“Truth is stranger than fiction, but it is because Fiction is obliged to stick to possibilities; Truth isn't.”

“The things you do for yourself are gone when you are gone, but the things you do for others remain as your legacy.”

Uterine Cancer

Most common malignancy in the female genital tract; the highest rate in developing countries while the lowest in India.

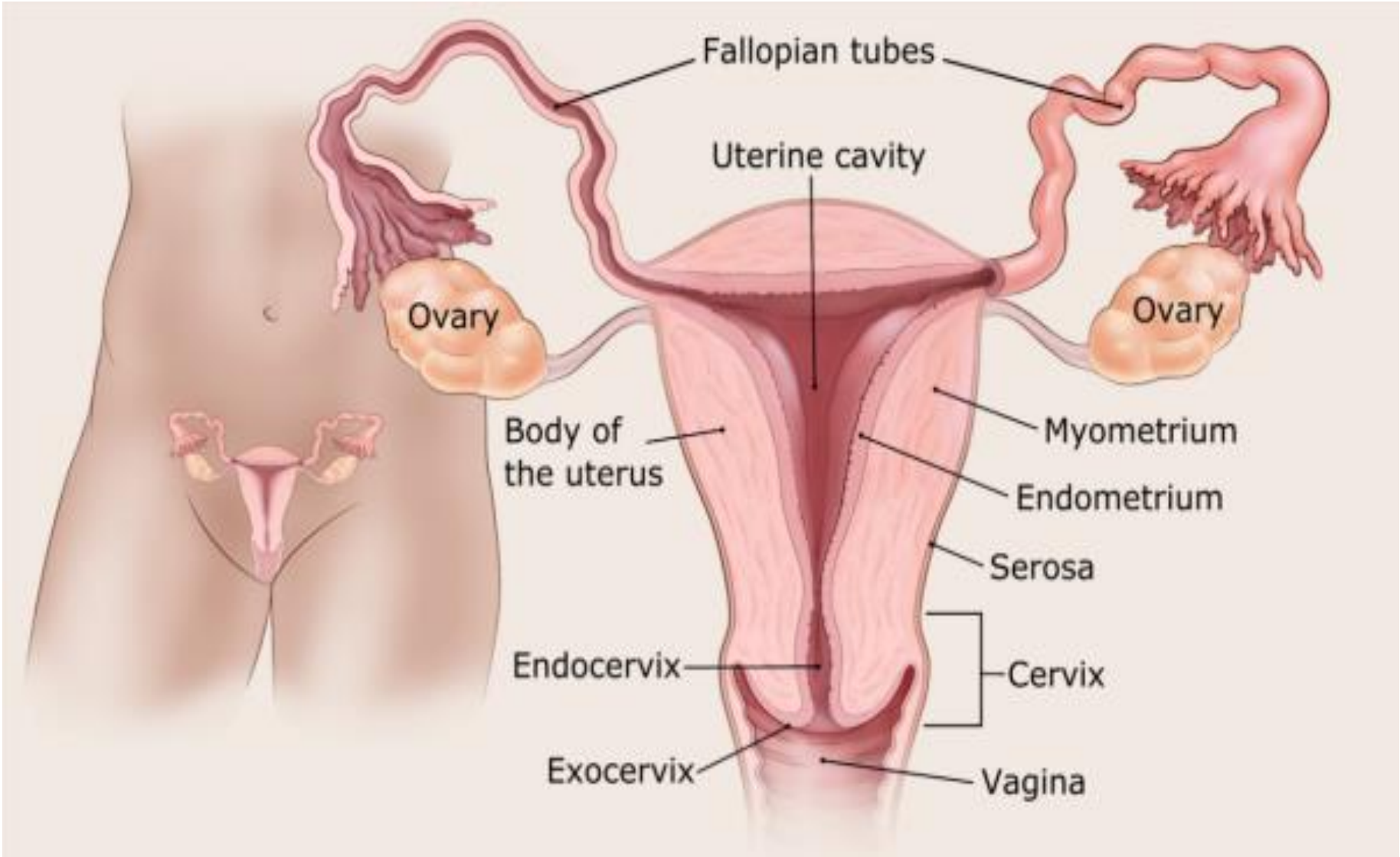
USA→ around 50%

JORDAN→ around 45%

Overall, about 2% to 3% of women develop endometrial cancer during their lifetimes.

Uterine cancer is the most common gynecologic malignancy in developed countries.

The second most common in developing countries (cervical cancer is more common).


Fallopian tubes
Uterine cavity
Ovary
Ovary
Body of
the uterus
Myometrium
Endometrium
Serosa
Endocervix
Cervix
Exocervix
Vagina

* Mean Age: 60 years; mostly between 50-59, 75% in women older than 50 years.
* Less than 5% are asymptomatic.
- Key: Increased circulating levels of unopposed estrogen
- Three to 20 percent of women with postmenopausal bleeding are found to have endometrial carcinoma.
- Another 5 to 15 percent have endometrial hyperplasia

Endometrial Cancer Risk Factors

Risk Factors	Risk
- Obesity	2.5-4.5x
- Nulliparity;	
compared with 1 child	2x
compared with 5 or more children	3x
- Late menopause	2.4x
- Diabetes mellitus	2.8
- Unopposed estrogen therapy	4-8
- Tamoxifen therapy	2-3
- Atypical endometrial hyperplasia	8-29
- Lynch II syndrome	20

↑ body fat → to ↓circulating progesterone,

and → to ↓SHBP → to ↑production of endogenous non-protien-bound estradiol → to endometrial hyperplasia and malignancy.

In D.M;

High levels of insulin-like growth factor I, coupled with elevated level of estrogen are thought to have neoplastic potential

Endometrial Hyperplasia

Proliferation of endometrial glands resulting in a greater gland-to-stroma ratio (>50 percent) than observed in normal proliferative endometrium. The proliferating glands vary in size and shape, and cells may have cytologic atypia.

The D-score is an integral part of the EIN classification.

- Simple hyperplasia consists of glands that are mildly crowded. They are frequently cystically dilated with only occasional outpouching. Mitoses are typically present in the glandular cells.

* Complex hyperplasia consists of glands that are crowded (>50 percent gland to stroma ratio); the gland-to-stroma ratio is higher in complex hyperplasia compared with simple hyperplasia. The glands appear disorganized and have luminal outpouching. Mitoses are typically present.

Nuclear atypia – Nuclear atypia is the presence of nuclear enlargement; the chromatin may be either evenly dispersed or clumped, and/or prominent nucleoli may be present. Gland crowding lined by atypical cells is the hallmark of endometrial intraepithelial neoplasia.

Diagnostic categories are based primarily upon two factors:

- -Nuclear atypia.
- -Degree of glandular crowding and complexity.

Lynch syndrome

- Oncology advises genetic assessment for Lynch syndrome for those who meet any of the following criteria:

- Endometrial cancer diagnosed prior to age 50
- Presence of synchronous or metachronous colorectal
- Endometrial cancer with tumor-infiltrating lymphocytes, peritumoral lymphocytes,
- lower uterine segment origin diagnosed in a patient less than age 60
- One or more first-degree relatives with a Lynch-associated tumor, with one of the cancers being diagnosed under age 50
- Endometrial or colorectal cancer diagnosed in two or more first- or second-degree relatives with Lynch-associated tumors regardless of age
- Patients with a first- or second-degree relative with a known

Warning

- PMW on exogenous estrogens.
- Women from families with hereditary nonpolyposis colorectal cancer syndrome.
- Premenopausal women with anovulatory cycles.
- High risk patients; current technologies could, at best, detected only 50%of frank endometrial cancer.
- Only 50% have malignant cells on Pap smear.

Screening

- Pap smear
- Transvaginal endometrial thickness with a cut off value of 9 mm.
- Tamoxifen therapy (cystic glandular dilatation, stromal edema, hyperplasia)

- endometrial thickness of 4 mm or less in PMW is consistent with atrophy.

Two different subtypes

- The estrogen-related (type I; endometroid type), 80%, younger age, perimenopausal women with a history of exposure to unopposed estrogen, either endogenous or exogenous; estrogen sensitive
- Usually begin as hyperplasic and progress to carcinoma.
- Typically are preceded by atypical endometrial hyperplasia.
- Better differentiated, more favorable prognosis.
- 5 year survival about 85%.

Non-estrogen related (type II, non-endometroid)

- No estrogen stimulation; no endometrial hyperplasia.
- May arise in a background of atrophic endometrium; not estrogen sensitive
- Less differentiated, high grade, poor prognosis.
- 20%, average age about 67 years, 5 year survival about 58%.
- May occasionally develop after radiation for cervical cancer.
- Carcinosarcomas fall into this group.

Symptoms

- Abnormal vaginal bleeding, (90%) → PMB.
- Intermenstrual bleeding.
- Heavy prolong bleeding in perimenopausal women.
- Anovulatory premenopausal women.
- Asymptomatic.

Post Menopausal Bleeding

Cause of bleeding	percentage
• Endometrial atrophy	60-80
• Exogenous Estrogen	15-25
• Endometrial cancer	15-20
• Endometrial or cervical polyps	02-12
• Endometrial hyperplasia	05-10

Signs

- ± Obese, hypertensive, postmenopausal women.
- ± Hematometra
- ± Uterine enlargement.
- ± breast findings.
- Recto-vaginal examination

Diagnosis

- Office endometrial biopsy is suspected women, 90% to 98% when compared to Hysteroscopy, D&C.
- Fractional D&C.
- A Pap Test is unreliable as only 30% to 50% of patients with endometrial cancer have abnormal test.

Preoperative evaluation /1

- **Complete history and physical examination.**

Routine……..

- Full blood count.
- Serum creatinine and electrolytes, blood sugar.
- Liver function tests
- Electrocardiography.
- Urinalysis
- Chest radiography; mandatory.

Preoperative Investigations/2

Non-routine…..Mostly in type II,

imaging is performed for the purpose of clinical staging;

- Pelvic sonography is often the first-line imaging study to evaluate for other etiologies of abnormal uterine bleeding.
- MRI to detect myometrial invasion or nodal metastases; this is the best tool
- CT scan of the pelvis, and abdomen.
- PET
- CA 125 levels.

If uterine size cannot be assessed with pelvic and abdominal examination (and if pelvic imaging was not done prior to evaluation), pelvic ultrasonography is usually the preferred modality to determine whether the patient is a candidate for minimally invasive hysterectomy.

Spread

- Direct
- Transtubal
- Lymphatic
- Hematogenous

Staging

* Clinical Staging: patients deemed not to be surgical candidates, MRI
* Surgical Staging:

- Identify patients with disseminated disease who are at high risk of recurrence.
- Target postoperative treatment.
- Reduce the number of patients potentially requiring postoperative treatment.
- Possibly eradicate lymphatic disease.

Staging

- Low-risk group:

- Grade 1 or 2 endometroid tumors confined to the inner 1/2 of the myometrium.

- **Intermediate-risk**

- Endometrial cancer includes women with uterine-limited cancer that invades the myometrium (stage IA or IB) or demonstrates occult cervical stromal invasion (stage II).

- High-risk group:

- Endometrial cancer includes women with stage III or higher endometrial cancer, regardless of histology or grade. women with a serous (USC) or clear cell (CC) carcinoma are deemed at high risk, regardless of stage.

  [These women are at a high risk of relapse and death]

- Stage I* Tumor confined to the corpus uteri.
- A* No or less than half myometrial invasion.
- B* Invasion equal to or more than half of the myometrium

- Stage II* Tumor invades cervical stroma, but does not extend beyond the uterus.

- Stage III* Local and/or regional spread of the tumor
  - IIIA* Tumor invades the serosa of the corpus uteri and/or adnexae#.
  - IIIB* Vaginal and/or parametrial involvement#

    » C= the status of lymph nodes

  - IIIC* Metastases to pelvic and/or par-aortic lymph nodes#
    - IIIC1* Positive pelvic lymph nodes.
    - IIIC2* Positive para-aortic nodes with or without pelvic lymph nodes.

- Stage IV* Tumor invades bladder and/or bowel mucosa, and/or distant metastases
- IVA* Tumor invades bladder and/or bowel mucosa
- IVB* Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes.

- * = G1, G2, or G3.
- #= Positive cytology has to be reported separately without changing the stage.

Treatment

- The cornerstone is surgery; TH + BSO
  ; laparotomy, vaginal, laparoscopic, robotic-assisted.
  ± pelvic lymphadenectomy
- ± Adjuvant radiation.
- Radiation therapy as primary treatment.

- Stage I and Stage II Occult: TAH (Type I) + BSO
- Clinical Stage II: Modified (type II) radical hysterectomy + BSO + PLA + surgical staging ± adjuvant radiation.
- Or Radical hysterectomy (type III) + BSO + PLA + surgical staging ± adjuvant radiation.

Surgical staging

- Patients with grade 3 lesions.
- Patients with grade 2 tumors >2 cm in diameter.
- Patients with clear cell or papillary serous carcinoma.
- Patients with greater than 50% of myometrial invasion.
- Patients with cervical extension.

Surgical Staging

* Cytology,
* Lymph nodes biopsy,
* Omental biopsy,
* Biopsy from peritoneal nodules,

Stage III

Radical hysterectomy + BSO + PLA + surgical staging ± adjuvant radiation ± adjuvant chemotherapy.

Or

Cytoreduction — Surgical cytoreduction for EC is typically performed in women who are found to have extrauterine pelvic or intra-abdominal disease or in situations where extrauterine disease is found at the time of initial surgical management.

- Stage IVA: modified pelvic exentration, with or without pelvic radiotherapy or chemotherapy.
- Stage IVB: cytoreductive surgery ± adjuvant radiation ± adjuvant chemotherapy.

Prognostic variables/1

- The stage of the disease: is the most significant prognostic variable.
- Age.
- Histologic type. [increased risk of recurrence, distant metastasis].
- Histologic grade.
- Nuclear grade.
- Vascular space invasion.

Prognostic variables/2

- Tumor size.
- Hormone receptor status.
- DNA ploidy: 2/3 have a diploid DNA; the proportion of nondiploid tumors increase with stage, poor differentiation, depth of myometrial invasion.
- Peritoneal cytology;……***
- Type of therapy.

Adjuvant Radiation

- Observation.
- Vault brachytherapy
- External pelvic irradiation
- Extended filed irradiation.
- Whole-abdominal irradiation.

Adjuvant Chemotherapy

Hormonal Therapy

Follow-Up

History and physical examination remain the most effective methods of follow up; every 3 months in the first 2 years, then every 6 months thereafter.

- Vault smear every 3 months for the first years,
- Vault smear every 4 months for the second years,
- Vault smear every 6 months until 5 years.
- Ca 125 , HE4
- CBC every visit if the primary level was high..
- Chest X-Ray.
- Annual CT scan.

5 Year survival rate

Stage	Rate
I	90%
II	75%
III	55%
IV	15%
NO stage	55%
Overall	75%

Five-year relative survival rates for women with clinical stage I and II endometrial cancer stratified by age

- ≤40 years old – 96 percent
- 41 to 50 years old – 95 percent
- 51 to 60 years old – 85 percent
- 61 to 70 years old – 75 percent
- 71 to 80 years old – 70 percent
- ≥80 years old – 55 percent

Distribution by Stage

Stage	Patients (%)
I	75
II	10
III	10
IV	05

Ovarian Preservation & Estrogen Replacement

- Twenty-five percent are premenopausal, and 5% are under the age of 40 years.
- About 25% of premenopausal may have a synchronous ovarian cancer.
- If both ovaries appear grossly normal, the risk drop down to 1%.
- Still, there is no clear agreement about the possible role of ovarian preservation or safety of estrogen replacement.

	Risk of developing		Risk of dying from	
	%	1 in	%	1 in
• Cervix	0.68	147	0.24	417
• Uterine corpus	2.61	38	0.54	185
• Ovary	1.40	71	1.02	98

A woman with cancer;

- Surgical therapy to remove cancer cells.
- Radiation therapy to kill cancer cells.
- Hormone therapy to block cancer growth.
- Chemotherapy to kill cancer cells.

“You know you're in love when you can't fall asleep because reality is finally better than your dreams.”

“It is better to be hated for what you are than to be loved for what you are not.”