue predominate; cartilage, bone, respiratory and intestinal epithelium are common)
- complications include torsion, rupture, infection etc.

Monodermal teratoma :

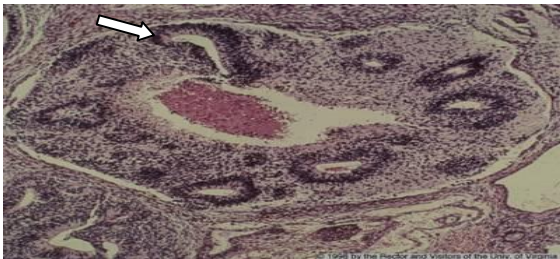
- a teratoma composed predominantly of **one tissue element**
- most common type is "**struma ovarii**", which is mature thyroid tissue(v.imp)



— Immature teratoma

- usually a unilateral, solid tumor
- similar to mature teratoma but contains immature or embryonal tissues, **mainly neuroepithelium.**

Microscopic: primitive **neuroepithelium** with multiple neural tubes



Krukenberg tumor(imp)

- **One of the most classic forms of metastatic carcinoma.** involving the ovaries is the Krukenberg tumor.
- This tumor is a metastatic carcinoma
- Composed of signet ring cells embedded within a hypercellular ovarian stroma that mimics sarcoma.
- **The most common sites of origin(GI) include stomach, colon and appendix.**

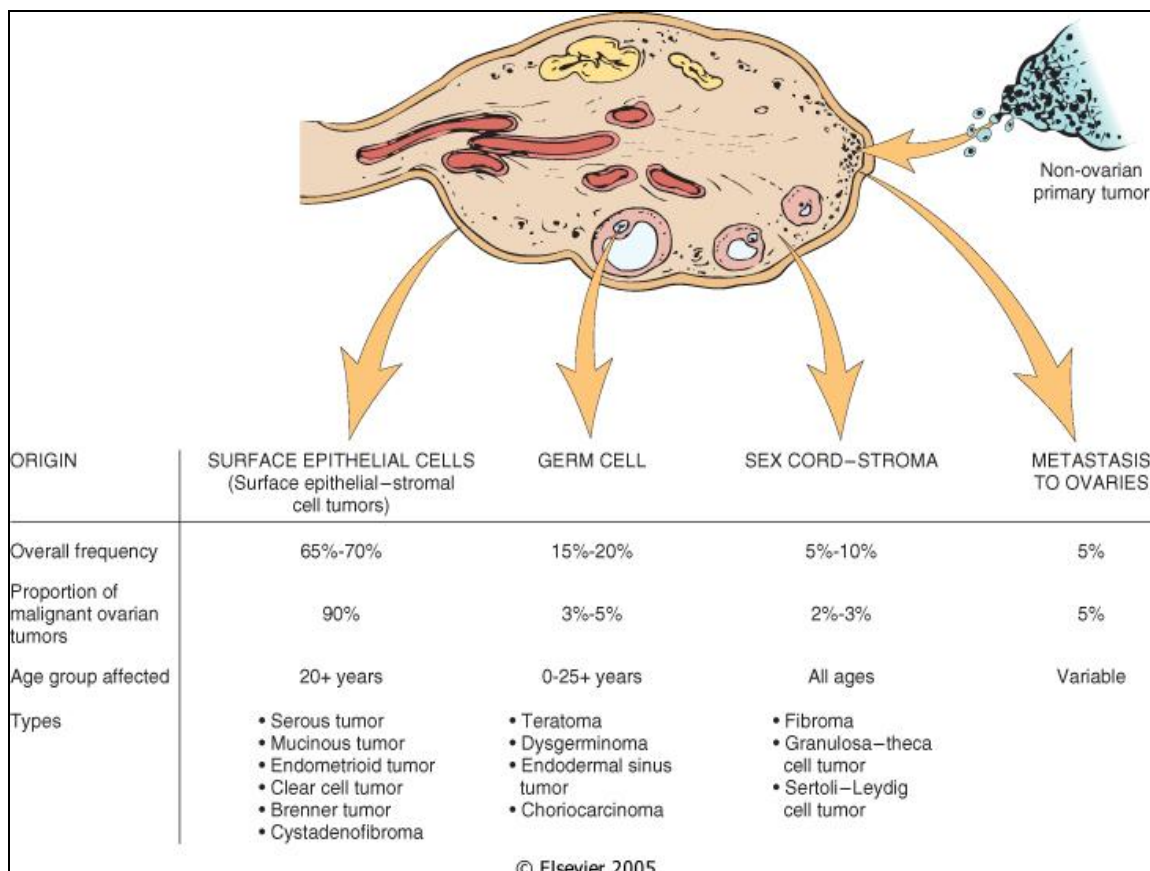


Krukenberg = = تفرقع =معدتي تفرقع من الجوع =
stomach



Summary:

Tumors may arise from any of the major components of the ovary: surface epithelium, ovarian stromal and follicle lining granulosa cells, or germ cells. **Epithelial tumors are the most common malignant ovarian tumors and are more common in women older than 40 years of age.** The major types of epithelial tumors are serous, endometrioid, and mucinous. Each has a benign, malignant, and a low malignant potential (borderline) counterpart. **Germ-cell tumors (mostly cystic teratomas) are the most common ovarian tumor in young women;** the majority are benign. Germ-cell tumors may differentiate toward oogonia (dysgerminoma), primitive embryonal tissue (embryonal), yolk sac (endodermal sinus tumor), placental tissue (choriocarcinoma), or multiple fetal tissues (teratoma). **Sex cord stromal tumors may display differentiation toward granulosa, Sertoli, Leydig, or ovarian stromal cell.** Depending on differentiation, they may produce estrogens or androgens.



Questions:

1-Which one of the following results from un-ruptured Graffian Follicle?

- A. Corpus luteum cyst
- B. Follicular cyst
- C. Chocolate cyst
- D. Serous cystadenoma

2-Patient came with bilateral masses the overall structure are solid with hemorrhage and necrosis,under microscopic examination we have seen stromal invasion by tall columnar ciliated cells.what is the diagnosis?

- A. Serous cystadenocarcinoma
- B. Serous cystadenoma
- C. Mucinous adenofibroma
- D. Dysgerminoma

3-Which one of the following tumors is common in pregnancies?

- A. Dysgerminoma
- B. Serous adenofibroma
- C. Sertoli-leydig cells tumor
- D. Embryonal carcinoma

Answers:

1-B

2-A

3-A