17-beta hydroxysteroid dehydrogenase 3 deficiency

Description

17-beta hydroxysteroid dehydrogenase 3 deficiency is a condition that affects male sexual development. 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 male sex hormone (androgen) called testosterone. Testosterone has a critical role in male sexual development, and a shortage of this hormone disrupts the formation of the external sex organs before birth.

Most people with 17-beta hydroxysteroid dehydrogenase 3 deficiency are born with external genitalia that appear female. In some cases, the external genitalia do not look clearly male or clearly female. Still other affected infants have genitalia that appear predominantly male, often with an unusually small penis (micropenis) or the urethra opening on the underside of the penis (hypospadias).

During puberty, people with this condition develop some male secondary sex characteristics, such as increased muscle mass, deepening of the voice, and development of male pattern facial and body hair. In addition to these changes typical of adolescent boys, some affected individuals may also experience breast enlargement (gynecomastia). Despite having testes, people with this disorder are generally unable to father children (infertile).

Children with 17-beta hydroxysteroid dehydrogenase 3 deficiency are often raised as girls. About half of these individuals adopt a male gender role in adolescence or early adulthood.

Frequency

17-beta hydroxysteroid dehydrogenase 3 deficiency is a rare disorder. Researchers have estimated that this condition occurs in approximately 1 in 147,000 newborns. It is more common in the Arab population of Gaza, where it affects 1 in 200 to 300 people.

Causes

Mutations in the *HSD17B3* gene cause 17-beta hydroxysteroid dehydrogenase 3 deficiency. The *HSD17B3* gene provides instructions for making an enzyme called 17-beta hydroxysteroid dehydrogenase 3. This enzyme is active in the testes, where it helps to produce testosterone from a weaker precursor androgen called

androstenedione.
Mutations in the *HSD17B3* gene result in a 17-beta hydroxysteroid dehydrogenase 3 enzyme with little or no activity, reducing production of testosterone from androstenedione. The shortage of the stronger androgen affects the development of the reproductive tract in the male fetus, resulting in the abnormalities in the external sex organs that occur in 17-beta hydroxysteroid dehydrogenase 3 deficiency.

At puberty, conversion of androstenedione to testosterone increases in various tissues of the body through processes involving other enzymes. The additional testosterone results in the development of male secondary sex characteristics in adolescents, including those with 17-beta hydroxysteroid dehydrogenase 3 deficiency.

A portion of the androstenedione is also converted to the female sex hormone estrogen. Since impairment of the conversion to testosterone in this disorder results in excess androstenedione in the body, a corresponding excess of estrogen may be produced, leading to breast enlargement in some affected individuals.

Learn more about the gene associated with 17-beta hydroxysteroid dehydrogenase 3 deficiency

- HSD17B3

Inheritance

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. Individuals who are genetically male and have two copies of a mutated gene in each cell are affected by 17-beta hydroxysteroid dehydrogenase 3 deficiency. People with two mutations who are genetically female do not usually experience any signs and symptoms of this disorder.

Other Names for This Condition

- 17-beta hydroxysteroid dehydrogenase III deficiency
- 17-ketosteroid reductase deficiency of testis
- 17-KSR deficiency
- Neutral 17-beta-hydroxysteroid oxidoreductase deficiency
- Pseudohermaphroditism, male, with gynecomastia
- Testosterone 17-beta-dehydrogenase deficiency

Additional Information & Resources

Genetic and Rare Diseases Information Center

- 46,XY disorder of sex development due to 17-beta-hydroxysteroid dehydrogenase 3 deficiency (https://rarediseases.info.nih.gov/diseases/5659/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- 17-BETA HYDROXYSTEROID DEHYDROGENASE III DEFICIENCY (https://omim.org/entry/264300)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%2817-beta+hydroxysteroid+dehydrogenase+deficiency%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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