Ovarian reserve testing
What is the ovarian reserve?

The number of eggs + The quality of eggs = Ovarian reserve

Ovarian responsiveness

Reproductive potential
Women’s chronological age is the most important factor in predicting reproductive potential
Number of eggs & Age

The age-related decrease in the number of primordial follicles (PF) within both human ovaries from birth to the menopause.

Why do we assessing ovarian reserve?

- Get more information for infertile couples
- Make decision about treatment options and expectation
- Prediction of ovarian response before ART
Methods assessing ovarian reserve
Correlated hormones for testing

Hypothalamus

Pituitary gland

GnRH

GAST

CCCT

EFORT

Ovary

FSH

Estrogen &
Inhibin

AMH
Ultrasound parameters of ovary

- Ovarian volume
- Ovarian blood flow
- AFC (Antral follicle count)
Ovarian reserve tests (ORT)

- Biological
  - Chronological Age
- Biochemical
  - Static
  - Dynamic
- Biophysical
- Histological
  - Ovarian Biopsy

Basal FSH

- Most widely use: easy, inexpensive
- On day 3 of menstrual cycle
- Diurnal, intra- and inter-cycle variability

- Normal reproductive potential
  FSH levels <10 IU/L
  Borderline 10-15 IU/L
- Failure to achieve live birth if level > 18 IU/L
Day 3 estradiol levels

- Combination with day 3 FSH level
- Check for accuracy of FSH level
- Day 3 estradiol level >60-80 pg/ml with normal FSH: negative feedback
  - Poor ovarian response
  - High cancelation rates
  - Lower pregnancy rates
Day 3 inhibin-B levels

- Hetereodimeric glycoprotein
- From granulosa cells
- Poor ovarian response to IVF
  Day 3 inhibin-B < 45 pg/ml
- Highly intra- and inter-cycle variability
- Routine use of inhibin-B as a measure of ovaria reserve is not recommended
AMH levels

- Mullerian inhibiting substance (MIS)
- Glycoprotein dimers consisted of 72 KD monomers (linked by disulphide bonds)
- Member of TGF superfamily
- No intra- and inter-cycle variability

Source: Clinical Endocrinol © 2006 Blackwell Publishing
AMH is produced by granulosa cells from growing follicles (primary to early antral follicles)

La Marca A et al. Hum Reprod Update 2010
AMH levels

- Chronological aging associated with low AMH levels

  Limit utility in PCOS and obesity

- High in PCOS
  - Poor follicular development
  - High risks of OHSS

- Decrease 70% in obesity

AMH: Anti-Mullerian Hormone. amh-test.com
ROC curve of AMH at time of presentation and live births involving 507 IVF cycles in 295 women with DOR

- ROC curves at ages 30–35, 36–40, and >40 years, all demonstrating the same point of maximal inflection between lower and higher live births.
- The value of 1.05 ng/mL thus represents a uniform cutoff between lower and higher live-birth chance, independent of age.

Norbert Gleicher. Fertil Steril. 2010
Clomiphene citrate challenge test (CCCT)

- Clomiphene citrate 100 mg/day on day 5-9 of menstrual cycle
- Day 3 and day 10 FSH levels
- Day 10 increase 10-22 IU/L = poor responders
GnRH agonist stimulation test (GAST)

- Triptorelin 100 micrograms on day 2 (subcutaneous)
- Day 2 and day 3 estradiol levels
- Rising of day 3 estradiol = good ovarian reserve
- Not superior to inhibin-B
Exogenous FSH ovarian reserve test (EFORT)

- FSH 300 units on day 3
- Day 3 FSH and estradiol levels
- Day 4 estradiol level
- Rising of day 4 estradiol = predict hyper responder
Antral follicle count (AFC)

- Antral follicles decline with age
- AFC predicts egg recovery at IVF

Female Fertility Screening Tests. advancedfertility.com

HSIEH, CHANG & TSAI 2001
- Women under 35: highest success rates in all of the "egg number" groups
- Women under 38: have acceptable live birth rates even with only 3 - 6 eggs, do better with >6 eggs, and do best with >10 eggs.
- Women 38-40 and 41-42 years old have low live birth rates with low egg numbers. Success rates are much better when relatively high egg numbers are obtained.
- All age groups have very low success rates with < 3 eggs retrieved.
Antral follicle count (AFC)

- Easy to measure
- Some variation between measurements
- Primarily reflects number of eggs recovery
- Related to outcome (quality)
Mean ovarian volume

- Ovarian volume
  \[ = D1 + D2 + D3 \times 0.52 \]
- Low ovarian volume: < 3 ml
  (high specificity: 80-90%)
- Limited value for detection of poor ovarian reserve
- AFC is better predictor
## The practice committee of ASRM: a committee opinion (2012)

<table>
<thead>
<tr>
<th>Test</th>
<th>Cutoff</th>
<th>Poor response (%)</th>
<th>Nonpregnancy (%)</th>
<th>Reliability</th>
<th>Advantage</th>
<th>Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FSH (IU/L)</strong></td>
<td>10-20</td>
<td>10-80</td>
<td>83-100</td>
<td>Limited</td>
<td>Widely use</td>
<td>Limitation of reliability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td></td>
<td>Low sensitivity</td>
</tr>
<tr>
<td><strong>AMH (ng/ml)</strong></td>
<td>0.2-0.7</td>
<td>40-97</td>
<td>78-92</td>
<td>Good</td>
<td>Reliability</td>
<td>Limit of detectibility</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 commercial assay</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Does not predict nonpregnancy</td>
</tr>
<tr>
<td><strong>AFC (n)</strong></td>
<td>3-10</td>
<td>9-73</td>
<td>73-100</td>
<td>Good</td>
<td>Reliability</td>
<td>Low sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Widely use</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inhibin-B (pg/ml)</strong></td>
<td>40-45</td>
<td>40-80</td>
<td>64-90</td>
<td>Limited</td>
<td></td>
<td>Reliability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Does not predict nonpregnancy</td>
</tr>
<tr>
<td><strong>CCCT, day 10 FSH (IU/L)</strong></td>
<td>10-22</td>
<td>35-98</td>
<td>65-98</td>
<td>Limited</td>
<td></td>
<td>Limitation of reliability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Higher</td>
<td></td>
<td>Higher sensitivity than basal FSH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>sensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>than basal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FSH</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Limited</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>additional</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>value to basal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FSH</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Requires drug</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>administration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Practice committee testing and interpretation measures of ovarian reserve. Fertil Steril 2012
Summary

• Age is an important factor in DOR

• All tests are designed to predict a woman’s ovarian response

• The purpose of ORT is to more accurately evaluate a couple’s chance of success with any given treatment, particularly IVF
No 100% accuracy of single ORT

Try to integrate all the test results together and give the best treatment options available
Thank you