CONDITION

Angelman syndrome

Learn how Angelman syndrome affects development, communication, movement, seizures, sleep, and long-term care, including genetic testing and supportive treatment.

WHAT IT IS
Rare genetic brain and nervous system condition

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Developmental delay, very limited speech, movement and balance problems, seizures

WHAT CAUSES IT
Reduced or absent maternal UBE3A activity

HOW IT IS DIAGNOSED
Chromosomal microarray, DNA methylation testing, UBE3A gene testing

MAIN TREATMENT
Supportive multidisciplinary care

CAN IT BE CURED?
No, no approved treatment corrects cause

IS IT AN EMERGENCY?
Sometimes, prolonged or repeated seizures without recovery

LONG-TERM OUTLOOK
Lifelong support usually needed into adulthood

Overview

Angelman syndrome is a rare genetic condition that affects the brain and nervous system. It causes developmental delay, major difficulty with speech, problems with movement and balance, and characteristic behavior. Seizures and sleep problems are also common.

The condition is usually caused by loss of function of a gene called UBE3A . In certain brain cells, the copy of UBE3A inherited from the father is normally switched off. The brain therefore depends mainly on the copy inherited from the mother. Angelman syndrome develops when this maternal copy is missing, changed, or inactive.

Children with Angelman syndrome usually need lifelong support. The amount and type of support vary. Most people have little or no spoken language, but many learn to communicate through gestures, pictures, communication boards, or electronic devices. Movement, sleep,

feeding, and seizure treatment may change over time.

There is currently no approved treatment that corrects the underlying genetic change. Care focuses on development, communication, safety, comfort, health, and participation in family and community life. Early recognition matters because it can lead to appropriate therapy, seizure care, educational support, and genetic counseling.

Symptoms

Signs often become noticeable during infancy or early childhood. A baby may feed slowly, have low muscle tone, or take longer than expected to reach milestones. Developmental delays may become clearer when the child does not sit, crawl, or walk at the expected time.

Angelman syndrome can cause:

The behavioral features do not mean that a person is always happy. People with Angelman syndrome experience pain, frustration, anxiety, and other emotions. Limited speech can make it harder for them to show what they need or where they hurt.

Feeding difficulties may include a weak suck, poor coordination of swallowing, reflux, or slow weight gain in infancy. Some older children and adults develop a strong interest in food or gain excess weight. Constipation is also common.

Other possible features include crossed eyes, sensitivity to heat, chewing or mouthing objects, drooling, and a curved spine called scoliosis. Some people have lighter skin, hair, or eye color when the genetic change also affects a nearby pigmentation gene.

Symptoms vary, including among people with the same genetic mechanism. A particular behavior or facial appearance cannot confirm or rule out the condition.

- Moderate to severe developmental and intellectual disability
- Very limited spoken language
- Problems with balance, coordination, or walking
- Trembling or jerky limb movements
- Frequent smiling, laughter, or an easily excited manner
- Hand-flapping or other repeated movements
- A short attention span or high activity level
- Seizures or an abnormal electroencephalogram, also called an EEG
- Difficulty falling asleep, staying asleep, or sleeping for long periods

- A smaller-than-expected head size, sometimes developing over time

Causes and risk factors

Angelman syndrome results from reduced or absent activity of the maternal UBE3A gene in the brain. This can happen in several ways.

The most common mechanism is a deletion, meaning that a section of the maternal chromosome 15 is missing. Other people inherit both copies of chromosome 15 from their father and no copy from their mother. This is called paternal uniparental disomy .

An imprinting defect can also cause the condition. Genomic imprinting is the process that marks certain genes according to which parent they came from. With an imprinting defect, the maternal UBE3A region may carry the wrong parent-specific mark and act like a paternal copy.

Some people have a disease-causing change within the maternal UBE3A gene itself. In a small number of people with a strongly suggestive clinical picture, available testing does not identify the cause.

Most cases happen as new genetic events and are not caused by anything a parent did before or during pregnancy. Angelman syndrome is not caused by diet, parenting, medicines used as directed, or ordinary environmental exposures.

The chance that it will occur again in a family depends on the exact genetic mechanism. For some families, the chance is low. For others, an inherited UBE3A variant or imprinting-center change can create a higher chance. A genetics professional can interpret the test results and discuss what they may mean for parents, siblings, and future pregnancies.

Diagnosis

A clinician may consider Angelman syndrome when a child has significant developmental delay, very limited speech, balance or movement problems, seizures, sleep difficulties, or characteristic behavior. Because these features overlap with other genetic and neurologic conditions, genetic testing is needed to confirm the diagnosis.

Testing may include:

No single test identifies every genetic mechanism. If initial testing is negative but concern remains, a clinical geneticist may recommend further testing or a broader test that examines many genes.

An EEG records the brain's electrical activity. It can help evaluate seizures and may show

patterns commonly seen in Angelman syndrome, but an EEG alone does not establish the diagnosis. Brain imaging, such as MRI, may be used to investigate other concerns, although it may not show a specific Angelman syndrome pattern.

The evaluation may also include hearing and vision tests, feeding and growth assessment, developmental testing, and physical examination of the spine, joints, and walking pattern.

- Chromosomal microarray , which looks for missing or extra sections of DNA, including a deletion in the Angelman syndrome region
- DNA methylation testing , which examines parent-specific chemical marks in the chromosome 15 region
- UBE3A gene testing , which looks for disease-causing changes within the gene
- Additional testing to determine whether an abnormal result came from a deletion, uniparental disomy, or an imprinting defect

Treatment and management

Care is usually coordinated across several specialties. The plan should reflect the person's age, symptoms, abilities, family priorities, and genetic test results.

Seizures are treated with anti-seizure medicine selected by a clinician familiar with the person's seizure type and EEG findings. Some people need more than one approach. Families may also receive a seizure action plan explaining what to do during a seizure and when to use prescribed rescue treatment. Medicines should not be started, stopped, or changed without clinical guidance.

Physical therapy can support balance, strength, posture, joint movement, and safe walking. Some people benefit from braces, adaptive seating, walkers, or wheelchairs. These devices can improve safety and participation rather than replace efforts to stay active.

Occupational therapy addresses daily activities such as dressing, eating, play, sensory needs, and use of the hands. Speech-language therapy should include augmentative and alternative communication , often shortened to AAC. AAC may involve signs, pictures, eye-gaze systems, communication boards, or speech-generating devices. It can be introduced even when a child makes sounds or says a few words.

Early-intervention services and individualized school support can help with learning and functional skills. Teaching often works best when it uses visual cues, repetition, consistent routines, and the person's interests.

Sleep management may begin with a regular schedule, a calming bedtime routine, and

attention to the sleep environment. A clinician should assess possible contributors such as seizures, reflux, constipation, pain, or breathing problems. If medication or a supplement is being considered, the choice should be discussed with the treating clinician because products and individual risks differ.

Feeding treatment may include assessment by a speech-language pathologist, dietitian, gastroenterology clinician, or feeding team. Changes in food texture, positioning, or mealtime equipment may improve safety. Significant swallowing difficulty may require further testing.

Behavioral support should focus on communication, triggers, environment, and unmet needs. Sudden behavior changes can be a sign of pain, illness, poor sleep, constipation, dental problems, or seizures and should not automatically be treated as a behavioral issue.

Complications

Seizures can interfere with sleep, learning, and safety. Prolonged seizures or repeated seizures without recovery require emergency care. Some seizure-like movements may not be epilepsy, so videos and careful descriptions can help the neurology team distinguish them.

Poor coordination and an unsteady walking pattern can lead to falls or injuries. Joint stiffness may develop, especially if mobility decreases. Scoliosis may progress during growth and sometimes requires bracing or surgery.

Swallowing problems can allow food or liquid to enter the airway. This is called aspiration and may contribute to coughing, choking, or lung infections. Reflux, constipation, dental disease, and weight changes can also affect comfort and behavior.

Chronic sleep disruption may affect the person and the entire household. A practical sleep plan and caregiver support are important parts of care.

Angelman syndrome does not usually cause ongoing loss of previously learned skills. However, health problems, pain, uncontrolled seizures, or reduced mobility can make abilities seem worse. Any clear loss of skills deserves medical assessment rather than being assumed to be part of the condition.

Many people live into adulthood, but they generally continue to need support with communication, personal care, health decisions, and daily activities.

Follow up

Routine follow-up may involve primary care, neurology, genetics, developmental or behavioral

specialists, rehabilitation therapists, and school or community services. The care team may monitor seizures, sleep, growth, nutrition, constipation, vision, dental health, mobility, joint range, and spinal curvature.

Medication reviews are important because seizure patterns, sleep, weight, and other health needs can change. Transition planning for adulthood should begin before pediatric services end. It may cover adult medical care, decision-making support, education, employment or day programs, transportation, housing, and caregiver planning.

Contact the usual care team promptly for non-emergency concerns such as:

Seek emergency help for a seizure that lasts longer than the person's seizure plan allows, repeated seizures without recovery, serious breathing difficulty, severe choking, a major injury, blue or gray skin color, or sudden unresponsiveness. Follow the person's emergency plan and local emergency-service instructions.

- New or more frequent brief seizures
- Increasing sleep, feeding, constipation, pain, or behavior problems
- Repeated coughing or choking with meals
- A change in walking, posture, or use of an arm or leg
- Loss of a previously stable skill
- Medication side effects

Sources

- Dagli AI, Mathews J, Williams CA. "Angelman Syndrome." GeneReviews . University of Washington, Seattle; NCBI Bookshelf.
- Wheeler AC, Sacco P, Cabo R. "Unmet clinical needs and burden in Angelman syndrome: a review of the literature." Orphanet Journal of Rare Diseases . 2017;12:164.
- Wheeler AC, et al. "A multidisciplinary approach and consensus statement to establish standards of care for Angelman syndrome." Molecular Genetics & Genomic Medicine . 2022;10(3):e1843.
- Buiting K, Williams C, Horsthemke B. "Angelman syndrome-insights into a rare neurogenetic disorder." Nature Reviews Neurology . 2016;12:584-593.
- U.S. National Library of Medicine. "Angelman syndrome." MedlinePlus Genetics .

- National Institute of Neurological Disorders and Stroke. "Angelman Syndrome." National Institutes of Health.