



## Müllerian aplasia and hyperandrogenism

Müllerian aplasia and hyperandrogenism is a condition that affects the reproductive system in females. This condition is caused by abnormal development of the Müllerian ducts, which are structures in the embryo that develop into the uterus, fallopian tubes, cervix, and the upper part of the vagina. Individuals with Müllerian aplasia and hyperandrogenism typically have an underdeveloped or absent uterus and may also have abnormalities of other reproductive organs. Women with this condition have normal female external genitalia, and they develop breasts and pubic hair normally at puberty; however, they do not begin menstruation by age 16 (primary amenorrhea) and will likely never have a menstrual period. Affected women are unable to have children (infertile).

Women with Müllerian aplasia and hyperandrogenism have higher-than-normal levels of male sex hormones called androgens in their blood (hyperandrogenism), which can cause acne and excessive facial hair (facial hirsutism). Kidney abnormalities may be present in some affected individuals.

### Frequency

Müllerian aplasia and hyperandrogenism is a very rare disorder; it has been identified in only a few individuals worldwide.

### Causes

Mutations in the *WNT4* gene cause Müllerian aplasia and hyperandrogenism. This gene belongs to a family of WNT genes that play critical roles in development before birth. The *WNT4* gene provides instructions for producing a protein that is important for the formation of the female reproductive system, the kidneys, and several hormone-producing glands. During the development of the female reproductive system, the WNT4 protein regulates the formation of the Müllerian ducts. This protein is also involved in development of the ovaries, from before birth through adulthood, and is important for development and maintenance of egg cells (oocytes) in the ovaries. In addition, the WNT4 protein regulates the production of androgens.

Mutations in the *WNT4* gene change single protein building blocks (amino acids) in the WNT4 protein. Researchers suspect that the altered protein cannot be released from cells as it normally would be; the trapped protein is unable to perform its usual functions. Loss of regulation by WNT4 likely disrupts development of the female reproductive system and induces abnormal production of androgens, leading to the features of Müllerian aplasia and hyperandrogenism.

## **Inheritance Pattern**

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Girls with Müllerian aplasia and hyperandrogenism do not inherit the mutation from their mother, because women with this disorder cannot have children. It is unknown, though, if an affected person inherits the mutation from her father or if the condition is caused by new mutations in the gene. Müllerian aplasia and hyperandrogenism may occur in people with no history of the disorder in their family.

## **Other Names for This Condition**

- Biason-Lauber syndrome
- Mayer-Rokitansky-Küster-Hauser-Biason-Lauber syndrome
- Mayer-Rokitansky-Küster-Hauser-like syndrome
- Mullerian aplasia and hyperandrogenism
- Müllerian duct failure
- WNT4 deficiency
- WNT4 Müllerian aplasia
- WNT4 Müllerian aplasia and ovarian dysfunction

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetic-testing](#)
- Genetic Testing Registry: Mullerian aplasia and hyperandrogenism  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2675014/>

### Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22Mullerian+aplasia%22>

### Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Excessive or Unwanted Hair in Women  
<https://medlineplus.gov/ency/article/007622.htm>
- MedlinePlus Encyclopedia: Ovarian Overproduction of Androgens  
<https://medlineplus.gov/ency/article/001165.htm>
- MedlinePlus Encyclopedia: Primary Amenorrhea  
<https://medlineplus.gov/ency/article/001218.htm>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Excessive or Unwanted Hair in Women  
<https://medlineplus.gov/ency/article/007622.htm>
- Encyclopedia: Ovarian Overproduction of Androgens  
<https://medlineplus.gov/ency/article/001165.htm>
- Encyclopedia: Primary Amenorrhea  
<https://medlineplus.gov/ency/article/001218.htm>
- Health Topic: Uterine Diseases  
<https://medlineplus.gov/uterinediseases.html>

### Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: Amenorrhea  
<https://www.nichd.nih.gov/health/topics/amenorrhea>

### Educational Resources

- Kids Health: Female Reproductive System  
<https://kidshealth.org/en/parents/female-reproductive-system.html>
- MalaCards: mullerian aplasia and hyperandrogenism  
[https://www.malacards.org/card/mullerian\\_aplasia\\_and\\_hyperandrogenism](https://www.malacards.org/card/mullerian_aplasia_and_hyperandrogenism)
- Orphanet: Müllerian aplasia and hyperandrogenism  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=247768](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=247768)

### Patient Support and Advocacy Resources

- AIS-DSD Support Group for Women  
<http://aisdsd.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/wnt4-deficiency/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mullerian+aplasia%5BTIAB%5D%29+OR+%28wnt4+deficiency%5BTIAB%5D%29+OR+%28WNT4%5BTIAB%5D%29%29+NOT+%28%28tendon%29+OR+%28muscle%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- MULLERIAN APLASIA AND HYPERANDROGENISM  
<http://omim.org/entry/158330>

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