SUPPORT | RESEARCH | AWARENESS

MPS VI

Maroteaux-Lamy disease

Information for individuals, parents and families

Society for Mucopolysaccharide Diseases
mpssociety.org.uk

In this booklet

There is huge variability within this condition. Some people may experience only some of the symptoms while the severity of those symptoms can also vary.

This booklet is produced by the **Society for Mucopolysaccharide Diseases (MPS Society)** and is designed to help those affected by MPS VI Maroteaux-Lamy and their families understand its causes and effects. While there is currently no cure for people affected by MPS VI, this booklet explores how best to understand and manage the disease. It draws on the experiences of patients, carers, families and medical professionals as well as medical literature.

MPS VI disease was first identified by Dr Maroteaux and Dr Lamy in 1963

What is MPS VI?

MPS VI, known as Maroteaux-Lamy, is a mucopolysaccharide disease. Mucopolysaccharides, also called glycosaminoglycans (GAGs), are long chains of sugar molecules used to build bones, cartilage, skin, tendons and other tissues in the body.

Glycosaminoglycans (GAGs) used to be called mucopolysaccharides, which is why these diseases are known as mucopolysaccharide diseases

Muco means jelly-like
poly means many
saccharides means sugar

In the course of normal life there is a continuous recycling process which consists of building new materials and breaking down old ones ready for disposal. This breakdown and recycling process takes place in a special part of the body's cells called the lysosomes, which is why MPS VI and other similar conditions are also known as lysosomal storage diseases. The process requires a series of special biochemical tools called enzymes.

What causes MPS VI?

MPS VI Maroteaux-Lamy is the result of a specific enzyme (called N-acetylgalactosamine-4-sulfatase) either not working correctly or not being produced at all. This occurs because there is a mistake (mutation) in the gene called arylsulfatase B (ARSB) that gives the body the instructions for making the enzyme.

This enzyme is essential in breaking down large sugar molecules called GAGs. When these are not completely broken down they remain stored in the body's cells and accumulate in many tissues and organs. The symptoms of MPS VI are a result of the build-up of dermatan sulphate in the body.

In general, the severity of MPS VI is related to the level of enzyme activity that remains.

Higher enzyme activity levels lead to less build up of dermatan sulphate within the body, resulting in milder signs and symptoms (sometimes called **attenuated disease**).

Lower or absent enzyme activity levels lead to build up of dermatan sulphate within the body, resulting in prominent signs and symptoms of MPS VI.

What can I expect in the future?

People affected by MPS VI may not experience all the symptoms. Where symptoms are present, they vary in severity from one person to another.

People with MPS VI may not experience every symptom and where symptoms are present, they vary in severity from one person to another. Life expectancy will depend on the severity of symptoms. Severely affected people may live only until early childhood or adolescence; those with milder forms usually live into adulthood although their life expectancy may be reduced.

How is MPS VI inherited?

Genes are the unique set of instructions inside our bodies that make each of us an individual

How common is MPS VI?

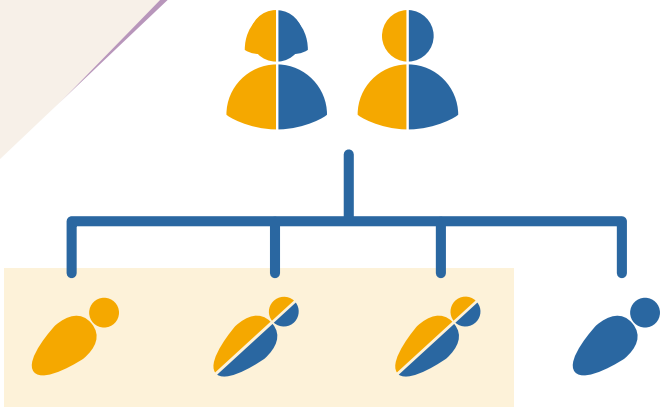
It is estimated that MPS VI affects between 1 in 250,000 to 1 in 600,00 newborns.

We have thousands of genes and they are the blueprint for our growth and development, as well as controlling how our bodies function. If a particular gene is faulty, or altered, then it will not work efficiently.

Genes are carried on structures called chromosomes. It is usual to have 23 pairs of chromosomes that are numbered in pairs from pair 1 to pair 22, plus one pair of sex chromosomes: XX for a female and XY for a male. A child will inherit one set of chromosomes from the mother in the egg, and one set from the father in the sperm, therefore we each have two copies of each gene, one of which is inherited from each parent.

In a person with MPS VI, both copies of the associated gene in each cell have mutations (mistakes). The parents each carry one copy of the mutated gene, but they do not show signs and symptoms of the disease. This is known as being a carrier.

A **carrier** will not show symptoms but can pass the defective gene to their child



Autosomal recessive

- **Affected by the disease 25%**
- **Carriers of affected gene 50%**
- **Unaffected by the disease 25%**

How is MPS VI diagnosed?

MPS VI diagnosis can take some time and typically requires looking at the person's medical history and symptoms and carrying out a physical exam and laboratory tests in order to make a diagnosis. People with MPS VI may experience some or all of the symptoms that are outlined in this booklet before receiving an actual diagnosis.

Following a diagnosis there will be medical tests and then usually a series of operations. This may be daunting for the child and the family, but treatments will be aimed at improving mobility and spinal stability.

There is a genetic test that can be used to confirm whether or not a person has MPS VI

How is MPS VI tested?

Diagnosis of MPS VI is usually a two-stage process: a screen test and a confirmation test.

- A urine analysis will usually show excessive amounts of heparan sulphate and dermatan sulphate present.
- Reduced enzyme activity from a blood test or a genetic test to identify the IDUA gene mutation will then be done to confirm the diagnosis.

There is no cure for MPS VI, but treatment in the form of ERT works to restore cell function and can help improve physical endurance.

Enzyme replacement therapy (ERT) is available in MPS IVA

Autosomal recessive pattern is when both parents are carriers of the defective gene

When both parents are carriers of the faulty MPS VI gene (autosomal recessive) for each pregnancy there is a 25% (1:4) chance of having a child with MPS VI. The chance of a baby inheriting MPS VI is the same for every pregnancy.

Brothers and sisters of a person affected by MPS VI might also be carriers of the disease and it is recommended that they seek advice from their local genetic department about the potential risks in future pregnancies.

Is there a test for MPS I in pregnancy?

Amniocentesis involves testing a small sample of amniotic fluid

Chorionic villus sampling involves testing a small sample of cells from where the placenta attaches to the uterus

In utero means that the tests are done while the baby is still in the womb

A **pre-implantation genetic diagnosis** (PGD) is an assisted fertility treatment

In vitro literally means 'in the glass', as the testing is done in a flat glass dish called a petri dish

Unless there is a known genetic risk of MPS VI in the foetus, it is unlikely that a test in pregnancy would be done. If you have a child with MPS VI or a known history in your family, it is possible to have tests during any subsequent pregnancy to find out whether the foetus is affected. It is important to contact your doctor as soon as you suspect that you may be pregnant if you wish for tests to be arranged. Both amniocentesis and chorionic villus sampling can be used to diagnose MPS VI *in utero*.

If an individual who is affected by MPS VI has a baby they will always pass on an altered copy of the gene associated with that condition. This means that all of their children will be carriers of the condition; but it does not mean that all of their babies will be affected. In order for their child to be affected the other parent would also need to pass on an altered copy of the gene. A genetic counsellor can support you to understand what the chance is of this happening.

It might also be possible to have PGD screening to avoid passing MPS VI to the baby. PGD is an assisted fertility treatment that involves checking the chromosomes of embryos *in vitro* before they are implanted in the womb, using IVF techniques. This is a complex process and requires referral from your regional genetics service.

What is the value of genetic screening and counselling?

MPS VI is a genetically inherited disease and there is a risk of recurrence in future pregnancies for a couple with an affected child. Therefore, all parents of children with MPS VI should consider asking for genetic counselling before having other children. The counsellor should be able to provide non-directive advice on the reproductive choices, the risk to close relatives, and to suggest whether the wider family should be informed.

There are several specialist centres in the UK where you can go to be tested and to see a specialist in MPS VI, the most up to date list can be found on the MPS website: **mpssociety.org.uk/our-friends**

What are the possible symptoms and how are they managed?

Symptoms are known as **clinical presentations**

It is important to note that people affected by MPS VI may not experience all the symptoms. Where symptoms are present, they vary in severity from one person to another.

Skeletal symptoms are usually among the first symptoms to develop and are broadly split into the spinal region and other joints in the body.

Initial diagnosis is usually made between six and 24 months of age, and life expectancy depends on the severity of symptoms and is around 20 to 30 years. People with MPS VI often begin to show signs and symptoms during early childhood. These include changes to the physical appearance as well as developing other clinical features in the cardiovascular and respiratory systems.

Following a new diagnosis there will be lots of medical tests and then usually a series of operations and this may be daunting for the child and the family, but treatments will be aimed at improving mobility and spinal stability.

MPS VI Maroteaux-Lamy does not cause intellectual disabilities

Spine and neck

Spinal involvement is common and spine abnormalities can include weakness in the neck and skeletal deformities.

Development and symptoms

The **cervical vertebrae** are the bones in the neck

The **cervical spine** (neck region) is often very underdeveloped making the neck unstable and putting the spinal cord at risk. Where the spinal cord is compressed or squeezed, there may be gradual worsening of nerve damage if left untreated.

This can lead to

- A gradual loss of power in arms and legs
- Unsteady gait
- Problems with urinary function
- Lower back pain
- Paralysis and even death in extreme cases

The bones of the **spinal column** (vertebrae) often have poorly formed bones that may not stably rest on top of each other. This can lead to short stature and curvature of the spine.

- **Scoliosis** – when the spine curves to one side
- **Kyphosis** – a hump on the upper back
- **Kyphoscoliosis** – a mixture of both scoliosis and kyphosis

The breastbone continues to grow normally but, as it is joined to the spine, it is forced to buckle outwards in a rounded curve and the chest appears bell-shaped.

A **bell-shaped** chest reduces breathing capacity making it difficult to cope well with chest infections

Testing and management

Magnetic resonance imaging (MRI) or x-rays are performed to monitor the development and progress of the disease. Cervical fusion surgery can be performed under the review and management of neurosurgeons. Skeletal involvement is progressive and typically requires multiple orthopaedic interventions to prevent malformations and to improve function.

A **cervical fusion** means fusing some bones of the spine to prevent possible damage to the spinal cord

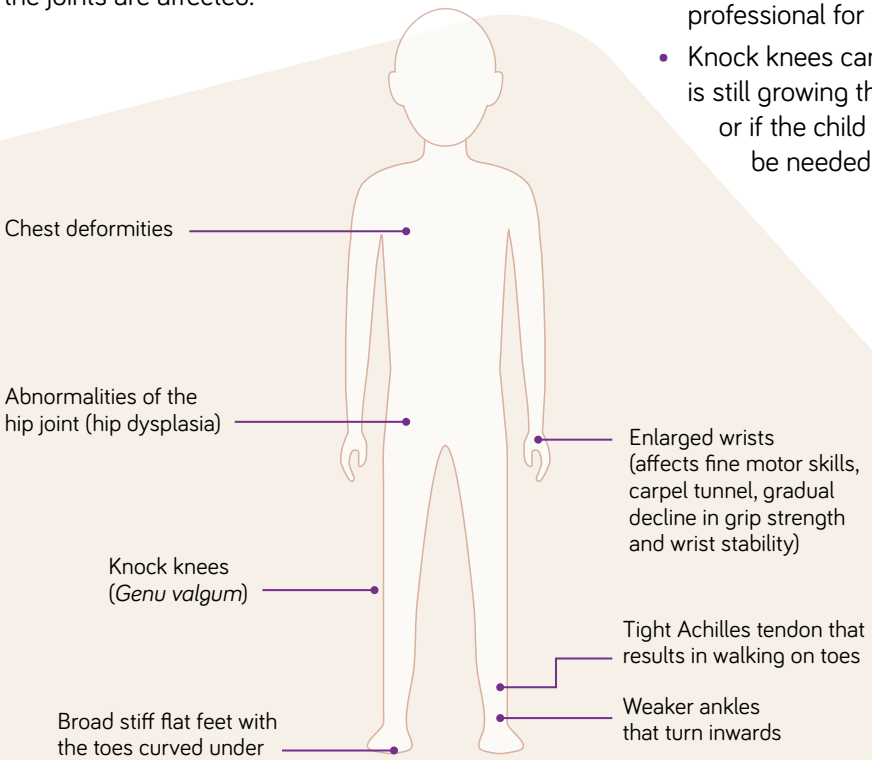
People with MPS VI Maroteaux-Lamy often have an abnormal way of walking (gait), standing and walking with their knees and hips flexed

Joints

Joint stiffness leads to limited movement in many areas of the body, including the shoulders, arms, hips and knees, and can sometimes cause aches and pain. Movement throughout the body is affected and increased muscle weakness compromises mobility. Some people with MPS VI may need to use walking aids or may become wheelchair-bound by adolescence.

Symptoms

Physical issues with the joints are most prevalent and are often seen before diagnosis. This diagram shows the areas of the body where the joints are affected.



Management

- Limited joint movement can make everyday activities like dressing difficult. Choose items of clothing that are easy to put on and take off to make getting dressed easier.
- Pain in the joints is a major symptom of MPS VI, but there are many ways this can be managed. For some people, pain may be relieved by applying warmth to the area, for example with a heat pack. Another option is painkillers. Speak with your doctor to select the most suitable treatment.
- There are alternative therapies such as hydrotherapy and physiotherapy programmes. Speak to a healthcare professional for advice.
- Knock knees can be treated with an operation. If the child is still growing this might involve **guided growth surgery**, or if the child has stopped growing other surgery may be needed.

There are many treatments available to manage pain, so speak to your doctor about options

Physical appearance

The skin is often thickened and lacking elasticity. Occasionally there may be more body hair than normal, which is called hirsutism.

Growth and height

- Babies grow normally until 18 months, thereafter growth slows significantly.
- Children who are severely affected usually stop growing around eight years old the final height may be between 90cm and 120cm.
- The height of children with a more attenuated form of the disease may not be as severely affected and they can reach around 150cm.

Facial features

- Very short neck
- Bridge of the nose is flattened
- Wider mouth with an enlarged tongue
- Teeth can be widely spaced and poorly formed with fragile enamel
- Chin may be prominent with a square jaw

People with MPS VI usually have a prominent lower face

The short stature is usually not in proportion; the trunk is relatively shorter than the legs

Heart

Slow and progressive valvular heart disease may develop without any obvious clinical effects. The heart valves are designed to close tightly as blood passes from one chamber of the heart to another in order to stop the blood flowing back in the wrong direction. Heart murmurs will occur if the valves become damaged by stored mucopolysaccharides.

Testing and management

An ECG test to measure the electronic activity of the heart, and an echocardiogram (ultrasound scan), are used to identify problems with heart muscle, function and valves. It is a painless procedure and is often carried out annually (or as often as your doctor thinks necessary) to show whether any problems are starting. An operation may be needed to replace damaged valves.

An **electrocardiogram** (ECG) is a test which measures the electrical activity of the heart

Lungs and breathing

Many people with MPS VI can struggle to maintain an open airway due to the narrowing of the airways and GAG deposits, which leads to breathing difficulties. In older teenagers and adults, the heart and lungs are squashed within a smaller area and make coping with chest infections harder. It is important to discuss any respiratory or breathing difficulties with your doctor so that the right treatment can be prescribed.

Bacterial **chest infections** may be treated with antibiotics

Symptoms

- Upper and lower respiratory infections
- Sleep apnoea, when breathing stops and starts during sleep
- Trouble breathing

Testing and management

Testing is done via overnight sleep studies. Regular reviews by a respiratory and ENT specialist can ensure that any necessary respiratory support is given. Some may benefit from the use of nebulisers and inhalers or an overnight **continuous positive airway pressure** (CPAP) or **bilevel positive airway pressure** (BiPAP), which pump air into the airway. Enlarged tonsils and adenoids may be removed to relieve upper airway obstruction and sleep apnoea.

Ear, nose, and throat (ENT) is a medical specialism

Liver, spleen and intestines

The liver, spleen and the lower abdominal are organs within the tummy (abdominal) area of the body. This area can look prominent for some people as the organs become enlarged.

Liver and spleen

The liver performs important tasks; it filters blood, produces a digestive liquid called bile to aid digestion, and stores energy. The spleen supports the immune system to help the body fight infections. An enlarged liver and spleen can develop from the build-up of mucopolysaccharide deposits (GAGs). Although these organs can continue to function normally, the abdomen may be distended and the pressure may affect eating and breathing.

An enlarged liver and spleen is known as **hepatosplenomegaly** (HSM)

Intestines

Occasionally, with a young child, diarrhoea can be present on its own or caused by severe constipation through leakage of loose stools from behind the solid mass of faeces. The problem may resolve itself as the child gets older, but it can be worsened by antibiotics prescribed for other problems. Constipation may become a problem as a child gets older as they may become less active and the muscles weaken.

Hernias are seen in people with MPS VI. This happens when an organ, such as the intestine, pushes through a weak spot in the muscle that holds it in place.

Depending on the type of hernia, surgery is needed in some cases

When making changes to your diet to improve digestive issues, make just one change at a time to see what is helping

Digestive issues

These issues are caused by enlarged organs. The rib cage restricts the stomach which means that people with MPS VI may need to eat little and often, and may vomit due to the pressure. Weight gain is also an issue for this group as they become less active and less mobile, so it is important to maintain a good balanced diet.

Symptoms

- Feeling sick, bloated, or vomiting after a meal
- Stomach cramps
- Changes in weight

Management

- Eating smaller meals at more regular intervals
- Sitting up straight while eating and taking small mouthfuls
- Avoiding spicy, high-fat foods and acidic foods
- Avoiding excesses of alcohol and caffeine
- Taking regular, gentle exercise
- Drinking plenty of water
- Gradually increasing fibre intake if constipated or eating less if experiencing diarrhoea

Eyes

Changes to the eyes are nearly always present and one common symptom is corneal clouding, which occurs when the cornea becomes scarred and stops light from passing through to the retina. The cornea may appear white or clouded. In early stages it does not generally impair or affect sight, it can be detected by eyecare professionals and provide an early sign that should be investigated before a diagnosis is made. A nightlight may be needed to help night vision.

Changes to the eyes are known as **opthalmological** changes

Dental

Because of potential problems with teeth and their enamel, good dental hygiene is especially important to avoid the need for extractions and other dental treatment. Using electric or battery-operated toothbrushes works better than a manual brush, especially for those with poor hand function.

Ears

Some degree of deafness is common. It may be conductive deafness, nerve deafness or both, called mixed deafness, and can be made worse by frequent ear infections.

Conductive deafness is when sound waves that travel through the ear canal, drum and the middle ear are impaired. Glue ear is where the middle ear fills with glue-like fluid instead of air, blocking the transmission of sound waves.
Nerve deafness is damage to the tiny hair cells in the inner ear. It may happen at the same time as conductive deafness; in which case it is referred to as **mixed deafness**.

Management

- Glue ear can be treated through surgery by inserting grommets into the ear. Small ventilation or tympanostomy tubes (T-tubes) are commonly used.
- Nerve deafness is usually managed by fitting hearing aids.
- Mixed deafness can be managed by grommets (small ventilation or T-tubes) or hearing aids.

The use of radio aids and the loop system can be helpful at school and at home.

Anaesthesia

When having an operation or procedure that requires an anesthetic, it is important that the patient is seen by an anesthetist experienced in MPS conditions or difficult airways. Pre-operative assessments should be carried out by those experienced in supporting MPS VI patients and the risks of every surgery explained.

For people with MPS VI, the airway can be very small and placing the tube in position for surgery can prove difficult. The doctor will use a flexible tube with a light and camera on the end in order to place the tube correctly.

The tube is known as an **endotracheal** tube

Equipped with a light and a camera, this is known as a **bronchioscope**

It is important that attempts are not made to extend the neck, especially when opening the airways. The cervical junction, the area where the skull and upper cervical spine connect, should always be considered unstable until proven otherwise. Attempts to adjust the area may compromise the spinal cord and be life threatening. The anaesthetist will be especially careful when repositioning the neck to avoid injury to the spinal cord.

Make medical staff aware of MPS VI and the anaesthetic risk for surgery and ask them to speak with your specialist team.

Living with MPS VI Maroteaux-Lamy

The MPS Society is able to provide more information on the following:

- Living independently
- Education and transition to employment
- Holistic approach, including well-being and mental health

Please contact us on **0345 389 9901** or visit our website **mpssociety.org.uk/advocacy** if you would like to find out more about how the MPS Society can support you.

Oliver talks about

My name is Ollie, I am 25 years old and have MPS VI which was diagnosed when I was four years old. Having MPS VI means it is necessary to manage time for hospital appointments, surgeries and infusions more than the average person.

living with MPS VI

Since the age of 11 I have been on a weekly enzyme replacement therapy (ERT) which is given intravenously over a four-hour period. This meant missing an afternoon of lessons each week throughout high school. Despite this I did manage 14 high-grade GCSEs. The ERT has been great at slowing the progression of the disease but I have still had problems that have cropped up over time that required treatment and surgery.

Throughout the majority of my time on ERT, a nurse would visit me at home once a week to insert the cannula, and my mum would do the rest of the treatment. This year, though, my mum has learned to do the cannulating too. This means that we have a lot more flexibility regarding my infusion each week and can fit it in when best suits us.

When I finished school, I spent a year in an accountancy apprenticeship and working full-time for a pneumatic company. After this year I found it quite difficult to maintain a full time role, due to having a few medical issues with my eyes that needed sorting and I was having my infusion each week after work, which finished quite late one night making me tired the next day. Due to this I decided to start a small online business of my own. And since then I have had a small mobile catering business and now for the past three years I have been trading stocks and shares and sports trading. Though it is not impossible for me to hold down a full-time role, I decided that if I was to become my own 'boss' I would not have to ask permission to have time off for hospital visits etc.

I am now awaiting a second cornea transplant and a possible operation on my legs to hopefully help with my mobility. I know my condition is a progressive one, but the ERT is helping to slow this. However, my aim now and always will be to lead a life as 'normal' as possible.

What kind of treatments and therapies are available for MPS VI?

Although there is currently no cure, management of MPS VI is outlined on pages 7 to 15 and the doctors will offer a range of treatments depending on the symptoms that the patient experiences. Because symptoms are highly individual, treatment will vary from person to person. Medical companies are looking into treatment of rare diseases and new treatments may become available in the future. Your specialist team will make you aware of any new trials or treatments.

The most common current treatment is enzyme replacement therapy (ERT). This uses a genetically engineered form of the missing or malfunctioning enzyme administered once a week by intravenous infusion over a number of hours.

If you would like more information on treatment options and clinical trials, then please contact your MPS VI specialist or the MPS Society.

More information about treatments is available here: **mpssociety.org.uk/treatments** and the latest information about clinical trials can be found here: **mpssociety.org.uk/clinical-research**

Because symptoms are highly individual, treatment will vary from person to person

Where can I get more information and support?

The Society for Mucopolysaccharide Diseases (MPS Society) is the only registered UK charity providing professional support to individuals and families affected by MPS and related lysosomal storage diseases throughout the UK.

Further information booklets and other resources about MPS, Fabry and related diseases are available from **mpssociety.org.uk**

Our Support and Advocacy team have specialist knowledge of these diseases and a background in social care. We are here for you whenever you need us.

Phone us on **0345 389 9901** Mon to Fri 9am–5pm

Outside these hours you can call us on **07712 653 258**
Mon to Fri 7am–9am and 5pm–10pm
Sat and Sun 7am–10pm

Email us at **advocacy@mpssociety.org.uk**

Members in Northern Ireland can contact our Northern Ireland based advocacy worker on **07786 258 336**

Every effort has been made to ensure that the information in this booklet was accurate and up to date at the time of going to press. This booklet is not intended as a substitute for professional medical advice and the MPS Society and other contributors cannot take responsibility for actions taken as a result of this information.

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