Antimullerian hormone (AMH)

Clinical information:

AMH is useful for:
- Assessment of ovarian reserve, including assessment of premature ovarian failure (such as in patients with Turner syndrome or treated with gonadotoxic cancer treatments)
- Prediction of ovarian responsiveness to assisted reproductive treatments
- A surrogate marker for antral follicle count in the assessment of polycystic ovarian syndrome (PCOS)
- Assessment of infants with disorders of sexual differentiation
- Evaluation of testicular function in infants/children
- Monitoring of granulosa cell tumours of the ovary

Antimullerian hormone (AMH) is produced by the granulosa cells of the ovary, and Sertoli cells of the testis.

In females AMH is produced by small growing follicles, and is correlated closely with age and antral follicle count. During infancy/early childhood there is a slight positive correlation with age, AMH levels are then relatively stable from mid childhood to early adulthood. From age 25 there is a strong inverse correlation with age, becoming undetectable by the time of menopause.

In males, longitudinal data shows that levels increase in the first few months of life, with a peak corresponding to mini-puberty. AMH levels subsequently decline and remain relatively stable from 12 months until puberty. During puberty AMH declines with increasing age, more steeply with increasing testicular volume to reach levels <5% of those during infancy. AMH then remains stable through late adolescence and adulthood. AMH is undetectable in anorchid males.

Reference intervals:

Adults:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age/Tanner stage</th>
<th>2.5th percentile</th>
<th>97.5th percentile</th>
<th>units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>20y to &lt;25y</td>
<td>8.7</td>
<td>83.6</td>
<td>pmol/L</td>
</tr>
<tr>
<td></td>
<td>25y to &lt;30y</td>
<td>6.35</td>
<td>70.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30y to &lt;35y</td>
<td>4.11</td>
<td>58.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>35y to &lt;40y</td>
<td>1.05</td>
<td>53.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40y to &lt;45y</td>
<td>0.19</td>
<td>39.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45y to &lt;51y</td>
<td>0.1</td>
<td>19.3</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>18y to &lt;110y</td>
<td>10.2</td>
<td>82.8</td>
<td>pmol/L</td>
</tr>
</tbody>
</table>

Children:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age/Tanner stage</th>
<th>2.5th percentile</th>
<th>97.5th percentile</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>Newborn (0 to 60 days)</td>
<td>0</td>
<td>24</td>
<td>pmol/L</td>
</tr>
<tr>
<td>Males</td>
<td>Newborn (0 to 60 days)</td>
<td>108</td>
<td>1903</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tanner stage 1</td>
<td>35</td>
<td>1032</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tanner stage 2</td>
<td>36</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tanner stage 3</td>
<td>19</td>
<td>542</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tanner stage 4</td>
<td>3</td>
<td>144</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tanner stage 5</td>
<td>14</td>
<td>151</td>
<td></td>
</tr>
</tbody>
</table>
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Source of reference intervals:

Adults: Roche AMH package insert.


Children:
Reference intervals are based on a study by Demirdjian et al (2016) using the Access AMH assay. There is evidence that the method used to test AMH in this study has good agreement with the Roche AMH assay, however reference intervals have not been verified locally and therefore can be used as a guide only when interpreting results.


Interpretation of results

Ovarian Reserve
AMH is very low or undetectable in menopausal women or those with premature ovarian failure. An abnormally low AMH may be helpful in the diagnosis of premature ovarian failure. AMH is also used as a marker of ovarian reserve in healthy women to assist with family planning. However, a normal result may only provide reassurance about the size of the cohort of growing follicles, while there are a number of other factors effecting the fertility, including the quality of the oocytes.

PCOS
Although not diagnostic, the correlation of AMH with antral follicle count has led to an argument that AMH could provide a useful surrogate for antral follicle count by transvaginal ultrasound in the assessment of PCOS. AMH concentrations have been found to be on average 2-3 times higher in patients with PCOS at all ages, however there is some overlap with the normal range.

Assisted reproduction
In patients being assessed for assisted reproductive therapies, AMH has been reported to help predict response to ovarian stimulation. With lower values, predicting a poor response, while higher levels predict an increased risk for ovarian hyperstimulation syndrome and therefore may warrant closer monitoring, or reduced doses of gonadotropin.

Chemotherapy effects
AMH has been used to assess chemotherapy and radiation induced gonadal damage in women and prepubertal girls undergoing treatment for cancer. A number of chemotherapeutic agents are gonadotoxic (particularly alkylating agents) resulting in increased risk of premature ovarian failure. AMH has been shown to fall rapidly after chemotherapy is commenced with variable recovery following treatment, depending (together with other factors) on the nature and dose of the chemotherapeutic agents used. Higher pre-treatment AMH levels have been shown to be predictive of higher AMH levels and recovery of ovarian function following chemotherapy. Following chemotherapy, even patients with regular menstrual cycles may have a reduced ovarian reserve as indicated by a reduced AMH compared to healthy women.
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Biological variation
Some studies have demonstrated variation in AMH throughout the menstrual cycle, with higher levels occurring in the follicular phase. Depending on the cut-offs used for assessment of likely poor/excessive response to fertility treatments, this variation may potentially result in different classification of women. Therefore caution should be used when applying these cut offs. Due to variation of results between different AMH test methods cut offs derived from the literature should also be carefully evaluated.

Variation between samples over time may be due to fluctuation during the menstrual cycle, and not necessarily reflect a change in ovarian reserve. This variation does not seem to occur in women with low AMH values, therefore this should not be a factor in the interpretation of low results.

AMH concentration has been demonstrated not to be affected by short term use of oral contraceptives, however several studies have shown lower AMH in users of the oral contraceptive pill. There is also conflicting data on the effect of pregnancy on AMH concentration, with some studies showing reduced concentration.

Disorders of sexual development
In infants/children with disorders of sexual differentiation or cryptorchidism, AMH is useful to determine the presence of absence of testicular tissue. An AMH concentration within the normal male reference limits is indicative of the presence of testicular tissue, while a low or undetectable value suggests anorchia, functional failure of the testis or ovarian tissue. The above provided reference interval for newborns 0-60 days did not provide further subdivision between birth and the time of mini-puberty. AMH levels increase significantly during mini-puberty, and the lower reference limit for this time period would be expected to be higher. A study by L Aksglaede et al (2010), found the 5-95% reference interval was 53-340 pmol/L for cord blood increasing to 749-1930pmol/L at mini-puberty (2.4 to 6 months).

Granulosa cell tumours
Granulosa cell tumors of the ovary may secrete AMH. Measuring AMH in these patients may be used to monitor treatment and indicate tumour recurrence or progression.

Cautions:

High dose biotin therapy may interfere with the immunoassay method used for measurement. Blood samples from patients on high dose biotin (>5mg/day) should not be taken until at least 3 days after the last dose. Heterophilic antibody interferences may also rarely occur, potentially causing erroneous results.

The AMH assay may report false-low results with very high AMH concentrations (hook effect). The Roche AMH assay is reported to be free from high-dose hook effect up to approximately 10,000 pmol/L. (up to 9996pmol/L)

The results should always be assessed in conjunction with the patient’s medical history, clinical examination and other findings. If test results are inconsistent with the clinical picture, please contact the laboratory.

Specimen:

Sample type:
Serum gel tube
Alternative, serum no gel
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Minimum volume:
250 ul of serum (approximately 0.5 ml sample)

Collection requirements:
Sample may be collected at any time of day.

Stability:
5 days at room temp
5 days at 2-8°C
6 months at -20°C

Transport:
Frozen serum (after separation) for samples collected externally.

Send samples to:
Department of Clinical Chemistry and Endocrinology
Level 4 Campus Centre
The Prince of Wales Hospital
Barker Street, Randwick, NSW 2031

Method:
AMH immunoassay, on a Roche cobas e411 analyser.

Testing frequency: Twice weekly on Tuesday and Thursday

Enquiries:

NSW Health Pathology
Department of Clinical Chemistry and Endocrinology
Level 4 Campus Centre
The Prince of Wales Hospital
Barker Street, Randwick, NSW 2031

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I Streuli et al. Serum antimullerian hormone levels remain stable throughout the menstrual cycle and after oral or vaginal administration of synthetic sex steroids. Fertil Steril; 2008; 90:395–400

D Wunder et al. Statistically significant changes of antimullerian hormone and inhibin levels during the physiologic menstrual cycle in reproductive age women. Fertil Steril; 2008; 89:927–933


C Bozza et al. Anti-Mullerian hormone: determination of ovarian reserve in early breast cancer patients. Endocrine-Related Cancer; 2014; 21: R51–R65