

Lecture 6

Topic:

Uterine Pathology

Anything added is written in italic
According to section 3 recording

ENDOMETRITIS



- Inflammation of the endometrium.
- Causes:
 - 1- pelvic inflammatory disease (PID)
 - 2- miscarriage or delivery
 - 3- *foreign body* : intrauterine contraceptive device (IUCD).
- acute or chronic
- fever, abdominal pain, menstrual abnormalities, infertility and ectopic pregnancy due to damage to the fallopian tubes.
- Rx: removal of cause, antibiotics, D&C.

Endometrium = the lining of the endometrial cavity (the uterus cavity), so it's the inner most layer (closest to the cavity).

Myometrium = smooth muscles inside the wall of the uterus.

D&C : Dilatation and curettage (توسيع عنق الرحم و تنظيفه), which is a procedure in which the cervix is dilated and an instrument is used to scrape the lining of the uterus (curettage), to make sure that after miscarriage, all the fetal tissue is removed to prevent potential inflammation caused by them.

ADENOMYOSIS

↓
glands

↓
muscles

- endometrial stroma, glands, or both embedded in **myometrium**.
- Thick uterine wall, enlarged uterus.
- Derived from stratum basalis → no cyclical bleeding.
Not responsive to hormonal stimulation.
- **menorrhagia, dysmenorrhea**

Although there is no cyclical bleeding but there is dysmenorrhea and menorrhagia, why? Because the uterus is enlarged so that the surface area of bleeding is bigger. And because the glands in the muscles might interfere with the muscles normal function

ENDOMETRIOSIS

- endometrial glands and stroma **outside the uterus**.
- *The most common location for endometriosis is the ovaries.*
- *Relatively common condition : 10% in reproductive yrs (the peak is in the 3rd decade).*
- ↑ infertility, *so there is an association between infertility and endometriosis (explanation in a couple of slides).*
- dysmenorrhea, and pelvic pain, pelvic mass filled with blood (**chocolate cyst**).
- Multifocal, multiple tissues in pelvis (ovaries, pouch of Douglas, uterine ligaments, tubes, and rectovaginal septum).
- Sometimes distant sites (*out side the pelvis*) e.g. umbilicus, lymph nodes, lungs, etc

This condition is not neoplastic because the origin of the cyst is not monoclonal (i.e. we have stroma and glands so 2 types of cells). Another reason is that they are well-differentiated cells.

Evidence on endometriosis : “Chocolate” cyst in an ovary



ENDOMETRIOSIS- Pathogenesis

- Three theories:

- **regurgitation theory.** (most accepted). Menstrual *bleeding during a menstrual cycle* backflow through tubes and implantation in an abnormal location in the pelvis.

***This theory is the best one in explaining the most common implantation location (ovaries).*

- **metaplastic theory** . Endometrial differentiation of coelomic epithelium.

→ *The cells that make the pelvic cavity, these cells are totipotential cells and can differentiate into endometrial cells .*

***This theory explains the multiple locations of endometriosis in the pelvis.*

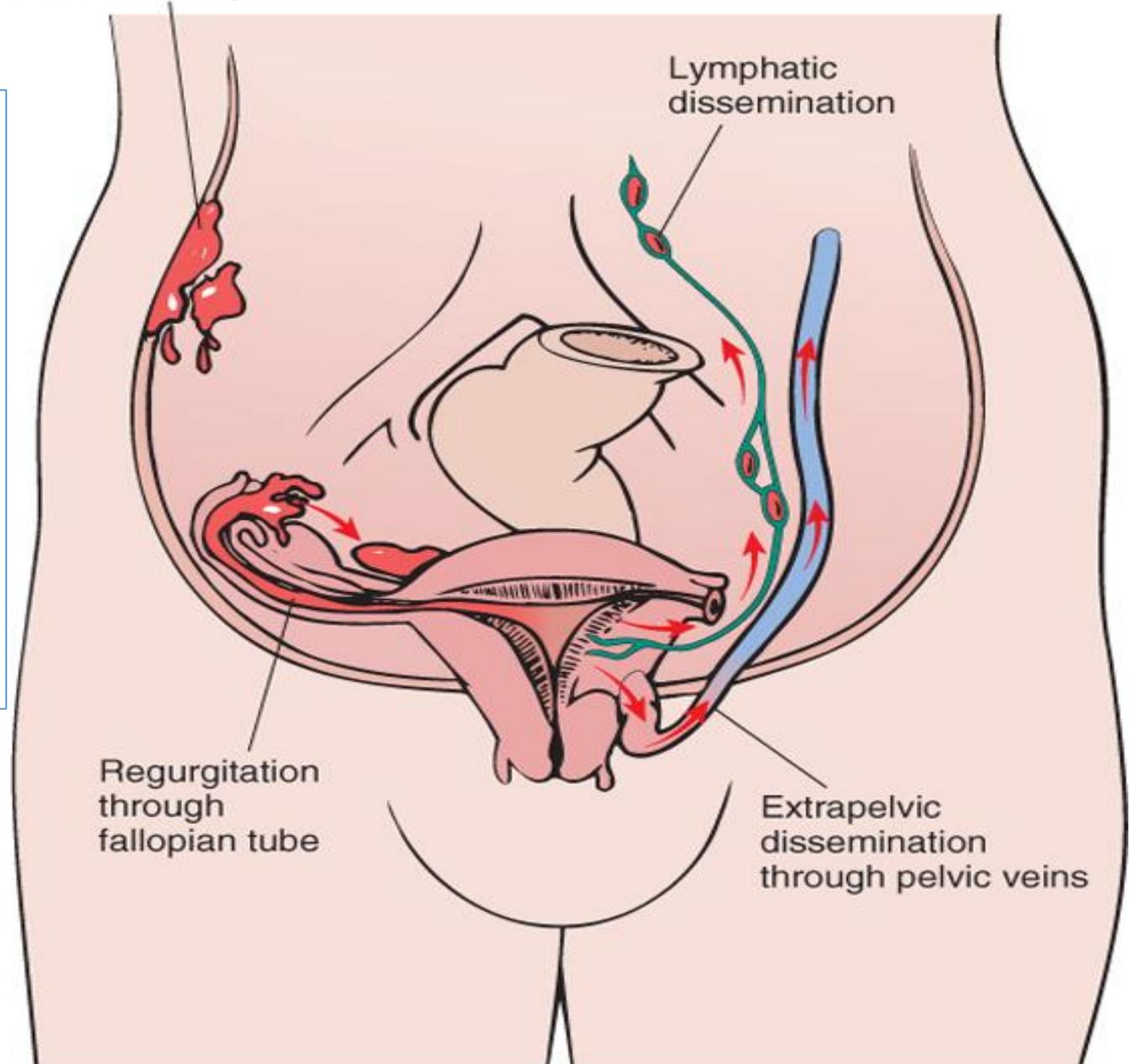
- **vascular or lymphatic dissemination theory.** *This theory states that some glands or stroma might go through the blood or lymphatic and implant in any tissue.*

May explain extrapelvic or intranodal implants.

***This theory explains the distal locations of implantation.*

Metaplastic differentiation
of coelomic epithelium

Conceivably,
all pathways
are valid in
individual
instances.



ENDOMETRIOSIS

- Contains/originate from **functionalis endometrium**, so undergoes **cyclic bleeding**.
- Consequences: *in every normal menstrual cycle, there will be hemorrhage in the affected organ, this hemorrhage will lead to damage and inflammation in the organ which might lead to: fibrosis, sealing of tubal fimbriated ends, and distortion of the ovaries and in the end might be infertility.*
- Diagnosis:

*The patient will seek medical help because of abdominal pain, abdominal masses(caused by hemorrhage) or infertility. After taking a biopsy and using histopathologic techniques, 2 of 3 the following features should be seen to diagnose: **endometrial glands, endometrial stroma, or hemosiderin pigment.***

Evidence of old bleeding.

DUB- Dysfunctional Uterine Bleeding

- *DUB means any abnormal menstruation whether it is prolonged, short, more frequent or less frequent normal (which is every 28 days) ...etc*
- causes:

1- Failure of ovulation *(anovulatory cycles)*. (most common).

- Usually hormonal dysfunction
- excess of estrogen
- Malnutrition, obesity, debilitating disease; severe physical or emotional stress.

- **2- Endomyometrial disorders**: *something that physically interferes with normal menstruation like : chronic endometritis, endometrial polyps, leiomyomas, endometrial hyperplasia and cancers.*

Dysfunctional Uterine Bleeding

Just know that there might be different causes of DUB in different age groups, and that failure of ovulation (anovulatory cycle) is present in most of the age groups.

Age Group	Cause(s)
Prepuberty	Precocious puberty (hypothalamic, pituitary, or ovarian origin)
Adolescence	Anovulatory cycle
Reproductive age	Complications of pregnancy (abortion, trophoblastic disease, ectopic pregnancy) Organic lesions (leiomyoma, adenomyosis, polyps, endometrial hyperplasia, carcinoma)
	Anovulatory cycle Ovulatory dysfunctional bleeding
Perimenopause	Anovulatory cycle Irregular shedding Organic lesions (carcinoma, hyperplasia, polyps)
Postmenopause	Organic lesions (carcinoma, hyperplasia, polyps)
	Endometrial atrophy

Endometrial Hyperplasia

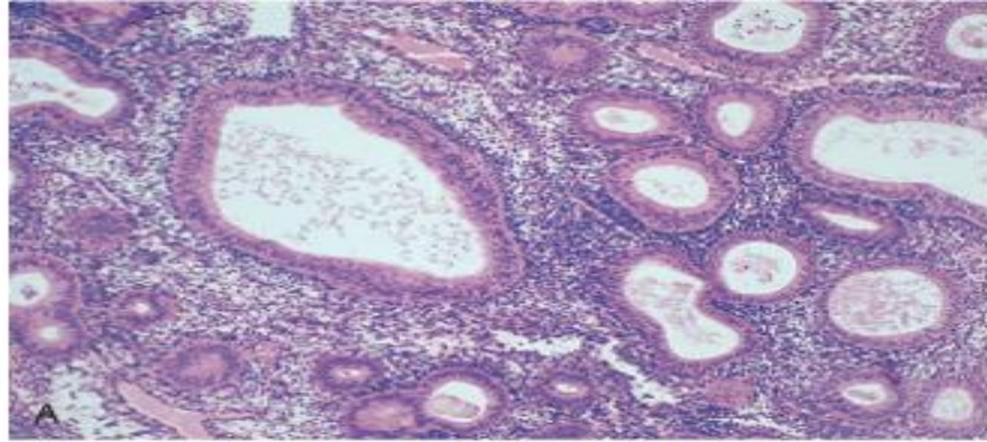
- prolonged or marked excess of **estrogen** relative to progestin → exaggerated proliferation (*hyperplasia*) → may progress to cancer
- Grading : severity is based on architectural crowding and cytologic atypia (*i.e. morphologic properties*), ranging from:
 - 1- Simple hyperplasia
 - 2- Complex hyperplasia
 - 3- Atypical hyperplasia (*high risk of cancer -20% risk of cancer-*).

The type of cancer that might develop after endometrial hyperplasia is probably of endometrioid type (later in the slide)

In all of them we have an increased glands to stroma ratio

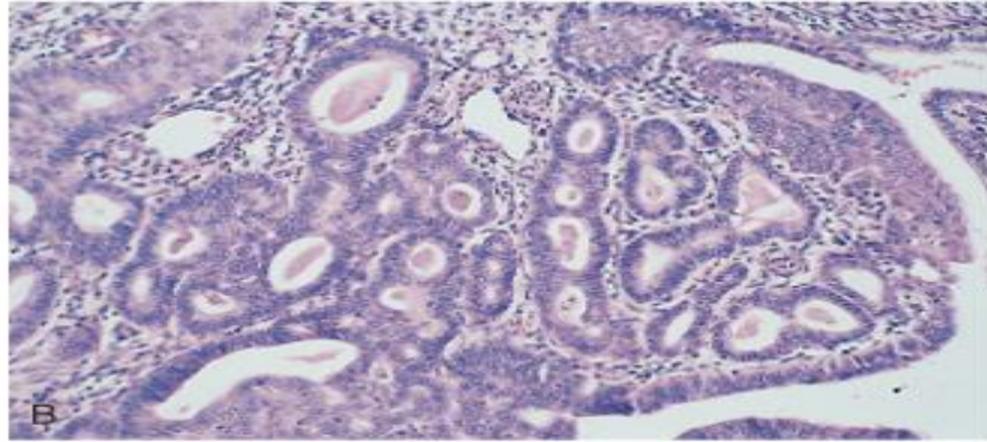
Simple hyperplasia

No changes in the morphology of the glands (just increase in number)



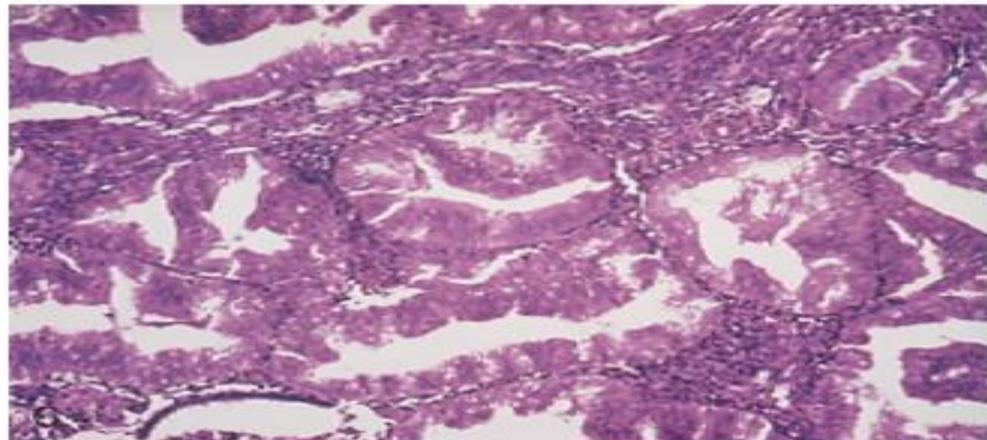
Complex Hyperplasia

The architecture of the glands is complex (the morphology of the glands is changed)



Atypical Hyperplasia

There is cytological atypia. This type has a higher potential to develop cancer making it the most significant.



TUMORS OF THE ENDOMETRIUM

❖ **Benign Endometrial Polyps**

- sessile or pedunculated
- *similar to GI tract polyps.*
- endometrial dilated glands, with small muscular arteries and fibrotic stroma.
- *They are not monoclonal so there is no risk of endometrial cancer.*

Endometrial Carcinoma

- **the most common cancer in female genital tract.**
- 50s and 60s.
- two clinical settings:
 - 1) perimenopausal women with estrogen excess
 - **similar to endometrial hyperplasia.*
 - 2) older women with endometrial atrophy.
 - These scenarios are correlated with differences in histology:
 - 1-endometrioid
 - 2-serous carcinoma , respectively.

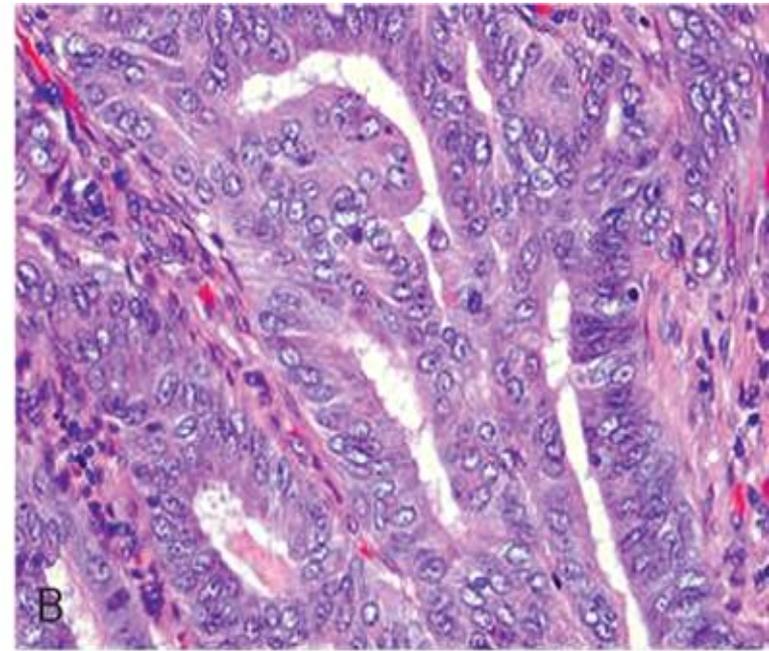
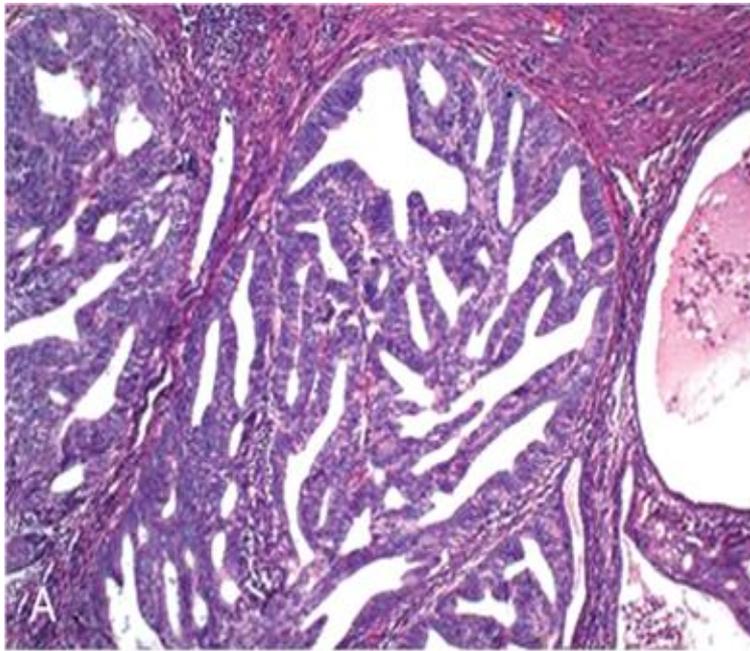
Endometrioid carcinoma:

- *The clinical setting is perimenopausal women with estrogen excess*
- Termed because similar to normal endometrium (*hence the suffix -oid*).
- risk factors: 1) **Diabetes; Hypertension** (mostly an association and not a true risk factors)
- 2) **True risk factors** (*these factors are related to increased estrogen*):
Obesity; Infertility; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors.
- **precancerous** lesion is atypical endometrial hyperplasia
- Mutations in **DNA mismatch repair genes** (*microsatellite instability*) and **PTEN** (*tumor suppressor gene*)
- **Prognosis: depends on stage.**
5-year survival in stage I = 90%; drops to 20% in stages III and IV.

Serous carcinoma

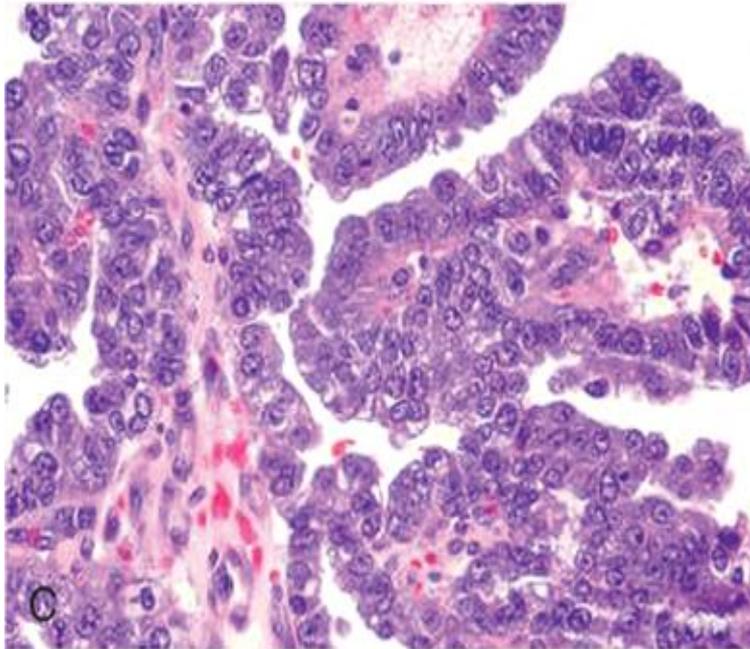
- *The clinical setting is older women with endometrial atrophy*
- **no relation with endometrial hyperplasia).**
- **mutations in *p53* tumor suppressor gene**, *here we will have over-expression of the mutated/not functional p53 protein.*
- Prognosis: depends on operative staging with peritoneal cytology. Generally worse than endometrioid ca.

Endometrioid carcinoma

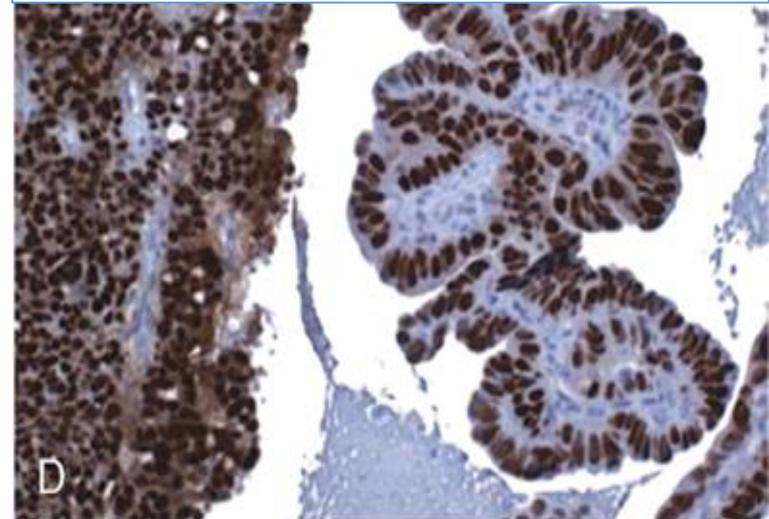


Serous carcinoma

They form papillary structures



*immunohistochemical stain for p53
(brown color = +ve RXN)*



Tumors of the myometrium

- Lieomyoma = fibroids (*another name for the tumor*)

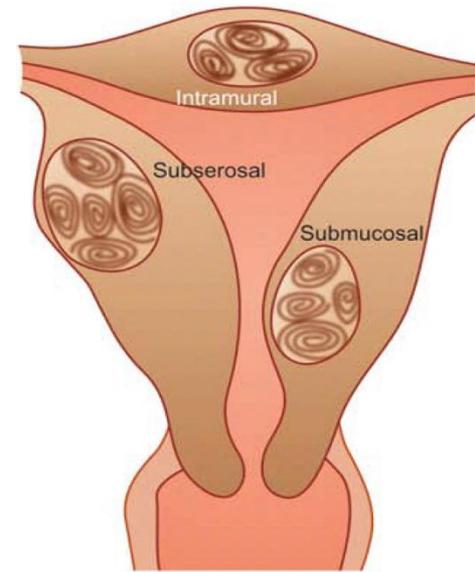
Smooth muscle *Benign*

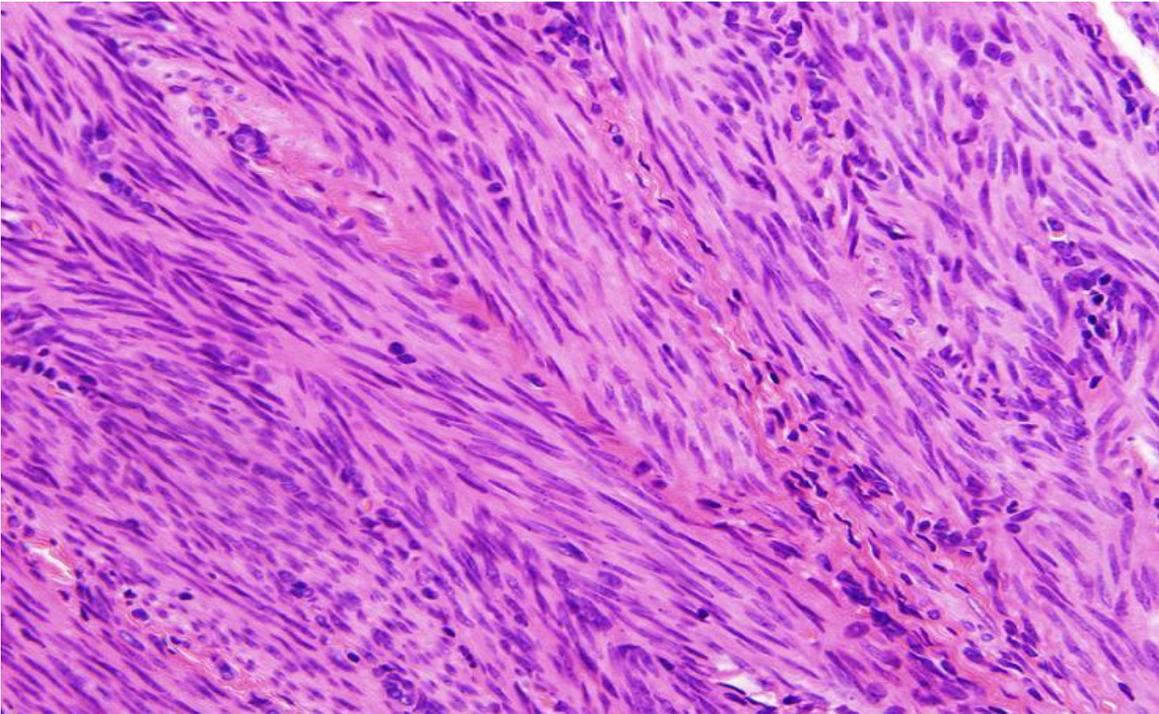
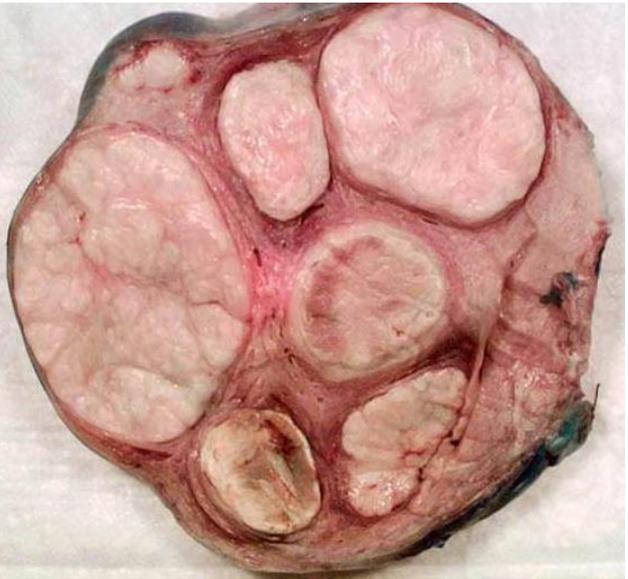
- Benign tumor of smooth muscle cells
- **most common benign tumor in females** (30% - 50% in reproductive life).
- Estrogen-dependent, shrink after menopause.
- circumscribed, firm gray-white masses with whorled cut surface.

Leiomyomas

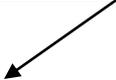
In the wall

- Location: (intramural), (submucosal), or (subserosal).
- may develop hemorrhage, cystic change or calcification.
- Clinically: *can be completely asymptomatic or have these symptoms* : menorrhagia; a dragging sensation.
- leiomyomas almost **never** transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.





Leiomyosarcoma



- Malignant counterpart of leiomyoma.
- not from preexisting leiomyomas.
- soft, hemorrhagic, and necrotic. Have infiltrative borders.
- diagnosis: **coagulative necrosis, cytologic atypia, and mitotic activity.**
- **Recurrence common, and metastasize, 5-year survival rate 40%.**

