

Genetic Testing for X-Linked Recessive Chondrodysplasia Punctata

Information for Parents

What is Chondrodysplasia Punctata?

Chondrodysplasia Punctata is a rare genetic bone disorder (skeletal dysplasia) that is usually diagnosed in babies or children. When you look at the bones on x-ray, there are small, circular white spots (punctate calcifications) seen at the end of the long bones in the regions of the growth plates (epiphyses) of the arms and legs, hands and feet, as well as the spine. These calcifications of the growth plates interfere with normal bone growth. People with this condition may be shorter than other children of the same age. These spots of calcification can also occur in the voicebox (larynx) and trachea. The trachea is the long tube that brings the air you breathe to the lungs. Calcifications in the airway tubes can cause breathing problems.

People with the X-linked recessive form of chondrodysplasia punctata (CDPX1), specifically, also can have flattening of the nose and of their midface or cheek region, shortening of the bones at the tips of the fingers, hearing loss, and heart defects. Most individuals with CDPX1 do not have learning problems. Not everyone with CDPX1 has all of the findings or is affected in the same way.

What causes CDPX1?

CDPX1 is caused by changes (mutations) in the Arylsulfatase E gene (*ARSE*) on the X chromosome. A female has two X chromosomes, and a male has one X chromosome and one Y chromosome. Females have two copies and males have one copy of the *ARSE* gene. In males, because they only have one copy of the *ARSE* gene, if that one copy does not work correctly, it causes the medical and physical findings associated with CDPX1. Because a female has two copies, if one of them has a change that causes the gene not to work correctly, the other gene can make up for the non-working one. Females with one gene change are called “carriers”. Carriers usually do not show any medical findings associated with CDPX1. Genes are the body’s instruction manuals, comprised of DNA, that tell the body to make proteins. The proteins are the workhorses that carry out the specific jobs of body development or maintenance. This protein is necessary for normal bone development and bone growth. When there is a change in the *ARSE* gene, the protein does not work correctly.

Why Genetic Testing?

Reasons for Genetic Testing

Genetic testing for CDPX1 is now available. Genetic testing is useful to confirm the diagnosis of CDPX1. If a specific gene change is identified, this allows the mother to have testing to determine if she is a carrier. This gives the family important information about the risk of having another boy with CDPX1. Knowing the exact gene change causing CDPX1 in the family allows for a pregnant couple to test a future pregnancy to

see if that baby also has the disorder. Prenatal genetic testing can be performed through a CVS (chorionic villus sampling) at approximately 10-11 weeks of pregnancy or through amniocentesis at approximately 16-18 weeks.

How to get genetic testing

Genetic testing requires a sample of blood from the child who the doctor thinks has CDPX1. Results are sent to your doctor. It will take 6 weeks to determine results for a new patient, and 2 weeks for testing a relative or performing a prenatal diagnosis for a known mutation. The cost of the test is 1500 USD. You should call your insurance company to find out if they will pay for the test. The ICD9 code used for this disorder is 756.59.

CDPX1 is a rare disorder and there is not a lot of information known about all the medical problems associated it. If *ARSE* gene testing is performed on your child, your doctor will be asked to fill out a form about your child's medical findings and your pregnancy history. Your child's name will be removed from his/her medical information and collected in a computer database at the National Center for Bioinformatics (NCBI). The goal is to get information that will help families and doctors learn more about medical problems and gene changes associated with CDPX1.

What a negative test result means

Not finding a gene change does not rule out the diagnosis of CDPX1, but does make it less likely. There are several reasons that a child might have a disorder that looks like CDPX1. A geneticist can help determine the next step of action if testing is negative.

What a positive test result means

A positive test result indicates that a change in the Arylsulfatase E gene was found that was considered to be a serious enough change to cause CDPX1 disease in a male patient.

Is there research on CDPX1?

Dr. Nancy Braverman at the McKusick-Nathan Institute of Genetics at the Johns Hopkins University in Baltimore, Maryland is studying the features of CDPX1 and other similar bone disorders. If you are interested in participating in, or learning more about these research studies, you can contact Dr. Braverman at nbraverm@jhmi.edu.

Is there more information about CDPX1 available?

There is also a parents' group who is willing to share more information, education, support and advice. If you are interested in contacting other CDPX1 families, or joining an email listserve for families with CDPX1, you can contact Beth and Dave Gillum at thegillums@cox.net