Clinical Applications of Anti-Müllerian Hormone Measurement

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What is anti-Müllerian hormone?

• Protein hormone
• TGF-β family
• Homodimeric protein
  • Two subunits linked by disulfide bonds
Müllerian Structures

• Derived from the Müllerian ducts
• Ducts atrophy in males during development
• Ducts persist in females
• Develop into:
  • Uterus
  • Fallopian tubes
  • Vagina
AMH Function in Males

- Sertoli cells in the testis produce high amounts of AMH
  - Suppresses formation of Müllerian structures
- AMH declines alongside rise in testosterone during puberty
AMH Function in Females

- AMH absent during development
- Absence allows formation of Müllerian structures
- Released by preantral and small antral follicles to inhibit recruitment of additional follicles
- Preserve primordial pool
How is anti-Müllerian hormone tested?

- Anti-Müllerian hormone is measured by two-site ("sandwich") immunoassays
- Manual or automated formats available
A Brief History of AMH Testing

- Immunotech (1999) and Diagnostic Systems Laboratories (2003) developed the earliest commercial AMH assays.
- Beckman purchased these companies and combined their assays in 2011.
- Stability studies showed increased recovery of AMH with storage time.
  - Ultimately attributed to complement interference.
- Current Beckman and Roche automated methods are not affected.\(^1\)
Clinical Uses for AMH Testing

- In vitro fertilization
- Assessing in-utero effects on ovary
- Impact of childhood disease
- PCOS
- Hypogonadotropin hypogonadism
- Primary ovarian insufficiency
- Ovarian surgery
- Granulosa cell tumors
- Pre- and post-cancer treatment
- Menopause
- Family planning
AMH is not a clinical measure of “fertility.”

- Don’t use AMH as a one-off measurement of “fertility”\(^3\)
- Women with low serum AMH become pregnant at similar rates to women with normal to high AMH\(^4\)
- Fecundability of women with AMH in the first quintile did not differ significantly with those in quintiles 2-4
  - Women in 5\(^{\text{th}}\) quintile had reduced fecundability\(^5\)
- Biomarkers of ovarian reserve do not predict fertility\(^6\)
Polycystic Ovarian Syndrome

• Characterized by
  • Hyperandrogenism
  • Ovulatory dysfunction
  • Polycystic ovarian morphology

• Metabolic derangements
  • Insulin resistance

• Affects 6-12% of women of reproductive age (CDC)
• Most common cause of infertility

At least 2/3 = PCOS$^7$
A role for AMH in diagnosis of PCOS?

- Polycystic ovarian morphology is currently assessed by ultrasound (antral follicle count)
  - Need to continually update cutoffs as ultrasound technology improves
  - AMH correlates well with antral follicle count
  - AMH is promising as a surrogate marker for follicle count

<table>
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<th>Threshold Follicle Number per Ovary (FNPO)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<td>36</td>
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</table>

Data from reference 9
Advantages and Limitations of AMH for PCOS

Advantages

- Good correlation with antral follicle count
- Elevated in PCOS
  - Correlates with symptom severity
- Consistent throughout menstrual cycle

Limitations

- Concentrations influenced by other factors
  - Weight
  - Age
  - Smoking
  - OCP use
  - Ethnicity
- Technical challenges
  - Standardization
  - Specimen handling
AMH in Management of Infertility

- AMH is predictive of ovarian response to stimulation
- Identifies women at risk of ovarian hyperstimulation syndrome
  - Life-threatening condition
  - “Third-spacing” of fluid
- Treatment of high-risk women can mitigate much of the risk of ovarian stimulation

Test AMH

- High: Co-administer GnRH antagonists
- Normal: Normal protocol (GnRH agonists)
- Low: “Flare” agonist protocol
Evaluation of Disorders of Sexual Development

• AMH is elevated in males at birth
  • Expressed solely in sertoli cells of the testis
• Can play a role in clarifying a patient’s status in a disorder of sexual development
  • Must be interpreted within the context of other findings (17-OH progesterone, karyotype, etc.)
• Elevation of AMH suggests testicular tissue and can inform decision to pursue gonadectomy
AMH as a Tumor Marker

- Granulosa cell tumors account for ~2% of ovarian cancers\textsuperscript{10}
- Traditionally inhibin B is the tumor marker of choice
- AMH is highly specific to granulosa cell tumors
- Combining AMH with inhibin B was superior to inhibin B alone for detection of recurrent disease\textsuperscript{11}
References

Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

▪ Employment or Leadership: No disclosures
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