SUPPORT | RESEARCH | AWARENESS

MPS I
Hurler 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 and their families to understand its causes and effects. While there is currently no cure for people affected by MPS I Hurler, 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?

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.

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

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?

MPS I Hurler 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 I Hurler are a result of the build-up of dermatan sulphate and heparan sulphate in the body. In general, the severity of MPS I Hurler is related to the level of enzyme activity that remains.

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**).

Lower or absent enzyme activity levels lead to a 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 Hurler inherited?

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

How common is MPS I Hurler?

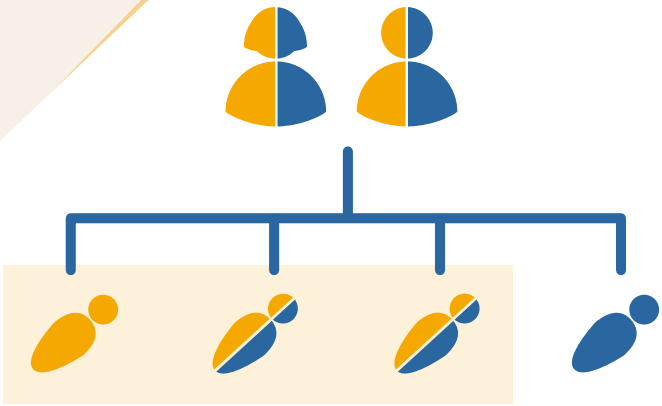
It is estimated that MPS I Hurler affects about 1 in 200,000 newborns in Europe.

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 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.

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%

There is a genetic test that can be used to confirm whether or not a child has MPS I Hurler

How is MPS I Hurler diagnosed?

MPS I Hurler 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 test results to make a diagnosis. Initial diagnosis is usually made between six and 24 months of age.

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.

What can I expect in the future?

MPS I Hurler is the severe form of the disease with many symptoms. Untreated, life expectancy may not be more than 11–12 years. When treated, it can be extended to around 30 years, depending on the severity of the symptoms.

How is MPS I Hurler tested?

Diagnosis of MPS I Hurler 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.

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

There is no cure for MPS I Hurler. Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for patients with MPS I Hurler syndrome under two and a half years of age and before developmental deterioration begins. Enzyme replacement therapy (ERT) may be used at diagnosis to prepare the child for HSCT, or it may be continued if HSCT is not suitable. ERT works to restore cell function and can help improve physical endurance.

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

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.

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 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**

People with MPS I Hurler often begin to show signs and symptoms of MPS I Hurler during early childhood. These include changes to the physical appearance as well as developing problems with the cardiovascular and respiratory systems.

MPS I Hurler can cause intellectual disabilities.

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

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 a 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

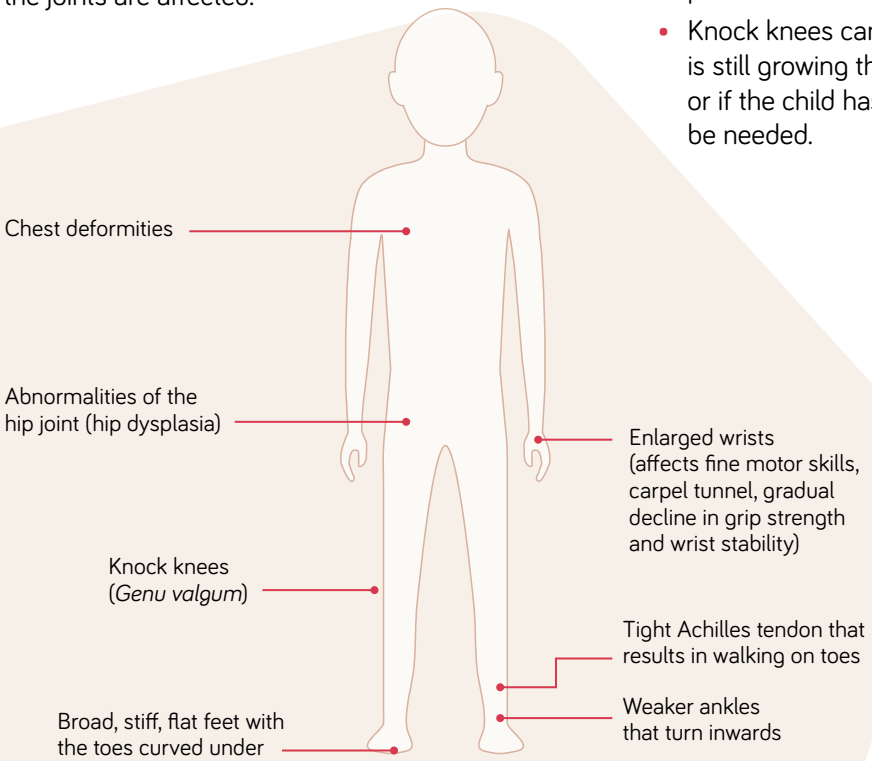
People with MPS I Hurler often have an abnormal way of walking (gait), standing and walking with their knees and hips flexed

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 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 is a major symptom of MPS I Hurler, but there are many ways this can be managed. For some people, pain may be relieved by applying warmth to the area, using a heat pack, for example. 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 develop signs of the disease during the first months of life.
- There may be delays in reaching normal developmental milestones such as sitting, crawling, walking.
- By three years, growth usually slows down significantly and intellectual and hearing problems become apparent.
- Children who are severely affected usually stop growing around eight years; the final height may be between 90cm and 120cm.

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 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 I Hurler can struggle to maintain an open airway due to the narrowing of the airways and GAG deposits which leads to breathing difficulties.
In older children and teenagers, the heart and lungs are squashed within a smaller area, which 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 pumps 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

With a young child, diarrhoea can be present on its own or can be 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. 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 may be 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 I Hurler 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
- 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 **ophthalmological** 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, especially for those with poor hand function.

Ears

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 I Hurler patients and the risks of every surgery explained.

For people with MPS I Hurler, 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 I Hurler and the anaesthetic risk for surgery and ask them to speak with your specialist team.

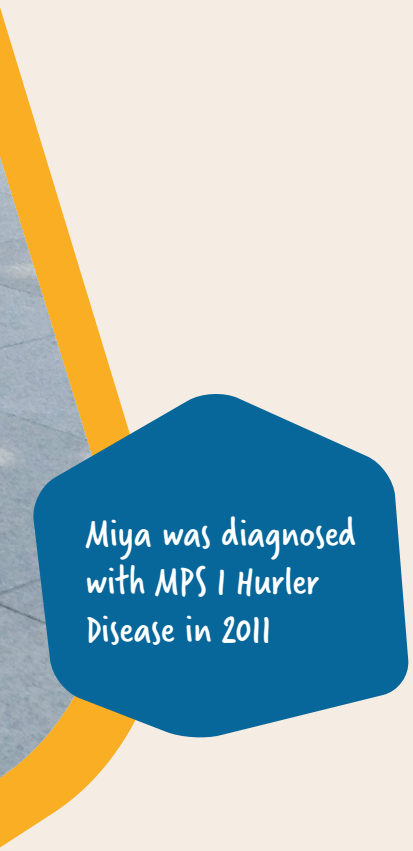
Living with MPS I Hurler

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.

Miya lives with MPS I Hurler



Miya was diagnosed with MPS I Hurler Disease in 2011

My husband and I got married in 2008 and I discovered I was pregnant a year later. Our little girl arrived after a smooth pregnancy and we called her Miya. Her birth had been a little bit rocky and she arrived face first, so at the time, I wasn't alarmed at the slightly "squished" look to her face, particularly her nose.

When Miya was two weeks old, she began showing signs that worried us. She wouldn't stop crying and she suffered terribly from silent reflux. Her breathing was noisy and I felt something wasn't right about the way she looked. Her face, particularly her eyes, forehead and nose struck me as being slightly off.

Her head was quite large and her neck was quite short. Her blue eyes were beginning to turn a cloudy grey colour. She was very floppy and her joints seemed to crack excessively. I took her to our GP about her noisy breathing and he advised she was young and her respiratory system was immature and just to keep an eye on it.

Miya has problems with her feet, and our orthopaedic doctor felt that perhaps this was a symptom of something greater and referred us to a paediatrician for testing. This doctor was the only medical professional who had the courage to say they thought something unusual was going on with Miya's health.

Miya was diagnosed with MPS I Hurler disease in 2011.

My husband and I are trying to stay strong. Now we know what Hurler disease is, we understand that we will need courage for the future. Chris is a serving soldier in the British Army, and they have been tremendously helpful in making sure that we are posted in the South West of England so we can be close to Miya's hospital. My family are all in Canada, and Chris's family are in Cumbria, so we are a little "island" of sorts.

The MPS Society has been very helpful in sending us supportive information and offering to put us in touch with other families who are affected by MPS. I know that in the difficult times to come, the MPS Society will be there for us as parents, and for Miya, offering us the support we will all need.

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

Although there is currently no cure, management of MPS I Hurler 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.

Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for patients with MPS I Hurler syndrome under two and a half years of age and before developmental deterioration begins. ERT is not routinely used after HSCT has been done, but may be used to prepare for HSCT or if HSCT cannot be done. The most common current treatment thereafter 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 specialist or the MPS Society.

More information is available on the website here: **mpssociety.org.uk/treatments** and **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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