



Purine nucleoside phosphorylase deficiency

Purine nucleoside phosphorylase deficiency is a disorder of the immune system called an immunodeficiency. Immunodeficiencies are conditions in which the immune system is not able to protect the body effectively from foreign invaders such as bacteria and viruses.

People with purine nucleoside phosphorylase deficiency have low numbers of immune system cells called T cells, which normally recognize and attack foreign invaders to prevent infection. Some affected individuals also have low numbers of other immune system cells called B cells, which normally help fight infections by producing immune proteins called antibodies (or immunoglobulins). These proteins target foreign invaders and mark them for destruction. The most severely affected individuals, who lack T cells and B cells, have a serious condition called severe combined immunodeficiency (SCID).

The shortage of immune system cells in people with purine nucleoside phosphorylase deficiency results in repeated and persistent infections typically beginning in infancy or early childhood. Infections most commonly affect the sinuses and lungs. These infections are often caused by "opportunistic" organisms that ordinarily do not cause illness in people with a normal immune system. The infections can be very serious or life-threatening, and without successful treatment to restore immune function, children with purine nucleoside phosphorylase deficiency usually do not survive past childhood.

Infants with purine nucleoside phosphorylase deficiency typically grow more slowly than healthy babies. About two-thirds of individuals with this condition also have neurological problems, which may include developmental delay, intellectual disability, difficulty with balance and coordination (ataxia), and muscle stiffness (spasticity). People with purine nucleoside phosphorylase deficiency are also at increased risk of developing autoimmune disorders, which occur when the immune system malfunctions and attacks the body's tissues and organs.

Frequency

Purine nucleoside phosphorylase deficiency is rare; only about 70 affected individuals have been described in the medical literature. This disorder accounts for approximately 4 percent of all SCID cases.

Causes

Purine nucleoside phosphorylase deficiency is caused by mutations in the *PNP* gene. The *PNP* gene provides instructions for making an enzyme called purine nucleoside phosphorylase. This enzyme is found throughout the body but is most active in specialized white blood cells called lymphocytes, which include T cells and B cells.

Lymphocytes are produced in specialized lymphoid tissues, including the thymus and lymph nodes, and then released into the blood. The thymus is a gland located behind the breastbone; lymph nodes are found throughout the body. Lymphocytes in the blood and in lymphoid tissues are a major component of the immune system.

Purine nucleoside phosphorylase is known as a housekeeping enzyme because it clears away waste molecules that are generated when DNA is broken down. Mutations in the *PNP* gene reduce or eliminate the activity of purine nucleoside phosphorylase. The resulting excess of waste molecules and further reactions involving them lead to the buildup of a substance called deoxyguanosine triphosphate (dGTP) to levels that can be toxic to cells. Immature T cells in the thymus are particularly vulnerable to a toxic buildup of dGTP, which damages them and triggers their self-destruction (apoptosis). B cells and T cells in other lymphoid tissues can also be damaged. The shortage of T cells and sometimes B cells results in the immune problems characteristic of purine nucleoside phosphorylase deficiency. Damage to brain cells caused by buildup of dGTP is thought to underlie the neurological problems that occur in some people with purine nucleoside phosphorylase deficiency.

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

- nucleoside phosphorylase deficiency
- PNP deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Severe Combined Immunodeficiency (SCID) and Conditions Associated with T Cell Lymphopenia
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/SCID.pdf>

Genetic Testing Information

- What is genetic testing?
</primer/testing/genetictesting>
- Genetic Testing Registry: Purine-nucleoside phosphorylase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268125/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22purine+nucleoside+phosphorylase+deficiency%22+OR+%22Severe+Combined+Immunodeficiency%22>

Other Diagnosis and Management Resources

- Baby's First Test: Severe Combined Immunodeficiency
<https://www.babysfirsttest.org/newborn-screening/conditions/severe-combined-immunodeficiency-scid>
- National Marrow Donor Program
<https://bethematch.org/patients-and-families/about-transplant/diseases-treated-by-transplant/severe-combined-immunodeficiency--scid/>

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Immune System and Disorders
<https://medlineplus.gov/immunesystemanddisorders.html>

Genetic and Rare Diseases Information Center

- Purine nucleoside phosphorylase deficiency
<https://rarediseases.info.nih.gov/diseases/4606/purine-nucleoside-phosphorylase-deficiency>

Additional NIH Resources

- National Human Genome Research Institute: Learning About Severe Combined Immunodeficiency
<https://www.genome.gov/Genetic-Disorders/Severe-Combined-Immunodeficiency>
- National Institute of Allergy and Infectious Diseases: Primary Immune Deficiency Diseases
<https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pidds>

Educational Resources

- MalaCards: purine nucleoside phosphorylase deficiency
https://www.malacards.org/card/purine_nucleoside_phosphorylase_deficiency
- Merck Manual Consumer Version: Immunodeficiency Disorders
<https://www.merckmanuals.com/home/immune-disorders/immunodeficiency-disorders/overview-of-immunodeficiency-disorders>
- Orphanet: Purine nucleoside phosphorylase deficiency
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=760

Patient Support and Advocacy Resources

- Immune Deficiency Foundation
<https://primaryimmune.org/>
- Jeffrey Modell Foundation
<http://www.info4pi.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28purine+nucleoside+phosphorylase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY
<http://omim.org/entry/613179>

Medical Genetics Database from MedGen

- Purine-nucleoside phosphorylase deficiency
<https://www.ncbi.nlm.nih.gov/medgen/75653>

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Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/purine-nucleoside-phosphorylase-deficiency>

Reviewed: April 2019

Published: May 14, 2019

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
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