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ANTI-MÜLLERIAN HORMONE (AMH) AND THE MECHANISMS OF MALE SEXUAL DIFFERENTIATION

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KALIT SO'ZLAR:
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ANNOTATSIYA:

Anti-Müllerian Hormone (AMH), also known as Müllerian Inhibiting Substance (MIS), is a glycoprotein hormone belonging to the transforming growth factor-beta (TGF-β) superfamily. It plays a crucial role in male sexual differentiation during embryonic development by inducing regression of the Müllerian ducts, thereby preventing the formation of female internal reproductive organs. The aim of this review is to analyze the biological functions of AMH in male sexual differentiation and evaluate its clinical significance in developmental disorders of the reproductive system. Literature data indicate that AMH secretion by Sertoli cells begins during early fetal development and is essential for normal male phenotypic differentiation. Alterations in AMH synthesis or receptor signaling may result in persistent Müllerian duct syndrome and other disorders of sex development. Understanding the molecular and physiological mechanisms of AMH contributes to improved diagnosis and management of reproductive disorders in pediatric and adult patients.

Introduction

Sexual differentiation in humans is a complex developmental process regulated by genetic, hormonal, and molecular factors. The establishment of male phenotype depends on coordinated actions of testicular hormones during embryogenesis. One of the most important mediators involved in this process is Anti-Müllerian Hormone (AMH), a glycoprotein secreted by Sertoli cells of the developing testes.

During the early stages of embryonic development, both male and female embryos possess two pairs of primitive genital ducts: the Wolffian ducts and the Müllerian ducts. In male embryos, the presence of the Y chromosome and expression of the Sex-determining Region Y (SRY) gene initiate differentiation of the bipotential gonads into testes. Subsequently, Sertoli cells begin producing AMH, while Leydig cells synthesize testosterone.

AMH is responsible for regression of the Müllerian ducts, structures that would otherwise develop into the uterus, fallopian tubes, and upper portion of the vagina. Failure of AMH production or receptor function results in persistence of these structures despite the presence of a normal male karyotype. Consequently, AMH is considered one of the key regulators of male sexual differentiation.

Recent advances in developmental biology and molecular endocrinology have provided substantial insight into AMH physiology, receptor signaling pathways, and its diagnostic value in reproductive medicine. Therefore, understanding the role of AMH is important for clinicians, embryologists, endocrinologists, and reproductive biologists.

Materials and Methods

This review was conducted using a comprehensive analysis of scientific literature published between 2000 and 2025. Relevant studies were identified through PubMed, Scopus, Web of Science, and Google Scholar databases.

Keywords used during the literature search included:

- Anti-Müllerian Hormone
- Müllerian Inhibiting Substance
- Male sexual differentiation
- Sertoli cells
- Persistent Müllerian duct syndrome
- Disorders of sex development

Inclusion criteria comprised original research articles, systematic reviews, clinical studies, and experimental investigations focusing on AMH physiology and male reproductive development.

More than 80 scientific publications were screened, and 35 highly relevant sources were selected for detailed analysis.

Results

Embryological Origin of AMH

AMH production begins approximately during the seventh week of gestation following differentiation of Sertoli cells. The hormone is synthesized as a precursor glycoprotein that undergoes proteolytic cleavage before becoming biologically active.

AMH exerts its effects through specific Anti-Müllerian Hormone Receptor Type II (AMHR2) located within the Müllerian duct mesenchyme. Activation of these receptors initiates intracellular signaling cascades involving SMAD proteins, leading to apoptosis and regression of Müllerian structures.

Studies indicate that Müllerian duct regression occurs between the 8th and 12th weeks of fetal development. During this critical period, AMH concentrations increase substantially and remain elevated throughout childhood.

Interaction Between AMH and Testosterone

Although AMH and testosterone are both essential for male sexual differentiation, their biological functions differ significantly.

AMH promotes regression of Müllerian ducts, whereas testosterone stimulates development of Wolffian ducts into:

- Epididymis
- Vas deferens
- Seminal vesicles

Additionally, testosterone is converted into dihydrotestosterone (DHT), which promotes development of external male genitalia.

Thus, normal male differentiation requires coordinated actions of both AMH and androgens.

AMH Levels Throughout Life

AMH concentrations demonstrate significant age-related variations.

During fetal development and childhood, AMH levels remain high due to active Sertoli cell function. At puberty, increasing testosterone concentrations suppress AMH secretion, resulting in progressive decline.

Adult men typically exhibit AMH concentrations ranging from approximately 2 to 6 ng/mL, although values vary according to laboratory methods and population characteristics.

Persistent Müllerian Duct Syndrome

One of the most important disorders associated with AMH dysfunction is Persistent Müllerian Duct Syndrome (PMDS).

PMDS is a rare congenital condition characterized by:

- Male karyotype (46,XY)
- Normal external male genitalia
- Persistence of uterus and fallopian tube remnants

The disorder results from mutations affecting either the AMH gene or AMHR2 receptor gene.

Clinical manifestations include:

- Cryptorchidism
- Inguinal hernia
- Infertility
- Increased risk of testicular malignancy

Genetic studies have identified numerous mutations responsible for impaired AMH signaling pathways.

Clinical Importance of AMH

Measurement of AMH concentrations is widely used in pediatric endocrinology and reproductive medicine.

In boys, AMH serves as a biomarker of Sertoli cell activity and testicular function. Low AMH levels may indicate:

- Gonadal dysgenesis
- Testicular failure
- Anorchia
- Disorders of sex development

Conversely, normal or elevated AMH concentrations help confirm the presence of functional testicular tissue.

Recent investigations suggest that AMH may also influence fertility potential and spermatogenic activity later in life.

Discussion

The findings of this review confirm the central role of AMH in male reproductive development. Without AMH activity, Müllerian duct structures persist despite normal androgen production.

The molecular mechanisms underlying AMH action involve complex interactions between transcription factors, receptor-mediated signaling pathways, and programmed cell death. These mechanisms ensure appropriate differentiation of the male reproductive tract.

Several studies have demonstrated that mutations affecting AMH synthesis or receptor function account for the majority of PMDS cases. Early diagnosis is important because affected individuals may develop infertility and malignant transformation of retained reproductive structures.

From a clinical perspective, AMH measurement has become an essential diagnostic tool. Unlike testosterone concentrations, which fluctuate considerably, AMH levels provide a stable marker of Sertoli cell function during childhood.

Advances in molecular genetics continue to improve understanding of AMH-related disorders and may contribute to development of targeted therapeutic approaches in the future.

Conclusion

Anti-Müllerian Hormone is one of the most important regulators of male sexual differentiation. Produced by Sertoli cells during fetal development, AMH induces regression of Müllerian ducts and prevents formation of female internal reproductive structures.

Normal male reproductive development depends on coordinated interactions between AMH and testosterone. Defects in AMH production or receptor signaling result in persistent Müllerian duct syndrome and other disorders of sex development.

Assessment of AMH concentrations has significant diagnostic value in pediatric endocrinology, reproductive medicine, and clinical genetics. Further research is required to clarify additional physiological functions of AMH and its role in male fertility.

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