

# Campomelic Dysplasia

## Overview

Campomelic dysplasia is a rare form of bent-bone skeletal dysplasia that affects an estimated 1 in 40,000-200,000 people. It is complicated by respiratory issues and has therefore historically been considered a lethal disease, with most individuals not surviving past infancy. With proper medical care and guidance, campomelic dysplasia can be managed, although not without lasting orthopaedic and miscellaneous concerns. Campomelic dysplasia may be detected using radiological techniques, physical exams and genetic testing. Clinical features include underdevelopment of the jaw, cleft palate, clubfoot, spine deformities and leg alignment issues. Treatment of symptoms may include monitoring and surgery by doctors who specialize in skeletal dysplasias.

## Heredity and genetics

Campomelic dysplasia is caused by mutations in the *SOX9* gene. This gene codes for a transcription factor — or protein — that attaches to genes to help them be expressed, particularly those involved in development of the skeleton and reproductive system. Under normal circumstances, there are two functioning copies of *SOX9*. Campomelic dysplasia occurs when one copy of the gene becomes defective — either through a point mutation on or near the gene, rearrangement of the chromosome or when the chromosome is deleted. Campomelic dysplasia tends to be less severe when the mutation involves a chromosomal abnormality instead of direct mutations of *SOX9*.

Most cases of campomelic dysplasia happen from spontaneous mutations during fetal development. However, the disease can be inherited in an autosomal dominant fashion, meaning one copy of the defective gene is sufficient to cause the disease in the offspring. If an affected individual survives past reproductive age, they have a 50 percent chance of passing on the mutation to their child.

## Diagnosis and testing

A diagnosis of campomelic dysplasia can be made using clinical assessments and radiological imaging, but genetic testing with chromosomal analysis should be performed to verify the type of mutation present and better predict the severity of the disease. Routine ultrasound can detect the presence of shortened limbs during pregnancy, but a formal diagnosis should be made after birth.

Clinical Features:

- Short stature
- Flat face
- Prominent eyes
- Cleft palate
- Micrognathia

- Scoliosis
- Kyphosis
- Hip dislocations
- Leg length discrepancy
- Clubfoot
- Sex reversal

#### Radiographic Features:

- Bowing of the femur and tibia
- Hypoplastic scapula
- Hip abnormalities (narrow iliac wings, hypoplastic pubic bones, shallow acetabula with hip dislocation)
- Non-mineralized thoracic vertebral pedicles
- Underdevelopment of the cervical vertebrae
- Underdevelopment of the mandible
- Radial head dislocation
- Constricted, bell-shaped thorax
- 11 pairs of ribs

#### **Orthopaedic problems and testing**

##### Growth monitoring

Because of the rarity and mortality rate of campomelic dysplasia, there are no campomelic-specific growth charts available in literature. Those who survive past infancy demonstrate small stature.

##### Spine deformities

Cervical (upper) spine instability may be likely, which can further complicate anesthesia during procedures and surgeries. This should be monitored beginning at six months of age using flexion/extension X-rays every six months during infancy and childhood and approximately yearly into adolescence.

Outward and/or side-to-side curvature of the spine (kyphosis and scoliosis) is common and should be monitored with clinical exams and radiologic imaging (AP and lateral spine X-rays). Treatment is not usually necessary, and bracing may complicate any respiratory issues.

##### Hip and forearm dislocation

The hip socket is shallower in people with campomelic dysplasia. That, in combination with other hip abnormalities, makes hip dislocations more common, particularly in infants. This can be monitored by a pediatric orthopaedist using routine AP and frog leg X-rays of the hips during infancy. Surgical treatment is generally not necessary.

Dislocations of the head of the radius (the bone that runs from the elbow to the thumb side of the wrist) are common and may limit the amount of elbow movement possible, but this does not generally require orthopaedic treatment or intervention.

### Clubfoot

Clubfoot deformities are present in nearly all infants diagnosed with diastrophic dysplasia. At MU Health Care, clubfoot deformities are treated using the Ponseti method, details for which can be found at <https://www.muhealth.org/conditions-treatments/pediatrics/orthopaedics> under the “Clubfoot” header.

## **Other problems and treatment**

### Respiratory problems and survival

Respiratory issues are the most severe concern for people with campomelic dysplasia during infancy and contribute to the low survival rate of people with the disease. There are several factors that contribute to the respiratory issues including chest constriction and small, weak airways. The lower jaw is typically smaller than average which can cause the tongue to shift backward (retroglossia), causing airway obstruction. Central sleep apnea, which disrupts the brain’s ability to send signals to the muscles that help with breathing, is also observed. All of these can cause death or lasting problems for newborns and infants. In survivors, these concerns can still pose a threat and should be managed accordingly.

A respiratory evaluation should be performed once the infant is older than four weeks and should include polysomnography to check for sleep apnea (central and obstructive) and a bronchoscopy to look at the airways. Treatment for respiratory symptoms may include supplemental oxygen, CPAP or BiPAP machines, tracheostomy, long-term ventilator support, etc. Primary care providers should be on alert for airway infections should they arise, so they can be treated aggressively. Immunizations should be given to reduce the risk of serious infections that may further compromise the respiratory system (i.e. pneumococcal conjugate vaccine). If a person with campomelic dysplasia needs surgery, surgical planning should consider risks with anesthesia because respiratory abnormalities.

### Cleft palate

Approximately one-third of people with campomelic dysplasia have a cleft palate, which can be evaluated and treated as with any other child with cleft palate. Careful surgical planning should be done to pay attention to respiratory risks and airway fragility. Click [here](#) for more information on cleft palates.

### Hearing

Hearing issues may be more common in those with cleft palates but can still happen in anyone with campomelic dysplasia. Hearing loss can contribute to speech delays, so it is important that a newborn hearing screening is done with periodic testing beginning around nine months to one year of age. Parents should be aware of the signs of ear infections (fussiness, ear tugging, etc.) and pediatricians

should treat all ear infections aggressively. Ear infections may be common, which may make tube placements necessary. Hearing aids may also be necessary for those with significant hearing loss.

### Cardiovascular conditions

Though less common, cardiovascular (heart and/or blood vessel) problems may be present in people with campomelic dysplasia. An echocardiogram (ECG) should be completed during infancy along with an assessment of the heart. Any abnormalities can be managed as usual.

### Kidney issues

Kidney problems may be present at birth or may be noticed throughout life. One such issue is vesicoureteral reflux, when the urine flows backward from the bladder back into the kidneys. An ultrasound of the kidneys during infancy can rule out kidney concerns, but it should be repeated yearly. Any kidney conditions can be managed by a urologist.

### Gastroesophageal reflux in infants

It is very common for infants to spit up after eating. This happens because the lower esophageal sphincter, or muscle between the esophagus and stomach, may be weak or not fully formed. This can be a problem in infants with campomelic dysplasia because of the risk of liquid coming back up from the GI tract and into the lungs. This can be a dangerous issue because campomelic dysplasia patients have increased respiratory issues. Monitor the infant during feedings and take precautions to limit the chances of aspiration. A gastroenterologist may be necessary to decide if medication, a swallow study, surgery, etc., is necessary.

## **Resources**

### **Campomelic Dysplasia General Information**

Pauli, R.M., Legare, J. Cartilage Hair Hypoplasia Natural History. Rev. 2009.

<http://www.lpaonline.org/natural-histories-of-dwarfism-types>

### **Little People of America**

<http://www.lpaonline.org/>

### **Adaptive Products**

<http://www.lpaonline.org/adaptive-products->