Zellweger spectrum disorder

Description

Zellweger spectrum disorder is a condition that affects many parts of the body. Cases of Zellweger spectrum disorder are often categorizes as severe, intermediate, or mild.

Individuals with severe Zellweger spectrum disorder usually have signs and symptoms at birth, which worsen over time. These infants experience weak muscle tone (hypotonia), feeding problems, hearing and vision loss, and seizures. These problems are caused by reduced myelin, which is the covering that protects nerves and promotes the efficient transmission of nerve impulses. The part of the brain and spinal cord that contains myelin is called white matter. Reduced myelin (demyelination) leads to loss of white matter (leukodystrophy).

Children with severe Zellweger spectrum disorder also develop life-threatening problems in other organs and tissues, such as the liver, heart, and kidneys, and their liver or spleen may be enlarged. They may have skeletal abnormalities, including a large space between the bones of the skull (fontanelles) and characteristic bone spots known as chondrodysplasia punctata that can be seen on x-ray. Affected individuals can have eye abnormalities, including clouding of the lenses of the eyes (cataracts) or involuntary, side-to-side movements of the eyes (nystagmus). Severe Zellweger spectrum disorder involves distinctive facial features, including a flattened face, broad nasal bridge, high forehead, and widely spaced eyes (hypertelorism). Children with severe Zellweger spectrum disorder typically do not survive beyond the first year of life.

People with intermediate or mild Zellweger spectrum disorder have more variable features that progress more slowly than those with the severe form. Affected children usually do not develop signs and symptoms of the disease until late infancy or early childhood. Children with these intermediate and mild forms often have hypotonia, vision problems, hearing loss, liver dysfunction, developmental delay, and some degree of intellectual disability. Most people with the intermediate form survive into childhood, and those with the mild form may reach adulthood. In rare cases, individuals at the mildest end of the condition spectrum have developmental delay in childhood and hearing loss or vision problems beginning in adulthood and do not develop the other features of this disorder.

The severe, intermediate, and mild forms of Zellweger spectrum disorder were once thought to be distinct disorders. The severe form was known as Zellweger syndrome, the intermediate form was neonatal adrenoleukodystrophy (NALD), and the mild form

was infantile Refsum disease. These conditions were renamed as a single condition when they were found to be part of the same condition spectrum.

Frequency

Zellweger spectrum disorder is estimated to occur in 1 in 50,000 individuals.

Causes

Variants (also called mutations) in at least 12 genes have been found to cause Zellweger spectrum disorder. These genes provide instructions for making a group of proteins known as peroxins, which are essential for the formation and normal functioning of cell structures called peroxisomes. Peroxisomes are sac-like compartments that contain enzymes needed to break down many different substances, including fatty acids and certain toxic compounds. They are also important for the production of fats (lipids) used in digestion and in the nervous system. Peroxins assist in the formation (biogenesis) of peroxisomes by producing the membrane that separates the peroxisome from the rest of the cell and by importing enzymes into the peroxisome.

Variants in the genes that cause Zellweger spectrum disorder prevent peroxisomes from forming normally. Diseases that disrupt the formation of peroxisomes, including Zellweger spectrum disorder, are called peroxisome biogenesis disorders. If the production of peroxisomes is altered, these structures cannot perform their usual functions. The signs and symptoms of severe Zellweger spectrum disorder are due to the absence of functional peroxisomes within cells. Intermediate and mild Zellweger spectrum disorder are caused by variants that allow some peroxisomes to form.

Variants in the *PEX1* gene are the most common cause of Zellweger spectrum disorder and are found in nearly 70 percent of affected individuals. The other genes associated with Zellweger spectrum disorder each account for a smaller percentage of cases of this condition.

Learn more about the gene associated with Zellweger spectrum disorder

- PEX1

Additional Information from NCBI Gene:

- PEX10
- PEX11B
- PEX12
- PEX13
- PEX14
- PEX16
- PEX19

- PEX2
- PEX26
- PEX3
- PEX5
- PEX6

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. 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

- Cerebrohepatorenal syndrome
- PBD, ZSS
- PBD-ZSD
- Peroxisome biogenesis disorders, Zellweger syndrome spectrum
- Zellweger spectrum
- Zellweger syndrome spectrum
- ZSD

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Peroxisome biogenesis disorder (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1832200/)
- Genetic Testing Registry: Peroxisome biogenesis disorder 2B (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3550234/)
- Genetic Testing Registry: Peroxisome biogenesis disorder 1A (Zellweger) (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4721541/)
- Genetic Testing Registry: Peroxisome biogenesis disorder 1B (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0282527/)

Genetic and Rare Diseases Information Center

- Peroxisome biogenesis disorder (https://rarediseases.info.nih.gov/diseases/11890/index)
- Zellweger syndrome (https://rarediseases.info.nih.gov/diseases/7917/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Zellweger spectrum disorder%22)

Catalog of Genes and Diseases from OMIM

- PEROXISOME BIOGENESIS DISORDER 2B; PBD2B (https://omim.org/entry/202370)
- PEROXISOME BIOGENESIS DISORDER 1A (ZELLWEGER); PBD1A (https://omim.org/entry/214100)
- PEROXISOME BIOGENESIS DISORDER 2A (ZELLWEGER); PBD2A (https://omim.org/entry/214110)
- PEROXISOME BIOGENESIS DISORDER 3B; PBD3B (https://omim.org/entry/266510)
- PEROXISOME BIOGENESIS DISORDER 1B; PBD1B (https://omim.org/entry/601539)
- PEROXISOME BIOGENESIS DISORDER 3A (ZELLWEGER); PBD3A (https://omim.org/entry/614859)
- PEROXISOME BIOGENESIS DISORDER 4A (ZELLWEGER); PBD4A (https://omim.org/entry/614862)
- PEROXISOME BIOGENESIS DISORDER 5A (ZELLWEGER); PBD5A (https://omim.org/entry/614866)
- PEROXISOME BIOGENESIS DISORDER 6A (ZELLWEGER); PBD6A (https://omim.org/entry/614870)
- PEROXISOME BIOGENESIS DISORDER 7A (ZELLWEGER); PBD7A (https://omim.org/entry/614872)
- PEROXISOME BIOGENESIS DISORDER 8A (ZELLWEGER); PBD8A (https://omim.org/entry/614876)
- PEROXISOME BIOGENESIS DISORDER 10A (ZELLWEGER); PBD10A (https://omim.org/entry/614882)
- PEROXISOME BIOGENESIS DISORDER 11A (ZELLWEGER); PBD11A (https://omim.org/entry/614883)
- PEROXISOME BIOGENESIS DISORDER 12A (ZELLWEGER); PBD12A (https://omim.org/entry/614886)
- PEROXISOME BIOGENESIS DISORDER 13A (ZELLWEGER); PBD13A (https://o

mim.org/entry/614887)

- PEROXISOME BIOGENESIS DISORDER 14B; PEX14B (https://omim.org/entry/614920)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28zellweger+spectrum%5BTIAB%5D%29+OR+%28zellweger+syndrome+spectrum%5BTIAB%5D%29+OR+%28zellweger+syndrome%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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