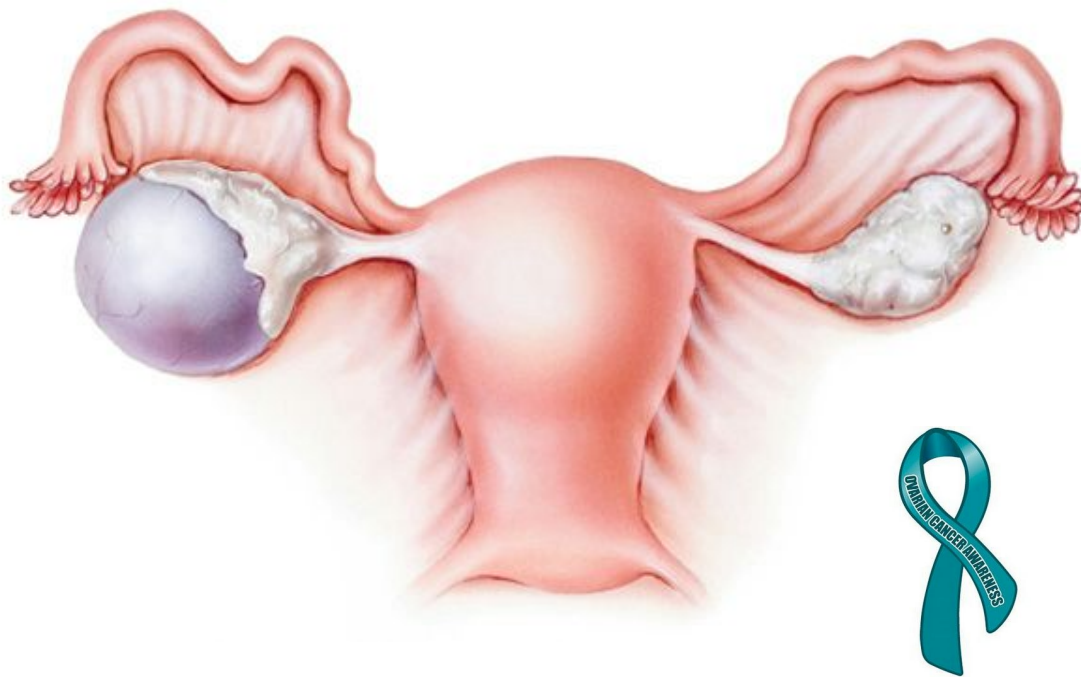


ovarian cysts & Tumors



Lecture outlines:

- ❖ The pathology of the major types of ovarian cysts (follicular and luteal).
- ❖ The classification and pathology of common ovarian tumors including surface epithelial, germ cell, stromal and metastatic neoplasms.

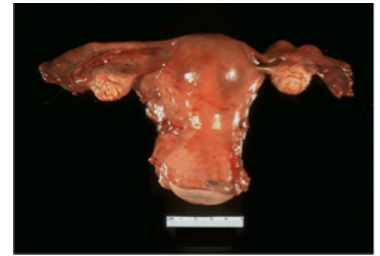
Important note: Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all or our work: [Pathology Edit.](#)

Grey = Extra
Red = Important

Introduction

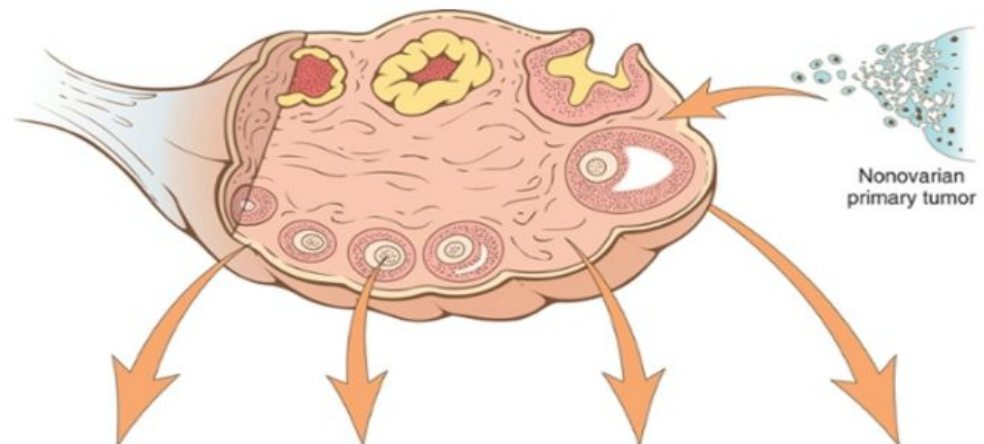
Ovarian Cysts and Tumors:

- **Non neoplastic cysts are common** but they are not serious problems.
- Inflammation of the ovaries is rare. It is usually associated with salpingitis of fallopian tubes¹ (salpingo-oophoritis).
- Frequently, the ovaries are affected by endometriosis².
- The most important medical problems in ovaries are the neoplasms.
- Death from ovarian cancers is more common than that of cervix and uterus together because ovarian tumors **grow silently** and are **usually diagnosed late**, which make them so dangerous. (because it's not palpable & there is no clear symptoms)



Ovarian Tumors:

- Leading cause of cancer death in women. (because → late diagnosis → metastasis)
- Ovarian cancers grow silently and go undetected in the early stage when it is still curable. Most of the patients already have metastasis at the time of diagnosis.
- The WHO Histological Classification for ovarian tumors divides ovarian neoplasms into primary and metastatic (secondary).



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 	

¹ In contrast, salpingitis only refers to infection and inflammation in the fallopian tubes.

² a condition resulting from the appearance of endometrial tissue in the ovaries.

Ovarian Tumors classification:

- **Primary** (classified into three main primary types of ovarian tumors based on the origin of the tumor cell):
 - **Surface epithelial ovarian tumors (65%).**
 - **Germ cell tumors (15%).**
 - **Sex cord stromal tumors (10%).**
- **Secondary/metastatic (5%):** Cancers from other organs can also spread to the ovaries.

1. Surface epithelial ovarian tumors (65%): derived from the cells on the surface of the ovary. This is the most common form of primary ovarian cancer and occurs in adults. Most common types are: **serous** or **mucinous** (both are usually cystic)

	Benign	Borderline tumors	Malignant
Serous tumors	cystadenoma	serous borderline tumor	serous adenocarcinoma
Mucinous tumors, endocervical-like and intestinal type	cystadenoma	mucinous borderline tumor	mucinous adenocarcinoma
Endometrioid tumors	cystadenoma	endometrioid borderline tumor	endometrioid adenocarcinoma
Clear cell tumors	Benign	Borderline	clear cell adenocarcinoma
Transitional cell tumors	Brenner tumor	Brenner tumor of borderline malignancy	1. Malignant Brenner tumor 2. Transitional cell carcinoma (non-Brenner type)
Others	-	-	-

2. Germ cell tumors (15%): Derived from the egg producing cells of the ovary, i.e. from the ovarian follicles. This occurs mainly in children, teens and young women. They are less common as compared to epithelial ovarian tumors.

A. Teratoma:

- Immature (malignant)
- Mature (benign)
- Solid
- Cystic (dermoid cyst)
- Monodermal (e.g., struma ovarii, carcinoid)

B. Dysgerminoma

C. Yolk sac tumor (endodermal sinus tumor)

D. Choriocarcinoma

E. Embryonal carcinoma

F. Mixed germ cell tumors³

³ mixture of germ cell tumors occurring together in one tumor mass.

3. Sex cord stromal tumors (10%): Derived from the ovarian stroma. Uncommon and this class of tumors often produces steroid hormones (especially estrogen).

Almost always Benign	With Malignant Potential
Fibromas/ Fibrosarcomas /Thecomas (have the same presentations)	<ul style="list-style-type: none"> ● Granulosa cell tumors ● Sertoli-Leydig cell tumors

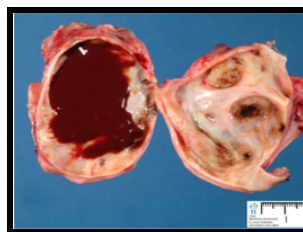
- These 3 main types are further divided into many subtypes (see later).

Non-Neoplastic Cysts of ovary

- More **common** than the neoplastic ones but usually cause no problems.
- Rarely can rupture and cause acute pain and intra-abdominal hemorrhage.

Common non-neoplastic cysts are as follows :

Follicular cyst	Arise from the ovarian follicles and are due to distension of unruptured Graafian follicle. Small and filled with clear serous fluid. Occasionally, they become significantly large to produce palpable masses and pelvic pain. When ruptured, producing intraperitoneal bleeding and peritoneal symptoms (acute abdomen).
Corpus luteum cyst	Results from hemorrhage into a persistent mature corpus luteum
Theca lutein cyst (hyperreactio luteinalis)	Are thin walled cysts lined by luteinized theca cells . They are associated with high levels of circulating gonadotropins (mainly estrogen, which is theca cell normal function) (e.g. pregnancy, hydatidiform mole ⁴ , etc).
Chocolate cyst (Endometriotic cyst)	Appearance of endometrial tissue inside the ovaries (endometriosis) → hemorrhage & bleeding inside the ovary → blood accumulates inside the ovary → formation of cyst filled with blood (chocolate cyst).



Chocolate cyst

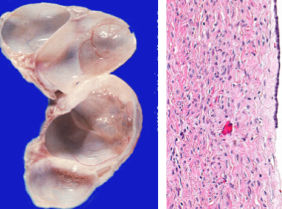
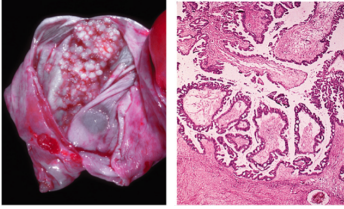
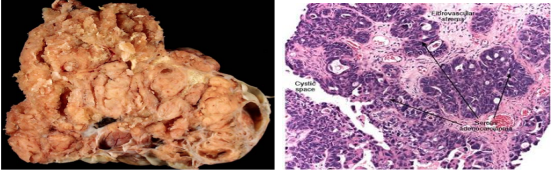
⁴ a growing mass of tissue inside uterus that will not develop into a baby.

Ovarian Tumors

Surface epithelial tumors.

❖ Serous Tumors

- most common type ovarian tumors.
- They are also the most common group of epithelial tumors. The tumor cells are of **serous nature**.
- Age is **30 -40**
- Usually cystic filled with clear serous fluid.
- Serous tumors are **often bilateral**.
- **Psammoma bodies** are commonly seen.
- Poor Prognosis.
- Mutation of BRCA1 increased the risk for development of serous tumors.

Benign ⁵ serous tumors (serous cystadenomas) (60%)	Borderline ⁶ serous tumors (15%)	Malignant ⁷ serous tumors (serous cystadenocarcinoma) (25%)
<p>Commonly large, single simple cystic and thin-walled, and unilocular. They are lined by serous cells and contain thin, clear yellow fluid. Most commonly seen in premenopausal women (30-40)</p>	<p>cystic with thin wall and smooth surface, but often have multiple papillary excrescences (grape-like clusters), protruding into the lumen in places. The feature between benign and malignant and has malignant potential</p>	<p>The tumors are partly complex cystic and partly solid with prominent excrescences, often with necrosis and hemorrhage . These tumors <u>usually present with ascites due to abdominal metastases</u> the commonest malignant ovarian tumor.</p> <ul style="list-style-type: none"> ● Treatment: surgery, chemotherapy and radiotherapy. ● Most commonly seen in postmenopausal women (60-70)
		

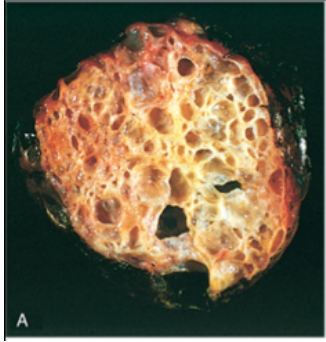
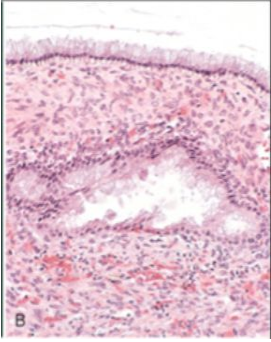
⁵ They do not spread and invade other tissues.

⁶ Tumors of low malignant potential: this is a gray zone. They are 'semi-malignant'. These appear to be low grade cancers with limited invasive potential. They have better prognosis than malignant. These tumors may seed or implant into the peritoneum.

⁷ are carcinomas and have potential to metastasize beyond the ovary.

❖ Mucinous Tumors

- Tumor cells are mucin-producing cells. (which are either endocervical type or intestinal type cells because both are formed of mucin-producing cells.)
- Form about 25% of all ovarian neoplasms.
- 80% are **benign**
- 10% are borderline
- 10% malignant. (Less likely to be malignant)
- **Bilaterality is uncommon.** (common in serous)
- Can be very large.

Grossly	Histologically
 <p>A</p>	 <p>B</p>
<p>They are typically cystic and multilocular (multiple cysts & nodules) and filled with thick sticky, viscous mucoid fluid.</p>	<p>The cyst is lined by columnar epithelium (mucin producing).</p>

❖ Endometrioid Tumors:

- They have tubular gland that resemble the endometrium so the name endometrioid (endometrial-like).
- Endometrioid tumors form 10 to 20% of all ovarian tumors.
- Most are **malignant** (carcinomas).
- Some endometrioid tumors are accompanied by an endometrial carcinoma in the uterus and/or endometriosis in the ovaries.

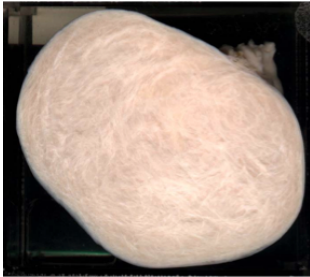
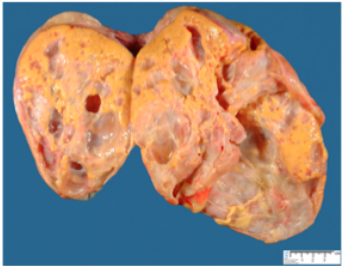
❖ Transitional Cell/ Brenner Tumor:

- Tumor cell are transitional cell type.
- Most are **benign**.

Sex Cord-Stromal tumors.

❖ Thecoma-Fibroma

- Any age.
- **Unilateral.**
- Almost always **benign**. Very rarely malignant.
- They are solid tumors, vary in color from white to yellow.
- About 40% cases are associated with **ascites** (fluid in abdomen) and **hydrothorax** (fluid in thorax) called as **Meig's Syndrome**.
- They can be either pure thecomas, pure fibromas or fibro-thecomomas (mixture of both).

Fibroma	Thecoma
 <ul style="list-style-type: none"> - Whiter, harder with whorled cut surface. - <u>Do not produce estrogen</u> (except when mixed with thecomas.) 	 <ul style="list-style-type: none"> - Yellower. - <u>Pure theca cell tumors produce estrogen.</u> (Patients present with signs of estrogen excess)

❖ Granulosa Cell Tumor:

- ❖ Unilateral, solid and cystic.
- ❖ Produce **estrogen** → Patients present with signs of estrogen excess such as **abnormal vaginal bleeding**.
- ❖ can be associated with endometrial hyperplasia and carcinoma.
- ❖ About 5 to 25% **show malignant behavior**. (usually metastasize)

Two forms:

- **Adult** form → is more common in postmenopausal women.
- **Juvenile** form → is seen the first three decades, can present with isosexual precocity

❖ Sertoli – Leydig cell tumor:

- Rare tumors of **low malignant potential**.
- All ages.
- Unilateral yellowish solid tumor.
- **Produces androgens** → **virilization** in 1/3 of cases (oligomenorrhea, amenorrhea, loss of female secondary sex characteristics with hirsutism, clitoromegaly, deepening of voice).

Germ Cell Tumors.

★ **NOTE: all ovarian GCTs are considered malignant except mature teratoma.**

★ 2nd most common tumors

Divided into:

<p>Dysgerminoma</p>	<ul style="list-style-type: none"> ● All malignant. ● Uncommon. ● Between 10 to 30yrs of age. ● Gross : Unilateral and solid mass. ● Microscopically: look exactly like its counterpart in testis (Seminoma) and brain (germinoma), large cells, clear cytoplasm and central nuclei. ● PLAP positive. ● Highly sensitive to radiation therapy. (good prognosis)
<p>Endodermal sinus tumor (yolk sac tumor)</p>	<ul style="list-style-type: none"> ● Can be pure or a component of a mixed germ cell tumor. ● Under 30 years of age. Most common tumors affects children. ● The tumor is associated with elevated serum α lpha-fetoprotein and α lpha-1-antitrypsin. ● Positive for immunostain for α lpha-fetoprotein. ● Histologic feature: Schiller-Duval bodies⁸ ● <u>Radioresistant</u> but responds to combination chemotherapy.
<p>Embryonal carcinoma</p>	<ul style="list-style-type: none"> ● Highly malignant, aggressive, early metastasis ● Rare (2nd and 3rd) decade (children and young adults). ● Similar to that in testis, usually occurs in combination with other GCTs (mixed GCT). ● Gross : Unilateral, solid tumor with hemorrhage and necrosis. ● CD30 immunostain positive. ● <u>Radioresistant</u> but responds to chemotherapy.
<p>Choriocarcinoma</p>	<ul style="list-style-type: none"> ● Highly malignant of placental like tissue, Rare aggressive, ● Metastasizes widely through bloodstream to the lungs, liver, bone etc. ● Similar to that in testis, usually occurs in combination with other GCTs (mixed GCT). ● Gross : Unilateral, solid, hemorrhagic tumor, composed of malignant cytotrophoblast and syncytiotrophoblast. ● Elevated serum hCG levels. ● HCG immunostain positive. ● <u>Radioresistant AND chemoresistant.</u>
<p>Teratoma</p>	<ul style="list-style-type: none"> ● Are 15-20% of ovarian tumors. ● Majority in the first 2 decades. ● The younger the patient, the greater the likelihood of malignant behavior. ● The tumors are subdivided into : <ol style="list-style-type: none"> 1. Mature cystic teratoma: benign and the most common. Divided into: <ul style="list-style-type: none"> - Cyst - Solid - Monodermal 2. Immature teratomas: Malignant and Rare.

⁸ Glomerulus like structures (looks like flowers under microscope)

Teratoma.

❖ Mature cystic teratoma (Benign)

Benign tumors composed mature elements such as ectoderm, endoderm and mesoderm. That's why the **Cystic tumor** filled with sebaceous material and hair and occasionally teeth. Cystic teratoma has no immature cells or somatic malignancy.

- ★ Occurs during reproductive years composed
- ★ Most common ovarian germ cell tumor and the most common type of ovarian teratoma.

Morphology:

- Skin, hair, Sebaceous glands
- Mature neural tissue
- Predominate; cartilage, bone, respiratory and intestinal epithelium are common.

Complications: Torsion⁹, Rupture, Infection.

❖ Immature teratoma (Malignant)

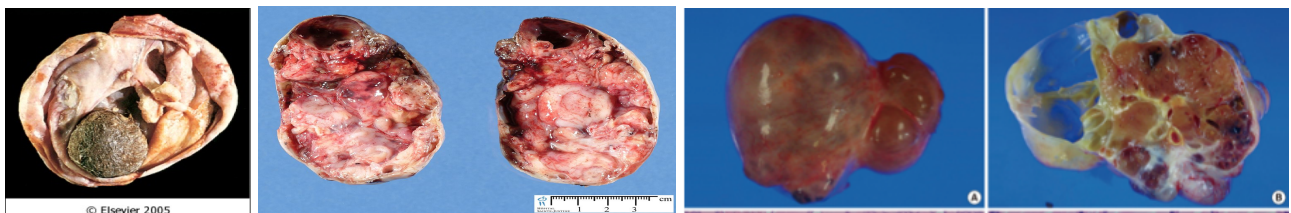
Malignant tumors similar to mature teratoma but in addition they **contain immature or embryonal tissues especially immature neuroepithelium.**

- Occurs in children and young adults.
- Usually a unilateral, solid tumor.
- They are graded based on the amount of immature tissue.

❖ Monodermal teratoma (Mono: One)

A teratoma composed predominantly of **one tissue element**

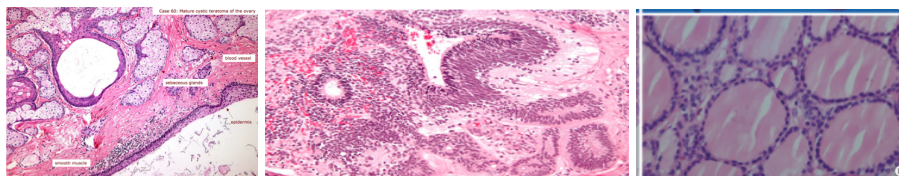
- Most common type is "**struma ovarii**", which is teratoma composed of thyroid tissue → Present with Hyperthyroidism .
- These thyroid tissue can sometimes become malignant such as carcinoid tumor(or Papillary thyroid carcinoma).



Mature

Immature

Monodermal



Mature

Immature

Monodermal

⁹ Twisting or rotation of a part on its long axis or on its mesentery; often associated with compromise of the blood supply.

Metastatic carcinoma in ovary.

- 5% of ovarian tumors.
- **Older ages.**
- Mostly Bilateral and sometimes very large.
- Primary tumor can be from Gastro-intestinal tract (most common), Breast and lung. Such as **Krukenberg tumor** and *pseudomyxoma peritonei*.

Krukenberg tumor:

- one of the most classic forms of metastatic carcinoma involving the ovaries
- This tumor is composed of **signet ring cells** in a fibrous background.
- The most common sites of origin is the **GIT** (stomach, colon and appendix).

Summary.

Ovarian Cysts.

Follicular cyst	Corpus luteum cyst	Theca lutein cyst/ hyperreactio (luteinalis)	Chocolate cyst /Endometriotic cyst
<ul style="list-style-type: none"> ● from the ovarian follicles. ● due to distension of unruptured Graafian follicle. 	Results from hemorrhage into a persistent mature corpus luteum.	<ul style="list-style-type: none"> ● Are thin walled cysts lined by luteinized theca cells ● ↑ circulating gonadotropins 	blood filled cyst. due to endometriosis in the ovary with hemorrhage.

Primary Ovarian Tumors:

1. Surface Epithelial Tumors	
Serous Tumors <ul style="list-style-type: none"> ● most common type ovarian tumors. ● Psammoma bodies are commonly seen. 	1. Benign Serous tumor: large, cystic and thin-walled, and unilocular. Lined by serous cells and contain thin, clear yellow fluid.
	2. Borderline serous tumors: multiple papillary excrescences.
	3. serous cystadenocarcinoma: partly cystic and partly solid with prominent excrescences, often with necrosis and hemorrhage usually present with ascites
Mucinous Tumors	Cystic and multilocular and filled with thick sticky, viscous mucoid fluid.
Endometrioid Tumors	<ul style="list-style-type: none"> ★ Mostly malignant. ★ Some are accompanied by an endometrial carcinoma in the uterus and/or endometriosis in the ovaries
TRANSITIONAL CELL/ BRENNER TUMOR	<ul style="list-style-type: none"> ★ Tumor cells are transitional cell type ★ Mostly benign

2. Sex Cord-Stroma Tumors	
Thecoma- Fibroma	<ul style="list-style-type: none"> ★ Unilateral, Solid tumors, Mostly Benign ★ Thecomas Produce Estrogen ★ 40% associated with ascites and hydrothorax called as Meig's Syndrome
Granulosa Cell Tumor	<ul style="list-style-type: none"> ★ Unilateral, solid and cystic, Produce estrogen ★ Adult form is common in postmenopausal women. juvenile form usually <30 , can present with isosexual precocity ★ abnormal vaginal bleeding ★ can be associated with endometrial hyperplasia and carcinoma
Sertoli – Leydig cell tumor	Rare. Produces androgens and present with virilization in 1/3 of cases

3. Germ Cell Tumors	
Teratoma	Mature: Benign, cystic tumor, filled with sebaceous material and hair and occasionally teeth. during reproductive years
	Immature: Malignant. occurs in children and young adults contain immature or embryonal tissues especially immature neuroepithelium
	Monodermal: most common type is "struma ovarii". Can be malignant.
Dysgerminoma	<ul style="list-style-type: none"> ★ Uncommon, Malignant. ★ PLAP positive ★ Highly sensitive to radiation therapy
Yolk Sac Tumor	<ul style="list-style-type: none"> ★ ↑ serum AFP and ↑ A1AT ★ Schiller-Duval bodies
Choriocarcinoma	<ul style="list-style-type: none"> ★ unilateral, solid, hemorrhagic tumor ★ composed of malignant cytotrophoblast and syncytiotrophoblast ★ metastasizes widely via bloodstream ★ Radioresistant, chemoresistant ★ ↑ serum hCG. HCG immunostain positive
Embryonal Carcinoma	<ul style="list-style-type: none"> ★ Rare, highly malignant, radioresistant but responds to chemotherapy. ★ Unilateral, solid tumor with hemorrhage and necrosis ★ CD30 immunostain positive.

MCQ's.

Q1:A 40-year-old woman presents with 6 months of increasing abdominal girth. Gynecologic examination reveals large bilateral ovarian masses. The patient undergoes bilateral oophorectomy. The pathology report reads “Krukenberg tumor”. Which of the following tests would likely provide the highest diagnostic yield?

- (A) Serum AFP level
- (B) Biopsy of the cervix and endometrial curettage
- (C) Laparoscopy
- (D) Serum hCG level
- (E) Gastric endoscopy

Q2:A 43-year-old woman presents with a 6-month history of increasing abdominal girth. On physical examination, there is pronounced ascites. Pelvic examination reveals a left adnexal mass.A 6-cm ovarian tumor is removed. The tumor is solid and white. Histologically, it is composed of cells resembling normal ovarian stroma surrounded by collagen fibers. Which of the following is the appropriate diagnosis?

- (A) Fibroma
- (B) Granulosa cell tumor
- (C) Leiomyosarcoma
- (D) Papillary cystadenoma
- (E) Sertoli-Leydig cell tumor

Q3:A 25-year-old woman presents with a 6-month history of increasing facial hair, deepened voice, and amenorrhea. Physical examination confirms virilization. A CT scan reveals a left ovarian mass. The tumor is surgically removed. It measures 10 cm in diameter and has a yellowish-tan appearance on cross section. The tumor is malignant and consists of two distinct cell populations. Some cells form solid nests, whereas others are arranged in trabecular and gland-like structures. Which of the following is the appropriate diagnosis?

- (A) Brenner tumor
- (B) Dysgerminoma
- (C) Granulosa cell tumor
- (D) Mature cystic teratoma
- (E) Sertoli-Leydig cell tumor

Q4:A 4-year-old girl is noted to have breast enlargement and vaginal bleeding. On physical examination, she is noted to have a 9-cm pelvic mass. Which of the following is the most likely etiology?

- (A) Cystic teratoma
- (B) Dysgerminoma
- (C) Endodermal sinus tumor
- (D) Granulosa cell tumor
- (E) Mucinous tumor

Q5: A 55-year-old woman presents with fatigue and malaise that have been worsening over the last 2 months. She has also noticed loss of appetite and early satiety. Evaluation finds an ulcerative mass located along the lesser curvature of the stomach along with bilateral ovarian masses. Which of the following is this patient most likely to have?

- (A) Barrett mucosa
- (B) Gastric leiomyosarcoma
- (C) Krukenberg tumor
- (D) Meigs syndrome
- (E) Ovarian dysgerminoma

Q6: A 54-year-old female has had weight loss accompanied by abdominal enlargement for the past 6 months. She is concerned because there is a family history of ovarian carcinoma. An abdominal ultrasound reveals a 10-cm cystic mass involving the left adnexal region, with scattered 1-cm peritoneal nodules. peritoneal fluid cytology reveals the presence of malignant cells, consistent with a cystadenocarcinoma. Which of the following mutated genes is most likely a factor in the development of this neoplasm?

- (A) Ras
- (B) C-erb-B2 (HER2)
- (C) BRCA1
- (D) myc
- (E) rb1

Ans: 1-E 2-A 3-E 4-D 5-C 6-C

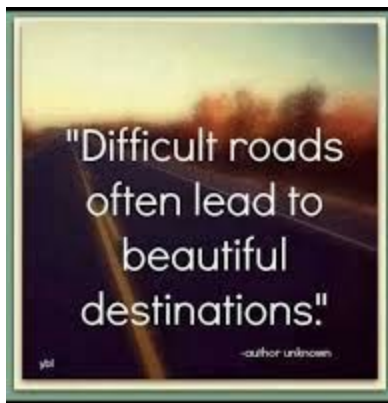
For any suggestions or questions please don't hesitate to contact us on:

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GOOD LUCK !!



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ريم لبني
نورة الهاللي
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