Uterine Pathology

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- Mucosal layer composed of glands and stroma.
- It covers the inner aspect of the uterine cavity.
- It's the part that undergoes cyclical bleeding as its hormonal dependent.

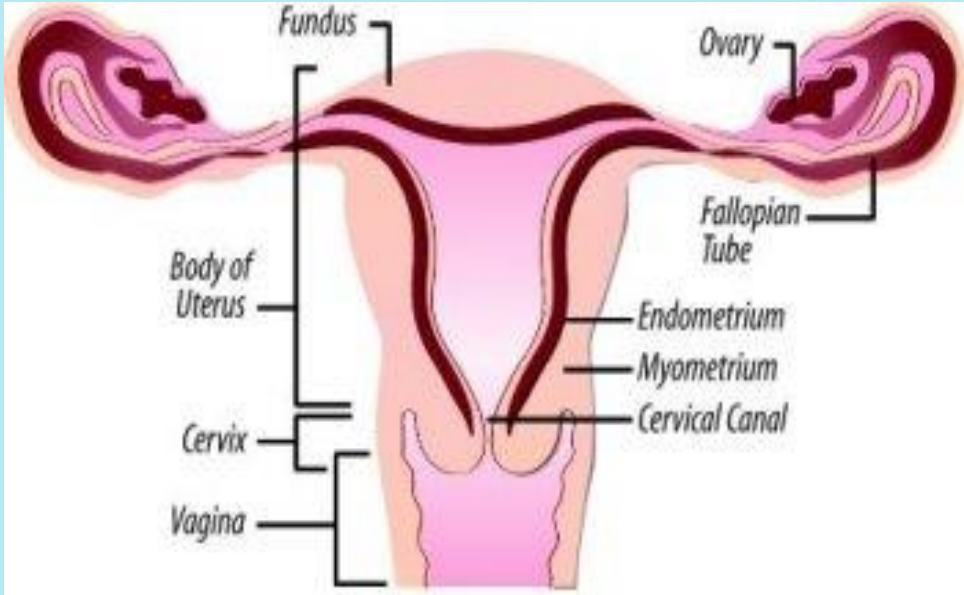
Endometrium

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

- Composed of smooth muscle fibers.
- Form the middle wall of the uterus.
- The function is support and contraction.

Myometrium

- Leiomyoma
- Leiomyosarcoma



ENDOMETRITIS

- Inflammation of the endometrium. May be infectious or non-infectious.
- Causes:

1- infections - pelvic inflammatory disease (PID)

2-miscarriage or delivery

3- intrauterine device (IUCD).

- acute or chronic
- fever, abdominal pain, menstrual abnormalities, infertility and ectopic pregnancy due to damage to the fallopian tubes.
  - Due to fibrosis and obstruction of the fallopian tubes.
  - Patients with chronic endometritis who have extensive inflammation and infection reaching the adnexal structure and leading to PID, this results in healing by fibrosis which is linked to infertility and higher risk to have ectopic pregnancies.
- Rx: removal of cause, antibiotics, D&C.
  - Dilatation and curettage.
  - An invasive procedure where there is scraping of endometrial tissue from the uterus (cleaning of the uterus).

First 3 are of acute, all are of chronic (but doctor didn't mention fever).

= Glands in muscles.

ADENOMYOSIS

- Invagination and embedding of endometrial statutes inside the myometrium.
- Meaning endometrial glands and stroma, one of them or both are embedded with the myometrium.
- This leads to a thick uterine wall, and globular enlarged uterus.
- The myometrium undergoes both hypertrophy and hyperplasia.
- Not cancer, merely endometrial structures present in an inappropriate place.

- endometrial stroma, glands, or both embedded in **myometrium**.
- Thick uterine wall, enlarged uterus.
- Derived from **stratum basalis → no** cyclical bleeding.

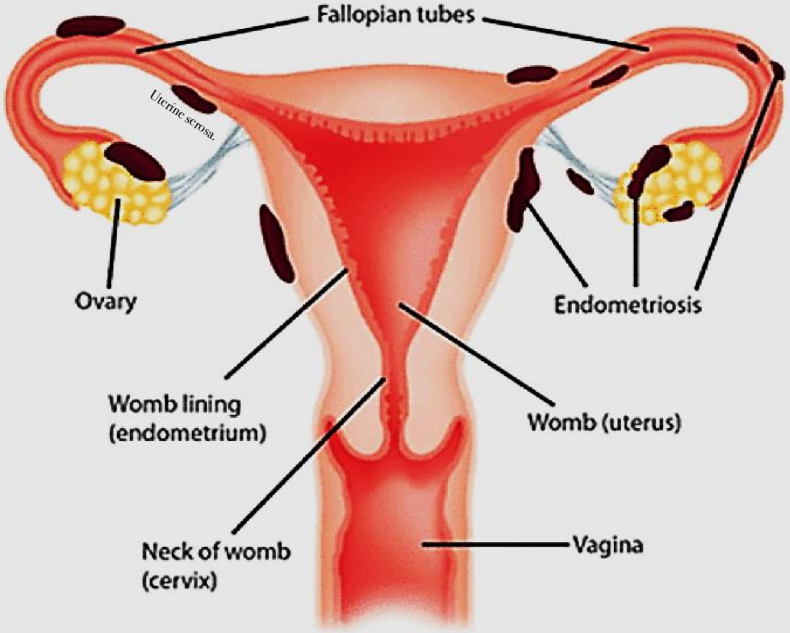
The endometrial tissue that is invaginating the myometrium is derived from stratum basalts which does not undergo cyclical bleeding.

- menorrhagia, dysmenorrhea (due to enlarged uterus, uterine contractions are exaggerated)

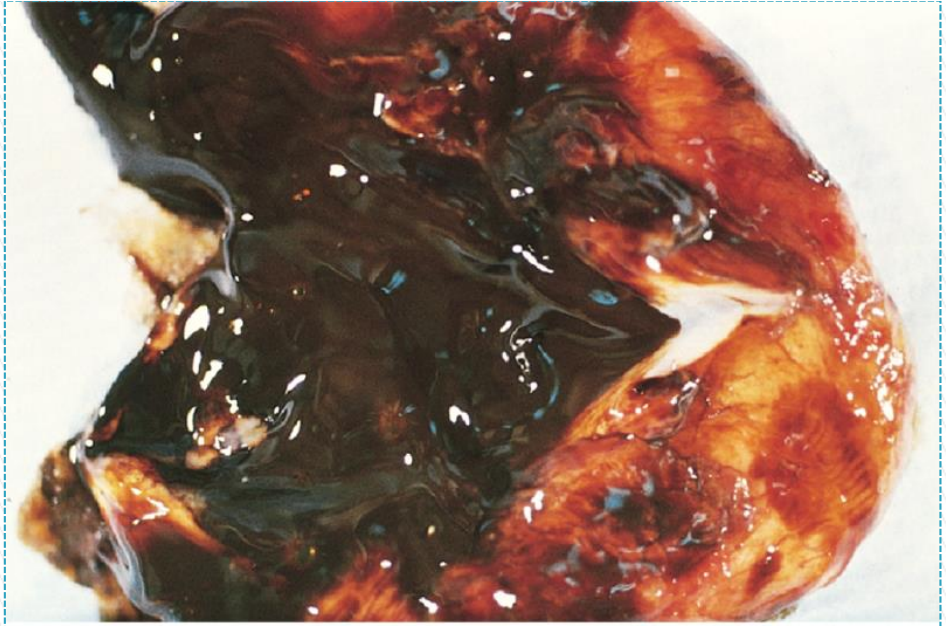
ENDOMETRIOSIS

- endometrial glands and stroma **outside the uterus (not cancer !)**.
- 10% in reproductive yrs; ↑ infertility.
- dysmenorrhea, and pelvic pain, pelvic mass filled with blood (chocolate cyst).
  - Called "chocolate cyst" due to the presence of old degenerated blood in the cycle giving a brownish color.
  - With every menstrual cycle, the blood further accumulates (has no drainage) and therefore changes color with time.
- Multifocal in pelvis (ovaries, pouch of Douglas, uterine ligaments, tubes, and rectovaginal septum).
- Sometimes distant sites (e.g. umbilicus, lymph nodes, lungs, ...)

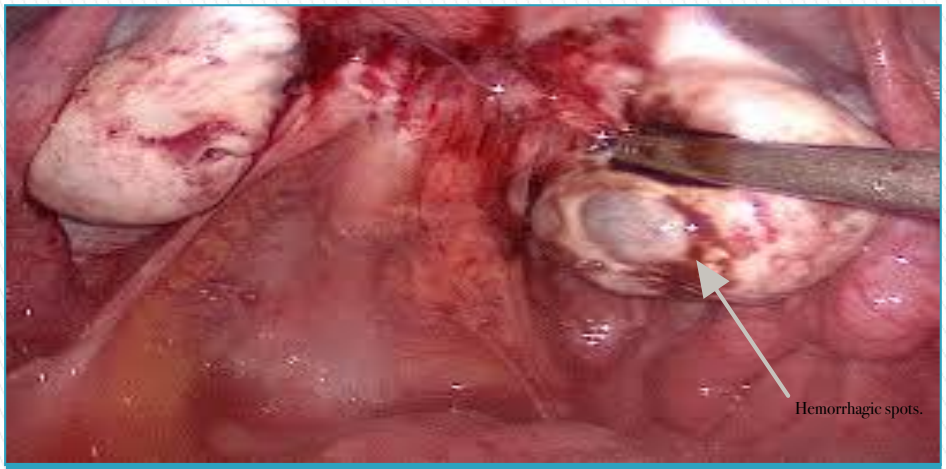
Sometimes they develop in surgical wounds/incisions, e.g. C-sections or appendectomies.



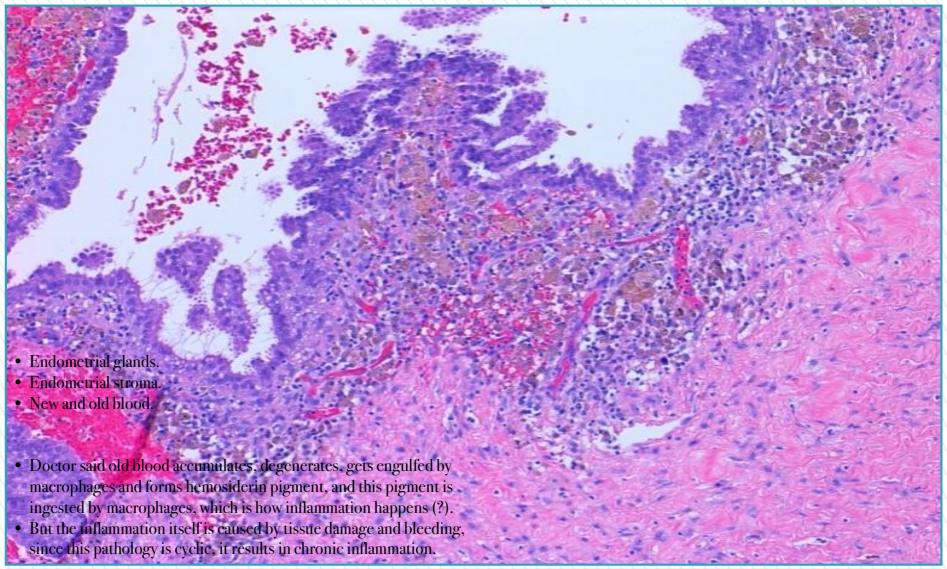
Common locations of endometriotic lesions



"Chocolate" cyst in an ovary



Intraoperative view of endometriosis



Microscopic view of endometriosis

ENDOMETRIOSIS- Pathogenesis

- 4 theories: All are valid depending on the case.
- ***Regurgitation theory.*** ***(***most accepted). Menstrual backflow through tubes and implantation..

  Explains the majority of cases, and suggests that fragments of endometrial glands and stroma get outside the uterus and implant somewhere else in intrapelvic structures.
- ***Metaplastic theory*** . Endometrial differentiation of coelomic epithelium.

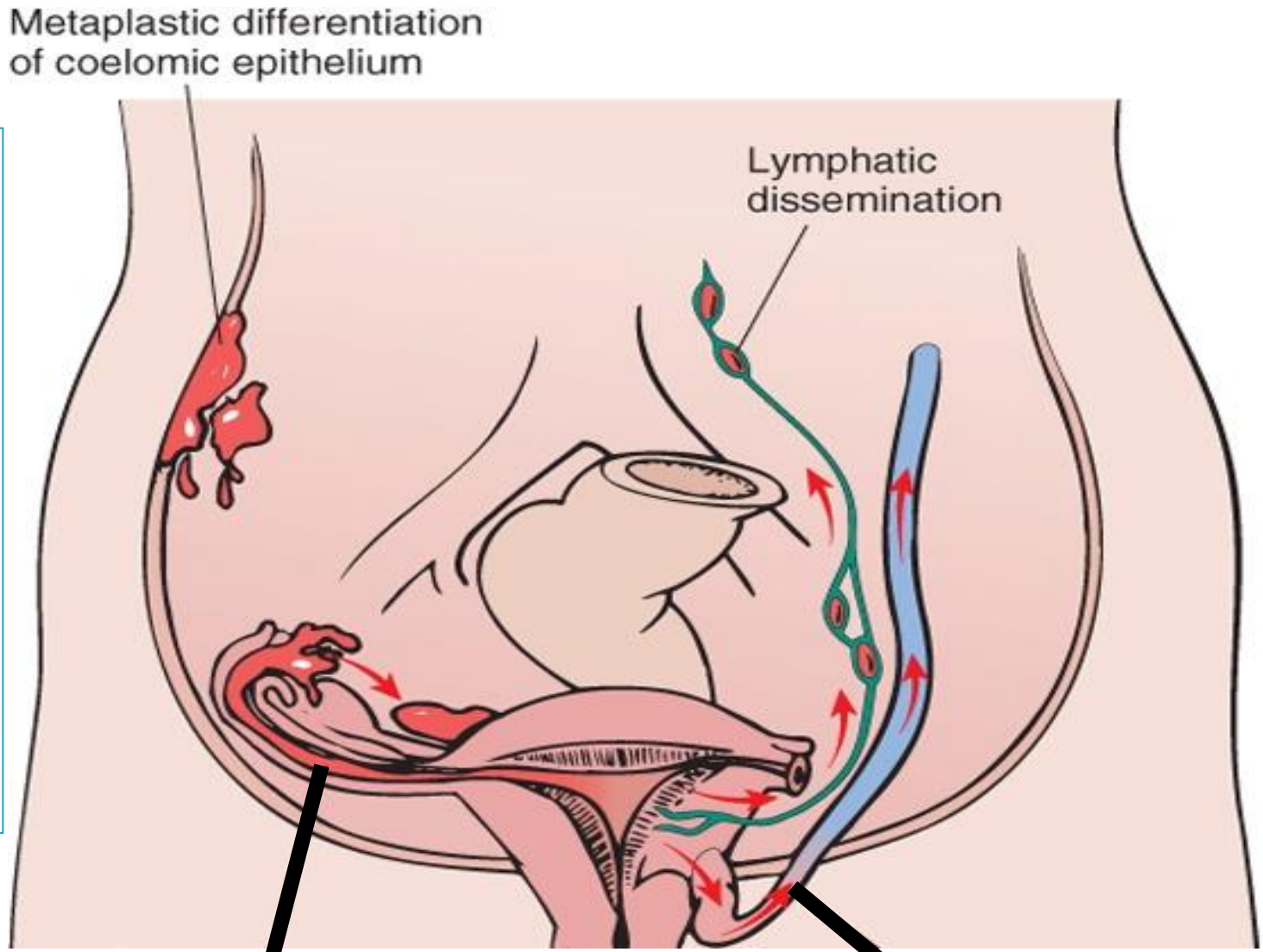
  Some coelomic epithelial cells within the peritoneum have the ability to differentiate into various cells of which one is endometrial cells, and therefore form endometrial tissue.
- ***Vascular*** **or** ***lymphatic dissemination theory.*** explain extrapelvic or intranodal implants.

  Fragments of endometrial glands and stroma get access to a blood vessel or a lymphatic vessel and travels with its flow to implant somewhere.
- ***Extrauterine stem/progenitor cell theory***, proposes that circulating stem/progenitor cells from bone marrow differentiate into endometrial tissue

  Most recent, explains distal (extrapelvic) endometriosis.

Conceivably, all pathways are valid in individual instances.

- Endometrial tissues forming lesions of endometriosis are composed of stratum functionalis, meaning it can undergo cyclical bleeding.
- "Functionalis" means it is functional, meaning it responds to cyclical changes of hormones.
- First half "proliferative" phase of the cycle: responds to estrogen and undergoes mitosis and growth of glands and stroma.
- Second half "secretory" phase of the cycle: responds to progesterone, causing it to function and release secretions.
- At the end of the second phase, endometrium will shed outside the uterine cavity and bleed, leading to dysmenorrhea and forms a pelvic mass (cyst that collects blood) over time.
- Over time, cysts, accumulation of blood, and the resulting inflammation leads to fibrosis, which causes infertility and increases the chances of ectopic pregnancy.



Regurgitation through fallopian tube

Extrapelvic dissemination through pelvic veins

ENDOMETRIOSIS

- contains **functionalis endometrium**, so undergoes **cyclic bleeding**.
- Consequences: fibrosis, sealing of tubal fimbriated ends, and distortion of the ovaries. Thus a major risk factor for ectopic pregnancy.
- Diagnosis; 2 of 3 features: endometrial glands, endometrial stroma, or hemosiderin pigment. That is the criteria for histological diagnosis.

- Relationship of estrogen with endometrial hyperplasia? Mitosis.
- That is, mitosis in the glandular cells.
- Progesterone's function is secretory, thus, estrogen is the more dangerous hormone in the context of cancer.
- The excess estrogen may be endogenous or exogenous (like estrogen medications or unbalanced contraceptives.
- The idea behind the mechanism is that the endometrium is being subjected to excessive amounts of estrogen, which cause proliferation (hyperplasia), and if left without removal, it may progress tor each cancer.

Endometrial Hyperplasia

Increased number of endometrial glands.

- prolonged or marked excess of **estrogen** relative to progestin →exaggerated proliferation → may progress to cancer
- risk factors: **Obesity; Diabetes; Hypertension**; (Metabolic syndrome.)

Infertility is related to anovulation and excess estrogen and thus (due to anovulation) a lack of progestin.

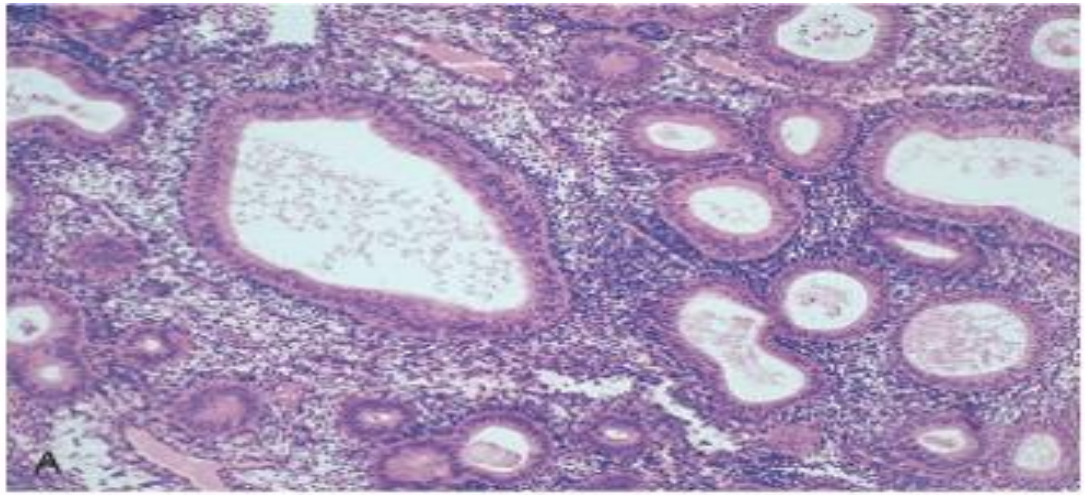
Infertility; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors. Those being risk factors for hyperestrinism.

- severity is based on architectural crowding and cytologic atypia, ranging from:

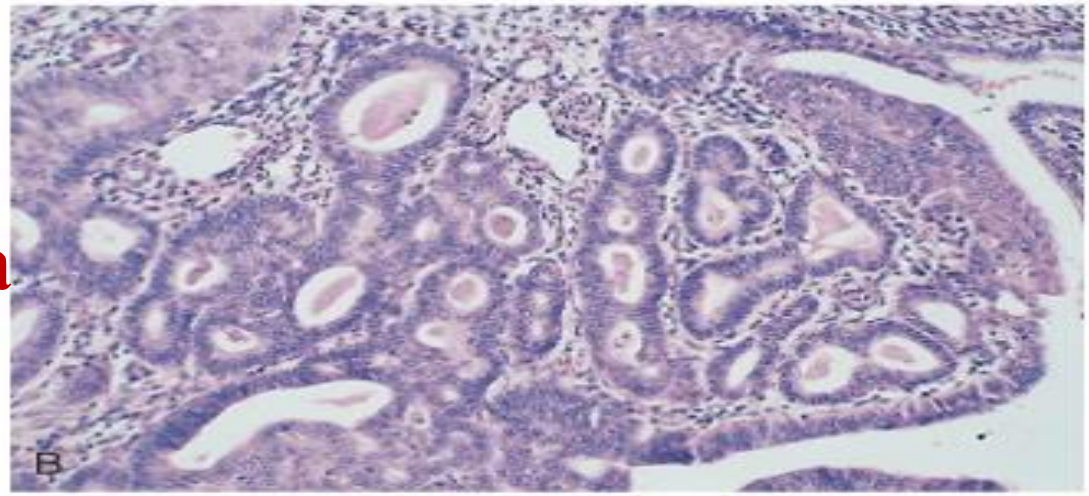
1- typical hyperplasia Without atypia.

2- Atypical hyperplasia (20% risk of cancer). With atypia, higher risk for cancer.

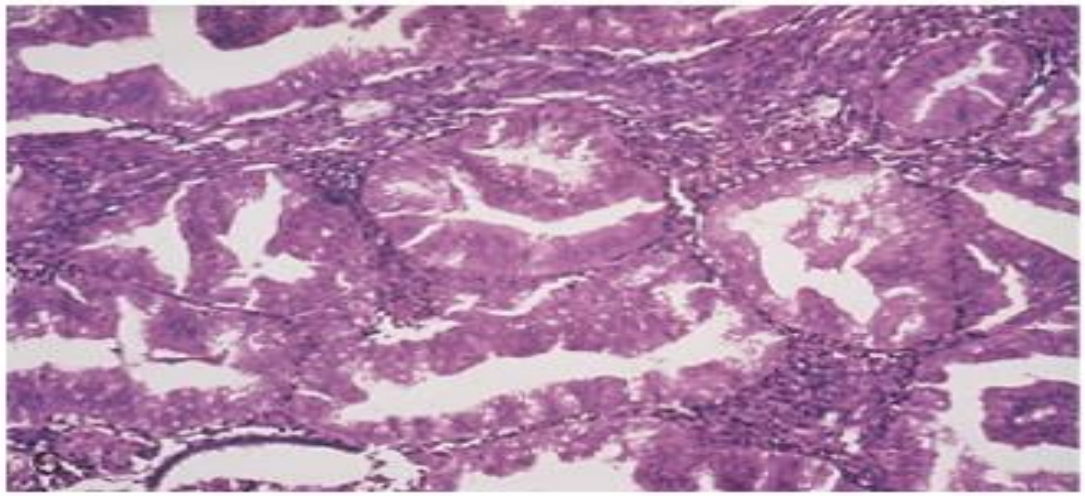
Simple hyperplasia



Complex Hyperplasia



Atypical Hyperplasia



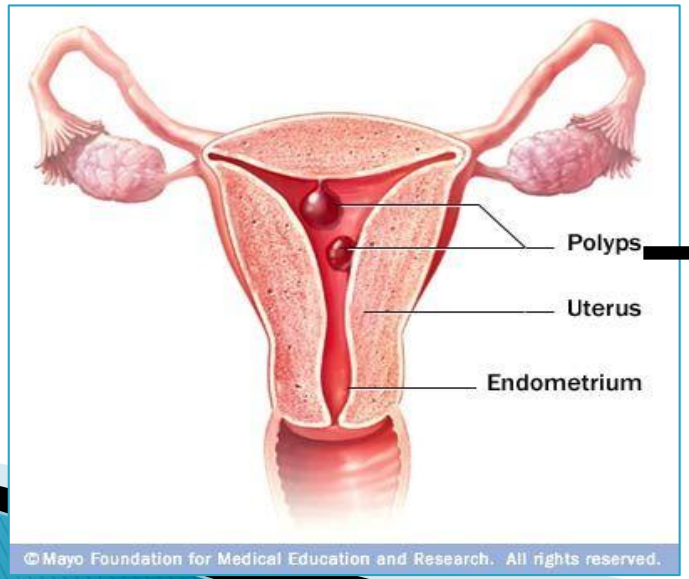
er. Kumar et al: Robbins Basic Pathology 8e - www.studentco

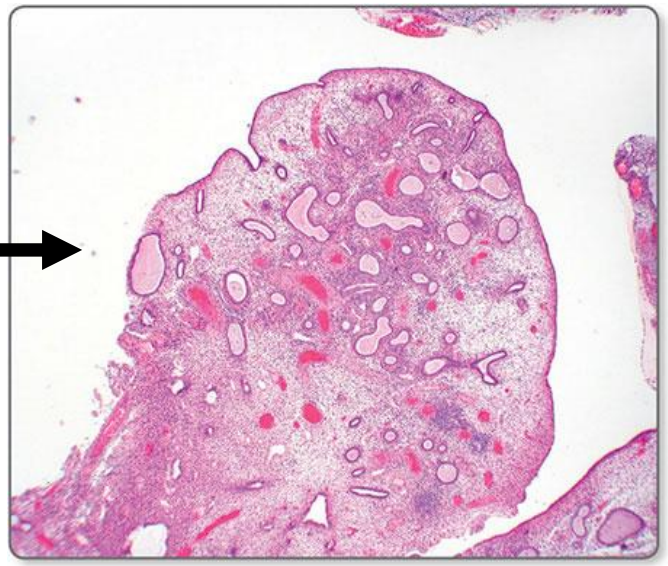
TUMORS OF THE ENDOMETRIUM

- They're similar to colonic hyperplastic polyps.
- Those are benign lesions, non-neoplastic, NOT a result of hyperplasia.
- They may undergo surface ulceration and bleeding.
- They may cause some symptoms for patients like menstrual irregularities. intermenstrual bleeding, spotting.

Benign Endometrial Polyps

- sessile or pedunculated
- endometrial dilated glands, with small muscular arteries and fibrotic stroma.
- no risk of endometrial cancer.





Endometrial carcinoma is classically divided into:

- **Type I (endometrioid carcinoma)**
  - Estrogen-related
  - Often preceded by hyperplasia
  - Better prognosis overall
- **Type II (serous carcinoma and others)**
  - Not estrogen-related
  - Arises in atrophic endometrium
  - More aggressive, worse prognosis

Endometrial Carcinoma

- **the most common cancer in female genital tract.**
- 50s and 60s.
- two clinical settings:

• The classic scenario (most common).
• Same mechanism discussed previously in endometrial hyperplasia, this time progressing to cancer.
• Typical > Atypical > Cancer.

1) perimenopausal women with estrogen excess
2) older women with endometrial atrophy.

A mutation developed in the cells causing this type of cancer.

- These scenarios are correlated with differences in histology:

"Looks similar to normal endometrium."

- 1-type I cancers: prototype is called ***endometrioid***
- 2- type II cancers: prototype is ***serous carcinoma*** , respectively.

Prototype = most important example.

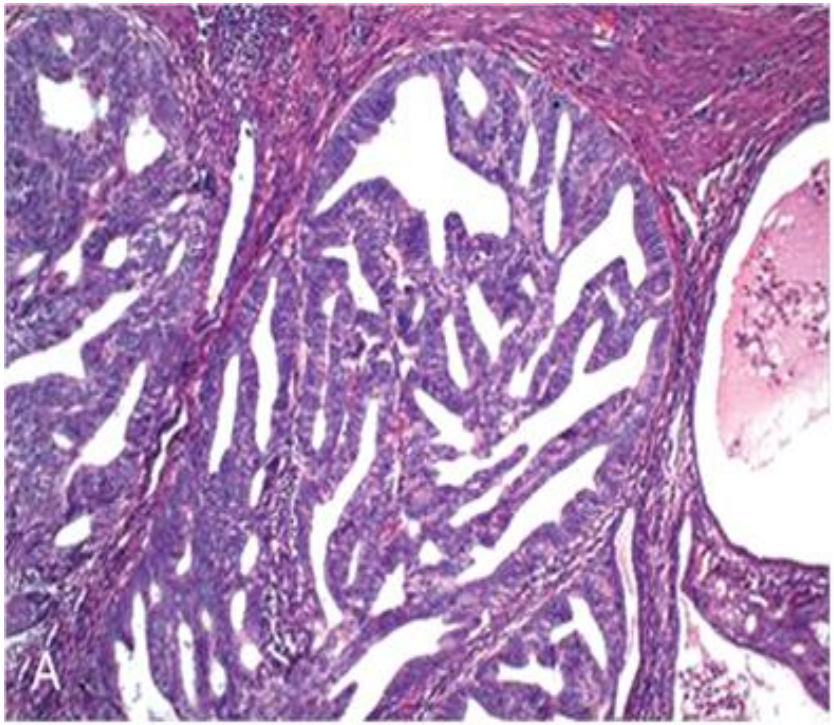
Endometrioid Carcinoma

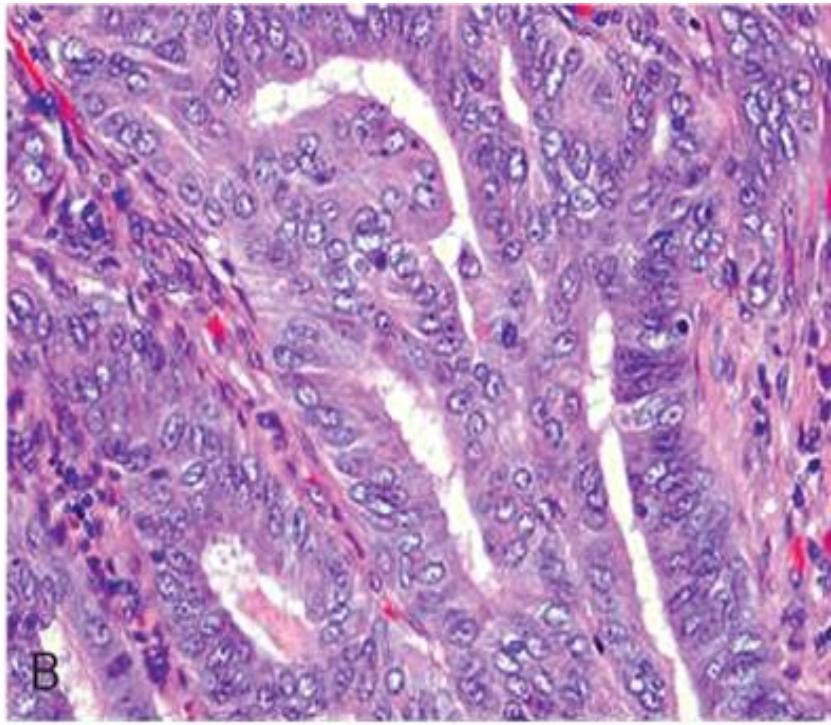
- similar to normal endometrium.
- risk factors: **Obesity; Diabetes; Hypertension**; **Infertility; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors**.
- ***precancerous*** *lesion is* ***atypical*** *endometrial hyperplasia*
- Mutations in DNA **mismatch repair genes** (MSI)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

Serous Carcinoma

- **No relation with endometrial hyperplasia**
- **Not hormone-dependent**
- **Mutations in *p53* tumor suppressor gene**.
- Prognosis: depends on operative staging with peritoneal cytology. Generally worse than endometrioid ca. Because they are often metastatic early.

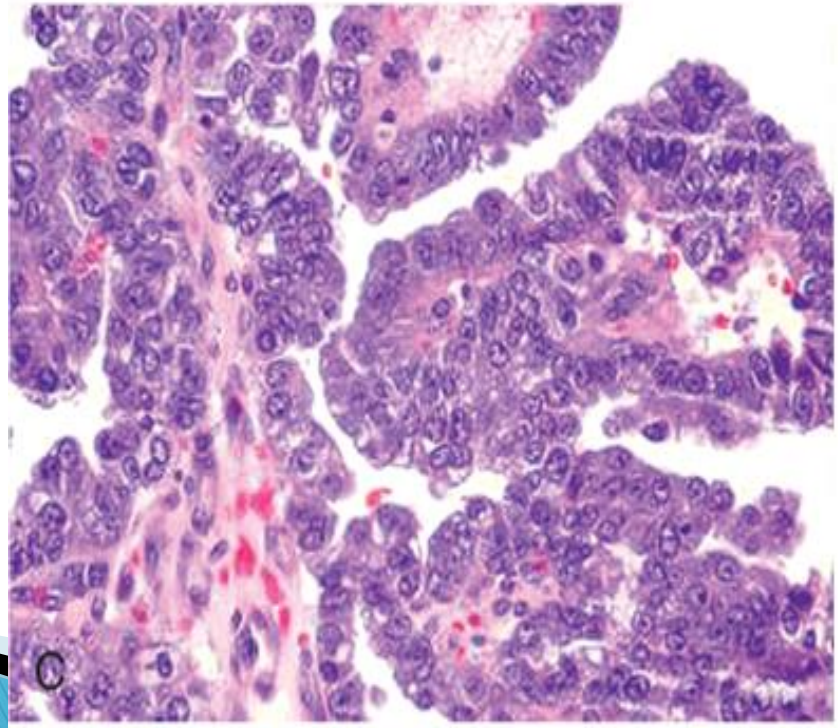
Endometrioid carcinoma



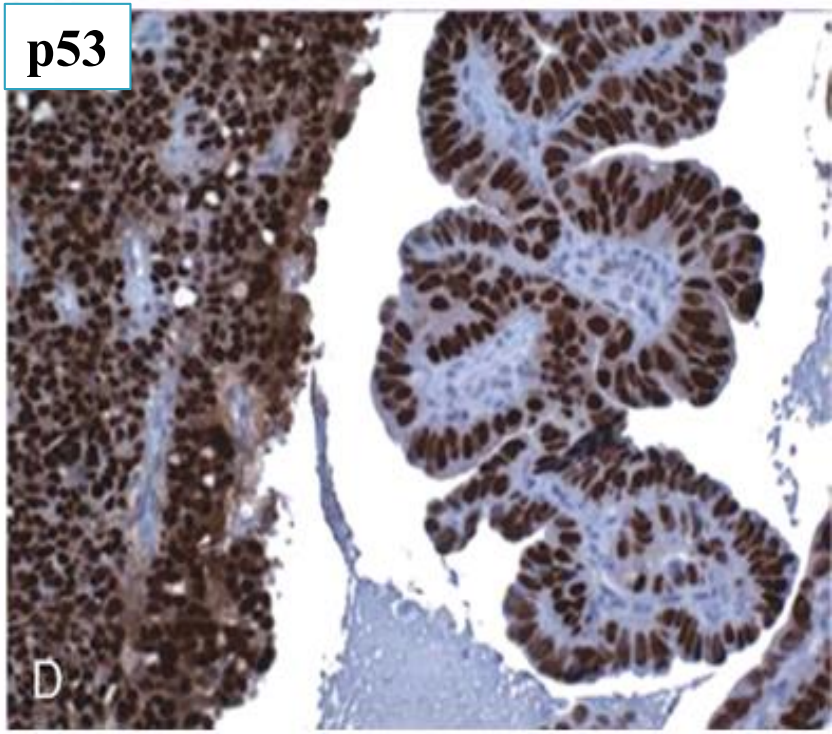


Serous carcinoma

- To detect p53 mutations, we perform immunostaining for the tissue of interest.
- The stain we use is to detect p53, which is counterintuitive but it is actually overexpressed despite being non-functional.
- The pattern here is all or none, either all cells are positive or all are negative.



p53



Tumors of the myometrium

Smooth Muscle Benign tumor

- **Lieomyoma = *fibroids***
- Benign tumor of smooth muscle cells
- most common benign tumor in females (30% - 50% in reproductive life).
- Estrogen-dependent; shrink after menopause.

Also means they get bigger with increase in estrogen.

- circumscribed, firm gray-white masses with whorled cut surface.

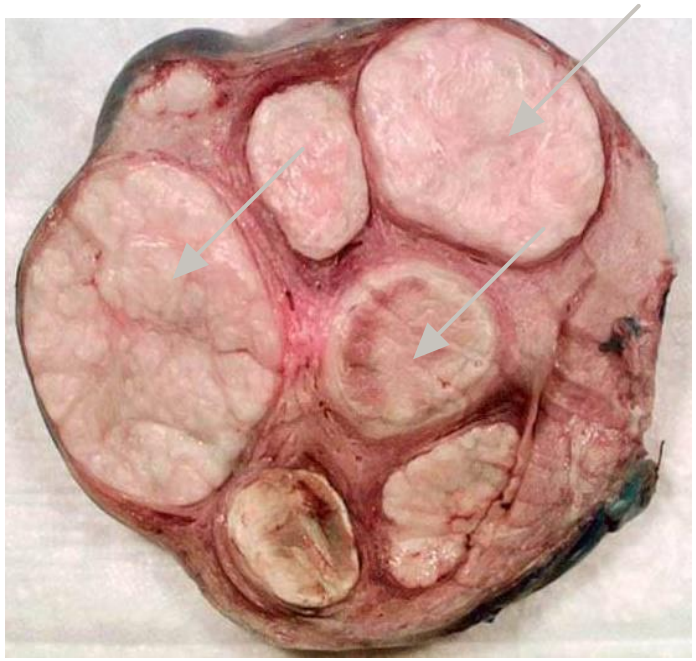
Because it is basically intersecting fascicles of smooth muscle.

Leiomyomas

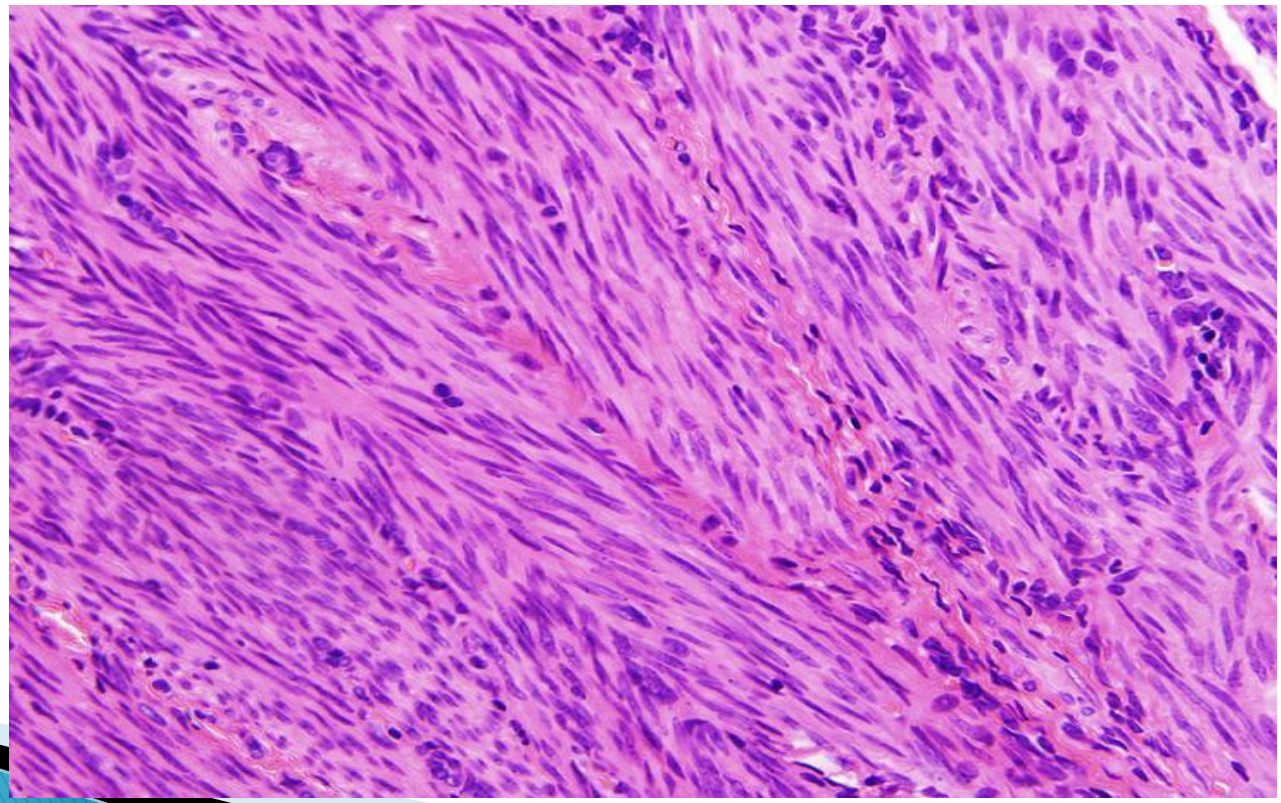
Meaning just beneath the endometrium (protruding into uterine cavity). Meaning below uterine serosa, the layer after myometrium.

- Location: (intramural), (submucosal), or (subserosal).
- may develop hemorrhage, cystic change or calcification.
- Clinically: asymptomatic or symptomatic; menorrhagia; a dragging sensation, anemia, etc... + dysmenorrhea.

  Depending on many factors like the location, the number, the size of the lesions.
- leiomyomas almost **never** transform into sarcomas, and the presence of multiple lesions *does not* increase the risk of malignancy.



- Well circumscribed.
- Whitish, fleshy lesion.
- Whorled cut surface.



Under microscope: intersecting fascicles of smooth muscle fibers.

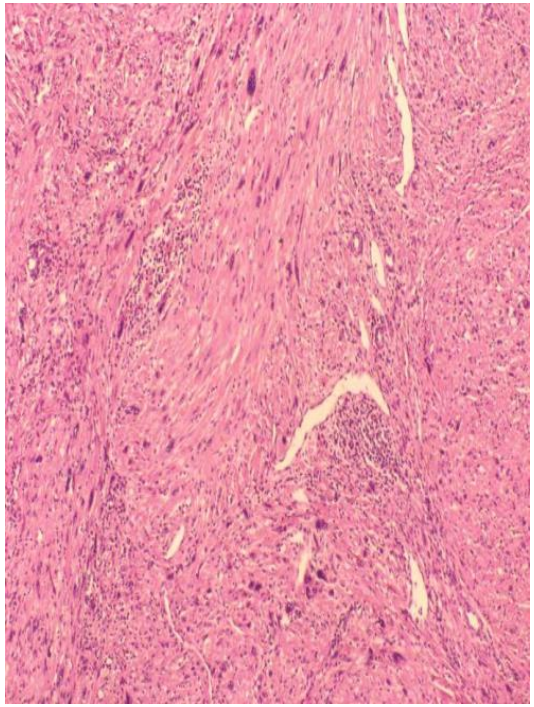
Lieomyosarcoma

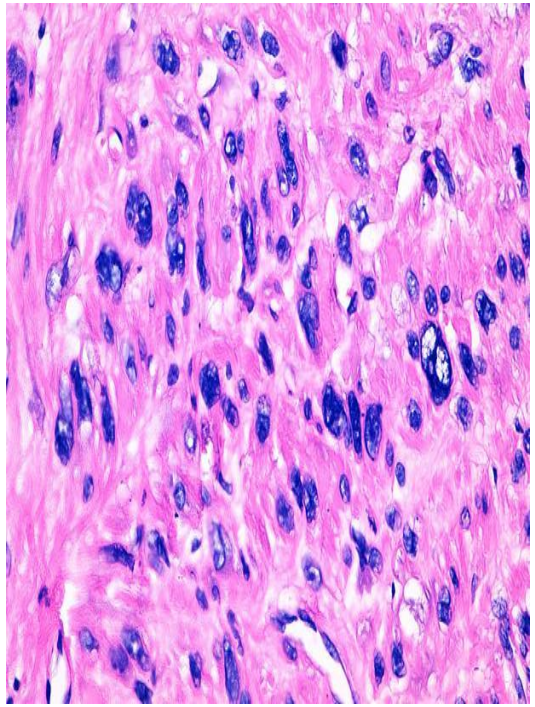
- Malignant counterpart of leiomyoma.
- not from preexisting leiomyomas.
- hemorrhagic, necrotic, infiltrative borders.
- diagnosis: coagulative necrosis, cytologic atypia, and mitotic activity.
- Recurrence common, and metastasize, 5-year survival rate 40%.

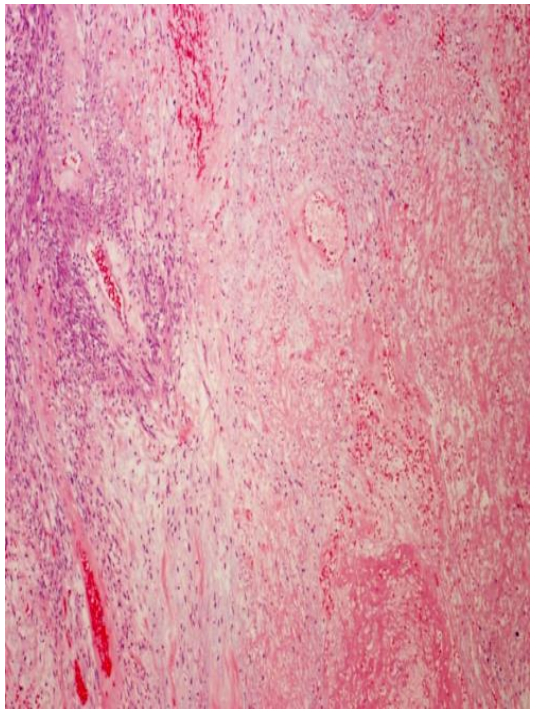
Not well demarcated like fibroids.

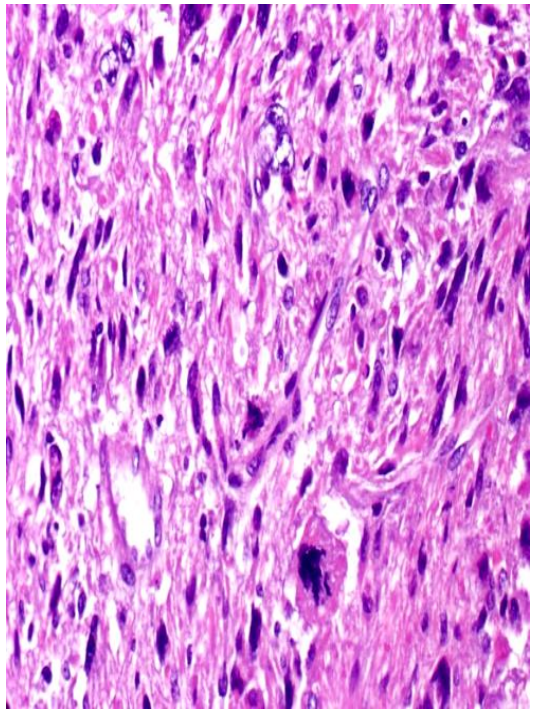
How to distinguish from fibroid:

- Aggressive.
- Grow rapidly.









Not like fibroids in that this one displays:

- Hemorrhage.
- Infiltration border.
- Yellowish areas surrounding the tumor indicating necrosis.
- Invasive (with hemorrhage and necrosis).