

## 17 alpha-hydroxylase/17,20-lyase deficiency

### Description

17 alpha( $\alpha$ )-hydroxylase/17,20-lyase deficiency is a condition that affects the function of certain hormone-producing glands called the gonads (ovaries in females and testes in males) and the adrenal glands. The gonads direct sexual development before birth and during puberty and are important for reproduction. The adrenal glands, which are located on top of the kidneys, regulate the production of certain hormones, including those that control salt levels in the body. People with 17 $\alpha$ -hydroxylase/17,20-lyase deficiency have an imbalance of many of the hormones that are made in these glands. 17 $\alpha$ -hydroxylase/17,20-lyase deficiency is one of a group of disorders, known as congenital adrenal hyperplasias, that impair hormone production and disrupt sexual development and maturation.

Hormone imbalances lead to the characteristic signs and symptoms of 17 $\alpha$ -hydroxylase/17,20-lyase deficiency, which include high blood pressure (hypertension), low levels of potassium in the blood (hypokalemia), and abnormal sexual development. The severity of the features varies. Two forms of the condition are recognized: complete 17 $\alpha$ -hydroxylase/17,20-lyase deficiency, which is more severe, and partial 17 $\alpha$ -hydroxylase/17,20-lyase deficiency, which is typically less so.

Males and females are affected by disruptions to sexual development differently. Females (who have two X chromosomes) with 17 $\alpha$ -hydroxylase/17,20-lyase deficiency are born with normal external female genitalia; however, the internal reproductive organs, including the uterus and ovaries, may be underdeveloped. Women with complete 17 $\alpha$ -hydroxylase/17,20-lyase deficiency do not develop secondary sex characteristics, such as breasts and pubic hair, and do not menstruate (amenorrhea). Women with partial 17 $\alpha$ -hydroxylase/17,20-lyase deficiency may develop some secondary sex characteristics; menstruation is typically irregular or absent. Either form of the disorder results in an inability to conceive a baby (infertility).

In affected individuals who are chromosomally male (having an X and a Y chromosome), problems with sexual development lead to abnormalities of the external genitalia. The most severely affected are born with characteristically female external genitalia and are generally raised as females. However, because they do not have female internal reproductive organs, these individuals have amenorrhea and do not develop female secondary sex characteristics. These individuals have testes, but they are abnormally located in the abdomen (undescended). Sometimes, complete 17 $\alpha$ -hydroxylase/17,20-

lyase deficiency leads to external genitalia that do not look clearly male or clearly female. Males with partial 17 $\alpha$ -hydroxylase/17,20-lyase deficiency may have a small penis ( micropenis), the opening of the urethra on the underside of the penis (hypospadias), or a scrotum divided into two lobes (bifid scrotum). Males with either complete or partial 17 $\alpha$ -hydroxylase/17,20-lyase deficiency are also infertile.

## Frequency

17 $\alpha$ -hydroxylase/17,20-lyase deficiency accounts for about 1 percent of congenital adrenal hyperplasia cases. It is estimated to occur in 1 in 1 million people worldwide.

## Causes

17 $\alpha$ -hydroxylase/17,20-lyase deficiency is caused by mutations in the *CYP17A1* gene. The protein produced from this gene is involved in the formation of steroid hormones. This group of hormones includes sex hormones such as testosterone and estrogen, which are needed for normal sexual development and reproduction; mineralocorticoids, which help regulate the body's salt and water balance; and glucocorticoids, which are involved in maintaining blood sugar (glucose) levels and regulating the body's response to stress.

Steroid hormones are produced through a series of chemical reactions. The CYP17A1 enzyme performs two important reactions in this process. The enzyme has 17 alpha( $\alpha$ )-hydroxylase activity, which is important for production of glucocorticoids and sex hormones. CYP17A1 also has 17,20-lyase activity, which is integral to the production of sex hormones.

17 $\alpha$ -hydroxylase/17,20-lyase deficiency results from a shortage (deficiency) of both enzyme activities. The amount of remaining enzyme activity determines whether a person will have the complete or partial form of the disorder. Individuals with the complete form have *CYP17A1* gene mutations that result in the production of an enzyme with very little or no 17 $\alpha$ -hydroxylase and 17,20-lyase activity. People with the partial form of this condition have *CYP17A1* gene mutations that allow some enzyme activity, although at reduced levels.

With little or no 17 $\alpha$ -hydroxylase activity, production of glucocorticoids is impaired, and instead, mineralocorticoids are produced. An excess of these salt-regulating hormones leads to hypertension and hypokalemia.

Loss of 17,20-lyase activity impairs sex hormone production. Shortage of these hormones disrupts development of the reproductive system and impairs the onset of puberty in males and females with 17 $\alpha$ -hydroxylase/17,20-lyase deficiency.

[Learn more about the gene associated with 17 alpha-hydroxylase/17,20-lyase deficiency](#)

- CYP17A1

## 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.

## Other Names for This Condition

- 17-alpha-hydroxylase deficiency
- 17-alpha-hydroxylase-deficient congenital adrenal hyperplasia
- Adrenal hyperplasia V
- Combined 17 alpha-hydroxylase/17,20-lyase deficiency
- Congenital adrenal hyperplasia due to 17-alpha-hydroxylase deficiency
- Congenital adrenal hyperplasia type 5
- Deficiency of steroid 17-alpha-monooxygenase

## Additional Information & Resources

### Genetic Testing Information

- Genetic Testing Registry: Deficiency of steroid 17-alpha-monooxygenase (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268285/>)

### Patient Support and Advocacy Resources

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

### Catalog of Genes and Diseases from OMIM

- ADRENAL HYPERPLASIA, CONGENITAL, DUE TO 17-ALPHA-HYDROXYLASE DEFICIENCY (<https://omim.org/entry/202110>)

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%2817alpha-hydroxylase/17,20-lyase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

## References

- Kim YM, Kang M, Choi JH, Lee BH, Kim GH, Ohn JH, Kim SY, Park MS, Yoo HW.

A review of the literature on common CYP17A1 mutations in adults with 17-hydroxylase/17,20-lyase deficiency, a case series of such mutations among Koreans and functional characteristics of a novel mutation. *Metabolism*. 2014 Jan;63(1):42-9. doi: 10.1016/j.metabol.2013.08.015. Epub 2013 Oct 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24140098>)

- Marsh CA, Auchus RJ. Fertility in patients with genetic deficiencies of cytochrome P450c17 (CYP17A1): combined 17-hydroxylase/17,20-lyase deficiency and isolated 17,20-lyase deficiency. *Fertil Steril*. 2014 Feb;101(2):317-22. doi:10.1016/j.fertnstert.2013.11.011. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24485502>)
- Miller WL. The syndrome of 17,20 lyase deficiency. *J Clin Endocrinol Metab*. 2012 Jan;97(1):59-67. doi: 10.1210/jc.2011-2161. Epub 2011 Nov 9. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22072737>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3251937/>)
- Rosa S, Steigert M, Lang-Muritano M, Allemand D, Schoenle EJ, Bion-Laubera A. Clinical, genetic and functional characteristics of three novel CYP17A1 mutations causing combined 17 $\alpha$ -hydroxylase/17,20-lyase deficiency. *Horm Res Paediatr*. 2010;73(3):198-204. doi: 10.1159/000284362. Epub 2010 Mar 3. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20197673>)

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