CONDITION

Achondrogenesis

Learn about achondrogenesis, a severe genetic disorder of bone and cartilage development, including prenatal diagnosis, inheritance, care options, and family support.

WHAT IT IS
Severe genetic disorder of bone and cartilage development

BODY SYSTEM
Bones and cartilage

MAIN SYMPTOMS
Very short limbs, very small chest, poor bone mineralization, fetal swelling

WHAT CAUSES IT
Genetic changes

HOW IT IS DIAGNOSED
Genetic testing, X-rays after delivery

MAIN TREATMENT
Palliative and comfort-focused care

CAN IT BE CURED?
No, development cannot be corrected

IS IT AN EMERGENCY?
Sometimes, major difficulty breathing

LONG-TERM OUTLOOK
Most pregnancies end in stillbirth or death shortly after birth

Overview

Achondrogenesis is a group of rare genetic conditions that severely affect the development of cartilage and bone before birth. Cartilage is the flexible tissue that forms the early framework of much of the skeleton. During typical development, much of this cartilage is gradually replaced by bone.

In achondrogenesis, this process is profoundly disrupted. The arms, legs, ribs, spine, and other bones do not grow or harden as expected. The chest is especially small, leaving too little room for the lungs to develop. This is called pulmonary hypoplasia , meaning the lungs are smaller and less developed than they need to be.

Achondrogenesis is considered a life-limiting skeletal dysplasia . Skeletal dysplasia is a broad term for genetic conditions affecting bone and cartilage growth. Most affected pregnancies

end in stillbirth, or the baby dies shortly after birth because the lungs cannot support breathing. The exact course can vary, and specialists use ultrasound findings, X-rays, and genetic testing to clarify the diagnosis.

The main forms are:

These forms have overlapping features but different inheritance patterns. Identifying the genetic cause can help a family understand the diagnosis and the chance of the condition occurring in a future pregnancy.

- Type 1A , usually caused by changes in the TRIP11 gene
- Type 1B , caused by changes in the SLC26A2 gene
- Type 2 , usually caused by a change in the COL2A1 gene

Symptoms

Features of achondrogenesis develop before birth. They may first be noticed during a prenatal ultrasound. Findings can differ by type and stage of pregnancy.

Common findings include:

The abdomen may appear relatively large compared with the chest. The neck may look short, and soft tissue around the body may appear unusually thick.

The small chest is the most medically important feature. When the lungs cannot develop fully, a newborn may be unable to breathe effectively even with intensive respiratory support. Some affected babies die before delivery. Others are born alive but survive only briefly.

These findings can also occur in other severe skeletal disorders. An ultrasound finding by itself does not always establish the exact diagnosis.

- Very short arms and legs
- A short trunk and very small chest
- A relatively large head
- Poor mineralization, meaning the bones do not harden normally
- A spine, skull, or pelvis that is difficult to see clearly on X-rays
- Short or fragile ribs
- Extra fluid under the skin, known as fetal edema
- A large amount of amniotic fluid, called polyhydramnios

- Reduced fetal movement in some pregnancies

Causes and risk factors

Achondrogenesis results from a disease-causing genetic change. It is not caused by something a pregnant person ate, did, or was exposed to during routine daily life.

In type 1A, changes in TRIP11 interfere with a protein involved in moving materials within cells. This disrupts the function of cartilage-producing cells and severely affects formation of the skeleton.

In type 1B, changes in SLC26A2 interfere with the movement of sulfate into cartilage cells. Sulfate is needed to build the supportive material around these cells. Without enough sulfate, cartilage and bone cannot form normally.

Types 1A and 1B usually follow an autosomal recessive inheritance pattern. This means the baby inherited one altered copy of the gene from each parent. Parents who carry one altered copy usually do not have symptoms.

When both parents carry a disease-causing change in the same recessive gene, each pregnancy has:

These chances start over with every pregnancy.

Type 2 is linked to COL2A1 , which provides instructions for making type II collagen. This collagen is an important structural part of cartilage and the developing skeleton. Type 2 usually results from a new genetic change in the egg, sperm, or early embryo. This is called a de novo change and is not usually inherited from either parent.

The chance of type 2 recurring is generally low when neither parent has the COL2A1 change in blood testing, but it is not zero. Rarely, a parent has the change in only some egg or sperm cells, known as germline mosaicism. A genetics professional can provide a recurrence estimate based on the family's test results.

- A 1 in 4 chance of being affected
- A 1 in 2 chance of producing an unaffected carrier
- A 1 in 4 chance of producing a child who is unaffected and not a carrier

Diagnosis

Achondrogenesis may be suspected during a second-trimester ultrasound, although severe

findings can sometimes be seen earlier. Ultrasound may show extremely short limbs, a small chest, limited bone mineralization, or fluid buildup around the fetus.

A specialist may perform a detailed ultrasound to evaluate:

Ultrasound can show that a skeletal dysplasia is severe, but several conditions can look similar before birth. Achondrogenesis may overlap with hypochondrogenesis, osteogenesis imperfecta, thanatophoric dysplasia, and other disorders. Expert review is often needed.

Genetic testing can confirm the cause. A fetal DNA sample may be obtained through chorionic villus sampling, which samples placental tissue, or amniocentesis, which samples amniotic fluid. These procedures have benefits and risks that should be discussed with a maternal-fetal medicine specialist.

Testing may focus on a suspected gene or use a panel that examines many skeletal dysplasia genes. Broader testing, such as exome sequencing, may be considered when targeted testing does not find an answer. Standard prenatal cell-free DNA screening does not usually diagnose achondrogenesis.

After delivery or pregnancy loss, X-rays can reveal patterns of bone development that help distinguish the different types. Examination of the placenta or body tissues may also provide useful information. If the family agrees, saving a DNA sample can be important when testing cannot be completed immediately.

- The length and shape of the long bones
- The size of the chest compared with the abdomen
- The appearance of the ribs, skull, spine, and pelvis
- Lung development
- Amniotic fluid levels
- Signs of fetal swelling or other abnormalities

Treatment and management

There is no treatment that can correct the underlying bone and lung development in achondrogenesis. Care therefore focuses on obtaining an accurate diagnosis, supporting the pregnant person, preparing the family, and keeping the baby comfortable.

A care team may include maternal-fetal medicine specialists, medical geneticists, genetic counselors, neonatologists, obstetric clinicians, palliative care professionals, nurses, social workers, and spiritual care providers.

After prenatal diagnosis, clinicians should explain the expected outcome and available pregnancy options in a clear and nonjudgmental way. Depending on the pregnancy stage, local laws, and the family's values, options may include continuing the pregnancy with planned comfort care, continuing with neonatal assessment after birth, or ending the pregnancy. Families may ask for additional imaging, genetic confirmation, or a second opinion before making decisions.

If the pregnancy continues, a perinatal palliative care plan can document the family's goals. Palliative care is not the same as doing nothing. It provides active treatment of discomfort and supports meaningful time between the baby and family.

The plan may address:

Some families request a brief trial of breathing support while the medical team evaluates the newborn. Others choose comfort-focused care from birth. Intensive ventilation cannot reverse severely underdeveloped lungs, but each baby should be assessed according to the confirmed diagnosis and the family's agreed goals.

Delivery planning should also protect the pregnant person's health. The diagnosis does not automatically determine the safest timing or method of delivery. Those decisions depend on obstetric circumstances and should be made with the care team.

- Where and how delivery will occur
- Which monitoring or procedures are wanted during labor
- Whether respiratory support will be attempted
- How warmth, pain, breathing discomfort, and feeding will be managed
- Opportunities for holding, bathing, photographs, keepsakes, or religious traditions
- Support for siblings and other family members
- Autopsy, imaging, tissue sampling, or genetic testing after death

Complications

The central complication is severe pulmonary hypoplasia. The small rib cage restricts the lungs, leading to life-threatening breathing failure after birth.

Other fetal or newborn complications may include fractures, widespread swelling, and difficulty with delivery because of the relatively large head, swollen tissues, or excess amniotic fluid.

Polyhydramnios can cause maternal discomfort, shortness of breath, early contractions, or

premature rupture of the membranes. Pregnancy loss, stillbirth, and newborn death can also have major emotional effects. Parents and siblings may experience grief, anxiety, depression, sleep problems, or traumatic stress. These responses deserve the same attention as physical complications.

Follow up

Routine follow-up usually involves maternal-fetal medicine and obstetric visits to monitor the pregnant person's health, amniotic fluid levels, fetal findings, and delivery plan. A genetics appointment can help the family review test results and decide whether parental testing is useful.

After delivery or pregnancy loss, follow-up may cover physical recovery, lactation concerns, emotional support, and final genetic or pathology results. Bereavement counseling, pregnancy-loss support groups, or mental health care may be helpful. Families do not need to wait for a crisis to request this support.

Seek prompt advice from the obstetric team for reduced fetal movement, possible fluid leakage, regular contractions, new shortness of breath, or symptoms that are concerning or different from what the care team has discussed.

Seek emergency care for heavy vaginal bleeding, severe or persistent abdominal pain, fainting, chest pain, major difficulty breathing, a seizure, or thoughts of self-harm.

Before a future pregnancy, a genetic counselor can review recurrence risk and testing options. If the familial genetic change is known, options may include testing during pregnancy or testing embryos created through in vitro fertilization. Early targeted ultrasound may provide additional information, but its timing and limits should be discussed with a specialist.

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