



National
MPS
Society

Support for Families. Research for a Cure.



A Guide to Understanding MPS IV

Morquio Syndrome

The National MPS Society exists to find cures for MPS and related diseases. We provide hope and support for affected individuals and their families through research, advocacy and awareness of these devastating diseases.

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2 Introduction

MPS IV is a mucopolysaccharide (MPS) storage disease, also known as Morquio syndrome. It takes its name from Dr. Morquio, a pediatrician in Montevideo, Uruguay, who in 1929 described a family of four children affected by this condition. As the same condition also was described in the same year by Dr. Brailsford from Birmingham, England, it is sometimes known as Morquio-Brailsford syndrome. MPS IV is characterized by short stature, severe bone disease and

The word “mucopolysaccharide” can be broken down into its parts: Muco refers to the thick jelly like consistency of the molecules; poly means many; and saccharide is a general term for a sugar molecule (think of saccharin).

preservation of intelligence. One of two enzyme deficiencies can cause MPS IV, each having a wide spectrum of clinical severity from mild to very severe disease.

If you are the parent of a newly diagnosed child, it is important to remember that MPS IV comprises a wide spectrum of severity and that individuals may be categorized anywhere from severe to attenuated (less severe). Even children from the same family may be affected differently. A range of possible problems is described

in this booklet, however this does not mean that your child will experience them all. Some complications arise early in childhood, while other present much later or may never occur.

As yet, there is no cure for individuals affected by this disease, but there are ways to manage the challenges they will have, and to ensure the best quality of life. Hematopoietic stem cell transplant (HSCT) has been attempted to treat MPS IV with little success. Scientists who study MPS continue to look for better and more effective ways to treat these diseases, and it is likely that individuals will have more options available in the future.

What causes MPS IV?

Glycosaminoglycans (GAG), previously called mucopolysaccharides, are long chains of sugar molecules used in the building of bones, cartilage, skin, tendons and many other tissues in the body. These sugar chains are submicroscopic and cannot be seen with the eye, but can be studied using special scientific instruments and analytical methods.

GAG form part of the structure of the body and also give the body some of the special features that make it work. For example, the slippery, gooey fluid that lubricates your joints contains GAG. The rubbery resilient cartilage in your joints is another example. All tissues have some of this substance as a normal part of their structure. However, individuals with MPS have too much GAG accumulation.

To understand how GAG accumulates and cause MPS IV, it is important to understand that in the course of the normal life process, there is a continuous process of building new GAG and breaking down old ones—a recycling process. The breaking down of GAG occurs in a part of the cell called the lysosome. That is why MPS IV is considered one of the approximately 40 different kinds of lysosomal storage diseases (LSDs). All LSDs are caused by the inherited deficiency of individual enzymes and are very rare. This ongoing recycling process is required to keep your body healthy. The breakdown and recycling process requires a series of special biochemical tools called enzymes. To break down GAG, a series of enzymes works in sequence one after another. The GAG chain is broken down by removing one sugar molecule at a time starting at one end of the GAG chain. Each enzyme in the process has its special purpose in the body and does one very specific action—just like a screwdriver works on screws and a hammer works on nails.

Individuals with MPS IV are missing one of two specific enzymes which are essential in the breakdown of certain GAG called keratan sulfate. The incompletely broken down keratan sulfate remain stored inside cells in the body and begin to build up, causing progressive damage. The GAG itself is not toxic, but the amount of it and the effect of storing it in the body lead to many physical problems.

Babies may show little sign of the disease, but as more and more GAG accumulates, symptoms start to appear. Sugar or foods normally eaten will not affect whether there is more or less buildup of GAG.

Individuals with MPS IV have a deficiency of an enzyme which results in the accumulation of glycosaminoglycans. This accumulation of GAG is responsible for numerous problems that affect individuals with MPS IV.

4 Are there different forms of MPS IV?

There are two different enzyme deficiencies that have been found to cause MPS IV; the disease is described as type A or B. The names of the enzymes are N-acetylgalactosamine 6-sulfatase (type A), also called galactose 6-sulfatase, and beta-galactosidase (type B). MPS IV A, the most common form, was first recognized to be a



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severe disease. MPS IV B was initially considered to be an attenuated form or late onset variant of Morquio syndrome. It is now recognized that the severe and attenuated forms of MPS IV are not caused by a unique enzyme deficiency, but rather that each form has a wide spectrum of clinical severity. It is now more appropriate to view MPS IV as a continuous spectrum of disease with the most severely affected individuals on one end, the less severely affected (attenuated) individuals on the other end, and a whole range of different severities in between.

In general, individuals with MPS IV B have similar problems, but tend to be mildly affected compared to MPS IV A individuals. Both enzymes are only involved with the breakdown of keratan sulfate, a type of GAG. Keratan sulfate is primarily found in the bones and connective tissues. The accumulation of keratan sulfate in the bones and connective tissues is responsible for the major problems that affect individuals with both types of MPS IV.

Currently there is no reliable way of telling from biochemical diagnostic tests how severe the disease will be. Detailed studies have shown that in individuals with attenuated MPS IV, a very tiny amount of active enzyme is working as designed resulting in the attenuated form of MPS IV.

DNA tests do not always correctly determine the severity of MPS IV. Many different kinds of mutations (defects in the makeup of genes) in the gene that produces the enzyme deficiency have been identified. This enzyme deficiency results in MPS IV disease. The gene has been studied extensively to see if there is any relationship between specific genetic mutations and the symptoms of the disease. There are some common mutations of the gene that result in

absolutely no enzyme being produced. If both copies of the defective gene inherited by an individual are of this kind, evidence suggests that the individual's condition is likely to be at the severe end of the spectrum. Other common mutations of the gene cause very small amounts of defective enzyme to be produced, and still other mutations are not common at all and may only occur in a single known family. In these cases, it is virtually impossible to predict severity of disease using DNA analysis.

Therefore, there is no perfectly reliable way to determine the exact course of disease for individuals with MPS IV. Even with the same small amount of enzyme activity, and even within the same family, there can be variations in severity of disease that cannot be explained by the enzyme level or DNA mutation. It is important to remember that whatever name is given to your child's condition, MPS IV is a spectrum with a variety of symptoms, and the disease is extremely varied in its effects. This booklet addresses a wide range of possible symptoms that individuals with MPS IV may encounter. However, parents are forewarned that your child may not experience them all or to the degree described herein.

MPS IV is a spectrum with a variety of symptoms, and the disease is extremely varied in its effects.

How common is MPS IV?

MPS IV is one of the rarest mucopolysaccharide diseases in the United States. Reliable incidence figures are not available, but estimates have varied between 1 in 200,000 live births to 1 in 300,000 live births. Although MPS IV is individually rare, the incidence of all MPS diseases is 1 in 25,000 births and the larger family of LSDs collectively occur in about 1 in every 5,000 to 7,000 births.

How is MPS IV inherited?

MPS IV is a genetic disease. When most individuals think of genetic disease, they think of a health problem that gets passed down from father or mother to child and so on. While many genetic diseases are passed down through generations in an obvious way, some genetic diseases are "hidden," or recessive, and only show up when

6 both genes in an individual are affected. MPS IV is this type of genetic disease. Most families who have a child with MPS IV do not have a family history of genetic problems. MPS IV seems to show up suddenly even though the genetic mutation can be traced up the family tree to earlier generations through DNA testing.

To understand this better, it is important to understand some basic concepts about genetics. All humans are formed with two complete sets of genes—one set from each parent. So any individual has half his genes from his mother and half from his father. Together, the individual has 100 percent of the genes required to live.

Each enzyme in the body is produced by two genes—one from the mother and one from the father. If one gene happens to be defective (as is the case for a carrier), then the body may produce only 50 percent of the normal level of enzyme associated with that gene. However, 50 percent of the normal enzyme level is enough enzyme to keep the individual who is a carrier from having any symptoms of MPS IV. If, however, the genes from both the mother and the father are not functioning correctly, the individual will have little or no enzyme in the body and will experience symptoms of MPS IV.

This is why MPS IV is a genetic recessive disease. Both parents are “carriers” of the defective gene—each parent has one normal copy of the gene that produces the enzyme and one defective copy of the gene that cannot properly produce the enzyme. However, one normal copy of the gene allows the carrier parents to be symptom free.

MPS IV is a genetic recessive disease.

All families of affected individuals should seek further information from their medical genetics doctor or from a genetic counselor if they have questions about the risk for recurrence of the disease in their family or other questions related to inheritance of MPS diseases.

Any child born of carrier parents has a three out of four (75 percent) chance of having at least one normal gene and therefore no disease. Each child also has a one in four (25 percent) chance of inheriting the defective gene from both the mother and from the father and thus being affected with MPS IV. There is a two in three (67 percent) chance that unaffected brothers and sisters of individuals with MPS IV will be carriers of the defective gene that causes MPS IV. This is why individuals who are related to each other

should not conceive children. The probability of related parents having similar recessive gene mutations increases dramatically.

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How is MPS IV diagnosed?

Doctors may consider testing for MPS IV when signs and symptoms of the disease are present and are not explained by other causes. All diagnostic tests should be overseen by a doctor with expertise in LSDs, as the tests are complicated and results may be difficult to interpret.

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To diagnose MPS IV, the doctor will typically first do a urine test to look for levels of GAG that are higher than normal. The results are compared to levels of GAG that are known to be normal for various ages. Most, but not all, individuals with MPS have GAG levels in their urine that are higher than those of individuals without MPS.

A urine test is only one of the first steps in diagnosing MPS IV; a clear diagnosis requires a test to measure levels of enzyme activity in the blood or skin cells. In healthy individuals, the tests show white blood cells, serum and skin cells that contain normal levels of enzyme activity. In individuals with MPS IV, the enzyme activity levels are much lower or absent.

Early diagnosis of MPS IV is critical. The earlier MPS IV is diagnosed, the sooner potential treatment options can be explored and supportive care may be started to help you or your loved one and potentially prevent some of the permanent damage that may be caused by the disease.

Prenatal diagnosis

If you have a child with MPS IV, it is possible to have tests during a subsequent pregnancy to find out whether the baby you are

8 carrying is affected. It is important to consult your doctor early in the pregnancy if you wish to perform these tests. The decision to have prenatal testing is complex and personal. Talking with your genetic counselor or doctor can help you explore these options and other strategies, such as egg or sperm donation, for having additional children while limiting the probability that they will have or be carriers for MPS IV.

Clinical problems in MPS IV

Growth

Children with MPS IV usually grow normally at first, but growth may start to slow down around 18 months. Those who are severely affected usually stop growing around the age of 8. Final height may be between 3 feet and 4 feet. Other individuals with MPS IV continue growing into their teens and can reach 5 feet. The trunk is relatively shorter than the limbs.

Intelligence

There is no storage of GAG in the brain of individuals with MPS IV, therefore intelligence is not normally affected.

Physical appearance

The face is altered to a certain extent by the disease. 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 it is in other MPS diseases. Individuals with MPS IV 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.

Eyes

The circular window at the front of the eye (cornea) can become cloudy due to storage of GAG, which disrupts the clear layers of the cornea. Corneal clouding tends to be mild and not particularly noticeable in most individuals with MPS IV and rarely interferes with vision. If corneal clouding is severe, it may reduce sight, especially in dim light. Some individuals cannot tolerate bright lights as the clouding causes uneven refraction of light. Wearing caps with visors or sunglasses can help.

Ears

Some degree of deafness is common in MPS IV. It may be conductive or nerve deafness or both (mixed deafness) and may be made worse by frequent ear infections. It is important that individuals with MPS IV have their hearing monitored regularly so that problems can be treated early to maximize their ability to learn and communicate.

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Conductive deafness

Correct functioning of the middle ear depends on the pressure behind the eardrum being the same as that in the outer ear canal and the atmosphere. This pressure is equalized by the Eustachian tube, which runs to the middle ear from the back of the throat. If the tube is blocked, the pressure behind the eardrum will drop and the drum will be drawn in. If this negative pressure persists, fluid from lining of the middle ear will build up and in time become thick like glue. This is called middle ear effusion.

If it is possible for the child to have a light general anesthetic, a small incision through the eardrum can be made (myringotomy) to remove the fluid by suction. A small ventilation tube 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. The tubes placed in the eardrum may quickly fall out. If this happens, the surgeon may decide to use T-tubes, which usually stay in place much longer. It is expected that, once a ventilation tube is in place, fluid should drain out and hearing should improve.



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Sensorineural (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 or conductive deafness can be managed by the fitting of a hearing aid or aids in most individuals. In general, it is felt that hearing aids are underutilized in MPS diseases.

Mouth and teeth

Individuals with MPS IV may have a prominent chin, wide mouth and enlarged tongue. The 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. Teeth should be

Teeth should be cleaned regularly, and if the water in your area has not been treated with fluoride the child should be given daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and avoid bad breath.

cleaned regularly, and if the water in your area has not been treated with fluoride the child should be given daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and help avoid bad breath. Even with the best dental care, an abscess around a tooth can develop due to abnormal formation of the tooth. Irritability, crying and restlessness can sometimes be the only signs of an infected tooth in a young child.

If an individual with MPS IV has a heart problem, it is advised that antibiotics

should be given before and sometimes after any dental treatment. This is because certain bacteria in the mouth may get into the bloodstream and cause an infection in the abnormal heart valve, potentially damaging it further. If teeth need to be removed while under an anesthetic, this should be done in the hospital under the care of both an experienced anesthetist and a dentist, never in the dentist's office.

Chest

Normally, the breastbone (sternum) is joined to the spine by the ribs. In MPS IV, the growth of the spine is affected. The breastbone continues to grow more normally, but as it is joined to the spine, it is forced to buckle outward 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. A breathing test, called a pulmonary function test, can be used by a lung specialist to assess the amount of breathing restriction the abnormal bones are causing.

Breathing difficulties

The windpipe (trachea) continues to grow while in some cases the cervical spine does not. This can mean that older teenagers and adults may need to tip their heads back to keep the trachea extended and prevent it from kinking and blocking the airway.

In addition, in older teenagers and adults the heart and lungs are compressed within a small thorax (area of the body between the neck and the diaphragm). This leads to difficulties in efficiently exchanging gases in the lungs, and restrictive respiratory failure can occur in adults. This is a difficult complication to treat, so it is important to treat additional chest problems, such as infections, very seriously.

Respiratory infections

Although children with MPS IV are not necessarily more prone to respiratory infections, their restricted chests mean they are less able to cope with an infection if it involves the lungs. Your doctor may advise you to contact him or her immediately if you think an infection might be starting so an antibiotic can be prescribed, if necessary.

Cases have been reported of individuals with MPS IV suffering from severe breathing problems after spending several days at high altitude. It would be wise to check with your doctor if you are planning a long airplane flight or a vacation in the mountains.

Treatment of respiratory infections

Although most individuals with colds do not require antibiotics, individuals with MPS IV almost always end up with secondary bacterial infections of the sinuses or middle ear. These infections should be treated with antibiotics. Poor drainage of the sinuses and middle ear worsens the problem in overcoming infections, therefore it is common to have infections improve on antibiotics and then promptly recur after the antibiotic course is completed. Chronic antibiotic therapy may be used to help some individuals with recurring ear infections. Ventilation tubes can be used to improve drainage from the ear and speed resolution of infections. It is important to consult an ear, nose and throat (ENT) specialist experienced with MPS diseases to determine which tube is best.

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12 Many people with MPS IV become allergic to antibiotics or may acquire resistant infections. Your doctor can prescribe other antibiotics to help manage this problem. While overusing antibiotics is not advised, most people with MPS will require some treatment for most infections. You will need a doctor with whom you can develop a good working relationship to manage the frequent infections.

Heart

Heart disease can occur in people with MPS IV but may not develop or cause any real problems until later in the individual's life.

Medications are available to help manage the heart problems that occur in MPS. Your doctor may hear heart murmurs (sounds caused

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by turbulence in blood flow in the heart) if the valves become damaged by stored GAG. Heart valves are designed to close tightly as blood passes from one chamber of the heart to another to stop blood from flowing back in the wrong direction. If a valve is weakened, it may not shut firmly enough and a small amount of

blood may shoot backward, leading to turbulence and a murmur. Many individuals with MPS IV have some degree of heart valve leakage or blockage. Some individuals with MPS IV may develop problems with the aortic or mitral valves. They may have slowly

progressive valvular heart disease for years without any apparent clinical effects. If the condition worsens, an operation may be needed to replace the damaged valves.

As heart problems occur in MPS IV, individuals should have a test known as an echocardiogram annually (or as often as your doctor thinks necessary) to show whether any problems are beginning. The test is painless, and similar to the ultrasound screening of babies in the womb.

It can identify problems with the heart muscle, heart function and heart valves, but like many tests it cannot detect all possible problems.

Because of the unusual special problems that can occur in these diseases, you should select a cardiologist with some knowledge of MPS IV. At a minimum, you should inform the doctor about heart problems commonly experienced by MPS IV individuals.



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Abdomen and hernias

13 Individuals with MPS IV develop an enlarged liver and spleen (hepatosplenomegaly) due to the storage of GAG. The enlarged liver does not cause problems or lead to liver failure but its volume can interfere with eating and breathing.

Occasionally part of the abdominal contents may push out behind a weak spot in the wall of the abdomen. This is called a hernia. The hernia can come from behind the navel (umbilical hernia) or in 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 are causing problems. It is very common to have a reoccurrence of an umbilical hernia after a repair has been made.

Bones and joints

People with MPS IV tend to have significant problems with bone formation and growth. The bone disease in MPS IV is different from that seen in other MPS diseases. The major clinical features of MPS IV are those related to the bones and their effect on the nervous system if nerves are compressed by abnormal bone movement.

Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. In individuals with MPS IV, the spine tends to be severely affected and its bones or vertebrae are abnormally flattened (platyspondyly). The vertebrae are often poorly formed and may not stably interact with each other. If this happens, the vertebrae can compress and injure the spinal cord. One or two of the vertebrae in the lower back are sometimes slightly smaller than the rest and set back in line.

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This backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not need surgical treatment. If curvature is not severe, bracing may be suggested. There are different opinions on whether surgery is needed or whether a brace can be used either to correct a curve or to support the back. If a brace is used, it should not be the kind that restricts the movement of the chest even further.

Neck (cervical spine)

Problems in this area are perhaps the most serious for individuals with MPS IV. Neck problems need to be discussed at the time of diagnosis, as serious problems can occur before 5 to 6 years of age. The difficulties arise from a structural defect in the upper vertebrae of the spine, which is worsened by very loose ligaments. The bones that stabilize the connection between the head and neck usually are malformed (odontoid dysplasia) in people with MPS IV. There should be a piece of bone called the odontoid process sticking up between the first and second vertebrae which gives support as the head moves backward and forward. With odontoid dysplasia, the neck can become unstable, which places the spinal cord at risk to life-threatening injury. The spinal cord is a big bundle of nerves that carries messages between the brain and the rest of the body. If the cord is compressed or squeezed (cervical myelopathy), there will be gradual worsening effects on the child with paralysis or death occurring if left untreated.

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MRI studies or X-rays will be performed with the head bent forward and with the neck straight (flexion and extension view) and will be repeated from year to year to monitor the situation. A baseline study of the neck is recommended at the time of diagnosis. If severe pain or pain associated with weakness or tremors in the lower legs occur, the child should

have studies of the neck (MRI and flexion-extension X-rays) to evaluate for slippage of the neck vertebrae.

Parents may be alarmed that their child may have weakness in such a vital place and may be harmed by a severe fall. The surgeon will be able to advise you on the risks. It is important to keep a balance between avoiding risks and letting the child lead as normal a life as possible, however activities such as somersaults, head stands or diving should be avoided completely.

The problem with the cervical spine can be corrected by an operation called a cervical fusion. Small pieces of bone are taken from the legs 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.

Fusion operations are often carried out on individuals with other conditions, but there are special problems with individuals with MPS IV and common methods may fail. Most orthopedic surgeons have minimal or no experience with individuals with MPS IV. One or two hospitals have taken a particular interest in individuals with MPS IV and have performed a number of fusion operations. The National MPS Society has information about orthopedic surgeons and hospitals where successful cervical fusions have been performed.

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After cervical fusion, it is essential to immobilize the neck in the correct position for more than four months while the grafted bone grows up to join the base of the skull. One method of achieving this successfully is known as the “halo” method.

A metal halo ring is attached to the skull, and bars leading from it are fixed to the body by a plaster cast. The operation usually involves a hospital stay of usually no more than one week. The halo is typically required for three to four months to allow healing and fusion of the spine. Although caring for a individual in a halo is hard work, individuals adjust remarkably well.

Scoliosis

Abnormal curvature of the spine, or scoliosis, also can occur and, if severe, may require intervention. In general, fusion with bone is the best alternative and hardware-like rods are not well tolerated. In any case, the soft bone makes the surgery and recovery difficult. Many individuals need multiple procedures.

Joints

Joint stiffness is common in MPS IV. All joints become stiff and their movement may become limited. Later in life this can cause pain which may be relieved by heat and prescribed analgesics. 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 MPS IV. Some individuals also may develop osteoarthritis.

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

16 the individual continues to be able to walk and pain occurs later in life, surgery may be considered.

Knock knees

As a child with MPS IV 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 fiber called ligaments. Individuals with MPS IV have ligaments that are often very lax. If this is the case, surgery may not achieve any noticeable improvement.

Ankles and feet

The ankles may be weak and turn inward as a result of ligaments being lax. Occasionally boots and splints are worn, but firm supportive shoes may be equally adequate. The bones composing the arches in the feet are held in position by ligaments and tendons. These are likely to be weakened resulting in flat feet. The toes may be misshapen.

Shoulders

The shoulders often are partially dislocated downward (subluxed) so the arms cannot be raised straight above the head. This rarely causes any discomfort.

Wrists

The wrists are enlarged and curved. They 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 strength in the hands. Attempts have been made to correct this problem surgically by grafting bone from another part of the body to the wrists, but unfortunately the technique has not yet been successful. Small plastic splints with wrist bands may be helpful in some cases.

Writing may be difficult and some individuals may find it easier to use a computer.



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Carpal tunnel syndrome is common in most forms of MPS diseases, but has not been a frequently reported problem in MPS IV.

Carpal tunnel syndrome is common in most forms of MPS diseases, but has not been a frequently reported problem in MPS IV. If your child seems to have pain or numbness in the hands, particularly at night, it would make sense to have an electrical test called a nerve conduction study performed. This test will show whether carpal tunnel syndrome is the cause. If your child has any weakness at all in the hand or has decreased muscle mass at the base of the thumb, ask for the test from your neurologist. Be persistent, as many physicians may not believe that carpal tunnel syndrome is present without the classic symptoms. Most individuals affected by MPS do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage.

General management of MPS IV

Diet

There is no scientific evidence that a particular diet has any helpful effect on people with MPS IV, and symptoms such as diarrhea tend to come and go naturally. Some parents, however, find that a change in their child’s diet can ease problems such as excessive mucus, diarrhea or hyperactivity. Reducing intake of milk, dairy products and sugar, as well as avoiding foods with too many additives and coloring, have helped some individuals. It would be advisable to consult your doctor or a dietician if you plan major dietary changes to make sure the proposed diet does not omit essential items. If your child’s problems are eased, you could try reintroducing foods one at a time to test whether any particular item appears to increase the child’s symptoms.

It is important to note that there is no diet that can prevent the storage of GAG because they are actually made by the body. So reducing sugar intake or other dietary components cannot reduce GAG storage.

Individuals with MPS IV should be as active as possible to maintain muscle strength and general health. Your child’s doctor or physical therapist may be able to suggest ways of achieving this.

Vomiting

Many of those with MPS IV 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

18 mean the stomach may be constricted and discomfort could be experienced after a large meal resulting in vomiting. Sometimes there is a feeling of finding it hard to breathe as the lungs also are constricted. A few children have had episodes of vomiting to such an extent that they become dehydrated. Consult your doctor if vomiting continues over several hours.

Drugs

Children with MPS may be affected differently by drugs, so it is essential to consult your doctor rather than using over-the-counter medications. 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. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for people with MPS IV.

Children with MPS may be affected differently by drugs, so it is essential to consult your doctor rather than using over-the-counter medications.

Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea by depressing muscle tone and respiration.

Physical therapy

Joint stiffness is not a feature of MPS IV, but loose joints can be a problem. Intensive physical therapy will be needed to help an individual with MPS IV start walking again after neck, spine or knee surgery. Individuals with MPS IV should be as active as possible to maintain muscle strength and general health. Your child's doctor or physical therapist may be able to suggest ways of achieving this. It is important to keep a balance between avoiding risks and letting the child lead as normal a life as possible. Activities such as somersaults, head stands or diving should be avoided completely because of risk to the neck.

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Mobility

Many individuals with MPS IV remain ambulatory into their teens and adult life. Others may need to use a wheelchair from an early age for longer periods of activity. An electric wheelchair is vital to encourage independence. Consult your physical therapist or occupational therapist for advice.

Anesthetics

19 Giving an anesthetic to an individual with MPS IV requires skill and should always be undertaken by an experienced anesthetist. If the cervical spine is unstable, the individual with MPS IV is at risk if the neck is flexed while unconscious, and special precautions must be taken. Inform your child's school or any other caregivers of this in case you cannot be contacted in the event of an emergency. If you have to go to a different hospital in an emergency, tell the anesthetist there may be problems with the neck and possibly with intubation (placement of the breathing tube). The airway can be very small and may require a very small endotracheal tube. Placing the tube may be difficult and require the use of a flexible bronchoscope to place it gently. In addition, the neck may be somewhat lax and repositioning the neck during anesthesia or intubation could cause injury to the spinal cord.

Giving an anesthetic to an individual with MPS IV requires skill and should always be undertaken by an experienced anesthetist.

For some individuals, it is difficult to remove the breathing tube after surgery is completed. Advise physicians of the critical nature of these problems, and that many problems have occurred during anesthesia of individuals with MPS. For any elective surgery in a child with MPS, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical center, not at a local hospital. See additional information on anesthesia in the booklet titled *Is Your Child Having an Anesthetic?* published by the National MPS Society.

Living with a child or adult with MPS IV

Education

The majority of children with MPS IV will attend mainstream school and achieve academically. Achieving an education through college is not unusual. For children with MPS IV to reach their full academic potential, it is important to ensure that the school is aware of the resources required. It is important to work with your

school system and develop the best Individualized Education Program (IEP) for your child. For more information on education, see the booklet titled *A Guide for Parents: Education Strategies and Resources* published by the National MPS Society.

Puberty and marriage

Adolescents with MPS IV will go through normal developments of puberty, although the onset of periods in girls may be delayed. Individuals with MPS IV are fertile. Women whose stature is significantly restricted may be advised not to become pregnant because of risks to her health. All children born to a parent with MPS IV are automatically carriers but none will have the disease unless the other parent also is a carrier.

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Independence

Individuals with MPS IV should be encouraged to be as independent as possible to lead full and enjoyable lives. The teenage years may be difficult if they have restrictions imposed by their disease. This may be helped by meeting or contacting other teenagers and adults who also have MPS IV. Individuals with short stature may find additional support and helpful information through Little People of America, www.lpaonline.org.

Employment

The physical disabilities of those suffering from MPS IV should not in themselves prevent people from accessing meaningful employment. The Americans with Disabilities Act provides assistance to both employees and employers.

Home adaptations

Appropriately adapted living accommodations will greatly enhance the ability of an individual with MPS IV to develop independent living skills. Where stature is severely restricted, kitchen and bathroom facilities at a low level will be required. If mobility is



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restricted to such an extent that a wheelchair is used, plans for any home adaptations will need to allow adequate space to accommodate this. Additional information about home adaptations can be found in the booklet published by the National MPS Society, *Daily Living with MPS and Related Diseases*.

Psychosocial issues

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

Currently there has been no research that explores the psychosocial development of individuals affected with MPS IV.

Some children and young adults with MPS IV may adapt socially and emotionally by becoming socially inhibited, or by internalizing problems or developing an aggressive, outgoing personality. Adolescence may be more of a challenge as they have to experience all of the physiological and psychosocial changes as well as any disease-related changes or limitations. Developing the necessary skills to lead independent adult lives can be challenging, although important, to achieving social maturity. Referral for counseling is recommended if problems such as depression are seen in teenagers and young adults with MPS IV.

Healthcare information

Assistance may be available from specialized agencies for the disabled and from genetic clinics. You might want to look into Social Services, Social Security, Medicaid Waivers and the Katie Beckett Law. Investigate these options and others in your state, or your Department of Health. If you have a social worker assigned to you, he or she should be able to locate additional information and/or resources for your family.

Assistance may be available from specialized agencies for the disabled and from genetic clinics.

Living with MPS IV

Disease severity varies significantly for individuals with MPS IV, and it is not possible to predict the expected life span for a given individual. Those on the more slowly progressing end of the disease spectrum may have a reasonably normal lifespan. However, the availability of new and ever-improving treatments as well as other surgical procedures provides hope for better future outcomes for individuals affected by MPS IV.

Specific treatment of MPS IV

Overview

The goals of managing MPS IV are to improve quality of life, to slow down the progression of the disease, and to prevent permanent tissue and organ damage. Currently there is no cure for MPS IV. However, early intervention may help prevent irreversible damage. Treatment options for MPS IV include those aimed at disease management and supportive or palliative care (care that makes a person with a disease that cannot be cured more comfortable).

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Hematopoietic Stem Cell Transplant (HSCT)

The goal of HSCT is to restore the activity of the deficient enzyme. HSCT does not, however, correct the skeletal structural defects, so at this time HSCT is not recommended for MPS IV.

Enzyme replacement therapy (ERT)

Currently there is not an approved ERT for MPS IV, although research in this area is promising.

Research for the future

The mission of the National MPS Society is to find cures for MPS and related diseases. As part of that mission, the Society funds research grants. The Society recognizes the need for targeted research for treatment of bone and joint problems and for treating the brain, and Society research funding has focused on those areas. Information about Society funded research and promising new areas of research can be obtained by contacting the Society's office.

This booklet is intended as an introduction into the nature of the disease, as well as to help families understand more about what is happening to those with MPS IV and what they can do to manage it. This booklet was updated by the National MPS Society in 2008.



This booklet is not intended to replace medical advice or care. The contents of and opinions expressed in A Guide to Understanding Mucopolysaccharidosis (MPS) IV do not necessarily reflect the views of the National MPS Society or its membership. This booklet may be reproduced or copies can be made available upon request and written authorization from the National MPS Society.

Common bonds unite the lives of those affected by MPS and related diseases—the need for support and the hope for a cure.

The National MPS Society is committed to making a difference in the lives of MPS families through support, research, education and advocacy. Families from around the world gain a better understanding of these rare genetically determined diseases through the Society's assistance in linking them with healthcare professionals, researchers and, perhaps most importantly, each other.

Individuals affected with an MPS or related disease and their families have a resource. One that stands ready to help—a resource that takes an active role in fostering the courage necessary to confront these diseases every day.

Benefits of membership in the National MPS Society:

- *Courage*, our quarterly newsletter containing stories and information about individuals with MPS and related diseases;
- Educational materials such as fact sheets and an MPS glossary;
- Conference and education scholarships;
- The Family Assistance Program, which provides financial support for durable medical goods;
- News about various Society sponsored conferences and gatherings, where families and leading MPS scientists, physicians and researchers join together for a common cause;
- Information on local events, such as regional social events and fundraisers. These events create opportunities for families to meet each other and help raise community awareness of these rare genetic diseases; and
- A listing in our annual directory of members that assists families with connecting with one another.



For more information or to join the National MPS Society:

Visit www.mppsociety.org

Contact us at **877.MPS.1001**

Or e-mail us at info@mppsociety.org