

cleidocranial dysplasia

Tamison Jewett, MD • Associate Professor, Department of Pediatrics, Section of Medical Genetics
• Wake Forest University School of Medicine • Winston-Salem, NC

Cleidocranial dysplasia, also known as cleidocranial dysostosis or CCD, is a genetic condition affecting bone growth. CCD is characterized by a larger-than-expected head with delayed closure of the soft spots (fontanel), underdevelopment or absence of one or both collar bones (clavicles) and short stature. This condition was first reported in 1760 and was later reported 1765. There is also evidence that it existed in prehistoric man. Greater than 1,000 cases of CCD have been reported in medical literature.

People with CCD have a characteristic facial appearance. They tend to have a short head from front to back (brachycephaly) and a prominent forehead ("frontal bossing"). There is typically delayed closure of the fontanel, and some adults with CCD have open fontanel. The eyes are widely spaced, and the nasal bridge is often flat. The neck appears long, and the shoulders are narrow and down-sloping.

Individuals with CCD often have abnormalities of the teeth, and many have extra teeth. The teeth may be unusually formed and positioned. Delayed eruption of the teeth, especially the permanent teeth, is common.

The clavicles may be completely absent on one or both sides, but more commonly, they are underdeveloped, usually deficient at the end closest to the shoulder. Occasionally, the clavicle is normally formed on each end with a gap in the middle. Because of these differences in the clavicle, individuals with CCD may have the ability to bring their shoulders together in front of their bodies. Additionally, the muscles attached to the clavicles may be unusually formed and placed.

People with CCD may have abnormalities in bones other than the skull and the clavicle. They may have unusual positioning of the hip joints, abnormalities of the bones of the spine, and unusual formation of the bones of the fingers and hands. The average height for an adult man with CCD is 156.6 (about 5'2") to 168.8 cm (about 5'6") and for a woman is 144.6 (about 4'9") to 148.5 cm (about 4'10"). Orthopedic care may be

warranted if there are concerns regarding the bones or joints.

Occasional abnormalities that are associated with CCD include scoliosis (curvature of the spine), extra ribs, a tendency to have bone fractures, cleft palate, small pelvis, hearing loss and respiratory problems (such as recurrent sinus infections or pneumonia). It is important that all women with CCD have adequate evaluation of their pelvic diameter prior to giving birth, as a cesarean section may be the preferred method of delivery. It is also important that individuals with CCD be monitored regularly for evidence of hearing loss. Hearing loss may be due to the structural and functional changes of the bones of the ear together with unusual formation of the palate, but it can also be due to abnormal function of the nerves of hearing.

Individuals with CCD typically have normal ability to learn. Affected, infants and children usually reach their developmental milestones as expected. Children may benefit from speech therapy, especially while undergoing treatment for dental problems.

CCD is usually inherited in an autosomal dominant fashion. Approximately

30 percent of cases are caused by a gene change occurring for the first time in the affected individual (spontaneous gene mutation), and 70 percent of people with CCD have an affected parent. The condition is highly variable from one affected person to another.

A brief review of chromosomes and genes may be helpful at this point. Genes are the basic units of heredity, and they are present in almost every cell of the body. Genes are located on larger structures called chromosomes. There are typically 46 chromosomes in almost every cell of the body. These chromosomes are arranged in 23 pairs. Twenty-two of the pairs are numbered from largest (#1) to smallest (#22) and are the same in males and females. The twenty-third pair is called the sex chromosomes because it determines if a

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person develops as a male or female. Females typically have two X chromosomes, while males typically have one X chromosome and one Y chromosome. Because our chromosomes come in pairs and the genes are located on the chromosomes, genes also occur in pairs. One gene of each pair comes from our mother and the other from our father. Likewise, we only contribute one gene from each pair to a child.

CCD follows an autosomal dominant pattern of inheritance. "Autosomal" means that the gene responsible for the condition is located on one of the numbered chromosomes, not the sex chromosomes. "Dominant" means that only a single gene change is necessary for an individual to show features of the condition. Therefore, people who have CCD have one gene of a pair that is unchanged and working properly and one gene that is changed and is not working properly. The gene that is altered "dominates" over the unchanged gene, causing the features of CCD.

The gene that causes CCD is denoted by the symbol RUNX2, and it directs the body to make a protein that helps to control the development of osteoblasts, which are cells that are important in the formation of bone. Gene testing is available on both a research and a clinical basis. While most individuals with CCD either inherited their "CCD gene" from an affected parent or are the first in their families to have a gene change, there are several reports of families in which two siblings with CCD were born to unaffected parents, suggesting that some parents may have a percentage of egg or sperm cells that carry the gene change. This phenomenon is referred to as "gonadal mosaicism."

Individuals with CCD should be followed by either a team of specialists or by individual specialists familiar with the problems that can be associated with this condition. In young children with CCD, the fontanelles may be so large as to warrant the wearing of a helmet to protect the brain. Hearing tests should be performed at birth and regularly (at least yearly) thereafter. Affected infants should receive their first dental evaluation by one year of age, preferably by a dentist who treats children with complex dental problems. Of note, it has been shown that extraction of primary teeth does not hasten the eruption of permanent teeth in this condition. Children with CCD may have recurrent otitis media (middle ear infection) related to abnormal formation of the palate and/or eustachian tube dysfunction; this may necessitate the

placement of tympanostomy tubes. Individuals with CCD are more likely to have upper airway obstruction, and sleep habits must be carefully monitored. Regular snoring and/or restless sleep may warrant a sleep study. Occasionally, an affected individual may have a very narrow chest that causes respiratory distress. Finally, it is important to note that people with CCD are expected to be shorter than their typical peers and family members. Nevertheless, with the proper anticipatory guidance, people with CCD usually lead healthy and productive lives.

Tamison Jewett, MD, is an associate professor in the Department of Pediatrics, Section of Medical Genetics, at Wake Forest University School of Medicine in Winston-Salem, NC. She is the director of Clinical Genetics Services.

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