FACTS ABOUT HEALTH CONDITIONS

CAUSED BY CHANGES IN THE *CTNNB1* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *CTNNB1* gene on your child and family. You can talk about the information in this fact sheet with your paediatrician or GP (family doctor). The links in the fact sheet may help you move forward with family life beyond receiving this rare diagnosis.

This fact sheet relates to health conditions that are due to small variants in the genetic code of the *CTNNB1* gene. These changes were identified by a genomic (DNA) test. This fact sheet does not relate to cancers that are due to acquired variants in the *CTNNB1* gene (changes that occur after a person is born).

Key points

- A change in the DNA code of the *CTNNB1* gene causes a condition called NEDSDV, which is an acronym for the most common problems seen in these children:
  NED = Neurodevelopmental disorder (slow development of the brain that affects learning and movement)
  SD = Spastic diplegia (tightness/stiffness in the muscles of the legs, often described as cerebral palsy)
  V = Vitreoretinopathy (visual problems such as farsightedness, squint and a lazy eye)
- Changes (variants) in the *CTNNB1* gene that cause health problems are almost always due to a new (*'de novo'*) change in a child and not inherited (passed down) from either parent. This means that the chance of future children having the same condition is low. Genetic counselling before any further pregnancies is recommended
- Supportive management is available
- You and your family are not alone in adjusting to life with the diagnosis of a change in the *CTNNB1* gene. Support is available from a number of different organisations and services

When a rare condition has been diagnosed

For some families, receiving a genetic diagnosis is a relief. Others may feel overwhelmed and sad. It is very common to have a mixture of thoughts and feelings about the news, and your hopes and expectations for the future may shift and change over time.

While experiences may be shared, individuals and families can respond in different ways and have different information and support needs. Many parents describe an ongoing process of adjusting to a different focus and finding ways to celebrate their child's gains made in their own way and time. It is very important to remember that the diagnosis is only one of many things that make your child unique.

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About the *CTNNB1* gene

Genes contain instructions that tell our body how to grow, develop and function. *CTNNB1* is a **gene** that tells the body to produce the protein beta-catenin. This protein is part of a signalling pathway between different parts of the body, but is especially important in the developing brain. Changes **(variants)** in the *CTNNB1* gene mean that these messages are not transmitted and brain cells do not grow and develop properly.

The *CTNNB1* gene is found on chromosome 3. Usually *CTNNB1*-related conditions are caused by a single spelling variation in the gene, which means the message is not read or received properly. In some individuals, a section of the chromosome that includes the *CTNNB1* gene is missing. This is called a deletion.

In most individuals with *CTNNB1*-related conditions, the gene change occurred when the baby was conceived (a new or *'de novo'* variant), and is not seen in the parents. In some of the milder forms, the variant is passed to the child from a parent.

CTNNB1-related conditions are **genetic conditions**. This means that the condition was not caused by anything the mother or father did before the baby was conceived, during pregnancy or birth, or after the baby was born. *CTNNB1*-related conditions are rare and currently the frequency is unknown.

What could a change in the *CTNNB1* gene mean for my child?

A change in the *CTNNB1* gene can affect children in different ways. Some are more severely affected than others. There may be a range of signs and symptoms even in children with the same genetic variant.

Children with a *CTNNB1*-related condition will generally have developmental delay that can range from mild to a more severe intellectual disability. They may also have some, all, or none of a number of different physical symptoms, including low muscle tone in the body (trunk) that starts when the children are very young (early onset hypotonia) and increased muscle tone/stiffness in the legs that gets worse over time (often described as cerebral palsy or spasticity).

Children may display repetitive behaviours and/or have trouble dealing with sensory information (sensory processing issues), and have problems adapting to new environments - symptoms of autism spectrum disorders. Going to sleep and staying asleep may also be a problem.

Head growth is often slow, which can lead to a small head size (microcephaly). Many children have a squint (strabismus), lazy eye, decreased eyesight, or long/far-sightedness. Children with NEDSDV may have fairer skin and lighter-coloured hair than other family members.

One of the less common problems that requires urgent treatment if it occurs is an eye condition called retinal detachment. This is when the gel-filled space (vitreous) between the lens at the front of the eye and retina at the back of the eye shrinks. The vitreous normally maintains the round shape of the eye and stops the retina from coming away from the back of the eye (retinal detachment). If retinal detachment is not treated quickly, there is a risk of permanent loss of sight.

At this point in time, it is not possible to reverse or directly repair this gene change. It is also not possible to accurately predict the level of care your child will require through to adulthood. Your child's individual needs and strengths will become more obvious over time, which will help with planning for the future.

While there is no single treatment or cure for NEDSDV at this time, each of the symptoms associated with the condition may be treated. Your child's development may be helped through early use of therapy services such as physiotherapy and treating symptoms if/when they arise. It is likely that many different health professionals will be involved in caring for your child. Your paediatrician or GP will arrange referrals to other health professionals as needed and help with applications for service funding through the **National Disability Insurance Scheme (NDIS)**.

Good communication with the health professionals caring for your child is important to establish common goals, trust and shared responsibility. We encourage you to ask questions and express your concerns as the primary carer for your child.

Management recommendations

As many health or developmental problems are not immediately obvious, your child will need to be checked by their paediatrician at diagnosis and then seen every 6–12 months or more often if needed. A visit to the ophthalmologist each year is also recommended. The list below includes many of the common problems, but others may arise. If you have any concerns about your child's health, please speak with your family doctor (GP) or paediatrician.

Possible health problems (% of children affected)	Management
Developmental delay/intellectual disability, including low muscle tone and speech delay (>90%)	Early intervention, including speech therapy, occupational therapy and physiotherapy Consider a formal developmental assessment before starting school or by school counsellor for school age children At least yearly checks by GP/paediatrician Early intervention and special education programs
Difficulty/delayed walking (>90%)	Physiotherapy/occupational therapy to help with using medical devices such as walking aids (e.g. frames), wheelchairs, if needed
Challenging behaviours (90%)	Diagnosis and management by paediatrician as appropriate
Autism spectrum disorder (70%)	Diagnosis and management by paediatrician as appropriate
Repetitive behaviours, especially of the hands (90%)	Diagnosis and management by paediatrician as appropriate
Small head size (microcephaly) (70%)	Regular review of height, weight and head size (circumference). No treatment is needed
Movement disorder of hands (dystonia [20%])	Consultation with paediatric neurologist
Disorders of sleep (20%)	Review by paediatrician, consider referral to sleep physician if severe symptoms
Muscle weakness and tightness (30–40%)	Orthopaedics/physiotherapy/occupational therapy, including stretching to help avoid fixed tightness of the muscles (contractures) and falls
Low muscle tone in the body (trunk) in infancy and increased muscle tone in the legs in later childhood (spasticity or cerebral palsy)	Physiotherapy/occupational therapy to help with mobility and function
Visual (eyesight) problems/vision loss (40%) **These include:** **- Lazy eye** **- Squint** **- Farsightedness** **- Retinal detachment**	Initial review by ophthalmologist for assessment of vision, retinal health and squint (strabismus) Yearly eye review by ophthalmologist A squint (strabismus) may require patching or glasses Long- or near-sightedness (refractive error) may require glasses Concern about sudden loss of sight in one eye (due to retinal detachment) requires urgent assessment and possible repair by an ophthalmologist
Feeding/gastrointestinal difficulty (20–30%)	Close monitoring of weight and growth by paediatrician Children with severe feeding problems may need to be referred to a paediatric gastroenterologist and may need a feeding (nasogastric or gastrostomy) tube

Detailed management recommendations for healthcare professionals can be found in the **GeneReviews article** and the **Human Disease Genes** website.

Resources, support and connecting with others

You may find it helpful to connect with other people who have personal experience of day-to-day life with a child who has a *CTNNB1*-related condition. You can make these connections through:

- Umbrella groups (e.g. **Genetic Alliance Australia** and **Rare Voices Australia**)
- Condition-specific groups (e.g. **CTNNB1 Connect & Cure** and **CTNNB1 Foundation**)
- Groups for individuals with common symptoms that may have many different causes (e.g. intellectual disability, hearing loss, autism).

Many organisations (e.g. **Carers NSW** and **Belongside Families**) can also offer general advice and support in caring for a family member with long-term needs.

It is important to know that you are not alone on this journey

More information about *CTNNB1*-related conditions

You can find further information about *CTNNB1*-related conditions by following the link below.

- National Organization for Rare Disorders (NORD): **CTNNB1 syndrome**

For more information about genetic conditions and to find your local Clinical Genetics services, visit the **NSW Centre for Genetics Education**.

Family planning

Genetic conditions are sometimes passed from a parent to their child. Even if the same variant was not found in one of the parents, it is still possible to have another child with the same condition. The chance of this happening is 1–2%.

If you are thinking about having more children, it is recommended that you talk with your local **Clinical Genetics service**. Some people may choose to have **genetic testing** before or during a pregnancy. Specialised health professionals such as **genetic counsellors** can advise you on your options.

You can also speak with your GP about options for **reproductive genetic carrier screening**. When planning a family, it is best to explore your options before becoming pregnant.

Research, registries and clinical trials

Some people with rare conditions are able to participate in research, which may be of benefit to your child. This may investigate how a particular variant causes health problems or it may be a clinical trial testing new treatments. Sharing information about your child's signs and symptoms through registries such as **IAMRARE** and those listed on the **CTNNB1 Connect & Cure** website can help build further knowledge about this condition.

Early research into **gene therapy** and small molecule treatments for *CTNNB1*-related conditions has started but no clinical trials are underway as yet. More details are available at the **CTNNB1 Foundation** and **CTNNB1 Connect & Cure** websites. Information about current clinical trials can be found by searching the international databases **ClinicalTrials.gov** or **EudraCT**. You may like to discuss this research with your child's health care team.

To print more copies of this fact sheet and access links to the underlined topics, go to **www.genetics.edu.au** and search for 'CTNNB1'.

This fact sheet should not replace a consultation with a specialist healthcare professional.