

Biochemical and Imaging Diagnostics in Endocrinology: Predictors of Fertility



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KEYWORDS

• Ovarian reserve • Ovulatory status • Gamete transport • Male factor • Infertility

KEY POINTS

- An appropriate diagnostic evaluation of the infertile couple includes ovarian reserve testing, determination of ovulatory status, evaluation of anatomy as it relates to gamete transport, and evaluation of the male, if applicable.
- In a couple who fulfills the criteria for the diagnosis of infertility, biochemical modalities are particularly useful for evaluating the ovaries and ovulatory status, and imaging is the appropriate way to evaluate transport.
- Although much has been elucidated about the diagnostic evaluation of the infertile couple, current testing has limited predictability for the ultimate achievement of a live birth.

INTRODUCTION

Infertility has traditionally been defined as the inability to achieve a successful pregnancy after 12 months or more of regular unprotected intercourse. This definition applies to heterosexual couples, because approximately 85% achieve a pregnancy within that time frame without medical assistance. Conversely, this means that 15% of heterosexual couples warrant an evaluation for causes of infertility. In women older than the age of 35, earlier evaluation is recommended (following 6 months of subfertility) because of the increased prevalence of ovarian reserve concerns in this group. Furthermore, an evaluation before 12 months may also be indicated for patients with clinical situations, such as oligomenorrhea or amenorrhea, known or suspected peritoneal disease, severe endometriosis, or male factor infertility.¹ In addition, same sex couples and single women may also benefit from a baseline evaluation to try and screen for potential fertility issues beyond lack of exposure to gametes.

One of the limiting factors of fertility testing is the relative inefficiency of human reproduction, because a couple without infertility has a fecundability rate of only

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15% to 20% per month.² A careful history and physical examination must be performed on each patient to inform the particular diagnostic tests that are chosen, and to create a meaningful treatment plan. The testing parameters, such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value, can help to interpret test results, although there is no perfect screening test for the various causes of infertility. This article describes the four major categories of testing for infertility: (1) ovarian reserve, (2) ovulatory status, (3) gamete transport, and (4) male factor (if applicable) (**Box 1**).

OVARIAN RESERVE
Review of Reproductive Physiology

Under normal circumstances, each month, a woman of reproductive age has a cohort of ovarian follicles. These follicles are destined for atresia, although one follicle is “rescued” from the group and is selected as the dominant follicle based on a variety of factors, such as the ability to express follicle-stimulating hormone (FSH) receptors, and to produce aromatase and estradiol. Inhibin B and estradiol from the follicle exert negative feedback on the hypothalamus and pituitary, until estradiol levels surpass a threshold, prompting a shift to positive feedback, inducing a luteinizing hormone (LH) surge and ovulation. The follicle remodels and becomes the corpus luteum, making progesterone, estradiol, and inhibin A. These hormones exhibit negative feedback with resultant suppression of gonadotropins. If a woman is not pregnant in a given cycle, the hormones from the corpus luteum rapidly decline to basal levels, which decreases the negative feedback, and FSH rises to start the process again.³

Ovarian follicle number and oocyte quality decrease continually from a midfetal peak until the loss of any ovulatory follicles around menopause. With ovarian aging, the corpus luteum function declines, with decrease in negative feedback. This results in an earlier rise in FSH, earlier recruitment of new follicles, and a shorter follicular phase. Antimüllerian hormone (AMH), produced by the total cohort of primary, secondary, and early antral follicles, decreases as the size of the cohort steadily decays. Although the exact role of AMH remains to be clarified, AMH is the least variable direct measure of follicular secretory activity and is constant throughout the menstrual cycle^{2,4} (**Table 1**).

Diminished Ovarian Reserve

Diminished ovarian reserve (DOR) is the most pressing concern in women of advanced maternal age. Unlike men, who produce new sperm on a daily basis, women reach peak oocyte number between 16 and 24 weeks of gestation with steady decline in numbers and quality until after menopause.³ Biochemical measures of ovarian reserve include AMH, a direct estimate of the total number of the primordial follicles, and early follicular FSH and estradiol, estimating the pituitary response to diminished negative feedback from a decreasing follicular pool. As of yet, there are no age-specific reference ranges for AMH, and lack of calibration among assays limits generalizability of

Box 1
Categories of testing for infertility
Ovarian reserve
Ovulatory status
Gamete transport
Male factor (if applicable)

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