What is Morquio Disease?
Morquio Disease is a Mucopolysaccharide storage disorder also known as MPS IV. The disease takes its name from Dr Morquio, a paediatrician in Uruguay, who described a family of four children affected by the condition in 1929.

Whilst there is no cure for individuals affected by Morquio Disease, this fact sheet explores its presentation and clinical management. This fact sheet is produced by the Society for Mucopolysaccharide Diseases (the MPS Society) drawing on the experiences of individuals affected by the disease, their families and doctors with reference to medical literature.

What Causes Morquio Disease?
Mucopolysaccharides are long chains of sugar molecules used in the building of bones, cartilage, 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.

The modern terminology for Mucopolysaccharides is glycosaminoglycans (GAGs) but the term Mucopolysaccharides 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. This process requires a series of biochemical tools called enzymes. Children and adults with Morquio Disease are missing an enzyme which is essential in the breaking down of Keratan Sulphate. Incompletely broken down Keratan Sulphate remains stored inside parts of cells called lysosomes.

The lysosomes become swollen and disrupt cell function causing progressive damage.

Does Morquio Disease Affect Individuals Differently?
There are two types of Morquio Disease which are referred to as MPS IVA and MPS IVB. The subtypes of this disease are as a result of the type of enzyme that is missing or malfunctioning within the cells of the body: A missing or malfunctioning enzyme known as ‘N-acetylgalactosamine 6-sulfatase’ results in MPS IVA. In MPS IVB the missing or malfunctioning enzyme is known as ‘beta-galactosidase’.

Morquio Disease comprises a wide spectrum of severity and clinical involvement. Some individuals may not achieve a height of one metre by adulthood, whilst others grow significantly taller and have fewer problems related to severely restricted growth.

A whole range of possible symptoms are outlined in this fact sheet, however, it is important to remember that although clinical features are similar in both types of the disease, they less appear less severe in Morquio Type B.

It is also important to keep in mind that individuals affected by either Morquio Type A and Morquio Type B may not experience all of the symptoms mentioned in this fact sheet. If symptoms are evident they will vary in severity from one individual to another.

In this fact sheet we will be using the term Morquio Disease to refer to both MPS IVA and MPS IVB. It is important to remember that not all symptoms will be experienced by individuals with either Type A or Type B as there is a wide spectrum of severity.
How Common is Morquio Disease?
The MPS Society, which co-ordinates the Registry for Mucopolysaccharide and Related Diseases, has shown that Morquio Disease is a rare condition, for example: between 1989 and 1999, 26 babies were born with Morquio Disease in the UK.

How is Morquio Disease Inherited?
Morquio Disease 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 IV 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 or 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.

There is a more detailed explanation of this complex subject in the booklet on inheritance available from the MPS Society.

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

Genetic Counselling
All parents of children with Mucopolysaccharide disease should consider asking for Genetic Counselling before having other children. The counsellor will be able to advise on the risk to close relatives and to suggest whether the wider family should be informed.

Life Expectancy
In the past, more severely affected patients did not survive beyond their late twenties, although those less severely affected have been known to live into their fifties, sixties and even seventies. Life expectancy is improving as a result of medical advances and better management of the disease.

Clinical Presentation of Morquio Disease

Growth
Babies with Morquio Disease usually grow normally at first. Growth then slows significantly around 18 months. Those who are severely affected usually stop growing around the age of eight and their final height may be between three feet (90 cms) and four feet (120 cm). Others continue growing into their teenage years and can reach five foot (150cms). The short stature is not in proportion and the trunk is relatively shorter than the legs.

Physical Appearance
The face of individuals with Morquio Disease is altered to a certain extent by the disease and the mouth tends to be wide, the jaw square and the bridge of the nose flattened. The neck is very short but the texture of the hair is not affected as in other MPS conditions.

Individuals with Morquio Disease may develop prominent tummies and a characteristic way of walking and holding their arms due to joint contractures at their shoulders, elbows, hips, knees and ankles.

Intellectual Ability
There is no storage of Mucopolysaccharides in the brain of individuals with MPS IVA and therefore intelligence is not usually affected. Individuals with MPS IVB often have significant learning disability.

Eyes
Clouding of the cornea caused by storage of Mucopolysaccharides is seen in children and adults with Morquio Disease. This rarely interferes significantly with vision and is not particularly noticeable.

Some individuals cannot tolerate bright lights as the clouding causes uneven refraction of light. Tinted glasses may be helpful in such circumstances.

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 Morquio Disease, the surgeon may decide to use T-tubes on the first occasion.
Mouth & Teeth

Individuals with Morquio Disease may have a prominent chin, a wide mouth and an enlarged tongue. Teeth can be widely spaced and poorly formed with fragile enamel. It is important that the teeth are well cared for as tooth decay can be a cause of pain.

Heart

Occasionally heart disease develops in late childhood but it does not usually cause problems until much later in life. Some individuals may develop problems with one of the heart 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 causing strain on the heart. This condition may be treatable.

Heart Problems

Some individuals with Morquio Disease may develop problems with the aortic or mitral valve having slowly progressive valvular heart disease for years without any apparent clinical effects.

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 may in certain circumstances 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.

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 Morquio Disease.

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. Some 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 Morquio Disease have found radio aids and the loop system helpful.

Breathing Difficulties

When individuals get older they can struggle to maintain an open airway which leads to breathing difficulties. In some cases the trachea continues to grow whilst the cervical spine does not. Many individuals need to tilt their heads backwards to prevent the blocking of the airway. This issue can cause problems when individuals try to do their schoolwork or whilst at the hairdressers.

In older teenagers and adults, the heart and lungs are squashed within the area between the head and abdomen (thorax) leading to difficulties exchanging gases in the lungs efficiently. As a result, restrictive respiratory failure can occur later in life. This is a difficult complication to manage so it is important to treat additional chest problems, such as infections, very seriously.

Chest

On looking at a skeleton or a diagram it is possible to see that the breastbone (sternum) is joined to the spine by the ribs. In Morquio Disease the growth of the spine is affected. The breastbone continues to grow normally but, as it is joined to the spine, it is forced to buckle outwards in a rounded curve or sometimes in a prominent beak shape.

The chest is bell-shaped and the ribs are held fixed in a horizontal position causing restriction of efficient breathing. This may mean that the affected individual does not cope well with chest infections.
An echocardiogram (ECG) should be carried out annually (or as often as the doctor thinks necessary) to show whether any problems are starting. This test is painless and similar to the ultra sound screening of babies in the womb. It can identify problems with heart muscles, valves and general function.

Liver, Spleen & Abdomen

Individuals with Morquio Disease may develop an enlarged liver and spleen due to the 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. Very occasionally 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 small and cause entrapment of the intestine, or are very large and problematic. Recurrence of an umbilical hernia is common even after a repair.

Bowel Problems

Many individuals with Morquio Disease 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 & Joints

Neck (Cervical Spine)

Difficulties can arise from a structural defect in the upper vertebrae of the spine. There should be a piece of bone called the ‘odontoid process’ sticking up between the second and first vertebrae and giving support as the head moves.

In individuals with Morquio Disease this piece of bone may fail to develop resulting in the spinal cord being insufficiently protected.

The spinal cord is a bundle of nerves which carries messages between the brain and the rest of the body.

Compression or squeezing of the spinal cord (cervical myelopathy) is a serious complication that requires careful clinical management. It can lead to sudden death or paralysis after a fall but more often, chronic damage leads to a gradual loss of power in arms and legs.

All individuals with Morquio Disease should be referred to an orthopaedic surgeon as soon as the diagnosis is made.

The condition of the cervical spine should be regularly assessed. If cervical instability is found most surgeons would recommend a cervical fusion to prevent possible damage to the spinal cord.

It is an alarming thought for parents that their child may have a weakness in such a vital place but it is important to keep a balance between leading a normal life and avoiding risks.

Treatment for the Cervical Spine

The problem with the cervical spine can be corrected by an operation called a ‘cervical fusion’. It is now thought advisable to treat patients before symptoms of cervical myelopathy occur as damage to the spinal cord may not heal or be repairable.

Small pieces of bone are taken from the patient (usually from the skull or the ribs) and fixed into the neck where they eventually grow to form a firm support joining the top two vertebrae to the base of the skull. Surgical fusion operations are often carried out on patients with other conditions but there are particular problems with individuals with Morquio Disease which mean that normal methods may fail. A few centres have taken a particular interest in patients with Morquio Disease and have developed a method of achieving successful cervical fusions.

It is essential to immobilise the neck in the correct position for three to four months post-operatively while the grafted bone grows up to join the base of the skull. A lightweight metal “halo” ring is attached to the skull using four screws and bars. This is fixed to the body by a jacket or plaster cast. The operation usually involves a stay of two to three weeks in hospital. Although caring for a patient in a halo may be hard work, the patients adjust remarkably well.
Lower Spine
The spine tends to be severely affected and its bones or vertebrae are abnormally flattened. Sometimes one or more of the vertebrae will slip back in position, narrowing the spinal canal. The spine may be curved to one side (scoliosis), hump-backed (kyphosis) or a mixture of the two (kyphoscoliosis).

The spine should be kept under regular review by an orthopaedic surgeon. In some cases it may be necessary to fuse some vertebrae in the spine to prevent damage to the spinal cord. This will involve one or two operations and some months in a plaster cast, jacket or brace to support the spine while the fusion takes place.

Knocked Knees (Genu Valgum)
As a child with Morquio Disease grows older the knees gradually become more “knocked” (genu valgum). It is sometimes possible for the legs to be straightened by an operation but it is usually considered best to wait until the child has stopped growing. Joints are held in place by strong bands of protein fibre known as ligaments. Individuals with Morquio Disease have ligaments which are often very lax. If this is the case, surgery may not achieve any noticeable improvement.

Ankles
The ankles may be weak and turn inwards as a result of ligaments being lax. Occasionally boots and splints are worn but firm supportive shoes may be equally adequate.

Feet
The bones composing the arches in the feet are held in position by ligaments and tendons. These are likely to be weakened with the result that the feet will be flat. The toes may be misshapen.

Shoulders
The shoulders are often partially dislocated downwards (subluxed) so that the arms cannot be raised straight above the head. This may make dressing or hair washing difficult. For younger individuals, attracting the teachers attention in the classroom may also prove problematic.

Hips
It is common for the hips to become dislocated but this is often not a problem and treatment may not be advisable or necessary. If the individual continues to be able to walk and pain occurs later in life, surgery may be considered.

Wrists
The wrists are enlarged and curved round. The wrists may become very loose and floppy as the tiny carpal bones fail to develop properly and the ligaments are lax. This can mean considerable loss of power in the hands. Surgery to correct this has not proven successful but small plastic splints may be helpful in some cases. Writing may be difficult and some individuals may find it easier to use a computer.

Joints
Joint stiffness is common in Morquio Disease. All the joints become stiff and their movement may become limited. Later in life this can cause pain which may be relieved by warmth and prescribed analgesics. The limited movement in the shoulders and arms may make dressing difficult. Aches and pains may commonly occur in various places due to the abnormal anatomy of individuals with Morquio Disease. Some individuals may also develop osteoarthritis.

General Management of Morquio Disease

Anaesthetic
Giving an anaesthetic to an individual with Morquio Disease requires skill and should always be undertaken by an experienced anaesthetist. Where a child is concerned this should be a paediatric anaesthetist. If the cervical spine is unstable, the individual is at risk if the neck is flexed while he or she is unconscious. Special precautions must be taken. 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 & Hydrotherapy
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.

Mobility
Many individuals with Morquio Disease remain walking into their teens and adult life. Others may need to use a wheelchair from an early age, at least for getting around outdoors.

An electric wheelchair is vital to encourage independence. Consult your physiotherapist, occupational therapist or ask the MPS Society for advice.

Roma (MPS IVA)
Diet
There is no scientific evidence that a particular diet has any beneficial effect and 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 such as diarrhoea. Cutting down on milk, dairy products and sugar as well as avoiding foods with too many additives and colourings 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 any particular food product appears to increase your child’s symptoms.

Vomiting
Many of those with Morquio Disease have a tendency to vomit easily, especially first thing in the morning, perhaps because mucus has built up overnight. Restricted space for internal organs in small bodies can mean that the stomach may be rather squashed and discomfort could be experienced after a large meal resulting in vomiting. Sometimes there may be a feeling of finding it hard to breathe as the lungs are also constricted. A few children have had episodes of vomiting to such an extent that they become dehydrated. You should consult your doctor if vomiting continues over several hours.

Medication
Children with MPS or a related disease 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 an Individual with Morquio Disease

Education
The majority of children with Morquio Disease will attend mainstream school and achieve academically. Achieving an education to degree level is not unusual. In order for children with Morquio Disease 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.

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Puberty
Adolescents with Morquio Disease will go through the normal developments of puberty although the onset of periods in girls may be delayed. There is no reason why individuals with Morquio Disease should not be fertile. They are inevitably carriers of the disease but would not pass it on to any offspring unless the other parent is also a carrier. Women whose stature is significantly restricted may be advised not to become pregnant because of the risks to their own health.

Independence
Individuals with Morquio 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 Morquio 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 condition. Ask the MPS Society to put you in touch through their Befriender Scheme. Adults with Morquio Disease have the potential to live independently claiming appropriate financial support to purchase the services needed including that of a Personal Assistant.

Employment
Physical disabilities should not prevent individuals from accessing meaningful employment. There is a considerable 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 to develop independent living skills. Where stature is restricted, kitchen and hygiene facilities should be at a low level. If mobility is restricted to such an extent that a wheelchair is used, plans for any home adaptations will need to allow adequate space to accommodate this. This may also be an important consideration for the future, even if a wheelchair is not required at the time. Provisions should also be made for a ceiling track hoisting to be installed in the future.
Consideration needs to be given in respect of taps, light switches, accessible furniture and handles. The process of achieving a home adaptation is means-tested and is a lengthy process. It is, therefore prudent to plan ahead whenever possible.

Psychosocial Issues

To date there has been no research carried out that explores the psychosocial development of individuals affected by Morquio Disease so it is not possible to make definitive statements about this subject. As a parent of a child or young person with Morquio Disease, however, it is important to consider how their disability may cause them to experience additional challenges in life.

Children and young adults with Morquio Disease adapt socially and emotionally in different ways and some may not differ greatly from their healthy peers in terms of mental health problems or achievements in developmental milestones. Other children and young adults, as they grow older, adapt to the challenges posed by their disability in other ways. This can be manifested as social inhibition, a tendency to internalise problems or an aggressive personality.

Adolescence may be more of a challenge for individuals with Morquio Disease as they have to experience all the physiological and psychosocial changes as well as any illness-related changes or limitations.

Developing the necessary skills to lead independent adult lives can be very difficult and some young people with Morquio Disease may experience difficulties establishing independence from their family - an important step in achieving social maturity.

Mental health problems such as depression are seen in teenagers and young adults with Morquio Disease so it is vital that steps are taken for an appropriate psychology referral as part of an on-going and comprehensive package of support.

Treatment of Morquio Disease

At this time there is no cure for Morquio Disease but doctors and scientists are working hard to find effective treatments. Enzyme Replacement Therapy (ERT) for Morquio Disease is being developed. A clinical trial of ERT for Morquio Disease is underway.

Enzyme Replacement Therapy (ERT)

Enzyme Replacement Therapy (ERT) works on the principal that the recombinant (enzyme manufactured externally from the body) form of the enzyme that is missing or malfunctioning in individuals with Morquio Disease is given via repeated intravenous infusions in order to reduce the symptoms and clinical manifestations associated with the disease.

ERT has been shown to reduce many of the non-neurological symptoms associated with Mucopolysaccharide and other lysosomal storage diseases. However, in developing ERT for Morquio Disease the question that remains unanswered is the role of the efficacy of ERT on the bones and growth in this disease.

Surgical Treatment

Most patients with the classical form of Morquio Disease have an abnormality of their second cervical vertebrae (in the neck). This bone, which is responsible for providing neck stability, is often very underdeveloped (known as hypoplastic).

This means that abnormal movement can occur between the upper bones in the neck and at the base of the skull leading to damage to the spinal cord if not detected and treated. The treatment consists of a surgical operation to fuse the upper bones in the neck to the base of the skull to prevent this abnormal movement. Problems may also develop lower down the spinal column and in addition many patients are severely “knock-kneed”. These complications may also require surgical attention.

About the MPS Society

The MPS Society is a voluntary support group founded in 1982 which represents over 1200 children and adults suffering from MPS and related diseases, their families, carers and professionals throughout the UK. It is a registered charity entirely supported by voluntary donations and fundraising and is managed by the members themselves.

The Society produces a range of publications which include: a quarterly MPS Magazine, a Fundraising Magazine, fact sheets on each MPS and related disease as well as 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 UK.

The Society’s advocacy team provides a unique, needs-led, individual advocacy service to individuals suffering from MPS and Related diseases, their families and carers. We provide 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 and out of hours helpline; 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.

The Society exists entirely on donations and fundraising from its members and the general public. Donations from companies and charitable trusts are sought through the MPS office.

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

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.