Age-related normograms of serum antimüllerian hormone levels in a population of infertile women: a multicenter study

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Objective: To produce age-related normograms for serum antimüllerian hormone (AMH) level in infertile women without polycystic ovaries (non-PCO).
Design: Retrospective cohort analysis.
Setting: Fifteen academic reproductive centers.
Patient(s): A total of 3,871 infertile women.
Intervention(s): Blood sampling for AMH level.
Main Outcome Measure(s): Serum AMH levels and correlation between age and different percentiles of AMH.
Result(s): Age-related normograms for the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of AMH were produced. We found that the curves of AMH by age for the 3rd to 50th percentiles fit the model and appearance of linear relation, whereas the curves of >75th percentiles fit cubic relation. There were significant differences in AMH and FSH levels and in antral follicle count (AFC) among women aged 24–33 years, 34–38 years, and ≥39 years. Multivariate stepwise linear regression analysis of FSH, age, AFC, and the type of AMH kit as predictors of AMH level shows that all variables are independently associated with AMH level, in the following order: AFC, FSH, type of AMH kit, and age.
Conclusion(s): Age-related normograms in non-PCO infertile women for the 3rd to 97th percentiles were produced. These normograms could provide a reference guide for the clinician to consult women with infertility. However, future validation with longitudinal data is still needed. (Fertil Steril® 2011;■:■–■. ©2011 by American Society for Reproductive Medicine.)

Key Words: Antimüllerian hormone, ovarian reserve, age, normogram

Received December 6, 2010; revised February 11, 2011; accepted February 25, 2011.
B.A. has nothing to disclose. F.S. has nothing to disclose. S.S. has nothing to disclose. H.H. has nothing to disclose. E.S.-P. has nothing to disclose. A.L.M. has nothing to disclose. S.M. has nothing to disclose. A.B. has nothing to disclose. R.H. has nothing to disclose. S.M.N. has nothing to disclose. J.S.C.-F. has nothing to disclose. T.E.-G. has nothing to disclose. E.J.M. has nothing to disclose. N.R.-F. has nothing to disclose. K.J. has nothing to disclose. M.M. has nothing to disclose. D.W. has nothing to disclose. T.F. has nothing to disclose. L.G.N. has nothing to disclose. J.B. has nothing to disclose. J.P. has nothing to disclose. J.S. has nothing to disclose. C.G. has nothing to disclose. E.G. has nothing to disclose. T.-H.L. has nothing to disclose. M.-S.L. has nothing to disclose. I.L. has nothing to disclose. R.G. has nothing to disclose. T.T. has nothing to disclose.
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TABLE 1

Correlation between the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of serum AMH level and age.

		Serum AMH level (ng/mL)						
Age (y)	No. of samples	3rd	10th	25th	50th	75th	90th	97th
<24	78	0.38	0.72	1.28	2.24	3.67	5.49	7.90
25	40	0.35	0.70	1.25	2.22	3.69	5.56	8.05
26	32	0.33	0.67	1.23	2.21	3.71	5.63	8.20
27	77	0.31	0.64	1.20	2.20	3.73	5.70	8.35
28	83	0.29	0.62	1.18	2.18	3.73	5.75	8.47
29	128	0.27	0.59	1.15	2.16	3.73	5.79	8.57
30	136	0.25	0.56	1.11	2.12	3.71	5.80	8.64
31	172	0.23	0.53	1.07	2.08	3.67	5.77	8.64
32	187	0.21	0.50	1.02	2.01	3.58	5.68	8.55
33	199	0.19	0.46	0.96	1.92	3.47	5.53	8.37
34	259	0.17	0.42	0.90	1.83	3.33	5.34	8.13
35	260	0.15	0.39	0.84	1.73	3.19	5.16	7.88
36	225	0.13	0.36	0.79	1.65	3.07	4.99	7.67
37	195	0.12	0.33	0.74	1.57	2.95	4.84	7.47
38	192	0.10	0.30	0.70	1.49	2.84	4.68	7.25
39	189	0.09	0.27	0.64	1.40	2.69	4.47	6.96
40	120	0.08	0.24	0.58	1.29	2.51	4.18	6.55
41	77	0.06	0.21	0.51	1.16	2.26	3.80	5.97
42	51	0.05	0.17	0.44	1	1.97	3.32	5.25
43	34	0.04	0.14	0.35	0.82	1.63	2.77	4.39
44	22	0.03	0.10	0.27	0.63	1.26	2.15	3.43
>45	14	0.02	0.07	0.18	0.43	0.87	1.50	2.41

Almog. Age-related normogram for antimüllerian hormone. Fertil Steril 2011.

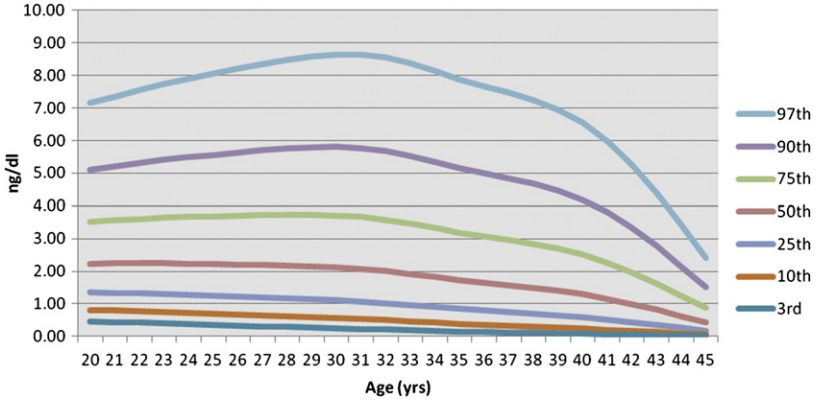
Antimüllerian hormone (AMH) is a member of the transforming growth factor-β superfamily (1). In females it is synthesized in the granulosa cells of preantral and small antral follicles (2–4). Antimüllerian hormone was previously thought to have a sole role in the embryonic life as a male sex differentiation factor (5). Today, it is recognized as a good indicator for ovarian reserve and potential fertility. Several studies have demonstrated the role of AMH to predict the quantitative and qualitative ovarian response in assisted reproductive technologies (ART) (6–19).

Antimüllerian hormone might also be used as a marker for ovarian failure, polycystic ovarian syndrome, ovarian hyperstimulation syndrome, and menopause (20–25). As some women tend to delay procreation and fertility declines with advancing age, ovarian reserve testing is becoming increasingly relevant. In addition, we can now preserve fertility by cryopreserving oocytes and/or embryos.

Ovarian aging is characterized by a gradual decrease in both quantity and quality of the oocytes residing within the follicles.

FIGURE 1

Correlation between the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of serum AMH level and age.



Almog. Age-related normogram for antimüllerian hormone. Fertil Steril 2011.

TABLE 2

Serum AMH and baseline FSH levels and AFC among women of different age groups.

Parameter	24–33 y	34–38 y	>39 y	*P* value (95% CI)[a]	*P* value (95% CI)[b]
AMH level (ng/mL)[c]	2.1 (1.1–3.4)	1.6 (0.8–2.9)	1.1 (0.5–2.3)	<.001 (0.2–0.5)	<.001 (0.2–0.5)
FSH level (IU/L)[c]	6.9 (5.5–8.3)	7.4 (6–9.4)	7.9 (6.2–10.6)	<.01 (0.4–0.9)	<.02 (0.2–0.8)
AFC [c]	11 (8–16)	10 (6–13)	7 (4–11)	.001 (1–3)	<.001 (2–3)

Note: CI = confidence interval.
[a] Age 24–33 y vs. age 34–38 y.
[b] Age 34–38 y vs. age >39 y.
[c] Median (interquartile range).

Almog. Age-related normogram for antimüllerian hormone. Fertil Steril 2011.

The availability of a test able to provide reliable information with respect to a woman's ovarian reserve within a given age category would help the clinician to provide an individually tailored treatment plan and prognosis (26). Different studies in the literature suggest that AMH is a potential marker of the ovarian follicle pool, thus reflecting the ovarian reproductive age (27, 28).

The purpose of our study was to create age-related normograms of AMH that could serve as a clinical tool for consulting infertile women without polycystic ovaries (non-PCO).

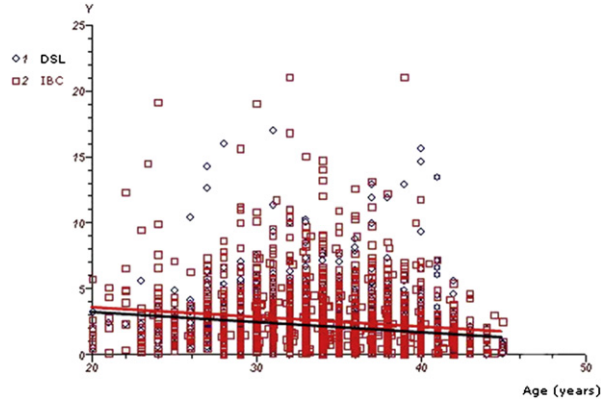
MATERIALS AND METHODS

Our study population included 3,871 infertile women from 15 academic reproductive centers mainly from Europe and North America. Blood samplings of AMH level were on day 3 of the cycle.

As we planned to study non-PCO infertile women, we excluded 1,101 cases with PCO. Exclusion criteria included women whose PCO status was unknown (n = 885) and women who were defined as having PCO by the Rotterdam criteria (n = 216) (29). The remaining 2,770 cases were available for analysis.

FIGURE 2

Grouped linear regression lines of AMH levels by age and by the type of AMH kit (IBC or DSL). Each kit creates a statistically different line parallel to the line of the other kit. The vertical difference between the lines is 0.4 ng/mL, with the IBC AMH kit higher than the DSL kit.



Almog. Age-related normogram for antimüllerian hormone. Fertil Steril 2011.

We created a database using Excel (Microsoft, Redmond, WA). It contained information from 15 reproductive centers on age of the patients, antral follicle count (AFC), baseline (day-3) levels of E_2, FSH, and LH, and AMH. Antimüllerian hormone was measured using either Immunotech–Beckman Coulter (Brea, CA) ELISA (IBC; n = 1,550) or Diagnostic System Laboratories (Webster, TX) (DSL; n = 1220). We converted AMH in SI units (pmol/L) to ng/mL by the conversion factor 7.14.

To construct a model that best described the percentile curves of AMH by age, we used the LMS method, whereby L stands for skewness, M for median, and S for coefficient of variation (30–32). Using LMS software (Institute of Child Health, London, United Kingdom), we constructed the centile curves. For each age, seven empirical percentiles (3rd, 10th, 25th, 50th, 75th, 90th, and 97th) were applied. To evaluate the independent effects of age, AFC, FSH, and the type of kit used for AMH measurements, we performed multivariate stepwise regression analysis.

The normality of data distribution was evaluated using the Shapiro-Wilk test. Because the data were not normally distributed, differences of AMH level, FSH level, and AFC by age group were analyzed using the Kruskal-Wallis test and Mann-Whitney *U* test.

Data were analyzed using the SPSS software package (SPSS, Chicago, IL). The differences were considered significant at $P<.05$.

RESULTS

The correlation between the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of AMH and age is demonstrated in Table 1 and Figure 1. The values presented were adjusted to obtain the minimal deviation for the percentile curves; in other words, the data were normalized to create the best fit to a smoothened curve. We found that the curves of AMH by age for the 3rd to 50th percentiles fit the model and appearance of linear relation, whereas the curves of >75th percentiles fit cubic relation.

Table 2 shows serum AMH, baseline FSH levels, and AFC among women of different age groups. There were significant differences in AMH, FSH levels, and AFC among women aged 24–33 years, 34–38 years, and ≥39 years. The correlation of AMH and age was significant ($P<.001$, $r = -0.15$), albeit with a low correlation coefficient. Higher correlation coefficients were seen between age and AFC ($r = 0.24$, $P<.01$) and FSH ($r = -0.19$, $P<.01$).

Multivariate stepwise linear regression analysis of FSH, age, AFC, and the type of AMH kit as predictors of AMH level showed that all variables were independently associated with AMH level, in the following order: AFC, FSH, the type of AMH kit, and age (Supplementary Table 1). Using group linear regression we found that the regression line of AMH results by IBC was different from

that of results by DSL. The vertical difference of the IBC AMH kit was 0.4 ng/mL higher than DSL (Fig. 2). The proportion of women with very low AMH level (<0.35 ng/mL) ranged from 2.9% at age <24 years to more than 40% at the age >44 years, suggesting decreased fertility with increasing age.

DISCUSSION

Antimüllerian hormone level is a potential predictor for menopause, poor ovarian reserve, and premature ovarian failure (14, 33–40). Unlike FSH, AMH level is independent of the time of menstrual cycle (8). In this study, we produced AMH percentiles normograms in a non-PCO infertile population. We found that the curves of AMH by age for the 3rd to 50th percentiles fit the model and appearance of linear relation, whereas the curves of >75th percentiles fit cubic relation.

The US Centers for Disease Control and Prevention suggest an approach to interpret growth normograms. One measurement is used as a screening tool and a series of measurement as a warning sign (41). This approach could be applied to our results. For example, a single measurement that places AMH level at the 3rd percentile in a 25-year-old woman suggests low ovarian response, whereas a 40-year-old woman with AMH at the 97th percentile indicates otherwise. A series of measurement in a 30-year-old woman showing AMH levels at the 90th percentile, 50th percentile, and then 25th percentile suggests rapidly declining fertility.

Our normagrams may also have an application in prediction and prevention of ovarian hyperstimulation syndrome and in creating individually tailored gonadotropins dose adjustment. We excluded women with PCO because of their higher levels of AMH (three times higher [22]) and higher AFC compared with non-PCO patients. Incorporating PCO results into the analysis would have created significantly higher deviation of the percentiles result and curves.

Our study population did not include normal fertile women. It is possible that their AMH levels are not the same and follow a different normogram. A comparison with such a group could be explored in a future study. At this time we are not aware of a large database of AMH tests results for fertile women.

Antimüllerian hormone levels were independently associated with the following order of variables: AFC, FSH, the type of AMH kit, and age. Currently there are two different kits for AMH measurement, IBC and DSL. The difference between the two assays is due to their dissimilarity in the antibodies, leading to differences in the assay sensitivities. Initial studies have shown that AMH levels seem to be four- to fivefold lower with the DSL assay compared with the IBC assay (42, 43). However, recent studies have demonstrated that the correlation between the two assays is very high (44, 45). We found the difference between the two assays to be 0.4 ng/mL (by grouped linear regression) to 0.5 ng/mL (by multivariate stepwise linear regression). In agreement with others, we found that compared with the DSL kit, the IBC kit resulted in higher levels. However, although developed independently, these assays are now both produced by a single company (Beckman Coulter), therefore suggesting that the methodologic problems mentioned by Bersinger et al. (42) should have been addressed and solved by the assay manufacturer (5).

Current tests of ovarian reserve, including AMH, are designed to predict how a woman is likely to respond to controlled ovarian stimulation and are better considered as evaluating "functional ovarian reserve" (24). It is also important to remember that although certain ovarian reserve tests, such as AMH and AFC, have been linked to the outcome of treatment and pregnancy, they do not predict the quality of oocytes in the ovarian pool, and they do not perform well enough in this respect. Thus couples should not be precluded from having ART on the basis of these tests alone. Women with ovarian reserve tests that imply a significant impairment in their follicle pool still maintain an ability to conceive both naturally and after fertility treatment, but they should be made aware that these chances seem to be reduced compared with women of similar age with more reassuring test results. We hope that the centile charts presented in this article help clinicians demonstrate this by providing patients with a graphic representation of how their results compare with these other women.

The weakness of our study is the use of cross-sectional data, making it difficult to distinguish the behavior of different cohorts over time. Thus, it is possible that the percentile curves merely represent the normal distribution of AMH levels. Accordingly, the analysis of rate of decline may be a rough estimation according to our data. Longitudinal studies are certainly needed to validate our normogram. However, longitudinal studies require a large cohort that could be followed for many years. As a result, other commonly used normograms, such as fetal growth and birth weight curves, are also based on cross-sectional data (30, 46, 47). Another weakness is that there are no data correlating the AMH levels with response to controlled ovarian stimulation, spontaneous pregnancy, and clinical outcome of ART. However, those subjects have been extensively studied (1–25, 48, 49).

We conclude that age-related normograms in non-PCO infertile women show that the curves of AMH by age for the 3rd to 50th percentiles fit a model and appearance of linear relation, whereas the curves of >75th percentiles fit cubic relation. These normograms could provide a reference guide for the clinician to consult women with infertility. However, future validation with longitudinal data is still needed.

REFERENCES

1. Cate RL, Mattaliano RJ, Hession C, Tizard R, Farber NM, Cheung A, et al. Isolation of the bovine and human genes for Mullerian inhibiting substance and expression of the human gene in animal cells. Cell 1986;45:685–98.
2. Weenen C, Laven JSE, von Bergh ARM, Cranfield M, Groome NP, Visser JA, et al. Anti-Müllerian hormone expression pattern in the human ovary: potential implications for initial and cyclic follicle recruitment. Mol Hum Reprod 2004;10:77–83.
3. Visser JA, Themmen APN. Anti-Müllerian hormone and folliculogenesis. Mol Cell Endocrinol 2005;234:81–6.
4. Themmen AP. Anti-Müllerian hormone: its role in follicular growth initiation and survival and as an ovarian reserve marker. J Natl Cancer Inst Monogr 2005;(34):18–21.
5. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artenisio AC, et al. Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). Hum Reprod Update 2010;16:113–30.
6. Seifer DB, MacLaughlin DT, Christian BP, Feng B, Shelden RM. Early follicular serum müllerian-inhibiting substance levels are associated with ovarian response during assisted reproductive technology cycles. Fertil Steril 2002;77:468–71.
7. Van Rooij IAJ, Broekmans FJM, Te Velde ER, Fauser BCJM, Bancsi LFJMM, De Jong FH, et al. Serum anti-Müllerian hormone levels: a novel measure of ovarian reserve. Hum Reprod 2002;17:3065–71.
8. Fanchin R, Schonäuer LM, Righini C, Frydman N, Frydman R, Taieb J. Serum anti-Müllerian hormone dynamics during controlled ovarian hyperstimulation. Hum Reprod 2003;18:328–32.
9. Muttukrishna S, Suharjono H, McGarrigle H, Sathanandan M. Inhibin B and anti-Mullerian hormone: markers of ovarian response in IVF/ICSI patients? BJOG 2004;111:1248–53.

10. Eldar-Geva T, Ben-Chetrit A, Spitz IM, Rabinowitz R, Markowitz E, Mimoni T, et al. Dynamic assays of inhibin B, anti-Mullerian hormone and estradiol following FSH stimulation and ovarian ultrasonography as predictors of IVF outcome. Hum Reprod 2005;20:3178–83.
11. Hazout A, Bouchard P, Seifer DB, Aussage P, Junca AM, Cohen-Bacrie P. Serum antimüllerian hormone/müllerian-inhibiting substance appears to be a more discriminatory marker of assisted reproductive technology outcome than follicle-stimulating hormone, inhibin B, or estradiol. Fertil Steril 2004;82:1323–9.
12. Peñarrubia J, Fábregues F, Manau D, Creus M, Casals G, Casamitjana R, et al. Basal and stimulation day 5 anti-Müllerian hormone serum concentrations as predictors of ovarian response and pregnancy in assisted reproductive technology cycles stimulated with gonadotropin-releasing hormone agonist-gonadotropin treatment. Hum Reprod 2005;20:915–22.
13. Fiçicioğlu C, Kutlu T, Baglam E, Bakacak Z. Early follicular antimüllerian hormone as an indicator of ovarian reserve. Fertil Steril 2006;85:592–6.
14. La Marca A, Giulini S, Tirelli A, Bertucci E, Marsella T, Xella S, et al. Anti-Müllerian hormone measurement on any day of the menstrual cycle strongly predicts ovarian response in assisted reproductive technology. Hum Reprod 2007;22:766–71.
15. Tremellen KP, Kolo M, Gilmore A, Lekamge DN. Anti-müllerian hormone as a marker of ovarian reserve. Aust N Z J Obstet Gynaecol 2005;45:20–4.
16. van Disseldorp J, Faddy MJ, Themmen AP, de Jong FH, Peeters PH, van der Schouw YT, et al. Relationship of serum antimullerian hormone concentration to age at menopause. J Clin Endocrinol Metab 2008;93:2129–34.
17. Silberstein T, MacLaughlin DT, Shai I, Trimarchi JR, Lambert-Messerlian G, Seifer DB, et al. Mullerian inhibiting substance levels at the time of HCG administration in IVF cycles predict both ovarian reserve and embryo morphology. Hum Reprod 2006;21:159–63.
18. Nardo LG, Gelbaya TA, Wilkinson H, Roberts SA, Yates A, Pemberton P, et al. Circulating basal anti-Mullerian hormone levels as predictor of ovarian response in women undergoing ovarian stimulation for in vitro fertilization. Fertil Steril 2009;92:1586–93.
19. Gnoth C, Schuring AN, Friol K, Tigges J, Mallmann P, Godehardt E. Relevance of anti-Mullerian hormone measurement in a routine IVF program. Hum Reprod 2008;23:1359–65.
20. Sowers MR, Eyvazzadeh AD, McConnell D, Yosef M, Jannausch ML, Zhang D, et al. Anti-mullerian hormone and inhibin B in the definition of ovarian aging and the menopause transition. J Clin Endocrinol Metab 2008;93:3478–83.
21. Van Disseldorp J, Faddy MJ, Themmen APN, De Jong FH, Peeters PHM, Van Der Schouw YT, et al. Relationship of serum antimüllerian hormone concentration to age at menopause. J Clin Endocrinol Metab 2008;93:2129–34.
22. Pigny P, Jonard S, Robert Y, Dewailly D. Serum anti-Müllerian hormone as a surrogate for antral follicle count for definition of the polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91:941–5.
23. La Marca A, De Leo V, Giulini S, Orvieto R, Malmusi S, Giannella L, et al. Anti-mullerian hormone in premenopausal women and after spontaneous or surgically induced menopause. J Soc Gynecol Invest 2005;12:545–8.
24. Jayaprakasan K, Campbell B, Hopkisson J, Johnson I, Raine-Fenning N. A prospective, comparative analysis of anti-Mullerian hormone, inhibin-B, and three-dimensional ultrasound determinants of ovarian reserve in the prediction of poor response to controlled ovarian stimulation. Fertil Steril 2010;93:855–64.
25. Jayaprakasan K, Deb S, Batcha M, Hopkisson J, Johnson I, Campbell B, et al. The cohort of antral follicles measuring 2-6 mm reflects the quantitative status of ovarian reserve as assessed by serum levels of anti-Mullerian hormone and response to controlled ovarian stimulation. Fertil Steril 2010;94:1775–81.
26. Broekmans FJ, Soules MR, Fauser BC. Ovarian aging: mechanisms and clinical consequences. Endocr Rev 2009;30:465–93.
27. Visser JA, de Jong FH, Laven JS, Themmen AP. Anti-Mullerian hormone: a new marker for ovarian function. Reproduction 2006;131:1–9.
28. Broekmans FJ, Visser JA, Laven JSE, Broer SL, Themmen APN, Fauser BC. Anti-Müllerian hormone and ovarian dysfunction. Trends Endocrinol Metab 2008;19:340–7.
29. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19:41–7.
30. Visser GH, Eilers PH, Elferink-Stinkens PM, Merkus HM, Wit JM. New Dutch reference curves for birthweight by gestational age. Early Hum Dev 2009;85:737–44.
31. Al-Qahtani A, Muttukrishna S, Appasamy M, Johns J, Cranfield M, Visser JA, et al. Development of a sensitive enzyme immunoassay for anti-Mullerian hormone and the evaluation of potential clinical applications in males and females. Clin Endocrinol (Oxf) 2005;63:267–73.
32. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. Stat Med 1992;11:1305–19.
33. Navot D, Rosenwaks Z, Margalioth EJ. Prognostic assessment of female fecundity. Lancet 1987;2:645–7.
34. Fanchin R, De Ziegler D, Olivennes F, Taieb J, Dzik A, Frydman R. Exogenous follicle stimulating hormone ovarian reserve test (EFORT): a simple and reliable screening test for detecting 'poor responders' in in-vitro fertilization. Hum Reprod 1994;9:1607–11.
35. Faddy MJ, Gosden RG. A model conforming the decline in follicle numbers to the age of menopause in women. Hum Reprod 1996;11:1484–6.
36. Lass A, Skull J, McVeigh E, Margara R, Winston RML. Measurement of ovarian volume by transvaginal sonography before ovulation induction with human menopausal gonadotrophin for in-vitro fertilization can predict poor response. Hum Reprod 1997;12:294–7.
37. Tomás C, Nuojua-Huttunen S, Martikainen H. Pretreatment transvaginal ultrasound examination predicts ovarian responsiveness to gonadotrophins in in-vitro fertilization. Hum Reprod 1997;12:220–3.
38. Hall JE, Welt CK, Cramer DW. Inhibin A and inhibin B reflect ovarian function in assisted reproduction but are less useful at predicting outcome. Hum Reprod 1999;14:409–15.
39. Bancsi LFJMM, Broekmans FJM, Eijkemans MJC, De Jong FH, Habbema JD, Te Velde ER. Predictors of poor ovarian response in in vitro fertilization: a prospective study comparing basal markers of ovarian reserve. Fertil Steril 2002;77:328–36.
40. Broekmans FJ, Kwee J, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF outcome. Hum Reprod Update 2006;12:685–718.
41. Centers for Disease Control and Prevention. Use and interpretation of the CDC growth charts. Available at: http://www.cdc.gov/nccdphp/dnpa/growthcharts/guide.htm. Accessed June 23, 2010.
42. Bersinger NA, Wunder D, Birkhäuser MH, Guibourdenche J. Measurement of anti-mullerian hormone by Beckman Coulter ELISA and DSL ELISA in assisted reproduction: differences between serum and follicular fluid. Clin Chim Acta 2007;384:174–5.
43. Fréour T, Mirallié S, Bach-Ngohou K, Denis M, Barrière P, Masson D. Measurement of serum anti-Müllerian hormone by Beckman Coulter ELISA and DSL ELISA: comparison and relevance in assisted reproduction technology (ART). Clin Chim Acta 2007;375:162–4.
44. Streuli I, Fraisse T, Chapron C, Bijaoui G, Bischof P, de Ziegler D. Clinical uses of anti-Müllerian hormone assays: pitfalls and promises. Fertil Steril 2009;91:226–30.
45. Taieb J, Belville C, Coussieu C, Guibourdenche J, Picard JY, Clemente ND. Deux dosages de l'hormone antimüllérienne: performances analytiques et cliniques [Two immunoassays for antimullerian hormone measurement: analytical and clinical performances]. Ann Biol Clin (Paris) 2008;66:537–47.
46. Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abrahamowicz M, et al. New and improved population-based Canadian reference for birth weight for gestational age. Pediatrics 2001;108:E35.
47. Olsen IE, Groveman SA, Lawson ML, Clark RH, Zemel BS. New intrauterine growth curves based on United States data. Pediatrics 2010;125:e214–24.
48. Gleicher N, Weghofer A, Barad DH. Anti-Müllerian hormone (AMH) defines, independent of age, low versus good live-birth chances in women with severely diminished ovarian reserve. Fertil Steril 2010;94:2824–7.
49. Iwase A, Hirokawa W, Goto M, Takikawa S, Nagatomo Y, Nakahara T, et al. Serum anti-Müllerian hormone level is a useful marker for evaluating the impact of laparoscopic cystectomy on ovarian reserve. Fertil Steril 2010;94:2846–9.

SUPPLEMENTARY TABLE 1

Multivariate stepwise linear regression analysis of FSH, age, type of AMH kit, and AFC as predictors of AMH level.

Model	Slope (B)	SE	Standardized coefficient	*P* value	95% CI
(Constant)	3.60	0.425		<.001	2.76, 4.43
AFC	0.105	0.008	0.348	<.001	−0.04, −0.007
FSH	−0.087	0.016	−0.149	<.001	0.08, 0.12
Age	−0.021	0.01	−0.069	<.008	−0.11, −0.05
Type of AMH kit	−0.515	0.088	−0.146	<.001	−0.68, −0.34

Note: CI = confidence interval.

Almog. Age-related normogram for antimüllerian hormone. Fertil Steril 2011.