

## Ovarian Assessment Test for Fertility Treatment

### **Background**

Knowledge of how patients' ovaries will respond to the hormone treatment we give during a 'cycle' is an important part of fertility treatment. An excessive response to the hormone drugs we administer increases the chances of suffering the dangerous condition of 'ovarian hyperstimulation syndrome' (OHSS), while an inadequate response is distressing for patients going through 2 to 3 weeks of daily injections resulting in a sub-optimal supply of eggs, or even cancellation of the cycle. Both these scenarios are experienced too frequently when we do not know how a patient is likely to respond. Unfortunately, we cannot avoid either of these end-points completely, but we can now use a test to reliably predict ovarian responses which allows us to modify our approach, resulting in a reduced incidence of both unexpected poor and excessive egg yields.

### The ovarian competence assessment

The test used to give us the information is the ovarian competence assessment which combines the ultrasound measurement of the number of small follicles present in the ovary (the antral follicle count: AFC), the total ovarian volume, and the concentration of the hormone "Anti-Mullerian Hormone" (AMH) in the blood. The ovarian follicles are the structures that contain the eggs. Using this information we can predict the likely response to a standard treatment programme, and therefore adapt the treatment modality according to the indicated best approach.

### Modified Strategies

Until recently, a patient would have to go through a complete treatment cycle before the best process could be determined, which would then be used in further treatment cycles. The ovarian competence assessment allows us to deploy different strategies in both poor and excessive responders for the first treatment cycle – with confidence.

### Poor responder women

Women who are likely to respond poorly to standard stimulation do so because their ovaries contain few eggs at advanced stages of development, (a low AFC, and AMH) as occurs when nearing the menopausal years of life. They respond poorly to standard treatment protocols, despite using large quantities of the hormone drugs, because there are simply insufficient follicles able to respond to the hormone treatment. There are different strategies which can be adopted.

We must acknowledge that these patients will not yield the 'normal' quantity of eggs – despite still having normal menstrual rhythm. Therefore we aim to obtain a more modest quantity of eggs through less stressful and less expensive methods.

### Excessive responder women

These patients have large numbers of follicles becoming hormone sensitive each day, and are at increased risk of developing OHSS after 2 weeks of hormone treatment. A shorter treatment cycle, controlled by a GnRH-antagonist (Cetrotide) is the usual approach to these cases. They can also be treated simultaneously with the drug metformin which can reduce the risk and severity of OHSS.

**“Anti-Mullerian Hormone” (AMH)**

The best single indicator of responses to fertility drugs is AMH. The information below explains how it is used here at GCRM, and it can provide you with knowledge to help make important decisions.

**The ultrasound scan**

The other component of the assessment is an ultrasound scan of the ovaries. This is used to examine a number of parts of the abdomen to check for the presence of cysts caused by endometriosis or cystic structures associated with the Fallopian tubes (hydrosalpinges), all of which can interfere with fertility, and influence the outcome of IVF. The detailed examination of the ovaries allows us to count the number of small follicles present (AFC), assess the ovarian volume, and check if there are indication of polycystic ovary syndrome. All of these are important pieces of information for us to have before we start treatment.

**THE CLINICAL VALUE OF AMH (anti-Mullerian hormone)**

It is now established that the hormone AMH (Anti-Mullerian Hormone) which is made by the ovarian follicle containing the egg, can tell us how a woman’s ovaries can respond to fertility drug treatment.

In young women, many eggs start to grow each day, and quite large numbers reach the final stages of development, where they can respond to fertility drugs. These women have high AMH values. In older women, there are fewer eggs left in the ovary, and few will reach these latter stages of development, and the AMH level will be low. The normal population has a considerable variation in AMH values and this is reflected in the wide range of responses to fertility drugs. Effectively, the blood level of AMH can tell us how many follicles (eggs) will be available when follicle stimulating hormone (FSH) is given.

A high value indicates a risk of excessive responses, and a very low value informs us that a patient should not undergo ovarian stimulation.

**When the AMH concentration is high**, it predicts excessive responses (see above) and indicates a risk of hyperstimulation syndrome when traditional treatment methods are used. We can modify our strategy to reduce this complication. If the scans, and other tests, show indications of polycystic ovary syndrome (PCOS), we can modify our treatment strategy and may recommend the use of another drug to further reduce risks.

**When the AMH concentration is low**, it indicates that the response to traditional treatment methods will be below average, and therefore the chances of success in IVF / ICSI will be reduced. This is common in older women (>37y), where it is well known that success rates are reduced. However, the predictive value of AMH is considerably better than a patient’s age. We use treatment strategies which achieve expected pregnancy rates with lower treatment burden than conventional protocols.

**TABLE OF INDICATOR CONCENTRATIONS OF AMH IN THE BLOOD**

Value (pmol/L)	Indication
>20	High responses to ovulation drugs expected <ul style="list-style-type: none"> <li>– risk of ovarian hyperstimulation syndrome</li> <li>– high pregnancy potential</li> </ul>
5 to 19.9	A normal response to drugs expected <ul style="list-style-type: none"> <li>– Low risk of ovarian hyperstimulation syndrome</li> <li>– Low risk of cycle cancellation</li> <li>– Good pregnancy potential</li> </ul>
1.0 to 4.9	Reduced responses to ovulation drugs. <ul style="list-style-type: none"> <li>– Expected yields of 1 to 6 eggs (normal average = 10 eggs)</li> </ul>
<1.0	Negligible responses to ovulation drugs. <ul style="list-style-type: none"> <li>– Treatment with own eggs rarely recommended.</li> </ul>

**GUIDE to the VALUE of AMH in PATIENTS UNDERGOING IVF / ICSI at GCRM**

(% values are outcomes as a proportion of all cycles started)

**Evaluation by Age and AMH category**

Age Group	AMH (pmol/L)	Treatment Information	CPR* (%)
<35y	≥ 5	AMH often greater than 15 pmol/L: High responder protocol often used – ie control with GnRH-antagonist - potential risk of OHSS - Twin rate >25 % (eSET reduces this)	45
	< 5	Reduced responder protocol used – ie control with Flare_ Agonist - negligible risk of OHSS	19
35 to 37y	≥ 5	Normal responder protocol usually used – ie control with GnRH-agonist - low risk of OHSS - Twin rate = 25 %	41
	< 5	Reduced responder protocol used – ie control with Flare_ Agonist - negligible risk of OHSS - Twin rate = 10 %	22
38 and 39y	≥ 5	Normal responder protocol usually used – ie control with GnRH-agonist - low risk of OHSS - Twin rate = 12 %	31
	< 5	Reduced responder protocol used – ie control with Flare_ Agonist - negligible risk of OHSS - Twin rate = 10 %	14
40 to 42y	≥ 5	Normal responder protocol usually used – ie control with GnRH-agonist - negligible risk of OHSS - Twin rate = 20 %	22
	< 5	Reduced responder protocol used – ie control with Flare_ Agonist - negligible risk of OHSS - Twin rate = 0 %	13
≥ 43y		Reduced responder protocol usually used – ie control with GnRH-antagonist - negligible risk of OHSS - Twin rate = 0 %	<5

- CPR = Clinical pregnancy rate – defined as foetal heart beat at 7 weeks as a proportion of the number of cycles started.

## **IMPLICATIONS OF LOW AMH VALUES.**

A low AMH value tells us that a patient will respond to fertility drugs with only a small number of eggs – or even none.

It does not tell us that she is at the menopause.

Some studies have suggested that a low AMH value tells us that the menopause is imminent, but recent studies have revealed that there is wide variation in older women, and that a low value is not a good marker for the menopause. On average, a woman with a low AMH value will enter the menopause before a woman with a high value. However, It is possible for a woman to maintain a normal menstrual pattern for some years after her AMH value is recorded as 'low'. On average, advancing age is associated with low AMH, but individual variation makes prediction imprecise.

As a woman gets older, over 37years, the ability of each egg to fertilize and implant declines dramatically. At 37 years this ability is approximately 30%, but over the next 6 years the effective ability for each normal egg declines to around 5%.

It is logical therefore that women of the older age-groups will require more eggs than younger women to achieve a pregnancy. Unfortunately, nature has provided the worse combination of lower number and lower quality. Therefore, older women should only consider treatment if they have a reasonable chance of producing at least 2 or 3 eggs.

AMH does not tell us about the quality of the eggs that we can obtain – only the number. This is a valuable piece of information for patients assessing their chances, and the table above helps in that guidance.