**Anti-Mullerian Hormone (AMH)**

**Fertility and Age**

The average age of first pregnancy in Australia is now over 30 years and over 20% of births are to women aged over 35. Fertility peaks in the early 20s and declines from the 30s to menopause. There is, however, large inter-individual variability; some women remain fertile significantly longer. Media attention is now focussed on Anti-Mullerian Hormone (AMH) in the hope this test can predict both current and future fertility, and thus allow postponement of pregnancy.

**AMH and Ovarian Reserve**

AMH, like antral follicle count (AFC) is a good measure of ovarian (follicular) reserve. Primordial follicles (the vast majority) mature sequentially via primary, pre-antral, antral, large antral stages and finally form a preovulatory (dominant) follicle.

AMH is produced by granulosa cells in primary, pre-antral and particularly small antral (<5mm) follicles and conserves the immature follicular pool by (a) inhibiting conversion of primordial to primary follicles and (b) inhibiting the (FSH stimulated) conversion of small antral to large antral follicles (see Figure 1).

The pool of AMH secreting follicles is proportional to the pool of primordial follicles; thus AMH levels usually reflect total ovarian follicular reserve.

Other blood tests (e.g. FSH, oestradiol and inhibin B) are unreliable and insensitive at predicting ovarian reserve as they only reflect large antral and preovulatory follicular function and thus only become abnormal late in ovarian ageing.

AMH levels parallel fertility; rising during puberty, peaking in the early 20s, and falling from 30 years on to undetectable levels post menopause.

The log scale on the y axis (Figure 2) is necessary to show the more than 40 fold decline in levels with ageing and the wide variation of AMH levels at 35-40 years age.

**Additional advantages of AMH over other markers**

AMH levels are remarkably stable in the short term and are only minimally affected by the menstrual cycle, oral contraception or pregnancy, thus blood samples can be taken at any time (unlike oestradiol, FSH and inhibin B levels). Commercial assays are now available in Australia (not reimbursed by Medicare). Unlike AFC, the levels are not affected by observer bias or inter-cycle variation.

![Figure 1. Ovarian Follicle Development](image1.png)

Adapted from Broekmans et al, Trends in Endocrinology and Metabolism vol. 19, No. 9, 2008

![Figure 2. The variation of AMH levels for women from 25-50 years.](image2.png)

Adapted from van Disseldorp et al J Clin Endocrinol Metab 93:2129-2134:2008
Present and future clinical roles for AMH

• **Role in predicting fertility**: As AMH is a new test, there are not yet prospective studies measuring AMH in the same individuals over time and current data consists of cross-sectional studies of AMH in different age groups. As a result, there is no confident ability to predict future fertility and onset of menopause from an individual’s AMH levels, and use for this purpose is generally premature. A low level would, however, indicate that attempted pregnancy should not be delayed and that if unsuccessful, referral for assisted reproductive technology (ART) should be prompt.

• **Role in ART**: Low AMH levels reliably predict a poor oocyte response (i.e. few oocytes retrieved) and also poor oocyte quality, and may be used to select a higher FSH stimulation dose; high AMH levels predict ovarian hyperstimulation syndrome and thus a lower FSH dose is favoured. AMH may also guide ART choices by providing a ‘reality check’ on likely ovulation success.

• **Role in PCOS**: AMH levels are 2-3 times higher in PCOS than in age matched controls (reflecting the 6x greater number of pre-antral follicles in PCOS) and levels decline less in PCOS with age (reflecting delayed ovarian ageing and delayed onset of menopause in PCOS); the elevated AMH may prevent follicular pool depletion. AMH elevation correlates with PCOS severity and is predictive of insulin resistance and anovulation. AMH may be useful to diagnose PCOS (67% sensitive, 92% specific) if AFC is unavailable. Lower baseline AMH levels predict a favourable response of menstrual irregularity to weight loss and also ovulation response to clomiphene. Metformin reduces both AMH and the number of antral follicles, thus AMH can be used to evaluate treatment with insulin sensitiser.

• **Role in premature ovarian failure**: This affects about 1% of women. AMH levels are low in the incipient failure stage (i.e. 3-10 years before cycle irregularity occurs). AMH is useful in differentiating amenorrhoea due to functional hypothalamic hypogonadism (normal levels) from ovarian failure (low levels).

• **Role post chemotherapy**: AMH helps guide fertility preservation strategies better than FSH levels can.

• **Synthetic AMH**: In the future, AMH may find uses in contraception or in delaying ovarian ageing.

Clinipath Pathology is pleased to be able to offer the AMH assay and the fee for this non-rebatable test under Medicare is $60.

**References available on request.**

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