UNIQUE

UNDERSTANDING GENES & CHROMOSOMES

Mosaic variegated aneuploidy 1 (MVA1) syndrome

(BUB1B gene variants)

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with MVA1 syndrome caused by variants in the BUB1B gene. 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 MVA1 syndrome?

MVA1 syndrome, also referred to as premature chromatid separation (PCS) syndrome or variegated aneuploidy related to premature centromere division (PCD) is a rare genetic condition associated with features such as having a small head (microcephaly), potentially developmental delays and intellectual disability, seizures, low muscle tone (hypotonia) and an increased chance of developing certain cancers.

MVA1 syndrome can be caused by changes (variants) in a gene called BUB1B, as well as several other genes (not covered in this leaflet). The genetic changes lead to some cells and tissues in the body having a different number of chromosomes than the expected 46 chromosomes. Mosaic means that not all cells are affected, variegated means the change in chromosome number can be different from cell to cell, and aneuploidy means there are more or fewer chromosomes than expected present in the cells.

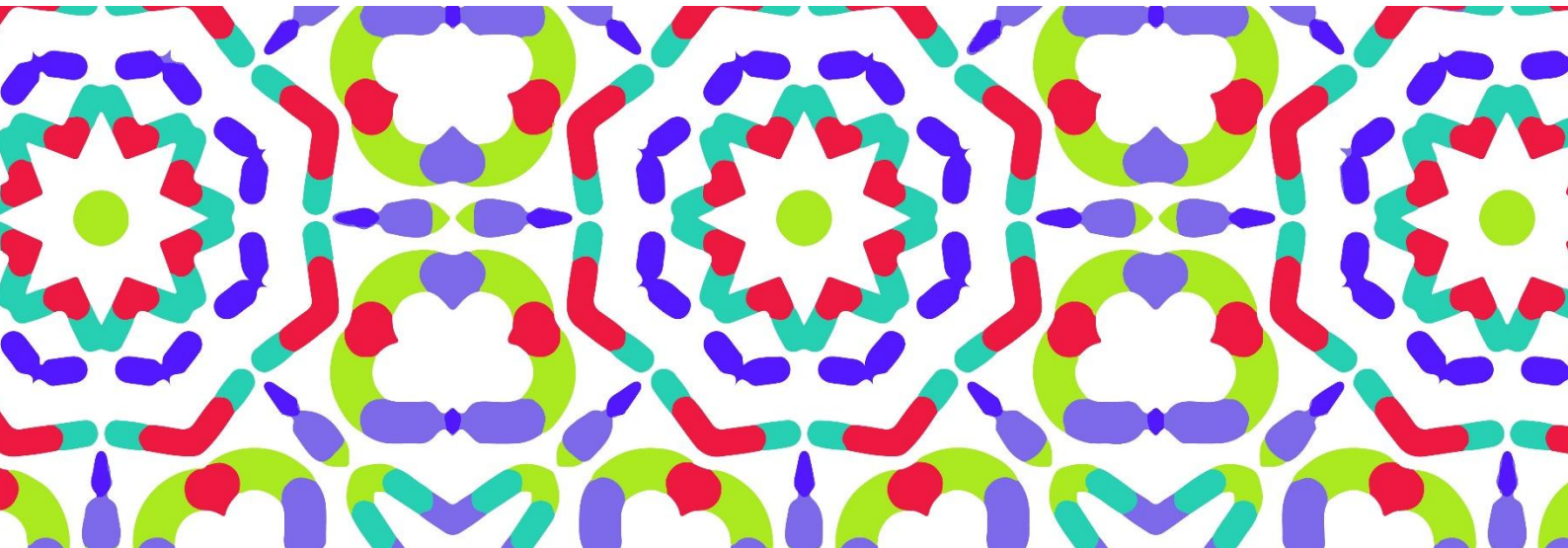
As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with MVA1 syndrome will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

How common is MVA1 syndrome?

MVA1 syndrome is extremely rare. Currently (2026) less than 50 individuals with MVA1 syndrome have been reported in the medical literature, but more are known to have been diagnosed. It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.

What features and symptoms do people with MVA1 syndrome have?

As is common with many genetic conditions, children and adults with MVA1 syndrome 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 MVA1 syndrome have:

- Slow growth before and after birth (pre- and post-natal growth retardation)
- An unusually small head (microcephaly)
- Intellectual and developmental delay, which can be variable in severity or mildness

Other possible features include:

- Eye anomalies, such as clouding of lenses (cataracts) and unusually small eyes (microphthalmia)
- Epileptic seizures, which may be unresponsive to medication
- Cancer, including cancer of the kidney (Wilms tumour) and soft tissue (rhabdomyosarcoma, including embryonal rhabdomyosarcoma) and blood (leukaemia)
- Structural brain anomalies
- Low muscle tone (generalised hypotonia)
- Feeding difficulties

Features that have been described in only a few people so far include:

(some of these features might not be related to MVA at all and coincidentally occur in a child or adult, or secondary to complications of surgery or one of the other core features of the condition)

- Heart anomalies
- Hormone (endocrine) dysfunction, such as hypothyroidism
- Kidney (renal) dysfunction, as well as a multicystic kidney
- Anaemia
- A benign tumour of blood vessels (hemangioma)
- Café-au-lait spots (a flat, pigmented birthmark)
- Cleft palate
- Gastrointestinal issues, such as duodenal atresia
- Urogenital anomalies in males, including undescended testicles (cryptorchidism) and ambiguous genitalia
- Paralysis of all four limbs (quadriplegia) (this has only been reported in one publication and it is unclear whether this is truly related to MVA1)

Pregnancy and birth

While some pregnancies are unremarkable and proceed without complication, concerns during pregnancy have been reported, often following mid-pregnancy anomaly scans. Where a cause for concern was noted, most often parents reported slow growth in the womb (intrauterine growth retardation IUGR), an unusually small head (microcephaly) or anomalies of the heart and brain. Other ultrasound findings can include, blocked/closed small intestine (duodenal atresia), increased fluid behind the neck (nuchal translucency), ovarian cysts and a build-up of fluid in the abdomen (ascitic fluid). Again, since the number of individuals reported with this condition is so small, some of these features might be coincidental and unrelated to the MVA.

The majority of pregnancies go to term but some babies are born prematurely. Many babies show some signs of difficulty at birth, including breathing problems (respiratory distress) requiring admission to a Neonatal Intensive Care Unit (NICU), difficulties with feeding due to a poor suckling reflex or a heart condition. Birth weights are usually below average. Often babies grow very slowly in the womb and are tiny at birth. Many new-born babies have generalised low muscle tone (hypotonia) and may be described as “unusually inactive and placid”, a feature that may alert doctors to an underlying condition. These growth and feeding challenges often persist after birth.

Appearance

Certain facial features are reported to be found more often in children with MVA1 syndrome than in other children. However, most of these features can occur in children without MVA as well, and in children with MVA they are probably over-reported. This means, that it is not common for a child with MVA to have unusual facial features that are sometimes associated with genetic conditions.

An unusually small head size (microcephaly), however, is a common finding. Other features related to the head and face shape can include a triangular-shaped face, a flattened back of the head (brachycephaly), underdevelopment of the middle part of the face (midface hypoplasia), and a small lower jaw (micrognathia).

It has not yet been documented if these features change or become more or less noticeable as a child gets older.

Development

Gross and fine motor skills

Developmental delay, which can be profound, has been reported in all children with MVA1 syndrome so far (2026) and is typically present from early infancy. Low muscle tone (generalised hypotonia) can be observed within the first few months of life and may affect mobility. A significant delay in reaching developmental milestones such as sitting, crawling and walking is expected and some individuals may not achieve these milestones. The strength, movement and coordination of facial muscles, including those of the mouth (oral-motor function) can also be affected from birth, leading to a poor suckling reflex.

Some children may have an unusual gait when walking because of balance issues (known as ataxia). Some individuals may also show recurrent stereotyped movements, such as upper arm waving. In the most severe and unusual form of this condition, motor impairment appears to have manifested as paralysis of all four limbs (quadriplegia), although it remains unclear whether this is truly related to MVA1. For some, independent walking may not be achieved, and many individuals require complete assistance from caregivers for all physical tasks and may need adaptive equipment such as specialised wheelchairs.

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Intellectual development and learning

Most children with MVA1-related disorders have learning (intellectual) disability (LD/ID) or learning difficulties ranging from mild to profound.

Most children will require significant additional support with their learning throughout their education. They are likely to require extensive and lifelong support to develop conceptual, social and practical living skills. 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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"Our son appears to be pretty OK when it comes to his mental development. He attends mainstream school. The only support he requires is physical help to get around the school due to his short stature."

Speech and language

Children with MVA1 syndrome typically experience some degree of speech and language delay and many may find it difficult to co-ordinate movement of their lips, jaw and tongue to make the right sounds (apraxia of speech). These challenges are linked to the child's low muscle tone and learning difficulties and may stem from a combination of physical and neurological factors. Some children may also have a cleft palate or hearing impairment which can affect speech development. The eventual range of speech and language achievement is broad.

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. For individuals with limited or no speech, Augmentative and Alternative Communication (AAC) methods, including pointing, pictograms, gestures, facial expression and simplified sign language and high-tech communication systems (aided communication) have enabled some to communicate their thoughts and needs effectively.

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Feeding

Feeding issues in the new-born period are common. Low muscle tone may contribute to difficulties with swallowing and some babies suck weakly or refuse to eat, so may need high energy milks to encourage weight gain. Some 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, medication, nutritional supplements or, for some children, insertion of a tube that is passed through the nose to the stomach (nasogastric tube (NGT)) or directly through the stomach wall (percutaneous endoscopic gastrostomy tube (PEG/G-tube)). Frequent episodes of vomiting during the first few months of life have also been reported.

In addition to these functional feeding difficulties, structural gastrointestinal anomalies have also been reported, including an obstruction of the small intestine (duodenal atresia) that requires surgical correction. Other issues that have been reported include aspiration (where fluid, food or saliva enters the airway or lungs).

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“Getting high calorific food into our son (and all children with MVA), is vital. It’s also often challenging as our son has a very small appetite. He tends to eat a little and often, rather than 3 square meals a day!”

Growth and stature

Most children with MVA1 syndrome are noted as having growth delay, which often begins before birth (intrauterine growth restriction or IUGR). Most of these children also have a smaller than expected head size (microcephaly). Beyond infancy, height and weight is variable and continued growth challenges or failure to thrive can be complicated by significant feeding difficulties. For some children, hormone (endocrine) dysfunction, such as hypothyroidism, may also be a contributing factor. In the end, most children with MVA are and remain of short stature.

Behaviour

Behavioural challenges can occur during infancy, but are common in all children, including refusal to eat. It is important to note that the literature currently lacks specific information on the prevalence of conditions such as autism spectrum disorder, attention-deficit/hyperactivity disorder, anxiety, or mood disorders, suggesting these areas have not yet been a focus of clinical research. These conditions are common in all children and might be more common in children with MVA, potentially secondary to their other medical problems and needs.

Unique publishes a separate guide to Challenging Behaviour

Puberty

There is limited information available about puberty in children with MVA1 syndrome. There is no direct evidence to suggest that differences in timing of puberty (such as delayed or early puberty) are typical features of MVA.

Unique publishes a separate guide to Puberty

Adulthood

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any learning disability or intellectual disability (LD/ID), possible on-going medical concerns and improvements in early intervention and therapies/treatments. Developmental delay can develop into learning difficulties and intellectual disability and in that case, will persist in adulthood.

Significant health concerns include an increased risk of developing cancer and kidney disease. This is a lifelong risk.

Currently (2026), there is not much information available in the medical literature about adults with MVA.

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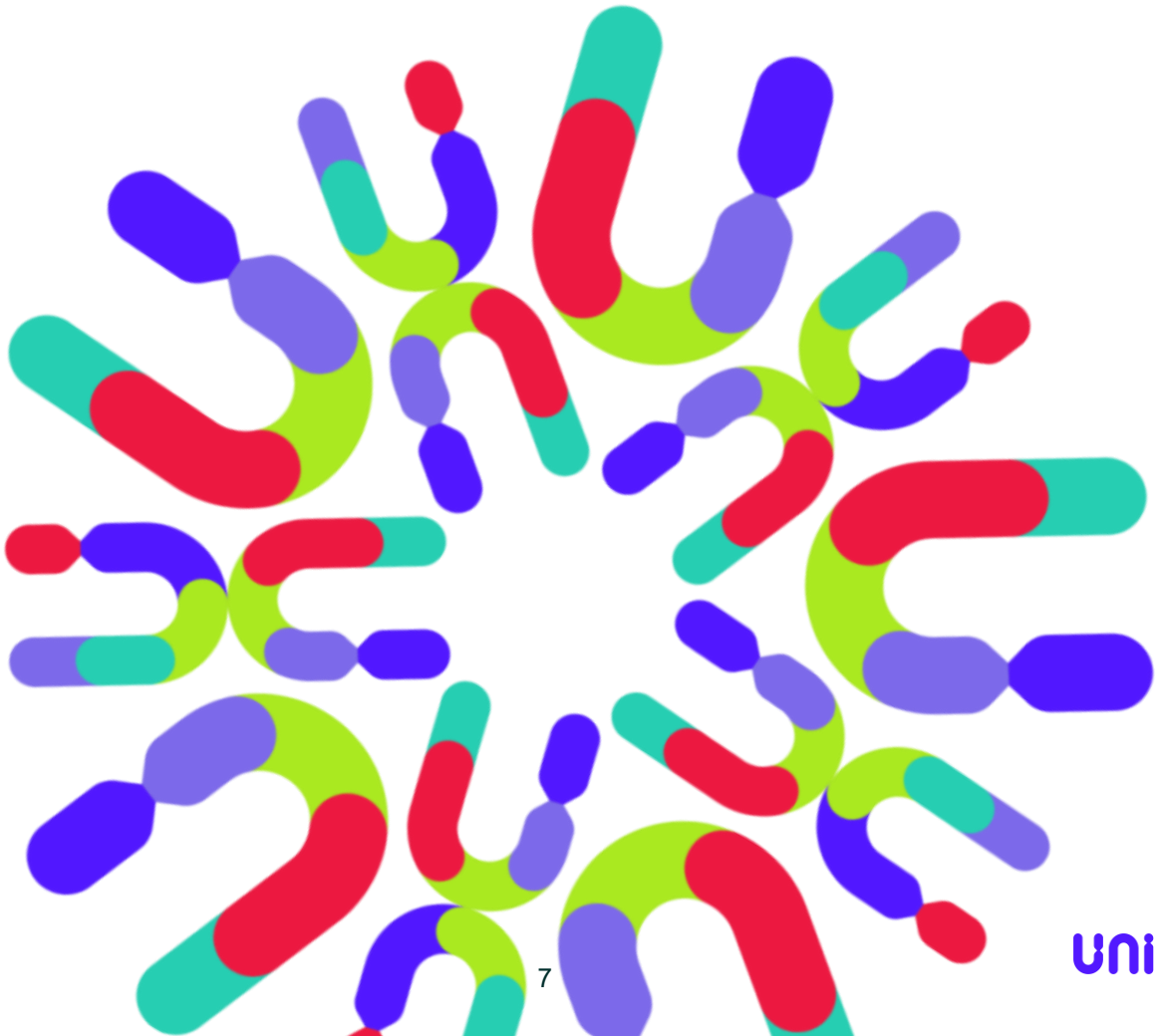

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Medical concerns

The following medical concerns have been found in children with MVA1 syndrome. They are not found in all children so not all children with MVA1 syndrome will be affected.

> ***Having a child with MVA is challenging on many fronts. The condition causes the need for medical input across multiple disciplines – oncology, nephrology, haematology (as, for our son, the cancer was in his liver), immunology and endocrinology. This takes its tole on the child and parents. On schooling and on your career. You need to devote a lot of time to hospitals!"***

Heart

A heart condition(s) has been found in a few people reported so far with MVA1 syndrome, which can be present at birth (congenital). The type of heart condition(s) is variable but include anomalies affecting the size and structure of the heart muscle and valves. The frequency of these heart conditions is not currently known.

Brain

Children with MVA1 syndrome can have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. Some of these changes may also be detected before birth on a fetal ultrasound scan. The changes seen vary, and their meaning is not always known, but they can be related to seizures.

Seizures

Children with MVA1 syndrome can experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Age of onset can vary considerably, with one report of a first seizure at seven months of age. Seizures may be isolated to a single incident or occur more regularly and more than one type of seizure may be present in the same individual.

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. Initial EEG recordings may not show any anomalies. Characteristic findings can include a disorganised background rhythm with multifocal spike and wave patterns, and these findings can change over time. Brain magnetic resonance imaging (MRI) is also used to look for any underlying structural brain anomalies.

Seizures can cause a lot of worry for families and can be frightening to observe, but in some 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.

Eyes and sight

Eye and vision anomalies have been reported in some children with MVA1 syndrome, and a thorough evaluation by a paediatric ophthalmologist is recommended at diagnosis. The most frequently reported conditions are clouded lenses at birth (congenital cataracts), which can affect one or both eyes, and uncontrolled repetitive eye movements (nystagmus). A less common finding is microphthalmia, where one or both eyeballs are atypically small.

Breathing

Babies and children with MVA1 syndrome can have respiratory concerns, which can be related to low birth weight or prematurity. This may become less frequent with age and maturity. In some children the respiratory distress at birth requires breathing support, such as intubation (where a flexible breathing tube is passed through the mouth or nose into the windpipe). In some older individuals, other issues such as the build-up of fluid around the lungs (pleural effusion and chylothorax) have occurred.

During childhood there may be an increased frequency of respiratory infection, which can be related to a low weight, dietary issues, hypotonia of breathing muscles and potentially (this has not been properly investigated yet) also to shortcoming of the immune system.

> ***We have begun to learn from other ultra-rare disease charities, who have kids with similar symptoms. For examples, kids with Bloom syndrome are put on low dose antibiotics to give them increased resilience over the winter months to respiratory infections. We have borrowed that approach for our son and it is working well!! We need to share more ideas between RD charities!!"***

Teeth

A small lower jaw (micrognathia) can lead to overcrowding of teeth and a misaligned bite (malocclusion). Discoloured teeth have also been reported. In general, but this counts for all children, a high standard of dental care is important.

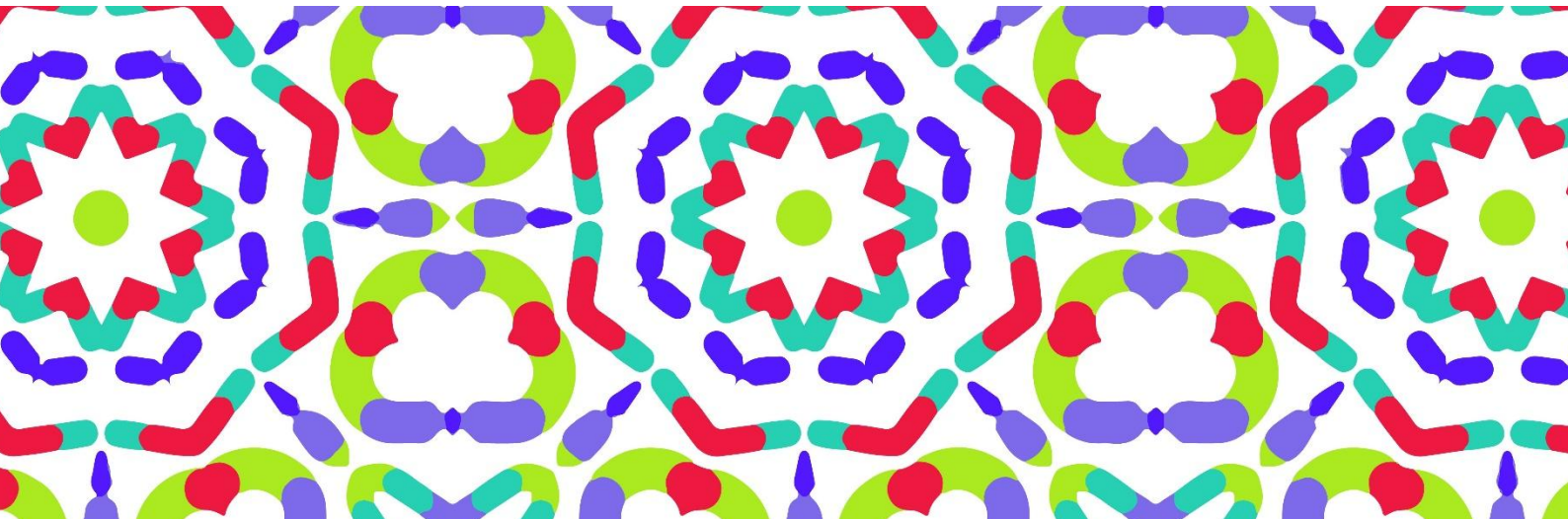
Kidney and urinary tract

A few babies are born with minor anomalies of the kidneys and/or urinary tract, which are not always clinically relevant. The main concern for the kidneys in childhood, is a high risk of developing a Wilms tumour (nephroblastoma), a type of kidney cancer.

Genitals

Anomalies of the genitals are not a frequent feature of MVA1 syndrome, but have been reported in a few individuals. Specific features that have been reported include:

- In males, ambiguous genitalia, undescended testes (cryptorchidism), a change in position of the whole normally at the end of the penis, to the underside (hypospadias), a curved penis and split (bifid) scrotum (that can be corrected by surgery if needed)
- In females, ovarian issues are notable, with reports of ovarian cysts and polycystic ovary syndrome (PCOS). Specific types of cancer have also been described in a few females (see the Cancer section of this guide below)



Tumour susceptibility

Children and adults with BUB1B syndrome have an increased risk of developing cancer. The age of onset can be very early, a matter of a few months or years. Childhood tumours are more common, especially rhabdomyosarcoma and Wilms's tumours. Some BUB1B gene variants may also predispose individuals to cancers of the stomach or intestines (gastrointestinal cancers) later in adulthood.

Different types of cancers reported in children and adults with MVA1 syndrome so far have been identified in many different parts of the body including:

- Soft tissue: this can occur at a very young age (embryonal rhabdomyosarcoma). These are tumours of muscle tissue and they can develop in different areas, such as the head, neck, bladder or genitals
- Stomach and intestines: known as gastrointestinal cancers
- Blood: different blood (haematological) cancers such as those that arise in bone marrow (leukaemia), or lymph nodes (lymphoma)
- Kidneys: e.g. Wilms tumour

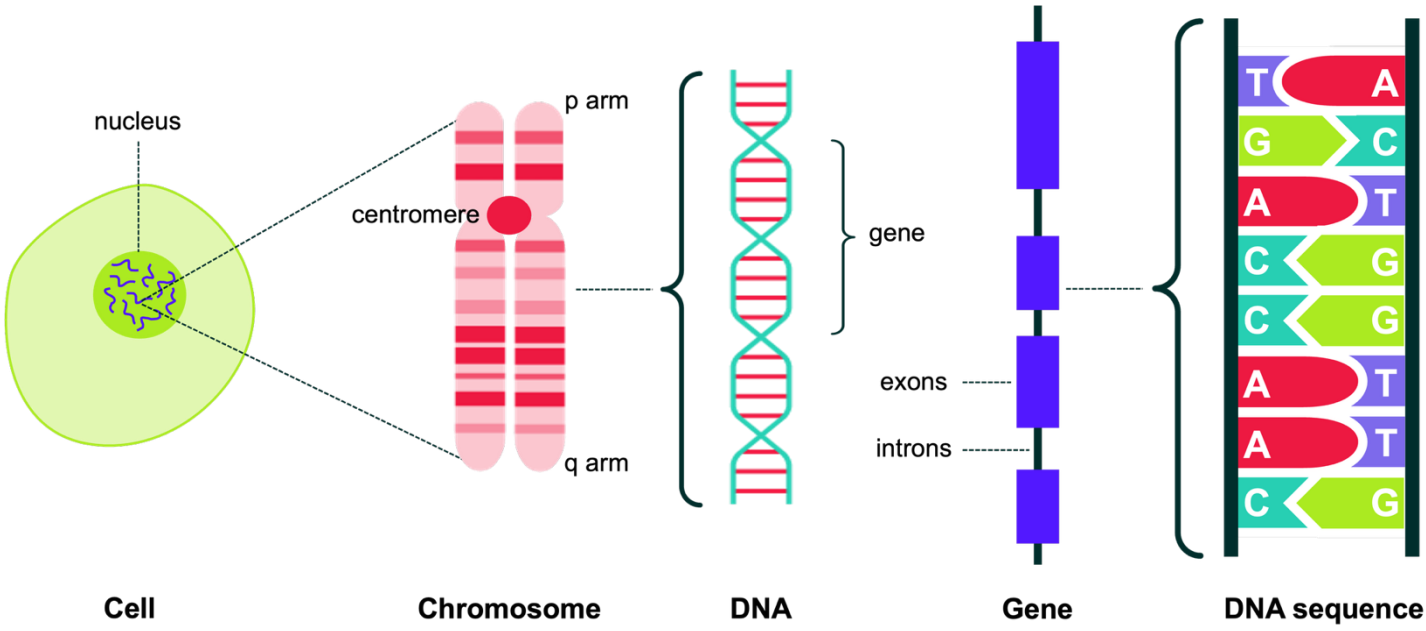
> ***We have 3 monthly scans for cancer".***

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.

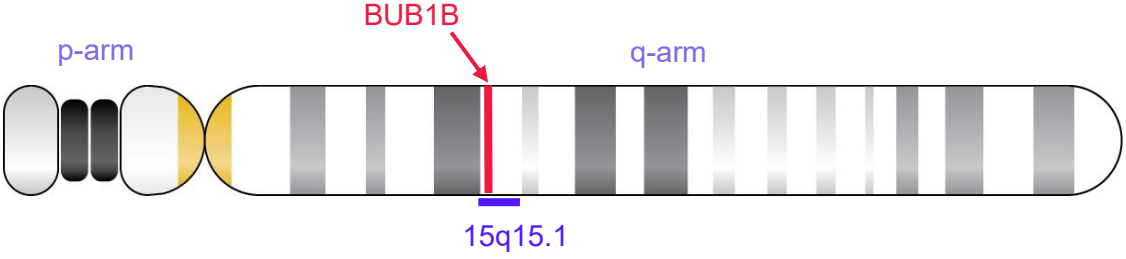


What causes MVA1 syndrome?

MVA1 syndrome is caused by specific changes (known as pathogenic variants) in the DNA sequence of a gene called BUB1B (also known as BUB1 Mitotic Checkpoint Serine/Threonine Kinase B). There are also other types of MVA that are caused by variants or deletions of different genes, that are not discussed in this guide.

The BUB1B gene is located in the q arm of chromosome 15 in a region called 15q15.1 as shown in the image below.

Chromosome 15

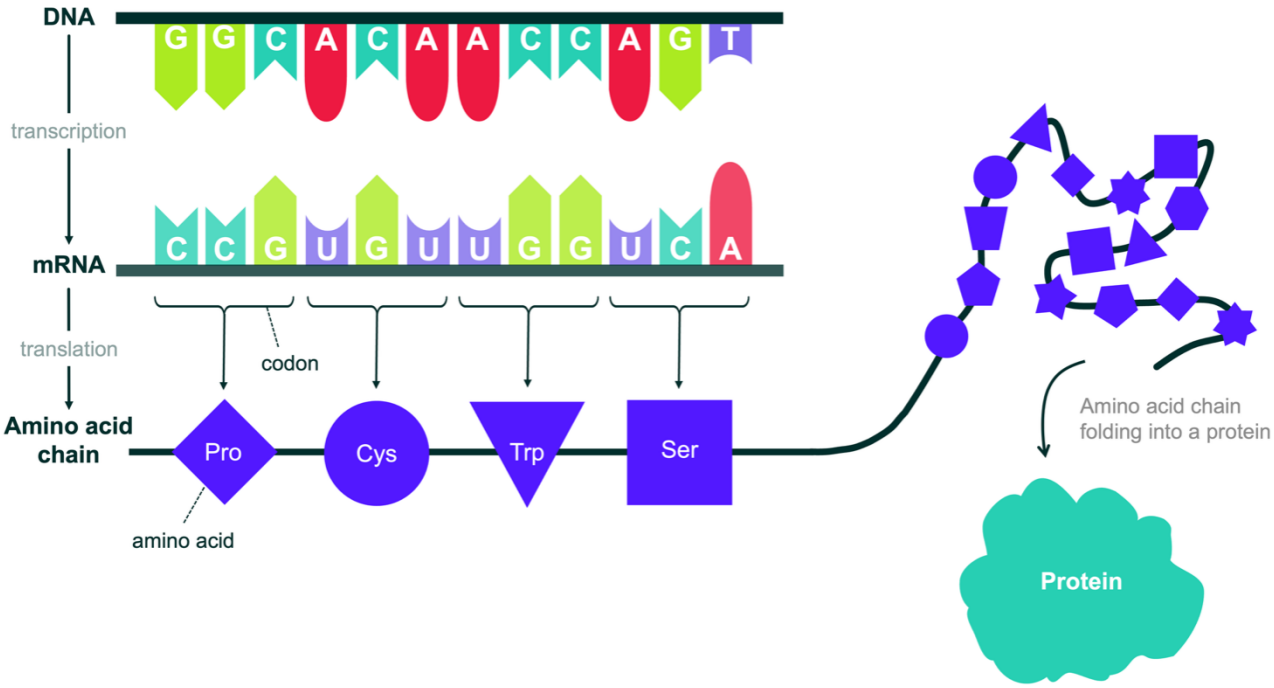


We have two copies of chromosome 15 in our cells, so we also have two copies of the BUB1B gene. MVA1 syndrome occurs when both copies of the BUB1B gene contain a change in the genetic code. This is known as autosomal recessive since all numbered chromosomes are called autosomes and genetic conditions that only occur when both copies of an autosomal gene are affected are known as recessive. Individuals with MVA1 syndrome do not necessarily have both copies of the BUB1B gene affected in the same way, they often have different changes to the gene, this is known as compound heterozygosity, meaning they have a different type of pathogenic DNA variant affecting each copy of the BUB1B gene.

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

Genes and proteins

Most genetic conditions are caused by changes to genes that provide instructions for making proteins; these are called protein-coding genes. BUB1B 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 BUBR1 protein

The BUB1B gene provides the instructions for making a protein called BUBR1. This protein is a key part of a monitoring system in our cells called the spindle assembly checkpoint (SAC) which is important during cell division (mitosis). As we grow and develop, our cells need to continuously make copies of themselves, they do this by creating a copy of our genetic material and then splitting in two, making sure that each new cell has exactly the same set of chromosomes. The SAC makes sure that when a cell divides into two cells, the correct number of chromosomes end up in each of the new cells.

Pathogenic DNA variants in the BUB1B gene can affect this monitoring system, which can lead to cells having an incorrect number of chromosomes (aneuploidy) after they divide. This is the underlying cause of MVA1 syndrome and the chromosomal instability is linked to cancer predisposition. Also, in the developing brain, a lack of functioning BUBR1 protein can mean that cells with the incorrect chromosome number are destroyed by the body (in a natural 'cleaning up' process), resulting in less cells available to divide correctly to form the brain and head (neural progenitor cells), which is thought to be a major cause of a smaller than expected head size (microcephaly).

Different types of genetic changes

Different types of pathogenic variants have been identified in the BUB1B gene. These include variants known as missense, truncating (nonsense and frameshift), splice-site, insertions and deletions as described below. These variants are often thought to be loss of function variants (LOFs), which means the smaller or altered protein is not able to perform its usual function or has reduced levels of the protein's activity.

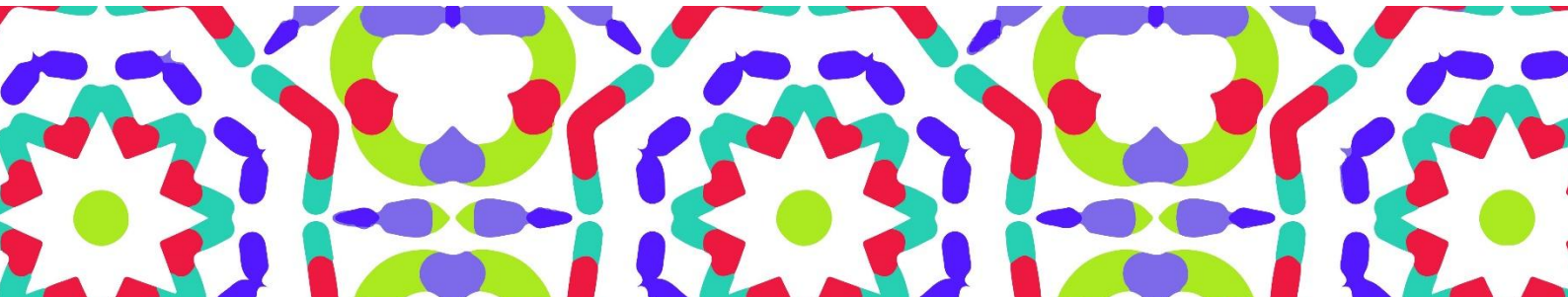
Gene sequence variants, loss of function (LOF): People with MVA1 syndrome are more commonly found to have a gene sequence variant, as opposed to a deletion of the entire gene. Such variants include:

- Nonsense variants: Where the amino acid change results in a premature 'stop' signal, stopping protein production too early, leading to a shorter, unfinished (truncated) protein
- Frameshift variants: Where the DNA coding sequence is shifted by the addition or deletion of individual DNA bases which means the incorrect amino acid sequence is used to produce the protein or there is a premature 'stop' signal
- Missense variants: Where one amino acid is replaced by another, producing an altered protein
- Splice-site variants: Where a genetic change occurs at the boundary of an exon and intron, which can affect the splicing process and lead to an anormal BUB1B protein
- Insertions: Where a piece of DNA is inserted into the gene, again leading to an abnormal BUB1B protein
- Deletion: Where a piece of DNA has been deleted, it's size can range from a single base-pair to a large deletion involving the entire gene (and possibly other genes in this region of the chromosome)

These different categories of gene changes are not mutually exclusive. Deletions and insertions are often frameshift variants.

The specific type of genetic change in the BUB1B gene is an important factor that could influence an individual's symptoms and features. Research suggests that different types of variants can affect the BUBR1 protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with MVA1 syndrome.

Often, individuals with MVA1 syndrome have two different types of variants (this is known as compound heterozygosity), often one truncating variant and one missense variant. This combination results in significantly reduced levels of functional BUBR1 protein, rather than a complete loss of the protein (the gene variant that allows for some form of functional protein is known as hypomorphic). A complete loss of BUBR1 protein is believed to be incompatible with life.



Genetic Tests

MVA1 syndrome caused by gene sequence variants or deletions, can be identified by a type of genetic test called DNA sequencing, such as whole exome sequencing (WES) or whole genome sequencing (WGS).

Unique publishes separate guides to DNA sequencing

Larger deletions involving the BUB1B gene can also be identified using a different type of genetic test called a chromosome microarray (CMA), also known as an arrayCGH or SNParray.

Unique publishes separate guides to DNA sequencing, arrayCGH and SNParrays

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. Depending on the test that was carried out, someone with MVA1 syndrome might have results that look like the example below.

An example result of a DNA sequencing test (e.g. WES or WGS), that can identify gene variants, is shown here for the BUB1B gene:

BUB1B c.2530 C>T p.L844F (NM_001211.6)

BUB1B	signifies the gene that is affected
c.2530	signifies the base pair position of the change within the gene sequence, 2530
C>T	signifies the gene sequence change: the C nucleotide has been replaced by a T nucleotide
p.L844F	signifies the change to the protein: the amino acid leucine (L) has been replaced by the amino acid phenylalanine (F) at position 844 in the sequence of amino acids that make up the protein
NM_001211.6	this is the specific 'reference sequence' or blueprint of the gene that scientists use to identify the location of the variant

Unique publishes a separate guide to Interpreting Genetic Test Results

Why did this happen?

In almost all people identified so far (2026) with MVA1 syndrome both parents passed on a copy of the MVA1 gene with a pathogenic variant to their child with MVA1 syndrome, so one variant was inherited from the biological mother and one from the biological father. There is nothing that happened before or during the pregnancy that caused this to happen. We all have small changes in our genes, and it is by chance that two parents have alterations in the same gene, or because the parents are related by blood and share a recent common ancestor. It is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when DNA changes are present in their child.

For many genes, including the BUB1B gene, having only one copy of the fully functional gene is enough for the body's healthy functioning. Therefore, when parents have only one copy of the BUB1B gene with a variant they are typically unaffected and do not know they are carriers of the variant.

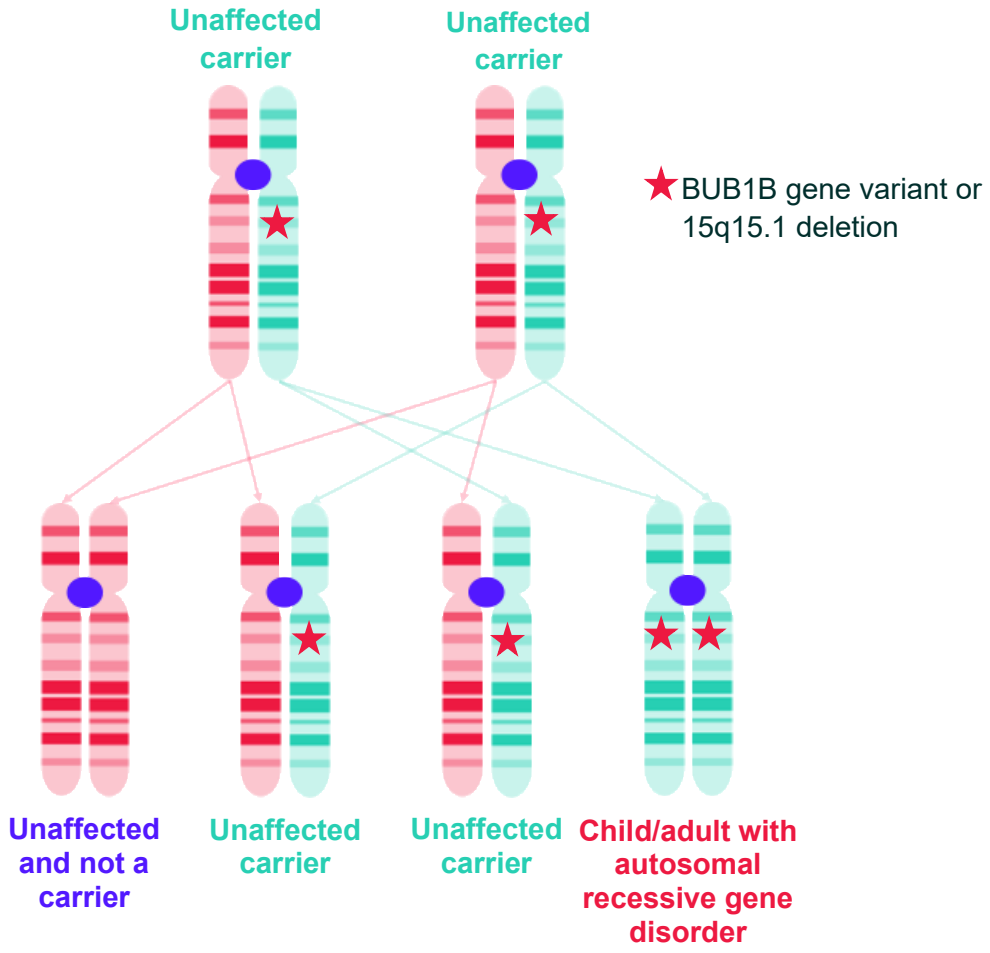
When children and adults are identified as having changes to both copies of the BUB1B gene, they are not necessarily the same type of genetic change. Some individuals with MVA1 may carry a gene variant in one copy of the gene and the other copy may be affected in a different way, such as being partially or fully absent due to a deletion or altered due to a different chromosomal rearrangement.

It is also possible, but incredibly rare, for children to inherit both copies of the same gene from one parent, and no copy of the gene form the other parent. This is known as uniparental disomy (UPD). If the parent form whom both BUB1B copies are inherited is a carrier of a BUB1B pathogenic variant, the child can have MVA without the other parent being a carrier. Again, this is incredibly rare.

Unique publishes a separate guides to UPD and deletions and microdeletions

Can it happen again?

The possibility of having another child affected by a rare autosomal recessive gene disorder is usually 25% (1 in 4) in each future pregnancy of the parents. Theoretically there is a one in four (25%) chance their child would have MVA1 syndrome, a one in two (50%) chance their child would be an unaffected carrier (like the parents) and a one in four (25%) chance of their child being unaffected and not a carrier. Carriers are typically healthy and do not show the clinical features of the syndrome. This chance resets for each pregnancy.



Once a person has been diagnosed with MVA1 syndrome, genetic testing can be carried out on relatives who may also carry the pathogenic variant in the BUB1B gene. This includes siblings of an affected child, who should be tested to determine if they are also affected (which is important for cancer monitoring) or if they are carriers for their own future family planning. Other relatives such as aunts, uncles and cousins also have an increased chance of being carriers. For couples who are carriers, there are reproductive and diagnostic options available to greatly decrease the risk of having another affected child. These include prenatal diagnosis during pregnancy, such as chorionic villus sampling (CVS) or amniocentesis, to determine if the foetus is affected. Prenatal ultrasound alone is not reliable to confirm or exclude a diagnosis of MVA in an unborn baby.). For couples using in vitro fertilisation (IVF), preimplantation genetic testing (PGT) can be used to test embryos for the specific familial BUB1B variants before they are transferred.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with MVA1 syndrome (MVA syndrome).

Unique publishes separate guides to Planning your next child, Prenatal genetic testing and diagnosis, A clinical genetics appointment and Supporting siblings of children with a rare genetic condition

Can MVA1 syndrome be cured?

There is no cure for MVA1 syndrome since a lot of the effects of the genetic change took place before or during a baby's formation and development. Instead, medical care is focused on managing symptoms and monitoring for complications, especially cancer.

Treatment is supportive and tailored to an individual's specific health issues. An important aspect of management is surveillance for cancer, as individuals with MVA have an increased predisposition to malignancies, often during childhood.

Management

No clinical practice guidelines for MVA1 syndrome have been published (2026). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with MVA1 syndrome, to improve quality of life and reduce complications.

Children and adults with MVA1 syndrome are likely to be under the care of a multidisciplinary team. The team should include a paediatrician and often in addition paediartic surgeons, oncologists and geneticists who can oversee care so that development and behaviour can be monitored, and the best help given in the form of different therapies.

> ***Finding out your child has MVA is quite a shock. Even more of a shock when you then find out there is no treatment available. The MVA Society is changing that. We are on a mission to find a treatment for this ultra-rare condition."***

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of MVA1 syndrome 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 MVA1 syndrome are present and how severe they are, and is used to initiate surveillance for the increased risk of cancer.

The following assessments are recommended:

- A physical examination to look for characteristic features. This should include measurement of weight, length and head circumference to assess for growth difficulties
- A cardiac assessment to look for congenital (present at birth) heart defects, which can include atrial septal defect (ASD) and atrioventricular septal defect (AVSD)
- A neurologic assessment to determine whether conditions such as developmental delay, intellectual disability, low muscle tone (generalised hypotonia) and seizures are present. Brain magnetic resonance imaging (MRI) or an electroencephalogram (EEG) do not need to be routinely done, they are usually requested when there are neurological symptoms such as seizures
- A gastroenterology assessment to evaluate feeding, as difficulties are common
- A kidney (renal) assessment to evaluate how well the kidneys are working
- An abdominal ultrasound to check for any internal anomalies
- A series of laboratory tests to establish a baseline, including measuring hormone levels to monitor for underactive thyroid (hypothyroidism)

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

How a person with MVA1 syndrome is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists, which may include a/an:

Cardiologist – a doctor who specialises in heart conditions.

Developmental paediatrician – to assess and manage developmental progress

Endocrinologist – a doctor who specialises in hormones and their effect on the body

Gastroenterologist/Nutritionist – to help address feeding difficulties, vomiting, and growth

Neonatologist – a doctor who provides specialised care for newborns

Nephrologist – a doctor who specialises in conditions affecting the kidneys

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment

Ophthalmologist – a doctor who specialises in conditions affecting the eyes

Paediatric oncologist/Haematologist – a doctor who specialises in cancer and blood conditions, and leads cancer surveillance

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood

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

Psychiatrist – a doctor who specialises in mental health

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

Treatments and therapies

As there is no treatment for the underlying genetic cause of MVA1 syndrome, care is supportive and multi-disciplinary, focusing on managing symptoms and proactive monitoring for complications, particularly malignancies.

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 MVA1 syndrome but may include:

- Physiotherapy for low muscle tone (hypotonia) and gross motor delays, which usually includes exercises to build core strength, improve balance, enhance coordination, improve head control, and prevent joint contractures to help children achieve motor milestones like sitting, crawling, and walking, and to improve overall mobility
- Occupational therapy for fine motor skill delays and feeding difficulties, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding and dressing) and strategies to improve oral motor skills for sucking and swallowing
- Speech therapy for a range of speech and language delays or difficulties and feeding/swallowing difficulties. For children with moderate to severe difficulties, this can include regular sessions focusing on Augmentative and Alternative Communication (AAC) methods (e.g. sign language, picture exchange systems and high-tech communication devices) and provides a functional means of communication for individuals who are non-verbal or have very limited speech
- Medications may be prescribed such as midazolam, valproate or levetiracetam to treat seizures and to help control or prevent seizures, though seizures can sometimes be difficult to control
- Hormone treatment for hypothyroidism to replace the deficient hormone
- Surgery, such as surgical excision or a renal transplant to remove tumours or for chronic renal failure
- Nutritional support, such as a nasogastric tube for infants with a poor suckling reflex and feeding difficulties
- Intensive care interventions, which may be required for acute respiratory infections, such as endotracheal intubation and oxygenation
- Cancer treatment will depend on the type of cancer diagnosed

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, including consistent tracking of weight, height and head circumference
- Consider an annual cardiac review, using electrocardiograms (ECG) and echocardiograms to assess heart function

- Consider a neurologic review (including MRI and EEG, if indicated by seizures), which includes ongoing examinations to evaluate muscle tone, motor skills, reflexes, and monitor for new movement anomalies
- Maintain a low threshold for suspicion for malignancies, with further investigation if relevant clinical symptoms arise

Cancer surveillance

Due to a significantly increased risk of cancer, a structured surveillance protocol is mandatory. Recommended screenings, especially for infants and young children, include:

- Abdominal ultrasound every three months to screen for tumours such as Wilms tumour and rhabdomyosarcoma
- Haematological (blood) check-up every three months to detect leukaemia

Research into new treatments for MVA1 syndrome

The genetic change causing MVA1 syndrome affects growth and development of a baby before birth. Therefore, a complete cure is unlikely, even in the future, since the body and organs have already been formed by the time a diagnosis is made. However, research into improved treatments and management for various features of MVA1 syndrome is ongoing. Currently (2026), there are no specific therapies to treat the underlying genetic cause, so clinical approaches centre on managing symptoms and proactive cancer surveillance. In addition, although MVA1 syndrome is a relatively rare condition, with fewer than 50 people described in the nmedical literature, the BUB1B gene is the subject of a lot of research. One avenue of research is to identify drugs or therapies that could limit the chromosomal instability and stabilise cell division. Other potential strategies include creating treatments that target the specific effects of the BUB1B gene changes or that adjust the immune system's response to cells with the wrong number of chromosomes (aneuploid cells). Genetically modified mouse models are also being used to study the condition, which is a crucial step for understanding how it progresses and for testing potential new therapies.

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

Families say ...

"Looking after a child with MVA takes grit and determination. It is a marathon not a sprint. There are no days off. Its 7 days a week. 52 weeks a year. It impacts your ability to do normal things – like go abroad on holiday. We now plan all of our vacations around hospitals! Hopefully this will ease as our son grows older and stronger. Hopefully!"

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. 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**.

References

- Hanks S et al (2004). Constitutional aneuploidy and cancer predisposition caused by biallelic mutations in MVA1. NATURE GENETICS, 36(11): 1159-61. PMID 15475955. **Link to article**
- Kato M et al (2017). PCS/MVA syndrome caused by an Alu insertion in the MVA1 gene. Human Genome Variation, 4: 17021. PMID 28611924. **Link to article**
- Laberko A et al (2019). Hematopoietic stem cell transplantation in a patient with type 1 mosaic variegated aneuploidy syndrome. Orphanet Journal of Rare Diseases, 14. **Link to article**
- Lin S et al (2020). Prenatal diagnosis and long-term follow-up of a Chinese patient with mosaic variegated aneuploidy and its molecular analysis. Clinical Case Reports, 8(8): 1369-1375. PMID 32884756. **Link to article**
- Malumbres M et al (2024). Mosaic variegated aneuploidy in development, ageing and cancer. Nature Reviews Genetics, 25(12): 864-878. PMID 39169218. **Link to article**
- Ochiai H et al (2014). TALEN-mediated single-base-pair editing identification of an intergenic mutation upstream of MVA1 as causative of PCS (MVA) syndrome. PNAS, 111(4): 1461–1466. PMID 24344301. **Link to article**
- Pavone P et al (2022). Pathogenic correlation between mosaic variegated aneuploidy 1 (MVA1) and a novel MVA1 variant: a reappraisal of a severe syndrome. Neurological Sciences, 43: 6529–6538. **Link to article**
- Rio Frio T et al (2010). Homozygous MVA1 Mutation and Susceptibility to Gastrointestinal Neoplasia. The New England Journal of Medicine, 363(27): 2628-37. PMID 21190457. **Link to article**

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Inform Network Support

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- MVA Society

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