

5-alpha reductase deficiency

Description

5-alpha reductase deficiency is a condition that affects sexual development before birth and during puberty. People with this condition are genetically male, with one X and one Y chromosome in each cell, and they have male gonads (testes). Their bodies, however, do not produce enough of a hormone called dihydrotestosterone (DHT). DHT has a critical role in male sexual development, and a shortage of this hormone disrupts the formation of the external sex organs before birth.

Many people with 5-alpha reductase deficiency are assigned female at birth based on their external genitalia. In other cases, affected infants are assigned male at birth based on their external genitalia, often an unusually small penis (micropenis) and the urethra opening on the underside of the penis (hypospadias). Still other affected infants may be assigned either female or male at birth as their external genitalia do not look clearly male or clearly female.

During puberty, an increase in the levels of male sex hormones leads to the development of some secondary sex characteristics, such as increased muscle mass, deepening of the voice, development of pubic hair, and a growth spurt. The penis and scrotum (the sac of skin that holds the testes) may grow larger. People with 5-alpha reductase deficiency do not develop much facial or body hair. Most affected individuals are unable to have biological children (infertile) without assisted reproduction.

Frequency

5-alpha reductase deficiency is a rare condition; the exact incidence is unknown. Large families with affected members have been found in several countries, including the Dominican Republic, Papua New Guinea, Turkey, and Egypt.

Causes

Variants (also called mutations) in the *SRD5A2* gene cause 5-alpha reductase deficiency. The *SRD5A2* gene provides instructions for making an enzyme called steroid 5-alpha reductase 2. This enzyme is involved in processing androgens, which are hormones that direct male sexual development. Specifically, the steroid 5-alpha reductase 2 enzyme is responsible for a chemical reaction that converts the hormone

testosterone to DHT. DHT is essential for the normal development of male sex characteristics before birth, particularly the formation of the external genitalia.

Variants in the *SRD5A2* gene prevent steroid 5-alpha reductase 2 from effectively converting testosterone to DHT in the developing reproductive tissues. These hormonal factors underlie the changes in sexual development seen in infants with 5-alpha reductase deficiency.

During puberty, the testes produce more testosterone. Researchers believe that people with 5-alpha reductase deficiency develop secondary male sex characteristics in response to higher levels of this hormone. Some affected people also retain a small amount of 5-alpha reductase 2 activity, which may produce DHT and contribute to the development of secondary sex characteristics during puberty.

[Learn more about the gene associated with 5-alpha reductase deficiency](#)

- *SRD5A2*

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the *SRD5A2* gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Although people who are genetically female (with two X chromosomes in each cell) may inherit variants in both copies of the *SRD5A2* gene, their sexual development is not affected. The development of female sex characteristics does not require DHT, so a lack of steroid 5-alpha reductase 2 activity does not cause physical changes in these individuals. Only people who have variants in both copies of the *SRD5A2* gene and are genetically male (with one X and one Y chromosome in each cell) will have the characteristic signs of 5-alpha reductase deficiency.

Other Names for This Condition

- PPSH
- Pseudovaginal perineoscrotal hypospadias
- Steroid 5-alpha-reductase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: 3-Oxo-5 alpha-steroid delta 4-dehydrogenase deficiency (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268297/>)

Genetic and Rare Diseases Information Center

- 46,XY disorder of sex development due to 5-alpha-reductase 2 deficiency (<https://rarediseases.info.nih.gov/diseases/5680/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%25-alpha reductase deficiency%22](https://clinicaltrials.gov/search?cond=%25-alpha+reductase+deficiency%22))

Catalog of Genes and Diseases from OMIM

- PSEUDO-VAGINAL PERINEOSCROTAL HYPOSPADIAS; PPSH (<https://omim.org/entry/264600>)

Scientific Articles on PubMed

- PubMed ([https://pubmed.ncbi.nlm.nih.gov/?term=\(5-alpha+reductase+deficiency%5BTIAB%5D\)+OR+\(steroid+5-alpha-reductase+deficiency%5BTIAB%5D\)+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+6000+days%22%5Bdp%5D](https://pubmed.ncbi.nlm.nih.gov/?term=(5-alpha+reductase+deficiency%5BTIAB%5D)+OR+(steroid+5-alpha-reductase+deficiency%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+6000+days%22%5Bdp%5D))

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