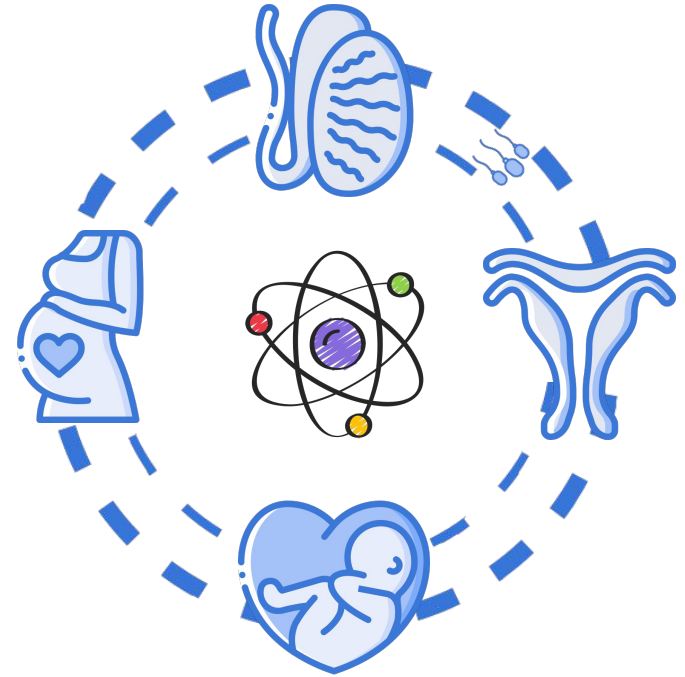


Biomarkers of Ovarian Cancer and Cysts



Color Index:

- Main Topic
- Main content
- Important
- Drs' notes
- Extra info



Objectives:

- ✓ Discuss the risk factors and possible causes of polycystic ovarian syndrome (PCOS) and ovarian cancer.
- ✓ Comprehend the role of insulin resistance and hypersecretion of androgens in the development of PCOS.
- ✓ Identify avenues for the diagnosis and treatment of PCOS and ovarian cancer.
- ✓ Assess the diagnostic significance of CA-125 in ovarian cancer.



Overview:



Polycystic ovarian syndrome (PCOS)

- Causes
- Endocrine changes
- Diagnostic criteria
- Treatment

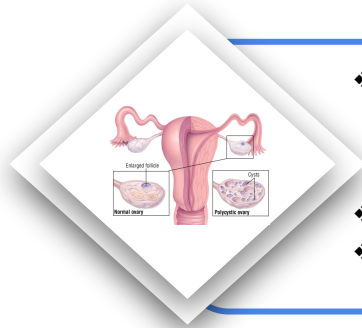


Ovarian cancer

- Types
- Risk factors
- Diagnosis
- CA-125 biomarker



1st. Polycystic Ovarian Syndrome



- ❖ Formation of multiple small cysts in the ovaries.
Multiple cysts which are formed of immature follicles with arrested growth during development (Due to constant secretion of LH rather than LH Surge) affecting menstrual cycle and causing infertility.
- ❖ Affects 5 -10% of women (20% in some populations).
- ❖ A major cause of infertility in women.

Strongly correlated to:

- ▶ Family History
- ▶ Obesity (40%)
- ▶ Hirsutism
- ▶ Chronic Anovulation
- ▶ Glucose Intolerance
- ▶ Insulin Resistance
- ▶ Hyperlipidemia
- ▶ Hypertension
- ▶ Menstrual disorders
- ▶ Hypersecretion of **LH** & **androgens** (testosterone).
- ▶ Low levels of **SHBG** (sex hormone binding globulin).

Causes:

- ❖ Exact cause of the syndrome is **unknown**, may be multifactorial (genetic & environmental).
Probable causes:
 - A) **Insulin resistance** (usually starts with obesity) causes excessive androgen production in ovaries (common).
 - B) **Abnormalities** in ovaries, adrenal and pituitary glands.

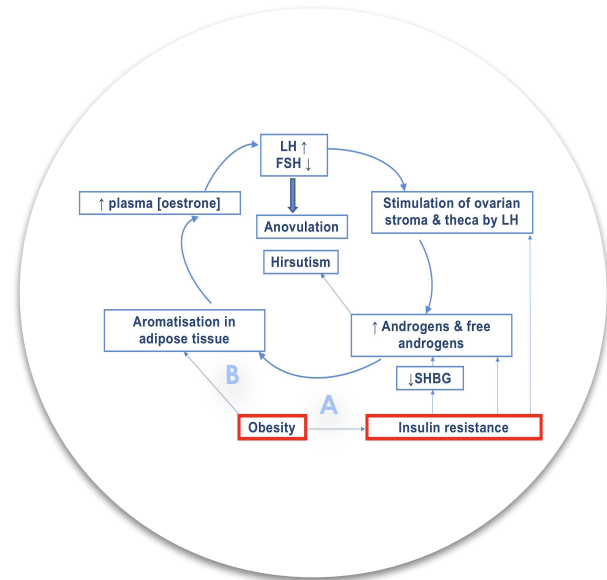
1st. Polycystic Ovarian Syndrome

Endocrine Changes in PCOS:

Doctor's explanation | **Obesity leads to two things:**

- A** Insulin resistance, which will lead to hyperinsulinemia. The hyperinsulinemia has **2** effects:
1. Insulin affects the ovary directly and **stimulates androgen** production.
 2. Affects the liver to **decrease** the formation of **SHBG**.
- **Net results:** **increase** in the amounts of **free androgens** leading to:
- Hirsutism and other symptoms such as acne.
 - **Increase** in the pulsatile secretion of GnRH, which favors the production of LH over FSH. **LH** will be very **high** while **FSH** is **low/normal**.
 - **Increase** in androgen conversion to estrogen in adipose tissue, which will **increase** estrogen → affects GnRH secretion → **decrease** the secretion of **FSH** from AP.
- So in PCOS, the ratio between FSH and LH is important. LH is at least double FSH.

- B** The increase in adipose tissue will **increase** aromatisation of androgens to estrone (by the **aromatase** present in adipose tissue).
- the continuous **high** levels of **LH** and the **decrease** in **FSH** & **progesterone** will lead to anovulation and arrested growth of the follicles leading to PCOS.



Diagnostic Criteria

European Society for Human Reproduction & Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) recommendation:

❖ **At least Two**¹ of the following features are required for **PCOS** diagnosis:

01 Oligo-ovulation or anovulation:

→ Manifested as **oligomenorrhea** or **amenorrhea**².

02 Hyperandrogenism:

→ Clinical & biochemical evidence of androgen excess³.

03 Polycystic ovaries:

→ As defined by ultrasonography.

Done by Measuring:

▶ **Free testosterone** (total testosterone is less sensitive; androgens are ↑ in PCOS)

▶ **Sex hormone-binding globulin** (SHBG; ↓ in PCOS).

▶ **Luteinizing hormone** (LH; high in 60% cases).

▶ **Follicle stimulating hormone** (FSH); usually normal in PCOS.

▶ **Fasting blood glucose** or 2H OGTT.

▶ **Insulin**

▶ **Lipids**

Ovarian Ultrasound:

▶ 30% of patients do **not** have ovarian cysts despite having symptoms.



Treatment of PCOS

Aim of the treatment:

→ Interrupt the cycle of obesity, insulin resistance, excess androgens. (**Break the cycle**⁴)

▫ **Decrease LH** levels⁴ (by oral contraceptives).

▫ **Decrease** body weight⁵.

▫ **Increase FSH** levels (by clomiphene, etc.)

▫ **Estrogen** replacement therapy⁶:

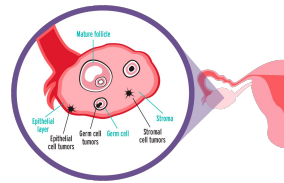
→ In select women after careful risk counseling "risk of cancer & Venous Thromboembolism".


- Give combined oral contraceptives which have estrogen & progesterone⁷.

- Provide metformin "oral hypoglycemic" for insulin resistance.

1. In **adults** two are enough, in **adolescence** all the three are required for diagnosis.
2. **Oligomenorrhea**: absence of menstrual periods for more than 6 weeks (less than 6 months)
3. **Amenorrhea**: absence of menstrual periods for more than 6 months.
4. **Clinical**: acne, hirsutism, alopecia. | **Biochemical**: hyperandrogenemia.
5. Can be done by decreasing androgens → decreases LH.
6. More sensitive to insulin → lower insulin levels in the blood - androgen excess decreased.
7. **Estrogens** include: estrone, estradiol, estriol. So we use estrogens other than estrone. Pills that contain estrogen and progestin decrease androgen production and regulate estrogen.

2nd. Ovarian cancer



 Most common type of ovarian cancer (the epithelial)

● A Leading cause of death because of gynecological cancer.

● Due to malignant transformation of ovarian epithelial cells.

Subtypes:

Serous (46%):
surface epithelial tumors

Mucinous (36%):
mucinous epithelial tumors

Endometrioid (8%):
endometrial tumors

History taking

Physical examination

Ultrasound

Measurement of serum **CA-125** level

Diagnosis includes:

Risk factors:

Carriers of **BRCA1** mutations have a cancer risk of 44%.

Mutations in **BRCA1 & BRCA2** genes.

Premenopausal breast cancer or ovarian cancer indicates higher risk for hereditary or breast cancer.

Ashkenazi Jews have higher risk of ovarian cancer

Family history of breast, ovarian, colorectal cancer.

Nulliparity (woman with no childbirth or pregnancy).

Biomarkers and diagnosis

❖ Epithelial ovarian cancer is commonly diagnosed at a later stage. *By chance during surgery for example*

❖ Due to non-specific symptoms such as: abdominal pain, bloating, early satiety, nausea, etc.

❖ Most patients (**75%**) have advanced-stage tumor upon diagnosis.

Cancer Antigen in 125 (CA-125)

A cell surface glycoprotein expressed in the epithelium of all tissues.
Normally absent in serum.

The **only** serum marker of epithelial ovarian cancer.

CA-125 is elevated in ovarian cancer.
>35 U/ml is considered positive.

CA-125 is **NOT** a marker of choice for ovarian cancer screening due to:

1 High false-positive rate

→ False positive CA-125 conc. are found in benign conditions and are usually not associated with postmenopausal women:

Endometriosis

During the first trimester of pregnancy

Uterine leiomyomas

During menstruation

Pelvic inflammatory disease

2 Low prevalence of ovarian cancer

01

02

03

04

05

06

Recommended as an annual test for women with family history of ovarian cancer.

CA-125 is associated with stages of ovarian cancer.

A **non-specific** marker.
Some patients (< 50 years) have elevated CA-125 due to **unrelated malignant mass**.
If a postmenopausal woman has a high serum level of CA125, she has a high chance of having an ovarian cancer .

Elevated in

50% of patients with **stage I**

90% of patients with **stage II**

>90% of patients with **stage III & IV**

Monitoring patient's response to chemotherapy.

Success of surgery (de-bulking procedures removing a tumor mass).

Annual testing for women with family history of ovarian cancer.

Useful in

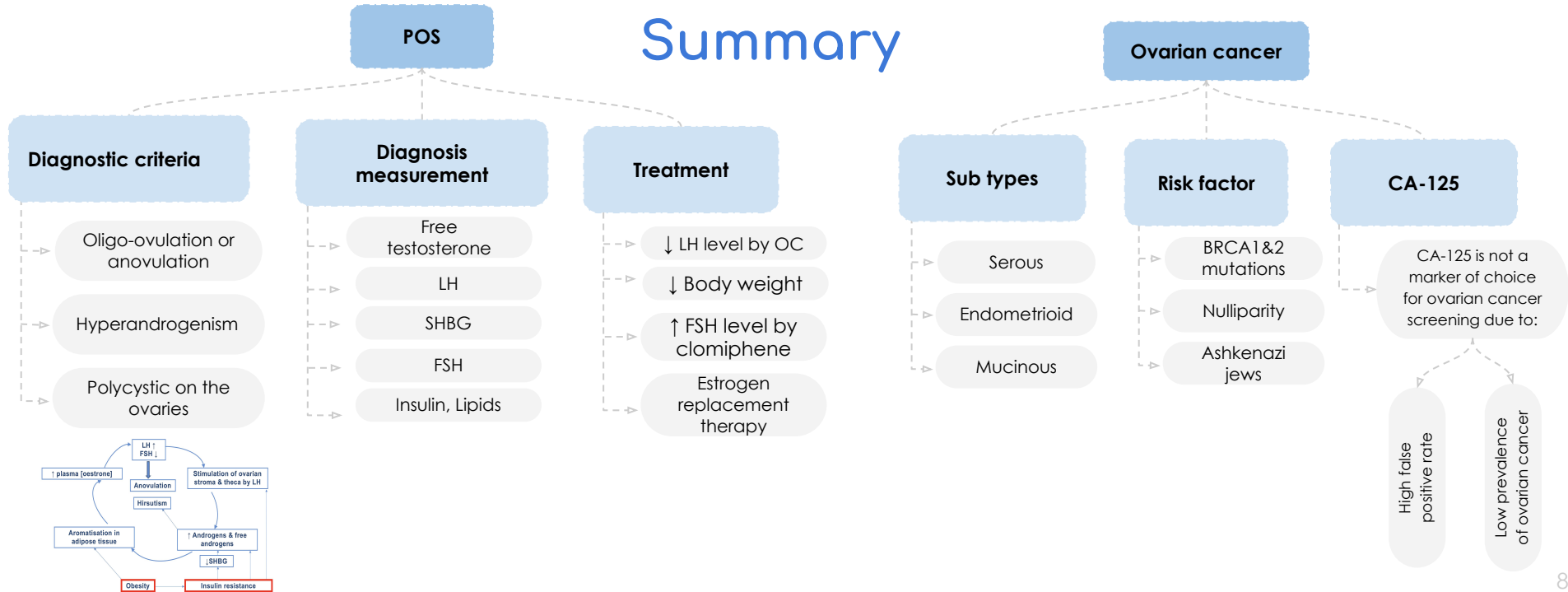
Take Home Messages



PCOS is strongly correlated to insulin resistance and endocrine abnormalities



Although a nonspecific biomarker, CA-125 is important for staging and follow-up of ovarian cancer treatment





Every journey ends eventually and our journey with **biochemistry** has finally come to an end, with all these mixed feelings of gratitude and appreciation we would like to thank each member of this amazing team for their hard work during the past 2 years in which they delivered everything they could possibly do to help our beloved batch, and we hope that we actually did.

Also we would love to thank our academic leader , the previous & the meantime team leaders:

Razan AlRabah

Ibrahim Aldakhil

Deema Almaziad

Raed Alojayri

Lina Alosaimi

Mohannad Alqarni

- Alwateen Albalawi
- Ajeed Al-rashoud
- Amira AlDakhilAllah
- Arwa Alemam
- Elaf Almusahel
- Haifa Alessa
- Haifa Alwaily
- Ghalia Alnufaie
- Leena Alnassar
- Lama Aldakhil
- Lamiss Alzahrani
- Lama Alassiri
- Rema Alkahtani

- Nouf Alhumaidhi
- Noura Alturki
- Nouran Arnous
- Reem Algarni
- Sara Alkhalife
- Shahd Alsalamh
- Taif Alotaibi
- Joud Alkhalifah
- Jude Alotaibi
- Sarah Alhilal
- Ghaida Albraithen
- Abeer Alkhodair
- Noura Almazrou

- Alkassem Binobaid
- Abdullah altuwaijri
- Khayyal Alderaan
- Fares aldokhayel
- Fahad Alsultan
- Mashal Abaalkhail
- Naif Alsolais
- Omar Alyabis
- Omar Saeed
- Omar Odeh
- Sultan Alhammad
- Rayyan Almousa
- Yazen Bajeaifer

- Saad Dammas
- Bader Alshehri
- Omar AlGhamdi
- Suhail Basuhail
- Nayef Alsaber
- Humaid Humaid
- Tariq Alanezi
- Abdulrahman Bedaiwi
- Rakan Alfaifi



Quiz

MCQs :

Q1: All the following are clinical Manifestations of PCOS, EXCEPT:

- a) Amenorrhea or Irregular Menses b) Facial Hair (Hirsutism)
c) Acne d) Weight Loss

Q2: When assessing a serum hormone levels, what would be consistent with PCOS?

- a) ↓ testosterone & estrogen b) ↑ testosterone & LH, ↓ FSH
c) ↓ LH, ↑ FSH d) ↓ SHBG

Q3: All the following are recommended treatment for PCOS, EXCEPT:

- a) Oral contraceptives b) Exogenic androgen intake
c) Reduce body weight d) Estrogen replacement therapy

Q4: which of the following mutation gene associated with the risk factor of ovarian cancer?

- a) BRCA1 b) BRCA4
c) BRCA2 d) A&C

Q5: a patient came to you with an ovarian cancer, you want to monitor the response of chemotherapy, which antigen you will look for?

- a) Androgen b) LH&FSH
c) CA-125 d) elevated estrogen

Q6: which one of the following in not a subtype of ovarian cancer?

- a) Mucinous b) serous
c) fibroid d) endometrioid

SAQs :

Q1: What are the two consequences of obesity that lead to PCOS?

Q2: What are the effects of hyperinsulinemia in PCOS?

Q3: 40 y.o patient came to you and you suspect ovarian cancer. the diagnosis will be based on what?

Q4: list 2 benign conditions where you will found a high false positive rate of CA-125?

★ MCQs Answer key:

1) D 2) B&D 3) B 4)D 5) C 6)C

★ SAQs Answer key:

- 1) A. Insulin resistance, which will lead to hyperinsulinemia.
B. The increase in adipose tissue will increase aromatisation of androgens to estrone.
- 2) The hyperinsulinemia has 2 effects: 1- Insulin affects the ovary directly and stimulates androgen production. 2- Affects the liver to decrease the formation of SHBG. [Slide 4](#)
- 3) History taking, physical examination, ultrasound, measurement of CA-125 serum level
- 4) During menstruation and endometriosis

Team members



- Ajeed Al-Rashoud
- **Nouf Alhumaidhi**
- **Noura Alturki**



- Mashal Abaalkhail
- Naif Alsolais



Team Leaders

Lina Alosaimi

Mohannad Alqarni

★ “Believe you can and you're halfway there.”
— Theodore Roosevelt.



We hear you