28 year old woman with amenorrhea

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Endorama

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History of Present Illness

- 28 yo Indian woman referred for secondary amenorrhea
  - Menarche at age 10
  - Regular menses
  - OCP from age 21-27
  - No menses in past 6 months

Past Medical History

- Exercise History:
  - High school: cheerleading
  - Current (last 5 years): runs 26 miles per week
- No history of eating disorders
- Lost 8 lbs over the past 5 years

Past Medical History

- Medical Problems:
  - None
- Medications:
  - None
- Allergies:
  - None
- Social History:
  - Married.
  - No children.
  - No history of tobacco use.
  - 1-2 glasses of wine per week

Past Medical History

- Family History:
  - Sister with PCOS.
  - Maternal grandparents with diabetes.

Physical Exam

- Height: 4’10”
- Weight: 89 lbs
- BMI: 18.6
- Pulse: 55
- Blood pressure: 96/54
- No hirsutism.
- No acanthosis nigricans.

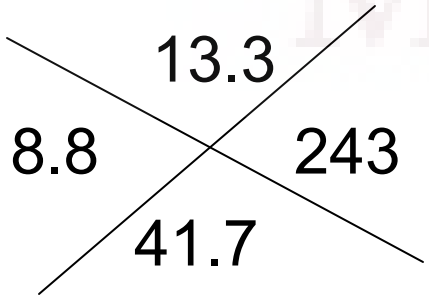
Labs

142	102	16	86
4.5	27	0.9	

Total protein 7, Albumin 4.8

AST 20, ALT 66

Alk phos 66, Total bili 0.2



- TSH 5.65
- A1c 5.2%
- PRL 5.4 ng/mL
- FSH 5.5 mIU/mL
- LH 3.2 mIU/mL
- Estradiol 43 pg/mL
- Total test 23 ng/dL
- Free test 0.8 pg/mL
- DHEA-S 119 uG/dL
- 17OH progesterone: 15 ng/dL
- AMH: 13.38 ng/mL

Follicular Ultrasound

- Left ovary:
  - 5 follicles 4-5 mm
  - >10 follicles <10 mm
  - Length: 34.3 mm
  - Volume: 7.69 cc
  - Height: 19.1 mm
  - Width: 22.4 mm
- Right ovary:
  - 5 follicles 4-5 mm
  - >10 follicles <10 mm
  - Length: 33.3 mm
  - Volume: 8.92 cc
  - Height: 23.6 mm
  - Width: 21.7 mm

Rotterdam 2004 criteria:
≥20 follicles measuring 2-9 mm in diameter or ovarian volume >10 cc

Assessment & Plan

- PCOS
  - Ultrasound results
  - Elevated AMH
  - Rec. Clomid or metformin
- Hypothalamic amenorrhea
  - Recommended cutting back on running

My Questions:

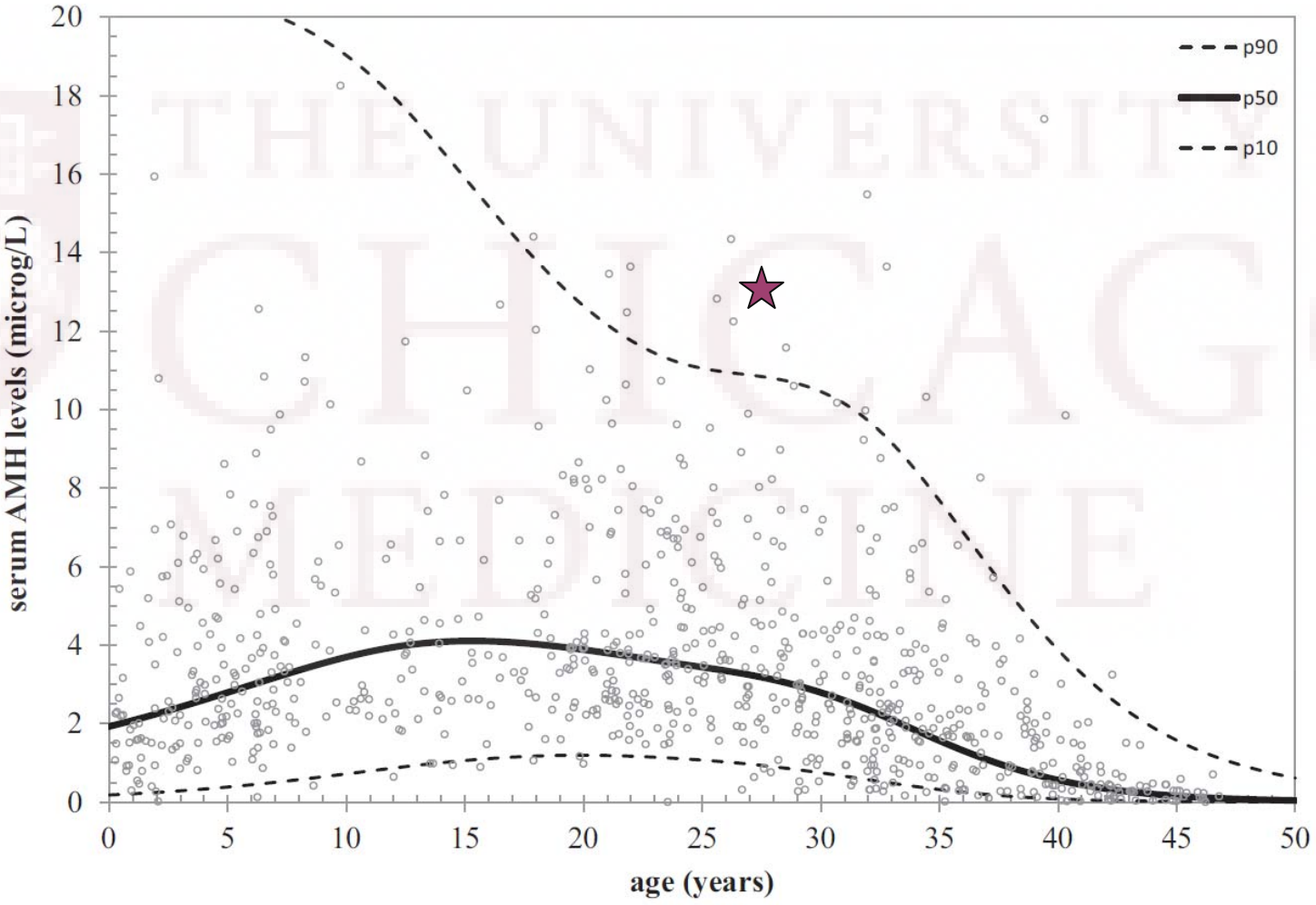
- What is AMH?
- What are normal levels of AMH?
- How is AMH used in the PCOS population?
- What are other causes of elevated AMH?

Anti-Mullerian Hormone

- Glycoprotein member of TGF-β family
- Only produced by granulosa cells in the ovary.
  - From primary follicular stage until early antral stage.
  - No further expression once the follicle 8-10 mm.
- Reflects ovarian reserve
  - >1 ng/mL reflects good ovarian reserve
  - <0.1 ng/mL suggests poor response to ovulation induction

Gurtcheff et al. Clin Obstet Gynecol. 2011 Dec;54(4):666-74.

AMH levels in healthy females



Fong et al. J Clin Endocrinol Metab. 2012 Dec;97(12):4650-5.

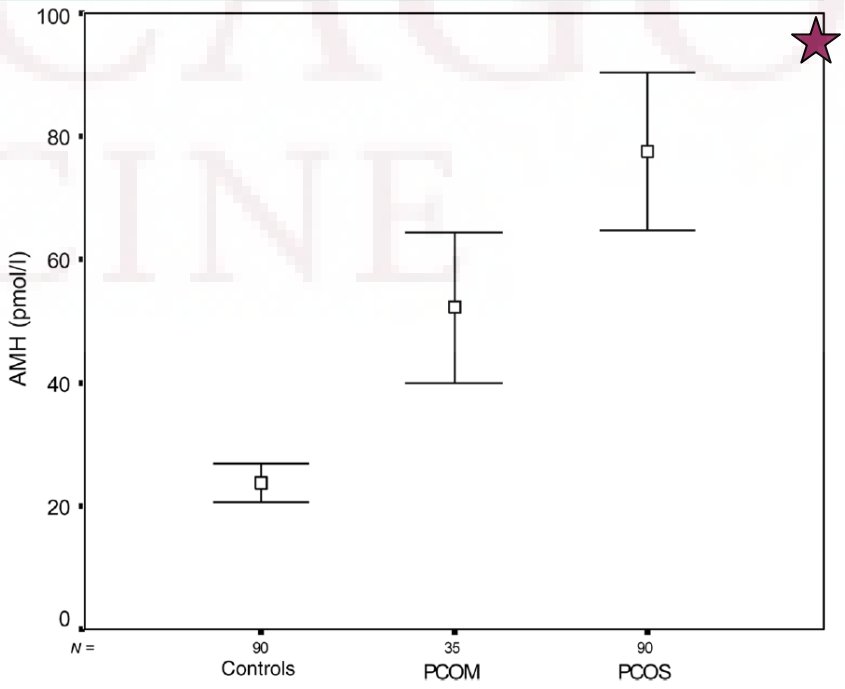
AMH and PCOS

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)

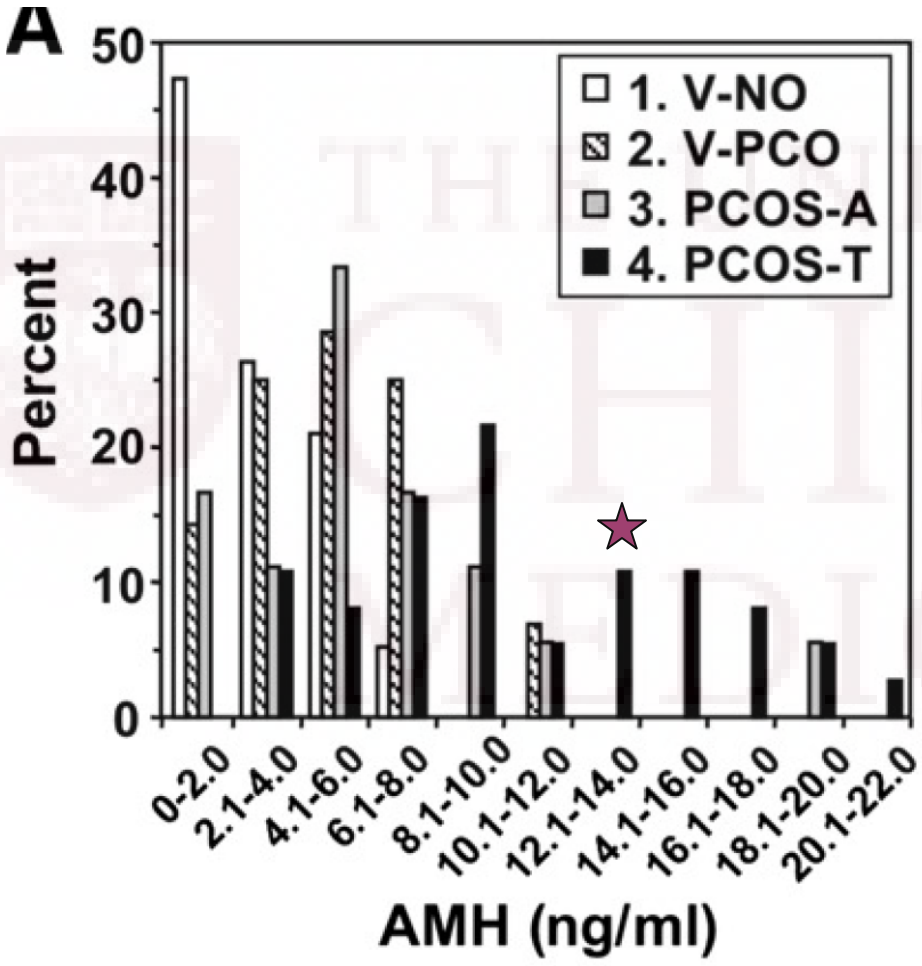
AMH, anti-Mullerian hormone; PCOM, polycystic ovary morphology; PCOS, polycystic ovary syndrome.
*$P < 0.001$ versus control.
**$P < 0.05$ versus PCOM.

- Diagnosis:
  - AUC 0.81
  - AMH >48 pmol/l:
    - sensitivity 60%
    - specificity 98.2%



Homburg et al. Hum Reprod. 2013 Apr;28(4):1077-83.

AMH and PCOS



- AMH correlated with presence of polycystic ovary, free testosterone, testosterone response to DAST, and 17OHP response to GnRH agonist.
- Very high AMH levels are specific but insensitive for PCOS.
- In the absence of hyperandrogenic anovulation, moderate AMH elevation in a woman with a polycystic ovary implies an increased oocyte pool size and suggests an increased reproductive lifespan, not PCOS.

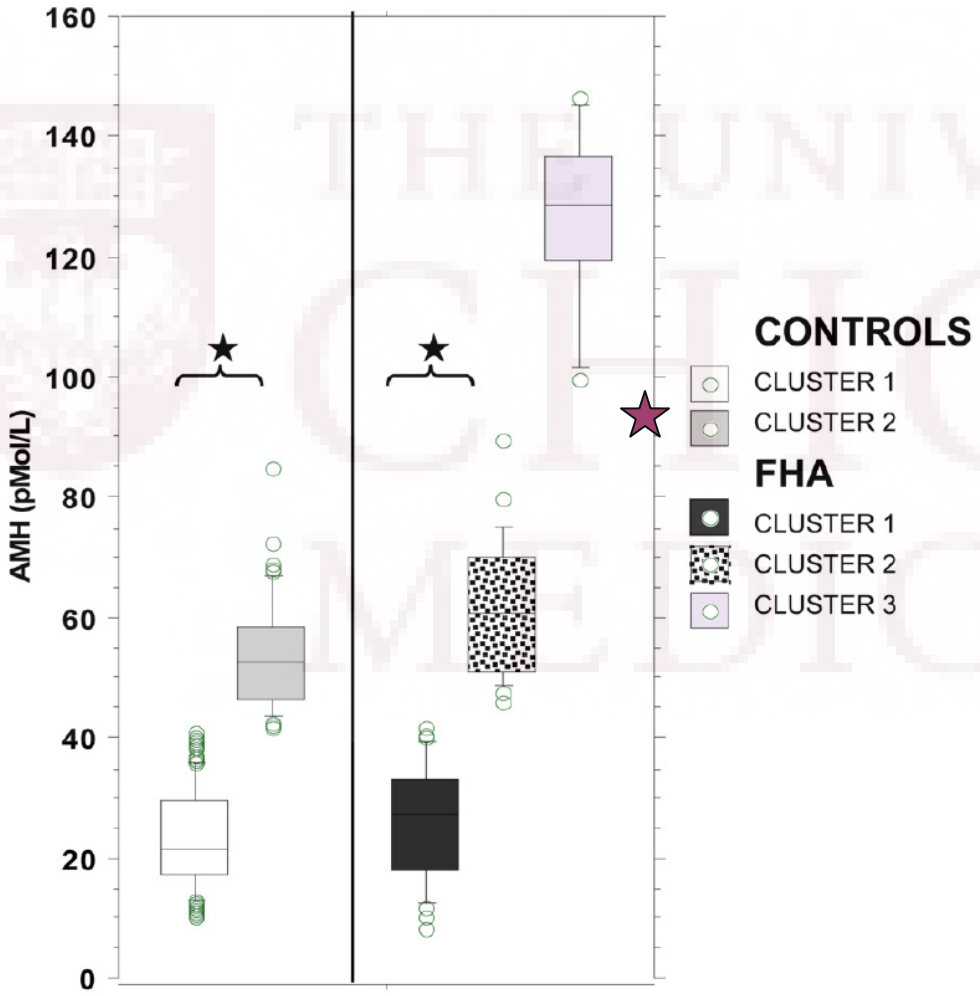
Rosenfield et al. Fertil Steril. 2012 Jul;98(1):242-9.

AMH and PCOS

- Pathogenesis: AMH inhibits FSH action, which leads to failure of follicle development
- Diagnosis: elevated AMH levels are specific but insensitive for PCOS
- Prognosis: elevated in proportion to clinical severity
- Treatment:
  - May need lower starting doses of FSH to avoid overstimulation.
  - Have not been found to help predict success of IVF.

Homburg et al. Hum Reprod. 2013 Apr;28(4):1077-83.
Sahmay et al. Gynecol Endocrinol. 2013 May;29(5):440-3.

AMH and Hypothalamic Amenorrhea



- Controls (n=219): PCOM in 15% and 72%
- FHA (n=58): PCOM in 17, 70, and 100%

Robin et al. J Clin Endocrinol Metab. 2012 Nov;97(11):4236-43.

AMH and Hypothalamic Amenorrhea

- PCO-L in normal adult women does not seem to translate to the development of PCOS.
- Conclude that the incidental finding of PCO-L in an amenorrheic woman with FHA should not lead to qualifying her for the diagnosis of PCOS.
  - A minority of patients with FHA seem susceptible to evolving into PCOS at the time of recovery, when serum LH and insulin levels return to normal.
    - AMH >90

Robin et al. J Clin Endocrinol Metab. 2012 Nov;97(11):4236-43.

Current status

- Decreased to 2-2.5 miles per day from 1 month.
- Had a menses following that month.
- Increased back to 3-4 miles/day.
- No further menses.
- Now considering metformin.

Take Home Points

- AMH indicates ovarian reserve.
- AMH is elevated in PCOS as well as PCOM.
- Elevated AMH levels or PCOM in normal women does not always translate to PCOS.

References

- Fong et al. J Clin Endocrinol Metab. 2012 Dec;97(12):4650-5.
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