

Ovarian Reserve Testing or Tests of Ovarian Function

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What is “ovarian reserve”?

Ovarian reserve refers to the number and quality of eggs that women have in their ovaries that could result in pregnancy.

To understand ovarian reserve, two important concepts in ovarian function must be understood. First, women are born with all of the oocytes (eggs) that they will ever have; they do not produce more oocytes. Although there are approximately six to eight million eggs at birth, many of these are lost during childhood so that by the time a female begins her periods she only has about 300,000 to 500,000 eggs left. During the typical menstrual cycle 10-30 eggs are recruited for growth on a daily basis, but only one of these dominates to become a mature follicle ready for fertilization on a natural cycle. The rest die off resulting in the loss of hundreds of eggs per year. This number of oocytes continues to decline month after month and is unaffected by being pregnant or being on birth control. This depletion continues month after month until the egg pool is nearly exhausted leaving a woman with only 100-500 eggs per ovary resulting in menopause.

The second concept is that not all the eggs in the ovaries are of the same quality. In fact, most of the eggs in storage are not capable of achieving a successful pregnancy. Of these, many are genetically abnormal and will either not fertilize with sperm or will result in an abnormal embryo that rapidly dies. It is believed that women tend to ovulate their best eggs when they are younger.

Testing ovarian reserve is a critical part of an infertility evaluation. There are several main factors to determine in completing this evaluation. In the case of abnormal findings, a diagnosis of diminished ovarian reserve or ovarian hypofunction might be made. This diagnosis suggests a decrease in the ability of the eggs to result in a healthy pregnancy.

In general, the better the ovarian reserve, the higher the chance of pregnancy, all other factors being equal (male factor, uterine factor, and tubal factor). There are several ways to estimate the ovarian reserve in individual women. Decreased fertility with aging is well documented and understood in every culture. Laboratory tests such as cycle day 3 follicle stimulating hormone (FSH), anti-mullerian hormone (AMH), and ovarian antral follicle count (AFC) are also useful and relatively easy tests used to evaluate a woman’s ovarian reserve. Finally, the way a woman responds to ovulation inducing medications is often the definitive test of ovarian reserve. Each of these factors will be discussed below.

Factors that affect ovarian reserve:

1. Female Age

The age of women is very important when calculating the probability of conceiving. It is well known that fertility decreases with maternal age. The trend of women waiting longer to start a family has contributed to the observation that more couples have fertility problems due to a decline in oocyte quantity and quality. Fertility starts decreasing for women in their late twenties and decreases more rapidly after age thirty-five. At age forty, fertility decreases significantly each year. Though age does play a part in women’s ovarian reserve, it is not definite. The quantity and quality of eggs can vary among women of the same age. Although advances in treatments for infertility, such as in vitro fertilization, have provided many couples with a family, egg quality is a significant factor that limits success.

2. Day 3 Follicle Stimulating Hormone (FSH)

Follicle stimulating hormone (FSH) is one of the most important blood tests in helping determine ovarian reserve. FSH is released by the pituitary gland in the brain to stimulate the ovaries produce a dominant follicle, which should contain a mature egg. FSH is also in many of the injectable gonadotropin medications used to mature multiple eggs in fertility treatments. Testing of FSH performed on menstrual cycle day 2,3, or 4 is known as one of the ovarian reserve baseline tests. At this time of the cycle, FSH should be low to prepare for the development of follicles. However, the lower the ovarian reserve, the higher levels of FSH are required to stimulate the follicle to grow.

Normal FSH levels can vary among labs and clinics. It is also important to understand that these levels can change slightly from month to month. The highest level obtained is considered to be the most accurate for reproductive potential. The

most accurate level is also determined by the normal range of some other hormones, for example Estradiol. If Estradiol is elevated it suppresses the level of FSH making it appear lower than it actually is. This test is not perfect and is not the only determining factor for infertility. It can still be possible to conceive with an elevated FSH.

Day 3 FSH level	FSH interpretation
<10	Normal FSH level. Expect a good response to ovarian stimulation.
10 - 12	Borderline FSH. Response to stimulation is somewhat reduced. Overall, a slightly reduced live birth rate.
13- 15	Elevated FSH. Reduced ovarian reserve. Reduced response to stimulation and some reduction in embryo quality with IVF. Reduced live birth rates on the average.
16 - 20	Markedly elevated FSH. Marked reduction in response to stimulation and usually a further reduction in embryo quality. Low live birth rates.
> 20	Very poor (or no) response to stimulation.

3. Antral Follicle Count (AFC)

Antral follicles are small, 2-8mm fluid filled cysts that are normally found in the ovaries. They are also referred to as resting follicles. The antral follicle count is obtained by having a vaginal ultrasound performed. During this cycle day 2,3,or 4 ultrasound, both ovaries are measured, and the number of resting follicles on each ovary is counted. A resting follicle contains an immature egg that could potentially develop in the future. A count of these antral follicles can help predict how many mature eggs could be released or retrieved after stimulation. This test is important in estimating how well the response to medications might be. In general, the more antral follicles present in the ovaries, the better the response a woman should have to gonadotropin injections.

Antral Follicle Count	Interpretation	Expected Response to FSH	Anticipated Cancellation with IVF	Anticipated Pregnancy Rate with IVF
<4	Very low	Very poor	Very high	Very low
4-6	Low	Poor	High	Low
7-10	Reduced	Reduced	Increased	Decreased
11-30	Normal	Good	Low	Excellent
>30	Above Normal(PCOS)	Increased risk of hyperstimulation	Low	Good

4. Anti-mullerian Hormone (AMH)

One of the most recent blood tests used to help determine ovarian reserve is called AMH. AMH, anti-mullerian hormone is a substance that is produced by the granulosa cells in small ovarian follicles. Therefore, AMH blood levels are thought to reflect the size of the remaining egg supply. AMH is likely to become the hormone of choice in determining ovarian reserve. The fact that AMH is secreted without dependence on other hormones makes it a more direct measurement than some other tests. AMH levels may be obtained on any day during the menstrual cycle. This is a vast difference in timing of other ovarian reserve tests. Though this test may be considered one of the most accurate, it is still not definitive and should not be used alone to determine ovarian reserve. Factors known to decrease AMH include age, prior chemotherapy

or radiation therapy, obesity, and surgical removal of one ovary. Below is a table that shows some insight into meaning of these blood levels.

AMH Level mg/ml	Interpretation	Expected Response to FSH	Anticipated Cancellation Rate with IVF	Anticipated Pregnancy Rate with IVF
>3.0	High, often PCOS	Very High	Low	Normal
1.0-3.0	Normal	Good	Low	Normal
0.4-0.9	Low	Reduced	Increased	Reduced
<0.4	Very Low	Very Poor	Very High	Very Low

5. Response to Gonadotropins (Injectable FSH)

The real test of ovarian reserve is considered by many to be the response of a woman's ovaries to stimulation with injectable gonadotropins (FSH). Some physicians call this a gonadotropin challenge. In this test, a woman uses injectable FSH and her response is measured based on number of follicles that grow and level of Estradiol production by the ovaries. The better response that a woman has, the better the chance of pregnancy. Very poor response often leads to the recommendation to use donor oocytes.

Summary

All tests of ovarian reserve are designed to predict a woman's response to injectable medications. The purpose of ovarian reserve testing is to more accurately evaluate a couple's chance of success with any given treatment, particularly IVF. Because the time commitment, stress level, and cost of IVF are high, physicians may discourage couples from attempting treatment based on poor results from ovarian reserve testing. No single test, however, is 100% accurate and there are always exceptions to these general guidelines. Your physician will try to integrate all the test results together and give the best treatment options available.