Biomarkers of ovarian cancer and cysts

Reproductive Block

1 Lecture

By: Reem Sallam, MD, MSc, PhD

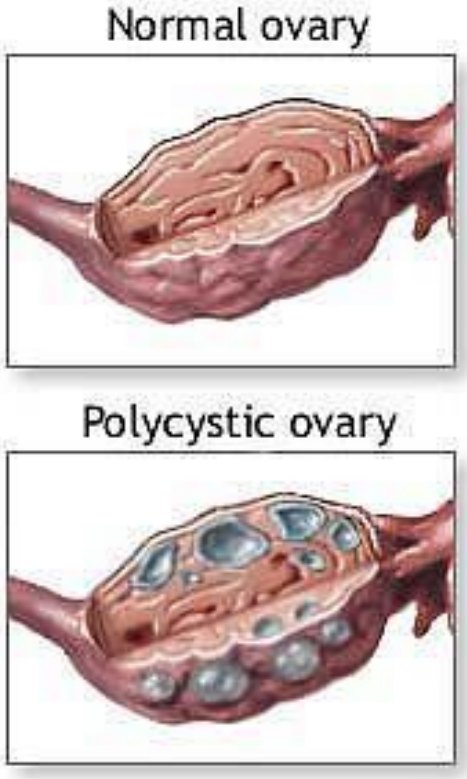
Overview

- Polycystic ovarian syndrome (PCOS)
  - Biomarkers and diagnosis
- Ovarian cancer
  - Types
  - Risk factors
  - Biomarkers and diagnosis (CA-125)

POLYCYSTIC OVARIAN SYNDROME (PCOS)

Polycystic ovarian syndrome (PCOS)

- Formation of multiple small cysts in ovaries
- Affects 5-10% of women *(or even higher: 20% in some populations)*
- A major cause of infertility in women



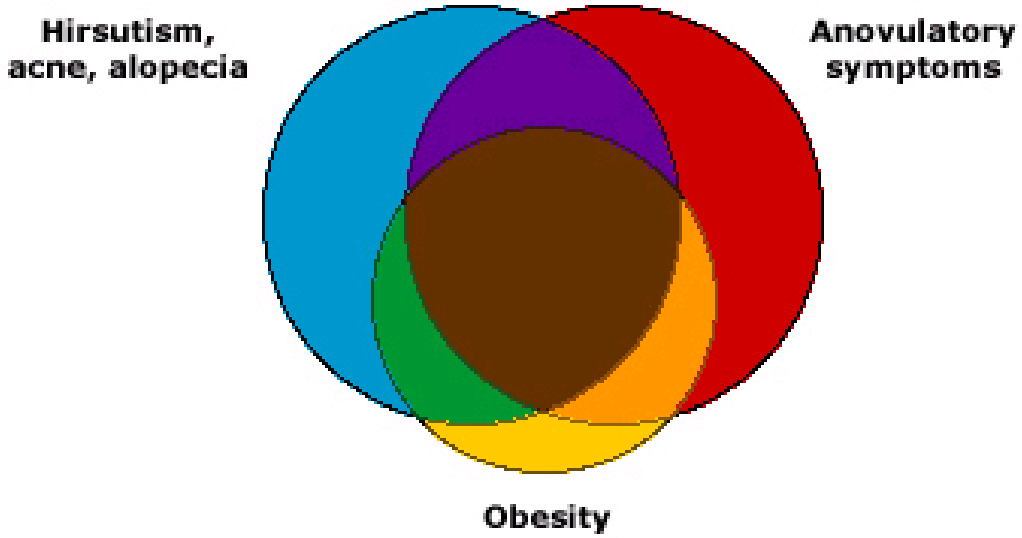
Polycystic Ovarian Syndrome

Polycystic ovarian syndrome, continued…

Associated with:

- Obesity (40% of cases)
- Hirsutism
- Chronic anovulation
- Glucose intolerance
- Hyperlipidemia
- Hypertension
- Menstrual disorders
- Hypersecretion of leutinizing hormone (LH) and androgens

Manifestations of polycystic ovary syndrome in approximate proportion to their relative incidence and coincidence



Cutaneous symptoms include hirsutism, acne or acanthosis nigricans. Anovulatory symptoms include amenorrhea, oligomenorrhea, dysfunctional uterine bleeding, and infertility.

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Polycystic ovarian syndrome, continued…

- Exact cause of the syndrome is unknown
- May be multifactorial:
  - Genetic factors and
  - Environmental factors
- Suggested causes:
  - Insulin resistance *(in 50% of patients)* and excessive androgen production are very common
  - Abnormalities in ovaries, adrenal & pituitary glands

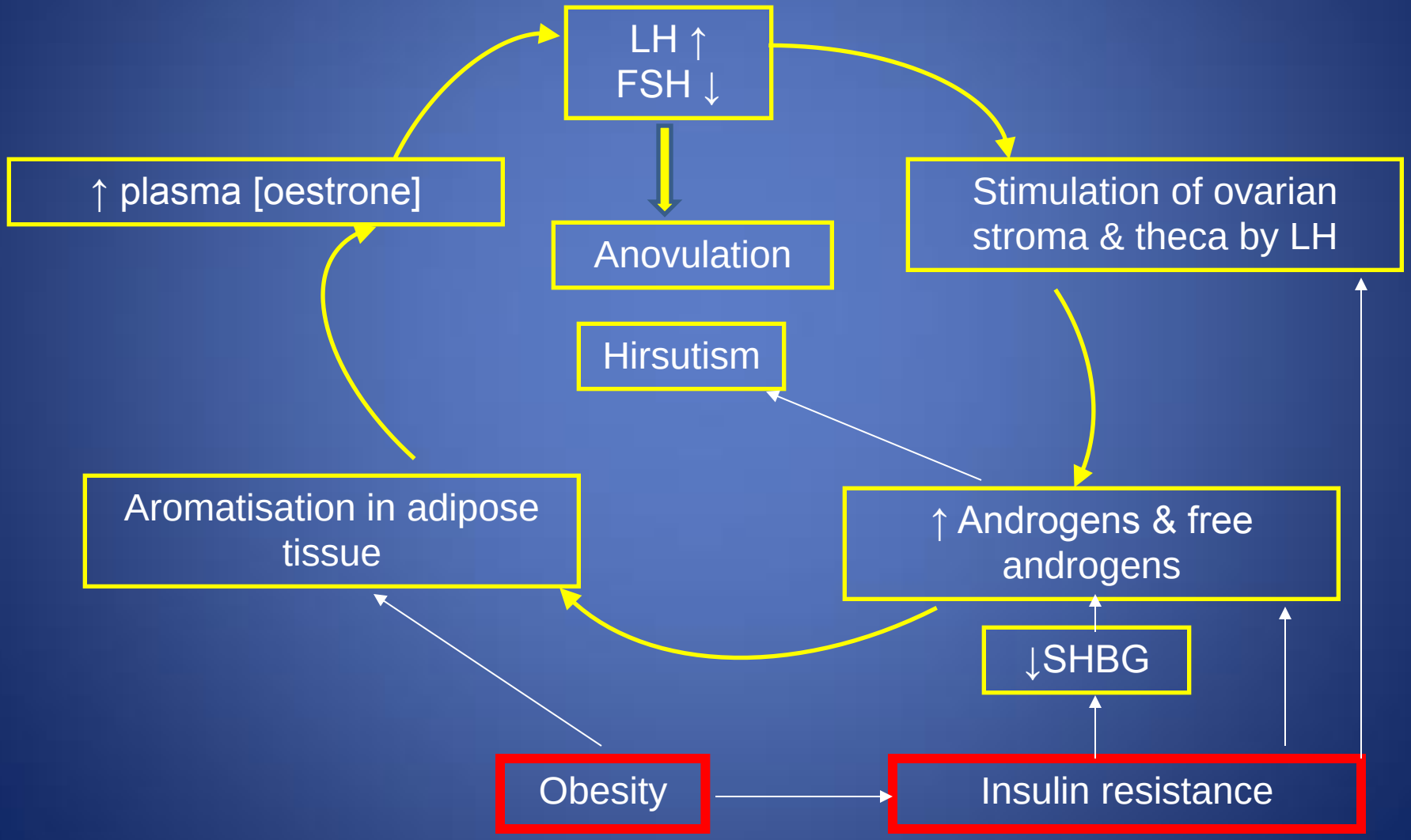
Polycystic ovarian syndrome, continued…

- Diagnosis done by measuring:
  - Free testosterone *(total testosterone is less sensitive than free testosterone, androgens often increase in PCOS)*
  - Sex hormone-binding globulin *(SHBG; often decreases in PCOS)*
  - Leutinizing hormone *(LH; ↑ in 60% of cases)*
  - Follicle stimulating hormone *(FSH; often normal in PCOS)*
  - LH/FSH Ratio *(↑ in > 90% of patients)*

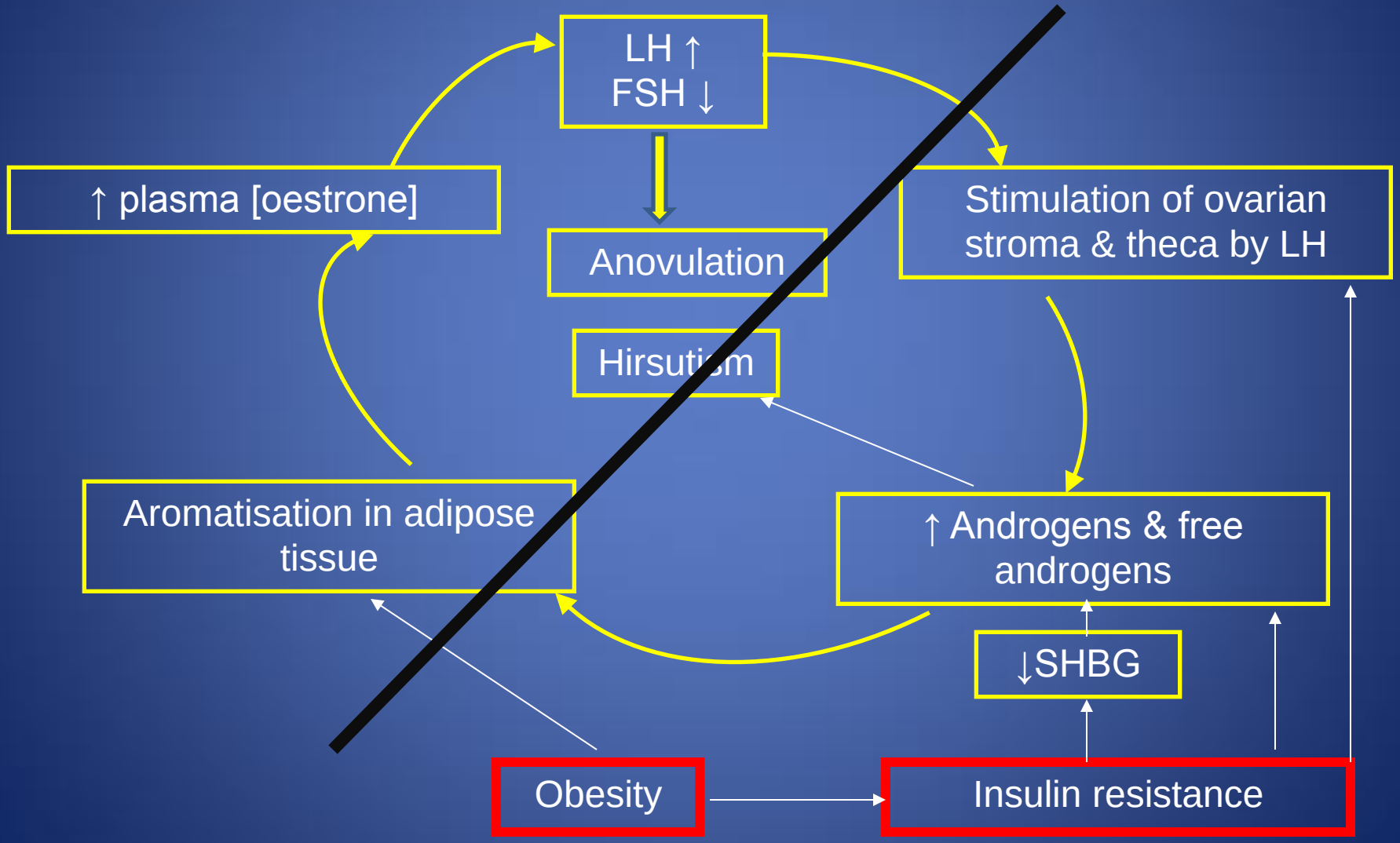
Polycystic ovarian syndrome, continued…

- Diagnosis, continued…:
  - Fasting glucose
  - Insulin
  - Lipids
- Ovarian ultrasound
  - 30% of patients do not have ovarian cysts despite having symptoms

Biochemical, metabolic & endocrine changes in PCOS



Treatment of PCOS: try to break the cycle



Treatment on PCOS

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

OVARIAN CANCER

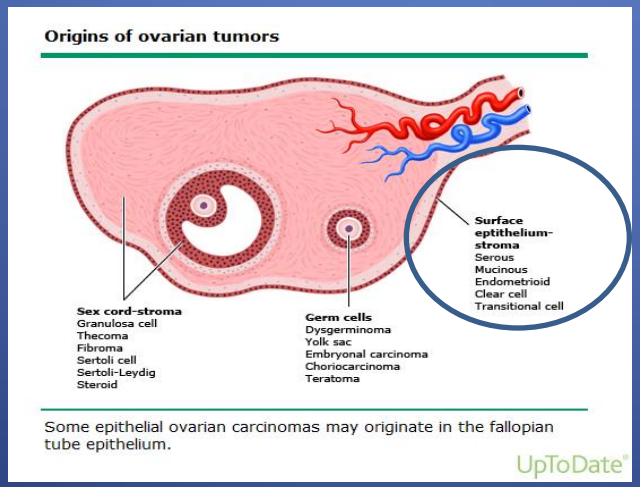
Ovarian cancer

- A leading cause of death from gynecologic cancer (in USA)
- Results from malignant transformation of ovarian epithelial cells *(Most common type of ovarian cancer)*

Ovarian cancer, continued…

Subtypes of epithelial ovarian cancer:

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



Ovarian cancer, continued…

Risk factors

- Nulliparity *(woman with no child birth or pregnancy)*
- Family history of ovarian cancer
- Family history of breast, ovarian, endometrial, or colon cancer *(may indicate a familial cancer susceptibility syndrome)*

Ovarian cancer, continued…

- Mutations in BRCA1 and BRCA2 genes are the most common inherited ovarian cancer susceptibility syndrome.
- Carriers of BRCA1 mutations have a risk of ovarian cancer approaching 44%

Ovarian cancer, continued…

- Premenopausal breast or ovarian cancer indicates higher risk for hereditary ovarian or breast cancer
- Ashkenazi Jews: have higher risk of ovarian cancer

Ovarian cancer, continued…

Biomarkers and diagnosis

- Epithelial ovarian cancer is commonly diagnosed at a later stage
- Due to non-specific symptoms such as abdominal pain, bloating, early satiety, nausea, etc...
- Most patients (75%) have advanced-stage tumor upon diagnosis

Ovarian cancer, continued…

- Diagnosis includes:
  - History taking
  - Physical examination
  - Ultrasound
  - Determination of serum CA-125 levels

Cancer antigen 125 (CA-125)

- A cell surface glycoprotein
- Normally absent in serum
- CA-125 is elevated in ovarian cancer
- >35 U/ml is considered positive

Cancer antigen 125 (CA-125)

- Recommended as an annual test for women with family history of ovarian cancer
- CA-125 correlates with ovarian cancer stage
- Elevated in:
  - 50% of patients with stage I
  - 90% of patients with stage II
  - >90% of patients with stage III and IV

Cancer antigen 125 (CA-125)

It is not specific enough:

- False positive CA-125 conc. are found in benign conditions:
  - Endometriosis
  - Uterine leiomyoma
  - Pelvic inflammatory disease
  - During the first trimester of pregnancy
  - During menstruation
- Some patients (< 50 years) have elevated CA-125 due to unrelated malignant mass

Cancer antigen 125 (CA-125)

- 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
- Useful in:
  - Monitoring chemotherapy
  - Monitoring success of surgery (de-bulking procedures)
  - Annual testing for women with family history of ovarian cancer

THANK YOU ☺