Ovarian Tumors

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Tumor-like conditions of the ovaries:

1-Pregnancy luteoma
2-corpus luteum cyst
3-lutein cyst
4-Follicular cysts
5-Germinal inclusion cysts
6-para- ovarian cysts
7-Multicystic ovary and PCOD
8-Endometrioma
9-Inflammatory mass.
10-Massive ovarian edema.
11-Hyperthecosis, hyperplasia of ovarian stroma.

Epidemiology

-**Ovarian cancer is the most common gynecological cancer in the U K ,while it is the 2rd common gynecological cancer in USA (after endometrial).**

-The life time risk of developing ovarian cancer is 1.5% (7.1% for breast cancer).

-About 90% of ovarian cancer are ***epithelial*** in origin (arising from coelomic epithelium).

-2/3 of diagnosed cases are *advanced* ovarian cancer (stage III & IV).

-The ovarian cancer-related deaths per annum outnumber those from cancer of the cervix & endometrium combined.

Epidemiology

Age incidence :

- *Epithelial carcinomas of the ovary are rare before the age of 30years,and the incidence increases with age (<20% diagnosed before the age of 50 years).the peak incidence is in 50 –70 years old group.
- Germ cell tumors are found in children & young women, usually before age of 30 years.

Epidemiology

- **Incidence/Morbidity/Mortality**
  - **Lifetime risk: approx 1/70**

Stage	Percent	Survival
I	24	>90%
II	6	70-80%
III	55	20-30%
IV	15	<5%
Overall		50%

Etiology

1-Continuous ovulation: "ovulation trauma":

This is supported by the following findings in ovarian cancer :

(a)Incidence is increased in women with early menarche ,late menopause & nulliparty.

(b)Incidence of ovarian cancer is reduced in women that taking the contraceptive pills , which suppress ovulation.

It thought that ovarian cancer starts at the fimbrial end of the fallopian tube

Etiology

2-Familial cancer: (5% of epithelial ovarian cancers, usually "serous")

-Lynch syndrome: Families with multiple cases of ovarian ,breast , colorectal or endometrial cancer ."***cancer family syndrome"*.

*Familial inheritance for ovarian & breast cancer is *"autosomal dominant"* & is due to the presence of mutations in the BRCA1 gene(breast cancer gene-1) → life time risk of >30% for ovarian cancer.

*Mutations in a second gene (BRCA2)→ low risk for developing ovarian cancer

Ovarian Cancer Risks

- **Increase Risk**
  - Age most important independent risk factor
  - Family history
  - BRCA1 (60x increased risk), BRCA2 (30x), HNPCC (13x)
  - Nulliparity, infertility, endometriosis
- **Decrease Risk**
  - Prophylactic oophorectomy
  - Oral contraceptive pills

WHO CLASSIFICATION OF OVARIAN NEOPLASMS

i. COMMON EPITHELIAL
ii. GERM CELL
iii. SEX-CORD STROMAL
iv. UNCLASSIFIED
v. METASTATIC

Epithelial ovarian tumors

Common epithelial tumors (benign ,border line, malignant): are the commonest type (85%)

1-Serous.

2-Mucinous.

3-Endometrioid.

4-Clear cell (mesonephroid).

5-Brenner.

6-Mixed epithelial.

7-Undifferentiated.

8-Unclassified

Sex-cord stromal tumors

1-*Granulosa - Stromal-cell tumors: (feminizing)*

A-Granulosa cell tumor

B-Tumors in thecoma –fibroma group:

(a)Thecoma (b)fibroma (c) unclassified.

2-Androblastomas ; sertoli- leydig -cell tumors; (virilizing)

A. Well differentiated :

(a) Sertoli cell tumor (b) Leydig cell tumor (=hilus cell tumor).

(c) Sertoli- Leydig cell tumor

B. Moderately differentiated.

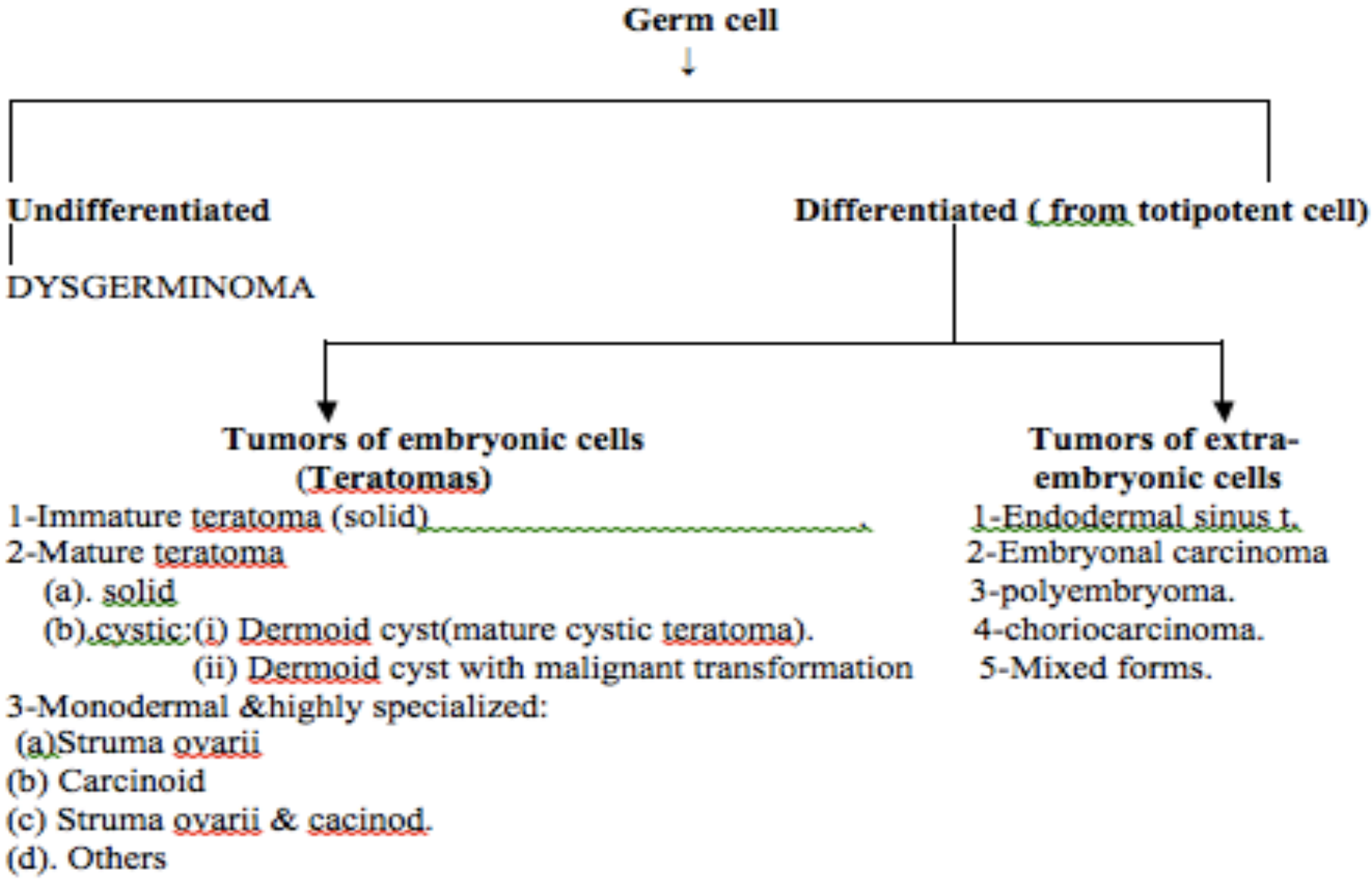
C. Poorly differentiated (Sarcomatoid).

D. With heterologous elements.

3- Gynandronblastoma (mixed).

4-Unclassified.

III. Germ cell tumors



Other ovarian tumors

IV. Soft tissue tumors not specific to ovary e.g. lymphomakin which is a non-Hodgin lympgoma.

V. Unclassified tumors.

VI. Metastatic tumors: Krukenberg tumor, bilateral kidney shaped with preservation of the ovarian contour, the origin may be breast, colon , stomach, or thyroid

FIGO Ovarian Cancer Staging

Effective Jan. 1, 2014- *(Changes are in italics.)*

STAGE I: Tumor confined to ovaries			
OLD		NEW	
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.	IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.
IB	Tumor involves both ovaries otherwise like IA.	IB	Tumor involves both ovaries otherwise like IA.
IC	Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.	*IC Tumor limited to 1 or both ovaries*	
		IC1	*Surgical spill*
		IC2	*Capsule rupture before surgery or tumor on ovarian surface.*
		IC3	*Malignant cells in the ascites or peritoneal washings.*

FIGO Ovarian Cancer Staging

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STAGE II: Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer				
OLD			NEW	
IIA	Extension and/or implant on uterus and/or Fallopian tubes		IIA	Extension and/or implant on uterus and/or Fallopian tubes
IIB	Extension to other pelvic intraperitoneal tissues		IIB	Extension to other pelvic intraperitoneal tissues
IIC	IIA or IIB with positive washings/ascites.			

Old stage IIC has been eliminated

FIGO Ovarian Cancer Staging

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STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes

OLD		NEW		
IIIA	Microscopic metastasis beyond the pelvis.	*IIIA (Positive retroperitoneal lymph nodes and /or microscopic metastasis beyond the pelvis)*		
		IIIA1	*Positive retroperitoneal lymph nodes only*	
			IIIA1(i)	*Metastasis ≤ 10 mm*
			IIIA1(ii)	*Metastasis > 10 mm*
		IIIA2	*Microscopic, extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes*	
IIIB	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm in greatest dimension.	IIIB	*Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.*	
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm in greatest dimension and/or regional lymph node metastasis.	IIIC	*Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.*	

FIGO Ovarian Cancer Staging

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STAGE IV: Distant metastasis excluding peritoneal metastasis				
OLD			NEW	
IV	Distant metastasis excluding peritoneal metastasis. Includes hepatic parenchymal metastasis.		*IVA*	*Pleural effusion with positive cytology*
			IVB	Hepatic and/or *splenic parenchymal* metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Other major recommendations are as follows:

- Histologic type including grading should be designated at staging
- Primary site (ovary, Fallopian tube or peritoneum) should be designated where possible
- Tumors that may otherwise qualify for stage I but involved with dense adhesions justify upgrading to stage II if tumor cells are histologically proven to be present in the adhesions

Diagnosis

I. CLINICAL DIAGNOSIS
II. INVESTIGATIONS
III. STAGING LAPAROTOMY

CLINICAL DIAGNOSIS

- Symptoms: non specific, vague
- Approximately 70% of patients are diagnosed when the ovarian cancer has advanced beyond the ovaries. This is due to the insidious nature of the symptoms & signs of carcinoma of the ovary (killing menace), but occasionally due to a rapidly growing tumor.

CLINICAL DIAGNOSIS

- **Signs:**

1- abdominal mass+ ascites is highly suggestive of malignancy especially if the mass is a fixed ,hard, irregular pelvic mass felt by bimanual examination.

2- Cachexia.

3-In very late cases supraelavicular or inguinal nodes may be palpable.

Clinical criteria suggesting malignancy

*ovarian **mass** plus the following*:

1-History: any patient but ovarian malignancy is most common in postmenopausal woman who was infertile or of low parity. Breast and/ or colon cancer may be found.

2-General exam:

-*Cachexia;* may be found in benign ovarian tumor(ovarian cachexia).

-*Unilateral lower limb edema* due to obstruction of venous return.

3- Abdominal exam:

heterogeneous consistency (solid + cystic areas). Ascites , detected by shifting dullness, or fluid thrill (if tense).

-Ovarian tumor which is; *bilateral*, *fixed*, slightly *tender*, with *ill-defined borders*.

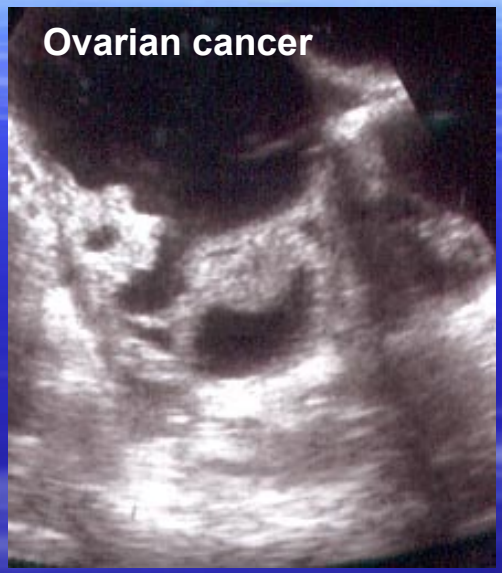
4-Pelvic exam:

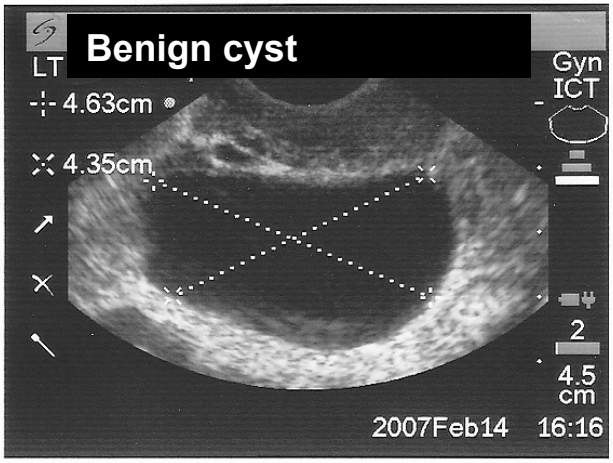
-There may be *multiple solid nodules* felt in cul-de-sac.

-The ovarian tumor (if small) it is felt as a hard, fixed, irregular pelvic mass.

IMAGING

- **Ultrasound**
  - Low positive predictive value for cancer
  - *Cancer*: excrescences, ascites, and mural nodules
  - *Benign*: unilocular, thin-walled sonolucent cysts with smooth, regular borders, regardless of menopausal status or cyst size
- **CT/MRI :**Better characterization of the tumor plus better evaluation of local, peritoneal, and nodal involvement





Ultrasound Criteria suggesting ovarian malign.:

1-*Ascites* 2- *Bilaterality*

3-*Multilocularity* (i.e. presence of intracystic septa dividing tumor into locules)

4-*Papillation*: papillae may be surface papillae or intracystic growths.

5-*Heterogeneous echogenicity* (i.e.solid [hyperechogenic] + cystic [hypoechogenic] parts).

6-TVS with Doppler ; decreased RI (resistance index) in abnormal blood vessels of the tumor.

7-Enlarged para-aortic & pelvic lymph nodes.

8-Parynchymal liver metastases can be detected.

Labs

- **Tumor markers**
  - ***Epithelial***: CA 125, elevated in 80%
    - 35 U/mL is upper limit of normal
    - Also elevated in many benign conditions
  - **Malignant *germ* cell tumors**: b-hCG, LDH, AFP
  - **Embryonal carcinoma**: AFP, BhCG
  - **Endodermal Sinus tumor**: AFP
  - **Granulosa cell tumors**: inhibin

SUMMARY OF TUMOR MARKERS

1. Tumor markers of ovarian malignancy include:
2. CA125 (cancer antigen 125)
3. HMFG 1&2 (human milk factor globulin 1&2).
4. M-CSF (macrophage colony simulating factor).
5. AFP (alpha feto protein)._
6. CEA (carcino-embryonic factor)
7. B-HCG (beta- human chorionic gonadotropin).
8. PLAP (placental alkaline phosphatase).
9. LDH (lactic dehydrogenase).
10. Inhibin
11. OVX-1 (ovarian – x-1).
12. NB /70 K (non-bound/ 70 kibdalton), in epithelial tumors.

*Staging Laparotomy : Technique:

Laparotomy is essential for both staging & treating ovarian cancer.

1-A satisfactory exposure is necessary in order to explorethe whole abdomen adequately and , there fore , a vertical incision is better than a transverse incision.

2-A sample of ascitic fluid or peritoneal washings , for cytological evaluation , is taken first .

3-Following this, a systematic examination of the omentum , subdiaphragmatic areas , anterior abdominal wall , para colic gatters , surface of small & large intestine , pelvic organ , and pelvic & paraaoatic nodes is made.

4-Biopsies of suspicious areas are taken in the absence of gross upper abdominal disease.

5-Using an Ayre´s spatula , a subdiaphragmatic scrape may be taken to check for microscopic peritoneal involvement.

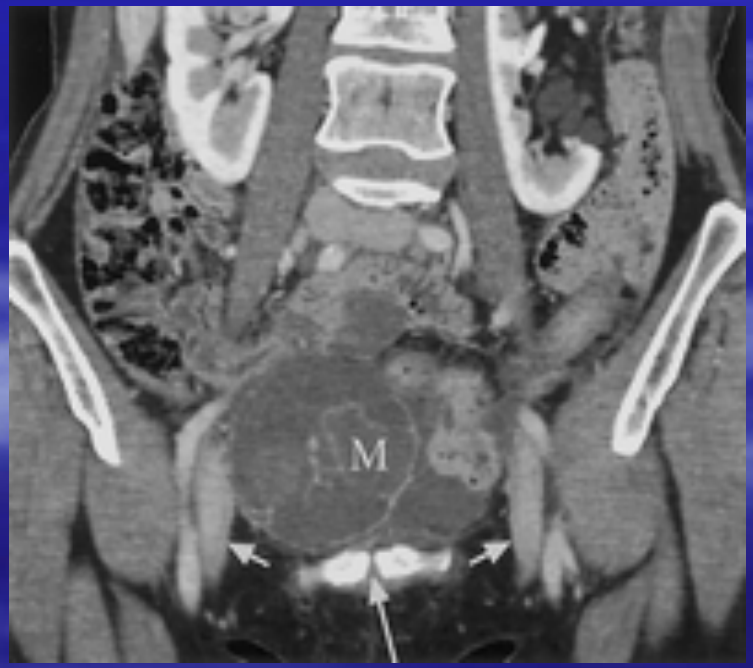
Signs of ovarian malignancy at laparotomy

At laparotomy ovarian malignancy is suspected if *one or more* of the following signs is found;

1- Solidity of the growth.
2-Bilaterality of tumor
3- Bloody ascites
4-Peritoneal nodules.
5- Surface papillae.
6-Omental involvement (omental nodules or omental cake).
7-Large blood vessels seen on the surface of the tumor.
8-The malignant tissue is seen fungating through the ovarian capsule.
9-The tumor is adherent to intestine or uterus (invasion).
10-Areas of hemorrhage & necrosis are seen through the outer wall of the growth.
11-Para-aortic lymph nodes are felt enlarged.
12-Frozen section reveals malignancy (most accurate here).

Treatment of Epithelial Ovarian Cancer

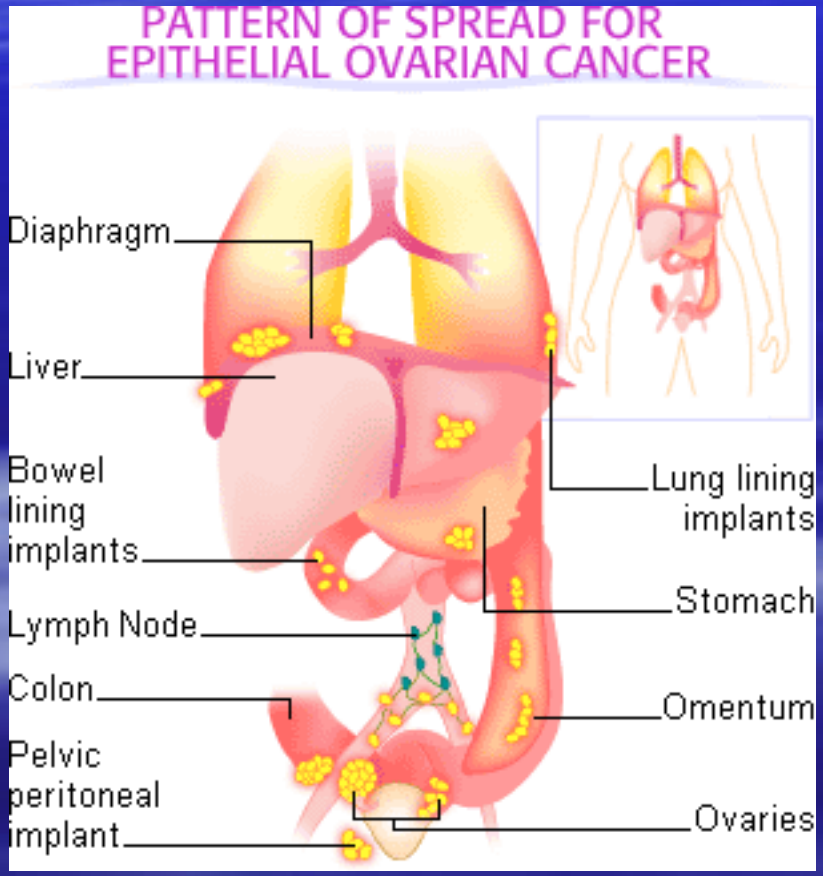
- Chemotherapy
- Cytoreductive surgery (debulking)

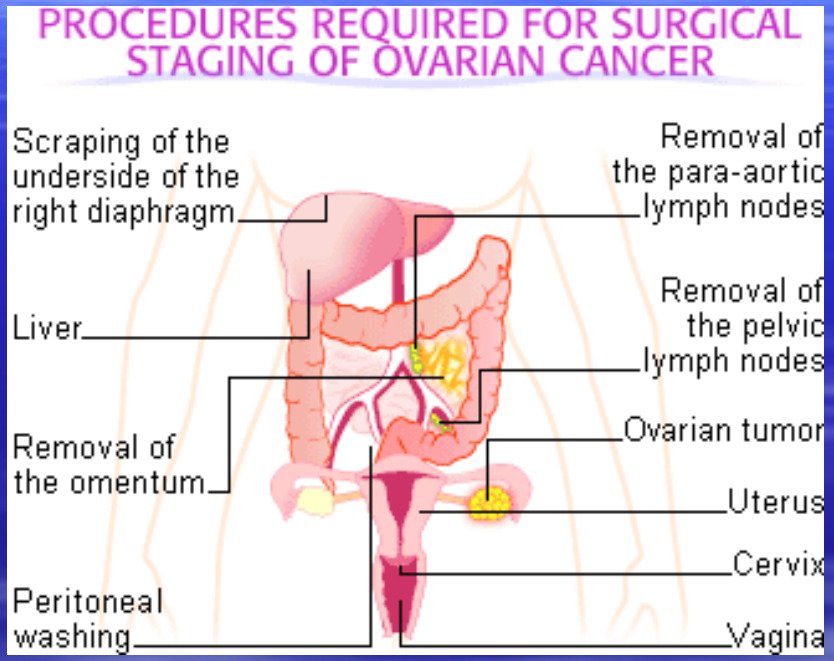


CT of ovarian mass

Treatment of Epithelial Ovarian Cancer

- Debulking





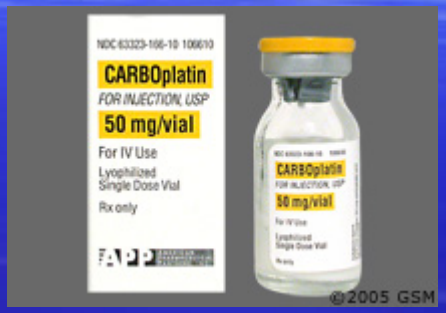
- Removal of: uterus, tubes, ovaries, omentum, pelvic and paraaortic nodes, all visible tumor

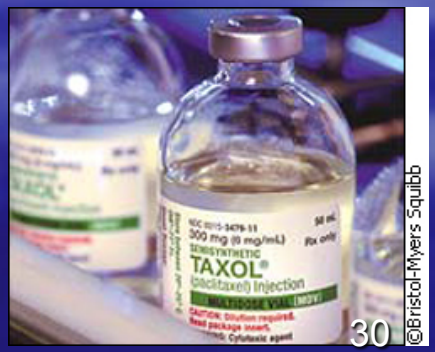
- Peritoneal washings

- Diaphragm biopsies

Treatment of Epithelial Ovarian Cancer

- **Carboplatin and Paclitaxel**
  - First line
  - Mechanism of action
    - Carbo: binds and crosslinks DNA
    - Taxol: promotes formation and inhibits disassembly of stable microtubules, inhibiting mitosis
  - Side effects
    - Carbo: thrombocytopenia, leukopenia, anemia, vomiting, hair loss
    - Taxol: neutropenia, leukopenia, anemia, hair loss, muscle pain, vomiting, diarrhea





THANKS