Endometrial Carcinoma

Amina Adel Al-Qaysi

RAK Medical & Health Sciences University

Objectives

- Introduction
- Epidemiology
- Risk Factors
- Protective Factors
- Classification
- Spread
- Clinical Presentation

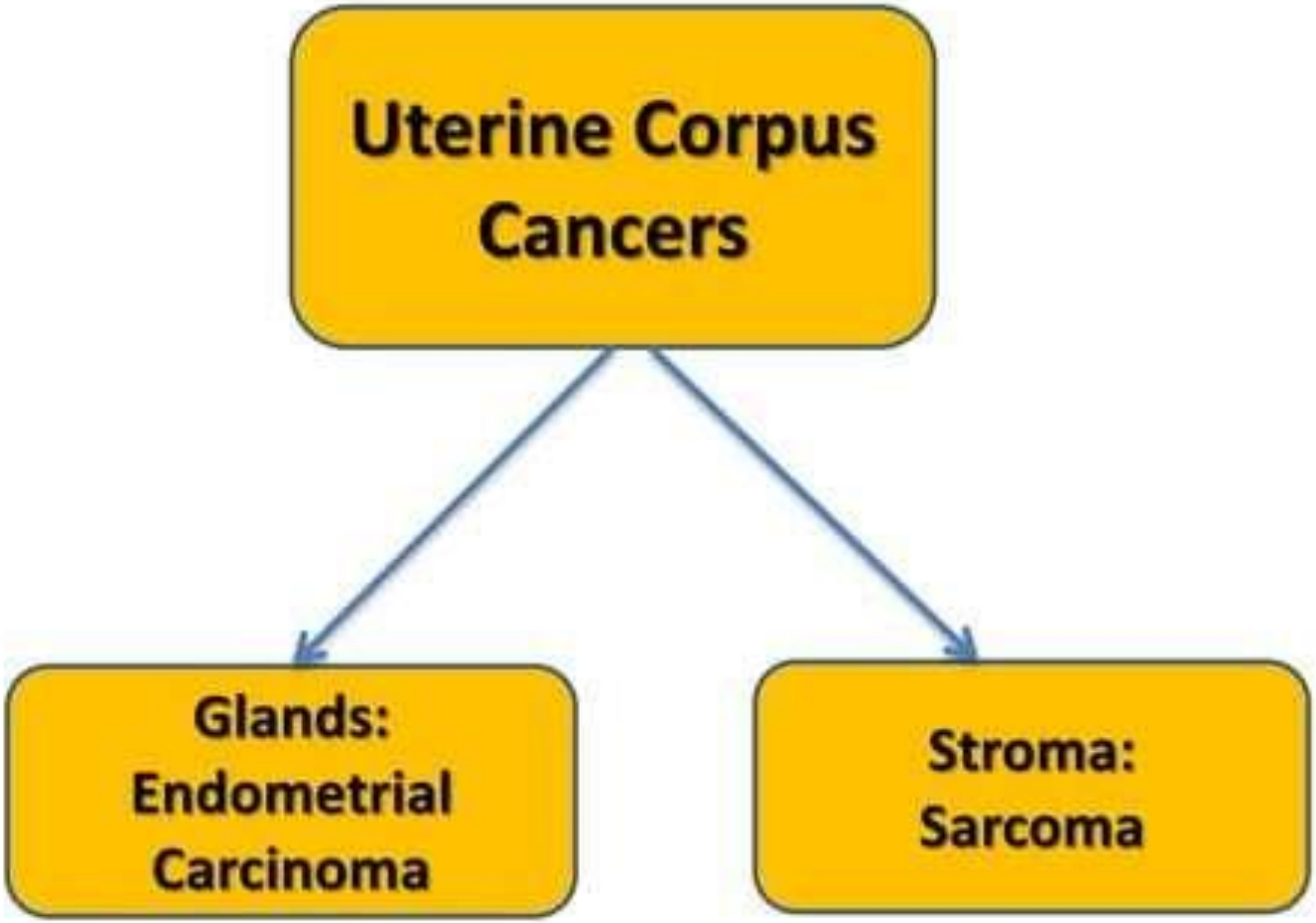
- Investigations
- Staging & Grading
- Treatment
- Follow Up
- Recurrence
- Prognosis
- Prevention
- Screening

Endometrial Carcinoma

- Carcinoma of the endometrial lining of the uterus.
- Most common gynaecological malignancy in postmenopausal women.
- 4th most common malignancy in women (following breast, bowel, & lungs).
- Majority are adenocarcinoma.

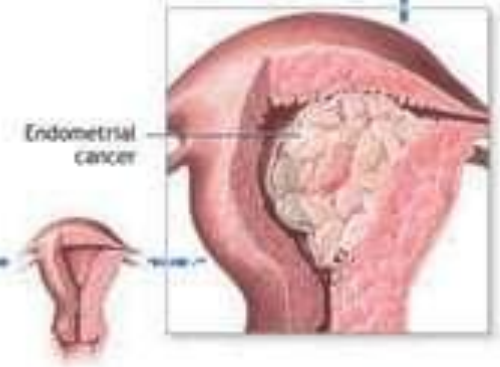
Incidence of Malignant Gynecological Lesions
endometrium > ovary > cervix > vulva > vagina > fallopian tube

Endometrial Carcinoma - Gross


Uterine Corpus Cancers
Glands: Endometrial Carcinoma
Stroma: Sarcoma

Epidemiology

- Most common gynaecological malignancy.
- 8th leading site of cancer-related mortality.
- 2-3% of women develop it in lifetime.
- Disease of postmenopausal women.
- 15%-25% of postmenopausal women with bleeding have endometrial cancer.
- Mean age is 60 years.
- Uncommon before age of 40 years.



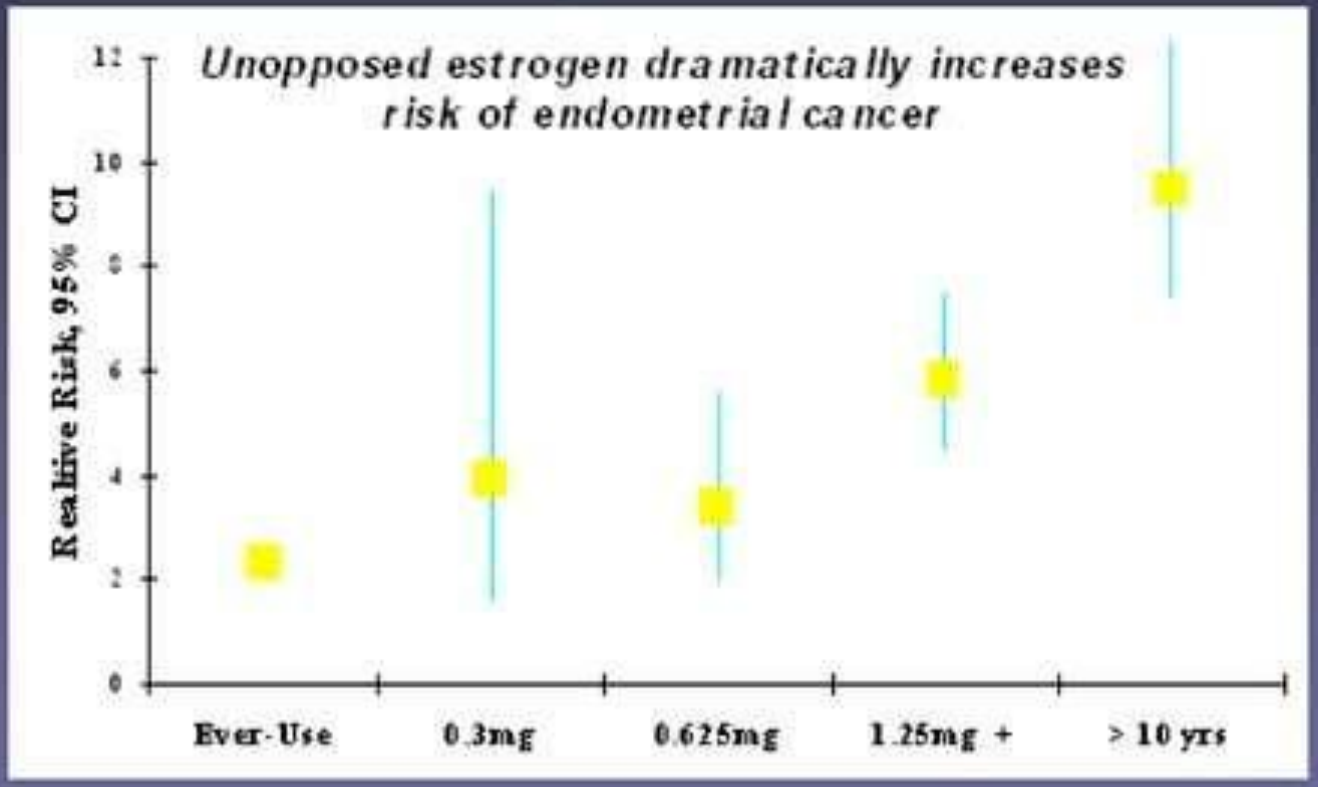
Risk Factors

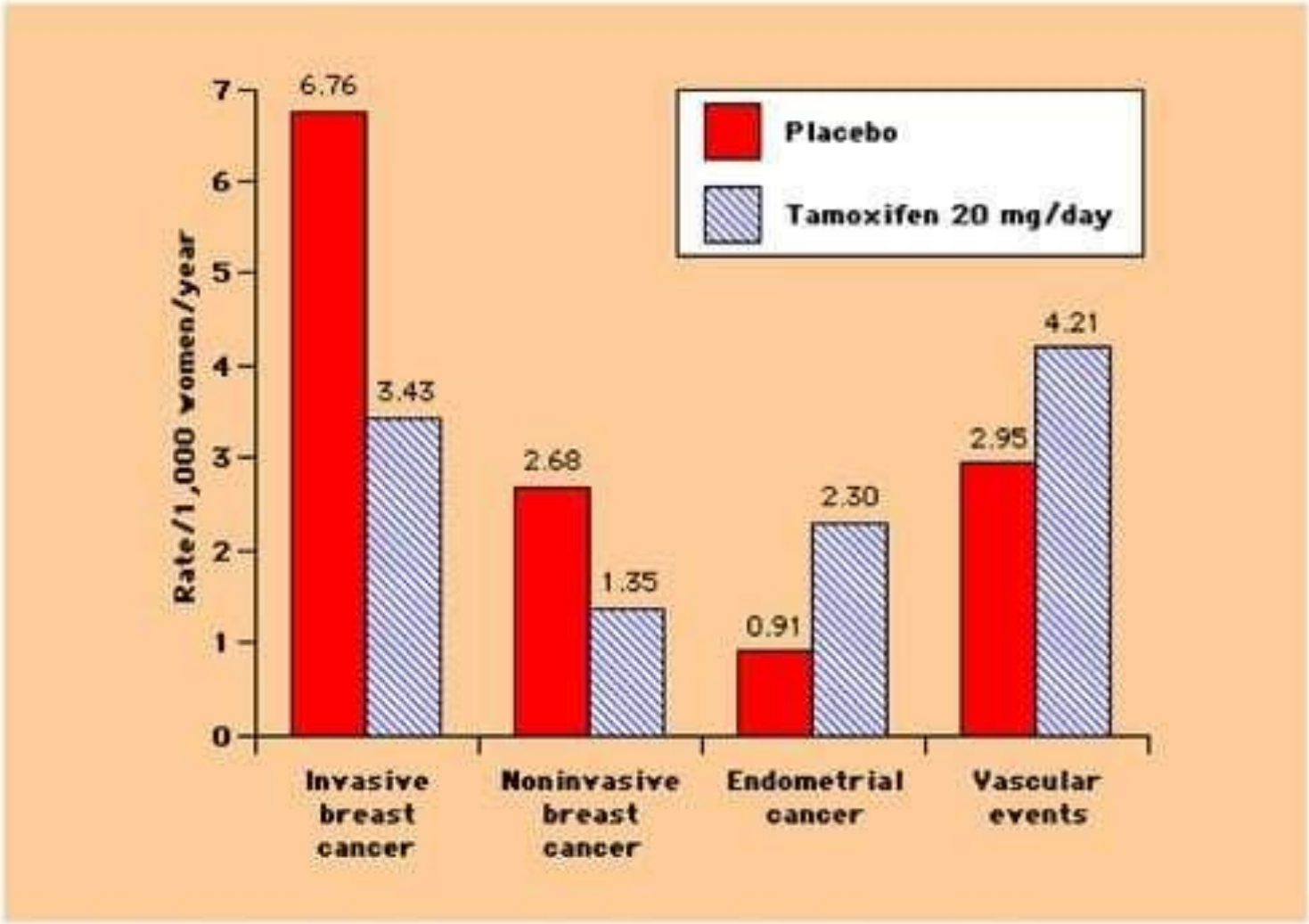
- Older age.
- Early menarche.
- Late menopause.
- Nulliparity.
- Unopposed estrogen (Obesity, PCOS, HRT).
- Chronic Tamoxifen use.
- Previous pelvic irradiation.
- Hypertension, Diabetes mellitus.

Any agent/factor that rises the level or time of exposure to estrogen is a risk factor for endometrial carcinoma

ERT and Endometrial Cancer

Meta-analysis, 30 studies





Varying effects of tamoxifen Tamoxifen decreased the average annual rate of breast cancer in the Breast Cancer Prevention Trial, but increased the rate of endometrial cancer and vascular events such as stroke, pulmonary embolism, and deep vein thrombosis. (Data from Fisher, B, Costantino, JP, Wikerham, DL, J Natl Cancer Inst 1998; 90:1371.)

Risk Factors Cont'd

- Hx of other estrogen-dependent neoplasm (breast, ovary).
- Family Hx of endometrial carcinoma.
- Estrogen-secreting ovarian cancer (e.g. granulosa cell tumor).
- Genetic: Lynch II $ (HNPCC).

Risk Factors for Endometrial Cancer
"COLD NUT"
Cancer, (ovarian, breast, colon)
Obesity
Late Menopause
Diabetes mellitus

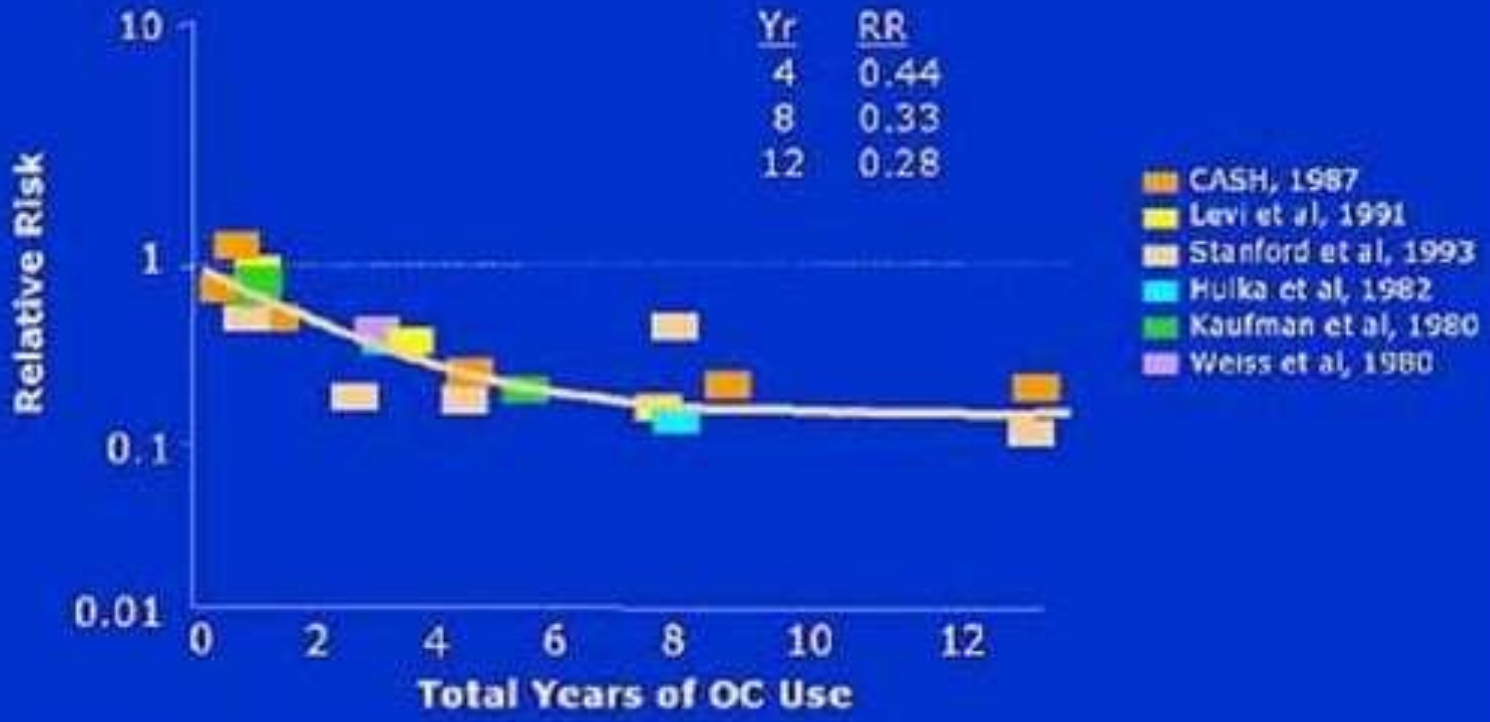
Nulliparity
Unopposed estrogen: PCOS, anovulation, HRT
Tamoxifen, chronic use

Protective Factors

- Multiparity.
- Smoking.
- COCP.
- Physical activity.

Any agent/factor that lowers the level or time of exposure to estrogen is a protective factor against endometrial carcinoma

OCs Reduce Risk of Endometrial Cancer
By Years of Use



Adapted from Schlesselman JJ. *Hum Reprod*. 1997;12:1851-1863.

Classification

TYPE 1

- Associated hyperestrogenism.
- Associated with hyperplasia.
- Patients usually peri-memopausal.
- Estrogen & progesterone receptors common.
- Usually endometrioid & mucinous subtypes.
- Favourable prognosis.

TYPE 2

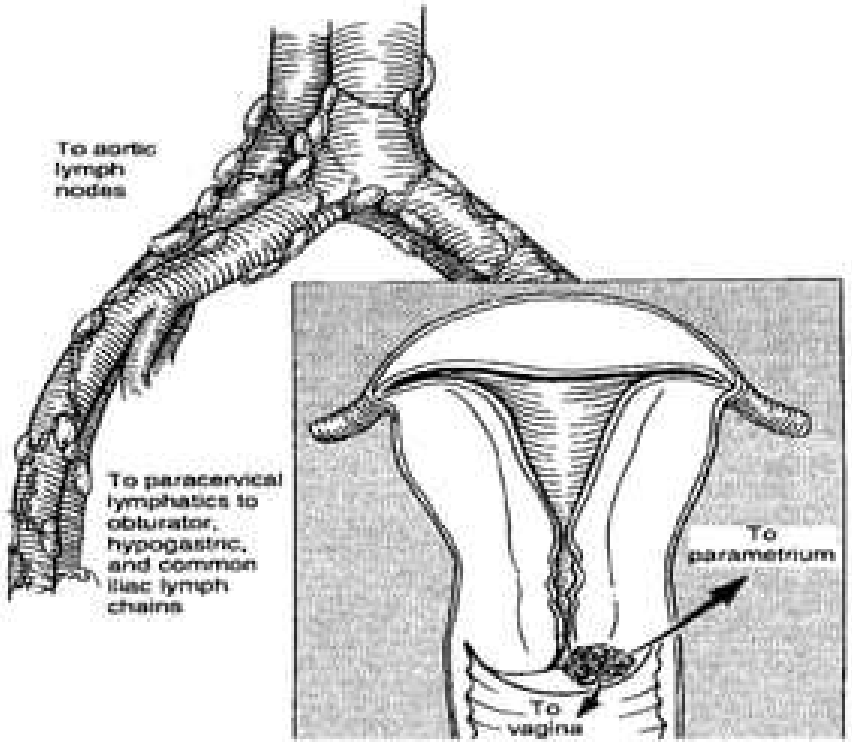
- Not related to hyperestrogenism.
- Usually atrophic endometrium.
- Postmenopausal patients.
- Estrogen & progesterone receptors uncommon.
- Usually serous or clear cell subtypes.
- Aggressive, poor prognosis.

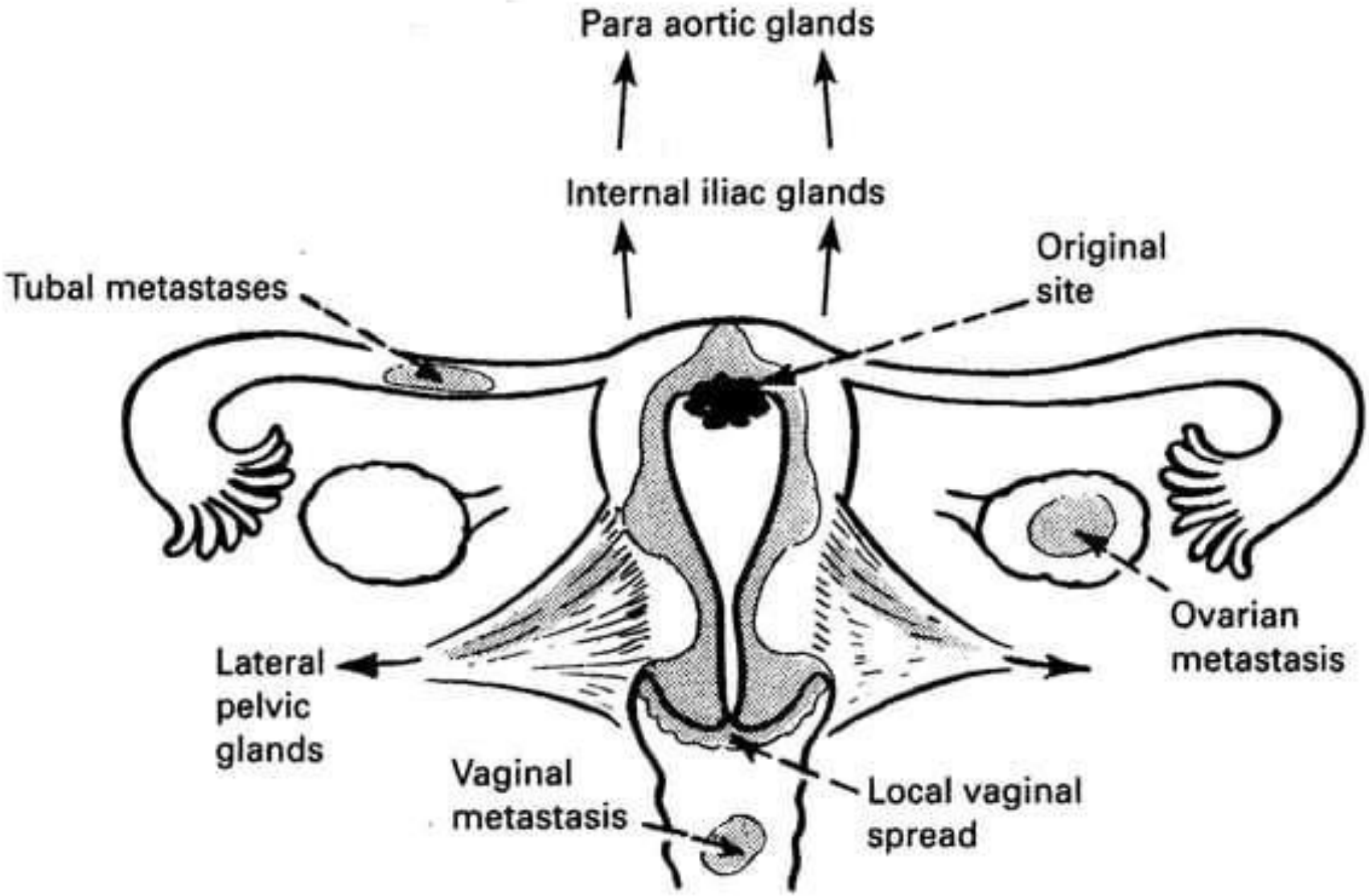
Classification Cont'd

- Endometrioid - Adenocarcinoma (most common 80%).
- Adenosquamous carcinoma (15%).
- Papillary serous carcinoma, Clear cell carcinoma (3-4% overall).

Spread

- Direct extension .. MC
- Lymphatics
- Transtubally
- Haematogenous (Lungs)





Most metastases occur in adjacent structures and peritoneum. In advanced cases distant metastases do occur, most commonly in lung, but occasionally in liver, vertebrae or other bones and in supraclavicular lymph nodes.

Clinical Presentation

Patient Profile

- Postmenopausal
- Nullipara
- Hx of early menarche & delayed menopause
- Obese
- Hypertension
- Diabetes mellitus

Clinical Presentation Cont'd

- Asymptomatic (< 5% of cases).
- **Abnormal bleeding:**
  - Postmenopausal bleeding *
  - Menorrhagia
  - Post-coital spotting
  - Intermenstrual bleeding

Postmenopausal bleeding is endometrial cancer until proven otherwise. 90% present with vaginal bleeding.

- Blood-stained vaginal discharge.
- If + cervical stenosis: Hematometra, Pyometra, purulent vaginal discharge.
- Colicky abdominal pain.

Clinical Presentation Cont'd

Signs:

- Patient's profile.
- Pallor (varying degree).
- **Pelvic examination:**

➢ **Speculum Exam**: Normal looking cervix, blood or purulent discharge through external os.

➢ **Bimanual exam:** Uterus either atrophic, normal, or enlarged. Uterus is mobile unless in late stage.

➢ Per-rectal examination.

➢ Regional lymph nodes & Breast examination.

Diagnosis

- Majority are diagnosed early, when surgery alone may be adequate for cure.

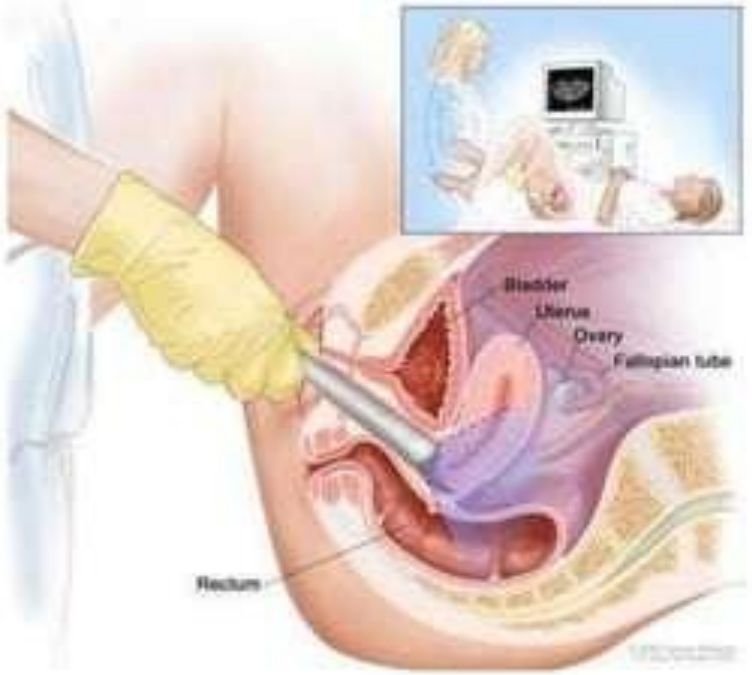
- History + Physical examination.

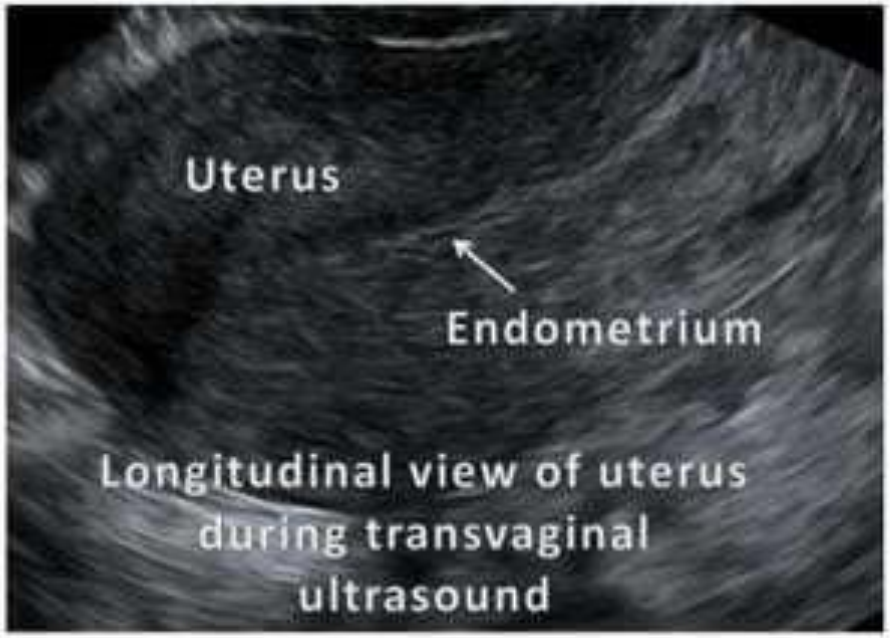
- CBC
- Transvaginal Ultrasound (endometrial thickness).
- Endometrial biopsy.
- Hysteroscopy & endometrial biopsy (Gold standard).

Transvaginal Ultrasound

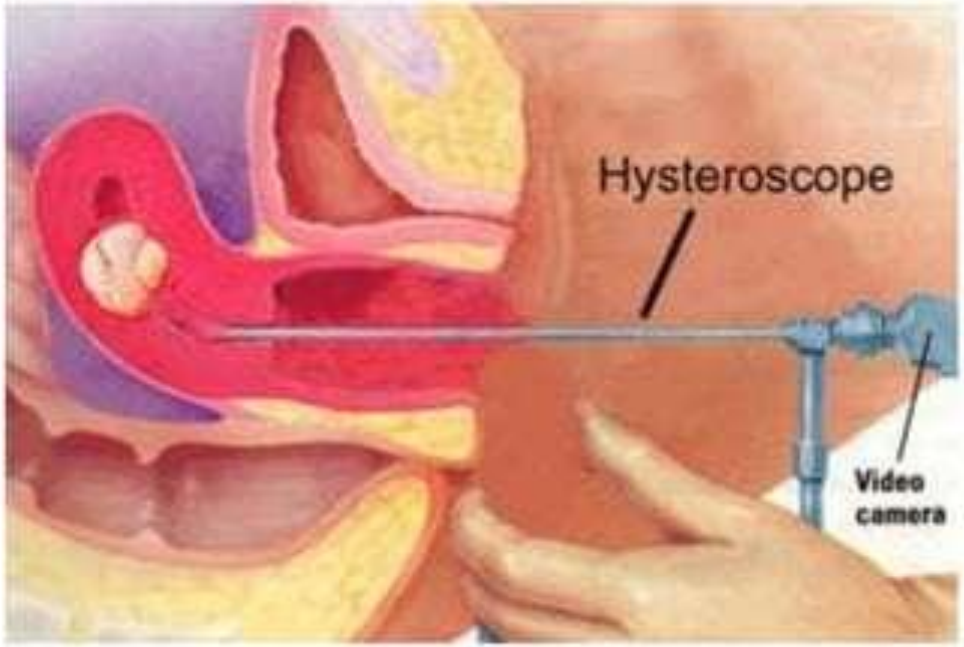
Findings suggestive of endometrial carcinoma:

- Endometrial thickness >5 mm.
- Hyper-echogenic endometrium with irregular outline.
- Increased vascularity with low vascular resistance.
- Intrauterine fluid.

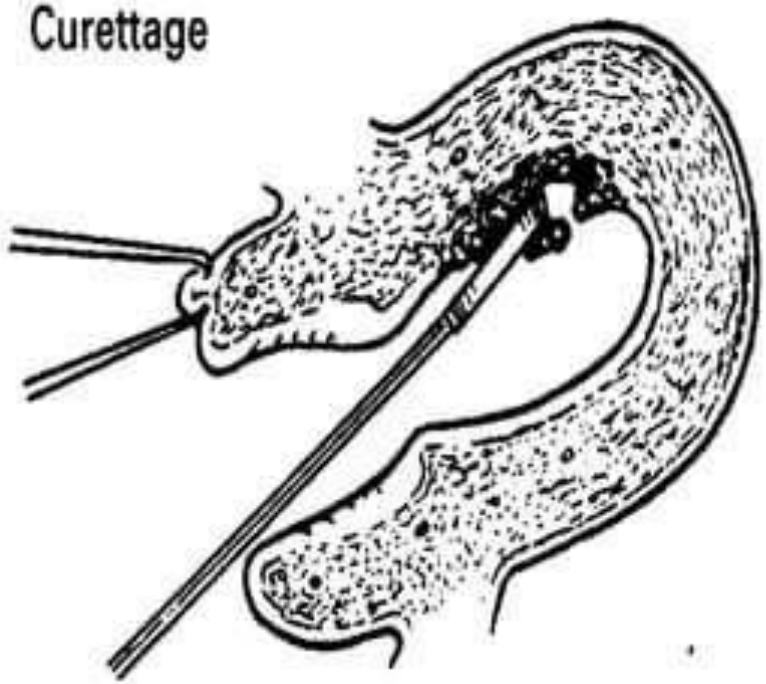

Bladder
Uterus
Ovary
Fallopian tube
Rectum


Uterus
Endometrium
Longitudinal view of uterus during transvaginal ultrasound

Hysteroscopy



Curettage



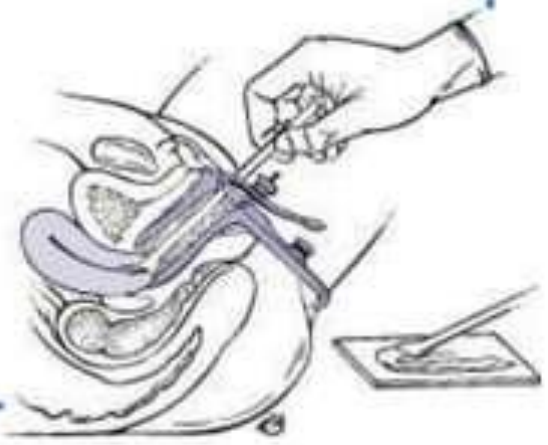
Diagnosis Cont'd

- Pap smear is **not diagnostic**, but a finding of abnormal glandular cells of unknown significance (AGCUS) leads to further investigations.
- Abnormal Pap smears is the presentation

Of **1-5%** of endometrial carcinoma cases.

- Pap smear/endocervical

curettage is required to evaluate cervical involvement.



Diagnosis Cont'd

Pre-operative Evaluation:

- Physical examination
- Blood: CBC, postprandial sugar, urea & creatinine, S.E, LFTs, CA-125.
- Urine: protein, sugar, pus cells.
- ECG
- Chest x-ray
- Pelvic USG
- Abdomeno-pelvic CT scan
- MRI
- PET

FIGO Staging

- ***Based on surgical & pathological evaluation.***

Stage 0: Atypical hyperplasia.

Stage I: Tumor limited to the uterus

I A: Limited to the endometrium

I B: Invasion < 1/2 of myometrium

I C: Invasion > 1/2 of myometrium

Stage II: Extension to cervix

II A: Involves endocervical glands only

II B: Invasion of cervical stroma

FIGO Staging Cont'd

Stage III: Spread adjacent to uterus

III A: Invades serosa or adnexa, or positive cytology

III B: Vaginal invasion

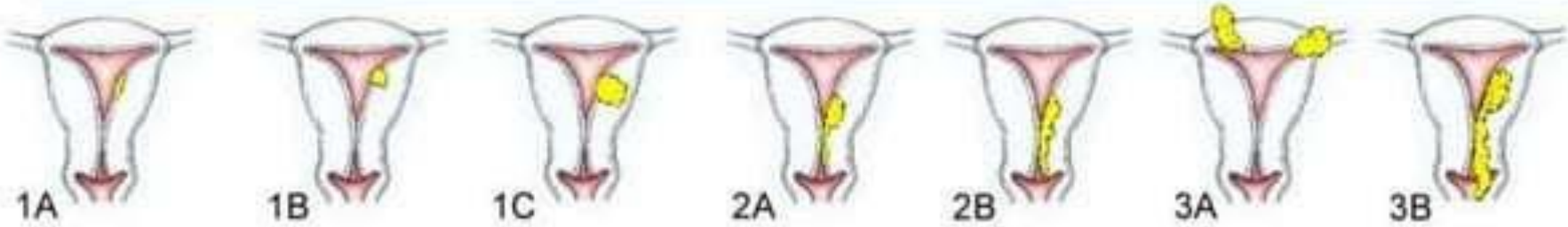
III C: Invasion of pelvic or para-aortic lymph nodes

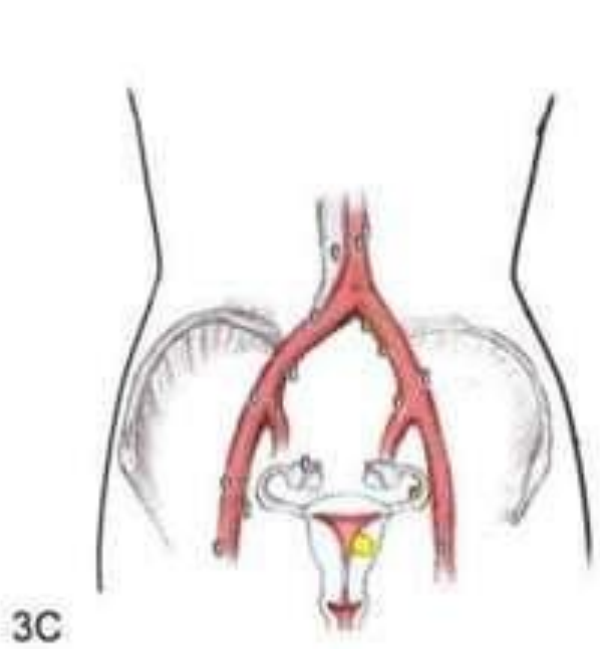
Stage IV: Spread further from uterus

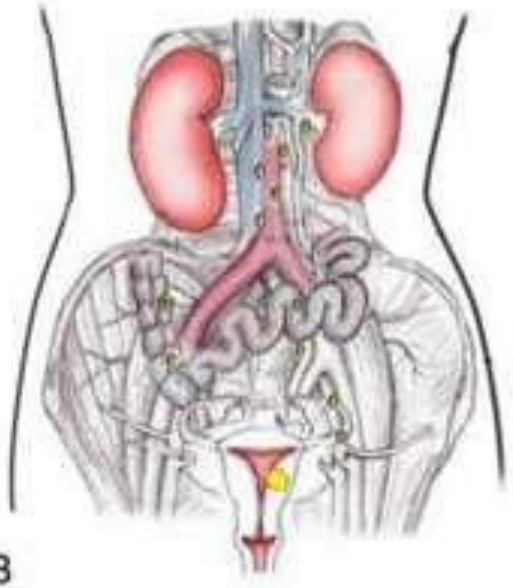
IV A: Involves bladder or rectum

IV B: Distant metastasis

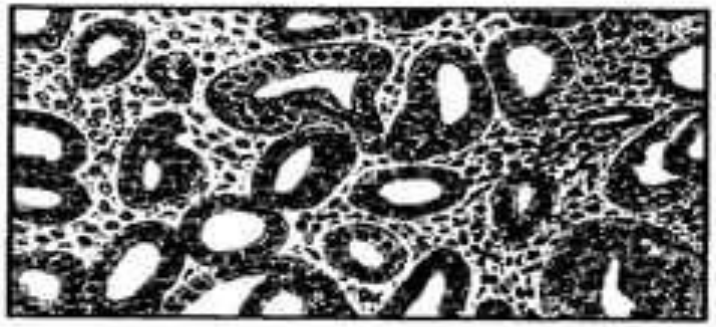
FIGO Staging



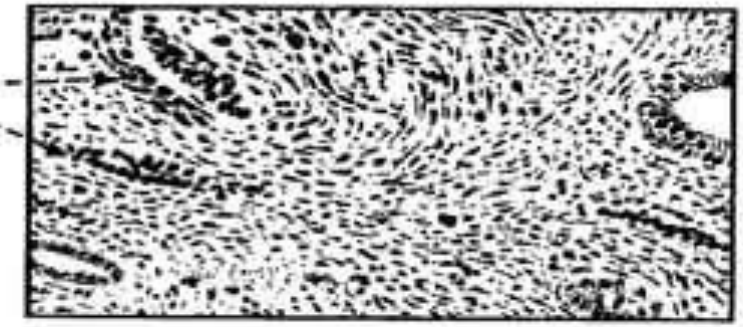




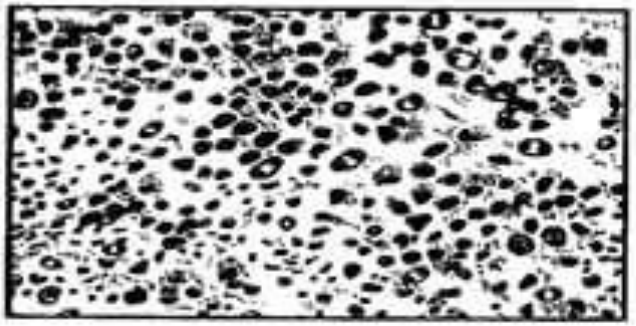
Grades



Grade 1 — well differentiated. Gland forms are conspicuous. Mitotic figures are moderately numerous.



Grade 2 — patchy differentiation. Gland forms are much less prominent and many deposits consist of infiltrating single cell columns or solid masses.



Grade 3. This type consists of solid masses of malignant cells of varying sizes and shapes with little or no stroma. Mitoses are numerous.

Treatment

- Surgery
- Chemotherapy
- Radiotherapy
- Hormonal therapy

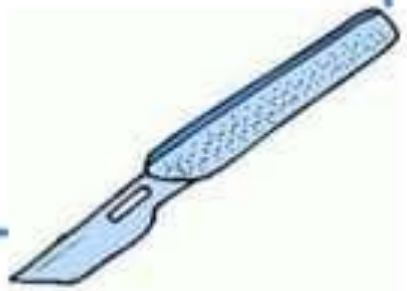
Treatment Cont'd

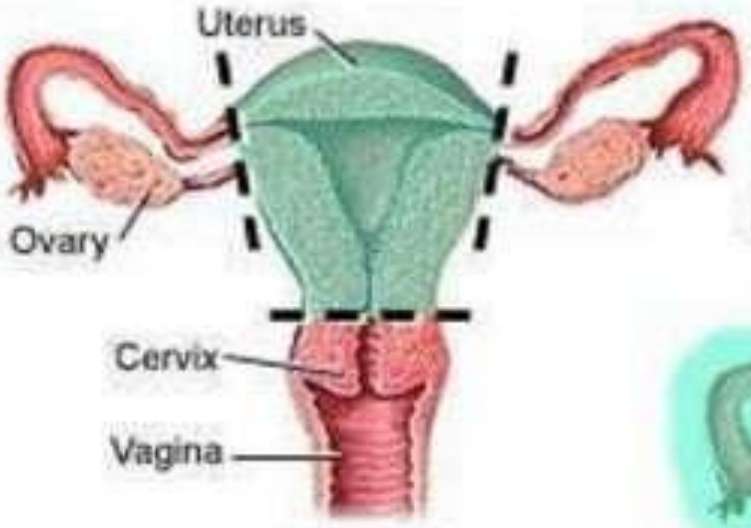
- Based on tumour grade and depth of myometrial invasion.
- ***Surgical:*** TAH+BSO and pelvic washings ± pelvic and periaortic node dissection

➢ Stage 1: TAH+BSO and washings.

➢ Stages 2&3: TAH+BSO and washings and node dissection.

➢ Stage 4: No surgical option.





Partial

Total

A hysterectomy removes the uterus and may also remove the cervix (total) and the vagina (radical)

Radical

Treatment Cont'd

- ***Hormonal therapy:*** Progestins for recurrent disease.
- ***Chemotherapy:*** In advanced, recurrent, or metastatic disease.

Treatment Cont'd

Radiotherapy:

- **Indications:**

➢ Patient medically unfit for surgery.

➢ Surgically inoperable disease.

➢ Those with high risk of recurrence

➢ Stage III or IV disease

- **Contraindications:** Pelvic kidney, pyometra, pelvic abscess, prior pelvic radiation, previous laparotomy/adhesions.

Follow Up

- Thorough physical examination, CXR.
- Regular serum CA-125 estimation.
- Mammography, CT, MRI: When indicated.

- Every 4 months for the first 2 years.
- Every 6 months for the next 2 years.
- Thereafter annually.

Recurrent Disease

- Most commonly in the vagina & pelvis.
- Majority (60%) present within 6 years of initial therapy.
- **Management:**

➢ Radiation therapy (for isolated recurrence)

➢ Hormonal therapy.

➢ Chemotherapy.

➢ Surgery: Of limited value.

Prognostic Factors

- Histologic grade (single most important).
- Depth of myometrial invasion (Second).
- Histologic type.
- Original tumor volume.
- Pelvic lymph nodes involvement.
- Extension to the cervix, adnexal metastasis, positive peritoneal washings.

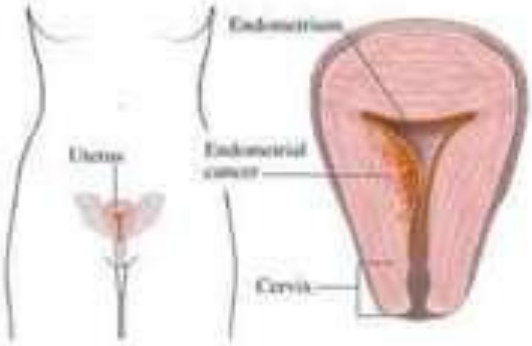
Prognosis Cont'd

5-years survival rate:

Stage	5-year survival (%)
Stage I	83
Stage II	71
Stage III	39
Stage IV	27

Screening

- There is no effective screening test.
- Occasionally, cervical smears contain endometrial cancer cells, or endometrial ultrasonic thickness of more than 5 mm indicates the need for endometrial sampling.



Prevention

- Controlling obesity, blood pressure, and diabetes help reduce risk.
- Restrict the use of estrogen after menopause in non-hysterectomised women.
- Estrogen + cyclical progesterone.
- Women report any abnormal vaginal bleeding or discharge to the doctor.
- Screening of high risk women in postmenopausal period.

References

- Obstetrics & Gynaecology, Beckmann.
- Hacker & Moore's Essentials of Obstetrics & Gynaecology.
- Textbook of Gynaecology, Dutta.
- Current diagnosis & treatment, Obstetrics & Gynaecology.
- Gynaecology By Ten Teachers, 18th edition.


Thank You!