SUPPORT | RESEARCH | AWARENESS

MPS I
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 Scheie and their families to understand its causes and effects. While there is currently no cure for people affected by MPS I 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 Scheie disease was first identified by Dr Scheie in 1962

What is MPS I 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.

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 Scheie?

MPS I 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 I Scheie are a result of the build up of dermatan sulphate and heparan sulphate in the body. In general, the severity of MPS I Scheie 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 a build up of dermatan sulphate and heparan sulphate within the body, resulting in varying moderate to severe symptoms in 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

How common is MPS I Scheie?

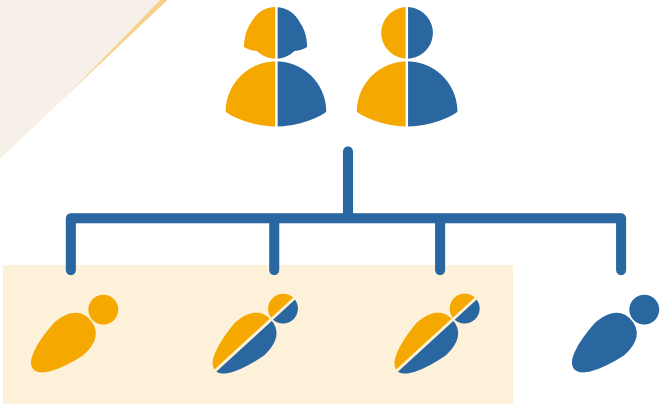
It is estimated that MPS I Scheie affects about 1 in 500,000 newborns.

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 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.

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 I Scheie diagnosed?

MPS I 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 Scheie may experience some or all the symptoms that are outlined in this booklet before receiving an actual diagnosis. MPS I Scheie diagnosis can happen from early childhood through to adulthood. Although symptoms may begin to appear by age five, affected children are often not diagnosed until after age ten.

What can I expect in the future?

Life expectancy for people with MPS I Scheie is only slightly affected and depends on the symptoms experienced. Symptoms usually occur after the age of five but are mild and diagnosis is often not considered until adulthood.

How is MPS I Scheie tested?

Diagnosis of MPS I Scheie 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 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 no cure for MPS I Scheie, 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 I Scheie

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.

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

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 Scheie may not experience all the symptoms. Where symptoms are present, they vary from one person to another.

Overall, there is slow disease progression affecting joints and bones. Hernias, some hearing and visual problems, and heart valve disease are the most frequent signs.

MPS I Scheie does not cause intellectual disabilities

Skeleton and joints

Skeletal and joint symptoms are common and can begin in childhood.

Development and symptoms

The **cervical spine** (neck region) stabilises the neck, which reduces risk the spinal cord. Where the spinal cord is compressed or squeezed, there may be gradual worsening of nerve damage if left untreated.

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

Joint stiffness affects movement in many areas of the body, including the shoulders, arms, hips and knees, and can cause aches and pain. Movement throughout the body is affected and increased muscle weakness compromises mobility. Physical issues are most prevalent and often present before diagnosis.

This can lead to

- A gradual loss of power in arms and legs
- Unsteady gait
- Lower back pain
- Standing and walking with knees and hips flexed
- Carpel tunnel
- Abnormalities of the hip joint (hip dysplasia)

The bones of the **spinal column** (vertebrae) may be poorly formed and may not stably rest on top of each other; for some people this may lead to short stature and curvature of the spine.

- **Scoliosis** – when the spine curves to one side
- **Kyphosis** – a hump on the upper back

Testing and management

Magnetic resonance imaging (MRI) or x-rays are performed to monitor the development and progress of the disease. Where surgery is needed it is normally performed under the review and management of neurosurgeons.

Management

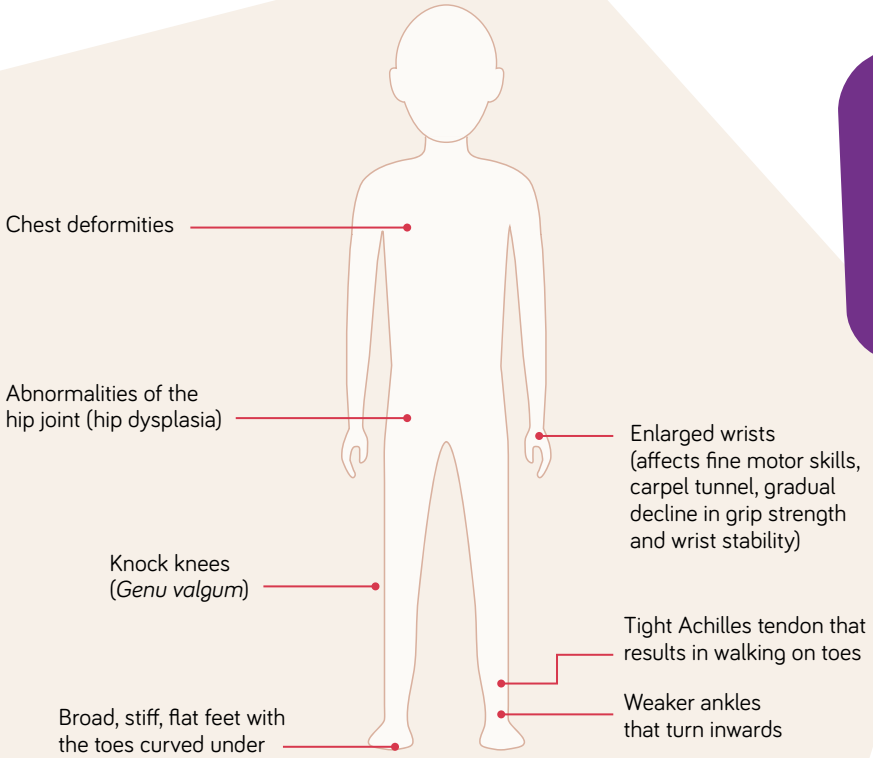
- For some people, pain in the joints may be relieved by applying warmth to the area such as a heat pack. Another option is painkillers. Speak with your doctor to select the most suitable treatment.
- There are alternative therapies such as hydrotherapy and physiotherapy programmes, speak to a healthcare professional for advice.

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

Physical appearance

Babies and children grow normally and by adulthood most usually reach normal height. Physical onset of symptoms varies between individuals ranging between five and 12 years for most features, including mild coarsening of facial features, such as a large mouth with thick lips and a square jaw.

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



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.

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

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.

Lungs and breathing

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

The lungs and breathing are relatively unaffected, and focus is on management of nasal secretions, coughs, colds and throat infections. It is important to discuss with your doctor any respiratory or breathing difficulties as soon as they develop so that the right treatment can be prescribed.

Management

Regular reviews by a respiratory and ENT specialist can ensure that any necessary respiratory support is given.

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

Liver, spleen and intestines

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

The liver and spleen 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.

Intestines

Hernias are fairly common among people with MPS I Scheie. 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 sometimes needed

Eyes

Changes to the eyes are known as **opthalmological** 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. A nightlight may be needed to aid night vision.

Ears

Some deafness may occur. This 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 is needed. Pre-operative assessments should be carried out by those experienced in supporting MPS I Scheie patients and the risks of every surgery explained.

For people with MPS I Scheie, the airway can be 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.

This tubeis 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 Scheie and the anaesthetic risk for surgery and ask them to speak with your specialist team.

Living with MPS I 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.

We provide a support network promoting understanding and awareness of the diseases

Support and Advocacy Lead, Steve Cotterell, shares his story

I am proud to head up the Support and Advocacy team. Having worked as a support officer for many years I understand the determination and expertise required to support our families and individuals living with these diseases.

Supporting children, young people and adults affected by MPS, Fabry and related conditions and their families is at the heart of what we do, and so we strive to provide a responsive service that gives people the help they need when they need it.

We are often able to make a positive difference to the lives of our community and this gives a real sense of achievement.

In particular, the rarity of these conditions means affected individuals and their families often experience difficulties accessing adequate needs-led support and services in their local area. We provide a support network promoting awareness and understanding of the diseases and we work in partnership with you and your family as well as developing professional relationships with local health professionals.

Each of our support officers has specialist knowledge in the particular diseases they look after so if you want to know anything about MPS I Scheie we can help and are here to provide emotional support, practical advice, information and guidance, and signposting where needed.

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

Although there is currently no cure, management of MPS I Scheie is outlined on pages 7 to 13 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 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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