Malignant tumours of the ovary

Dr.Nadia Mudher Al-Hilli
FICOG
Department of Obs&Gyn
College of Medicine
University of babylon

Objectives of lecture

- Learn how malignant disease of the ovary presents.
- Learn how ovarian cancer is investigated and staged.
- Learn how ovarian cancer is managed.

Epidemiology:

- The lifetime risk is 1.4 %
- Mean age of presentation is 64 years.
- More prevalent in developed nations
- incidence vary with ethnicity, Caucasian have higher incidence than Asian.
- large proportion of ovarian cancers may originate in the Fallopian tube, rather than the ovarian surface epithelium.
- There is a significant genetic aspect to ovarian cancer.
- hereditary cancer present early, with a mean age at diagnosis of 54 years.

Classification of malignant ovarian tumours

1 Epithelial ovarian tumours (80%)	**High-grade serous (75%)** **Endometrioid** **Clear cell** **Mucinous** **Low-grade serous** **(Borderline)**
2 Sex cord stromal tumours (10%)	Granulosa cell Sertoli–Leydig Gynandroblastoma
3 Germ cell tumours (10%)	Dysgerminoma Endodermal sinus (yolk sac) Teratoma Choriocarcinoma
	Mixed
4 Metastatic (including Krukenberg tumours	

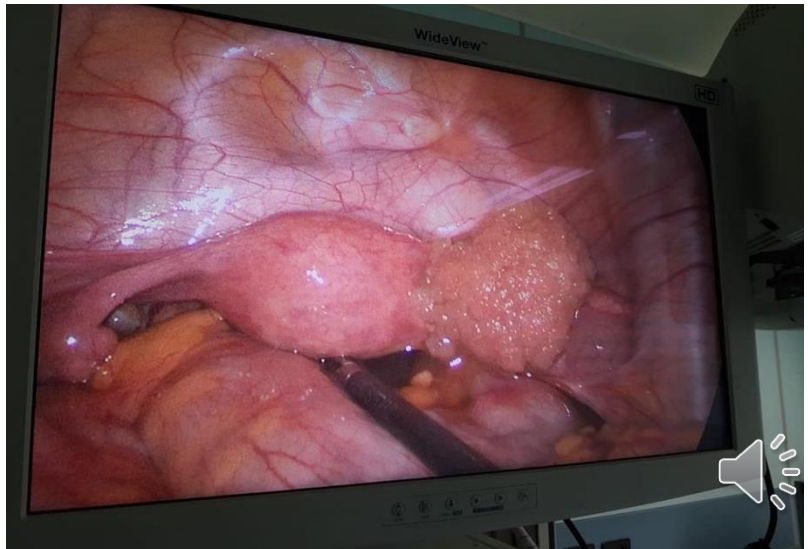
Borderline epithelial tumours:

- well differentiated, with some features of malignancy (nuclear pleomorphism, cellular atypia) but do not invade the basement membrane.
- constitute 10% of epithelial ovarian tumours.
- May spread to pelviabdominal structures but not recur after initial

surgery.

- The majority of BOTs are

serous tumours.



Etiology of Epithelial tumours:

- Incessant ovulation theory:
- Subfertility treatment:
- Genetic factors:

Risk factors in ovarian cancer:

Decreased risk of ovarian cancer	Increased risk of ovarian cancer
Multiparity	Nuliparity
Oral contraceptive pill (RR reduced by 20% per 5 years use)	Intrauterine device (RR 1.76)
Tubal ligation	Endometriosis
Hysterectomy	Cigarette smoking (mucinous tumours only)
	Obesity

High-grade pelvic serous carcinomas:

- most present with advanced disease involving the ovary, Fallopian tube and peritoneal surfaces, making it impossible to establish the anatomical site of origin.

- This term incorporate all high-grade serous tumours arising from the ovary, Fallopian tube and/or peritoneum.

- New data suggest a Fallopian tubal precursor lesion for high-grade pelvic serous tumours. These precursors are called serous tubal intraepithelial carcinoma (STIC) lesions.

Familial ovarian cancer:

- Constitute 10–15 % of epithelial ovarian cancer.
- mutations in BRCA1, BRCA2 and Lynch syndrome
- The lifetime risk rises to 5 % if one family member affected and increases to 40–50 % if two first degree relatives are affected.
- it occur 10 years earlier than sporadic cancers

- 90% of hereditary cancer is the breast ovarian cancer syndrome (BRCA)
- The defective gene is most commonly the tumour-suppressor gene BRCA1 (80%), BRCA2 (15%).
- Lynch syndrome is hereditary non-polyposis colorectal cancer (HNPCC) and is associated with endometrial cancer and a 10 per cent risk of ovarian cancers.

Preventing ovarian cancer

- Women test positive for a BRCA mutation are offered risk-reducing prophylactic BSO after completing their families.
- reduces risk of ovarian cancer by 90% and premenopausal breast cancer by 50%.
- should be carried out prior to the age-related surge in ovarian cancer.
- bilateral salpingectomy with delayed oophorectomy in the 30s and early 40s may offset the morbidity associated with a surgical menopause in young women.
- opportunistic removal of the Fallopian tubes during hysterectomy for benign indications, tubal ligation (sterilization) and hysterectomy with ovarian conservation, also reduces ovarian cancer risk.
- Chemoprevention using COCP reduces ovarian cancer risk by up to 50%.

Screening:

- Screening using transvaginal ultrasound scan (TVUSS) and CA125 measurement has not been shown to improve survival in women with a familial predisposition to ovarian cancer.
- because the high grade serous tumours that are associated with BRCA mutation carrier status develop rapidly and most are at an advanced stage before they can be picked up by screening.

Clinical features of epithelial ovarian cancer

- symptoms are nonspecific and often vague. The difficulty with clinical diagnosis is the main reason that patients with ovarian carcinoma present with late stage disease

Common symptoms are:

- persistent pelvic and abdominal pain
- increased abdominal size/persistant bloating
- difficulty eating and feeling full quickly.

Other frequent symptoms:

- change in bowel habit
- urinary symptoms
- back ache
- irregular bleeding
- fatigue

Clinical Examination:

- Pelvic and abdominal examination may reveal a fixed, hard mass arising from the pelvis. with or without ascites
- Chest examination is important to assess pleural fluid and the neck and groin should be examined for enlarged nodes.

The differential diagnosis:

- Non epithelial ovarian cancer
- Tuboovarian abscess
- endometriomas
- fibroids

Investigations:

- TVUSS is the initial imaging modality of choice to check for pelvic pathology.
- US characteristics:
  - Size
  - Consistency
  - the presence of solid elements
  - bilaterality
  - ascites
  - extraovarian disease, including peritoneal thickening and omental deposits.

In conjunction with Ca125 measurement and menopausal status, a risk of malignancy (RMI) is calculated.

Tumour markers used in ovarian carcinoma

Tumour Marker	Tumour type	Uses
Ca 125	Epithelial ovarian cancer (serous), borderline ovarian tumours	Preoperative, follow up
Ca 19-9	Epithelial ovarian cancer (mucinous), borderline ovarian tumours	Preoperative, follow up
Inhibin	Granulosa cell tumours	Follow up
β-hCG	Dysgerminoma, choriocarcinoma	Preoperative, follow up
AFP	Endodermal yolk sack, teratoma	Preoperative, follow up

- Pelvic pathology at intermediate or high risk of malignancy is further imaged using computed tomography (CT) for extrapelvic disease & staging and/or magnetic resonance imaging (MRI) scans help define tissue planes & operability.

Other investigations required for preoperative work-up include:

- chest X-ray,
- electrocardiography (ECG)
- full blood count
- urea and electrolytes
- liver function tests.

Other investigations:

- Endometrial biopsy, especially if conservative surgery is to be undertaken.
- If the patient presents with gross ascites or pleural effusion, paracentesis or pleural aspiration may be required for relief of symptoms or for diagnosis.
- barium enema or colonoscopy if bowel symptoms are present or there is a possibility of a primary colorectal tumour.

- **Metastatic spread:**
- pelvic peritoneum & pelvic organs are involved by direct spread. malignant cells on all intra-abdominal structure surfaces.

- Lymphatic spread involve pelvic & para-aortic lymph nodes, nodes in the neck & inguinal region.

- Haematogenous spread occurs late in the course of disease involving liver & lung, sometimes bone & brain.

Clinical staging:

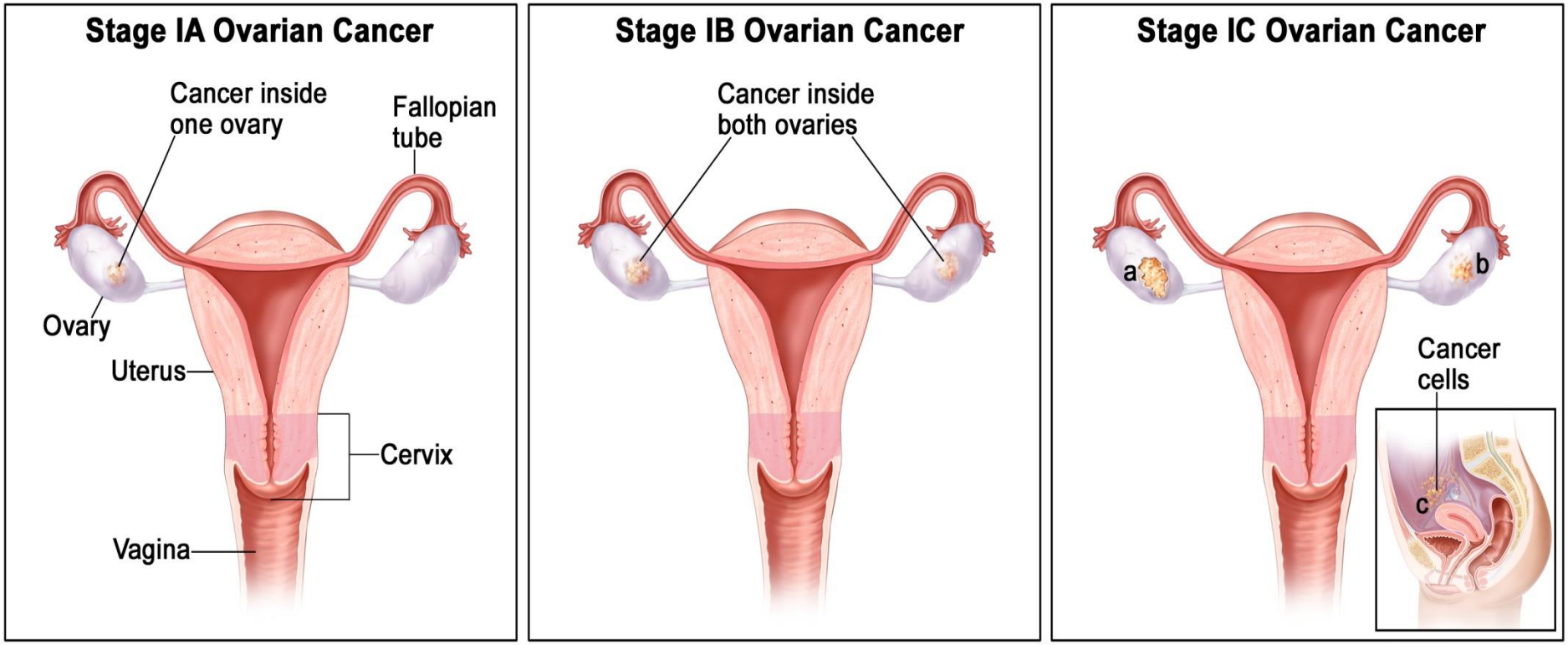
Stage FIGO definition

I growth limited to ovaries

Ia growth limited to one ovary, no ascites, no tumour on external surface, capsule intact.

Ib growth limited to both ovaries, no ascites, no tumour on external surfaces, capsule intact

Ic tumour either stage Ia or Ib but tumour on surface of one or both ovaries or with capsule rupture or with ascites present containing malignant cells or with positive peritoneal washing

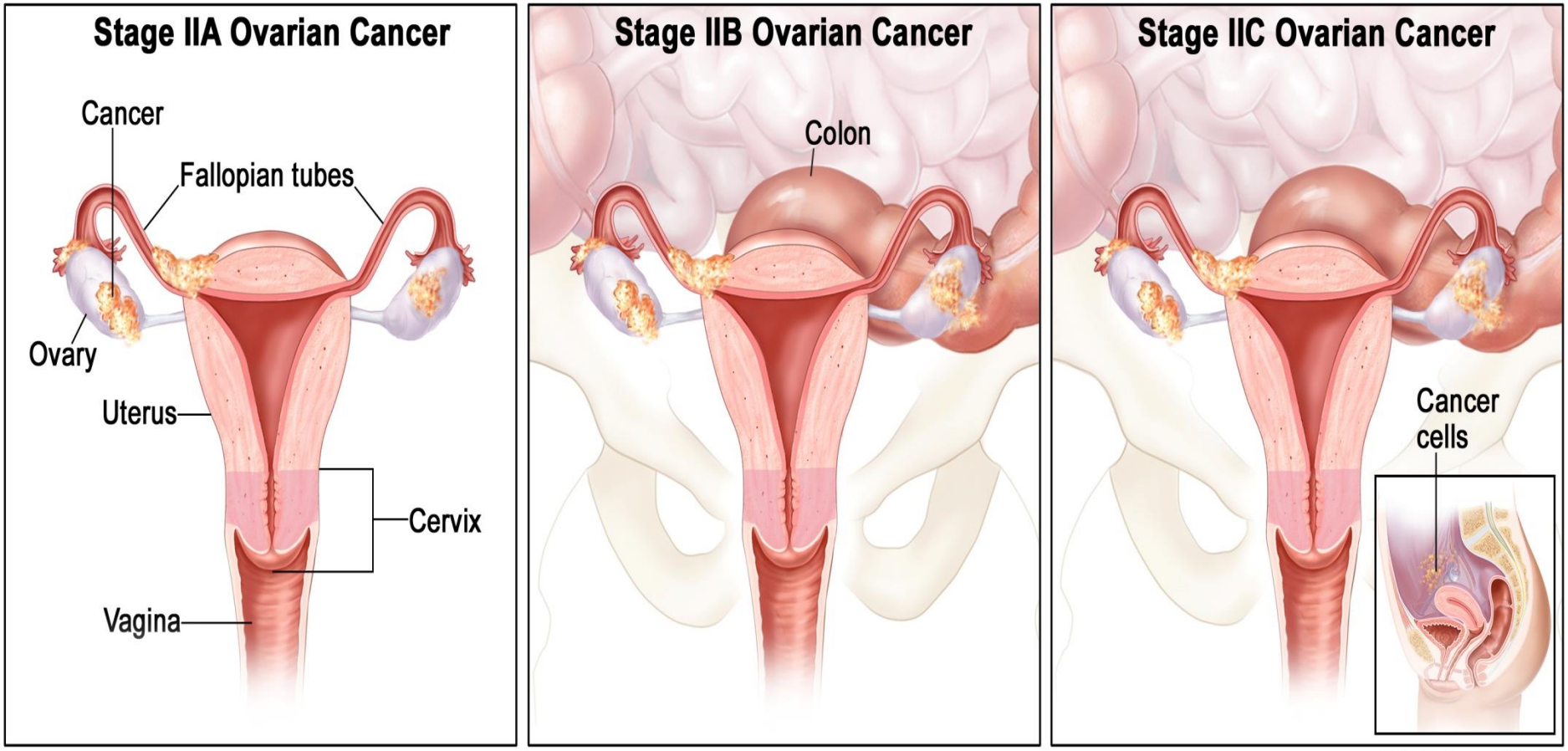


II growth involving one or both ovaries with pelvic extension

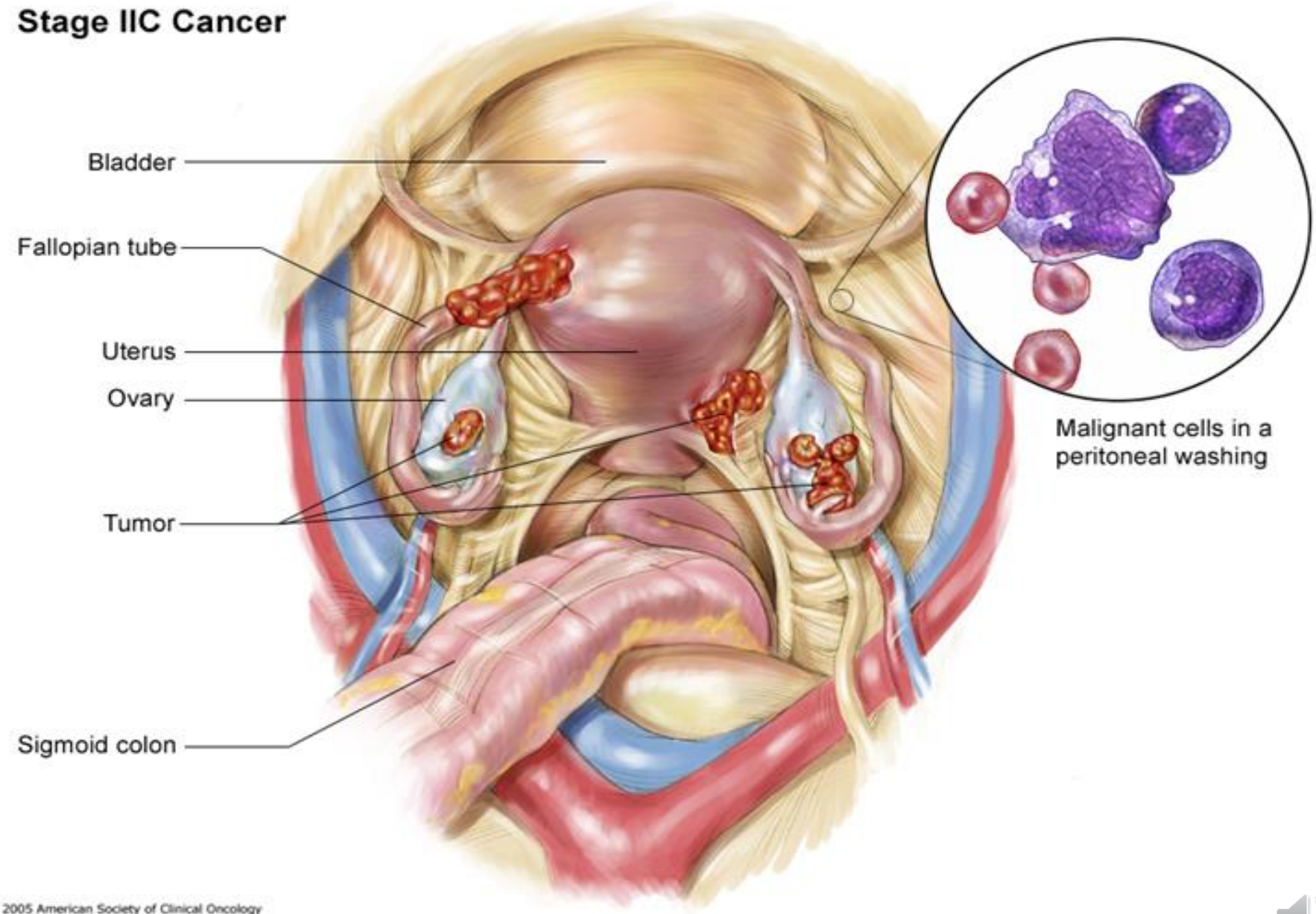
IIa extension &/or metastasis to the uterus or tubes

IIb extension to other pelvic tissues

IIc tumour either stage IIa or IIb but tumour on surface of one or both ovaries or with capsule rupture or with ascites containing malignant cells or with positive peritoneal washing



Stage IIC Cancer



III tumour confined to abdominal peritonium or positive retroperitoneal or inguinal nodes

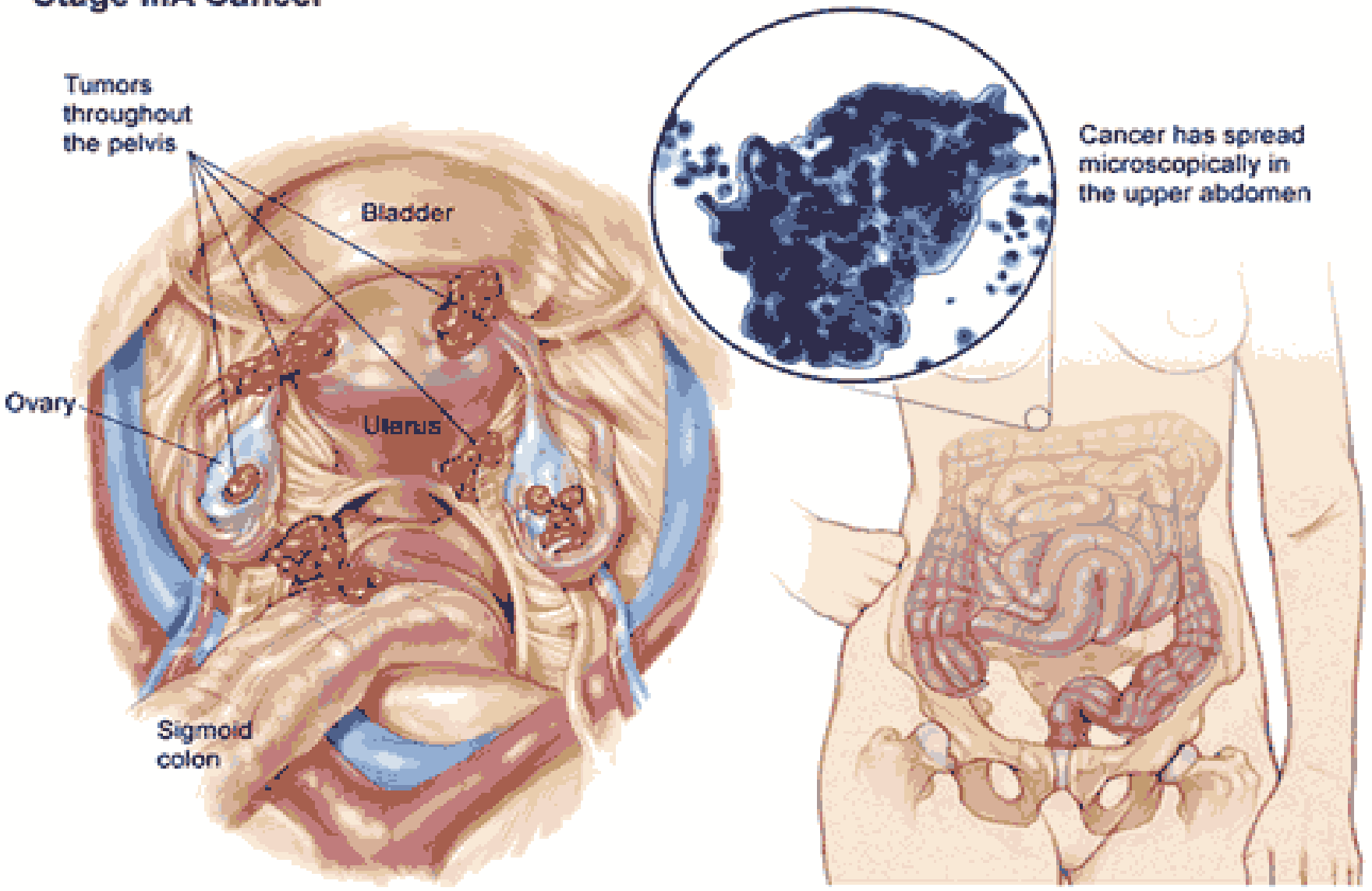
IIIa tumour grossly limited to the true pelvis with negative nodes but with histologically confirmed microscopic seeding of abdominal peritoneal surfaces

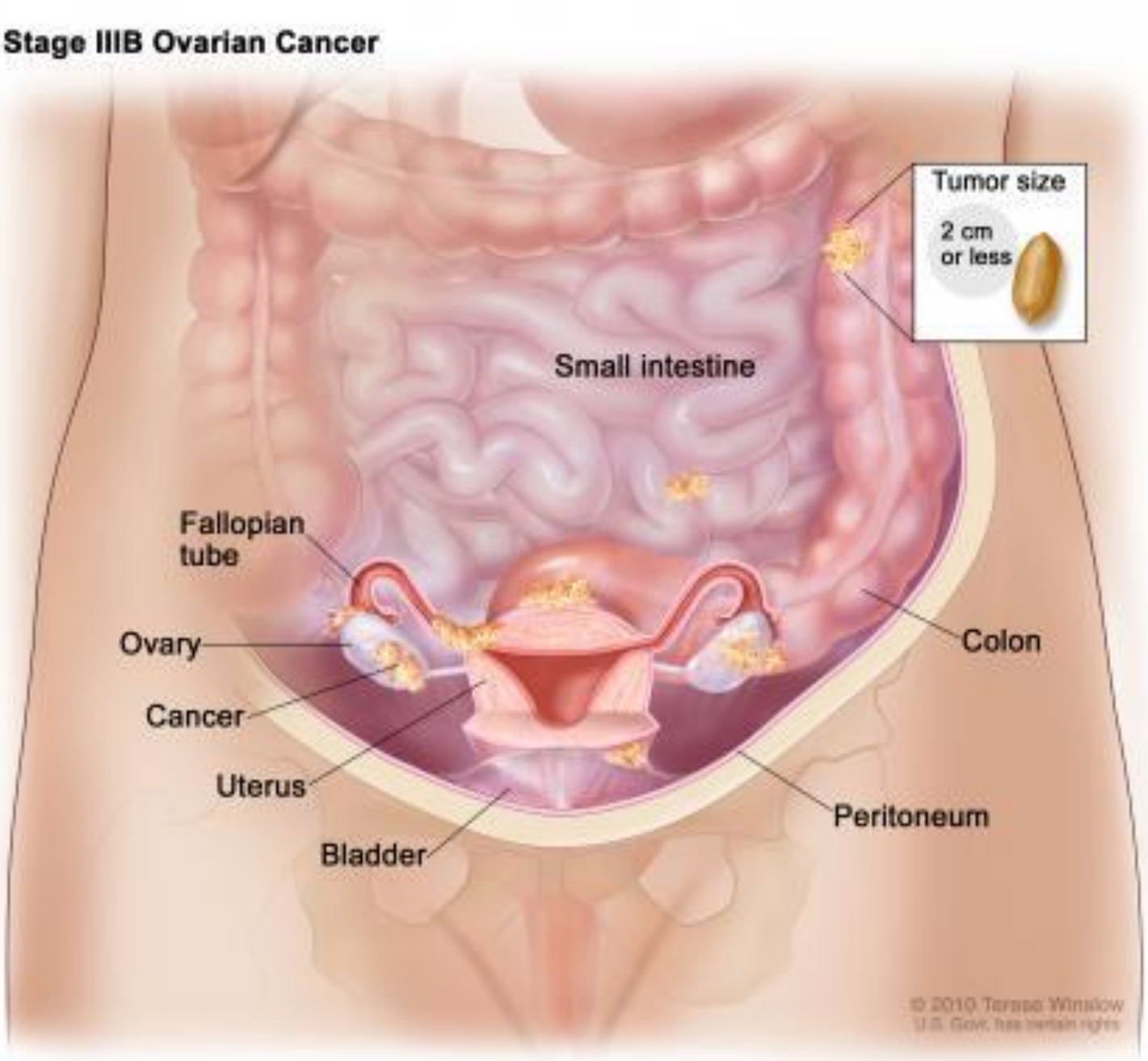
IIIb Abdominal implants <2 cm in diameter, nodes are negative.

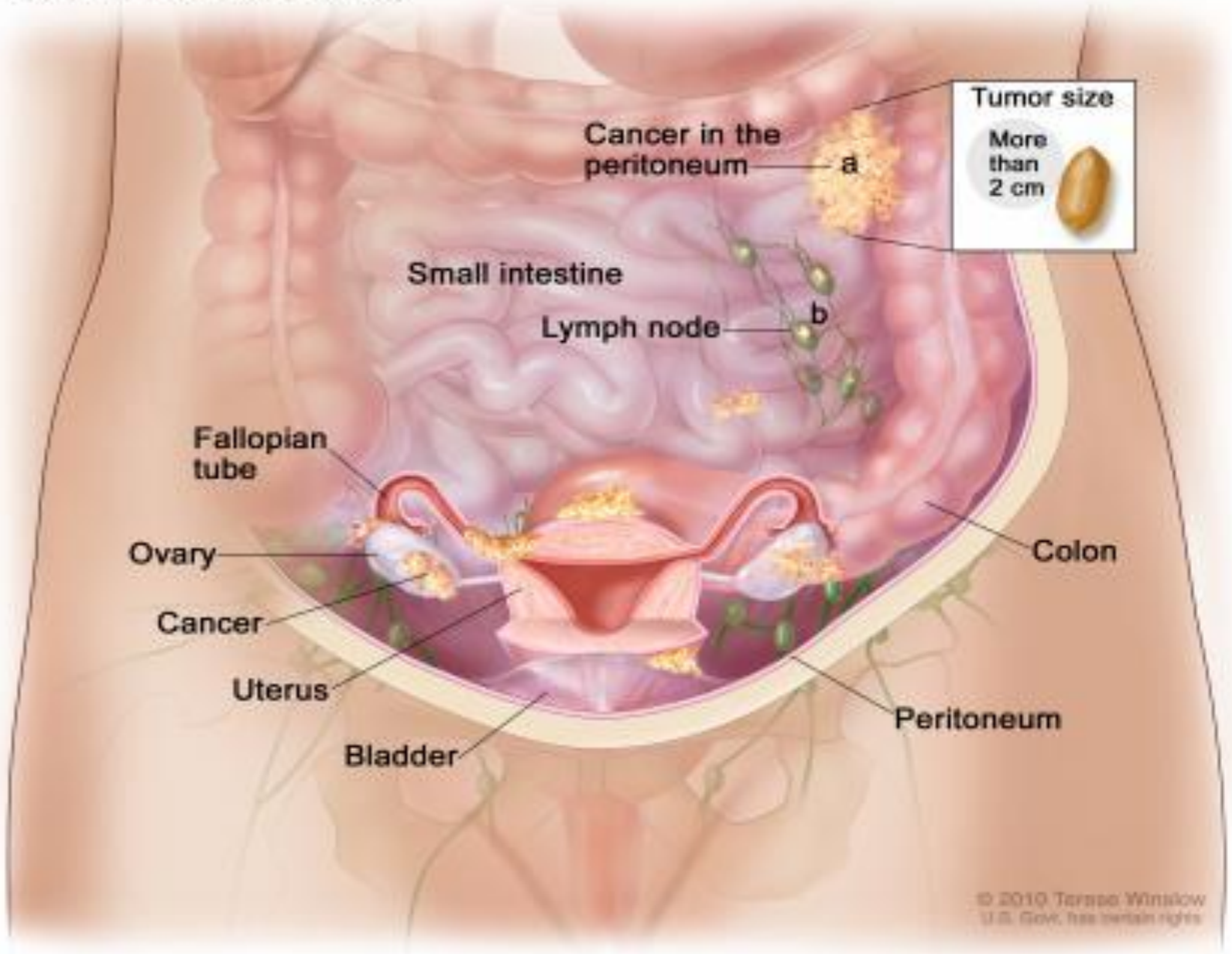
IIIc abdominal implants > 2cm in diameter or positive retroperitoneal or inguinal nodes.

IV distant metastasis, if pleural effusion is present, there must be positive cytology to allot a case to stage IV

Stage IIIA Cancer




Stage IIIB Ovarian Cancer
Tumor size
2 cm
or less
Small intestine
Fallopian
tube
Ovary
Cancer
Uterus
Bladder
Colon
Peritoneum


Stage IIIC Ovarian Cancer
Tumor size
More than 2 cm
Cancer in the peritoneum
a
Small intestine
Lymph node
b
Fallopian tube
Ovary
Cancer
Uterus
Bladder
Colon
Peritoneum
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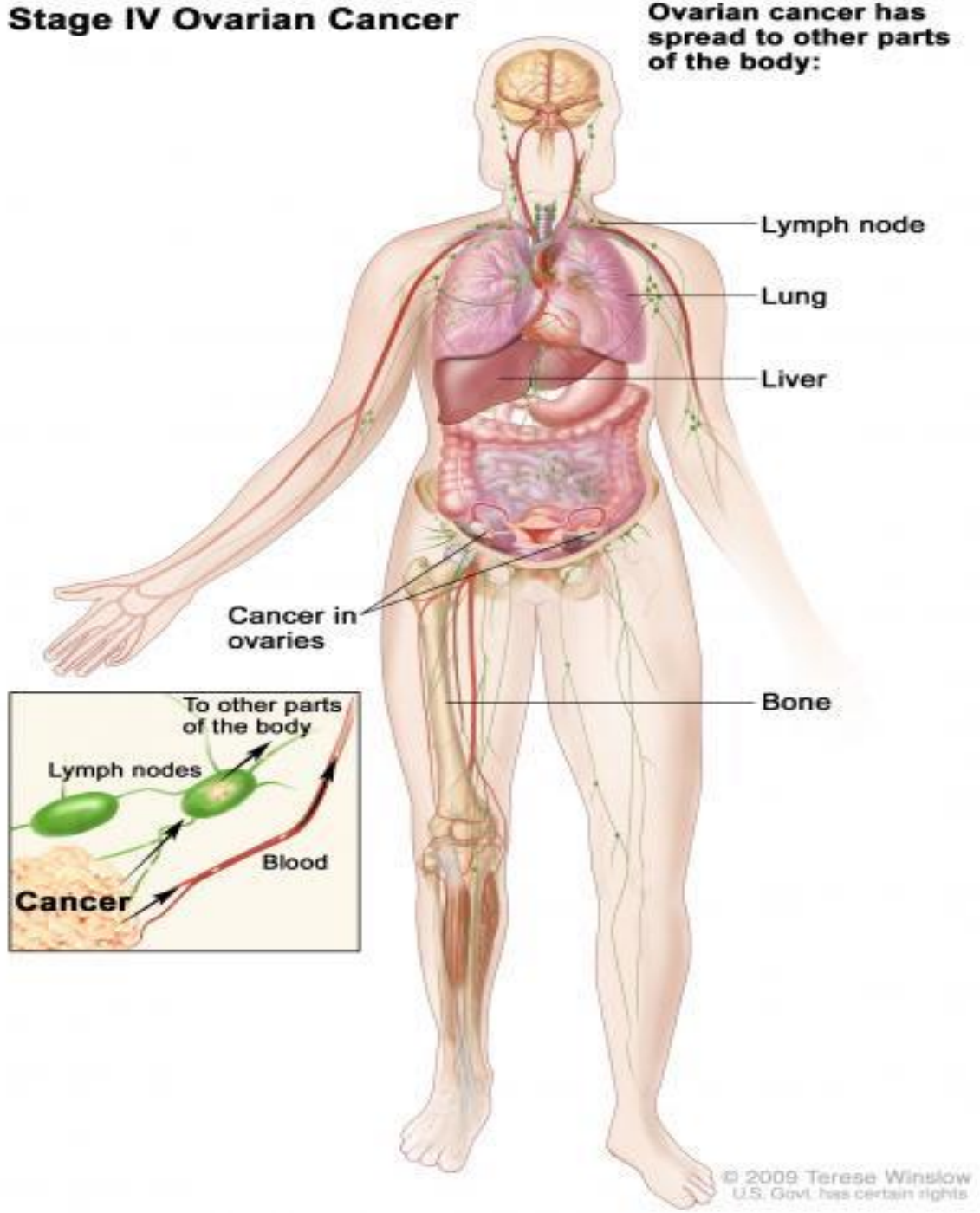
Stage IV Ovarian Cancer
Ovarian cancer has spread to other parts of the body:
Lymph node
Lung
Liver
Cancer in ovaries
Bone
To other parts of the body
Lymph nodes
Blood
Cancer
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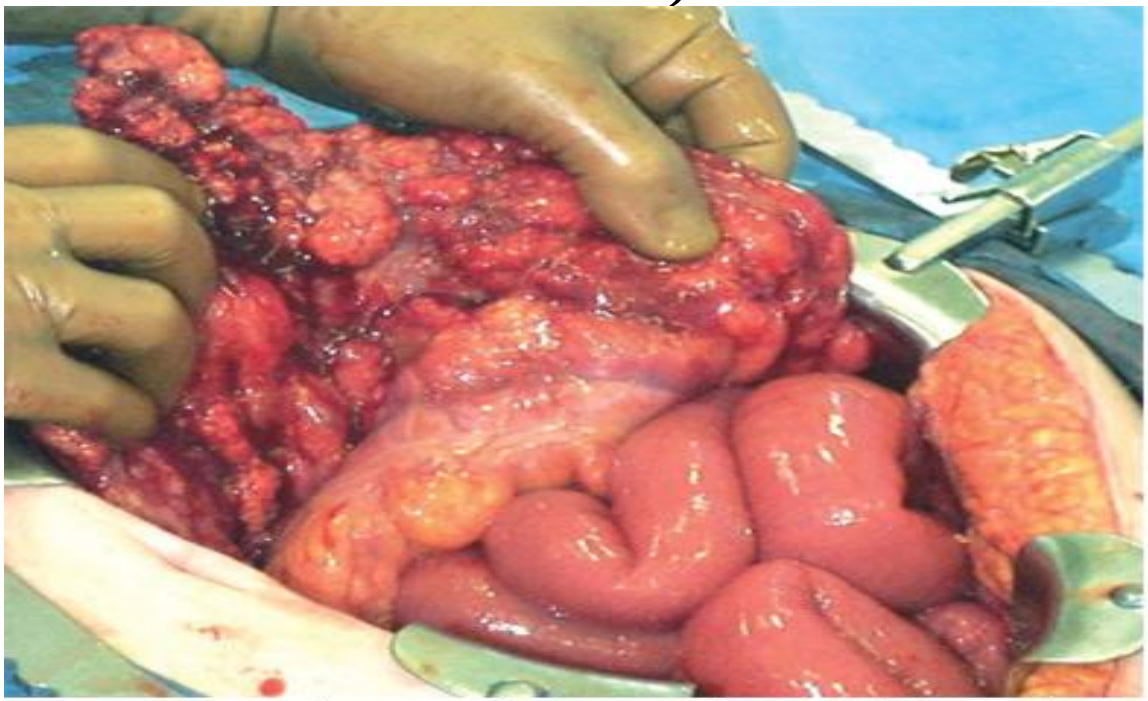
Surgery:

- surgery remains necessary for diagnosis, staging and treatment of epithelial ovarian cancer.
- Surgery includes total hysterectomy, bilateral salpingo-oophorectomy & infracolic omentectomy.
- The aim of surgery is complete or optimal cytoreduction (where <1 cm of residual macroscopic disease is left behind).



Source: B. Y. Karlan, R. E. Bristow, A. J. Li: Gynecologic Oncology: Clinical Practice and Surgical Atlas
www.obgyn.mhmedical.com

- In young nulliparous woman with unilateral tumour & no ascites, unilateral salpigo-oophorectomy may be justified after exploration to exclude metastatic disease & curettage of the uterine cavity to exclude synchronous endometrial tumour.

- If the tumour is subsequently found to be poorly differentiated or the washing is positive, a second operation to clear the pelvis will be necessary.

- Interval debulking surgery: When bulky disease remains after initial surgery, chemotherapy should be given in two to four courses then a second laparotomy is performed after which chemotherapy is resumed as soon as possible.

- If a patient is unfit or unwilling to have surgery, or if preoperative assessment indicates that complete debulking is unlikely to be achievable, primary chemotherapy may be offered. If the patient responds to the chemotherapy, interval surgery can be carried out after three cycles.

- In borderline tumours ovarian cystectomy or oophorectomy are adequate in young women while hysterectomy & bilateral salpingo-oophorectomy is advisable for older women.

Chemotherapy:

- stage II-IV & stage Ic.
- given as primary treatment, as an adjunct following surgery or for relapse of disease.
- given to prolong clinical remission & survival, & for palliation in advanced & recurrent disease.
- 3 weeks apart for six cycles.
- The platinum drugs, cisplatin & its analogue carboplatin are heavy metal compounds which cause cross-linkage of DNA strands.

- Carboplatin is the drug of choise, as effective as cisplatin with lesser side effects.
- Paclitaxel works by causing microtubular damage to the cell thus prevents replication and cell division.
- Bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF), inhibits angiogenesis, clinically effective at improving recurrence free and overall survival when given in combination with carboplatin and paclitaxel in advanced ovarian cancer

- Follow-up of patients includes clinical examination and CA125 measurement

Prognosis: The overall 5-year survival from ovarian cancer is 46%

Prognostic factors
Stage of diseae
Volume of residual disease post surgery
Histological type and grade of tumour
Age at presentation

FIGO stage	5-year survival (%)
1	80–90%
2	65–70%
3	30–50%
4	15%

Primary peritoneal carcinoma

- PPC is a high-grade pelvic serous carcinoma, histologically indistinct from tumours arising from the Fallopian tube or ovary.
- Criteria for diagnosis includes:
  - Normal sized or slightly bulky ovaries.
  - More extraovarian disease than ovarian disease.
  - Low volume peritoneal disease.
- The clinical behaviour, prognosis and treatment is the same as for other high-grade pelvic serous carcinomas, with a trend towards using primary chemotherapy as complete surgical debulking is difficult.

Sex cord stromal tumours:

- they are tumours of low malignant potential with a good long-term prognosis.
- morbidity may arise from the oestrogen (granulosa, theca cell) or androgen production (Seroli–Leydig)
- Presentation
- staging system is the same as for epithelial tumours. Most present as stage I.
- Treatment: surgical treatment is the same as for epithelial tumours. Unilateral oophorectomy is indicated in young women with stage Ia disease.

Malignant Germ cell tumours: mainly in young women.

- Dysgerminomas account for 50% of all germ cell tumours. occasionally secrete human chorionic gonadotrophin (hCG).
- Endodermal sinus yolk sac tumours are the second most common germ cell tumours, accounting for 15% of the total. secrete α-fetoprotein (AFP). present with a large solid mass that often causes acute symptoms with torsion or rupture.
- Immature teratomas account for 15–20% of malignant germ cell tumours
- Non-gestational choriocarcinomas are very rare, usually presenting in young girls with irregular bleeding and very high levels of hCG.

Clinical features:

- Present in young woman with a large solid ovarian mass that is rapidly growing.
- Tumour markers are measured preoperatively.
- MRI is helpful to assess morphology, particularly within teratomas.
- CT scaning of the abdomen allows assessment of the liver and lymph nodes.
- All patients should have a chest X-ray to exclude pulmonary metastases

Treatment:

- fertility-sparing treatment may be preferred for young patients.
- exploratory laparotomy, remove the tumour and assess contralateral ovary. Careful inspection of the abdominal cavity, peritoneal biopsies and sampling of any enlarged pelvic or para-aortic nodes.
- Postoperative chemotherapy depends on stage of disease. combination of bleomycin, etoposide and cisplatin (BEP), given as a course of three to four treatments, 3 weeks apart. This regime gives long-term cure rates of over 90% and also preserves fertility if required.

Thank you for listening