CONDITION

Canavan disease

Learn about Canavan disease, including its genetic cause, symptoms, diagnosis, supportive treatment, complications, and recommended follow-up care.

WHAT IT IS
Rare inherited disorder damaging brain white matter

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Delayed development, poor head control, low muscle tone, rapid head growth

WHAT CAUSES IT
Inherited ASPA gene variants

HOW IT IS DIAGNOSED
ASPA genetic testing, NAA testing, brain MRI

MAIN TREATMENT
Supportive care

CAN IT BE CURED?
No, no treatment reverses white-matter damage

IS IT AN EMERGENCY?
Sometimes, significant breathing difficulty or prolonged seizures

LONG-TERM OUTLOOK
Infantile form is progressive and life-limiting; milder forms retain more abilities

Overview

Canavan disease is a rare inherited disorder that damages the brain's white matter. White matter contains nerve fibers and the protective covering around them, called myelin. Myelin helps signals travel efficiently through the brain and spinal cord.

Canavan disease is one type of leukodystrophy , a group of genetic conditions that affect white matter. It is caused by changes in the `ASPA` gene. These changes reduce or eliminate the activity of an enzyme called aspartoacylase. Without enough of this enzyme, a substance called N-acetylaspartic acid, or NAA, builds up in the brain. This contributes to abnormal myelin development and a sponge-like breakdown of brain tissue.

The most common and severe form begins during infancy. Affected babies may initially appear healthy but later have delayed development, poor head control, weak muscle tone, and rapid

head growth. Less common, milder forms may begin later and cause learning, movement, or speech difficulties.

Canavan disease affects people differently. The infantile form is usually progressive and can be life-limiting, while people with milder forms may retain more abilities. Early diagnosis matters because it allows families to begin supportive care, address feeding and breathing concerns, receive genetic counseling, and consider appropriate research studies.

Symptoms

Symptoms depend on the form of Canavan disease and how much enzyme activity remains. In the severe infantile form, signs usually become noticeable during the first several months of life.

Early findings may include:

As the condition progresses, low muscle tone may be followed by stiffness or spasticity. Spasticity means that muscles remain unusually tight, making movement and positioning difficult. Some children develop rigid limbs, abnormal posture, or involuntary movements.

Other possible symptoms include seizures, sleep difficulties, reduced vision, and limited speech. A child may respond to light even when they cannot clearly track objects or recognize what they see. Hearing is often better preserved than vision, although responses may be hard to assess when movement and communication are limited.

Feeding problems may become more noticeable over time. A child may cough, choke, take a long time to eat, or have difficulty gaining weight. These symptoms can indicate swallowing problems and should be discussed promptly with the care team.

Mild or juvenile Canavan disease is less common. It may cause delayed speech, learning difficulties, poor coordination, mild weakness, or behavioral concerns. Head enlargement and severe loss of movement may be absent. Because these signs overlap with many other conditions, symptoms alone cannot confirm Canavan disease.

- Delayed development, such as difficulty rolling, sitting, or reaching for objects
- Poor head control
- Low muscle tone, also called hypotonia
- Reduced movement or unusual limpness
- Feeding or swallowing difficulty
- Irritability or unusually reduced responsiveness

- Rapid increase in head size, called macrocephaly

Causes and risk factors

Canavan disease results from disease-causing variants in both copies of the `ASPA` gene. The `ASPA` gene provides instructions for making aspartoacylase, the enzyme that breaks down NAA. Reduced enzyme activity allows NAA to accumulate and interferes with the health of white matter.

The condition follows an autosomal recessive inheritance pattern. A person who has one altered copy of the gene is known as a carrier. Carriers generally do not develop Canavan disease because their other gene copy provides enough enzyme activity.

When both biological parents are carriers, each pregnancy has:

These chances are the same for each pregnancy. They do not depend on the sex of the child or what happened in an earlier pregnancy.

Canavan disease can occur in any ethnic or racial group. Certain `ASPA` variants are more common among people with Ashkenazi Jewish ancestry, so the condition has historically occurred more often in that population. Some variants are also seen more often in other specific populations. Ancestry alone does not confirm or rule out the condition.

The main risk factors are having two carrier parents, having an affected sibling, or having a known family history. Canavan disease is not caused by anything a parent did during pregnancy, and it is not contagious.

- A 25% chance that the child will have Canavan disease
- A 50% chance that the child will be an unaffected carrier
- A 25% chance that the child will inherit neither familial variant

Diagnosis

A clinician may consider Canavan disease when an infant has developmental delay, low muscle tone, poor head control, and increasing head size. However, these findings can have many possible causes. Diagnosis usually combines clinical assessment with laboratory, imaging, and genetic tests.

Brain magnetic resonance imaging, or MRI, can show widespread changes in white matter. MRI uses a magnetic field to create detailed images and does not use ionizing radiation. A related test called magnetic resonance spectroscopy may detect unusually high NAA levels in the

brain.

Laboratory testing can measure NAA in urine. NAA may also be measured in blood or cerebrospinal fluid in selected situations. A clearly elevated level supports the diagnosis, particularly in the severe infantile form. Mild disease may produce a smaller increase.

Molecular genetic testing can identify disease-causing variants in both copies of the `ASPA` gene. Genetic confirmation helps distinguish Canavan disease from other leukodystrophies and provides information for family testing.

Evaluation may also include a neurological examination, developmental assessment, vision testing, hearing testing, and an assessment of feeding and swallowing. An electroencephalogram, or EEG, may be performed if seizures are suspected. An EEG records the brain's electrical activity.

After a diagnosis, parents and other relatives may be offered carrier testing. If familial variants are known, prenatal testing or preimplantation genetic testing may be possible for future pregnancies. A genetic counselor can explain the benefits, limitations, and possible results of these options without directing a family's reproductive decisions.

Treatment and management

There is currently no established treatment that reverses the underlying white-matter damage caused by Canavan disease. Care focuses on comfort, function, nutrition, communication, and prevention or treatment of complications. Management is usually coordinated across several specialties.

Physical and occupational therapy can support mobility, positioning, comfort, and participation in daily activities. Gentle stretching and properly fitted equipment may help reduce stiffness and protect joints. Seating systems, supportive strollers, standing devices, or wheelchairs may be considered based on the person's needs.

Speech-language specialists can help assess communication and swallowing. Communication support may include pictures, switches, eye-gaze technology, or other assistive devices. A person's ability to understand language may be greater than their ability to speak or move.

Nutrition management is especially important. A feeding assessment can determine whether food or liquid is entering the airway, a problem called aspiration. Adjusting food texture, eating position, or feeding pace may help some children. If eating by mouth is unsafe or does not provide enough nutrition, the team may discuss tube feeding. This decision should consider safety, comfort, growth, and family goals.

Seizures are treated with antiseizure medicines selected by the treating clinician. Muscle

stiffness, sleep problems, pain, constipation, reflux, and excess saliva may also be treated when present. Medication choices depend on the person's symptoms, other health conditions, and possible side effects.

Respiratory care may include airway-clearance techniques, treatment of infections, and support for weak coughing. Vaccination and routine preventive care remain important and should be discussed with the primary care clinician.

Gene therapy and other treatments aimed at the cause of Canavan disease are being studied. Research participation may provide access to an investigational treatment, but potential benefits are uncertain and risks may not yet be fully known. Families considering a clinical trial should discuss eligibility, travel demands, follow-up requirements, costs, and alternatives with both the research team and their regular specialists.

Palliative care can be added at any stage. It is not limited to end-of-life care. Pediatric palliative care teams help manage symptoms, support family decision-making, coordinate services, and focus on quality of life alongside other treatment.

Complications

Canavan disease can affect several aspects of health. The type and severity of complications vary.

Swallowing weakness can allow food, liquid, or saliva to enter the lungs. This may lead to aspiration pneumonia. Poor intake can also cause dehydration, inadequate growth, or nutritional deficiencies.

Reduced movement and increased muscle tone may contribute to joint tightening, known as contractures. Other possible orthopedic problems include scoliosis, hip displacement, and discomfort from prolonged positioning. Regular assessment can identify these concerns before they become severe.

Weak coughing and reduced mobility may make it harder to clear mucus. This can increase the effect of respiratory infections. Sleep-related breathing problems may also occur.

Seizures range from brief, subtle episodes to prolonged convulsions. Changes such as repeated staring, sudden stiffening, rhythmic jerking, or unexplained loss of awareness should be reported to a clinician. Families of someone with diagnosed seizures should have a written seizure-response plan.

The severe infantile form can shorten life expectancy, often because of respiratory or feeding-related complications. Prognosis cannot be predicted from the diagnosis alone. Genetic findings, symptom severity, medical complications, and access to supportive care all

influence a person's course.

Follow up

Regular follow-up helps the care team respond to changing needs. Visits may involve primary care, neurology, rehabilitation medicine, genetics, nutrition, speech and swallowing specialists, pulmonology, ophthalmology, orthopedics, and palliative care.

Routine follow-up commonly reviews development, growth, nutrition, swallowing safety, seizure control, breathing, sleep, vision, muscle tone, joint movement, equipment needs, pain, and caregiver support. Families should also ask whom to contact between visits and how to replace or adjust equipment as the child grows.

Contact the clinical team promptly for increasing coughing during meals, worsening feeding, poor weight gain, new seizure-like episodes, increased sleepiness, new pain, reduced movement, skin breakdown, constipation that does not improve, or a change in breathing during sleep.

Seek urgent medical help for significant breathing difficulty, bluish or gray lips, severe dehydration, repeated choking, a serious injury, or a seizure that lasts longer than directed in the person's emergency plan. Emergency care is also appropriate when seizures occur back-to-back without recovery or when a first seizure is prolonged. Follow the individual's emergency plan and local emergency instructions.

Sources

- Matalon R, Michals-Matalon K. "Canavan Disease." In: Adam MP, Feldman J, Mirzaa GM, and colleagues, editors. GeneReviews . University of Washington, Seattle.
- National Library of Medicine. "Canavan disease." MedlinePlus Genetics . National Institutes of Health.
- National Center for Advancing Translational Sciences. "Canavan disease." Genetic and Rare Diseases Information Center .
- Orphanet. "Canavan disease." ORPHA:141. INSERM and the Orphanet network.
- National Institute of Neurological Disorders and Stroke. "Leukodystrophy." National Institutes of Health.