What causes ARID1B syndrome?

ARID1B syndrome is caused by changes in the DNA (genetic material) in the *ARID1B* gene, or by loss of the gene. Genes provide the instructions to make proteins. The ARID1B protein is one component of a large assembly of proteins called the BAF-complex. This complex plays an important role in the formation of nerve cells (neurons). We do not understand yet the precise way this causes intellectual disability or the other features of ARID1B syndrome, but research is ongoing.

Why did this happen?

In most families the DNA change in *ARID1B* occurs out of the blue (de novo). When children are conceived their parents' 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. These types of change happen naturally in all species - humans, plants and animals - and are not due to your lifestyle or anything you did.

In a few families, one parent may have the same genetic change as their child, but this is very rare.

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. For ARID1B syndrome where parents do not carry the same *ARID1B* change as their child, the chances of having another child are almost certainly no higher than for anyone else in the population. If the genetic analysis of the parents of a child with ARID1B syndrome shows that they carry the same change in the *ARID1B* gene, the chances of it happening again are much higher.

It is possible in theory that either the mother or father could carry this gene change in just some of their eggs or sperm, which is known as gonadal mosaicism. This risk is likely to be very small (less than 1%).

Each family situation is different and a clinical geneticist or genetic counsellor can give you specific advice for your family.

Families say ...

"There is a strong possibility that other children will be diagnosed with the same condition and it is a help to share experiences with other parents to find out what works, and what doesn't. We have hopes that if there is a similar adult case we may have some idea of her future outcomes or whether specialist training may prevent her having future problems. She is an incredibly happy child and brings joy to family and school, popular with the other children, and has started to become more engaged and to cuddle, hug and laugh with us demonstrating a sense of humour." - 6 years

"Happy, friendly. Loves exploring, being busy." - 8 years

Inform Network Support

Rare Chromosome Disorder Support Group,
GI, The Stables, Station Road West, Oxted, Surrey RH8 9EE, UK
Tel/Fax: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

There is a FB site for Coffin-Siris syndrome at: www.facebook.com/pages/Coffin-Siris-Syndrome/389657281170288

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ARID1B syndrome

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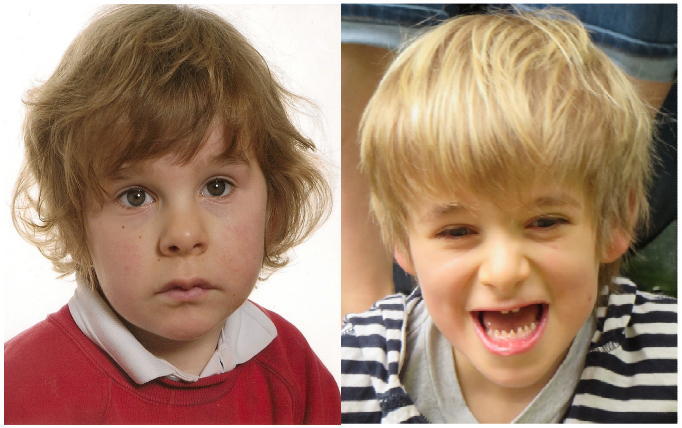

What is ARID1B syndrome?

ARID1B syndrome is a recently discovered condition. The term used by clinical geneticists is ARID1B-related intellectual disability. Intellectual disability can be shortened to ID. In this guide we use the name ARID1B syndrome. *ARID1B* (pronounced a-rid-one-bee) is the name of the gene involved. A change in the gene or loss of the gene can cause the syndrome. ID stands for intellectual disability, but the degree of learning difficulty is very variable.

Typical features

- Some difficulty with learning
- Delay in development, and speech
- Feeding difficulties
- Short sight

Knowledge about ARID1B syndrome is only just emerging, and much remains to be learnt. This is because most people with ARID1B syndrome were first diagnosed with a different disorder (Coffin-Siris syndrome, or CSS) and this may have somewhat different effects to ARID1B syndrome. Fewer than 20 people with a change in the *ARID1B* gene or loss of the gene without a CSS diagnosis have been reported. What has become clear is that the effect of a change in *ARID1B* is very variable. It is likely that many other individuals with learning difficulties have ARID1B syndrome but have not been recognised yet.

For the time being, for our knowledge about ARID1B syndrome we have to rely partly on information about people who also have CSS, and this may give a biased picture.

Can the syndrome be cured?

It is not possible to repair the change in the *ARID1B* gene, but careful screening, early intervention with the right therapies and regular monitoring will give your child the best chance of reaching their full potential. Treatments can be offered for some of the symptoms such as seizures.

The *ARID1B* gene is found on chromosome 6.
It is on the long arm of the chromosome,
in the band known as 6q25.3.

Medical concerns

Seizures Recently seizures were reported in 14/59 (24%) people. The first seizure usually occurred in childhood and most seizures responded well to treatment. If you are worried that your child is having seizures, we recommend you try to video these episodes and talk about this to your child's doctor.

Eyesight Short sight (myopia) is reported in about half of the people with an *ARID1B* mutation. About one third of these have severe myopia (more than -4 D, sometimes even up to -20 D). We therefore strongly recommend vision testing, particularly when there are indications that your child appears not to see very well. Strabismus (squint) is also often reported in people with an *ARID1B* mutation.

Hearing Hearing problems have been noted in a minority (about 1/6) of people. Only 3/54 (5%) were reported to have hearing loss in both ears. So far, all children had mild hearing loss only. There is no evidence that hearing loss gets worse with time. Once babies have passed their neonatal hearing test, hearing problems are therefore not expected. However, if you have any doubt about your child's hearing ability, this should be tested.

Feeding difficulties Feeding problems are reported in about half the babies with an *ARID1B* mutation. Usually, these difficulties show shortly after birth, and resolve within a few months. However, there is a group of children who need tube feeding direct to the stomach by gastrostomy for up to several years. We therefore recommend that any feeding difficulties are taken very seriously, and dietary advice and feeding management offered promptly.

Frequent infections There have been reports of frequent infections in people with Coffin-Siris syndrome. Frequent infections have been reported in about one third of children, though no confirmed abnormalities of the immune system have been reported. At the moment, there is no clinical evidence to support taking extra precautions to prevent infections.

Heart/kidneys A small proportion of babies with an *ARID1B* change have had heart or kidney problems. In young children heart and kidney screening is therefore recommended. However, if patients are diagnosed when they are older, and do not display any symptoms, screening may not be needed.

Malignancies Although mutations in ARID1B have been described in cancer, there is no clinical evidence to support an increased risk of malignancies in ARID1B syndrome. So there is no recommended screening..

Development

Physical development

Physical development is delayed in most children with an *ARID1B* change. The vast majority of children learn to walk without support. On average children learn to walk around 30 months, but the known range is between 15 months and 5 years.

Learning

Children with an *ARID1B* change usually need learning support. Most are reported to have moderate intellectual disability, but some have a low-normal IQ, and others are more severely affected. Some children with an *ARID1B* change are able to read and write, most are able to use tablets or computers, among other things to watch movies.

Speech

Most children with an *ARID1B* change do develop speech. The age at which this occurs is variable, but around half speak some words before their fourth birthday. Because it appears that expressive speech is particularly affected, it may help to offer alternative forms of communication such as sign language and picture-based systems.

Behaviour

Children with an *ARID1B* change are often considered very friendly. However, they may become frustrated and develop aggressive behaviour especially when they have difficulty communicating. There are also reports of autistic features in some of the children.

Growth

Children with an *ARID1B* change are on average shorter than their peers. However, there is wide variation and your child might be a normal height. People are usually of a normal weight relative to their height.

Managing ARID1B syndrome

At Diagnosis

- Kidney and heart ultrasound scans
- Hearing and eyesight tests if needed
- Consider EEG (test of the brain's electrical activity) if seizures are suspected
- Feeding management and dietary advice for any feeding problems

After Diagnosis

- Yearly evaluation by a developmental paediatrician
- Early intervention with speech and/or physical therapy where needed
- Regular eyesight tests