SUPPORT | RESEARCH | AWARENESS

MPS II
Hunter 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 II Hunter and their families understand its causes and effects. While there is currently no cure for individuals affected by MPS II, 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 II disease was first identified by Dr Hunter in 1971

What is MPS II Hunter?

MPS II, known as Hunter disease, 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 II 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 II?

MPS II is the result of a specific enzyme (iduronate 2-sulphatase) either not working correctly or not being produced at all. This occurs because there is a mistake (mutation) in the gene called iduronate 2-sulphatase (IDS) 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 II are a result of the build-up of dermatan sulphate and heparan sulphate in the body.

In general, the clinical picture of MPS II for any individual is related to the level of enzyme activity that remains.

Higher enzyme activity levels, often referred to as attenuated, lead to less build up of dermatan sulphate and heparan sulphate within the body, resulting in milder signs and symptoms.

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

What can I expect in the future?

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

The life expectancy depends 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 II Hunter inherited?

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

How common is MPS II?

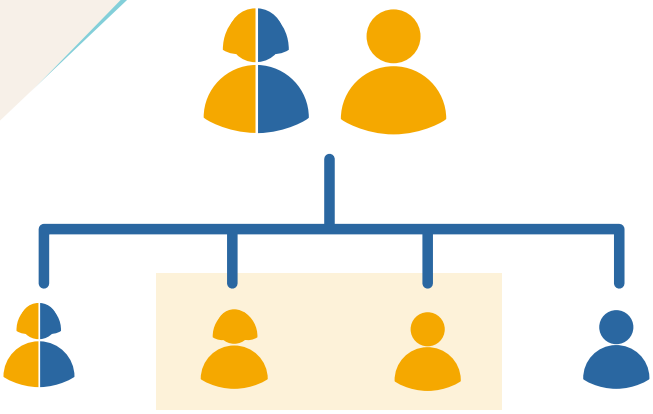
It is estimated that MPS II affects between 1 in 100,000 to 1 in 170,000 males. MPS II is almost exclusively found in males, although cases of affected females have been reported.

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.

MPS II is the only mucopolysaccharide disease in which the mother alone can pass the affected IDS gene to a son, called X-linked recessive.

X-linked recessive pattern is when the mother alone passes the defective gene to a son



X-linked recessive

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

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

For each pregnancy with a female carrier of MPS II there is a 50% (1:2) risk that any male born to her will have the disease. There is a 50% (1:2) risk that any female born to her will be a carrier for the disease. The chance of a baby inheriting MPS II is the same for every pregnancy. There have been cases of MPS II men having children, this means that any girl born to them would be carriers and a son would not have MPS II.

It is not always the case that the mother is a carrier; there are cases where the gene alteration has occurred for the first time and no link back to the mother has been found.

The sisters and maternal aunts of a male with MPS II may be carriers of the disease and would also have the same risk of passing the affected gene to any male born to them. It is recommended that they seek advice from their local genetic department about the potential risks in future pregnancies.

How is MPS II Hunter diagnosed?

MPS II 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. Males with MPS II may experience some or all of the symptoms that are outlined in this booklet before receiving an actual diagnosis.

How is MPS II tested?

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

- A urine analysis will usually show excessive amounts of dermatan sulphate and heparan sulphate in the urine.
- Reduced enzyme activity from a blood test or a genetic test to identify the IDS 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 II

There is no cure for MPS II, but treatment in the form of ERT works to restore cell function and can help improve physical endurance. Hematopoietic stem cell transplantation (HSCT) can be an option for patients under two years.

Enzyme replacement therapy (ERT) is available in MPS II

Is there a test for MPS II 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 II in the foetus, it is unlikely that a test in pregnancy would be done. If you have a child with MPS II 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 II *in utero*. Some families choose to have a blood test at week seven of the pregnancy to determine sex before amniocentesis and chorionic villus sampling.

It might also be possible to have PGD screening to avoid passing MPS II 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 II 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 II 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 II. 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 II Hunter experience a wide range of symptoms. Where symptoms are present, they vary in severity from one person to another.

MPS II Hunter can affect intellectual and physical development. Children with the more severe form (neuronopathic) of MPS II will most likely experience delays in intellectual and social development, and physical characteristics are more prominent with overall rapid disease progression.

Children with a less severe form (non-neuronopathic) of MPS II are much less affected by intellectual and social development, and physical characteristics are less obvious; disease progression is also slower.

In the non-neuronopathic form of the disease intelligence may be normal or only slightly impaired

Brain and nervous system

Children with no neurological involvement tend to have normal or near normal intelligence. Many go on to college, university and employment.

Children with neurological involvement experience progressive storage of GAGs in the brain. This can cause progressive learning difficulties and gradual loss of skills. There is huge variation in how the storage affects the brain and the severity of the learning disabilities, with some children only learning a few words whilst others are able to speak in sentences and read books.

In the severe form, children can develop abnormal behaviours: some can be hyperactive and have trouble paying attention or following directions, while others behave aggressively and seem unable to sense danger.

- Mental development will become affected between the ages of two and six.
- Sometimes fluid builds up around the brain leading to increased pressure and severe headaches that interfere with vision.
- Seizures may also occur and need to be managed with anti-convulsant medication.

Hydrocephalus is caused by build-up of fluid around the brain

Testing and management

Speak to your doctor about anticonvulsant medication to manage seizures. Tests to confirm hydrocephalus can be done using a computed tomography (CT) or magnetic resonance imaging (MRI) scan, or a lumbar puncture. If hydrocephalus is confirmed it can be treated by an insertion of a small tube in the spinal cord which drains fluid from the brain.

Physical development

Growth and height

The symptoms of MPS II Hunter are generally not apparent at birth but start to become noticeable before two years of age as the GAGs accumulate in the cells. Diagnosis is not usually made until the age of two to four years. Typically features are;

- Children are shorter, though in milder cases normal or near-normal height can be reached.
- Hands are short and broad with stiff curled fingers.
- Feet are flat and broad, and toes can curl under.
- Pubertal development is normal but may be delayed in some males.
- Skin is thick and tough with more hair on the back and torso.

Hirsutism is when there is more hair on the body than normal

CT and MRI scans are used to help diagnose hydrocephalus

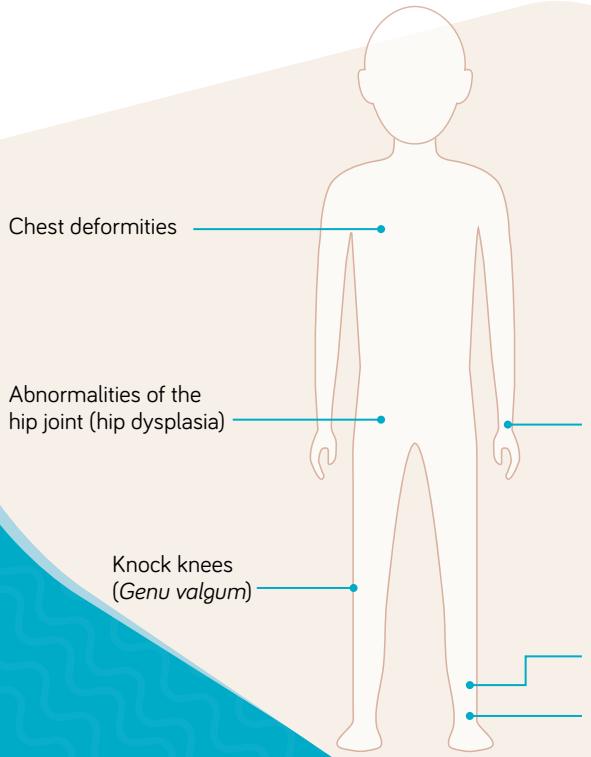
Facial features

- Coarseness in facial features
- Large head with prominent forehead
- Short neck
- Nose with a flattened bridge
- Enlarged tongue
- Coarse hair and bushy eyebrows
- Deep, hoarse voice

Skeleton and joints

Problems with the skeleton will get worse over time and typically require multiple orthopaedic, spinal or neurosurgical interventions to prevent abnormalities and to improve function. Often people with MPS II Hunter walk on their toes because of tendon shortening and they have reduced flexibility in their joints. Fine motor skills may be affected by carpel tunnel syndrome and a decline in grip strength and wrist flexibility. It it best to get expert advice on how to manage these symptoms. As in all areas of medicine, new developments come into use all the time and discussing this with an expert is the best way to find out if some of these are suitable.

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



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

Testing and management

- MRI or x-rays are performed to monitor the development and progress of the disease.
- Limited joint movement and weakness 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 II Hunter, 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, so 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.

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

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

Many people with MPS II Hunter can struggle to maintain an open airway due to the narrowing of the airways and collapsing airways, which leads to breathing difficulties. In older teenagers and adults, the heart and lungs are squashed within a smaller space, 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.

Symptoms

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

Testing and management

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

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.

Liver, spleen and intestines

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.

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

Intestines

In males with the severe form of MPS II, incontinence is common and this can be from the start or later as the disease progresses. For others, 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 II Hunter. 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 II Hunter 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
- Frequent heartburn
- 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
- Some medications can help if symptoms are severe, so discuss this with your expert

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.

Eyes

Occasionally visual problems exist caused by changes in the retina or by glaucoma. Some children may find a night light helpful for night vision.

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

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. Chronic glue ear can lead to damage to the ear drums which contributes to hearing loss and recurrent ear canal infections. **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.
- Newer hearing aids, like bone-anchored hearing aids and cochlear implants, can be used in special circumstances.

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 II patients and the risks of every surgery explained.

For people with MPS II, 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 camera and light, 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 II and the anaesthetic risk for surgery and ask them to speak with your specialist team.

Living with MPS II Hunter

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.

Louis talks about living with MPS II Hunter

Louis says he doesn't like to talk or think about his condition too much, and tries to keep it just as a 'label' rather than a burden. But when he does discuss it, he approaches the subject lightly and with good humour.

Louis has been on enzyme replacement therapy for MPS II Hunter since the age of eight, having taken part in the clinical trial resulting in the licensing of Elaprase. He was able to go into mainstream education and then onto university. While at school he was advised not to play contact sports such as rugby, but he enjoyed hockey and tennis.

Having got a place at university, Louis took a gap year and worked in an outdoor retail store to raise money to take a trip abroad. The staff were understanding of his condition, allowing him to take short breaks off the shop floor if he had joint pains. In addition Louis learned to give himself his own ERT infusions, so that he wouldn't be reliant on a nurse while travelling.

He travelled around Australia, New Zealand and Thailand, taking two months of enzyme with him, making sure there were friends or relatives close by in case he had any issues with his infusions. He made many friends on his travels.

At university he enjoyed sharing a flat with friends and graduated with a degree in mechanical engineering.

'The more people you meet the more you're going to find those who accept you for who you are.'

He does admit life hasn't always been easy, as he has joint pains and is often fatigued. He's had various operations along the way including recent heart surgery.

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

Although there is currently no cure, management of MPS II 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 II 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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