11.2.4

Disorders of the Ovary

Watch this video on PCOS

Polycystic Ovary Syndrome (PCOS)

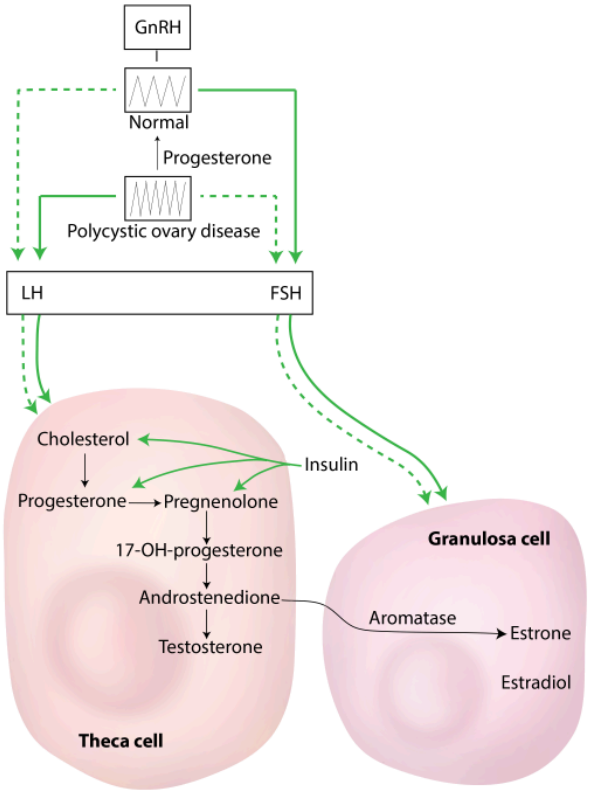

Image by Becky T F19

Polycystic Ovarian Syndrome (PCOS) occurs when follicles repeatedly do not ovulate. Follicles that do not ovulate are called **cysts**. Multiple cysts that represent past failed follicular ovulation events are characteristic of PCOS. If a follicle does not ovulate, a corpus luteum is not created and without a corpus luteum, there is no surge in progesterone. PCOS is characterized by an increase in the frequency of pulsatile GnRH release. This increase in GnRH appears to be a result of the lack of high progesterone during a luteal phase since progesterone is a powerful inhibitor of GnRH. This increased frequency of GnRH release leads to an increase in the amount of LH over FSH because LH secreting cells are more responsive to GnRH than FSH. FSH is needed to help follicles mature to the point of ovulation. If LH is higher than FSH, then a follicle may develop but not mature sufficiently to be a functional Graafian follicle that can ovulate. Also,

excessive LH stimulation of theca cells can increase the production of androgens. As a result, common symptoms of PCOS include menstrual irregularity because of hormone imbalance, hyperandrogenism that leads to **hirsutism** (excessive hair growth in unexpected areas) and acne, and infertility due to anovulation.

Insulin is a hormone that can also stimulate steroidogenesis in the ovary and the adrenal cortex. When insulin increases steroidogenesis in these cells, even more androgens are released. The androgens can have a negative feedback effect on the hypothalamus and pituitary which makes hormone imbalances even more complicated and ovulation even more difficult. Androgens also cause decreased sensitivity to insulin. This creates an environment of insulin resistance where the pancreas will produce and secrete more insulin in order to maintain proper blood glucose levels. Then, with elevated insulin levels, we see even more stimulation of steroidogenesis in theca cells and the vicious cycle continues.

Let us recap briefly what we know to this point:

- Without ovulation, there is no progesterone surge as seen in a normal luteal phase and GnRH release is not inhibited. GnRH pulse frequency increases.
- LH secreting cells are more sensitive to higher GnRH pulse frequency.
- Increased LH stimulates theca cells to make more androgens.
- Among many effects, androgens cause hirsutism, acne, and insulin resistance.
- Insulin resistance causes more insulin to be released and thus increase androgen production and perpetuate the dysfunctional cycle.
- These various hormone imbalances decrease the likelihood of a successful ovulation.

Looking through this list, it becomes apparent that there is a kind of “chicken or the egg” paradox. What comes first – insulin resistance or excessive androgen production? We don’t really know what triggers these hormone imbalances or which comes first. We do know that increased androgens and insulin resistance are found together in women with PCOS. In fact, more than half of women with PCOS develop type II diabetes by the time they are 40. See the following link if you are interested in learning more about the correlation between diabetes and PCOS.
https://www.cdc.gov/diabetes/basics/pcos.html

Women with PCOS are at increased risk for developing endometrial cancer because of their prolonged exposure to estrogen. Without the progesterone surge and subsequent loss in the second half of the uterine cycle, estrogen abounds and can lead to endometrial hyperplasia. Administering progestins (synthetic forms of progesterone) through various contraceptives can inhibit the higher pulse frequency of GnRH. Other treatments for PCOS include weight loss, administering spironolactone (inhibits androgen receptors, but also inhibits aldosterone receptors), and metformin (anti-diabetic drug).

Ovarian Cancer

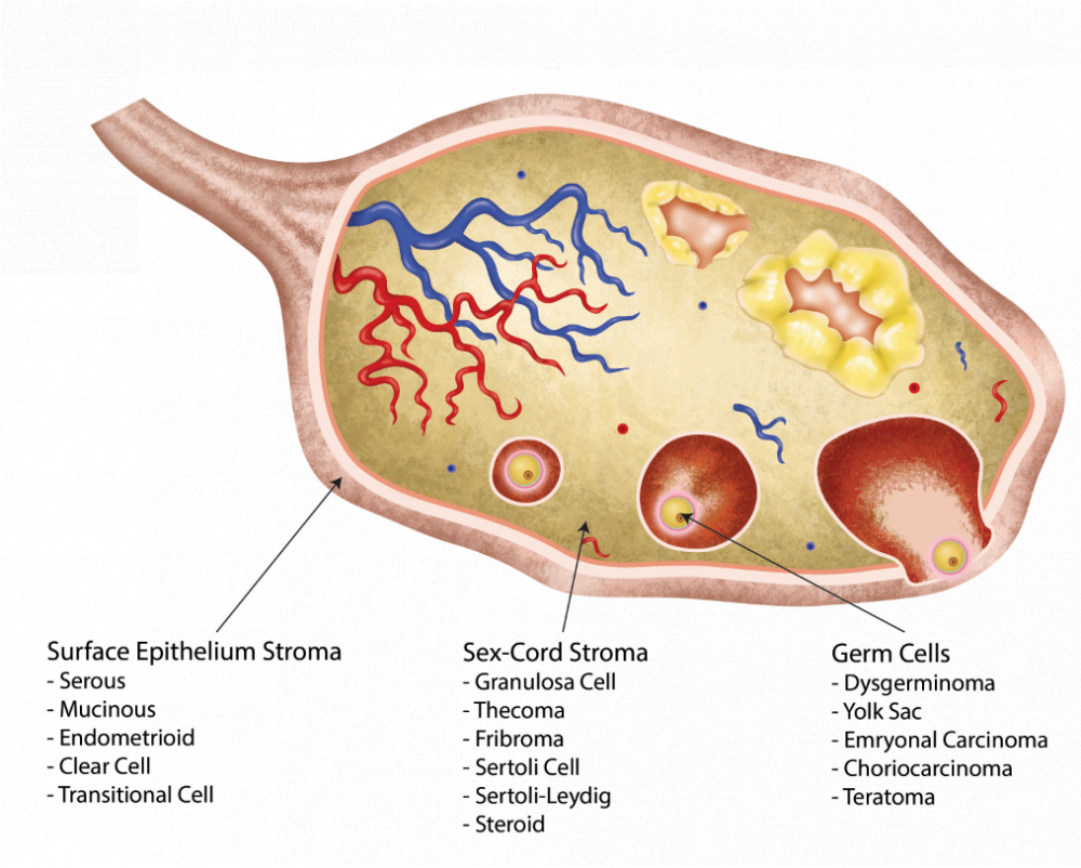

Image by Becky W10

Types of Ovarian Cancer

After endometrial cancer, **ovarian cancer** is the second most common gynecologic malignancy and it is the most lethal because it is usually discovered late in the disease process. Ovarian cancer can occur in the surface epithelium, germ cells and in stromal cells of the ovaries, but it occurs most often in the epithelial cells (90% of cases). The germ cell tumors and the stromal cell tumors appear more often in younger women and are generally discovered earlier in the progression, leading to a better prognosis.

The most significant risk factor for ovarian cancer is **ovulatory age**, which is how long a woman's body has been exposed to high estrogen levels. Pregnancy, lactation, and oral contraceptives all suppress the ovarian cycle temporarily and therefore have a diminishing effect on the overall ovulatory age. Mutations of the tumor suppressing genes, **BRCA1** and **BRCA2** significantly increase the risk of ovarian cancer (as well as breast cancer). Mutations in both of these genes can create a lifetime risk of ovarian cancer that is nearly 30-50%. A high fat western diet and the use of talcum powders in the genital area also correlate with increased risk of ovarian cancer.

Cancers of the ovary produce vague GI symptoms such as abdominal bloating, early satiety, and diarrhea. It is believed that women with ovarian cancer have these GI symptoms because the cancer can change the biochemical nature of the peritoneal fluid in a way that may irritate the bowel. Pain and discomfort from the ovaries may also cause referred pain to the bowel that can be erroneously interpreted as GI problems.