بسم الله الرحمن الرحيم

Uterine Pathology

FINAL | Lecture 2

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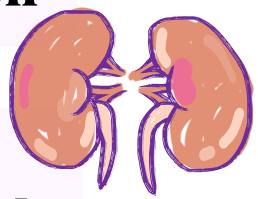
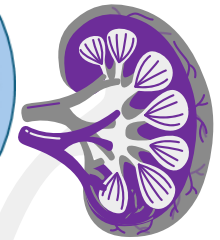
﴿ قُلْ بِفَضْلِ ٱللَّهِ وَبِرَحْمَتِهِۦ فَبِذَٰلِكَ فَلْيَفْرَحُوا۟ هُوَ خَيْرٌ مِّمَّا يَجْمَعُونَ ﴾





Uterine Pathology

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Uterus Histology

- The inner aspect of the uterus is lined by a mucosal layer called the endometrium. It is composed of glands and stroma. The endometrium is the part that undergoes cyclical bleeding because it is hormone-dependent and responds to changes in estrogen and progesterone levels during each ovarian cycle.

- The second layer is called the myometrium, which forms the wall of the uterus. It consists of smooth muscle fibers, and its main functions are support and contraction.

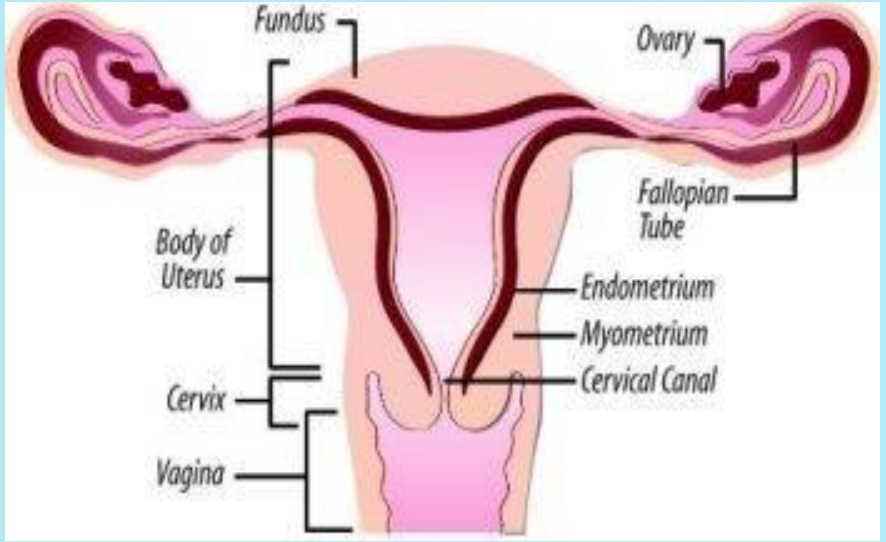
- In this lecture, we will discuss diseases affecting the endometrium and myometrium.

Endometrium

- Endometritis
- Adenomyosis
- Endometriosis
- Endometrial Polyps
- Endometrial Hyperplasia
- **Endometrial Carcinoma**

Myometrium

- Leiomyoma
- **Leiomyosarcoma**



Endometritis

- Inflammation of the endometrium.
- Causes:

1- infections - pelvic inflammatory disease (PID)

2-miscarriage or delivery may lead to contamination and serve as a source of infection.

3- intrauterine device (IUCD).

- acute or chronic
- fever (in acute form), abdominal pain, menstrual abnormalities, infertility and ectopic pregnancy due to fibrosis, damage, and obstruction of the fallopian tubes are seen in chronic cases .
- Rx: removal of cause, antibiotics, D&C.

D&C stands for dilation and curettage, which is a surgical procedure used to clean the endometrium.

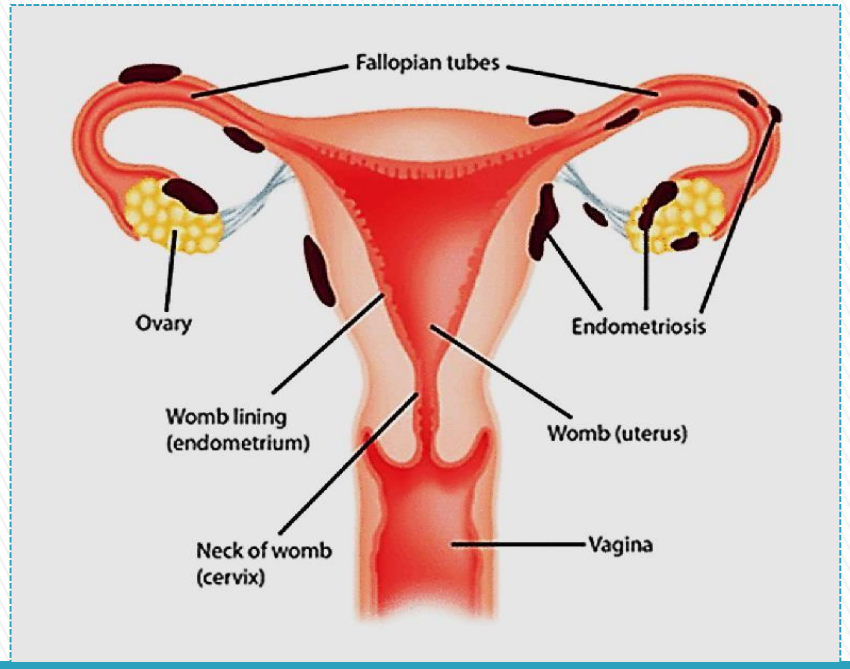
Adenomyosis

- Adenomyosis means “glands within the muscle.” In this condition, there is abnormal invagination and embedding of endometrial tissue into the myometrium.
- Adenomyosis is not a cancerous condition. It is simply the presence of normal endometrial tissue in an abnormal location within the myometrium.
- endometrial stroma, glands, or both embedded in **myometrium**..
- Derived from **stratum basalis → no cyclical bleeding**.
- However, the presence of endometrial tissue in this abnormal location causes changes in the myometrium, including hyperplasia and hypertrophy leading to Thick uterine wall, globular enlarged uterus.
- menorrhagia(heavy menstrual bleeding), dysmenorrhea (severe pain during mensis); due to enlarged uterus, uterine contractions are exaggerated

Endometriosis

- endometrial glands and stroma **outside the uterus (not cancer !)** there is no monoclonal proliferation.
- Instead, there is a mixture of two types of polyclonal cells: endometrial glands and stroma. One theory suggests that it originates from the coelomic epithelium in the peritoneum
- Histologically, it contains functional endometrium
- 10% in reproductive yrs; ↑ infertility.
- dysmenorrhea, and pelvic pain, pelvic mass filled with blood (chocolate cyst). It is called a "chocolate cyst" because it contains old degenerated blood, which gives it a brownish color
- Multifocal in pelvis (ovaries, pouch of Douglas, uterine ligaments, tubes, and rectovaginal septum).
- Sometimes distant sites (e.g. umbilicus, lymph nodes, lungs, ...)

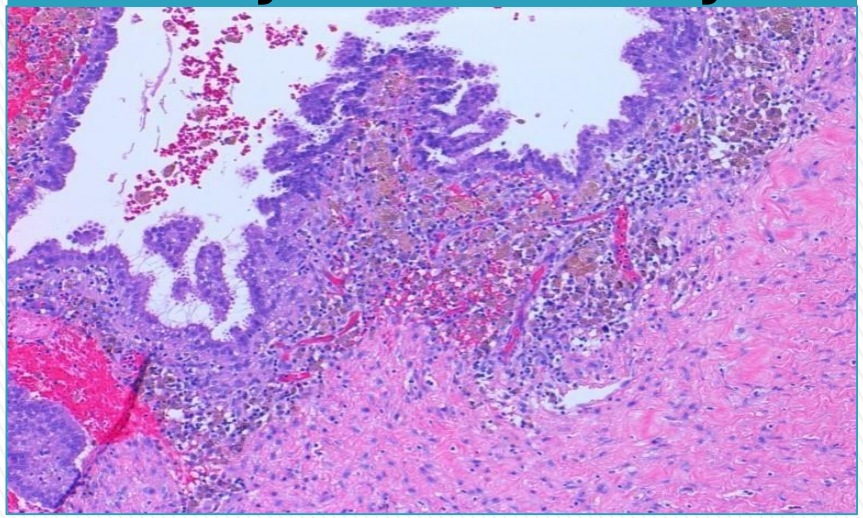
there is a black region. These black regions represent the locations of endometriosis, where endometrial glands and stroma grow outside the uterus



Common locations of endometriotic lesions

"Chocolate" cyst in an ovary

Intraoperative view of endometriosis



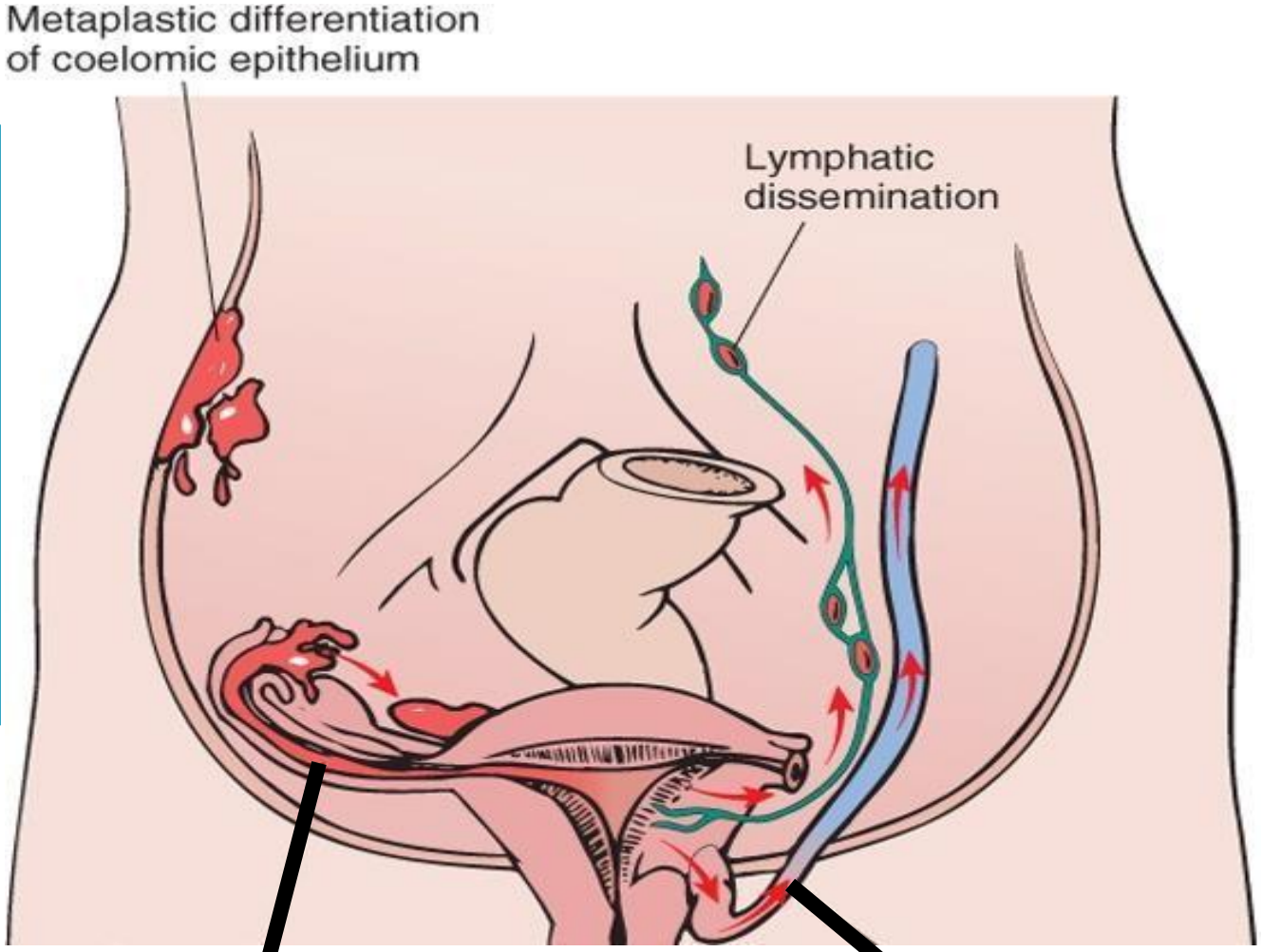
Microscopic view of endometriosis

ENDOMETRIOSIS- Pathogenesis

4 theories: All four theories are considered valid

- ***Regurgitation theory.*** ***(***most accepted). Menstrual backflow through tubes and implantation..
- ***Metaplastic theory*** . Endometrial differentiation of coelomic epithelium.
- ***Vascular*** **or** ***lymphatic dissemination theory.*** explain extrapelvic or intranodal implants.
- ***Extrauterine stem/progenitor cell theory***, proposes that circulating stem/progenitor cells from bone marrow differentiate into endometrial tissue

Conceivably, all pathways are valid in individual instances.



Regurgitation through fallopian tube

Extrapelvic dissemination through pelvic veins

Endometriosis

- contains *functionalis endometrium*, as the name indicates, this layer has a function and therefore responds to hormonal cyclic changes, particularly estrogen and progesterone so undergoes cyclic bleeding.
- In the first half of the menstrual cycle, known as the proliferative phase, the tissue responds to estrogen and grows.
- In the second half of the cycle, it responds to progesterone, which stimulates secretory activity.
- At the end of the second phase, the endometrium sheds. If shedding occurs outside the uterine cavity, as in the black regions, it causes pain and dysmenorrhea

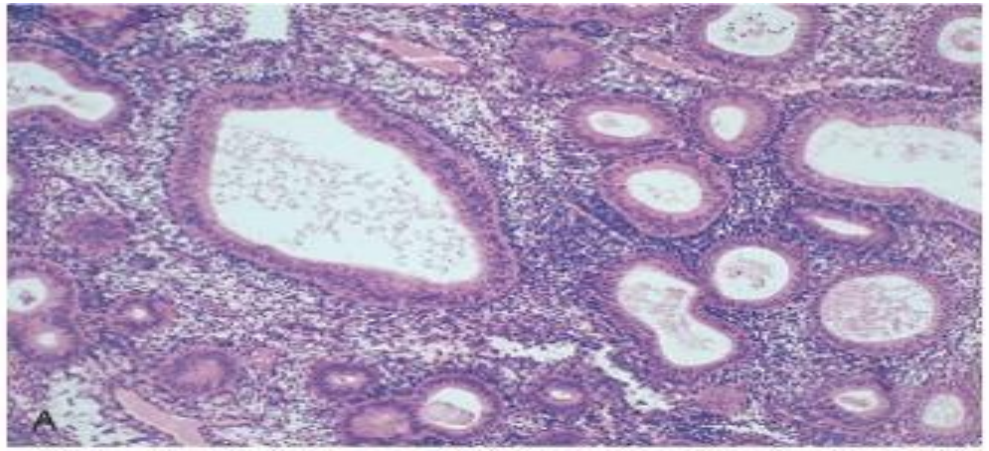
- It may also cause menstrual abnormalities and pelvic masses if these regions enlarge and form cysts that collect blood over a long period of time.
- Over several months or years, this process can lead to pelvic masses and chronic inflammation
- Chronic inflammation may result in Consequences: fibrosis leading to infertility and an increased risk of ectopic pregnancy, sealing of tubal fimbriated ends, and distortion of the ovaries.

- Diagnosis; 2 of 3 features: endometrial glands, endometrial stroma, or hemosiderin pigment
  Hemosiderin pigment forms because blood accumulates, degenerates, and is then engulfed by macrophages.

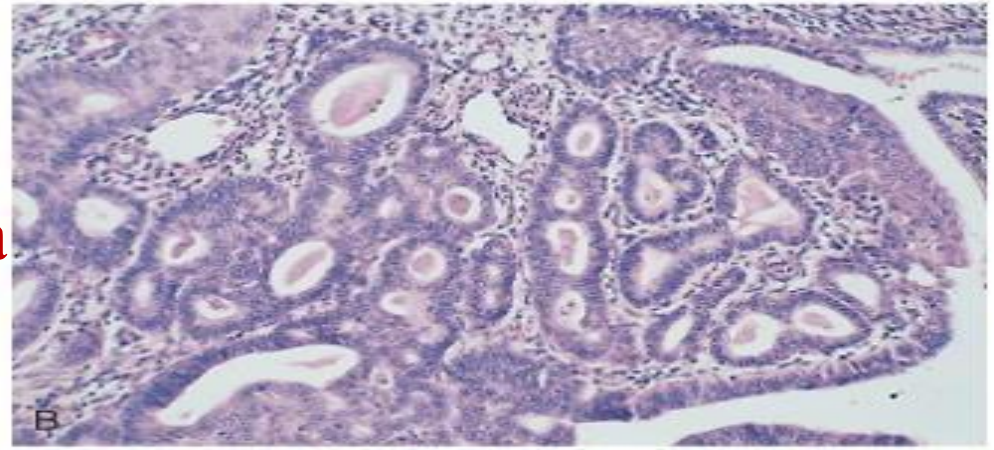
Endometrial Hyperplasia

- Endometrial Hyperplasia is increase in cells number of endometrial glands (epithelial cells)
- Caused by prolonged or marked excess of estrogen, which is responsible for inducing mitosis in glandular cells, relative to progestin →exaggerated proliferation →may progress to cancer
- Excess estrogen either endogenous or exogenous (unbalanced Contraceptive pills) → exaggerated proliferation
- risk factors for the condition are those of hyper-estrinism : **Obesity; Diabetes; Hypertension; Infertility (that is related to excess estrogen, anovulation and lack of progesterone) ; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors**
- severity is based on architectural crowding and cytologic atypia, ranging from:
  - typical hyperplasia
  - Atypical hyperplasia (20% risk of cancer).

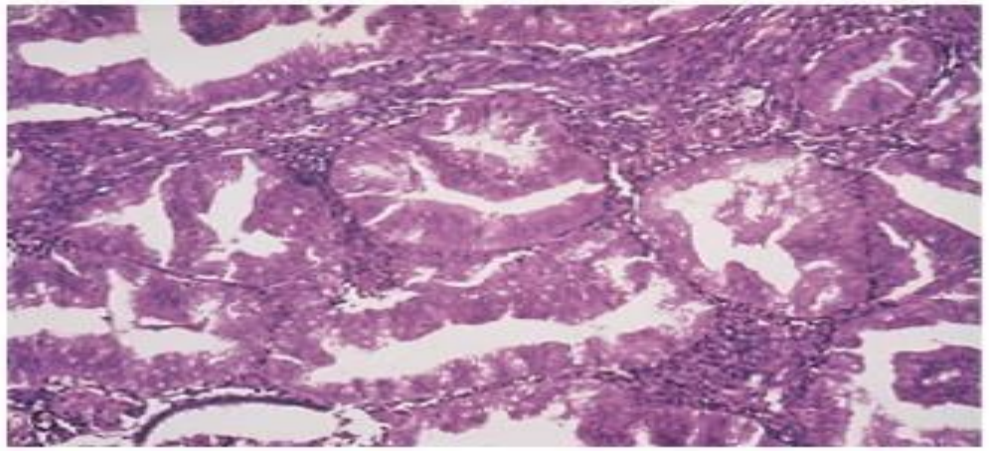
Simple hyperplasia



Complex Hyperplasia



Atypical Hyperplasia



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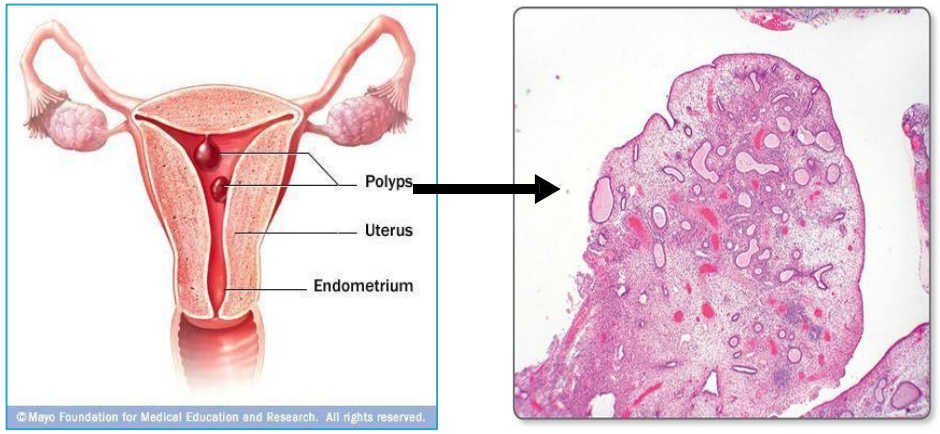
Benign Endometrial Polyps

- Like polyps seen in colon (hyperplastic polyps)
- Can be sessile or pedunculated
- endometrial dilated glands, with small muscular arteries and fibrotic stroma
- They are benign lesions that are not neoplastic, and they don't develop to cancers so no risk of endometrial cancer
- may undergo surface ulceration and bleeding
- symptoms: menstrual irregularity, intermenstrual bleeding or spotting (light vaginal bleeding outside of a normal period)



Endometrial Carcinoma

The most common cancer in all parts of female genital tract.

- Patients develop it in their 50s and 60s.
- Two clinical settings, are correlated with differences in histology:
  - Perimenopausal women with **estrogen excess**, prototype is called ***endometrioid*** (type I) , the suffix –ioid means like, and that indicates that it has developed from a previously normal endometrium that have undergone hyperplasia due to excess stimulation by estrogen then it develop to cancer.
    - The precursor lesion: Atypical endometrial hyperplasia
    - Most frequent
  - older women with endometrial atrophy, prototype is ***serous carcinoma*** (type II) which is less frequent, not related to estrogen level, but rather it is related to **genetic mutation** in the cells of endometrium

Endometrioid carcinoma

- similar to normal endometrium.
- risk factors: Obesity; Diabetes; Hypertension; Infertility; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors. Just like those of endometrial hyperplasia
- precancerous lesion is **atypical** endometrial hyperplasia
- Mutations in DNA mismatch repair genes and PTEN
- Prognosis: depends on **stage**. (5-year survival in stage I= 90%; drops to 40% in stages III and IV.)

Gra**d**e → related to **d**ifferentiation, higher grade less differentiation
Stage→ **S**pread (metastasis), higher stage means higher spread

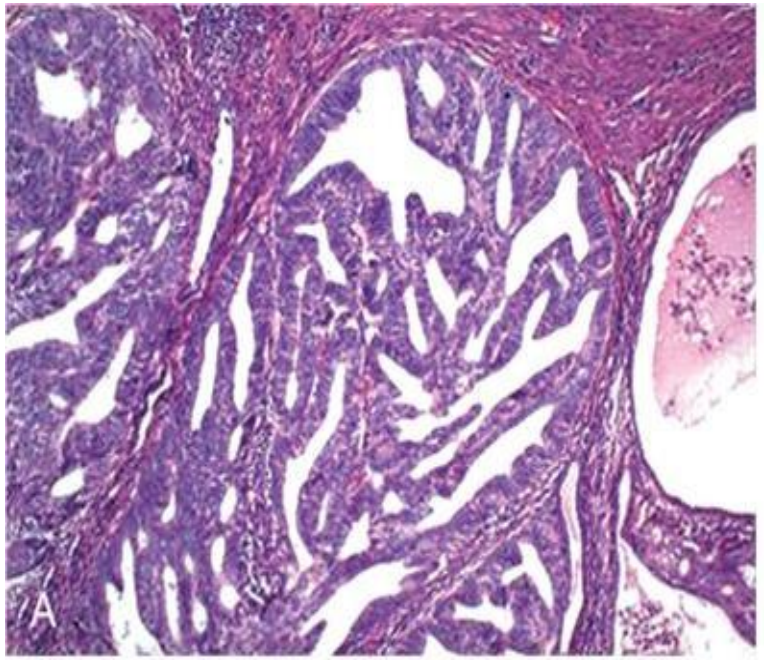
serous carcinoma

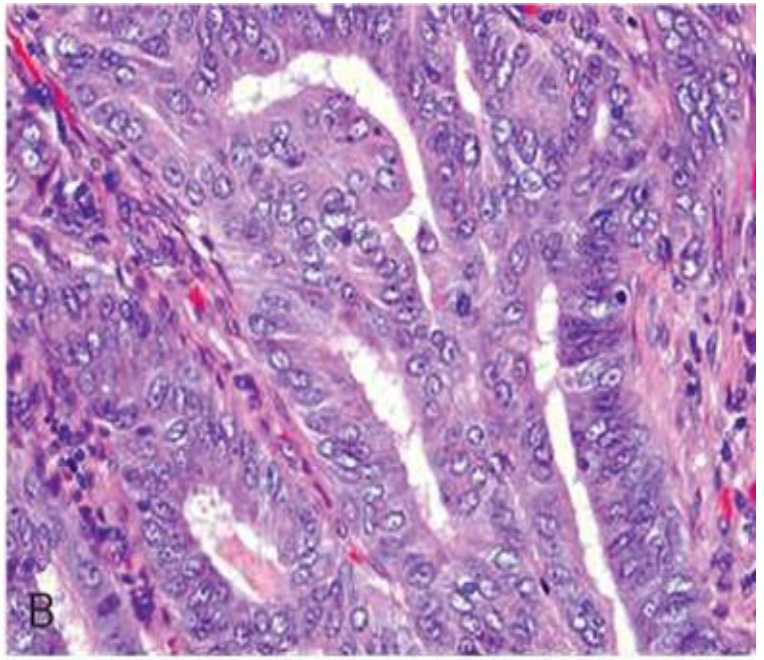
- No relation with endometrial hyperplasia
- Not hormone-dependent
- Mutations in p53 tumor suppressor gene. Detected in more than 90% of patients
- Prognosis: depends on operative **staging** with peritoneal cytology.
- Generally worse than endometrioid carcinoma; because they are metastatic early.

- Immunohistochemical stains for p53 can tell the type of carcinoma, where it is over expressed in serous carcinoma

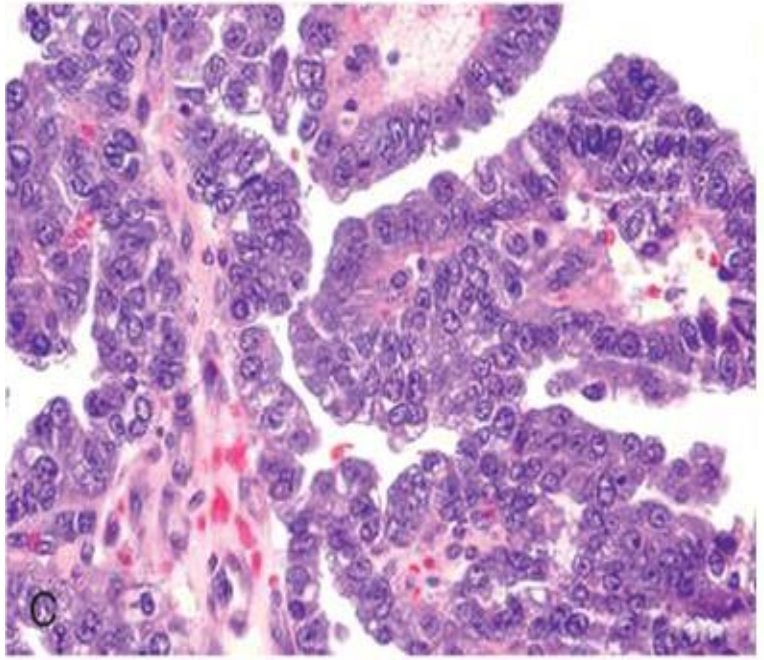
- It shows “All or None” pattern of detection where **all** tumor cells retain positive result or none of them indicate so.

Endometrioid carcinoma

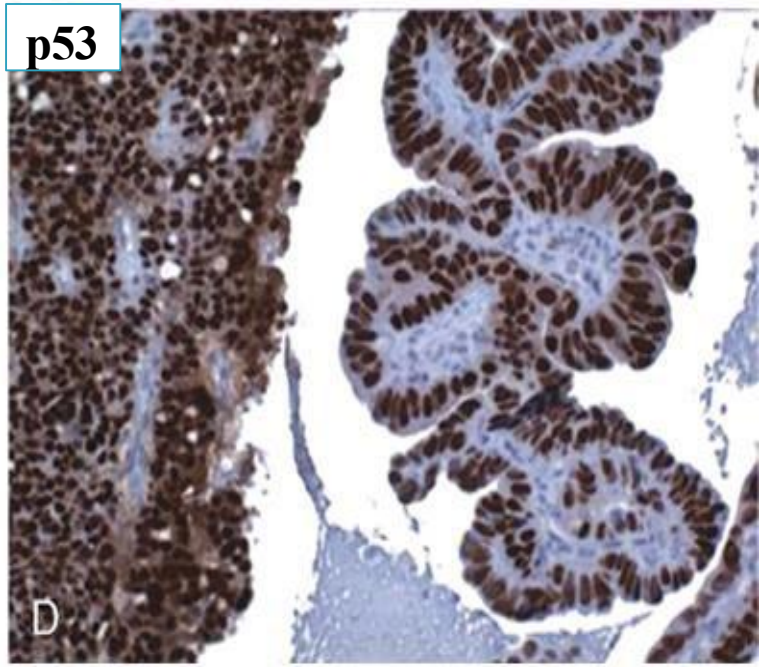




Serous carcinoma



p53

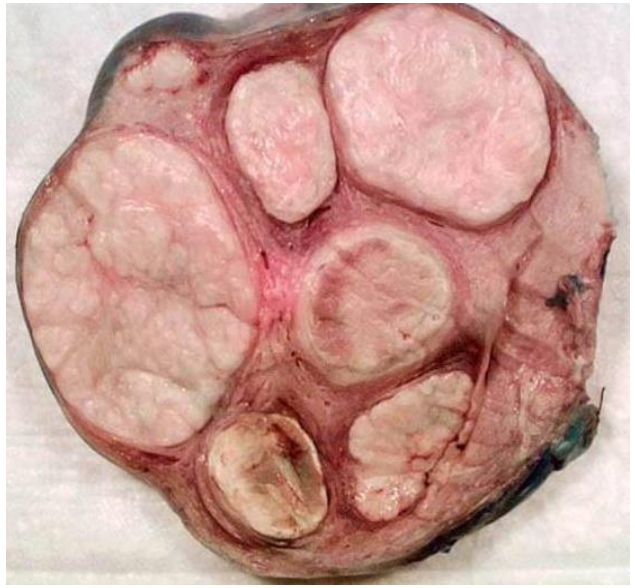


Tumors of myometrium

- **Lieomyoma** = fibroids a commoner name "التَلَيُّف"
  lieo = smooth, myo = muscle, -oma indicates benign tumor
- Very common Benign tumor of smooth muscle cells
- Most common **benign tumor** in females (30% - 50% in reproductive life). Not to be confused with that fact the endometrial carcinoma is the most common **cancer** in female genital tract
- Estrogen-dependent, enlarges with hyper-estrinism ; shrink after menopause.
- well circumscribed, firm gray-white masses with whorled "دوامة" cut surface.

Lieomyoma

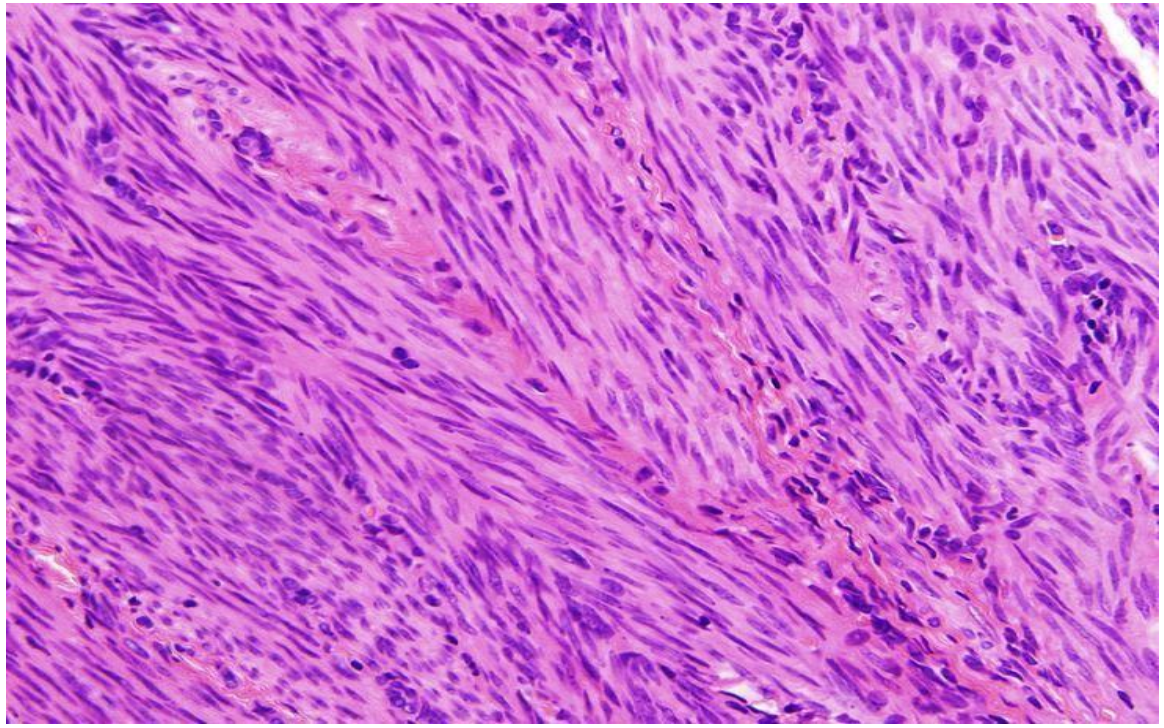
- Location: (intramural, inside the wall), (submucosal, just beneath the endometrium), or (subserosal, serosa is the layer beneath myometrium).
- may develop hemorrhage, cystic change or calcification.
- Clinically: asymptomatic or symptomatic;
  depending on size and location, when there are symptoms they show menorrhagia; a dragging sensation, anemia; due to excessive bleeding, etc...
- leiomyomas almost **never** transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.



Intramural

subserosal

Submucosal



Intersecting fascicles of smooth muscle fibers

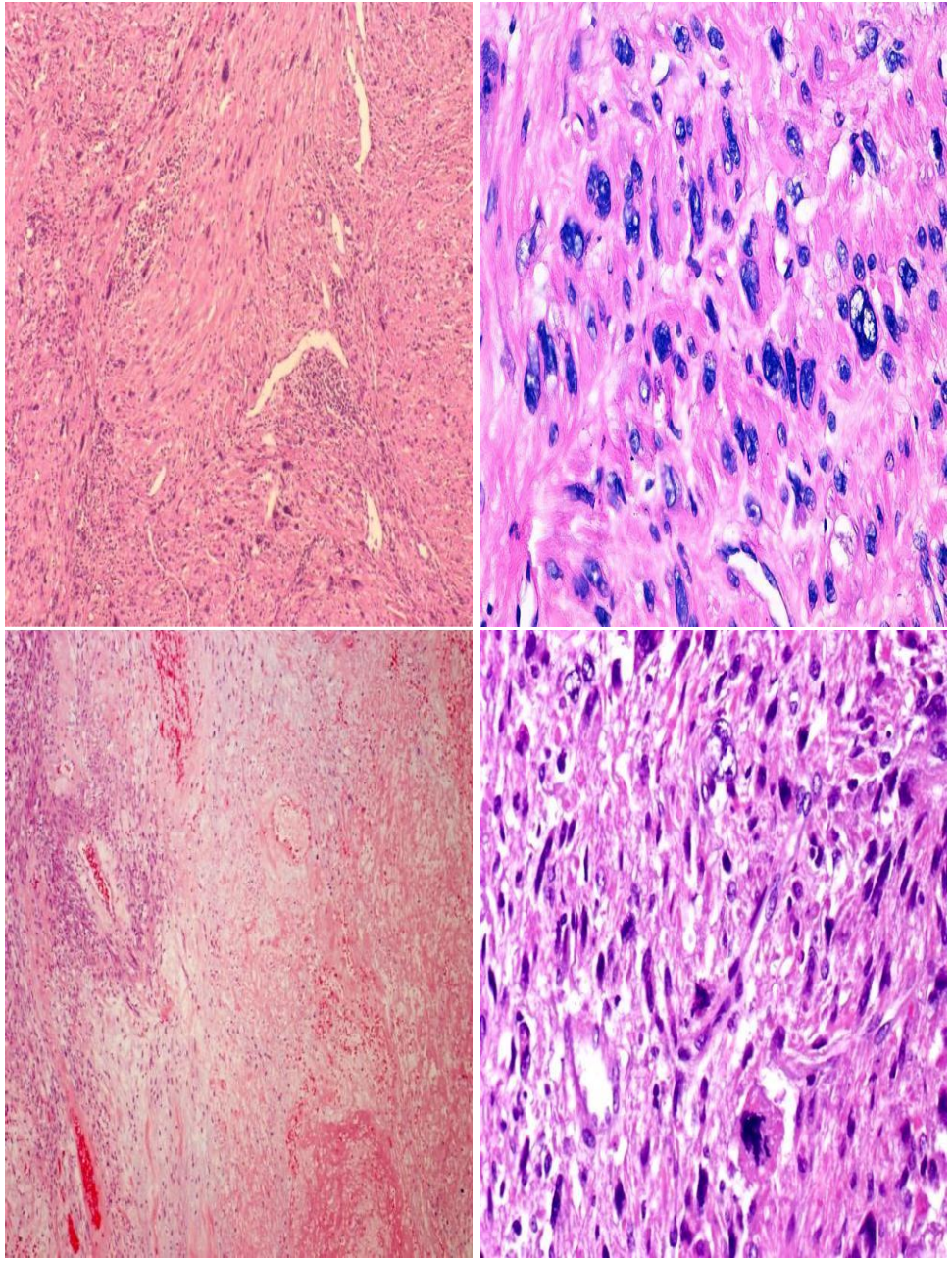
Lieomyosarcoma

Malignant counterpart of leiomyoma.

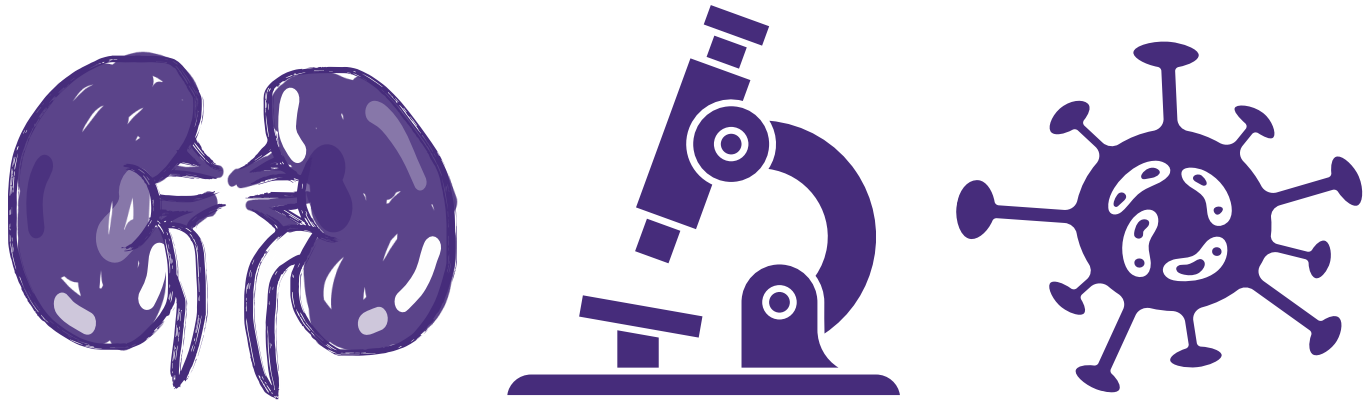
- do not arise from preexisting leiomyomas.
- clues: hemorrhagic, necrotic, infiltrative borders.
- diagnosis: presence coagulative necrosis, cytologic atypia, and mitotic activity.
- aggressive tumors Recurrence common,

Lieomyosarcoma

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



- Please appreciate how this morphology totally differs from that seen in leiomyoma
- Hemorrhage, infiltrative borders, necrosis (the yellowish areas) are seen



PATHOLOGY QUIZ LECTURE 2

External Resources

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Versions	Slide # and Place of Error	Before Correction	After Correction
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