PATHOLOGY

- SHEET NO. 9
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Uterine Pathology

Quick recap of uterine histology:

The uterus has 3 layers:

1- **Endometrium** : is a special kind of mucosa [composed of glands/ epithelial cells and stroma in between].It's the inner layer lining the cavity of the uterus and this layer undergoes shedding during menstruation and the embryo implants in it in normal pregnancy.

There are two layers within the endometrium :

1) stratum basale (Basal layer)
2) stratum functionale (Functional layer): is the one that responsive to hormone ; it's the part of the endometrium that undergoes cyclic changes and bleeding

2- **Myometrium**: Muscular layer/ muscles of the uterus. Smooth muscle fibers that cause contractions that are important for the menstrual cycle and delivery/ labor.

3- **Perimetrium** (The external layer)

In this lecture, we are going to discuss diseases that affect the endometrium and myometrium.

Endometrium Pathology:

1- Endometritis:

As the name implies, it is inflammation of the endometrium because of [infectious and non infectious causes]:

1- infections –pelvic inflammatory disease (PID)
2- miscarriage or delivery/ labor
3- intrauterine contraceptivedevice (IUCD).

This process can be localized to the endometrium or generalized that involved the whole female genital tract . (If the process is generalized they tend to used the term pelvic inflammatory disease (PID))

We know that pelvic inflammatory disease (PID) is caused by infections in many cases. Also, miscarriage or delivery and usage of intrauterine contraceptive device can increase the risk of getting infections and therefore inflammation (endometritis).

Endometritis can be acute (up to several weeks) or chronic (more than several weeks).

Symptoms: **fever**, lower **abdominal pain** (especially in acute phase), **menstrual abnormalities**. If endometritis is chronic, it may lead to [complications] **infertility** and **ectopic pregnancy** due to damage tothe Fallopian tubes.

Treatment: removal of cause, antibiotics, D&C.

Dilation and curettage (D&C) is a procedure to remove tissue from inside uterus (endometrium).

2- Adenomyosis:

Adeno = glands, myo = muscles. That indicates the presence of glands inside the muscles and of course it is abnormal because the myometrium is a muscular layer that shouldn't contain glands.

As we said previously, the endometrium is the layer that contain glands, and in this disease these glands are leaving the endometrium invading the myometrium.

➔ Adenomyosis: endometrial stroma, glands, or both embedded in **myometrium**.

These glands are derived from **stratum basalis** (one of the endometrial layers).

Glands derived from stratum basalis **don't normally undergo cyclical bleeding** but their abnormal presence in the myometrium will cause irritation of the surrounding muscles + muscular hypertrophy => **thickening of the uterine wall and enlargement of the uterus** which will be globular in shape. => Symptoms: **menorrhagia**, **dysmenorrhea** (**due to enlarged uterus, uterine contractions are exaggerated**).

Menorrhagia: heavy or prolonged bleeding. Dysmenorrhea: pain with menstruation or menstrual cramps

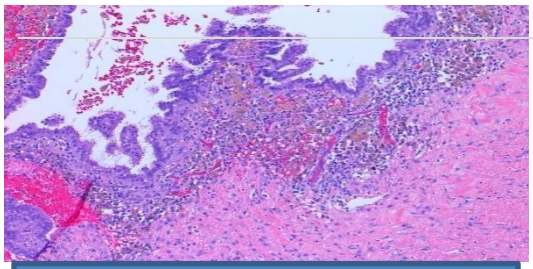
3- endometriosis: بطانة الرحم المهاجرة

Endometrial glands and stroma **outside the uterus (NOT CANCER)**.

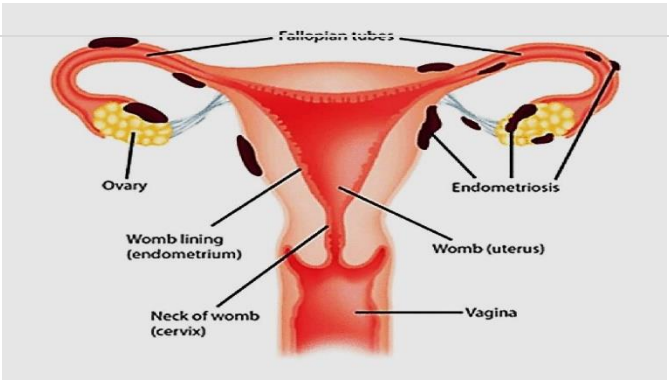
The endometrium leaves its normal place and goes outside the uterus.

Where does it go?

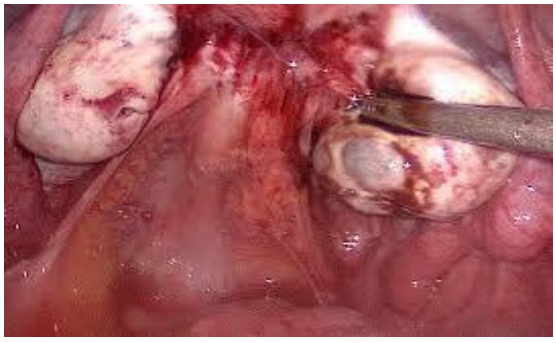
* it may go anywhere inside the peritoneal cavity (**ovaries**, **pouch of Douglas**, **uterine ligaments**, fallopian **tubes**, **rectovaginal septum**, and serosa of the organs inside the peritoneal cavity). these are the common locations because they are surrounding the uterus.



Intraoperative view of endometriosis



Common locations of endometriotic lesions



Microscopic view of endometriosis

And in this case, they are usually **multifocal = present in multiple tissues in the pelvis**. The most common location ➔ ovaries

* **sometimes** it may reach **distant sites** not related to the female genital tract **e.g., umbilicus, lymph nodes, lungs,** skin wounds, fingers, brain, **etc.**

➔ it's common (**10% of women in reproductive years;↑ infertility**).

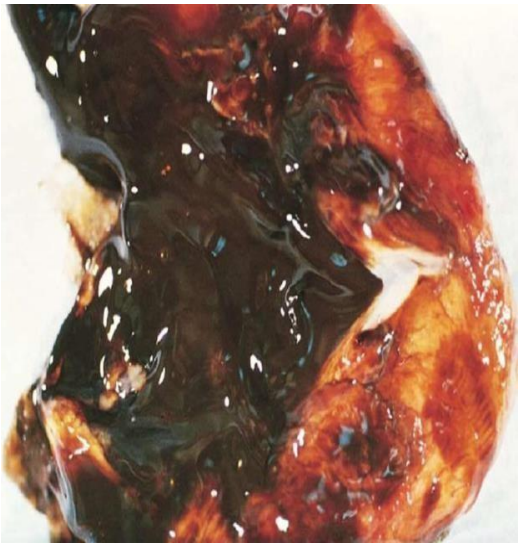
➔ it's benign. It's not cancerous because it doesn't have monoclonal growth [consist of two types of tissue].

Symptoms: **dysmenorrhea, pelvic pain, pelvic mass filled with blood (chocolate cyst)**

Dysmenorrhea: pain with menstruation or menstrual cramps

Why does it cause symptoms? Endometrial tissue doesn't get implanted outside the uterus without doing anything. It continues its own function. Glands will work as if they are inside the uterus and will be affected by the hormonal changes happing during menstrual cycle (hormonal dependent). So, in every menstrual period (bleeding), the endometrial tissue will experience shedding, break down and bleeding.

Let's assume that endometriosis occurred above the **ovaries** in Douglas' pouch, with time and recurrent bleeding, it will be converted to mass / cyst filled with blood from more than one menstrual cycle which will be thick and brown in color ➔ **chocolate cyst.**



➔ Endometriosis contains **<u>functionalis endometrium</u>** (one of the endometrial layers), so undergoes **<u>cyclic bleeding</u>.**

Pathogenesis:

Four theories:

A. Regurgitation theory (**most accepted**): menstrual blood backflow through tubes and implantation. This blood contains remnants of glands and stroma that contain viable cells. It explains a high percentage of endometriosis cases especially those in the ovaries, Fallopian tubes, and peritoneal surfaces.

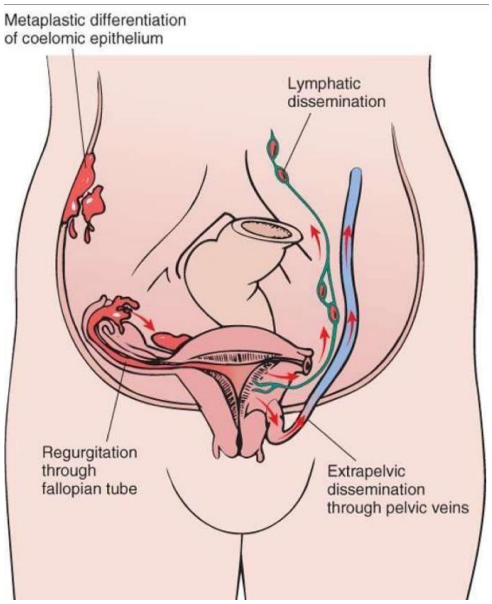
B. Metaplastic theory: endometrial differentiation of coelomic epithelium.

Coelomic epithelium = peritoneal cavity and surfaces covered by peritoneum.

Metaplasia = normal mature tissue starts transforming into another **benign** mature tissue because of environmental changes.

3- vascular or lymphatic dissemination theory: may explain extra-pelvic or intranodal implants because it may enter inside the blood (most likely veins) or lymphatic vessels perhaps due tears that occur duringmenstruation.

4- Extrauterine stem/progenitor cell theory, proposes that circulating stem/progenitor cells from bone marrow differentiate into endometrial tissue.(This theory may explain the distant sites of endometriosis)

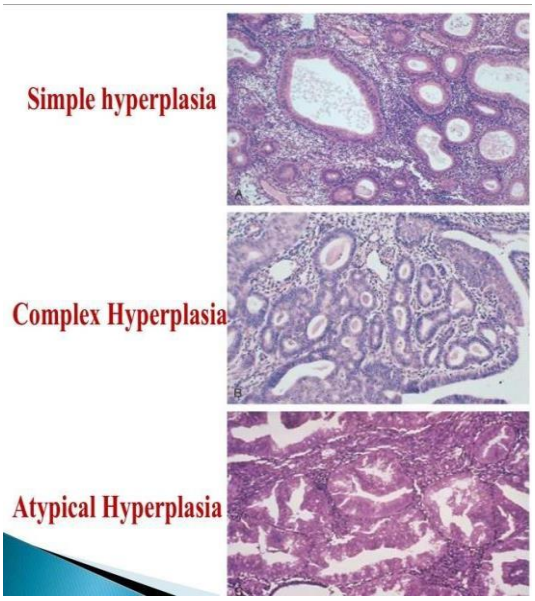


Conceivably, all pathways are valid in individual instances.

Consequences: inflammation --> fibrosis, sealing of tubal fimbriated ends and distortion of the shape and function of the ovaries → increase the risk of infertility

Diagnosis: (histopathological conformation) 2 of 3 features: endometrial glands, endometrial stroma, or hemosiderin pigment.

4-Endometrial hyperplasia (increase number of cells (Endometrial glands))



Prolonged or marked excess of **estrogen** (exogenous/ endogenous) relative to progestin → exaggerated proliferation of endometrial glands → may progress to cancer.

risk factors: Obesity; Diabetes; Hypertension; Infertility; Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors.

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

In the past , they are classified into simple , complex and atypical hyperplasia

1- Typical hyperplasia

2- atypical hyperplasia (20% risk of cancer)→(Has the highest risk to progress to cancer)

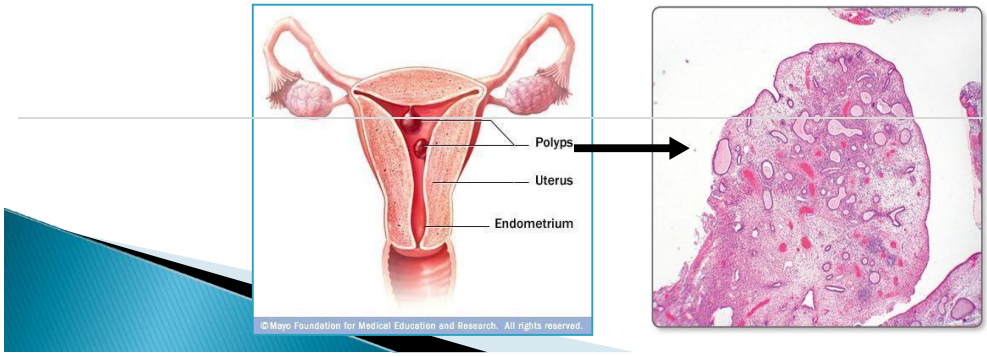
Tumors of the Endometrium:

5-benign endometrial polyps:

Sessile or pedunculated.

Endometrial dilated glands, with small muscular arteries and fibrotic stroma.

No risk of endometrial cancer.



6-endometrial carcinoma:

The most common cancer in female genital tract

50s and 60s.

Two clinical settings correlated with differences in histology:

A) **Perimenopausal women with estrogen excess → endometrioid carcinoma**:

Precancerous lesion is atypical endometrial hyperplasia.

Termed so because it is similar to normal endometrium (-oid) with much more glands.

Mutations in **DNA mismatch repair genes** and **PTEN**

risk factors: (same as the risk factors for endometrial hyperplasia)

obesity [true risk factor because morbid obesity increases estrogen]

diabetes and **hypertension** [mostly an association and not a true risk factor]

infertility

prolonged estrogen replacement therapy [exogenous]

Estrogen-secreting ovarian tumors

Prognosis: **depends on stage**. 5-year survival in stage 1= 90%; drops to 40% in stages 3 and 4

B) Older women with endometrial atrophy → serous carcinoma

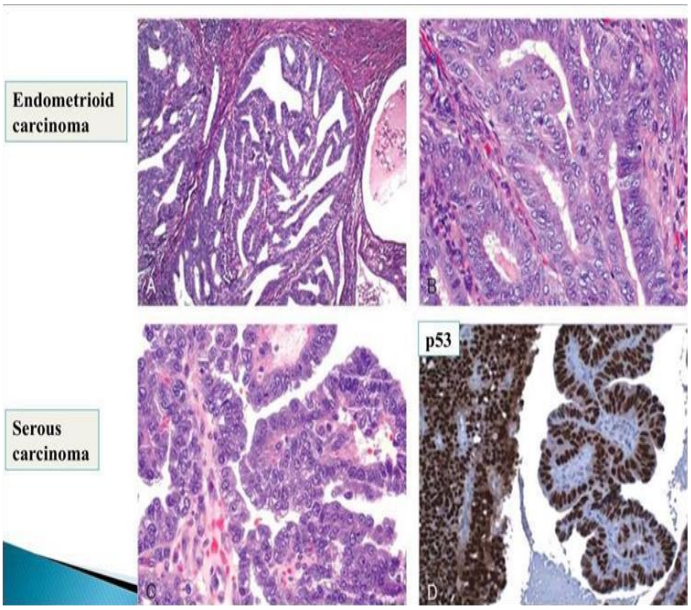
No relation with endometrial hyperplasia (no relation with estrogen)

Not hormone-dependent

Mutations in p53 tumor suppressor gene.

Prognosis**:** depends on operative staging with peritoneal cytology.

Generally worse than endometrioid carcinoma. (more aggressive, less common).



Myometrium pathology:

Tumors of myometrium:

1- Leiomyoma: (Fibroids)

Leio = smooth, myo = muscles, oma = benign

➔ benign tumor of smooth muscle cells

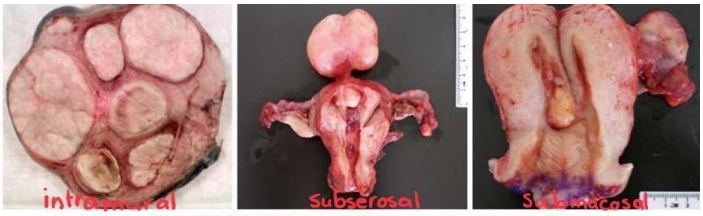
Most common benign tumor in females (30 – 50% in reproductive life)

Estrogen-dependent; enlarge during reproductive years and shrink after menopause.

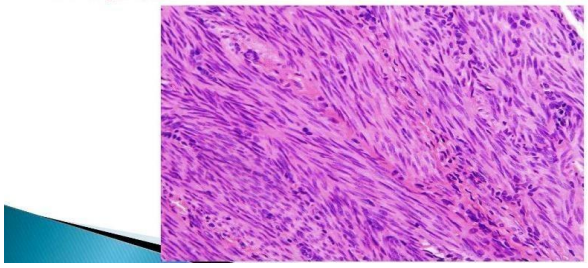
Circumscribed, firm gray-white masses
with whorled cut surface.

Might be single or multiple.

Location: **intramural** => inside the wall of the uterus, **submucosal** => under the endometrium or **subserosal** => under the serosa



May develop hemorrhage, cystic change, or calcification. (no necrosis)



Clinically: (depend on the size and location of the tumor) **asymptomatic** or **symptomatic**; menorrhagia; a dragging sensation, anemia, etc.

Leiomyomas almost never transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.

2- Leiomyosarcoma:

Malignant counterpart of leiomyoma.

Not derived from preexisting leiomyomas.

Macroscopically: Hemorrhagic, necrotic, infiltrative borders.

Diagnosis: (under microscope) **coagulative necrosis**, **cytologic atypia**, and **mitotic activity**.

Recurrence common, and metastasize, 5-year survival rate 40%.