



# Lecture 7: Polycystic Ovarian Disease and Endometriosis

Objectives:

At the end of this lecture, the student should be able to:

- Know the clinicopathologic features of endometriosis with special emphasis on: definition, typical sites and theories behind its pathogenesis.
- Understand the clinical manifestations and pathologic features of polycystic ovarian disease.



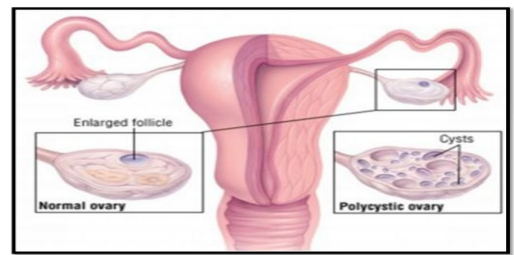
MED437  
KING SAUD UNIVERSITY



TEAM 437

**Important**  
**Terminology**  
**Doctor's Notes**  
Extra Information

# Polycystic ovarian disease



- It is characterized by:
  - **bilateral enlargement** of ovaries by multiple small cysts
  - chronic **anovulation**
  - clinical manifestations secondary to excessive production of estrogens and androgens, mainly **androgens**.
- Other names for this disease include **polycystic ovarian syndrome** and **Stein-Leventhal syndrome**.
- The initial abnormality resulting in the syndrome is **not known** but is believed to be related to hypothalamus-pituitary dysfunction leading to over-secretion of **luteinizing hormone (LH)**.
- **LH** in turn stimulates the ovary to produce excess **androgens**. The secretion of follicle stimulating hormone (**FSH**) is **inhibited** leading to suppression of ovulation and formation of cystic follicles in the ovary.

## Patients have:

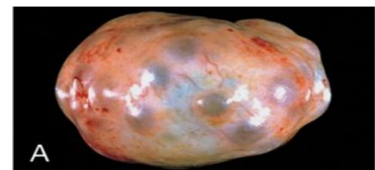
↑ LH

↓ FSH

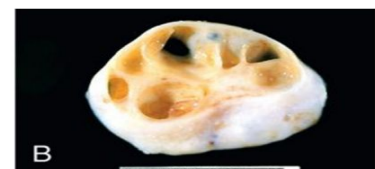
↑ Testosterone

↑ Estrogen

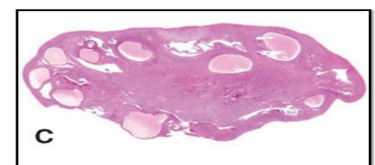
**A:** The ovarian surface reveals numerous nodular elevations of **clear cysts**.



**B:** Cut section shows several **subcortical cystic follicles** in the ovary.

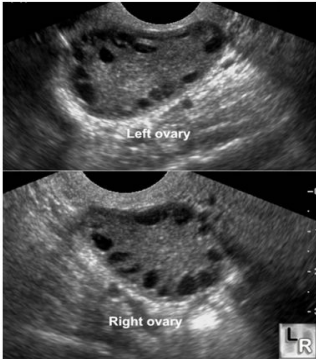


**C:** **Cystic follicles** seen in a low-power microphotograph.



# Polycystic ovarian disease

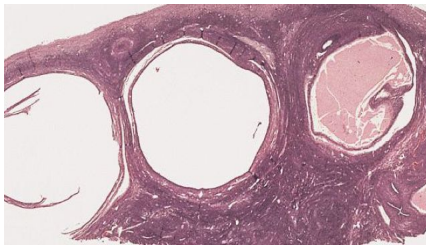
## Clinical presentation



It usually affects **young women** (between 15 and 30 years) and present with:

- secondary amenorrhea with anovulation
- oligomenorrhea or irregular menses
- infertility
- hirsutism
- virilism due to increased androgenic (masculinizing) hormones
- obesity
- acne

## Microscopic features (Ovaries)



- Ovaries are **2 times** the normal size with many subcortical cysts measuring 0.5 to 1.5 cm in diameter.
- The outer portion of the cortex is **thickened and fibrotic** (cortical stromal fibrosis) with multiple cysts underneath. The follicular cysts usually have a **prominent theca interna layer**. "Theca layer produces androgen"
- **Corpora lutea** are frequently **absent** (because **no ovulation**, women with PCOD have anovulatory cycles).

## Microscopic features (Endometrium)

**Chronic anovulation** > unopposed estrogen > hyperestrogenic state > **endometrium** may develop estrogen associated **hyperplasia** and show any of the following:

- simple with or without atypia
- complex hyperplasia, with or without atypia
- or even endometrial adenocarcinoma

# Polycystic ovarian disease

Women with PCOD are at risk for the following:

Endometrial hyperplasia and endometrial cancer

Insulin resistance/Type II diabetes

High blood pressure

Depression/Anxiety

Dyslipidemia

Cardiovascular disease

Strokes

Weight gain

Miscarriage

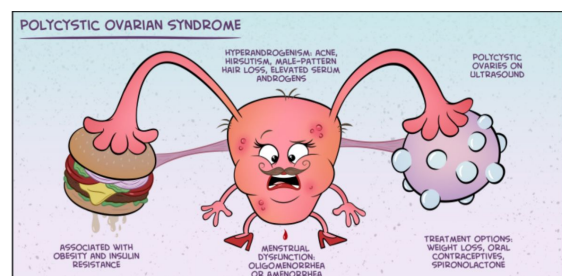
Autoimmune thyroiditis

Acanthosis nigricans (patches of darkened skin under the arms, in the groin area, on the back of the neck)

## Treatment:

- **Life-style modifications**
- Treatment with drugs that either **induce ovulation (clomiphene or hCG)** or regulate the menstrual cycle restores fertility.
- **In refractory cases** Reduction of ovarian volume by **wedge resection of the ovaries** is also successful in initiating ovulation and restoring fertility.
- The endometrial change usually regress once ovulation is achieved.

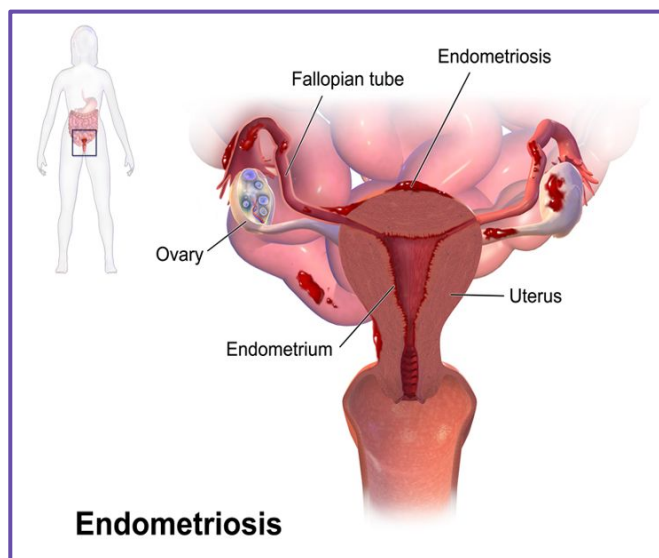
Changes in endometrium are reversible if it's in hyperplasia stage (not adenocarcinoma)



# Endometriosis بطانة الرحم المهاجرة

**Reminder** (Layers of uterus):  
Endometrium - Myometrium -  
Serosa.

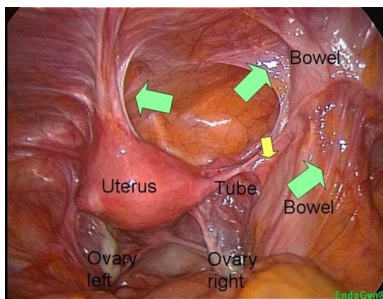
- ★ Normally endometrial glands and endometrial stroma are found in the endometrium of the uterus.
- ★ Endometriosis is the presence of ectopic **endometrial glands** and **stroma** **outside** the uterus.
- ★ It is **non-neoplastic** condition.
- ★ Endometriosis is usually found on the peritoneal surfaces of the reproductive organs and adjacent pelvic organs. The most frequent locations are:
  - **ovary** (the most common site, approx. 50%).
  - Pouch of Douglas “**between uterus and rectum**” and uterine ligaments (second most common).
  - Occasionally: cervix, vagina, perineum, bladder, large bowel and umbilicus.
  - Rarely: small bowel, kidneys, lungs, nose and brain.
- ★ It has been reported in men. The sites involved have been the bladder, scrotum and prostate. **How it's affect male? By genetic abnormality.**



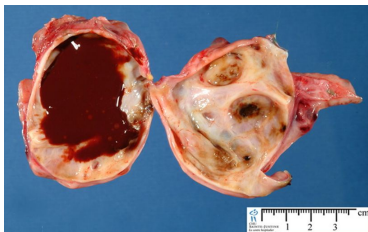
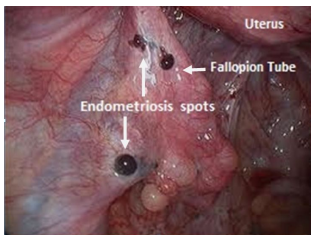
# Endometriosis

- ★ Like the uterine endometrium it is responsive to the hormonal variations of the menstrual cycle, and **bleeds during menstruation**. It will **proliferate in proliferative phase**. It will **has secretory changes in secretory phase**.
- ★ Therefore in endometriosis there is menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. **chocolate cysts**).

## Clinical presentation



Fibrous adhesions

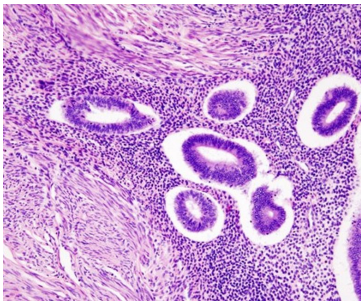
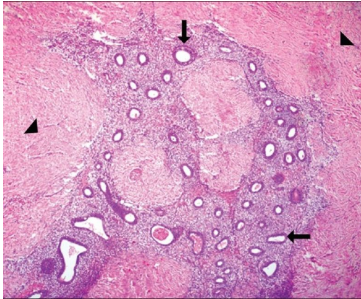


Chocolate cyst of ovary (endometriotic cyst)

- ★ The clinical presentation depends on the site of endometriosis:
  - Dysmenorrhea **pain during menstrual cycle**
  - Dyspareunia **pain during intercourse**
  - Cyclic abdominal pain (there is usually a severe menstrual-related pain)
  - **Infertility**
  - **Fibrous adhesions** **one of the causes of infertility**
- ★ The behavior of endometriosis is **benign with no malignant potential**. It may recur after surgical excision but the risk is low.
- ★ Endometriosis usually appears as multiple **red** or **brown** (due to hemosiderin) 1 mm to 5 mm nodules (some may form larger masses or cysts). Dense fibrous adhesions may surround the foci.
- ★ Repeated hemorrhage into the ovary with each menstrual cycle produces cysts, filled with chocolate-brown material. The cyst is called "chocolate cyst".
- ★ With time the ovaries become totally cystic and turn into large cystic masses filled with chocolate brown fluid.

# Endometriosis

## Microscopic features

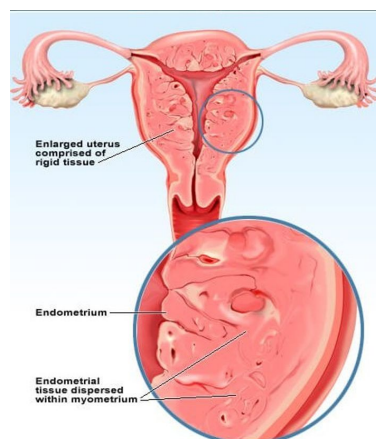


## Very important!

- ★ Ectopic endometrial glands and endometrial stroma are present.
- ★ Denatured blood from previous bleeding is present.
- ★ Macrophages containing hemosiderin (siderophages) are present. Hemosiderin is a golden granular material inside the cytoplasm of macrophages.
- ★ When endometriosis develops in a muscular organ, the smooth muscle around it is often hyperplastic.

# Adenomyosis

- ★ This is defined as the presence of **endometrial glands** and endometrial **stroma** in the **myometrium** of the uterus.
- ★ It is more common in the posterior wall than the anterior wall (but it may affect both walls in the same uterus).
- ★ The disease is primarily a disorder of parous women and is uncommon in the nullipara or single female.



# Adenomyosis

## Clinical presentation



- ★ It is associated with menorrhagia “**excessive bleeding**” and severe dysmenorrhea, however it is asymptomatic in 1/3 of the patients. **Why there is menorrhagia? Because there is no more control of the muscle that normally contract to stop this bleeding at some point, all of it is infiltrated by bleeding endometrium.**
- ★ When extensive, the lesions cause myometrial thickening with small yellow or brown cystic spaces containing fluid or blood.
- ★ The behavior of this conditions is **benign** with no known malignant potential and it usually regresses after the menopause.
- ★ Cross section through the wall of a hysterectomy specimen of a 30-year-old woman who reported chronic pelvic pain and abnormal uterine bleeding. The endometrial surface is at the top of the image, and the serosa is at the bottom. **All of these cysts within the myometrium are endometrial foci or adenomyotic foci → Islands of endometrium infiltrating the myometrium.**



# Doctors notes

## PCOD

- It is characterized by **bilateral** enlargement of ovaries by multiple small cysts, chronic anovulation and clinical manifestations secondary to excessive production of estrogens and androgens, mainly **androgens**.
- It is believed to be related to hypothalamus-pituitary dysfunction leading to over-secretion of **luteinizing hormone LH** (more androgen > less FSH > anovulation > multiple cysts > estrogen but no ovulation because of deficiency of FSH).
- Clinical presentation: secondary amenorrhea, infertility, hirsutism, obesity, acne, irregular menses.
- Cut section shows **several** subcortical **cystic follicles** in the ovary.
- On microscope: Ovaries are **2 times** the normal size with many **subcortical** cysts, The follicular cysts usually have a prominent **theca interna** layer.
- Women at high risk for **Acanthosis nigricans**, **Autoimmune thyroiditis**.
- Treatment with Clomiphene or wedge resection.

## Endometriosis

- Endometriosis is the presence of ectopic endometrial **glands** and **stroma** outside the uterus, Its non neoplastic.
- Most common site is the **ovary** then **pouch of douglas** and uterine ligaments.
- there is menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. **chocolate cysts**).
- Endometriosis usually appears as **multiple red or brown** (due to hemosiderin).
- **On microscope we see ectopic endometrial glands and endometrial stroma, Denatured blood from previous bleeding is present, macrophages containing hemosiderin (siderophages).**

## Adenomyosis

- presence of endometrial glands and endometrial stroma in the **myometrium** of the uterus.
- It is associated with **menorrhagia** and severe **dysmenorrhea**, however it is asymptomatic in 1/3 of the patients.
- It is **benign** with no known malignant potential and it usually regresses after the menopause.

# Pathoma summary

## I.ENDOMETRIUM

### I. ENDOMETRIOSIS

- A. Endometrial glands and stroma outside of the uterine endometrial lining
  - 1. Most likely due to retrograde menstruation with implantation at an ectopic site
- B. Presents as dysmenorrhea (pain during menstruation) and pelvic pain; may cause infertility
  - 1. Endometriosis cycles just like normal endometrium.
- C. Most common site of involvement is the ovary, which classically results in formation of a 'chocolate' cyst
  - 1. Other sites of involvement include the uterine ligaments (pelvic pain), pouch of Douglas (pain with defecation), bladder wall (pain with urination), bowel serosa (abdominal pain and adhesions), and fallopian tube mucosa (scarring increases risk for ectopic tubal pregnancy); implants classically appear as yellow-brown 'gun-powder' nodules. Involvement of the uterine myometrium is called adenomyosis.
- D. There is an increased risk of carcinoma at the site of endometriosis, especially in the ovary.

## II.OVARY

### I. BASIC PRINCIPLES

- A. The functional unit of the ovary is the follicle.
- B. A follicle consists of an oocyte surrounded by granulosa and theca cells
  - 1. LH acts on theca cells to induce androgen production.
  - 2. FSH stimulates granulosa cells to convert androgen to estradiol (drives the proliferative phase of the endometrial cycle).
  - 3. Estradiol surge induces an LH surge, which leads to ovulation (marking the beginning of the secretory phase of the endometrial cycle).
- C. After ovulation, the residual follicle becomes a corpus luteum, which primarily secretes progesterone (drives the secretory phase which prepares the endometrium for a possible pregnancy).
  - 1. Hemorrhage into a corpus luteum can result in a hemorrhagic corpus luteal cyst, especially during early pregnancy.
- D. Degeneration of follicles results in follicular cysts. Small numbers of follicular cysts are common in women and have no clinical significance.

### II. POLYCYSTIC OVARIAN DISEASE (PCOD)

- A. Multiple ovarian follicular cysts due to hormone imbalance
  - 1. Affects roughly 5% of women of reproductive age
- B. Characterized by increased LH and low FSH (LH:FSH > 2)
  - 1. Increased LH induces excess androgen production (from theca cells) resulting in hirsutism (excess hair in a male distribution).
  - 2. Androgen is converted to estrone in adipose tissue.
    - i. Estrone feedback decreases FSH resulting in cystic degeneration of follicles.
    - ii. High levels of circulating estrone increase risk for endometrial carcinoma.
- C. Classic presentation is an obese young woman with infertility, oligomenorrhea, and hirsutism; some patients have insulin resistance and may develop type 2 diabetes mellitus 10-15 years later.

# Questions

1- A 36-year-old woman presents with infertility. She complains of having had dull pelvic pain for 9 months, which is accentuated during menstruation. Physical examination and endocrinological studies are normal. Laparoscopy reveals multiple, small hemorrhagic lesions over the surface of both ovaries and fallopian tubes and abundant pelvic scarring. Which of the following is the most likely diagnosis?

- (A) Borderline serous tumor
- (B) Ectopic pregnancy
- (C) Endometriosis
- (D) Metastatic cervical carcinoma

2- A 25-year-old woman is referred to the gynecologist for treatment of infertility. The patient is obese (BMI = 32 kg/m<sup>2</sup>) and has pronounced facial hair. She states that she has always had irregular menstrual periods. On gynecologic examination, both ovaries are found to be symmetrically enlarged. This patient's ovaries would likely show which of the following pathologic findings?

- (A) Bilateral Endometriomas
- (B) Cystic teratoma
- (C) Serous Cystadenoma
- (D) Subcapsular cysts

3- Endocrine studies of the woman described in Question 2 would most likely show which of the following results in the serum?

- (A) High levels of corticosteroids
- (B) High levels of follicle-stimulating hormone
- (C) High levels of luteinizing hormone
- (D) Low levels of estrogens

4- What is the most common site of endometriosis?

- (A) Myometrium
- (B) Perimetrium
- (C) Fallopian tubes
- (D) Ovaries

- 1- C
- 2- D
- 3- C
- 4- D

5- Are women with endometriosis in risk of cancer?

- (A) Yes, slightly.
- (B) Yes, up to 80%.
- (C ) Not at all.

6- Which of the following is not associated with PCOS?

- (A) Obesity
- (B) Hirsutism
- (C ) Adhesions
- (D) Infertility

7- Which of the following is correct about endometriosis?

- (A) Most common site is the pouch of Douglas
- (B) Presence of hemosiderin pigment is diagnostic
- (C ) Lesion seen in myometrium
- (D) Associated with high malignant potential

8- Women with PCOS are at high risk of developing:

- (A) Diabetes type 2
- (B) Hypotension
- (C) UTI
- (D) Weight loss

9- Corpora lutea are frequently:

- (A) present
- (B) Absent

10- Chocolate cysts are filled with:

- (A) mucos
- (B) Air
- (C) Water
- (D) Blood

5- C

6- C

7- B

8- A

9- B

10- D



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References:



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