UNIQUE

UNDERSTANDING GENES & CHROMOSOMES

Bachmann-Bupp syndrome (BABS)

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with Bachmann-Bupp 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 Bachmann-Bupp syndrome?

Bachmann-Bupp syndrome, also referred to as BABS, is a rare neurodevelopmental disorder associated with developmental delay, hair loss that is not present at birth (non-congenital alopecia), low muscle tone (hypotonia), recurring hair follicle cysts, an unusually large head circumference (macrocephaly), and a larger body size than is typical (macrosomia).

Bachmann-Bupp syndrome is caused by certain changes (variants) in the ODC1 gene. As is common with genetic conditions, each person can be affected differently. Not everyone with Bachmann-Bupp 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 Bachmann-Bupp syndrome?

Bachmann-Bupp syndrome is extremely rare, and its exact prevalence is unknown. Currently (2026), about 11 individuals worldwide with Bachmann-Bupp syndrome have been reported in medical literature. 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 Bachmann-Bupp syndrome have?

As is common with many genetic conditions, children and adults with Bachmann-Bupp 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.

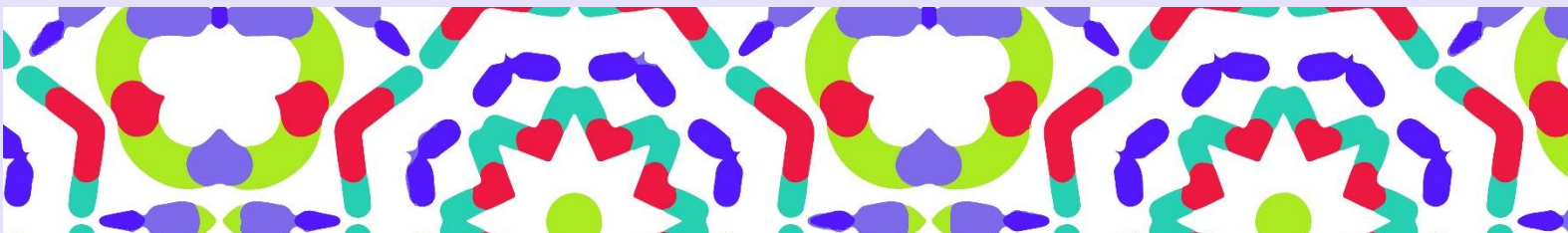
Common features

Most people with Bachmann-Bupp syndrome have:

- Developmental delay
- Speech delay
- Low muscle tone (hypotonia) from birth
- Loose (hypermobile) joints
- Large head and body size (macrocephaly and macrosomia)
- Hair loss (non-congenital alopecia)
- Brain anomalies
- Feeding difficulties
- Hair follicle cysts
- Brain MRI anomalies
- Characteristic facial features
- Undescended testes in males (cryptorchidism)
- Prenatal history of excessive amniotic fluid (polyhydramnios)

Other possible features include:

- Behavioural differences e.g. autism spectrum disorder (ASD) / ADHD / anxiety
- Skin condition(s)
- Heart condition(s)
- Seizures
- Musculoskeletal conditions
- Eye/vision anomaly
- Hearing loss



Pregnancy, birth and newborns

While experiences of pregnancy may be unremarkable and proceed without complication, some concerns during pregnancy have been reported, sometimes following mid-pregnancy anomaly scans. Where a cause for concern was noted, these included reduced fetal movements and an unusually large head size (macrocephaly). An excessive amount of amniotic fluid (polyhydramnios) is common.

The majority of pregnancies go to term, but some babies are born prematurely. Babies may show some signs of difficulty at birth. One child experienced significant breathing difficulties after birth (respiratory distress), requiring oxygen support. Birth weights are usually above average (macrosomia), with an unusually large head size (macrocephaly) and increased body length being more consistent features than a high birth weight. Many new-born babies have low muscle tone (hypotonia) and have been described as “unusually inactive and placid”, a feature that may alert doctors to an underlying condition.

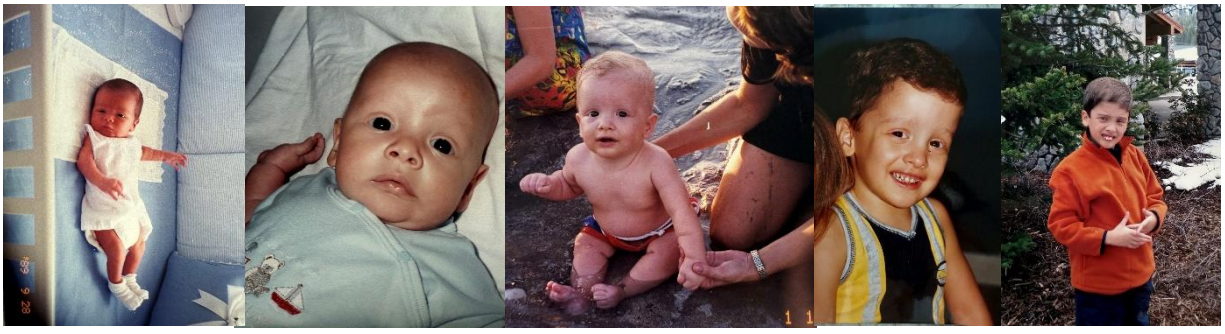
“Mom’s pregnancy was typical until around 30 weeks, when she was diagnosed with polyhydramnios without any clear cause. At birth it was very apparent she had significant neurological deficits. As a newborn, she was unable to regulate her blood sugar, body temperature, required oxygen support and lacked the suck/swallow reflex so had an inability for any oral intake. Her hair completely fell out with her first bath.

An MRI showed that she had suffered an intraventricular haemorrhage during the pregnancy. From the MRI scan she was diagnosed with periventricular leukomalacia (PVL). After a month in the NICU and failure to progress with feeding therapy, a gastrostomy tube (G-tube) was placed for nutritional support, and she was able to go home. As an infant she was very calm and quiet. Limited interaction with her environment and slept for 10-12 hours a night from just a couple months old. She seemed to have a very poor immune system. A lot of congestion and fevers. She had multiple bouts with pneumonia.”

Appearance

Certain facial features are found more often in children with Bachmann-Bupp syndrome than in other children. These features may mean that you see unexpected similarities between your child and others with Bachmann-Bupp syndrome. The most common characteristic features include wide-set, down-slanting and deep-set eyes; a high, broad forehead; a pointed chin; a short space between the nose and upper lip; and a low hairline.

In addition to these features, individuals with Bachmann-Bupp syndrome often have a large head size (macrocephaly) and a distinctive pattern of hair loss.



1 month | 3 months | 8 months | 2 years | 6 years

Hair

A characteristic feature of Bachmann-Bupp syndrome is a specific pattern of hair loss (alopecia) that is not present at birth. Babies are typically born with hair, which can be plentiful and sometimes an unusual colour, such as silver or blonde. One baby was noted to have had hair in their meconium (the first stool that is passed by a newborn) after birth. Hair then typically falls out within the first few weeks or months of life. This hair loss can be complete, affecting the scalp, eyebrows and eyelashes. Some children may experience regrowth of hair on the head, but eyebrows and eyelashes often remain sparse. Treatment with a medication known as α-difluoromethylornithine (DFMO) has been shown to lead to significant regrowth of hair, eyebrows and eyelashes (See 'Research into new treatments for Bachmann-Bupp syndrome' section).

> ***She lacked eyebrows, eyelashes and all hair on her head except about 30 strands."***

Body

Babies are often large for their gestational age at birth and may continue to have a large body size (macrosomia). Low muscle tone (hypotonia), muscle weakness and unusually flexible joints (hypermobility) are common. Skeletal and orthopaedic conditions have been noted in some individuals, including funnel or pigeon chest (pectus carinatum/excavatum), winged shoulder blades (scapulae), long fingers with broad tips, curvature of the spine (scoliosis) and a partially dislocated hip (hip subluxation).

Hands and feet

Children with Bachmann-Bupp syndrome occasionally have anomalies of the hands and feet. Most common among these are fingers that curve inwards (clinodactyly) and unusually long fingers with wide tips (broad terminal phalanges).

Skin and Nails

Some individuals have a skin condition(s), notably rough patches and small bumps (keratosis pilaris), dry skin and recurrent hair follicle cysts on the head, neck, back and ears. The cysts can be large (up to 2.5 cm (1 inch) in diameter. Differences in the nails have also been observed in some individuals, including brittle, underdeveloped (hypoplastic) or misshapen nails.

Development

Gross and fine motor skills

So far, developmental delay has been reported in most children with Bachmann-Bupp syndrome. The degree of delay ranges from mild to profound. Developmental 'milestones', including sitting, walking and using cutlery, are often delayed, although there is a wide range of eventual ability. For some, independent sitting began as early as 11 months or was delayed until after three years of age. Walking began for some at around 17 months while some older children are not able to walk independently. Low muscle tone (hypotonia) is common and may affect mobility. Some children may have an unusual gait when walking because of stiffness (spasticity), a lack of motor coordination, weakness in the upper legs, bow-leggedness (genu vara) or balance issues (known as ataxia). Fine motor skills, such as using cutlery, zips and buttons, and playing with toys, can also be significantly affected. Toilet training is also likely to be delayed.

We began with conventional therapies and later attended [an Institute that works in the field of child brain development]. Their philosophy had a profound impact on our family. We were taught that every day mattered and that waiting for a diagnosis should never delay intervention. For four consecutive years, I personally carried out an intensive home program that focused on following the normal developmental sequence of the human body, including crawling, creeping, standing, and walking. Our son made significant progress and eventually learned to walk."

Unique publishes separate guides to Therapies and Toilet training and continence

Intellectual development and learning

Most children with Bachmann-Bupp syndrome have learning (intellectual) disability (LD/ID) or learning difficulties. Intellectual disability may become more apparent as a child's cognitive and behavioural development progresses. LD/ID ranges from mild to profound but is usually in the moderate range. Most children will require significant additional support with their learning throughout their education.

Our son attended school, but looking back, I feel there were periods when the educational setting was not fully adapted to his needs. Today there are many more specialized programs, therapies, and educational resources available than there were when he was growing up. My advice to parents is to seek environments that truly maximize their child's potential and encourage meaningful learning and development."

Unique publishes separate guides to Education and Further education, training and work

Speech and language

Children with Bachmann-Bupp 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), with specific difficulties including elocution, articulation and word retrieval. The onset of speech is typically delayed, with first words appearing between two and three years of age, but the eventual range of achievement is broad and some may remain non-verbal. For those with limited or no speech, sign language, sounds or augmentative and alternative communication (AAC) methods may allow them to communicate their thoughts and needs effectively. A common observation is that a child's understanding of language (receptive language) is significantly better than their ability to speak (expressive language).

Unique publishes a separate guide to Communication

Feeding

Feeding issues in the new-born period are common, with poor feeding sometimes leading to a failure to thrive (poor weight gain). One of the causes of feeding issues may be difficulty in coordinating the muscles required for eating and drinking (oro-motor dyspraxia). Some babies also suffer from gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), which may require treatment, including in some cases insertion of a percutaneous endoscopic gastrostomy tube (PEG/G-tube). Other gastrointestinal issues are also seen, including easy vomiting in the new-born period and constipation, which can be severe. Low muscle tone (hypotonia) may be a contributing factor to constipation. It is important that possible causes of constipation are discussed with a health visitor or doctor, who may recommend adapting diet or giving stool softeners or laxatives.

"She appeared malnourished and underweight as a toddler. Even with the G-tube it seemed we couldn't get her enough calories to add weight. Feeding therapy minimally helped her to get her oral intake of pureed foods increased, but we were still struggling to get weight on her."

Unique publishes a separate guide to Feeding

Growth and stature

Children with Bachmann-Bupp syndrome are noted as having growth ranging from that within the expected range, to overgrowth or growth delay. Birth measurements are typically within the expected to large range and most children also have larger than expected head size (macrocephaly). For one infant, the absence of a larger head size was explained by early fusion of the skull bones (craniosynostosis). Beyond infancy, height and weight are variable. Reported height measurements have ranged from the 29th to above the 97th percentile at different ages.

Behaviour

Children with Bachmann-Bupp syndrome 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), anxiety, self-harming (self-injurious) behaviours, aggressive behaviours, and poor social and coping skills have also been reported. It is important to note that not all children will have behavioural differences.

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.

Unique publishes a separate guide to Challenging Behaviour

Puberty

There is limited information available about puberty in children with Bachmann-Bupp syndrome. 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

Information about experiences of adulthood is exceptionally limited. Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of learning (intellectual) disability, possible on-going medical concerns and improvements in early intervention and therapies/treatments.

Current insights are derived from a small number of individuals in late adolescents and young adults who consistently demonstrate profound developmental delay. The neurological and cognitive features in adulthood include moderate intellectual disability and significant communication impairments. Behavioural and psychiatric issues appear to be prominent and include diagnoses of ADHD, anxiety, disruptive behaviour, aggression and self-injurious behaviour.

Adults with Bachmann-Bupp syndrome are likely to continue to live with their parents or in supported settings such as a group/residential care home, with caregivers who can provide support. Poor social and coping skills have also been noted in some individuals, which collectively impact the skills required for independent living.

> ***Even today, at 29 years of age, our son continues to participate in therapy. He still works on language, communication, and physical abilities. We continue because we believe that learning and development do not stop in childhood. Progress is still possible, even in adulthood."***

Unique publishes a separate guide to Transition

Medical concerns

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

Brain

Most children with Bachmann-Bupp syndrome have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. A brain scan is typically carried out due to developmental delay and a larger head size.

The changes seen vary but include:

- Anomalies of the brain's white matter
- Cysts
- Dilated fluid-filled spaces that surround blood vessels in the brain (perivascular or Virchow-Robin spaces)
- Abnormal organization and development or brain cells (neurones) in a specific part of the brain (focal cortical dysplasia), which can cause seizures
- Underdevelopment (hypoplasia) or partial/complete absence (agenesis) of the white matter connecting the two halves of the brain (corpus callosum)
- Enlarged fluid-filled cavities (ventricles) in the brain (ventriculomegaly)

Less commonly reported changes include:

- Loss of brain tissue volume in the main part of the brain (parenchymal volume loss) or in the area of the brain associated with memory (hippocampal volume loss)
- Deposits of calcium in the brain (intracranial calcification)
- A mildly unusually shaped part of the cerebellum (dysmorphic cerebellar vermis)
- Pituitary gland anomalies, which could lead to hormone deficiency

Seizures

Rarely, children with Bachmann-Bupp syndrome experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). To date, epilepsy has only been reported in the oldest known individual, with an onset at 14 years of age. This late onset suggests there is a chance that children may develop seizures as they age.

Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. 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 seizures(s) experienced.

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. Management has proven challenging in one individual reported. General anti-epileptic drug treatment had a limited impact on seizure control, and the seizures were also resistant to a ketogenic diet and vagus nerve stimulation (VNS). 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.

Seizure types reported in individuals with Bachmann-Bupp syndrome include:

Absence seizures: A change in behaviour as if the child 'switches off', sometimes with staring, eyelid flickering or lip smacking. Absences are very brief, often lasting less than half a minute.

Atypical absence seizures: The child may appear confused and unresponsive for minutes (very different from a typical absence seizure).
Atonic seizures: Involving a sudden loss of muscle tone, causing the individual to go limp and fall if standing
Generalised tonic-clonic seizures: At the onset of a seizure, the abnormal electrical activity involves both sides of the brain. The seizure involves a phase of stiffening followed by jerking of the body

When our son was an infant, we were referred to hospital because of his large head circumference. An MRI was performed and was reported as normal. However, no EEG was ever obtained. His first recognized seizure, an absence seizure, did not occur until he was approximately 14 years old. Looking back, I believe that obtaining a baseline EEG earlier in life might have provided useful information, even if no seizures were evident at the time. For children with Bachmann-Bupp syndrome, especially those with macrocephaly and developmental concerns, early neurological monitoring may be worth considering."

Heart

A heart condition(s) has been found in a few people with Bachmann-Bupp syndrome, which can be present at birth (congenital). The type of heart condition(s) is variable but includes anomalies affecting the size and structure of the heart muscle and valves. Other heart anomalies that have been reported include a hole between the bottom two chambers of the heart (ventricular septal defect, VSD), narrowing of the vessel carrying blood from the heart to the lungs (pulmonary stenosis) and narrowing of the main artery of the body (coarctation of the aorta). These conditions may be relatively minor and resolve naturally in time, as was the case for the one instance of VSD.

Ears and Hearing

A few children with Bachmann-Bupp syndrome have a hearing impairment. A hearing loss may be sensorineural, where there are problems with the inner ear, sometimes with the cochlea or auditory nerve (the nerve that sends signals to the brain about sound). Hearing loss that was present at birth (congenital) and affected one ear (unilateral sensorineural hearing loss) was reported in one individual.

As children are at risk of speech delay, parental concerns should be acted on early and home- or school-based therapy provided. Identifying and managing any hearing impairment is important to help with development and communication.

Spine

Some babies are born with or develop a spinal curvature, a sideways curve of the spine (scoliosis). The curvature can be treated with physiotherapy and exercises, or a support brace or surgery may be needed. Additionally, a fluid-filled cyst in the spinal cord (syringohydromyelia) has been seen in one individual, which resolved on its own.

Joints and bones

Joint anomalies are a known feature of Bachmann-Bupp syndrome. These include extremely loose (hyper-mobile) joints. This often occurs alongside low muscle tone (hypotonia) and muscle weakness. While this may cause no problems, hyper-mobility is sometimes associated with joints that come out of position (dislocate) easily. In one individual, increased muscle tone (spasticity) was noted. Some children have a degree of hip dysplasia, in which the hip joints are easily dislocated. Weaker, thinner bones (osteoporosis) have also been reported. A reduced sensitivity to pain has also been seen in a small number of individuals.

Our son was eventually diagnosed with severe osteoporosis, but unfortunately this diagnosis came very late, around age 25 or 26. Prior to that, he had experienced several fractures that were never fully investigated. It was only after an orthopaedic evaluation that we were advised to perform a bone

density study, which revealed advanced osteoporosis. Based on our experience, I believe it would be valuable to consider baseline bone density evaluations in individuals with Bachmann-Bupp Syndrome at an earlier age, even if they are not routinely performed in children. Earlier monitoring could help identify problems before severe bone loss develops."

Skin

Skin conditions are a key characteristic of Bachmann-Bupp syndrome, although the symptoms and features can be very different between individuals, and some people may been unaffected.

When skin conditions are present, they may include:

- Dryness
- A common, harmless skin condition that causes dry, rough patches and tiny bumps, usually on the upper arms, thighs, cheeks or buttocks (keratosis pilaris)
- A condition that causes redness and small bumps on the eyebrows (ulerythema ophryogenes)
- A red (erythematous follicular) pattern on the face
- An unusual build-up of blood vessels on or under the surface of the skin that can look like a red-coloured birthmark (cutaneous haemangioma)

Various non-cancerous (benign) lesions have also been reported, including:

- Recurrent follicular cysts on the head, ears, armpits (axilla), neck and back
- A pigmented mole (nevus) on the back of the head
- Multiple small, flat, darkened patches of skin (hyperpigmented macules) on the abdomen, back and inner thigh

"She got frequent massive skin cysts that were impossible to heal and had to be surgically removed. These were painful and lasted for months."

Palate

Anomalies of the palate (roof of the mouth), such as a high arched palate, have been reported in a few individuals with Bachmann-Bupp syndrome.

Genitals

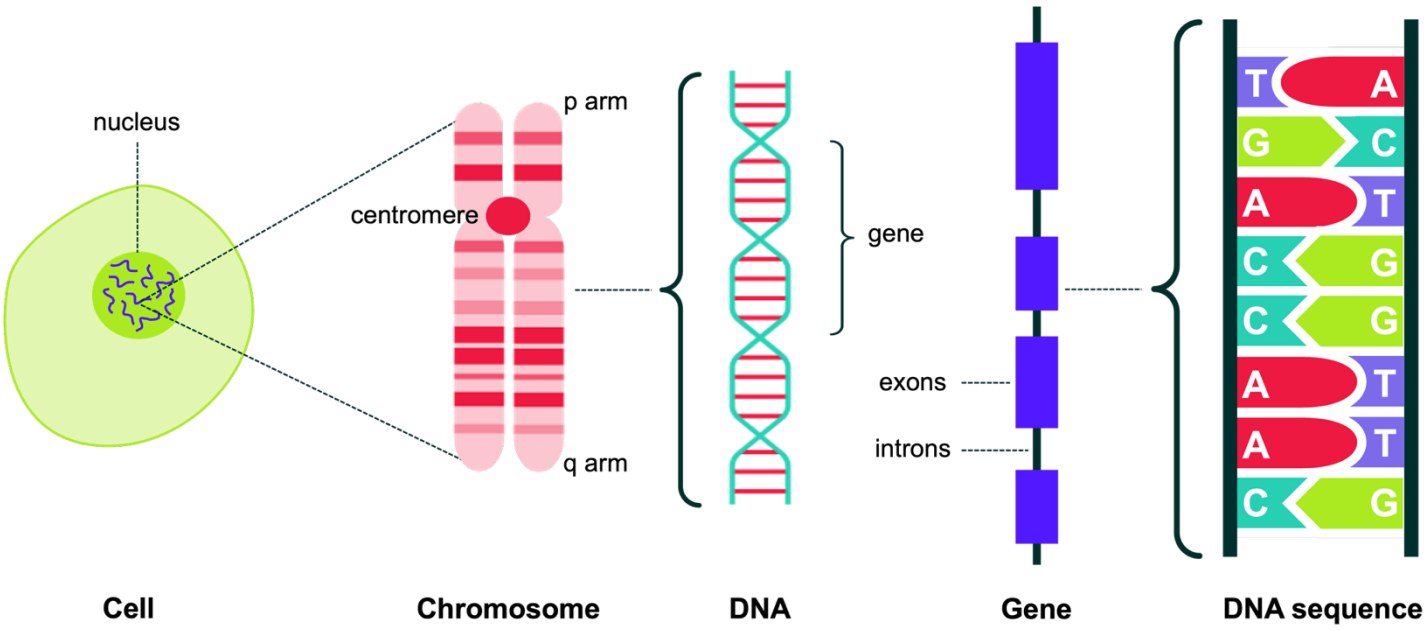
Minor anomalies of the genitals in boys have been reported, including undescended testes (cryptorchidism). This condition can also be seen in children without Bachmann-Bupp syndrome and is not usually of major concern. If necessary, cryptorchidism can be corrected with surgery. There is currently no information available about genital anomalies in girls with the syndrome.

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.

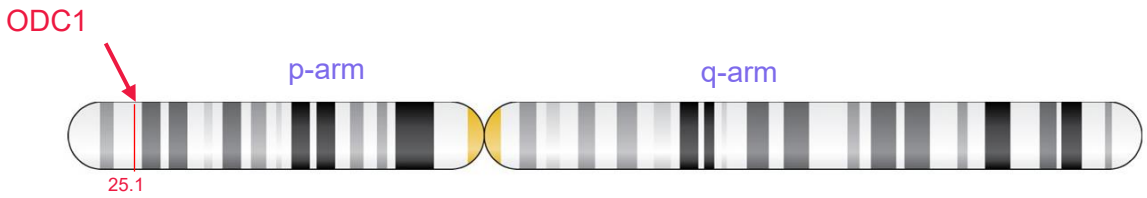
DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes 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 Bachmann-Bupp syndrome?

Bachmann-Bupp Syndrome is caused by specific changes (known as pathogenic variants) to the DNA sequence of a gene called ODC1 (ODC1 is an abbreviation of the gene's full name, Ornithine Decarboxylase 1). The ODC1 gene is located in the short 'p' arm of chromosome 2 in a region called 2p25.1 as shown in the image below.

Chromosome 2

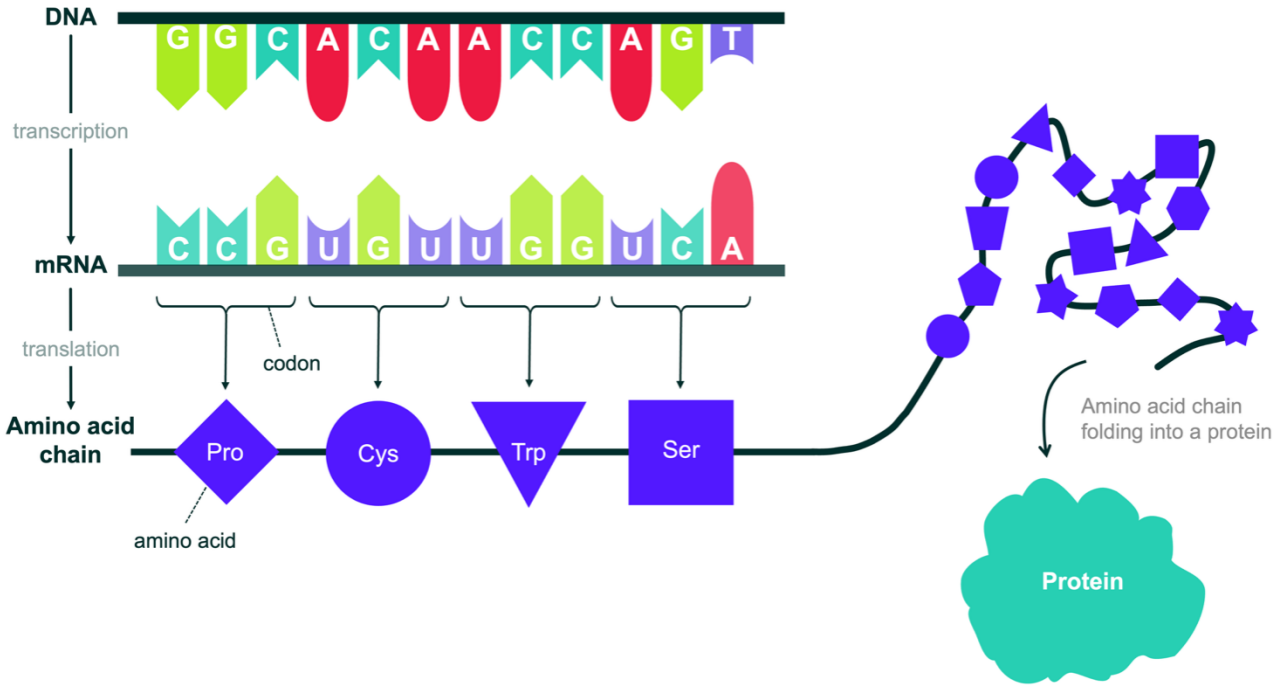


We have two copies of chromosome 2 in our cells, so we have two copies of the ODC1 gene. Bachmann-Bupp Syndrome occurs when only one copy of the ODC1 gene is affected; the second copy is fully functional.

This 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

Most genetic conditions are caused by changes to genes that provide instructions for making proteins; these are called protein-coding genes. ODC1 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 ODC protein

The protein made by the ODC1 gene is called ornithine decarboxylase. This protein is an enzyme that plays a critical role in the process of making polyamines. Bachmann-Bupp syndrome is classified as a polyaminopathy, which is a disorder of the polyamine pathway. Polyamines are compounds essential for many cellular activities, including cell growth and division, embryonic development, and the synthesis of DNA, RNA and proteins. In Bachmann-Bupp syndrome, changes in the ODC1 gene lead to a shortened version of the ODC protein being produced that cannot be broken down by the cell. This leads to a build-up of the ODC protein within cells and abnormal polyamine levels, which in turn causes the features of the syndrome.

Different types of genetic changes

The specific type of genetic change in the ODC1 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 ornithine decarboxylase protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with Bachmann-Bupp syndrome. People with Bachmann-Bupp syndrome are more commonly found to have a gene sequence variant, as opposed to a deletion of the entire gene.

Bachmann-Bupp syndrome is caused by pathogenic changes in the gene that act like gain of function variants (GOFs). The GOF variants associated with Bachmann-Bupp syndrome result in a shortened (truncated) protein that cannot be broken down, leading to a build-up of the protein in the body. 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, have not yet been reported as a cause of Bachmann-Bupp syndrome (2026).

Genetic Tests

Bachmann-Bupp syndrome 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 found 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

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 here for the ODC1 gene:

p.Lys448* (K448*): c.1342 A>T in exon 12 of the ODC1 gene (NM_002539.3)

p.Lys448Ter (K448*)	signifies the change to the protein: the amino acid lysine (Lys) has been replaced by a stop codon at position 448 in the sequence of amino acids that make up the protein
A>T	signifies the gene sequence change: the A nucleotide has been replaced by a T nucleotide
c.1342	signifies the base pair position of the change within the gene sequence (the position where the A nucleotide has been replaced by the T nucleotide)
exon 12	signifies which part of the gene has been altered, in this case exon 12
ODC1	signifies the gene that is affected
NM_002539.3	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?

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 ODC1 gene then a child will have Bachmann-Bupp Syndrome.

In everyone identified so far (2026) with Bachmann-Bupp Syndrome, the genetic change was a random (or 'de novo') change, meaning the change occurred for the first time in that family in the affected individual. It is important to recognize 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. In everyone reported with Bachmann-Bupp syndrome so far, the genetic alteration has been found to be de novo (dn), which means neither parent was found to have the same ODC1 gene change as their child. Therefore, the chance of having another child with Bachmann-Bupp syndrome is usually less than 1%.
One reason why there is some residual chance of recurrence 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 (2026) no instances of germline mosaicism have been reported in the literature for Bachmann-Bupp syndrome.

If your child with an ODC1 variant goes on to have children of their own, the chances of passing on the variant to their child are 50% in each pregnancy. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with Bachmann-Bupp syndrome.

Can Bachmann-Bupp syndrome be cured?

There is no cure for Bachmann-Bupp syndrome since most of the effects of the genetic change took place during a baby's formation and development. However, knowing the diagnosis means that appropriate monitoring and interventions can be put in place.

Management

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

Children and adults with Bachmann-Bupp syndrome 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 Bachmann-Bupp 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 Bachmann-Bupp syndrome are present and how severe they are.

The following assessments are recommended:

- A physical examination to look for features such as such as an unusually large head size (macrocephaly) and hair loss (alopecia). This should also include growth measurements (head circumference, height and weight) and an assessment for other skin conditions such as keratosis pilaris, dry skin and differences in nails
- A gastroenterology and nutrition assessment to evaluate feeding and swallowing
- A referral to physical, occupational and speech therapists to support motor and language skills
- A neurologic assessment to determine whether conditions such as developmental delay, low muscle tone (hypotonia), muscle weakness and seizures are present
- A cardiac assessment to look for a heart conditions(s)
- An orthopaedic assessment to monitor for skeletal conditions such as hip subluxation, scoliosis and osteoporosis
- An audiological (hearing) assessment to determine the severity of any hearing loss and ensure early intervention
- An ophthalmology (eye) assessment to screen for any vision differences

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 Bachmann-Bupp syndrome 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, motor skills and evaluate for seizures.

Cardiologist – a doctor who specialises in heart conditions.

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.

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.

Audiologist – a health care professional who diagnoses, treats and helps manage a condition that involves hearing or balance.

Dermatologist – a doctor who specialises in conditions of the skin, hair and nails.

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 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/Psychologist – doctors and healthcare professionals who specialise in mental health and can help with behavioural concerns.

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

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 Bachmann-Bupp Syndrome but may include:

Physiotherapy for low muscle tone (hypotonia), joint hypermobility 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 scoliosis.

Occupational therapy for fine motor skill delays, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding, dressing and personal care), and introducing adaptive strategies and equipment to promote independence.

Speech therapy for a range of speech and language delays or feeding/swallowing difficulties (dysphagia). Receptive language (comprehension) is often stronger than expressive language, and therapy aims to enhance verbal communication, articulation and word retrieval.

Medications may be prescribed such as α-difluoromethylornithine (DFMO), also known as eflornithine, which directly addresses the underlying cause of the condition by inhibiting the overactive ODC enzyme.

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, including tracking height, weight and head circumference
- Neuropsychiatric and learning assessments every few years to optimise the EHCP/IEP. This should include tracking key developmental milestones, evaluating communication methods and monitoring for anxiety, disruptive behaviour and aggression
- Consider an annual cardiac review

- Consider annual audiologic assessments
- Consider a skeletal review for issues such as scoliosis and osteoporosis
- On-going examinations by an ophthalmologist
- Regular dermatological and physical examinations to monitor for changes in hair (alopecia) and skin (such as recurring follicular cysts, keratosis pilaris, pigmented macules)
- For individuals on specific treatments (such as eflornithine), biochemical and metabolomic analysis of plasma samples may be required to monitor treatment response

Research into new treatments for Bachmann-Bupp syndrome

The genetic changes that cause Bachmann-Bupp syndrome 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 Bachmann-Bupp Syndrome is ongoing.

Although there is no treatment for the underlying genetic basis of the condition, a repurposed and highly effective drug called eflornithine (also known as DFMO) can help manage the symptoms. This drug works by blocking the overactive ODC enzyme, which helps to normalise the polyamine levels in the body. In four paediatric individuals treated with DFMO, this has led to significant improvements (Afrin 2023; Rajasekaran 2021), including:

- Full regrowth of hair, eyebrows, and eyelashes
- Considerable improvement in low muscle tone
- Notable developmental progress

In addition, although Bachmann-Bupp syndrome is a rare condition, the ODC1 gene is the subject of a lot of research. The International Center for Polyamine Disorders (ICPD) was founded at Corewell Health West and Michigan State University in 2020. The ICPD offers an IRB-approved research study that aims to advance our understanding of Bachmann-Bupp syndrome and other polyaminopathies through a state-of-the-art biobank and clinical data registry. You can learn more about the ICPD and/or the research study here.

Currently (2026), there is no evidence of gene therapy being explored for this condition.

“As she progressed through infancy and toddlerhood, she failed to meet all milestones. She was completely non-verbal. She had very low muscle tone and couldn’t even hold her head up as a 4-year-old. We continued with speech, physical and occupational therapy and continued to give her all the support to help her advance and it was just never enough.

At 4 years old, the world completely changed for her. And us. Receiving the diagnosis of Bachmann Bupp syndrome helped us to understand her a little. However, once we began the medication DFMO (at 4 years and 9 months), it became so apparent that her imbalance of polyamines was the cause of so many of her issues. Within the first few months, she was back on a healthy weight chart and was no longer appearing so malnourished. Her immune system improved and the winter following the initiation of DFMO her respiratory illnesses seemed to come, be less severe and leave quicker. She has not had a diagnosis of pneumonia since starting DFMO.

Her cognitive abilities were some of the most significant changes. She completely woke up. She was more engaged with the world around her. This did begin to cause some pretty significant agitation issues as she still struggled with a way to communicate, so she was very frustrated.

Within the first 3 months of beginning DFMO treatment, she started to grow eyelashes, eyebrows and hair on her head.

Her physical strength, muscle tone and coordination have improved greatly. Still significant deficits are present, but she's able to propel herself in her manual wheelchair, she can do some walking with the assistance of a person or her gait trainer.

Communication continues to be a major challenge. We have made minimal progress with her being able to express herself. She has a few American Sign Language (ASL) words that she uses, and has had some advancement using a communication device, mostly appropriate yes/no responses utilizing her device. She can however follow commands, and she understands us quite well. The pride that she gets from completing tasks around the house is so fulfilling to see!

Present day, she is the happiest and most social girl. She meets friends everywhere she goes. She loves going grocery shopping and waving at every single human she sees. She is a typical moody pre-teen and loves to harass her little brother. One of my favorite characteristics has become her sense of humor. It's been so cool to watch that develop over the last few years!"

"As a BABS parent the point that stands out most, is how fortunate our daughter is to have a treatment for the genetic disorder that she was diagnosed with. The early diagnosis (2 weeks old) and the early start on treatment (3 months) are what really provided her with a chance at life. The devotion and dedication of [her medical team] is beyond what words can describe, and the impact that it has on her life will forever be felt."

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

Families say ...

“Our daughter’s journey with Bachmann-Bupp syndrome has shown us a strength we didn’t know was possible. Every milestone, no matter how small, is a victory worth celebrating. She continues to teach us resilience, love, and the power of never giving up.”

“I recall the confusion when we first received the diagnosis, and how dire things looked then. Seeing our daughter today, at the level that she manages to function is no less than an open miracle.”

“One of the most important things I would like to share is that it took us approximately 23 to 24 years to finally learn what condition our son had. For most of his life, we did not have a diagnosis or a name for what he was experiencing. However, from the time he was about four months old, we knew something was different. He had significant macrocephaly, hypotonia, and developmental delays.

Looking back, one of the best decisions we made as parents was not to allow the lack of a diagnosis to stop us from helping him. Rather than waiting for answers, we focused on what we could do for him at that moment. We started therapies as early as possible and worked intensively to help him develop. Throughout his childhood and adulthood, we never stopped searching for answers. We explored physical therapy, behavioral therapy, speech and language therapy, educational interventions, and every available resource that might help him.

One lesson I would like to share with other parents is that progress does not have to wait for a diagnosis. Children still need support, therapy, education, and opportunities to develop regardless of whether a diagnosis has been identified. Over the years, I have maintained a complete logbook of our son’s life and medical history. This information has been invaluable when meeting new physicians and specialists. Parents observe things in daily life that may not be apparent during a brief medical appointment. Maintaining open communication with healthcare providers and becoming an active participant in your child’s care can make a significant difference. Our son continued to improve over the years because we never stopped working with him.

Our family’s experience has taught us that persistence matters and, most importantly, give your child love, patience, and support. Ultimately, the greatest advice I can offer to parents facing Bachmann-Bupp Syndrome - or any rare disorder - is simple: do not give up.”

Sources

The information in this booklet is drawn from the published medical literature. In 2026, Unique had no members with Bachmann-Bupp syndrome.

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/).

References

Afrin A (2023). Improvement of dermatological symptoms in patients with Bachmann-Bupp syndrome using difluoromethylornithine treatment. Pediatric dermatology, *40*(3): 528–531. PMID 36443247. **Link to article**

Bachmann A (2024). Bachmann–Bupp syndrome and treatment. Dev Med Child Neurol., 66(4): 445–455. PMID 37469105. **Link to article**

Bupp C (2018). Novel de novo pathogenic variant in the ODC1 gene in a girl with developmental delay, alopecia, and dysmorphic features. Am J Med Genet.: 1-6. **Link to article**

Bupp C (2022). Bachmann–Bupp syndrome. GeneReviews®. **Link to article**

Bupp C (2025). Repurposing With Purpose: Treatment of Bachmann–Bupp syndrome With Eflornithine and Implications for Other Polyaminopathies. American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 0(3): 183-188. PMID 40167220. **Link to article**

Michael J (2023). Two New Cases of Bachmann–Bupp syndrome Identified through the International Center for Polyamine Disorders. Med. Sci., 11(2): 29. PMID 37092498. **Link to article**

Rajasekaran S (2021). Repurposing eflornithine to treat a patient with a rare ODC1 gain-of-function variant disease. eLife, 10, e67097. PMID 34282722. **Link to article**

VanSickle E (2021). Expanding the phenotype: Four new cases and hope for treatment in Bachmann-Bupp syndrome. American Journal of Medical Genetics Part A, 185A(7): 3485–3493. PMID 34477286. **Link to article**

unique

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

Join Unique for family links, information and support:

Become a member

Please help us to help you!

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation:

Donate via our website

Websites, Facebook groups and other links:

Bachmann-Bupp Family Coalition

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change.

This guide was reviewed by Caleb Bupp, MD, FACMG; Elizabeth VanSickle, PhD, MS; Julianne Michael, MS, CGC; Cari Flynn, MS, CGC; Corewell Health Helen DeVos Children's Hospital, Michigan, US and the International Center for Polyamine Disorders, Michigan, US.

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 (CA/AP) [2026]

unique

UNDERSTANDING GENES
& CHROMOSOMES

rarechromo.org