CONDITION

# GAN

GAN is a rare inherited condition that progressively damages nerves controlling movement, sensation, and other functions.

**WHAT IT IS**
Rare inherited condition causing progressive nerve damage

**BODY SYSTEM**
Nervous system

**MAIN SYMPTOMS**
Muscle weakness, walking difficulty, reduced sensation, tightly curled hair

**WHAT CAUSES IT**
Inherited changes in the GAN gene

**HOW IT IS DIAGNOSED**
Genetic testing showing two disease-causing GAN variants

**MAIN TREATMENT**
Supportive multidisciplinary care and rehabilitation

**CAN IT BE CURED?**
No - current care manages symptoms

**IS IT AN EMERGENCY?**
Sometimes - severe breathing or choking symptoms

**LONG-TERM OUTLOOK**
Usually progressive, with increasing mobility and breathing support needs

## Overview

GAN stands for giant axonal neuropathy , a rare inherited condition that progressively damages the nervous system.

The condition mainly affects axons, the long extensions of nerve cells that carry electrical signals. In GAN, some axons become unusually enlarged and stop working properly.

Damage can involve the peripheral nerves , which connect the brain and spinal cord to the muscles, skin, and organs, and the central nervous system , meaning the brain and spinal cord. This can affect movement, balance, sensation, speech, swallowing, breathing, and sometimes learning or thinking.

Symptoms often begin in early childhood. A child may initially develop normally and then

become unsteady, fall frequently, or lose physical abilities. Some people have milder disease that appears later.

GAN is also the name of the gene linked to the condition. It provides instructions for making gigaxonin, a protein involved in maintaining a cell's internal support system.

## Symptoms

Early symptoms often involve walking and coordination. A child may appear clumsy, have difficulty running, or fall more than expected. Weakness usually begins in the legs and later affects the arms and other muscles.

Possible symptoms include:

Many affected children have pale, tightly curled, or "kinky" hair that differs from their parents' hair. This can be a useful clue, but not everyone with GAN has it, and hair appearance cannot confirm the condition.

As nerve damage progresses, a person may need braces, walking aids, or a wheelchair. Weak breathing muscles can make it harder to cough, clear mucus, or breathe effectively during sleep. The symptoms and rate of progression vary.

- Progressive muscle weakness and reduced muscle tone
- An unsteady, wide-based walk and poor coordination
- Reduced reflexes or loss of sensation in the hands or feet
- Tight joints, shortened muscles, or curvature of the spine
- Difficulty speaking clearly or controlling eye movements
- Problems chewing or swallowing
- Hearing or vision changes
- Seizures in some people
- Changes in learning, memory, or thinking

## Causes and risk factors

GAN is caused by harmful changes, called pathogenic variants, in the GAN gene . These changes reduce or prevent normal gigaxonin function. Proteins involved in a cell's internal structure then build up, causing axons to swell and transmit signals less effectively.

GAN usually follows an autosomal recessive inheritance pattern. A person generally has a harmful variant in both copies of the GAN gene, one inherited from each biological parent.

Parents of an affected child are usually carriers. Carriers have one altered copy and one working copy and generally do not have symptoms. When both biological parents are carriers, each pregnancy has:

These chances apply separately to every pregnancy. A family history may not be apparent because healthy carriers usually have no symptoms.

- A 1 in 4 chance of the child having GAN
- A 1 in 2 chance of the child being an unaffected carrier
- A 1 in 4 chance of the child inheriting neither familial variant

## Diagnosis

GAN cannot be diagnosed from symptoms or hair appearance alone. Several neurological conditions can cause weakness, poor coordination, or loss of sensation.

Assessment usually includes a neurological examination of muscle strength, reflexes, balance, coordination, sensation, and eye movements. The clinician also reviews development, symptom progression, and family history.

Tests may include:

A nerve biopsy can show enlarged axons, but because it is invasive, it is generally reserved for cases that remain unclear after other testing.

After genetic testing, a genetics professional can explain what the results mean for the person and their relatives. Testing relatives is most informative when the family's specific variants are known.

- Genetic testing: Harmful variants in both copies of the GAN gene confirm most cases
- Nerve conduction studies and electromyography: Measure nerve signalling and muscle responses
- MRI scanning: May identify changes in the brain or spinal cord
- Vision, hearing, swallowing, and breathing assessments: Identify functions needing support

## Treatment and management

There is no established cure that reverses GAN-related nerve damage. Treatment aims to maintain function, support comfort and independence, and address complications early.

Care may involve specialists in neurology, rehabilitation, respiratory care, nutrition, orthopaedics, speech and communication, and genetics. Mental health and social support may also help affected people and their families.

Physical and occupational therapy can support movement and make daily activities safer. Stretching, positioning, braces, supportive seating, walking aids, and wheelchairs may reduce strain and improve participation. Equipment should be reviewed as needs change.

Speech and language therapy can assess communication and swallowing. Communication devices may help if speech becomes difficult. If swallowing causes repeated choking or does not provide enough nutrition, the team may discuss alternative feeding support.

Breathing care may include regular lung-function testing, sleep assessment, help clearing mucus, or non-invasive ventilation through a mask. These measures support breathing but do not correct the genetic cause.

Other treatments may address seizures, pain, muscle tightness, constipation, sleep problems, or bone and joint complications. Orthopaedic procedures may be considered for severe scoliosis or contractures.

Gene-replacement approaches have been studied in clinical trials, but they remain investigational rather than established cures. Eligibility, possible benefits, and risks must be discussed with an appropriate research centre.

## Complications

Weakness and poor balance increase the risk of falls and injuries. Reduced movement can contribute to joint contractures, weak bones, pressure injuries, and spinal curvature.

Swallowing problems can cause weight loss, dehydration, or aspiration, in which food or liquid enters the airway. Aspiration may lead to coughing, choking, or chest infections.

Weak respiratory muscles can make deep breathing and coughing less effective. Breathing may become shallow during sleep before daytime problems appear. Morning headaches, restless sleep, unusual daytime sleepiness, or repeated chest infections can be warning signs.

GAN may also affect hearing, vision, communication, and thinking, influencing education, relationships, and independence. Not everyone develops every complication, and timing varies.

## Prevention

GAN cannot be prevented through diet, exercise, vaccination, or changes during pregnancy. It results from inherited gene variants and is not caused by anything a parent did.

Once familial GAN variants are known, carrier testing can identify relatives who may carry one altered copy. A genetics professional can explain reproductive options, including testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices, not required steps.

Supportive care cannot prevent the condition, but monitoring may reduce the effects of complications. Examples include treating swallowing problems before significant weight loss and providing breathing support when testing shows it is needed.

## Living with it and what to expect

GAN is usually progressive, meaning nervous system function declines over time. Changes generally occur over months or years rather than from one day to the next.

Many children gradually lose the ability to walk independently and later need help with transfers and daily activities. Arm strength, speech, swallowing, and breathing may also be affected. Some people have a slower or milder course, so one person's experience cannot precisely predict another's.

Mobility equipment is not a sign that rehabilitation has failed. A wheelchair, supportive seat, or communication device can conserve energy, reduce falls, and improve access to school, family activities, and community life.

Children may continue attending school but may need accessibility changes, writing or communication assistance, rest periods, and an individual learning plan. Thinking skills are affected in some people but relatively preserved in others.

Regular follow-up commonly reviews movement, joint range, spine shape, nutrition, swallowing, breathing, sleep, hearing, vision, communication, and emotional well-being. This is important because swallowing and breathing changes may develop gradually.

Families may benefit from respite care, accessible transport, home adaptations, financial guidance, and peer support. Palliative care can be provided alongside active treatment to support comfort, communication, and family goals; it is not limited to the final stage of life.

## When to get medical help

Contact the regular care team promptly for new or worsening symptoms, including:

These concerns need timely assessment but are not automatically emergencies.

Seek emergency help for severe trouble breathing, blue or grey lips, choking with inability to breathe or clear the airway, or marked difficulty waking. Emergency assessment is also needed for a seizure lasting more than five minutes, repeated seizures without recovery, or a first seizure.

Follow any individual emergency plan provided by the person's care team.

- More falls, weakness, pain, or difficulty with transfers
- Coughing during meals or a change in swallowing
- Weight loss, dehydration, or longer mealtimes
- Morning headaches, poor sleep, or unusual daytime sleepiness
- New vision, hearing, speech, or behaviour changes
- Equipment that no longer fits or causes skin pressure

## Common questions

Is GAN the same as giant axonal neuropathy?

Yes. GAN is the standard abbreviation for giant axonal neuropathy. GAN is also the gene's name, so the full condition name may be used for clarity.

Is GAN fatal?

GAN can shorten life, mainly because progressive weakness may affect breathing and swallowing. Respiratory monitoring, nutrition support, rehabilitation, and infection treatment address important risks but do not remove the underlying condition.

Can someone with GAN walk?

Many affected children learn to walk but later develop increasing weakness and poor balance. Some remain mobile longer. Therapy, braces, walkers, and wheelchairs can support safe movement and participation.

Does curly hair mean a child has GAN?

No. Unusually textured hair can occur with GAN, but many people have curly hair for unrelated reasons, and some people with GAN do not have this feature. Genetic testing is needed to confirm the diagnosis.

Can gene therapy cure GAN?

Gene therapy is being studied but is not an established cure. Clinical trials are needed to determine its safety and whether it meaningfully changes long-term function.

Can a person with one GAN gene variant develop the condition?

A person with one harmful variant is usually an unaffected carrier. GAN generally occurs when both gene copies have harmful variants. A genetics professional can interpret unusual or uncertain results.

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