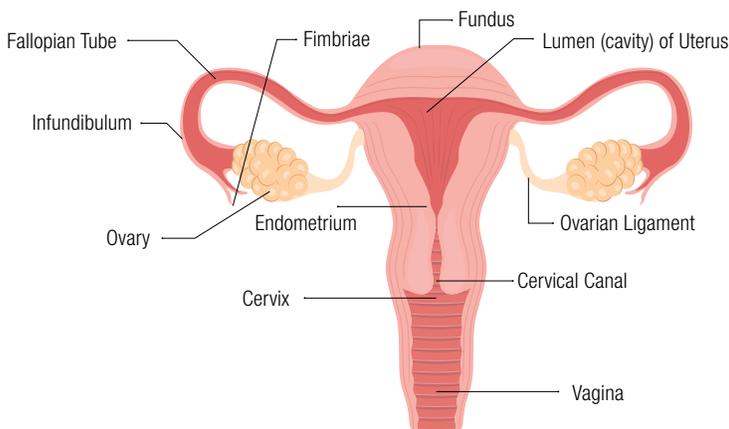


LABORATORY TESTS RELATED TO OVARIAN DISEASES AND CANCER

WHAT IS THE OVARY?

The ovaries are female reproductive glands located on either side of the uterus. Each ovary is typically 3-5 centimeters long. The ovaries are responsible for producing the hormones progesterone and estrogen as well as ovulation (producing ova or eggs). Progesterone and estrogen play a crucial role in female reproductive development and control the menstrual cycle.

THE UTERUS



OVARIAN DISEASES

Ovarian diseases, which are classified as human endocrine disorders, affect the reproductive system of women. The three main ovarian diseases include endometriosis, ovarian cysts and polycystic ovary syndrome (PCOS). Irregular menstrual cycles and infertility are some of the effects of ovarian diseases.

ENDOMETRIOSIS

Endometriosis is a disease where the tissue that lines the uterus (endometrium) grows outside of the uterus. The ovaries, fallopian tubes and the pelvic tissue lining are commonly affected by endometriosis as cysts and fibrous tissues are more likely to grow there. Endometriosis can cause severe pain and fertility issues. During the menstrual cycle, the endometrial tissue outside of the uterus behaves in the same manner as the uterus lining as it thickens, sheds and bleeds during the menstrual cycle. Due to the endometrial tissue being outside the uterus, it cannot shed through the vagina. Only women and people assigned female at birth who have menstrual periods are affected by endometriosis.

OVARIAN CYSTS

An ovarian cyst is a fluid-filled sac that forms inside or right outside the ovary. Common symptoms of ovarian cysts include painful menstrual cycles, pelvic pain, pain during intercourse and bloating. Functional ovarian cysts that develop during the menstrual cycle are the most common types of ovarian cysts, and they rarely cause pain. Pathological ovarian cysts are not related to the menstrual cycle and are a result of abnormal cell growth. They are often benign.

POLYCYSTIC OVARY SYNDROME (PCOS)

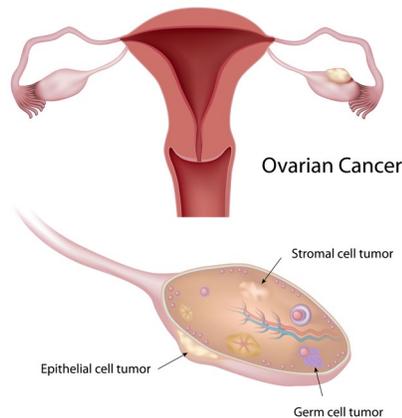
PCOS is a condition that affects hormone levels and impacts the function of ovaries resulting in enlarged ovaries and irregular periods. PCOS can cause cysts on the ovaries, which prevents the release of eggs (anovulation). The hormonal imbalance caused by PCOS can result in excess hair growth on the face and body, irregular menstrual cycles, infertility, pelvic pain and increased risk of developing diabetes.

OVARIAN CANCER

Ovarian cancer is a type of malignant growth that begins in or on the surface of the ovaries. In the early stages, ovarian cancer often goes undetectable due to lack of symptoms until the later stages. There are three different types of ovarian tumors which are epithelial, germ cell and stromal tumors.

OVARIAN EPITHELIAL CANCER

Ovarian epithelial cancer develops when malignant growth begins in the tissue covering the outer surface ovary. This type of cancer can also develop in the lining of the fallopian tube. It is the most common type of ovarian cancer in women with about 85-90% of ovarian cancer cases starting in the epithelial cells. The signs and symptoms include abdominal pain and bloating, the need to urinate often, constipation and feeling full quickly.



OVARIAN GERM CELL TUMORS

Ovarian germ cell tumors are growths that develop in the egg cells of the ovary. Most of the tumors are benign but malignant tumors contribute to 2% of ovarian cancers. Swelling in the abdomen and vaginal bleeding can be signs of ovarian germ cell tumors.

OVARIAN STROMAL TUMORS

Ovarian stromal tumors are growths that develop in the connective tissue cells that may produce progesterone and estrogen. The tumors can be either benign or malignant. Ovarian stromal cell tumors contribute to about 1% of ovarian cancer cases. Symptoms of ovarian stromal tumors include abnormal vaginal bleeding and abdominal pain.

STAGES OF OVARIAN CANCER

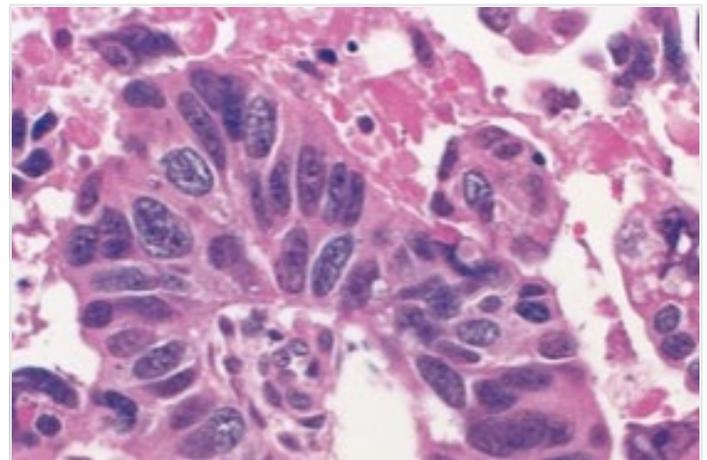
The stages of ovarian cancer determine how far the cancer has spread and what parts of the body it has spread to. Your treatment plan and prognosis will depend on the staging portion of your diagnosis. Below is a short description of each stage:

STAGE 1: The cancer has invaded one or both ovaries

STAGE 2: The cancer has invaded the ovaries or the fallopian tubes and has spread to organs within the pelvis (e.g. bladder, uterus)

STAGE 3: The cancer has spread outside of the pelvis and into the lymph nodes or the abdominal cavity

STAGE 4: The cancer has spread to other parts of the body such as the liver; the cancer has metastasized



UNDER THE MICROSCOPE

Papillary serous adenocarcinoma, as shown in this image, gets its name from the formation of rounded or tufted structures with central blood vessels (papillary), the production of watery fluid (serous), the formation of glands (adeno), and the invasive and metastatic nature of its behavior (carcinoma).

LAB TESTS RELATED TO OVARIAN DISEASES

**Please note that reference ranges are set by individual laboratories for their specific populations so reference ranges might differ slightly.*

17-HYDROXYPROGESTERONE: The test measures the level of the hormone 17-Hydroxyprogesterone which is produced in the adrenal glands when cortisol is made. This test is important because it can indicate whether you have congenital adrenal hyperplasia which affects the adrenal glands. The typical reference range* for adults is 200 ng/dL.

A1C: This test measures the average blood sugar levels over the past 2 to 3 months. This test is important because it helps determine the risk of developing diabetes. The typical reference ranges* for adults are below 5.7%.

ANDROSTENEDIONE: This test measures the level of androstenedione, an androgen, in the blood to determine whether the ovaries and adrenal glands are working properly. This test is important because high levels of androstenedione can be a sign of PCOS. The typical reference range* for women is between 30-200 ng/dL.

ANTI-MÜLLERIAN HORMONE (AMH): This test measures the level of AMH in your blood, which is also produced by the ovaries. This test is important because it AMH supports the female's eggs prior to fertilization. A typical reference range* for fertile women is between 1.0-4.0 ng/mL. Levels below 1.0 ng/mL is considered low and indicates a diminished reserve of eggs.

CORTISOL: This test measures the levels of cortisol in the blood, saliva or urine to determine whether the adrenal glands are functioning properly. This test is important because it helps rule out the chances of having Cushing syndrome, a condition where the body produces too much cortisol, since it has similar symptoms to PCOS. The typical reference range* for adults vary depending on time as follows;

- 6 to 8 a.m.: 10 to 20 mcg/dL
- Around 4 p.m.: 3 to 10 mcg/dL

DHEAS: This test measures the level of the hormone, dehydroepiandrosterone sulfate (DHEAS), in the blood to determine whether the adrenal glands are working properly.

“This test is important because it helps indicate whether you have a high level of androgens (testosterone). The typical reference ranges* for females vary by age. The ranges by age group are as follows;

- Ages 18 to 19: 145 to 395 µg/dL or 3.92 to 10.66 µmol/L
- Ages 20 to 29: 65 to 380 µg/dL or 1.75 to 10.26 µmol/L
- Ages 30 to 39: 45 to 270 µg/dL or 1.22 to 7.29 µmol/L
- Ages 40 to 49: 32 to 240 µg/dL or 0.86 to 6.48 µmol/L
- Ages 50 to 59: 26 to 200 µg/dL or 0.70 to 5.40 µmol/L
- Ages 60 to 69: 13 to 130 µg/dL or 0.35 to 3.51 µmol/L
- Ages 69 and older: 17 to 90 µg/dL or 0.46 to 2.43 µmol/L

ESTRADIOL: This test measures the levels of estradiol levels, which is one type of estrogen. This test is important because a hormonal imbalance of estrogen can indicate fertility or pregnancy issues. A typical reference range* for menstruating women is between 15-350 pg/mL. However, the levels can vary widely through the menstrual cycle. During the follicular phase, the typical reference range* is between 19-140 pg/ml; just prior to ovulation, the typical reference range* is between 110-410 pg/ml; during the end of the cycle, the luteal phase, the typical reference range* is between 19-160 pg/ml. During pregnancy, the estradiol levels will continue to increase until the fetus is 32 weeks.

FOLLICLE STIMULATING HORMONE (FSH): This test measures the health of a woman's ovaries, as well as measuring the amount of FSH in the blood. This test is important because FSH regulates the reproductive processes. A typical reference range* for menstruating women is between 4.7-21.5 mIU/mL.

GLUCOSE: This test measures the amount of glucose (blood sugar) in the blood. This test is important because high levels of glucose in the blood indicate whether you are at risk for diabetes. The typical reference range* for adults when fasting is between 72- 99 mg/dL and less than 140 mg/dL two hours after eating.

HUMAN CHORIONIC GONADOTROPIN (HCG): This test measures the amount of hCG in your blood, which indicates if you are pregnant. HCG is produced by cells in the placenta, indicating if you are pregnant and if the pregnancy is advancing accordingly. For negative pregnancy tests, the HCG level is less than 5.0mIU/mL; a HCG level between 6- 24 mIU/mL is indeterminate of pregnancy; a level above 25 mIU/mL is positive for pregnancy.

IGF-1: This test measures the amount of insulin-growth factor hormone in the blood that helps with tissue and bone growth. This test is important because it indicates excess hormone growth and can be used to rule out pituitary tumors as the cause of symptoms. The typical reference ranges* for IGF-1 is highly dependent on age and biological sex.

INHIBIN: This test measures the levels of inhibin A and inhibin B hormones in the blood. This test is important because high levels of inhibin can indicate whether you have an ovarian tumor. The typical reference ranges for premenopausal women * are as follows;

- Follicular: <139 pg/mL
- Luteal: <92 pg/mL
- Postmenopausal: <10 pg/mL

LIPID PANEL: This test measures the fats and fatty substances used by your body as a source of energy called lipids. Lipids include cholesterol, high-and low-density lipoprotein, and triglycerides. This test is important because it indicates your chances of developing cardiovascular disease.

Lipid Test	Role in Health	Recommended Reference Ranges*
High-Density Lipoprotein (HDL) Cholesterol	The “good” cholesterol that removes fatty deposits	60 mg/dL and above
Low-Density Lipoprotein (LDL) Cholesterol	The “bad” cholesterol that reduced blood flow associated with depositing “plaques”	Below 70-100 mg/dL
Total Cholesterol	Sum of your cholesterol	Below 200 mg/dL
Triglycerides	Type of fat in the blood related to recent meals	Below 150 mg/dL

*Please note that reference ranges are set by individual laboratories for their specific populations so reference ranges might differ slightly.

LUTEINIZING HORMONE (LH): This test also measures the health of a woman’s ovaries by measuring the amount of LH in the blood. This test is important because it may indicate an issue with the production of LH, which is related to fertility. This test also indicates which phase of the menstrual cycle a woman is in, indicating when she is ovulating. A typical reference range* for women is between 1.68-15 IU/L during the mid-cycle peak, around 21.9-56.6 IU/L during the middle of the cycle (ovulation) and 0.61-16.3 IU/L during the end of the cycle, the luteal phase.

SEX HORMONE BINDING GLOBULIN (SHBG): This test measures the level of SHBG, a protein that binds to sex hormones, in the blood. This test is important because it measures androgen excess in the body and high levels of excess androgens in women can be a sign of ovarian diseases such as PCOS. A typical reference range * for SHBG for women is between 8-144 nmol/L.

TESTOSTERONE: This test measures the level of testosterone in your blood, which is a critical part of both female and male fertility. This test is important because high testosterone levels in women can indicate a potential fertility issue or ovarian tumor. A typical reference range* for women is between 15-70 ng/dL.

THYROID-STIMULATING HORMONE (TSH): This test measures if the thyroid is performing optimally. This test is important because it can indicate whether your thyroid is under or over performing. Typical reference ranges for adults* are between 0.4-4.0 mIU/L

ADDITIONAL LAB TESTS RELATED TO OVARIAN CANCER MONITORING

ALPHA-FETOPROTEIN (AFP): This test measures the amount of AFP in the blood. This test is important because high levels of AFP in non-pregnant women can indicate ovarian cancer and can be used to monitor how well the treatment is working. The typical reference ranges* for women are between 10-20 ng/mL.

CANCER ANTIGEN 125 (CA-125): This test measures the levels of CA-125 protein in the blood. The test is important because it is used as a tumor marker to see how well the treatment plans are working. The typical reference range* for CA-125 is less than 35 units per milliliter.

CARCINOEMBRYONIC ANTIGEN (CEA): This test measures the amount of CEA in the blood. This test is important because it can indicate whether there is a tumor present and can be used to monitor cancer treatment. The typical reference ranges* are between 0-2.5 ng/mL.

ESTRADIOL: This test measures the levels of estradiol levels, which is one type of estrogen. The test is important because it is used to monitor antiestrogen therapies that are used to treat cancer. A typical reference range* for menstruating women is between 15-350 pg/mL. However, the levels can vary widely through the menstrual cycle. During the follicular phase, the typical reference range* is between 19-140 pg/ml; just prior to ovulation, the typical reference range* is between 110-410 pg/ml; during the end of the cycle, the luteal phase, the typical reference range* is between 19-160 pg/ml. During pregnancy, the estradiol levels will continue to increase until the fetus is mature.

HUMAN CHORIONIC GONADOTROPIN (HCG): This test measures the amount of HCG in your blood. This test is important because HCG is produced by abnormal tissues, tumors and cancers so the test is used as a tumor marker. High levels of hCG can be a sign of ovarian cancer. The typical reference range* is less than 5.0mIU/mL.

HUMAN EPIDIDYMIS PROTEIN 4 (HE4): This test measures the amount of the protein, HE4, which is produced by epithelial ovarian cancer cells, in the blood. This test is important because it indicates whether the treatment for epithelial ovarian cancer is working. The typical reference range* for women is less than 140 pmol/L.

LACTATE DEHYDROGENASE (LDH): Lactate Dehydrogenase (LDH): This test measures the levels of the enzyme, LDH, in the blood. This test is important because increased levels of LDH can indicate tissue damage in the body such as cancer and can be used to monitor the effectiveness of treatment. The typical reference ranges* for adults are between 140-280 units/L.

ASK YOUR DOCTOR

- What screening tests do you recommend for ovarian diseases and/or cancer?
- What is the course of action based on my lab results?
- What are all my treatment options?
- Why do you recommend this particular treatment option?
- How do we know the procedure was successful/what lab tests and which results indicate successful treatment?
- What are the markers we are monitoring? What are the levels we are hoping for? What happens if the markers are higher than we would like to see?
- What are the follow-up tests and what are we looking for?
- Are there additional tests that could be used to better understand my disease and prognosis?
- Should I get genetic testing to see if I have mutations such as the *BRCA* mutation?

MEET ILANA



“With the rise in personalized medicine, the more information a patient and their doctor can know about the tumor, the better it can be treated.”

Given her family history, Ilana knew that she was at risk for breast cancer and ovarian cancer. She had taken the necessary precautionary steps by getting her ovaries removed but at age 45, she was diagnosed with Stage 2 ovarian cancer. During the surgery to remove her ovaries, a cancerous tumor developing from her fallopian tubes was found. The pathologists and lab professionals were able to determine the type and stage of her cancer while she was still in surgery. Today, Ilana is an ovarian cancer survivor and an advocate for her community.

To learn more about Ilana, go to www.ascp.org/patients

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