Ovarian Assessment Report
OAR™ with Egg Supply Score (ESS™)

PATIENT: Example, Patient
PHYSICIAN: Benjamin Leader MD
DATE OF REPORT: 12/01/2014

PRIVATE AND CONFIDENTIAL
Ovarian Assessment Report 1.5

Patient: Example, Patient
Gender: F Age: 28 years Date of Birth: 01/01/1986
Specimen: 00190326 Reported: 12/01/2014
Received: 11/14/2014 Time: 09:00 Approx
Collected: 11/13/2014 Time: 09:00

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Address: ReproSource Fertility Diag
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Tests:

<table>
<thead>
<tr>
<th>Patient Values</th>
<th>FSH</th>
<th>Estradiol</th>
<th>LH</th>
<th>AMH</th>
<th>Inhibin B</th>
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</thead>
<tbody>
<tr>
<td>Values</td>
<td>8.0</td>
<td>30</td>
<td>2.2</td>
<td>0.51</td>
<td>30</td>
</tr>
<tr>
<td>Follicular Day 2,3</td>
<td>3.0 to 14.4</td>
<td>ND to 84</td>
<td>1.1 to 11.6</td>
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<tr>
<td>Midcycle</td>
<td>5.8 to 21.0</td>
<td>34 to 400</td>
<td>17.0 to 77.0</td>
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<tr>
<td>Menopausal</td>
<td>21.7 to 153.0</td>
<td>ND to 30</td>
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</tbody>
</table>

RANGE

Egg Supply Score (ESS)

Increased Chance

Reduced Chance

Egg Supply Score

The ESS estimates likelihood of good egg supply (quantity) by optimizing the combination of age with multiple ovary-related hormones such as AMH and FSH10,11.

Egg Quality & Your Age

Increased Chance

Reduced Chance

Age in Years

Currently, age is the best predictor of good egg quality. The bar above shows, based upon age alone, how aging decreases the chance of good egg quality.

Egg Supply Score Compared to 26,125 Women from Fertility Centers

The graph displays bars with the ESS range containing the middle 70% of women (“average”) by year of age in 26,125 women evaluated at fertility centers. Women with an ESS in the lowest 15% are defined as “below average” while those with an ESS in the highest 15% are “above average.” Bar color indicates chance of good egg supply based upon ESS. Note: Women from fertility centers are not randomly selected from the general population but are comprised of both fertile and infertile women with low, intermediate, and high egg supply.

Note: Ranges calibrated to egg supply defined by ovulatory response during egg retrieval.1

RESULTS AND AGE SUGGEST A REDUCED CHANCE OF A GOOD EGG SUPPLY AND A GOOD CHANCE OF GOOD EGG QUALITY. GIVEN EGG SUPPLY AND QUALITY DIMINISH WITH TIME, WOMEN EXPERIENCING DIFFICULTY WITH CONCEPTION OR CONSIDERING EGG PRESERVATION SHOULD DISCUSS TREATMENT OPTIONS WITH A FERTILITY SPECIALIST.

Low age specific AMH is associated with premature ovarian insufficiency, earlier menopause, and autoimmunity, while high AMH is associated with PCOS and later menopause. Hormonal contraceptives may lower AMH within the first 8 weeks of use with increasing AMH observed within 8 weeks after discontinuing use. NOTE: Consider repeat testing to confirm concerning serum AMH results. In some women retested within 1 year, AMH can show substantial biological fluctuations. AMH results and ranges are specific to ReproSource. 2-9
Egg Supply Score Clinical Ranges:
Historically, an accurate egg supply assessment was difficult to obtain. The number of eggs obtained through an IVF egg retrieval procedure is considered to be the gold standard for measuring egg supply, but this procedure is not a practical diagnostic test. Although many studies demonstrate the ability of various blood tests to correlate with eggs retrieved, general clinical testing laboratories do not calibrate their test results to this clinical outcome.

The Egg Supply Score (ESS) calibrates age and blood test results from ovary related hormones including AMH and FSH to the number of eggs obtained in an egg retrieval. The ESS ranges from 1 to 20, with likelihood of good egg supply increasing as the score increases.

Note: No single test can predict a woman's ability to have a child and the ESS does not assess egg quality.

Study Calibrating ESS to Egg Supply:
Objective: To provide the most accurate and easily interpreted assessment of a woman's current egg supply from a blood test.

Methods: In a blinded study, blood samples from women undergoing a total of 454 egg retrievals were tested by ReproSource, and included women with likely excellent egg supply (79 egg donors and 26 female partners of infertile men) and with likely poor egg supply (139 infertile women). ReproSource conducted testing for ovary related hormones, such as AMH and FSH, and for calculation of the ESS. A third party unblinded and analyzed results.

Results: The results (graph to upper right) showed that women with lower ESS values were more likely to have a low egg supply (0 to 4 eggs retrieved, red bars) and women with higher ESS values were more likely to have a good egg supply (12 or more eggs retrieved, dark green bars).

Conclusions: The Egg Supply Score (ESS) is highly correlated with the gold standard measurement of a woman's egg supply: the number of eggs obtained in an egg retrieval procedure. The ESS can be a useful tool to help clinicians and patients better understand a woman's likely egg supply.

AMH Level Compared to 65,128 Women* Evaluated at Fertility Centers

AMH and Women’s Health
If appropriately calibrated to clinical outcomes, age specific serum AMH testing can provide helpful information for a number of conditions in women’s health. Although population average AMH level declines steadily from 25 years of age until undetectable, individual AMH levels vary considerably amongst women of the same age (graph, above right). The more elevated the age-specific AMH, the higher the likelihood of polycystic ovary syndrome (PCOS) and later menopause. Conversely, lower age-specific AMH values are associated with premature ovarian insufficiency/failure (POI/POF), earlier menopause, and autoimmune conditions such as systemic lupus erythematosus and Crohn’s disease. Importantly, clinical now conclude that hormonal contraceptives can lower AMH values as can ovarian related surgery and chemotherapy.

Note: AMH levels are not standardized across laboratories. Thus, AMH results from different laboratories cannot be compared. Secondly, while there is clear clinical benefit from AMH testing, especially as values approach the extremes of high and low, definitive cut points for the general population are still the subject of active research. Therefore, interpretation of AMH results in the general population should be directional rather than definitive, prompting further investigation rather than establishing diagnoses.

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① Most Up To Date Ovarian Reserve Testing for Clinical Use

ReproSource provides the latest testing related to egg supply and ovarian reserve. Historically FSH has been the blood test most frequently used as a marker of egg supply, but it has a high frequency of falsely reassuring results. AMH, which is secreted from the granulosa cells surrounding each egg, has emerged as a more accurate blood test. ReproSource has demonstrated AMH is more accurate than other hormones in assessing egg supply, declines gradually with age, and identifies many women at risk for poor egg supply missed by FSH testing (1 in 11 women tested under age 35 are missed which rises to 1 in 3 women above 39 years of age).

② Mathematical Formula Calibrates Results to Egg Supply for Easier Interpretation

ReproSource provides the latest testing related to egg supply but generally do not calibrate to egg supply. Thus, it is often unclear how reported results link to clinical outcomes or how to weight the results of individual tests together. By conducting clinical outcomes research in egg supply testing, ReproSource is able to directly calibrate testing results to egg supply and mathematically optimize the combination of results to provide the Egg Supply Score: a single, easy to use assessment of egg supply.

③ Continuous Improvement of Clinical Information Through Clinical Research

The field of fertility medicine is complex and rapidly evolving with hundreds of studies published each year, many of which rely upon diagnostic testing to categorize patients. Therefore, clinicians need a fertility focused laboratory which calibrates to clinical outcome, and maintains the link between the reported test result and new clinical information. ReproSource provides this service. Recent advancements in egg supply testing, especially related to AMH, have important consequences to women’s health. The biggest barrier to the clinical utility of this testing is the frequently changing test methodology, and cut points not calibrated to egg supply. For example, laboratories that provide results for routine tests such as FSH or newer tests such as AMH, generally do not use the same testing methodologies employed in the clinical studies that reported the interpretative ranges of clinical utility. By both conducting clinical outcomes research and providing testing for clinical use, ReproSource provides a reliable source for appropriately calibrated ovarian reserve and other fertility testing used by hundreds of fertility specialists.

References (** ReproSource Publications)**


11. Index outperforms AMH, inhibin B, and FSH in predicting poor egg supply. Leader B, Quinn E, Sullivan L, Yin L, Riggs R, Stadtmueller L. Fertility and Sterility 2008 Sep; 90(1);5263-5264.

