UNIQUE
UNDERSTANDING GENES & CHROMOSOMES

KCNK9 imprinting syndrome (KIS)

(Birk-Barel syndrome (BIBARS))

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with KCNK9 imprinting syndrome. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition.

What is KCNK9 imprinting syndrome?

KCNK9 imprinting syndrome (KIS), which encompasses the Birk-Barel syndrome (BIBARS), is a rare genetic condition associated with developmental delay, varying degrees of learning (intellectual) disability, low muscle tone (hypotonia) and severe feeding difficulties.

KIS is caused by certain changes (variants) in the KCNK9 gene. As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with KIS will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

How common is KIS?

KIS is extremely rare. Currently (2026), approximately 50 individuals with KIS have been reported in the medical literature. The majority are children, but more recently older aged adults including a 64-year-old woman have been reported.

What features and symptoms do people with KIS have?

As is common with many genetic conditions, children and adults with KIS can have a range of features and symptoms. As more people are diagnosed, and information is shared, the range of features, and the likelihood of a child or adult having these features, will become clearer.

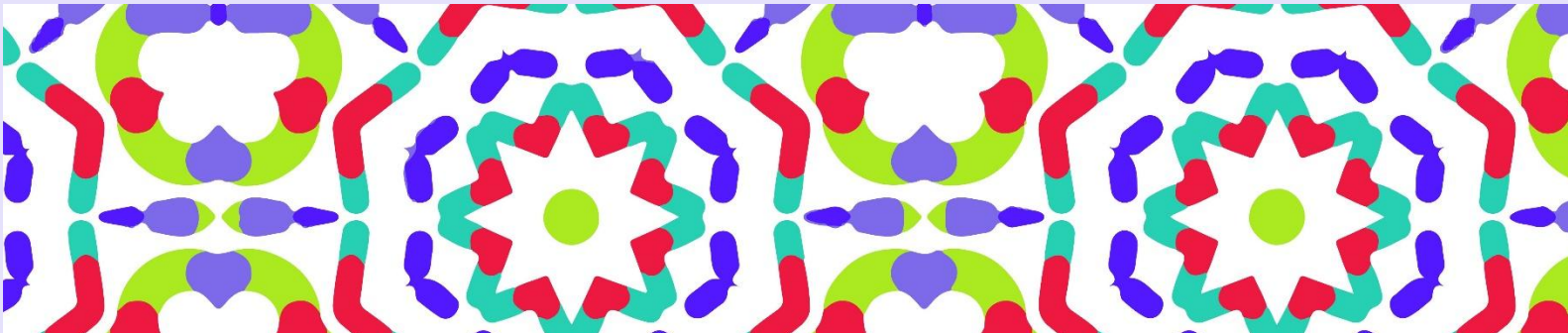
Common features

Most people with KIS have:

- Low muscle tone (hypotonia) from birth
- Severe feeding difficulties
- Some degree of learning (intellectual) disability (LD/ID)
- Speech delay
- Developmental delay
- Behavioural differences
- Characteristic facial features
- A slender build with a long neck and tapered chest (asthenic body habitus)
- Tapered fingers with prominent fetal fingertip pads

Other possible features include:

- Cleft palate
- Seizures
- Temporary low blood sugar in the newborn period (transient neonatal hypoglycaemia)
- Weakness in specific muscle groups
- Reduced tear production (decreased lacrimation)
- Rhythmic, involuntary muscle contractions (clonus)
- Pauses in breathing during sleep (sleep apnoea)



Pregnancy and birth

While many pregnancies are unremarkable and proceed without complications, some concerns during pregnancy have been reported. Where a cause for concern was noted, most often parents reported slow growth in the womb (intrauterine growth retardation or IUGR) and reduced fetal movements, which can be caused by the baby's low muscle tone (congenital hypotonia). A reduced amount of amniotic fluid (oligohydramnios) has also been noted.

Birth weights are usually below average, and a small number of babies grow very slowly in the womb and are tiny at birth. The low muscle tone that is characteristic of the syndrome can result in the baby being positioned bottom-first for birth (a breech presentation), which may mean a caesarean section is required for delivery. Many new-born babies have been described as alert, but with very low tone and reduced movements, features that may alert doctors to an underlying condition.

Many babies show some signs of difficulty at birth related to difficulties with feeding, due to a combination of facial weakness, anomalies of the roof of the mouth (palatal anomalies), a poor sucking reflex and poorly coordinated swallowing. To manage these feeding difficulties and ensure adequate nutrition, interventions such as a nasogastric (NG) tube or a gastrostomy (G-tube) are often required. Reports of temporary low blood sugar (transient neonatal hypoglycaemia) have also been noted, which resolved with treatment.

> ***My pregnancy was normal, save from an element of extra fluid (polyhydramnios) which was monitored but never crossed the threshold for further investigation. Our daughter was a good size and I felt movements despite having my placenta at the front. Quite quickly after birth it was noticed that our daughter had no suck reflex, shallow breathing and overlapping fingers. She was transferred to NICU where multiple tests were carried out including the genetic testing which found the variant in her KCNK9 gene."***

Appearance

Certain facial features are observed more often in children with KIS than in other children and can become more pronounced with age. These features may mean that you see unexpected similarities between your child and others with KIS.

The most common characteristic features include:

- A long head shape (dolichocephaly) with a narrow forehead
- Reduced facial movement (myopathic face)
- Drooping of the upper eyelids (ptosis), with arched eyebrows and long lashes
- A high, narrow nasal bridge and a broad nose with a bulbous tip
- A short space between the nose and upper lip (philtrum)
- A mouth with down-turned corners, a tented upper lip and sometimes a thin upper lip in infancy
- A small or recessed jaw (micro/retrognathia)
- A narrow, high-arched palate. A cleft palate is seen in almost half of individuals

Other physical characteristics may include:

- A slender build with a long neck and tapered chest
- Tapered fingers with prominent foetal fingertip pads
- A dimple or small channel (pilonidal dimple or sinus) at the base of the spine

> ***Our daughter still has a lot of similarities to our son, who doesn't have the syndrome, but there are some noticeable differences such as her head shape, muscle weakness around the mouth and***

nose shape. She also has very long eyelashes which always attract comments. Given her likeness in a lot of areas to her brother, we were surprised when we first saw other children with the condition that they also look like they could be siblings."

Development

Gross and fine motor skills

Developmental delay has been reported in most children with KIS. The degree of delay ranges from mild to profound. Developmental 'milestones', including sitting, and walking are often delayed, although there is a wide range of eventual ability. A few children acquire mobility and other skills around the same age as 'typically-developing' children, but most show delays. Low muscle tone (hypotonia) is common and may affect mobility and may be accompanied by occasional involuntary muscle contractions (clonus). Some children may have an unsteady or wide-based gait when walking because of balance issues (known as ataxia). Fine motor skills are also affected, which can be made more challenging by generalised hypotonia, muscle weakness close to the centre of the body (proximal muscle weakness), and the potential for joints to become fixed in one position (joint contractures). A number of individuals demonstrate easy fatiguability with exertion.

Many benefit from early intervention with treatments or therapies such as orthotics e.g. insoles, braces, splints and callipers; occupational therapy (OT); and physiotherapy (PT).

"Sleepiness/lethargy is a big problem in trying to implement therapies. [Before the age of one] we hadn't seen any of the typical milestones such as smiling or head control, but we were hopeful they would come. Since turning one, she's showing very small signs of gaining more strength every day and is now showing signs of intermittent head control and wanting to roll over. The early days can be hard, but our children are amazing and will do what they can in their time."

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Intellectual development and learning

All children with KIS have learning (intellectual) disability (LD/ID) and/or learning difficulties, which ranges from mild to profound, but is often in the moderate to severe range and is often accompanied by limited speech. Most children will require significant additional support with their learning throughout their education. Early intervention can prove particularly beneficial and formal testing to assess specific, individual needs is recommended to help each child reach their full potential.

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Speech and language

Children with KIS typically experience some degree of speech and language delay, and many find some difficulty with planning speech (apraxia) as well as with co-ordinating movement of their lips, jaw and tongue to make the right sounds (dysarthria). As a result, expressive language is often limited. Features such as cleft palate, frequently contribute to these challenges in articulation.

An assessment by a speech therapist should be able to identify your child's specific difficulties, allowing regular therapy sessions tailored to your child's specific areas of need. Assessment by a cleft/craniofacial team may also be recommended.

"Our daughter has never cried, which many would think is a dream but is actually very scary when your baby can't communicate with you. However, you learn to read their other signs of distress or contentment and there's always hope. Our daughter started making whimpers and groans at around one year and now has a range of noises of different tones and has recently started her version of crying'."

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Feeding

Severe feeding issues in the new-born period are common and can sometimes lead to poor weight gain. Some babies will suck weakly. Low muscle tone, difficulties with swallowing (dysphagia) and easy fatigability, which can persist until near puberty, also often contribute to feeding difficulties. Other issues that have been reported include aspiration (where fluid, food or saliva enters the airway or lungs). Many babies also suffer from gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), which may require treatment, including careful positioning for feeds or, in some cases, insertion of a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy tube (PEG/G-tube).

Many children have benefited from attending a feeding clinic where an assessment can be made, and advice to help treat any eating and drinking difficulties provided. Due to the impact on growth, routine surveillance of nutritional status is also recommended.

"Our daughter has been tube fed since birth. She had an NG tube until 7 months when she had her Mic-key button fitted. Her growth and weight have come on leaps and bounds with the button. She has also had bad reflux since birth, but we have recently found splitting her Omeprazole into a morning and an evening dose has been more beneficial for her."

Unique publishes a separate guide to Feeding

Growth and stature

Many children with KIS described in the medical literature are noted as having growth delay and a short stature. Growth issues can begin before birth, with some reports of babies being born smaller than expected for their gestational age (intrauterine growth restriction). Failure to thrive during infancy is also frequently observed. Beyond infancy, height and weight are variable and may remain below average. Other physical characteristics may develop gradually, such as a long neck and a difference in leg length.

Behaviour

Children with KIS typically tend to have behaviour in keeping with their overall degree of developmental delay. Some children have an autism diagnosis or traits. Other behaviours including attention deficit hyperactivity disorder (ADHD), aggressive behaviours (which are particularly prominent), obsessive compulsive disorder (OCD) and sleep disturbances, have also been reported.

Understanding this complex profile is key to providing effective support. Management strategies should focus on addressing the root causes of challenging behaviours - such as providing sensory supports, using strategies to manage anxiety and creating structured environments to help with attention. Efforts to take into account and introduce strategies to tackle communication and other difficulties can also be beneficial. For example, treating sleep apnoea in one instance led to progressive improvements in social milestones, including better alertness, increased interaction with caregivers and more frequent smiling.

Unique publishes a separate guide to Challenging Behaviour

Puberty

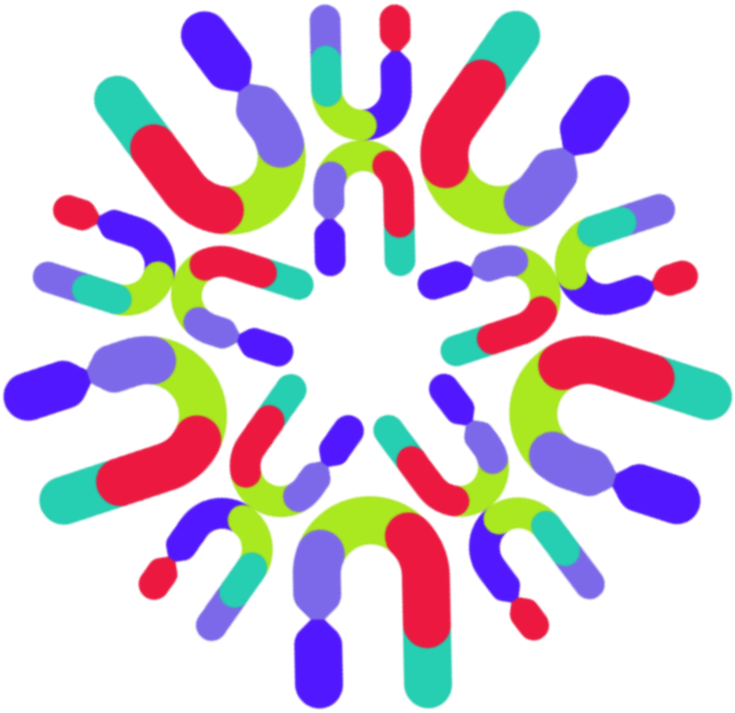
There is limited information available about puberty in children with KIS. To date, there are no reports of significant differences in the timing of puberty, such as it starting particularly early (precocious puberty) or late (delayed puberty). Some families of children with genetic disorders and behavioural difficulties or learning disability can be particularly concerned at their daughter's ability to cope with menstruation, and for some discussing menstrual regulation options with a paediatrician may be beneficial.

Unique publishes a separate guide to Puberty

Adulthood

Experiences of adulthood are likely to vary and will depend on many factors. These include the level of any learning (intellectual) disability, possible on-going medical concerns and improvements in early intervention and therapies/treatments. Since reported adult cases are extremely rare at present, long-term outcomes are not yet well understood.

Unique publishes a separate guide to Transition



Medical concerns

The following medical concerns have been found in children with KIS. They are not found in all children so not all children with KIS will be affected.

Breathing

Babies and children with KIS have a higher rate of significant and often early-onset respiratory concerns, which are likely to require treatment.

Newborns can experience severe breathing difficulties immediately after birth, which may include a bluish discolouration of the skin (cyanosis) and very low oxygen levels (hypoxaemia), sometimes leading to a diagnosis of suspected acute respiratory distress syndrome (ARDS). The cause of these respiratory issues is complex. A primary factor is low muscle tone from birth, which weakens the breathing muscles as well as those around the windpipe (trachea) and can contribute to a weak airway that can collapse during breathing (tracheomalacia). This can be made worse by specific facial features such as a small or set-back lower jaw (micrognathia or retrognathia) and a cleft palate. Other contributing factors can include a floppy voice box (laryngomalacia), joint stiffness (contractures) and curvature of the spine (scoliosis).

For some people, an abnormal breathing pattern during sleep (central and obstructive sleep apnoea) is a major concern, since recurrent pauses in breathing (apnoea) can lead to low oxygen levels and, in some cases, respiratory failure. Consequently, night-time respiratory support is often required.

> ***"Our daughter was diagnosed with obstructive sleep apnoea at 11 months old and started on continuous positive airway pressure (CPAP), which has given us a lot of reassurance about her safety overnight."***

Heart

A heart condition has been reported in a few people with KIS, specifically a hole between the top two chambers of the heart (secundum atrial septal defect, ASDII) and a small opening between the two upper chambers of the heart (patent foramen ovale, PFO). Where a heart condition is found, it is recommended that further genetic testing to rule out other genetic causes of the heart condition is carried out as part of the diagnostic process.

Seizures

Often, children with KIS experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain), including cases of seizures that occur in the absence of a fever (afebrile seizures). Age of onset can vary considerably, with the typical age of onset for afebrile seizures being between two and eight years, although febrile seizures have been reported as early as one month of age. In some individuals, a pattern has been observed where febrile seizures (seizures that only occur when a child has a high temperature) precede the onset of afebrile seizures. Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Absence seizures, where there is a change in behaviour as if the child 'switches off', sometimes with staring, eyelid flickering or lip smacking, have also been suspected. Absences are very brief, often lasting less than half a minute.

Electroencephalograph (EEG) and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced. Seizures can cause a lot of worry for families and can be frightening to observe, but in the majority of cases they self-

resolve or resolve with medical treatment. If your child has a seizure for the first time, it is important to remove nearby hazards so they can't hurt themselves and contact a medical professional.

"Our daughter has had a variety of seizures since she was 3 months old and has more recently been commenced on medication for infantile spasms. Other than the spasms her seizures have always been very short (under a minute)."

Constipation

Constipation is common among children with KIS and can be related to low muscle tone, among other reasons that are not fully understood. It is important that possible causes are discussed with a health visitor or doctor.

Hormones

Children with KIS may have conditions that affect their hormones. One hormone-related concern is temporary low blood sugar (transient neonatal hypoglycaemia) in the newborn period. This can sometimes be associated with high levels of insulin (hyperinsulinism).

Eyes and sight

Eye and vision anomalies are relatively common in children with KIS. A thorough evaluation by a paediatric ophthalmologist is recommended at diagnosis. Known concerns include a squint, where one or both eyes turn inward, outward, up, or down (strabismus); drooping of the upper eyelid (ptosis); and skin folds of the upper eyelid covering the inner corner of the eye (epicanthal folds). Notably, individuals may experience a decreased production of tears (decreased lacrimation), which can lead to dry eyes (corneal dryness).

Hands and feet

Children with KIS often have differences of the hands and feet including:

- Fingers or toes that curve inwards (clinodactyly)
- Flat feet (pes planus)
- Club foot (talipes)
- Tapered fingers
- Prominent fingertip pads
- Long fingers
- Small hands
- Short feet
- A single, straight crease across the palm of the hand (single transverse palmar crease)
- Long toes

Some children are only mildly affected and may not require treatment. Others may benefit from orthotics, such as ankle-foot orthoses (AFOs), and physical and occupational therapy. Some may also require a gait trainer to aid mobility.

Spine

Some children develop a spinal curvature, either a sideways curve of the spine (scoliosis) or a rounding of the upper back (kyphosis). The curvature can be treated with physiotherapy, exercises and occupational therapy, but a support brace (orthosis) or surgery may be needed.

A sacral dimple (also known as a pilonidal dimple or sinus) is a more common feature, seen in many individuals. A sacral dimple may be deep and, in rare cases, may be associated with underlying conditions such as a filar cyst or a non-cancerous growth made of fat cells (a lipoma). If there is any concern about this, a spinal ultrasound is recommended.

Joints

Joint differences are common to KIS. These may be present from birth (congenital) and include extremely loose (hyper-mobile) joints. Children with very loose joints may need physiotherapy or additional braces (supports, splints). In some cases, joints are unusually tight (joint contractures). Contractures have also been reported at birth, including in the hips, and have also been seen to develop over time from low muscle tone (hypotonia) and muscle weakness. Management includes occupational therapy (OT) and regular evaluation by a specialist, such as an orthopaedist, to monitor for any emerging mobility limitations.

> ***Our daughter has had orthotics for her hands and feet to try and stretch tight tendons. She has also had serial casting of her foot and is due to have surgery for developmental dysplasia of the hip (DDH).”***

Palate

Anomalies of the palate (roof of the mouth), ranging from those that may be invisible to the casual onlooker such as a high/arched palate to more obvious conditions such as a cleft palate, have been reported. This can include a full cleft, a submucous cleft, or velopharyngeal insufficiency (an issue where the soft palate does not close tightly against the back of the throat. Anomalies of the palate, particularly clefting, can cause difficulties in feeding and breathing. These difficulties can result in failure to thrive during infancy if not managed appropriately. As well as helping aesthetically, surgical repair, such as cleft palate repair and a procedure to lengthen the jawbone, eases these problems and may even eliminate them altogether.

CLAPA (Cleft Lip and Palate Association) offers support for people affected by cleft lip and palate

Skin

Skin and connective tissue features in children with KIS typically appear gradually after the newborn period and can change throughout childhood. These features can vary in how much they affect a person but include prominent fetal fingertip pads, fair skin, reduced fat under the skin (decreased subcutaneous fat) and mild wasting of the chewing muscles (mild atrophy of the temporalis and masseter muscles).

Teeth

Dental concerns are common. A number of issues described include the misalignment of teeth (malocclusion), which may appear gradually after the newborn period; an undersized jaw (retromicrognathia), which has been seen in many individuals; and wide or thick alveolar ridges (the bones in the mouth that hold the teeth).

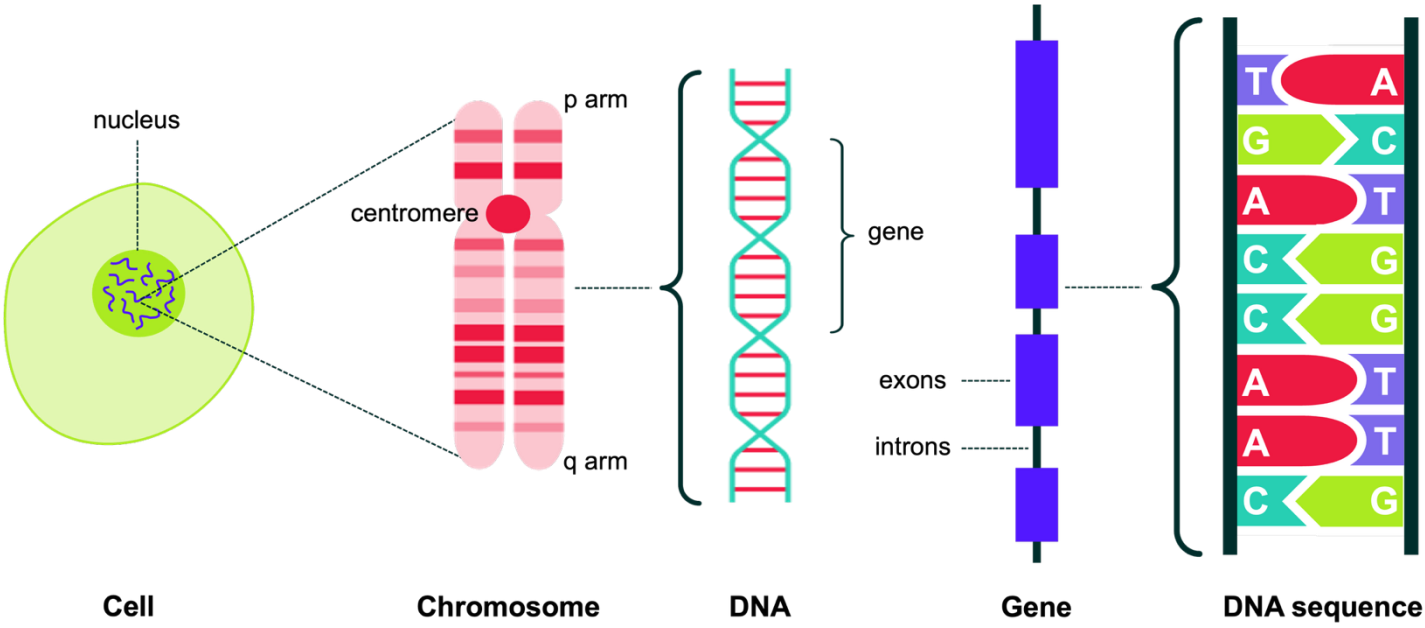
Children and adults may also benefit from specialist hospital dental services and may require treatment under general anaesthesia. In some cases, a surgical procedure to lengthen the jaw (mandibular distraction osteogenesis) may be considered.

This section includes some more complicated scientific terms and concepts - don't worry if it's a lot to take in, you can always come back to this section later if you want to.

Genes and chromosomes

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes, therefore, contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.

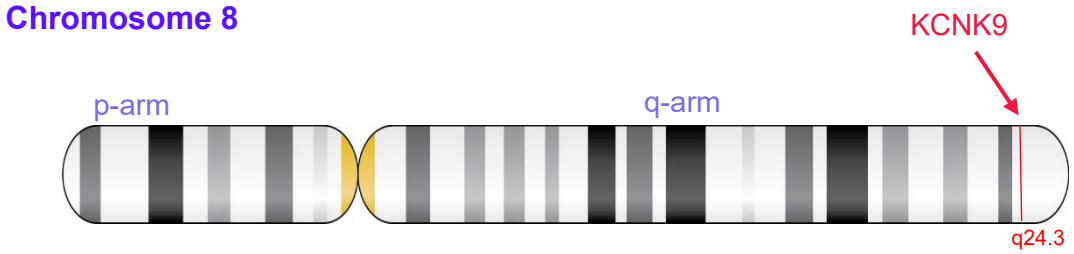
DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes in the DNA sequence (variants) present in everyone's genes. It is variants in our genes that make each one of us unique individuals.



What causes KIS?

KIS is caused by specific changes (known as pathogenic variants) to the DNA sequence of a gene called KCNK9 (KCNK9 is an abbreviation of the gene's full name, derived from Potassium channel subfamily K member 9).

The KCNK9 gene is located in the long 'q' arm of chromosome 8 in a region called 8q24.3 as shown in the image below.

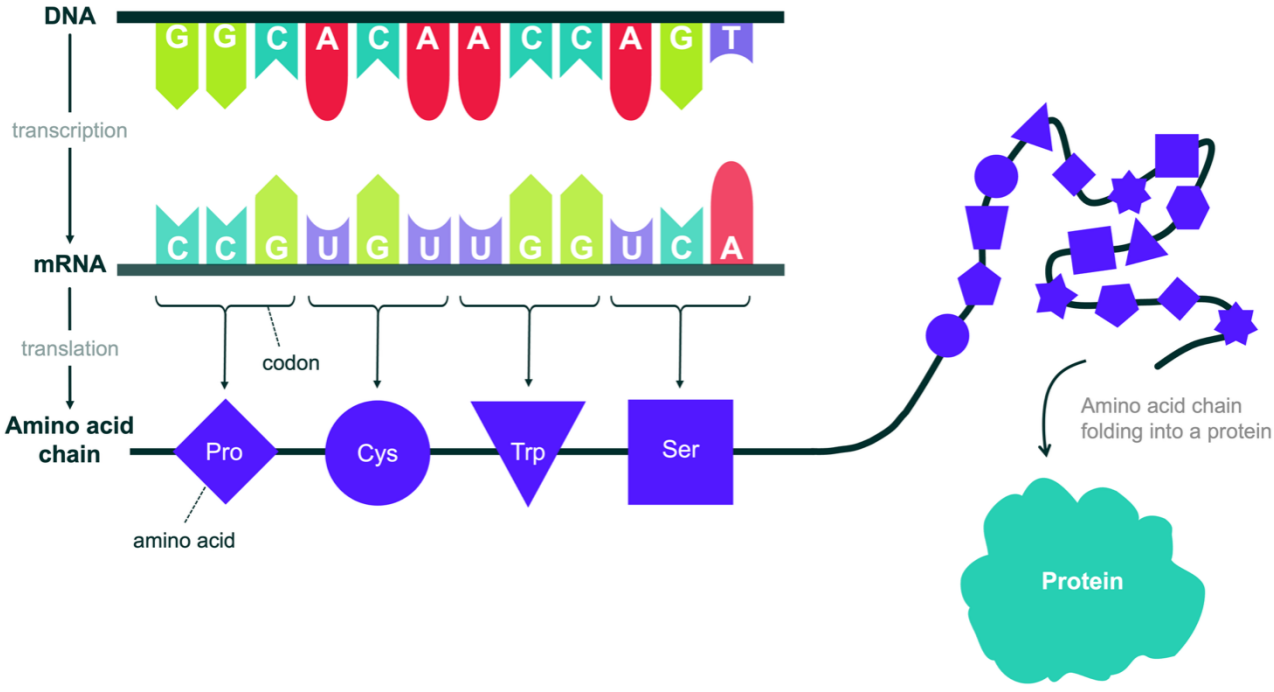


We have two copies of chromosome 8 in our cells, so we also have two copies of the KCNK9 gene. KIS occurs when only one copy of the KCNK9 gene is affected. This type of inheritance is known as autosomal dominant since all numbered chromosomes are called autosomes and genetic conditions that occur when only one copy of an autosomal gene is affected are known as dominant.

Unique publishes a separate guide to single gene disorders – autosomal dominant inheritance

However, the KCNK9 gene is also subject to a process called genomic imprinting. This means that only the copy of the gene inherited from the mother is active; the copy inherited from the father is silenced. For this reason, KCNK9 imprinting syndrome only occurs when the pathogenic variant is on the maternally inherited copy of the gene.

Most genetic conditions are caused by changes to genes that provide instructions for making proteins; these are called protein-coding genes. KCNK9 is one of thousands of these protein-coding genes. Proteins are molecules that are made up of long chains of chemicals called amino acids and play critical roles in the body. This is because proteins are essential for lots of processes, such as breaking down food, moving our muscles, and growing the body's organs and making sure they function properly. To make these amino acids, a copy of the DNA sequence is created, called messenger RNA (mRNA). mRNA uses the same A, C and G bases as DNA, but the 'T' bases are swapped to 'U' bases. Within a gene, each three-letter sequence (codon) of mRNA bases provides the instructions for one amino acid. Changes to the amino acid sequence can affect the function of the protein.



The role of the TASK3 protein

The protein made from the KCNK9 gene is called TASK3. This protein forms a channel that is mainly found in the brain and nervous system where it is important for controlling the activity of nerve cells (neurons) and is important for brain development. It does this by creating a channel that helps to stabilise the resting electrical state (resting membrane potential) of neurons, which is critical for controlling their activity.

Different types of genetic changes

The specific type of genetic change in the KCNK9 gene that a person has is an important factor that could influence an individual's symptoms and features. Research suggests that different types of variants can affect the TASK3 protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with KIS.

People with KIS typically have a gene sequence variant type called a missense variants, as opposed to a variant that causes the loss of the entire gene.

- Missense variants: Where one amino acid is replaced by another, producing an altered protein (see Genetic test results).

These variants are often thought to result in altered protein that is produced as a result of the missense variant is not able to perform its usual function or has reduced levels of activity. Sometimes a variant may cause a gain of function (GOF), which means the altered proteins resulting from the missense variant can gain a new or increased level of activity. Depending on the genetic variant, the way the change alters the function of the TASK3 potassium channel may therefore vary, resulting in either a 'gain-of-function' (where the channel is too active) or a 'loss-of-function' (where the channel is not active enough).

Despite some variants leading to a loss of function and others to a gain of function, they all cause forms of KIS. This has important implications for potential treatments. A treatment that stimulates the channel might be effective for an individual with a loss of function variant but could be unhelpful for someone with a gain of function where the variant causes typical or increased channel function. Therefore, understanding the specific functional impact of an individual's KCNK9 variant is a vital step in developing therapeutic strategies.

Genetic tests

KIS caused by gene sequence variants, can be identified by a type of genetic test called sequencing, such as whole exome sequencing (WES) or whole genome sequencing (WGS). Gene deletions can also be identified by a sequencing test but are more commonly detected using a different type of genetic test called a chromosome microarray (CMA), also known as an arrayCGH or SNParray.

Genetic Test Results

The results of genetic (genomic) testing are likely to be provided by a geneticist, a genetic counsellor or the clinician who ordered the test. An example result of a DNA sequencing test (e.g. WES or WGS), that can identify gene variants, is shown on the next page for the KCKN9 gene encoding the TASK3 protein:

p.Gly236Arg: c.706G>A in exon 2 of the KCNK9 gene (NM_001282534.2)

p.Gly236Arg	signifies the change to the protein: the amino acid glycine (Gly) has been replaced by the amino acid arginine (Arg) at position 236 in the sequence of amino acids that make up the protein
G>A	signifies the gene sequence change: the G nucleotide has been replaced by an A nucleotide
c.706	signifies the base pair position of the change within the gene sequence (the position where the G nucleotide has been replaced by the A nucleotide)
exon 2	signifies which part of the gene has been altered, in this case exon 2
KCNK9	signifies the gene that is affected
NM_001282534.2	this is the specific 'reference sequence' or blueprint of the gene that scientists use to identify the location of the variant

Why did this happen?

When children are conceived, their parents' genetic material (DNA) is copied in the egg and sperm that makes a new child. The biological copying method is not perfect, and random changes occur in the genetic code of all children that are not seen in the DNA of their parents. This happens naturally and is not due to the parents' diet, environment or lifestyle. Most of these DNA changes have no obvious effect. But in rare instances these random DNA changes can lead to health issues or affect development. When such a random change disrupts the function of the KCNK9 gene then a child will have KIS.

KIS is caused when there is a pathogenic variant in the copy of the KCNK9 gene that is inherited from the mother. The condition's mode of inheritance is due to a mechanism called genomic imprinting. For the KCNK9 gene, the copy inherited from the father is typically silenced or 'imprinted', meaning only the copy inherited from the mother is active, particularly in the brain. Consequently, the syndrome develops only if the active maternal copy has a pathogenic variant; a variant on the silenced paternal copy does not cause the condition. Usually, the pathogenic variant is inherited from an unaffected mother, who does not have any features of KIS. Occasionally, the pathogenic variant occurs as a new, random (or 'de novo') change on the maternal copy of the gene, meaning the change occurred for the first time in that family in the affected individual. It is important to recognise that no one should be blamed for variants in their DNA and no parent is at fault when a new DNA change occurs in their child.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. For KIS, the chance depends largely on the genetic status of the mother. This is because the condition is caused by a pathogenic variant on the copy of the KCNK9 gene that is inherited from the mother; the copy of the gene from the father is typically silenced.

Where the genetic alteration has been found to be de novo, or not seen in the blood testing of either parent, the chance of having another affected child is usually less than 1%. One reason why there is some residual chance of recurrence in de novo cases is due to the rare phenomenon called germline mosaicism. This is

when a parent carries a genetic change, but it is limited to some of their egg or sperm cells. The genetic change would not, therefore, be detected in the parents' blood tests. However, to date, no instances of maternal germline mosaicism have been reported for KIS.

In families where the KCNK9 pathogenic variant has been inherited from the mother, the possibility of having another child - either a girl or a boy - with KIS is 50% (1 in 2) in each subsequent pregnancy.

A female who inherits the pathogenic variant from her father will typically be an unaffected carrier and she would have a 50% (1 in 2) chance of having an affected child for each pregnancy. A male who inherits the pathogenic variant from his father will also be an unaffected carrier; he can pass the variant to his daughters, who are typically unaffected carriers but will have a 50% (1 in 2) chance of having an affected child for each pregnancy.

To date, no individual with KIS has been reported to have children.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with KIS. They can also discuss reproductive options such as prenatal testing during pregnancy and preimplantation genetic testing (PGT) for in vitro fertilisation (IVF).

Can KIS be cured?

Currently, there is no cure for KIS. However, knowing the diagnosis means that appropriate monitoring and interventions can be put in place.

Management

No clinical practice guidelines for KIS have been published (2026). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with KIS, to improve quality of life and reduce complications.

Children and adults with KIS should be under the care of a multidisciplinary team. The team should include a geneticist and paediatrician (for children) who can oversee care so that development and behaviour can be monitored, and the best help given in the form of different therapies. Individuals may also have evaluations with various specialist doctors.

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of KIS that are present in the child or adult who has been diagnosed with this genetic condition is recommended. This can determine which of the features of KIS are present and how severe they are. Management of this condition is supportive and requires a multidisciplinary team of specialists.

The following assessments are recommended:

- A physical examination to look for features such as joint contractures, scoliosis and cleft palate
- A feeding and swallowing evaluation to assess for feeding difficulties and investigate for gastro-oesophageal reflux disease (GERD)
- A respiratory (pulmonary) assessment, which may include a sleep study (polysomnogram) to investigate for obstructive or central sleep apnoea
- An eye (ophthalmology) assessment to check for reduced tear production (decreased lacrimation) and the associated chance of corneal dryness

- An ENT (otorhinolaryngology) assessment to evaluate for upper airway obstruction
- A neurologic assessment to determine the degree of low muscle tone and whether conditions such as global developmental delay are present. An electroencephalogram (EEG) may be performed if seizures are suspected
- An endocrine assessment to check for low blood sugar (hypoglycaemia), particularly during the newborn period and infancy
- A developmental assessment to screen for global developmental delay and to arrange early referral for therapies, including physical, occupational and speech therapy

Genetic counselling for affected individuals and their families should also be offered together with the provision of signposting to family support and resources.

Supportive care

Care for individuals with KIS is supportive and tailored to specific symptoms, as no formal management guidelines have been established. How a person with KIS is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists, which may include:

Clinical geneticist and genetic counsellor – to confirm the diagnosis and support families with informed decision-making.

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood; this may include a developmental paediatrician who conducts developmental assessments.

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system, who will assess strength, muscle stamina, motor skills and evaluate for seizures.

Gastroenterologist – a doctor who specialises in the digestive system and may help to manage feeding and swallowing difficulties, gastro-oesophageal reflux disease (GERD) and constipation.

Pulmonologist – a doctor who specialises in the respiratory system and may assess for issues such as obstructive and central sleep apnoea.

Otorhinolaryngologist (ENT) – a doctor who specialises in conditions of the ear, nose and throat and may evaluate for upper airway obstruction.

Endocrinologist – a doctor who specialises in hormones and their effect on the body, who will assess for hypoglycaemia (low blood sugar).

Orthopaedist – a doctor who specialises in musculoskeletal issues like joint contractures and curvature of the spine (scoliosis)

Ophthalmologist – a doctor who specialises in conditions affecting the eyes and will conduct assessments for decreased tear production (lacrimation) and subsequent possible corneal dryness.

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment to assist with fine motor skills and activities of daily living.

Physiotherapist/physical therapist (PT) – a health care professional who uses exercise, movement, manual therapy, education and advice to help with the body's strength and mobility to address low muscle tone (hypotonia) and delayed motor milestones.

Speech and language therapist (SALT) – a health care professional who helps with speech, language communication and sometimes feeding/swallowing difficulties, including managing severe feeding difficulties, swallowing problems (dysphagia) and oro-sensory disorders.

Psychiatrist – a doctor who specialises in mental health and may be involved in neurodevelopmental or neuropsychiatric evaluations.

Surgeon – a doctor who is specially trained to perform medical operations.

Plastic surgeon – who assesses and provides management for features such as cleft palate, bifid uvula and a recessed jaw (retrognathia).

Treatments and therapies

Early intervention can be beneficial and formal testing to assess specific, individual needs is recommended. An education, health and care plan (EHCP) in the UK, individualized education plan (IEP) in the US, or equivalent document in other countries, may be issued after a child has undergone an assessment, to help ensure that the educational, health and social provisions deemed necessary to support the child's needs are delivered.

Treatment will depend on the specific features and symptoms experienced by the person with KIS but may include:

Physiotherapy for low muscle tone (hypotonia), easy fatigability and gross motor delays, which usually includes exercises to build core strength, improve balance and enhance coordination to help children achieve motor milestones like sitting, crawling and walking, and to improve overall mobility. It also helps to manage musculoskeletal issues like joint contractures and scoliosis.

Occupational therapy for fine motor skill delays, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding and dressing).

Speech therapy for a range of speech and language delays or feeding/swallowing difficulties (dysphagia).

Cognitive therapy as part of a comprehensive developmental support plan to address intellectual disability.

Special bottles and teats to help manage feeding difficulties resulting from facial weakness and a poor suck.

Assistive devices such as ankle-foot orthoses (AFOs) to help with mobility and contractures.

Respiratory support, such as a continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) machine, for obstructive and central sleep apnoea.

Medications may be prescribed such as anti-seizure medications (ASMs), standard treatments for GERD or to treat transient neonatal hypoglycaemia (low blood sugar), or to manage acid reflux.

Surgery, such as the placement of a gastrostomy tube (G-tube) or repair of a cleft palate.

Surveillance

It is recommended that the following evaluations are carried out/considered to monitor an individual's existing symptoms, how they respond to care and treatment and whether any new symptoms emerge over time:

- Monitor for growth and adequate nutritional intake
- Evaluations by ENT for presence of micrognathia and cleft palate
- Gastroenterology (recommended every six months until age two, then annually)
- Learning and neuropsychiatric assessments to optimise the EHCP/IEP, including for behavioural differences such as ADHD and ASD
- Consider a neurologic review (including MRI and an EEG, if indicated for seizures)
- Consider a skeletal evaluation for issues such as joint contractures and scoliosis

- On-going examinations by an ophthalmologist to check for reduced tear production (decreased lacrimation) and risk of corneal dryness
- Consider regular meetings with an endocrinologist to monitor serum glucose levels for hypoglycaemia (low blood sugar).
- Consider need for a sleep study (polysomnogram) if obstructive sleep apnoea is suspected or if there is a history of sleep disturbance
- Assessment of the need for social support, such as respite care and home nursing care, or genetic counselling and family planning advice

Specialist nurses and/or other healthcare professionals may need to systematically and comprehensively plan a child or adult's treatment.

Research into new treatments for KIS

The genetic changes causing KIS affect development of the brain and other parts of the body before birth. Therefore, a complete cure is unlikely, even in the future, since the brain has already formed by the time a diagnosis is made. However, research into improved treatments and management for various features of KIS is ongoing.

Although KIS is a relatively rare condition, the KCNK9 gene has been the subject of a lot of research. One avenue of research is to find drugs that can rescue the function of the faulty TASK3 potassium channel, which is encoded by the KCNK9 gene. Preclinical studies have shown that a class of non-steroidal anti-inflammatory drugs (NSAIDs), including flufenamic acid and mefenamic acid, can partially rescue function of channels. Several children with KIS have been treated with oral mefenamic acid, and reports indicated they experienced increased energy and showed improved developmental milestones, although core clinical features of the syndrome remained. This approach remains investigational, and long-term studies and larger clinical trials are necessary to understand its effectiveness and potential outcomes. Currently (2026), there are no established gene therapy treatments for the syndrome.

Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

"We are aware of research in relation to the TASK3 potassium channel and are hopeful that advances will be made to help improve the quality of life for our daughter and others with the condition."

Families say ...

Our experience with KCNK9 imprinting syndrome touches almost every part of our son's daily life; muscle tone, feeding, speech, and learning; but it does not define who he is. Yes, there are real challenges: appointments, therapies, equipment, and the constant balancing act between safety and independence. There are also incredible strengths - determination, a unique sense of humor, deep empathy, and the way they push us to slow down and celebrate every small step.

We wish we had known earlier that progress can be slow but still meaningful, and that it is okay if your child's timeline looks very different from anyone else's. We wish someone had told us that using feeding tubes, wheelchairs, or communication devices is not a failure; it is just another way of meeting needs and unlocking potential. Make peace, as much as you can, with the fact that you will not have all the answers about the future, and instead focus on building a strong care team, saying yes to help from others, and protecting time for joy and rest.

If you are reading this soon after diagnosis, you may be scared and exhausted. That is normal. You do not have to become an expert overnight. Start with one thing at a time; find a trusted medical provider, connect with at least one other KCNK9 family, and remember that you are allowed to feel whatever you feel. Your love and advocacy matter more than any single test result. There will be hard days, but there will also be days when your loved one surprises you, and those moments are worth holding onto."

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. In 2026, Unique had 2 members with KIS. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (pubmed.ncbi.nlm.nih.gov/).

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Inform Network Support

Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted, Surrey, RH8, 9EE, UK
Tel: +44(0)1883 723356
help@rarechromo.org I rarechromo.org

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Websites, Facebook groups and other links:

KCNK9 Foundation
KCNK9 Facebook group

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This guide was produced as part of a collaborative project between the Manchester Rare Condition Centre, Shorthills AI and Unique (CA/AP). We thank the North West Genome Medicine Service Alliance for supporting the project.

Version 1.1 (CA/AP) [2026]

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