Biochemistry Bandits 434

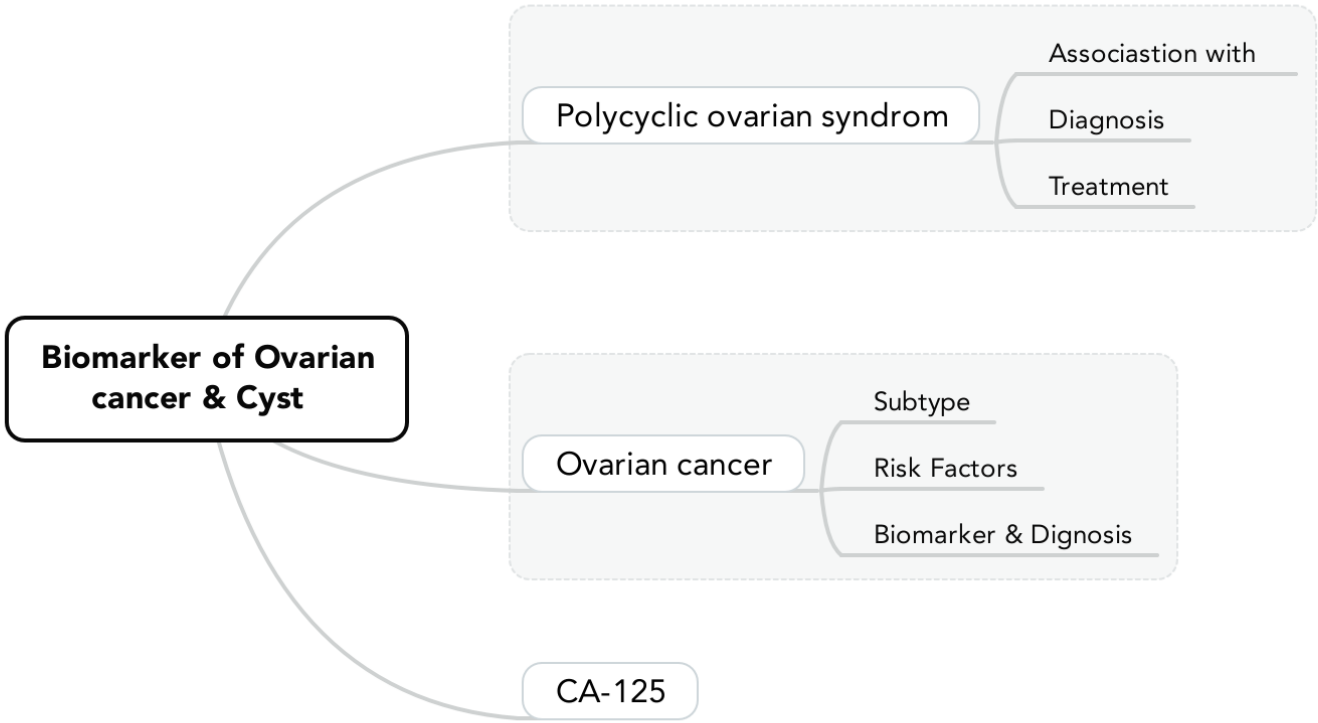
BIOMARKERS OF OVARIAN CYSTS & CANCERS

Overview:

- Polycystic ovarian syndrome
- Biomarkers and diagnosis
- Ovarian cancer
- Types, risk factors
- Biomarkers (CA-125) and diagnosis

❖ **Important** ❖ Extra ❖ Biochemistry Edit

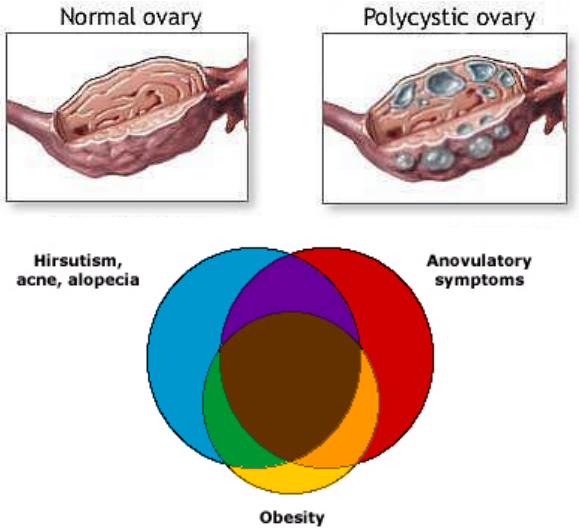
MIND MAP


Biomarker of Ovarian cancer & Cyst
Polycyclic ovarian syndrom
Associastion with
Diagnosis
Treatment
Ovarian cancer
Subtype
Risk Factors
Biomarker & Dignosis
CA-125

POLYCYSTIC OVARIAN SYNDROME

- Formation of **multiple small cysts in the ovaries**.
- Affects 5-10% of women (20% in some populations).
- Exact cause of the syndrome is **unknown**
- May be multifactorial (**genetic and environmental**)

A major cause of infertility in women



➢ **Suggested causes**:

1. **Insulin resistance** causes excessive **androgen** production in ovaries (common).

2. **Abnormalities** in **ovaries**, **adrenal** and **pituitary glands**

➢ **Associated with:**

Obesity (40%)

Hirsutism

Chronic anovulation

- Glucose intolerance
- Insulin resistance

- Hyper-lipidemia
- Hyper-tension

Menstrual disorders

POLYCYSTIC OVARIAN SYNDROME

➢ **Associated with:**

Hypersecretion:
- LH
- androgens (testosterone)

Low levels of SHBG (sex hormone-binding globulin)

➢ **Diagnosis done by measuring:**

Free testosterone

total testosterone is less sensitive; androgens are increased in PCOS

INCREASING

SHBG

Sex hormone-binding-globulin (decreased in PCOS)

DECREASING

LH
(high in 60% cases)

INCREASING

FSH
usually normal in PCOS

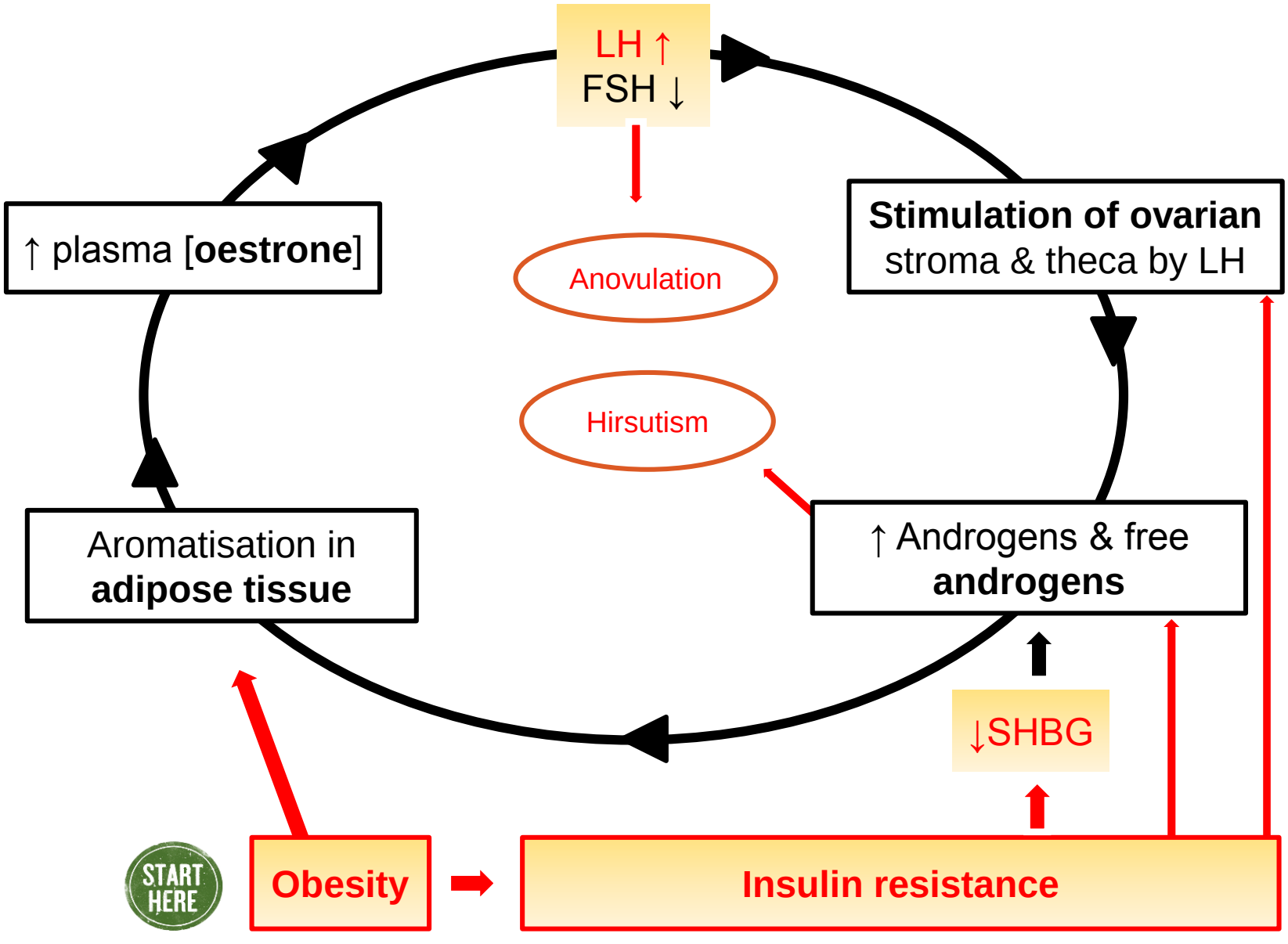
NORMAL

- **Fasting blood glucose**
- **Insulin**
- **Lipids**

Ultrasound

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

BIOCHEMICAL, METABOLIC & ENDOCRINE CHANGES IN PCOS



We just need to break the cycle at any step to prevent PCOS

TREATMENT OF PCOS

Aim: **Interrupt the cycle**
(obesity, insulin resistance, excess androgens…)

↓ [LH] with oral contraceptives

↓ weight

↑ [FSH] with clomiphene, etc

Estrogen replacement therapy in select women after careful risk counseling

OVARIAN CANCER

- A leading cause of **death** because of **gynecologic cancer.**
- Cancrs due to **malignant transformation of ovarian** epithelial cells being the Most common type of ovarian cancer.

mucinous epithelial tumors

Endometrioid (8%):

endometrial tumors

Mucinous (36%):

Serous (46%):

surface epithelial tumors

Subtypes

➢ **Risk factors:**

Nulliparity (woman with no child birth or pregnancy)	**Family history** of breast, ovarian, colorectal cancer	**Mutations** in BRCA1 and BRCA2 genes (**most common**). • Carriers of BRCA1 mutations have a cancer risk of 44%	• **Premenopausal** breast cancer, ovarian cancer: indicates higher risk for hereditary or breast cancer	**Ashkenazi Jews** have higher risk of ovarian cancer

BIOMARKERS AND DIAGNOSIS OVARIAN CANCER

- **Epithelial ovarian cancer is commonly diagnosed at a later stage**
- Most patients (75%) have advanced-stage tumor upon diagnosis

- Due to **non-specific symptoms** such as abdominal pain, blotting, early satiety, nausea, etc.

➢ **Diagnosis includes:**

✓ History taking

✓ Ultrasound

✓ Physical examination

✓ Determination of serum CA-125 levels

CANCER ANTIGEN 125
(CA-125)

The only serum marker of epithelial ovarian cancer

A cell surface glycoprotein expressed in the epithelium of all tissues

Normally **absent** in serum

CA-125 is elevated in ovarian cancer

>35 U/ml → considered positive

- Recommended as **an annual test** for **women** with family history of ovarian cancer.
- CA-125 is associated with **stages** of ovarian cancer:
  - **Elevated in:**

50% of patients with	**stage I**
90% of patients with	**stage II**
>90% of patients with	**stage III**

CANCER ANTIGEN 125
(CA-125)

- **A non-specific marker.**

➢ False positive CA-125 conc. are found in benign conditions:
  - **Endometriosis**
  - **Uterine leiomyomas**
  - **Pelvic inflammatory disease**
  - **During the first trimester of pregnancy**
  - **During menstruation**

- Some patients (< 50 years) have **elevated CA-125** due to **unrelated malignant mass**

- **CA-125 is not a marker of choice** for ovarian cancer screening due to:
  1. Low prevalence of ovarian cancer
  2. High false-positive rate

Useful in:

1. Monitoring patient's response to **chemotherapy.**
2. Success of **surgery** (de-bulking procedures).
3. **Annual testing for women** with **family history** of ovarian cancer

Summary:

Polycystic ovarian syndrome (Formation of multiple small cysts in ovaries)

Associated with:

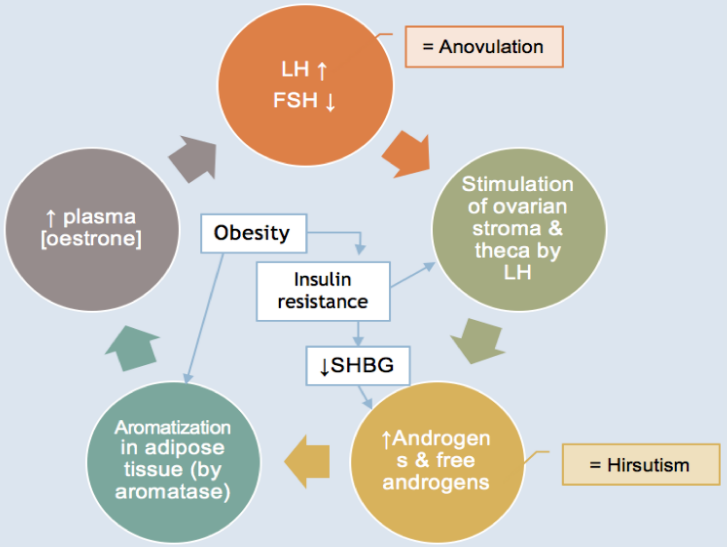
1. Obesity (40% of cases)
2. Chronic anovulation/infertility/Menstrual disorders
3. Glucose intolerance
4. Hyperlipidemia/Hypertension
5. Hypersecretion LH and androgens/Hirsutism

Diagnosis done by measuring:

- ❖ Free testosterone
- ❖ Sex hormone-binding globulin (SHBG) often decreases in PCOS → tends to ↓ [total testosterone] & ↑[free testosterone]
- ❖ LH; ↑ in 60% of cases. FSH; often normal.
- ❖ LH/FSH Ratio (↑ in > 90% of patients)
- ❖ Fasting glucose
- ❖ Insulin
- ❖ Lipids

Treatment:

↓ LH with oral contraceptives
↓ weight
↑ FSH with clomiphene.
Estrogen replacement therapy.



Ovarian Cancer

Subtypes:

–Serous (46%)
–Mucinous (36%)
– Endometrioid (8%)

Risk Factors:

1. Nulliparity
2. Family history of ovarian cancer
3. Family history of breast, ovarian, endometrial, or colon cancer
4. Mutations in BRCA1 and BRCA2

Diagnosis includes:

–History taking
–Physical examination
–Ultrasound
–Determination of serum CA-125 levels

Cancer antigen 125

A cell surface glycoprotein/The only serum marker of epithelial ovarian cancer/Normally absent in serum

- ❖ >35 U/ml is considered positive
- ❖ Elevated in:
  50% of patients with stage I
  90% of patients with stage II
  >90% of patients with stage III and IV
- ❖ Patients (< 50 years) have elevated CA-125 due to unrelated malignant mass

False positive CA-125 conc. are found in benign conditions:

1. Endometriosis
2. Uterine leiomyoma
3. Pelvic inflammatory disease, peritonitis, cirrhosis, ascites
4. First trimester of pregnancy
5. Menstruation

Useful in:

- ❖ Monitoring chemotherapy
- ❖ Monitoring success of surgery
- ❖ Annual testing for women with family history of ovarian cancer

CA-125 isn't a marker of choice for ovarian cancer screening in asymptomatic individuals due to:
↓prevalence of ovarian cancer
↑false-positive rate

MCQS

1) Which of the following associated with polycystic syndrome?

A. Obesity
B. Glucose intolerance.
C. Hypertension.
D. All of them

2) The most common subtype of ovarian cancer is

A. Mucinous .
B. Serous.
C. Endometroid.
D. Non of them.

3) When the CA-125 considered positive :

A. Above 35 U/ml.
B. Below 35 U/ml.
C. Above 35 U/L.
D. Non of them.

4) 20 % of patient doesn't have cystic despite they have the symptoms.

A. True
B. False.

5) In ovarian cancer the patient have specific symptoms.

A. True, abdominal pain blotting & nausea
B. True, weight loss & dehydration & dysuria.
C. False non specific, abdominal pain blotting & nausea.
D. False non specific, weight loss & dehydration & dysuria.

6) CA-125 is marker of choice for ovarian cancer screening . And mention the reason

A. True.
B. False.

Because of low prevalence of ovarian cancer & high prevalence of false positives

SAQs

❖ **Mention 4 signs associated with polycystic ovarian syndrome.**

1. Hyperlipidemia.
2. Hirsutism.
3. Low level of SHBG.
4. Hyperscreation of LH & FSH.

❖ **Mention 3 risk factors of ovarian cancer.**

1. Nulliparity.
2. Mutation in BRCA1 & BRCA2.
3. Ashkenazi Jews.

❖**CA-125 sometimes the result become false positive, mention 3 condition that could render the test to become false positive.**

1. Endometriosis.
2. Uterine leiomyoma.
3. Pelvic inflammatory disease

❖**CA-125 useful for :**

1. Mentoring patient's respond to chemotherapy .
2. The Success of surgery.

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

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Thank you

DONE BY:

HAITHAM ALASIM
ABDULAZIZ ALSAUD
Najla Aldraiweesh

REVIEWED BY:

Mohammad Alotaibi
Elham Alghamdi

For questions and comments contact us: Biochemistry434@gmail.com