CONDITION

Acrodysostosis

Learn how acrodysostosis affects bone growth, development, and hormone response, and how specialists diagnose, monitor, and manage this rare genetic condition.

WHAT IT IS
Rare genetic bone development condition

BODY SYSTEM
Bones and hormones

MAIN SYMPTOMS
Short fingers and toes, short stature, distinctive facial features, developmental differences

WHAT CAUSES IT
Genetic, inherited or new variant

HOW IT IS DIAGNOSED
X-rays and genetic testing

MAIN TREATMENT
Symptom-based supportive care

CAN IT BE CURED?
No, genetic change cannot be reversed

IS IT AN EMERGENCY?
Sometimes, seizures or sudden weakness

LONG-TERM OUTLOOK
Widely variable with lifelong monitoring

Overview

Acrodysostosis is a rare genetic condition that affects the development of bones, especially those in the hands, feet, and face. People with acrodysostosis often have short fingers and toes, short stature, and distinctive facial features. Some also have developmental or learning differences.

The condition can interfere with the body's response to certain hormones. Hormones are chemical messengers that help control processes such as growth, thyroid function, and calcium balance. A person may make enough of a hormone, but the body's tissues may not respond to it properly. This is called hormone resistance .

Acrodysostosis varies widely. Some people mainly have skeletal differences, while others have endocrine problems, developmental disabilities, or complications related to the spine. Features

may become more noticeable as a child grows.

There is no cure that reverses the underlying genetic change. Treatment instead focuses on managing hormone problems, supporting development, maintaining movement and function, and identifying complications early. Care often involves genetics, endocrinology, orthopedics, developmental services, and other specialties.

Symptoms

The signs of acrodysostosis can be present at birth or become clearer during childhood. Not everyone has every feature.

Common skeletal and growth-related findings include:

The bones in the hands may mature earlier than expected for the child's age. Doctors call this an advanced bone age . On X-rays, the ends of certain bones may have a cone-like shape.

Facial features may include a small or underdeveloped nose, a flat nasal bridge, or underdevelopment of the middle part of the face. These features differ from person to person and may change with age.

Developmental effects can include delayed speech, delayed motor skills, learning disabilities, or intellectual disability. Some children have behavioral or attention-related concerns. Other people have typical intellectual development.

When hormone resistance is present, symptoms depend on the hormone involved. Resistance to parathyroid hormone can disturb calcium and phosphate levels. Low calcium may cause tingling around the mouth or in the fingers, muscle cramps, stiffness, twitching, or, in severe cases, seizures.

Resistance to thyroid-stimulating hormone can contribute to an underactive thyroid. Possible symptoms include tiredness, constipation, feeling unusually cold, dry skin, slower growth, or difficulty concentrating. These symptoms have many possible causes, so laboratory tests are needed to determine whether thyroid function is affected.

Other reported concerns include recurrent ear problems, hearing loss, dental crowding, sleep-related breathing problems, and symptoms caused by narrowing around the spinal cord or nerves.

- Short fingers and toes, known as brachydactyly
- Broad or unusually shaped fingers and toes
- Small hands and feet

- Short stature
- Limited movement in some joints
- Curvature or narrowing of parts of the spine
- Bone changes visible on X-rays, including short hand and foot bones

Causes and risk factors

Acrodysostosis is caused by a disease-causing change, also called a pathogenic variant, in one of two genes: PRKAR1A or PDE4D . These genes help regulate signaling inside cells. When this signaling is disrupted, it can affect bone development, hormone response, and brain development.

Acrodysostosis related to a PRKAR1A variant has often been called acrodysostosis type 1. It is more commonly associated with resistance to hormones such as parathyroid hormone and thyroid-stimulating hormone.

Acrodysostosis related to a PDE4D variant has often been called acrodysostosis type 2. Developmental and learning differences may be more prominent in some affected people. However, the features overlap, and the gene involved does not predict every symptom.

The condition follows an autosomal dominant inheritance pattern. This means one altered copy of the gene is enough to cause the condition. Many affected people have a new genetic change that was not found in either parent. This is known as a de novo variant and is not caused by anything a parent did during pregnancy.

If a parent has the genetic variant, each pregnancy has a 1 in 2 chance of inheriting it. When the variant appears de novo, the chance that the parents will have another affected child is usually lower, but it may not be zero because of the possibility of germline mosaicism. A genetic counselor can explain recurrence risks based on the family's test results.

There are no known lifestyle choices that cause acrodysostosis.

Diagnosis

Diagnosis begins with a detailed medical and developmental history and a physical examination. A clinician may look at growth patterns, hand and foot shape, facial development, joint movement, and neurologic function.

X-rays can identify the characteristic skeletal pattern. Findings may include shortened bones in the hands and feet, cone-shaped bone ends, advanced bone age, and changes in the skull or

spine. Because some features overlap with other genetic skeletal conditions, X-rays alone may not establish the diagnosis.

Blood and urine tests may be used to check for hormone resistance. Testing may include:

A high parathyroid hormone level can indicate that the body is working harder to maintain calcium balance. Calcium may be normal early in the condition, so a normal result does not always exclude hormone resistance.

Genetic testing can look for pathogenic variants in PRKAR1A and PDE4D. Testing may use a focused gene panel, a broader skeletal-disorder panel, or exome or genome sequencing. Testing the parents can help determine whether the variant was inherited or occurred de novo.

Doctors may also evaluate hearing, vision, dental health, development, and the spine. Magnetic resonance imaging, or MRI, may be considered if there are signs of spinal cord or nerve compression. An MRI uses magnets to produce detailed images and does not use ionizing radiation.

Conditions that can resemble acrodysostosis include pseudohypoparathyroidism, other forms of brachydactyly, and several rare skeletal dysplasias. A clinical geneticist can help interpret the combination of physical, X-ray, laboratory, and genetic findings.

- Calcium, phosphate, and parathyroid hormone levels
- Thyroid-stimulating hormone and free thyroxine levels
- Kidney function and urine calcium when calcium-related treatment is used
- Other endocrine tests based on growth and symptoms

Treatment and management

Treatment is based on the person's specific symptoms and test results. There is no single treatment plan that applies to everyone with acrodysostosis.

An endocrinologist can monitor hormone function. If parathyroid hormone resistance causes low calcium or an abnormal phosphate level, treatment may include calcium and an active form of vitamin D. These treatments require careful laboratory and urine monitoring because too much calcium can contribute to kidney stones or calcium deposits in the kidneys.

Thyroid hormone replacement may be used when testing confirms inadequate thyroid function. The dose is adjusted by a clinician using symptoms, growth, and blood test results.

Growth should be followed on a regular chart. A pediatric endocrinologist may investigate poor growth for treatable causes, including thyroid dysfunction or growth hormone deficiency. Growth hormone treatment has been used in selected patients, but evidence in acrodysostosis

is limited. It requires an individualized discussion of likely benefits, burdens, and uncertainties.

Developmental assessment can identify support needs early. Depending on the person, services may include physical therapy, occupational therapy, speech and language therapy, educational accommodations, or behavioral support.

Orthopedic care may help with painful joints, reduced mobility, limb alignment, or spinal problems. Physical therapy may support strength and movement but cannot change the underlying bone structure. Surgery is considered only for specific problems, such as significant nerve compression or functional limitations.

Hearing evaluations are appropriate when there are recurrent ear infections, delayed speech, or concern about hearing. Dental care may address crowding, abnormal tooth development, or difficulty cleaning closely spaced teeth.

If a procedure or surgery is planned, the medical team should know about possible neck, spine, airway, and endocrine concerns. This allows the surgeon and anesthesia team to plan positioning, airway care, and laboratory monitoring safely.

Complications

Possible complications depend on the severity of the skeletal, endocrine, and developmental features.

Hormone resistance may lead to persistent thyroid dysfunction or abnormal calcium and phosphate levels. Untreated low calcium can affect muscles and nerves. Long-term treatment also requires monitoring to prevent excess calcium in the urine and kidney-related complications.

Narrowing of the spinal canal can place pressure on the spinal cord or nerves. Possible symptoms include neck or back pain, numbness, weakness, balance problems, or changes in walking. Joint stiffness and altered bone structure may also affect mobility and daily activities.

Developmental or learning differences can influence communication, education, independence, and emotional well-being. Early support and an individualized education plan may improve participation at school and in the community.

Hearing loss, dental problems, and sleep-related breathing difficulties may affect speech, sleep quality, and overall health. These concerns are treatable or manageable when recognized.

The condition can also affect self-image and social experiences because of short stature or visible physical differences. Psychological support and connections with rare-disease

communities may be helpful for affected people and their families.

Follow up

Routine follow-up is usually coordinated by a primary care clinician, geneticist, or endocrinologist. The schedule depends on age, symptoms, laboratory results, and treatment.

Ongoing care may include:

Contact the care team promptly about new muscle cramps, tingling, worsening fatigue, changes in walking, persistent neck or back pain, new numbness, or possible sleep-related breathing pauses. These concerns may require earlier assessment but are not always emergencies.

Seek emergency care for a seizure, loss of consciousness, severe or sustained muscle spasms, sudden weakness, difficulty breathing, or a sudden loss of bladder or bowel control. These symptoms may indicate severely low calcium or pressure on the spinal cord and require immediate evaluation.

Genetic counseling can be revisited during adolescence or adulthood, particularly when discussing family planning. Prenatal and preimplantation genetic testing may be possible when the family's specific variant is known.

- Tracking height, weight, development, and school progress
- Checking calcium, phosphate, parathyroid hormone, and thyroid function
- Monitoring urine calcium and kidney health during calcium-related treatment
- Reviewing mobility, joint function, pain, and neurologic symptoms
- Periodic hearing, dental, and vision care
- Reassessment by genetics when new information or testing becomes available

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