

## Why did this happen?

When children are conceived the genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. This happens naturally and is not due to your lifestyle or anything you did to cause a change in the *CTNNB1* gene. In most families there is only one affected child and the sequence change in *CTNNB1* occurred out of the blue (de novo). There is one family with two affected siblings reported. Neither parent was found to carry the change in *CTNNB1* (in blood), suggesting that part of the egg cells of the mother or part of the sperm cells of the father carries the change in *CTNNB1* ('germline mosaicism').

## Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. *CTNNB1* syndrome occurs almost always de novo, which means that the parents were not found to carry the change in *CTNNB1*. The chance of having another child with *CTNNB1* syndrome is in this case very low (less than 1%). The risk for healthy brothers and sisters of having a child with *CTNNB1* syndrome is not increased and is the same as for anyone else in the population. In rare cases it can happen that parents have another child with *CTNNB1* syndrome while neither parent was found to carry the change in *CTNNB1*. Up to now this has been reported once. If the genetic analysis of the parents of a child with *CTNNB1* syndrome shows that one of them carries the same variant, the chance of it happening again is much higher. Each family situation is different and a clinical geneticist can give you specific advice for your family.

## How many people have *CTNNB1* syndrome?

*CTNNB1* syndrome is rare, but might be not as rare as we think. Up to now, more than 20 individuals with *CTNNB1* syndrome have been reported in the medical literature. With the increasing use of the latest 'gene sequencing' technology, it is expected that many more people will be diagnosed with this condition over the next few years.

## Families say ...

*" Our son Cas is a very happy, enthusiastic and sociable boy. He can also get very scared when seeing people or children he is unfamiliar with or when he is confronted with unexpected situations. He can also get completely beside himself if he is not understood properly. From birth, Cas' legs have had high muscle tone, but his motor development still keeps progressing. He is able to crawl, he can climb the stairs to a certain level, and can stand independently at the table. Moreover, he is very handy with his walker that we take everywhere. What the future will bring for Cas we do not know exactly, but due to his very positive attitude we have every trust that it will bring all the best for him! "*  
3½ years

## Inform Network Support

### Rare Chromosome Disorder Support Group,

The Stables, Station Road West, Oxted, Surrey RH8 9EE, UK

Tel: +44(0)1883 723356

info@rarechromo.org | www.rarechromo.org

Facebook *CTNNB1* syndroom [in Dutch, with English speaking members]: [www.facebook.com/groups/787268954682708](https://www.facebook.com/groups/787268954682708)

Website for *CTNNB1* Syndrome Awareness Worldwide:  
[www.ctnnb1.org](http://www.ctnnb1.org)

Unique lists external websites and webpages in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This guide was compiled by Dr Tjitske Kleefstra, Clinical Geneticist, Nijmegen Medical Center, Netherlands, with contributions from Marjolein Willemsen. 2015

Version 1 [PM] Copyright © Unique 2015

Rare Chromosome Disorder Support Group Charity Number 1110661  
Registered in England and Wales Company Number 5460413



**CTNNB1  
syndrome**  
rarechromo.org



## What is CTNNB1 syndrome and how is it caused?

CTNNB1 syndrome is a recently discovered condition with developmental delay/intellectual disability. The first people with CTNNB1 syndrome were reported in 2012. Since then several people with the same condition have been identified and it seems a relatively common syndrome.

CTNNB1 syndrome occurs when one of the two copies of the *CTNNB1* gene has lost its normal function. This can be caused by a spelling mistake in the gene or a loss of one copy of the gene. Genes are instructions, which have important roles in our growth and development. They are made of DNA and are incorporated along with many other genes into organised structures called chromosomes. The *CTNNB1* gene is on chromosome 3 in band 3p22.1 at base pairs 41236328 to 41301587 [hg19 genome assembly].

*CTNNB1* is important in the development and maturation of the brain and loss of its function causes learning and memory problems. This is why CTNNB1 syndrome is primarily associated with developmental delay/intellectual disability.



### Can CTNNB1 syndrome be cured?

There is no cure as the effects of the genetic change took place during your baby's formation and development. However, knowing this diagnosis means that appropriate monitoring and treatment can be put in place for your child.

### Most people with CTNNB1 syndrome have

- Developmental delay or intellectual disability
- Speech impairment
- Low muscle tone in the trunk and altered tone in the legs making walking difficult
- Small head circumference (microcephaly)
- Vision problems
- Specific facial features, including a broad tip to the nose and thin upper lip

### Medical concerns

#### Low muscle tone in the trunk and altered limb tone

Most babies have low muscle tone [hypotonia] at birth, and this leads to a delay in reaching their motor milestones and sometimes feeding difficulties. In addition, most babies develop an increased muscle tone in the legs and sometimes the arms during the first year of life. Many are diagnosed with cerebral palsy or pyramidal tract disorder. The raised tone and spasticity can be progressive, leading to spinal curvature [scoliosis], foot deformities and heel cord tightness. Only 40% of children can walk without support. They often walk on tiptoes and can have a broad-based or unsteady [ataxic] way of walking. Most people need the support of a walker frame, or are not able to walk.

#### Eyes and eyesight

Most people have eye and eyesight problems, which are quite varied and can include longsightedness, nearsightedness and a squint [strabismus].

#### Neuroimaging abnormalities

Most people have normal brain MRI scans. A minority have abnormal findings on neuroimaging, which are diverse and include dilated ventricles [fluid-filled parts] of the brain, underdevelopment of the corpus callosum [the band of nerve fibres between the two sides of the brain] and brainstem, abnormal wrinkles and folds on the surface of the brain, and/or delayed myelination (delay in the normal formation of the white matter in the brain and spinal cord). In addition in a few patients spinal cord abnormalities are seen.

#### Healthy heart and kidneys

No structural heart or kidney problems have been reported.

## Development

### ■ Growth

All babies are a normal length at birth and most have a normal birth weight. Half of the babies have a small head circumference at birth. Head growth often stays behind and eventually most children have a small head circumference. Height and weight are mostly normal.

### ■ Sitting, moving and walking

Most children show significant delay in reaching motor milestones due to low truncal muscle tone and the abnormal tone in the legs and sometimes the arms. Four children in 10 learn to walk unsupported, albeit mostly very late (over 6 years) and with an unusual style. The majority need a walker frame. Some need a wheelchair.

### ■ Speech

Some children eventually acquire the ability to speak in simple sentences. More than half, however, have a severe speech impairment and use no or only single meaningful words. Speech is usually affected more than language, which can be in the [low] normal range. Understanding can be much better than speaking.

### ■ Learning

Children have learning difficulties/intellectual disability, sometimes severe, sometimes less so. They usually need the support of special education. Most of them are not expected to be able to live fully independently as adults. In a few cases some kind of loss of acquired skills (regression) has been seen.

### ■ Behaviour

Most children generally have a friendly disposition. About half have behaviour problems, which can include sleep problems, autistic behaviour, ADHD [attention deficit and hyperactivity], and aggression to others or themselves.

## Management recommendations

Children with CTNNB1 syndrome should be followed up by a general paediatrician who can oversee care so that development, behaviour, and complications of spasticity can be monitored and the best help in the form of physiotherapy, orthopaedic shoes, bracing, occupational, behaviour and speech therapies given. Eyesight should be checked at diagnosis and follow-up.