

Phosphoribosylpyrophosphate synthetase superactivity

Description

Phosphoribosylpyrophosphate synthetase superactivity (PRS superactivity) is characterized by the overproduction and accumulation of uric acid (a waste product of normal chemical processes) in the blood and urine. The overproduction of uric acid can lead to gout, which is arthritis caused by an accumulation of uric acid crystals in the joints. Individuals with PRS superactivity also develop kidney or bladder stones that may result in episodes of acute kidney failure.

There are two forms of PRS superactivity, a severe form that begins in infancy or early childhood, and a milder form that typically appears in late adolescence or early adulthood. In both forms, a kidney or bladder stone is often the first symptom. Gout and impairment of kidney function may develop if the condition is not adequately controlled with medication and dietary restrictions. People with the severe form may also have neurological problems, including hearing loss caused by changes in the inner ear (sensorineural hearing loss), weak muscle tone (hypotonia), impaired muscle coordination (ataxia), and developmental delay.

Frequency

PRS superactivity is believed to be a rare disorder. Approximately 30 families with the condition have been reported. More than two thirds of these families are affected by the milder form of the disease.

Causes

Certain mutations in the *PRPS1* gene cause PRS superactivity. The *PRPS1* gene provides instructions for making an enzyme called phosphoribosyl pyrophosphate synthetase 1, or PRPP synthetase 1. This enzyme helps produce a molecule called phosphoribosyl pyrophosphate (PRPP). PRPP is involved in producing purine and pyrimidine nucleotides. These nucleotides are building blocks of DNA, its chemical cousin RNA, and molecules such as ATP and GTP that serve as energy sources in the cell. PRPP synthetase 1 and PRPP also play a key role in recycling purines from the breakdown of DNA and RNA, a faster and more efficient way of making purines available.

In people with the more severe form of PRS superactivity, *PRPS1* gene mutations

change single protein building blocks (amino acids) in the PRPP synthetase 1 enzyme, resulting in a poorly regulated, overactive enzyme. In the milder form of PRS superactivity, the *PRPS1* gene is overactive for reasons that are not well understood. *PRPS1* gene overactivity increases the production of normal PRPP synthetase 1 enzyme, which increases the availability of PRPP. In both forms of the disorder, excessive amounts of purines are generated.

Under these conditions, uric acid, a waste product of purine breakdown, accumulates in the body. A buildup of uric acid crystals can cause gout, kidney stones, and bladder stones. It is unclear how *PRPS1* gene mutations are related to the neurological problems associated with the severe form of PRS superactivity.

[Learn more about the gene associated with Phosphoribosylpyrophosphate synthetase superactivity](#)

- PRPS1

Inheritance

This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell sometimes causes the disorder.

In most reported cases, affected individuals have inherited the mutation from a parent who carries an altered copy of the *PRPS1* gene. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons. PRS superactivity may also result from new mutations in the *PRPS1* gene and can occur in people with no history of the disorder in their family.

Other Names for This Condition

- Gout, PRPS-related
- PRPP synthetase overactivity
- PRPP synthetase superactivity
- PRPS1 superactivity
- PRS overactivity
- PRS superactivity

Additional Information & Resources

[Genetic Testing Information](#)

- Genetic Testing Registry: Phosphoribosylpyrophosphate synthetase superactivity (h

<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970827/>

Genetic and Rare Diseases Information Center

- Phosphoribosylpyrophosphate synthetase superactivity (<https://rarediseases.info.nih.gov/diseases/4337/index>)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Phosphoribosylpyrophosphate synthetase superactivity%22](https://clinicaltrials.gov/search?cond=%22Phosphoribosylpyrophosphate%20synthetase%20superactivity%22))

Catalog of Genes and Diseases from OMIM

- PHOSPHORIBOSYLPYROPHOSPHATE SYNTHETASE SUPERACTIVITY (<https://omim.org/entry/300661>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28phosphoribosylpyrophosphate+synthetase+superactivity%29+OR+%28prps1+superactivity%29+OR+%28prps+superactivity%29+OR+%28prps+overactivity%29+OR+%28prps-related+gout%29+OR+%28prpp+synthetase+superactivity%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

References

- Ahmed M, Taylor W, Smith PR, Becker MA. Accelerated transcription of PRPS1 in X-linked overactivity of normal human phosphoribosylpyrophosphate synthetase. *JBiol Chem.* 1999 Mar 12;274(11):7482-8. doi: 10.1074/jbc.274.11.7482. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10066814>)
- Becker MA, Smith PR, Taylor W, Mustafi R, Switzer RL. The genetic and functional basis of purine nucleotide feedback-resistant phosphoribosylpyrophosphate synthetase superactivity. *J Clin Invest.* 1995 Nov;96(5):2133-41. doi: 10.1172/JCI118267. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7593598>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC185862/>)
- Becker MA, Taylor W, Smith PR, Ahmed M. Overexpression of the normal phosphoribosylpyrophosphate synthetase 1 isoform underlies catalytic superactivity of human phosphoribosylpyrophosphate synthetase. *J Biol*

Chem. 1996Aug 16;271(33):19894-9. doi: 10.1074/jbc.271.33.19894. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/8702702>)

- de Brouwer APM, Christodoulou J. Phosphoribosylpyrophosphate Synthetase Superactivity. 2008 Sep 23 [updated 2022 Feb 17]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews (R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1973/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301734>)
- Garcia-Pavia P, Torres RJ, Rivero M, Ahmed M, Garcia-Puig J, Becker MA. Phosphoribosylpyrophosphate synthetase overactivity as a cause of uric acid overproduction in a young woman. *Arthritis Rheum.* 2003 Jul;48(7):2036-41. doi: 10.1002/art.11058. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12847698>)
- Nyhan WL. Disorders of purine and pyrimidine metabolism. *Mol Genet Metab.* 2005 Sep-Oct;86(1-2):25-33. doi: 10.1016/j.ymgme.2005.07.027. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16176880>)

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