



Educational Discussion: Anti-Müllerian hormone (AMH)

2017-B Antimüllerian Hormone (AMH)

The 2017 AMH-B Survey comprised three challenges encompassing a continuation of the previously established analytes for this Survey. The AMH-B Survey challenges are **prepared using a spike of hAMH material**. Results are provided in the AMH-B 2017 participant summary by measurement procedures used by participating laboratories.

Anti-Müllerian hormone (AMH) is a biochemical marker garnering more clinical attention in laboratory medicine. AMH is produced by Sertoli cells of the testes in males and by ovarian granulosa cells in females. It is expected that AMH reference intervals for normal males and females will exhibit the highest differences early in life. Expression of AMH in the male fetus prevents Müllerian duct development, and subsequently, promotes male reproductive tract development *in utero*. In the absence of AMH, Müllerian ducts develop into female internal genitalia.

AMH measurement has been shown to assist in the clinical assessment of infants with ambiguous genitalia. Studies evaluating the intersex conditions in children demonstrate that AMH concentrations reflect the function of Sertoli cells, and are often assessed with other clinical findings and testosterone measurement. In males, AMH concentrations have also been shown to distinguish undescended testes, which have normal male AMH concentrations, from anorchia, which have extremely low or undetectable AMH concentrations. Testicular dysgenesis is characterized by low concentrations of both AMH and testosterone compared to normal males. AMH has also been studied in conjunction with the measurement of FSH, LH, and testosterone for precocious and delayed puberty in adolescent males.

At birth, levels of AMH are undetectable in females, and slowly begin to increase, reaching a maximum level after puberty, until progressively declining to undetectable levels by menopause. After puberty in females, AMH concentrations are ovarian cycle-independent, tightly correlated with antral follicle count (AFC), and have been demonstrated to be reflective of the size of the remaining egg supply. Therefore, AMH is a clinically attractive tool for the early identification of decreasing ovarian reserve and timely referral of patients to fertility clinics, as well as assessing ovarian reserve to help identify patients most likely to respond to assisted reproductive technologies (ART). Approximately 11% of women are estimated to use some form of fertility service, thus additional diagnostic tools, such as AMH measurement, may provide important information that has the potential to improve outcome and reduce missed fertility opportunities. As a woman ages, the concentration of AMH will fall to undetectable levels at menopause and most determinations of AMH in females is primarily to provide an assessment of menopausal status, including premature ovarian failure. Additional clinical uses of AMH in assessing polycystic ovary syndrome (PCOS) have been demonstrated. However, to our knowledge there are no consensus guidelines for using AMH in this clinical context.



There is currently no international standard reference material or reference measurement procedure for AMH, and no consensus on the threshold value of AMH suggestive of reduced fertility potential. Therefore, a clinician's interpretation of AMH values should always be guided using reference intervals from the laboratory testing their patient's sample. However, in general, it is accepted clinically that a reciprocal relationship exists between AMH concentration and inadequate ovarian reserve. As AMH concentrations decrease, the probability of diminished ovarian reserve progressively increases. A level well-above normal suggests adequate ovarian reserve. The levels targeted for the AMH Survey challenges represent relevant concentrations observed in clinical practice. Consider the results for challenge AMH-06 in the AMH-B 2017 Survey. If using these values to assess reduced fertility potential, the results (depending on the laboratory's reference intervals) could suggest adequate ovarian reserve and likely a good response to ovarian stimulation. In contrast, the results for challenge AMH-04 could suggest a reduced ovarian reserve. In general, the analytical concordance of results across method peer groups in the AMH-B 2017 Survey is good. It is also interesting to note the largest CV and spread across AMH results was observed in the ELISA method peer group, which may be due to the manual steps in the ELISA process causing an increase in result variability.

The importance of AMH in providing insight clinically cannot be understated. It is involved in sex differentiation during fetal development and can be used in assessing testicular presence and intersex conditions. In women it is a very useful marker for ovarian dysfunction and provides important information regarding ovarian reserve, ovarian response as well as progression of menopause. Future CAP AMH Surveys will strive to challenge higher, clinically relevant, AMH concentrations.

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