[lecture 2]

Biomarkers of ovarian cancer and cysts

Biochemistry Team

Teams

The Objectives

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

Red = Import-ant

Blue = explain

Green = addition notes

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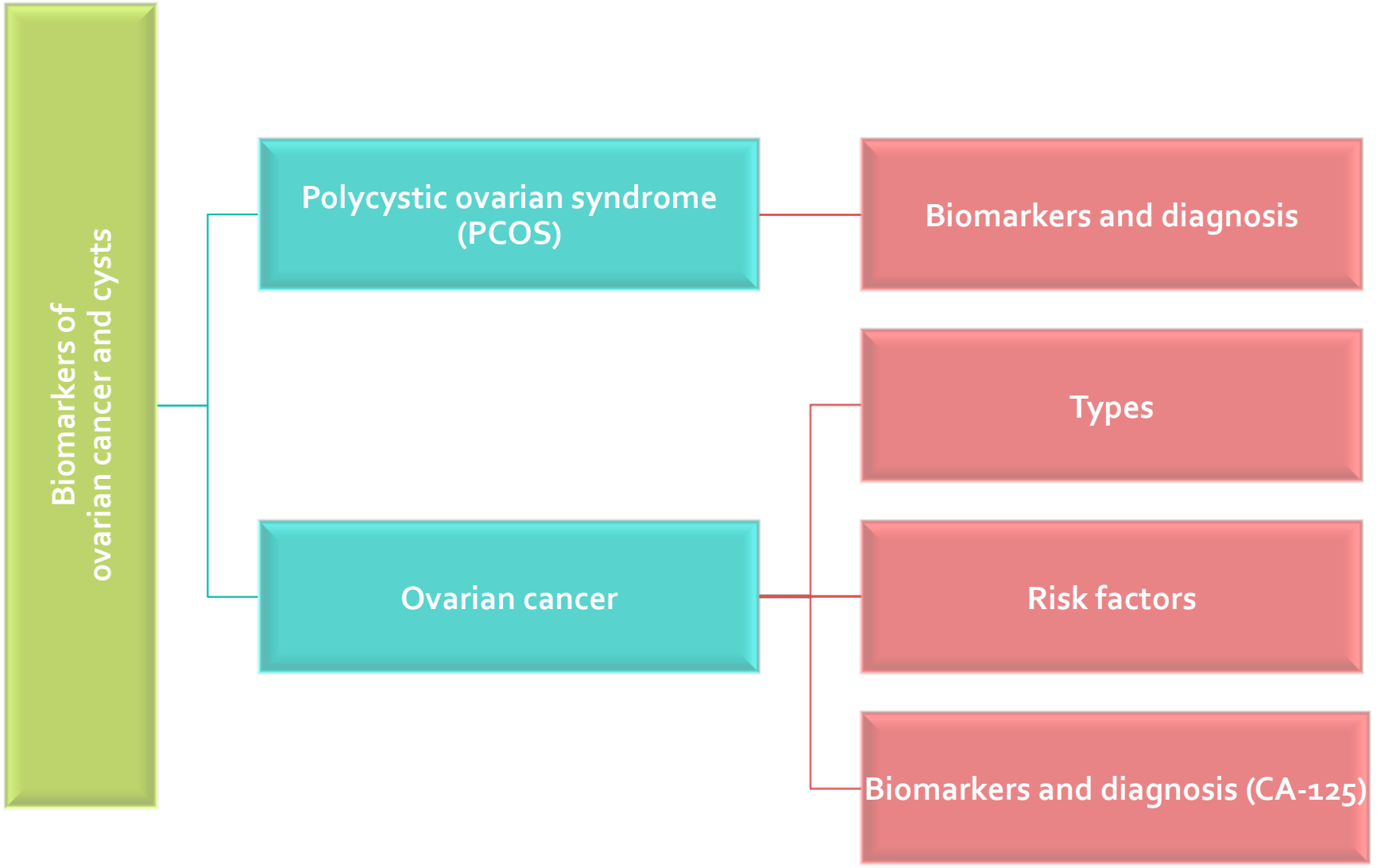
Biochemistry Team

Mind Map

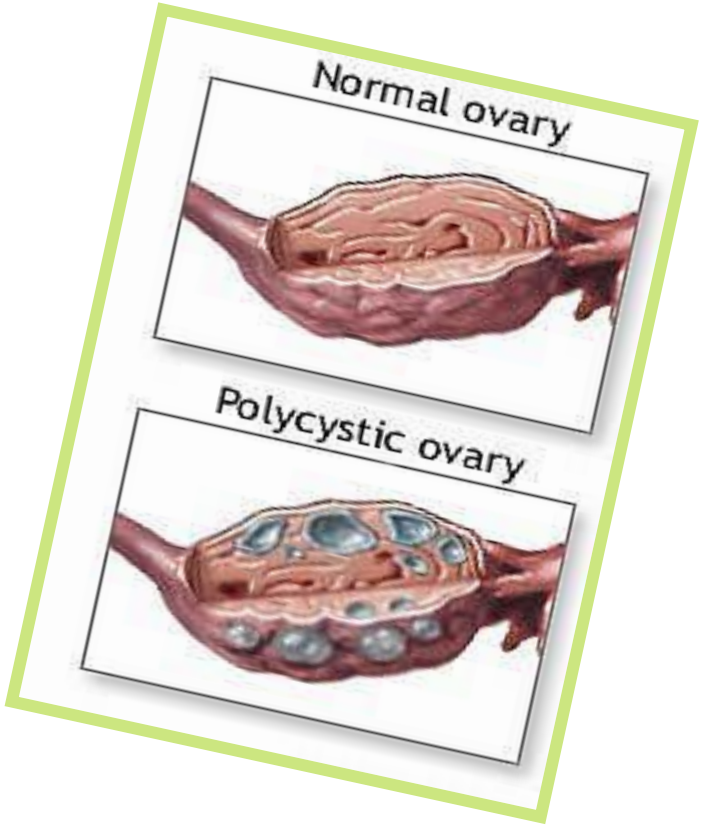


Polycystic ovarian syndrome

Formation of multiple small cysts in the ovaries.
Affects 5-10% of women.
A major cause of infertility in women.

Associated with:

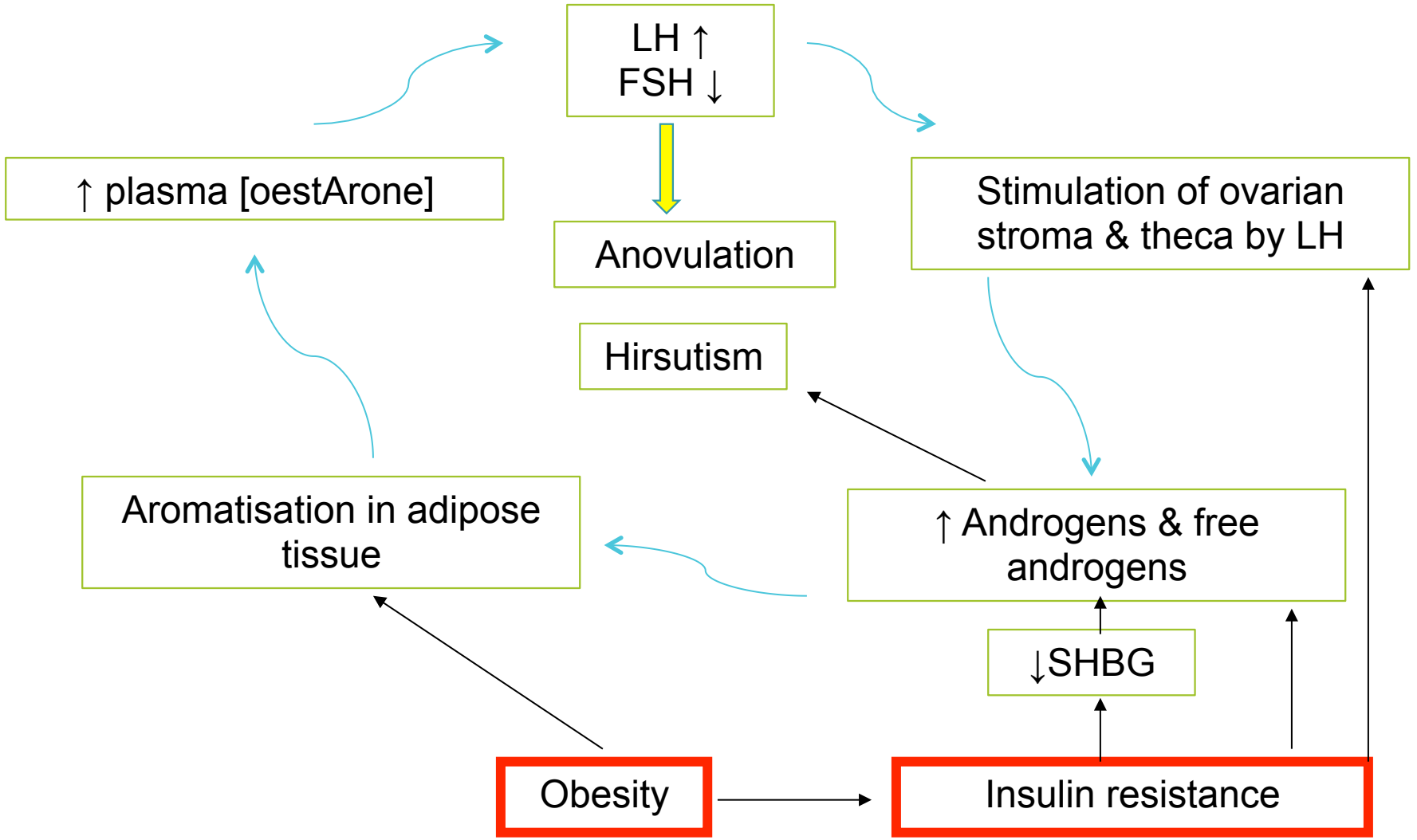
- Obesity(or overweight) 40% of the cases
  Hirsutism
- Chronic anovulation (with or without normal menstruation)
  Glucose intolerance
- Insulin resistance
- Hyperlipidemia (high LDL&VLDL, low HDL)
  Hypertension
- Menstrual disorders



Hormonal Changes:

- Hypersecretion of leutinizing hormone (LH)
- and androgens (testosterone). (causing hirsutism)
- Low levels of SHBG (sex hormone-binding globulin).

Biochemical, metabolic & endocrine changes in PCOS



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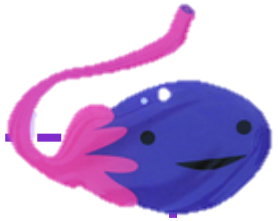

Exact cause of the syndrome is unknown
May be multifactorial (genetic and environmental)
Suggested causes:

- Insulin resistance causes excessive androgen production in ovaries
- Abnormalities in ovaries, adrenal and pituitary glands are also observed

Diagnosis done by measuring:

- Free testosterone (total testosterone is less sensitive than free testosterone, androgens often **increase** in PCOS)
- , SHBG (Sex hormone-binding globulin often **decreases** in PCOS)
- , FSH (normal or decreased), LH (**increased**) , fasting glucose, insulin, lipids

Ovarian ultrasound

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

Treatment:

Aim: interrupt the previous 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

- Diagnosis cannot be based on TOTAL testosterone levels only. Free (active) testosterone is more sensitive.
- Calculating LH\FSH ratio is more sensitive than measuring LH or FSH separately.
- Hormones are usually measured in the mid-follicular phase.

Ovarian cancer

Types

A leading cause of death because of gynecologic cancer
Due to malignant transformation of ovarian epithelial cells
Most common type of ovarian cancer.

Subtypes:

- Serous (46%): surface epithelial tumors
- Mucinous (36%): mucinous epithelial tumors
- Endometrioid (8%): endometrial tumors

Other types of ovarian cancer:

① Sex cord tumors
② Stromal tumors
③ Germ cell tumors

Risk Factors

- Nulliparity (woman with no child birth or pregnancy)
- Family history of breast, ovarian, colorectal cancer
- Mutations in BRCA1 and BRCA2 genes
- Carriers of BRCA1 mutations have a cancer risk of 44%
- Premenopausal breast cancer
- Ashkenazi Jews(endogamous ethnoreligious group*):

have higher risk of ovarian cancer>
*endogamy: is the custom of marrying within the limits of a clan or tribe .

Biomarkers and diagnosis:

- Epithelial ovarian cancer is commonly diagnosed at a later stage(it is a silent cancer) . So, 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:

① History taking
② Physical examination
③ Ultrasound
④ Determination of serum CA-125 levels (see the next slide)

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 (or low)
- **CA-125 is elevated in ovarian cancer**
- >35 U/ml is 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:	False positive in	Useful in
1. 50% of patients with stage I(NOT elevated in the other 50%) 2. 90% of patients with stageII(NOT elevated in the other 10%) 3. >90% of patients with stage III and IV	1. Endometriosis 2. Uterine leiomyomas 3. Pelvic inflammatory disease 4. During the first trimester of pregnancy 5. During menstruation Some patients (< 50 years) have elevated CA-125 due to unrelated malignant mass	1. Monitoring patient's response to chemotherapy 2. Success of surgery (debulking procedures)"decrease the tumor load" 3. Annual testing for women with family history of ovarian cancer

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

- Low prevalence of ovarian cancer
- High false-positive rate (not specific and not sensitive)

Summary

- PCOS is a major cause of infertility in women .
- Associated with: Obesity , Chronic anovulation , Hyperlipidemia and Menstrual disorders .
- Diagnosis done by measuring:
  - Free testosterone .
  - Sex hormone-binding globulin (SHBG).
  - LH & FSH .
  - Fasting glucose , Insulin and Lipids .
  - Ovarian ultrasound : 30% of patients **do not** have ovarian cysts .
- Ovarian cancer : Results from malignant transformation of ovarian epithelial cells .
- Risk factors :
  - Nulliparity .
  - Family history of ovarian ,breast, endometrial or colon cancer .
  - Mutations in BRCA1 and BRCA2 genes
- Cancer antigen 125 (CA-125) :
  - Normally absent in serum
  - CA-125 is elevated in ovarian cancer
  - CA-125 correlates with ovarian cancer stage :
  - 50% of patients with stage I
  - 90% of patients with stage II
  - >90% of patients with stage III and IV
- CA-125 is not a marker of choice for ovarian cancer screening in asymptomatic individuals due to:
  - Low prevalence of ovarian cancer
  - High false-positive rate

Test your knowledge ..!

1. The biomarker of ovarian cancer is:

a)AFT
b)CA-125
c) HCG
d) CEA

2. Breast cancer and ovarian cancer is commonly caused due to mutation in which one of the following genes:

a) p35
b) PTEN
c) HER2
d) BRCA 1&2

3. All of the following are elevated in Polycystic ovarian syndrome EXCEPT:

a) LH
b) Androgens
c) SHBG (Sex hormone-binding globulin)
d) b+c

Test your knowledge ..!

4. Regarding the serum marker of epithelial ovarian cancer (CA125), which ONE of the following statements is correct:

a) Normally present in serum
b) Less 35 U/ml is considered positive
c) CA-125 is not elevated in ovarian cancer
d) CA-125 is associated with stages of ovarian cancer

5. False positive CA-125 concentration are found in all of the following conditions EXCEPT:

a) Endometriosis
b) Uterine leiomyoma
c) Ovarian cancer
d) Pelvic inflammatory disease

1.B 2-D 3-C 4-D 5-C

Biochemistry
Team

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Thank you