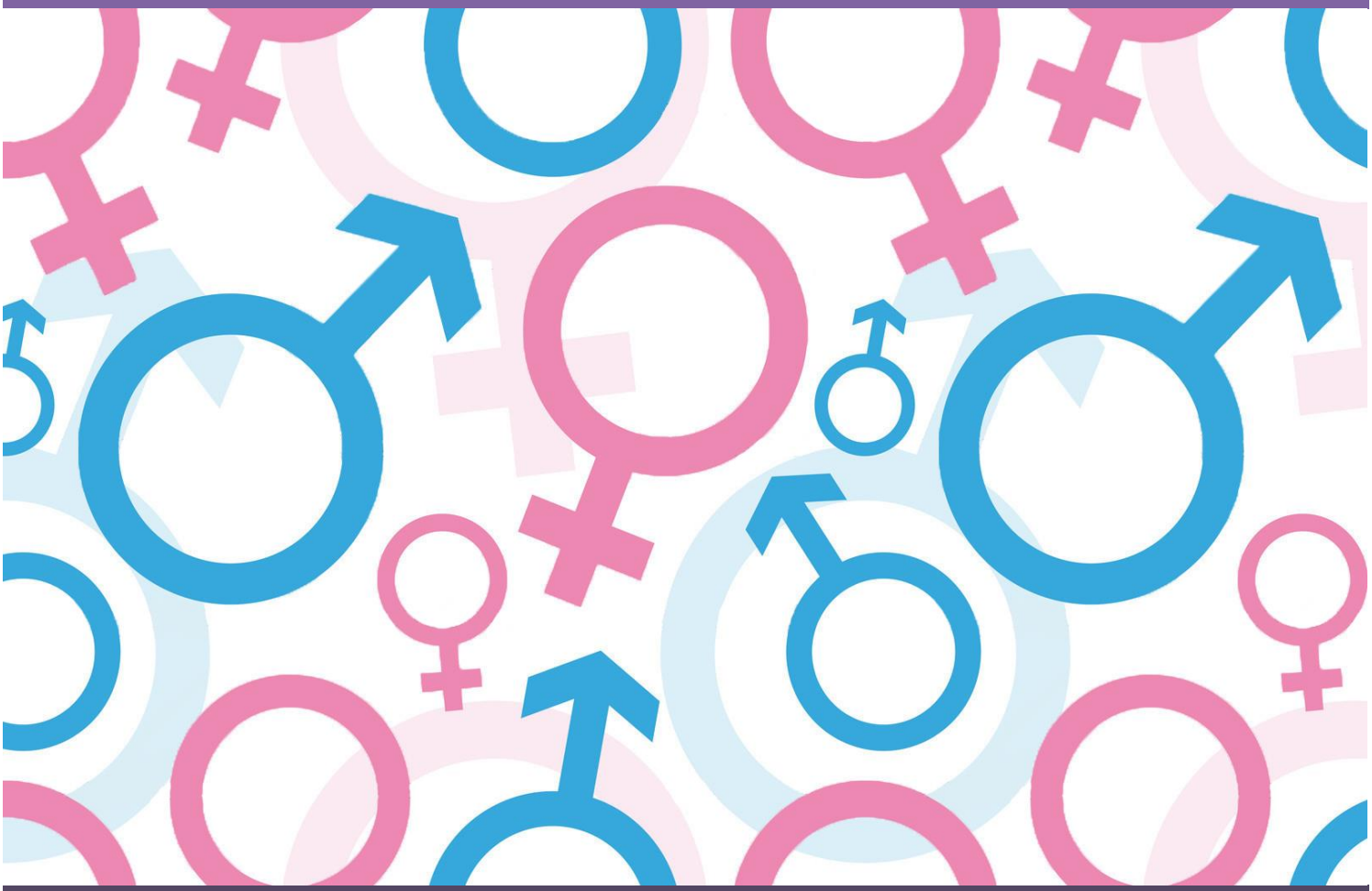

Lecture 3

The Uterine Corpus

432 ***Pathology*** *Team*

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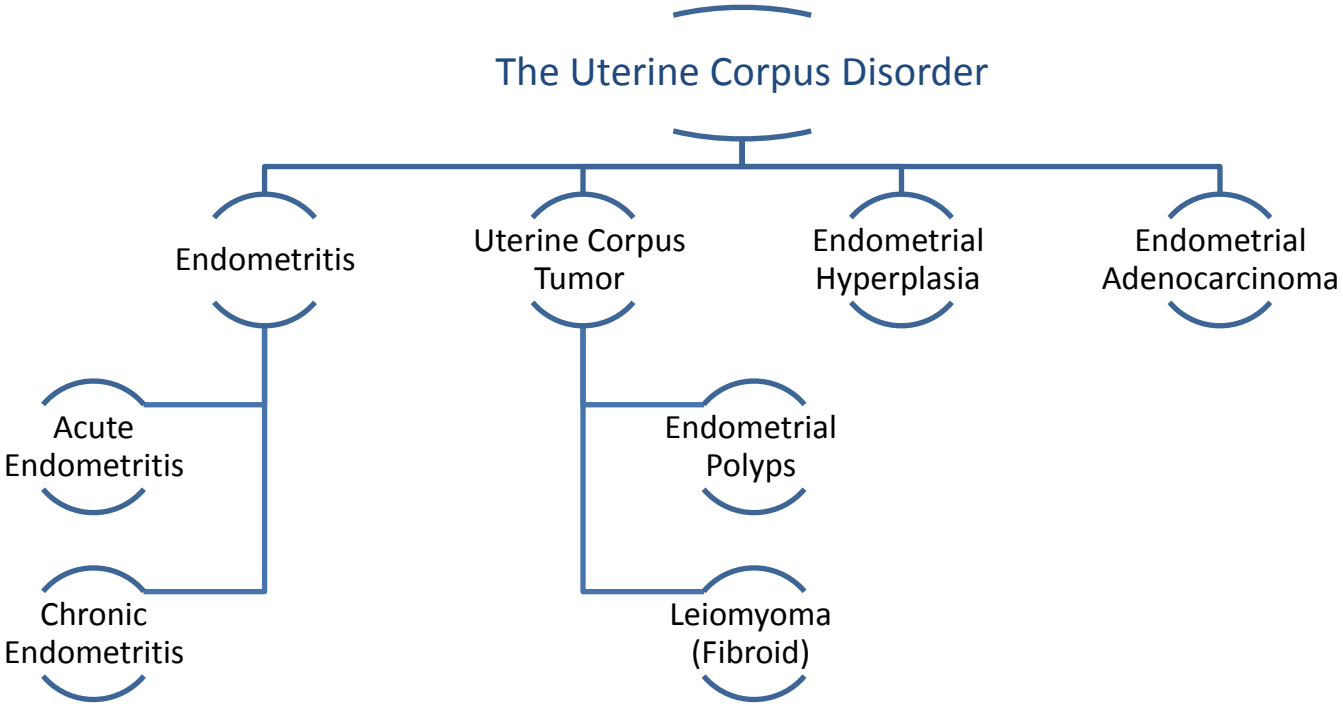
Reviewed By: Hamad *Adel Almohsen*

Reproductive Block

Color Index: Female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

The Uterine Corpus

Mind Map:



Female Genital system disorders (Body of the Uterus)

Introduction:

The uterine corpus is composed of endometrial mucosa and the underlying smooth muscle myometrium. The more frequent and significant disorders of the uterus are considered here:

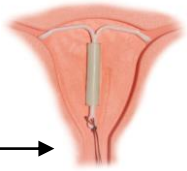
1- Endometritis:

- Inflammation of the endometrium is classified as (Acute or Chronic) depending on whether a neutrophils or plasma cells predominate respectively.

Acute Endometritis:

- 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. For example: women used to delivered baby at home and using unsterile instruments.
- Is most often caused by Staphylococci, Streptococci. And it get worse if the causative micro-organism is MRSA (methecillin resistance staphylococcus aureus)
- Others like N. gonorrhoeae, gram-negative bacilli and occasionally fungi and viruses can also cause infection.

Chronic Endometritis:



- Chronic endometritis is associated with :
  *Intrauterine contraceptive device (The coil) use = is an effective method of contraception. It is a T shape and sits inside the uterus. Once fitted, it can stay in the womb for up to ten years.
  * Pelvic inflammatory disease = Pelvic inflammatory disease (PID) is an infection of the female reproductive organs. It usually occurs when sexually transmitted bacteria spread from the vagina to the uterus and upper genital tract.
  * 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.
- Patients present with irregular bleeding. Or complaining of infertility, so when Dr do D&C* and send it to the lab, the pathologist Weight it and Process it by using stain and the observation under the microscope 2 main characteristics:
- Histologically, the presence of plasma cells in the endometrium is diagnostic even if it only ONE plasma cell. The stromal cells become spindled and swirl around the glands.
- Sometimes granulomatous endometritis is noted in patients with tuberculosis.
  In case of tuberculosis not necessary to have necrosis, granulomatous is enough to diagnose, because the uterus renew its cells every month, so no necrosis.

NOTE:

- **D&C = Dilatation And Curettage, is a procedure to remove tissue from inside the uterus. Doctors perform dilation and curettage to diagnose uterine conditions such as (heavy bleeding \ post-menopausal bleeding) or use D&C in treatment such as (Remove cervical or uterine polyps, which are usually benign \ Remove fibroid tumors, which are benign tumors formed on the uterine wall that sometimes bulge into the uterine cavity \ clear the uterine lining after a miscarriage or abortion.)**
  To see the procedure: http://www.youtube.com/watch?v=1IwrAyonFA4

- **Tubeculous endometritis is common in countries where TB is endemic such as KSA, so should be included in differential diagnosis for pelvic inflammatory disease in women who have recently emigrated from endemic areas.**
- **Endometritis clinically :**
  All forms of endometritis may manifest with fever, abdominal pain and menstrual abnormalities. In addition there is increased risk of infertility and ectopic pregnancy as a consequence of damage and scarring of the fallopian tubes.

2- Endometrial Polyps:

- Is a localized benign overgrowth of endometrial tissue covered by epithelium.
- Endometrial polyps are most common in women between 40 and 50 years. Usually detected around the time of menopause.
- The polyp may cause irregular bleeding. During menstruation or between cycles.
- 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.

Histology

- Composed of glands of variable size and shape, **fibrotic and loose stroma that tend to give the stroma spindle shape, and thick-walled blood vessels. And polyps lined by epithelium.**

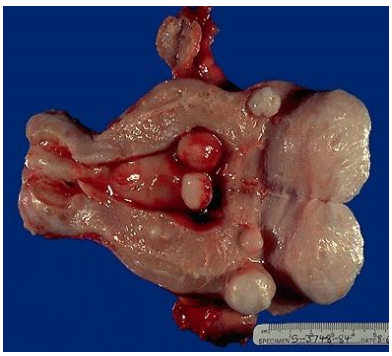
Clinical behavior:

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

3- Leiomyoma (fibroid):

- Leiomyoma is a benign tumor of smooth muscle origin.
- 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



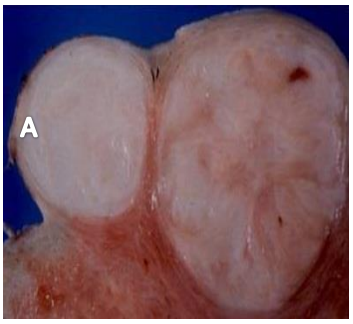
*Patients may present with irregular bleeding, pelvic pain, pelvic mass, infertility.

*The tumor is estrogen responsive and often increases in size during pregnancy and decreases in size during menopause. Estrogens and possibly oral contraceptives stimulate the growth of leimyomas; conversely it shrinks post-menopausally women if they are not in hormonal {estrogen} therapy.

*It can be single or multiple. Mostly it is multiple. If multiple: leiomyomata.

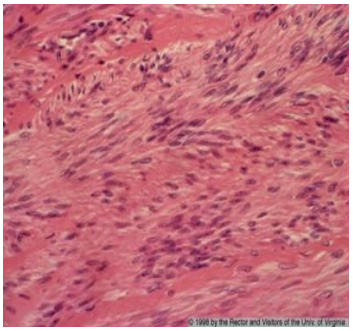
- Leiomyoma may be located anywhere in the myometrium.
- Submucosal tumors: are present immediately below the endometrium, may be pedunculated and occasionally protrude though the cervix.
- Intramural tumors: the most common, lie within the myometrium.
- Subserosal fibroids: lie beneath the serosal covering 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 (A in the image), spherical, dense and firm-to-hard masses with whorled, tan-white cut surfaces.

Microscopy:



- Composed of interlacing fibers of bland smooth muscle with collagenous stroma between bundles.

Leiomyoma (Fibroid) Degenerative changes:

1. Atrophy — the tumor reduces in size at menopause or after pregnancy following drop in estrogen level.
2. Hyaline change (hyalinization) — usually occurs as the tumor "ages".
3. Myxoid and cystic change.
4. Calcification — common in menopausal women.
5. Septic with necrosis of the center due to circulatory inadequacy.
6. 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:

1. This is a benign tumor with no appreciable malignant potential (incidence of malignant transformation is 0.1-0.5%). Even the presence of multiple lesions does not increase the risk of malignancy.
2. It may cause anemia from heavy bleeding or urinary or bowel obstruction (subserosal or parasitic tumors).
3. In pregnant women it may cause spontaneous abortion, precipitate labor, obstructed labor, post-partum hemorrhage (due to interference with uterine contraction), and red degeneration.

4- 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 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).
- It may also be caused by excessive endogenously produced estrogen in:
  - Polycystic ovary syndrome including Stein-Leventhal syndrome.
  - Granulosa cell tumors of the ovary "because it's hormonally active tumor".
  - Excessive ovarian cortical function (cortical stromal hyperplasia).
- Prolonged exogenous administration of estrogenic steroids without counter balancing progestins.

  So, patient with menstrual irregulation prone to have endometrial hyperplasia due to Estrogen stimulation & may proceed to carcinoma.

REMEMBER:

Estrogens in treating osteoporosis for example; in case of If hystrectomy (no uterus) or given with progestins if uterus present
(Estrogen increases the risk for breast cancer + endometruim cancer in menopausal women so progestins must be co-administered.

NOTE:

Polycystic ovarian syndrome; formerly called (Stein – leventhal syndrome); is a condition in which a woman's levels of the sex hormones estrogen and progesterone are out of balance. This leads to the growth of ovarian cysts.

Clinical:

- Milder forms of hyperplasia tend to occur in younger patients.
- The great majority of mild hyperplasia regresses, 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.

Microscopy:

- Characterized by proliferation of both glands and stroma. (we asked the doctor and she told us that only the glands are going to proliferate)
- 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**.**

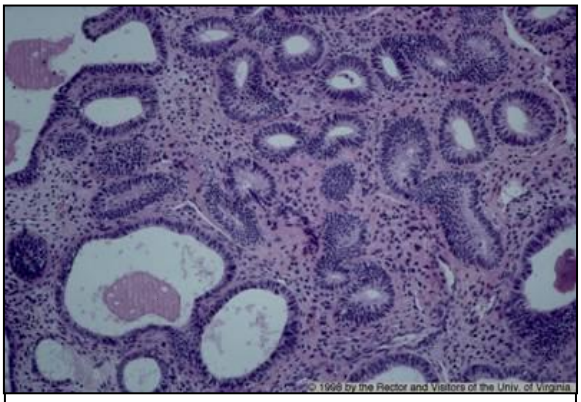
Classification:

Simple hyperplasia: with atypia or without atypia.

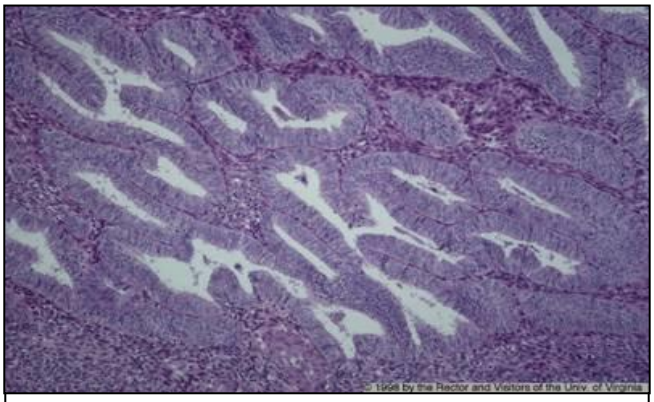
Complex hyperplasia: with atypia or without atypia.

Microscopy:

- Simple hyperplasia (cystic hyperplasia) — glands are cystically dilated and dispersed within abundant cellular stroma and give a "Swiss Cheese" appearance.
- Complex hyperplasia —characterized by complex crowded glands with papillary infoldings and irregular shapes.
- 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 reverts to normal spontaneously or with medical treatment, 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:

- Obesity, - adipose tissues convert steroids precursor to estrogen.
- Western diet – high dietary animal fat intake gives 2.1 fold increased risk.
- Nulliparity – due to failure of ovulation which potentially causes the estrogen excess.
- Diabetes Mellitus – studies have found in type 2 higher than type 1 due to hyperinsulinemia and insulin resistant which play a role in endometrial proliferation.
- Hypertension – independent risk factor.
- Hyperestrinism – due to high estrogen level.

NOTE: The appearance of the hyperplasia resemble the Carcinoma, so before diagnosing carcinoma u have to look at the (Patient's Age + History – medications affecting the hormones and aggressively induce hyperplasia like some drugs that treat infertility) so, instead of (hysterectomy in treating carcinoma, we do "cessation of these kind of drugs and she will be Normal.

5-Endometrial adenocarcinoma

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:

- 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 (breast cancer therapy, need to monitor the patient.. cause it's act on breast as " anti-estrogen , but pro-estrogen effect on the uterus and bones)
- High socioeconomic status.

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

Clinical presentation:

- Most patients are between 50 and 59 years.
- Endometrial adenocarcinoma manifests as marked leukorrhea and abnormal vaginal bleeding.
- The tumor may grow in a diffuse or polypoid pattern.

It often involves multiple areas of the endometrium.

Morphology:

1- May closely resemble normal endometrium
2- May be exophytic
3- May be Infiltrative
4- May be polypoid

Histology:

The commonest type is: Endometrioid adenocarcinoma.

Other types include:

1- Clear cell 2- Adeno-squamous 3- Papillary serous carcinoma

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

In adenosquamous carcinoma both glandular and squamous components appear malignant.

Prognosis:

- Clinical behavior depends on the histologic type, the grade (degree of differentiation) and the stage (extent of spread).
- Endometrioid carcinoma has a better prognosis than the other histological types, which tend to occur at a higher stage.

Staging is based on:

- Degree of myometrial invasion, cervical, adnexal and adjacent pelvic organ invasion,
- Result of peritoneal fluid cytology and
- Distant organ metastasis.
- 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

- 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 from Robbins

Uterine Smooth Muscle Neoplasms

- Benign smooth muscle tumors, called leiomyomas, are common and frequently multiple; they may manifest with menorrhagia or as a pelvic mass or may be detected as a cause of infertility.
- Malignant smooth muscle tumors, called leiomyosarcomas, arise de novo, not from leiomyomas.
- Criteria of malignancy include necrosis, cytologic atypia, and mitotic activity

Endometrial Hyperplasia and Endometrial Carcinoma

- Endometrial hyperplasia results from excess endogenous or exogenous estrogen.
- Risk factors for developing endometrial hyperplasia include anovulatory cycles, polycystic ovary syndrome, estrogen-producing ovarian tumor, obesity, and estrogen therapy without counterbalancing progestin.
- The severity of hyperplasia is graded on the basis of architectural (simple versus complex) and cytologic (normal versus atypical) criteria. The risk of developing carcinoma is predominantly related to cytologic atypia.
- Stage is the major determinant of survival in both types.

Summary

	Findings	Factors	Clinically
Acute Endometritis	Neutrophils	1- Fever 2- Abdominal pain 3- Menstrual abnormalities. 4- Increase risk of infertility and ectopic pregnancy	
Chronic Endometritis	Plasma cells & Spindle stroma cells		
Endometrial polyp	- Benign overgrowth of endometrial tissue covered by epithelium. - Composed of glands of variable size and shape, fibrotic and loose stroma and thick-walled blood vessels.	1- Irregular bleeding. 2- Almost No risk to develop malignancy.	
Leiomyoma	benign tumor of smooth muscle origin **Grossly:** the tumors are circumscribed, spherical, dense and white cut surfaces. **Microscopically:** fibers of bland smooth muscle with collagenous stroma between bundles.	Estrogen responsive Almost No risk to develop malignancy.	1- irregular bleeding 2- Pelvic pain. 3- Pelvic mass 4- Infertility. 5- Anemia 6- Urinary or bowel obstruction. 7- In pregnant women it may cause spontaneous abortion, precipitate labor, obstructed labor, post-partum hemorrhage.
Endometrial Hyperplasia	Proliferation of endometrial glands & The endometrial hyperplasia Simple hyperplasia (cystic hyperplasia) — glands are cystically dilated and give a "Swiss Cheese" appearance. Complex hyperplasia — characterized by complex crowded glands with papillary infoldings and irregular shapes. Both simple and complex hyperplasia can be with or without atypia.	- It is induced by persistent, prolonged estrogenic stimulation - A common cause is a succession of anovulatory cycles	Abnormal uterine bleeding
Endometrial Carcinoma	May closely resemble normal endometrium or exophytic or Infiltrative or polypoid		Marked leukorrhea and abnormal vaginal bleeding.

Questions

1/ A 45-year-old obese woman (BMI = 32 kg/m2) with a history of diabetes and poorly controlled hypertension complains of increased menstrual blood flow of 3 months in duration. An endometrial biopsy is done. Which of the following most likely accounts for the pathogenesis of endometrial hyperplasia in this patient?

(A) Excess estrogen stimulation
(B) Exposure to exogenous progestational agents
(C) History of chronic endometritis
(D) History of oral contraceptive use

2/ A 33-year-old woman with a history of menorrhagia presents with a 6-month history of increasing fatigue. A CBC reveals a hypochromic, microcytic anemia (hemoglobin = 8 g/dL). Bimanual pelvic examination reveals an enlarged uterus with multiple, irregular masses. A hysterectomy is performed, and a sharply circumscribed fleshy tumor is found within the uterine wall. Which of the following is the most likely cause of vaginal bleeding and anemia in this patient?

(A) Adenomyosis
(B) Uterine leiomyoma
(C) Endometrialc arcinoma
(D) Endometriosis

3/ A 50-year-old woman complains of having intermenstrual bleeding for 4 months. A Pap smear is normal. An ultrasound examination shows a mass in the endometrial cavity. The patient elects to undergo a hysterectomy. A large polyp is found upon opening the endometrial cavity. Histologic examination of this polyp will most likely show which of the following pathologic findings?

(A) Atypical endometrial hyperplasia
(B) Chronic endometritis
(C) Complex endometrial hyperplasia
(D) Endometrial glands and fibrous stroma

For more questions please refer to Revision Team files

Answers:

- 1- A
- 2- B
- 3-D

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us on: 432PathologyTeam@gmail.com

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*Good Luck ^_^*