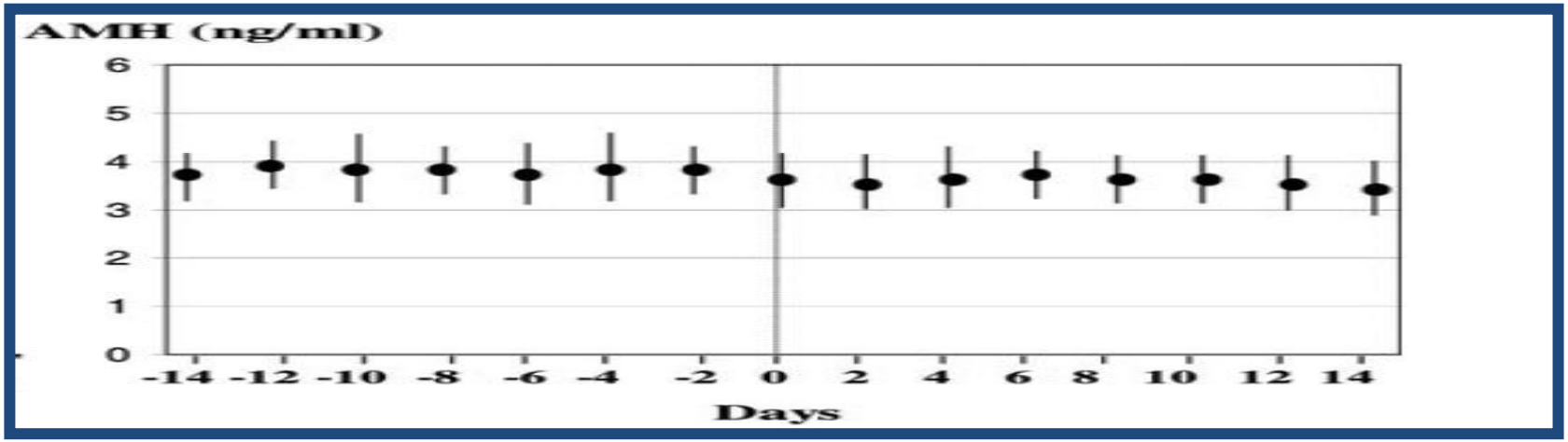
PCOS and AMH

Prof. Dr. Cem S. Atabekoğlu

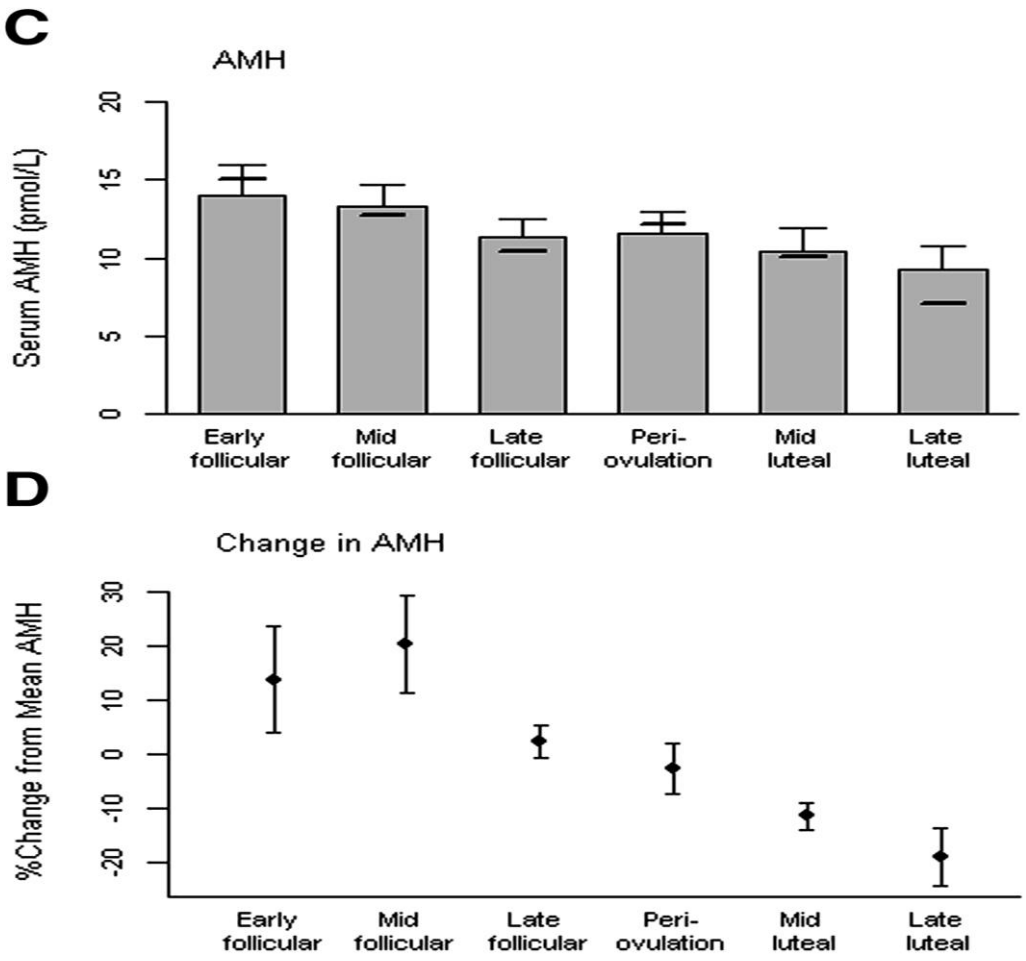
ANKARA UNIVERSITY

AMH

- Member of the transforming growth factor- b (TGF-b) superfamily.
- Produced by the granulosa cells of preantral and small antral follicles.
- Low inter- and intra-cycle variability in serum.



AMH: menstrual cycle variability

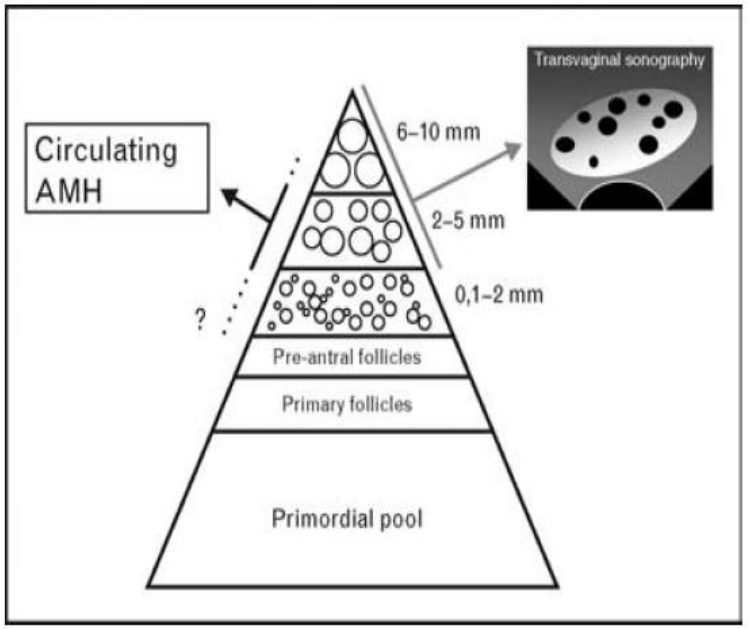


AMH levels in the follicular phase appear to be 20-30% greater than in the luteal phase

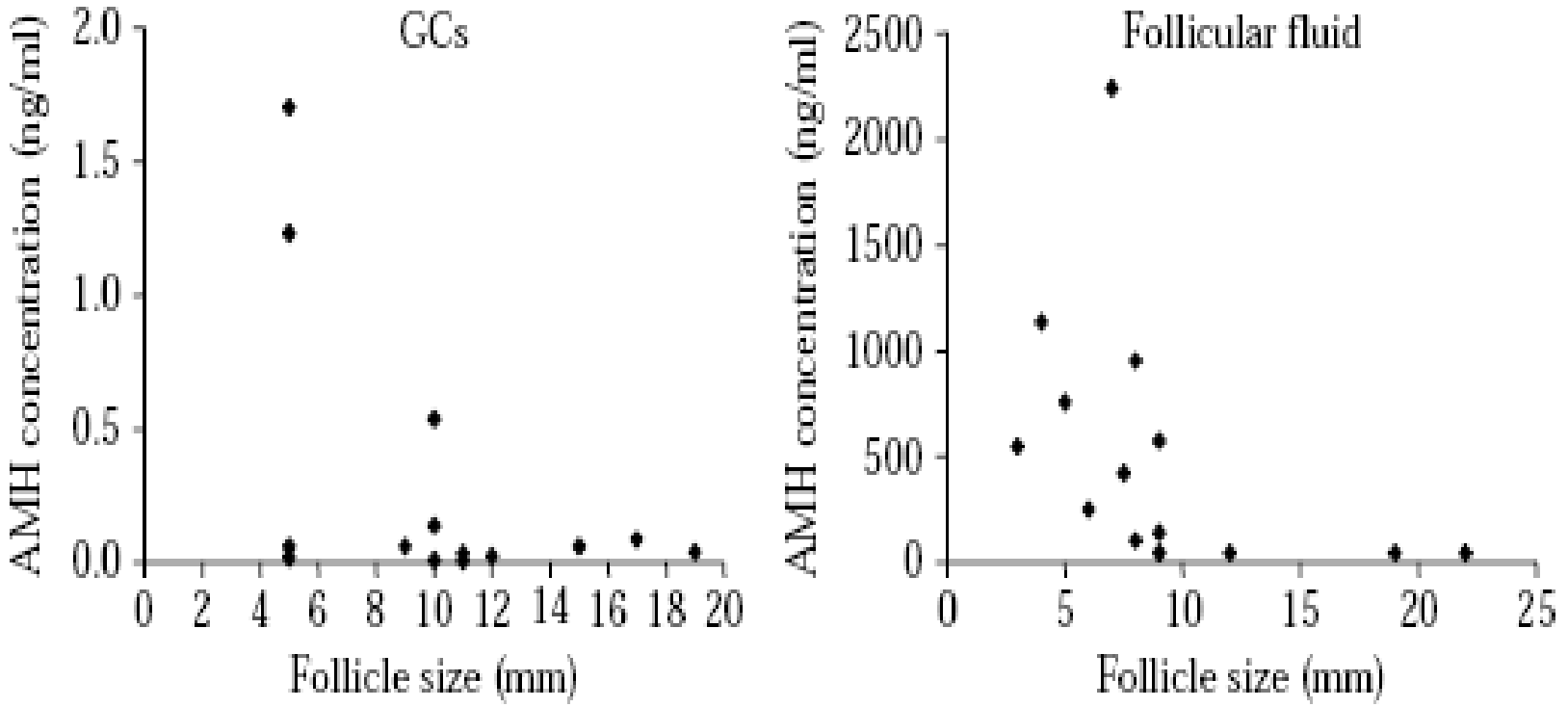
Hadlow et al, Fertil Steril 99:1791, 2013

AMH

- Shynthesis starting from the primary follicular stage
- The initial antral follicles (up to 2 mm of diameter) which are not detected by ultrasound, secrete large amounts of AMH.
- Expression is maximal in granulosa cells of preantral and small antral follicles (up to 6mm in diameter).
- After follicular growth has become FSH-dependent (8mm), AMH expression diminishes and becomes undetectable
- AMH is not expressed in atretic follicles



Levels of AMH declined as the follicle size increased.



Pellatt L et al. Journal of Clinical Endocrinology and Metabolism 2007.

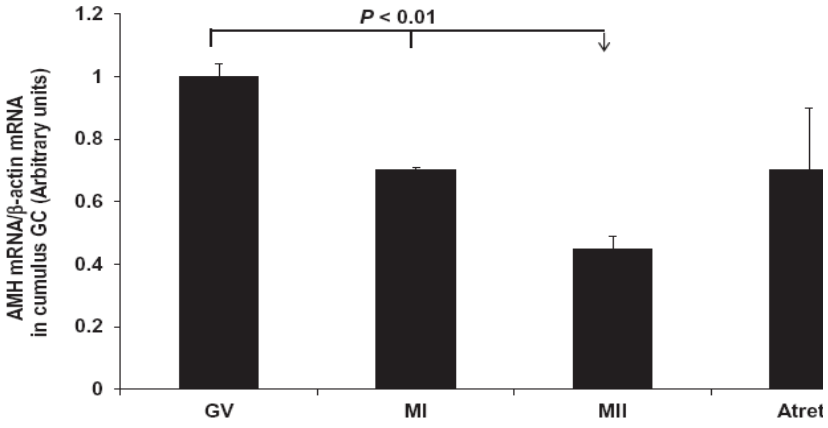
Reproductive BioMedicine Online (2012) 24, 540–546

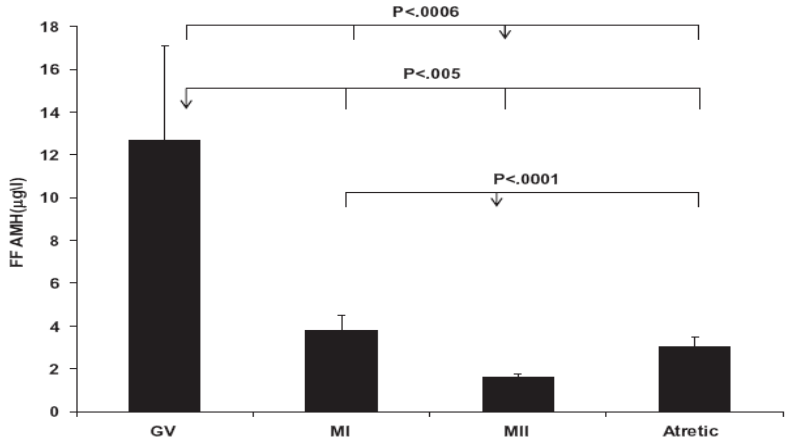
www.sciencedirect.com
www.rbmonline.com

ARTICLE

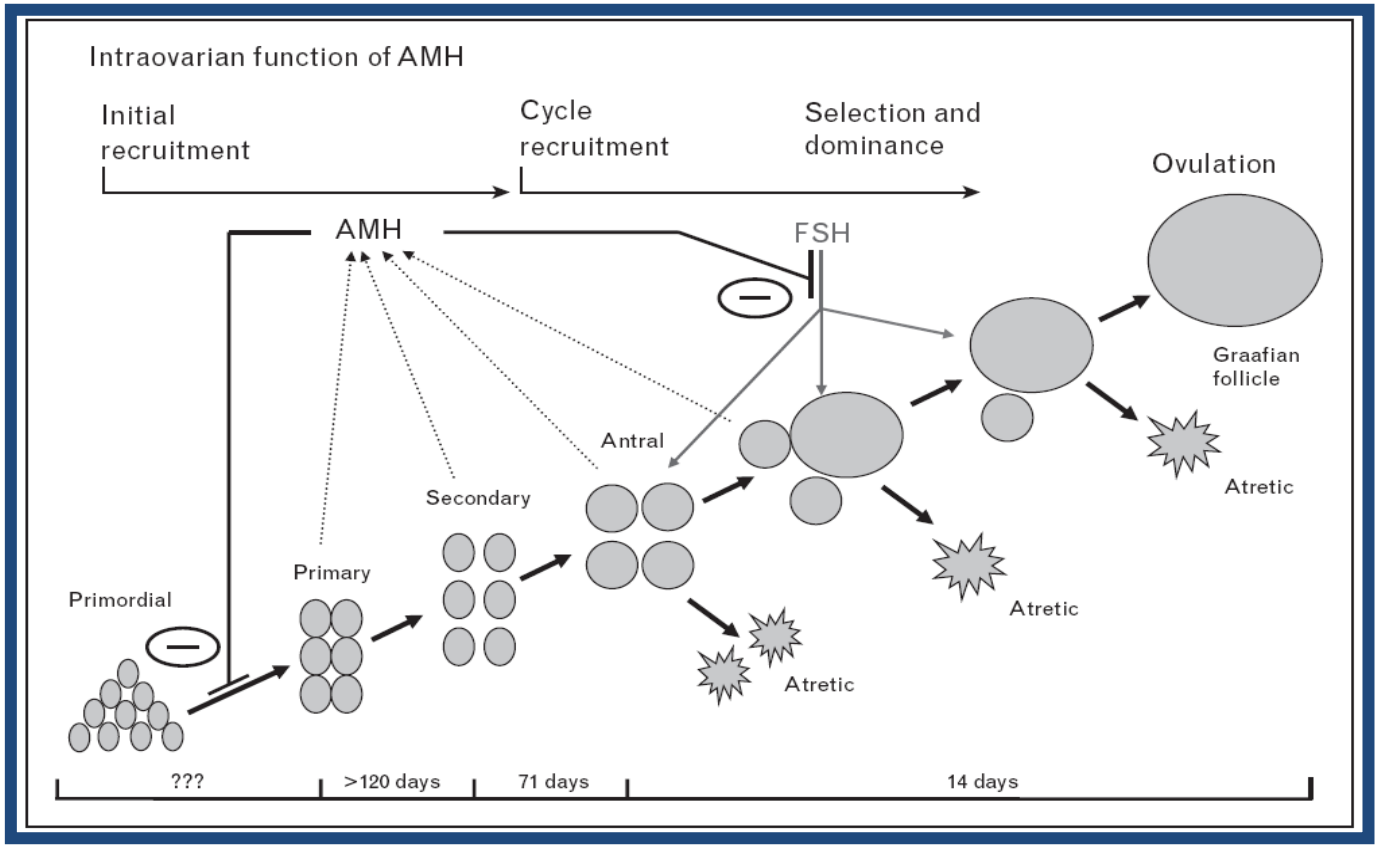
Anti-Müllerian hormone is highly expressed and secreted from cumulus granulosa cells of stimulated preovulatory immature and atretic oocytes

Alon Kedem-Dickman [a,*], Ettie Maman [a], Yuval Yung [a], Gil M Yerushalmi [a], Rina Hemi [b], Mirit Hanochi [b], Jehoshua Dor [a], Ariel Hourvitz [a]





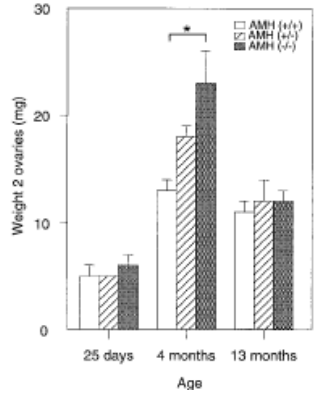
AMH



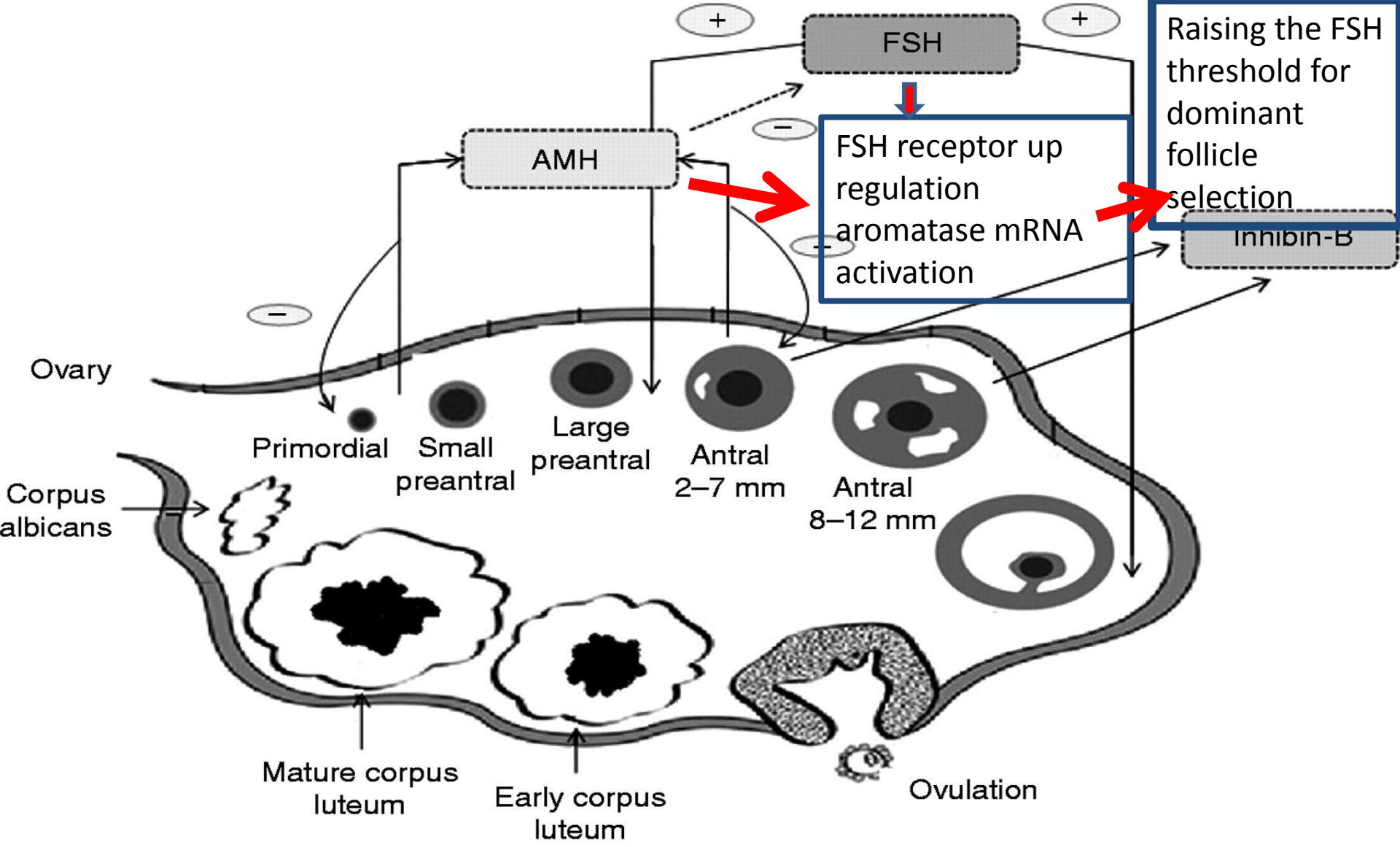
AMH plays crucial role in preservation ovarian reserve via inhibition of recruitment of resting follicles from the primordial follicle pool.

AMH knockout mice

- AMH knockout (AMHKO) mice are fertile
- AMH-knockout female mice have more growing pre-antral and small antral follicles than wild-type mice
- 4th month → double size ovary
- 4th month → less primordial folicle.
- 13th month → nothing primordial folicle .



- Premature cestation of cyclic mensturation .
- Their stock of primordial follicles is depleted earlier in life

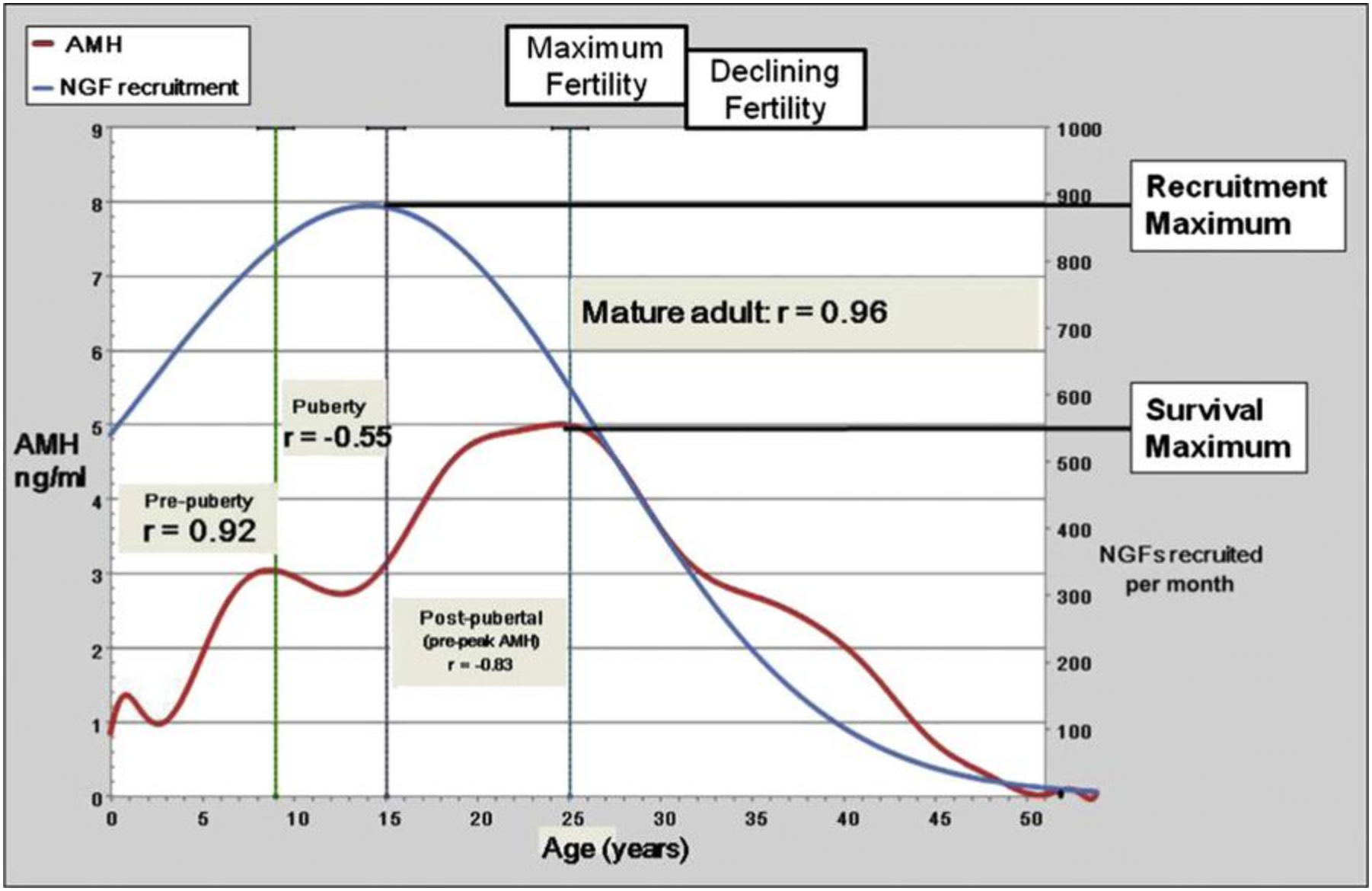


AMH plays crucial role in folliculogenesis via decreases the sensitivity of ovarian follicles to FSH.

AMH may play role in monofollicular development !!!!!

AMH / Granulosa Cell Cultures

- Anti-Mullerian hormone (AMH) inhibits FSH stimulated aromatase activity.
- Anti-Mullerian hormone (AMH) inhibits FSH-dependent expression of luteinizing hormone (LH) receptor
- Anti-Mullerian hormone (AMH) inhibits Granulosa-luteal cell proliferation



Fleming. Folliculogenesis, AMH, and human fertility. Fertil Steril 2012.

ORIGINAL ARTICLE

Endocrine Research

Elimination Half-Life of Anti-Müllerian Hormone

G. Griesinger, K. Dafopoulos, N. Buendgen, I. Cascorbi, P. Georgoulias, A. Zavos, C. I. Messini, and I. E. Messinis

Circulating AMH is solely of ovarian origin in women
T1/2= 27.6 h

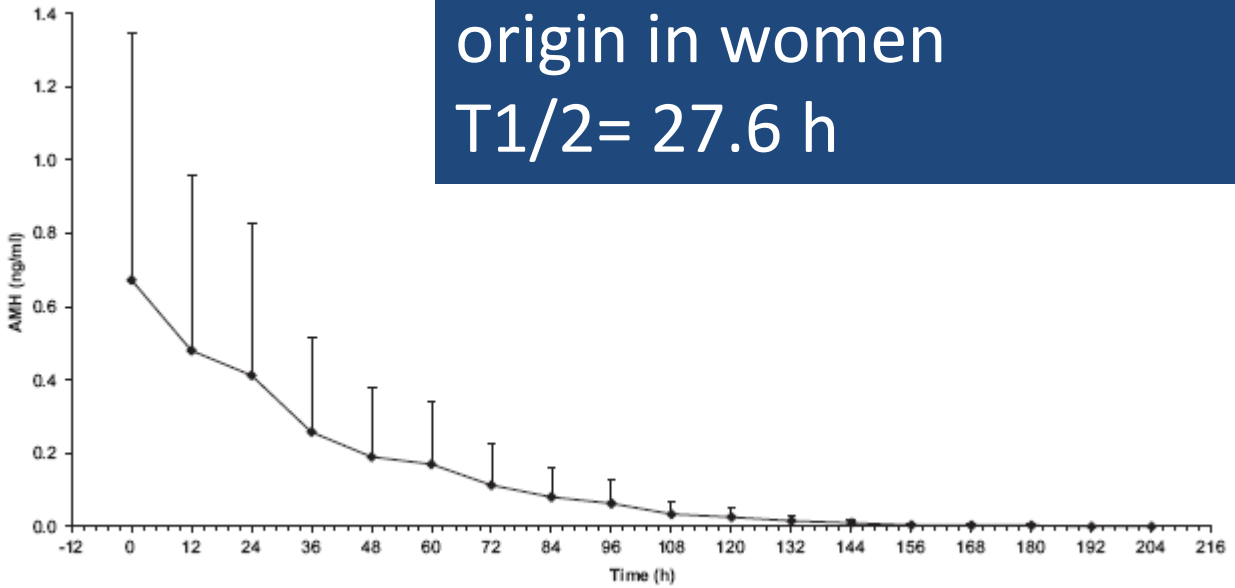
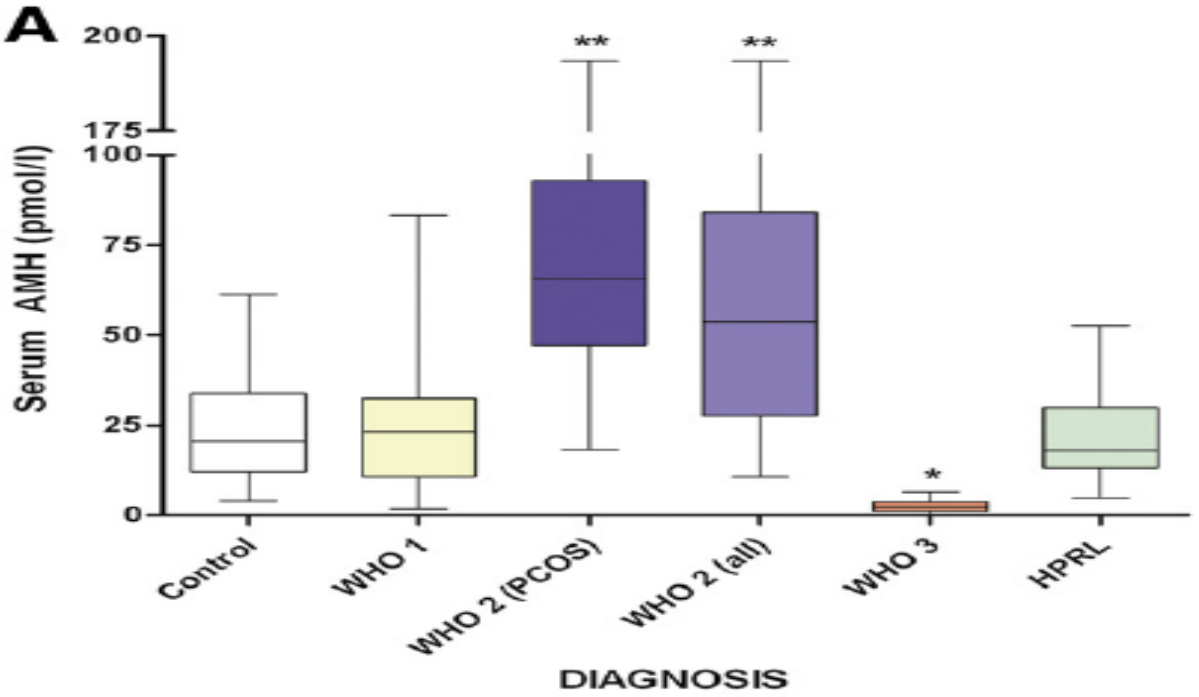


FIG. 1. AMH kinetics after bilateral salpingo-oophorectomy (means and SD).

J Clin Endocrinol Metab **97: 2160–2163, 2012**

Evaluation of serum antimullerian hormone and inhibin B concentrations in the differential diagnosis of secondary oligoamenorrhea

Hang Wun Raymond Li, M.R.C.O.G.,[a] *Richard A. Anderson, M.D., Ph.D.,*[b] *William Shu Biu Yeung, Ph.D.,*[a] *Pak Chung Ho, M.D.,*[a] *and Ernest Hung Yu Ng, M.D.*[a]



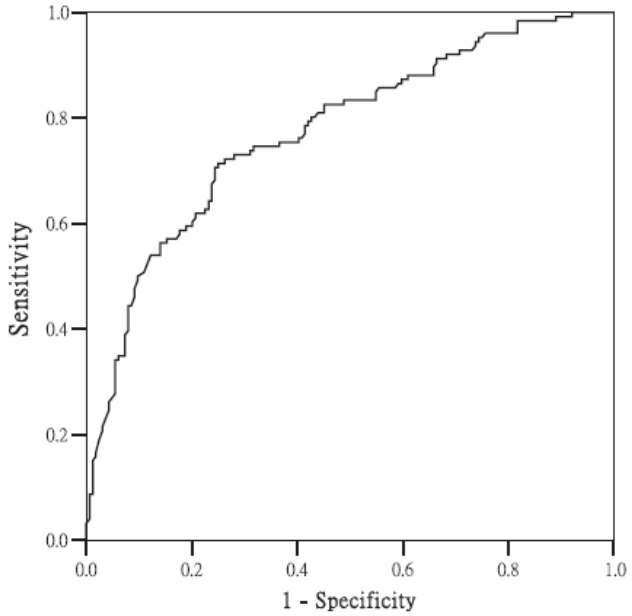
Fertil Steril 2011;96:774–9.

Antimüllerian hormone and polycystic ovary syndrome

Yi-Hui Lin, M.D.,[a] Wan-Chun Chiu, Ph.D.,[c] Chien-Hua Wu, Ph.D.,[b,e] Chii-Ruey Tzeng, M.D.,[d] Chun-Sen Hsu, M.D.,[a] and Ming-I Hsu, M.D.[a]

	PCOS prevalans
AMH (<4 ng/mL)	%21
AMH (4–11 ng/mL)	%37
AMH (>11 ng/mL)	%80

Receiver-operating characteristic (ROC) curves of antimüllerian hormone (AMH) levels for the evaluation of polycystic ovary syndrome (PCOS).



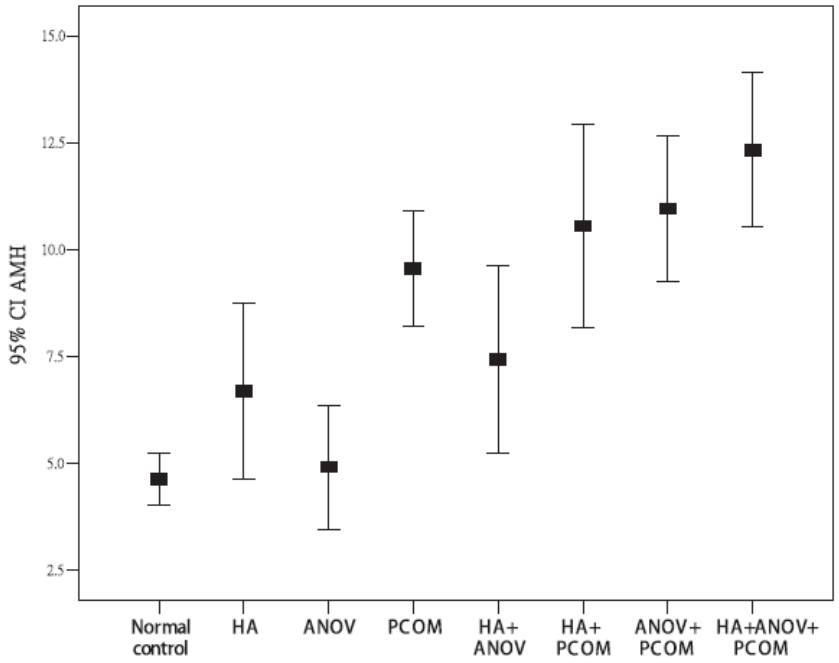
Lin. Antimüllerian hormone and PCOS. Fertil Steril 2011.

There is a correlation between elevated AMH level and the risk of PCOS.

Antimüllerian hormone and polycystic ovary syndrome

Yi-Hui Lin, M.D.,[a] *Wan-Chun Chiu, Ph.D.,*[c] *Chien-Hua Wu, Ph.D.,*[b,e] *Chii-Ruey Tzeng, M.D.,*[d] *Chun-Sen Hsu, M.D.,*[a] *and Ming-I Hsu, M.D.*[a]

The mean serum antimüllerian hormone (AMH) levels of various polycystic ovary syndrome–related phenotypes. Error bars represent 95% confidence intervals. ANOV = oligoanovulation; HA = hyperandrogenism; PCOM = polycystic ovary morphology.



Lin. Antimüllerian hormone and PCOS. Fertil Steril 2011.

There is positive correlation with serum AMH levels and severity of the syndrome.

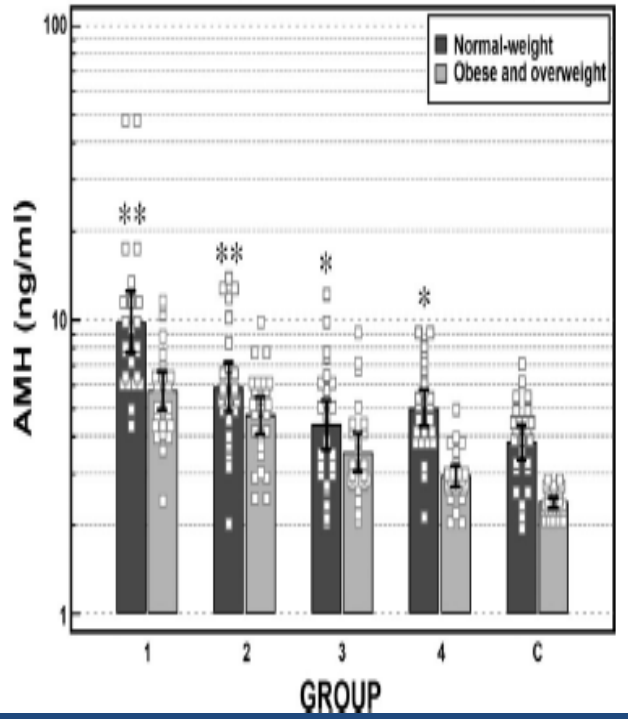
Am J Physiol Endocrinol Metab 296: E238–E243, 2009.
First published October 28, 2008; doi:10.1152/ajpendo.90684.2008.

Anti-Müllerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels

Athanasia Piouka,[1] Dimitrios Farmakiotis,[1] Ilias Katsikis,[1] Djuro Macut,[2] Spiros Gerou,[3] and Dimitrios Panidis[1]

Table 1. *Definition of the five groups studied*

	ANOV	HA	PCO	Epidemiology in Greece
PCOS				
1	+	+	+	Severe ~46.4%
2	+	+	−	Anovulation and hyperandrogenemia ~39.6%
3	−	+	+	Ovulatory ~7.2%
4	+	−	+	Mild ~6.8%
Control	−	−	−	

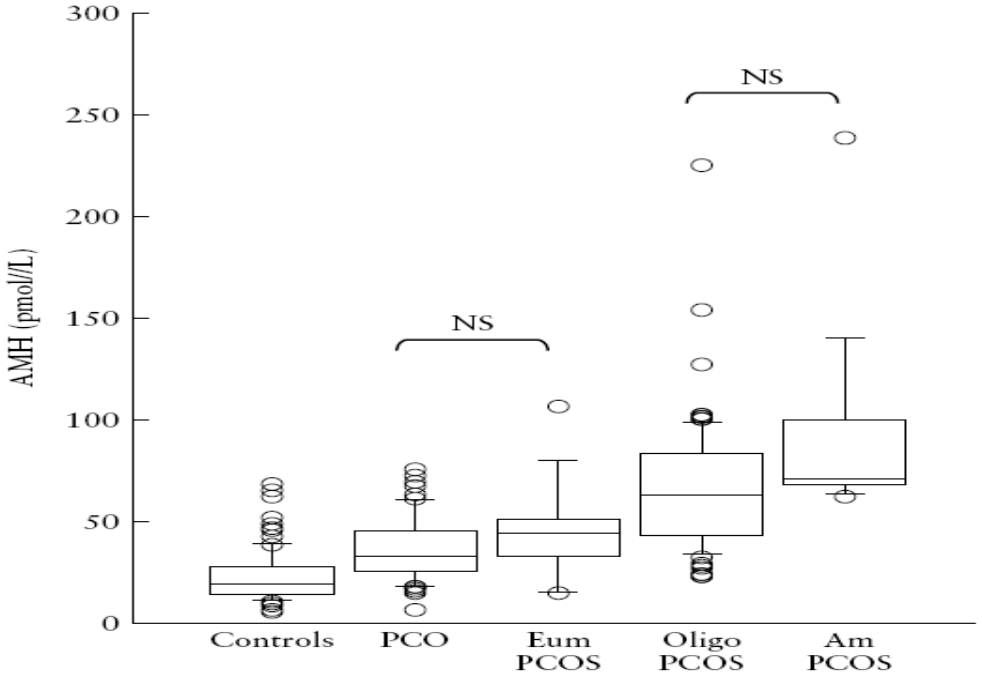


There is positive correlation with serum AMH levels and severity of the syndrome

Ultrasound Obstet Gynecol 2012; **40**: 223–229
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.11202

Polycystic ovaries at ultrasound: normal variant or silent polycystic ovary syndrome?

S. CATTEAU-JONARD*†, J. BANCQUART*†, E. PONCELET†‡, C. LEFEBVRE-MAUNOURY*†, G. ROBIN*† and D. DEWAILLY*†

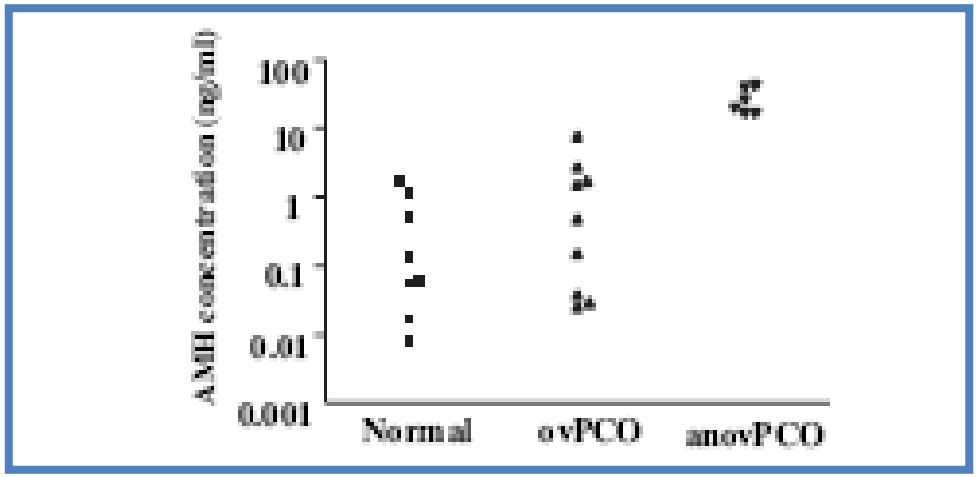


There is positive correlation with serum AMH levels and severity of the syndrome

PCOS ve AMH

- **<u>Serum AMH levels three times higher in women with Polycystic Ovary Syndrome</u>**
- PCO has similar number primordial follicle but two- to six-fold number preantral and small antral follicles.
- AMH is mostly expressed from preantral and small antral follicles

AMH production is 75 times higher per granulosa cell in PCOS patients !!!!!!!



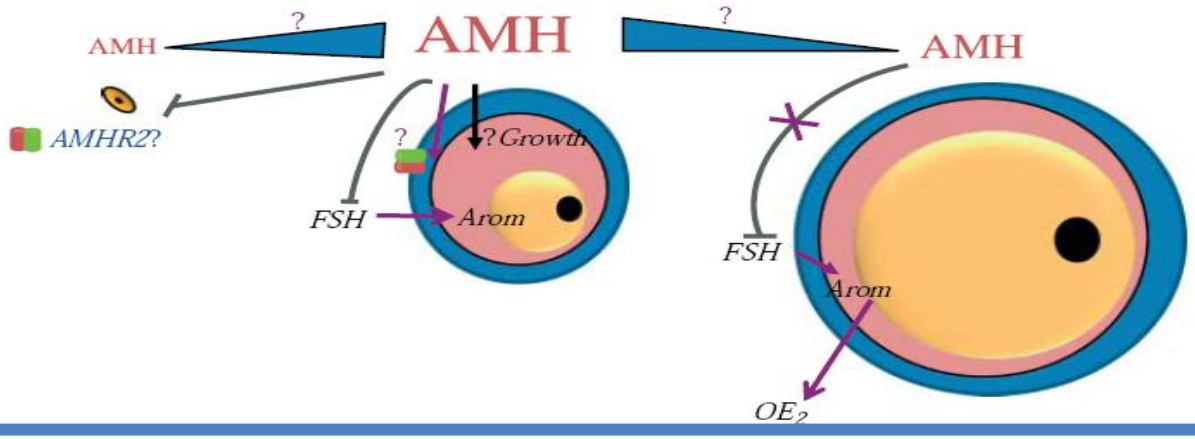
Pellatt L, J Clin Endocrinol Metab 2007;92:240–5. 13.

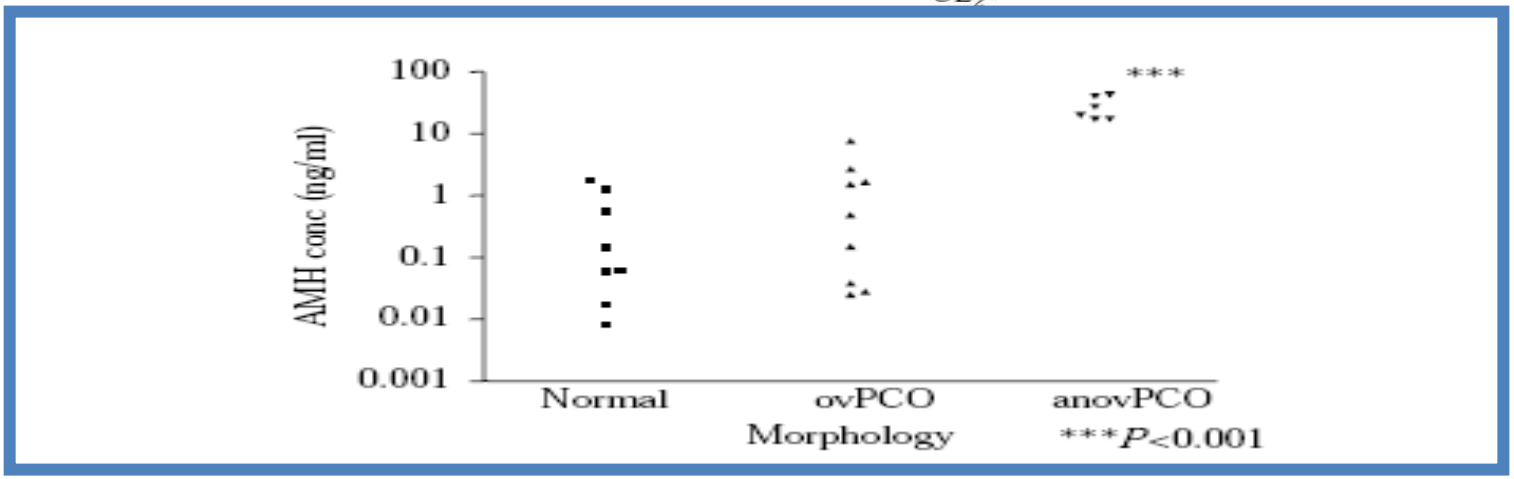
High production of AMH by the polycystic ovary may have an important role in the pathophysiology of the syndrome.

- AMH plays a role in the control of follicle growth via paracrine and autocrine effects.
- AMH can reduce FSH- and cAMP-stimulated aromatase activity.
- Reduced aromatase activity may lead to hyperandrogenism.
- AMH inhibits FSH-stimulated FSH receptor production
- Raising the FSH threshold for dominant follicle selection

Cause or Consequence ???

AMH & Follicle Growth

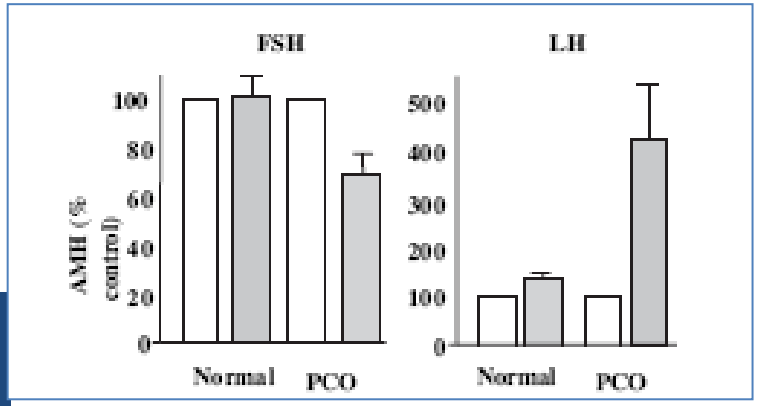




GCs from anovPCOs produced on average 18 times more AMH than GCs from ovPCOs

High LH

(Granulosa cells cultures)



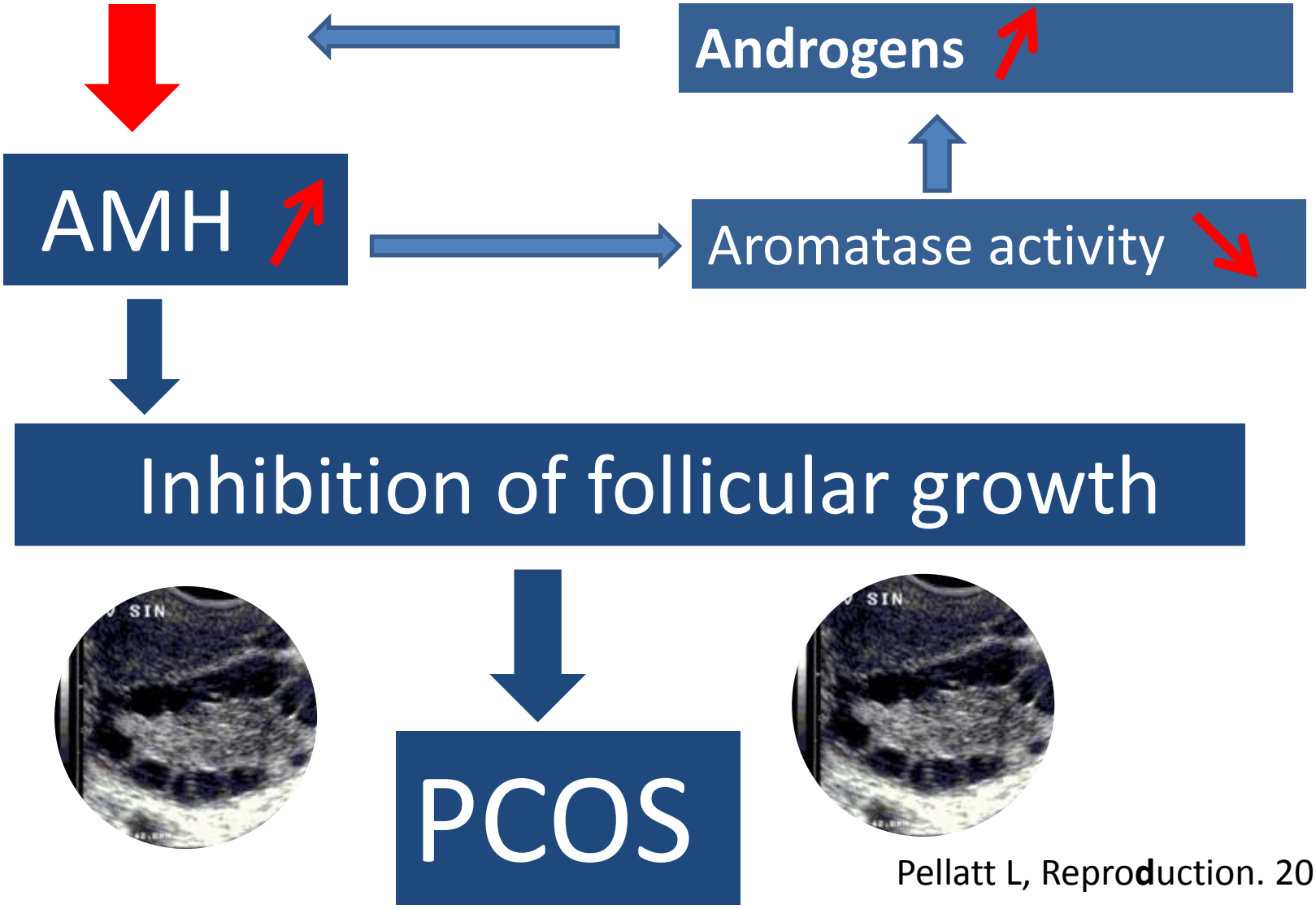
Pellatt L. JCEMetab. 2007;92 (1):240–5.

Increased AMH production

follicular growth inhibition

PCOS

Androgens induce the recruitment of small follicles



Pellatt L, Reproduction. 2010;

J Assist Reprod Genet (2012) 29:1147–1151
DOI 10.1007/s10815-012-9839-2

GONADAL PHYSIOLOGY AND DISEASE

Different diagnostic power of anti-Mullerian hormone in evaluating women with polycystic ovaries with and without hyperandrogenism

Yi Li · Yun Ma · Xianghong Chen · Wenjun Wang · Yu Li · Qingxun Zhang · Dongzi Yang

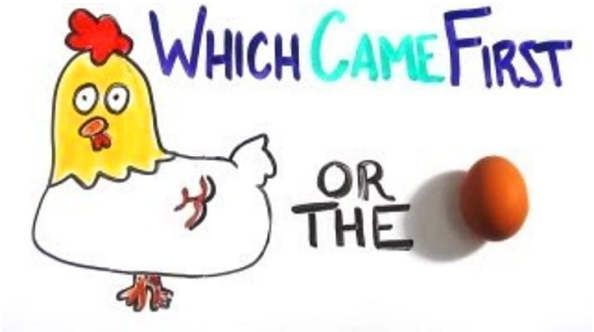
Basal parameters	HA+	HA−	Control
N	62	69	61
AMH (ng/ml)	8.41±4.57[ab]	5.81±3.85[c]	3.74±2.25

Table 2 Diagnostic power of AMH for PCOS patients of different subtypes

Groups	AUC	*P* value	Threshold (ng/ml)	Sensitivity	Specificity
All types	0.68 (0.60–0.76)	<0.01	3.92	65 %	62 %
HA+	0.82 (0.72–0.92)	<0.01	4.23	82 %	64 %
HA−	0.66 (0.56–0.75)	<0.01	3.76	64 %	62 %

HA+: PCOS patients with hyperandrogenism, HA−: PCOS patients without hyperandrogenism

AMH



Anovulation

Hyperandrogenism

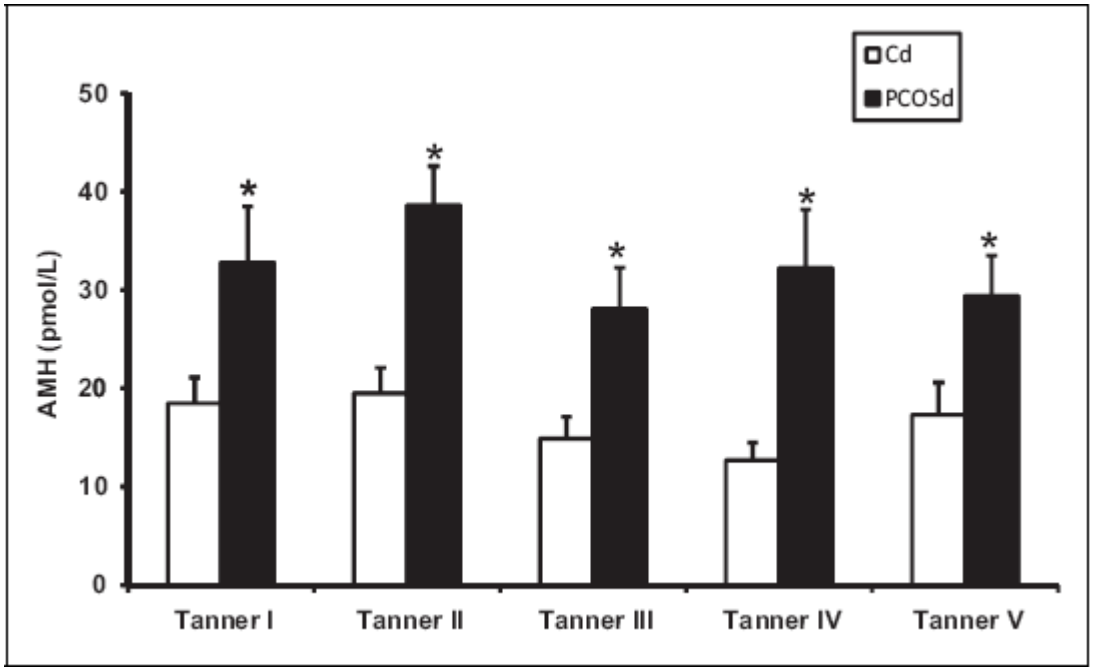
Insulin resistance

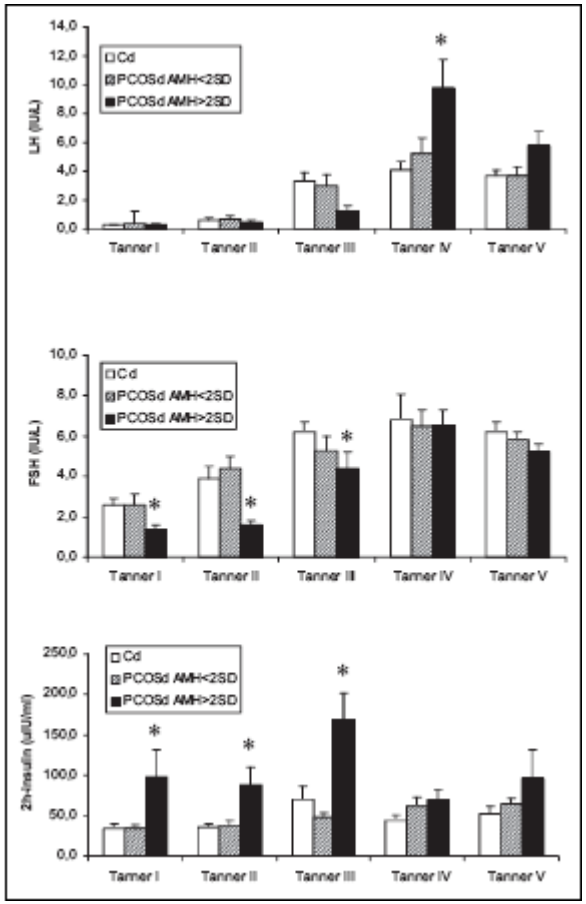
Reproductive Sciences
19(4) 383-390

DOI: 10.1177/1933719111424444
http://rs.sagepub.com
SAGE

Relationship Between Anti-Müllerian Hormone (AMH) and Insulin Levels During Different Tanner Stages in Daughters of Women With Polycystic Ovary Syndrome

Teresa Sir-Petermann, PhD, MD[1],
Amanda Ladrón de Guevara, MD[1], Ethel Codner, PhD, MD[2],
Jessica Preisler, MD[1], Nicolás Crisosto, PhD, MD[1],
Bárbara Echiburú, PhD[1], Manuel Maliqueo, PhD[1],
Fernando Sánchez, MD[1], Francisco Perez-Bravo, PhD[3], and
Fernando Cassorla, PhD, MD[2]

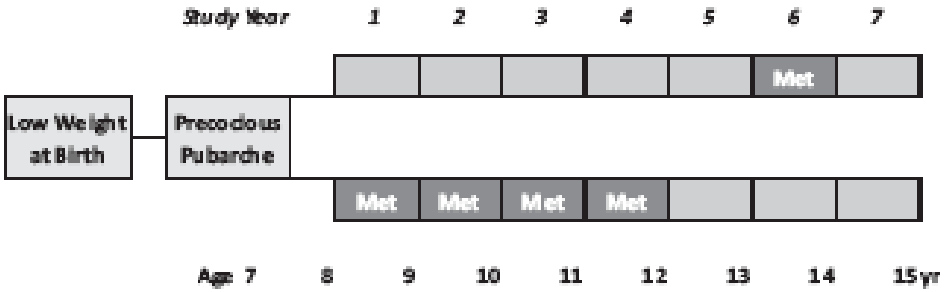




The follicular alterations related to PCOS may appear in adolescent stage or younger!

Early Metformin Therapy (Age 8–12 Years) in Girls with Precocious Pubarche to Reduce Hirsutism, Androgen Excess, and Oligomenorrhea in Adolescence

Lourdes Ibáñez, Abel López-Bermejo, Marta Díaz, Maria Victoria Marcos, and Francis de Zegher



	Early metformin (n = 19)		Late metformin (n = 19)	
	n	%	n	%
Androgen excess				
Ferriman Gallwey score >8	2	11[a]	12	63
Serum testosterone above +2 SD (>48 ng/dl)[b]	6	32[c]	12	63
Total (clinical and/or biochemical)	6	32[c]	13	68
Menstrual irregularity				
Amenorrhea (no menses for >3 months)	0	0	0	0
Oligomenorrhea (cycles >45 d)	1[d]	5[e]	7[d]	37
Total (amenorrhea or oligomenorrhea)	1[d]	5[e]	7[d]	37

J Clin Endocrinol Metab, August 2011, 96(8):E1262–E1267

Human Reproduction, Vol.26, No.10 pp. 2861–2868, 2011
Advanced Access publication on July 21, 2011 doi:10.1093/humrep/der223

human reproduction ORIGINAL ARTICLE *Reproductive endocrinology*

Polycystic ovarian morphology in adolescents with regular menstrual cycles is associated with elevated anti-Müllerian hormone

C. Villarroel[1], P.M. Merino[1,2], P. López[1,3], F.C. Eyzaguirre[1], A. Van Velzen[1], G. Iñiguez[1], and E. Codner[1,*]

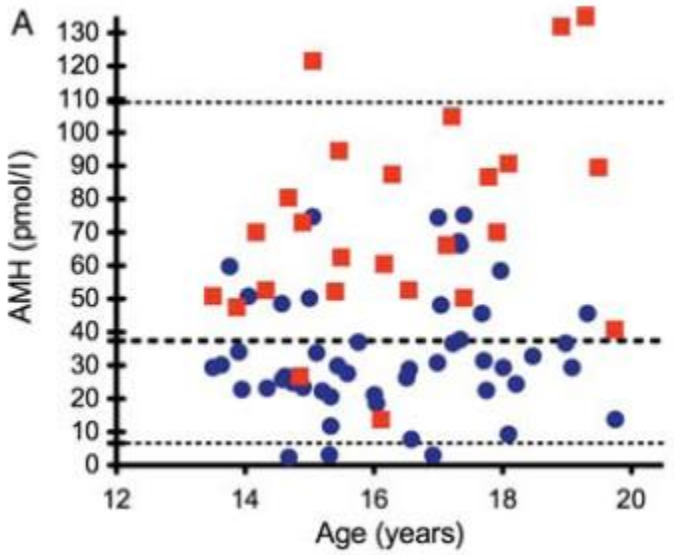


Table III Relationships between AMH, inhibin B, FSH levels and insulin, androgens and ovarian parameters.

		AMH	Inhibin B	FSH
Age	r	0.195	−0.068	−0.131
BMI-SDS	r	−0.151	0.119	−0.100
Ovarian volume	r	0.396**	0.339**	−0.281*
Follicle number	r	0.376**	0.183	−0.141
2–5 mm follicles number	r	0.299**	0.205	−0.170
6–9 mm follicle number	r	0.132	0.004	−0.079
FSH	r	−0.193	0.164	–
Testosterone	r	0.124	0.150	−0.179
FAI	r	0.081	0.074	−0.145
Insulin	r	−0.311**	0.040	−0.035
HOMA-IR	r	−0.306**	0.095	−0.041

European Journal of Obstetrics & Gynecology and Reproductive Biology 158 (2011) 254–259

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Is the plasma anti-Müllerian hormone (AMH) level associated with body weight and metabolic, and hormonal disturbances in women with and without polycystic ovary syndrome?

Piotr Skałba [a], Anna Cygal [a], Paweł Madej [a], Anna Dąbkowska-Huć [a], Jerzy Sikora [b], Gayane Martirosian [c], Małgorzata Romanik [c], Magdalena Olszanecka-Glinianowicz [d,*]

Serum concentrations of hormones in analyzed groups of PCOS and Non-PCOS.

	All PCOS	Normal weight PCOS	Overweight PCOS	All Non-PCOS	Normal weigh Non-PCOS	Overweight Non-PCOS
FSH (mIU/mL)	$6.8 \pm 2.1^{\%}$	$6.9 \pm 2.0^{\#}$	$6.6 \pm 2.1^{\&\&,\^,\$}$	8.4 ± 3.2	8.5 ± 3.2	8.3 ± 3.2
LH (mIU/mL)	$12.7 \pm 6.2^{\%\%\%}$	$12.7 \pm 6.2^{\#\#\#,+++}$	$12.5 \pm 6.4^{\&\&\&,\^\^\^,\$\$\$}$	5.5 ± 2.4	5.7 ± 2.5	5.1 ± 2.3
Androstendione (ng/mL)	$3.4 \pm 1.4^{\%\%\%}$	$3.5 \pm 1.5^{\#\#\#,+++}$	$3.2 \pm 1.2^{\&\&,\^\^,\$\$}$	1.4 ± 0.3	1.5 ± 0.4	1.4 ± 0.3
Total testosterone (ng/mL)	$3.7 \pm 2.5^{\%\%\%}$	$3.7 \pm 3.0^{\#\#\#,+++}$	$3.7 \pm 1.5^{\&\&\&,\^\^\^,\$\$\$}$	1.6 ± 0.4	1.7 ± 0.4	1.6 ± 0.5
Free testosterone (pg/mL)	$7.9 \pm 4.5^{\%\%\%}$	$7.1 \pm 4.3^{*\#\#\#,+++}$	$9.2 \pm 4.6^{\&\&\&,\^\^\^,\$\$\$}$	1.4 ± 0.4	1.4 ± 0.4	1.3 ± 0.4
Estradiol (pg/mL)	$54.3 \pm 26.0^{\%\%\%}$	$50.2 \pm 19.3^{+++}$	$61.2 \pm 33.5^{\&\&\&,\^\^\^,\$\$\$}$	82.1 ± 26.7	81.7 ± 26.3	82.5 ± 27.7
SHBG (nmol/l)	$42.8 \pm 21.4^{\%\%\%}$	$50.0 \pm 21.9^{***,\#}$	$30.2 \pm 13.1^{\&\&\&,\^\^\^,\$\$\$}$	56.7 ± 12.6	57.8 ± 12.7	55.2 ± 12.7
FAI	$11.0 \pm 8.2^{\%\%\%}$	$8.7 \pm 7.0^{***,\#\#\#,+++}$	$14.8 \pm 8.8^{\&\&\&,\^\^\^,\$\$\$}$	3.1 ± 1.0	3.1 ± 0.9	3.0 ± 1.1
AMH (ng/mL)	$10.2 \pm 3.7^{\%\%\%}$	$9.6 \pm 3.5^{\#\#\#,+++}$	$11.2 \pm 4.5^{\&\&\&,\^\^\^,\$\$\$}$	2.4 ± 0.7	2.5 ± 0.8	2.3 ± 0.7

There is no correlation between plasma AMH level and body weight.

Antimüllerian hormone and polycystic ovary syndrome

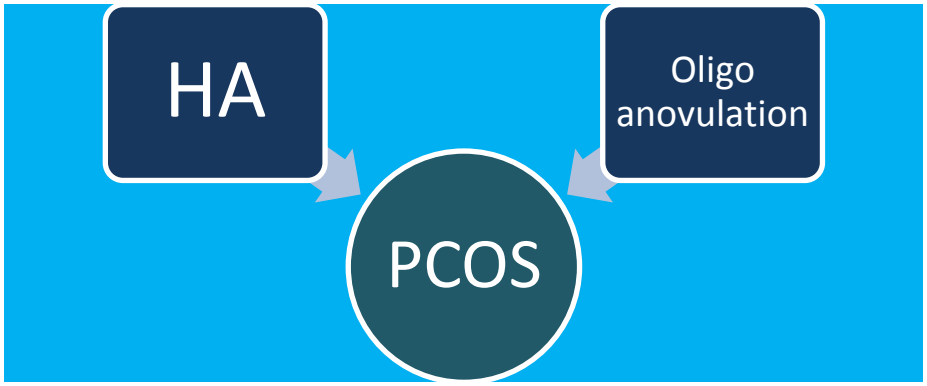
Yi-Hui Lin, M.D.,[a] *Wan-Chun Chiu, Ph.D.,*[c] *Chien-Hua Wu, Ph.D.,*[b,e] *Chii-Ruey Tzeng, M.D.,*[d] *Chun-Sen Hsu, M.D.,*[a] *and Ming-I Hsu, M.D.*[a]

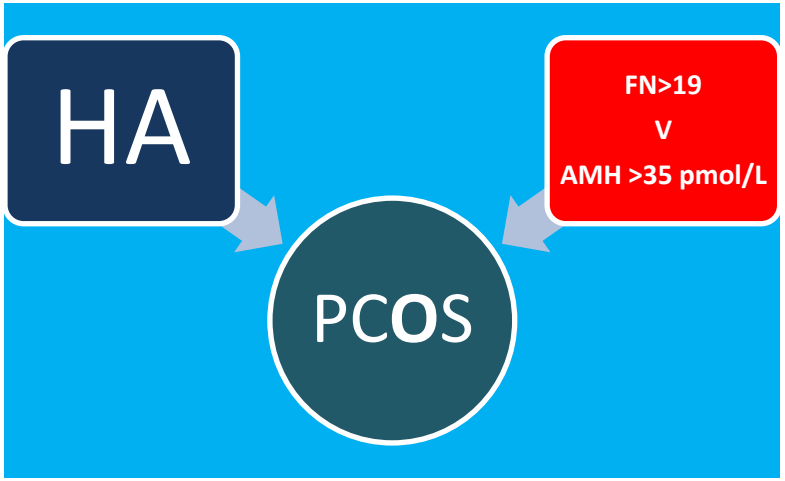
Biochemical and clinical characteristics of women in their reproductive age with low, moderate, and high levels of AMH.

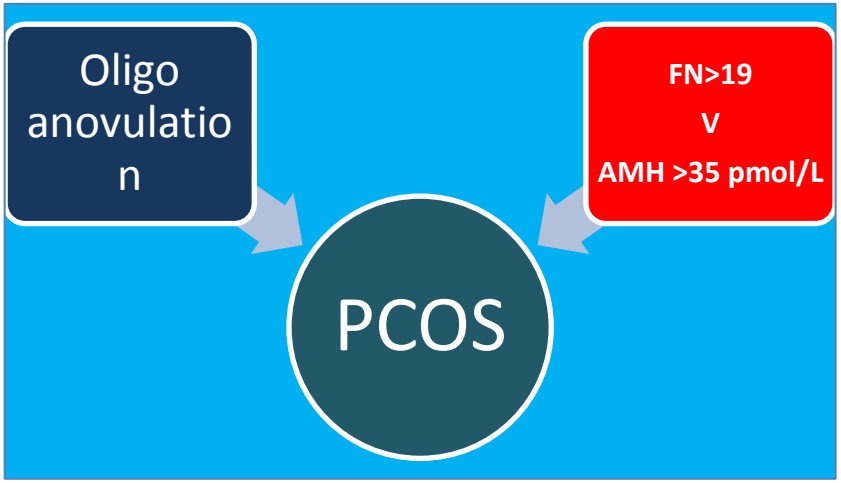
	Total	AMH <4 (L)	AMH 4–11 (M)	AMH >11 (H)	*P* value		
					L vs. M	L vs. H	M vs. H
Insulin sensitivity and glucose tolerance							
Fasting insulin (uIU/mL)	1.8 ± 13.5	13.1 ± 16.4	9.3 ± 9.1	11.6 ± 17.2	.194	.929	.661
Fasting glucose (mg/dL)	92.7 ± 16.8	95.7 ± 18.3	92.5 ± 17.1	9.0 ± 13.9	.514	.110	.582
2-hour glucose (mg/dL)	114.2 ± 45.3	12.8 ± 51.1	112.1 ± 41.5	112.0 ± 46.6	.515	.638	1.000
HOMA-IR	2.6 ± 3.6	3.4 ± 4.9	2.2 ± 2.6	2.7 ± 4.0	.159	.680	.789
Impaired glucose tolerance	21%	29%	20%	16%	.608	.374	.893
Diabetes	5%	7%	4%	6%	.783	.987	.939

Elevated serum AMH levels are not correlated with an increased risk of insulin resistance and metabolic syndrome.

PCOS -DIAGNOSIS/ AMH







AMH may be a good substitute for PCOM in diagnosing PCOS

PCOS -DIAGNOSIS/ AMH

Table III Adaptation of the previous classifications for the diagnosis of PCOS, proposing an excessive FN of >19 or serum AMH concentration >35 pmol/l or >5 ng/ml as a surrogate when either oligo-anovulation or HA is missing.

Oligo -anovulation	Clinical and/or biological HA	FN > 19 and/or serum AMH[a] > 35 pmol/l (5 ng/ml)	Diagnosis
+	+	(+/−)[b]	PCOS
+	−	+	PCOS
−	+	+	PCOS
−	−	+	Normal woman with PCOM[c]
+	−	−	Idiopathic anovulation
−	+	−	Idiopathic hyperandrogenism

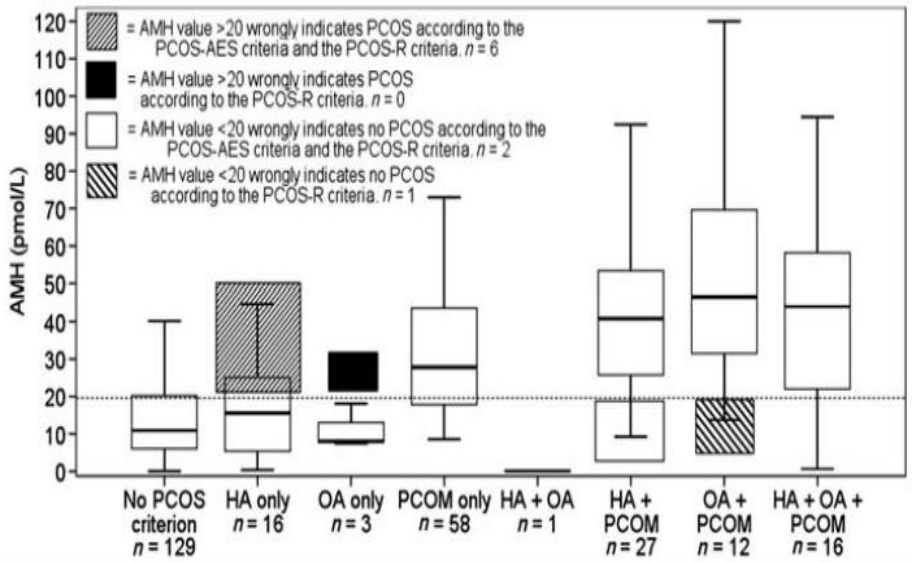
Human Reproduction, Vol.27, No.8 pp. 2494–2502, 2012
Advanced Access publication on June 12, 2012 doi:10.1093/humrep/des213

human reproduction

ORIGINAL ARTICLE *Reproductive endocrinology*

Anti-Mullerian hormone in the diagnosis of polycystic ovary syndrome: can morphologic description be replaced?

Tina B. Eilertsen[1,2,*], Eszter Vanky[2,3], and Sven M. Carlsen[4,5]



Assay[a] (total, *n* = 262)	Actual state: PCOS-R	
	Sensitivity (%) [Yes (*n* = 56)]	Specificity (%) [No (*n* = 206)]
AMH-based PCOS-R[b] (pmol/l)		
10	98.2	94.8
20	94.6	97.1
25	85.7	98.1
30	75.0	98.5
40	69.6	99.5

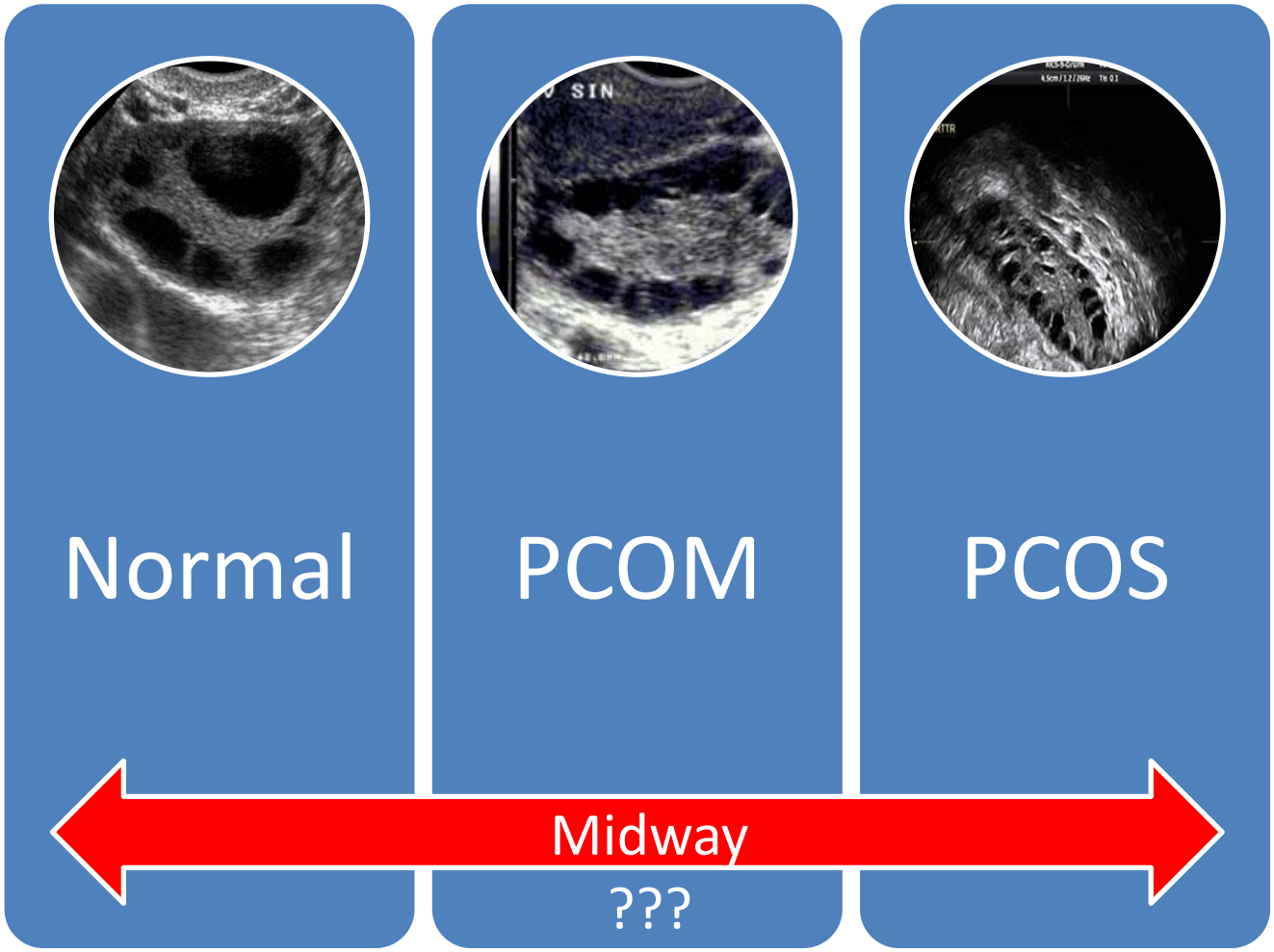


Table I Details of the 215 participants expressed as means (± SD). Between-group differences calculated by one way ANOVA or Kruskal–Wallis with a *post hoc* test, Bonferroni or Tamhane's T2, depending on the distribution of the data.

	n	Age	BMI	FSH (IU/l)	LH (IU/l)	AMH (pmol/l)
Controls	90	32.5 (3.3)	24.8 (2.6)	6.3 (2.0)	4.9 (3.0)	23.6 (15.0)
PCOM	35	32.1 (4.2)	24.7 (2.6)	5.6 (1.4)	5.3 (3.0)	52.2* (35.0)
PCOS	90	31.6 (4.4)	24.9 (2.4)	5.1* (1.4)	8.8* (5.2)	77.6*** (61.0)

Hum. Reprod. Advance Access published February 1, 2013
Human Reproduction, Vol.0, No.0 pp. 1–7, 2013
doi:10.1093/humrep/det015

human reproduction ORIGINAL ARTICLE *Reproductive endocrinology*

The relationship of serum anti-Mullerian hormone with polycystic ovarian morphology and polycystic ovary syndrome: a prospective cohort study

R. Homburg[1,2,*], A. Ray[1,2], P. Bhide[1,2], A. Gudi[1,2], A. Shah[1,2], P. Timms[1,2], and K. Grayson[1,2]

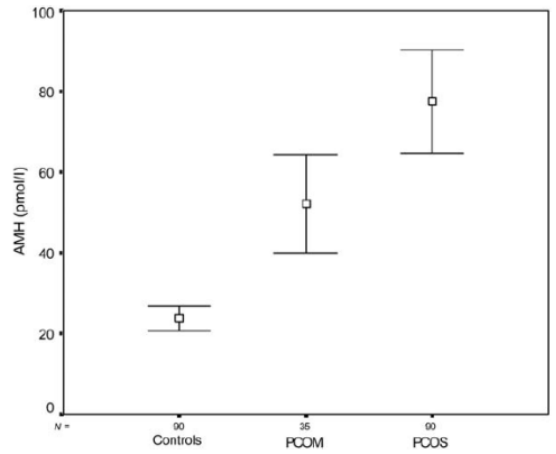
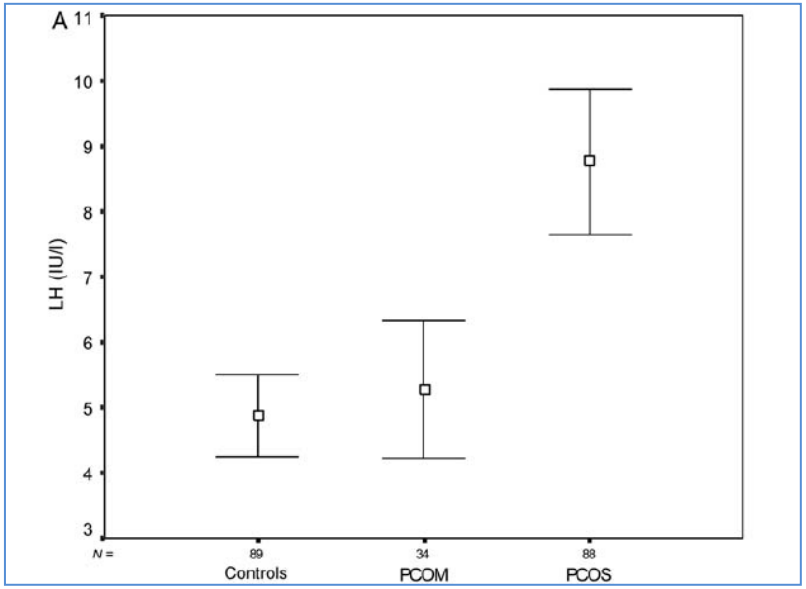


Figure 1 Mean values and 95% confidence intervals for AMH (pmol/l) in the group of controls, PCOM and PCOS.



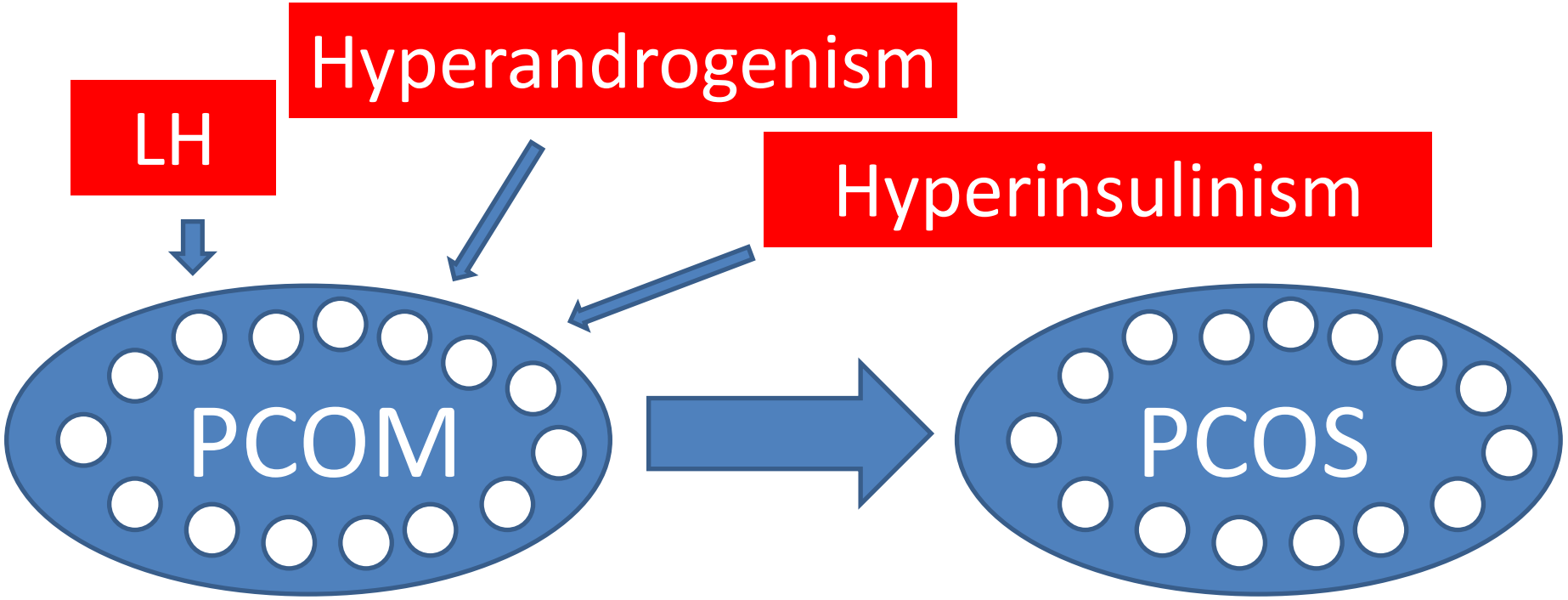


Table II Total dose of FSH required (IU) and number of eggs retrieved in the 171 women who underwent IVF expressed as means (± SD).

	n	Total dose FSH	Eggs retrieved
Controls	66	4215 (2010)	11.2 (6.8)
PCOM	35	2841* (1156)	16.5** (8.4)
PCOS	70	2848* (1144)	18.8* (9.1)

Does the level of serum antimüllerian hormone predict ovulatory function in women with polycystic ovary syndrome with aging?

Enrico Carmina, M.D.,[a] Anna Maria Campagna, M.D.,[a] Pasquale Mansuet, M.D.,[b] Giustina Vitale, M.D.,[b] Daniel Kort, M.D.,[c] and Roger Lobo, M.D.[c]

[a] Department of Medical and Biological Sciences and [b] Department of Clinical Medicine, University of Palermo, Palermo, Italy; and [c] Department of Obstetrics and Gynecology, Columbia University, New York, New York

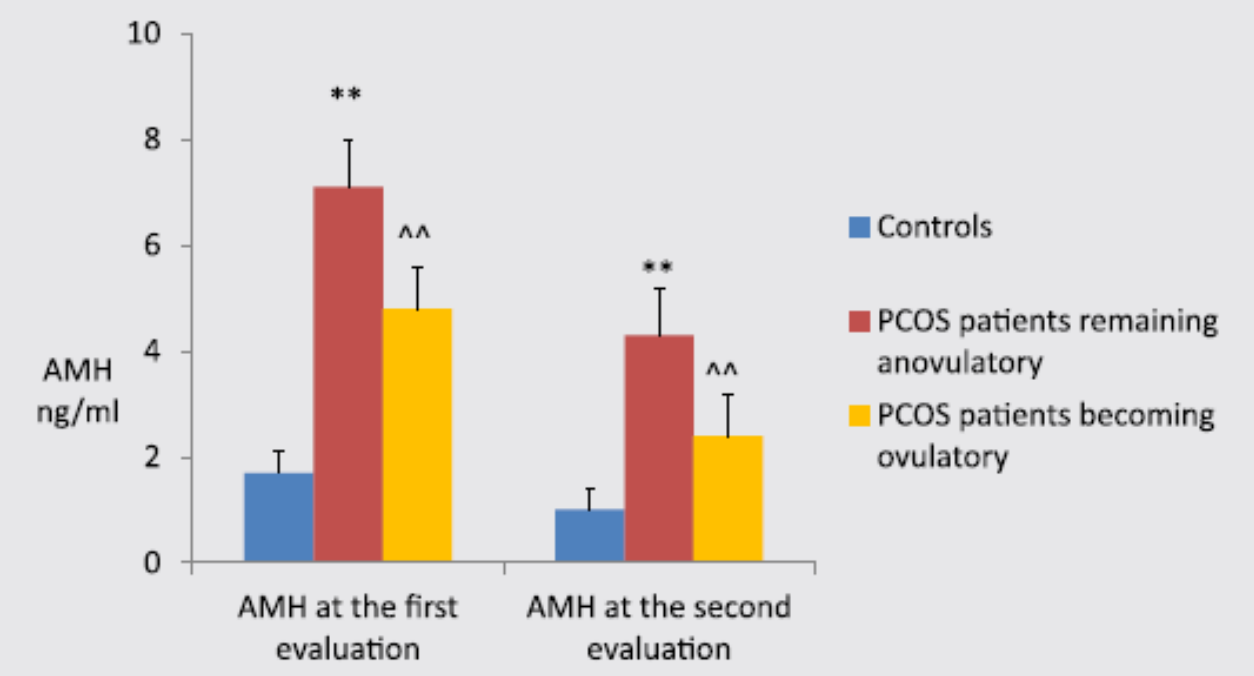
Some clinical and endocrine parameters in 54 PCOS women and 20 control subjects aged 35–40 years and 5 years later.

	Age, y	AMH, ng/mL
PCOS	37 ± 1	6.7 ± 2.1
Control	37 ± 1	1.7 ± 0.7
PCOS	42 ± 1	3.9 ± 1.2
Control	42 ± 1	1 ± 0.7

Does the level of serum antimüllerian hormone predict ovulatory function in women with polycystic ovary syndrome with aging?

Enrico Carmina, M.D.,[a] Anna Maria Campagna, M.D.,[a] Pasquale Mansuet, M.D.,[b] Giustina Vitale, M.D.,[b] Daniel Kort, M.D.,[c] and Roger Lobo, M.D.[c]

[a] Department of Medical and Biological Sciences and [b] Department of Clinical Medicine, University of Palermo, Palermo, Italy; and [c] Department of Obstetrics and Gynecology, Columbia University, New York, New York



Carmina. AMH and normalization of menses in PCOS. Fertil Steril 2012.

Some women with PCOS may become ovulatory with aging. Serum AMH may help predict ovulatory function with aging in anovulatory women with PCOS.

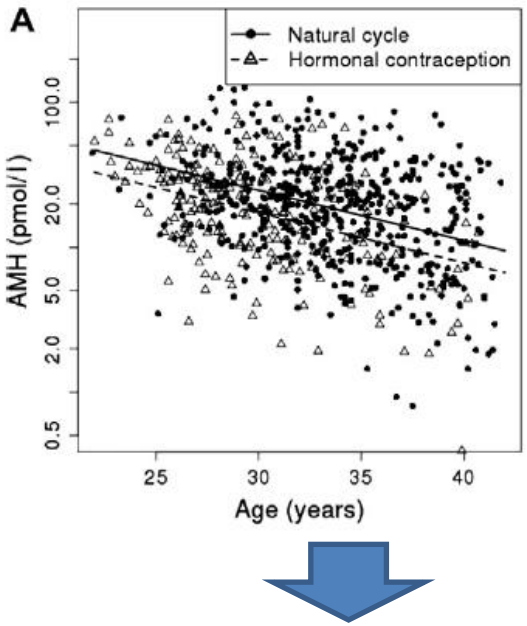
Reproductive BioMedicine Online (2012) 25, 612–619

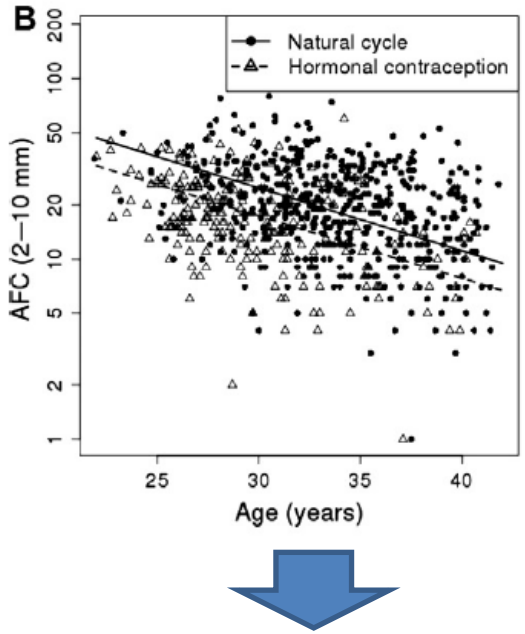
www.sciencedirect.com
www.rbmonline.com

ARTICLE

Ovarian reserve parameters: a comparison between users and non-users of hormonal contraception

JG Bentzen [a,*], JL Forman [b], A Pinborg [a], Ø Lidegaard [c], EC Larsen [a], L Friis-Hansen [d], TH Johannsen [d,e], A Nyboe Andersen [a]





Hormonal contraception may decrease value of the ovarian reserve markers. Duration ?? Doses ??

Gynecological Endocrinology, August 2011; 27(8): 587–592

informa
healthcare

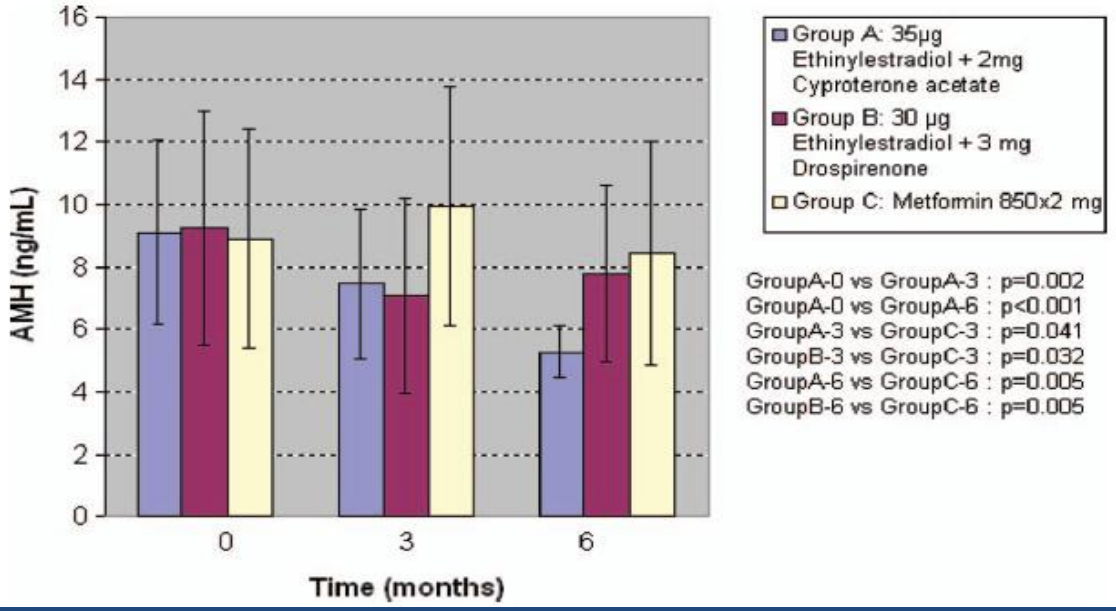
PCOS

The impact of oral contraceptives and metformin on anti-Müllerian hormone serum levels in women with polycystic ovary syndrome and biochemical hyperandrogenemia

DIMITRIOS PANIDIS[1], NEOKLIS A. GEORGOPOULOS[2,3], ATHANASIA PIOUKA[1], ILIAS KATSIKIS[1], ALEXANDROS D. SALTAMAVROS[2,3], GEORGE DECAVALAS[3], & EVANTHIA DIAMANTI-KANDARAKIS[4]

[1]*Division of Endocrinology and Human Reproduction, Second Department of Obstetrics and Gynaecology, Aristotle University of Thessaloniki, Thessaloniki, Greece,* [2]*Division of Reproductive Endocrinology,* [3]*Department of Obstetrics and Gynaecology, University of Patras Medical School, Patras, Greece, and* [4]*Division of Endocrinology, First Department of Medicine, Laiko Hospital, Medical School, University of Athens, Athens, Greece*

(Received 17 February 2010; revised 25 June 2010; accepted 5 July 2010)



Using COC decreases AMH levels, may be due to decrease in androgens and suppression of gonadotropins.

	Non-PCOS n = 8		PCOS n = 7		Mean difference between PCOS and non-PCOS (95 % CI)	Effect of time(p)	Effect of PCOS status over the intervention(p)
	Pre Wk 0	Post Wk 12	Pre Wk 0	Post Wk 12			
Age (years)	35.3 ± 5.2	–	30.6 ± 7.1	–	–	–	–
Weight (kg)	99.4 ± 15.3	97.0 ± 12.7	90.4 ± 10.8	90.1 ± 11.5	−2.1 (−5.2, 1.0)	0.090	0.169
BMI (kg/m^2)	36.9 ± 5.9	35.9 ± 5.0	33.1 ± 3.6	32.9 ± 4.0	−0.8 (−1.9, 0.4)	0.044	0.178
Lean mass (kg)	45.3 ± 3.6	45.9 ± 2.5	45.3 ± 5.6	45.0 ± 5.8	0.8 (−1.4, 3.0)	0.767	0.436
Fat mass (kg)	49.9 ± 12.6	47.0 ± 11.5	41.5 ± 6.8	41.0 ± 8.1	−2.3 (−5.3, 0.7)	0.028	0.120
Android mass (kg)	4.5 ± 1.3	4.2 ± 1.3	4.0 ± 0.1	3.9 ± 1.0	−0.2 (−0.5, 0.08)	0.006	0.154
Visceral fat (cm^2)	135.1 ± 41.5	132.7 ± 48.0	126.4 ± 67.4	118.4 ± 63.2	5.7 (−16.3, 27.6)	0.319	0.583
Testosterone (nmol/l)	1.4 ± 0.6†	1.8 ± 1.0	2.9 ± 0.6	2.9 ± 0.9	0.4 (−0.2, 1.0)	0.231	0.140
SHBG (nmol/l)	51.7 ± 35.6	54.3 ± 30.0	29.7 ± 10.5	31.1 ± 11.5	−1.2 (−11.1, 13.5)	0.499	0.835
FAI	3.5 ± 2.0†	4.1 ± 3.2†	10.8 ± 4.6	9.9 ± 4.1	1.5 (−0.7, 3.8)	0.835	0.165
GIR (mg·m^{-2}·min^{-1})	240.4 ± 53.0†	297.5 ± 91.9†	178.7 ± 120.2	199.3 ± 106.3	36.4 (−25.5, 98.3)	0.018	0.224
AMH (pmol/l)*	14.9 ± 9.9†	16.3 ± 12.0†	59.1 ± 20.5	45.9 ± 15.3	14.6 (4.7, 24.4)	0.022	0.007

Moran LJ et al. Exercise, AMH, and PCOS … Horm Metab Res 2011; 43: 977–979

Exercise Decreases Anti-Müllerian Hormone in Anovulatory Overweight Women with Polycystic Ovary Syndrome

European Journal of Obstetrics & Gynecology and Reproductive Biology 163 (2012) 185–189

Contents lists available at SciVerse ScienceDirect

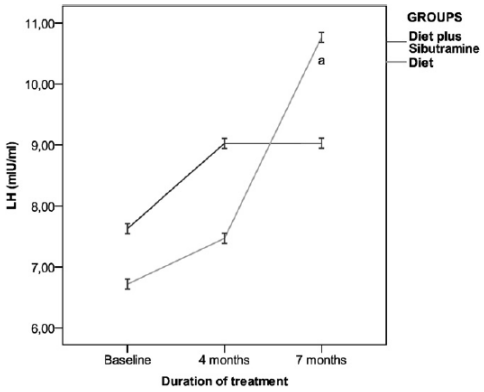
European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

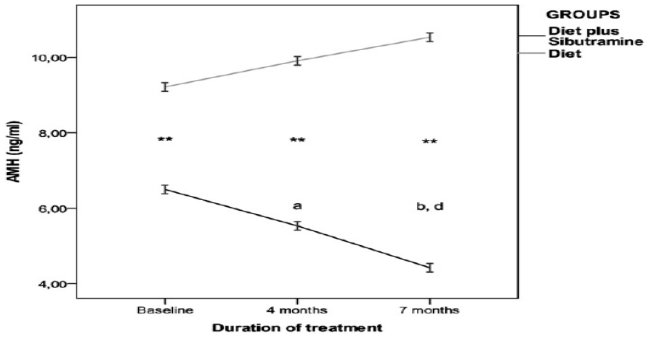
Sibutramine administration decreases serum anti-Müllerian hormone (AMH) levels in women with polycystic ovary syndrome

Christos Vosnakis [a], Neoklis A. Georgopoulos [b,*], Anastasia K. Armeni [b], Efstathios Papadakis [a], Nikolaos D. Roupas [b], Ilias Katsikis [c], Dimitrios Panidis [c]

	Diet and physical exercise plus sibutramine (group S) ($n=57$)			Hypocaloric diet and physical exercise (group D) ($n=19$)		
	Baseline	4 months	7 months	Baseline	4 months	7 months
Age	25.72 ± 6.08			25.45 ± 5.77		
Body weight (Kg)	94.76 ± 13.25	83. ± 13.85[b]	80.4 ± 14.69[b,d]	93.53 ± 17.57	85.63 ± 16.98[b]	85.93 ± 18.05[b]
BMI (Kg/m^2)	34.12 ± 4.78	29.88 ± 4.97[b]	28.95 ± 5.20[b,d]	34.08 ± 5.88	31.19 ± 5.71[b]	31.27 ± 5.95[b]
WHR	0.84 ± 0.07	0.82 ± 0.06[b]	0.81 ± 0.06[b]	0.84 ± 0.07	0.82 ± 0.08	0.81 ± 0.08[a]
AMH (ng/ml)	6.50 ± 3.25[**]	5.53 ± 3.41[a]	4.42 ± 2.37[b,d]	9.21 ± 3.67	9.91 ± 4.88	10.53 ± 5.00



Direct ovarian act



Anti-Müllerian Hormone in Women with Polycystic Ovary Syndrome Before and After Therapy with Metformin

Tomova A et al. AMH in Women with PCOS… Horm Metab Res 2011; 43: 723–727

Authors A. Tomova[1], F. Deepinder[2], R. Robeva[1], G. Kirilov[1], Z. Mechandjiev[3], P. Kumanov[1]

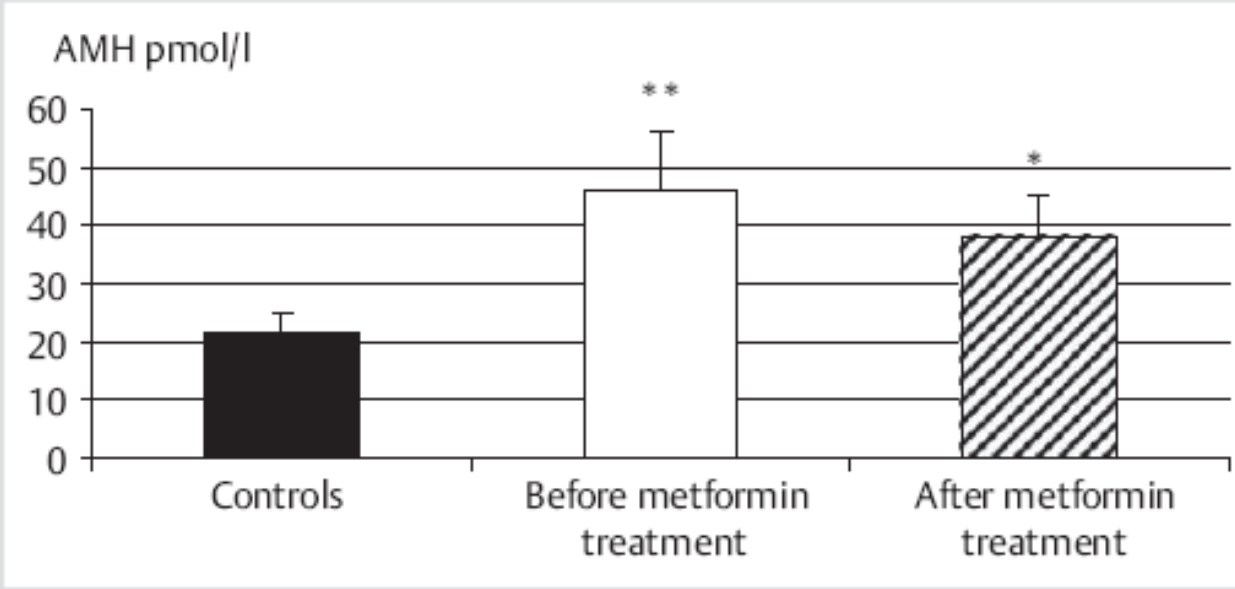


Fig. 1 AMH levels in 13 patients before and after metformin treatment in comparison with the controls (**p<0.01; *p<0.05) (mean ± SEM).

Gynecological Endocrinology, 2012; Early Online: 1–4

ISSN 0951-3590 print/ISSN 1473-0766 online
DOI: 10.3109/09513590.2012.736563

informa
healthcare

ORIGINAL ARTICLE

Effects of metformin on serum insulin and anti-mullerian hormone levels and on hyperandrogenism in patients with polycystic ovary syndrome

Areana Diogo Nascimento[1], Lucia Alves Silva Lara[1], Ana Carolina Japur de Sá Rosa-e-Silva[1], Rui Alberto Ferriani[2] & Rosana Maria Reis[2]

Table II. Serum AMH and insulin levels of patients with PCOS, before and after metformin treatment.

	PCOS group ($N = 16$)		
	Pretreatment	Post-treatment	
Variable	(Mean ± SD)		p
Insulin	16.4 ± 2.6	12 ± 1.9*	0.01
QUICKI	0.33 ± 0.01	0.35 ± 0.01*	0.001
AMH (pmol/l)	49.9 ± 6.1	41.5 ± 5.6	0.06

AMH, anti-mullerian hormone; PCOS, polycycstic ovary syndrome; QUICKI, quantitative insulin check index.

J Clin Endocrinol Metab 96: E821–E824, 2011

JCEM ONLINE

Brief Report—Endocrine Research

The Metabolic Status Modulates the Effect of Metformin on the Antimullerian Hormone-Androgens-Insulin Interplay in Obese Women with Polycystic Ovary Syndrome

D. Romualdi, S. De Cicco, V. Tagliaferri, C. Proto, A. Lanzone, and M. Guido

Normo-insulinemic

AMH unchanced

hyperinsulinemic

AMH decrease 29.5%

Metformin decrease serum AMH level only in the hyperinsulinemic patient .

Impact of laparoscopic ovarian drilling on anti-Müllerian hormone levels and ovarian stromal blood flow using three-dimensional power Doppler in women with anovulatory polycystic ovary syndrome

Ashraf I. Elmashad, M.D.

Department of Obstetrics and Gynecology, Benha Faculty of Medicine, Benha University, Egypt

Variable	Control group (n = 20)	PCOS group (n = 23)	
		Pre-LOD	Post-LOD
Age (y)	27.4 ± 2.8	28.8 ± 3.1	–
BMI (kg/m^2)	26.7 ± 2.4	29.2 ± 2.6	28.4 ± 2.3
LH (IU/L)	4.9 ± 1.2	11.7 ± 1.3[a]	10.8 ± 1.8
FSH (IU/L)	3.9 ± 1.1	4.2 ± 1.3	4.1 ± 1.4
LH:FSH	1.2 ± 0.2	2.8 ± 0.4[a]	2.5 ± 0.6
T (nmol/L)	1.1 ± 0.3	4.2 ± 0.4[a]	2.6 ± 0.6[b]
SHBG	48	31	34
FAI	2.3	11.6	7.6
AMH (ng/mL)	1.9 ± 0.3	7.4 ± 4.6[a]	4.2 ± 2.5[b]
Ovarian volume (mL)	6.9 ± 1.1	13.8 ± 2.1[a]	7.4 ± 2.9[b]
Mean number of follicles (both ovaries)	13.0 ± 1.9	29.0 ± 2.4[a]	15.0 ± 2.2[b]
Vascularization index	1.7 ± 0.34	4.8 ± 1.3[a]	2.4 ± 0.75[b]
Flow index	43.9 ± 5.9	52.4 ± 4.3[a]	44.3 ± 2.5[b]
Vascularization flow index	0.97 ± 0.38	2.9 ± 0.43[a]	1.2 ± 0.59[b]

Fertil Steril 2011;95:2342–6.

Preoperative and postoperative plasma levels of AMH, power Doppler flow studies, and other hormones in women with PCOS who ovulated in response to LOD (responders) versus nonresponders.

LOD	Variable	Responders (n = 17)	Nonresponders (n = 6)	*P* value[a]
Pre-LOD	AMH (ng/mL)	6.3 (5.1–6.9)[b]	11.9 (11.1–13.6)	.003
	FSH (IU/L)	4.8 (2.8–5.1)	4.7 (2.7–5.2)	.437
	LH (IU/L)	11.8 (8.1–13.2)	12.4 (11.31–6.8)	.243
	T (nmol/L)	3.4 (3.2–3.6)	4.1 (3.8–4.2)	.116
	SHBG	36.0 (34.1–38.0)	34.7 (34.1–37.1)	.721
	FAI	9.7 (8.4–10.3)	11.0 (10.3–11.3)	.218
	Vascularization index	4.7 (4.5–4.9)	5.1 (4.5–5.2)	.183
	Flow index	50.9 (49.4–53.4)	51.3 (49.7–53.9)	.872
	VFI	2.8 (2.3–3.1)	3.1 (2.8–3.2)	.170
Post-LOD	AMH (ng/mL)	4.2 (2.6–4.9)[b]	11.2 (10.4–14.0)	.002
	FSH (IU/L)	4.7 (2.7–5.2)	4.9 (4.2–5.4)	.129
	LH (IU/L)	10.9 (7.8–12.7)	12.1 (11.1–17.5)	.241
	T (nmol/L)	3.3 (3.1–3.5)	3.8 (3.6–4.1)	.578
	SHBG	38.1 (35.1–39.2)	36.2 (35.3–38.5)	.258
	FAI	8.8 (7.9–9.9)	10.3 (9.7–10.9)	.063
	Vascularization index	2.4 (2.2–2.7)	2.5 (2.3–2.7)	.610
	Flow index	44.3 (42.1–45.2)	44.8 (41.7–45.8)	.364
	VFI	1.3 (1.2–1.4)	1.7 (1.4–1.1.8)	.412

After LOD serum AMH level reduce significantly especially in responders.

Women who ovulated in response to LOD (responders) have a significantly lower preoperative AMH .

REPRODUCTION
REVIEW

Anti-Müllerian hormone and polycystic ovary syndrome: a mountain too high?

Laura Pellatt, Suman Rice and Helen D Mason

Basic Medical Sciences, St George's, University of London, Cranmer Terrace, London SW17 0RE, UK

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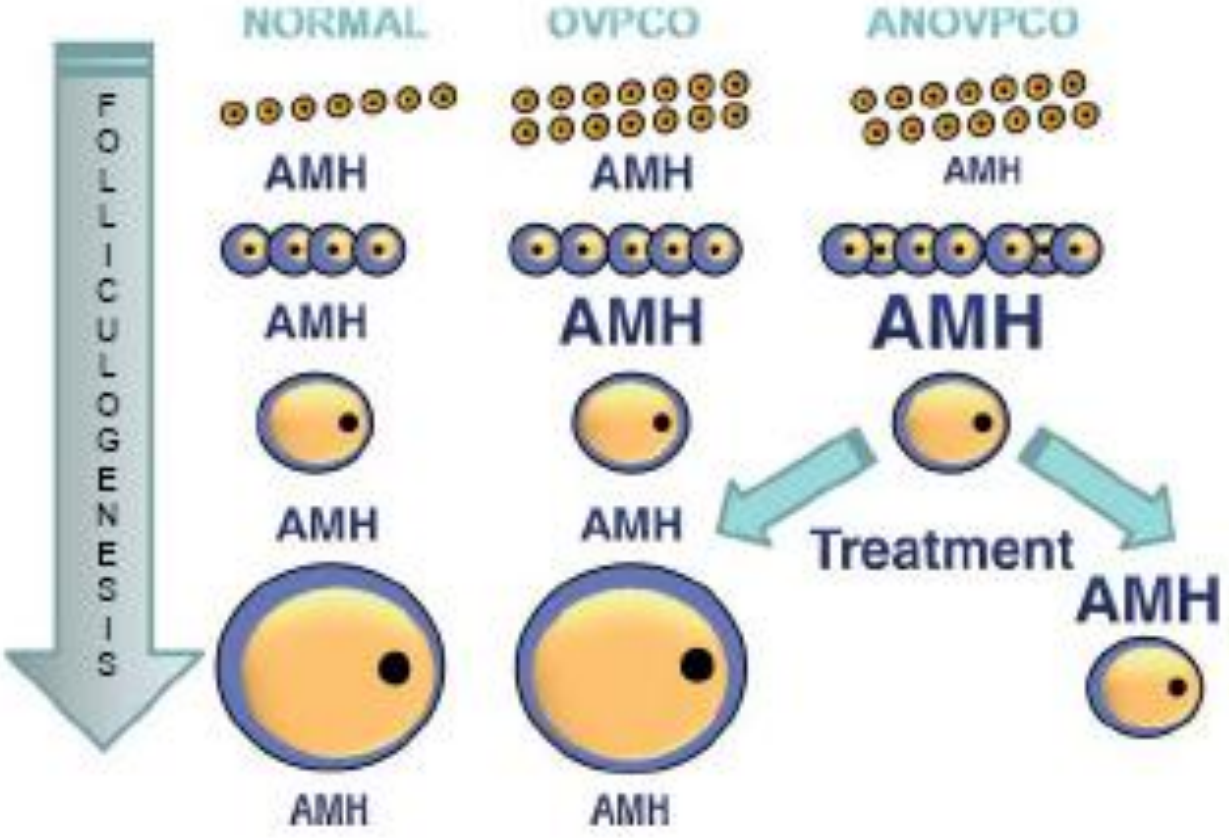
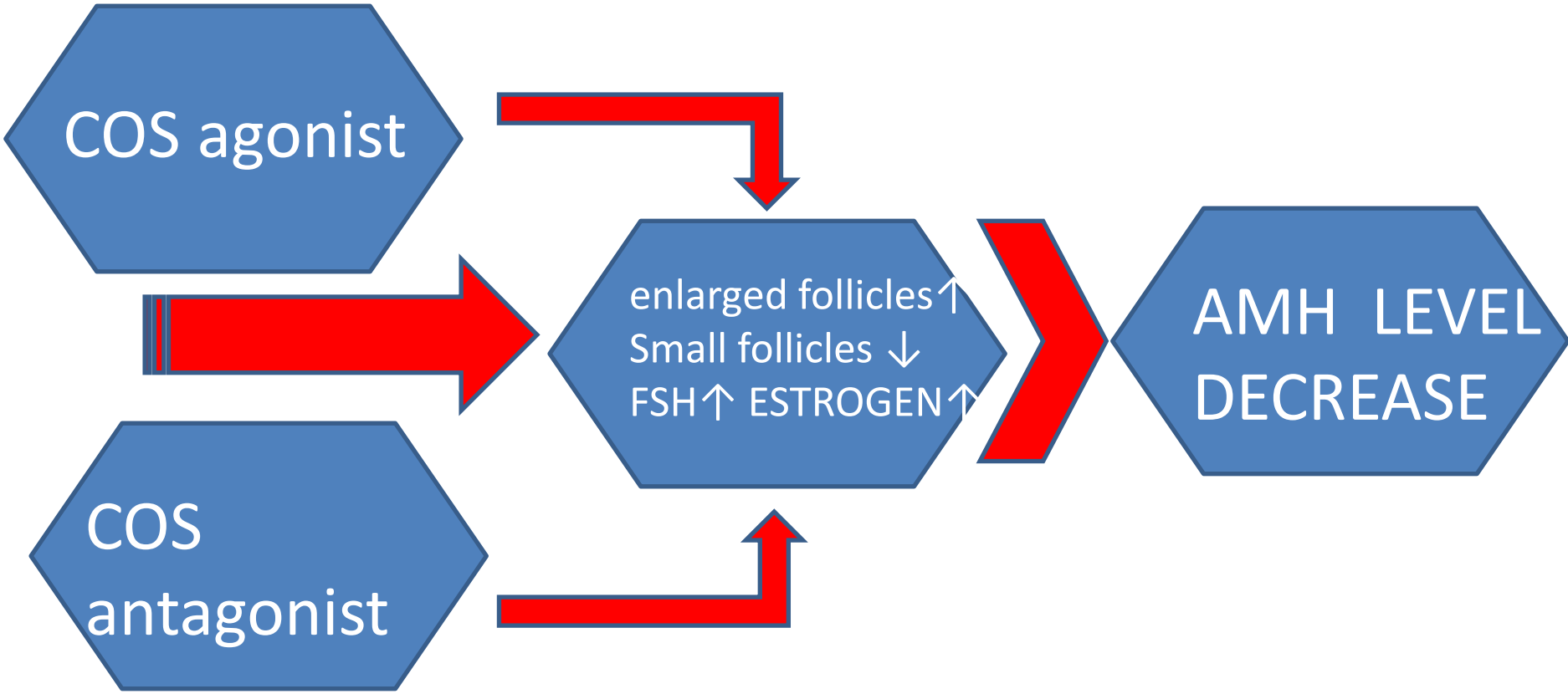


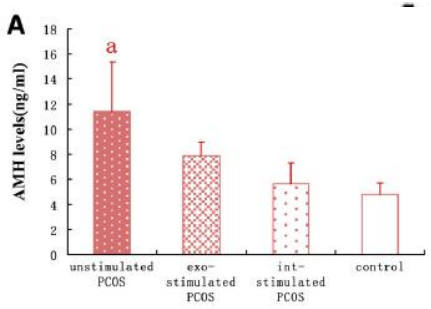
COS and AMH

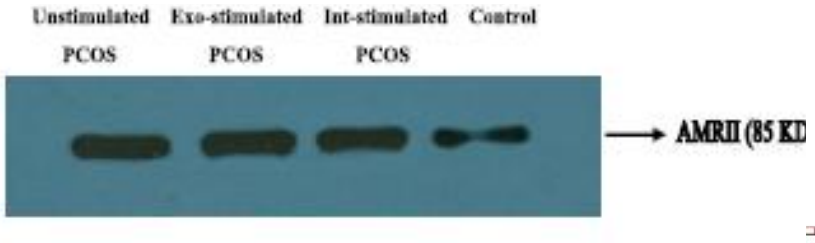

COS agonist
COS antagonist
enlarged follicles↑
Small follicles ↓
FSH↑ ESTROGEN↑
AMH LEVEL DECREASE

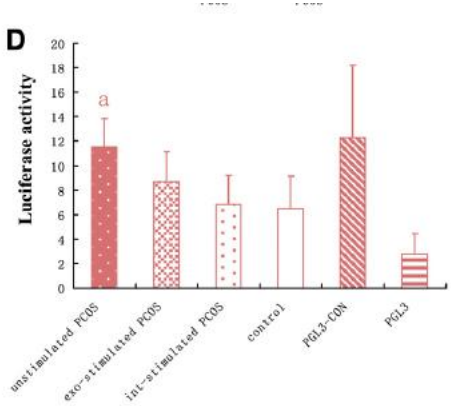
Follicle-stimulating hormone suppressed excessive production of antimullerian hormone caused by abnormally enhanced promoter activity in polycystic ovary syndrome granulosa cells

Yi Li, Ph.D., Li-Na Wei, Ph.D., and Xiao-Yan Liang, M.D.

Center for Reproductive Medicine, Sixth Affiliated Hospital, Sun Yat-sen University, Guangz







Result(s): Both the secretiory level and mRNA abundance of AMH were significantly enhanced in PCOS granulosa cells. They could be partially suppressed by FSH. The mRNA and protein levels of AMHRII in PCOS granulosa cells were significantly increased. However, they were not affected by FSH. The luciferase activity of AMH in PCOS granulosa cells was significantly amplified but could be suppressed by FSH.

Conclusion(s): Enhanced promoter activity can cause excessive production of AMH in PCOS granulosa cells. FSH may inhibit the excessive secretion of AMH by suppressing the luciferase activity of AMH promoter, but it has no effect on AMHRII expression. (Fertil Steril® 2011;95:2354–8. ©2011 by American Society for Reproductive

If an inhibitor of AMH promoter activity can be created in the future, this may provide a new direction for treating PCOS follicular developmental retardation

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Reproductive BioMedicine Online (2013) xxx, xxx–xxx
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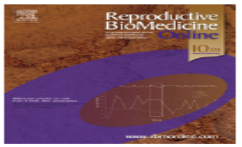


ARTICLE

Anti-Müllerian hormone as a predictor of pregnancy following IVF

Priya Bhide [a,*], Anil Gudi [a], Amit Shah [a], Peter Timms [a], Kate Grayson [b], Roy Homburg [a]

Table 1 Clinical pregnancy rate according to quartiles of AMH.

AMH quartile (pmol/l)	Not pregnant	Pregnant
<10.28	155 (75.6)	50 (24.4)[a]
10.29–20.02	136 (66.3)	69 (33.7)
20.03–35.38	139 (67.8)	66 (32.2)
>35.38	123 (60.0)	82 (40.0)[b]
Total	553 (67.4)	267 (32.6)

AMH is a poor predictor for CPR

But in conjunction with older age, AMH may be independent predictive for negative outcome

Table 2 Age-stratified clinical pregnancy rate according to quartiles of AMH.

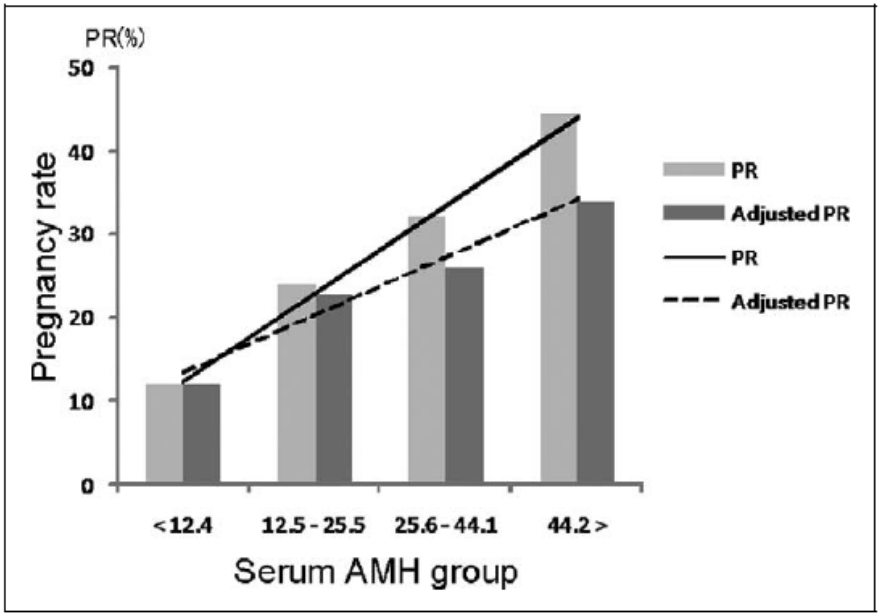
Age (years)	Overall	AMH quartile				Chi-squared tests[a]
		1st	2nd	3rd	4th	
<30	43/124 (34.7)	5/15 (33.3)	9/21 (42.9)	9/36 (25.)	20/52 (38.5)	2.449, 3, NS
30–34	96/270 (35.6)	17/54 (31.5)	17/59 (28.8)	28/70 (40.0)	34/87 (39.1)	2.637, 3, NS
35–39	110/316 (34.8)	23/82 (28.0)	36/94 (38.3)	27/82 (32.9)	24/58 (41.4)	3.387, 3, NS
≥40	18/110 (16.4)	5/54 (9.3)	7/31 (22.6)	2/17 (11.8)	4/8 (50.0)	9.743, 3, $P = 0.021$

Serum Anti-Mullerian Hormone Levels Affect the Rate of Ongoing Pregnancy After In Vitro Fertilization

Reproductive Sciences
20(1) 51-59

DOI: 10.1177/1933719112450329
http://rs.sagepub.com
SAGE

Hiroyuki Honnma, MD, PhD[1], Tsuyoshi Baba, MD, PhD[2], Masahiro Sasaki, MD, PhD[1], Yoshiki Hashiba, MD, PhD[1], Hisanori Oguri, MD, PhD[1], Takanori Fukunaga, PhD[1], Toshiaki Endo, MD, PhD[2], and Yoshimasa Asada, MD, PhD[1]

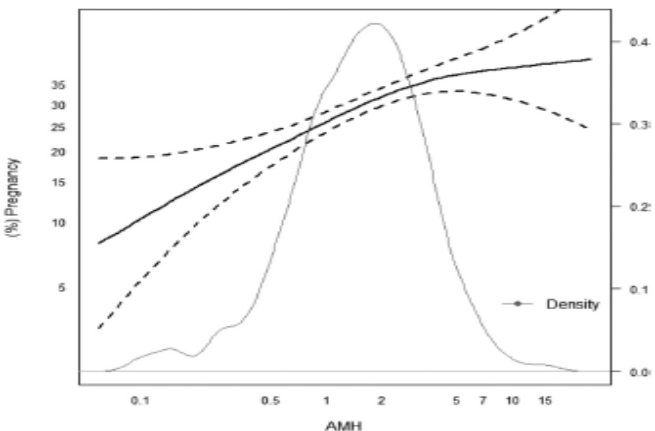


J Clin Endocrin Metab. First published ahead of print February 13, 2013 as doi:10.1210/jc.2012-3676

ORIGINAL ARTICLE
Endocrine Care

Antimüllerian Hormone Levels Are Strongly Associated with Live-Birth Rates After Assisted Reproduction

Thomas Brodin, Nermin Hadziosmanovic, Lars Berglund, Matts Olovsson, and Jan Holte



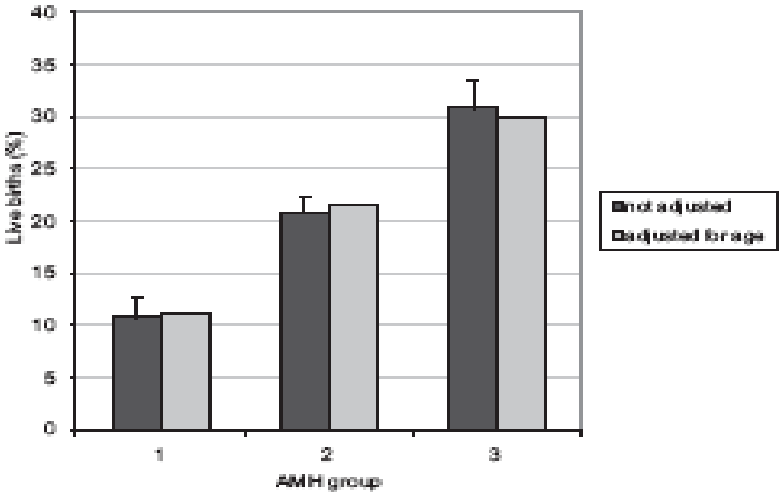


Figure 2. Live-birth rate per started cycle, without (mean values ± SEM, *black*) and with age adjustment (*gray*). Group 1: antimüllerian hormone (AMH) < 0.84 ng/mL (25th percentile); group 2: AMH 0.84 to 2.94 ng/mL; group 3: AMH > 2.94 ng/mL (75th percentile). N = 1230 in vitro fertilization-intracytoplasmic sperm injection treatment cycles.

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Reproductive BioMedicine Online (2013) xxx, xxx–xxx

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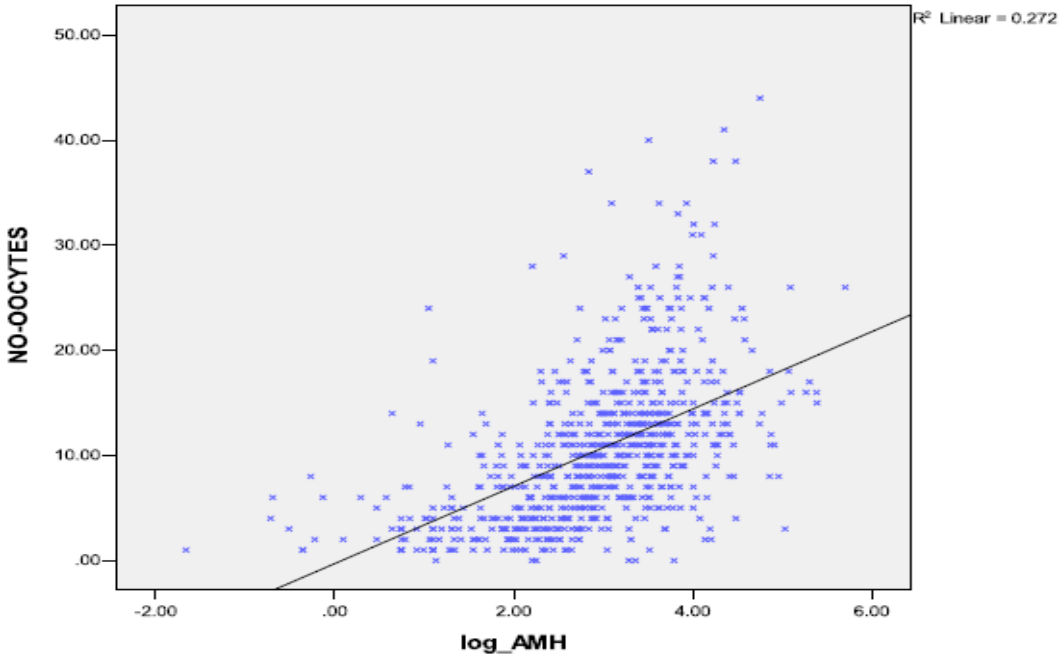
ARTICLE

Anti-Müllerian hormone as a predictor of pregnancy following IVF

Priya Bhide [a,*], Anil Gudi [a], Amit Shah [a], Peter Timms [a], Kate Grayson [b], Roy Homburg [a]



Correlation of log AMH and number of oocytes retrieved (r = 0. 522; n = 820; p<0.001).

AMH is sensitive predictor of overresponse to COH

Table III Basal AMH levels in women with normal response, hyper-response to controlled ovarian stimulation (COS) and ovarian hyperstimulation syndrome (OHSS)

Author	Design	*n*	Mean AMH levels		
			Normal response	Excessive response	OHSS
Tremellen *et al.* (2005)	Prosp	75	15.47 pmol/l	21.53 pmol/l[a]	
Eldar-Geva *et al.* (2005)	Prosp	56	14.1 pmol/l	37.8 pmol/l[b]	
Nakhuda *et al.* (2006)	Retro	30	0.63 ng/ml		3.6 ng/ml
La Marca *et al.* (2007)	Prosp	48	5.98 ng/ml	10.13 ng/ml[c]	
Nelson *et al.* (2007)	Prosp	340	10 pmol/l	27 pmol/l[d]	
Nardo *et al.* (2008)	Prosp	165	3.04 ng/ml	5.56 ng/ml[b]	

Table IV AMH cut-off values for the prediction of hyper-response to COS and OHSS

Author	*n*	Study design	Cut-off value	Sensitivity (%)	Specificity (%)	Prediction of hyper-response	Prediction of OHSS
Kwee *et al.* (2007)	110	Prosp	5 mcg/l	53	91	√[a]	
Nelson *et al.* (2007)	340	Prosp	25 pmol/l	60	94.9	√[b]	
Lee *et al.* (2008)	262	Prosp	3.36 ng/ml	90.5	81.3		√
Nardo *et al.* (2008)	165	Prosp	3.5 ng/ml	88	70	√[a]	

La Marca et al. 2010

Human Reproduction Update, Vol.17, No.1 pp. 46–54, 2011
Advanced Access publication on July 28, 2010 doi:10.1093/humupd/dmq034

human reproduction update

AMH and AFC as predictors of excessive response in controlled ovarian hyperstimulation: a meta-analysis

S.L. Broer [1,*], M. Dólleman [1], B.C. Opmeer [2], B.C. Fauser [1], B.W. Mol [3], and F.J.M. Broekmans [1]

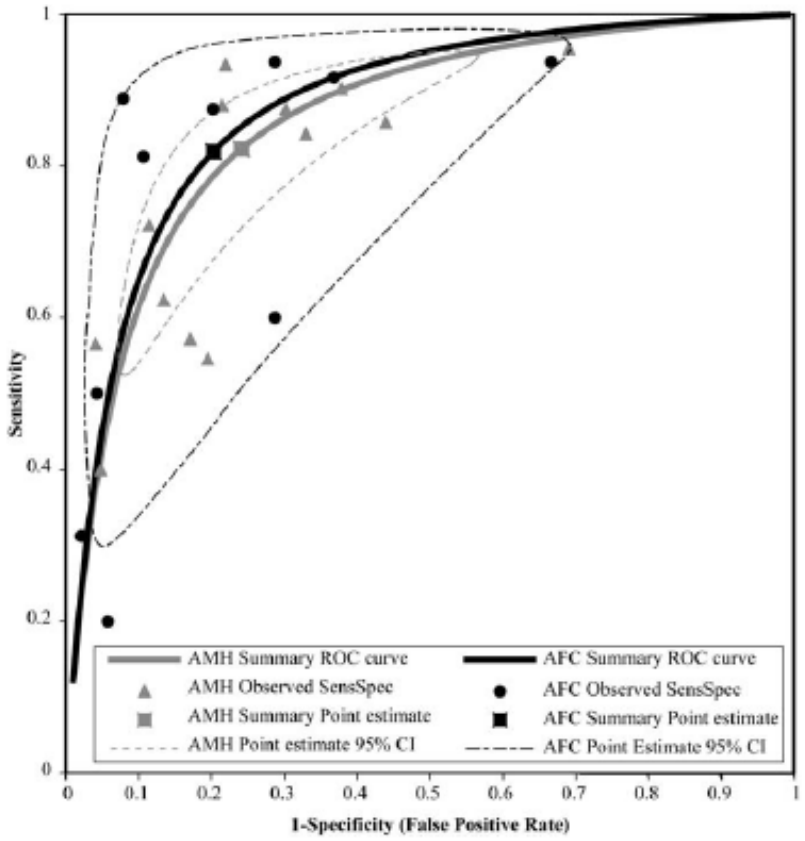


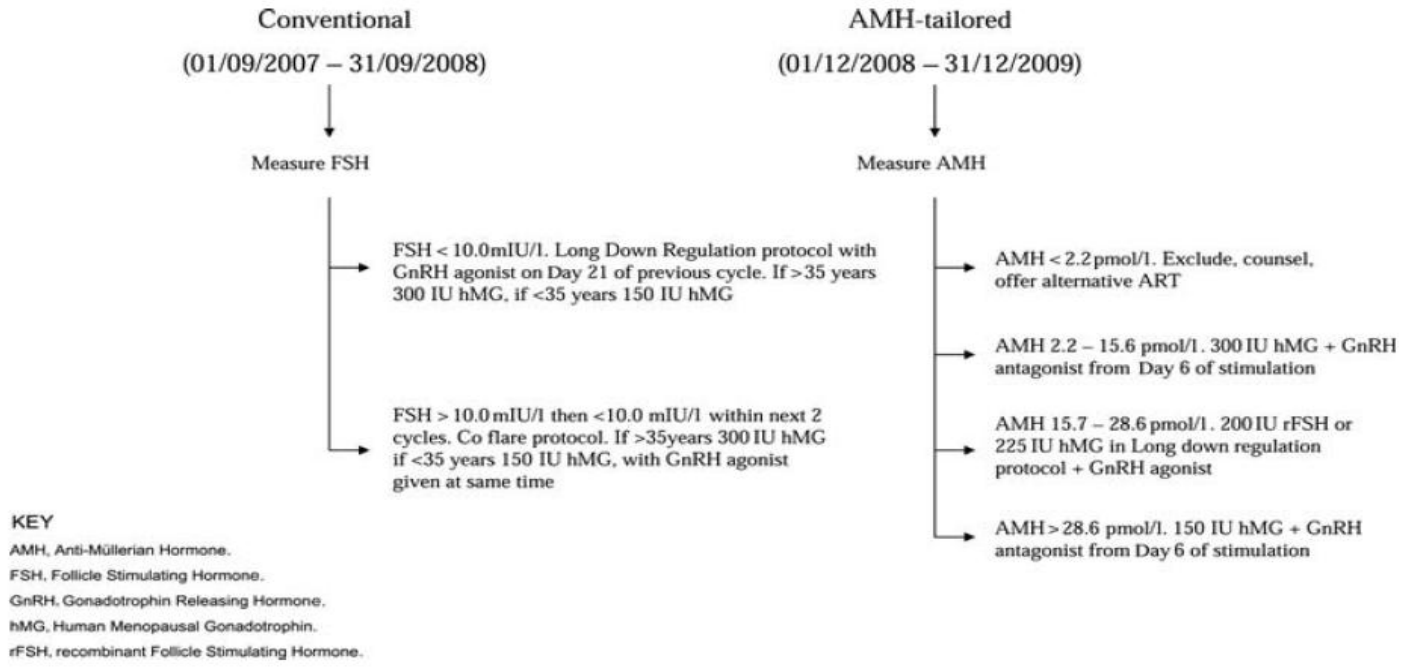
Figure 2 AMH and AFC in the prediction of an excessive response. *Note:* Regardless of the number of cut-offs mentioned per study, only one cut-off was taken into analysis. For the observed values of sensitivity–specificity points, all cut-offs are displayed.

Hum. Reprod. Advance Access published June 13, 2011
Human Reproduction, Vol.0, No.0 pp. 1–10, 2011
doi:10.1093/humrep/der182

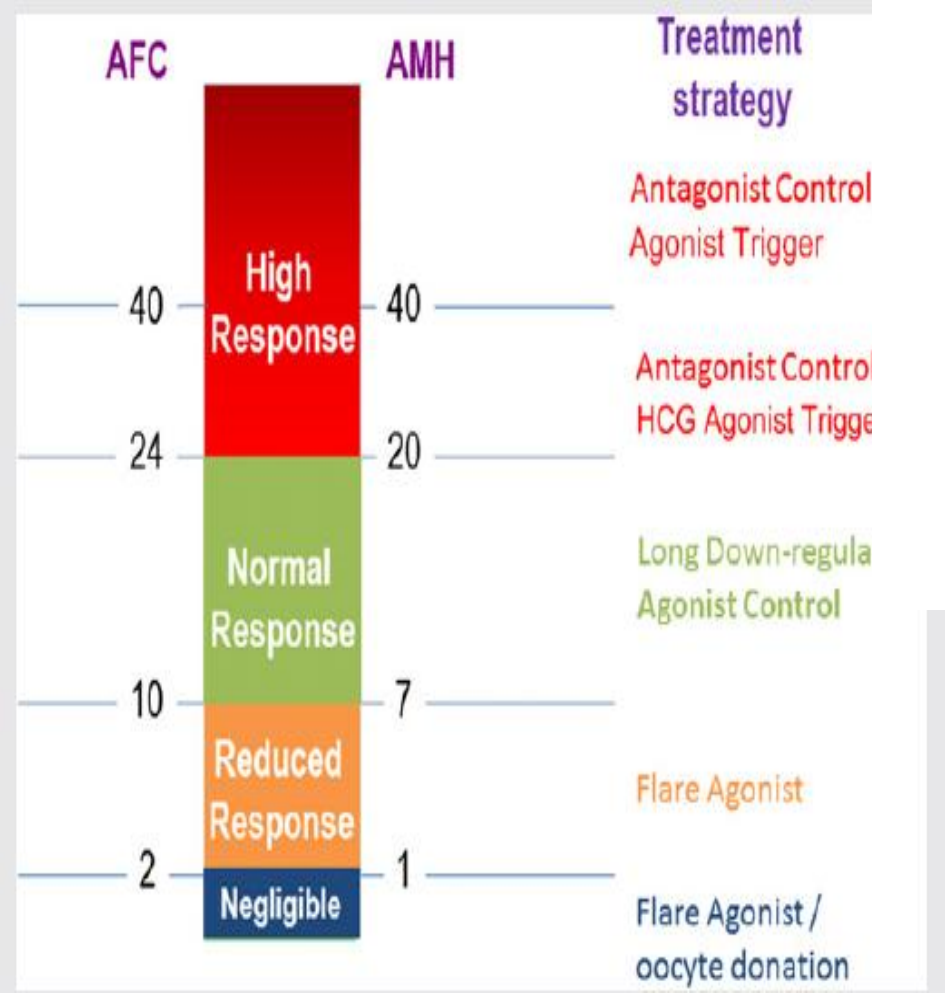
human reproduction ORIGINAL ARTICLE *Reproductive endocrinology*

Anti-Müllerian hormone-tailored stimulation protocols improve outcomes whilst reducing adverse effects and costs of IVF

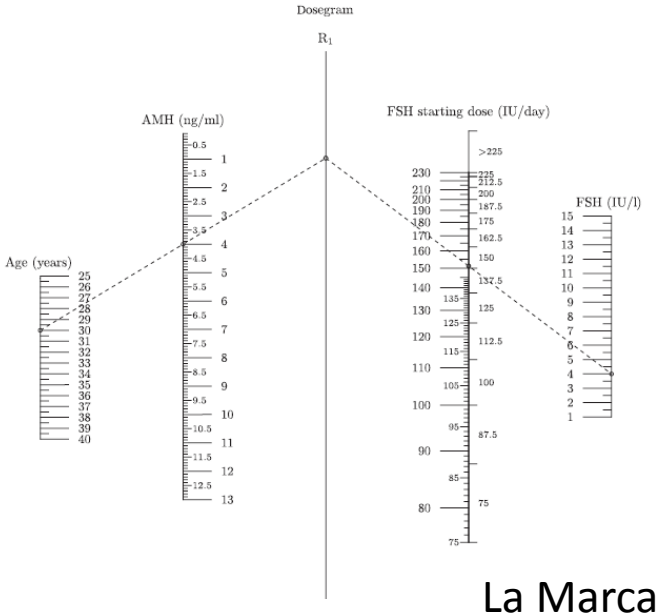
A.P. Yates[1,*], O. Rustamov[2], S.A. Roberts[3], H.Y.N. Lim[2], P.W. Pemberton[1], A. Smith[1], and L.G. Nardo[2]



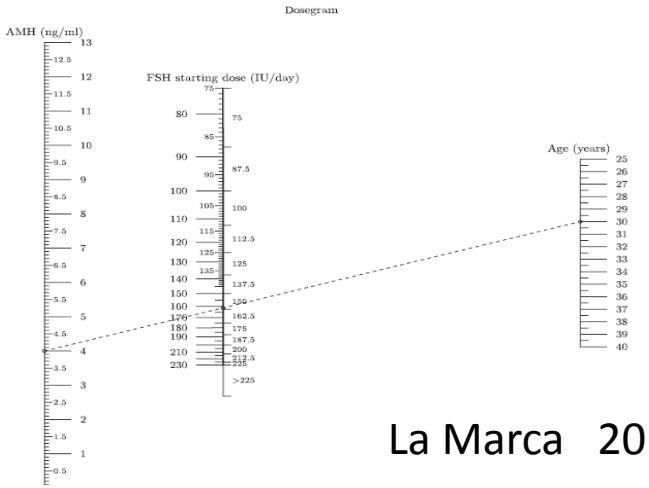
Clinical outcomes	Conventional protocol (n = 346)	AMH-tailored protocol (n = 423)	Unadjusted P-value[a]	Adjusted P-value[b]
Cancelled cycles due to				
Poor response	14 (4.0%)	14 (3.3%)	0.70	0.57
Elective freeze all	0	3 (0.7%)	0.26	0.066
Other reasons	4 (1.2%)	4 (0.9%)	1	0.80
Number (SD) of oocytes	12.4 ± 7.8	10.6 ± 6.9	0.001[c]	0.007[c]
OHSS leading to				
Cycle cancellation and/or freeze all	24 (6.9%)	10 (2.3%)	0.002	0.004
Hospital admission	10 (2.9%)	5 (1.2%)	0.12	0.15
Fertilization				
Incidence of failed fertilization	27 (7.8%)	19 (4.5%)	0.066	0.11
Absence of normal embryos	4 (1.2%)	3 (0.7%)	0.71	0.54
Embryo transfer				
Women who had embryo transfer (based on outcome data)	273 (78.9%)	370 (87.5%)	0.002	0.003
Pregnancy				
Pregnancy per cycle started	62 (17.9%)	117 (27.7%)	0.002	0.002
Live births per cycle started	55 (15.9%)	101 (23.9%)	0.007	0.003
Twin births per cycle started	9 (2.6%)	20 (4.7%)	0.13	0.15
Live birth per ET	20.1%	27.3%	0.041	0.012



Nelson. 2013.



La Marca 2012.



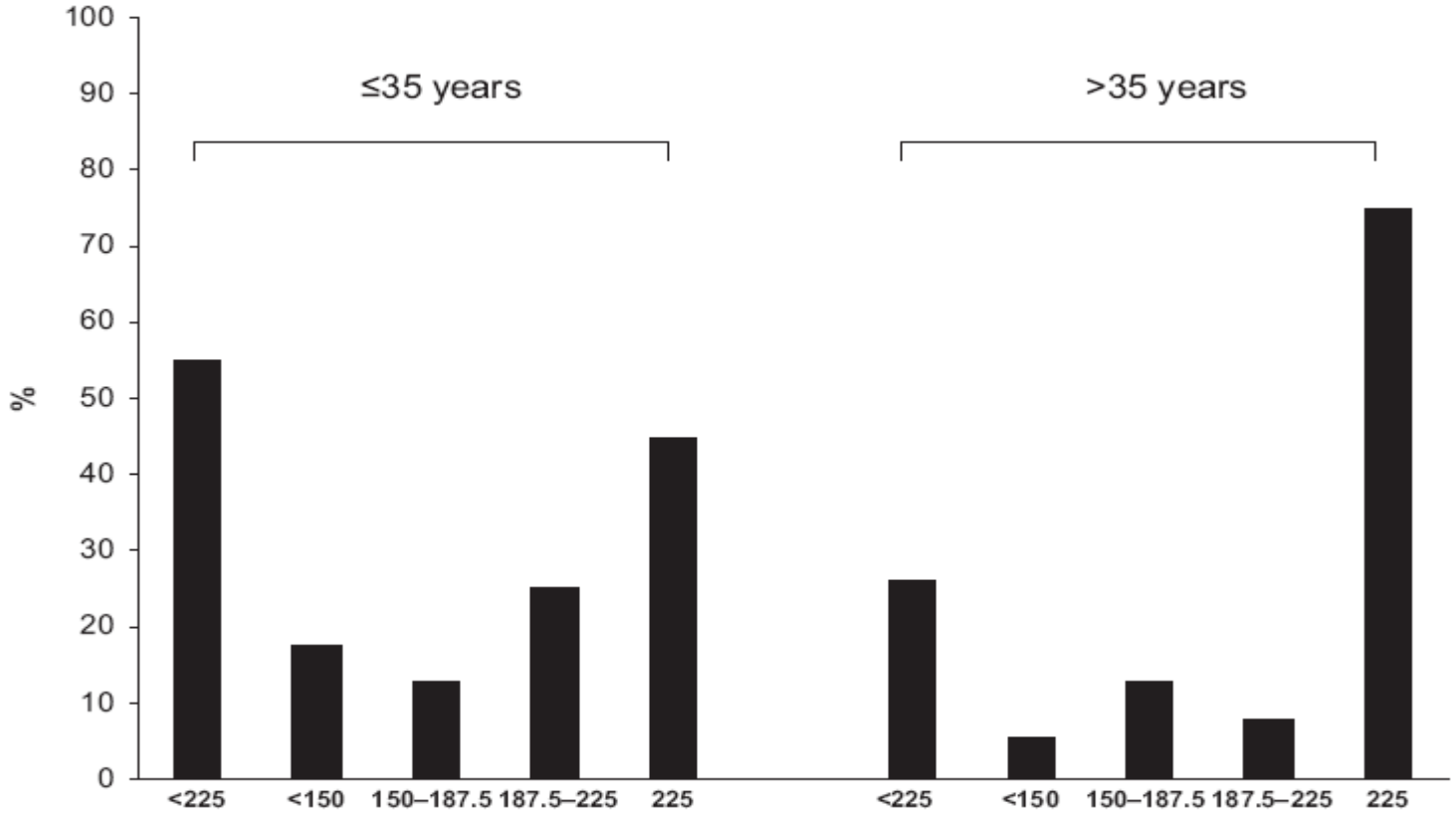
La Marca 2012.

The measurement of AMH before IVF cycles may be useful for individualization of COS protocol .

DOI: 10.1111/j.1471-0528.2012.03412.x
www.bjog.org

Development of a nomogram based on markers of ovarian reserve for the individualisation of the follicle-stimulating hormone starting dose in *in vitro* fertilisation cycles

A La Marca,[a] E Papaleo,[b] V Grisendi,[a] C Argento,[a] S Giulini,[a] A Volpe[a]



J Assist Reprod Genet (2012) 29:597–602
DOI 10.1007/s10815-012-9759-1

ASSISTED REPRODUCTION TECHNOLOGIES

Serum anti-Mullerian hormone levels correlate with ovarian response in idiopathic hypogonadotropic hypogonadism

M. Sönmezer · B. Özmen · C. S. Atabekoglu · E. G. Papuccu · S. Ozkavukcu · B. Berker · R. Pabuccu

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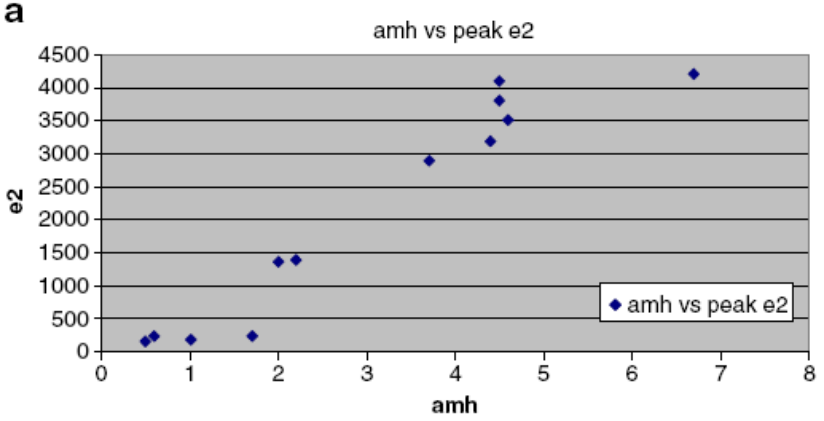

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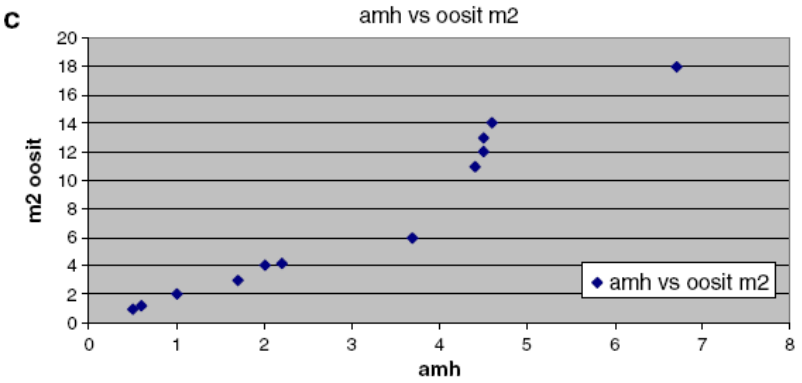


Table 2 Correlations between serum AMH levels, and COH outcome parameters and embryologic data

AMH	Serum Peak E2	MII oocytes	hCG day		Total hMG Dose	Grade A embryos
			Follicle >14 mm	Follicle >17 mm		
r	0,8766	0,8395	0,8287	0,8142	−0,6918	0,8516
p value	0.001	0.002	0.003	0.003	0.0506	0.002

European Journal of Obstetrics & Gynecology and Reproductive Biology 158 (2011) 254–259

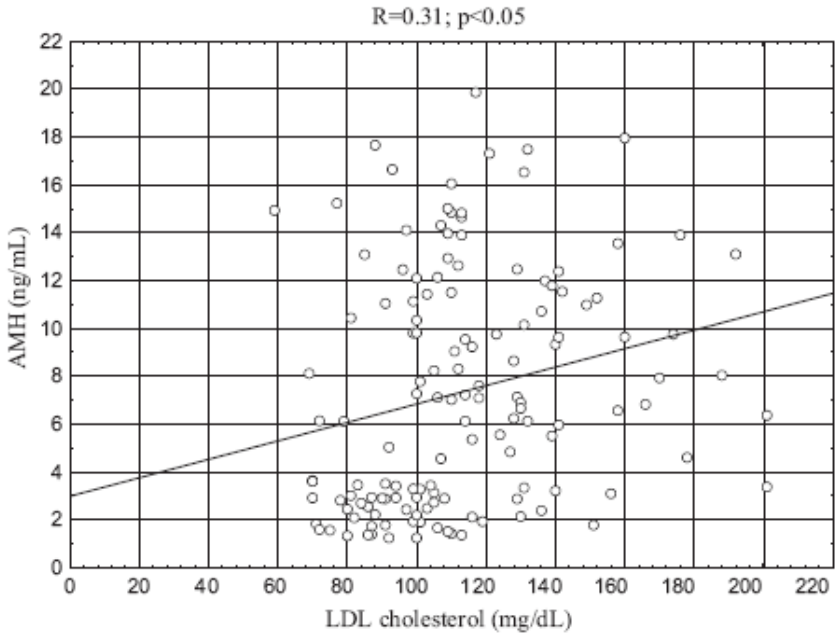
Contents lists available at ScienceDirect

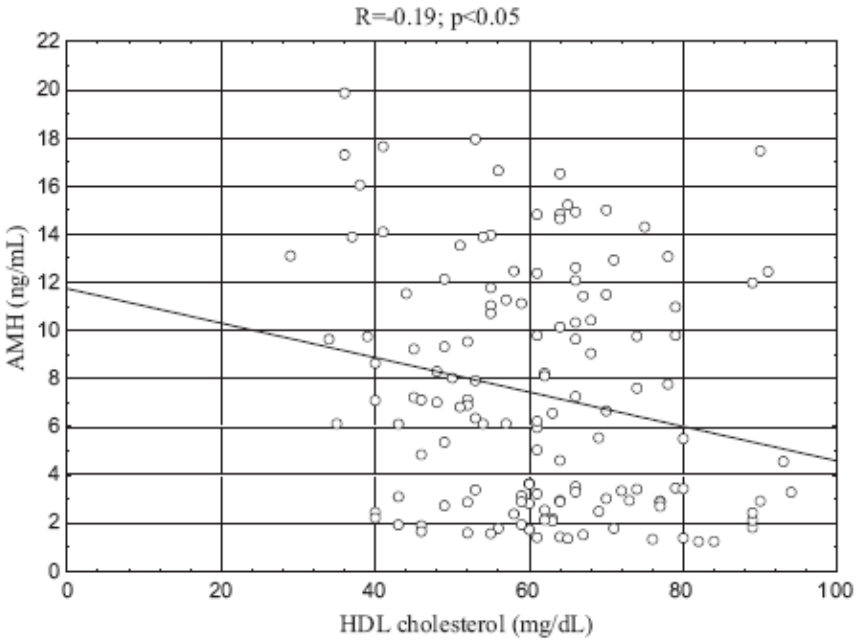
European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

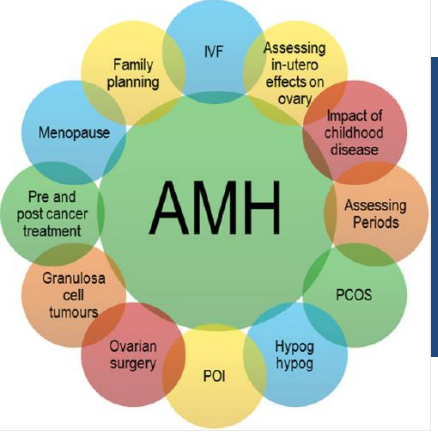
Is the plasma anti-Müllerian hormone (AMH) level associated with body weight and metabolic, and hormonal disturbances in women with and without polycystic ovary syndrome?

Piotr Skałba [a], Anna Cygal [a], Paweł Madej [a], Anna Dąbkowska-Huć [a], Jerzy Sikora [b], Gayane Martirosian [c], Małgorzata Romanik [c], Magdalena Olszanecka-Glinianowicz [d,*]

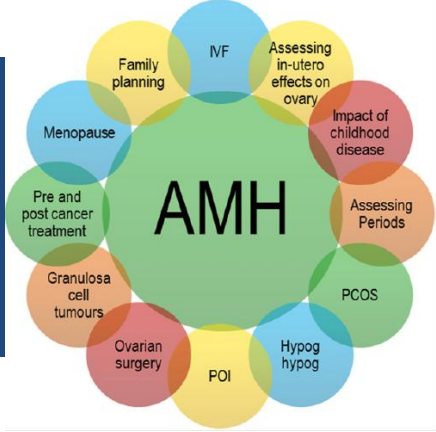




AMH may be useful marker for cardiovascular risk .



Conclusions



- **AMH plays crucial role in preservation ovarian reserve via inhibition of recruitment of resting follicles from the primordial follicle pool.**
- **AMH plays crucial role in folliculogenesis via decreases the sensitivity of ovarian follicles to FSH.**
- **AMH may play role monofollicular development**
- **AMH may play an important part in the pathophysiology of PCOS.**
- **AMH levels may reflect the severity of the syndrome AMH**
- **AMH may be use for diagnosis of PCOS ????**
- **AMH may be use for evaluate the respons of the treatment**
- **There is a correlation between retrieved oocyte number and AMH levels in IVF cycles**
  - The measurement of AMH levels can be useful for predicting hyperresponse,
  - Not useful for pregnancy prediction

THANK YOU