SUPPORT | RESEARCH | AWARENESS

MPS I
Hurler-Scheie 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 I Hurler-Scheie and their families to understand its causes and effects. While there is currently no cure for people affected by MPS I Hurler-Scheie, 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 I Hurler-Scheie disease displays a spectrum of symptoms

What is MPS I Hurler-Scheie?

MPS I 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.

Muco means jelly-like
poly means many
saccharides means sugar

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

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 I and other similar conditions are also known as lysosomal storage diseases. The process requires a series of special biochemical tools called enzymews.

MPS I includes Hurler, Hurler-Scheie and Scheie diseases. These diseases differ in severity across a spectrum of symptoms. Hurler disease (severe form), was first identified by Dr Hurler in 1919; later in 1962 Dr Scheie identified MPS I Scheie disease (mild form). People with MPS I who appear not to fit clearly at either end of the spectrum of Hurler or Scheie are classified with Hurler-Scheie disease.

What causes MPS I Hurler-Scheie?

MPS I Hurler-Scheie is the result of a specific enzyme (called iduronidase) either not working correctly or not being produced at all.

This occurs because there is a mistake (mutation) in the gene called IDUA 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 Hurler-Scheie are a result of the build up of dermatan sulphate and heparan sulphate in the body. The severity of MPS I is related to the level of enzyme activity.

Higher enzyme activity levels lead to less build up of dermatan sulphate and heparan sulphate within the body, resulting in milder signs and symptoms (sometimes called **attenuated disease**). This is what happens in MPS I Scheie.

Lower or absent enzyme activity levels lead to build-up of dermatan sulphate and heparan sulphate within the body, resulting in varying moderate to severe symptoms of MPS I Hurler-Scheie and MPS I Hurler.

How is MPS I inherited?

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

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

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

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.

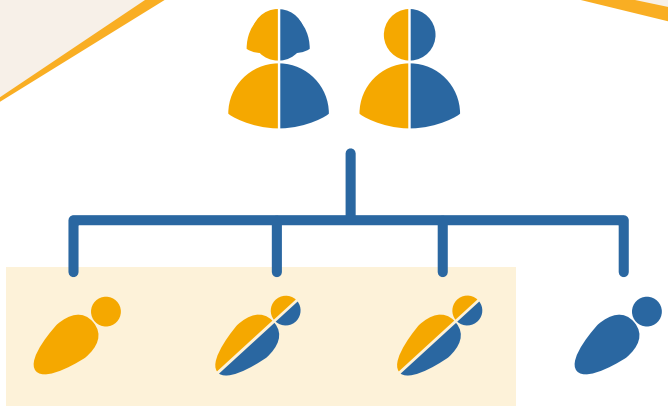
Genes are carried on structures called chromosomes. It is usual to have 23 pairs of chromosomes that are numberedin pairs from pair 1 to pair 22, plus one pair of sex chromosomes: XX for a female and XY for a male. A child will inherit one set of chromosomes from the mother in the egg, and one set from 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 I, 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.

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

Brothers and sisters of a person affected by MPS I 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.



Autosomal recessive

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

How common is MPS I Hurler-Scheie?

It is estimated that MPS I Hurler-Scheie affects about 1 in 100,000 newborns.

Life expectancy can vary between individuals and is dependent on the symptoms they experience and how they are managed. How it will affect individuals is unpredictable and if more advice is needed, please contact your specialist. To give a general idea, initial diagnosis is usually made between six and 24 months of age and life expectancy may be around 20 to 30 years, but could be longer. Severely affected people may live only until early childhood or adolescence; those with milder forms usually live into adulthood.

How is MPS I Hurler-Scheie diagnosed?

MPS I Hurler-Scheie 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 to make a diagnosis. People with MPS I Hurler-Scheie may experience some or all the symptoms that are outlined in this booklet before receiving an actual diagnosis. Where symptoms are present, they vary in severity from one person to another.

Following a new diagnosis there will be lots of medical tests and some people with MPS I Hurler-Scheie may undergo 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.

How is MPS I Hurler-Scheie tested?

Diagnosis of MPS I Hurler-Scheie is usually a two-stage process involving a screening test and a confirmation test.

- A urine analysis will usually show excessive amounts of heparan sulphate and dermatan sulphate present in the urine.
- 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 a genetic test that can be used to confirm whether or not a person has MPS I Hurler-Scheie

Enzyme replacement therapy (ERT) is available in MPS I Hurler-Scheie

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

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 I in the foetus, it is unlikely that a test in pregnancy would be done. If you have a child with MPS I, 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 I *in utero*.

If an individual who is affected by MPS I 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 I 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 I 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 I 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 I, 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 I Hurler-Scheie may not experience all the symptoms. Where symptoms are present, they vary in severity from one person to another.

People with MPS I Hurler-Scheie 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.

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

MPS I Hurler-Scheie is unlikely to affect intelligence

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) may be poorly formed and 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

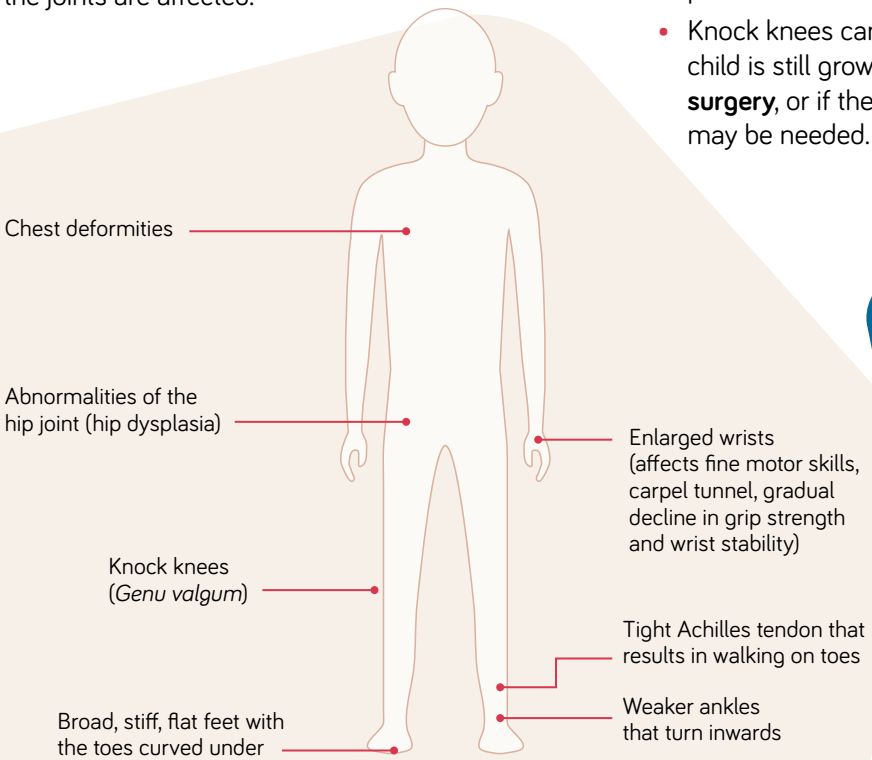
People with MPS I Hurler-Scheie often have an abnormal way of walking (gait), standing and walking with their knees and hips flexed

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 I Hurler-Scheie 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 getting dressed difficult. Choose items of clothing that are easy to put on and take off to make dressing easier.
- Pain in the joints can be a major symptom of MPS I Hurler-Scheie and there are many ways this can be managed. For some people pain may be relieved by applying warmth to the area, for example, by using 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 till 18 months, thereafter growth slows significantly.
- Children who are severely affected usually stop growing around eight years old and 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 I Hurler-Scheie 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

People with MPS I Hurler-Scheie 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 this makes 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** should 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 and spleen are organs within the tummy (abdominal) area of the body. This area can look prominent 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 disappear 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 commonly seen in people with MPS I Hurler-Scheie. This happens when an organ, such as the intestine, pushes through a weak spot in the muscle that holds it in place.

Surgery may be needed for some types of hernia

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 I Hurler-Scheie 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 known as **ophthalmological** changes

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. Some children may need a nightlight to help night vision.

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, 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, an anesthetist experienced in MPS conditions or difficult airways is needed. Pre-operative assessments should be carried out by those experienced in supporting MPS I Hurler-Scheie patients and the risks of every surgery explained.

For people with MPS I Hurler-Scheie, 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.

These are 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, therefore the anaesthetist will be especially careful when repositioning the neck to avoid injury to the spinal cord.

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

Living with MPS I Hurler-Scheie

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.

Elizabeth talks about living with MPS I Hurler-Scheie

If you are reading this booklet then I already know two things about you.

The first is that your child or someone close to you has just been diagnosed with MPS I Hurler-Scheie. The second is that you are feeling worried, confused and scared that your life and that of your loved one will never be normal once again.

Well, I want to tell you it will. Believe me. How do I know this?

Well, 15 years ago, my parents were in the exact same situation as you. And we all got through it. I picked up a few surgical scars along the way, but my diagnosis of MPS I Hurler-Scheie Attenuated when I was four years old did not herald the end of my life, or that of my parents. It definitely made it more challenging but such was their determination that I should not be defined by MPS, they went to great lengths to normalise every aspect of my condition as much as possible.

MPS certainly meant some practical adjustments needed to be made at home, plus surgeries were needed as and when and medical treatment plans needed putting in place, but the most important bit was this. My family welcomed this new, rare, incurable condition into their lives and into their home. They made friends with MPS and vowed to educate themselves on every aspect of this rare condition in order to ensure the very best medical treatment and life options for me. Every act, every surgery, and every decision was made – purely and simply – with my life, my welfare and my future in mind. For that, I will be eternally grateful. They did not allow MPS to limit their hopes and dreams for my life and my potential.

It is very important to remember that every diagnosis of MPS I Hurler-Scheie is unique, just like your child. No two cases are the same but there are similarities and varying degrees of severity. As you know by now, there is a spectrum of Hurler-Scheie that spans from severe to mild. Depending on your child's level of severity, you will have to deal with the unique symptoms they present with, or those they go on to develop.

Growing up, I have no recollection of being 'told' that I had MPS I Hurler-Scheie. I wasn't treated any differently to my sister, nor was I regarded as special. I was just me. I was expected to do all the things my friends and sister did. I just did them my way. I really enjoyed being a kid. School, friends, drama groups and harp and piano lessons kept me really busy. Mixed in with all that fun stuff was my weekly enzyme infusion (ERT). It wasn't my favourite part of my week, but it was something that had to be done and was certainly made easier with lots of treats and a ready supply of chocolate.

It is very important to remember that every diagnosis of MPS I Hurler-Scheie is unique – just like your child

Regular hospital check-ups with my specialists in Manchester became part of our normal family routine and as the years rolled on, I notched up a few surgeries, including vascuport insertion, carpal tunnel, trigger finger release, and cervical spine decompression. In fairness, all of these surgeries were a bit of a nuisance but we just got on with everything – after all, they were for my benefit and would help secure my ability to live a quality, independent life.

I am now 19 years of age and am about to set off to study Law at university. My journey to where I am now hasn't been easy but nor has it been impossible. The challenges I have overcome with the help of my family, have made me who I am today. And regardless of MPS, my parents never lost sight of their vision that I would live a full, happy life.

I really want to impart some important advice to you, the parent. For one moment, I want to be the voice of your child's future. I have walked this path that you now find yourself on. Although this journey may seem very dark and frightening right now, I want to shine a light to make your journey easier. And I would like you to know this. The only thing your child needs right now is your love and your support. Your child will thrive in spite of MPS and they will live a happy and fulfilling life alongside MPS as long as they are surrounded by your help, guidance and creativity.

As someone with Hurler-Scheie I know that every child needs warrior parents who will tirelessly oversee every appointment with every specialist involved in their care, to proactively manage their medical or surgical needs. Every child needs school support and a statement of educational needs in order to protect their ability to reach their academic and developmental potential and help them realise their ambitions within the remits of their abilities. Every child needs exposure to everything that brings joy into their lives. Every child needs boundless praise to feed their self-esteem and their confidence with unceasing praise and needs to celebrate every single achievement, no matter how small. Strengthen and build your child up and help them to be the very best version of themselves possible. You, the parent, have already created a phenomenal human being. MPS has not changed that. As the parent, you can help your child to become exceptional and to live an amazing life and make their mark.

Living with MPS is indeed challenging but it it is not impossible. It will, however, be unbearably harder if it is combined with unrealised potential.

What kind of treatments and therapies are available for MPS I Hurler-Scheie?

Although there is currently no cure, management of MPS I Hurler-Scheie 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 I Hurler-Scheie 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**

We also have a number of resources and lots of information available on our website: **mpssociety.org.uk**

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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