



## Cornelia de Lange syndrome

Other Names: Brachmann-de Lange syndrome

*Cornelia de Lange syndrome is a rare genetic condition with characteristic facial features and birth defects. In most cases it is caused by mutations in the NIPBL gene which makes a protein called delangin.*

### Characteristics of Cornelia de Lange syndrome

The characteristic facial features seen in Cornelia de Lange syndrome (CdLS) include arched eyebrows that often meet over the bridge of the nose (synophrys), long eyelashes, low-set ears, small widely spaced teeth, and a small upturned nose. Their heads are often smaller than average (microcephaly). Individuals with CdLS also tend to have multiple congenital anomalies (i.e., birth defects) such as fewer than five fingers, and some may be missing the entire forearm. More often, CdLS causes a person to have small hands, with the thumb closer to the elbow than usual.

One of the major health concerns in this condition is feeding. Growth is reduced, both before and after a baby is born, so people with CdLS are always smaller than usual. Virtually all children with CdLS have reflux, which can cause problems with feeding. People with CdLS can have other health problems as well, including congenital heart defects, seizures, cleft palate, hearing loss, eye problems such as near-sightedness or glaucoma, or kidney problems. Boys with CdLS are likely to have undescended testes.

Almost everyone with CdLS has intellectual disabilities, although a few people have a normal IQ. The average IQ is about 53, but ranges from less than 30 to 102. Some children with CdLS may also have behaviors (e.g., social impairments such as social anxiety) commonly observed in children with autism.

### Diagnosis/Testing

Diagnosis of CdLS is often made through a clinical evaluation by a medical geneticist. The diagnosis can be confirmed by genetic testing for a change or mutation in the NIPBL, SMC1A or SMC3 genes. Approximately 65% of individuals with CdLS have a mutation in one of these genes. This suggests that there are other genes yet to be identified that can also cause CdLS.

The NIPBL, SMC1A, and SMC3 genes make proteins that are thought to be important in early development of the face, limbs, and other parts of the body. Mutations in these genes do not allow the proteins to work properly, thus affecting important stages of early development.

### Management/Surveillance

It is recommended that all children with CdLS be evaluated for gastroesophageal reflux and possible malrotation (i.e., where the bowel has been twisted during growth in the uterus). Effective and thorough treatment of reflux is essential to avoid growth and feeding problems. Supplemental formulas or placement of a G-tube (i.e., a feeding tube surgically inserted through the abdomen that delivers nutrition directly to the stomach) may be necessary. Physical therapy, occupational therapy, and speech therapy are needed to help children communicate as effectively as possible. Other health conditions should be treated if present, such as surgery if necessary for heart defects.

Guidelines have been developed for surveillance of CdLS and include regular evaluations for appropriate growth, yearly developmental assessments, hearing and vision evaluations, at least one heart ultrasound (echocardiogram) to rule

out any problems with the heart, a kidney ultrasound to rule out structural problems with the kidneys, a neurological exam and EEG, an x-ray of the arms and hands, as well as a blood test if there are any concerns about anemia, bruising, bleeding, or repeated infections.

### **Mode of inheritance**

CdLS may be inherited in one of two patterns of inheritance: autosomal dominant, and X-linked recessive.

Autosomal dominant inheritance:

CdLS is most often inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be affected and show signs of CdLS. The mutation can be inherited from an affected parent, however in the majority of individuals it occurs brand new (de novo) in an affected child.

X-linked recessive inheritance:

Infrequently, CdLS can also be caused by a mutation in the X-linked SMC1A gene. This follows an X-linked recessive inheritance pattern. This means that in females, both copies of the SMC1A (i.e., one on each X chromosome) must have a mutation, whereas in males, only one copy of the SMC1A gene must have a mutation to be affected. A female with a mutation in one copy of the SMC1A gene is said to be a "carrier."

### **Risk to family members**

The risk to family members depends on the pattern of inheritance.

Autosomal dominant inheritance:

The risk to family members depends on whether or not the individual with CdLS has a parent affected with CdLS. Since the vast majority of individuals with CdLS have a de novo mutation, the risk of other siblings being affected is very low.

X-linked recessive inheritance:

If a mother is a carrier of CdLS, each daughter has a 1 in 2 chance (i.e., 50%) of being a carrier and each son has a 1 in 2 (i.e., 50%) of being affected with CdLS

### **Special considerations**

The smaller airways in children with CdLS may make it more difficult to provide sedation for surgery or other procedures. It is recommended that care be provided by a pediatric anesthesiologist with experience working with these conditions. In addition, there have been occasional reports of severe reactions, such as malignant hyperthermia, to anesthetic agents.

### **Resources**

Cornelia de Lange Syndrome Foundation, Inc.

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

Management and Treatment Guidelines for CdLS

<http://www.cdlsusa.org/docs/treatment-guidelines.pdf>

Genetics Home Reference: Cornelia de Lange syndrome

<http://ghr.nlm.nih.gov/condition/cornelia-de-lange-syndrome>

### **References**

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