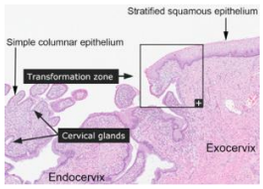
Dr. Kamil lecture notes:

Endometrial, ovarian & cervical cancers



- Ectocervix, vagina, vulva & perineum are lined by stratified squamous cell epithelium.
- Endocervix & endometrium is lined by simple columnar epithelium.
- The transition zone is the area in the cervix where the columnar epithelium of the endocervix meets the stratified squamous epithelium of the ectocervix. This junction is dynamic and changes with age and hormonal status.
  Clinical importance: Site of metaplasia and cervical cancer.
- The endosalpinx of the fallopian tube is lined by ciliated epithelium, which plays a crucial role in facilitating sperm movement & transport of the fertilized egg to the endometrial cavity.

Endometrial cancer

Presentation	Risk factors	Diagnosis	Treatment
○ The most common gynecologic malignancy in developed countries. ○ The most common presentation is abnormal bleeding (time, amount, presentation, …). ○ Mostly affects peri-menopausal & early post-menopausal women. 2 types: ○ The estrogen-related (type I; endometroid type): 80%, younger age, perimenopausal women with a history of exposure to unopposed estrogen, either endogenous or exogenous. Usually begin as hyperplasic and progress to carcinoma. Better differentiated, more favorable prognosis. 5 year survival about 85%. ○ Non-estrogen related (type 2): May arise in a background of atrophic endometrium; not estrogen sensitive. Less differentiated, high grade, poor prognosis, average age about 67 years, 5 year survival about 58%. May occasionally develop after radiation for cervical cancer	Any situation cause unopposed effect of estrogen (increased estrogen exposure) >> risk of endometrial growth & type 1 endometrial cancer: ✓ Low parity or nullparity or old age at first birth. ✓ Early menarche & late menopause. ✓ Anovulatory cycle: mcc is PCOS [extra note: it is genetic syndrome disorder, no complete cure]. ✓ Obesity, highest incidence. ✓ Diabetes mellitus type 2. ✓ Exogenous exposure of estrogen (HRT without progestin). ✓ Tamoxifen therapy (used in breast cancer treatment, anti-estrogenic on breast, estrogenic on the endometrium). ✓ Endometrial hyperplasia (gland to stroma ratio >50%). ✓ Lynch syndrome *Postmenopausal bleeding with an endometrial thickness of 10 mm (normal is typically <4-5 mm in postmenopausal women not on HRT) is highly suspicious for endometrial carcinoma until proven otherwise. *Protective factors: parity & OCP.	❖ History taking (ask about menstrual history and hormonal history). ❖ Physical examination. ❖ Investigations: ✓ The best tool for diagnose endometrial cancer is MRI. ✓ Definitive diagnosis: hystrescopic endometrial biopsy. *Surgical staging (cytology, LN biopsy, omental biopsy, peritoneal nodules nodules) is done in: 1. Grade 3 tumor 2. Grade 2 tumor >2cm in diameter 3. Clear cell or papillary serous carcinoma 4. > 50% of myometrial invasion 5. Cervical extension *Prognostic variables: Stage (the most important),histology type, nuclear grade, vascular invasion, size, hormone receptor status, DNA ploidy, type of therapy.	❖ First line: hysterectomy & bilaterally salpingo-oophorectomy. ○ Stage I and Stage II Occult: TAH (Type I) + BSO. ○ Clinical Stage II: Modified (type II) or radical hysterectomy (type III) + BSO + PLA + surgical staging ± adjuvant radiation. ○ Stage III Radical hysterectomy + BSO + PLA + surgical staging ± adjuvant radiation ± adjuvant chemotherapy. ○ Stage IVA: modified pelvic exentration, with or without pelvic radiotherapy or chemotherapy. ○ Stage IVB: cytoreductive surgery ± adjuvant radiation ± adjuvant chemotherapy. ❖ The role of chemotherapy just to help the action of radiotherapy (no primary role in Tx). ❖ 5-10% of cases at the early presentation there is micrometastasis in the ovaries. ❖ 5-10% of cases they will devolve another primary ovarian cancer within 5-10 years.

Extra note:

- There are 4 types of estrogen:
  1. **Estrone E1** [in adipose tissue, highest in post-menopause].
  2. **Estradiol E2** [the most potent, highest in the reproductive years].
  3. **Estriol E3** [the weakest, estrogen of pregnancy].
  4. **Estetrol E4** [produced by the fetal liver, one of the markers that is used to assess a healthy pregnancy].

FIGO Stage	Description
IA	Tumor confined to uterine corpus, <50% myometrial invasion
IB	Tumor confined to uterine corpus, >50% myometrial invasion
II	Tumor invades cervical stroma but does not extend beyond the uterus
IIIA	Invasion of uterine serosa and/or adnexa
IIIB	Tumor involves vagina and/or parametrium
IIIC1	Metastases to pelvic lymph nodes
IIIC2	Metastases to para-aortic lymph nodes, with or without pelvic nodal involvement
IVA	Invasion of bladder or bowel mucosa
IVB	Distant metastases, including intra-abdominal metastases and/or inguinal nodes

- The most common gynecological cancer in the **developed** countries: **endometrial cancer**
- The most common gynecological cancer in the **developing** countries: **cervical cancer**

Cervical cancer

Presentation	Risk factors	Diagnosis	Treatment
○ The third most common gynecologic cancer. ○ Mean age 50. ○ 85 % of cervical neoplasm arise from ectocervix. ○ Cervical cancer presents with abnormal bleeding (usually postcoital bleeding) and malodorous discharge. ○ The most common laboratory finding is an abnormal Pap smear test result. ○ Adenocarcinoma: younger age, HPV 18 (more). ○ SCC: 85%, older age, HPV 16, high parity, associated more with early age of sexual activity, multiple sexual partners, high gravidity. ○ Prevention: ➢ HPV vaccine . ➢ Regular speculum examination including Pap smear (negative pap smear does not exclude the diagnosis).	HPV-related risks factors: any situation increase the chance of infection: ✓ Early marriage ✓ First coitus at a younger age (<17 yo). ✓ Multiple sexual partners. ✓ Married to man with multiple sexual partners. ✓ Immunosuppressants drugs. ✓ High parity. ✓ Lower socioeconomic status Non-HPV risk factors: ✓ Smoking (cause damage to langerhans cells which is a part of local immunity system at the level of the cervix). ✓ OCP if used more than 5 years continuously; unopposed action of estrogen.	❖ History (ask about menstrual history and hormonal history). ❖ Physical examination (speculum is the most important). ❖ Investigations: ✓ The best tool for diagnose cervical cancer is MRI. ✓ Biopsy for definitive Dx. ✓ Cystoscopy, sigmoidoscopy, hysteroscopy, colonoscopy to r/o invasion. ✓ Pan-CT for metastasis. ✓ PET scan	❖ Up to stage 2A (involvement of the cervix, upper 1/3 vagina, without involvement of myometrium) >> surgery is the first line ❖ Up to 2A = no parametrial invasion ❖ Surgery (hysterectomy) followed by radiotherapy +/- chemotherapy. ❖ Beyond stage 2A >> radiotherapy -/+ chemotherapy ❖ To know if there is parametrial invasion or not: (1) Reactovaginal exam (2) MRI ❖ The role of chemotherapy is to help the action of radiotherapy. ❖ No primary role for chemotherapy in treatment.

Ovarian cancer

Presentation	Risk factors	Diagnosis	Treatment
○ The second most common cancer after endometrial cancer. ○ Ovarian cancer may presents with non-specific GI symptoms (gastric upset, ~~abdominal destination~~, nausea, vomiting, loss appetite).abdominal distension).	✓ Early menarche & late menopause. ✓ Late first pregnancy. ✓ Nullparity. ✓ Infertility. ✓ PCOS. ✓ Hormone secreting tumor. ✓ Exogenous estrogen.	❖ History taking (ask about menstrual history and hormonal history). ❖ Physical examination ❖ Investigations: ✓ The best tool to diagnose ovarian cancer is ultrasound (abdominal or vaginal US, but the vaginal US is better because it will shows the: fiber-like projections, high vascularity, septations, nodularity, mass criteria). ✓ Pan-CT, MRI, PET scan for metastasis.	❖ First line is surgery: cytoreductive surgery (also called radical debulking surgery), resection of uterus, ovaries, fallopian tubes, parametrium, broad ligaments, supporting ligaments, omentum, pelvic lymph nodes // with biopsy from the peritoneal cavity & peritoneal wall, mesentery & any suspensions lesion. ❖ Alternatives if there is contraindications: neoadjuvant chemotherapy followed by surgery. ❖ No role for radiotherapy or hormonal therapy.

Follow up for all of them

❖ Every 3 months in the first 2 years
- ✓ Ovarian cancer history of constipation, diarrhea & vomiting >> Abdominal US
- ✓ Cervical & endometrial cancer >> vault smear every 3 months for 2 years, then every 4 months every 2 years, then 6 months every 1 year, ca 125, CBC & chest X-ray every visit, annual CT.
- ✓ 80-90% of cases the recurrence comes within the first 18 months after the primary treatment.

Shahed Atiyat