Diseases of the corpus (body) of the uterus:

1- Inflammation (endometritis)
2- Benign conditions (endometriosis & adenomyosis)
3- Dysfunctional uterine bleeding
4- Neoplasms (Benign & Malignant)
    I) Endometrial polyp
    II) Endometrial carcinoma (endometrial origin)
    III) Leiomyoma & Leiomyosarcoma (myometrial origin)

1- Endometritis:

- Causes (mainly):

a) pelvic inflammatory disease: which may involve inflammation of the uterus, uterine tube, ovary & surrounding tissue. (As a part of it)

b) retained products of conception: because it will be considered as a foreign material.

c) Intrauterine contraceptive devices (IUD)

- It is classified as:

a) acute:

neutrophils are the main cells

b) chronic:

Macrophages (in general), lymphocytes & plasma cells are the main cells, especially the plasma cells, because lymphocytes are part of normal mucosa. So, lymphocytes alone doesn't mean the presence of inflammation, we must see plasma cells as well.

{P.S. TB can cause tuberculous endometritis}

- Clinically:

fever, pain, loss of function (infertility and menstrual abnormalities).

2- Benign conditions (endometriosis & adenomyosis)

(not neoplastic)

I) Adenomyosis:

- Means the presence of abnormal glands and stroma outside their normal locations (ectopic).
  The uterine wall involve the **endometrium** which composed of glands and stroma, the **myometrium** which composed of smooth muscles, and the **serosa**.
  If some of these glands and/or stroma are present deep in the muscle (abnormal location), this is called Adenomyosis.
- In Adenomyosis the whole uterine wall (muscles wall mainly) is usually thickened, in response to this foreign tissue.
- These glands are derived from stratum basalis (the basal layer of the endometrium), so **they are non-functional and don't undergo cyclic changes** during menstrual cycle (important to differentiate **adenomyosis** from **endometriosis**).
- If there is marked Adenomyosis**,** it can cause menorrhagia, dysmenorrhea & pelvic pain, especially at the onset or before the onset of menstruation.

II) Endometriosis:

- Means the presence of endometrial tissue in other places, but outside the uterus, for example in the ovaries, abdominal cavity, in a scar, in the lungs or other sites. So, anywhere in the body outside the uterus, if you find endometrial glands and stroma, it means that it is an endometriosis.
- Usually 10% of women in the reproductive age have endometriosis, however 50% of infertile women have endometriosis. (it is associated with infertility)
- It is a common cause of dysmenorrhea, pelvic pain, and it can cause pelvic masses.
- The glands here are derived from stratum functionalis (the functional layer of the endometrium), so **they are functional and undergo cyclic changes** during menstrual cycles such us bleeding (important to differentiate it from **adenomyosis**).
- So it appears as a cyst or a mass with blood inside, that is called a **chocolate cyst,** which is very characteristic and most commonly seen in the ovaries.
- It can be multi-focal.
- To diagnose endometriosis histologically we need 2 out of 3 things:
  1) endometrial glands
  2) endometrial stroma
  3) blood either fresh or old (hemosiderin macrophages)

- Pathogenesis - we have two main theories:

1) Regurgitation theory:

- Most acceptable theory
- During menstruation, the endometrium which is being shed out will not go down it will go up, from the uterus to the fallopian tube, to the ovaries, then to the abdominal cavity. But the problem of this theory, that it doesn't explain the endometriosis in other sites.

2) Metaplastic theory:

- Metaplasia means, the process in which an epithelium change to another type of epithelium.
- Endometrial epithelium is derived from coelomic epithelium, which can be found in other sites in the body; lungs, pleura, pericardium … etc.
  This coelomic epithelium can undergo metaplastic changes and become endometrial tissue. This explain how endometriosis can occur in other sites of the body that have coelomic epithelium.
- An important point to know that it is not the coelomic epithelium itself will undergo transformation, but the stem cells that give us the coelomic epithelium will do (dedifferentiation).

{P.S. There is a third theory "**vascular and lymphatic dissemination of endometrial tissue**"

3- Dysfunctional uterine bleeding (DUB)

- It means abnormal menstrual bleeding
- Causes:

I) Functional causes:

Hormonal imbalance: clinicians consider it the only cause that refers to DUB

a) Failure of ovulation: (the most common cause Of DUB)
common in premenopausal & before the onset of menstruation
→ causes : 1) dysfunction of the hypothalamic-pituitary access (FSH & LH related)
2) increase in estrogen (unopposed by progesterone) can be endogenous (tumor-secreting estrogen) or exogenous (drugs).
3) malnutrition (anorexia nervosa) either decrease or increase of bleeding
4) obesity (estrogen related)
5) severe physical & emotional stress

b) Inadequate luteal phase:
the corpus luteum fail to mature (lack of progesterone)

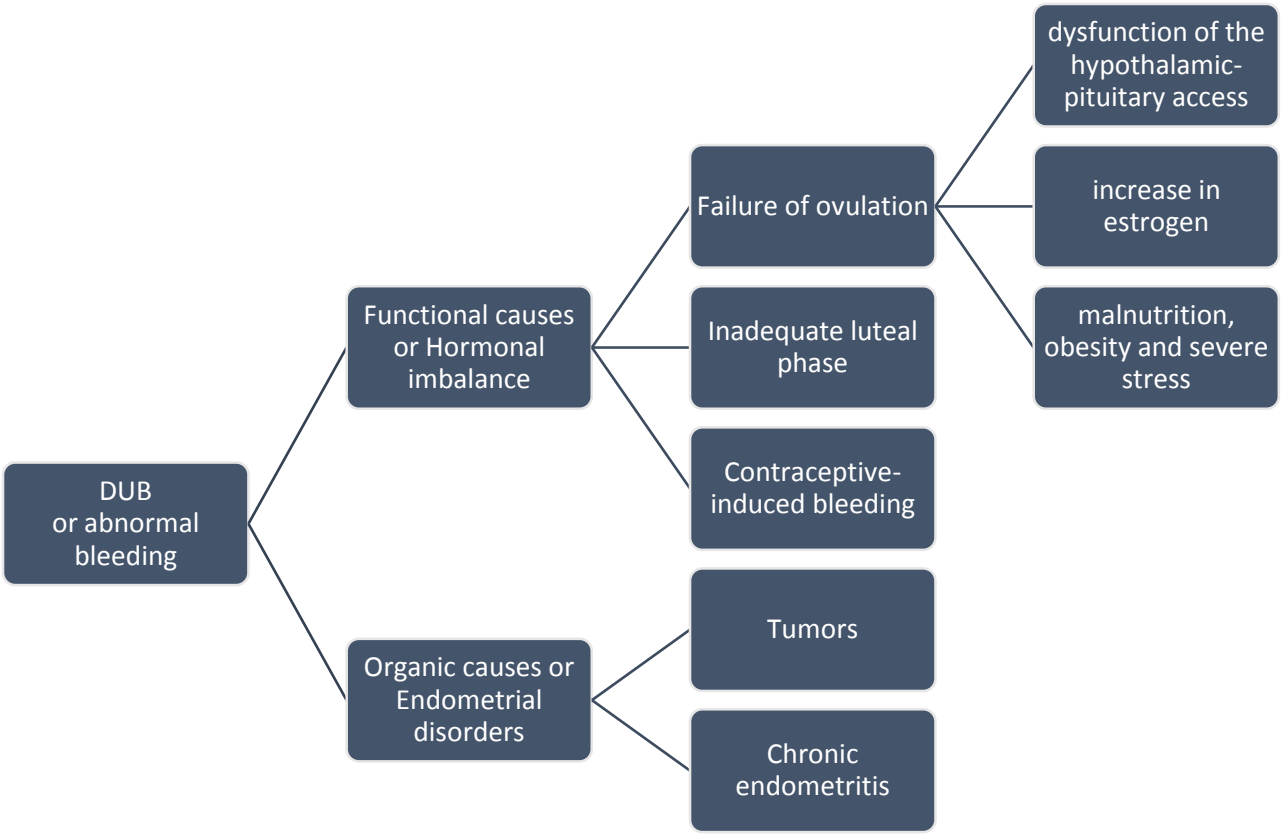
c) Contraceptive-induced bleeding

II) Organic causes

Endometrial disorders: clinicians don't consider it as a cause of DUB, but it really can cause abnormal menstrual bleeding.
(مجرد خلاف على الأسماء)

1) Tumors (benign/polyps or malignant/carcinomas): leiomyomas, endometrial hyperplasia,cancer … etc

2) Chronic endometritis



4- Neoplastic conditions of the endometrium:

I) Endometrial hyperplasia:

- **Hyperplasia** in general can be physiological or pathological. Hyperplasia during pregnancy occurs in the muscles of the uterus not in the endometrium, however **endometrial hyperplasia** is caused by hormonal imbalances (prolonged increase in estrogen without an increase in progesterone), and is always pathological.
  {P.S. Endometrium during follicular phase of menstrual cycle, undergo proliferation, so we don't call it hyperplasia, although it has somehow the same basic meaning.}

- Hyperplasia can be a predisposing factor for endometrial carcinoma, so it is a premalignant condition.

- Classification of hyperplasia: depending on; its origin, estrogen level and its morphology:

1) Simple hyperplasia: there is dilatation in the glands and increase in the endometrial cells. So, ratio between glands and stroma increased (more glands than stroma), because it is epithelial hyperplasia not stromal hyperplasia.

a) <u>increase in endometrial cells (glands)</u>
b) <u>no structural abnormalities</u>
c) <u>no atypia</u>

2) Complex Hyperplasia: as glands increase their no. it will begin to make folding and papillary structures.

a) <u>increase in endometrial cells (glands)</u>
b) <u>structural abnormalities</u>
c) <u>no atypia</u>

3) Atypical Hyperplasia: we have atypia.
(Atypical features: pleomorphism, hyperchromasia … etc)

a) <u>increase in endometrial cells (glands)</u>
b) <u>structural abnormalities</u>
c) <u>atypia</u>

- Atypical hyperplasia: in the nuclei of the cell, we have atypical features. E.g: polymorphism, hyperchromasia and other atypical signs.

There are 20% risk of developing endometrial carcinoma from hyperplasia, especially in atypical hyperplasia.

And the risk of malignant transformation increases from complex to atypical type, while there are **no risk of malignant transformation in simple hyperplasia**.

Keep in mind that simple hyperplasia could transform to complex or atypical hyperplasia and from there to cancer, but in general we still deal with it as non-precancerous.

Morphology :

Simple hyperplasia:

- Glands are crowded (increase in the number of the glands)
- Some of the glands are cysticlly dilated.
- The lining epithelium is proliferative (as it was induced by increasing estrogen) so it appears crowding with stratification.

Complex hyperplasia:

- Architectural abnormalities (glands are too close to each other with no stroma in between).
- And other morphological features of hyperplasia like what we see inn simple type.

Atypical hyperplasia:

- Structural and nuclear atypia .
- other morphological features of hyperplasia like what we see inn simple type.

Endometrial tumors

And here we have :

1- benign tumors
2- malignant tumors

The most important and the most common benign tumor in the endometrium is endometrial polyp.

Endometrial polyp.

Polyps are usually small in size : up to 3 cm.

They could be :

a- sessile : have a lare fat base (stock).
b- pedunculated : attached to the uterus by an elongated pedicle(wiki.).

Morphology:

- cysticlly dilated glands
- **the stroma is fibrotic**
- no increase in the gland-stroma ratio (one of the signs which differentiate it from hyperplasia)
- sometimes we could find small foci of hyperplasia within the polyp, but we ignore them, because what causes the hyperplasia (estrogen increase) is also causing the polyp, so we still dealing with it as a polyp not a hyperplasia.

  * remember that hyperplasia is diffused through all the endometrium (not focal as here).

- hypertrophied blood vessels.

Endometrial polyps are completely benign and don't predispose to cancers.

Question: all the following are precancerous **except**:

a- simple hyperplasia
b- complex hyperplasia
c- atypical hyperplasia
d- endometrial polyp
e- a and d

Endometrial carcinoma

It's the **most common** carcinoma of the female genital tract .

It's very common in postmenopausal females especially at the age of 50s and 60s.

We have two types of endometrial carcinoma:

1- **Endometrioid adenocarcinoma**: in the perimenopausal women and its related to excess estrogen (so associated with hyperplasia).
2- **Serous carcinoma**: in older ages, postmenopausal women, (not related to estrogen) and associated with endometrial atrophy.

Endometrioid carcinoma

Morphologically:

- Similar to endometrial tissue. So, easily appeared that it's derived from the endometrium.
- Architecture of the glands are altered
- Necrosis
- Anaplastic features like mitosis, hyperchromasia, irregularity polymorphism…

Risk factors:

1- Estrogen & hyperplasia. (the most important risk factors)
2- Obesity

3- Diabetes
4- Hypertension
5- Infertility
6- Estrogen secreting tumors

Although we don't really know whether if obesity, diabetes and hypertension are risk factors or just associations, obesity is the most Candidate to be a risk factor because of its association with estrogen.

- Regarding risk factors there are nothing confirmed except the relation between smoking and lung cancer, as all the other risk factors are based on epidemiological evidence not experimental.

Serous carcinoma

- Usually arise on a background of endometrial **atrophy**.
- Sometimes it arise on a background of endometrial polyp. That doesn't mean that it arise **from** it, it's just an association.
- **No** relation with hyperplasia
- **P53** mutation is associated with serous not Endometrioid carcinoma (diagnostic feature).

Morphologically:

- similar to the serous carcinoma in the ovaries
- papillary architecture (figure like with a vascular core)
- very high nuclear atypia
- P53 positive

Usually it have poorer prognosis than endometrioid carcinoma.

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We grade endometrial carcinoma into 4 stages:

- **remember that prognosis depends on the extent (stage) of involvement**

Stage I : tumors are in the corpus (uterus) only (not involving the cervix)

Stage II : tumors are in the corpus and cervix

Stage III : tumors reach the pelvic cavity

Stage VI : tumors go outside the pelvic cavity

Tumors of myometrium

Myometrium is a muscle, so we are going to see tumors that arise in the muscular tissues.

Leiomyomas

- We call them fibroids
- They are **benign** smooth muscle tumors
- The **most common tumor in females** (almost 50% of females at certain age will have fibroids, a high percentage of them are asymptomatic)
- Estrogen increases their growth, so we usually see a peek of them in the reproductive age, pregnancy
- Usually they shrink after menopause
- No atypia, no polymorphism
- Leiomyomas do **NOT** transform to leiomysacromas (they do **NOT** carry a malignant potential).

Leiomyosarcoma

- Arise **de novo**
- They are malignant tumors
- Necrosis, high mitosis, cellular atypia
- Grossly not like leiomyomas (nice white color), it's hemorrhagic and necrotic.

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