

# **Adenocarcinoma of the uterine corpus**

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# Objectives:

- Incidence.
- Epidemiology.
- Risk factors.
- Diagnosis.
- Pathology.
- Prognostic factors.
- Treatment.

# Incidence:

- Most common malignancy unique to women.
- The 4th most common cancer in women.
- Incidence is increasing; may be related to increasing prevalence of overweight and obesity.

# Epidemiology:

- Most patients between the ages 50-59 years.
- The mean age is 63 years.
- 20-25% diagnosed before menopause.
- 5% before the age of 40 years.
- Two pathogenic types of endometrial cancer.

# Pathogenic types of endometrial cancer:

Type I	Type II
Obesity, hyperlipidemia, signs of hyperestrogenism	None, not clearly defined
Well- moderately differentiated	Poorly differentiated
Superficial myometrial invasion	Deep myometrial invasion
High sensitivity to progestins	Decreased sensitivity to progestins
Favorable prognosis (85% 5-year survival rate)	Poor prognosis (58% 5-year survival rate)

# Risk factors:

- Variants of normal anatomy and physiology:
- Frank abnormality or disease:
- Exposure to external carcinogens:

# **Risk factors:**

## **Variants of normal anatomy and physiology:**

- Obesity.
- Nulliparity.
- Late menopause: at age 52 or older.

# Variants of normal anatomy and physiology:

## Obesity:

- Upper body fat localization.
- Diet:
  - increased association with total energy intake.
  - More risk with more consumption of eggs, meats, beans, added fat and sugar.
  - Protection: elevated intake of vegetables, fresh fruits, whole grain bread and pasta.

## **Variants of normal anatomy and physiology:**

### **Obesity:**

- Decreased circulating levels of progesterone and SHBG.
- Higher endogenous production of non protein bound estradiol.

## **Variants of normal anatomy and physiology:**

- Diabetes and hypertension are frequently associated with endometrial cancer.
- Diabetes : high levels of insulin-like growth factor I, coupled with elevated estrogen levels.
- High blood pressure is relevant in older obese patients. Not appear to be a significant factor by itself.

# Risk factors:

Exposure to external carcinogens:

- **Unopposed estrogen:**
  - Relationship is well documented.
  - Addition of progestin appears to be protective.
  - Adequacy of progestins is important.
  - Stage of disease and histologic grade lower in estrogen users.
  - Survival rates are better: with correction of stage and grade.

# Risk factors:

Exposure to external carcinogens:

- Oral contraceptives:
  - Decrease the risk of developing endometrial cancer.
  - Used for at least for 12 months.
  - Protection continued for at least 10 years after use.
  - Most notable for nulliparous.
  - About 2000 cases of endometrial cancer are prevented in the USA.

# Risk factors:

Exposure to external carcinogens:

- Smoking:
  - Decrease the risk of developing endometrial cancer.
  - This advantage is strongly outweighed by the increased risk of lung cancer and other major health hazards.

# Risk factors:

Exposure to external carcinogens:

- Tamoxifen:
  - Used to treat and prevent breast cancer: decrease in the incidence of a second cancer in the opposite breast, lower recurrence and lower mortality compared with no adjuvant therapy.
  - Antiestrogen with estrogenic properties.
  - Protection against osteoporosis and heart disease.
  - Increased risk of endometrial cancer while receiving tamoxifen.

# Risk factors:

## Exposure to external carcinogens:

## Tamoxifen:

- However it is well known that women who developed breast cancer are at increased risk of endometrial cancer.
- Benefit of tamoxifen is apparent, 121 fewer breast related events\1000 women with tamoxifen compared with 6.3 endometrial cancers\1000 women.
- Reduce: 2nd cancer on the other breast, recurrence, mortality.

- Hereditary endometrial CA:
- Most cases sporadic.
- Identified in association with hereditary nonpolyposis colon cancer( HNPCC), Lynch II syndrome.
  - Autosomal dominant.
  - Mutation in DNA mismatch repair gene family.
  - Lifetime risk 30% of developing endometrial cancer.

# Diagnosis:

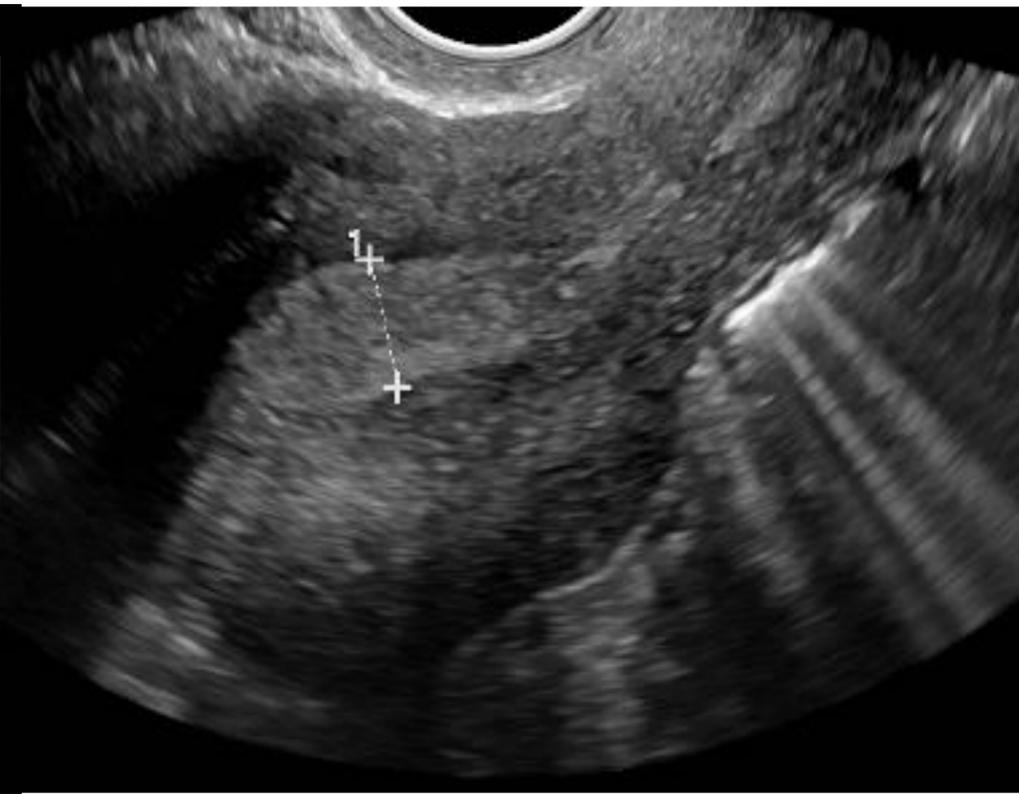
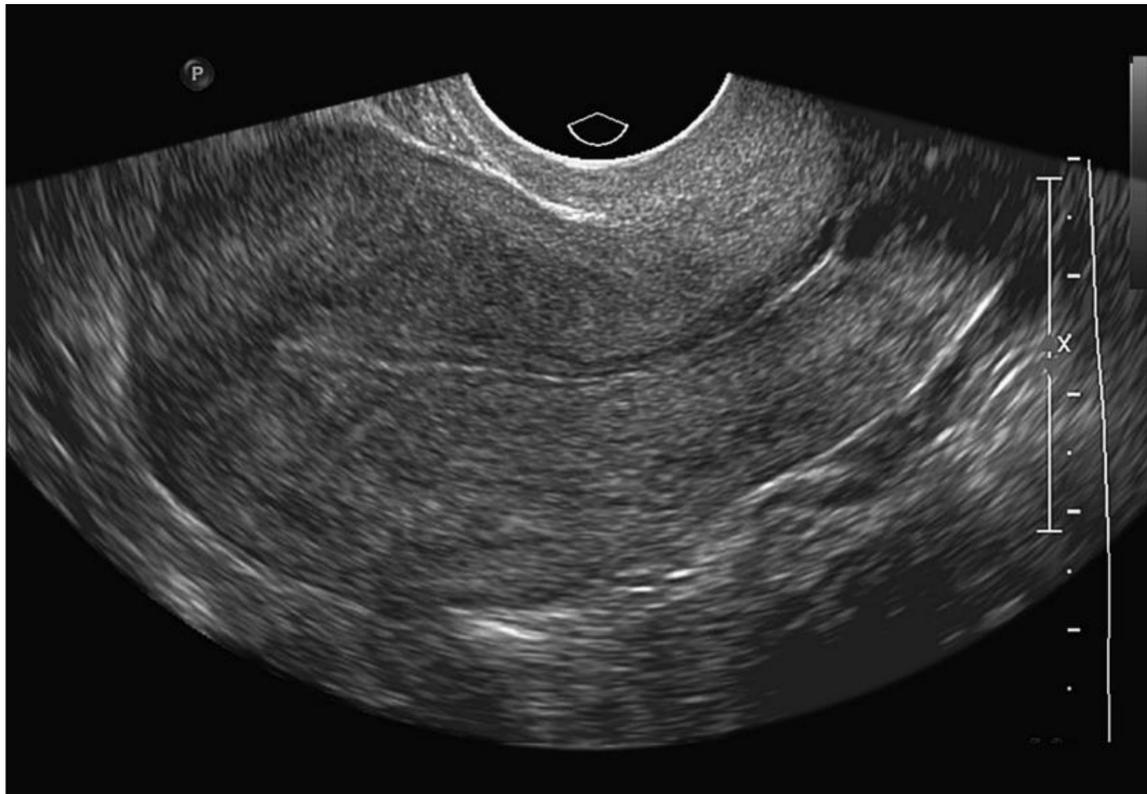
- Routine screening is not recommended. Even before during HRT, unless abnormal bleeding occurred.
- All post menopausal women with uterine bleeding must be evaluated for endometrial cancer.
- 20% will have malignant genital neoplasm.
- Probability that the bleeding is caused by endometrial cancer increases with the age after menopause.

# Diagnosis:

- Perimenopausal women with abnormal bleeding indicative of endometrial cancer.
- Menstrual cycle should become lighter and further and further apart , any other bleeding must be evaluated.
- High index of suspicion in young patient with prolonged and heavy menstrual periods and intermenstrual spotting, esp: obese, anovulatory cycles.

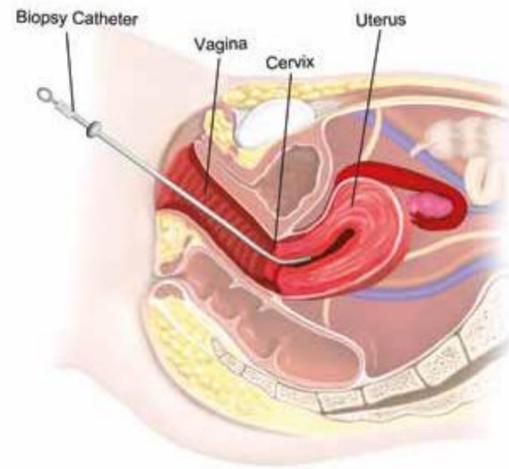
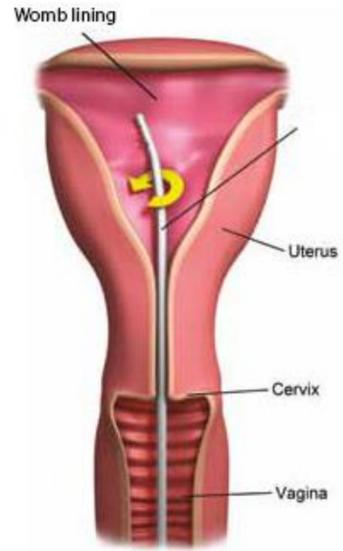
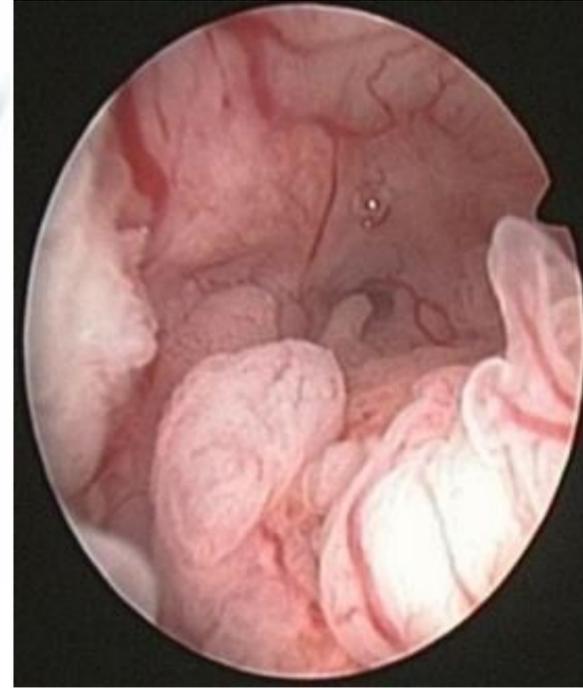
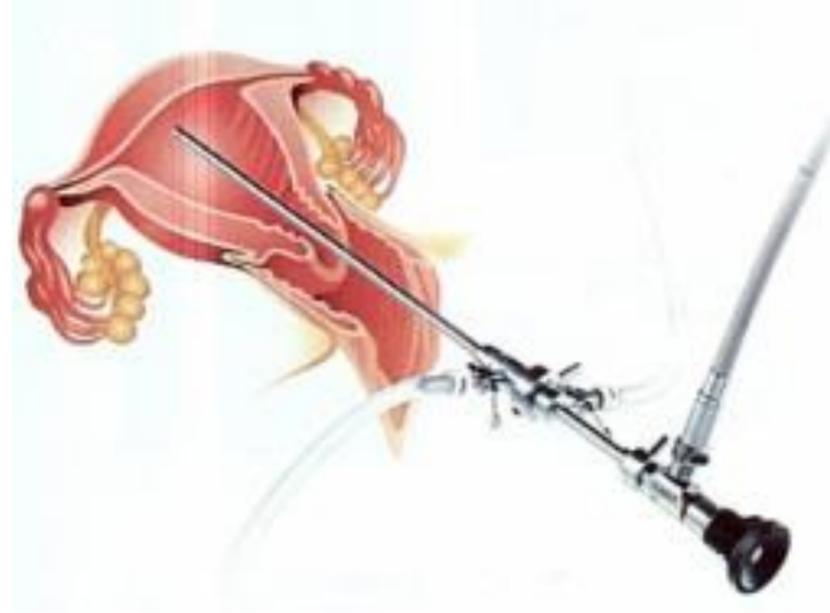
# Diagnosis:

- Ultrasound:
  - Using cut off 4 mm used.
  - Several studies suggest that if thin endometrial stripe, no need for histological diagnosis; atrophic endometrium.



# Diagnosis:

- Endometrial biopsy:
  - Office procedure: avoid hospitalization, minor surgical procedure.
    - Pipelle: accuracy in detecting endometrial carcinoma is 90%.
    - Hysteroscopy: Adjuvant in making diagnosis, direct view of the endometrium.  
Allow to see pathological lesion and direct biopsy, and evaluation of endocervical canal.



Endometrial sampling to test cells in the lining of the womb.

- Factors that affect endometrial thickness:
  - Estrogen use.
  - E+P use.
  - BMI.
  - Diabetes.
  - Poor histotype: may use other parameters; intracavitary fluid or lesion, myometrial mass, enlarged uterus, or adnexal mass.
  - Race.
  - Postmenopausal status.

- Reliability determining endometrial thickness in PM women not applicable to patients on Tamoxifen.

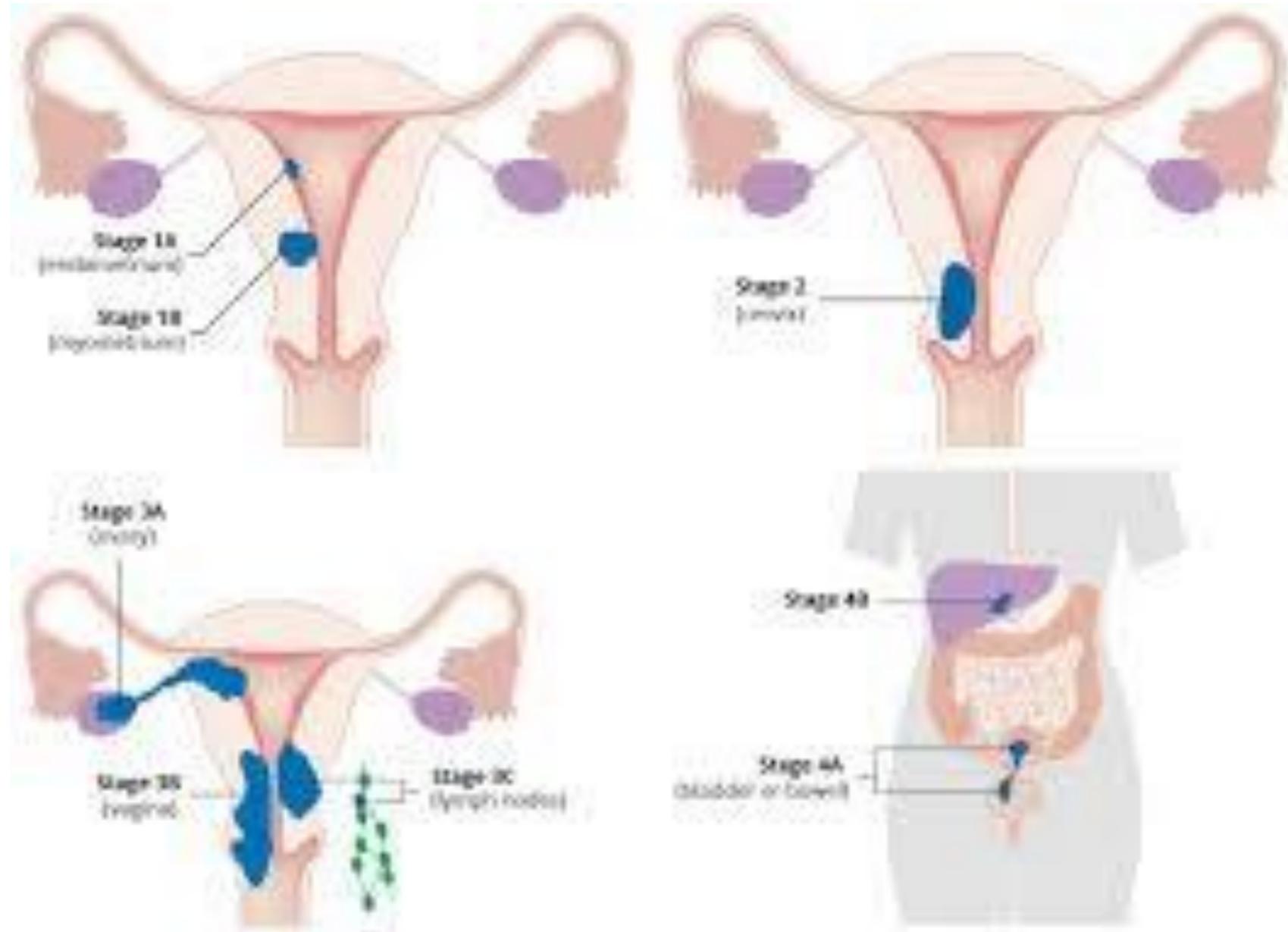
# Pathology:

- Can disseminate: - Lymph nodes.
  - Direct extension.
  - Hematogenous.
- Most common histological type:
  - Adenocarcinoma: usually preceded with atypical hyperplasia.

- Endometrial carcinoma Subtypes.

Type	Number (%)
Endometrioid	6231 (85)
Aden-squamous	317 (4.2)
Mucinous	74 (0.9)
Uterine papillary serous	335 (4.5)
Clear cell	185 (2.5)
Squamous cell	28 (0.04)
Other	285 (3.8)

# Stages:



- Tumor grade:
  - Tumor differentiation.
  - Important prognostic factor.

# Prognostic factors:

- Stage.
- Tumor grade.
- Lymph-vascular space involvement.
- Peritoneal cytology.
- Molecular indices: hormone receptors.

# Treatment

- Surgical management of endometrial cancer:
  - Assessment: CBC, metabolic profile, and metastatic evaluation with Chest radiography.
  - Routine CT or MRI scans not shown to be useful, reserved for unusual situations.
  - Most patients are candidates for definitive surgery: Extrafascial hysterectomy and BSO +/- lymphadenectomy.

- Radiation therapy:
  - Mainstay of adjuvant therapy.
  - Adjuvant often used in early-stage (stage I or II)
  - Vaginal brachytherapy (VVB) - preferred route due to its reduced toxicity, or external beam radiotherapy (EBRT)
  - VVB is used to treat any remaining cancer in the vagina, EBRT can be used to treat remaining cancer elsewhere in the pelvis following surgery
  - The benefits are controversial.
  - EBRT significantly reduces the rate of relapse in the pelvis, overall survival. Metastasis rates are not improved.
  - VVB provides a better quality of life than EBRT

- Chemotherapy:
  - Its role is evolving.
  - Consisting of some combination of paclitaxel, and platins (particularly cisplatin and carboplatin)
  - Adjuvant chemotherapy has been found to increase survival in stage III and IV cancer more than radiotherapy.
  - In cases where surgery is not possible, palliative chemo is an option
- Hormones:
  - Progestins.

Thank you