FACTS ABOUT HEALTH CONDITIONS

CAUSED BY CHANGES IN THE *KIF1A* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *KIF1A* 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 *KIF1A* gene. These changes were identified by a genomic (DNA) test. It does not provide information about conditions caused by chromosome deletions or duplications that involve the *KIF1A* gene.

Key points

- *KIF1A* stands for kinesin family member 1A
- Children with a *KIF1A*-related condition often have developmental delay, intellectual disability, stiffness in their legs, abnormal muscle tone and eye problems
- Changes (variants) in the *KIF1A* gene that cause health problems may be inherited from a parent or may be a new (*'de novo'*) change in a child. This means that future children may also have this variant. Genetic counselling before any further pregnancies is recommended
- Symptomatic management is available
- You and your family are not alone in adjusting to life with the diagnosis of a change in the *KIF1A* gene. Support is available from a number of different organisations and services

Other names this condition may be referred to as

- *KIF1A* syndrome
- KAND (*KIF1A*-Associated Neurological Disorder)
- Kinesin-3 family member 1A syndrome
- Hereditary Sensory Neuropathy type IIc
- NESCAV syndrome (Neurodegeneration and Spasticity with or without Cerebellar Atrophy or Cortical Visual Impairment)
- Hereditary Spastic Paraplegia type 30 (HSP30)

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 *KIF1A* gene

Genes contain instructions that tell our body how to grow, develop and function. *KIF1A* (said as "kiff-one-ay") is a **gene** that directs cells to make the protein KIF1A, which is found in brain cells (neurons). KIF1A helps to transport proteins and other cargo to the very end of neurons to help the brain work in the usual way.

The *KIF1A* gene is found on chromosome 2. Usually *KIF1A*-related conditions are caused by a single spelling variation in the gene. This means the message is not read or received properly. *KIF1A*-related conditions are not yet fully understood.

Individuals with *KIF1A*-related conditions may have symptoms that are mild or more severe. The differences are thought to be due to the specific change (**variant**) in the gene, as well as other factors that have not yet been worked out. Depending on the specific variant, *KIF1A*-related conditions can occur when there is a change in both copies of the *KIF1A* gene (one from each parent) or a change in a single copy (from one parent only). These variants can either be passed down (inherited) from a parent or for those individuals where the condition is due to a change in a single copy of the gene, it can occur for the first time in the person with the condition (a new or *'de novo'* variant).

KIF1A-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 at birth, or after the baby was born. *KIF1A*-related conditions are rare, affecting about 300 children worldwide.

The symptoms of *KIF1A*-related conditions often appear at birth or early childhood, and some children may pass away during childhood. Because the clinical features of *KIF1A*-related conditions overlap with those of other neurological problems, many children are probably either not diagnosed, or given a different diagnosis by mistake. For this reason, it is likely that many more than 300 children worldwide have this genetic condition.

What could a change in the *KIF1A* gene mean for my child?

A change in the *KIF1A* gene can affect children in different ways. Some are more severely affected than others, and there may be a range of signs and symptoms even in different children with the same genetic variant. Mildly-affected children may only have difficulty walking, with no other problems. Moderately- or severely-affected individuals may have developmental delay/intellectual disability that can range from mild to very severe. Many of these children do not learn to talk, or only speak a little.

Over time, some nerves may stop working, causing numbness and/or pain. Children may have problems with their movement (motor) skills, which may worsen rather than improve. Eyesight (vision) may become worse over time because of problems with the lens or the nerves at the back of the eye. Many children have problems keeping their body at the correct temperature, and have unexplained fevers. Up to half of all children with *KIF1A*-related conditions have seizures (epilepsy).

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.

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 obvious straight away, your child will need to be checked by their paediatrician at diagnosis and then seen every year or more often if needed. 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
Development delay and/or intellectual disability (90%)	• Early intervention, including speech therapy, occupational therapy and physiotherapy • Consider a formal developmental assessment before starting school or by a school counsellor for school age children • At least yearly checks by GP/paediatrician
Autism spectrum disorder, hyperactivity disorder and anxiety (20%)	• Diagnosis and management by paediatrician as appropriate
Muscle weakness and tightness (progressive spasticity) (80%)	• Orthopaedics/rehabilitation/physiotherapy/occupational therapy, including stretching to help avoid contractures and falls
Difficulty keeping the body at the correct temperature (frequent fevers unrelated to infection) (50%)	• Anti-fever (antipyretic) medication such as paracetamol
Visual (eyesight) problems/vision loss (40%)	• Annual review by ophthalmologist to check for breakdown (atrophy) of the optic nerve, lens clouding (cataract), retinal changes and squint (strabismus)
Seizures (epilepsy) (40%) **Many seizure types may occur, including atonic drop seizures, petit mal/absence seizures, infantile spasms and generalised tonic-clonic seizures**	• Review and management by paediatrician or neurologist • Standard investigations and treatments, including EEG and anti-epileptic medications • Consider overnight EEG monitoring (telemetry) as seizures often occur at night and may not be detected using routine daytime EEG
Damage to the peripheral nerves (peripheral neuropathy) (30%)	• There is no treatment or cure for nerve damage. Some medications can relieve the pain
Structural brain abnormality including microcephaly (small head)/ corpus callosum abnormality	• Brain MRI if clinically indicated. • Most structural differences do not require any specific treatment
Digestive problems including gastroesophageal reflux, constipation and diarrhoea (20–40%)	• Review and management by paediatrician • Gastroesophageal reflux may respond to upright posture, thickened feeds, early introduction of solids and/or medications • Constipation can be treated with a high fibre diet, adequate fluid intake and/or laxatives
Difficulty swallowing (dysphagia) (30%)	• Investigation for swallowing difficulties or reflux where appropriate • Children with severe feeding problems may need to be referred to a paediatric gastroenterologist and may need a feeding (nasogastric or gastrostomy) tube

Possible health problems (% of children affected)	Management
Excessive salivation (sialorrhoea) (30%)	• Review by paediatrician as needed • Medication such as anticholinergics may be helpful. These medications block the action of a brain chemical messenger (neurotransmitter) known as acetylcholine in brain cells. These agents can reduce saliva production but may cause some level of sedation (causing increased calmness and/or drowsiness) • Injection of botulinum toxin (botox) into the salivary glands or other types of surgery
Curved spine (scoliosis) (15%)	• May progress, particularly during puberty. Stabilises if treated • Yearly monitoring by GP/paediatrician until growth is complete
Short stature (10%)	• Measurement of the child's height at least once each year by GP/paediatrician • Consider investigation for hypothyroidism and growth hormone deficiency if height is less than the third centile and children do not grow as expected • Children with either partial or complete growth hormone deficiency may benefit from growth hormone therapy
Genitourinary malformations (10%)	• Physical examination by paediatrician • If the testicles cannot be felt (palpated), a surgical consultation is required • If the opening of the tube that lets urine out of the body (urethra) is underneath rather than at the end of the penis (hypospadias), a surgical consultation is required

More detailed clinical management recommendations can be found at the US **National Organization for Rare Diseases (NORD)**.

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 *KIF1A*-related condition. You can make these connections through:

- KIF1A.org **website** and **Facebook page**
- Umbrella groups (e.g. **Genetic Alliance Australia** and **Rare Voices Australia**)
- Condition-specific groups
- 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 **Reframing Disability**) 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 *KIF1A*-related conditions

You can find further information about *KIF1A*-related conditions by following the links below.

- MedlinePlus: **Hereditary sensory and autonomic neuropathy type II**
- UNIQUE: **KIF1A syndrome**
- KIF1A.org: **KIF1A gene**
- National Organization for Rare Disorders (NORD): **KIF1A-related disorder**

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 may be passed from a parent to their child. The chance of having another child with a *KIF1A*-related condition can range from very low to as high as 50% (1 in 2 chance), depending on whether the biological parents also have a *KIF1A* variant.

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 **KIF1A.org** and **IAMRARE** can help build further knowledge about this condition.

Information about current clinical trials can be found by searching the international databases **ClinicalTrials.gov** or **EudraCT**.

To print more copies of this fact sheet and access links to the underlined topics, go to **www.genetics.edu.au** and search for 'KIF1A'.

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