

## Gonadotropin role & administration strategies in 2009: bases & new trends

Salvador, Brazil – May 8-9, 2009

# AMH to assess follicle health and custom- tailor gonadotropin treatment

Renato Fanchin





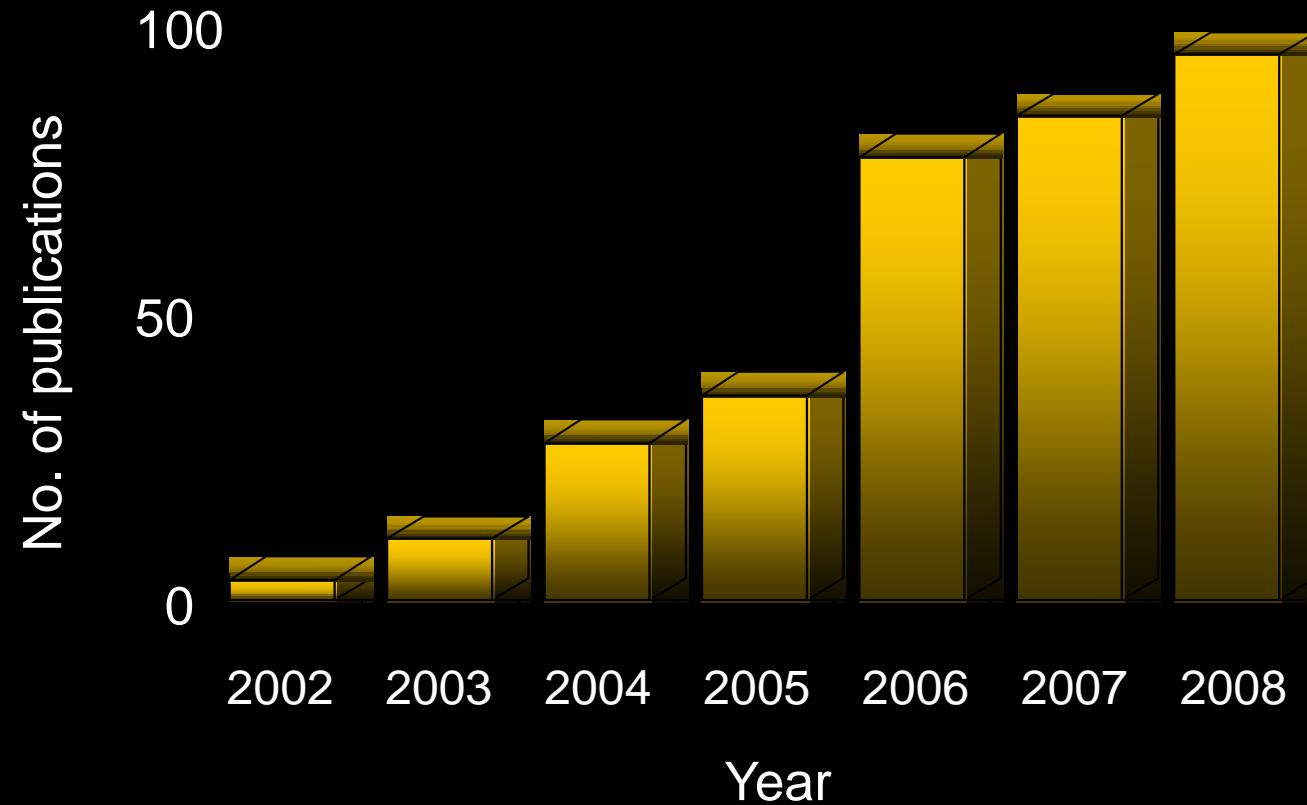
*AMH  
to assess follicle health and  
custom-tailor gonadotropin treatment*

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INSERM U782  
Clamart-France



# *AMH in adult women*

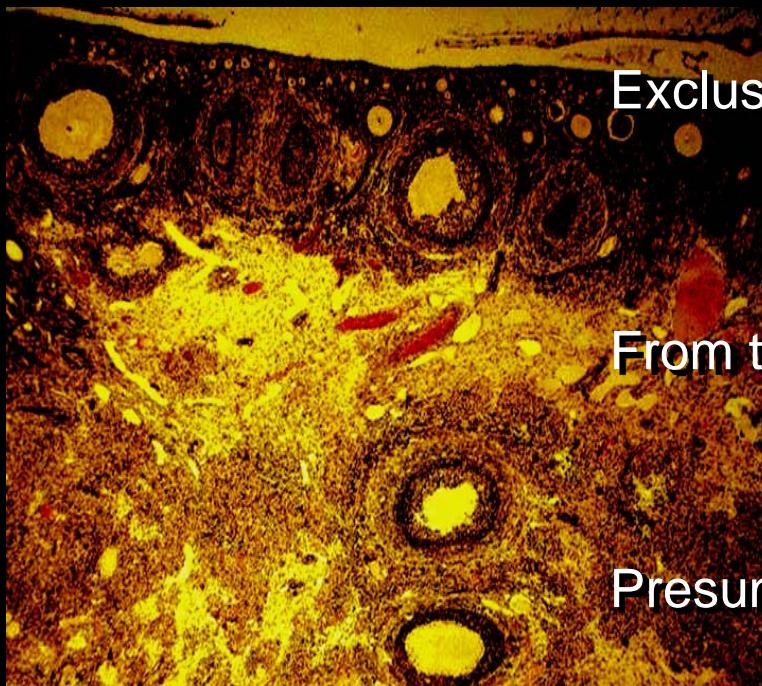


Source: PubMed



# *Clinically relevant features*

*AMH*



Exclusively produced by granulosa cells

Vigier et al, Endocrinology, 1984

From the primary to the small antral stages

Weneen et al, Mol Hum Reprod, 2004

Presumably with little or no FSH-dependency

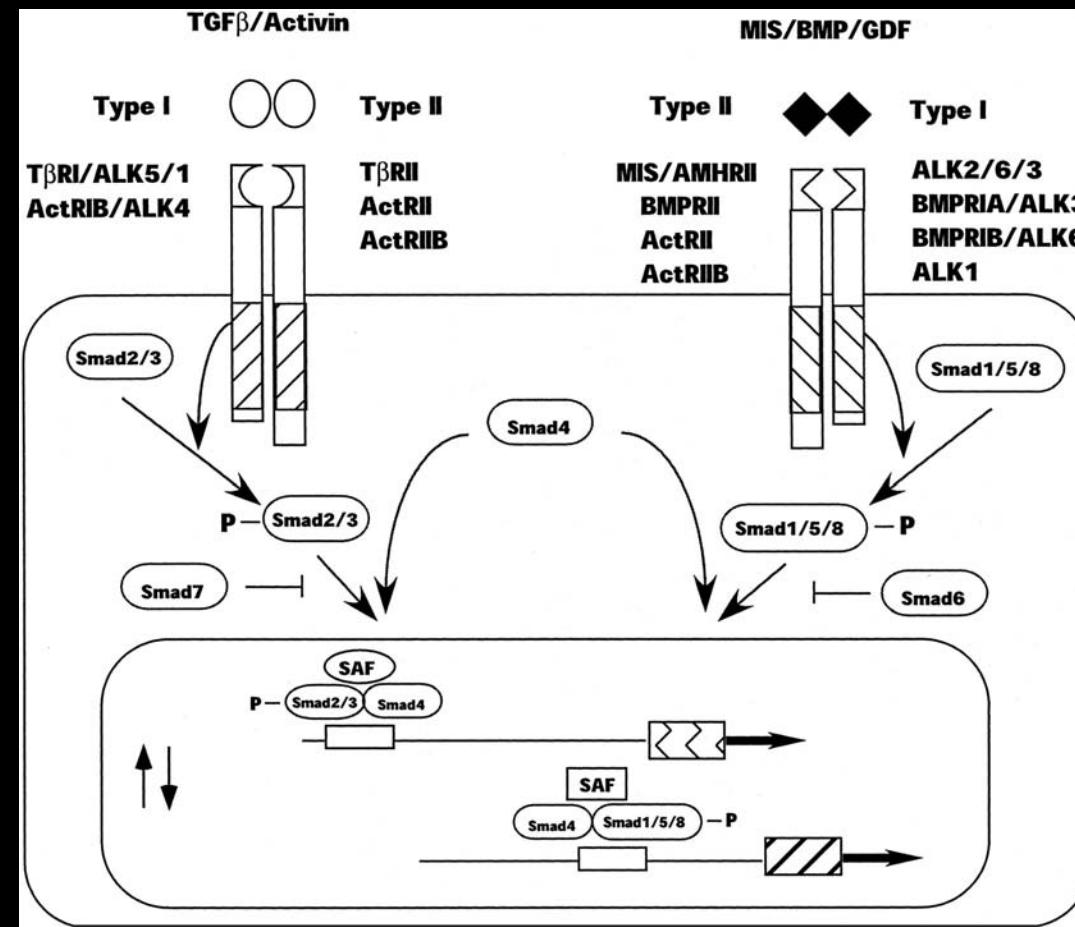
Bath et al, Hum Reprod, 2003

Eldar-Geva et al, Hum Reprod, 2005

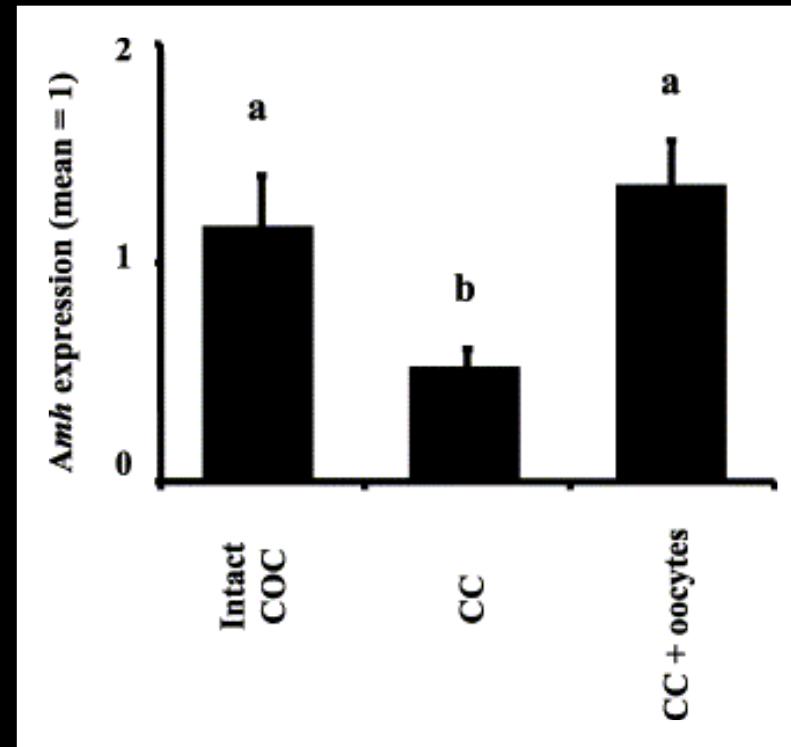
Wachs et al, JCE&M, 2007

Unique marker of the ovarian follicular status

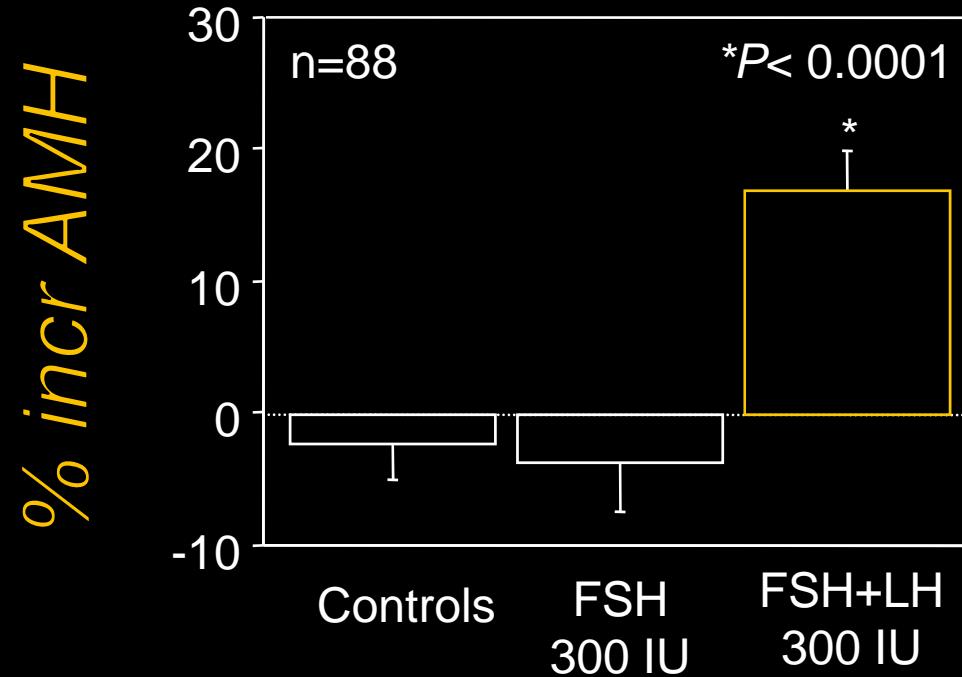
# Signaling pathway



Role on normal and altered ovarian function and folliculogenesis?



Oocyte up-regulates AMH in preantral, preovulatory follicles?



Direct LH/hCG action or via downstream androgen increase?



# AMH: regulation

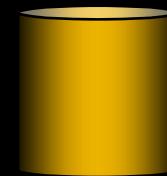
*Early foll*

*Late foll*

*Mid lut*



-56%



-65%



+20%

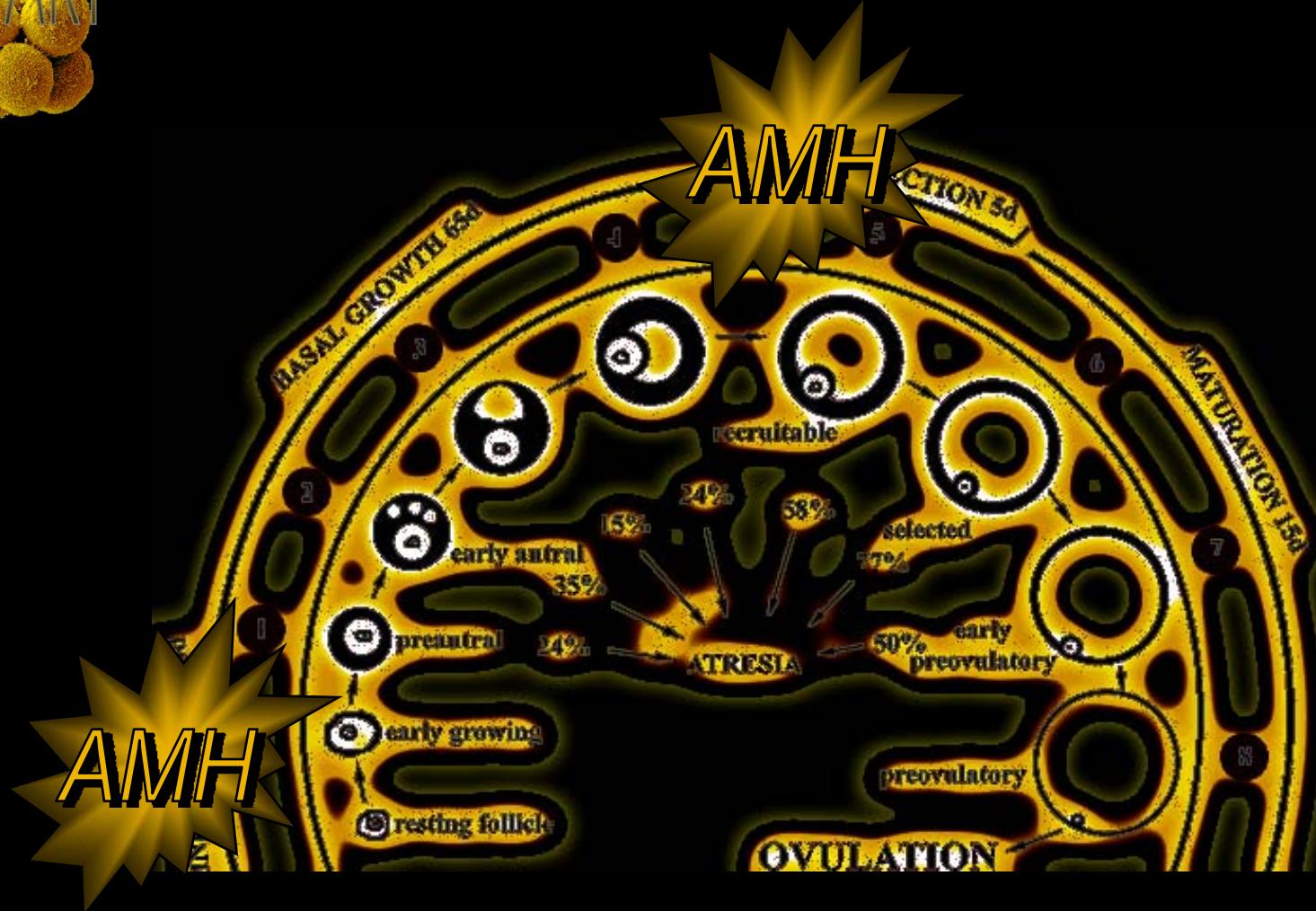


*Serum AMH levels*

Fanchin et al, Hum Reprod, 2003 & 2005



# Physiological role



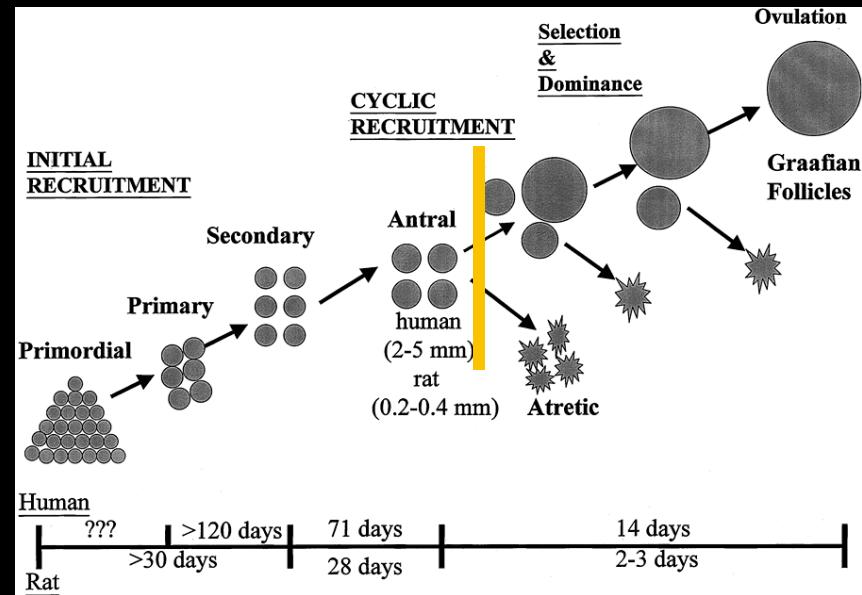
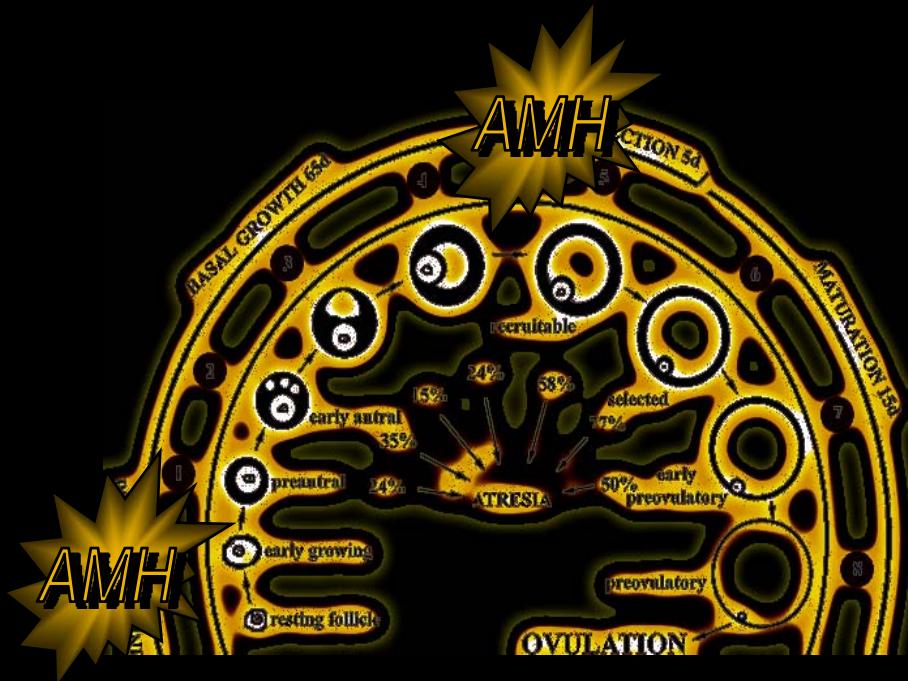
Inhibition of initial recruitment ?

Inhibition of follicular responsiveness to FSH ?



# Polycystic ovary syndrome

2 major features of PCOS



Role on altered folliculogenesis?



Follicular excess



Follicular arrest



# Relationship with ovarian ageing

## Sensitivity to ovarian ageing

Screening variable	Visit 1	Visit 2	P value <sup>a</sup>
Antimüllerian hormone level (µg/L)	2.1 (0.1–7.4)	1.3 (0.0–5.0)	<.001
FSH level (IU/L)	6.0 (1.4–13.5)	5.8 (2.4–13.4)	.29
Inhibin B level (pg/L)	112 (12–213)	110 (4–206)	.92
E <sub>2</sub> level (pmol/L)	151 (64–404)	161 (70–620)	.52
No. of antral follicles	14 (6–28)	14 (2–24)	.27

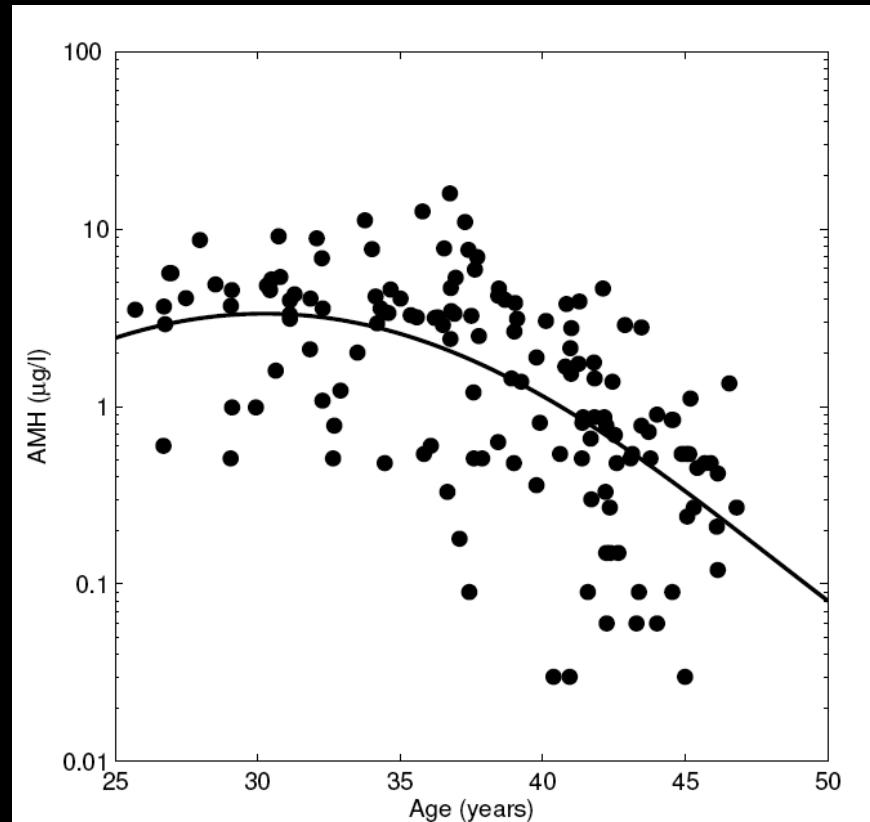
{

2.6 ± 1.7 years

de Vet et al. Fertil Steril 2002

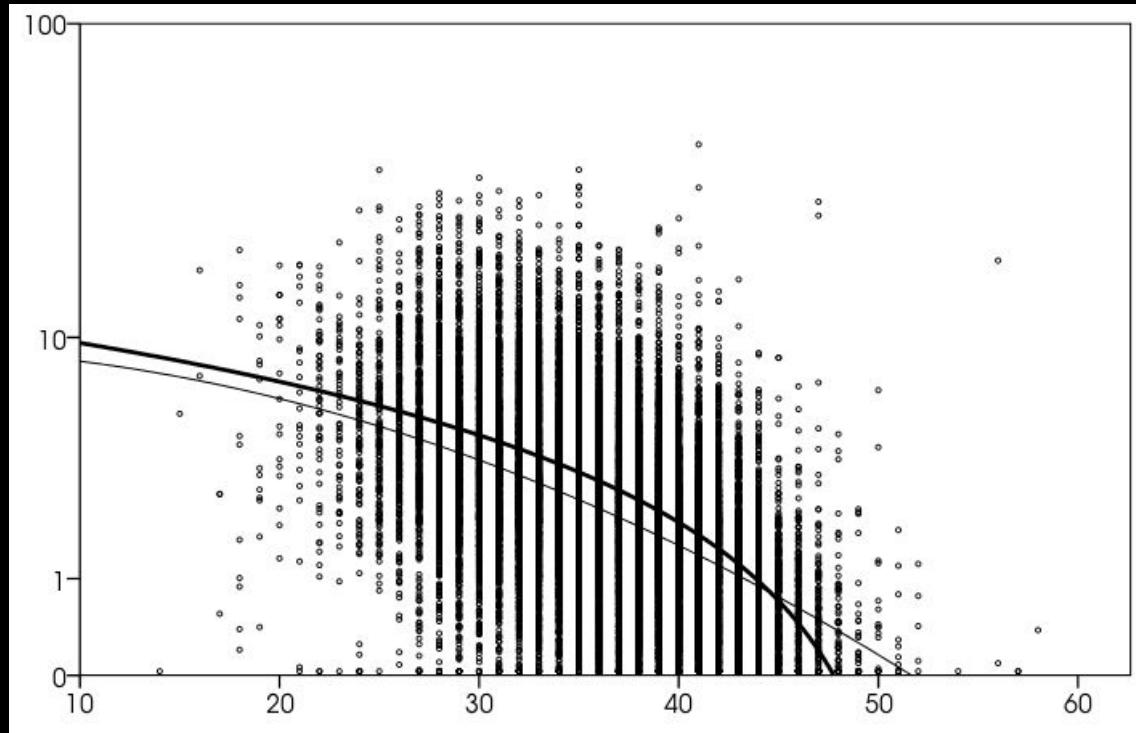
van Rooij et al. Hum Reprod 2002

# *Relationship with ovarian ageing*



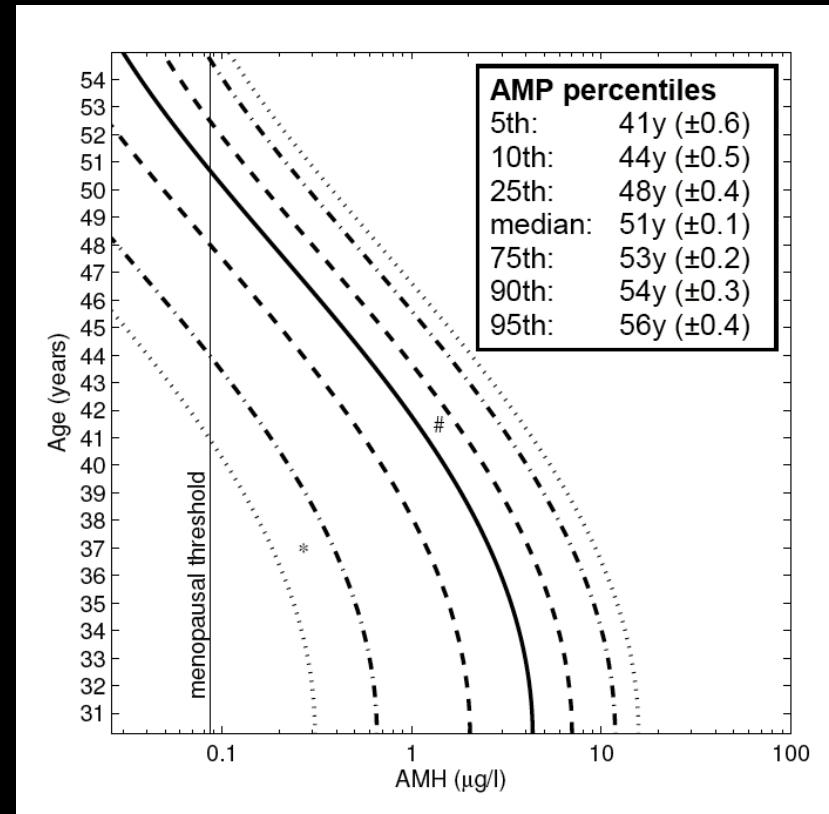
Relationship between AMH & age

# *Relationship with ovarian ageing*



Relationship between AMH & age

# Relationship with ovarian ageing

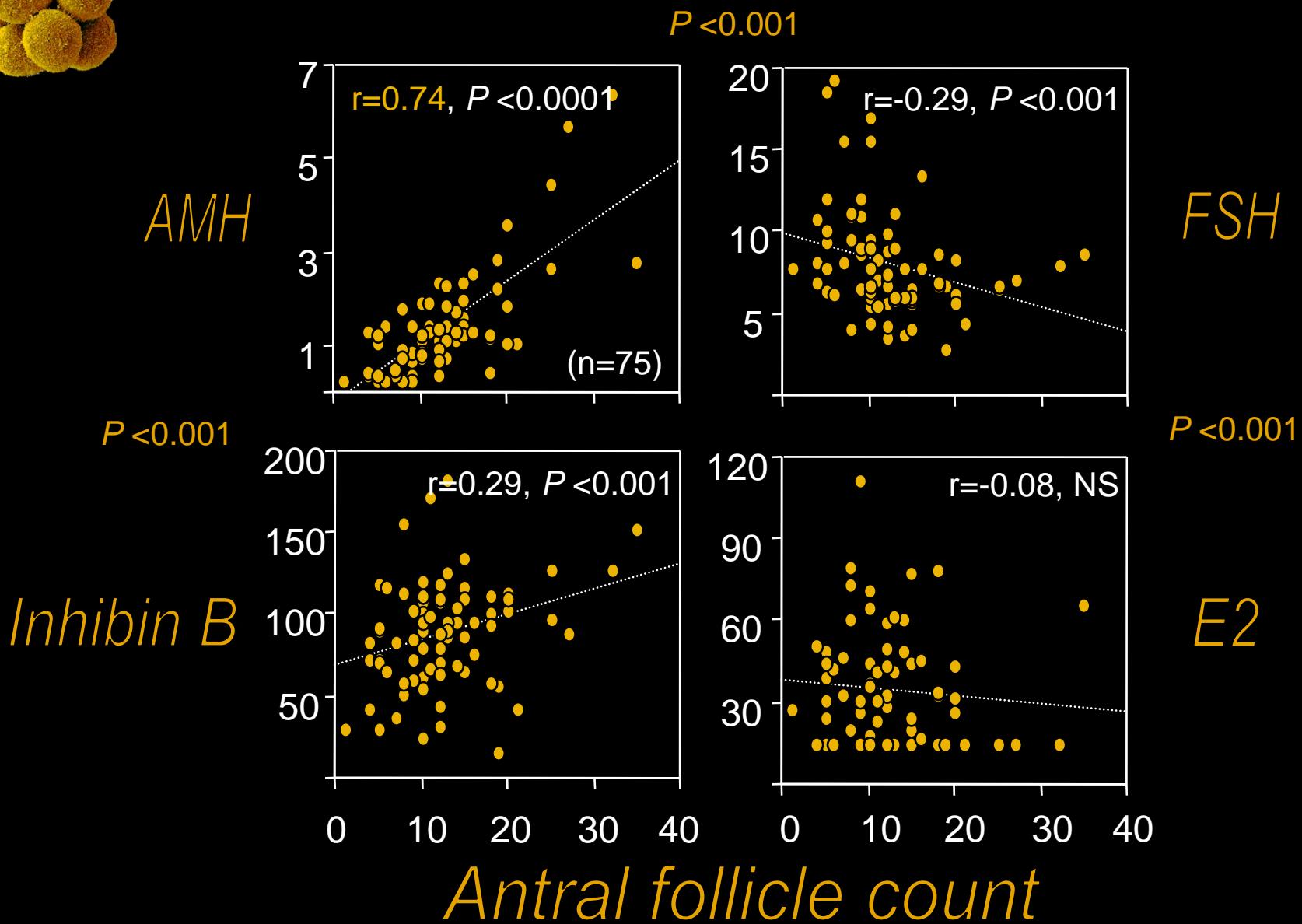


Relationship between AMH & age

Women with lower AMH may experience earlier menopause



# Relationship with follicle pool





# *Relationship with follicle pool*

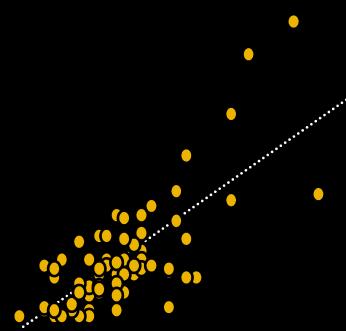
*Early foll*

*Late foll*

*Mid lut*

$r=0.74, P < 0.0001$

AMH



AFC



AMH

?

AFC



AMH

?

AFC



Dynamic antral follicle rearrangements (growth waves)?

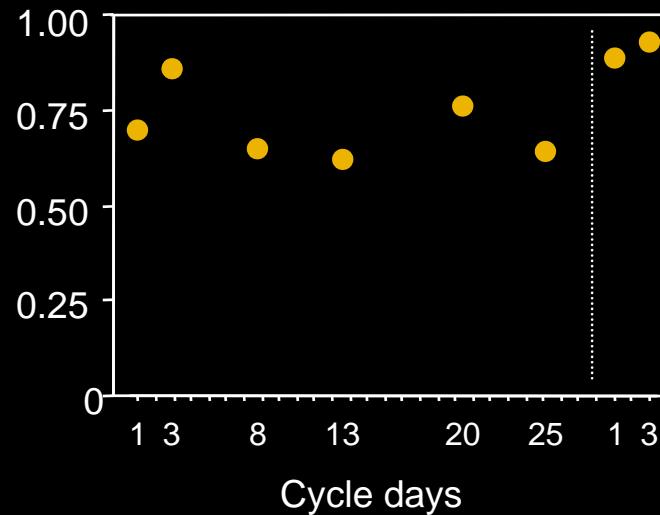
Baerwald et al, Biol Reprod, 2003

# *Relationship with follicle pool*

Evolvement of the relationship AMH x AFC

*Rho values*

Spearman's correlation



- 8 normoovulating volunteers
- Daily blood samplings for 34 days
- 8 ovarian utz scans

Fanchin et al, unpublished data



# *Multi-staged follicle production*

Clinically relevant issue:

AMH as a marker of “non-cyclic” follicles



Improved intercycle & intracycle consistency?



# *Multi-staged follicle production*

Variable	ICC (3 consecutive cycles)	# repeats to steadiness
E <sub>2</sub> :	0.22 (0.03-0.41)	14 (6-120)
FSH:	0.55 (0.39-0.71)	3 (2-6)
Follicle count (2-12 mm):	0.73 (0.41-0.72)	1 (1-2)
Inhibin B:	0.76 (0.66-0.86)	1 (1-2)
AMH:	0.89* (0.83-0.94)	1 (0-1)

47 patients, 3 consecutive cycles

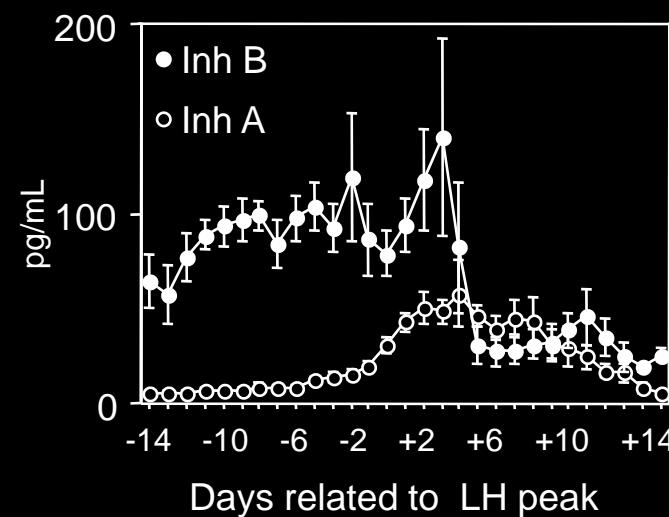
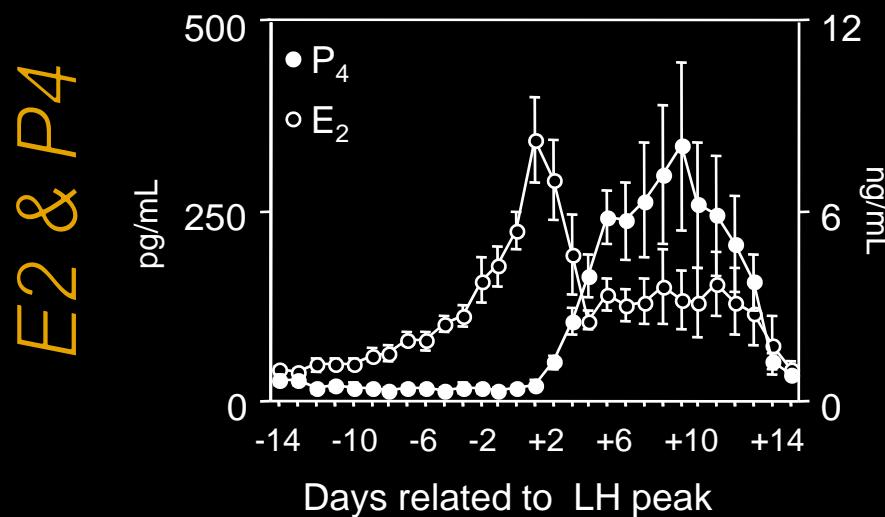
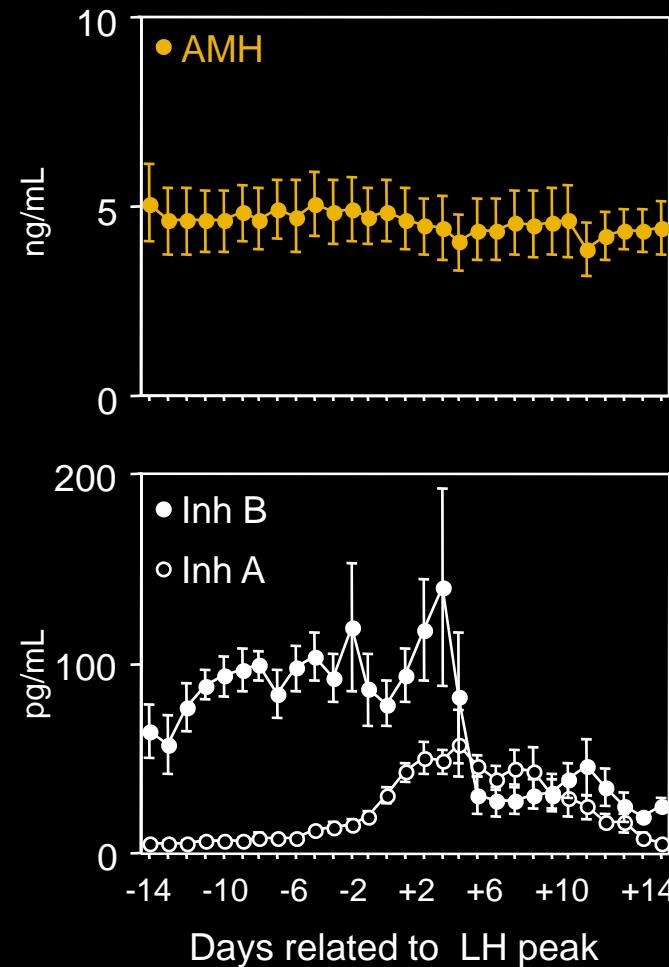
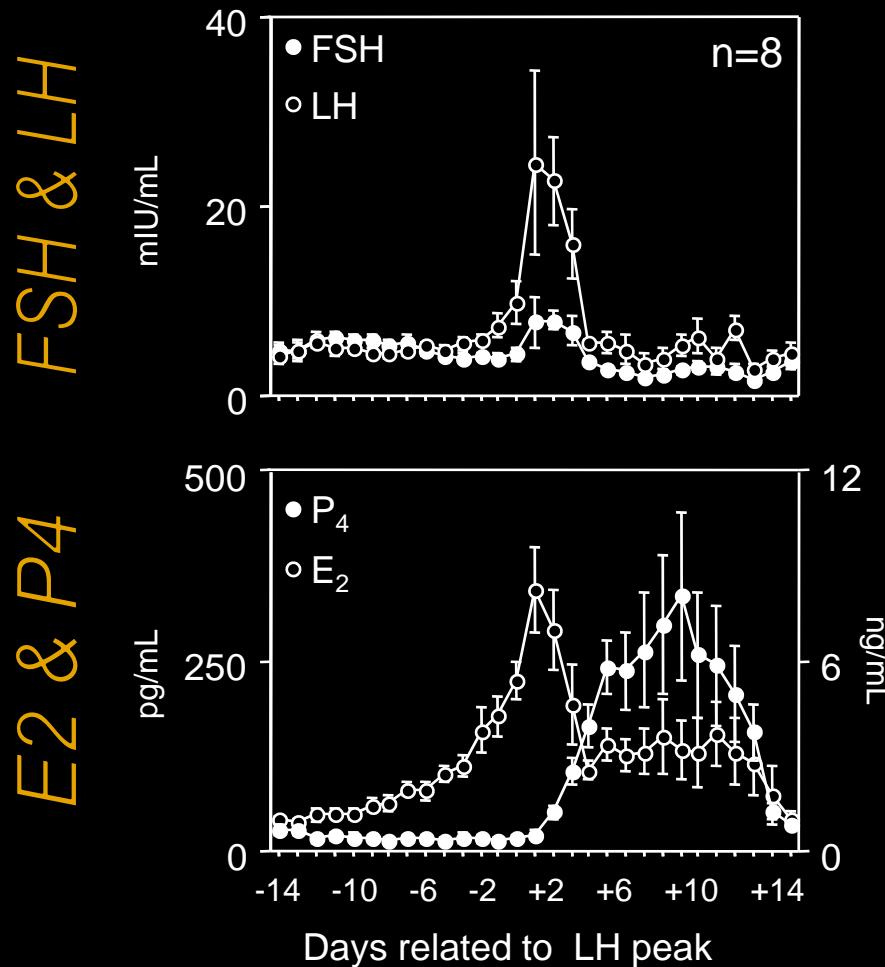
\*P < 0.03

Fanchin et al, Hum Reprod, 2005a



# Multi-staged follicle production

## AMH dynamics during the menstrual cycle





# *Multi-staged follicle production*

Steadiness...

Hehenkamp et al, JCE&M, 2006

LaMarca et al, Hum Reprod, 2006

Tsepelidis et al, Hum Reprod, 2007

Post-ovulatory decrease...

Lahlou et al, ASRM, 2006

Wunder et al, Fertil Steril, 2007



# *Prediction of ovarian response to FSH*

AMH: a good predictor ovarian response to COH

Seifer et al. Fertil Steril 2002

Fanchin et al. Hum Reprod 2003

Hazout et al. Fertil Steril 2004

Muttukrishna et al. BJOG 2004

Penarrubia et al. Hum Reprod 2004

Fleming et al. Hum Reprod 2006

Ebner et al. Hum Reprod 2006

La Marca et al. Hum Reprod 2007

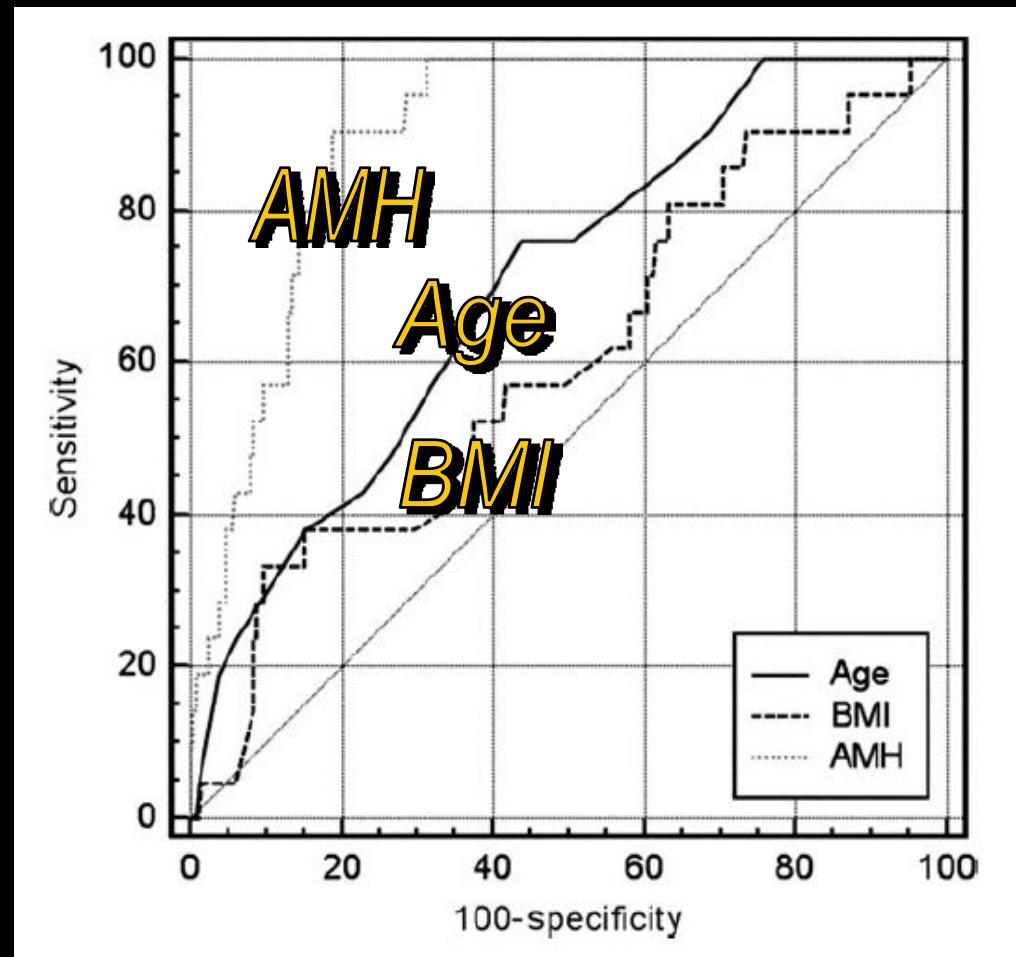
Nelson et al. Hum Reprod 2007



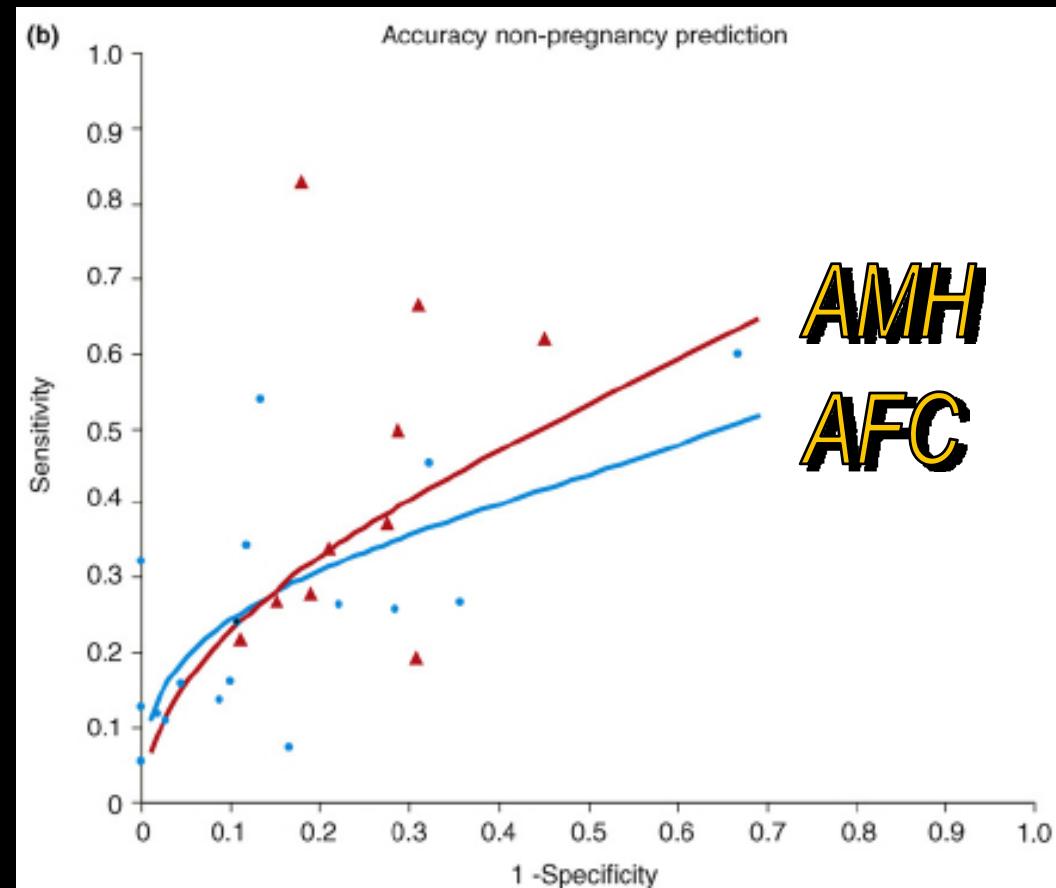
# *Prediction of ovarian response to FSH*

AMH

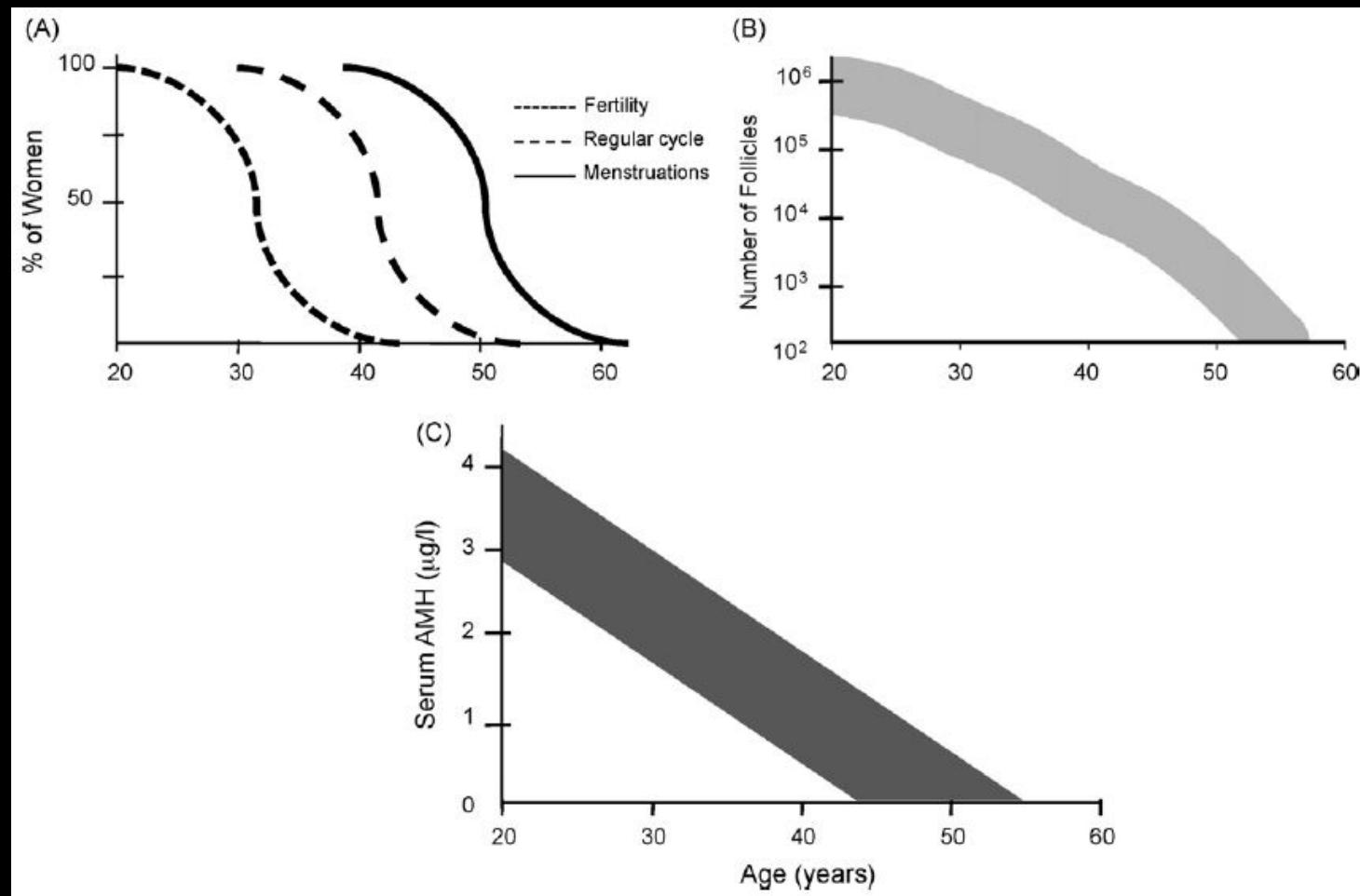
AFC



# *Prediction of pregnancy*



# *Prediction of pregnancy*





# *Choosing COH regimen*

human  
reproduction

ORIGINAL ARTICLE *Infertility*

## **Anti-Müllerian hormone-based approach to controlled ovarian stimulation for assisted conception**

**Scott M. Nelson<sup>1,2</sup>, Robin W. Yates<sup>2</sup>, Helen Lyall<sup>2</sup>, Maybeth Jamieson<sup>2</sup>, Isabel Traynor<sup>2</sup>, Marco Gaudoin<sup>3</sup>, Paul Mitchell<sup>3</sup>, Pat Ambrose<sup>3</sup>, and Richard Fleming<sup>1,3,4</sup>**

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ClamART



*Concept*

*Heterogeneous follicle competence*

CASE REPORT

## Undetectable serum anti-Müllerian hormone levels and occurrence of ongoing pregnancy

*Timothée Fraisse, M.D., Victoria Ibecheole, M.D., Isabelle Streuli, M.D., Paul Bischof, Ph.D., and Dominique de Ziegler, M.D.*

Unité d'Endocrinologie Gynécologique et Médecine de la Reproduction, Hôpitaux Universitaires de Genève, Département de Gynécologie et d'Obstétrique, Geneva, Switzerland

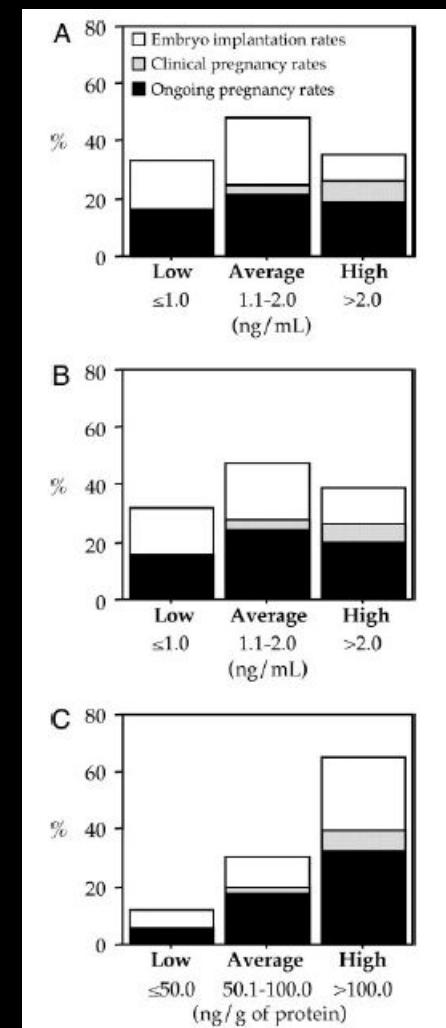
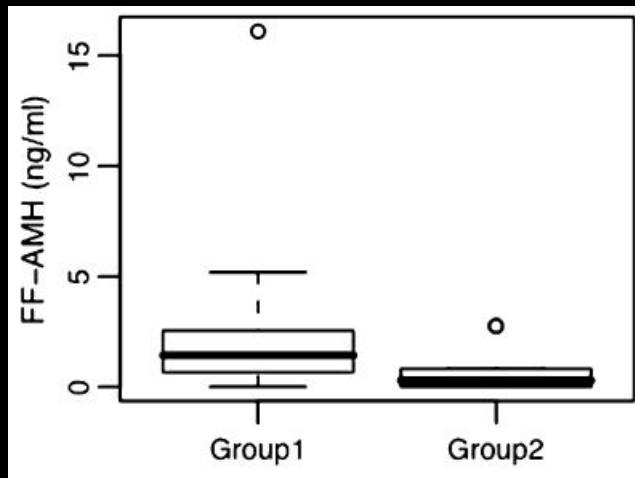


*Concept*

*Going down to the follicular level...*



# Follicular fluid AMH levels





# Conclusions

1. AMH: a quantitative marker of antral follicles

Better than other hormonal markers

2. AMH: a marker of hypo and hyperresponse to FSH

Improved intra & intercycle consistency

3. AMH: a marker of a larger span of follicles

Improved intra & intercycle consistency

4. AMH: a marker of follicle quality

Role in the selection of best embryos to transfer?



AMH team at



& INSERM  
U782:

INSERM U-569 Epidemiology:

Laboratoire Eylau, Paris:

Joëlle Taieb

Michael Grynberg

Yaël Lazimy

Nathalie di Clemente

Nelly Frydman

Jean-Yves Picard

René Frydman

Jean Bouyer

Béatrice Ducot

Paul Cohen-Bacrie

Stéphanie Belloc