



The Uterine Corpus

Lecture 1

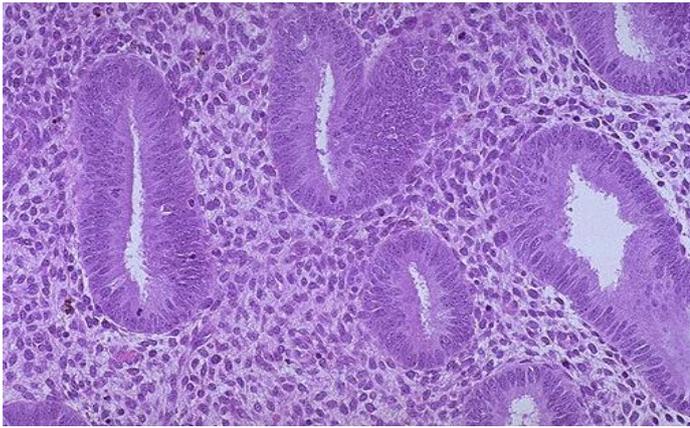
430 Pathology Team

Seham AlArfaj

Nora AlRajhi

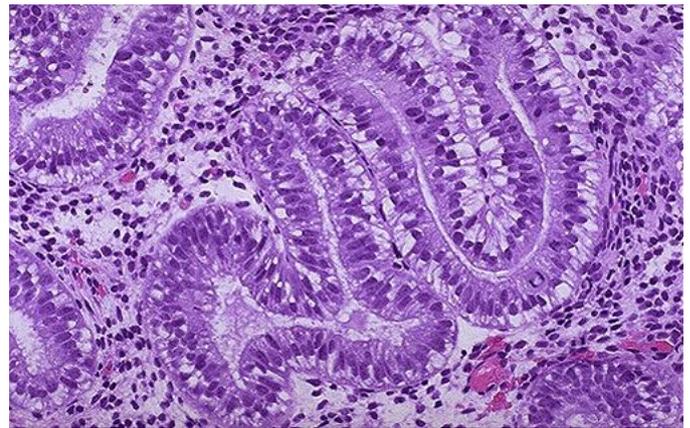
Red: Doctors' and important notes.
Green: Team notes.

Physiology:



Proliferative Endometrium (1st half of menstrual cycle):

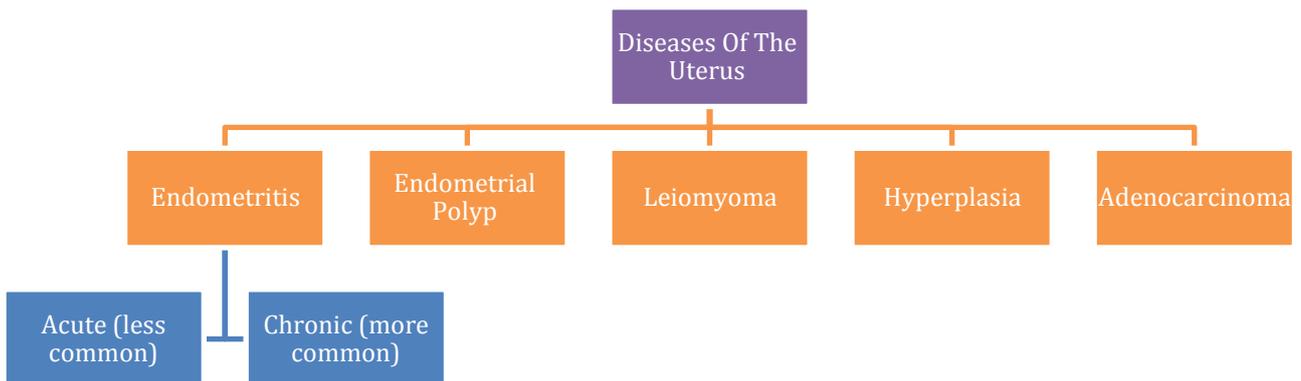
In this phase there is normal mitosis both in glands and stroma and it is under the control of estrogen.



Secretary Endometrium (2nd half of menstrual cycle):

You'll see subnuclear vacuolization as well as vacuoles in the epithelium of the gland. And it is under the control of progesterone

Pathology:



N.B: most common clinical presentation of all the previous diseases is uterine bleeding

Acute Endometritis:

Definition: it is an acute inflammation that is **rare**.

Etiology:

- ✧ It is most often related to intrauterine **trauma** e.g. after an abortion either spontaneous or induced, complications of pregnancy, medical instrumentation or intrauterine contraceptive devices.
- ✧ It is most often caused by Staphylococci, Streptococci.
- ✧ Others like *N. gonorrhoeae*, gram-negative bacilli and occasionally fungi and viruses can also cause infection.

Chronic endometritis :

It is more common than the acute form and it is associated with (in descending order):

- ✧ Intrauterine contraceptive device use (most common cause)
- ✧ Pelvic inflammatory disease
- ✧ Retained products of conception following an abortion or delivery.

The etiologic agent is often not apparent and the patient is said to have non-specific chronic endometritis.

Clinical presentation: patients present with irregular bleeding around the menopausal age and sometimes with pelvic (lower abdominal) pain.

Histologically:

1. Presence of **plasma cells in the endometrium is diagnostic.**
2. The stromal cells become spindled and swirl around the glands.
3. Sometimes granulomatous endometritis is noted in patients with tuberculosis.

Endometrial polyp:

Definition: it is a localized benign overgrowth of endometrial tissue **covered by epithelium (it should be covered by epithelium to say that it is a polyp).**

Age group: endometrial polyps are most common in women between 40 and 50 years.

Clinical presentation: the polyp may cause irregular bleeding.

Characteristics:

- ✧ It may be broad-based and sessile, pedunculated or attached to the endometrium by a slender stalk.
- ✧ The size is variable from 1mm to a mass that fills the endometrial cavity.
- ✧ Occasionally a polyp may protrude through the external os (**external orifice of the uterus**)

Histologically:

1. Composed of **glands of variable size and shape.**
2. **Fibrotic stroma.**
3. **Thick-walled blood vessels.**

Clinical behavior:

Endometrial polyps are **benign** with no malignant potential **but** sometimes malignant tumors may be found in them.

Leiomyoma (Fibroid):

Definition: Leiomyoma is a **benign tumor** of smooth muscle origin.

Epidemiology:

- ✧ It is the most common neoplasm of the female genital tract and probably **the most common neoplasm in women**.
- ✧ Is more common in women of African lineage.

Clinical and gross appearances:

- ✧ Patients may present with **heavy irregular bleeding with clotting**, pelvic pain, pelvic mass, **infertility** (especially with intramural type).
- ✧ The tumor is **estrogen responsive** and often increases in size during pregnancy and decreases in size during menopause.
- ✧ It can be single or multiple. Mostly it is multiple.

Classifications:

May be located anywhere in the **myometrium** and it is classified according to the site into:

- Submucosal tumors are present immediately below the endometrium, may be pedunculated and occasionally protrude through the cervix.
- Intramural tumors, the most common, **lie within the myometrium**.
- Subserosal fibroids lie beneath the serosal covering of the uterus or are pedunculated and attached to the serosa.

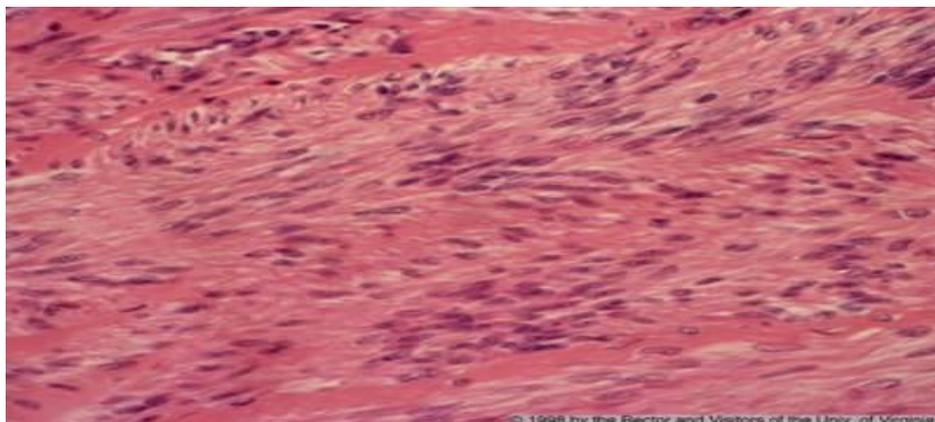
Pedunculated ones may undergo torsion and infarction or lose their connection to the uterus and become attached to another pelvic organ forming a "**parasitic leiomyoma**".

Grossly:

The tumors appear as **well circumscribed**, spherical, dense and firm-to-hard masses with **whorled**, tan-white cut surfaces.

Histologically:

Composed of **interlacing** fibers of bland **smooth muscle** with **collagenous (fibrous) stroma** between bundles.



Degenerative changes:

- ✧ Atrophy : the tumor reduces in size at menopause or after pregnancy following drop in estrogen level.
- ✧ Hyaline change (hyalinization) :Usually occurs as the tumor "ages".
- ✧ Myxoid and cystic change.
- ✧ Calcification : common in menopausal women.
- ✧ Septic with necrosis of the center due to circulatory inadequacy (**this is rare**).
- ✧ Red degeneration: **venous thrombosis** and congestion with interstitial hemorrhage may occur, **most commonly in pregnancy**. This is usually accompanied by pain, which may produce a clinical picture of acute abdomen.

Clinical behavior:

- ✧ This is a benign tumor with no appreciable malignant potential (**incidence of malignant transformation into leiomyosarcoma is 0.1-0.5%**).
- ✧ It may cause **anemia from heavy bleeding**, or urinary or bowel obstruction (subserosal or parasitic tumors)
- ✧ In pregnant women it may cause **spontaneous abortion**, precipitate labor, obstructed labor ,post partum hemorrhage (due to interference with uterine contraction), and red degeneration.

Endometrial Hyperplasia:

- ✧ It refers to a process in which there is a **proliferation of endometrial glands**.
- ✧ The glands are irregular size and shape with an **increase in gland/stroma ratio** compared to the normal proliferative endometrium.
- ✧ It is induced by persistent, prolonged estrogenic stimulation of the endometrium.
- ✧ **The endometrial hyperplasia may progress to endometrial carcinoma.**
- ✧ The development of cancer is based on the level and duration of the **estrogen excess**.
- ✧ The risk depends on the severity of the hyperplastic changes and **associated cellular atypia**.

Causes:

- ✧ A common cause is a succession of anovulatory cycles (**failure of ovulation = no progesterone**).
- ✧ It may also be caused by excessive endogenously produced estrogen in :
 1. Polycystic ovary syndrome including Stein-Leventhal syndrome.
 2. Granulosa cell tumors of the ovary.
 3. Excessive ovarian cortical function (cortical stromal hyperplasia).
- ✧ Prolonged exogenous administration of estrogenic steroids without counter balancing progestins

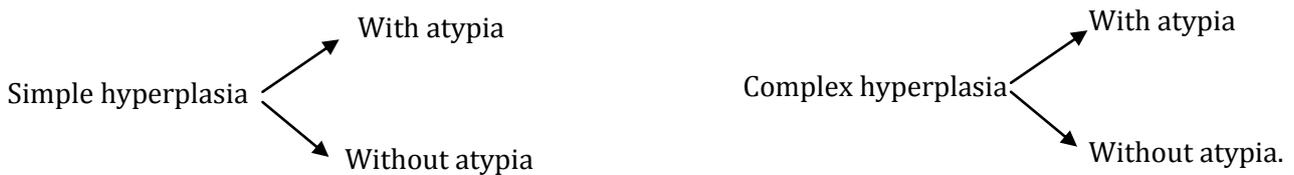
Clinically:

- ✧ Milder forms of hyperplasia tends to occur in younger patients.
- ✧ The great majority of mild hyperplasia regress , either spontaneously or after treatment .
- ✧ The **more severe forms occur predominantly in peri- and postmenopausal women .This form has a significant premalignant potential.**
- ✧ Patients usually present with abnormal uterine bleeding .

Histologically:

- ✧ Characterized by proliferation of both glands and stroma.
- ✧ In spite of proliferation of both components, **glandular overcrowding occurs.**
- ✧ Endometrial hyperplasia is histologically classified according to:
 1. Architecture as: simple or complex depending on the degree of glandular complexity and crowding.
 2. Cytologic features as: with or without atypia (**abnormality in a cell**).

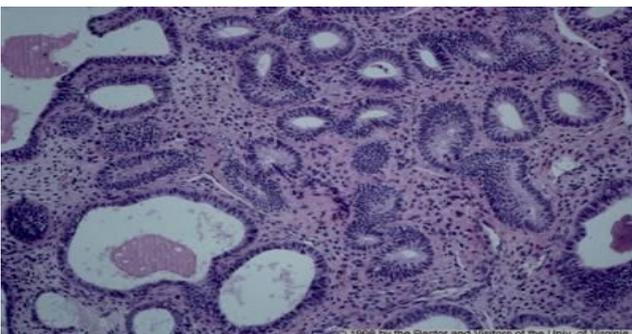
Classification:



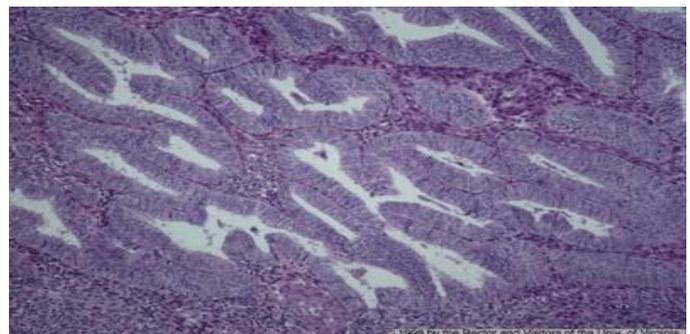
Histologically:

- ✧ Simple hyperplasia (cystic hyperplasia): **glands are round, cystically dilated** and dispersed within abundant cellular stroma and give a "Swiss Cheese" appearance.
- ✧ Complex hyperplasia:
 1. complex crowded glands with papillary infoldings (**finger-like projection**)
 2. **The glands are irregular in shape.**
 3. The crowded glands are **back-to-back** with very little intervening stroma.

Both simple and complex hyperplasia can be with or without atypia.



Simple hyperplasia with dilated glands.



Complex atypical hyperplasia with back-to-back arrangement of glands and papillary tufting.

Clinical behavior and premalignant potential:

- ✧ Some endometrial hyperplasia revert to normal spontaneously or with medical treatment (Sometimes as a treatment option they perform hysterectomy which is an operation where the uterus is taking out), others persist as hyperplasia, and a few progresses to endometrial adenocarcinoma.
- ✧ Generally, patients who have hyperplasia with atypia are more likely to develop carcinoma than those without atypia.

The risks for developing adenocarcinoma in each are as follows:

- Complex atypical : 30%
- Simple atypical : 10%
- Complex : 3%
- Simple : 1%

Atypical hyperplasia in postmenopausal women appears to have a higher rate of progression to adenocarcinoma.

Risk Factors:

1. Obesity
2. Western diet
3. Nulliparity (the condition in a woman of never having given birth)
4. Diabetes Mellitus
5. Hypertension
6. Hyperestrinism (a condition marked by the presence of excess estrins (an estrogenic hormone) in the body and often accompanied by functional bleeding from the uterus)

Endometrial adenocarcinoma:

Epidemiology:

- ✧ It is the **most common invasive tumor of the female genital tract** in the U.S.
- ✧ Worldwide, it is the **fifth** commonest cancer in women.

Risk Factors (same as endometrial hyperplasia):

- ✧ Obesity (women with upper body fat have 3 times the risk of women with lower body fat),
- ✧ Estrogen therapy
- ✧ Nulliparity (as a result of infertility due to chronic anovulation),
- ✧ Chronic anovulation

- ✧ Late menopause
- ✧ Hypertension
- ✧ Diabetes
- ✧ Tamoxifen therapy side effect (this is an estrogen suppressor which is used in treatment of breast cancer)
- ✧ High socioeconomic status.

The disease may follow atypical hyperplasia but may occur independently (de novo) of it especially in older patients.

Clinical presentation

- ✧ Most patients are between 50 and 59 years (post-menopausal)
- ✧ Endometrial adenocarcinoma manifests as abnormal vaginal bleeding.
- ✧ The tumor may grow in a diffuse or polypoid pattern.
- ✧ It often involves multiple areas of the endometrium

Morphology:

- ✧ May closely resemble normal endometrium
- ✧ May be exophytic = grows into the endometrium
- ✧ May be Infiltrative = grows into the myometrium
- ✧ May be polypoid

Histologically:

The commonest type is: Endometrioid adenocarcinoma.

Other types include:

1. Clear cell
2. Adeno-squamous : both glandular and squamous components appear malignant.
3. Papillary serous carcinoma.

Endometrioid carcinoma may show areas of benign looking squamous epithelium known as (adenoacanthoma).

Prognosis:

- ✧ Clinical behavior depends on the histological type, the grade (degree of differentiation) and the stage (extent of spread).
- ✧ Endometrioid carcinoma has a better prognosis and it is usually a stage one disease while the other histological types tend to occur at a higher stage.

Staging is based on:

1. Degree of myometrial invasion, cervical, adnexal and adjacent pelvic organ invasion,
 2. Result of peritoneal fluid cytology and
 3. Distant organ metastasis.
 4. Lymph node status is an important prognostic factor.
- ◇ 75% of patients present with stage I disease and these have 95% 5-year survival.
 - ◇ The tumors associated with unopposed estrogen tend to have low histologic grade and clinical stage, hence tend to have better prognosis.
 - ◇ These usually occur in young women.
 - ◇ 20% of endometrial carcinoma there is no association with hyperestrinism or preexisting hyperplasia ,these cancers tend to occur late in life and have a poor prognosis.

Grading and staging:

- ◇ Grading is from 1 to 3
- ◇ Staging is from 1 to 4 (it is used in assisting prognosis)
 - Stage 1 : Confined to uterus corpus
 - Stage 2 : Cervix involvement
 - Stage 3 : beyond the uterus ,but within the true pelvis
 - Stage 4 : Distant metastasis/ extrapelvic extension.

Summary

- **Acute endometritis:** is a rare condition most commonly caused by Staphylococci or Streptococci organisms and it is most often related to trauma during abortion or complication of pregnancy.
- **Chronic endometritis:** is diagnosed histologically by the presence of plasma cells and most common etiology is Intrauterine contraceptive device use.
- **Endometrial polyp:** is benign with no malignancy potential and microscopically we find: glands of variable size and shape, fibrotic stroma, thick-walled blood vessels.
- **Leiomyoma (Fibroid):** is a benign tumor of smooth muscle origin. It is the most common neoplasm in women. It is estrogen responsive. The incidence of malignant transformation into leiomyosarcoma is 0.1-0.5%. It is classified into: submucosal tumors , intramural tumors which is the most common, and subserosal fibroids. Grossly it is forming whorled while under the microscope we see interlacing fibers of smooth muscle with collagenous (fibrous) stroma between bundles. One of the degenerative changes is red degeneration which is seen in pregnancy in the presence of venous thrombosis.
- **Endometrial Hyperplasia:** is proliferation of endometrial glands that increase the gland/stroma ratio compared to normal proliferative endometrium. It is induced by persistent, prolonged estrogenic stimulation. Classification depends on: is it simple or complex with/out atypia. It may progress to endometrial carcinoma depending on association of cellular atypia (mostly if it is complex with atypia).
- **Endometrial adenocarcinoma:** is the most common invasive tumor of the female genital tract found in high socioeconomic status. Most common type is Endometrioid adenocarcinoma. Adenoacanthoma is when the endometrioid carcinoma show areas of benign looking squamous epithelium while Adeno-squamous is when both glandular and squamous components appear malignant.
- Staging is used to assest the prognosis. 75% of patients present with stage I disease and these have 95% 5-year survival.
- Remember that the common clinical presentation of all the previous diseases is uterine bleeding