



3-beta-hydroxysteroid dehydrogenase deficiency

3-beta (β)-hydroxysteroid dehydrogenase (HSD) deficiency is an inherited disorder that affects hormone-producing glands including the gonads (ovaries in females and testes in males) and the adrenal glands. The gonads direct sexual development before birth and during puberty. The adrenal glands, which are located on top of the kidneys, regulate the production of certain hormones and control salt levels in the body. People with 3β -HSD deficiency lack many of the hormones that are made in these glands. 3β -HSD deficiency is one of a group of disorders known as congenital adrenal hyperplasias that impair hormone production and disrupt sexual development and maturation.

There are three types of 3β -HSD deficiency: the salt-wasting, non-salt-wasting, and non-classic types. In the salt-wasting type, hormone production is extremely low. Individuals with this type lose large amounts of sodium in their urine, which can be life-threatening. Individuals affected with the salt-wasting type are usually diagnosed soon after birth due to complications related to a lack of salt reabsorption, including dehydration, poor feeding, and vomiting. People with the non-salt-wasting type of 3β -HSD deficiency produce enough hormone to allow sodium reabsorption in the kidneys. Individuals with the non-classic type have the mildest symptoms and do not experience salt wasting.

In males with any type of 3β -HSD deficiency, problems with male sex hormones lead to abnormalities of the external genitalia. These abnormalities range from having the opening of the urethra on the underside of the penis (hypospadias) to having external genitalia that do not look clearly male or female (ambiguous genitalia). The severity of the genital abnormality does not consistently depend on the type of the condition. Because of the hormone dysfunction in the testes, males with 3β -HSD deficiency are frequently unable to have biological children (infertile).

Females with 3β -HSD deficiency may have slight abnormalities of the external genitalia at birth. Females affected with the non-salt-wasting or non-classic types are typically not diagnosed until mid-childhood or puberty, when they may experience irregular menstruation, premature pubic hair growth, and excessive body hair growth (hirsutism). Females with 3β -HSD deficiency have difficulty conceiving a child (impaired fertility).

Frequency

The exact prevalence of 3β -HSD deficiency is unknown. At least 60 affected individuals have been reported.

Causes

Mutations in the *HSD3B2* gene cause 3 β -HSD deficiency. The *HSD3B2* gene provides instructions for making the 3 β -HSD enzyme. This enzyme is found in the gonads and adrenal glands. The 3 β -HSD enzyme is involved in the production of many hormones, including cortisol, aldosterone, androgens, and estrogen. Cortisol has numerous functions such as maintaining energy and blood sugar levels, protecting the body from stress, and suppressing inflammation. Aldosterone is sometimes called the salt-retaining hormone because it regulates the amount of salt retained by the kidney. The retention of salt affects fluid levels and blood pressure. Androgens and estrogen are essential for normal sexual development and reproduction.

3 β -HSD deficiency is caused by a deficiency (shortage) of the 3 β -HSD enzyme. The amount of functional 3 β -HSD enzyme determines whether a person will have the salt-wasting or non-salt-wasting type of the disorder. Individuals with the salt-wasting type have *HSD3B2* gene mutations that result in the production of very little or no enzyme. People with the non-salt-wasting type of this condition have *HSD3B2* gene mutations that allow the production of some functional enzyme, although in reduced amounts.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 3 beta-HSD deficiency
- 3 beta-ol dehydrogenase deficiency
- 3-beta–hydroxysteroid dehydrogenase deficiency
- 3b-hydroxysteroid dehydrogenase deficiency
- 3 β -HSD deficiency
- 3 β -HSD deficiency congenital adrenal hyperplasia
- 3 β -hydroxysteroid dehydrogenase deficiency
- type II 3 β -hydroxysteroid dehydrogenase deficiency

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
[/primer/testing/genetictesting](#)
- Genetic Testing Registry: 3 beta-Hydroxysteroid dehydrogenase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342471/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%223-beta-hydroxysteroid+dehydrogenase+deficiency%22+OR+%22Adrenal+Hyperplasia%2C+Congenital%22>

Other Diagnosis and Management Resources

- Great Ormond Street Hospital for Children: Cortisol Deficiency
<https://www.gosh.nhs.uk/conditions-and-treatments/conditions-we-treat/cortisol-deficiency>
- MedlinePlus Encyclopedia: Ambiguous Genitalia
<https://medlineplus.gov/ency/article/003269.htm>
- MedlinePlus Encyclopedia: Congenital Adrenal Hyperplasia
<https://medlineplus.gov/ency/article/000411.htm>
- MedlinePlus Health Topic: Assisted Reproductive Technology
<https://medlineplus.gov/assistedreproductivetechnology.html>
- National Institutes of Health Clinical Center: Managing Adrenal Insufficiency
https://www.cc.nih.gov/ccc/patient_education/pepubs/mngadrins.pdf

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Ambiguous Genitalia
<https://medlineplus.gov/ency/article/003269.htm>
- Encyclopedia: Congenital Adrenal Hyperplasia
<https://medlineplus.gov/ency/article/000411.htm>
- Health Topic: Adrenal Gland Disorders
<https://medlineplus.gov/adrenalglanddisorders.html>
- Health Topic: Assisted Reproductive Technology
<https://medlineplus.gov/assistedreproductivetechnology.html>
- Health Topic: Infertility
<https://medlineplus.gov/infertility.html>

Genetic and Rare Diseases Information Center

- 3-beta-hydroxysteroid dehydrogenase deficiency
<https://rarediseases.info.nih.gov/diseases/9152/3-beta-hydroxysteroid-dehydrogenase-deficiency>

Educational Resources

- Boston Children's Hospital: Congenital Adrenal Hyperplasia
<http://www.childrenshospital.org/conditions-and-treatments/conditions/c/congenital-adrenal-hyperplasia-cah>
- CARES Foundation: FAQs
<https://www.caresfoundation.org/faqs/>
- MalaCards: 3-beta-hydroxysteroid dehydrogenase deficiency
https://www.malacards.org/card/3_beta_hydroxysteroid_dehydrogenase_deficiency
- March of Dimes: Genital and Urinary Tract Defects
<https://www.marchofdimes.org/baby/genital-and-urinary-tract-defects.aspx>
- Orphanet: Congenital adrenal hyperplasia due to 3-beta-hydroxysteroid dehydrogenase deficiency
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=90791

Patient Support and Advocacy Resources

- CARES Foundation
<https://www.caresfoundation.org/>
- National Organization for Rare Disorders (NORD): Congenital Adrenal Hyperplasia
<https://rarediseases.org/rare-diseases/congenital-adrenal-hyperplasia/>
- RESOLVE: The National Infertility Association
<https://resolve.org/>
- The MAGIC Foundation: Congenital Adrenal Hyperplasia
<https://www.magicfoundation.org/Growth-Disorders/Congenital-Adrenal-Hyperplasia/>
- University of Kansas Medical Center Resource List: Sexuality and Sexual Differentiation Syndromes
<http://www.kumc.edu/gec/support/ambig.html>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%283+beta+hydroxysteroid+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%283+beta+HSD+deficiency%5BTIAB%5D%29+OR+%283beta+hydroxysteroid+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%283beta+HSD+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- ADRENAL HYPERPLASIA, CONGENITAL, DUE TO 3-BETA-HYDROXYSTEROID DEHYDROGENASE 2 DEFICIENCY
<http://omim.org/entry/201810>

Medical Genetics Database from MedGen

- 3 beta-Hydroxysteroid dehydrogenase deficiency
<https://www.ncbi.nlm.nih.gov/medgen/452446>

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