



Board Certified in Reproductive
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Fertility Facts

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Making Families a Reality

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Using anti-mullerian hormone to evaluate ovarian reserve

Various tests are used to assess a woman's ovarian reserve, including 1) the Clomid challenge test, in which early follicular phase serum levels of FSH and estradiol are obtained, and repeat testing of FSH is done after five days of clomiphene citrate, and 2) early follicular phase serum levels of FSH, estradiol, and inhibin B. Unfortunately these markers remain interdependent and procurement remains cycle-dependent. Some people contend that the best predictor of ovarian reserve is the antral follicle count (AFC). But this evaluation is also cycle dependent and requires some degree of operator expertise and transvaginal ultrasonography. Obviously a serum marker that reflects the nascent follicle pool, but is independent of gonadotropins, would be useful to both couples and their physicians. Antimullerian hormone (AMH) may be that marker.

What is AMH?

Antimullerian hormone, also called mullerian inhibiting substance, is directly secreted into the circulation by growing ovarian follicles. The hormone is synthesized and secreted by preantral and early antral follicles, and expression almost disappears once follicles become larger than 8 mm. By the time a follicle establishes dominance, the granulosa cells no longer show AMH expression. At any given time, serum AMH levels reflect the number of pre-antral follicles that are undergoing FSH-independent growth, which is proportional to the size of the entire primordial follicle pool.

AMH levels appear to be stable until adulthood and then decrease with aging as preantral follicles become exhausted. In women, AMH is exclusively made in the ovary and it has a short half-life of only several days.

Throughout the menstrual cycle, serum AMH tends to remain constant. This is consistent with the finding that there is continuous noncyclical growth of small preantral follicles. As a result, AMH can be measured at any point during a woman's menstrual cycle, obviating the need for collection in the early follicular phase. This is clearly an advantage of using AMH as a marker of ovarian reserve. Furthermore, the cycle-independent testing of AMH is extremely useful for the oligo-ovulatory or anovulatory patient with irregular or absent cycles.

Since oral contraceptives have little effect on primary and preantral follicular growth, AMH can even be obtained in women as they remain on hormonal contraceptives. AMH is not affected by changes in gonadotropin levels or by estrogen and progesterone administration.

AMH appears to be a more sensitive marker of ovarian reserve than FSH, inhibin B, estradiol, and AFC. Serum AMH levels have been shown to correlate well with age, FSH, and the number of antral follicles, but the levels have been shown to decrease over relatively short periods of time in young ovulatory

women. One research team performed an observational study in women who had AMH drawn at two distinct intervals 2.6 +/- 1.7 years apart, and found a 38% reduction in AMH, whereas the AFC and levels of FSH and estradiol did not change. In a separate observational study, AMH was the only marker that consistently declined over four years in both younger women (<35 years) and in women over 40 years.

The clinical use of AMH is becoming more popular as a way to determine ovarian reserve. The main advantage of AMH over FSH seems to be ease of collection and interpretation, and greater sensitivity to detect declining ovarian reserve.

Clinical use of AMH in the infertility practice

AMH has proven more useful than day 3 FSH and estradiol to determine that diminished ovarian function is likely responsible for unexplained infertility or unexplained habitual abortion, and AMH levels predict exogenous gonadotropin requirements in superovulation. In our practice, AMH has evolved as the sole prerequisite test used to gauge ovarian function and determine the exogenous FSH requirement in women undergoing IVF or controlled ovarian hyperstimulation. AMH has been shown to closely predict the ovarian response in these cycles. Higher levels of AMH are associated with a greater number of retrieved oocytes. AMH has been shown to be the best single marker to predict ovarian response to gonadotropin stimulation, compared to FSH and inhibin B. Although multiple studies confirm the predictive value of AMH in ovarian responsiveness, it appears to be less predictive of pregnancy rates.

AMH levels will also corroborate findings during the evaluation of secondary hypogonadism. AMH, as expected, is normal in women with hypogonadotrophic hypogonadism in which FSH levels may be low or normal, but AMH is evidently undetectable in over 80% of women with hypergonadotrophic amenorrhea.

In the future, normal AMH levels will become better standardized for specific age ranges of reproductive women since it is natural for AMH levels to decline with increasing age. We, along with others, have discovered that AMH values <1ng/mL are associated with decreased ovarian reserve. Values >1.5 ng/mL are reassuring, while those between 1 and 1.5 are considered borderline. Low AMH levels, while predictive of decreased numbers of eggs in younger women are less predictive of concomitant poor egg quality. AMH cut offs to determine the absolute chance of pregnancy outcome with IVF, like with other hormones, are impractical. There have been cases of spontaneous pregnancies when AMH levels are undetectable. However we predict that the clinical usefulness of AMH will surpass that of the current markers of ovarian reserve.

About Us: Carolina Conceptions is the fastest growing infertility center in the southeast and is the only private practice of its kind in the Triangle area where all doctors are board certified in both OB/GYN and Reproductive Endocrinology and Infertility. The physicians share more than 45 years experience in the infertility field and have achieved some of the highest success rates in both the region and country. The practice offers a fully comprehensive range of treatment options along with a highly trained staff who are dedicated to delivering friendly and compassionate care.