# Pyridoxal phosphate-responsive seizures

## Description

Pyridoxal phosphate-responsive seizures (sometimes called pyridoxamine 5'-phosphate oxidase deficiency or PNPO deficiency) is a condition in which repeated seizures ( epilepsy) typically begin within the first two weeks of life. In approximately 10 percent of individuals with PNPO deficiency, the seizures have a later onset, beginning after the first month of life. The seizures typically involve irregular involuntary muscle contractions (myoclonus), abnormal eye movements, or convulsions. In some cases, the seizures may last for several minutes or the seizures may occur too close together to allow for recovery between episodes (status epilepticus). Some babies with PNPO deficiency will experience seizures before birth, and some will experience a slow heart rate and a lack of oxygen before delivery (fetal distress).

Anticonvulsant medications, which are usually given to control seizures, are not effective in people with PNPO deficiency. Instead, individuals with PNPO deficiency require lifelong treatment with one of the following forms of vitamin B6: pyridoxal 5'-phosphate (PLP) or pyridoxine. If untreated, people with this condition can develop severe brain dysfunction (encephalopathy), which can lead to death. Even though seizures can be controlled with PLP or pyridoxine, people with PNPO deficiency may still experience neurological problems such as developmental delays, learning disorders, and uncontrolled movements (dystonia).

## Frequency

PNPO deficiency is a rare condition; as of 2022, approximately 90 individuals with PNPO deficiency have been described in the scientific literature.

## Causes

Variants (also called mutations) in the *PNPO* gene cause PNPO deficiency. The *PNPO* gene provides instructions for producing an enzyme called pyridox(am)ine 5'-phosphate oxidase. This enzyme is involved in the breakdown (metabolism) of vitamin B6 into pyridoxal 5'-phosphate (PLP), the active form of vitamin B6. PLP is necessary for protein metabolism and the processing of chemicals that transmit signals in the brain ( neurotransmitters).

Variants in the *PNPO* gene cause the gene to produce a version of the pyridox(am)ine 5'

-phosphate oxidase enzyme that is unable to metabolize vitamin B6, leading to a deficiency of PLP. A shortage of PLP can disrupt the function of many other proteins and enzymes that need PLP in order to be effective. Because PLP plays an important role in neurotransmitter metabolism, a lack of PLP is believed to cause the seizures that are characteristic of PNPO deficiency.

Learn more about the gene associated with Pyridoxal phosphate-responsive seizures

- PNPO

## Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

## Other Names for This Condition

- PNPO deficiency
- PNPO-related neonatal epileptic encephalopathy
- PNPOD
- Pyridoxal phosphate-dependent seizures
- Pyridoxamine 5'-oxidase deficiency
- Pyridoxamine 5-prime-phosphate oxidase deficiency
- Pyridoxine-5'-phosphate oxidase deficiency
- Pyridoxine-resistant seizures, PLP-sensitive

## Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Pyridoxal phosphate-responsive seizures (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1864723/)

Genetic and Rare Diseases Information Center

- Pyridoxal 5'-phosphate-dependent epilepsy (https://rarediseases.info.nih.gov/diseases/10730/pyridoxal-5-phosphate-dependent-epilepsy)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Pyridoxal phosphate-responsive seizures%22)

Catalog of Genes and Diseases from OMIM

- PYRIDOXAMINE 5-PRIME-PHOSPHATE OXIDASE DEFICIENCY; PNPOD (https://omim.org/entry/610090)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28pyridoxal+5'-phosphate+dependent+epilepsy%29+OR+%28pyridoxine+5'-phosphate+oxidase+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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