



FEMALE GENITAL SYSTEM PATHOLOGY

Lec. 4

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Case scenario

A 65-year-old nulliparous woman complain with light vaginal bleeding. Her last period was at the age of 55 years while her menarche was at 12 years old. She is sexually active but has noticed vaginal dryness on intercourse recently.

She is hypertensive on anti hypertension.

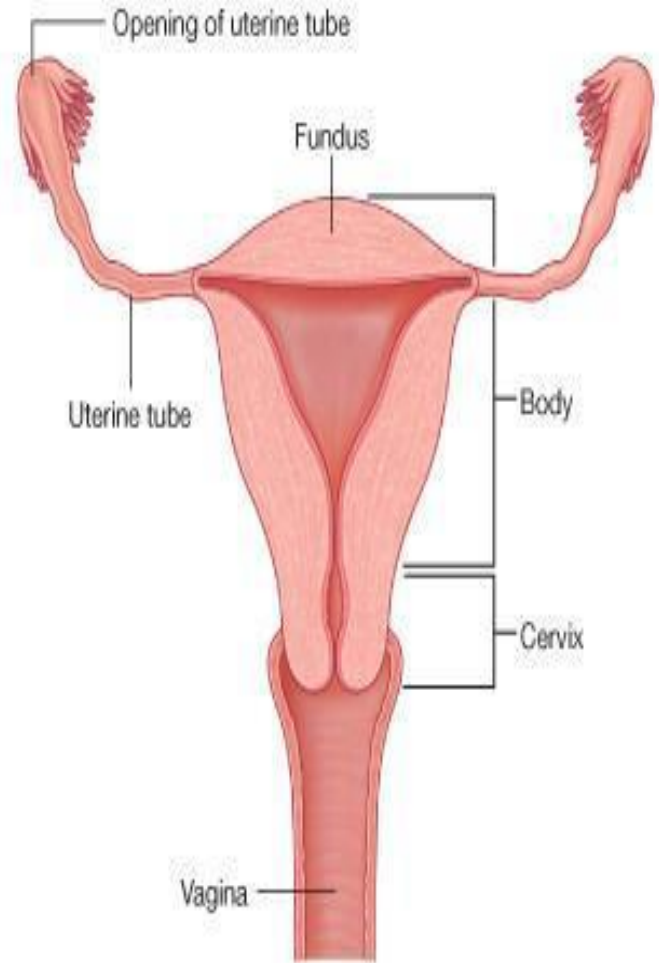
Examination

She is **overweight**. Abdominal examination is normal. The vulva and vagina appear thin and atrophic (post menopausal changes) , the cervix is normal & the uterus is small with no palpable adnexal masses. Transvaginal ultrasound scan revealed thickening of endometrium.

Objectives of this lecture

At the end of the lecture

- Anatomy and normal histology of uterus (rapid revision)
 - Classification of uterine pathological disorders
 - Proliferative lesion of endometrium and myometrium
 - Neoplastic disorders
-
- ❖ Types
 - ❖ Presentation
 - ❖ Histopathological finding



PROLIFERATIVE LESIONS OF THE ENDOMETRIUM AND MYOMETRIUM

- The most common proliferative lesions of the uterine corpus are:
 1. Endometrial hyperplasia.
 2. Endometrial polyps.
 3. Endometrial carcinomas.
 4. Smooth muscle tumors: leiomyoma & leiomyosarcoma
- All tend to produce **abnormal uterine bleeding** as their earliest manifestation.

Endometrial Hyperplasia

- increased proliferation of the endometrial glands relative to the stroma resulting in an increased gland-to-stroma Ratio when compared with normal proliferative Endometrium an important cause of abnormal bleeding
- Excess of estrogen, can induce exaggerated endometrial proliferation (hyperplasia), which is an **important precursor of endometrial carcinoma.**
- **Causes of estrogen excess include**
 1. Anovulation
 2. Polycystic ovarian disease
 3. Functioning granulosa cell tumors of ovary
 4. Estrogen replacement therapy
 5. Obesity, as adipose tissue converts steroid precursors into estrogens.

Classification of endometrial hyperplasia

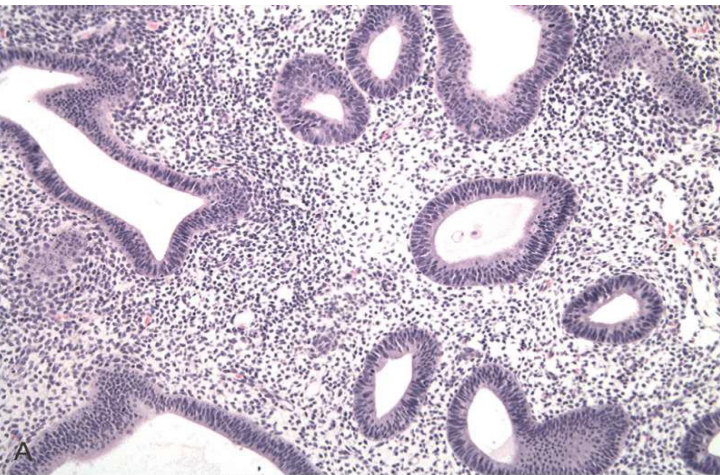
1. Hyperplasia Without Atypia (low grade)

- Simple hyperplasia: exhibits benign cystically dilated glands; these rarely progress to adenocarcinoma.
- Complex hyperplasia: closely apposed glands of varying size crowded together into clusters; the epithelium remains cytologically normal
Less than 5% progress to carcinoma

2. Atypical Hyperplasia (high grade)

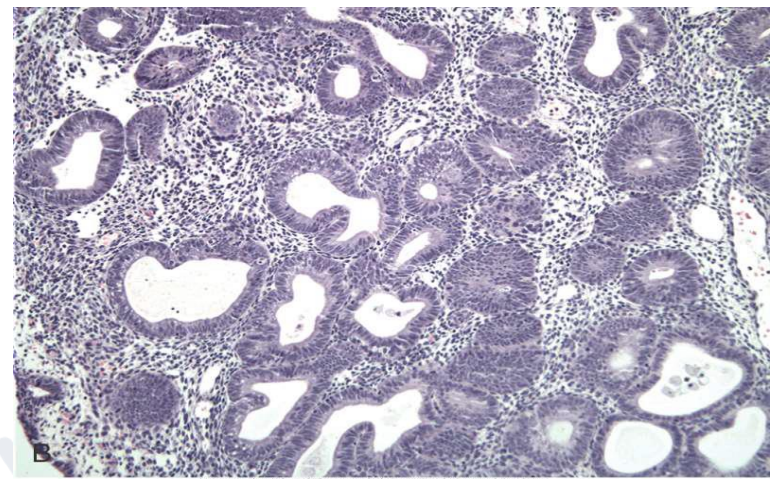
- shows gland crowding and cytologic changes with atypical cellular and nuclear features.
Approximately 25% progress to carcinoma

MORPHOLOGY



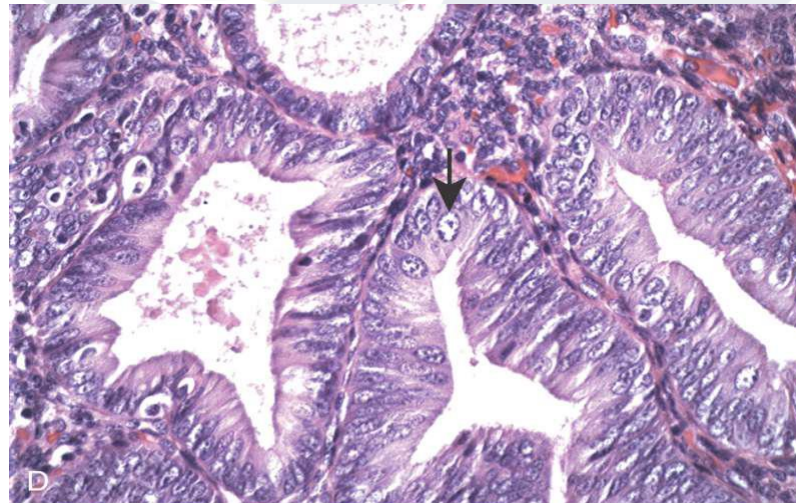
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Simple hyperplasia without atypia with architectural abnormalities including mild glandular crowding cystic glandular dilatation



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Complex hyperplasia without atypia increased glandular crowding with areas of back-to-back glands cytologic features similar to proliferative endometrium



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Complex hyperplasia with atypia similar to complex hyperplasia without atypia but the cytologic features have changed

Endometrial Polyps

Are exophytic masses of endometrial glands and stroma that project into the endometrial cavity;

Range from 0.5 to 3 cm in diameter arising from endometrium.

They may be associated with elevated **estrogens** or **tamoxifen** therapy.

These polyps are usually benign and manifest primarily with abnormal bleeding, but they occasionally develop into adenocarcinoma.

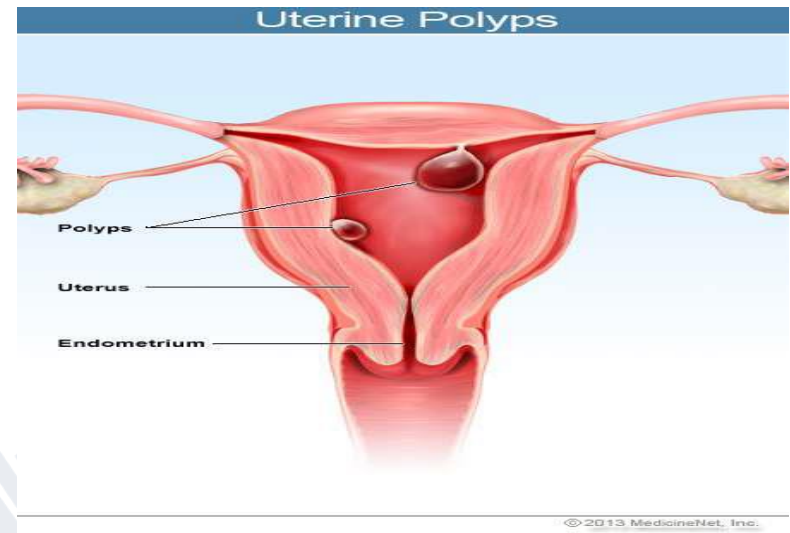
Diagnosis

History

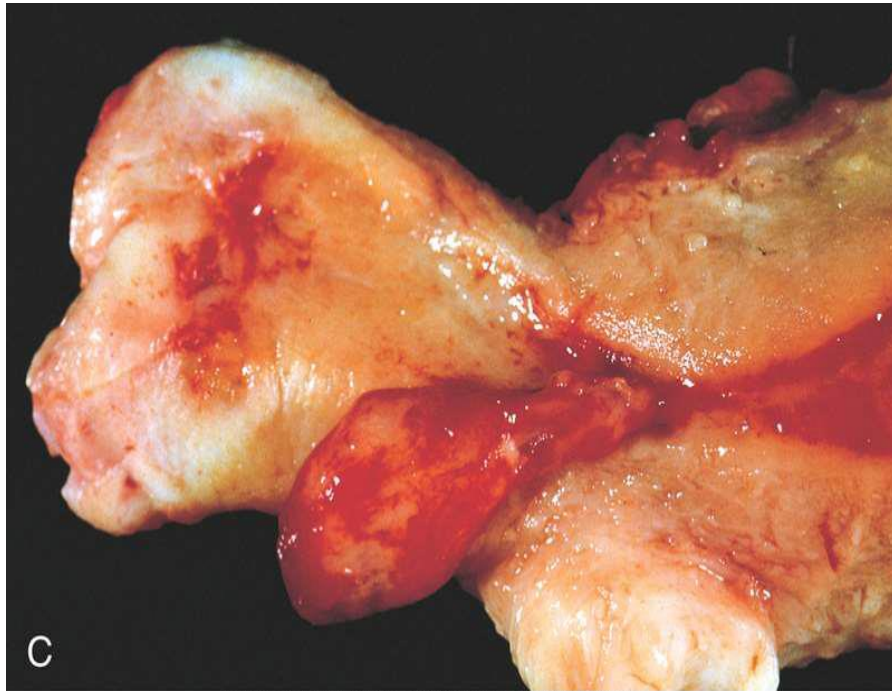
Ultrasound

Hysterosonography

Histopathology

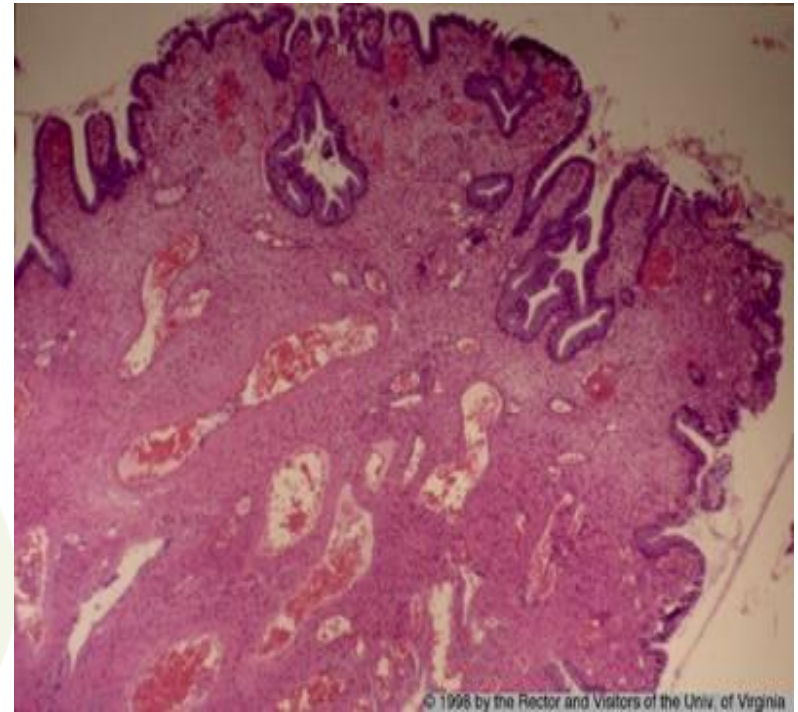


Morphology



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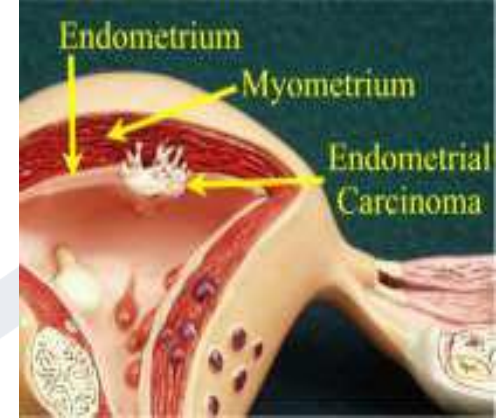
single or multiple
usually sessile, measuring from 0.5 to 3
cm in diameter
occasionally large and pedunculated



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On histologic examination,
they are composed of
endometrium resembling
the basalis, frequently with
small muscular arteries.

Endometrial Carcinoma



- Carcinoma of the endometrial lining of the uterus.
- Most common gynaecological malignancy in postmenopausal women accounts for 7% of all invasive cancers in women.
- 4th most common malignancy in women (following breast, bowel, & lungs).
- 8th leading site of cancer-related mortality.
- 2-3% of women develop it in lifetime.
- 15%-25% of postmenopausal women with bleeding have endometrial cancer.
- Peak incidence of 55 to 65 years.
- Uncommon before age of 40 years.
- Majority are adenocarcinoma.

• Risk factors :-

- Older age.
- Early menarche.
- Late menopause.
- Nulliparity.
- Unopposed estrogen (Obesity, PCOS, HRT).
- Chronic Tamoxifen use.
- Family Hx of endometrial carcinoma.
- Genetic: Lynch II (HNPCC).
- 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

❖ Prolonged estrogen replacement therapy and estrogen-secreting ovarian tumors increase the risk of endometrioid type of endometrial carcinoma.

• 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

Classification

Type I Carcinomas

- Are the most common (80%);
- And are well differentiated (endometrioid carcinoma)
- Typically arise in the setting of endometrial hyperplasia (with the same overall risk associations).
- PTEN mutations are seen in 30% to 80% of endometrioid carcinomas . It often exhibit microsatellite instability
- p53 mutations may be late events.

Type II Carcinomas

Typically arise a decade later than type I tumors and Occur in the setting of endometrial atrophy;

Are poorly differentiated tumors. The most common subtype is **serous carcinoma, so-called due to biologic overlaps with similar ovarian lesions;**

p53 mutations are present in at least 90% and appear to be early oncogenic events.

Endometrial intraepithelial carcinoma (EIC) without invasion is a precursor to serous carcinoma.

Types

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

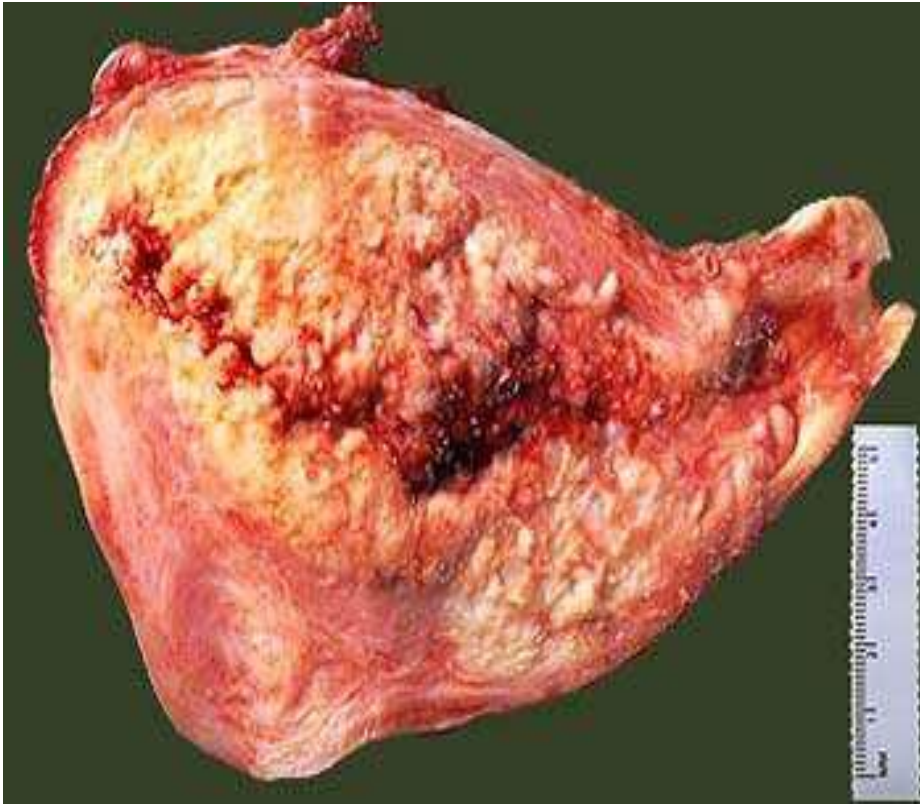
Clinical course :-

- Asymptomatic (< 5% of cases).
- **Abnormal bleeding:**
 - Postmenopausal bleeding
 - Menorrhagia
 - Post-coital spotting
 - Intermenstrual bleeding
- **Blood-stained vaginal discharge.**
- **If + cervical stenosis:**
Hematometra, Pyometra,
purulent vaginal discharge.
- **Colicky abdominal pain.**

Patient Profile

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

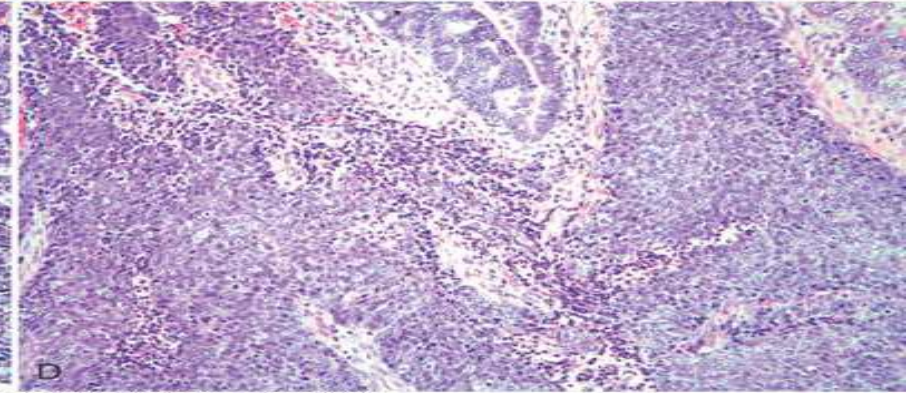
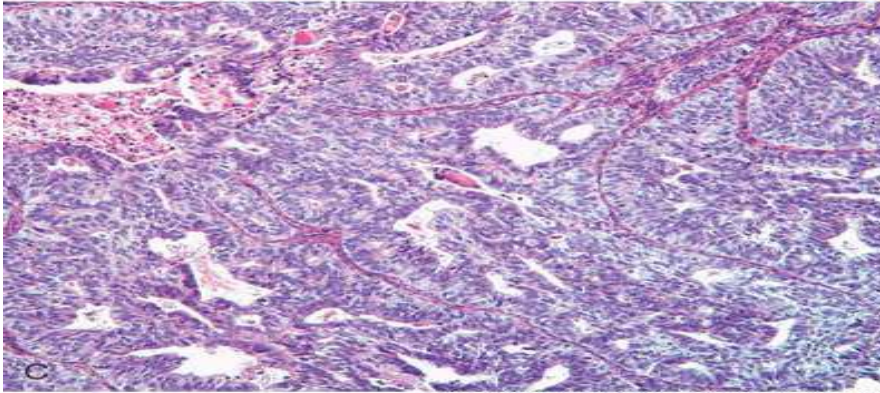
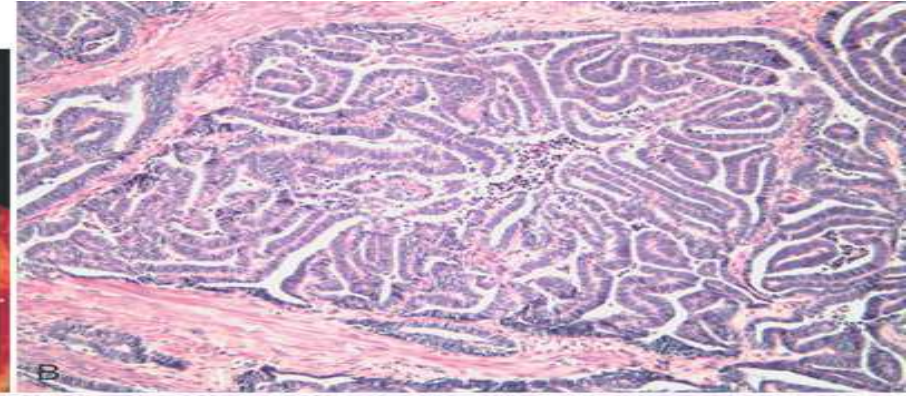
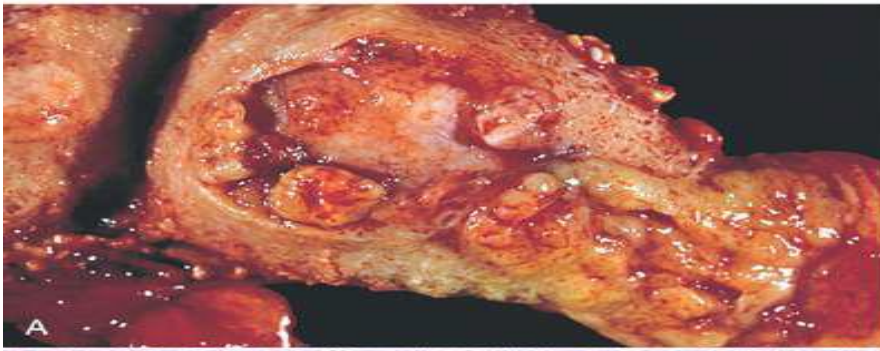
MORPHOLOGY



Sagittal section of the uterus shows a friable, tan-yellow tumor that is filling the uterine cavity and extending into the myometrium



- Obvious Irregular masses of white tumor are seen over the surface of this uterus that has been opened anteriorly. The cervix is at the bottom of the picture.**

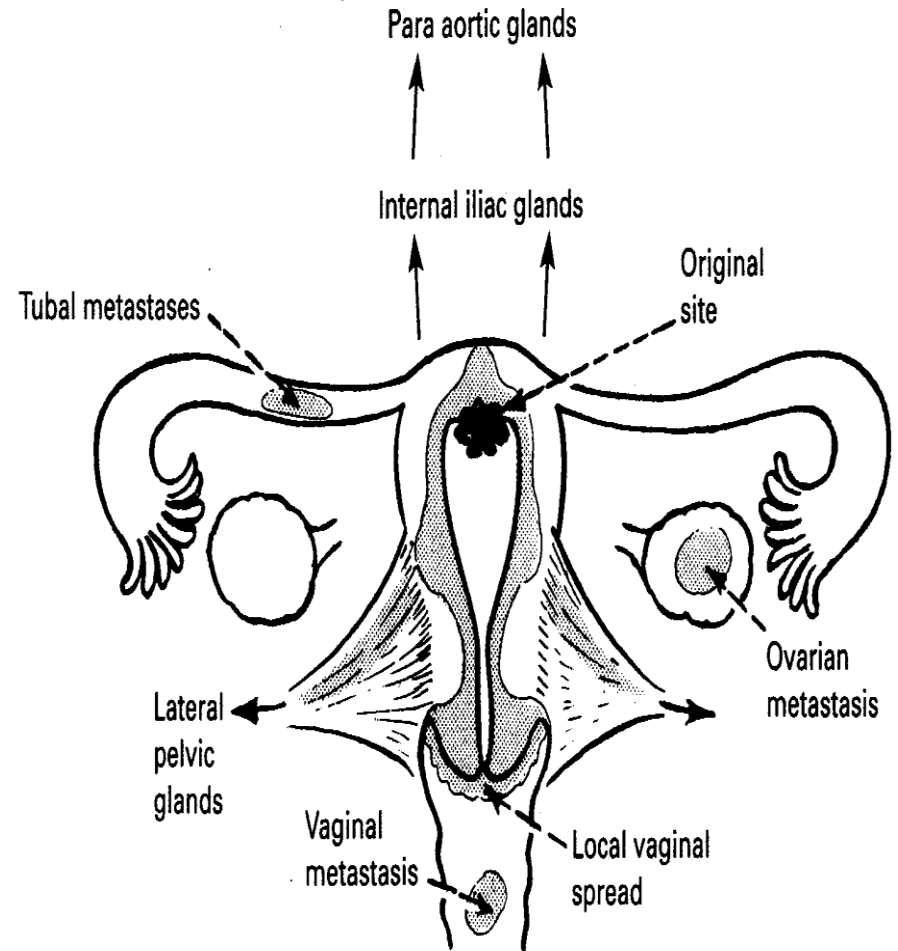


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- A-- Endometrial adenocarcinoma a fungating mass in the fundus of the uterus**
- B-- Well-differentiated (grade 1) endometrioid adenocarcinoma preserved glandular architecture lack of intervening stroma.**
- C-- Moderately differentiated (grade 2) endometrioid adenocarcinoma glandular architecture admixed with solid areas.**
- D-- Poorly differentiated (grade 3) endometrioid adenocarcinoma with predominantly solid growth**

Spread

- Direct extension to Myometrium
- 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.

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

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

THANK YOU
FOR YOUR
ATTENTION