What is MPS I?

Hurler, Hurler Scheie and Scheie Disease are Mucopolysaccharide storage disorders also known respectively as MPS IH, IHS and IS. In the past these diseases were described solely on the presence of symptoms and were simply named after the doctors that first identified them. Hurler Disease takes its name from Gertrud Hurler, the doctor who first described a boy and girl with the condition in 1919.

In 1962 Dr Scheie, an American consultant ophthalmologist, identified a patient with an attenuated form of MPS I. Patients who appear not to fit clearly at either end of the disease spectrum are classified with Hurler Scheie Disease.

However, current understanding of the enzyme and its gene defect shows that MPS I comprises a wide spectrum of severity and symptom involvement. The traditional classification of Hurler, Hurler Scheie and Scheie does not adequately reflect this wide spectrum. Whilst there is no cure for individuals affected by MPS I this booklet explores the presentation and clinical management of MPS I. Bone Marrow Transplant, Haematopoietic Stem Cell Transplantation, Umbilical Cord Blood Transplant and Mobilised Peripheral Blood Stem Cell Transplant are addressed in this fact sheet (see specific treatment of MPS I).

This factsheet is produced by the Society for Mucopolysaccharide Diseases (MPS Society) drawing on the experiences of parents and doctors with reference to medical literature.

What causes Hurler Disease?

Mucopolysaccharides are long chains of sugar molecules used in the building of bones, cartilage, skin, tendons and many other tissues in the body. “Muco” refers to the thick jelly-like consistency of the molecules, “poly” means many, and “saccharide” is a general term for the sugar part of the molecule.

An alternative word for Mucopolysaccharides is glycosaminoglycans or GAG’s but the term Mucopolysaccharide will be used for continuity throughout this fact sheet.

In the course of normal life there is a continuous recycling process of building new Mucopolysaccharides and breaking down old ones. The breakdown and recycling process requires a series of special biochemical tools called enzymes.

Children and adults with Hurler Disease are missing, or are deficient in, an enzyme called ‘alpha-L-iduronidase’, which is essential in the breaking down of dermatan and heparan sulphate.

The incompletely broken down dermatan and heparan sulphate remain stored inside the cells of the body and begin to build up causing progressive damage. Babies may show little sign of the disease but as more and more cells become damaged by accumulation of Mucopolysaccharides, symptoms start to appear.
Does Hurler Disease Affect Individuals Differently?

MPS I comprises a wide spectrum of severity and clinical involvement. Children with the classic, severe form of Hurler Disease have progressive developmental delay, severe progressive physical problems and early advancement of the disease. Children and adults with Scheie Disease do not have progressive developmental delay and their physical problems advance more slowly. There are others whose disease pattern will fall between the two ends of the spectrum. It is important to remember that MPS I is extremely varied in its effect. A whole range of possible symptoms are outlined in this booklet, however, an affected individual may not experience all of them.

Spectrum of Disease for MPS I

Severe
a) Facial Dysmorphism
b) Progressive Physical Problems
c) Developmental Delay
d) Profound, Progressive Mental Retardation

Intermediate
a) Normal or Near Normal Intelligence
b) Milder, Less Progressive Physical Problems

Attenuated
a) Normal Intelligence
b) Milder, Less Progressive Physical Problems
c) Normal Life Span

How common is Hurler Disease?
The MPS Society, which coordinates the Registry for Mucopolysaccharide and related diseases, has shown that MPS I is a rare condition affecting approximately 1 in 100,000 live births. In the UK, between 1989 and 1999, 68 babies were born with MPS IH, 16 were born with MPS IHS and 4 were born with MPS IS.

How is Hurler Disease Inherited?
MPS I is an autosomal recessive disease whereby both parents must carry the same defective gene and each pass this same defective gene to their child. Where both parents are carriers of the MPS I gene there is a 25% (1:4) chance of having an affected child in each pregnancy. There is a 50% (1:2) chance of a child receiving only one copy of the defective gene and therefore being a carrier. A carrier will not be affected but can pass the defective gene to his/her offspring. The remaining 25% (1:4) will be neither affected nor a carrier. Using information from an affected individual’s DNA, it may be possible to determine whether brothers and sisters are carriers of, or are affected by MPS I. There is a more detailed explanation of this complex subject in the booklet on inheritance available from the MPS Society.

Can you Test for MPS I in Pregnancy?
For each pregnancy the chances of a baby inheriting MPS I are totally independent of whether a previous child was affected with MPS I. Pre-natal tests can be arranged early on during a pregnancy for those families who already have a child with MPS I. Both amniocentesis and chorionic villus sampling can be used to diagnose MPS I in utero.

Genetic Counselling
All parents of children with a lysosomal storage disease should consider asking for genetic counselling before having other children. The counsellor will be able to provide non directive advice on the risk to close relatives and to suggest whether the wider family should be informed.

Clinical Presentation of MPS I

Growth
Babies with classic Hurler Disease may be larger than average and may grow relatively fast during the first year of life. Growth then slows significantly, stopping altogether around the age of 3 years. Children do not usually achieve a height of more than 100cms.

In contrast, individuals with Scheie Disease usually grow to a relatively normal height. The height of other individuals affected with MPS I is variable. The short stature is not in proportion and the trunk is relatively much shorter than the legs.

Physical Appearance
Children with classic Hurler Disease ultimately look very similar and when together can resemble carbon copies of each other. Chubby faces with rosy cheeks, large heads with prominent foreheads are typical. The neck is short and the nose is broad with a flattened bridge and wide upturned nostrils. Eye sockets are shallow and the eyes may protrude slightly. The lips are often thickened and the tongue enlarged. Hair tends to be thick and coarser than usual, with bushy eyebrows and above average body hair. Children with Hurler Disease have prominent bellies and a characteristic way of walking and holding their arms due to joint contractures at their shoulders, elbows, hips, knees and ankles.

The appearance of individuals with the attenuated form is variable. Children may look no different to their healthy peers. Adults are usually shorter than average, have a characteristic way of walking due to joint contractures and their trunk is often shorter than their limbs. The neck is short, the lips may appear thickened and the jaw square. Others may eventually have the same physical features as those seen in classic Hurler Disease but with a greatly reduced rate of progression.

Lauren (MPS IH)
Correct functioning of the middle ear depends on the pressure behind the ear drum being the same as that in the outer ear canal and the atmosphere. This pressure is equalised by the eustachian tube which runs from the middle ear to the back of the nose. If this tube is blocked, the pressure behind the eardrum will drop, the drum will be drawn in and the transmission of sound waves will be impaired. If this negative pressure persists, fluid from the lining of the middle ear will build up and in time will become thick like glue, hence the condition being known as “glue ear”.

Conductive Deafness (Glue Ear)
Under general anaesthetic a small incision behind the eardrum can be made (myringotomy) and the fluid sucked out. A small ventilation tube called a “grommet” may then be inserted to keep the hole open and allow air to enter from the outer ear canal until the eustachian tube starts to work properly again. Grommets will eventually fall out. If the Conductive Deafness recurs the surgeon may decide to use T-tubes, a type of grommet which stays in place longer. In view of the anaesthetic risks for individuals with Hurler Disease, the surgeon may decide to use T-tubes on the first occasion.

Sensorineural Deafness (Nerve Deafness)
In most cases the cause of nerve deafness is damage to the tiny hair cells in the inner ear. It may accompany conductive deafness, in which case it is referred to as “mixed deafness”. Nerve Deafness is managed by the fitting of hearing aids in most individuals with Hurler Disease. More severely affected children may keep pulling out their hearing aids at first but it is important to persevere at wearing them so that communication can be maintained. Other children and adults with Hurler Disease have found radio aids and the loop system helpful at school and at home.

Brain
The brain and spinal cord are protected from jolting by the fluid that circulates around them (known as the cerebrospinal fluid). In some individuals with classic and attenuated forms of MPS 1, fluid circulation may become blocked over time. The blockage (known as obstructive hydrocephalus) causes increased pressure in the head which can press on the brain causing headaches and delayed development.

Hydrocephalus
Hydrocephalus (also known as “water on the brain”) can be confirmed using a CT or MRI scan. A lumbar puncture with pressure is another way to assess if hydrocephalus exists. If hydrocephalus is confirmed it can be treated by an insertion of a small tube (shunt) which drains fluid from the brain. The shunt has a pressure sensitive valve which allows spinal fluid to be drained when the pressure around the brain becomes too high. A lack of swelling around the optic disc does not rule out hydrocephalus in an individual suffering from Hurler Disease.
Nose and Throat
The problems described in this section are common to children with classic Hurler Disease and, to a lesser extent, those with Hurler Scheie. Those with Scheie Disease can be relatively unaffected.

Frequent coughs, colds and throat infections are common problems. The tonsils and adenoids often become enlarged and can partly block the airway. For this reason they may be removed (see breathing difficulties). The windpipe (trachea) becomes narrowed by storage material and is often more floppy or softer than usual due to abnormal cartilage rings in the trachea. Nodules or excess induration of tissue can further block the airway.

Typically, the bridge of the nose is flattened and the passage behind the nose is smaller than usual due to poor growth of the bones in the mid-face and thickening of the mucosal lining. The combination of abnormal bones and storage of Mucopolysaccharide in the soft tissues in the nose and throat can cause the nose to become easily blocked. One of the common features of children with classic Hurler Disease is the chronic discharge of clear mucus from the nose (rhinorrhea) and sinus infections.

Mouth and Teeth
The lips are thick, the gum ridges are broad and the tongue becomes enlarged. Teeth are widely spaced and poorly formed with fragile enamel. It is important that the teeth are well cared for as tooth decay could be a cause of pain.

Skin
Individuals with Hurler Disease tend to have thickened and tough skin which lacks elasticity. Both sweating and cold hands and feet become common problems in Hurler Disease later in life due to poor temperature control, as the centre of the brain which regulates temperature becomes damaged.

Night Time C-PAP
(Continuous Positive Airway Pressure)
A Night time C-PAP may be recommended where a sleep study has shown that an individual is experiencing sleep apnoeas (where the individual stops breathing for short periods whilst sleeping). This leads to day time drowsiness and headaches.

C-PAP involves placing a mask or canula on the face each night and having air pumped into the airway to prevent it from collapsing. This may seem an extreme measure but it can greatly improve the quality of sleep as well as help prevent or reduce the risk of heart failure caused by low oxygen levels at night. In severe cases of sleep apnoea with heart failure, a tracheostomy (a hole in the airway made in front of the neck) may be needed. Most individuals with Hurler Disease will try to avoid a tracheostomy because it is invasive and seemingly destructive of normal function. In fact, those who have received an early tracheostomy claim to feel much better after improving their night time breathing.

Dental Hygiene
Teeth must be well cared for to avoid the need for extractions. If the water in your area has not been treated with fluoride, your child should have fluoride tablets or drops daily. Cleaning around the mouth with a small sponge or a stick soaked in mouthwash will help keep the mouth fresh and avoid bad breath. Dribbling is a common problem and a plastic backed bib under the clothes may prevent soreness.

If your child is severely affected it may be safer for any treatment to be carried out in hospital. The dentist should be informed if your child has a heart problem and you will probably be advised that s/he should be given antibiotics before and after any dental treatment. This is because certain bacteria in the mouth may get into the blood stream and cause an infection of the heart valves. If teeth need to be removed under anaesthetic this should be carried out in hospital under the care of an experienced anaesthetist and never in the dental surgery.

Chest
In classic Hurler the shape of the chest is abnormal and the junction between the ribs and the breastbone (sternum) is not as flexible as it should be. The ribs are abnormally straight and shaped like oars with narrow necks and wide ends. The chest is therefore rigid and cannot move freely to allow the lungs to take in a large volume of air. The muscle at the base of the chest (diaphragm) is pushed upwards by the enlarged liver and spleen, further reducing the space for the lungs. The tissue of the lungs becomes thickened by storage material and stiffer than usual. It becomes like a balloon which has never been blown up before and which therefore needs much greater force to expand it.
There is an increase in secretions which are harder to clear as the restricted lungs make it difficult for sufferers to take a deep enough breath to cough properly. When the lungs are not fully cleared there is an increased risk of infection which can lead to scarring of the airways causing further obstruction.

**Breathing Difficulties**

Many children with MPS I breathe very noisily even when there is no infection. At night they may be restless and snore. Sometimes the child may stop breathing for short periods while asleep (sleep apnoea). This noisy breathing which stops and starts can be very frightening for parents to hear and they may fear that their child is dying. In fact many children may breathe like this for years.

**Respiratory Infections**

Medication may affect individuals with MPS differently so it is essential to consult your doctor rather than using over the counter medication.

Medication for controlling mucus production may not help. Medication such as antihistamines may dry out the mucus making it thicker and harder to dislodge. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for individuals with Hurler Disease. Cough medicines that have a sedating effect may cause more problems with sleep apnoea by depressing muscle tone and respiration. Individuals with Hurler Disease commonly end up with secondary bacterial infections which should be treated with antibiotics.

**Heart**

Heart Disease is common in classic Hurler Disease but may not develop or cause major problems until later in life when drugs can be prescribed to help relieve the condition. Some Scheie sufferers may develop problems with one of the heart valves but they may have valvular Heart Disease for years without any ill effects. If the condition worsens an operation may be possible to replace the damaged valves.

‘Heart murmurs’ will occur if the valves become damaged by stored Mucopolysaccharides. The heart valves are designed to close tightly as blood passes from one chamber of the heart to another in order to stop it flowing back in the wrong direction. If a valve is weakened or changed in shape it may not shut firmly enough and a small amount of blood may leak back.

In severely affected patients the muscle of the heart may be damaged by storage of Mucopolysaccharides (cardiomyopathy) and the heart may also be put under strain by having to pump blood through stiffened and inefficient lungs (cor pulmonale). A number of affected children have high blood pressure. Occasionally the coronary arteries of Hurler patients may become narrowed and cause episodes of chest pain (angina). If your child is distressed and crying and is at the same time pale and sweating while keeping still, you should consult your doctor who may refer your child for further tests.

**Heart Problems**

Some individuals with MPS I may develop problems with the aortic or mitral valve having slowly progressive valvular Heart Disease for years without any apparent clinical effects. An ECG (electrocardiogram) is a test that measures the electrical activity of the heart and should be carried out annually (or as often as your doctor thinks necessary) to show whether any problems are starting. The test is painless and similar to the ultra sound screening of babies in the womb. It can identify problems with heart muscle, function and valves.

**Liver, Spleen and Abdomen**

In most individuals with MPS I the liver and spleen become enlarged by storage of Mucopolysaccharides (hepatosplenomegaly). The enlarged liver does not actually cause problems or lead to liver failure but its volume can interfere with eating and breathing. In children with classic MPS I and sometimes in the attenuated forms, the abdomen bulges out due to the child’s posture as well as weakness of the muscles and the enlargement of the liver and spleen. Part of the abdominal contents may push out behind a weak spot in the wall of the abdomen. This is called a hernia.

**Hernias**

A hernia can come from behind the navel (umbilical hernia) or from the groin (inguinal hernia). Inguinal hernias should be repaired by an operation but hernias will sometimes recur. Umbilical hernias are not usually treated unless they are large and cause entrapment of the intestine. It is very common to have a recurrence of an umbilical hernia after a repair has been made.

**Bowel Problems**

Many individuals with MPS I suffer periodically from loose stools and diarrhoea. Occasionally it is caused by severe constipation and leakage of loose stools from behind the solid mass of faeces. However, parents often describe it as “coming straight through”. It is thought there may be a defect in the autonomic nervous system which controls those bodily functions usually beyond voluntary control. Examination by a paediatrician or physician, supplemented by an X-ray if needed, will establish the cause. The problem may disappear as the child gets older but it can be worsened by antibiotics prescribed for other problems.

If there is diarrhoea (and it is not secondary to constipation) simple medication, for example loperamide (Imodium), can be very useful. A diet low in roughage may also be helpful. Constipation may become a problem as a child gets older, less active and the muscles weaken. If an increase in roughage in the diet does not help or is not possible, the doctor may prescribe laxatives or a disposable enema.
Bones and Joints

Spine
The bones of the spine are called vertebrae. In Hurler and Hurler Scheie Disease the vertebrae are poorly shaped. One or two of the vertebrae in the middle of the back become slightly smaller than the rest and set back in line. This develops into an angular curve (kyphosis) which is unlikely to need treatment. Some patients with Scheie or Hurler Scheie Disease develop lower back pain. This seems to be due to the lower vertebrae slipping on one another (spondylolisthesis). This can be readily diagnosed by X-rays.

Some children with Hurler Disease appear to have pain occasionally in the back of the neck. This can be relieved by rubbing and many children enjoy having their neck gently massaged. Very rarely the bones at the top end of the neck are unstable. X-rays can detect if this problem is present or likely to develop.

Joints
Joint stiffness is common in all forms of the disease. All the joints become stiff and their movement may become limited. Later in the child’s life this can cause pain which may be relieved by warmth and ordinary painkillers. The limited movement in the shoulders and arms may make dressing difficult.

Carpal Tunnel Syndrome
Although a child or adult with Hurler Disease may not complain of pain they may already have Carpal Tunnel Syndrome. Doctors may advise this to be monitored with a nerve conduction study which will show whether the syndrome is present. This test would also be carried out if there is any weakness or numbness in the hand or decreased muscle mass at the base of the thumb. This disorder can be treated by a minor operation.

Skeletal abnormalities
a) Gibbus (deformity of spine)
b) Spinal Deformity
c) Poorly Formed Pelvis
d) Abnormal Cavicles & Ribs
e) Hip Dysplasia
   (Deformity or Misalignment of the Hip Joint)
f) Knock Knees
g) Joint Stiffness
h) Growth Retardation

Hips
Individuals with MPS I may suffer from dislocated hips but treatment may not be advisable or necessary.

Legs and Feet
Many individuals with Hurler Disease stand and walk with their knees and hips flexed. Combined with the tight Achilles Tendon this may cause them to walk on their toes. Sometimes these individuals have ‘knock knees’ but this is very unlikely to need treatment. The feet are broad and may be stiff with the toes curved under, rather like the hands.

Hands
The shape of the hands is very noticeable and has been used as the symbol of the MPS Society. They are short and broad with stubby fingers which gradually become curved over or “clawed”.

Individuals with Scheie Disease sometimes experience pain and loss of feeling in the fingertips caused by Carpal Tunnel Syndrome. The wrist, or carpus, consists of eight small bones known as the carpals which are joined by bands of protein fibre called ligaments. Nerves have to pass through the wrists in the space between the carpals and the ligaments. Thickening of the ligaments causes pressure on the nerves. This can be relieved by an operation.

It is now known that Hurler and Hurler Scheie children may also have this problem. If your child seems to have pain in the hands, particularly at night, it would be sensible to have an electrical test called a ‘Nerve Conduction Study’ which will show whether Carpal Tunnel Syndrome is the cause.

General Management of MPS I
Anaesthetic
Giving an anaesthetic to an individual with Hurler Disease requires skill and should always be undertaken by an experienced anaesthetist. Where a child is concerned this should be a paediatric anaesthetist. The airway can be very small and may require a very small endotracheal tube. Placing the tube may prove difficult and require the use of a flexible bronchoscope. In addition, the neck may be somewhat lax and repositioning the neck during anaesthesia or intubation could cause injury to the spinal cord. For some individuals, it is difficult to remove the breathing tube after surgery is completed. There is a more detailed explanation of this complex subject in the specialist anaesthetic booklet published by the MPS Society.

Physiotherapy and Hydrotherapy
Physiotherapy and hydrotherapy can be useful to help individuals with MPS I achieve specific and realistic goals in daily life or to drain mucus from the chest. Individuals should be as active as possible to improve their general health and a physiotherapist may be able to suggest ways of achieving this. For children the best forms of physiotherapy are exercises that are introduced through play. In adults it is important to remember that passive stretching may be painful and should only be used with caution.
Diet
There is no scientific evidence that a particular diet has any beneficial effects. Symptoms, such as diarrhoea, tend to come and go naturally. Some parents, however, find that a change in their child’s diet can ease problems with excessive mucus, diarrhoea or hyperactivity. Cutting down on milk, dairy products and sugar as well as avoiding foods with too many additives have all been said to help individual children.

It would be advisable to consult your doctor or a dietician if you plan major changes to ensure that the proposed diet does not leave out any essential nutrients. If your child’s problems are eased you could try reintroducing foods one at a time to test out whether anything in particular tends to increase your child’s symptoms.

Drugs
Children with MPS may be affected differently by drugs so it is essential to consult your doctor rather than purchase over-the-counter medication. Drugs may be tried for controlling mucus production but some may make the mucus thicker and harder to dislodge or they may make the child more irritable. The use of sedatives can increase the problem of sleep apnoea by depressing respiration.

It is now recognised that frequent use of antibiotics may make them less effective when really needed. Repeated use can also cause thrush (a fungal infection which commonly affects the mouth or vagina and produces a white curd-like deposit). It causes irritation and discomfort and will need to be treated. Your doctor may, therefore, wish to limit the number of times when antibiotics are prescribed for coughs and colds.

Living with a Child with Classic Hurler Disease
Hurler children are usually happy, friendly children who mix well and are popular at school. They are much loved by all who know them and many are very easy to manage. Some are easier to please than other children. They may be mischievous and often laugh heartily at other people’s misfortunes.

Although Hurler children are placid and cheerful most of the time, some do have fits of crying and screaming which may be linked to frustration at being unable to communicate.

Once a diagnosis of classic Hurler Disease is confirmed, families find it to be a very painful process coming to terms with the news that their child’s life will be so very different from what they had hoped. Over the years their child will lose skills that have been learnt, sight and hearing will deteriorate and any control over bodily functions will be lost.

Feeding
Most children with classic Hurler Disease enjoy their food although some are reluctant to try anything new. In the later stages, your child may find it harder to chew properly and food may have to be liquidised.
Education
Whilst some children with severe Hurler Disease may benefit from having a mainstream education in their primary school years and enjoy the social interaction with peers, a majority will equally benefit from a Special Educational Needs placement with small class sizes and a range of communication systems in place. Children with Hurler Disease may have a Statement of Special Educational Needs or need an Individual Education Plan (IEP) with regular reviews.

Many will need the help of a classroom assistant during the school day to ensure that the child is able to access all the educational opportunities that are available to them. This provision will enable the class teacher to set specific tasks for the child and will help maintain concentration in order to keep the child on course.

The classroom assistant will also be on hand during breaks and lunch times in order to ensure that the child’s health and safety is maintained throughout the day.

Home Adaptations
Children with severe Hurler Disease will become progressively less mobile and increasingly dependent on their parents and carers to meet their everyday needs in areas of incontinence, personal hygiene and nutrition. It is important to give thought early on to the ways in which the families and carers will manage when weight bearing and walking or climbing the stairs is no longer possible. An ensuite bathroom and bedroom is ideal with plenty of space for a buggy and carer to manoeuvre around in. When weight bearing is no longer possible a hoist is beneficial with tracking from bed to bath directly in line for ease of use. Adaptations can often take a long time so it is prudent to plan ahead as far as possible. The MPS Society has considerable experience of the options available to families caring for a child with severe Hurler Disease.

Having a Break
Caring for a child severely affected by Hurler Disease is hard work and parents or carers need a break to rest and enjoy activities which may not be possible when in their caring role. Many families use the children’s hospices, social services respite care or have a friend or family member close by who can regularly help out at busy times.

Further details of hospices throughout the UK offering respite care to families are available from the MPS Society.

Palliative Care
Palliative care is provided to the family and child with a life limiting disease in situations where curative treatment is not an option. This support encompasses aspects such as respite care, symptom management and bereavement support and may extend over a considerable period of time. In addition, considerable personal care may be required which can take up a large amount of time. This will include feeding and personal hygiene. The stress involved can put a family under immense strain. An assessment of medical needs and a care plan should lead to an approved package of support being provided to both the child and the family and enable both to experience a better quality of life.

Life Expectancy
Sadly, children with the classic form of Hurler Disease rarely live more than 10 or 12 years. Some individuals die much younger. Parents often worry about their child’s death, how it will happen and whether their child will suffer. Many Hurler children have a peaceful death after an infection or from the heart’s gradual failure. You may find it helpful to prepare yourself for this time. If you would like to discuss this please contact the MPS Society.

Living with a Child or Adult with the Attenuated form of MPS I
Education
The majority of children with the attenuated form of MPS I will attend mainstream school and achieve academically. In order for such children to reach their full academic potential it is important to ensure that the education authority and the school are aware of the resources required. This may include a one to one classroom assistant, appropriate classroom furniture and access to an individual computer.

Independence
Individuals with Hurler Scheie and Scheie Disease should be encouraged to be as independent as possible in order to lead full and enjoyable lives. The teenage years may be difficult; if ordinary adolescents worry about a pimple on the chin, think how much more teenagers with Hurler Scheie and Scheie Disease must worry about their appearance and the restrictions imposed by their condition.

They may be helped by meeting or being put in touch with other teenagers and adults with the same conditions.
Ask the MPS Society to put you in touch with other individuals and families who are affected by MPS and related diseases through their ‘Befriender Scheme’. This encourages those who find themselves in similar circumstances to get in touch with one another for mutual support.

Employment
The physical disabilities of those suffering from an attenuated form of MPS I should not in themselves prevent people from accessing meaningful employment. There is a considerable amount of responsibility on the part of employers under the Disability Discrimination Act to meet the needs of employees with a disability.

Home Adaptations
Appropriately adapted living accommodation will greatly enhance the ability of an individual with Hurler Scheie or Scheie Disease to develop independent living skills. Where mobility is restricted, particularly for individuals with Hurler Scheie Disease, a wheelchair may be required for mobility outdoors whilst mobility indoors could be reduced to only a few metres due to the pain and joint constrictures resulting from the disease. Furthermore, this pain may impact on the individual’s ability to undertake personal care and daily living tasks and a carer may be required to assist. Appropriately adapted living accommodation will therefore greatly enhance independence.

Life Expectancy
Life expectancy for individuals with MPS I is very varied. Individuals with Scheie should expect to have a reasonably normal life span. Severely affected Hurler Scheie patients may die in childhood but others will live into adulthood.

Specific Treatment of MPS I
Haematopoietic Stem Cell Transplantation (HSCT) is the collective name for Bone Marrow Transplant (BMT), Cord Blood Transplant (CBT) and Mobilised Peripheral Blood Stem Cell Transplant (PBSCT). BMT has been used to treat children with MPS I Hurler Disease since 1980. CBT and PBSCT were introduced later as a treatment option to overcome the difficulty when a suitable bone marrow donor could not be found.

Bone Marrow Transplant
Bone Marrow Transplant requires the availability of an appropriate tissue matched donor. This donor may be a family member or an unrelated donor from a bone marrow donor panel. Having a Bone Marrow Transplant, a Cord Blood Transplant or a Mobilised Peripheral Blood Stem Cell Transplant is rather like having a blood transfusion.

Cord Blood Transplant
A Cord Blood Transplant is carried out using umbilical cord blood. Cord blood is collected from the afterbirths (placenta) of new born babies with their parent’s consent. The baby donors are not normally related to the patient although the cord blood needs to provide a suitable match. In all other aspects the procedures and outcomes are the same as having a bone marrow transplant.

Mobilised Peripheral Blood Stem Cell Transplant (PBSCT)
In PBSCT drugs are given to the donor to stimulate their bone marrow to produce high numbers of stem cells. These cells are then separated from the blood by apheresis using a machine that separates the white blood cells for processing and the red blood cells which are given back to the donor.

HSCT has been shown to have a positive outcome in altering the progression of Hurler Disease and improving life expectancy. Harshness of facial features, hearing, enlargement of the liver and spleen and heart function have all improved following transplant. However, HSCT has less effect on skeletal structure and problems such as kyphosis, severe joint stiffness and pain, carpal tunnel syndrome and compression of the spinal cord can be significant post HSCT complications. Specific orthopaedic care should be offered to patients after HSCT.

In terms of neurological outcome, HSCT is most effective in individuals who are transplanted early in life and usually before the age of 2 years. Children who show advanced developmental delay before transplant are not likely to benefit from the treatment.

It is important to remember that Haematopoietic Stem Cell Transplantation is a treatment for the symptoms of MPS IH, not a cure. Individuals post HSCT still experience a wide range of problems which are not just physical in origin but also psychological and may impact on their development as they get older. The majority of post HSCT children will attend mainstream school but will need individual support both with their learning and social skills in order to achieve their full educational potential.

Joanna (MPS IS)
To address the ongoing problems experienced by individuals post HSCT a comprehensive package of support is vital to ensure cohesion between medical professionals, schools and anybody else involved in the child’s care and development. As the number of adults who underwent HSCT in childhood is still relatively small, knowledge of the range and extent of the problems they will face as adults is limited. Some will go on to lead independent lives whilst others will need significant support, for example, with personal care.

HSCT is a complex procedure that may involve lengthy periods in hospital and in isolation. There are risks involved in a undergoing a HSCT including graft rejection, infection, graft vs. host disease and other complications all of which will be explained to you in great detail by your child’s MPS doctor or treating haematologist.

It is important to give yourselves time to understand the risks and to ask all the questions you might have. Securing the support of family and friends to help with domestic and practical issues whilst your child is in hospital is recommended.

Enzyme Replacement Therapy (ERT)
ERT for MPS I is based on the principle that the recombinant form of the enzyme that is missing or malfunctioning in individuals with MPS I is given via repeated intravenous infusion in order to reduce the symptoms and clinical manifestations associated with the disease.

Following the success of ERT in the treatment of other lysosomal storage disorders, ERT for patients with MPS I has been developed. The generic name for ERT in MPS I is laronidase and the product brand name is Aldurazyme®. Aldurazyme® has undergone extensive clinical trials including a double blind, placebo controlled study involving weekly intravenous infusions in 45 patients. Part of this study took place in the UK. Most patients included on the clinical trial programme had the attenuated form of MPS I, Hurler Scheie Disease. Aldurazyme® was licensed as an ERT in 2003. ERT has been shown to reduce many of the non-neurological symptoms associated with MPS I, such as improving mobility and lessening joint stiffness. Significant improvement has also been seen in respiratory function, one of the major symptoms in all forms of MPS I.

Following marketing approval of Aldurazyme® from the Food and Drug Administration (FDA) and the European Medicines Evaluation Agency (EMEA) patients aged under five years of age and diagnosed with the classic form of Hurler Disease were entered into a safety and efficacy clinical trial for Aldurazyme® and subsequently ERT is used routinely for 3 months pre HSCT and is continued until engraftment. The rationale for this is to improve the child’s physical condition prior to BMT or CBT and to lessen the risk of primary graft failure. In England ERT is funded centrally through the National Commissioning Group (NCG) subject to the patient meeting the NCG clinical guidelines.

There are different arrangements for funding ERT in Wales, Scotland and Northern Ireland.

There are still a number of questions that remain unanswered over the role and efficacy of ERT. It is known that the enzyme cannot cross the blood-brain barrier and that any improvement seen in children with MPS I Hurler Disease using ERT alone may be limited to an improved quality of life through alleviation of non-neurological symptoms, such as improved respiration and mobility and a reduction in the size of the liver and spleen.

About the MPS Society
The Society for Mucopolysaccharide Diseases (MPS Society) is a voluntary support group founded in 1982 which represents over 1200 children and adults suffering from MPS and related diseases including Fabry, their families, carers and professionals throughout the UK.

The Society produces a range of publications of which include: a quarterly MPS Magazine, a Fundraising Newsletter, Fact Sheets and various literature for children, adults, parents, siblings and individuals that are affected by MPS or a related disease.

Regional clinics, information days and conferences are arranged throughout the United Kingdom.

The MPS Society provides a range of services including:
- Advocacy Support to individuals suffering from MPS and related diseases, their families and carers;
- Ongoing Advocacy support for affected families following bereavement; telephone support including an out of hours helpline; a ‘Befrienders Scheme’ putting individuals suffering from MPS and their families in touch with each other for mutual support;
- Financial Assistance Scheme: Funds research and treatment into MPS and related diseases.

Membership to the MPS Society is open to all individual residents in the UK who meet the agreed criteria. Other individuals wishing to belong to the UK MPS Society can become ‘Friends of MPS’.

The Society exists entirely on donations and fundraising from its members and the general public.

For further information about the work of the MPS Society and the service we provide please contact us.

Please note that this fact sheet is not intended to replace medical advice or care.

The Society has received unrestricted grants from a number of pharmaceutical companies with an interest in Lysosomal Storage Disorders for a range of projects.

Society for Mucopolysaccharide Diseases
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