Prader-Willi syndrome

Prader-Willi syndrome is a complex genetic condition that affects many parts of the body. In infancy, this condition is characterized by weak muscle tone (hypotonia), feeding difficulties, poor growth, and delayed development. Beginning in childhood, affected individuals develop an insatiable appetite, which leads to chronic overeating (hyperphagia) and obesity. Some people with Prader-Willi syndrome, particularly those with obesity, also develop type 2 diabetes (the most common form of diabetes).

People with Prader-Willi syndrome typically have mild to moderate intellectual impairment and learning disabilities. Behavioral problems are common, including temper outbursts, stubbornness, and compulsive behavior such as picking at the skin. Sleep abnormalities can also occur. Additional features of this condition include distinctive facial features such as a narrow forehead, almond-shaped eyes, and a triangular mouth; short stature; and small hands and feet. Some people with Prader-Willi syndrome have unusually fair skin and light-colored hair. Both affected males and affected females have underdeveloped genitals. Puberty is delayed or incomplete, and most affected individuals are unable to have children (infertile).

Frequency

Prader-Willi syndrome affects an estimated 1 in 10,000 to 30,000 people worldwide.

Causes

Prader-Willi syndrome is caused by the loss of function of genes in a particular region of chromosome 15. People normally inherit one copy of this chromosome from each parent. Some genes are turned on (active) only on the copy that is inherited from a person's father (the paternal copy). This parent-specific gene activation is caused by a phenomenon called genomic imprinting.

Most cases of Prader-Willi syndrome (about 70 percent) occur when a segment of the paternal chromosome 15 is deleted in each cell. People with this chromosomal change are missing certain critical genes in this region because the genes on the paternal copy have been deleted, and the genes on the maternal copy are turned off (inactive). In another 25 percent of cases, a person with Prader-Willi syndrome has two copies of chromosome 15 inherited from his or her mother (maternal copies) instead of one copy from each parent. This phenomenon is called maternal uniparental disomy. Rarely, Prader-Willi syndrome can also be caused by a chromosomal rearrangement called a translocation, or by a mutation or other defect that abnormally turns off (inactivates) genes on the paternal chromosome 15.

It appears likely that the characteristic features of Prader-Willi syndrome result from the loss of function of several genes on chromosome 15. Among these are genes that

provide instructions for making molecules called small nucleolar RNAs (snoRNAs). These molecules have a variety of functions, including helping to regulate other types of RNA molecules. (RNA molecules play essential roles in producing proteins and in other cell activities.) Studies suggest that the loss of a particular group of snoRNA genes, known as the SNORD116 cluster, may play a major role in causing the signs and symptoms of Prader-Willi syndrome. However, it is unknown how a missing SNORD116 cluster could contribute to intellectual disability, behavioral problems, and the physical features of the disorder.

In some people with Prader-Willi syndrome, the loss of a gene called *OCA2* is associated with unusually fair skin and light-colored hair. The *OCA2* gene is located on the segment of chromosome 15 that is often deleted in people with this disorder. However, loss of the *OCA2* gene does not cause the other signs and symptoms of Prader-Willi syndrome. The protein produced from this gene helps determine the coloring (pigmentation) of the skin, hair, and eyes.

Researchers are studying other genes on chromosome 15 that may also be related to the major signs and symptoms of this condition.

Inheritance Pattern

Most cases of Prader-Willi syndrome are not inherited, particularly those caused by a deletion in the paternal chromosome 15 or by maternal uniparental disomy. These genetic changes occur as random events during the formation of reproductive cells (eggs and sperm) or in early embryonic development. Affected people typically have no history of the disorder in their family.

Rarely, a genetic change responsible for Prader-Willi syndrome can be inherited. For example, it is possible for a genetic change that abnormally inactivates genes on the paternal chromosome 15 to be passed from one generation to the next.

Other Names for This Condition

- Prader-Labhart-Willi syndrome
- PWS
- Willi-Prader syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Prader-Willi syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0032897/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Prader-Willi+syndrome%22

Other Diagnosis and Management Resources

- GeneReview: Prader-Willi Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1330
- MedlinePlus Encyclopedia: Hypotonia
  https://medlineplus.gov/ency/article/003298.htm
- MedlinePlus Encyclopedia: Prader-Willi Syndrome
  https://medlineplus.gov/ency/article/001605.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hypotonia
  https://medlineplus.gov/ency/article/003298.htm
- Encyclopedia: Prader-Willi Syndrome
  https://medlineplus.gov/ency/article/001605.htm
- Health Topic: Prader-Willi Syndrome
  https://medlineplus.gov/praderwillisyndrome.html
- Medical Tests: Obesity Screening
  https://medlineplus.gov/lab-tests/obesity-screening/

Genetic and Rare Diseases Information Center

- Prader-Willi syndrome
  https://rarediseases.info.nih.gov/diseases/5575/prader-willi-syndrome

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development
  https://www.nichd.nih.gov/health/topics/prader-willi

Educational Resources

- International Prader-Willi Syndrome Organisation (UK): What is Prader-Willi Syndrome
  https://www.ipwso.org/what-is-prader-willi-syndrome
- MalaCards: prader-willi syndrome
  https://www.malacards.org/card/prader_willi_syndrome
- Orphanet: Prader-Willi syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=739

Patient Support and Advocacy Resources

- International Prader-Willi Syndrome Organisation (UK)
  https://www.ipwso.org/
- Medical Home Portal
  https://www.medicalhomeportal.org/diagnoses-and-conditions/prader-willi-syndrome
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/prader-willi-syndrome/
- Prader-Willi Syndrome Association (USA)
  https://www.pwsausa.org/
- The Foundation for Prader-Willi Research
  https://www.fpwr.org/

Clinical Information from GeneReviews

- Prader-Willi Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1330

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Prader-Willi+Syndrome%5BMAJR%5D%29+AND+%28Prader-Willi+syndrome%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- PRADER-WILLI SYNDROME
  http://omim.org/entry/176270

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