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# Benign and Malignant ovarian mass

## Objectives:

- Compare Describe the initial management of a patient with an adnexal mass
- the characteristic of functional cyst, benign ovarian neoplasm and ovarian cancer
- List the risk factors and protective factors for ovarian cancer
- Describe the symptoms and physical findings associated with ovarian cancer
- Describe the three histological categories of ovarian neoplasms

**References*:* team 433, APGO video and kaplan lecture note 2018, Hacker and moore (p440-448)**

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# Adnexal mass

**Adnexal mass:** in gynecology it is anything next to the uterus usually involving the **fallopian tubes and ovaries.** The term adnexal mass is often used interchangeably with the term pelvic mass.

Any pelvic mass could be :

| Gynecologic | Non-gynecologic |
|---|---|
| Ovarian cyst | Appendicitis |
| Malignant neoplasms | Diverticular abscess |
| Benign neoplasms | Gastrointestinal carcinoma |
| Ectopic pregnancy | Peritoneal cyst |
| Leiomyoma | |
| Tubo-ovarian abscess | |

### when the patient presents with adnexal mass:

1- detailed history and do pregnancy test to exclude ectopic pregnancy.

2- You must do a thorough pelvic exam:

- For Premenarche girls the ovaries should not be palpable.
- For Reproductive age women normally the ovary is palpable about half of the time .
- For Postmenopausal women the ovaries usually not palpable.

3- Pelvic ultrasound is the primary component of evaluation of an adnexal mass.

# Classification of ovarian mass

Ovarian cancer is the 5th most common cause of cancer death in USA. it has the highest mortality rate among gynecological malignancies, 55% of patients will die 5 years after diagnosis. 25% of ovarian tumors in postmenopausal women are malignant, 10% of ovarian tumors in reproductive age women are malignant.

## Classification:

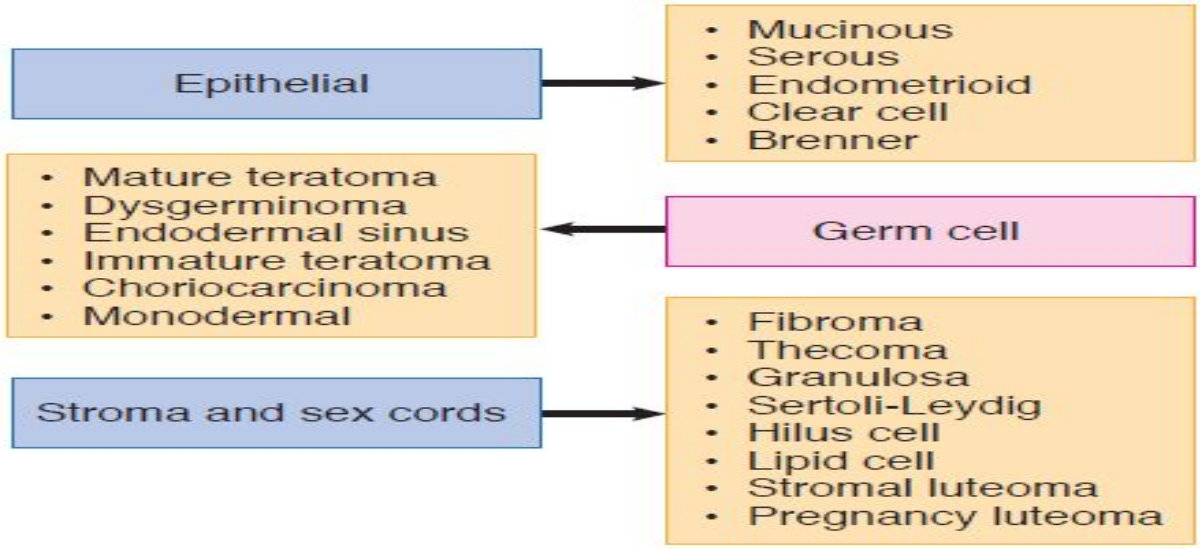
**1- functional cyst:**

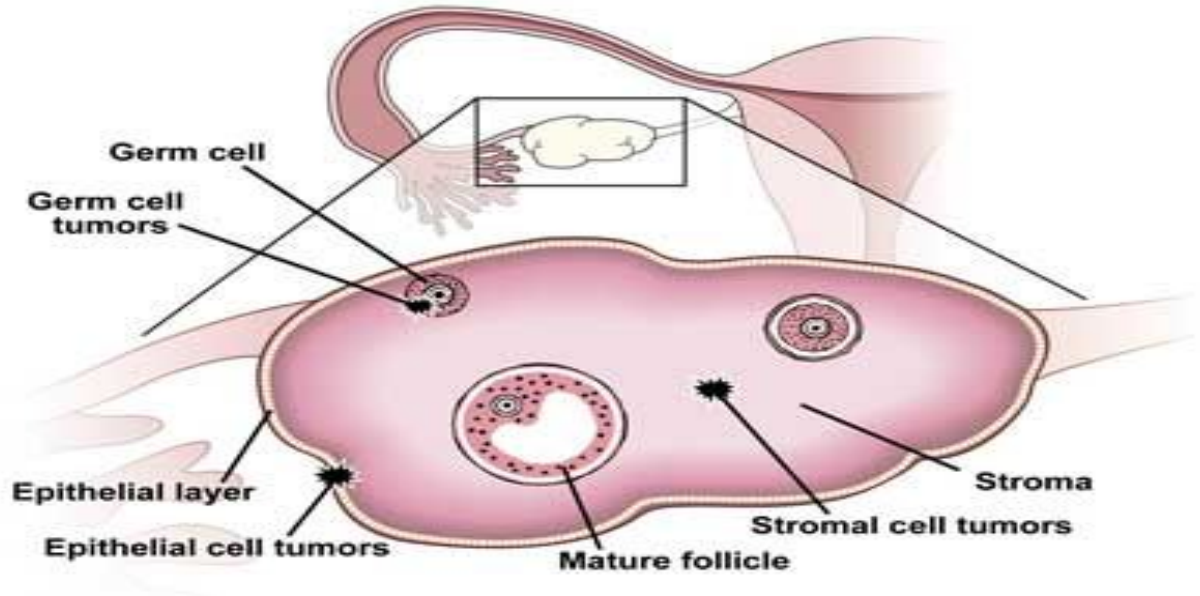
are physiologic and formed from normal ovulatory function. Composed of Follicular cell and Corpus Luteum cells and with time will **spontaneously resolve .** During the reproductive years the ovaries are functionally active, producing a dominant follicle in the first half of the cycle and a corpus luteum after ovulation in the second half of the menstrual cycle. Either of these structures, the **follicle or corpus luteum**, can become **fluid-filled and enlarged**, **producing a functional cyst.**

Only if symptomatic it requires surgical intervention: **if the size[1] becomes large**, **if there is torsion**, or if there is **uncontrolled bleeding into the cyst (hemorrhagic cyst)**. **Functional cysts should not form if the patient has been on oral contraception for at least 2 months because gonadotropins should have been suppressed.**

**2- Benign and malignant ovarian neoplasms:**

- The 3 histological cell types that give arise of benign and malignant ovarian neoplasm:




[1] Physiologic cysts do not usually get larger than 7 cm in diameter.

| HISTOGENETIC CLASSIFICATION OF PRIMARY OVARIAN NEOPLASMS | |
|---|---|
| **Derivation** | **Type of Tumor** |
| Epithelial origin (80-85%) | "Common" epithelial tumors: benign, borderline, malignant<br>Serous tumor<br>Mucinous tumor<br>Endometrioid tumor<br>Clear cell (mesonephroid) tumor<br>Brenner tumor<br>Undifferentiated carcinoma<br>Carcinosarcoma or malignant mixed mesodermal tumors |
| Germ cell origin (10-15%) | Teratoma<br>Mature teratoma<br>Solid adult teratoma<br>Dermoid cyst<br>Struma ovarii<br>Malignant neoplasms secondarily arising from teratomatous tissues (squamous carcinoma, carcinoid tumor, sarcoma)<br>Immature teratoma<br>Dysgerminoma<br>Endodermal sinus tumor<br>Embryonal carcinoma<br>Choriocarcinoma<br>Gonadoblastoma*<br>Mixed germ cell tumors |
| Specialized gonadal-stromal origin (3-5%) | Granulosa-theca cell tumors<br>Granulosa cell tumor<br>Thecoma<br>Sertoli-Leydig tumors<br>Arrhenoblastoma<br>Sertoli cell tumor<br>Gynandroblastoma<br>Lipid cell tumors |
| Nonspecific mesenchymal origin (<1%) | Fibroma, hemangioma, leiomyoma, lipoma<br>Lymphoma<br>Sarcoma |

Data from Hart WR, Morrow CP: The ovaries. In Romney SL, Gray MJ, Little AB, et al, editors: *Gynecology and obstetrics: the health care of women,* ed 2, New York, 1981, McGraw-Hill.
*Combined germ cell and specialized gonadal-stromal elements.

- **Benign ovarian neoplasms:**

25% of adnexal masses in the reproductive age women are benign.

**Types:**

A) **Epithelial cell type:** the largest class of benign ovarian tumours.
   - Serous
   - Mucinous
   - Endometrioid

B) **Germ cell type:** are derived from the primary germ cell and that may contain relatively differentiated structures such as: hair and bone.
   - Mature cystic teratoma (Dermoid): most common tumor of women of all ages but it is often in pre-menopausal women. It demonstrates tissues of all three embryological cell types (ectodermal, mesodermal and endodermal).

C) **Stromal cell type:** derived from specialized sex-cord stroma of the developing gonads.
   - Thecoma
   - Fibroma : **MEIG's Syndrome: Benign ovarian fibroma + Ascites + pleural effusion** right, left or both.

- **Malignant ovarian neoplasms:**

A) **Epithelial cell type:** 90% of all ovarian malignancies.
   - Serous (most common): • Postmenopausal woman • Pelvic mass • ↑ CEA or CA-125 level
   - Mucinous
   - Clear cell
   - Endometrioid

B) **Germ cell type[2]:** most common ovarian cancer in women <20 yo. It may become functional producing: (□-hCG) or ( $\alpha$ -fetoprotein).
   - Dysgerminoma (most common) • ↑ LDH
   - Endodermal sinus tumor (yolk sac)
   - Immature teratoma

C) **Sex-cord stromal cell type:**rare tumor, produces hormones:
   - Granulosa cell tumor: secrets large amount of estrogen[3].
   - Sertoli Leydig tumor: secrets large amount of androgens. Postmenopausal pelvic Mass • **Masculinization** • ↑ testosterone level

Benign cystic teratoma (kaplan)

Dermoid cysts are benign tumors. They can contain cellular tissue from all 3 germ layers. The most common histology seen is ectodermal skin appendages (hair, sebaceous glands), and therefore the name "dermoid." Gastrointestinal histology can be identified, and carcinoid syndrome has been described originating from a dermoid cyst. Thyroid tissue can also be identified, and if it comprises more than 50% of the dermoid, then the condition of struma ovarii is identified. Rarely, a malignancy can originate from a dermoid cyst, in which case the most common histology would be squamous cell carcinoma, which can metastasize.

[2] It is uniquely x-ray sensitive
[3] can cause bleeding from endometrial hyperplasia

# Patient presentation

**Age:** women most commonly present in their 5th decade of life.

**Symptoms:**

- abdominal bloating
- abdominal distension (mass effect)
- abdominal or pelvic pain
- early satiety (mass effect)
- urinary urgency (mass effect)
- decreased energy'
- Constipation (mass effect)

**the most common symptoms are GastroIntestinal not gynecological symptoms**

Approximately 1/70 women develops ovarian cancer during her life.

| Risk factors | Protective factors |
|---|---|
| Family history | Hx of hysterectomy |
| Endometriosis | Hx of tubal ligation |
| Inherited mutations (BRCA and HNPCC) | OCP for at least 5 years |
| Prolong interval of ovulation[4] | |
| White race | |
| Late age at menopause | |

Last 3 risk factors + last protective factor for epithelial

# Evaluation

It is very important for the patient and her clinician to be aware of early warning signs.

**1-Qualitative b-human chorionic gonadotropin ( $\beta$ -hCG) test. If negative, this will rule out pregnancy.**

**2- Radiological imaging**

**pelvic ultrasound[5] is the best first line test**. if there is mass We check for US hints for malignancy : calcification, no clear borders, nodularity, septated or multilobulated masses and finally perform doppler looking for high vascularity. Transvaginal is most accurate after that:

**Chest radiograph and Abdominal CT rule out metastasis**

[4] continuous ovulation not interrupted by pregnancy OCP > Nulliparity Primary infertility or secondary

Sonogram. A complex mass on ultrasound appearance is incompatible with a functional[5] cyst

**3- CA-125 Levels (elevated in 50% of stage 1)**

most helpful in postmenopausal women with a pelvic mass, because in premenopausal women the CA-125 levels may increase for other reasons such as: (fibroids, PID, Endometriosis) (Which makes it less useful during this age, although it is very important to be done for postmenopausal patients).

We can use it as screening test with transvaginal US for women with strong family history of epithelial ovarian tumors

Other tumor markers include:

- LDH, hCG, and $\alpha$-fetoprotein should be drawn for the possibility of germ cell tumors.
- Estrogen and testosterone should be drawn for the possibility of stromal tumors.
- CEA for the possibility of mucinous and serous tumors.

**4- Others :**

**Fecal occult blood test and may Barium enamea is used and clonoscopy (rule out colon cancer which is one of DDx sometimes is metastasize to ovary)**

**Patient with significant GI symptoms Upper GI endoscopy is done krukenberg tumor in stomach is DDx)**

**Mammograms (breast cancer can metastasize to ovary)**

**5- Surgical exploration**

It is definitive next step in the evaluation if there is high suspicion.

Surgical staging. Even if the cyst is simple in appearance, surgical evaluation should be Performed. Absolute indication: if the cyst is >7 cm or if patient had been on prior steroid contraception.

| | |
|---|---|
| Stage I: | Spread limited to the **ovaries** |
| IA. | Limited to one ovary, capsule intact, negative cytology |
| IB. | Limited to both ovaries, capsules intact, negative cytology |
| IC. | One or both ovaries but ruptured capsule, positive cytology |
| Stage II: | Extension to the **pelvis** |
| IIA. | Extension to uterus or tubes |
| IIB. | Extension to other pelvic structures |
| IIC. | Extension to pelvis with positive cytology |
| Stage III: | **Peritoneal** metastases or positive nodes. This is the **most common** stage at diagnosis. |
| IIIA. | Microscopic peritoneal metastases |
| IIIB. | Macroscopic peritoneal metastases ≤2 cm |
| IIIC. | Macroscopic peritoneal metastases >2 cm |
| Stage IV: | **Distant** metastases |
| IVA. | Involves bladder or rectum |
| IVB. | Distant metastasis |

## Management

Ovary tumour can be benign or malignant or borderline
Borderline Cancers: Another entity of ovarian cancer is the borderline tumors also known as tumors of low malignant potential. These are characterized by no invasion of the basement membrane and can also be treated conservatively.

• Conservative surgery: A patient who desires further fertility with a unilateral borderline cancer of the ovary can be treated with a USO[6] with preservation of the uterus and the opposite adnexa.
• Aggressive surgery: If the patient has completed her family then the most acceptable treatment would be a TAH[7] and BSO[8]. debaliking sometimes used.
• Chemotherapy: Patients with borderline cancer of the ovary do not require chemotherapy unless they have metastasis, and this is a rare occurrence.very effective in sensitive tumors (germ cell) can cure matastisizes.
Sometimes used before debulking surgery in patient with effusion to make surgery easier and shrink the tumor and stabilize aggressive tumors.

## Follow-Up

Depend on pathology report of the enlarged adnexa.

**Benign**: followed up in the office on a yearly basis for regular examination. If the pathology report is defined.

**carcinoma**: followed up every 3 months for the first 2 years and then every 6 months for the next 2 years with follow-up of the CA-125 tumor marker.

[6] Unilateral salpingo-oophorectomy
[7] Total abdominal hysterectomy
[8] Bilateral salpingo-oophorectomy

# Case

CASE: A 48 year-old G3P3 woman comes to the office for a health maintenance exam. She is in good health and has no concerns. She had three normal vaginal deliveries and underwent a tubal ligation after the birth of her third child 15 years ago. She has no history of abnormal Pap smears or sexually transmitted infections. Her cycles are regular and her last menstrual period was 18 days ago. She is not taking any medications. Her family history is significant for a maternal aunt who was diagnosed with ovarian cancer at age 60. On examination, she has normal vital signs. Her heart, lung and abdominal exams are normal. On pelvic examination, she has normal external genitalia, vagina and cervix. On bimanual exam, she has a slightly enlarged uterus and a palpable 6 cm mobile, nontender right adnexal mass which is confirmed on the rectovaginal exam.

### 1. What is the next step in the management of this patient?

- **Start by taking history and performing an examination**

- **Pelvic transvaginal ultrasound** is essential to evaluate the characteristics of the adnexal mass. Categorization as to whether this is a simple (cystic) or complex adnexal mass is crucial to the management.

- If **cystic, mobile, and less than 10 cm, observation** is reasonable in the premenopausal patient who is asymptomatic (and with no family history of ovarian cancer). A repeat ultrasound in 8-12 weeks will assist in determining if this is persistent or increasing, at which point surgical exploration would be advisable. In this case, this is most likely a neoplasm. If the cystic ovary resolved or is smaller, then this likely represents a functional cyst.

- If the adnexal **cystic mass is solid or complex, fixed, size >10 cm, or bilateral, then surgical exploration** is recommended.

- **CA125**: tumor marker often **elevated in women with advanced epithelial ovarian cancer.** CA 125 was developed originally to **follow up response to chemotherapy treatment** (as surrogate marker for response), but now used to assess for relapsed disease and to triage women with a pelvic mass (to gyn oncologist or gynecologist for further investigations). Non-specific elevations seen among premenopausal women with gynecologic and non-gynecologic conditions (endometriosis, fibroids, benign cystic neoplasms, infection/inflammation, cirrhosis). More likely to be discriminating among postmenopausal women with adnexal masses.

- Other tumor markers to consider: **CEA** (mucinous tumors), **AFP** (yolk sac germ cell tumors), **LDH** (dysgerminoma), **beta-HCG** (choriocarcinoma, mixed germ cell tumors)

**2. How would your approach be different if the patient was postmenopausal at 62 years of age?**

Any postmenopausal patient with a complex cystic/solid mass requires **surgical exploration and removal**. If the cyst is simple in nature, then observation is reasonable provided the patient is asymptomatic, there is no significant family history of ovarian cancer, and CA125 is normal.

**3. You obtain an ultrasound which shows a 6 cm right complex ovarian cyst. What is your differential diagnosis?**

Benign:

- Functional cyst (follicular, corpus luteum, theca lutein)
- Endometrioma
- Tubo-ovarian abscess
- Serous/mucinous cystadenoma
- Gonadal stromal tumors (fibroma/thecoma)
- Germ cell tumors (teratomas)

Malignant:

- Epithelial tumors (serous, mucinous, clear cell, endometrioid, Brenner)
- Germ cell tumors (dysgerminoma, endodermal sinus tumor, immature teratoma)
- Sex cord stromal tumors (Sertoli-Leydig, Granulosa)

**4. What risk factors does this patient have for ovarian cancer?**

- This patient's risk factors include a **family history** of ovarian cancer.
- Other risk factors include: **family history of breast cancer, personal history of breast cancer, BRCA 1/2 genetic mutation, increasing age, nulliparity, infertility.**
- **Protective factors include: oral contraceptive use, tubal ligation, increasing parity**.

**5. List elements of the history and physical examination, which would help support the diagnosis of ovarian cancer:**

1- Presenting symptoms for epithelial ovarian cancer include:

- Abdominal discomfort/bloating (50%)
- Gastrointestinal disturbances (20%)
- Urinary symptoms (15%)
- Vaginal bleeding/menstrual irregularities (15%)
- Weight loss (15%)
- Germ cell tumors may present with acute pain. Precocious pseudopuberty and virilization may be seen with some germ cell and sex cord/stromal tumors.

2- Physical exam findings typically include the presence of an adnexal/pelvic mass. In advanced stages, abdominal distension with ascites and/or an abdominal mass may be noted.