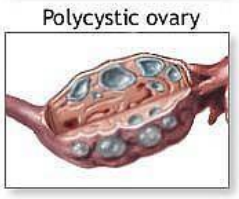
Biomarkers of ovarian cancer and cysts

POLYCYSTIC OVARIAN SYNDROME (PCOS):



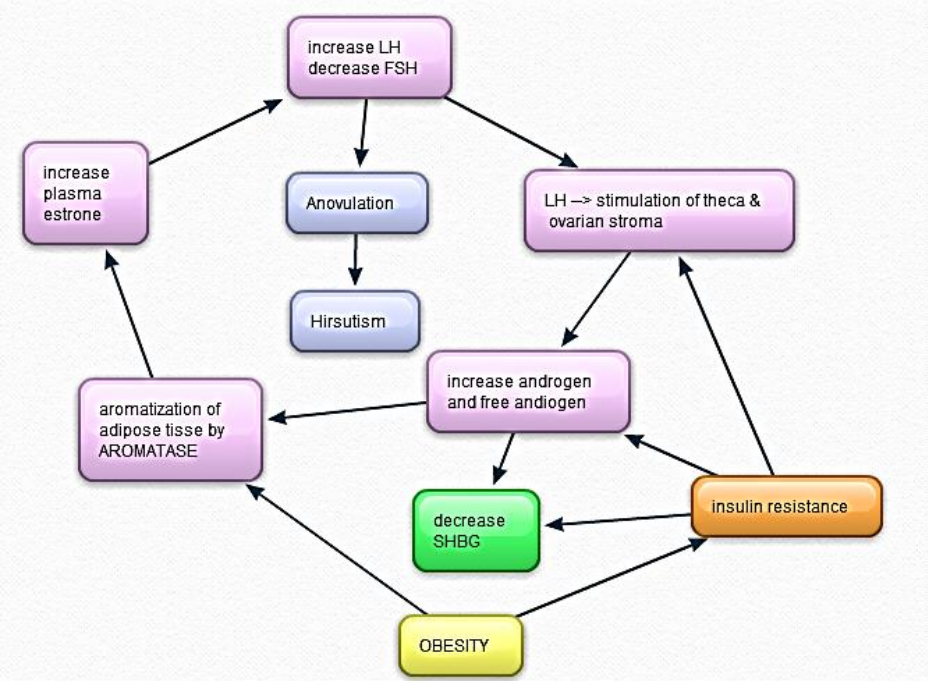
- Formation of multiple **small cysts** in ovaries
- Affects 5-10% of women (up to 20% in some populations)
- A major cause of **infertility** in women
- **Associated with:** **Obesity (40% of cases) – Hirsutism - Chronic anovulation - Glucose intolerance – Hyperlipidemia – Hypertension - Menstrual disorders - Hypersecretion of leutinizing hormone (LH) and androgens**
- 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**

	Free testosterone	Sex hormone-binding globulin	LH	FSH	LH/FSH Ratio
Dx	**(total testosterone is less sensitive than free testosterone, androgens often increase in PCOS)**	**often decreases in PCOS → tends to ↓ [total testosterone] & ↑ [free testosterone]**	**↑ in 60% of cases**	**often normal in PCOS**	**↑ in > 90% of patients**
	Ovarian ultrasound • **The presence of cysts (size: 2-6 mm) in the central stoma.** • **30% of patients do not have ovarian cysts despite having symptoms**		**Insulin**	**Lipids**	**Fasting Glucose**

Treatment on PCOS: Aim: interrupt 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 from gynecologic cancer (in USA)
- Results from 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
- **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)
  - 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%
  - Premenopausal breast or ovarian cancer indicates higher risk for hereditary ovarian or breast cancer
  - **Ashkenazi Jews:** have higher risk of ovarian cancer

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

Cancer antigen 125 (CA-125)

- The only serum marker of epithelial ovarian cancer
- **A cell surface glycoprotein**
- Normal ovarian epithelial cells do not express CA-125
- **Normally absent in serum**
- 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 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**
- **It is not specific enough:**
  - **False positive CA-125 conc. are found in benign conditions:**
    - Endometriosis
    - Uterine leiomyoma
    - Pelvic inflammatory disease, peritonitis, cirrhosis, ascites
    - 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 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**