# Lecture 1: Endometrial Hyperplasia, Uterine Cancer, and Fibroids

Objectives:

- **Lesions of endometrium of uterus:** know the risk factors, clinical presentation, macroscopic and histological features of
  - **Endometrial hyperplasia**
  - **Endometrial carcinoma**
- **Lesions of myometrium of uterus:**
  - **Leiomyoma :** understand the pathology and clinical features of uterine leiomyomas andis aware that leiomyoma (fibroid) is the commonest neoplasm arising in the female genital tract.
  - **Leiomyosarcoma**

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PATHOLOGY
TEAM 437

Important
Terminology
Doctor's Notes
Extra Information

# Endometrial Hyperplasia

- Endometrial hyperplasia is a process in which there is a proliferation of endometrial glands resulting in an **increase in the gland/stroma ratio** of the endometrium when compared to normal.
- It is induced by persistent, prolonged stimulation of the endometrium by high levels of estrogen. Exogenous intake
- The endometrial hyperplasia **may progress to endometrial carcinoma.**
- The risk of developing carcinoma depends on:
  -level and duration of the estrogen excess
  -severity of the endometrial hyperplasia
  -associated cellular atypia.
- In endometrial hyperplasia there is proliferation of both glands and stroma but the proliferation of the glands is much more leading to overcrowding of glands.

## Causes

Anything that increases Estrogen level

Anovulatory menstrual cycles (such as in perimenopause)

Ovulation is important because it produces progesterone.
No ovulation → No progesterone → Unopposed estrogen "estrogen works without progesterone"

Excessive endogenous production of estrogen (by the body) e.g. in:
1. Polycystic ovary syndrome (Stein-Leventhal syndrome).
2. Granulosa cell tumors of the ovary.
3. Cortical stromal hyperplasia (excessive ovarian cortical function).

LH stimulate thecal cells (which convert cholesterol → androgens) then FSH stimulate granulosa cells (convert androgens → estrogen)

Exogenous administration or intake of estrogenic steroids without counter balancing progestins, over a long period of time.

taking progesterone with estrogen reduce the risk of endometrial hyperplasia and carcinoma

## Clinical presentation

**Mild type** of hyperplasia tends to occur in **younger** patients. Most of the mild hyperplasia cases **regress**, either spontaneously or after treatment.

The more **severe type** of hyperplasia occur mainly in **perimenopausal or postmenopaus**al women. This form has a significant **premalignant potential.**

Patients with endometrial hyperplasia usually present with abnormal uterine bleeding.

## CLASSIFICATION OF ENDOMETRIAL HYPERPLASIA

1) Based on the architecture of the endometrial glands, i.e. depending on the degree of glandular complexity and crowding it can be:

- Simple
- Complex

2) Based of the presence or absence of atypia of the cells lining the endometrial glands

Presence of atypia is more dangerous than complexity

- Without atypia
- With atypia

### I. Simple hyperplasia

• Without atypia • With atypia

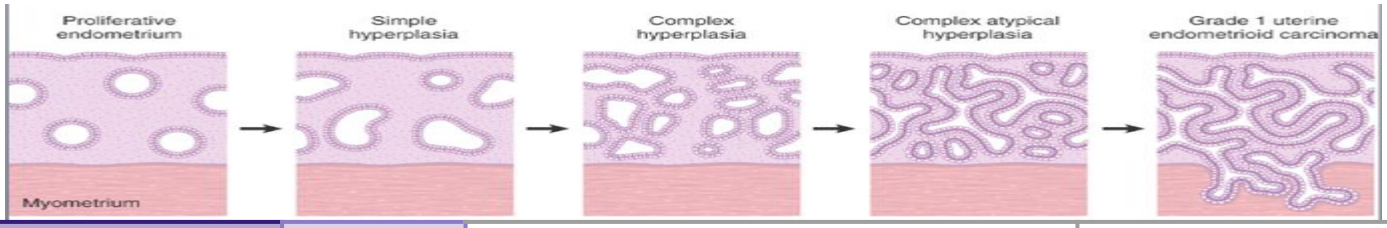
### II. Complex hyperplasia

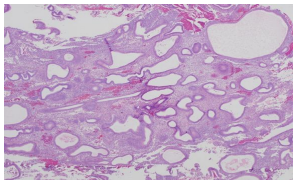
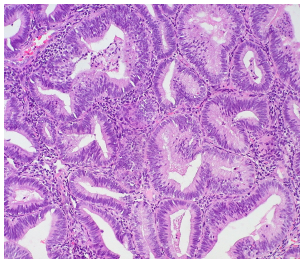
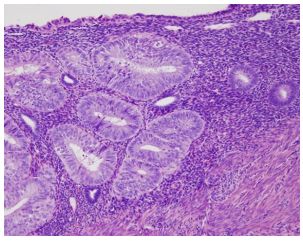
• Without atypia • With atypia

## Endometrial Hyperplasia Risk Factors :

-Obesity -Western diet -Nulliparity -Diabetes Mellitus -Hypertension -Hyperestrinism

Note: atypia/ pleomorphism = loss of polarity, vesicular nuclei, prominent nucleoli, rounded cells.




| | | | |
|---|---|---|---|
| **SIMPLE HYPERPLASIA** | Without Atypia | • Simple hyperplasia (cystic hyperplasia): glands are variably shaped and sized and cystically dilated.<br><br>• There is a **mild increase in the gland-to-stroma ratio** | rarely progress to adenocarcinoma<br>  |
| | With Atypia | • Uncommon.<br><br>• It has the **Architecture of simple hyperplasia**, but there is cytologic **atypia** within the glandular epithelial cells. | 10% of such lesions progress to carcinoma |
| **COMPLEX HYPERPLASIA** | Without Atypia | • Proliferation of endometrial glands resulting in **complex crowded glands** with **papillary infoldings** and irregular shapes. The crowded glands are **back-to-back** with very little intervening stroma.<br><br>• The epithelial cells remain **cytologically normal**. No atypia | 3% progression to carcinoma<br>  |
| | With Atypia | • Complex proliferation of endometrial glands **(back-to-back irregular glands)** with **atypia**.<br><br>• The nuclei show **loss of polarity** and are enlarged and rounded and may have irregular nuclear membranes.<br><br>• Commonly about 30% of women with this diagnosis have carcinoma somewhere in the uterus when a hysterectomy is performed. | About 30% progress to carcinoma<br>  <br>Notice that presence of atypia related to higher risk of carcinoma |

# Endometrial Hyperplasia: Clinical behavior and premalignant potential

- Some endometrial hyperplasia **revert** to normal **spontaneously** or with **medical treatment**
- others **persist as hyperplasia.**
- and a few progresses to endometrial **adenocarcinoma**.

- The risks for developing adenocarcinoma in each are as follows:

1. Simple hyperplasia without atypia — 1%
2. Complex hyperplasia without atypia — 3%
3. Simple hyperplasia with atypia (simple atypical hyperplasia) — 10%
4. Complex hyperplasia with atypia (complex atypical hyperplasia) — 30% (HIGHEST)

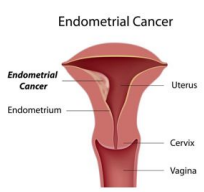
- Atypical hyperplasia in **postmenopausal** women appears to have a **higher rate of progression to adenocarcinoma.**

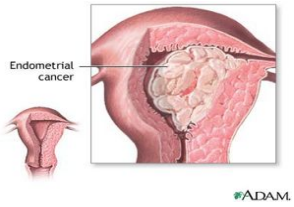
## Robbins 10the ed

- Endometrial hyperplasia is placed in two categories based on the presence of **cytologic atypia**: hyperplasia without atypia and hyperplasia with atypia.
- The importance of this classification is that the **presence of cytologic atypia** correlates with the development or **concurrent finding of endometrial carcinoma.**
- Hyperplasia **without cellular atypia carries a low risk** (between 1% and 3%) for progression to endometrial carcinoma, whereas **hyperplasia with atypia,** also called endometrial intraepithelial neoplasia (EIN), is associated with a much **higher risk** (20%–50%).
- When hyperplasia with atypia is discovered, it must be carefully evaluated for the presence of cancer and usually warrants a hysterectomy in patients no longer desiring fertility. In **younger patients, treatment with high- dose progestins** may be used in an attempt to preserve the uterus.

# Endometrial adenocarcinoma

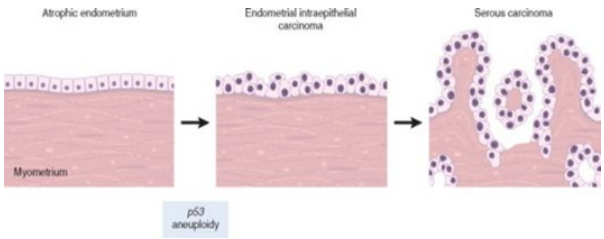
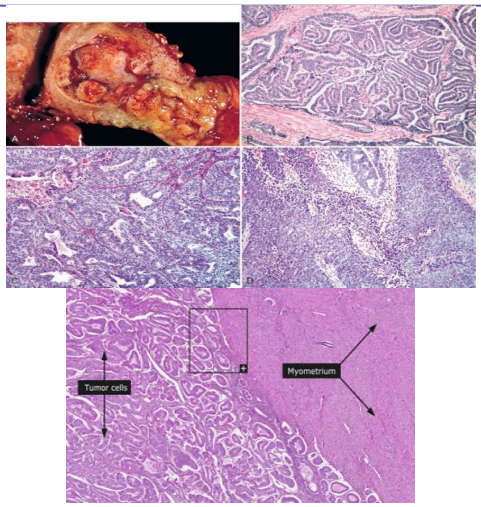
- This is a **common** neoplasm in women. Overall it is the fifth commonest cancer in women.
- Endometrial cancers arise mainly in **postmenopausal** women
- They cause postmenopausal bleeding
- Early detection and cures are possible




These tumors are classified into two broad categories:

| | Type I carcinomas | Type II carcinomas |
|---|---|---|
| Notes | also known as **endometrioid carcinoma** it looks like exactly the endometrium | they are papillary **serous** carcinoma and clear cell carcinoma. Papillary serous is the more common form of type II carcinoma. |
| Epidemiology | - accounts for 80% of endometrial cancers.<br>- It is the most **common** type. e.g. endometrioid adenocarcinoma and its variants. | -They represent 15% of cases of all endometrial carcinoma<br>-They occur in **late in life**, about one decade later than type I carcinoma |
| What is it? | - Endometrioid carcinoma is associated with estrogen excess and endometrial hyperplasia.<br>- The disease may follow atypical hyperplasia but **may occur independently** of it especially in **older patients.** | - Serous carcinoma arises in older women, with endometrial atrophy (**small atrophic uterus**).<br>-There is **no** association with hyperestrinism or preexisting hyperplasia |
| precursor | **Endometrial hyperplasia** is a precursor to endometrioid carcinoma | The precursor of serous carcinoma is serous endometrial intraepithelial carcinoma (its like carcinoma in situ) (SEIC) in which **TP53** mutations are often detected, suggesting an early role for such mutations in the development of this form of endometrial carcinoma. |

| | | |
|---|---|---|
| genetics | -Mutations in **mismatch repair genes** and the **tumor suppressor gene PTEN** are early events in the stepwise development of endometrioid carcinoma.<br><br>1-Women with germline mutations in PTEN (Cowden Syndrome) and<br><br>2-germline alterations in DNA mismatch repair genes (Lynch Syndrome) are at high risk for this cancer.<br><br>3-TP53 mutations (seen in half of the poorly differentiated endometrioid carcinomas) occur but are relatively **uncommon** and are late events in the genesis of this tumor type. | Mutations in **p53** are present in at least 90% of **serous endometrial carcinoma** |
| other | - Risk factors are they same as that of endometrial hyperplasia and include:<br>" Obesity - Western diet- Nulliparity - Diabetes Mellitus- Hypertension- Hyperestrinism- Estrogen therapy- chronic anovulation - Late menopause- Tamoxifen therapy "<br>- High socioeconomic status.<br><br>- The majority of the carcinomas are **well differentiated** | - These tumors are large bulky **poorly differentiated** tumors which invade early into the myometrium and have a **poor prognosis.**<br><br>- Extrauterine extension is common.<br><br>  |
| Pics |  | |

EXTRA EXPLANATION

Endometrial can develop by two different pathways:

1- hyperplasia pathway "type1": there is increase in the estrogen production "whatever the cause" → endometrial hyperplasia → endometrial carcinoma "this pathway has classical histological findings ENDOMETRIOID which means that the cancer cells look much like the normal endometrium"

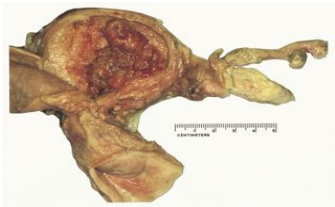
2- sporadic pathway "type2": atrophic endometrium "**not** related to either increase estrogen or hyperplasia" → endometrial carcinoma "classic histological findings SEROUS and often this serus has papilly so we call it sometimes papillary serous also it's very common to find **p53** mutation in these patients"

## Summary

### CHARACTERISTICS OF TYPE I AND TYPE II ENDOMETRIAL CARCINOMAS

| FEATURES | TYPE I | TYPE II |
|---|---|---|
| **HISTOLOGIC TYPE** | Endometriod adenocarcinoma | Serous or clear cell carcinoma |
| **AGE** | Premenopausal and perimenopausal (50-60 yrs) | Post menopausal (~ 70 yrs) |
| **UNOPPOSED ESTROGEN** | Present | Absent |
| **PRECURSOR LESION** | Hyperplasia with atypia | Endometrial intraepithelial carcinoma |
| **GROWTH** | Slow growing | Rapidly progressing |
| **GRADE** | Low | High |
| **MYOMETRIAL INVASION** | Usually superficial | Usually deep |
| **PROGNOSIS** | Favorable | Poor |
| **GENETIC ALTERATIONS NOTED** | PTEN, microsatellite instability | P53 mutations |

# Endometrial adenocarcinoma
## clinical features



- Most patients are between 50 and 60 years. Old age group
- Many of the patients tend to be nulliparous "never given birth" and obese.
- Patients have abnormal vaginal bleeding and excessive leucorrhea.
- Elderly women present with postmenopausal bleeding.
- The diagnosis of endometrial cancer must be confirmed by **biopsy** or **curettage** and **histologic examination** of the tissue.

# Endometrial carcinoma
## basic morphology

**Grossly**

- May look **close to normal** or **exophytic** or **infiltrative**

**Microscopy**

- Both type I and II are adenocarcinomas.
- In both cases tumors **originate in the endometrium** and can eventually **infiltrate the underlying myometrium**, enter **vascular** spaces and metastasize to **lymph nodes.**
- **Serous carcinoma** "type2" has much greater cytologic **atypia** and are more **poorly differentiated** and is therefore more **aggressive**

**Tumor spreads by**

- Direct **myometrial invasion** with extension to the periuterine structures.
- Through **lymphatics** to lymph nodes.
- In the late stages, metastasize to the lungs, liver, bones, others

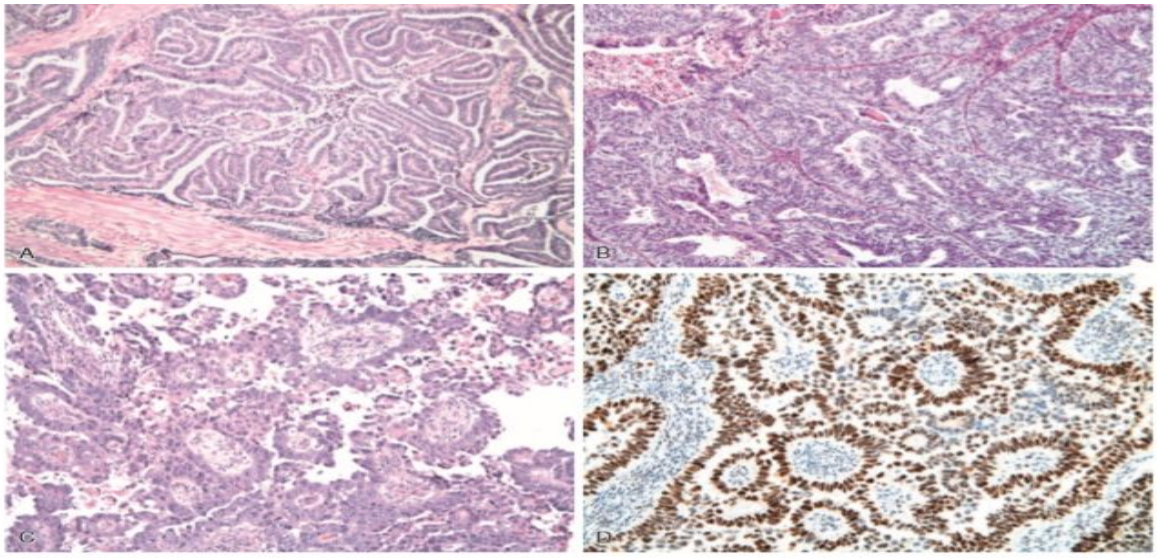


Fig. 19.12 Endometrial carcinoma. (A) Endometrioid type, grade 1, infiltrating myometrium and growing in a glandular pattern. (B) Endometrioid type, grade 3, has a predominantly solid growth pattern. (C) Serous carcinoma of the endometrium, with papilla formation and marked cytologic atypia. (D) Immunohistochemical staining shows accumulation of p53, a finding associated with *TP53* mutation.

# Endometrial adenocarcinoma

## prognosis

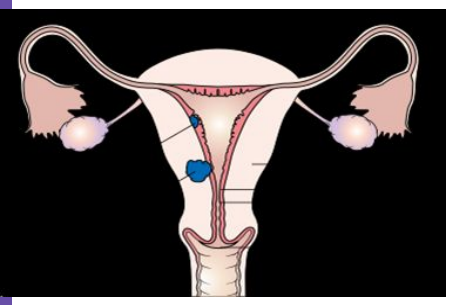
- Clinical behavior of endometrial adenocarcinoma depends on:

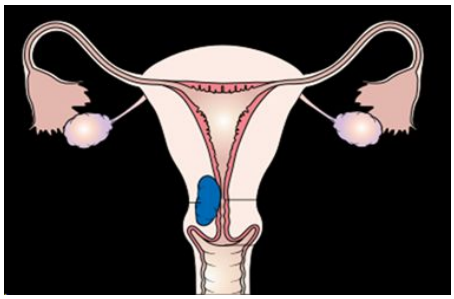
| the histologic type | the grade (degree of differentiation) | the stage (extent of spread) |
|---|---|---|

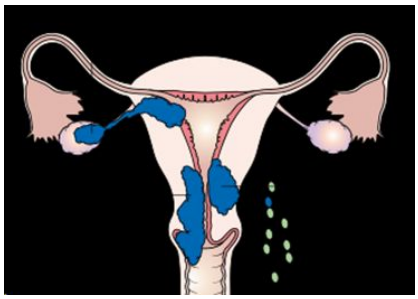
- **Endometrioid carcinoma** (type I) has a **better prognosis** than the other histologic types.
- **Serous carcinomas** (type II) have **poorer prognosis.**
- Stage is the major determinant of survival.

## How endometrial carcinoma can spread

(stages 1, 2 and 3 of endometrial carcinoma) :







# LEIOMYOMA

## Leiomyoma (fibroid) of uterus

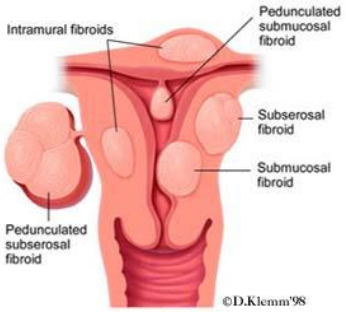
- **Benign tumors** that arise from the **smooth muscle** cells in the myometrium are properly termed leiomyomas, but **because of their firmness often are referred to clinically as fibroids.**
- Leiomyomas are the most **common** benign tumor in **females**, affecting 30% to 50% of women of **reproductive age**, and are considerably more frequent in black women.
- These tumors are associated with several different recurrent chromosomal abnormalities, including rearrangements of chromosomes 6 and 12 that also are found in a variety of other benign neoplasms, such as endometrial polyps and lipomas.
- Mutations in the MED12 gene, which encodes a component of the RNA polymerase transcription complex, have been identified in up to 70% of leiomyomas. The mechanism by which MED12 mutations contribute to the development of leiomyomas is not presently understood.
- **Estrogens** and possibly oral contraceptives **stimulate the growth of leiomyomas**; conversely, these tumors shrink postmenopausally. "In pregnancy→ high estrogen→larger leiomyoma
- The tumor is estrogen responsive. Estrogen stimulates their growth. Leiomyomas often increases in size during pregnancy and decrease in size after menopause.
- About 40% of leiomyomas have an associated chromosomal abnormality.
- They are benign tumors with no appreciable malignant potential (incidence of malignant transformation to sarcoma is 0.1-0.5%).

## Clinical features

- Leiomyomas of the uterus often are **asymptomatic**, being **discovered incidentally** on routine pelvic examination.
- The most frequent presenting sign is menorrhagia, with or without metrorrhagia.
- Leiomyomas rarely, if ever, transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.
- It can be single or multiple (mostly multiple).
- Irregular abnormal bleeding and sometimes pelvic pain.
- It may cause anemia from heavy bleeding.
- Can have urinary frequency if the fibroid is compressing the urinary bladder.
- It may interfere with implantation and therefore cause infertility.
- In pregnant women it may cause abortion, obstructed labor, postpartum hemorrhage etc.

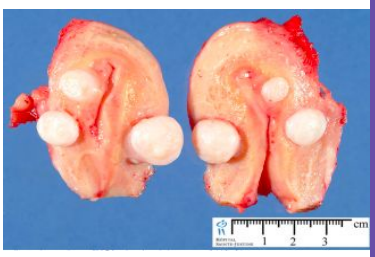
# LEIOMYOMA (cont.)

## Uterine Leiomyoma




- Leiomyomas are **typically sharply circumscribed**, firm **gray white masses** with a characteristic **whorled cut surface.**
- They may occur singly, but more often occur as **multiple tumors** that are scattered within the uterus, ranging from small nodules to large tumors that may dwarf the uterus.

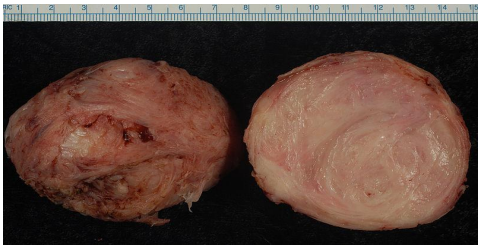
Leiomyoma may be located anywhere in the myometrium:



- **Submucosal** tumors are present immediately below the endometrium.
- **Intramural** tumors, the most common, lie within the myometrium.
- **Subserosal** fibroids lie beneath the serosal surface of the uterus or are pedunculated and attached to the serosa.
- **Pedunculated** ones may loose their connection to the uterus forming a "parasitic leiomyoma".
- others are (Pedunculated) ones may loose their connection to the uterus forming a "parasitic leiomyoma".

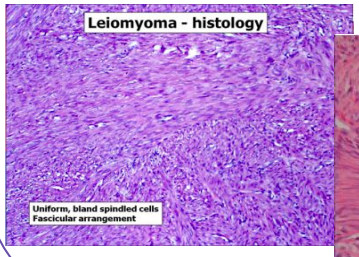
## Grossly:

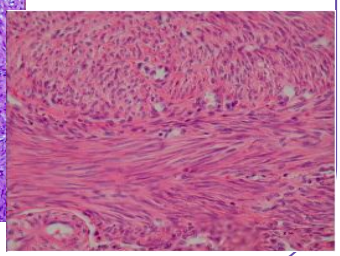
- **Well circumscribed,** spherical, dense and firm-to- hard masses.
- Cut section shows **whorled**, **tan-white** cut surfaces.



## Microscopically:

- Interlacing bundles of smooth muscle cells.
- Collagenous stroma between bundles.
- Individual muscle cells are uniformj in size and shape.
- Characteristic oval to elongated nucleus.
- Mitotic figures are scarce.



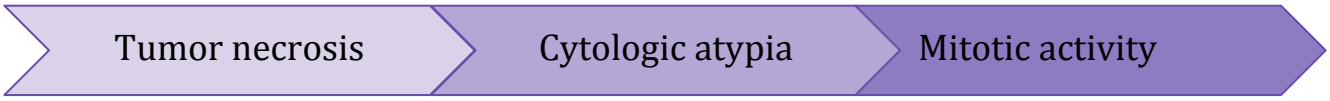



# LEIOMYOSARCOMA (osmosis)

- It is the malignant tumor of the smooth muscle with increased mitosis and necrosis.
- It is rare.
- Sites include the uterus and soft tissue
- Poor prognosis.
- Leiomyosarcomas of the uterus virtually always **arise de novo** "has no precursor/not a progression of leiomyoma" from the mesenchymal cells of the myometrium.
- They are almost always **solitary** and most often occur in **postmenopausal** women, in contradistinction to leiomyomas, which frequently are multiple and usually arise premenopausally.
- **Recurrence** after surgery is common with these cancers, and many **metastasize**, typically to the lungs.

## Morphology:

- The diagnostic features of leiomyosarcoma include:




- Because increased mitotic activity is sometimes seen in benign smooth muscle tumors, particularly in young women, an assessment of all three features is necessary to make a diagnosis of malignancy

# Summary

| | LEIOMYOMA | LEIOMYOSARCOMA |
|---|---|---|
| Origin | Smooth muscle cell of myometrium | Mesenchymal cells of the myometrium. |
| Age | Premenopausally | Postmenopausally |
| Features | • Multiple<br>• Grey white mass<br>• Whorled cut surface (characteristic) | • Solitary<br>• Necrotic<br>• Hemorrhagic |
| Metastasis | -- | **Lung most commonly** |
| Histopathology | • Mitotic figures are scarce.<br>• Characteristic oval to elongated nucleus.<br>• Interlacing bundles of smooth muscle cells. | • Tumor necrosis<br>• Cytologic atypia<br>• Mitotic activity |
| Malignancy potential | • Rarely transform to sarcoma<br>• Multiple lesions do NOT increase risk of malignancy | Assessment of:<br>• Tumor necrosis<br>• Cytologic atypia<br>• Mitotic activity |

# Doctors notes

- Endometrial hyperplasia is placed in two categories based on the presence of cytologic atypia: hyperplasia without atypia and hyperplasia with atypia. “This is the new classification”.
- Hyperplasia without cellular atypia carries a low risk (between 1% and 3%) for progression to endometrial carcinoma, whereas hyperplasia with atypia, also called endometrial intraepithelial neoplasia (EIN), is associated with a much higher risk (20%–50%).
- We take a biopsy of the endometrium by curettage.
- If we see atypia we consider the very high chance for cancer, so if the women is old we do a hysterectomy but if she is young we treat her with progestins and follow up.
- Endometrial cancers arise mainly in postmenopausal women.
- Endometrioid carcinoma is associated endometrial hyperplasia.
- Women with germline mutations in PTEN (Cowden Syndrome) and germline alterations in DNA mismatch repair genes (Lynch Syndrome) are at high risk for this cancer.
- Mutations in p53 are present in at least 90% of serous endometrial carcinoma نادر يجي مع النوع الاول يجي دايم هنا!
- serous endometrial carcinoma is more aggressive and has poor prognosis compared to endometrioid carcinoma.
- Stage is the major determinant of survival and prognosis.
- How to differentiate between complex and endometrial carcinoma?1-architecture is more complex in carcinoma 2-invasion (the glands invade myometrium).
- Leiomyoma is a benign tumor arise from smooth muscle, it could be anywhere but the uterus is the most common place.
- Estrogens and possibly oral contraceptives stimulate the growth of leiomyoma; conversely, these tumors shrink postmenopausally.
- The most frequent presenting sign of leiomyoma is menorrhagia, with or without metrorrhagia, also back pain.
- On cut section of leiomyoma it shows whorled, tan-white cut surfaces.
- The most common place of Leiomyosarcoma for metastasis is the lung.
- The diagnostic features of leiomyosarcoma include tumor necrosis, cytologic atypia, and mitotic activity, assessment of all three features is necessary to make a diagnosis of malignancy.

Why? Because increased mitotic activity alone is sometimes seen in benign smooth muscle tumors.

# Pathoma summary

## I.ENDOMETRIAL HYPERPLASIA

A. Hyperplasia of endometrial glands relative to stroma
B. Occurs as a consequence of unopposed estrogen (e.g., obesity, polycystic ovary syndrome, and estrogen replacement)
C. Classically presents as postmenopausal uterine bleeding
D. Classified histologically based on architectural growth pattern (simple or complex) and the presence or absence of cellular atypia
l. Most important predictor for progression to carcinoma (major complication) is the presence of cellular atypia; simple hyperplasia with atypia often progresses to cancer (30%); whereas, complex hyperplasia without atypia rarely does (<5%).

## II. ENDOMETRIAL CARCINOMA

A. Malignant proliferation of endometrial glands
l. Most common invasive carcinoma of the female genital tract
B. Presents as postmenopausal bleeding
C. Arises via two distinct pathways: hyperplasia and sporadic
D. In the hyperplasia pathway (75% of cases), carcinoma arises from endometrial hyperplasia.
l. Risk factors are related to estrogen exposure and include early menarche/late menopause, nulliparity, infertility with anovulatory cycles, and obesity.
2. Average age of presentation is 60 years.
3. Histology is endometrioid (i.e., normal endometrium-like)
E. In the sporadic pathway (25% of cases), carcinoma arises in an atrophic endometrium with no evident precursor lesion.
l. Average age at presentation is 70 years.
2. Histology is usually serous and is characterized by papillary structures (Fig. 13.9C) with psammoma body formation; p53 mutation is common, and the tumor exhibits aggressive behavior.

## III. LEIOMYOMA (FIBROIDS)

A. Benign neoplastic proliferation of smooth muscle arising from myometrium; most common tumor in females
B. Related to estrogen exposure
l. Common in premenopausal women
2. Often multiple
3. Enlarge during pregnancy; shrink after menopause
C. Gross exam shows multiple, well-defined, white, whorled masses that may distort the uterus and impinge on pelvic structures.
D. Usually asymptomatic; when present, symptoms include abnormal uterine bleeding, infertility, and a pelvic mass.

## IV. LEIOMYOSARCOMA

A. Malignant proliferation of smooth muscle arising from the myometrium
B. Arises de novo; leiomyosarcomas do not arise from leiomyomas.
C. Usually seen in postmenopausal women
D. Gross exam often shows a single lesion with areas of necrosis and hemorrhage; histological features include necrosis, mitotic activity, and cellular atypia.

# Questions

1- A 50-year-old nulliparous woman with a history of diabetes complains that her menstrual blood flow is more abundant than usual. During the last two menstrual cycles, she noticed spotting throughout the entire cycle. The patient is obese (BMI = 32 kg/m2), and her blood pressure is 160/100 mm Hg. An ultrasound examination reveals a thickened endometrial stripe with a polypoid mass in the uterine fundus. The patient undergoes a hysterectomy. The uterus is opened to reveal a partially necrotic mass (shown in the image). A biopsy of the mass shows moderately differentiated adenocarcinoma. Which of the following represents the most likely precursor of this patient's malignant disease?

A - Adenomyosis
B - Atypical hyperplasia
C - Chronic endometritis
D - Complex hyperplasia
E - Glandular metaplasia

2 - Neoplastic cells obtained from the patient described in Question 1 would most likely show loss of function of which of the following cell cycle control proteins?

A - p53
B - PTEN
C - Rb
D - RET

3 - 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 shown in the image. 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

1: B
2: B
3: A

4 - 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 (shown in the image). Which of the following is the most likely cause of vaginal bleeding and anemia in this patient?
A - Adenomyosis
B - Cervical cancer
C - Endometrial carcinoma
D - Uterine leiomyoma

5 - A 52-year-old woman presents with chronic pelvic discomfort. A CT scan of the pelvis shows a 10-cm, well-circumscribed uterine mass. A hysterectomy is performed. On gross examination, the mass is soft with areas of necrosis and irregular borders extending into the myometrium. Histologic examination demonstrates large zones of necrosis surrounded by a rim of disorganized spindle cells that display numerous mitoses. Immunohistochemical staining for smooth muscle actin is positive. Which of the following is the most likely diagnosis?
A - Adenomyosis
B - Carcinosarcoma
C - Endometrial stromal sarcoma
D - Leiomyosarcoma

6 - Obesity, Hypertension and diabetes are risk factors for Endometrioid carcinomas. Why is that?
A - They are part of Metabolic syndrome.
B - They increase estrogen levels.
C - They decrease mortality. D- A&C.

7 - Which of the following endometrial lesions carries the greatest risk of progression to endometrial carcinoma
A - Polyp
B - Simple hyperplasia
C - Atypical hyperplasia
D - Complex hyperplasia

4: D
5: D
6: B
7: C

8 - Serous carcinoma arises in older women with:
A- excess estrogen levels
B- endometrial atrophy
C - endometrial hyperplasia

9 - Intramural uterine leiomyomas are located:
A- within the myometrium
B- immediately below the endometrium
C -beneath the serosal surface of the uterus

10 - Leiomyomas are monocolonal tumors associated with different chromosomal abnormalities including rearrangement of chromosomes:
A - 10 and 11
B - 6 and 8
C - 4 and 6
D - 6 and 12

8: B
9: A
10: D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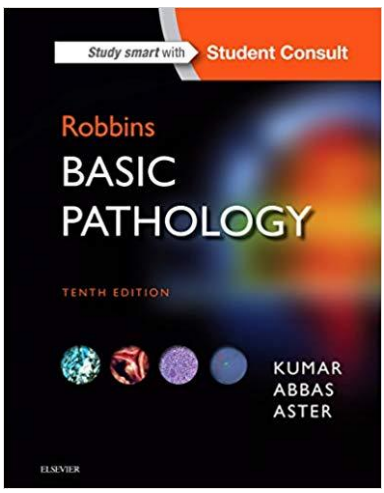


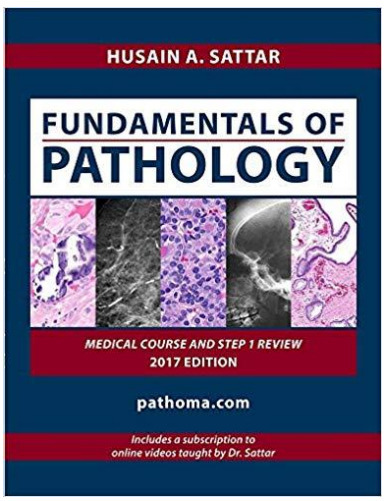


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