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Ovarian reserve testing: A review of the options, their applications, and their limitations

Nicole D Ulrich, MD¹ and Erica E Marsh, MD, MSCI, FACOG¹

¹Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI

INTRODUCTION

Ovarian reserve traditionally refers to the store of eggs a woman has in her ovaries that have the potential to produce mature follicles for ovulation to sustain the menstrual cycle and/or create a pregnancy. However, in clinical application ovarian reserve is a complex concept that has two distinct windows of interpretation. It can be broken down to the biological concept of ovarian reserve, or that which we can measure in a laboratory or with an ultrasound machine and the clinical concept of ovarian reserve, that which we can measure with outcome data. These two concepts are, of course, inter-related but also distinct in their definitions and evaluation.

The biological concept of ovarian reserve is based on the accepted notion that the number of oocytes within a woman's ovary declines over time. This natural decline is influenced by a number of different factors including age, genetics, and environmental factors.^{1,2} Unlike sperm generation in the male, the follicular pool in women is unidirectional and the rate of decrease accelerates as a woman ages.³ The total number of oocytes is thought to peak in fetal life at 20 weeks of gestation with approximately 5–7 million.¹ This number has already decreased to 500,000 to 1 million primordial follicles at birth.¹ By menarche only approximately 400,000 follicles are estimated to be present. This number continues to decrease throughout early adult life and begins to decline more rapidly as a woman enters her mid-30s. By the late-30s the total number is less than 50,000.^{1,3} There is no accepted way to predict this decline over time in an individual woman, and women of the same age can have very different biological measures of ovarian reserve and reproductive potential.^{4,5} The biological measures available to us only provide an estimate of the general number of viable oocytes remaining, and they have limited utility in terms of predicting a woman's clinically relevant ovarian reserve. In addition, it is important to note that while we have testing that can measure the estimated oocyte quantity, age is the only current marker of oocyte quality.⁶

When we discuss the clinical aspects of ovarian reserve, the most relevant question for patients is whether or not they can achieve pregnancy and ultimately a live birth. An

Corresponding author: Dr. Erica Marsh L4000 University Hospital South, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-5276, Phone: (734) 232-5029, Fax: (734) 936-5948, marsh@med.umich.edu.

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additional clinical benefit of ovarian reserve testing is to help us anticipate the ovarian response to stimulation, specifically the number of oocytes that can be retrieved in an IVF cycle. Other clinical outcomes of interest include identifying those patients at risk for either a very low response to stimulation or an over response leading to ovarian hyperstimulation syndrome (OHSS). The clinical measures of ovarian reserve are not always solely dictated by the biological measures of ovarian reserve. In this review we will discuss ovarian reserve in the context of its biological evaluation and highlight where the data support or don't support its use as a clinical predictor.

One of the challenges of any discussion of ovarian reserve is the lack of a gold standard in terms of assessment of ovarian reserve. In addition, no universally accepted clinical cut off has been established to define a normal vs an abnormal result for any available measure of ovarian reserve. As we discuss the tools available to assess ovarian reserve, we will discuss the data that support the values that are most often used clinically. It has become clear that certain tests have better positive predictive value while others have better negative predictive value. We will also discuss how these findings can be applied clinically.

BIOLOGICAL MEASURES OF OVARIAN RESERVE

There are several biological measures of ovarian reserve, both biochemical and imaging based. The biochemical assessments include serum measurement of anti-mullerian hormone (AMH) and early follicular levels of estradiol, follicle stimulating hormone (FSH), and inhibin B. In addition to basal measures, the provocative clomiphene citrate challenge test (CCCT) measures FSH in response to ovarian stimulation. The ultrasonographic measures available include the antral follicle count (AFC) and ovarian volume measurements.⁴ The tests most commonly used in clinical practice today, and the ones we will focus on in this review are early follicular estradiol/FSH, AMH, and AFC. The CCCT, inhibin B, and ovarian volume as markers of ovarian reserve are no longer as well supported by the current literature and are less widely utilized.⁴

FSH AND ESTRADIOL

Early follicular FSH in combination with estradiol has been used for more than 30 years as an indirect measure of ovarian reserve.^{2,7} At the beginning of the menstrual cycle feedback inhibition from estradiol and inhibin B are at the lowest point and allow the basal, unsuppressed FSH to be measured. Women with normal ovarian reserve produce enough estradiol and inhibin B from the granulosa cells in the ovary during the early cycle to keep the FSH low.^{2,7,8} However, as the follicular pool declines, the early follicular FSH increases due to insufficient production of estradiol and inhibin B to fully inhibit FSH production.⁷ Therefore, when the early follicular phase FSH is elevated it is highly suggestive of diminished ovarian reserve (DOR). It is important measure the estradiol level at the same time for an accurate interpretation of the FSH. In women with DOR the incompletely suppressed FSH can drive estradiol levels higher (>60–80pg/mL), which in turn will then suppress FSH levels to normal ranges.⁴ In this case if only the FSH were measured, it could be falsely interpreted as a normal result. Therefore, a normal FSH with elevated estradiol should also prompt concern for DOR.⁵

Elevated FSH values are associated with but not always predictive of poor ovarian response and failure to conceive.^{4,5} FSH values can also vary significantly from cycle to cycle, which can limit its reliability.^{4,9} Using FSH cut off levels of 10–20 IU/L can be somewhat specific for predicting poor response to stimulation, defined as less than 2–3 follicles or less than or equal to 4 oocytes retrieved or cycle cancellation.^{2,4,5} However, sensitivity is poor and widely variable for poor ovarian response and failure to conceive.⁴ Given that elevated FSH can suggest a poor outcome with IVF and FSH does vary between cycles, there has been some thought that repeating FSH monthly to attempt to select a cycle when the level falls below a desired cut point before proceeding with IVF in that specific month may improve results. However, when evaluated using an FSH of 10 IU/L or greater as an elevated value, this selection process does not improve live birth rate or ART outcomes including number of oocytes collected, oocytes fertilized, or embryos transferred.⁹ Among women with less than 3 months of attempted conception, an elevated FSH (10mIU/mL or greater) did not predict a difference in probability of achieving pregnancy after 6 or 12 attempted cycles.⁸ Though the majority of young, reproductive aged women tested will not have an elevated FSH, the test is still clinically useful because it is fairly certain that a woman with an elevated FSH will have DOR.⁴ However, given that there is significant variability from cycle to cycle, the positive predictive value is higher in older women.⁴ False positives are higher when FSH is tested in a low risk population of young women. Consequently, one elevated FSH level in a women younger than 40 may not predict a poor response to stimulation or failure to achieve pregnancy.^{2,4} Currently, it is not known whether elevated FSH can predict an earlier menopause among women of reproductive age.⁴

ANTRAL FOLLICLE COUNT

The antral follicle count (AFC) describes the number of antral follicles measuring between 2–10mm noted on early follicular phase ultrasound of the ovaries.⁴ AFC measures have a good inter-cycle and inter-observer reliability in centers with experienced sonographers.^{2,4,10} In a comparison of early follicular phase AFC using a 3-D ultrasound with FSH and ovarian volume, the AFC showed the least variability between two observed IVF cycles.¹¹ The IVF cycles were separated by at least two menstrual cycles with a mean interval of 5.4 months, suggesting stability in the AFC over at least that length of time.¹¹ One limitation of the AFC is that it is possible that the count would overestimate the amount of follicles able to respond to FSH in a given cycle, as atretic follicles would also be included in the total number visible with ultrasound.²

AFC has been shown to be a reliable predictor of ovarian response to stimulation for IVF, including over response.^{4,10,11} However, it is a generally a poor predictor of pregnancy outcomes.^{2,4} Using a cut off value of 3–4 follicles in both ovaries is highly specific but less sensitive for predicting IVF cycle cancellation or a low number of oocytes retrieved (<3–4). That same cut off value is moderately specific but retains a low sensitivity for predicting failure to conceive.⁴ Furthermore, the positive and negative predictive values for predicting poor response vary widely among studies.⁴ AFC is also a strong predictor of those at highest risk for OHSS. A meta-analysis included 5 studies with cut off values ranging from 9 to 18 found that AFC had a good discriminatory capacity to separate normal and excessive responders, and it can be used to help drive dosing decisions to attempt to prevent a

dangerous over response to stimulation.¹⁰ The authors proposed that a cut off for AFC should be determined by the individual physician as the results can vary based on ultrasound equipment, dedicated personnel, and systematic visualization and counting process. While this would certainly improve internal consistency, it does limit the generalizability of AFC across centers.¹⁰ AFC can be a useful adjunct for evaluating a woman's overall picture of ovarian reserve given its stability across menstrual cycles and ability to accurately predict respond to stimulation. However, AFC is limited in its ability to predict pregnancy outcomes.

AMH

Anti-mullerian hormone (AMH) is a glycoprotein hormone that belongs to the transforming growth factor beta superfamily. During fetal sex differentiation, AMH precipitates the degeneration of the Mullerian structures (including the oviducts, uterus, and upper part of the vagina) when it is produced by testicular Sertoli cells in the male fetus.¹² In adult women, it is produced by the granulosa cells in the preantral and small antral follicles in the ovary.¹³ These follicles and their production of AMH are gonadotropin independent, which, in general, keeps the AMH relatively stable within and between menstrual cycles.^{11,13} Though, there is debate on this topic with some suggesting that the small variations that have been noted have little clinical relevance and are limited to younger women and those with higher basal AMH levels.^{2,4} AMH was first detected in follicular fluid in the mid-1990s and was later demonstrated to be involved in folliculogenesis.^{14,15} In follicles up to 6mm in size, AMH acts as a negative paracrine regulator inhibiting recruitment of follicles early in folliculogenesis by preventing selection of follicles by FSH and inhibiting FSH stimulated expression of aromatase.^{2,14} AMH expression declines as the follicles increase in size and is absent in large (>8–10mm) follicles in women without other pathology (i.e. PCOS).¹⁴ The expression of AMH in these early follicles is thought to prevent maturation and ovulation in most of the antral follicles and consequently prevents early depletion of ovarian follicles.¹⁴ AMH levels decline as a woman's age increases and are strongly correlated with the remaining number of early antral follicles, making it a useful test as a marker of ovarian reserve.^{5,15} Over the last 20 years, AMH has become one of the most commonly ordered tests of ovarian reserve and is now an integral part of the work up of the infertile couple in most centers.

While AMH can be very useful as a component of the fertility work up and a prediction tool for ovarian response to medical stimulation, caution must be exercised when attempting to further generalize the interpretation of the value. AMH does not appear to have any predictive value for pregnancy or live birth in a fertile patient. A recent study by Steiner and colleagues suggests that AMH may not be useful for prediction in the general population of women attempting to conceive. Their evaluation included 750 women age 30–44 within no known infertility diagnosis who had been attempting to conceive for 3 months or less. They found no association between AMH levels and reduced fecundability or a lower cumulative probability of conceiving by 6 or 12 cycles of pregnancy attempt. This suggests that AMH testing is not a helpful way to assess natural fertility for women that do not yet have a diagnosis of infertility and argues against using AMH as a fertility screening test in the general reproductive aged population trying to conceive.⁸

AMH cannot accurately predict pregnancy outcomes in the general fertile population and there are similar difficulties in using AMH to predict pregnancy in those couples undergoing IVF.^{4,5,16} For women with a diagnosis of infertility, AMH is not a reliable predictor of clinical pregnancy or live birth following ART.^{4,5,16} Some studies have found that AMH can correlate with pregnancy outcomes during IVF cycles.^{5,12} However larger analyses, including two meta-analyses, found that AMH is a poor predictor of clinical pregnancy and live birth for couples undergoing ART.^{2,16} In addition, a more recent study including 85,062 cycles pulled from the SART database, AMH was noted to be a poor independent predictor of clinical pregnancy in both autologous fresh and frozen-thaw embryo transfer cycles.¹⁶ They suggest that because AMH is well known to predict ovarian response, it would seem logical that AMH might be associated with clinical outcomes, including pregnancy and live birth. However, the data do not support this assumption, indicating that there may be other factors contributing to overall success including sperm/egg genetic integrity, embryo quality, stimulation protocol, transfer technique, and endometrial receptivity.¹⁶

While AMH's value in predicting pregnancy and live birth is limited, AMH does have a strong ability to predict response to stimulation including both poor response and an over response or ovarian hyperstimulation syndrome (OHSS).^{2,5,12} Daney de Marcillac and colleagues evaluated ovarian response to stimulation in an IVF cycle by AMH level. They used a cut off of AMH level of 1.0 ng/mL or less to define a low AMH and found that those women with a decreased AMH level had a lesser number of oocytes retrieved and a higher cancellation rate in comparison to those with a normal AMH. AMH can also be used to identify who may be at risk for an exaggerated to stimulation and potentially allow for dose adjustments ahead of an IVF cycle to attempt to mitigate this risk.^{4,5} A meta-analysis including 9 studies which evaluated AMH as a predictor of excessive ovarian response suggests that AMH can reliably be used to determine patients at high risk of excessive ovarian response. However, given the differences in AMH assays used in the included studies, they could not determine a generalizable cut-off value.¹⁰ In cycles with an over response, it is possible that the oocyte yield will be high but this does not necessarily translate to good quality embryos and may be related to a lower chance of pregnancy.¹⁰

AMH is well known to be a strong predictor of response to ovarian stimulation during IVF. There has also been interest in using AMH as a predictive test for timing of menopause or a marker of risk for early or late menopause. Menopause occurs when the number of remaining follicles falls below a critical threshold and the ovaries are no longer able to generate mature oocytes or maintain a menstrual cycle.¹⁷ It appears that the end of natural fertility occurs at some point, approximately 10 years, before this point, though the ovaries maintain normal hormone secretion until 3–4 years before the menopausal transition.^{3,17} Several studies have suggested that using AMH in addition to age can possibly predict timing of menopause in late reproductive-age women.^{2,17} However, other studies have suggested that these predictions may be too broad and less accurate at the extremes of age of menopause, limiting their clinical utility.^{2,17} Depmann and colleagues recently published a meta-analysis using data from 2596 women from several different countries to create models assessing time to early menopause and time to late menopause. They determined that AMH percentile category was one significant predictor of time to menopause. This effect was especially evident for time to early menopause (less than or equal to 45 years) in younger

women. They comment that as age increased, the addition of AMH did not increase the predictive effect of age alone, as menopause becomes inevitable at a certain point. However, attempting prediction of the age at menopause for an individual had a limited precision due to a wide prediction interval. Therefore, the clinical application of AMH for prediction of time to menopause or reproductive lifespan for the individual, low-risk patient may be limited.^{2,17}

Another area in which AMH has potential clinical benefit in the diagnosis of PCOS. AMH has consistently been demonstrated to be elevated in PCOS.^{2,8,14} Given that a normal AMH level is thought to inhibit maturation and ovulation in early folliculogenesis, an abnormally elevated AMH level in PCOS may prevent the FSH stimulated growth of the dominant follicle, leading to anovulation.^{8,14} Though the exact mechanism for elevated AMH in PCOS is not well defined, it is suggested that the increased number of antral follicles producing AMH contributes to an increase in the total value. PCOS is, of course, also associated with insulin resistance. Liu and colleagues recently described increased expression of AMH within the granulosa cells and increased AMH levels in the follicular fluid of women with PCOS in response to a high dose of insulin, suggesting this may be another possible mechanism for elevated AMH in PCOS.¹⁴ There is strong evidence that AMH level correlates with severity of PCOS including abnormal ovarian morphology, hyperandrogenism, and oligo/anovulation, and it is also thought that AMH can predict a poor response to treatments for PCOS including weight loss, ovulation induction, and laparoscopic ovarian drilling.² While there is general agreement in the literature that PCOS is associated with an elevated AMH level, determining what level that may be is similar to the “Normal AMH” conundrum. There is currently no consensus on what cut off for elevated AMH would be highly suggestive of PCOS. In summary, while AMH offers a good biological lens into ovarian reserve and certainly has clinical relevance, it is, similar to other markers of ovarian reserve, predictive ability for the outcomes that matter most to providers and patient, live birth and pregnancy outcomes, is limited.

FACTORS THAT AFFECT OVARIAN RESERVE AND ITS MARKERS

There are several lifestyle factors which have been evaluated for their potential effect on ovarian reserve including oral contraceptive medications, obesity, smoking, vitamin D level, and alcohol use.^{1,2,18} A history of ovarian surgery, chemotherapy, and endometriosis have also been shown to decrease AMH.² Race and ethnicity may play a role in measures of ovarian reserve as well.¹⁹ The majority of studies evaluating the effect of oral contraceptives on ovarian reserve have shown lower AMH levels and a decreased AFC in women on birth control pills.^{2,13,20} Oral contraceptives decrease gonadotropins through direct suppression on the pituitary.²⁰ The combination of estrogen and progestin components inhibit FSH and therefore follicle growth dependent on FSH. Though, the degree of suppression of gonadotropins is variable in individual patients and does depend on the type of type and dose of steroids used. Use of oral contraceptives decrease the size of the ovary and therefore might decrease gonadotropin independent follicle recruitment and functionality as well, thus lowering AMH.^{13,20} The suppressive effect on gonadotropins resolves very quickly after cessation of daily administration of oral contraceptives, and it appears that the suppressive effect on AMH and AFC is resolved within 3–6 months of discontinuation of use.^{2,20} In a

study including women from 4 different race/ethnic groups, the past use of oral contraceptives was not associated with a difference in AMH, suggesting no long term effect of oral contraceptive use on AMH levels.¹⁹ It is important to note that any measure of ovarian reserve including AMH, AFC, or early follicular FSH and estradiol will mostly likely not reflect an entirely accurate measure of ovarian reserve in a current user of oral contraceptive pills and a full reversal of the effect on AMH and AFC may take several months to be evident.

Race and ethnicity have been evaluated for their potential implication on ovarian reserve markers, given the observed differences in menopausal timing among these groups.¹⁹ There are a small number of studies that have looked at ovarian reserve markers across race and ethnic groups. The majority focus on AMH levels. However, one study of ovarian reserve markers in healthy, cycling women aged 25–45, not attempting pregnancy, included 200 African-American and 232 Caucasian women and found that FSH levels were similar but AMH levels were lower in the African-American group.⁷ The authors also point out that in the African-American group, the AMH, AFC and FSH levels were more variable and less strongly correlated with age.⁷ In a recent study of 947 healthy, regularly cycling, pre-menopausal women aged 25–45 AMH levels were compared in women of 4 different race/ethnic backgrounds (white, African American, Latina, and Chinese). They also found lower AMH levels among African American women at younger ages, but higher levels in this group at older ages. They suggest that African American women may have a lower AMH but experience less of a reduction in AMH with aging. In addition, Latina and Chinese women had lower AMH levels when compared with white women, suggesting a possibly increased risk for earlier menopause in these groups.¹⁹ Though more work is clearly needed to fully understand these differences and what may be contributing to them, it is important for the provider to be aware of these subtle differences as they evaluate and care for women of different racial and ethnic backgrounds.

Though race and ethnicity do appear to have implications for ovarian reserve, the effect of obesity on ovarian reserve markers is somewhat unclear.^{2,19} Anovulation is more common in obese women and this may increase the number of small antral follicles secreting AMH. However, obesity also increases adipokines and/or other inflammatory markers in ovaries, which could lead to decreased follicular pool.²¹ There have been several studies published that report no effect of obesity on AMH, as well as several that report a negative effect of obesity on AMH.^{13,19,21,22} Though AFC is generally stable across menstrual cycles, it has been demonstrated to have some variability at high levels.¹¹ Possibly related to this, inter-cycle variability in AFC appears to be higher in overweight and obese women, which can limit the predictive utility in this population.² Bleil and colleagues evaluated AMH across 4 different race/ethnic groups and found a BMI related decrease in AMH. Other studies have evaluated African-American women alone and observed a significant inverse effect.^{21,22} Among African Americans, AMH was negatively correlated with current BMI²² as well as current BMI, BMI at age 18, and highest lifetime BMI.²¹ Though, the effect of BMI on ovarian reserve is debated, it is worth noting that race and ethnicity may have implications for the observed effects as well.

Additional lifestyle factors such as smoking and alcohol used have also been evaluated for a potential effect on ovarian reserve. Smoking is of a particular interest given the previously observed association between smoking and earlier menopause.⁷ There is evidence that smoking can decrease ovarian reserve, though data are somewhat mixed.¹³ A histology based study counting the number of follicles from ovaries removed in surgery found no difference in the measurable follicular pool in current smokers.¹ The authors proposed that associations between smoking and earlier menopause might be related to some effect not involving direct toxicity to the follicles in the ovary.¹ When African American women were evaluated alone, smoking did not appear to have an effect on AMH.¹⁸ However, this was a young cohort, who may not have had as much time for regular smoking to show its full effect. In another study, previous and current smoking did not affect the AFC but did trend toward higher FSH levels, supporting the notion of a toxic effect on the follicular pool that could lead to earlier menopause. One study also examined binge drinking among African American women and demonstrated a significantly decreased AMH level among those who binge twice weekly or more frequently compared to current drinkers who never binged.¹⁸ Interestingly, on histologic evaluation of the surgically removed ovary, there was a slight increase in the follicular number in light and moderate alcohol use, corresponding to the previously reported delayed age of menopause in these groups.¹ In addition, the authors did not report a significant association between heavy drinking and the size of the follicular pool.¹ While there does appear to be an effect of smoking on long term reproductive function, in particular, additional evaluation is needed to further determine its full effect and the mechanism behind its potential ovarian toxicity.

DIMISHED OVARIAN RESERVE

An estimated 10% of the general female population will experience an accelerated loss of ovarian reserve, presumably from a more rapid rate of follicular atresia, leading to a loss of fertility in the mid-30s and early menopause by age 45.^{2,6} This discrepancy in ovarian reserve between women of similar ages has become more clinically relevant in recent years as the average age of first birth has increased to the age of 30 in the Western world with 1 in 5 women not having attempted pregnancy by the age of 35.^{1,2} Diminished ovarian reserve (DOR) is a distinct process, different from either menopause or primary ovarian insufficiency (POI).^{2,4} In most cases a cause for the expedited decline is not determined. However, several factors including, exposure to systemic chemotherapy, pelvic radiation, and genetic abnormalities (45, X mosaicism, FMR1 premutation) are related to a more rapid decline in number of available oocytes and fertility potential and would be indications for testing of ovarian reserve (Table 1.).^{4,11}

While an elevated FSH and advancing age correspond to a decrease in oocyte quality among women with a normal trajectory for decline in ovarian reserve, there does not appear to be as strict of a correlation between early elevated FSH and oocyte quality among women with DOR at younger ages.^{6,8} DOR is used clinically to describe a woman of a traditional reproductive age with regular menses who has a decreased response to stimulation or a decreased ability to conceive when compared to women of the same age.⁴ However, the biochemical diagnosis of DOR is more difficult to define. In their study of IVF/ICSI outcomes, Daney de Marcillac and colleagues define DOR as AMH < 1.1 ng/mL and FSH >

10 mIU/mL. Steiner and colleagues also selected a FSH cut off of 10 mIU/mL but chose an AMH cut off of 0.7 ng/mL to define DOR. They also comment that a very low AMH of 0.1ng/mL or lower likely reflects DOR more consistent with the late perimenopause transition.⁸ Though the follicular pool is depleted, a diagnosis of DOR does not necessarily equate with a decreased ability to conceive, as discussed previously, or increased pregnancy loss.^{6,8} In younger women with DOR (defined by elevated FSH >10mIU/mL), there is no difference in the miscarriage rate when compared to women of the same age without a diagnosis of DOR.⁶ As ovarian reserve testing becomes more common in a younger, ostensibly low risk population, providers and patients should be aware that a biochemical diagnosis of DOR does not necessarily correlate directly to clinical outcomes.

CONCLUSION

As we have discussed there are several windows through which we can view a woman's ovarian reserve, including the biological tests of age, both serum biomarkers and ultrasound based measurements, in addition to the clinical outcomes of ovarian response to stimulation, achieving pregnancy, and ultimately live birth. Each of these yields a unique contribution to the overall picture of potential ovarian response and functionality. The most common biological tests of ovarian reserve used today are the AMH, early follicular measurements of FSH and estradiol, and ultrasound assessment of the AFC. Given the ease of a single serum based test that does not need to be drawn at a specific time in the cycle and the inconsistencies in FSH and estradiol measurements across cycles, AMH has become very popular as a potential "fertility screening test". However, the proven utility of AMH is for prediction of ovarian response to stimulation, not as an overall test of fertile potential or ability to conceive. One recent publication reports on the potential negative psychological effect that an AMH result, either normal or abnormal, can have on a patient, whether ordered as a part of an infertility work up or as a screening test.²³ AMH has a unique role in the evaluation of the infertile couple and helps to guide decisions on therapy recommendations. However, based on the current data, it cannot reliably be used to predict those who may have difficulty conceiving or the timing of an individual's menopausal transition. If the test is being ordered in these contexts, care must be taken to ensure the patient understands the significant limitations that affect the interpretation of that result.

In summary, while ovarian reserve testing has significant clinical benefits, it also has significant interpretive limitations and can even cause psychological harm. Given this, it is important for providers to be judicious in their use and interpretation.

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Table 1.

Indications for evaluation of ovarian reserve and cases where ovarian reserve testing is not recommended. ART, assisted reproductive technology; POI, premature ovarian insufficiency; FMR1, fragile X mental retardation 1. (Table compiled from Practice Committee of the American Society for Reproductive Medicine, 2015; Steiner et al, 2017; and Tal & Seifer, 2017)

Ovarian reserve testing indicated
Evaluation of the infertile couple
Selecting stimulation protocol and dosing in women undergoing ART
Women considering elective oocyte cryopreservation
Before and after gonadotoxic treatment
Counseling regarding Perimenopause
Evaluation for POI
Women with BRCA-1
Ovarian reserve testing not recommended
Evaluation of fertility potential in women prior to attempting pregnancy
As a screening tool for diminished ovarian reserve in a low-risk population
As a predictor of pregnancy or live birth prior to ART
As inclusion or exclusion criteria for use of ART
Individualized counseling on reproductive lifespan