bioscientia

lab.bulletin

Nr. 2/2008

Anti Mullerian Hormone (AMH) is an indicator of ovarian functional reserve

Marc Beineke

Anti Mullerian Hormone (AMH), also called Mullerian Inhibiting Substance (MIS), is a homodimeric glycoprotein from the TGFβ family. It plays a major role in cell growth and differentiation. With a molecular weight of 140 kDa, it is four times larger than LH or FSH.

Physiology of AMH's action

AMH plays a role in gender differentiation during embryo development.

Under the influence of the AMH formed in the Sertoli cells, the Mullerian ducts degenerate in male fetuses. This leads to the normal development of the male genitals. Female fetuses do not have AMH, and so develop the internal female genital organs.

In women, at the onset of puberty AMH, like inhibin B, is formed by the granulosa cells of the maturing ovarian follicle, but not by the primordial follicles and also not by the antral follicles under direct FSH regulation in the final stage of follicular growth. AMH is the biological regulator of folliculogenesis and of primordial follicular rupture. It reduces the rate of follicle conversion from the primordial to the growing stage and regulates follicle growth by inhibiting FSH-induced conversion from the early to the late stage (Fig. 1) [1].

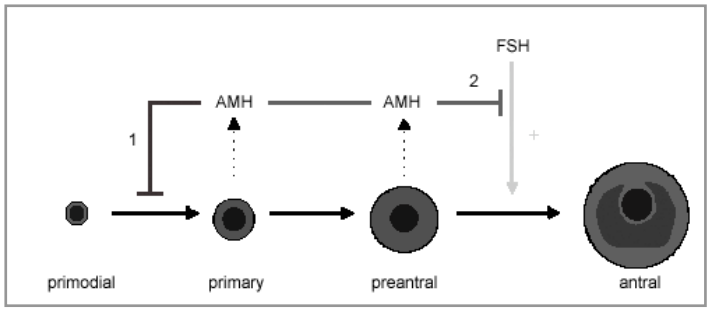

Fig. 1: Formation and action of AMH, from [4]

Clinical significance and indications

AMH is an ideal marker for ovarian functional reserve because it is formed only by the primary follicles, which are potentially capable of maturation, and the secondary follicles. There is thus a very good correlation between the serum AMH level and the number of follicles potentially capable of maturation and thus also the ovarian functional reserve [2, 3].

In women over 30 and particularly those over 35 years of age, AMH can be used as a screening test to assess fertility status. Women wishing to have children can thus be assisted in their family planning [4].

As regards the rate of response to ovarian stimulation, AMH is of much greater value than inhibin B [2]. In addition, AMH is not subject to the same cycle-dependent fluctuations as inhibin B and FSH in the assessment of ovarian functional reserve.

AMH can thus be used at any point during the menstrual cycle, whereas days 3-5 of the cycle should be selected when testing FSH and inhibin B [5, 6].

The AMH level falls continuously with increasing age, corresponding to the loss of ovarian functional reserve; a significant decrease is detectable considerably earlier than a clear rise in FSH [2].

Reduced levels point to restricted ovarian functional reserve and a poor response to ovarian stimulation. Over 80% of women show reduced ovarian functional reserve, with a level of < 1 µg/l, and an inadequate ovarian response to stimulation is seen in 90%. For this reason, patients with low AMH levels require much higher rFSH doses for stimulation than women with normal or high levels [6].

Patients who developed Ovarian Hyper Stimulation Syndrome (OHSS) during stimulation treatment were found to have levels six times higher than those in normal controls [7]. The AMH concentration should therefore be determined before every IVF/ICSI treatment. This allows treatment to be tailored to the individual [4, 8, 9].

With AMH levels of < 0.025 µg/l the patient is already in the infertile phase [10]. With AMH levels of < 0.1 µg/l, IVF treatment is no longer advisable. With AMH levels of < 0.5 µg/l, a maximum of 2 oocytes can generally be obtained on stimulation with an adjusted, increased dose of rFSH [4].

Clearly elevated AMH concentrations are measured in the serum of patients with PCO (Polycystic Ovaries) syndrome. The concentration is also greatly increased in anovulatory cycles.

AMH suppresses follicle growth in the ovaries. The increased formation of AMH in cystic ovaries could be partly responsible for the failure of follicle growth and ovulation [11, 12, 13].

AMH level in women	
Fertile phase	1.0-8.0 µg/l
Reduced fertility	< 1.0 µg/l
Infertile phase	< 0.025 µg/l

Table 1: With AMH levels below 1 µg/l, over 80% of all women have reduced ovarian functional reserve

The analysis of AMH in combination with the analysis of inhibin B and other tumour markers may be useful in the treatment and follow-up of granulosa cell tumours after surgical tumour removal.

Use of AMH in males

In males, the determination of AMH may be useful in the investigation of gonadal function, the differential diagnosis of intersexuality and cryptorchidism/anorchism and in the diagnosis of precocious/late puberty. AMH can be used to detect the presence of testes in cryptorchidic boys [14].

AMH – possible clinical applications

Patient group	Application
Women of reproductive age	■ Assessment of the ovarian reserve ■ Prognostic factor for IVF ■ Assessment of the stimulability of the ovaries and adjustment of hormonal stimulation ■ Perimenopause ■ Premature ovarian failure (POF) ■ Follow-up of granulosa cell tumour, detection of ovarian toxicity in chemotherapy ■ Assessment of ovarian response in obesity and PCO ■ Identification of patients at increased risk of OHSS
Men	■ Male infertility, testicular function
Children	■ Gonadal function in prepubertal children (cryptorchidism, gender differentiation, onset of puberty, etc.)

Table 2: AMH measurement provides information about a range of clinical conditions [8]

Reference range:

Adult women, fertile phase: 1-8 µg/l
Values > 1 µg/l indicate adequate residual ovarian function.

For age-dependent reference ranges for girls and boys and for men, see individual reports or available on request

Material:

2 ml serum, FROZEN.

Author:

Dr. Marc Beineke, M.D., MSc.
Clinical Pathologist

Published by:

Bioscientia
Institute für Medizinische Diagnostik GmbH
Konrad-Adenauer-Strasse 17
55218 Ingelheim, Germany
Tel. +49-6132-781 – 203/224/165
Fax + 49-6132-781 – 236
Email: int.support@bioscientia.com
www.bioscientia.com

References

1) Durlinger A L et al.: Regulation of ovarian function: the role of anti-Müllerian hormone. Reproduction 124: 601–609, 2002.
2) de Vet A et al.: Antimüllerian hormone serum levels: a putative marker for ovarian aging, Fertil Steril 77(2): 357–62., 2002.
3) Visser J A et al.: Anti-Müllerian hormone: a new marker for ovarian function. Reproduction 131: 1–9, 2006.
4) Gnoth C et al.: Relevance of anti-Mullerian hormone measurement in a routine IVF program. Human Reprod. 23: 1359–65, 2008.
5) Tsepelidis S et al.: Stable serum levels of anti-Müllerian hormone during the menstrual cycle: a prospective study in normo-ovulatory women. Human Reproduction 22: 1837–1840, 2007.
6) La Marca et al.: Serum anti-Mullerian hormone throughout the human menstrual cycle. Human Reproduction 21: 3103–3107, 2006.
7) Nakhuda GS et al.: Elevated serum müller-inhibiting substance may be a marker for ovarian hyperstimulation syndrome in normal women undergoing invitro fertilization. Fertil Steril 85: 1541–1543, 2006.
8) Nelson SM et al.: Serum anti-Müllerian hormone and FSH: prediction of live birth and extremes of response in stimulated cycles – implications for individualization of therapy. Human Reprod 22: 2414– 421, 2007.
9) Ebner T et al.: Basal level of anti-Müllerian hormone is associated with oocyte quality in stimulated cycles. Human Reprod 21: 2022-2026, 2006.
10) Katzorke T.: AMH – ein neuer ovarieller Marker mit zunehmender klinischer Bedeutung. Frauenarzt 49: 406–408, 2008.
11) Chu MC et al.: Müllerian-inhibiting substance reflects ovarian findings in women with polycystic ovary syndrome better than does inhibin B. Fertil Steril 84: 1685–1688, 2005.
12) Cook C et al.: Relationship between serum müller-inhibiting substance and other reproductive hormones in untreated women with polycystic ovary syndrome and normal women. Fertil Steril 77: 141– 146, 2002.
13) Pellat L et al.: Granulosa cell production of antimüllerian hormone is increased in polycystic ovaries. J Clin Endocrinol Metab 92: 240 – 245, 2007.
14) Muttukrishna S et al.: Serum anti-Müllerian hormone and inhibin B in disorders of spermatogenesis. Fertil Steril 88: 516-518, 2007.