Canadian MPS Society
for Mucopolysaccharide & Related Diseases

September 2016

Dear Friends,

The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society) is pleased to provide you with with this resource binder entitled *MPS IV: A resource for individuals and families living with MPS IV.*

The resource binder is designed to give you a reliable, comprehensive source of information on the symptoms and treatment of MPS IV, also known as Morquio syndrome. It also provides space for you to record your appointments or concerns, making it easier for you to track your own unique experiences and to share them with others.

On July 2, 2014, VIMIZIM® (elosulfase alfa) was approved by Health Canada for the treatment of MPS IVA. Since approval, a 52 week study of the safety of VIMIZIM in patients under 5 years of age has been completed. In this study, 15 paediatric patients under 5 years of age were treated with 2.0 mg/kg of VIMIZIM once per week resulting in reduction of urinary glycosaminoglycan levels. Side effects of treatment were similar in this study of patients less than 5 years of age to the side effects experienced in other studies of patients older than 5 years of age

Based on the results of this study, VIMIZIM was approved for all ages on March 24, 2016. The product monograph recommends that treatment with VIMIZIM be initiated as early as possible, before the appearance of non-reversible symptoms of MPS IVA.

The enclosed section on treatment options includes important updates about this enzyme replacement therapy (ERT) with VIMIZIM. You may wish to discuss this treatment with your doctor.

We encourage you to ask your doctors for copies of your medical reports and evaluations and include them in your binder. Having all this information in one place may make it easier to answer questions from the various specialists you will likely see.

We hope this MPS IV resource binder is a useful and beneficial tool for your family. If you have comments or suggestions on how we might improve our resources, please contact us at anytime.

Sincerely,

Kim Angel
Executive Director

Disclaimer

Mucopolysaccharidosis (MPS) IVA and IVB are two separate and distinct diseases. Although there are similarities, the differences between the two may be significant, especially with regards to treatment options such as enzyme replacement therapy (ERT), which is now available for MPS IVA but not MPS IVB. Many publications about MPS IVA have recently become available due to research into ERT. The following sections of your MPS IV binder have been updated based on these recent publications. New content has been indicated with a yellow box around the content, such as the yellow box that appears around this disclaimer section.

This binder is a resource designed to support people with MPS IV understand their disease and its management. While the updates may be informative for all people with MPS IV, not all information will be relevant to people with MPS IVB, especially the updates to the treatment section. You should discuss the information contained in this binder with your doctor to determine how it impacts your personal disease management and treatment.

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Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Mucopolysaccharidosis IV (MPS IV)

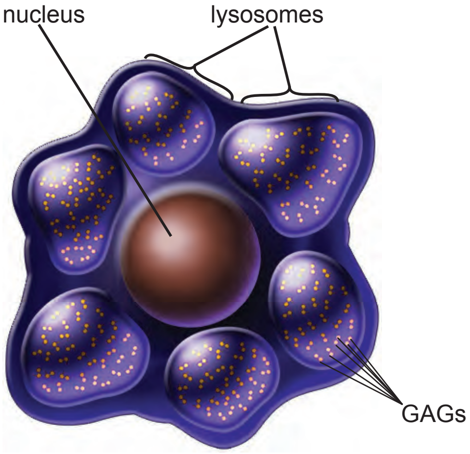
Contents

Mucopolysaccharidosis IV (MPS IV)

What is MPS IV disease?

Mucopolysaccharidosis IV (MPS IV; pronounced **mew**·ko·**pol**·ee·**sak**·ah·ri·**doh**·sis **four**) is a rare genetic disorder that affects many body systems and may lead to the damage of different body organs such as the bones, joints, and heart. MPS IV is also known as Morquio syndrome. There are two types of MPS IV. MPS IVA is caused by a defect in the gene that instructs the body to make the enzyme N-acetylgalactosamine-6-sulfatase (GALNS, pronounced en-a·**see**·tyl·ga·lak·**tose**·amine-six-**sul**·fate sul·fa·tace), which is also called galactosamine-6-sulfatase. MPS IVB is caused by a defect in the gene that instructs the body to make the enzyme beta-galactosidase (GLB1). Because of this gene defect, cells either produce the enzyme in low amounts or not at all. Both the enzymes are needed to break down substances called glycosaminoglycans (GAGs; pronounced **gly**·cose·a·**mee**·no·**gly**·cans). If GAGs are not broken down, they build up in the cell, eventually leading to damage in cells, tissues, and organs.

Mucopolysaccharidosis IV (MPS IV) is a rare genetic disorder that affects many body systems and may lead to damage of body organs.



Cell with GAG buildup

Courtesy of Genzyme Corporation

GAGs, previously called mucopolysaccharides, are long chains of sugar molecules joined together, and are located mostly on the outside surface of cells. The body uses them in the building of bones, cartilage, skin, tendons, and many other tissues in the body. GAGs 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 joint fluid that lubricates your joints contains GAGs. The rubbery 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 IV have too great an amount of GAGs in their body.

To understand how GAGs accumulate and cause MPS IV, it is important to understand that in the course of normal life, there is a continuous process of building new substances like GAGs and breaking down old ones. This ongoing process is required to keep your body healthy. The breakdown and rebuilding of GAGs requires a number of different enzymes, which are chemicals that are made by the body.

To break down GAGs, a series of enzymes work in sequence one after another. Each enzyme in the process has its own special purpose in the body and does one very specific action, just like a screwdriver works on screws and a hammer works on nails. As mentioned earlier, people with MPS IV are missing one of two specific enzymes (either N-acetylgalactosamine-6-sulfatase or beta-galactosidase), needed for the breakdown of certain GAGs called keratan sulfate and chondroitin-6-sulfate. If these GAGs are not completely broken down, they remain stored inside cells throughout the body and begin to accumulate. This buildup of GAGs interferes with how the cell normally works and causes damage that worsens with time.

Some individuals with MPS IV may initially show few signs of the disorder, but as more and more GAG accumulates, signs of too much GAG in the body's tissues start to appear. GAGs are produced in the body, not obtained from sugar in foods, so it is not possible to reduce the buildup by eating a special diet.

How is MPS IV related to other MPS syndromes?

The enzymes involved in breaking down GAGs are contained inside special parts of the cell, called lysosomes. The GAGs that accumulate as a result of the missing enzyme, therefore, are all stored within the lysosomes in the cells. It is for this reason that MPS IV is part of a larger family of diseases called the "lysosomal storage disorders" (or "LSDs" for short).

There are more than 40 different conditions that are known to be caused by lysosomal storage disorders. These disorders have some features in common: they are genetic; most are caused by a deficiency in a particular enzyme normally present in lysosomes; and they cause by-products of chemical reactions to build up in the body's cells, leading to symptoms in a variety of body systems. However, because the exact enzyme is different in each case, individual LSDs can cause completely different types of symptoms and affect different organ systems. Individual LSDs can also vary in terms of the age at which they begin to cause symptoms and how they affect life expectancy.

Within the larger family of LSDs, however, there are certain groups of conditions that have many clinical features in common. The mucopolysaccharidoses (MPS) are an example of such a group. The MPS disorders include seven main types: MPS I, MPS II, MPS III, MPS IV, MPS VI, MPS VII, and MPS IX. All MPS disorders result in the buildup of various GAGs in the lysosomes. Each type of MPS is caused by a deficiency of a different specific enzyme. Although each of the individual MPS disorders can cause a variety of different symptoms, the disorders collectively have many symptoms in common (which are explained later in this resource). These include, for example, short stature, bone and joint problems, speech and hearing problems, hernias, runny nose, and heart problems.

How common is MPS IV?

MPS IV is a rare disease, but it is hard to say exactly *how* rare because there are so few studies. The incidence of MPS IVA varies significantly. It is estimated to occur in 1 of every 76,000 to 640,000 live births.

It is worth noting that while MPS IV is rare, the larger family of lysosomal storage diseases collectively occurs in about 1 in every 5,000 live births.

Because MPS IV is an inherited disorder, family screening is extremely important.

How do people inherit MPS IV?

MPS IV is a genetic disorder. When most people 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 the generations in an obvious way, some genetic diseases are "hidden," or recessive, and only show up when both genes in an individual are affected. MPS IV is one such disease.

Most families with a child with MPS IV do not have a family history of any genetic problem – MPS IV seems to show up suddenly. To understand this better, it is important to understand some basics of genetics.

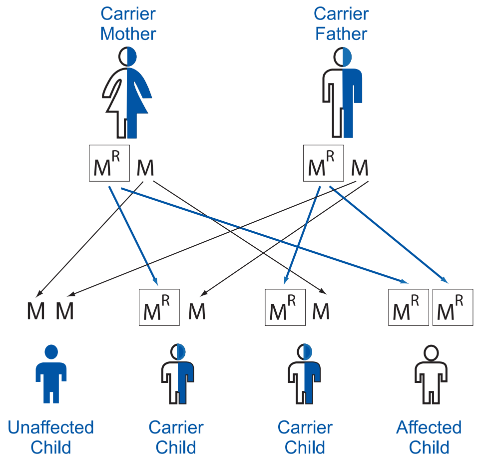
All humans are formed with two complete sets of genes, one set from each parent. So any individual has half his genes from his mother and half from his father. Together, the individual has 100% of the genes required to live. Our genes carry the instructions for traits like eye colour, as well as instructions for our bodies to work properly.

For each enzyme made in the body, there are two copies of the same gene that carry instructions to produce it, one from the mother and one from the father. If one gene happens to be defective, then the body may only produce 50% or less of the normal level of enzyme associated with that gene. The body is quite resilient, however, and even a 50% level of enzyme is more than enough to keep the person healthy. Basically, half the enzyme can do twice the usual amount of work. However, if both genes for the enzyme from the mother and the father are not functioning correctly, then the individual will have little or no enzyme in the body and then will suffer from the disease.

MPS IV is a recessive disorder. This means the disorder occurs only if both copies (one from each parent) of the galactosamine-6-sulfatase (for individuals with MPS IVA) or beta-galactosidase (for individuals with MPS IVB) enzyme gene inherited by the individual are defective. This can happen when each parent is a “carrier”of the defective gene; i.e., each parent has one normal version of the gene that can produce the necessary enzyme but also “carries” one defective version of the gene that cannot produce the enzyme properly. Unfortunately, individuals do not usually know they are carriers until, by chance, the condition occurs in their child.

The figure in the next column shows how the MPS IV gene may be passed from one generation to the next.

Because of the way genetic inheritance works, in a family with no previous history of MPS it is impossible to predict in advance of a pregnancy whether parents are carrying the defective gene for MPS IV and if they will have an affected child. However, it is possible to calculate the probability that this will occur if the parents are known to be carriers. As the figure above illustrates, each child born of carrier parents has a 3 out of 4 (or 75%) chance of having at least one normal gene and therefore no disease. Each child born also has a 1 out of 4 (or 25%) chance of inheriting the defective gene from each parent and thus being affected with the disorder. There is a 2 in 3 (or 67%) chance that unaffected brothers and sisters of individuals with MPS IV will still be carriers. Carriers have one good gene and one defective gene.



Courtesy of Genzyme Corporation

Legend:

M – copy of gene that properly controls production of the enzymes that break down GAGs

M^R – faulty copy of gene, one that does not properly control production of the enzymes that break down GAGs in MPS IV

Because MPS IV is an inherited disorder, family screening is extremely important. When a diagnosis for an individual is made, it is important to find out whether other siblings may also be affected. A genetic counsellor can be a valuable resource in helping you understand how MPS IV is inherited and in determining whether other family members also wish to pursue genetic testing for MPS IV. Testing for MPS IV is done by measuring the enzyme level in a blood or skin sample, and your doctor can arrange for this test. With an early diagnosis, the disease may be better managed.

Prenatal testing allows pregnant women who have already had a child with MPS IV to find out if the baby they are carrying is also affected by MPS IV. There are two tests that can be used: chorionic villus sampling (taking a sample of the placenta) and amniocentesis (taking a sample of the amniotic fluid). Your doctor can advise you on your specific prenatal testing options. The decision to have prenatal testing is complex and personal. It is important to consult your doctor early in the pregnancy if you wish tests to be arranged. Talking with your genetic counsellor or doctor can help you explore these options and other strategies for having additional children while limiting the probability that they will have MPS IV.

Is it possible to predict the severity of MPS IV?

There is currently no test that reliably indicates how severe an individual's MPS IV will eventually become. As MPS IV is a condition that worsens over time, all individuals will experience a progression of symptoms. Patients cannot be classified into different subgroups based on their symptoms, the severity of the disease, or rate of progression. This is because individuals with MPS IV may experience severe disease symptoms in one area (e.g., respiratory problems), but not in another (e.g., their height may be unaffected).

People with MPS IV either completely lack the enzyme needed to break down GAGs or only produce small amounts. Many different kinds of mutations in the genes (i.e., defects in the make-up of genes) that produce the enzymes galactosamine-6-sulfatase or beta-galactosidase have been identified, all of which have reduced enzyme activity. This enzyme deficiency results in MPS IV disease. The gene has been studied 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, but there are also other kinds of mutations that cause the enzyme to be produced in very small amounts or to be defective. And then there are still other mutations that are not common at all. 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. Possible symptoms are outlined to a large extent later in this resource, but any given person may not experience them all or to the degree presented in those sections.

MPS IV is a progressive disease with a broad spectrum of symptoms.

4 years *10 years* *28 years* *30 years*

MPS IV disease leads to progressive multisystemic disease manifestations.

Courtesy of BioMarin Pharmaceutical Inc.

Is it possible to predict lifespan?

MPS IV disease varies significantly for people with MPS IV and it is not possible to predict the expected lifespan for a given individual. Lifespan depends on many factors, such as if and when an affected person receives treatment for MPS IV, and the specific kinds of symptoms a person experiences. Some patients are likely to have a shortened lifespan, and often do not live beyond their teens or twenties. However, there have been patients who have lived into their sixties. 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.

A clear diagnosis requires enzyme tests conducted by experts. Early diagnosis is critical to initiate management of MPS IV.

How is a diagnosis made?

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. This can potentially prevent some of the permanent damage that may be caused by the disease. Early diagnosis is especially critical for those with MPS IVA as they now have an enzyme replacement therapy (ERT) available called VIMIZIM™ (elosulfase alfa), which replaces the deficient GALNS enzyme and restores cell function. VIMIZIM has been shown to improve endurance and walking ability for people with MPS IVA. ERT is not a cure for MPS IVA. Other management options for MPS IVA and IVB include those aimed at disease management and supportive or palliative care. Treatment and management options for MPS IV are explained in more detail later in this resource.

Doctors may consider testing for MPS IV when signs and symptoms of the condition are present and are not explained by other causes. As diagnosis of MPS IV may be difficult and rely on clinician interpretation, all diagnostic tests should be overseen by a doctor with expertise in lysosomal storage disorders. This is because the tests are complicated and the results may be challenging to interpret.

VIMIZIM™ (elosulfase alfa) Product Monograph, BioMarin Pharmaceutical (Canada) Inc. 2014

Typically, a doctor will first send a person for x-rays to determine if the individual has skeletal abnormalities commonly associated with MPS IV. If a doctor already has a strong suspicion of MPS IV being present, the individual may be sent for urine glycosaminoglycan (GAG) analysis and enzyme activity analysis at the same time or may send the person for enzyme activity testing alone, without performing a urine GAG assessment at all. Results of the individual's urine GAG test is compared to levels of GAGs that are known to be normal for various age groups. Most, but not all, individuals with MPS have GAG levels in their urine that are higher than those of people without MPS. As the GAGs associated with MPS IV are difficult to analyze, there is a chance that a urine GAG test may falsely indicate that an individual does not have MPS IV. This is called a false-negative test result. The doctor may send an individual for enzyme analysis even with a negative urine GAG assessment if MPS IV is suspected based on x-rays and other symptoms.

A clear diagnosis of MPS IV requires a test that measures the levels of enzyme activity in the blood or skin cells. An individual should be assessed for other lysosomal enzymes at the same time to rule out the presence of other enzyme deficiencies, which may cause mucolipidosis II and III, MPS VI, and multiple sulfatase deficiency. 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, enzyme activity levels are much lower or absent. For some, the enzyme analysis may also be inconclusive. For these people, genetic testing will be required for conclusive diagnosis.

Genetic testing identifies the underlying mutations causing MPS IV. It may be done on all individuals with MPS IV, but may also be the final stage in definitive diagnosis for some. In addition to diagnosis, identifying the underlying mutations can help to contribute to the understanding of the disease for healthcare professionals, and will assist with the family's future genetic counselling.

An update on newborn screening

Newborn screening is the testing of newborn babies to see whether they have specific disorders. The goal is to help with early diagnosis and treatment. Each province makes its own decisions about which health conditions should be included in their newborn screening programs.

The factors that are considered when deciding on newborn testing include:

- Is the disorder clearly defined?
- Does the disorder occur fairly often?
- Does early diagnosis help?
- Are tests available to diagnose the disorder accurately and cost-effectively?
- Can the tests be done quickly or is there a long waiting time for results?

Lysosomal storage disorders (such as MPS IV) meet some of these criteria:

- Lysosomal storage disorders occur in about 1 in every 5,000 live births, which is more frequent than some conditions already included in newborn screening.
- Early diagnosis helps affected people get interventions sooner.
- There are a number of "markers" (substances that can be measured, such as GAGs in the urine) for lysosomal storage disorders that could potentially be used to develop screening tests.

Currently, there is growing movement promoting newborn screening for MPS disorders such as MPS IV. It is now more widely recognized that for many families, just knowing about the diagnosis is helpful, along with the opportunity for genetic counselling and education about additional medical help and management options.

Considering the potential benefits, the current aim is to develop a test that would allow for these options for children with lysosomal storage disorders. To develop a good screening strategy, researchers have identified features common to all lysosomal storage disorders. This is important because there would not be enough time, money, and labour available to measure each enzyme that is deficient in each individual disorder, which is the usual method of making a diagnosis. Thus, different methods for screening are being studied.

There is a growing movement promoting newborn screening for MPS.

Some researchers suggest a tiered, or step-by-step, screening strategy. The first screening would involve measuring certain markers to identify a person who is at risk for the condition. For the person identified as "at risk," a second test would be performed to identify higher levels of stored materials. A positive result on both tests would need to be found before a family was referred for counselling, additional testing, and management.

Research into newborn screening for LSDs is still in early stages. Important questions remain about the screening process and the testing methods. There will likely continue to be debate over the appropriateness of screening. There may also be concern about the effect on the parent-child relationship when a newborn is identified with

Courtesy of BioMarin Pharmaceutical Inc.

a condition before symptoms appear. This will leave many questions for families and healthcare professionals who want to choose the best treatment. As a community, those whose lives have been touched by MPS IV will likely continue to become more involved in the promotion of newborn screening.

Signs and symptoms of MPS IV and their management

Overview

MPS IV has a wide range of symptoms. Most people will experience reduced endurance, pain, and decreased quality of life, often related to the other symptoms experienced. As each person will experience different stages of disease progression and disability, the management of the disease will differ depending on each person's symptoms.

Guidelines have recently been published for MPS IVA* (entitled "International Guidelines for the Management and Treatment of Morquio A Syndrome"), much of which may also be applicable for people with MPS IVB. These guidelines were developed with the input and consensus of leading medical experts experienced in managing the full range of symptoms associated with MPS IV. Whether you have MPS IV or you are caring for someone with MPS IV, these guidelines are a powerful resource to help you and your doctors manage this condition.

Table 1: MPS IV signs and symptoms

General symptoms
- reduced endurance
- pain

Gastrointestinal system (abdomen and intestines)
- enlarged liver and spleen (hepatosplenomegaly)
- umbilical and inguinal hernias*
- loose stools, diarrhea, constipation, abdominal pain

Physical appearance
- short neck
- large head (macrocephaly)
- short stature
- uneven, swaying gait

Mouth and teeth
- prominent chin, wide mouth, and enlarged tongue
- abnormal teeth (widely spaced with small sharp pointed cusps and very thin enamel)

Eyes, ears, nose, and throat
- vision problems, such as corneal clouding and vision impairment
- hearing loss
- frequent ear infections (otitis media)
- frequent upper respiratory tract infections (e.g., tonsillitis)

Brain and nerves
- pressure on the neck area of the spinal cord from abnormal tissue growth nearby (cervical spinal cord compression)
- normal intelligence

Musculoskeletal system (bones and joints)
- skeletal abnormalities (dysostosis multiplex with odontoid hypoplasia)
- abnormal hip formation (hip dysplasia)
- lax joints and loose ligaments
- bone deformities in the spine (scoliosis, gibbus, kyphosis), knees (knock-knees or genu valgum), and ankles (valgus deformity)

Respiratory system
- lung problems and reduced lung function
- sleep apnea
- frequent lung infections

Heart and blood vessels
- heart abnormalities

**Hernias: When part of an organ (such as the intestine) protrudes from a weak spot in the muscular wall surrounding the abdomen, producing a bulge in the skin, this is called a hernia. With an umbilical hernia, the bulge is in the belly-button area. With an inguinal hernia, the bulge is in the groin area*

**Christian J. Hendriksz, Kenneth I. Berger, Roberto Giugliani, Paul Harmatz, Christoph Kampmann, William G. Mackenzie, Julian Raiman, Martha Solano Villarreal, and Ravi Savarirayan. International Guidelines for the Management and Treatment of Morquio A Syndrome. Am J Med Genet Part A. 2014. DOI: 10.1002/ajmg.a.36833*

Given the diverse symptoms of MPS IV, patients will need to see different specialists to manage their care. These specialists should be coordinated by a doctor experienced in MPS IV. This coordinating doctor, often a pediatrician or a geneticist, will provide continuity in monitoring of the progression of the disease as well as the individual's overall care. This coordinating doctor will need to regularly educate other members of the healthcare team (such as other specialists, dentists, and physiotherapists) about the disease, and discuss the risks, benefits, and necessary precautions associated with different interventions and treatments. Additionally, this coordinating doctor will offer guidance to people with MPS IV and their family on healthcare decisions. With the publication of these guidelines, doctors who have less experience with MPS IV can access expert medical guidance on the multisystemic effects of the disorder and the best ways to manage the condition.

Table 1 on the previous page provides an overview of the signs and symptoms that may occur in individuals who have MPS IV. The content in later parts of this section provides more details about some of these signs and symptoms. Where possible, symptoms that are similar or linked or that relate to a common organ system have been included together. Within the content details, there is also information about disease management and surgical procedures devoted to each symptom or group of symptoms.

It is important to note that many individuals with MPS IV may never experience some of the symptoms described in this section, and that those who do experience such symptoms will not necessarily do so to the degree presented.

Gastrointestinal system

Individuals with MPS IV may experience abdominal or gastrointestinal issues including enlargement of the liver and spleen, hernias, chronic constipation, and diarrhea. However, gastrointestinal symptoms are less common and severe for individuals with MPS IV when compared to what may be experienced by individuals with other forms of MPS disease.

Liver

Accumulation of GAGs causing enlargement of the liver (hepatomegaly) or spleen (splenomegaly) has been rarely reported in people with MPS IV, but does occur. The large liver does not usually cause liver problems or lead to liver dysfunction.

Abdomen and hernias

In individuals with MPS, the abdomen may bulge out due to their posture, the weakness of the muscles, and the enlarged 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. The hernia can come from behind the navel (umbilical hernia) or in the groin (inguinal hernia). Inguinal (groin) hernias should be repaired by an operation, but hernias will sometimes recur. Umbilical (navel) hernias are not usually treated unless they cause entrapment of the intestine (the intestine gets caught in the abdominal opening, which cuts off its blood supply) or are very large and are causing problems. It is very common for an umbilical hernia to reappear after it has been repaired.


Hernia in a child with MPS VI

Courtesy of the National MPS Society

Bilateral diaphragmatic hernias have also been reported in MPS IV. This hernia affects a small part of the diaphragm (a muscle that stretches across the bottom of the rib cage and plays an important role in respiration) on the right side of the body. Laproscopic surgery may be recommended for individuals with this type of hernia, even when they are not experiencing symptoms, due to the increase of recurrent chest infections and gastrointestinal symptoms for individuals with bilateral diaphragmatic hernias.

Physical appearance

Stature

At birth, those affected usually initially grow at the same rate as other children who do not have MPS IV, their growth may start to slow down around 18 months of age. The majority of individuals with MPS IV will be greater than the 85th percentile for weight, yet under the 3rd percentile for height with a short torso and neck. Due to their physical limitations (such as short stature) and musculoskeletal problems, people with MPS IV tend to move less than their peers and, therefore, are prone to obesity.

Facial features

Some individuals with MPS IV have similar facial features, which may include a wide mouth, a square jaw, and a broad nose with a flat bridge. Typically, the neck is very short. The texture of the hair is not affected as it is in other MPS disorders, as the GAG accumulation in MPS IV occurs mostly in the joints and bones, rather than the skin.

Mouth and teeth

People with MPS IV tend to have a prominent chin, wide mouth, and enlarged tongue. The teeth are generally small, widely spaced, and poorly formed, with fragile enamel (outer layer). It is important that the teeth be well cared for, as people with MPS IV are prone to tooth decay, which can be a cause of pain.

People with MPS IV should be referred to a dentist at diagnosis and should be monitored at least annually by a dentist. Teeth should be cleaned regularly, and if the tap water in your area has not been treated with fluoride, a person with MPS IV should have daily fluoride tablets or drops. Dental sealants may be considered to prevent decay. Even with the best dental care, an abscess (infection) around a tooth can develop due to the tooth not having formed properly.

If an individual with MPS IV has a heart valve problem, antibiotics may be considered before and 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. Depending on the antibiotic used, side effects could differ. Some common side effects of antibiotics include diarrhea, nausea, and vomiting. Antibiotics may also cause skin rashes and allergic reactions. Consult a cardiologist before the procedure to determine if antibiotics are necessary.

If teeth need to be removed while under anesthesia, this should be done in the hospital under the care of both an experienced anesthesiologist and a dentist, never in the dentist's office.

Eyes

Symptoms related to the eye can occur in individuals with MPS IV. These symptoms include the following:

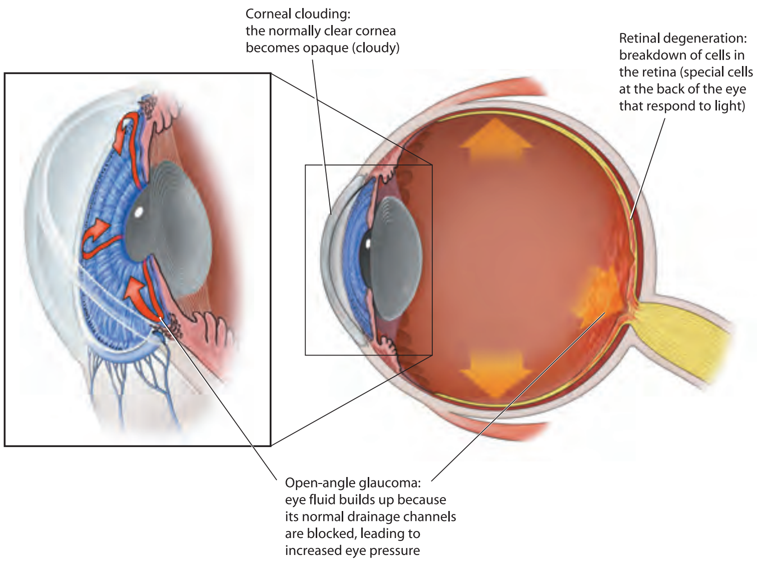
- *Corneal clouding*: The circular window at the front of the eye (known as the cornea) becomes cloudy due to storage of GAGs, which disrupts the clear layers of the cornea. If corneal clouding is severe, it may reduce sight, especially in dim light. Some people with MPS IV cannot tolerate bright lights, as the clouding causes uneven refraction (bending) of the light. Wearing sunglasses or caps with visors can temporarily help. Many people with MPS IV have had a corneal transplant, which usually improves vision. Possible risks of a corneal transplant include infection, rejection of the transplanted cornea, or an allergic reaction to the medication used for local anesthesia (numbing the eye before surgery). It may take up to one year for vision to return to normal after such complications. It

MPS IV affects many areas of the body. Because its signs and symptoms are so variable, it affects each individual differently.

is important to be aware that the clouding may recur, as has been reported with other MPS diseases, and that retinopathy, glaucoma, and wasting of the optic nerve (all described below) may impact the success of the corneal transplant.

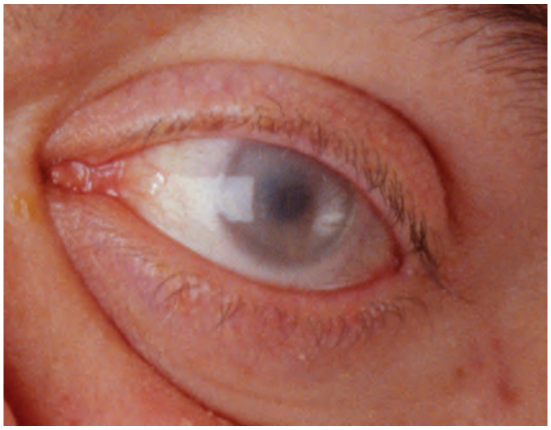
- *Refractive error problems:* Astigmatism, myopia, and hyperopia are commonly found in individuals with MPS IV and can impact visual acuity and sensitivity to light. These can be assessed for during an eye examination.
- *Glaucoma*: There may be problems with vision caused by glaucoma (increased pressure in the eye) that should be checked during an eye examination.
- *Retinal degeneration*: There may be problems with vision caused by changes to the retina (the light-sensitive tissue that lines the inner surface of the eye). For example, GAG storage in the retina can result in night blindness and loss of peripheral vision (ability to see things that are at the side while looking straight ahead). Night blindness can result in an individual not wanting to walk in a dark area at night or waking up at night and being afraid. Sometimes the addition of a night light in a hall or bedroom is helpful.

Other eye problems that are occasionally experienced by individuals with MPS IV include cataracts (clouding of the lens inside the eye that can lead to impaired vision), which may be surgically corrected, swelling of the optic disc (the beginning of the optic nerve), wasting of the optic nerve (the nerve that carries information from the eye to the brain), and eyes that appear to bulge due to shallow orbits or eye sockets.



Eye problems in MPS IV

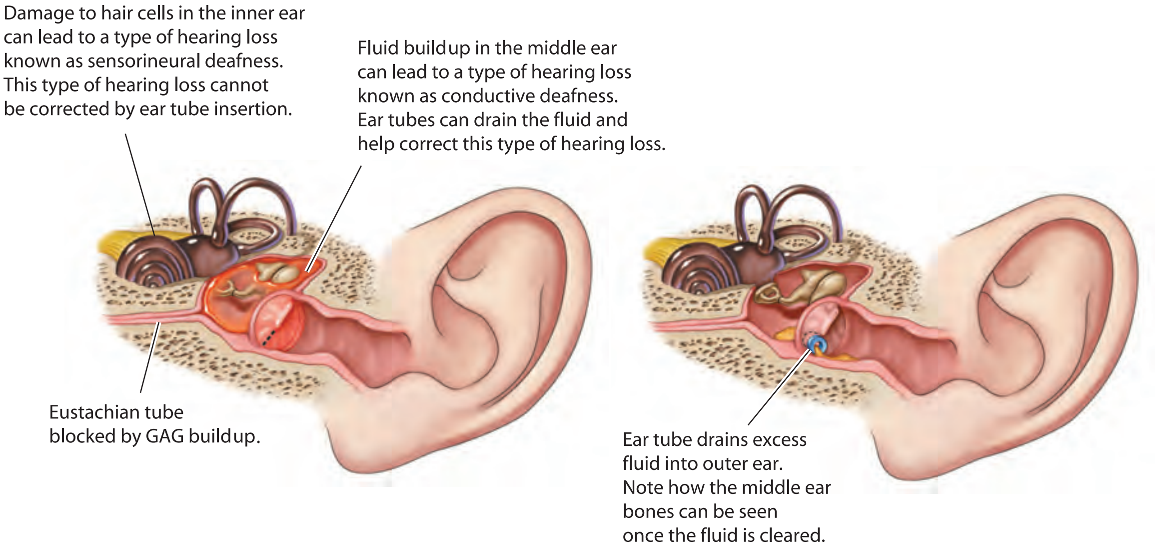
Courtesy of Genzyme Corporation



Corneal clouding

Courtesy of BioMarin Pharmaceutical Inc.

Visual acuity (how clearly a person can see) can be affected by these symptoms. It is often difficult to determine which combination of problems is responsible for the decrease in eyesight. An ophthalmologist (eye specialist) can perform special studies to help determine whether the problem with vision in an individual with MPS IV is due to how light gets in the eye (i.e., related to the cornea) or how the eye responds to light (i.e., related to the retina or optic nerve). Corrections for issues with visual acuity such as astigmatism are possible with prescription eyeglasses (corrective lenses). If an individual has issues with sensitivity to light, hats, and sunglasses can help.



Ear problems in MPS IV

Courtesy of Genzyme Corporation

Nose and throat

As with all symptoms associated with MPS IV, the following problems related to the nose and throat may not occur for all individuals with MPS IV.

In some cases, the adenoids (tissues at the back of the nasal cavity) and tonsils may become enlarged and partly block the airway. As the neck of a person with MPS IV is usually short, this can contribute to breathing problems. The windpipe (trachea) may become narrowed by stored GAGs and may be floppy or softer than usual due to abnormal cartilage rings in the trachea. Bumps or folds of excess tissue can further block the airway.

For some people with MPS IV, the bridge of the nose is flattened and the passage behind the nose may be smaller than usual due to the bones in the mid-face not having grown well and the nose lining being thicker. GAG buildup in the soft tissues of the nose and throat, combined with abnormal bones, can cause the airway to become easily blocked. Some individuals may have a chronic (long-term) discharge of thick mucus from the nose, which can contribute to chronic ear and sinus infections.

Ears

Deafness

Some degree of deafness is a common and underestimated issue for individuals with MPS IV. Hearing loss usually begins in adolescence but may begin anytime in childhood, and is found in almost all adult patients over the age of thirty years. Hearing loss is progressive and may be made worse by frequent ear infections. It is important that individuals with MPS IV have their hearing checked regularly so that problems can be treated early to maximize their ability to learn and communicate.

Deafness in people with MPS IV may be conductive deafness, sensorineural deafness, or both (see definitions below). Hearing aids may be helpful if hearing loss is present.

- *Conductive deafness:* Conductive deafness occurs when the transmission of sound through the outer and middle ear is blocked. In order for the middle ear to work properly, the pressure behind the eardrum has to be 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 the lining of the middle ear will build up and, over time, become thick like glue. This is called middle ear effusion, and is an important factor contributing to hearing loss in people with MPS. A small incision through the eardrum can be made (myringotomy) to remove the fluid. 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. However, 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 the ventilation tube is in place, fluid should drain out and hearing should improve.

- *Sensorineural (nerve) deafness:* Sensorineural deafness occurs from damage to the sensory hair cells in the inner ear or to the nerves that transmit sound to the brain. It may accompany conductive deafness, in which case it is referred to as mixed deafness. In most cases, nerve or conductive deafness can be managed with a hearing aid or aids.

Otitis media is the medical term for an infection of the middle ear.

Otitis media
For parents of children with MPS IV

What is otitis media?

Otitis media (OM) is the medical term for an infection of the middle ear. OM is a common problem encountered by healthy children, but it is one of the more stubborn problems for children with MPS IV. In children unaffected by MPS IV, ear infections are usually caused by blockage of the Eustachian tubes (the tube that runs from the middle ear to the throat and helps equalize the pressure in the middle ear) due to large adenoids or problems with drainage of fluid from the middle ear. In children affected by MPS IV, this is also complicated by the buildup of GAGs in the middle ear, nose, mouth, and throat.

There are two types of otitis media:

- *Acute otitis media:* This occurs when fluid is present in the middle ear, along with signs or symptoms of ear infection including a bulging eardrum often with pain, as well as ear tugging, fever, irritability, decreased appetite, vomiting, and diarrhea. Complications, although rare, can include tympanic membrane perforation (broken eardrum), acute mastoiditis (an inflammation in the area surrounding the middle and inner ear), cholesteatoma (a mass of cells and cholesterol in the middle ear), meningitis (a serious, potentially life-threatening inflammation of the membranes covering the brain), and epidural abscess (an inflammation of the area between the skull bone and the membranes covering the brain). Language development can also be affected by repeated ear infections.
- *Otitis media with effusion (OME):* OME is diagnosed when there is fluid in the middle ear without signs or symptoms of middle ear infection.

For some individuals with MPS IV, a number of middle ear infections may occur before MPS IV is diagnosed. The child may not have any symptoms of OM, but hearing can be affected. Any child who has fluid in the middle ears for at least three months should have a hearing test. Ear, nose, and throat (ENT) specialists, also called otolaryngologists, can help diagnose MPS IV by identifying children with recurrent infections and abnormalities seen under examination. Once a diagnosis of MPS IV has been made, the ENT specialist can be very helpful with many of the issues regarding managing the symptoms associated with the ears, nose, and throat.

Medication

Children with MPS IV tend to have many ear infections that can be very difficult to treat. If your child has ear infections that are hard to get rid of, it may be necessary for the doctor to do a "culture" of the fluid in the middle ear. The doctor will take a sample of this fluid and test it to see which bacteria, viruses, or fungi are living in the fluid. Identifying the bacteria, virus, or fungus that may be causing the infection allows the doctor to prescribe the appropriate medication. If the infection is fungal, frequent antibiotic use will only worsen the situation.

Antibiotics are the usual treatment for OM. There is a wide array of antibiotics available for treatment. Some require refrigeration or frequent dosing. Antibiotic injections can be considered for a child who has difficulty taking medications by mouth. Some common side effects of antibiotics include diarrhea, nausea, and vomiting. Antibiotics may also cause skin rashes and allergic reactions.

Occasionally, older children may have infections caused by other bacteria (such as *Pseudomonas aeruginosa* or *Staphylococcus aureus*) that can be more difficult to treat. If the child has tympanostomy tubes as described in the next section, ear drops may be used to treat the infection. Corticosteroid medications (drugs like prednisone that reduce inflammation) may also be helpful.

In most cases of repeated ear infections, inserting tubes into the eardrum is recommended to allow the fluid to drain.

Use of ear tubes

In most cases of repeated ear infections, inserting tubes into a hole in the eardrum (tympanostomy) is recommended to allow the fluid to drain. Insertion of tympanostomy tubes (ear tubes) is a 10–15 minute procedure usually performed under general anesthesia. The tubes help the child by keeping the middle ear ventilated.

There are several different types of ear tubes. Long-lasting tubes are preferred for individuals with MPS IV. Ear tubes may become blocked or infected. They may also damage or scar the eardrum. It is important to consult with an ear, nose, and throat (ENT) specialist experienced with MPS IV to determine which tube is best. (Please note that many experts recommend that ear tube insertion should always be done at a properly equipped hospital and only after consultation with the anesthesiologist due to anesthesia concerns for individuals with MPS IV. These concerns are covered in detail in the "Anesthesia considerations" section of this resource). After the procedure, a culture should be made from the drained fluid to identify the offending organism.

Removal of the adenoids (tissues at the back of the nasal cavity) and tonsils might also be useful for children who have recurrent acute OM. If the child is to have general anesthesia for the placement of ear tubes, removal of the adenoids and tonsils should also be considered at the same time. This avoids some of the risk by reducing the number of procedures requiring anesthesia.

Prevention

Some experts feel that children may benefit from a vaccine for *Streptococcus pneumoniae,* which is one of the bacteria that cause ear infections. This might help reduce the number of future bacterial infections. Vaccines may cause a fever or pain, redness, or swelling at the site of injection. More serious side effects include allergic reactions, but these are rare.

Some children may benefit from eliminating common food allergens from the diet. These can include soy, citrus, peanuts, wheat, fish, eggs, corn, and tomatoes. Some parents report positive results from supplementation with cod liver oil or other fish oils. Check with your doctor about adding a multivitamin to the child's diet. Exposure to second-hand cigarette smoke is recognized as a risk factor for OM, and every effort should be made to keep children away from smoke exposure.

Ear infections can be a persistent problem in children with MPS IV, and anything that can help relieve the symptoms may be warranted. Each child may respond differently to various treatments, so every option should be tried if needed. Speak to your doctor before trying a new treatment, including herbal or alternative treatments.

Frequent ear infections, hearing loss, and blocked airways may lead to speech and language problems. A speech therapist may help those with MPS IV with their speech. Hearing aids and sign language may also be useful for people with hearing loss.

Brain and central nervous system (CNS)

Unlike certain other mucopolysaccharidoses, MPS IV does not affect intelligence. For some patients with MPS IV who have severe physical and sensory disabilities, psychomotor performance may be impaired. Psychomotor performance is the ability to coordinate mental activity with physical activity. For example, catching a ball, driving, and dancing are all examples of activities requiring good psychomotor performance.

For those with MPS IV, the spinal cord is a component of the central nervous system that is frequently affected. As the management of spinal cord symptoms is directly related to the management of the spine and neck, this is discussed in the following section which covers the musculoskeletal system.

Musculoskeletal system (bones and joints)

The major clinical features of MPS IV are related to the bones and joints and their effect on the nervous system, if nerves are compressed by abnormal bone movement. Orthopedic complications are critical for individuals with MPS IV. The direct bone involvement and pain can lead to significant physical disability, with many individuals with MPS IV requiring walking aids and wheelchairs for mobility and major surgical procedures on the neck, hip, knee, and leg by the age of 10 years.

At the time of diagnosis, individuals with MPS IV should be referred to an orthopedic surgeon experienced in treating people with MPS. This is because significant problems can occur before the age of six years. Regular assessments are also needed to monitor the progression of orthopedic symptoms and to determine the appropriate care.

Musculoskeletal assessments for an individual with MPS IV should include:

- x-rays of the hips and lower extremities to monitor for progressive dysplasia, genu valgum (knock knees), and ankle valgus (ankles angled towards each other)
- MRIs (magnetic resonance images) of the spine to monitor for spinal cord stenosis, instability, and compression.

More information about these and other assessments is available in Table 2, which shows the recommended schedule of medical assessments for individuals with MPS IV.

Dysostosis multiplex

People with MPS IV tend to have significant problems with bone formation and growth. This leads to bone problems (called dysostosis multiplex) as well as neurological problems if nerves are squeezed by bone. The term “dysostosis multiplex” means “multiple abnormally shaped bones.” Dysostosis multiplex occurs when bones do not form correctly at cartilage growth centres throughout the body (growth centres are near the ends of the bones).

Spine, neck, and spinal cord compression

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. In individuals with MPS IV, the spine, including the neck, 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. Additionally, one or two of the vertebrae in the lower back are sometimes slightly smaller than the rest and set back from the others. This backward slippage of the vertebrae can occur causing an angular curve called kyphosis or gibbus to develop.

Gibbus in a child with MPS I

Courtesy of Dr. Emil Kakkis

Spinal symptoms, especially those associated with the neck and spinal cord, need to be discussed at the time of diagnosis of MPS IV. A study of the neck is also recommended at this time (baseline study). This will involve MRI studies or x-rays, performed with the child's head bent forward and with the neck held straight (flexion and extension views). These tests will be repeated regularly with results compared to the baseline results to track the condition of the spine, neck, and spinal cord.

Gibbus or kyphosis

Gibbus refers to a bump in the person's lower back, which is actually an abnormal curvature of the spine. This forward bend, or kyphosis, in the lower spine often occurs in children with severe MPS IV. The orthopedic term for gibbus is thoracolumbar kyphosis. It develops from poor bone growth in the upper front part of the vertebrae, which results in a wedging of the vertebrae (bones are smaller in the front than in the back). A large number of people with MPS IV who have gibbus will require surgery to stop it from getting worse.

Scoliosis

Some children with MPS IV may also have scoliosis of the spine. Scoliosis occurs when the spine curves from side to side rather than front to back. Scoliosis may also require surgery. When not treated, scoliosis can progress to the point that children have difficulty expanding their chest wall for breathing. Occasionally, children may suffer from both kyphosis and scoliosis, making surgical procedures more likely and more complicated. Bracing may slow the progression of both spinal kyphosis and scoliosis, delaying—but not preventing—surgery. Bracing can be uncomfortable for children, and they rarely tolerate it, especially young children. Consequently, bracing is usually not recommended.

Odontoid dysplasia

Most patients with MPS IV have odontoid dysplasia, which occurs when the bones that stabilize the connection between head and neck are malformed, making the neck unstable (called atlanto-axial instability). This is the most serious skeletal manifestation of MPS IV that puts people with MPS IV at risk of spinal cord compression (a condition where fluid or tissues such as bones are pressing on the spinal cord).

Individuals with MPS IV should be cautious about how the area of the spine around the neck is handled. Parents of children with MPS IV may be alarmed that their child may have weakness in such a vital area and may be harmed by a severe fall. While it is important to keep a balance between minimizing risks and letting your child lead as normal a life as possible, individuals with MPS IV should avoid "high-risk" activities such as contact sports and gymnastics. In addition, these children should be treated with caution when undergoing positioning for anesthesia. If there is severe pain or pain associated with weakness or tremors in the lower legs, the person should have studies of the neck to evaluate for slippage of the neck vertebrae.

Spinal cord compression

Spinal cord compression is a serious complication of MPS IV that can lead to unsteady gait, upper and lower extremity weakness, dysesthesias, urinary dysfunction, paralysis and even sudden death. In all people, the length of the spinal cord is surrounded by a system of tissue and ligaments and bones that is intended to protect it from damage when there is movement. However, as a result of GAG accumulation, over time these very tissues and ligaments may gradually become thicker and start pressing against the spinal cord. The underdevelopment of parts of the first two vertebrae of the neck (odontoid hypoplasia) adds to this problem by causing spinal instability. With spinal instability, spinal cord compression can result. This can cause a range of symptoms, including neck pain, weakness or numbness in the limbs, poor balance, and dizziness.

Spinal cord compression, particularly in the cervical (neck) region of the spinal column is quite common in individuals with MPS IV. If left untreated, spinal cord compression can lead to serious injury, including paralysis and even death.

The symptoms experienced depend on where the the spine is compressed. If it is compressed in the upper spinal cord area, symptoms may include loss of endurance, diminished walking distance, and gait instability. The loss of strength in an individual's arms and hands that can be expected may be difficult to assess for a person with MPS IV due to the joint laxity that may already impair grip and pinch strength.

If the spinal cord compression occurs lower in the spine, symptoms will be confined to the lower extremities, with the individual potentially experiencing loss of endurance, diminished walking distance, and gait instability.

Some individuals with MPS IV may have spinal cord compression without experiencing any symptoms, and still be at the same risk for spinal cord injury as those who experience symptoms. Doctors can usually detect spinal cord compression with an x-ray or MRI evaluation. As MRI studies may over- or underestimate the risk of spinal cord compression for individuals with MPS IV, a neurosurgeon should assist with this assessment.

Surgical correction of spinal problems

Conditions determining a need for surgery vary, depending on the needs of the individual and the desires of the family. The overall goals for spinal surgery are to protect the spinal cord from potential injury, relieve compression and its related symptoms, provide stability, reduce deformity, and relieve pain.

Surgery to correct spinal problems involves an incision in the back and sometimes from the front (through the flank or ribcage). Surgery for scoliosis usually involves an incision from the back, while surgery for kyphosis almost always requires incisions from the front and back.

Generally, surgical interventions are required to relieve spinal cord compression. This includes spinal decompression, fusion, or a combination of both. Fusion surgeries are also used to correct for scoliosis and kyphosis. The "fusion" involves taking bone from one area of the body and placing it in the area that requires stabilizing. Metal hardware (typically stainless steel or titanium) holds the piece of bone in place, providing temporary support to the spine until the fusion heals. Once placed, the hardware is not usually removed unless there is a complication related to its presence, such as an infection.

Most individuals will require some combination of a cast or brace for anywhere from three months to a year following surgery. If everything is done properly and effectively, the extra bone will heal to form a strut between the vertebrae, preventing the spine from curving further. An unsuccessful fusion (one where the bone strut does not form) can be painful and may require a repeat surgery. Instability can also recur in the same area as the fusion, making ongoing assessments for spinal cord compression necessary for individuals with MPS IV.

Spinal surgery comes with a number of risks, including the risks associated with anesthesia (see "What can be done to reduce the risks?" in "Anesthesia considerations"), infection, bleeding, blood clots, and damage to the spinal cord. It is important for an individual with MPS IV to be treated by an orthopedic surgeon who is experienced with MPS IV. Most orthopedic surgeons have minimal or no experience with MPS IV; however, a few hospitals have taken a particular interest in this disorder and have conducted a number of fusion operations. The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society) can provide you with information about finding orthopedic surgeons and hospitals that have performed successful cervical fusions on individuals with MPS.

Extremities

Joints

In contrast with other MPS disorders, individuals with MPS IV are not affected by joint stiffness. Rather, they generally have loose and hypermobile joints resulting from bone deformities, small bones (hypoplasia), and degradation of the connective tissue around the joint. This is partially responsible for the characteristic posture of a person with MPS IV, with hips flexed and knees in a "knock-kneed" position.

Hips

Like the spine, the hip joints suffer from altered bone formation that may lead to mobility issues requiring wheelchair and walking aids for many people with MPS IV. The hip joints are ball-and-socket joints situated at either side of the pelvis. The "ball" is the head of the femur (thigh bone) and the "socket" is the cupped part of the pelvis (the acetabulum) that surrounds the ball. In abnormal formation of the hip, or hip dysplasia, there is a shallow acetabulum, the head of the femur is underdeveloped, and the top of the thigh bone at the neck of the femur is straightened (a condition called coxa valga). Individuals with MPS IV commonly experience hip dysplasia and dislocation (resulting from the bone defects). Destructive arthritis can also have a significant effect on MPS IV patients, leading to restriction of motion.

Hip dysplasia is found in many individuals with MPS IV. Most children with hip dysplasia eventually require corrective hip surgery. Surgery on the hips is done more easily at a younger age, around ages five to seven, for the best results. Successful surgery (i.e., surgery that is able to correct the hip dysplasia) becomes much more difficult at older ages. If the hips have already dislocated, the surgery becomes technically very difficult, and the results are much less predictable.

Although prosthetic hip surgery is a challenge for individuals with MPS IV, hip surgery for dysplasia with precise bone cuts, or osteotomies, which allow the surgeon to reposition the bones and optimize the working of the hip, are useful in preventing the progression of osteoarthrosis. Cuts are made in the pelvis and sometimes the femur. The surgery on the bones may be performed in conjunction with tightening the soft tissues around the hip. Without hip surgery, the affected person will experience progressive pain and eventually dislocation of the hips, resulting in a greatly decreased ability to walk.

Hip surgery carries a number of risks, including the risks associated with anesthesia (see "What are the special considerations when planning an anesthetic for a child with MPS IV or a similar condition?" in "Anesthesia considerations"), infection, bleeding, and blood clots. Physical therapy may also be helpful for hip-related problems. It can help preserve hip-joint function and should be started while the child is young.

Legs and feet

Individuals with MPS IV typically develop "knock-knees" (genu valgum). Genu valgum, a condition where the legs angle inward, with the knees but not the ankles touching) is often found in individuals with MPS IV by the age of three years with varying degrees of severity. Although less common, individuals with MPS IV may also have ankle valgus, when the ankles angle inwardly. The degree of severity of these conditions may be assessed by observing how the individual walks using gait analysis. This technique assesses the impact of the disease on a person's ability to walk.

Courtesy of BioMarin Pharmaceutical Inc.

Many individuals with MPS IV will undergo surgery to correct genu and ankle valgum by the age of ten. Surgical intervention may improve the conditions, but recurrences requiring additional surgeries are common for individuals with MPS IV.

In the body, joints are held in place by strong bands of protein fibre called ligaments. However, individuals with MPS IV often have ligaments that are very lax. If this is the case, surgery may not provide much help. Occasionally, boots and splints may be needed, but often firm supportive shoes are just as effective. And as the bones composing the arches in the feet are held in position by ligaments and tendons, these too are likely to be weakened, which can result in flat feet (pes planus). The toes may also be affected and misshapen.

Hands

The wrists of people with MPS IV are typically enlarged and curved. They may become very loose and floppy as the tiny carpal bones in the wrist fail to develop properly, and because the ligaments are lax. Naturally, this can mean a considerable loss of strength and fine motor skills 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. Some people find that small plastic splints with wrist bands provide help. Those who find writing by hand challenging may find it easier to type on a computer. To ensure timely interventions to preserve hand function, individuals with MPS IV should have regular assessments of grip and pinch strength and the fine motor skills using the nine-hole peg test.

Physical therapy may help relieve symptoms and improve the person's ability to function.

Physical and occupational therapy

As discussed earlier in this section, loose joints can cause problems for people with MPS IV. Intensive physical therapy will be needed to help someone with MPS IV start walking again after neck, spine, or knee surgery. As is true for everyone, people 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 to achieve this. It is important to keep a balance between avoiding risks and letting your child lead as normal a life as possible.

Respiratory system

Overview

The respiratory system of individuals with MPS IV is often impaired. A combination of these issues can prevent an individual with MPS IV from breathing in adequate amounts of oxygen and can lead to difficulty breathing while awake or asleep. This can impact quality of sleep and significantly impacts the endurance experienced by people with MPS IV.

Individuals with MPS IV experience combinations of obstructive (blockage) and restrictive (compressed) respiratory disease. The abnormal chest shape commonly associated with MPS IV is caused by impaired growth of the spine combined with normal growth of the breastbone, which is joined to the spine. As the growth of the spine slows, the breastbone is forced to buckle outward in a rounded curve or occasionally in a prominent beak shape. This results in a “bell” shape to the chest, with the ribs being held fixed in a horizontal position. The junction between the ribs and the breastbone (called the sternum) is not as flexible as it should be. This makes the chest rigid, so it cannot move freely to allow the lungs to take in a large volume of air. This restricts efficient breathing, and may also cause instability of the spine and, potentially, weakness of respiratory muscles.

Additionally, MPS IV often results in upper and lower airway obstruction (blockage) due to GAG accumulation throughout the respiratory system. The adenoids (tissues at the back of the nasal cavity) and tonsils may become enlarged and can partly block the airway for individuals with MPS IV. The windpipe (trachea) becomes narrowed by stored GAGs and may be floppy or softer than usual. Folds of excess tissue can further block the airway. When the lungs cannot fully clear out, there is an increased risk of infection (pneumonia). Many affected individuals breathe very noisily even when there is no infection. People may take on a "sniff" position, with their neck extended and their nose raised to maintain an open airway.

Chest x-ray of child with MPS I

Courtesy of Hodder Arnold Publishers

Early signs of breathing difficulties often occur at night, when an individual with MPS IV may be restless and snore. Sometimes the individual may stop breathing for short periods (usually 10–30 seconds) while asleep (sleep apnea). This noisy breathing, which stops and starts, can be very frightening for parents or bed partners to hear. They may fear that the person is dying. If there is noisy breathing, the individual's oxygen level may be low when sleeping, which can cause problems with the heart. If a parent or bed partner notices significant choking or episodes of interrupted breathing, a sleep specialist should evaluate the individual with MPS IV using a sleep study (for more information, see "Sleep disordered breathing" on this page). It is important to know that many people may breathe like this for years, and that these respiratory issues also directly impact the individual's endurance.

A breathing test, called a pulmonary function test, can be conducted by a lung specialist to assess the extent of the breathing restriction. Individuals with MPS IV should have regular influenza (flu) and pneumococcus (pneumonia) vaccinations. Obstructive respiratory disease can be treated in some cases with bronchodilators (inhaled medication) to help open the airway of a person with MPS IV or by removing the adenoids (adenoidectomy) and tonsils (tonsillectomy) to help improve blockage in the upper airway. This may also help treat sleep apnea. Opening up the airway with nighttime CPAP (continuous positive airway pressure), BiPAP (bi-level positive airway pressure), or tracheostomy may be required to treat sleep apnea (for more information, see "Sleep disordered breathing" on this page).

Upper respiratory tract infections (URTI)

People with MPS IV are more prone to recurrent upper respiratory tract infections. Bacterial infections of the airways may be treated with antibiotics as prescribed by your doctor. There are many different antibiotics that may be used, and each one has side effects. Some common side effects of antibiotics include diarrhea, nausea, and vomiting. They may also cause skin rashes and allergic reactions. Since the airways may not drain properly for individuals with MPS IV, overcoming infections can be difficult. It is common to have infections seem to go away while the individual is taking antibiotics and then come back after the antibiotic course is over.

Some people become allergic to antibiotics or may develop resistant infections. Your doctor can prescribe other antibiotics to help manage this problem. You will need a doctor with whom you can develop a good working relationship to manage the infections.

Drugs may affect individuals with MPS IV differently than unaffected individuals, so it is imperative that you consult your doctor before using any medications, even those that are available over the counter (i.e., off the shelf) to treat respiratory infections. For example, drugs such as antihistamines (allergy medications) may dry out mucus, making it thicker and harder to dislodge. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels. Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea by decreasing muscle tone and breathing rates.

Sleep disordered breathing

Sleep disordered breathing is an early sign that a person with MPS IV is experiencing respiratory impairment (having trouble breathing). Sometimes the person with MPS IV may stop breathing for short periods while asleep (sleep apnea). Obstructive sleep apnea (OSA) is a common airway problem for individuals with MPS IV. It is defined as temporary breathing interruptions during sleep that occur when the airway in the neck becomes blocked due to muscles in the airway relaxing. The risk of the airway becoming blocked is increased by some of the physical effects of MPS IV, including a narrow airway, and enlarged tonsils and adenoids. A person with MPS IV may also experience sustained hypoventilation (not getting enough oxygen) while sleeping. Over time, these issues can cause serious cardiovascular issues, which can result in cardio-respiratory failure.

Sleep disordered breathing can be improved in some individuals by opening the airway with nighttime CPAP (continuous positive airway pressure) or BiPAP (bi-level positive airway pressure).

If you or your child with MPS IV are experiencing signs of sleep disordered breathing, your doctor may ask for a sleep study to be performed. Monitors are placed on the skin and connected to a computer to measure the levels of oxygen in the blood, breathing effort, brain waves during sleep, and other indicators of the body's function. From this study, doctors can assess how much blockage to breathing is present, how much trouble the person is having moving air into the lungs during sleep, and how much effect this has on the body.

A sleep specialist can use a sleep study to determine the presence and severity of sleep apnea as well as decreases (desaturations) in the person's oxygen level.

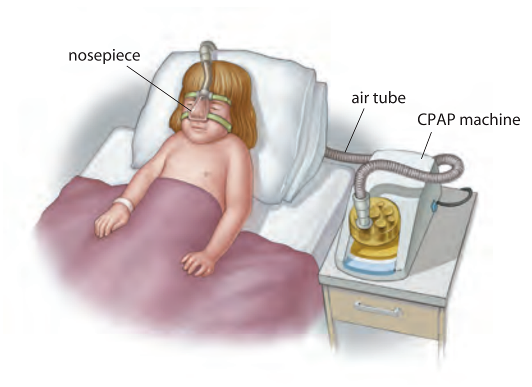
Managing sleep disordered breathing

Sleep disordered breathing can be treated in some cases by removing the tonsils and adenoids and/or opening up the airway with nighttime CPAP (continuous positive airway pressure) or BiPAP (bi-level positive airway pressure), or tracheostomy. Nighttime CPAP or BiPAP can open the airway at night using air pressure, which can help the person's airway stay open. In severe cases of sleep apnea, a tracheostomy (a hole into the airway made in the front of the neck; for more information, see "Tracheostomy" in this section) may be needed to keep an airway open. Before considering any therapy or treatment, consult your respirologist (lung doctor).

CPAP and BiPAP

An abnormal sleep study may suggest that CPAP or BiPAP would be helpful to maintain an open airway during the night. Both CPAP and BiPAP are non-invasive. This means that they do not involve surgery, breaking the skin, or inserting a device into a body cavity. Instead, the treatments require that the individual wear a mask covering the nose and sometimes the mouth while sleeping in order to receive the positive airway pressure needed to keep the airway open. CPAP and BiPAP are very effective treatments for sleep apnea, but they do not cure the underlying problem.

While CPAP and BiPAP are generally very similar, there are slight differences between them. BiPAP differs from CPAP in that the pressure during expiration (breathing out) may be



CPAP device *Courtesy of Genzyme Corporation* adjusted separately from the pressure delivered during inspiration (breathing in). CPAP means there is a continuous supply of air at the same pressure being delivered to the patient with each breath. Nasal CPAP delivers air pressure through the nose. The mask is placed securely over the person's nose and slight positive air pressure is used to increase the amount of air being inhaled without making the work of breathing more difficult. The mask does not breathe for the person. The airflow creates enough pressure during inspiration to keep the airway open. Another method for delivering air involves placing a tube into the nose in order to supply gentle air pressure to the airway.

Occasionally, CPAP can increase the work involved in breathing. In those cases, BiPAP is used instead. As mentioned, BiPAP stands for "bi-level positive airway pressure." It is also called non-invasive face mask ventilation. Bi-level means that the air pressure rises during inhalation and drops during exhalation, making breathing easier. BiPAP therapy is usually prescribed for people with sleep apnea if the CPAP therapy is too difficult. Occasionally the BiPAP machine will be spontaneously timed (BiPAP SP), meaning that if for some reason the patient does not take a breath, the machine will automatically start a breath for them.

Obstacles to using CPAP and BiPAP

The major obstacle that most people must overcome is getting used to the CPAP or BiPAP system. The person must get used to sleeping while wearing the mask and mouthpiece. Approximately 20% of people never adjust or get accustomed to the treatment method. Some people feel that the device makes them feel claustrophobic. Others find that it is difficult to take with them when travelling.

Some complications can arise through the use of positive airway pressure devices. These complications can be associated with the equipment or with the person's condition. Mucus can build up in the nasal tubes. The person can also become uncomfortable if the pressure is set too high.

Tracheostomy

A tracheostomy (**tray**-kee-**oss**-ta-mee; also called an artificial airway or "trach," pronounced "trake") is a surgically created opening through the neck into the trachea (windpipe). A tube is usually placed through the opening into the trachea. This tube is referred to as a tracheostomy tube or a "trach" tube. The function of the tube is to open an airway and to remove secretions from the lungs.

A tracheostomy is usually performed under general anesthesia. After the area is cleaned, incisions are made to expose the outer wall of the trachea, which is made up of tough cartilage rings. A surgeon inserts the tracheostomy tube into the trachea after creating an opening through the cartilage rings.

There are three parts to the tracheostomy tube: the outer cannula, the inner cannula, and the obturator. The obturator is used for inserting the tube. The outer cannula is a tube that stays in the trachea all of the time, except for cleaning. The inner cannula is a safety valve to keep the airway open. This can be removed for cleaning.

How well a person does following a tracheostomy procedure depends greatly on their well-being prior to the surgery and on the specific reason the tracheostomy was performed. A person can expect to spend approximately 3–5 days in the hospital after a tracheostomy operation and usually an additional two weeks recovering.

A tracheostomy is generally a routine procedure; however, as with any other surgical procedure, there are risks. With the anesthesia, there is a risk of adverse reactions to medications and problems with breathing. Because people with MPS IV are at a higher risk of problems with


Tracheostomy in an individual with MPS VI

Courtesy of the Canadian MPS Society

anesthesia, the tracheostomy should be done in a hospital that is fully equipped to deal with these issues. Make sure that the anesthesiologist for the procedure has experience with MPS. See "Anesthesia considerations" for more information about anesthesia and MPS IV. With the surgery, there is a risk of bleeding, pneumothorax (presence of air or gas in the space between the ribs and the lungs), low blood pressure, infection, vocal cord paralysis, damage to the trachea, and buildup of scar tissue in and around the trachea.

Adjusting to a tracheostomy

Having a tracheostomy may also lead to significant differences in a person's lifestyle during the adjustment to having a trach placed. It is important to discuss trach care in detail with the doctors. The surgical incision needs to be cleaned frequently as it heals, perhaps as many as four to five times per day. Once the skin heals, it should be kept clean and dry. Most people use soap and water to clean the skin. Some people use a small amount of water-soluble antibiotic ointment around the skin incision.

Mucus secretions or blood can block the tracheostomy tube and interfere with breathing. The tube may be blocked if you notice bubbles in the trach tube, if you hear loud gurgles coming from the trach tube, or if the individual with the tube seems to be having difficulty breathing (for babies, the signs may include agitation, flared nostrils, increased heart rate, or pale or blue skin). If this occurs, the tube should be suctioned. People with tracheostomies can learn to suction their trach by using a suction machine and catheter as needed. If a child in your care has a tracheostomy, you may need to suction the trach tube for them.

From time to time, the tracheostomy tube will need to be changed. Changing an old tube for a fresh new tube can be challenging but becomes easier with time. Shortly after surgery, if the entry site has not healed properly, it may cave in when the tube is removed and block the trachea. When the new tube is being inserted, there is also a risk of the tube accidentally entering incorrectly. As the wound heals, the chance that either situation will occur will decrease. Many people are eventually able to change their trach tubes in their home. If your child has a trach tube, you may need to change the tube for them.

One of the biggest challenges that people face following the insertion of the trach is adjusting to new breathing patterns and the changes to the vocal cords. Communication is perhaps the biggest adjustment because it may be impossible for the person to talk or make sounds. However, with proper training, many individuals can learn to speak with a tracheostomy tube.

Water-related activities can be hazardous to the person with a trach because there is not an easy way to hold their breath underwater and water could enter their lungs. Tub baths may be a reasonable solution for bathing. If a shower is preferred, it can be done with special care to shield the tracheostomy tube opening from the water.

A person with a trach also may benefit from using a cotton cover or scarf as a protection from inhaling dust and other particles.

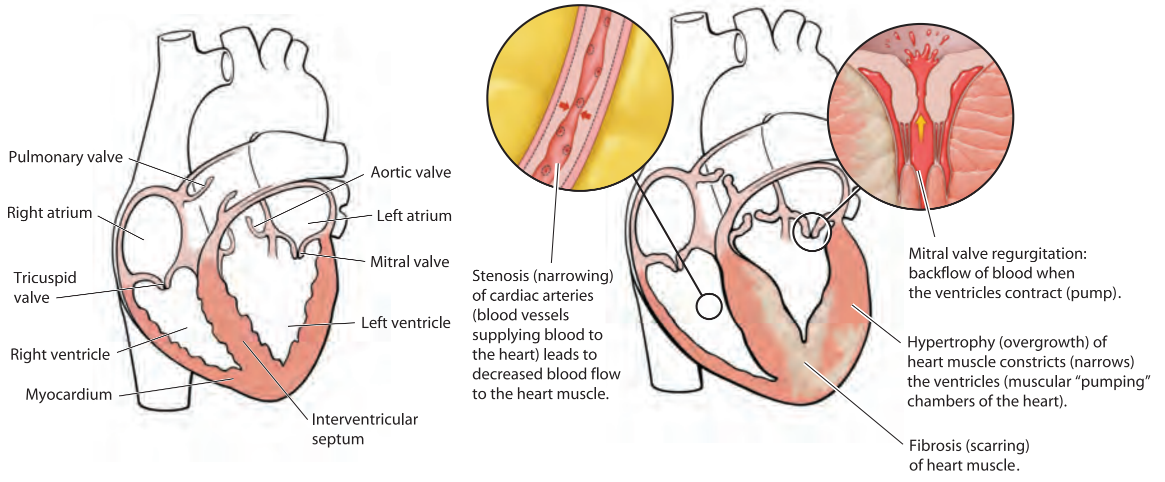
With proper planning, discussion with doctors, and after-surgery care, a tracheostomy may significantly help individuals with MPS IV whose upper airway is blocked.

Heart and blood vessels

Heart disease is a major cause of death in individuals with all MPS disorders, occurring in 60% to 100% of those patients who have been studied. Heart disease is more common for MPS disorders that involve dermatan sulfate, which include MPS I, II, and VI. However, individuals with MPS IV also experience heart abnormalities although it may not develop or cause any real problems until later in the individual's life. Medications are available to help manage this condition.

Effects on the heart muscle

Cardiomyopathy (abnormal heart muscle) may occur in some individuals with MPS IV. This type of heart damage is caused by the storage of GAGs. There are many different types of cardiomyopathy, and the type of cardiomyopathy



Heart problems in MPS

Courtesy of Genzyme Corporation

seen in some individuals with MPS IV is called hypertrophic cardiomyopathy. The terms "hypertrophic" and "hypertrophy" refer to an abnormal thickening of the heart muscle. Eventually a type of cardiomyopathy called "dilated cardiomyopathy" can occur. This condition causes the heart to become enlarged (cardiomegaly is another term that is sometimes used – it means "enlarged heart"). It also causes the heart to pump more weakly. The heart may also be put under strain by having to pump blood through abnormal lungs.

Effects on the blood vessels of the heart

GAG storage in the heart blood vessels (coronary arteries) can damage these vessels. The damage seen is similar to the coronary artery disease experienced by older people and can lead to death. Coronary artery disease has been reported in all MPS disorders, but is most common in MPS I and II, and not common in MPS IV. Occasionally, the coronary arteries may become narrowed and cause episodes of chest pain (angina). If you have MPS IV and notice these symptoms, consult your doctor. If your child has MPS IV and you notice that he or she is distressed, crying, pale, sweating, and keeping still, consult your doctor. The doctor may refer your child for an electrocardiogram (ECG). A number of affected individuals also have high blood pressure.

Effects on the blood vessels of the lungs

People with MPS IV may occasionally suffer from pulmonary or systemic hypertension, a condition that causes high blood pressure in the blood vessels which respectively supply the lungs or the body. Pulmonary hypertension is considered common in MPS I and II, but is not often found in other MPS disorders such as MPS IV.

Effects on the heart valves

Individuals with MPS IV may develop problems with their heart valves. Heart valves may leak or become narrowed because of GAG storage.

There are four valves in the heart:

- The *tricuspid valve* is on the right side of the heart between the atrium (a collecting chamber for blood flowing back from the body) and ventricle (a muscular pumping chamber that pumps blood to the lungs). The valve prevents blood from flowing backwards into the right atrium when the right ventricle of the heart contracts.
- The *mitral valve* is on the left side of the heart between the atrium (a collecting chamber for blood flowing back from the lungs) and the ventricle (a muscular pumping chamber that pumps blood to the rest of the body). The

valve prevents blood from flowing backwards into the left atrium when the left ventricle of the heart contracts.

- The *pulmonary valve* sits between the right ventricle and the pulmonary artery (the vessel that brings blood from the heart to the lungs). The valve prevents blood from flowing backwards into the heart between its contractions.
- The *aortic valve* sits between the left ventricle and the aorta (the vessel that brings blood from the heart to the rest of the body). The valve prevents blood from flowing backwards into the heart between its contractions.

The doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAGs. The heart valves are designed to close tightly in order to stop blood from flowing back in the wrong direction as blood passes from one chamber of the heart to another. If a valve is damaged by GAG accumulation, two different conditions may occur:

- *Regurgitation:* This occurs when the weakened valve cannot shut firmly enough and a small amount of blood may shoot backwards, leading to turbulence and a murmur. Conditions that involve regurgitation include mitral valve regurgitation (where the valve within the left side of the heart does not shut firmly enough) and aortic valve regurgitation (where the valve between the left side of the heart and the rest of the body does not shut firmly enough).
- *Stenosis:* This term refers to a stiffened heart valve. A stiffened heart valve may not be able to open completely. This means that the opening through which the blood is pumped will be smaller.

Many individuals with MPS IV have some degree of heart-valve leakage or blockage, and some develop problems with aortic or mitral valves. A person can have slowly progressive heart disease for years without any apparent clinical effects. Eventually, however, the damaged heart valves may need surgical replacement.

The importance of regular heart checkups

Since people with MPS IV may experience heart disease, it is important to have a test known as an echocardiogram regularly (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 disorders, you should choose a cardiologist with some knowledge of MPS IV. If this is not possible, you should inform the doctor about the heart problems experienced by individuals with MPS IV. Medications are available to help manage the heart problems that occur as a result of MPS IV.

Reduced endurance

Frequently, individuals with MPS IV have reduced endurance in comparison with individuals who are not affected by MPS IV. Short stature, respiratory impairment, and cardiac symptoms all contribute to limitations in endurance.

Measuring endurance has always been important in evaluating disease progression and the effectiveness of some treatment options for MPS, such as enzyme replacement therapy (ERT). Recently an ERT has been approved for treating individuals with MPS IVA. VIMIZIM™ (elosulfase alfa) has been shown to positively impact the distance walked after 24 weeks of treatment for individuals with MPS IVA (see the "Treatment options" section of this resource for more information). Monitoring endurance on an ongoing basis can assist in determining the effectiveness of VIMIZIM for people with MPS IVA. Assessing endurance can also assist in determining how effective surgical interventions have been for people with MPS IV.

The six-minute walk test (6MWT) is a standardized assessment that evaluates the distance an individual can walk in six minutes. This endurance

VIMIZIM™ (elosulfase alfa) Product Monograph, BioMarin Pharmaceutical (Canada) Inc. 2014 test measures the ability of the musculoskeletal and cardiopulmonary systems. The 6MWT will always be done at the same location to ensure consistency over time. If an individual is unable to perform a 6MWT, a timed 25-foot walk test (T25FW) will be used to evaluate the amount of time the individual needs to walk 25 feet. Blood saturation, heart rate, and respiratory rate will be measured immediately before and after each endurance test, and again two minutes after the test has been completed to determine the effect the physical exertion has had, providing important information about the impact of disease progression and treatment.

Pain and quality of life

Pain and reduced quality of life are interrelated symptoms associated with MPS IV. Although it is common for individuals with MPS IV to experience pain, which is generally related to the musculoskeletal system, it is often underreported. Pain may result in the need for mobility aids, including walking aids and wheelchairs. Pain may reduce an individual's ability to perform activities of daily living, such as walking, getting dressed, and living independently. Pain, endurance, mobility, dependence on caregivers, frequent surgical interventions, and fatigue are reported to have a significant impact an individual's quality of life.

Assessments of the quality of life and the pain experienced by an individual with MPS IV should be done regularly through self- and parent-reported questionnaires. Simple interventions can have a significant impact on quality of life, and can be tailored to the age of the individual. For example, assessments can spur improved communication about MPS IV with teachers and peers, which may improve quality of life for children, and can help indicate if a person requires information about mobility aids (see the "Living with MPS IV" section of this resource for more details).

Courtesy of BioMarin Pharmaceutical Inc.

Table 2: Recommended schedule of assessments in patients with MPS IVA, adapted from Hendriksz et al. 2014

Assessment	At diagnosis	Follow-up frequency	Pre-ERT[a]
Medical history	X	Every visit	
Physical examination	X	Every visit	X
Upper limb function • Standardized upper extremity function test	X	Annually	X
Hips and lower extremities			
• Hips/pelvis: AP pelvis radiograph	X	As clinically indicated	
• Lower extremities: standing AP radiographs	X	As clinically indicated	
Spine/spinal cord compression			
• Plain radiograph spine	X	Every 1–3 years	
• Magnetic resonance imaging of the spine	X	Annually	
• CT neutral region of interest		As clinically indicated[b]	
Cardiac function			
• Electrocardiogram[d]	X	Every 1–3 years[c]; As clinically indicated[b]	
• Echocardiogram	X	Every 2–3 years[c]; As clinically indicated[b]	
• Heart rate	X	Annually[e]	
Respiratory function			
• FVC and MVV	X	Annually[f]	X
• Respiratory rate	X	Annually[e]	X
• Oxygen saturation[g]	X	Annually[e]	
• Overnight sleep study	X	Annually[h]	
Neurological exam	X	Every visit (at minimum every 6 months)	X
Ophthalmological function			
• Slit-lamp biomicroscopy of cornea	X	As clinically indicated	
• Intraocular pressure	X	As clinically indicated	
• Refractive error	X	As clinically indicated	
• Examination of posterior segment	X	As clinically indicated	
• Scotopic and photopic electroretinogram		As clinically indicated	
Hearing • Audiology assessment (multimodal)	X	Annually	
Dental evaluation by a dentist	X	Annually	
Endurance • 6-minute walk test, T25FW[e]	X	Annually; As clinically indicated[b]	X
Growth			
• Height and weight	X	Every visit	X
• Head circumference (infants ≤ 3 years)	X	Every visit	
• Pubertal stage (age 9 until mature)	X	Every visit	X
Disease burden			
• Pain assessment	X	Every 6 months	X
• Quality of life questionnaire	X	Annually	X
• Functional test[j]/ADL questionnaire	X	Annually	X
Evaluation by physiotherapist	X	Annually; As clinically indicated[b]	

ADL: activities of daily living; AP: anteroposterior; FVC: forced vital capacity; MVV: maximum voluntary ventilation; T25FW: timed 25-foot walk

[a] If not done within 3–6 months, these assessments should be done before treatment with enzyme replacement therapy (ERT) is started

[b] E.g., pre- and/or post-operative planning

[c] ECG and echocardiogram at diagnosis and after 1 year. If no signs of cardiac involvement, assessments can be repeated every 3 years, otherwise follow-up in expert centres according to standard of care

[d] In symptomatic patients (e.g., suspicious ECG) or post-pubertal patients, prolonged ECG (Holter monitoring for 5–7 days including normal exercising) should be done in expert centres at diagnosis and every 1–3 years

[e] Heart rate, respiratory rate, and oxygen saturation should be measured before and after each endurance test; choice of endurance measure depends on patient's physical and developmental abilities (for the 6MWT, consistently use the same hallway)

[f] Annual follow-up only required until children stop growing or when patient is on treatment. Once growth has stopped, testing frequency can be decreased to every 2 to 3 years provided that respiratory symptoms remain unchanged

[g] Oxygen saturation can be determined either by pulse oximetry or by arterial blood gas analysis

[h] Screening studies should be done in the home on an annual basis. Full polysomnography should be performed at diagnosis in an expert centre, then every 3 years, unless clinically indicated (or before major surgery). Patients with a positive test and those who need ventilatory support should be evaluated by a sleep expert

[i] Pubertal stage can be assessed using 2 scores: genitalia (male), breast (female), pubic hair (male and female) as described by Marshall and Tanner [Marshall and Tanner, 1969; Marshall and Tanner, 1970] E.g. 6MWT / T25FW, pinch / grip test, functional dexterity test

Christian J. Hendriksz, Kenneth I. Berger, Roberto Giugliani, Paul Harmatz, Christoph Kampmann, William G. Mackenzie, Julian Raiman, Martha Solano Villarreal, and Ravi Savarirayan. International Guidelines for the Management and Treatment of Morquio A Syndrome. Am J Med Genet Part A. 2014. DOI: 10.1002/ajmg.a.36833

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Treatment options

Contents

Treatment options

Overview

There is currently no cure for mucopolysaccharidosis IV (pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis four), also called MPS IV and often referred to as Morquio syndrome. There are two types of MPS IV: MPS IVA, also called Morquio A syndrome, and MPS IVB, also called Morquio B syndrome.

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). For MPS IVA, there is treatment targeted to replace the deficient enzyme that uses an enzyme replacement therapy (ERT) called VIMIZIM® (elosulfase alfa).

In MPS IVA, enzyme replacement therapy (ERT) is designed to address the underlying deficiency of the enzyme N-acetylgalactosamine-6-sulfatase (GALNS), which leads to GAG buildup in the cells of various organs.

The decision of which interventions and treatments are best for you or your child is an important and complex one. The information in this section is not intended to be medical advice or recommendations. Decisions about interventions and treatments for you or your child are best discussed with medical professionals who have experience with MPS.

Importance of multidisciplinary care

As described earlier in this resource, people with MPS IV usually have a wide range of signs and symptoms. As a result, they often need to see a large number and variety of medical specialists, including orthopedic surgeons, physical therapists, cardiologists, gastroenterologists, respirologists, otolaryngologists, ophthalmologists, and speech therapists. All health professionals involved in the care of people with MPS IV should have a basic understanding of the disease and how the condition may affect treatment decisions.

However, it can also be very helpful to have a single physician with experience in MPS IV who takes responsibility for overseeing the overall care across medical specialties and who keeps track of the “big picture.” This physician can then refer the person with MPS IV to other specialists as needed and help make sure the individual is receiving the best possible care. For people with MPS IV, the physician who performs this role is usually either their primary care physician (who might be a pediatrician) or a geneticist.

Disease management and supportive care

Supportive and disease management therapies may improve quality of life for people with MPS IV and their caregivers, and may increase the lifespan of the person with the disease. Supportive care measures – such as the use of walking aid or wheelchair – are described earlier in this learning guide, as are descriptions of the symptoms they are intended to address. For people who plan to have surgical and medical interventions, it’s important that the health professionals involved in the intervention, especially the anesthesiologist, have a good understanding of the potential risks and complications for individuals with MPS IV.

Enzyme replacement therapy (ERT)

Overview of ERT

People with MPS have a deficiency in certain enzymes that break down glycosaminoglycans (GAGs). These deficiencies lead to GAG buildup in the cells of various organs. Enzyme replacement therapies (ERTs)* provide

VIMIZIM® (elosulfase alfa) Product Monograph, BioMarin Pharmaceutical (Canada) Inc. March 3, 2016 an external source of the deficient enzymes. ERT is designed to work by replacing the deficient enzyme and restoring the cell function, and is given weekly via an intravenous (IV) infusion. The enzyme travels through the bloodstream and enters cells in various organs, such as the liver and heart, where it helps break down GAG buildup. Current forms of ERT do not effectively penetrate the blood-brain barrier (BBB) and thus do not enter the brain. Therefore ERT does not alter the neurocognitive disease that leads to intellectual decline in some of the MPS subtypes. Since individuals with MPS IVA do not have direct neurocognitive involvement, this is not a factor in this disorder.

ERT is currently available for infusion in hospital and home infusion settings for people with MPS I, II, and VI. An ERT for individuals with MPS IVA has been found to be safe and effective. VIMIZIM® (elosulfase alfa) is a manufactured version of the body's natural *N*-acetylgalactosamine-6-sulfatase (GALNS), the enzyme that is deficient in MPS IVA. VIMIZIM was approved for use in Canada by Health Canada on July 2, 2014.

How VIMIZIM® (elosulfase alfa) works

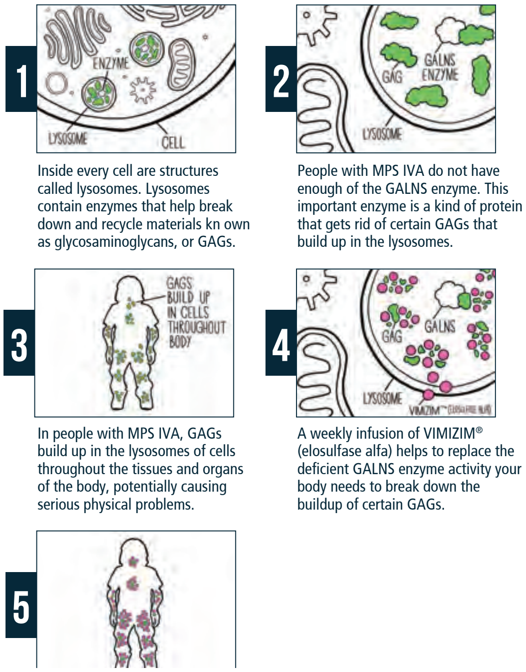
VIMIZIM® (elosulfase alfa) is an enzyme replacement therapy (ERT) for people with a confirmed diagnosis of MPS IVA. VIMIZIM is the only ERT available for individuals with MPS IVA. As with all lysosomal storage disorders, it is important to start treatment with VIMIZIM as early as possible for people with MPS IVA, before the appearance of non-reversible symptoms of the disease.

**Enzyme replacement therapy: A therapeutic approach for a genetic disorder whereby the missing protein is manufactured outside the body and given intravenously (injected into a vein) to the individual on a regular basis.*

VIMIZIM® (elosulfase alfa) is a laboratory-made version of GALNS, the natural enzyme which is lacking in people with MPS IVA. VIMIZIM is given via an intravenous (IV) infusion. The enzyme travels through the bloodstream and enters

VIMIZIM® (elosulfase alfa)

Courtesy of BioMarin Pharmaceutical (Canada) Inc.



Inside every cell are structures called lysosomes. Lysosomes contain enzymes that help break down and recycle materials known as glycosaminoglycans, or GAGs.

People with MPS IVA do not have enough of the GALNS enzyme. This important enzyme is a kind of protein that gets rid of certain GAGs that build up in the lysosomes.

In people with MPS IVA, GAGs build up in the lysosomes of cells throughout the tissues and organs of the body, potentially causing serious physical problems.

A weekly infusion of VIMIZIM® (elosulfase alfa) helps to replace the deficient GALNS enzyme activity your body needs to break down the buildup of certain GAGs.

ERT reduces GAG accumulation

Courtesy of BioMarin Pharmaceutical Inc.

VIMIZIM® (elosulfase alfa) improves endurance and walking ability in people with MPS IVA.

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cells in various organs of the body. By providing the body with an external source of GALNS, VIMIZIM replaces the deficient GALNS enzyme and restores cell function.

The recommended dosage regimen of VIMIZIM is 2 mg per kg of body weight given once weekly through an IV infusion. Each vial (bottle) of VIMIZIM contains 5 mg of elosulfase alfa in 5 mL of solution, and the number of vials used is rounded up to the next whole vial. For example, a person weighing 32 kg would be given 65 mg (13 vials) of VIMIZIM. The infusion should be given over a period of time of approximately four hours. Your doctor may adjust the rate of infusion according to your body weight or any infusion reactions.

Safety and efficacy of VIMIZIM® (elosulfase alfa)

By reducing GAG levels in the body in those with MPS IVA, VIMIZIM® (elosulfase alfa) improves endurance in people living with MPS IVA, as measured by the six-minute walk test (6MWT), and helps improve walking ability. In a six-month clinical study, people who took VIMIZIM once a week walked an average of 23.9% farther than at the start of the study. Improvement occurred within 24 weeks of treatment initiation.

VIMIZIM® (elosulfase alfa) improves endurance and helps improve walking ability. As with all lysosomal storage disorders, it is important to start treatment with VIMIZIM as early as possible for people with MPS IVA, before the appearance of non-reversible symptoms of the disease.

Starting treatment with VIMIZIM as early as possible and before the appearance of non-reversible symptoms of the disease is important. VIMIZIM will not cure MPS IVA and is a life-long treatment. The benefits of VIMIZIM have been established through clinical studies. VIMIZIM does not treat all signs and symptoms of MPS IVA.

The safety and efficacy of VIMIZIM® (elosulfase alfa) were assessed in a clinical study of 176 patients with MPS IVA. The ages of the patients ranged from five to 57 years, with the majority in the range of five to 17 years of age. Serious adverse events were more frequent in children younger than 12 years of age. The majority of these patients (82%) studied had a medical history of musculoskeletal conditions, including knee deformity (52%), kyphosis (31%), hip dysplasia (22%), prior spinal fusion surgery (22%), and arthralgia (20%). At the start of the study, all could walk more than 30 m but less than 325 m in six minutes.

During this study, some patients received VIMIZIM 2 mg/kg once per week, some received 2 mg/kg once every other week, and some received a placebo (an infusion without any medication).

The study measured the change at Week 24 in the distance walked in a six-minute walk test by those who had received VIMIZIM compared with those who had received the placebo. The study also looked at the change at Week 24 in the rate of stair climbing in a three-minute stair climb test, as well as levels of keratan sulfate (KS), the GAG that is excreted in the urine of people with MPS IVA.

At Week 24, the change in the distance walked in six minutes, compared to the placebo group, was 22.5 m in those who had received VIMIZIM 2 mg/kg once per week. There was no difference in the rate of stair climbing between those who had received VIMIZIM 2 mg/kg once per week and those who had received the placebo. Patients who received VIMIZIM 2 mg/kg once every other week performed similarly in the walking and stair-climbing tests as those who received placebo. The reduction in urinary KS levels was higher in the VIMIZIM® (elosulfase alfa) treatment groups compared to the placebo group. However, the relationship between KS levels in the urine and

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other measures of clinical response has not been established.

All patients treated with VIMIZIM 2 mg/kg once per week in the placebo-controlled trial developed anti-drug antibodies and tested positive for neutralizing antibodies at least once during the clinical trial. The relationship between the presence of neutralizing antibodies and long-term therapeutic response could not be determined.

These same 176 patients who participated in this clinical trial were eligible to continue treatment in an extension trial. Of this group, 173 enrolled in the extension trial in which some received VIMIZIM 2 mg/kg once per week and others received VIMIZIM 2 mg/kg once every other week. Patients who continued to receive VIMIZIM 2 mg/kg once per week for another 48 weeks (for a total of a 72-week exposure to the medication), showed no further improvement in walking ability beyond the first 24 weeks of treatment.

In clinical studies, cases of anaphylaxis occurred as early as 30 minutes from the start of infusion and up to three hours after infusion. Anaphylaxis occurred as late into treatment as the 47th infusion.

The safety and efficacy of VIMIZIM in patients less than 5 years of age is being assessed in an ongoing study. In the first 52 weeks of this study, 15 paediatric patients under 5 years of age were treated with 2.0 mg/kg of VIMIZIM once per week. Due to the age of patients, the 6MWT was not possible, but treatment resulted in a mean reduction of urinary KS levels.

Patients under the age of 5 reported more pyrexia (100%), vomiting (80%) and cough (73%), abdominal pain (40%) and diarrhea (47%) as compared to the pivotal placebo controlled study. Serious and severe adverse events in children less than 5 years of age were enlarged tonsils resulting in tonsillectomy, cervical cord compression, hypersensitivity, sepsis and staphylococcal skin infection, spinal cord edema, and joint instability. Other side effects occurring in two or more patients were diarrhea, abdominal pain, throat pain, headache, and nausea. These results are similar to the study results from patients older than 5 years of age being treated with VIMIZIM® (elosulfase alfa).

Based on the results of this study, VIMIZIM was approved for all ages on March 24, 2016. The product monograph recommends that treatment with VIMIZIM be initiated as early as possible, before the appearance of non-reversible symptoms of MPS IVA.

Every individual responds differently to treatment and so it is important to set realistic treatment goals. Regular tests and assessments by a doctor who is an expert in MPS IVA disease are important to help understand each individual's response to treatment over time. Before starting VIMIZIM, baseline assessments must be completed to ensure that you and your doctor are able to measure your response to treatment. This information may also be required for reimbursement purposes at a later date.

Important safety information for VIMIZIM® (elosulfase alfa)

VIMIZIM® (elosulfase alfa) is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of mucopolysaccharidosis IVA (Morquio A syndrome, or MPS IVA).

Warning: Risk of anaphylaxis and hypersensitivity

Life-threatening anaphylactic reactions have occurred in some patients during VIMIZIM® (elosulfase alfa) infusions. Anaphylaxis, a serious allergic reaction that presents as cough, redness of the skin, throat tightness, hives, flushing, an appearance of a bluish colour to the skin or mucus membranes, low blood pressure, rash, shortness of breath, chest discomfort, and gastrointestinal

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symptoms (e.g., nausea, abdominal pain, retching, and vomiting) in conjunction with hives, have been reported during VIMIZIM infusions, regardless of the duration of the course of treatment. A healthcare professional should closely observe patients during and after VIMIZIM administration and should be prepared to manage anaphylaxis. Patients and parents/caregivers should be informed of the signs and symptoms of anaphylaxis and severe hypersensitivity reaction, which occurs from a normal immune system and may include anaphylaxis, hives, swelling, cough, shortness of breath, and flushing, and should seek immediate medical care should symptoms occur. Patients with acute respiratory illness may be at increased risk of serious acute exacerbation due to hypersensitivity reactions, and require additional monitoring and/or delaying infusion.

Serious warnings and precautions

Anaphylaxis and hypersensitivity reactions

Treatment with this medication should be supervised by a doctor who has experience with MPS. Administration of VIMIZIM® (elosulfase alfa) should be carried out by an appropriately trained health professional with the ability to manage medical emergencies. Home administration by a health professional trained in recognizing and managing serious infusion reactions may be considered only for patients who are tolerating their infusions well under the direction of the practicing physician. As with all lysosomal genetic disorders, it is important to initiate treatment as early as possible, before appearance of non-reversible manifestations of the disease.

Due to the potential for life-threatening anaphylactic reactions, appropriate medical support should be readily available during and after VIMIZIM® (elosulfase alfa) administration. In clinical studies, cases of anaphylaxis occurred as early as 30 minutes from the start of infusion and up to three hours after infusion. Anaphylaxis occurred as late into treatment as the 47th infusion.

In clinical trials, hypersensitivity reactions occurred as early as 30 minutes from the start of infusion but as late as six days after infusion. Frequent symptoms of hypersensitivity reactions (occurring in more than 2 patients) included anaphylactic reactions, urticaria, peripheral edema, cough, dyspnea, and flushing.

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Because of the potential for hypersensitivity reactions, a health professional should administer antihistamines with or without antipyretics before the infusion. Management of hypersensitivity reactions should be based on the severity of the reaction and include slowing or temporary interruption of the infusion and/or administration of additional antihistamines, antipyretics, and/or corticosteroids for mild reactions. However, if severe hypersensitivity symptoms occur, a health professional should immediately stop the infusion of VIMIZIM and initiate appropriate treatment.

Infusion reactions can occur at any time during VIMIZIM treatment. The majority of infusion reactions were mild to moderate. Severe adverse events during infusion have included anaphylactic reaction, rash, chills, hypersensitivity, and severe breathing problems. The most common infusion reactions included headache, nausea, vomiting, fever, chills, and abdominal pain. Other infusion reactions reported were hives, shortness of breath, low blood pressure, an appearance of a bluish colour to the skin or mucus membranes, difficulty breathing, and loss of consciousness.

Consider the risks and benefits of re-administering VIMIZIM following a severe anaphylactic or hypersensitivity reaction. Re-administration after a severe reaction should proceed with caution and close monitoring.

Illnesses with fever or breathing problems

Patients with an acute febrile or respiratory illness at the scheduled time of the VIMIZIM® (elosulfase alfa) infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Careful consideration should be given to the patient's clinical status prior to administering or delaying the VIMIZIM infusion.

Sleep apnea

Sleep apnea is common in MPS IVA patients. Evaluation of airway patency should be considered prior to initiation of treatment with VIMIZIM® (elosulfase alfa). Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an acute reaction, or extreme drowsiness/ sleep induced by antihistamine use.

Spinal/cervical cord compression

Spinal or cervical cord compression (SCC) is a known and serious complication of MPS IVA and may occur due to the natural disease process. In clinical trials, SCC was observed both in patients receiving VIMIZIM® (elosulfase alfa) and in patients receiving placebo. Patients with MPS IVA should be monitored for signs and symptoms of SCC, including back pain, paralysis of limbs below the level of compression, and loss of bladder and bowel control, and be provided with appropriate clinical care.

Antibodies

All patients treated with VIMIZIM® (elosulfase alfa) at 2 mg/kg once per week in the placebo-controlled trial developed anti-drug antibodies and tested positive for neutralizing antibodies at least once during the clinical trial. The relationship between the presence of neutralizing antibodies and long-term therapeutic response could not be determined.

Pregnant and nursing women

There are no studies with VIMIZIM® (elosulfase alfa) in pregnant women. VIMIZIM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if VIMIZIM® (elosulfase alfa) is present in human milk. Exercise caution when administering VIMIZIM to a nursing mother. There is a Morquio A Registry that collects data on pregnant women and nursing mothers with MPS IVA who are treated with VIMIZIM. Contact MARS@BMRN.com or call 1-800-983-4587 for information and enrollment.

Paediatric patients

The safety and efficacy of VIMIZIM® (elosulfase alfa) have been demonstrated in MPS IVA patients 9 months to 57 years of age. The safety and efficacy of VIMIZIM has been established in a clinical trial in children aged 9 months to 4.9 years of age. The majority of patients who received VIMIZIM during clinical studies were in the pediatric and adolescent age range (5 to 17 years). Serious adverse events were more frequent in children less than 12 years of age.

Common adverse reactions

In clinical trials, the most common adverse reactions (≥10%) that occurred during infusion included fever, vomiting, headache, nausea, abdominal pain, diarrhea, mouth pain, shortness of breath, dizziness, chills, hypersensitivity, and muscle pain. The acute reactions requiring intervention were managed by either temporarily interrupting or discontinuing infusion, and administering additional antihistamines antipyretics, or corticosteroids.

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by any of the three following ways:

- Report online: www.healthcanada.gc.ca/medeffect
- Call toll-free: 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage-paid labels, the Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the

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MedEffect™ Canada website at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, please contact your health professional. The Canada Vigilance Program does not provide medical advice.

Dosage and importance of regular treatment

The recommended dosage regimen of VIMIZIM® (elosulfase alfa) is 2 mg per kg of body weight given once weekly through an intravenous (IV) infusion. The infusion should be given over a period of time of approximately four hours. Your doctor may adjust the rate of infusion according to your body weight.

As MPS IVA is a lifelong illness, regular infusions are essential for reducing the buildup of GAGs. Therefore, even if individuals with MPS IVA begin to notice improvements, it's important that they continue to receive regular infusions of VIMIZIM as recommended by the doctor.

If an infusion session is missed, talk to your doctor about rescheduling the next dose. Support may be available to help individuals continue to receive regular infusions even when travelling for work or vacation. Discuss your infusion schedule with the infusion team before finalizing your travel plans.

Some people prefer to have a permanent catheter (port) surgically implanted under the skin to reduce the trauma each week of having to find a vein for the intravenous (IV) infusion. With the port, one end is stitched into a major vein while the other end has a large rubber septum, where medication is injected into the catheter. This can be easier for the injection of medication than the traditional method of finding a new IV site each week.

It is possible to receive VIMIZIM® (elosulfase alfa) at home once you are well established on treatment. It is important to note that not everyone receiving VIMIZIM will be eligible for home infusions. Your doctor and healthcare team will determine whether home infusions are an appropriate treatment option for you. Individuals with MPS IVA will still need to keep regular appointments with their healthcare team, regardless of where they receive their infusions. However, receiving infusions at home may allow for additional comfort. Talk to your doctor about whether home infusions are right for you.

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Accessing VIMIZIM® (elosfulase alfa) treatment

BioMarin RareConnections™: BioMarin Pharmaceutical (Canada) Inc. has established this program to provide support for individuals with MPS IVA in accessing treatment with the medication VIMIZIM® (elosulfase alfa). Administered through BioMarin's partner, Innomar Strategies Inc., BioMarin RareConnections™ is a private, confidential, free support service for individuals with MPS IVA, their families, caregivers, and healthcare providers.

BioMarin RareConnections™ provides:

- Assistance with drug plan coverage and reimbursement
- Coordination and delivery of VIMIZIM
- Clinic and home infusion services
- Educational information on MPS IVA and VIMIZIM

For more information on BioMarin RareConnections™, call 1-877-597-6744, between 8:00 a.m. and 8:00 p.m. EST, Monday to Friday (excluding statutory holidays).

Where can I get more information and help?

Whether you are still making a decision regarding treatment options, or you have already made a decision and have subsequent questions, the following sources of information can be of help:

The Canadian Society for Mucopolysaccharide & Related Diseases Inc.

The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society) provides support for individuals and families living with MPS IV and other MPS disorders. The Society can connect you with other families affected by MPS IV. The staff can talk with you about disease and treatment information. Please call 1-800-667-1846 or visit www.mpssociety.ca. The Society also offers a variety of other services that are not related to treatment. These are described in the "Living with MPS IV" section of this learning guide.

Other organizations

Various other organizations can provide you with more information about your current and future treatment and management options.

These resources include:

- **Canadian Organization for Rare Disorders:** This national network represents all Canadians with rare disorders. www.raredisorders.ca
- **ClinicalTrials.gov:** This registry and database, maintained by the U.S. National Institutes of Health, includes a listing of active clinical studies, of treatment options for individuals with MPS IV. www.clinicaltrials.gov.
- **Communauté Morquio du Québec** is a group devoted to helping Quebecers with Morquio A by raising awareness of Morquio syndrome and becoming the Quebec centre of information and resources for patients and their families. www.morquioquebec.org
- **MedlinePlus:** This service, provided by the U.S. National Library of Medicine, offers a summary of information about MPS IV, including causes, symptoms, medical tests, treatment, and prognosis. www.nlm.nih.gov/medlineplus/ency/article/001203.htm
- **Morquio In Canada:** A site that provides information about Morquio A disease and management options. www.morquio.ca
- **MPS Emergency:** A site that provides medical information for emergency healthcare professionals who may encounter patients with MPS. www.mpser.com
- **National MPS Society (USA):** This American organization offers information on MPS, including an MPS IV booklet that provides information on the features and treatment of MPS IV. www.mpssociety.org
- **Online Mendelian Inheritance in Man (OMIM):** This database provides detailed information on inherited conditions such as MPS IV. MPS IVA at www.omim.org/entry/253000 and MPS IVB at www.omim.org/entry/253010
- **Orphanet:** This organization, which has a Canadian portal, offers information and services related to rare diseases and orphan drugs; its resources are provided for individuals and families affected by MPS IV, and physicians. www.orpha.net/national/CA-EN/index/homepage/
- **Regroupement québécois des maladies orphelines (RQMO):** RQMO has partnered with people in Quebec impacted by Morquio A on a site that advocates for government funding for treatment. www.mylifecantwait.ca
- **The Carol Ann Foundation:** This American foundation serves patients and families affected by MPS IV; it collects and shares information on MPS IV and promotes a support network for families. www.morquio.com
- **The Isaac Foundation:** This organization helps families of individuals suffering from MPS advocate for government funding for treatments. They also raise money for research projects that aim to find a cure for MPS. www.theisaacfoundation.com

Rare disease research

There are many types of ongoing research for a host of rare diseases. This research is considered investigational, as evidence does not exist that the treatment(s) being studied will be safe or effective. Please check with the Canadian MPS Society or your healthcare provider for the most up-to-date information. The websites listed in the previous

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section may also offer information on the latest studies.

The Canadian MPS Society aims to find cures for MPS and related diseases, and as part of that mission, the Society funds research grants. The Society recognizes the need for targeted research for treating bone and joint problems, and for treating the brain. Recent research funding from the Society has focused on these areas as well as on biomarker research. Information about the Society's research program can be obtained through the Society office by calling 1-800-667-1846, or by visiting its website at www.mpssociety.ca.

Notes

A resource for individuals and families living with MPS IV

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Anesthesia considerations

Contents

Anesthesia considerations

Overview

Various management options and surgical procedures to manage the symptoms of MPS IV have been described in this resource. For many of these procedures, a person with MPS IV may require an anesthetic. General anesthesia uses a medication or gas that "puts the person to sleep" before surgery. To make sure the person under anesthesia (i.e., getting an anesthetic) receives enough oxygen during surgery, a laryngeal mask airway (LMA) is used, if possible. In some cases, a LMA may not be possible and a tube is then placed into the throat and connected to a machine that helps the person breathe.

Courtesy of the Canadian MPS Society

Individuals with MPS IV are at a higher risk of complications when under anesthesia.

Individuals with MPS IV – especially those at the more rapidly progressing end of the disease spectrum – are at a particularly high risk of complications from anesthesia. One reason for this is that it can be difficult to insert the necessary breathing tube, as the airways of such individuals may be narrow as a result of the underlying disease. In addition, the spine needs to be protected during placement of the breathing tube, which can also complicate the process of inserting it.

It is important for individuals with MPS IV to be properly assessed by an anesthesiologist, with a full evaluation of their heart and their airways, complete with x-rays, prior to undergoing any medical procedures that may require anesthesia. It is also important for such interventions to be performed at a hospital where there is knowledge of and experience with MPS IV (or with MPS disorders in general) in order to reduce the risk of potentially serious complications. In addition, it is recommended that consideration be given to performing multiple procedures under a single anesthesia session in order to minimize the number of times an anesthetic needs to be given.

This section is intended to describe anesthesia and its use for individuals with MPS IV in more detail, and is intended primarily for individuals with MPS IV or the parents of children with MPS IV.

What is anesthesia?

"Anesthesia" means a loss of feeling, particularly the sensations of pain and touch. Usually, the term is used to refer to the use of medication to temporarily suppress sensations, especially before surgery.

There are three main types of anesthesia:

- *Local and regional anesthesia*
    - Only the relevant area of the body is numb and experiences no pain.
    - The individual remains awake and aware of what is going on during the medical treatment.
    - No breathing assistance is required.
    - *Local anesthesia* refers to the local anesthetic or "freezing" that is given around the affected area to keep it pain-free.
    - *Regional anesthesia* involves blocking the nerve supply to the affected area to keep it pain-free.
    - People sometimes use the terms "local" or "regional" anesthesia interchangeably.
    - Use of local or regional anesthesia is recommended whenever possible, with sedation if necessary, when anesthesia is required.

It is important for individuals with MPS IV to be properly assessed by an anesthesiologist prior to undergoing medical interventions that may require anesthesia.

- *General anesthesia*
    - The entire body is numb and experiences no pain.
    - The individual remains unconscious and unable to move for the duration of the medical treatment.
    - Mechanical help is required to breathe. To assure safe oxygen levels while the individual under general anesthesia is unconscious, the airway needs to be kept open. Some anesthesiologists use a laryngeal mask airway in combination with a flexible bronchoscope. While such techniques have been found to be beneficial for individuals with MPS IV, they require an anesthesiologist who is skilled with these newer methods. The typical way to manage this problem is to pass a tube through the larynx (voice box) and into the trachea (airway). The tube remains in the airway during the procedure but is removed at the end before the person fully awakes.

Normal procedure for general anesthesia

1. Gas or a medication given by injection is used to make the patient go to sleep.
2. A muscle relaxant is introduced, which paralyzes all the muscles, including the breathing mechanism.
3. Oxygen is given by squeezing a bag linked to a face mask. This is a temporary supply until a breathing tube is inserted.
4. An instrument known as a laryngoscope is passed over the tongue and down the back of the throat so that the anesthesiologist can view the entrance to the larynx.
5. A tube (endotracheal) is put into the trachea through the larynx and the laryngoscope is removed.
6. Sometimes a laryngeal mask airway (LMA) may be used. Other times, though, the endotracheal tube is connected to a machine that breathes for the patient during the procedure.
7. At the end of the surgical procedure, the anesthetic is stopped. The patient should start to wake up once the anesthetic begins wearing off.
8. The endotracheal tube is usually removed before the individual is fully awake.

What is different for individuals with MPS IV?

The impact of underlying symptoms

Anything that makes it difficult for an anesthesiologist to perform the steps required to deliver anesthesia will increase the risks associated with a medical intervention. For people with MPS IV, the effect of the storage of GAGs in many soft tissues, as well as the effects on bone formation, can create such difficulties. For example:

- The storage of GAGs narrows the nasal passages; enlarges the tonsils and adenoids; and causes loose extra tissue and thick secretions to form around the larynx. These problems have the collective effect of severely limiting an anesthesiologist's ability to view the larynx in order to insert a breathing tube.
- The muscle relaxation produced by pre-medications and/or by general anesthesia leads to further obstruction of the airway.
- The under-development of the joint between the first and the second neck vertebrae (odontoid hypoplasia) results in instability of the cervical (i.e., the neck) portion of the spine. The risk of spinal cord compression for individuals with MPS IV increases due to flexing or extending their neck, which is required for an anesthesiologist to view the larynx. The limited ability to manipulate the neck for individuals with MPS IV makes it difficult for even a very skilled anesthesiologist to see the larynx.

Individuals with MPS IV have other symptoms that can also contribute to the increased risks associated with general anesthesia. For example:

- The under-development of the rib cage restricts lung movement, and the accumulation of GAGs in airways leads to poor ventilation in the lungs. These two factors contribute to respiratory problems.
- The storage of GAGs in the heart and blood vessels of the heart can add to the overall burden to the cardiovascular system.

Potential risks and complications

As a result of the burden of symptoms described earlier, individuals with MPS IV may experience some of the following complications while under general anesthesia:

- Spinal issues
  - There is the potential for injury to the spine during insertion of breathing tubes, causing paralysis and death.
  - The spine needs to be protected during placement of the breathing tube, which can complicate the process of inserting the tube.
  - The spine also needs to be protected when the individual is turned or moved in any way on the operating table during the procedure.
- Airway (breathing) problems:
  - There may be difficulty in placing the breathing tube into the trachea.
  - There may be difficulty in keeping the airway open after the breathing tube has been removed.
  - The breathing tube may have to remain in place after the surgery if the initial placement was very difficult or traumatic.
  - Emergency tracheostomy (making an incision in the neck and inserting a tube directly into the trachea) may be necessary if the airway becomes compromised during intubation (putting the tube in) or extubation (taking the tube out).
  - The restricted movement of the chest may cause individuals with MPS IV to have difficulty expelling phlegm by coughing, leading to lung infections.
- Cardiac (heart) problems
  - Heart failure may occur.
  - Heart rhythm may become irregular.
  - There may be large changes (up or down) in blood pressure.

It is important to remember that this list does not imply that all persons with MPS IV will experience these problems. It should be noted that the risk of heart-related problems is much less than that of spinal injury or airway problems in individuals with MPS IV under general anesthesia.

What can be done to reduce the risks?

Assessing the risks prior to a procedure

If you are worried about the proposed surgery, discuss it with your primary care doctor, surgeon, or medical geneticist. He or she may suggest seeking a second opinion. The risks of general anesthesia should be weighed against the advantage to be gained from the surgery or procedure.

For many individuals with MPS IV, it is possible to determine before they undergo anesthesia whether they have a significantly increased risk associated with such a procedure. Though anesthetic complications may not be entirely preventable, a preoperative consultation with an anesthesiologist experienced in providing care to individuals with MPS and/or managing difficult airways could help in planning for the unusual or unexpected and may help reduce the risk of anesthetic-related complications.

An evaluation by a respirologist (lung doctor) and cardiologist (heart doctor) can be helpful in determining preoperative risks. The respirologist may recommend a sleep study and a pulmonary (lung) function test. He or she may also want to look at the structure of the airway using a flexible bronchoscope, which is a small tube that can be used to view the airway.

Choosing and meeting the anesthesiologist

For both children and adults with MPS IV, it is safer to have medical interventions at a major hospital experienced with treating people with MPS. This usually entails travelling to a regional medical centre or university hospital. Therefore, it is important for parents or individuals with MPS to understand which hospitals in their area are most experienced treating patients with MPS IV.

As there are no minor anesthetics for most patients with MPS IV, planned procedures should always involve careful assessment by a pediatric or general anesthesiologist with appropriate skills and training. In fact, for many surgical procedures it may be important to identify the anesthesiologist even *before* choosing the surgeon.

Anesthesiologists should be consulted during the planning process for a surgical intervention as well as for examination just prior to the intervention.

The anesthesiologist is responsible for deciding the best method of anesthetizing the patient who is undergoing medical intervention. There are several aspects to this:

- Because people with MPS IV present the anesthesiologist with difficult airways and often an impossible intubation using usual methods, other methods need to be used. For example, the flexible bronchoscope can be used to pass the breathing tube into the trachea at the start of the procedure. Some anesthesiologists use a laryngeal mask airway in combination with a flexible bronchoscope. While such techniques have been found to be beneficial for individuals with MPS IV, they require an anesthesiologist who is skilled with these newer methods.
- For some procedures, a local anesthetic may be an option. The anesthesiologist or a member of the team may visit the individual before the procedure and prescribe the medication needed to prepare for the anesthetic.
- Difficult-airway tools that are rigid and displace excess soft tissue may be helpful for use in children with MPS IV. Video laryngoscopes provide clear, ongoing images of the airway and tube placement with minimal cervical movements, which are dangerous for those individuals with MPS IV who have instability of the cervical spine
- There are steps that can be taken to try to make the overall process safer, such as avoiding particular anesthetic drugs or stabilizing the neck of an individual who has problems with the cervical spine.

The anesthesiologist should be aware of your or your child's condition and possible problems. Inform the medical team of any disabilities or hearing or vision problems, and bring hearing aids or glasses to assist the medical team in

The risks of anesthesia should be weighed against the advantage to be gained from the surgery or procedure.

Courtesy of BioMarin Pharmaceutical Inc.

communicating with you or your child. It may be useful to provide the anesthesiologist with information and experience from prior operations. For example, some people are afraid of injections or dislike the smell of the gas.

What does the overall process look like?

Preparation

Below are some of the steps involved in preparing the patient for general anesthesia.

Consent

The surgeon or members of the medical team will explain what is planned for the operation or procedure. The parent or individual will be asked to sign an official form of consent. The individual and/or parent should continue to ask questions until completely comfortable with what is being agreed to. If the person having anesthesia is a child and is able to understand, he or she could also be asked to sign the consent form.

"Nothing by mouth (NPO)"

The individual undergoing surgical intervention will be asked to not eat or drink anything for usually six to eight hours before receiving the anesthetic (the abbreviation "NPO" comes from the Latin for "nothing by mouth"). It is important to have the stomach empty, as patients undergoing general anesthesia are at risk of vomiting, and it is best to reduce the risk of such problems as food entering the lungs and making breathing even more difficult than is already the case for people with MPS IV.

Pre-medication

Pre-medication is the medication that is given to people before the general anesthetic. This can vary with the age of the individual and the type of procedure. Medication is usually given to help people relax, to dry up moisture in the mouth and throat, and to make it easier for the anesthetic to be given. Such pre-medication may be consumed by mouth (for example, via a drink) or it may be given by intravenous (IV) injection or by an intramuscular (IM) injection in the thigh or buttocks. Some individuals may be irritable until the medication has had a chance to work properly. People can also become suddenly wobbly on their feet. It is safer for them to rest on their bed or sit with a caregiver. If the individual falls asleep, it is recommended that they lie on the bed or be held in a horizontal position, as blood pressure may drop while they are standing upright. Occasionally, some of the pre-medication given to people with MPS IV will have a reverse effect and make them more energetic rather than drowsy. If this has happened previously, be sure to tell the anesthesiologist about it, as well as the type of medication that produced this effect.

Anesthetic cream

If the anesthetic is to be given by IV injection, an anesthetic cream may be applied to the site of injection an hour before the operation. This may numb the area so that the person may not feel the needle going in. Unfortunately, the cream numbs only the skin and does not help with an IM injection given as part of the pre-medication.

Courtesy of BioMarin Pharmaceutical Inc.

In the operating room

A nurse always accompanies the individual into the operating room. For a child, a favourite teddy bear, doll, or blanket could accompany the individual too.

Sometimes parents accompany their child to the operating room and remain there until he or she is asleep; this should be discussed and agreed with the anesthesiologist ahead of time. The parent may be asked to put on a gown and shoe coverings before going into the sterile operating area.

The anesthesiologist will explain the procedure being used. As mentioned earlier, sometimes an IV injection is used to initially put the individual to sleep, or the person is asked to breathe in an anesthetic through a mask.

Occasionally, small children can be anesthetized on their parent's knee while the gas tube is held near their face. Once the child is asleep, parents are asked to leave. It is important to go as soon as asked, as the anesthesiologist has many things to do very quickly to ensure the safety of the child being anesthetized. The nurse will estimate how long a person is likely to be in the operating room. Many parents or caregivers like to go for a walk or have a meal during this time. If the individual is going to the intensive care unit afterwards, you could be taken to see the ward beforehand. Many operations take longer than planned, and people usually spend a period of time in the recovery room before going back to their room or being discharged. If you are worried, you can ask the nurse to check how the individual is doing. In most children's hospitals, parents will be able to join their child once he or she has been taken to the recovery room.

Back in the recovery room

After having an anesthetic, individuals may be drowsy and unaware of their surroundings. For a child, hearing a familiar voice will help him or her relax and sleep more deeply. The nurse will indicate when it is safe for the person to drink something.

It may be necessary for the individual to remain intubated (with a breathing tube in place) and on a ventilator (breathing machine) for a period of time following surgery, so in the case of a young person, choosing a hospital with a pediatric intensive care unit is essential. For both children and adults, even minor procedures may require a stay in the intensive care unit so that breathing may be monitored.

Outpatient surgery (where the person returns home on the same day of the surgery) may not be suitable for severely affected individuals, even when having routine operations.

Conclusion

Local or regional anesthesia is preferable to general anesthesia when a choice is given; however, in many circumstances general anesthesia is the only option for many patients with MPS IV requiring surgery. This section has outlined some of the risks and complications that are associated with general anesthesia in individuals with MPS IV, as well as steps to potentially minimize them. This material is intended to help individuals, caregivers, and doctors better prepare for anesthesia. With that comes the hope that these individuals can safely receive medical interventions intended to improve long-term health outcomes.

Canadian MPS Society
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Living with MPS IV

Contents

Living with MPS IV

Overview

The objective of this section is to provide recommendations, guidance, and support resources on a number of different topics. Many sections are most appropriate for the caregivers of individuals with MPS IV, but some are also specifically included for individuals with MPS IV.

Getting organized

MPS IV Journal

Because you will be seeing multiple doctors, it's vital to maintain a thorough record of medical visits, treatments, appointments, and impressions over time. You can use the MPS IV journal included with this learning guide to help you keep all of this information in one convenient place. It's easy to use, and if you start to run out of space, you can make copies or download extra copies from the website of The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society): www.mpssociety.ca. You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Use the MPS IV Journal to help you keep track of medical visits, treatments, appointments, and impressions — all in one convenient place!

Emotional support

For parents of a child with MPS IV

As a parent of a child with MPS IV, you devote a great deal of time and energy to helping your child. But what happens when you need help yourself? When their child is first diagnosed, parents may have a variety of feelings, including fear, grief, uncertainty, and "information overload." They may also feel relieved that there is finally a diagnosis for the problems their child has been having. As time goes on, parents may also feel frustrated, isolated, stressed, and worn out.

If you feel this way, you are not alone. Many services are available to help parents cope, including respite care, counselling, funding, and support groups. There is no single "best choice" for everyone, as everyone's needs and personality are different. Here are a few ways to get emotional support:

Courtesy of the Canadian MPS Society

- **Talk to other families affected by MPS IV.** The Canadian MPS Society may be able to match you up with families who have volunteered to share their experiences and offer emotional support to other families affected by MPS IV. The Canadian MPS Society publishes an annual Family Referral Directory, enabling affected families to contact others in the same region or in the same circumstances. Some families have created websites to share their experiences with others. Visit www.mpssociety.ca for more information. You may also attend MPS meetings and family events or conferences. Attending these events can help parents connect with other families affected by MPS IV and get a new sense of hope from ongoing research.
- **Contact the Canadian MPS Society (1-800-667-1846) to find out more.** Many people find that talking to someone who understands may help them feel less alone and ease their fears.

- **Draw strength from your family, friends, or religious community.** Although they may not have experience with MPS IV, these are the people who care about you and would like to help. Keep in touch with your “support network” on a regular basis. Think of a few specific things they could do to help you, such as just coming over to talk, running some errands for you, babysitting, or bringing over some food. Getting a break, even on the small things, might really help.
- **Apply for a Respite Grant through the Canadian MPS Society’s Family Assistance Program.** Details are available on the Society’s website or by calling 1-800-667-1846.
- **Be good to yourself.** Although your role as a caregiver is very important, try to keep your own needs in mind too. Arrange for respite care or other help so that you are able to take some time for yourself on a regular basis. Continuing to do the activities you enjoy can help you hold onto your sense of self.
- **Take a break.** Caring for any child is hard work. Parents need a break to rest and enjoy activities, and this may not be possible when their child with MPS IV is with them. Brothers and sisters also need their share of attention, and to be taken on outings that may not be feasible for a rapidly progressing child with MPS IV. Organizations such as Kids Up Front Foundation (http://kidsupfront.com) and Starlight Children’s Foundation Canada (www.starlightcanada.org) run free programs to help families affected by diseases such as MPS IV go on recreational outings, such as visiting the zoo or attending a theatrical or sporting event. Many parents use some form of respite care or have someone come in regularly to help at busy times. Slowly progressing individuals may need help to become more independent from their families and may benefit from a vacation, perhaps with others who have disabilities.
- **Apply for a wish to be granted:** Several foundations work to help bring joy to children and families affected by diseases such as MPS IV. They do this by making a dream of the child come true, be it a special trip or a chance to meet a favourite celebrity. Examples of such organizations include Make-A-Wish® Canada (http://www.makeawish.ca), Children’s Wish Foundation of Canada (http://www.childrenswish.ca), and Starlight Children’s Foundation Canada (http://www.starlightcanada.org).

It’s not always easy to ask for help. But help is out there – try one of these forms of emotional support if you are feeling overwhelmed.

Though parents cannot control having to accept the diagnosis of MPS IV, they do control how the diagnosis affects their child and the rest of the family.

For adults with MPS IV

As an adult with MPS IV, you are faced with another set of challenges. MPS IV is a family affair in many ways. While you may be the one with the disease, it ultimately affects everyone in the family. If you are married or living with a partner, your spouse or partner may need to pick up more of the household responsibilities. It is important to talk to one another and learn how to communicate about how these changes make you feel. If you have children, or if your spouse or partner does, remember that children might have trouble understanding why you tire so easily. Children might also think that you are dying or that they did something to cause you to get sick. Talk openly with your children about your disease, how it will change your family, and what they can do to help.

Daily living with MPS IV

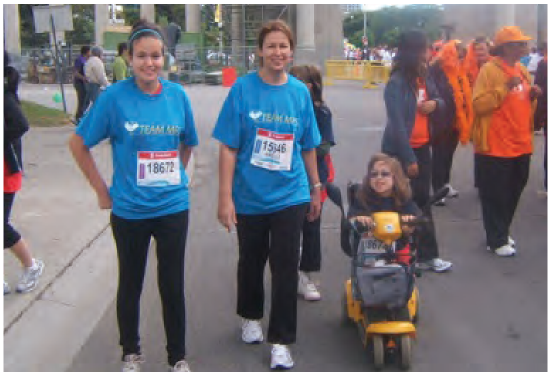
Challenges associated with MPS IV symptoms can have an impact on the abilities of an individual to cope with activities and stresses of daily living. Here are some coping strategies for common issues that you can try.

- **Home modifications.** Making changes to accommodate the needs of a person with MPS IV can reduce daily stress and put the individual more at ease. A one-level home is ideal for accessibility, but wheelchair lifts for stairs or vertical home lifts can be used in multi-level homes. Modifications that can be made outside the home include wide walkways, ramps to doorways, and handrails adjusted for the height of the individual with MPS IV. Inside, hallways and doors should be wide, and fixtures such as light switches and doorknobs should be adjusted to appropriate heights. Bathrooms should be large enough to accommodate wheelchair access, and grab bars should be placed in bath and toilet areas. In the bedroom, a mattress can be placed directly on the floor if the individual with MPS IV is at risk of falling out of bed. The Canadian MPS Society has Family Assistance Program (FAP) grants available that may be used to offset the costs associated with home renovations. Please visit www.mpssociety.ca for FAP guidelines and application forms.

- **Managing questions from strangers.** At times, strangers may ask questions or stare at people with MPS IV. Your response depends entirely on what you are comfortable with. Two basic strategies that may be used to deal with this situation are ignoring the individual and trying to explain the situation. However, smiling and answering questions will help spread MPS news and awareness. You can take along booklets and brochures wherever you go to help educate people. When dealing with stares, you might say something like "Thank you for noticing our beautiful daughter. If you have any questions about her, we'd be happy to answer them." Remember that your dignity and the dignity of your child are not bestowed upon you by strangers.

- **Travel tips.** Travelling can be a challenge for any family with children. When travelling with a child with MPS IV, remember to take breaks during long trips and give your child one-on-one attention. If your child is prone to wandering, ensure that clothing has important contact information sewn on the labels. If travelling by airplane, be sure to inform the airline a day or two before the flight if you will need boarding assistance, and explain if you have a need for a wheelchair or stroller. It is a good idea for teens and adults with MPS IV to wear MedicAlert bracelets and carry medical wallet cards to ensure medical personnel are aware of any crucial health concerns in the case of an emergency.

The Canadian government publishes information in English and French on accessible transportation and travel and related service standards. The websites listed on the following page provide information on local transportation as well as travel between Canadian cities by air, rail, ferry, and intercity bus.



Courtesy of the Canadian MPS Society

Answers to questions should be honest and straightforward, yet age-appropriate.

- **Access to Travel:** http://www.accesstotravel.gc.ca/1.aspx?lang=en
- **Voyage accessible:** http://www.accesstotravel.gc.ca/1.aspx?lang=fr
- **FAQ: Accessible Transportation:** https://www.otc-cta.gc.ca/eng/faq-accessible-transportation
- **FAQ: Transports accessibles:** https://www.otc-cta.gc.ca/fra/faq-transports-accessibles
- **Accessible Transportation:** http://www.tc.gc.ca/eng/policy/acc-accf-menu.htm
- **Transports accessibles:** http://www.tc.gc.ca/fra/politique/acc-accf-menu.htm

Much more information as well as tips for daily living with MPS can be found in the document "Daily Living with MPS and Related Diseases," published together by the Canadian MPS Society and the National MPS Society (USA). It can be accessed at http://www.mpssociety.ca/page/publications.aspx.

Courtesy of the Canadian MPS Society

Courtesy of the Canadian MPS Society

Talking with your family

Your immediate family

For parents of a child with MPS IV

Receiving a diagnosis of MPS IV can be a life-altering event for families. After the initial feelings of shock, despair, sorrow, hopelessness, and anger somewhat subside, parents generally regain their footing and consider how to deal with this new aspect of their lives. They realize that though they cannot control having to accept the diagnosis of MPS IV, they do control how the diagnosis affects their child and the rest of the family. Please consider the following suggestions as you create your family's plan for coping with MPS IV.

Keeping the child's brothers and sisters informed makes them feel important and involved, can minimize resentment, and can help facilitate healthy parental and sibling relationships.

Talk about MPS IV with both your affected child and their unaffected siblings. Parents of children with MPS IV may have a difficult time deciding how much information to give their affected and unaffected children about the disease. Although there may be a tendency to conceal information from children to avoid causing unnecessary anxiety, it is often best to be as open and honest as possible. Keep in mind that your child with MPS IV and his or her brothers and sisters can be very perceptive. They will likely know if their parents are not being completely honest with them, and they may develop feelings of confusion and mistrust. Age-appropriate information can be delivered in small doses and should be geared toward the children's level of understanding. Parents should make sure their affected child and his or her brothers and sisters know that the parents are available to answer any questions that may result from these discussions. Answers to questions should be honest and straightforward, yet age-appropriate.

Help your children deal with their feelings about the disease. Parents of children with MPS IV are faced with the difficult task of helping both their affected and unaffected children deal with the wide array of emotions associated with living with MPS IV. Providing support by listening and discussing these feelings is essential. Younger children may believe that MPS IV is a punishment for something they have done. Older children may resist discussing their concerns or feelings in order to protect their parents from becoming upset. It is important to reassure affected children and their siblings that they did not cause MPS IV. They must also know that they can talk to their parents about any concerns or feelings without fear of being judged negatively or causing parents to become overly upset. Remember that children's thoughts and feelings about MPS IV and their impact may change over time. As such, keeping the lines of communication open should be an ongoing task.

Just like other children, children with MPS IV need discipline from parents according to their ability.

Prepare your children for medical procedures. Children need to know what to expect in their lives. Although parents may think they are protecting their child with MPS IV by withholding information about procedures that may be painful or uncomfortable, this approach may increase anxiety. It is usually a good idea for parents to take the time to prepare both the affected child and their brothers and sisters for upcoming procedures. Parents should explain why the procedure is being done, who will be performing the procedure, what equipment will be used, whether or not there will be pain or discomfort, and what type of recovery period to expect.

Courtesy of the Canadian MPS Society

While most pediatric hospitals have staff experienced in helping to prepare children for hospitalization, surgery, and various medical procedures, the responsibility of preparing the siblings often falls on the parents. Siblings may experience anxiety related to parents spending increased time away from home, getting less attention from parents, fear of outcome of the procedure being performed, and missing planned events in their own lives due to parental time and resource constraints. Keeping the child's brothers and sisters informed makes them feel important and involved, can minimize resentment, and can help facilitate healthy parental and sibling relationships. Keep in mind that the information provided does need to be geared toward the age level of the children, and that the children should be encouraged to ask questions until they understand.

Give your children some choices. At times, children with MPS IV and their siblings may feel they have little control over their lives. Therefore, it is important for parents to help foster a greater sense of control. This can be accomplished by offering children choices whenever possible. When it is appropriate, children with MPS IV may enjoy being given the choice as to which arm the IV will go into, what they will eat, or when they will do homework or play. Likewise, siblings may enjoy having a choice over which caregiving tasks they will perform and the timing of these tasks.

Help your children lead as normal a life as possible. Parents should try as much as possible to treat their child with MPS IV and siblings like any other child. While recognizing that children with MPS IV do have special needs, it is important that parents encourage them and their siblings to participate in activities that involve other children of the same age. Parents should make sure siblings and playmates understand what types of activities are considered appropriate for the child with MPS IV.

Talking about MPS IV can help both you and your family.

Don’t be afraid to discipline your child who has MPS IV. Many parents are reluctant to set the same kind of limits for affected children as they do with their unaffected siblings. However, just like other children, children with MPS IV need discipline from parents according to their ability. When the parents maintain structure and consistency, it helps the children to feel safe and secure. Adequate discipline also helps children learn to control their own behaviour. When possible, parents should make sure that discipline is consistent – no matter what the day or time, who is disciplining (parents and caregivers), or who is being disciplined. Consistent discipline among children with MPS IV and their brothers and sisters in the household helps to foster healthy sibling relationships. Recommended discipline techniques include praising appropriate behaviour, using time-outs for young children, and restricting privileges of older children for inappropriate behaviour.

Give your children responsibilities. Just as children need discipline, they also need to be given responsibilities. Encouraging responsibility is one way to help a child with MPS IV lead as normal a life as possible. Parents must use judgment in assigning tasks to affected children that can be carried out with success. The requirements for the tasks should be clear and consistent. Parents should also remember to acknowledge and offer praise for tasks that have been done well. Siblings can be empowered to help care for their brother or sister with MPS IV and may actually enjoy providing care if the tasks are communicated in a clear and consistent manner and praise is given when appropriate.

Develop and maintain family routines as much as possible. Children typically prefer daily routines that are predictable and consistent. Although this is not always possible in an MPS IV family, an effort should be made to maintain regular routines and schedules for all family members.

Be mindful of what your children can overhear. Parents should be mindful about what is said within earshot of their affected and unaffected children. It is important that children receive consistent and age-appropriate information from their parents. They also should not be exposed to conflicts related to MPS IV and its management that may take place in the home or medical environment. This can lead to feelings of insecurity and mistrust.

Prepare your children for the reaction of others. Children with MPS IV and their siblings often don’t know how or what to tell others about the disease. Parents can help their children by suggesting various age-appropriate explanations of what MPS IV is and how it affects people. The issue of how to handle any teasing should also be discussed with children. Role-playing may be useful in helping children to craft responses to questions or teasing that may come from those unfamiliar with MPS IV.

Your extended family

For parents of a child with MPS IV

Speaking with your extended family

Talking about MPS IV can help both you and your family. Because MPS IV is genetic, your other family members may be carriers. Unless other family members have children with partners who also have a family history of MPS IV, it is unlikely that they will have children affected by MPS IV. However, making them aware that MPS IV may run in your family will give them the chance to have genetic testing. Telling your family can help them understand what you are going through. The more they know about MPS IV, the more likely they will be able to help. For more information on genetic testing, see "How do people inherit MPS IV?" in the "Mucopolysaccharidosis IV (MPS IV) disease" section.

Getting ready to talk to your extended family

Telling your family about MPS IV isn't easy. It may help to plan a few things in advance. First, decide when and where to tell your family. Make an outline of things you would like to say. Think of what reactions they may have and how you may deal with them. The information below will help you with each of these steps.

When is the best time to tell them?

Give yourself some time after the diagnosis to take in the new information and deal with it within your immediate family first. Then you can begin telling other relatives. There is no "best time," but try to choose a time when you can meet face-to-face if possible, and a time when they are not stressed about issues of their own.

What should you tell them?

There are no hard-and-fast rules for what to say to your family. Before talking to them, develop an outline of what you would like to say. This will help you decide which points to focus on and which things you would like to keep private. It's OK if you are uncomfortable talking about certain things and would rather not discuss them.

Courtesy of the Canadian MPS Society

Here are some points that you may want to consider including in your outline:

- What is MPS IV? Explain that there is a variable range of disease progression in MPS IV, and not all affected individuals have all the medical problems seen in MPS IV.
- When did the symptoms start? How did they affect your life?
- Where did you go for help and how did you finally get a diagnosis?
- How is your or your child's health now?
- What treatments are available for MPS IV? Have you made a decision on which treatments will be best for you? Will you be starting treatment soon, and what will that mean for your family?
- How are you and your family keeping a positive attitude?
- Where can relatives find out more information on MPS IV?
- How can your family help?
- What does this mean to your relatives? Should they be tested for MPS IV?

This list is just a guide to help you put together your outline. You do not have to talk about any of these topics if you are not comfortable with them. The answers to these questions depend on your individual situation. You can turn to your doctor, this learning guide, or the Canadian MPS Society for more information.

Possible reactions and tips for dealing with them

It's impossible to predict the reactions that your family will have to your news. However, there are a few common reactions that people may have:

- They may want to know how they can help you. To be prepared for this, think in advance about a few things they could do to help (such as house-sitting or running the occasional errand).
- They may want to learn more about MPS IV. You may wish to plan ahead by making a list of a few resources (see "Source of support and information," later in this section) and bringing information materials with you.
- They may be concerned about whether they or their children are at risk of MPS IV. To help, you may want to explain how MPS IV is inherited (see "How do people inherit MPS IV?" in the "Mucopolysaccharidosis IV (MPS IV) disease" section).

Getting involved in treatment means having a good partnership with your doctor.

Moving forward as a family

Telling your family about MPS IV can be difficult, but it may help both you and your family. Your family may want to learn more about MPS IV so that they can understand what is happening and how to help. If other people in the family have MPS IV, they may finally have an explanation for their symptoms. Family members may choose to be tested to see if they are carriers for MPS IV. These things will all help you to cope with the diagnosis of MPS IV as a family.

Talking to doctors

Why it's important to talk to your doctor

Getting involved in treatment means having a good partnership with your doctor. This section suggests some steps you may take to build this partnership and increase your understanding of MPS IV.

MPS IV can cause many challenges, including difficulties with mobility. Parents of a child with MPS IV may feel helpless and uncertain about their child's future. Older individuals with MPS IV may feel frustrated when unable to participate in certain activities or unable to make certain lifestyle choices. You may want to consider becoming an active participant in your care and working with your doctor to make the choices that are right for you or your child.

Finding the right doctor

Whether you are newly diagnosed or just changing doctors, it's important to choose a general practitioner (GP) or pediatrician that you, or you and your child, feel comfortable with. Consider the qualities that are important to you. If you are changing doctors, think of the qualities you liked in the previous doctor. Were there things about the doctor you didn't like? Are there attributes you think would be helpful for your next doctor? Make a list of those qualities. For example, do you prefer a doctor who uses clinical language or one who speaks in layperson's (everyday) terms? MPS IV is a rare condition, so many doctors may not have extensive experience with the condition. Finding a doctor who is knowledgeable about MPS or is willing to work through the issues with you is very important.

Once you've thought these things through, it's time to look for a doctor in your area who meets your criteria. You may want to meet with several doctors before making a final decision on one that you feel communicates in a manner appropriate for you and understands your needs and concerns. If over time, you feel you are not satisfied with the care you receive from your doctor, remember that you have the option to seek a new practitioner.

Preparing for your visit to the doctor

Plan ahead

You may find it helpful to plan ahead for your visit to the doctor. Consider preparing a list of questions and concerns before every visit. Your list might include your goals for the visit, any new information about your or your child's condition, such as new symptoms or treatments, and any questions or concerns you may have.

If you are seeing a new doctor for the first time, you might also want to include:

- all symptoms, when they began, how often they occur, and how they have changed over time
- any medications taken
- your or your child's medical history, including a list of your other doctors and previous medical procedures
- any problems with daily activities
- a copy of the doctor's handout from this resource guide which includes a recommended schedule of assessments and reference to the publication of the guidelines for treating MPS IV

MPS IV is a lifelong condition. Staying well informed can help you play a role in your or your child's health. Your doctor may be a source of information on MPS IV and current treatment options. During the visit, write down the information your doctor gives you so that you'll have a record of it, and ask for a letter from the doctor summarizing the visit.

Ask your doctor for any brochures or videos that provide information about your symptoms or the treatment of your symptoms. If your doctor makes any recommendations for treatment or therapy, be sure to write them down or ask your doctor to write down the instructions for you.

Keep up to date

To stay informed between your visits to the doctor, you can find more information by reading books on MPS IV, searching websites, or attending support groups. For a list of relevant websites, see "Websites" at the end of this section. If you think of a question you'd like to ask or information to share on your next visit, keep a running list so it will be available when you're preparing for the next visit.

When in doubt, ask

Don't be embarrassed to ask your doctor questions if you need more information or if there's anything you don't understand. If something doesn't make sense, ask your doctor to explain it again differently and to define any new words. You may want to try repeating what your doctor has told you in your own words so you can be sure you've understood.

Courtesy of BioMarin Pharmaceutical Inc.

Keep an open line of communication

Open and honest communication will help create and maintain your partnership with your doctor. Some symptoms or problems may be hard to talk about, or it may be difficult to admit that you have not understood something. However, knowing about these things helps your doctor give you better care. You'll both benefit in the long run: your doctor will understand your needs, and you will gain more control over your care.

Know your treatment options

It's important to understand the treatment options that are available. Here are a few questions to ask your doctor about treatment:

- What treatment and management options are available?
- Of these, which may be appropriate for me (or my child)?
- How will it interact with other medications and treatments?
- How much will it cost?
- Who will pay for the treatment?
- How long until it starts to work?
- For symptoms that cannot be treated, how else might I be able to manage them?

Your doctor is your partner in managing MPS IV. Good communication will help you get the most out of your visits to the doctor and strengthen your ongoing partnership.

Young adulthood — a time of transition

Healthcare

As you reach your teen years, it is helpful to start a gradual transition to advocate for your own medical care. Eventually as an adult, you will be responsible for communicating with your doctors and navigating the healthcare system as needed. Some first steps in this process toward independence are to know how to explain your condition and to know who your doctors are and what medications you take.

Having this knowledge and the skills to communicate it will be of especial benefit when you reach the age of 18. At this point, you may find that some changes to your medical team must take place. For instance, if you have been attending a pediatric hospital, you may be told that you are now of an age that you need to seek care elsewhere.

The Hospital for Sick Children (SickKids) in Toronto runs a service to help youth transition from pediatric to adult care. Called the "Good 2 Go Transition Program," it helps young adult patients with ongoing medical needs develop the necessary skills to navigate the adult healthcare system. Many of this program's resources are available online at http://www.sickkids.ca/Good-2Go. You may wish to ask your doctor if such a program is available to you locally. Another useful online resource is the "Got Transition?" website (http://www.gottransition.org) run by the National Health Care Transition Center in the U.S. It offers tools and information for youth and families to better manage this important period of transition in a young adult's medical care.

Life planning

If you're living with MPS IV, you may be asking yourself, "How will this condition affect my life and career choices as I transition into adulthood?" If your friends and other people around you aren't familiar with MPS IV, you may feel like no one understands how you're feeling. But take some inspiration from the stories of other young adults and adults with MPS IV who have made successful choices in life.

Making new friends and dating

It's normal to feel shy sometimes, and making new friends or dating can be challenging and intimidating for just about everyone. Remember, most friendships aren't created overnight – they take some time and effort. Having MPS IV may seem like a barrier to making new friends, but it shouldn't. Here are a few ways you can try to reach out and make friends:

- Find people who share your interests (like movies, music, or sports). For example, try joining after-school clubs, sports, or activities that you like.
- To meet someone new, smile at them and introduce yourself. You may want to start with a compliment (like "Hi, I really like your jacket, where'd you get it?") or a comment about an experience you have just shared (like "Hey, what did you think of that test?").
- Ask questions to help you get to know your new friend(s) better. People love to talk about their interests to someone who is genuinely listening.
- Make plans to meet up and do something you can enjoy together.
- As your friendship develops with a special someone, dating may occur as a natural progression.
- Your friends may ask you questions about MPS IV. Answer questions that you're comfortable with. You can also refer them to the Canadian MPS Society website (www.mpssociety.ca) for more information.

> *A career counsellor can help you explore a type of work that you might enjoy and that is well suited to your individual strengths and interests.*

Networking

You may also want to make friends with other young adults who have MPS. Since MPS is rare, your friends with MPS may be located all over the world. You can keep in touch in many different ways online, as well as through texting and talking on your phone.

Here are a few ways to meet others with MPS:

- Contact the Canadian MPS Society (www.mpssociety.ca) to see if they can put you in touch with people your age who have MPS.
- Visit the Canadian MPS Society on Facebook.
- Attend MPS activities such as regional meetings, family events, and national conferences. Contact the Canadian MPS Society for more information.
- Join the MPS Forum (www.mpsforum.com) – a forum for those affected by MPS and related diseases.

Education

Careful planning is needed to ensure that your education takes into account your preferences and interests as well as your goals for the future. Resources such as the Canadian Education Association (www.cea-ace.ca), the National Educational Association of Disabled Students (www.neads.ca), and Inclusive Education Canada (www.inclusiveeducation.ca) can help. Post-school goals may include post-secondary education, vocational training, integrated employment (including supported employment), continuing and adult education, independent living, and community participation.

Long-range planning for the transition from school to post-secondary education or work should focus on helping you improve skills related to employment, independent living, and community participation. The following is a transition checklist that can help you prepare for the future:

- ✓ Identify personal learning styles and the necessary accommodations to be a successful learner and worker.
- ✓ Identify career interests and skills, complete interest and career inventories, and identify additional education or training requirements.
- ✓ Explore options for post-secondary education and admission criteria.
- ✓ Identify interests and options for future living arrangements as well as possible supports.
- ✓ Learn to effectively communicate your interests, preferences, and needs.
- ✓ Be able to explain your disability and the accommodations you need.
- ✓ Match career interests and skills with vocational course work and community work experiences.
- ✓ Determine the need for financial support (such as from provincial, territorial, or federal funding programs).
- ✓ Practice independent living skills such as budgeting, shopping, cooking, and housekeeping.

Choosing a career

Many individuals with MPS IV do well at a variety of different jobs. Begin your search for the right job by assessing your physical capabilities. Try to be realistic about what you can and cannot do. Ask yourself these questions:

- How much standing, walking, and sitting are you comfortable doing?
- How much lifting and reaching can you do?
- What is your fatigue level?
- Can you hold objects or open car doors easily?

Consider your abilities on both “good” and “bad” days while making these judgments. If the job you are interested in requires you to do activities you find difficult, you have two choices: try to find ways to do the job comfortably, or make the decision to find a job that is more suitable for you.

With or without MPS IV, most people find it challenging to choose a career. It is usually a complex process that involves matching your skills and desires with the realities of the business world.

You know your own abilities and limitations. It is important to be practical about what you can and cannot do. Instead of using your limitations as a restriction, use them as a guide to finding the right career.

If you are interested in an occupation but feel it is not suited to you, consider other opportunities in the same field. For example, if you've always wanted to be a nurse but feel you don't have the strength it requires, other careers in healthcare such as nutrition or health education might give you as much satisfaction.

A career counsellor can help you explore a type of work that you might enjoy and that is well suited to your individual strengths and interests.

Learning from others with MPS

It often helps to hear how others with MPS deal with the challenges associated with daily living. The following are some quotes from young adults with MPS, as they discuss various aspects of their life journey.

"Having others who believe in you can make all the difference in the world."

"My advice for keeping a positive attitude is to not let anyone ever make you give up on your dreams and goals. Just because we have MPS does not mean that we should stop trying to achieve what we want."

"I believe the world needs to know that just because we have MPS, it does not mean we let the disease define who we are. We are the ones who define who we are!"

"I would have to say that MPS has affected my social life more now than when I was younger. I do not drive so that makes it more difficult at times to try to meet up with friends. But I am blessed because most of my friends realize that and will come and get me. My mother also offers to take me to places. I have lived at home throughout college so I have not made as many friends at college, but I am fine with that."

"I am a person who does not mind if people help me with doors. Some get offended when someone tries to help them, but I really appreciate the assistance. I look at it as people helping people whether or not someone is short, tall, in a wheelchair, or walking. It is just the polite thing to do as a person."

"Hopefully in a couple of years I will have the opportunity to live in my own apartment with or without a roommate. I know that I tend to not make quick decisions when it comes to big decisions. Just like there being different levels of severity in the MPS conditions, there are different levels of life's personal independences. It is all up to what works best for the individual with MPS."

Talking to employers

For parents of children with MPS IV

The information in this section is meant to be informative only and does not constitute legal advice. Individual situations should be discussed with a legal professional to determine the extent to which these laws may apply to you.

Meeting the demands of the workplace and caring for an ill child is extremely difficult. It is important to explain to your employer what MPS IV is and what implications it has on your life.

There are programs to help working parents cope with MPS IV.

Some companies have employee assistance programs that can connect employees to a qualified professional who can help parents deal with the stress of having a child who is ill, and direct them to other services that can help, such as respite care. The Canadian MPS Society can connect you to other families who have experienced similar problems and who can provide helpful information.

Other companies may offer daycare facilities, but these may not be equipped to assist children with special health needs. Check with your employer to see whether they offer any daycare services and, if so, whether they could accommodate your child.

For individuals with MPS IV

Talking to your employer about MPS IV
The information in this section is meant to be informative only and does not constitute legal advice. Individual situations should be discussed with a legal professional to determine the extent to which these laws may apply to you.

You may be concerned that having MPS IV may raise questions in an employer's mind about your ability to do your job. You may be reluctant to talk about your condition for fear you will not be hired or considered for a promotion. You should know that Section 15 of the Canadian Charter of Rights and Freedom guarantees equality rights plus freedom from discrimination for people who have a physical or mental disability. The Employment Equity Act (EEA) of 1995 ensures that persons with disabilities are granted full and equal access to employment and opportunity. An employer must accommodate the disabilities of employees, prospective employees, and clients or customers.

In order to avoid particular actions in this regard, the employer must prove that accommodation of the needs of an individual or a particular class of individuals would impose undue hardship on the organization or on the people who would have to accommodate those needs, considering factors such as health, safety, and cost.

Protection from discrimination occurring at the private employment level would be provided by provincial or territorial legislation. You can find information on employment standards in your jurisdiction by visiting http://www.hrsdc.gc.ca/eng/labour/employment_standards/ministries.shtml. To learn more about disability-related policies in Canada, see http://www.disabilitypolicy.ca/index_english.php. If, when, or how you decide to talk with your employer about your condition is a personal decision.

You may find that you need special accommodations to do your job. If so, your employer needs to know about your condition in order to make the necessary accommodations. Open communication is the key to a healthy work relationship.
If you are unable to work for a time because of illness, you may be entitled to sickness benefits under Employment Insurance (EI). To learn more, visit http://www.servicecanada.gc.ca/eng/sc/ei/benefits/sickness.shtml.


Courtesy of the Canadian MPS Society

Working successfully
Working successfully depends greatly on having proper management of your disease. This includes care from an experienced doctor, working with your healthcare team to plan a treatment program of proper medication and exercise, and self-management skills.

Be flexible and creative. Flexibility can help you balance work responsibilities with the demands of MPS IV. By figuring out your energy patterns during the day and what kind of activities hurt or help you, you can arrange your work schedule accordingly.

Create an efficient work environment. Arrange your area to limit the amount of lifting, reaching, carrying, holding, or walking necessary.

Talking to educators

Educators can play a critical role in your development and the development of your child. They need to provide you with accommodations, but first need to understand the special issues that could affect your educational needs. Please see "Educational strategies" and "An overview of MPS IV for teachers" for information on this very important issue.

Sources of support and information

Resources from the Canadian MPS Society

Founded in 1984, The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society) provides support to individuals and families affected with MPS and related diseases. It seeks to educate medical professionals and the general public about MPS and to raise funds for research so that one day there will be cures for all types of MPS and related diseases. The Society supports individuals and families affected by MPS through all stages of their journey, from diagnosis onward. Its website (www.mpssociety.ca) offers a wide range of resources.

The Canadian MPS Society provides support for individuals and families living with MPS IV.

The Society has booklets available online that contain valuable information on MPS symptoms, management, and care. Together with the National MPS Society (USA), the Society has published a booklet called "Daily Living with MPS & Related Diseases," which offers helpful tips for parents by parents. Other resources include an annual family directory, which helps families affected with the same syndrome or living in the same region of the country get in touch with each other, and a quarterly newsletter, the Connection, which also helps members connect and stay informed of MPS-related news and events.

Additionally, the Society runs a Family Assistance Program that provides financial support to help offset the costs of living with a chronic health condition. It also makes available travel stipends to help member families attend its regional family meetings and national family conferences, as well as international MPS symposia. These regional and national events supply families an opportunity not only to learn more about new research, treatments, and care strategies, but also to meet with other families and share common experiences. For some people, these events are their first opportunity to meet others affected by the same disease.

The Society funds research into MPS, and it advocates to ensure its members receive the treatment and care they need. It also provides bereavement support to those dealing with the devastating loss of a child or family member to MPS. The Society works with other MPS patient organizations through the International MPS Network, and with various Canadian patient organizations through the Canadian Organization for Rare Disorders (CORD).

For more information on the Canadian MPS Society, or to find information or support for living with MPS and related diseases, call 1-800-667-1846 or visit www.mpssociety.ca.

Resources for adaptive living

There are many resources that may help you overcome physical limitations due to MPS IV. Seek advice and recommendations from professionals such as your doctor, nurse, physical therapist, occupational therapist, or other healthcare provider.

An occupational therapist is trained to make a complete evaluation of the impact of MPS IV has on your home and work activities. The therapist will review your situation by conducting an interview, asking questions about hygiene, grooming, eating, drinking, dressing, getting in and out of bed, driving, cleaning, cooking, shopping, and working. The therapist will also conduct a physical examination. After a thorough assessment, the therapist will develop a plan, which may include physical therapy and adaptive equipment.

Adaptive equipment includes tools and devices that help you perform your daily tasks, such as getting dressed and eating, more easily. They also help you maintain a more active lifestyle.

Some adaptive tools that might be helpful for MPS IV include:

- **thick grips or handles:** These handles can make it easier for you to grasp small objects. They can be used on a variety of objects including utensils, toothbrushes, hairbrushes, pens and pencils, or combs.
- **extended handles and other tools to give you extra leverage:** These tools help you with tasks like opening jars, turning doorknobs, or twisting dials on your stove.
- **graspers and reachers:** These aids can help you pick up objects without bending or reaching. Extended shoehorns called donners can be used to help you pull up your socks.
- **slip-on shoes or Velcro closures:** These shoe styles are easier to take on and off than the lace-up kind.
- **zipper pullers and button grippers:** These devices can help you get dressed by making it easier to pull your zippers and fasten buttons. Sewing on buttons with elastic thread makes them easier to use and less likely to break off while you are fastening them. You can also opt for clothing with an elastic waist and Velcro tabs to make dressing less painful or difficult.

Websites

The Canadian MPS Society, www.mpssociety.ca, has a listing of websites that includes information on general health, government agencies, advocacy and education, support, and helpful products.

Resources that can help you:

- www.mpsforum.com (owned and operated by a family affected by MPS)
- www.raredisorders.ca (Canadian Organization for Rare Disorders)
- www.lhsc.on.ca/programs/medgenet (Canadian Directory of Genetic Support Groups)
- www.goldinfo.org (Global Organization for Lysosomal Diseases)
- www.wsfc.ca/family.html (Western Society for Children with Birth Disorders)
- www.siblingsupport.org (Sibling Support Project)
- www.cacl.ca (Canadian Association for Community Living)
- www.neads.ca (National Education Association of Disabled Students)
- www.pwd-online.ca (Government of Canada – Persons with Disabilities Online)
- www.inclusiveeducation.ca/english/index.asp (Inclusive Education Canada)
- http://www.ldac-taac.ca (Learning Disabilities Association of Canada)
- www.cea-ace.ca (Canadian Education Association)
- www.cailc.ca (Canadian Association of Independent Living Centres)
- http://www.ccdonline.ca (Council of Canadians with Disabilities [CCD])
- http://www.reach.ca (Reach Canada)
- www.vracanada.com (Vocational Rehabilitation Association of Canada)
- www.rhdcc-hrsdc.gc.ca (Human Resources and Skills Development Canada)
- www.geneticalliance.org (Genetic Alliance)
- www.climb.org.uk (Children Living with Inherited Metabolic Diseases)
- www.lysosomallearning.com (Lysosomal Learning)
- www.abilities.ca/agc/disability_organization/view_disability_organizations.php?pid=&cid=&show=all&subid=169 (Access Guide Canada – Disability organizations)
- www.respitelocator.org (ARCH National Respite Network – National Respite Locator)

- www.ablelink.org/public/new/index.html (Ability Online)
- www.cra-arc.gc.ca/tx/ndvdls/tpcs/rdsp-reei/menu-eng.html (Canada Revenue Agency – Registered Disability Savings Plan)
- www.cra-arc.gc.ca/cdb (Canada Revenue Agency – Child Disability Benefit)
- www.raredisorders.ca (CORD – Canadian Organization for Rare Disorders)
- www.theisaacfoundation.com (The Isaac Foundation)
- www.makeawish.ca (Make-A-Wish® Canada)
- www.childrenswish.ca (Children's Wish Foundation of Canada)
- www.starlightcanada.org (Starlight Children's Foundation Canada)
- www.starlight.org (Starlight Children's Foundation)
- www.sickkids.ca/Good2Go (Good 2 Go Transition Program at The Hospital for Sick Children)
- http://www.morquio.com (The Carol Ann Foundation)
- http://www.orpha.net (Orphanet)
- http://www.rqmo.org (Regroupement québécois des maladies orphelines)
- http://www.lpaonline.org (Little People of America)
- http://www.gottransition.org (Got Transition? — a resource of the National Health Care Transition Center)

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For parents of children with MPS IV

Introduction

Both parents and educators want the best for their children. Understanding how to work together with the education system can help parents of children with MPS IV ensure that their child has the best possible education.

This section is designed to be a source of information for parents and educators. It is not meant to be an exhaustive resource; it attempts to pull together some information on strategies and resources that can be used to help devise an appropriate educational program for children with MPS IV. There has been very little research on the educational aspects of MPS IV. This section brings together the experiences of parents and educators who have developed successful educational programs (programs that provide the child with the best possible education) and techniques and who have addressed difficulties commonly experienced by children with MPS IV.

Courtesy of the Canadian MPS Society

Understanding how to work together with the education system can help parents of children with MPS IV ensure that their child has the best possible education.

How schools work

Understanding how schools are organized can help parents work together with educators. Parents of children with MPS IV must often ask school personnel to do something different from the norm. Give them time to adjust to your requests. See how you can support them as they adjust to the new expectations you are requesting. Compliment them on what they do well.

Schools as organizations

All organizations have a particular way they operate. Schools have a division of labour based on specialization. Education is organized to meet the needs of the group, and education programs are conducted by regular or general education teachers. Special education was developed for those students who do not do well in general education classes. General education teachers have been told for years to refer children to special education when their educational needs cannot be met in a general classroom.

The classroom teacher and others cannot make school operational changes without getting approval from their superiors. Change generally occurs from the top down, meaning that school policy changes usually result from directives from central office administrative staff. This limits how easily changes can occur in normal school operations, and teachers may not be free to independently make necessary changes in the material they teach and how they teach it. Difficulties developing an individual educational program (IEP) often result from problems with school policies or from getting permission from superiors to make changes.

A teacher’s life

Your child’s teacher is there to help. Like you, their goal is to provide the best possible education for your child. By working together, parents and teachers can provide valuable resources for each other. Parents can share information with teachers regarding MPS IV, their child’s strengths and preferences, and their goals for their child’s education. Teachers can share with parents the child’s progress and help the child meet his or her educational goals. Having a strong relationship with your child’s teacher can help your child benefit as much as possible from education.

The role of parents

Parents may be in a position of asking teachers to do things that go against the norm of the school. Without approval from their supervisors, teachers may not be able to make changes that both parents and teachers are recommending. Teachers’ superiors may not always be knowledgeable about special needs children. The job of parents is to understand and then help the school system plan for developing an IEP.

Relevant laws

The information in this section is meant to be informative only and does not constitute legal advice. Individual situations should be discussed with a legal professional to determine the extent to which these laws may apply to a particular child.

Canadian human rights laws specify a “right to reasonable accommodation for a disability.” This means that schools and other education authorities have a legal obligation to take appropriate steps to eliminate discrimination resulting from a rule, practice, or barrier that has, or can have, an adverse impact on individuals with disabilities. This is referred to as the “duty to accommodate.” Adjustment for a disability is legally required if the accommodation is needed to ensure that the person has the opportunity to participate fully and equally. Examples of accommodations that may be necessary include those that address access barriers or the need to create IEPs for students.

Planning for educational programs and supports

Educational needs: The big picture

Parents can help their school plan for their child’s education by providing resources (such as “A teacher’s guide to MPS IV”) to help school personnel become more familiar with MPS IV. This section covers some of the “big picture” issues schools should consider when developing an individual educational program (IEP) for a child with MPS IV. It is difficult to write specific guidance that covers every child with MPS IV, as the spectrum of severity varies widely between rapidly and slowly progressing forms of the disease. All children are legally entitled to a free and appropriate public education, regardless of any disabilities they may have, and you and your school can work together to help your child have a positive educational experience.

Parents of children with MPS IV must often ask school personnel to do something different from the norm.

Overall planning and monitoring considerations

Schools should monitor changes in the needs of children with MPS IV so the IEP can be adapted as needed to support a child whose physical limitations are affecting learning. The IEP should be developed to encourage social and academic participation and development. Teachers may need additional support to understand the child’s physical capabilities and to cope with any limitations due to the child’s disease progression or missed school. This will assist them in tailoring their teaching and expectations to the child. Planning and goal development may be difficult for school personnel who do not have experience with children whose disorders are progressive. The traditional focus is on improvement in skills and tapering support as improvement occurs rather than on maintaining skills.

Medical care needs

Mobility problems, hearing loss, and vision difficulties may need the special attention of school personnel in program planning. All schools should have teachers who specialize in working with children with vision or hearing impairments. These teachers help the IEP team develop alterations to deal with these problems. Mobility problems and physical limitations caused by the disorder can be addressed by consulting physical and occupational therapists. Class assignments and projects (such as art projects) can be modified to allow children with physical limitations to participate in similar projects with their peers.

Classroom integration and social skills

School attendance and socialization should be encouraged and fostered through integrating the child into the classroom and through interventions for specific social skills. Independence should be supported. Teachers can do much to improve the acceptance of the child through instructional activities such as cooperative learning and encouraging support for all children in the classroom. Additional support and education is necessary during adolescence.

Teacher education and support

Teachers should be educated about the child's disorder, abilities, and special needs. Teachers may be unsure of their ability to teach children with MPS IV, but many skills they use in teaching non-disabled students will enable them to work well with children with MPS IV. Teachers and classmates may also need support in dealing with feelings of loss if the child's condition worsens.

Academic and career expectations

Teachers need appropriate expectations for learning that are balanced by an awareness of the child's physical limitations. It's important for teachers to be aware that the outward physical manifestations of the disorder do not mean that the child has a delay in intellectual development.

There is no reason that an individual with MPS IV should not succeed academically. Appropriately high expectations of academic achievement will foster realistic self-appraisal and enhanced academic achievement. Academic and vocational programming for the child should foster independence, and career goals should be set realistically high. Achieving post-secondary education is highly possible; however, it is important to ensure that the school is aware of the resources required. Planning for the transition from school to post-secondary education or work should focus on helping children and adolescents with MPS IV pursue vocations in a manner similar to that of their peers. For more information, please see the section, "Post-secondary education."

Special services

Overview

A Supreme Court ruling on the Charter of Rights and Freedoms established that education for students with disabilities should be provided in a regular class environment with reasonable but not excessive adaptation provided to promote equal opportunity in the classroom. In addition, provincial education laws require that school boards make education available to all school-aged persons in a district.

One of the most vexing issues in devising an educational plan for children is deciding how any needed special education services will be delivered.

It should first be determined what types of adaptive equipment and services would enable the child to be educated in the regular classroom. This list could include devices to assist in writing and hearing, special desks or seats, or extra time to finish computer and writing projects. An occupational therapist should be included in determining what tools would help integrate your child into a normal classroom setting. See "Assistive Technology," later in this section, for more information and adaptive resources that support the school setting.

A resource that you or your child's teacher may find useful is a book that is written by special education expert Dr. Darlene Perner and published by the United Nations Educational, Scientific and Cultural Organization (UNESCO). Entitled *Changing Teaching Practices*, the book is designed to help teachers carry out instructional strategies that support the inclusion of students with disabilities and special needs. It is available online at http://www.inclusiveeducation.ca/documents/Changing%20Teaching%20Practices%20Perner%20136583e.pdf.

Socialization

In determining the proper placement, parents should consider their child's socialization needs. To aid in this, they should do the following:

- Form a social network in an inclusive setting. Meet with small groups of classmates and have them develop a list of ideas on how to involve the special needs student in the school. Students who volunteer to get involved with these activities can form a peer network. Although the peers will first consider themselves to be advocates, this role may evolve into a friendship between the special needs student and other students.
- Match your child with another child according to their preference for certain activities that improve the interaction between your child and others. These activities may take place in the school cafeteria, library, computer lab, or gym.

The individual education plan (IEP)

If you feel that your child with MPS IV needs an IEP, the following information will help you work with your school to set an appropriate plan.

IEP goal setting

The first step in creating an IEP is to develop some broad goals for the child. While these will vary from child to child, here are some examples:

Courtesy of the Canadian MPS Society

- Develop relationships with adults and children in school.
- Achieve as many self-help skills as possible.
- Be as self-directed as possible.
- Be happy with himself/herself and his/her school.
- Develop the desire to be independent.
- Behave acceptably at school.
- Be accepted by others – both students and adults.

The next step is to look at the child's current performance and needs in a variety of educational areas, including:

- **academic/cognitive skills:** Setting appropriate academic learning goals such as reading, math, and social studies. These will vary according to the child's level of academic skill and potential.
- **emotional development:** Developing satisfaction with school, life, and self, improving self-control, and enhancing feelings of personal effectiveness.
- **social development:** Developing friendships, interacting with peers, feeling part of a group, contributing to the good of the school and classroom, and having models of appropriate social behaviour.
- **communication skills:** Building skills that develop understanding and communication with others, such as improving language skills, learning compensatory communication skills, and being exposed to and practicing appropriate language skills.

- **sensory skills:** Dealing with the effects of vision and hearing loss, providing a satisfactory and stimulating environment, and protecting the child from an environment that is too stimulating.
- **mobility/physical development:** Maintaining and improving mobility, coordination, and physical skills. This includes regular and adaptive physical education activities and activities with other children.
- **medical/health needs:** Finding and maintaining supports that meet the medical and health needs of the child to enable him or her to benefit from his or her educational program.

Strength-based planning – child

Considering your child's strengths provides a new focus that can be built into the IEP program. Strengths and likes can be used as learning tools, and a focus on these can enhance motivation and allow everyone to enjoy the experience.

Courtesy of the Canadian MPS Society

Parents should ask the IEP team to focus on the child's strengths and likes. The team can refer to these when composing the IEP. Below are questions to ask about the child. Be open to new ideas as the meeting progresses.

- What is the child's favourite thing to do?
- What areas have had the most improvement?
- What has the child most improved on from earlier in the year?
- Who does the child like best in school (teachers, peers, other school staff)?
- What was the best day the child had this year? What activities and events occurred on that day?
- What activities do the parent and child enjoy doing together?
- What does the child do well?
- What are the child's strongest physical and motor skills?
- If the child could do anything, what would it be?
- What are the child's favourite foods?

There are many more questions parents can ask to help the IEP team identify the child's strengths and likes. Encourage other team members to brainstorm and think about specific times and events in the past few months that remind them of strengths and likes.

Strength-based planning – school

This approach also can be used when planning the classroom setting. Some professionals who work with children often refer to the "wraparound" approach to developing plans. The idea is to think in terms of what supports the teacher would need in order to help this student be successful (i.e., meet his or her educational goals). Parents can do a strengths and likes assessment of the teacher and classroom, too! Here are some ideas to get started on a school strength assessment:

- What are the best aspects of the classroom?
- What does the teacher do for fun in the classroom?
- With what types of children with special needs is the school most successful (that is, providing the child with the best possible education)?
- What are some things children enjoy doing in the classroom?
- What aspects of teaching does the teacher do best?
- What types of students respond well to the teacher?
- What is most exciting for the teacher on the first day of school each year?
- Who are the most supportive individuals in the school?
- What are the teacher's favourite subject areas?

This also can be an illuminating process for the teacher. It gets people thinking about how to use their strengths to educate children. It may identify things that people haven't thought of in a long time. It also gets people to think about developing supports to better serve the children. It helps if parents have identified a few strengths of the teacher and the school before the IEP meeting.

Courtesy of the Canadian MPS Society

Preparing for the IEP meeting

Be an advocate for your child. Prepare ahead of time for the IEP meeting and keep the focus on what your child's needs and goals are. Review the child's records. Read over the last IEP. Make notes on areas where the child has improved and areas where there needs to be more work. Review any classroom work or progress notes received since the last review. Review reports or evaluations from outside professionals. Bring these reports to the meeting. Make a list of the child's strengths and a list of his/her needs. Think of academic, social, emotional, and physical strengths. Involve the child and other family members. Make a list of the things that need to be done to meet the child's needs. Think in terms of classroom size, peers, accommodations, curriculum, modifications, related services, assistive technologies, and transition. Make a list of the main points to be discussed at the meeting. Be sure to specifically discuss assistive technologies and adaptive physical education (discussed later in this section). Read materials on IEPs and work with the school so you are prepared. Parents may want another person to attend the meeting for support or to have another professional attend who can better explain the child's needs.

Having a successful IEP meeting

- Remember to bring all the information to the meeting.
- If something is difficult to understand, ask to have it explained. Ask questions.
- Keep emotions in check. It may be difficult, but it is best to remain calm. It is helpful to have another person present to provide support. If the meeting seems to be too emotional, ask for a break or reschedule another meeting.
- Keep in mind that the parent is a full member of the IEP team, and by working together the team can help the child have the best possible education.
- Listen to what others have to say and agree with what is reasonable.
- Make sure all of what is decided is written down on the IEP and get a copy.
- If you disagree with the school, attach a written statement of the disagreement to the IEP and don't forget your right to appeal.

Many people don't consider the fact that children with serious disabilities have strengths.

Managing disagreement with the IEP

If the parent(s) and school personnel don't agree on the IEP, focus on areas of agreement and work from there.

- Try to agree on as much of the IEP as possible so the school can begin implementing the plan.
- Look for others to help (other parents, special education law centres, advocates for the disabled, and organizations for children with disabilities). Take someone else with you to meetings who can observe and can assist you.
- Work hard at keeping cool during meetings.
- Write down goals and plans before going to meetings and provide evidence that backs the claims.

Courtesy of the Canadian MPS Society

If the experience is difficult, hang in there. Remember, most of the time the local school district has the burden of proof that its programs are meeting the child's needs. And it's also important to keep in mind that you and the school share the same goals – to help your child have the best possible education.

If parents cannot come to an agreement through discussion, negotiation, or mediation, and they feel that their child is being discriminated against by the school board, a complaint may be lodged with their provincial or territorial human rights commission or agency. After the investigation is complete, a commission or agency will issue a report, and usually try to facilitate a negotiated settlement. If a settlement is not reached, the case may be referred to a specialized tribunal, board of inquiry, board of adjudicators, or human rights court. A decision will then be made as to whether or not there has been discrimination in violation of the law. If there is a hearing, the human rights commission or agency will supply a lawyer to the complainant. It may take months, however, before the hearing occurs.

Monitoring progress with the IEP

It is important to monitor the progress of your child's education:

- Keep in touch with the child's teachers, principal, and other related personnel. Visit the school as often as possible.
- Keep a record of the child's progress on the IEP goals.
- Ask for a review of the IEP as the child's needs change.
- Make sure the IEP is being followed.
- Make sure that school personnel provide documentation that goals have been met or needs have changed.

Consider the following areas:

Academic achievement
- Is the child making academic progress?
- Is he/she meeting the goals of the IEP?
- Does the teacher believe that academic goals are important for the child?
- Does the teacher encourage the child's best performance?
- Does the child have appropriate expectations of his or her academic performance?
- Does he/she try hard to reach the goals?

Social development
- Does the child have a variety of friends in the class (a close friend, some acquaintances)? How many friends and how often the child plays with them may be related to the child's basic temperament and ability level.
- Does the teacher promote social interaction between all students in the classroom?
- Does the child get to work cooperatively with other students during learning activities?
- Does the child participate in non-academic activities (sports, socials, etc.)?

Emotional development
- Does the child like school? Is this a change?
- Does the child feel that he/she can master his/her environment at school?
- Does the child have strong negative feelings at school (anger, sadness, anxiety)?
- Does the child manage his/her feelings satisfactorily at school (anger, sadness, etc.)?

School environment
- Is the child getting an appropriate amount of assistance or support to reach his/her emotional, social, and academic goals?
- Does the teacher understand the child's needs?
- Does the teacher want to teach exceptional children in the classroom?

- Are the classroom and other areas easily accessible for the child?
- Are school-related tasks modified where appropriate but still similar to tasks other children do?

Courtesy of the Canadian MPS Society

Adaptive physical education

Children with MPS IV, like all children, must have a physical education program.

The teacher responsible for developing the adaptive physical education program should assess the child's physical education needs and develop an adaptive physical education program as part of the child's IEP. Adaptations can be made in existing games to include children with disabilities. Some possibilities include the following:

- using a batting tee instead of pitching in a softball game
- having designated runners
- decreasing the distances in games
- using real teams where children assist each other in parts of activities
- allowing children in wheelchairs to hold the ball on their lap while being pushed by another child
- changing rules of games
- modifying equipment
- adapting the layout of the game space
- developing new games that emphasize interaction rather than competition

Evaluate the effectiveness of the goals and activities at each IEP update, and have the adaptive physical educator present at the IEP meeting.

Parents can ask for an IEP team meeting if they aren't sure how things are going or if they aren't happy with the current status of their child's physical education plan.

Assistive technology

It is important to consider whether a child needs assistive technology devices and services to accomplish the educational goals in the IEP. An assistive technology device is a piece of equipment or system used to maintain or improve the functional capabilities of a child with a disability. These devices can be homemade or commercially available. Some devices may be specifically designed for persons with a disability; others may be commonly available.

Assistive technology helps compensate for limitations in functional skills caused by a disability. These devices can be used to help communicate, control the environment, get around, and do other activities of daily living. They have been commonly used for children with a variety of disabilities. Few devices are likely to be available off the shelf for children with complex physical disabilities, so it may take some creativity to modify already existing devices, or create homemade devices, to fit the particular situation. Each school district should have an assistive technology specialist on staff or available as a consultant to help you.

The following are examples of assistive technology devices for different areas of activity:

Communication

- Augmentative communication devices can provide a "voice" for communication. Ever-improving software and mobile apps also facilitate communication in many ways.

Transportation

- Scooters (power wheelchairs with joy-stick controls) can assist children with getting to and between classes.
- Motor vehicle adaptive equipment combined with a driver's licence can offer teens and older students greater independence in getting to school and other destinations.

Daily activities

Courtesy of the Canadian MPS Society

- Devices can make it easier for a person to turn something on and off. "The Clapper" is one such device that allows a child with mobility difficulties to turn a light on and off without getting up.
- Mobility aids can help a person get around or participate in an activity that otherwise requires a motor skill the child finds difficult because of mobility or motor control difficulties.
- Specially designed recreational equipment can allow a child to participate in games or sports. For example, a ball ramp can allow children to bowl who cannot pick up and move a bowling ball.

Educational activities

- Large-button calculators can assist with math.
- Speech recognition software and other assistive technology software and hardware can enable a child to enter and read text.

To successfully use assistive technology for your child's IEP, make sure:

- the assistive technology device doesn't inhibit the child's development or reduce his/her skill level, but extends his/her capabilities
- the parent, child, and school personnel receive adequate training on the use of the device
- service and maintenance are available for the device
- back-up plans exist if crucial devices break down
- the child's assistive technology needs are monitored regularly
- all assistive technology devices are written into the IEP
- the IEP team considers the child's assistive technology needs only after determining his/her educational goals
- a person knowledgeable about assistive technology is on the IEP team
- the device is sent home if the child needs the assistive technology at home
- the child has a monitored trial period with the device to ensure it is functioning properly

Post-secondary education

All students who pursue post-secondary education need to independently self-advocate to ensure they receive the support and resources available to them in their new academic environment. Self-advocacy skills are especially critical for persons with MPS IV as it is the student's responsibility to identify and request any needed accommodations from their post-secondary institution. The earlier requests can be placed, the better the results for the student.

In Canada, post-secondary institutions have a legal obligation (under the Canadian Charter of Rights and Freedoms and various provincial and territorial legislation) to provide reasonable accommodation. These accommodations may include note-taking services, oral exams, transportation, special parking permits or other tools required for accessible education. Your college or university's disabilities service office can work with you to arrange and customize the necessary tools. While certain services may involve a fee, funding programs and tax exemptions may help offset these expenses. Your college or university disabilities service office can offer details for your specific circumstance.

Choosing courses

All students selecting courses should consider the goal of their post-secondary education. Is it meant to open a particular career path? Is that area of work realistic in terms of one's strengths, weaknesses, and physical requirements—on both good and bad days? As not everyone is suited for every type of work, a career counsellor may help identify what coursework could lead to appropriate employment and help uncover alternative options when tough decisions are faced. While still in high school, students can consult their guidance counsellors for advice and information to plan ahead, and, once embarked on post-secondary studies, students can turn to academic advisors and career-counselling services for direction.

Housing considerations

Deciding where to live is an important aspect of transitioning to post-secondary education. For persons with MPS IV, considerations will include practical concerns such as wheelchair and other physical accessibility requirements, proximity to key physicians and healthcare, and transportation options. Your college or university can provide information about housing both on- and off-campus to help you decide what is right for you. You may wish to contact other individuals with MPS who have experience with post-secondary education to see what housing situations worked for them. Contact The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society; www.mpssociety.ca) to see if they can help connect you to someone with a similar experience or visit the Facebook page of the Canadian MPS Society to reach out to others directly.

Resources for more help

- Canadian Education Association: http://www.cea-ace.ca
- Persons with Disabilities Online: www.pwd-online.ca
- The National Educational Association of Disabled Students: www.neads.ca
- Inclusive Education Canada: www.inclusiveeducation.ca
- Learning Disabilities Association of Canada: http://www.ldac-acta.ca
- You2Youth (Learning Disabilities Association of Canada): http://www.youth2youth.ca
- College Committee on Disability Issues: http://www.disabilityissues.ca
- Inter-University Disability Issues Association: http://www.idia.ca/web
- Canadian Association of Independent Living Centres: www.cailc.ca
- Council of Canadians with Disabilities (CCD): http://www.ccdonline.ca
- Reach Canada: http://www.reach.ca
- Canadian Heritage: Human Rights and Disabilities: http://www.pch.gc.ca/pgm/pdp-hrp/canada/abl-eng.cfm
- Patrimoine canadien: Les droits de la personne et l'incapacité: http://www.pch.gc.ca/pgm/pdp-hrp/canada/abl-fra.cfm
- School-Aged Therapy Program (B.C. Ministry of Children and Family Development): www.mcf.gov.bc.ca/spec_needs/school_aged_therapies.htm
- Adult Special Education (B.C. Ministry of Advanced Education): www.aved.gov.bc.ca/adultspecialed/welcome.htm)
- Everyone Belongs in Our Schools: A Parent's Handbook on Inclusive Education (British Columbia Association for Community Living): http://www.bcacl.org/resources/everyone-belongs-our-schools-parents-handbook-inclusive-education-bcacl
- Wrightslaw Special Education Advice and Resources: www.wrightslaw.com
- Project INSPIRE at Texas Woman's University: www.twu.edu/inspire
- Council for Exceptional Children: http://www.cec.sped.org/am/template.cfm?section=Home
- PE Central at Virginia Tech (see a variety of lesson plans and activities): www.pecentral.org
- University of Virginia, M.Ed in Kinesiology – Adapted Physical Education (see what areas of study are covered in this field): www.teach.virginia.edu/overview-ape-324
- RESNA (Rehabilitation Engineering and Assistive Technology Society of North America): www.resna.org
- AbleData (sponsored by the National Institute on Disability and Rehabilitation Research, part of the U.S. Department of Education): www.abledata.com
- National Association of School Psychologists: www.nasponline.org
- Little People of America: www.lpaonline.org
- Neil Squire Society: http://www.neilsquire.ca/
- Tetra Society of North America: http://www.tetrasociety.org/
- Adaptech Research Network: http://www.adaptech.org/
- OCAD University, Inclusive Design Research Centre: http://idrc.ocad.ca/index.php/services

MPS IV journal

Introduction

How can this journal help?

This journal has been designed to help you organize your schedule and records for monitoring tests, supportive care, medications, and infusions. There is also a section that helps you keep track of the members of your medical team, and a section to help you prepare for medical visits. There's even a diary where you can record thoughts, observations, and questions. Using the journal helps you keep all important medical information in one convenient place for easy reference. And it's simple to use!

How do I use the journal?

Just fill in each section as you have a new medical test, visit, or infusion, or whenever you add a new member to your medical team (e.g., doctor, physical therapist, speech therapist). You can write in the diary as often as you wish. You may also wish to make extra copies of the journal pages so that you don't run out of space.

See the "What this section is for, and how to use it" box in each section for more details on how you can get the most out of using the journal.

If you start to run out of space, you can make copies or download extra copies from the website of The Canadian Society for Mucopolysaccharide & Related Diseases Inc. (Canadian MPS Society): www.mpssociety.ca. You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

The journal contains the following sections:

- My portable medical summary
- My medical team
- Preparing for medical visits
- Recommended assessments
- Monitoring test log
- Supportive care log
- Medication log
- Observation diary
- Notes
- Glossary of terms used in this journal

Why are regular doctor's visits and medical tests so important for individuals with MPS IV?

The effects of MPS IV and responses to MPS IV treatment vary from person to person. All individuals with MPS IV should have certain medical tests on a regular basis. Regular medical appointments help the doctor keep track of your health and response to treatment. You can play a role in monitoring progress as well by keeping track of tests your doctor has ordered. Open communication with your team of healthcare specialists is important to ensure appropriate care.

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

My portable medical summary

This medical summary provides a way for you to keep all your key medical information in one place and carry it with you. It is a good idea revisit and revise the summary on a regular basis so that the information stays current.

You may wish to make extra copies as needed. You can also download extra copies from the Canadian MPS Society's website (www.mpssociety.ca) or you can call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Date summary updated: MM/DD/YY

Name ______________________ Date of birth MM/DD/YY

Parent/caregiver (if applicable) ______________________

Address ______________________

Phone ______________ Email ______________________

Emergency contact ____________ Phone ____________ Relationship ____________

Diagnoses: Primary: __________ Secondary: __________ Secondary: __________

Allergies

Allergies (e.g., penicillin)	Reactions

Medications

Medication	Dose	How often it is taken	How it is taken (e.g., by mouth)

My main medical team

Name/Profession	Location	Phone/Email

The following special situations apply:

- ☐ Restricted airway
- ☐ Tracheostomy
- ☐ Supplemental oxygen: Amount ______________
- ☐ Wheelchair assistance
- ☐ Limited ability to move head/neck
- ☐ Difficulties with intubation
- ☐ Other medical assistance required:

____

____

____

Surgeries

Type of surgery	Date	Health professional's name/location

Supportive care treatments

Type of supportive care (e.g, physical therapy, tracheostomy)	Date received	Health professional's name/location

Assistive technologies

Types of assistive technology used (e.g., scooter, communication device)

My medical team

What this section is for, and how to use it:

This section will help you keep track of the different health professionals who are part of your or your child's medical team. Because MPS IV affects many different aspects of the body, a number of different health professionals may be involved. For example, your medical team may include specialists such as anesthesiologists, cardiologists, and ophthalmologists. It may also include other health professionals such as physiotherapists, occupational therapists, or speech therapists. Keeping track of all of these different professionals can be a challenge, but this section helps you keep all of your information organized in one convenient place.

To use this section, simply fill in the information on each medical professional on your team. Use the business card holders provided to store the business cards from your health professionals.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Name/Profession	Address	Phone/Email	Notes
Example: Dr. John Doe Cardiologist	123 Main Street, Edmonton, AB A1A 1A1	111-123-4567 jdoe@cardiocare.ca	No appointments available on Fridays. Best way to reach him is by phone.

Name/Profession	Address	Phone/Email	Notes

Preparing for medical visits

What this section is for, and how to use it:
This section helps you prepare for your medical visits to ensure that you get the most out of each visit. Review this section before each medical visit.

You or your child will get more out of your visit if you are prepared ahead of time. Here are a few tips:

Before your medical visit

- Write down any questions you may have for your health professional (e.g., doctor, nurse, physical therapist). Put your most important questions first. See the list below ("Questions to ask your health professional") for some ideas to get you started.
- Make a note of any concerns you would like to discuss at the appointment (e.g., new symptoms).
- Think about what you would like to achieve from the visit (e.g., "During this visit, I would like to gather the information I will need to decide about hip surgery for my child.")
- If you don't already have one, put together an up-to-date list of your or your child's medical conditions, medications, recent procedures, and medication allergies. You can use the journal to keep track of this information and then bring it to your medical appointment.
- Confirm the time, date, and location of your appointment. If you have not been there before, make sure you have directions on how to get to your appointment.

Going to your visit

- Bring your journal with you so that you will have all of your medical information in one place. The journal will also help the various medical professionals involved in your care share information, which can save you time and ensure that everyone has the complete picture.
- Bring what you need to take notes (or use a recording device, with your medical professional's permission).
- Leave plenty of extra time to get to the appointment so you don't have to worry about being late. Plan to arrive a bit early to give yourself time to park, find the office, and check in at the desk.
- You may wish to bring a friend or family member with you to the visit for support. They can help you take notes and remind you to ask your questions.

At your visit

- If the health professional says anything you don't understand, ask them to explain it to you again. Sometimes having it explained in a different way can help.
- Ask the health professional the questions from your list. To make the most of your time during the visit, make sure you ask your most important questions first.
- Take notes, have a family member or friend take notes, or record the visit (with the health professional's permission). Ask if there are any written materials you can take with you.
- Find out if and when you should follow up with your health professional after the visit, and ask about the best way to contact your health professional to follow up.

After your visit

In some cases, you may need to follow up with your health professional after your visit. Reasons to follow up may include:

- getting the results of medical tests done during the visit
- asking questions that came up after the visit
- reporting on how a new treatment is working for you
- getting help if your symptoms get worse or you have side effects from the treatment

Questions to ask your health professional:

The questions you will want to ask during your visit will depend on your individual situation, the type of health professional you are seeing, and the nature of your visit. Use this list as a guide to develop your own personal list of questions.

1. What is causing my symptoms? Are these symptoms related to MPS IV or to another condition?
2. Do I need to have any medical tests?
3. Are treatments available to correct the underlying enzyme deficiency in MPS IV?
4. What treatments are available for supportive care (which helps with symptoms or improves quality of life but does not affect the underlying enzyme deficiency)?
5. Which treatments do you recommend and why?
6. For a specific treatment:
    a. What are the benefits of this treatment?
    b. What are the risks of this treatment (including long-term safety information, if available)?
    c. How will this treatment affect my daily life (e.g., frequency of treatment, how the treatment is given, where you will need to go to receive the treatment)?
    d. Are there any possible interactions between this treatment and my other medications, treatments, or medical conditions?
    e. What will the treatment help with, and how much of an improvement can I expect?
    f. When will the treatment start to work?
    g. How long will I need to use the treatment?
    h. When should I seek medical attention (e.g., if you experience certain side effects or if your symptoms get worse)?
    i. Who will pay for the treatment?
7. Are there any modifications I can make to my home or workplace to make my daily activities easier?
8. What else can I do to improve my health?
9. What other resources are available to help me learn about MPS IV?
10. When can I expect to get the results of any medical tests that were done?
11. When should I come back for another visit?
12. Other:______________________________
____
13. Other:______________________________
____
14. Other:______________________________
____
15. Other:______________________________
____

These questions may not apply to everyone. When putting together your list of questions, select the ones that apply to you or your child, and add any additional questions you may have.

Recommended assessments

What this section is for, and how to use it: MPS IV can affect many different areas of the body. For this reason, you may be referred to different specialists. These specialists may order regular medical tests to get a complete picture of how the condition is affecting your body over time. That's why you may have tests even for body areas that aren't giving you any problems right now. For example, your cardiologist (heart doctor) may recommend an echocardiogram, a test that checks for heart problems, even if you're not having any trouble with your heart. Your ophthalmologist may recommend vision tests even if your vision seems fine, just to keep track of your vision over time and catch any problems early.

This list of tests (assessments) was developed to help you keep track of the routine medical tests that your doctors may order to monitor your condition. The list shows some of the most common medical tests for people with MPS IV. You may not have all of the tests listed here, and you may have some tests that are not on this list. It is up to your doctor to decide which tests are appropriate.

You can look up unfamiliar terms in the glossary at the end of this section.

Table 1: A list of possible medical assessments for individuals with MPS IV

✓ Complete medical history review

✓ Height, weight and, for infants, head circumference

✓ Glycosaminoglycan (GAG) levels in urine

✓ Missing enzyme levels in dried blood spot (DBS)

✓ Urinary protein levels

✓ Photographs for general appearance

✓ Electrocardiogram

✓ Echocardiogram

✓ Electrophysiology

✓ Vision tests

✓ Hearing tests

✓ MRI

✓ Sleep study

✓ Pulmonary (lung) function tests

✓ X-rays

✓ Endurance measurements (walk and stair-climbing tests)

Appointment log

What this section is for, and how to use it:

This section helps you keep track of the appointments that you have made as well as ones you still need to schedule. After each medical appointment, place an asterisk (*) in the month where the follow-up with that health professional should take place. Once this has been scheduled, replace the asterisk with the date and time.

Start a new appointment log for every calendar year. You may wish to store past appointment logs in one place so you can easily refer to them if need be.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Period: MM/DD/YY **to** MM/DD/YY

Health professional	Phone number	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec

Monitoring test log

What this section is for, and how to use it:
This section gives you a place to write down the results of medical tests. Simply write down the test name, date, and results in the spaces of the table (or if you have a printout, you can staple it to the journal).

You may wish to make extra copies of the monitoring test log pages so that you don't run out of space.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Period: *MM/DD/YY* ***to*** *MM/DD/YY*

Test/Assessment	Date	Comments/Observations
Example: Visual acuity	August 1, 2012	Vision is 20/60 in the left eye, and 20/100 in the right eye. Some corneal clouding is present.

Test/Assessment	Date	Comments/Observations

Supportive care log

What this section is for, and how to use it:
"Supportive care" refers to important treatments and interventions that are used to manage the symptoms of MPS IV, but do not affect the underlying enzyme deficiency. Examples of supportive care include physical therapy, speech therapy, respiratory therapy, CPAP or BiPAP machines for sleep apnea or tracheostomies. This section helps you keep a record of your supportive care treatments. It will also inform medical professionals of the supportive care treatments that have been received.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

*Please note that individuals should always consult their physicians before starting any form of supportive therapy. Persons requiring diagnosis or treatment or with questions specific to a single individual are urged to contact their local healthcare providers.

Type of supportive care	Date	Health professional's name and location	Results/Health professional's observations
Example: Insertion of ventilation ear tubes	August 7, 2012	Dr. Anna Sample, Memorial Hospital, Montreal, QC	Ventilation ear tubes successfully inserted. If tubes fall out, contact Dr. Sample's office.

Type of supportive care	Date	Health professional’s name and location	Results/Health professional’s observations

Medication log

What this section is for, and how to use it:
This section helps you keep a record of medications and medication allergies. Keeping a current medication list is important for your health and safety. The list will ensure that all medical professionals are aware of any medication allergies and can avoid potentially dangerous drug interactions. In the "Details" space, you can write the dosage and any observations you may have about the effects of the medication. Remember to contact your doctor if there are any side effects.

To learn more about medication safety, visit the Health Canada website at www.hc-sc.gc.ca.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Current medications (include name, dose, how it is given, and how often it is taken)	Date started	Date stopped	Details
Example: Clarithromycin (Biaxin®) 250 mg (5 mL) by mouth once daily	September 28, 2012	October 12, 2012	Cleared up my child's sinus infection. Caused some nausea and a funny taste in her mouth.

Current medications (include name, dose, how it is given, and how often it is taken)	Date started	Date stopped	Details

Medication allergies (include a brief description of the allergy)

Example:
penicillin (hives, swelling of face and throat)

Additional comments

Observation diary

What this section is for, and how to use it:
The diary is your place to write down any thoughts, feelings, or questions you may have. Not only can it help you keep track of progress over time (e.g., improvements in symptoms or abilities), it can also give you somewhere to write about feelings and concerns as you go through the care journey.

You may wish to make extra copies of these pages so that you have plenty of space in which to write.

If you start to run out of space, you can make copies or download extra copies from the Canadian MPS Society's website (www.mpssociety.ca). You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Date: MM/DD/YY

Comments: ____________________

Date: MM/DD/YY

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Notes

Glossary of terms used in this journal*

cornea: The transparent circular part of the front of the eye.

corneal: Of the cornea.

echocardiogram: Ultrasound of the heart to evaluate heart valve and heart muscle function.

electrocardiogram (ECG or EKG): A study of the currents in the heart that control its contraction.

ERT: Enzyme replacement therapy (for more information on ERT, see the "Rare disease research" section in "Treatment options").

GAG: Glycosaminoglycan (for more information on GAGs, see "What is MPS IV disease?" in "Mucopolysaccharidosis IV (MPS IV)").

GALNS: N-acetylgalactosamine-6-sulfatase, the enzyme that is deficient in MPS IVA

GLB1: beta-galactosidase, the enzyme that is deficient in MPS IVB

MRI: Magnetic resonance imaging (a technique used to view tissues inside the body, including the brain).

pulmonary: Of the lung, or relating to the lung.

sleep study: An analysis of your sleep patterns. Sleep studies are used to identify sleep-related problems such as sleep apnea (where breathing repeatedly stops for short periods during the night). Sleep studies are usually done in a special sleep lab where you stay overnight so that information can be recorded about your sleeping patterns.

urinary: Of the urine, or found in the urine.

visual acuity: The ability to see in detail (checked with a vision test).

*For further information on medical terms used in the journal and the binder, please consult the main Glossary of the binder.

An overview of MPS IV for doctors

Information handout

Additional copies of this handout are available for download on the website of The Canadian Society for Mucopolysaccharide & Related Diseases (Canadian MPS Society): www.mpssociety.ca. You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

Definition, causes, and incidence

Mucopolysaccharidosis IV (MPS IV; pronounced **mew**·ko·**pol**·ee·**sak**·ah·ri·**doh**·sis **four**) is a rare genetic disorder that affects many body systems and may lead to the damage of different body organs such as the bones, joints, and heart. MPS IV is also known as Morquio syndrome. There are two types of MPS IV. MPS IVA is caused by a defect in the gene that instructs the body to make the enzyme N-acetylgalactosamine-6-sulfatase (GALNS, pronounced en-a·**see**·tyl·ga·lak·**tose**·amine-six **sul**·fa·tace), which is also called galactosamine-6-sulfatase. MPS IVB is caused by a defect in the gene that instructs the body to make the enzyme beta-galactosidase (GLB1). Because of this gene defect, cells either produce the enzyme in low amounts or not at all. Both the enzymes are needed to break down substances called glycosaminoglycans (GAGs; pronounced **gly**·cose·a·**mee**·no·**gly**·cans). If GAGs are not broken down, they build up in the cell, eventually leading to damage in cells, tissues, and organs. The incidence of MPS IVA varies significantly. It is estimated to occur in 1 of every 76,000 to 640,000 live births.

Clinical presentation and prognosis

MPS IV is a progressive disease involving multiple organ systems. Disease severity varies significantly for people with MPS IV and it is not possible to predict the expected lifespan for a given individual. Table 1 on the following page describes the clinical manifestations of MPS IV.

Diagnosis

More common childhood conditions are usually ruled out before considering a diagnosis of MPS IV. The first step in diagnosis is either an analysis of a dried blood spot (DBS) to measure enzyme levels or urinary GAG levels. However, urinary GAG analysis is problematic for MPS IV and it is strongly recommended to proceed to enzyme activity testing even if urine

MPS IV is a rare, progressive disease genetic disorder that affects many body systems.


4 years *10 years* *28 years* *30 years*

MPS IV disease leads to progressive multisystemic disease manifestations.

Courtesy of BioMarin Pharmaceutical Inc.

Table 1: Clinical manifestations of MPS IV

General symptoms
- reduced endurance
- pain

Gastrointestinal system
- hepatosplenomegaly
- umbilical and inguinal hernias
- loose stools, diarrhea, constipation, abdominal pain

Physical appearance
- short neck
- macrocephaly
- short stature
- uneven, swaying gait

Mouth and teeth
- prominent chin, wide mouth, and enlarged tongue
- abnormal teeth (widely spaced with small sharp pointed cusps and very thin enamel)

Eyes, ears, nose, and throat
- vision problems, such as corneal clouding and vision impairment
- hearing loss
- otitis media
- frequent upper respiratory tract infections (e.g., tonsillitis)

Brain and nerves
- cervical spinal cord compression
- normal intelligence

Musculoskeletal system
- skeletal abnormalities (dysostosis multiplex with odontoid hypoplasia)
- hip dysplasia
- lax joints and loose ligaments
- bone deformities in the spine (scoliosis, gibbus, kyphosis), knees (knock-knees or genu valgum), and ankles (valgus deformity)

Respiratory system
- obstructive airway disease
- restrictive airway disease
- sleep apnea
- reduced pulmonary function
- recurrent pulmonary infections

Cardiovascular
- valvular disease
- cardiomyopathy
- cardiac arrhythmia

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appears normal when there is clinical suspicion of MPS IV. Enzyme activity tests are essential for a definitive diagnosis. If enzyme activity levels are abnormally low, the diagnosis of MPS IV is confirmed. DNA testing may be considered to determine the specific genetic mutations, especially when enzyme activity levels are inconclusive, and also for those with confirmed diagnosis as it is helpful information if others in the family are to be tested. Testing may also be considered for others in the family. Families are encouraged to visit a genetic counsellor.

Recommended schedule of assessments

Guidelines with a recommended schedule of assessments have recently been published for MPS IVA (entitled "International Guidelines for the Management and Treatment of Morquio A Syndrome"*), much of which may also be applicable for people with MPS IVB. These guidelines provide recommendations from physicians experienced in treating individuals with MPS IV and are valuable for all healthcare professionals who may encounter individuals with MPS IV. Although the guidelines support management decisions, the actual frequency of assessments and management decisions should be based on the individual's disease progression, existing symptoms, age and other factors that may arise. However, all individuals with MPS IV should be monitored for some symptoms, such as spinal cord compression.

Spinal/cervical cord compression (SCC) is a known and serious complication of MPS IV and may occur due to the natural MPS IV disease progression. Individuals with MPS IV should always be monitored for signs and symptoms of SCC, including back pain, paralysis of limbs below the level of compression, and loss of bladder and bowel control.

Some assessments, such as brain and spine magnetic resonance imaging (MRI) may require sedation or anesthesia, and thus manipulation of the neck and spine. As individuals with MPS IV are at a higher risk for complications during anesthesia, such as airway emergencies and spinal cord injury, the individual should be referred to an anesthesiologist experienced with these special circumstances. It may also be helpful to involve an otolaryngologist due to upper respiratory abnormalities.

**Christian J. Hendriksz, Kenneth I. Berger, Roberto Giugliani, Paul Harmatz, Christoph Kampmann, William G. Mackenzie, Julian Raiman, Martha Solano Villarreal, and Ravi Savarirayan. International Guidelines for the Management and Treatment of Morquio A Syndrome. Am J Med Genet Part A. 2014. DOI: 10.1002/ ajmg.a.36833*

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Table 2: Recommended schedule of assessments in patients with MPS IVA, adapted from Hendriksz et al. 2014

Assessment	At diagnosis	Follow-up frequency	Pre-ERT[a]
Medical history	X	Every visit	
Physical examination	X	Every visit	X
Upper limb function • Standardized upper extremity function test	X	Annually	X
Hips and lower extremities			
• Hips/pelvis: AP pelvis radiograph	X	As clinically indicated	
• Lower extremities: standing AP radiographs	X	As clinically indicated	
Spine/spinal cord compression			
• Plain radiograph spine	X	Every 1–3 years	
• Magnetic resonance imaging of the spine	X	Annually	
• CT neutral region of interest		As clinically indicated[b]	
Cardiac function			
• Electrocardiogram[d]	X	Every 1–3 years[c]; As clinically indicated[b]	
• Echocardiogram	X	Every 2–3 years[c]; As clinically indicated[b]	
• Heart rate	X	Annually[e]	
Respiratory function			
• FVC and MVV	X	Annually[f]	X
• Respiratory rate	X	Annually[e]	X
• Oxygen saturation[g]	X	Annually[e]	
• Overnight sleep study	X	Annually[h]	
Neurological exam	X	Every visit (at minimum every 6 months)	X
Ophthalmological function			
• Slit-lamp biomicroscopy of cornea	X	As clinically indicated	
• Intraocular pressure	X	As clinically indicated	
• Refractive error	X	As clinically indicated	
• Examination of posterior segment	X	As clinically indicated	
• Scotopic and photopic electroretinogram		As clinically indicated	
Hearing • Audiology assessment (multimodal)	X	Annually	
Dental evaluation by a dentist	X	Annually	
Endurance • 6-minute walk test, T25FW[e]	X	Annually; As clinically indicated[b]	X
Growth			
• Height and weight	X	Every visit	X
• Head circumference (infants ≤ 3 years)	X	Every visit	
• Pubertal stage (age 9 until mature)	X	Every visit	X
Disease burden			
• Pain assessment	X	Every 6 months	X
• Quality of life questionnaire	X	Annually	X
• Functional test[i]/ADL questionnaire	X	Annually	X
Evaluation by physiotherapist	X	Annually; As clinically indicated[b]	

ADL: activities of daily living; AP: anteroposterior; FVC: forced vital capacity; MVV: maximum voluntary ventilation; T25FW: timed 25-foot walk

[a] If not done within 3–6 months, these assessments should be done before treatment with enzyme replacement therapy (ERT) is started

[b] E.g., pre- and/or post-operative planning

[c] ECG and echocardiogram at diagnosis and after 1 year. If no signs of cardiac involvement, assessments can be repeated every 3 years, otherwise follow-up in expert centres according to standard of care

[d] In symptomatic patients (e.g., suspicious ECG) or post-pubertal patients, prolonged ECG (Holter monitoring for 5–7 days including normal exercising) should be done in expert centres at diagnosis and every 1–3 years

[e] Heart rate, respiratory rate, and oxygen saturation should be measured before and after each endurance test; choice of endurance measure depends on patient's physical and developmental abilities (for the 6MWT, consistently use the same hallway)

[f] Annual follow-up only required until children stop growing or when patient is on treatment. Once growth has stopped, testing frequency can be decreased to every 2 to 3 years provided that respiratory symptoms remain unchanged

[g] Oxygen saturation can be determined either by pulse oximetry or by arterial blood gas analysis

[h] Screening studies should be done in the home on an annual basis. Full polysomnography should be performed at diagnosis in an expert centre, then every 3 years, unless clinically indicated (or before major surgery). Patients with a positive test and those who need ventilatory support should be evaluated by a sleep expert

[i] Pubertal stage can be assessed using 2 scores: genitalia (male), breast (female), pubic hair (male and female) as described by Marshall and Tanner [Marshall and Tanner, 1969; Marshall and Tanner, 1970] E.g. 6MWT / T25FW, pinch / grip test, functional dexterity test

Christian J. Hendriksz, Kenneth I. Berger, Roberto Giugliani, Paul Harmatz, Christoph Kampmann, William G. Mackenzie, Julian Raiman, Martha Solano Villarreal, and Ravi Savarirayan. International Guidelines for the Management and Treatment of Morquio A Syndrome.
Am J Med Genet Part A. 2014. DOI: 10.1002/ajmg.a.36833

Treatment

There is currently no cure for MPS IV. For MPS IVA, an enzyme replacement therapy (ERT) called VIMIZIM™ (elosulfase alfa) is available, which replaces the deficient GALNS enzyme and restores cell function, allowing people with MPS IVA to have improved endurance and walking ability. ERT is not a cure for MPS IVA. Other management options for MPS IVA and IVB include those aimed at disease management and supportive or palliative care.

Supportive care includes physical therapy, occupational therapy, walking aids or wheelchairs, tracheostomies for breathing difficulties, CPAP/BiPAP for sleep apnea, speech therapy, hearing aids, mobility aids, and educational interventions. Physicians play an important role in patient support for referral and insurance coverage issues.

Enzyme replacement therapy for MPS IVA

With ERT for MPS IVA, a recombinant version of GALNS called VIMIZIM™ (elosulfase alfa) is given as a weekly intravenous infusion. This can replace the natural enzyme which is lacking in MPS IVA patients.

VIMIZIM is indicated for long-term use in patients with a confirmed diagnosis of MPS IVA. VIMIZIM is the only ERT available for MPS IVA. For patients with MPS IVA, treatment has been shown to improve endurance and walking ability—in clinical trials, patients walked 23.9% farther on VIMIZIM 2mg/kg/week—and to reduce the levels of GAGs in the body.

The safety and efficacy of VIMIZIM™ (elosulfase alfa) were assessed in a clinical trial of 176 patients with MPS IVA. The ages of the patients ranged from five to 57 years. The majority of the patients (82%) had a medical history of musculoskeletal conditions. At the start of the trial, all could walk more than 30 m but less than 325 m in six minutes.

During the trial, some patients received VIMIZIM 2 mg/kg once per week, some received 2 mg/kg once every other week, and some received a placebo. The study measured the change at Week 24 in the distance walked in a six-minute walk test by those who had received VIMIZIM compared with those who had received the placebo. The study also looked at the change at Week 24 in the rate of stair climbing in a three-minute stair climb test, as well as in levels of keratan sulfate (KS), the GAG that is excreted in the urine of people with MPS IVA.

At Week 24, the change in the distance walked in six minutes, compared to the placebo group, was 22.5 m in those who had received VIMIZIM 2 mg/kg once per week. There was no difference in the rate of stair climbing between those who had received VIMIZIM 2 mg/kg once per week and those who had received the placebo. Patients who received VIMIZIM 2 mg/kg once every other week performed similarly in the walking and stair-climbing tests as those who received placebo. The reduction in urinary KS was higher in the VIMIZIM treatment groups compared to the placebo group. However, the relationship between urinary KS and other measures of clinical response has not been established.

Of these 176 patients, 173 enrolled in an extension trial in which some received VIMIZIM 2 mg/kg once per week and others received

VIMIZIM™ (elosulfase alfa) improves endurance in those with MPS IVA. In clinical trials, patients walked 23.9% farther on VIMIZIM 2mg/kg/week.

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VIMIZIM™ (elosulfase alfa) 2 mg/kg once every other week. Patients who continued to receive VIMIZIM 2 mg/kg once per week for another 48 weeks (for a total of a 72-week exposure to the medication), showed no further improvement in walking ability beyond the first 24 weeks of treatment.

Important safety information

VIMIZIM™ (elosulfase alfa) is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of mucopolysaccharidosis IVA (Morquio A syndrome, or MPS IVA).

Warning: Risk of anaphylaxis and hypersensitivity

Life-threatening anaphylactic reactions have occurred in some patients during VIMIZIM™ (elosulfase alfa) infusions. Anaphylaxis, presenting as cough, redness of the skin, throat tightness, hives, flushing, an appearance of a bluish colour to the skin or mucus membranes, low blood pressure, rash, shortness of breath, chest discomfort, and gastrointestinal symptoms (e.g., nausea, abdominal pain, retching, and vomiting) in conjunction with hives, have been reported during VIMIZIM infusions, regardless of the duration of the course of treatment. Closely observe patients during and after VIMIZIM administration and be prepared to manage anaphylaxis. Inform patients and parents/caregivers of the signs and symptoms of anaphylaxis and severe hypersensitivity and have them seek immediate medical care should symptoms occur. Patients with acute respiratory illness may be at increased risk of serious acute exacerbation due to hypersensitivity reactions, and require additional monitoring and/or delaying infusion.

Serious warnings and precautions

Anaphylaxis and hypersensitivity reactions

Treatment with this medication should be supervised by a doctor who has experience with MPS. Administration of VIMIZIM™ (elosulfase alfa) should be carried out by an appropriately trained health professional with the ability to manage medical emergencies. Home administration by a health professional trained in recognizing and managing serious infusion reactions may be considered only for patients who are tolerating their infusions well under the direction of the practicing physician.

Due to the potential for life-threatening anaphylactic reactions, appropriate medical support should be readily available during and after VIMIZIM™ (elosulfase alfa) administration. In clinical studies, cases of anaphylaxis occurred as early as 30 minutes from the start of infusion and up to three hours after infusion. Anaphylaxis occurred as late into treatment as the 47th infusion.

In clinical trials, hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as six days after infusion. Frequent symptoms of hypersensitivity reactions (occurring in more than two patients) included anaphylactic reactions, urticaria, peripheral edema, cough, dyspnea, and flushing.

Because of the potential for hypersensitivity reactions, a health professional should administer antihistamines with or without antipyretics prior to infusion. Management of hypersensitivity reactions should be based on the severity of the reaction and include slowing or temporary interruption of the infusion and/or administration of additional antihistamines, antipyretics, and/or corticosteroids for mild reactions. However, if severe hypersensitivity symptoms occur, a health professional should immediately stop the infusion of VIMIZIM and initiate appropriate treatment.

Infusion reactions can occur at any time during VIMIZIM treatment. The majority of infusion reactions were mild to moderate. Severe adverse events during infusion have included anaphylactic reaction, rash, chills, hypersensitivity, and status asthmaticus. The most common infusion reactions were headache, nausea, vomiting, pyrexia, chills, and abdominal pain. Other infusions reactions reported were urticaria, dyspnea, hypotension, cyanosis, bronchospasm, and syncope.

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Consider the risks and benefits of re-administering VIMIZIM™ (elosulfase alfa) following a severe anaphylactic or hypersensitivity reaction. Re-administration after a severe reaction should proceed with caution and close monitoring.

Patients with acute febrile or respiratory illness at the time of VIMIZIM infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Careful consideration should be given to the patient's clinical status prior to administration of VIMIZIM and consider delaying the VIMIZIM infusion.

Sleep apnea is common in MPS IVA patients. Evaluation of airway patency should be considered prior to initiation of treatment with VIMIZIM. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an acute reaction, or extreme drowsiness/sleep induced by antihistamine use.

Spinal or cervical cord compression (SCC) is a known and serious complication of MPS IVA and may occur as part of the natural history of the disease. In clinical trials, SCC was observed both in patients receiving VIMIZIM and in patients receiving placebo. Patients with MPS IVA should be monitored for signs and symptoms of SCC (including back pain, paralysis of limbs below the level of compression, urinary and fecal incontinence) and given appropriate clinical care.

All patients treated with VIMIZIM 2 mg/kg once per week in the placebo-controlled trial developed anti-drug antibodies and tested positive for neutralizing antibodies at least once during the clinical trial. The relationship between the presence of neutralizing antibodies and long-term therapeutic response could not be determined.

There are no studies with VIMIZIM in pregnant women. VIMIZIM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if VIMIZIM™ (elosulfase alfa) is present in human milk. Exercise caution when administering VIMIZIM to a nursing mother. There is a Morquio A Registry that collects data on pregnant women and nursing mothers with MPS IVA who are treated with VIMIZIM. Contact MARS@BMRN.com or call 1-800-983-4587 for information and enrollment.

The safety and efficacy of VIMIZIM have been demonstrated in MPS IVA patients five years of age and older. The safety and efficacy of VIMIZIM have not been established in children younger than five years of age. The majority of patients who received VIMIZIM during clinical studies were in the pediatric and adolescent age range (five to 17 years). Serious adverse events were more frequent in children <12 years of age.

In clinical trials, the most common adverse reactions (≥10%) occurring during infusion included pyrexia, vomiting, headache, nausea, abdominal pain, and chills. The acute reactions requiring intervention were managed by either temporarily interrupting or discontinuing infusion, and administering additional antihistamine, antipyretics, or corticosteroids.

Reporting suspected side effects

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by any of the three following ways:

- Report online: www.healthcanada.gc.ca/medeffect
- Call toll-free: 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

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Notes to my doctor:

Every person with MPS IV and their family has different experiences with the disease and its management. Here are some insights into our experiences, which may include information about severity, treatment experiences and goals, complications encountered, feelings about MPS IV, and topics we'd like to discuss with you.

Notes

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An overview of MPS IV for teachers

Information handout

Additional copies of this handout are available for download on the website of The Canadian Society for Mucopolysaccharide & Related Diseases (Canadian MPS Society): www.mpssociety.ca. You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

What is MPS IV?

Mucopolysaccharidosis IV (MPS IV; pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis **four**) is a rare genetic disorder. It is an inherited autosomal recessive disease in which a child gets two faulty copies of a gene, one from each parent. It is caused by a deficiency of the enzyme N-acetylgalactosamine-6-sulfate sulfatase (which results in MPS IVA) or a deficiency of the enzyme beta-galactosidase (which results in MPS IVB). These enzymes are needed to break up substances called glycosaminoglycans (GAGs; pronounced **gly**-cose-a-**mee**-no-**gly**-cans), which are long chains of sugar molecules. Without enzymes, GAGs build up in cells throughout the body, leading to damage in many body systems and organs.

The severity of the condition varies widely between affected individuals. MPS IV signs and symptoms also vary and may include:

- abnormal bone structure
- looseness in the joints and movement problems
- "thickened" facial features, a large head, and a very short stature
- hearing loss and vision problems
- breathing problems
- heart damage

See Table 1 below for a more detailed list of MPS IV signs and symptoms.

Table 1: Clinical manifestations of MPS IV

General symptoms
- reduced endurance
- pain

Gastrointestinal system (abdomen and intestines)
- enlarged liver and spleen
- umbilical and inguinal hernias
- loose stools, diarrhea, constipation, abdominal pain

Physical appearance
- short neck
- macrocephaly
- short stature
- uneven, swaying gait

Mouth and teeth
- prominent chin, wide mouth, and enlarged tongue
- abnormal teeth (widely spaced with small sharp pointed cusps and very thin enamel)

Eyes, ears, nose, and throat
- vision problems, such as corneal clouding and vision impairment
- hearing loss
- frequent ear infections (otitis media)
- frequent upper respiratory tract infections (e.g., tonsillitis)

Brain and nerves
- spinal cord compression
- normal intelligence

Musculoskeletal system (bones and joints)
- skeletal abnormalities (dysostosis multiplex with odontoid hypoplasia)
- hip dysplasia
- lax joints and loose ligaments
- bone deformities in the spine (scoliosis, gibbus, kyphosis), knees (knock-knees or genu valgum), and ankles (valgus deformity)

Respiratory system (lungs and breathing)
- obstructive airway disease
- restrictive airway disease
- sleep apnea
- reduced pulmonary function
- recurrent pulmonary infections

Heart and blood vessels
- valvular disease
- cardiomyopathy
- cardiac arrhythmia

**Hernias: When part of an organ (such as the intestine) protrudes from a weak spot in the muscular wall surrounding the abdomen, producing a bulge in the skin, this is called a hernia. With an umbilical hernia, the bulge is in the belly-button area. With an inguinal hernia, the bulge is in the groin area.*

How can MPS IV affect a child's school performance?

Children with MPS IV have normal intelligence, but those with severe physical and sensory disabilities may have impaired psychomotor performance. Psychomotor performance is the ability to coordinate mental activity with physical activity (e.g., catching a ball, playing an instrument, or dancing).

Children with MPS IV have normal intelligence, but those with severe physical and sensory disabilities may have impaired psychomotor performance.

Changes in physical appearance (such as the bone and joint problems and thickened facial features) make children with MPS IV look different from their peers, which could lead to feelings of isolation, or teasing.

Physical symptoms such as limited mobility, heart problems, and breathing problems may make it hard for children with MPS IV to do the physical tasks and activities that their classmates find easy, such as handwriting, artwork, putting on a coat, or attending gym class.

Serious injury to the spinal cord is a known complication of MPS IV that can occur during regular physical activities. People with MPS IV are monitored for signs and symptoms of spinal cord complications and should be aware of any personal physical limitations. Should a person with MPS IV fall and not be able to get up independently, you should not assist the person as there is the potential for causing further injury to the spinal cord. You should immediately call for assistance from a trained healthcare professional, explaining that the child is at risk for serious injury to the spinal cord due to MPS IV.

If the physical problems are severe, a child with MPS IV may require a personal care worker or nurse on an ongoing basis.

Relevant legislation

Canadian legislation stipulates that educational facilities have a "duty to accommodate." Inclusive education is legally required in Canada; therefore, schools must have a means of identifying those students who are not completely able to adjust to a standard classroom situation as a result of a disability. Canadian human rights laws imply that schools and other education authorities have a legal obligation or "duty to accommodate," which ensures they take appropriate steps to eliminate discrimination resulting from a rule, practice, or barrier that has, or can have, an adverse impact on individuals with disabilities.

How teachers can help children with MPS IV

Teachers are part of the educational team for the child with MPS IV. It is important to be aware that for people with MPS IVA, a treatment is available that restores the deficient enzyme. This medication, called VIMIZIM$^{\text{TM}}$ (elosulfase alfa), is delivered through a weekly intravenous (IV) infusion that takes approximately four hours. This medical treatment may require the child to be regularly absent from school. Ensuring that a child with MPS IVA has homework assigned in advance or is aware of required school work may help the child to better keep up with the class.

Here are a few additional ways that teachers may be able to help children with MPS IV:

- Teachers may want to encourage children with MPS IV to socialize with healthy children by organizing group activities where students work together and support each other.
- Teachers may want to monitor changes in school behaviour and performance so the individualized education program (IEP) can be adjusted if necessary.
- Class assignments and projects (such as art projects) can be modified to allow children with physical limitations to participate in similar projects with their peers.

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- Keep in mind that children with MPS IV have normal intelligence, even though they may appear to be severely affected physically. Academic and vocational programming for the child should foster independence, and career goals should be set realistically high. Planning for the transition from school to post-secondary education or work should focus on helping children with MPS IV pursue vocations in a manner similar to that of their peers. Although children and adults with MPS IV may have difficulties with heavy manual labour such as picking up heavy objects, they may excel in careers like computer programming. Encouraging pursuit of appropriate career objectives may help a child with MPS IV feel more confident in his or her abilities.
- For severely affected children, most behaviour problems are likely caused by lack of understanding, difficulty with communication, or sensory limitations. There should be an emphasis on modifying the classroom environment and using reinforcements to promote appropriate behaviour. Teachers may wish to request a consultation with a professional experienced in dealing with these behaviour issues.
- Children with MPS IV should be disciplined consistently and appropriately according to their age and abilities. Teachers and parents should arrange to coordinate discipline strategies in advance to maintain consistency between home and school.
- Teachers need support too! The child with MPS IV may have a personal care worker or nursing assistant if required. Your school may have access to physical and occupational therapists as well as specialists in developmental disorders and speech therapists. Having a teacher's aide for the student may also be an option.

For more information on IEPs, placement issues and support for children with MPS IV, see the publication, *Education Strategies and Resources: A Guide for Parents*, available at http://www.mps-society.org/wp-content/uploads/2011/07/Education_2008.pdf. The British Columbia Association for Community Living publishes a handbook called *Everyone Belongs in Our Schools*. This resource is helpful for those involved in the care of children with MPS IV. It is available free of charge at www.bcacl.org. The British Columbia government also provides a guide for educational transition planning entitled *Your Future Now: A Transition Planning and Resource Guide for Youth with Special Needs and Their Families*. It can be found at www.mcf.gov.bc.ca/spec_needs/adulthood.htm.

Resources

- Canadian Education Association: www.cea-ace.ca
- Persons with Disabilities Online: www.pwd-online.ca
- The National Educational Association of Disabled Students: www.neads.ca/en
- Inclusive Education Canada: www.inclusiveeducation.ca
- Learning Disabilities Association of Canada: www.ldac-acta.ca
- School-Aged Therapy Program (B.C. Ministry of Children and Family Development): www.mcf.gov.bc.ca/spec_needs/school_aged_therapies.htm
- Adult Special Education (B.C. Ministry of Advanced Education): www.aved.gov.bc.ca/adultspecialed/welcome.htm
- Everyone Belongs in Our Schools: A Parent's Handbook on Inclusive Education (British Columbia Association for Community Living): www.bcacl.org/resources/everyone-belongs-our-schools-parents-handbook-inclusive-education-bcacl
- RESNA (Rehabilitation Engineering and Assistive Technology Society of North America): www.resna.org
- Wrightslaw Special Education Advice and Resources: www.wrightslaw.com
- Project INSPIRE at Texas Woman's University: www.twu.edu/inspire
- PE Central at Virginia Tech (a variety of lesson plans and activities): www.pecentral.org
- National Association of School Psychologists: www.nasponline.org
- Family Guide to Assistive Technology (by Parents, Let's Unite for Kids): www.pluk.org/AT1.html

For additional information, please call the Canadian MPS Society at 1-800-667-1846 or visit www.mpssociety.ca.

Notes to my teacher:

Every person with MPS IV and their family has different experiences with the disease and its management. Here are some insights into my experiences that we want to share with you.

Notes

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Notes to my class:

Every person with MPS IV has different experiences with the disease and its management. Here are some insights into my experiences that I want to share with you!

My Family Photo

Put your favourite family photo here to share with your class.

My favourite things to do are ______

My favourite foods are ______

I like to play ______

I don't like to play ______

Some things I want you to know about MPS are ______

______

______

Some things I want you to know about me are ______

______

______

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An overview of MPS IV for case managers and support workers

Information handout

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MPS IV is inherited when a child gets two faulty copies of a gene, one from each parent.

The severity of the condition varies widely between affected individuals. MPS IV signs and symptoms also vary and may include:

- abnormal bone structure
- looseness in the joints and movement problems
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Services that may help MPS IV families

Individuals with MPS IV and their families may need help from case managers and support workers to access a variety of services, including physical supportive care, emotional support, and financial or practical support.

Physical supportive care

Depending on the severity of the condition, the doctor may request access to physical therapy, occupational therapy, respiratory therapy and devices such as CPAP or BiPAP machines; hearing aids, speech therapy, or sign language tutoring; and home nursing care, personal care workers, or special education experts.

Emotional support

Parents and family members may need emotional support to help them cope. Families may need access to respite care, individual counselling, and support groups.

Financial assistance

Many families may benefit from financial assistance from health insurance or government programs to help cover the costs of medical treatment and devices for MPS IV. There are also services available to help with expenses that are not covered by public or private insurance plans, and to provide respite funding.

MPS IV resources and relevant legislation

Federal, provincial, or territorial legislation may affect access to healthcare, education, and services for families affected by MPS IV. See Table 2 for details about legislation that may assist you in supporting a person with MPS IV and their family. The following organizations and resources may also help you assist families affected by MPS IV.

The Canadian Society for Mucopolysaccharidosis and Related Diseases (Canadian MPS Society)

The Canadian MPS Society provides programs and services to families affected by all forms of MPS and related diseases, including:

- Providing information and education for affected families and health care providers
- Providing emotional support
- Advocating for and helping gain access to appropriate care and treatment
- Facilitating personal connections to other affected families
- Overseeing the *Family Assistance Program* to help offset costs associated with respite care, home renovations, durable medical goods, or other costs associated with disease management and caring for someone living with MPS

Visit our website at www.mpssociety.ca for more information about our programs, including guidelines and applications for the *Family Assistance Program*. We are also available toll-free at 1-800-667-1846 for more information about our available resources.

BioMarin Pharmaceutical (Canada) Inc.

BioMarin Pharmaceutical (Canada) Inc. has established the Reimbursement and Patient Services (RPS) program to provide support for individuals with MPS IVA in accessing treatment with the medication VIMIZIM™ (elosulfase alfa). This program is administered through BioMarin's partner, Innomar Strategies Inc. RPS is a private, confidential, and free support service for individuals with MPS IVA and their families, caregivers, and healthcare providers. RPS provides:

- Assistance with drug plan coverage and reimbursement
- Coordination and delivery of VIMIZIM
- Clinic and home infusion services
- Educational information on MPS IVA and VIMIZIM

For more information on RPS, call 1-877-597-6744 between 8:00 am and 8:00 pm EST, Monday to Friday (excluding statutory holidays).

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Table 2: Workplace legislation, educational legislation, and social support

Workplace legislation	• Section 15 of the Canadian Charter of Rights and Freedom guarantees equality rights plus freedom from discrimination for people who have a physical or mental disability. The Employment Equity Act (EEA) of 1995 ensures that persons with disabilities are granted full and equal access to employment and opportunity. An employer must accommodate the disabilities of employees, prospective employees, and clients or customers. In Canada, compassionate leave legislation is overseen at the provincial and territorial level. A summary of the elements of the compassionate care leave provisions in employment standards in legislation published by Human Resources and Skills Development Canada can be found online at http://www.hrsdc.gc.ca/eng/labour/employment_standards/publications/compassionate.shtml.
Educational legislation	• Inclusive education is legally required in Canada. Therefore schools must have a means of identifying those students who are not completely able to adjust to a standard classroom situation as a result of a disability. • Canadian human rights laws imply that schools and other education authorities have a legal obligation or "duty to accommodate," which ensures they take appropriate steps to eliminate discrimination resulting from a rule, practice, or barrier that has, or can have, an adverse impact on individuals with disabilities.
Social support	The Service Canada website offers links to a number of financial programs to support people with disabilities. See details at www.servicecanada.gc.ca/eng/audiences/disabilities/index.shtml. The following are some of the programs available in Canada that provide financial assistance for people with disabilities and/or their families: • Child Disability Benefit (Canada Revenue Agency): http://www.cra-arc.gc.ca/cdb • Registered Disability Savings Plan (Canada Revenue Agency): http://www.cra-arc.gc.ca/E/pub/tg/rc4460/rc4460-e.html • Grant for Students with Permanent Disabilities (Service Canada): http://www.servicecanada.gc.ca/eng/goc/grant_disabilities.shtml • Residential Rehabilitation Assistance Program for Persons with Disabilities (Canada Housing and Mortgage Corporation): http://www.cmhc-schl.gc.ca/en/co/prfinas/prfinas_003.cfm • Children's Medical Equipment Recycling Loan Service: http://www.redcrossequipment.com/ • Canadian Bar Association — Financial help for people with disabilities: http://www.cba.org/bc/public_media/employment/289.aspx • Planned Lifetime Advocacy Network: www.plan.ca/ • President's Choice® Children's Charity: http://www.presidentschoice.ca/LCLOnline/aboutUsCharity.jsp • Canada Revenue Agency - Persons with disabilities (information on tax relief benefits): http://www.cra-arc.gc.ca/disability • Human Resource and Skills Development Canada - Disability Issues: http://www.hrsdc.gc.ca/eng/disability_issues/index.shtml • March of Dimes (Canada): http://www.marchofdimes.ca • Fuel Tax Refund for Persons with Disabilities (British Columbia): http://www.sbr.gov.bc.ca/documents_library/bulletins/mft_004.pdf • Easter Seals Ontario: http://www.easterseals.org/

Other organizations and resources

Vocational Rehabilitation Association Canada is a national organization of professionals who work to deliver timely and effective vocational rehabilitation services. The association supports and advocates for its members. Details on its provincial chapters can found online at www.vracanada.com/societies.php

The British Columbia government provides a guide called *Transition Planning for Youth with Special Needs: Community Support Guide*. This guide was developed to provide community partners (school personnel, social workers, and community members) with useful information and practical tips for supporting successful transition planning for youth with special needs. It is available at www.mcf.gov. bc.ca/spec_needs/pdf/support_guide.pdf

Notes

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An overview of MPS IV for employers

Information handout

Additional copies of this handout are available for download on the website of The Canadian Society for Mucopolysaccharide & Related Diseases (Canadian MPS Society): www.mpssociety.ca. You can also call the Canadian MPS Society's office at 1-800-667-1846 to receive hard copies by mail.

What is MPS IV?

Mucopolysaccharidosis IV (MPS IV; pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis **four**) is a rare autosomal recessive genetic disorder caused by a deficiency of the enzyme N-acetylgalactosamine-6-sulfate sulfatase (which results in MPS IVA) or a deficiency of the enzyme beta-galactosidase (which results in MPS IVB). This disorder can damage many systems and organs of the body. MPS IV is inherited when a child gets two faulty copies of a gene, one from each parent.

The severity of the condition varies widely between affected individuals. MPS IV signs and symptoms also vary and may include:

- abnormal bone structure
- looseness in the joints and movement problems
- "thickened" facial features, a large head, and a very short stature
- hearing loss and vision problems
- breathing problems
- heart damage

See Table 1 for a more detailed list of MPS IV signs and symptoms.

Table 1: Clinical manifestations of MPS IV

General symptoms

- reduced endurance
- pain

Gastrointestinal system (abdomen and intestines)

- enlarged liver and spleen
- umbilical and inguinal hernias
- loose stools, diarrhea, constipation, abdominal pain

Physical appearance

- short neck
- macrocephaly
- short stature
- uneven, swaying gait

Mouth and teeth

- prominent chin, wide mouth, and enlarged tongue
- abnormal teeth (widely spaced with small sharp pointed cusps and very thin enamel)

Eyes, ears, nose, and throat

- vision problems, such as corneal clouding and vision impairment
- hearing loss
- frequent ear infections (otitis media)
- frequent upper respiratory tract infections (e.g., tonsillitis)

Brain and nerves

- spinal cord compression
- normal intelligence

Musculoskeletal system (bones and joints)

- skeletal abnormalities (dysostosis multiplex with odontoid hypoplasia)
- hip dysplasia
- lax joints and loose ligaments
- bone deformities in the spine (scoliosis, gibbus, kyphosis), knees (knock-knees or genu valgum), and ankles (valgus deformity)

Respiratory system (lungs and breathing)

- obstructive airway disease
- restrictive airway disease
- sleep apnea
- reduced pulmonary function
- recurrent pulmonary infections

Heart and blood vessels

- valvular disease
- cardiomyopathy
- cardiac arrhythmia

**Hernias: When part of an organ (such as the intestine) protrudes from a weak spot in the muscular wall surrounding the abdomen, producing a bulge in the skin, this is called a hernia. With an umbilical hernia, the bulge is in the belly-button area. With an inguinal hernia, the bulge is in the groin area.*

Meeting the needs of persons with MPS IV, or families of persons with MPS IV

Whether it is your employee who is affected by MPS IV, or one of their children, it is important for you as an employer to understand your responsibilities as well as your opportunities to assist your employee and their family.

It is important to understand that unlike many other MPS diseases, MPS IV does not affect the intelligence of the individual. Many people with MPS IV disease have above average ability.

Workplace legislation

Section 15 of the Canadian Charter of Rights and Freedom guarantees equality rights plus freedom from discrimination for people who have a physical or mental disability. The Employment Equity Act (EEA) of 1995 ensures that persons with disabilities are granted full and equal access to employment and opportunity. An employer must accommodate the disabilities of employees, prospective employees, and clients or customers.

In Canada, compassionate leave legislation is overseen at the provincial and territorial level. The Canadian government provides compassionate care benefits for up to six weeks for people who need temporary time off work to care for a family member who is gravely ill and who has a significant risk of death within 26 weeks. The legislation that governs job security in these situations is managed at the provincial and territorial level. For details on what compassionate care leave and job protection legislation exist in your jurisdiction, please see the links provided.

For more information on Compassionate Care Leave (part of Employment Insurance), please visit www.servicecanada.gc.ca/eng/ei/types/compassionate_care.shtml#Definition.

For more information on job protection in your region, please visit:

Alberta:
[At the time of publication of this learning guide, Alberta has no legislation for job protection in the case of a compassionate care leave. The Government of Alberta provides this information on Family leaves: www.albertahumanrights.ab.ca/employment/employee_info/accommodation/family_leave.asp]

British Columbia:
www.labour.gov.bc.ca/esb/facshts/ccl.htm

Manitoba:
www.gov.mb.ca/labour/standards/doc,compassionate-leave,factsheet.html

New Brunswick:
www.gnb.ca/0062/PDF-acts/e-07-2.pdf

Newfoundland and Labrador:
www.gov.nl.ca/lra/faq/ls_compassionatecare.html

Nova Scotia:
www.gov.ns.ca/lwd/employmentrights/compassionatecarefaq.asp

Nunavut:
www.gov.nu.ca/hr/site/HR_Manual/1300_Leave/1317-Compassionate_Care_Leave/1317%20-%20Compassionate%20Care%20Leave%20-%20March%2031%202009.pdf

Northwest Territories:
www.hr.gov.nt.ca/policy/hrm/0800%20-%20Leave/814/default.htm

Ontario:
www.labour.gov.on.ca/english/es/pubs/guide/family.php

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Prince Edward Island:
www.gov.pe.ca/labour/index.php3?number=1022358&lang=E

Quebec:
www.cnt.gouv.qc.ca/en/situations-of-life-at-work/work-and-family-obligations/index.html

Saskatchewan:
www.lrws.gov.sk.ca/rights-responsibilities

Yukon:
www.community.gov.yk.ca/es/spleave.html

A summary of the elements of the compassionate care leave provisions in employment standards in legislation published by Human Resources and Skills Development Canada can be found online at www.hrsdc.gc.ca/eng/labour/employment_standards/publications/compassionate.shtml.

Treatment of MPS IV

Although there is currently no cure for MPS IV, treatment options include those aimed at disease management and supportive care. For people with MPS IVA, there is treatment targeted at the underlying enzyme deficiency (enzyme replacement therapy, or ERT).

In ERT for people with MPS IVA, a synthetic version of the body's natural enzyme is given by weekly intravenous infusion. The medication delivered by the infusion is called VIMIZIM™ (elosulfase alfa) and has been shown to improve endurance with respect to walking ability in people with MPS IVA.

Financial assistance

Service Canada offers links to a number of financial programs to support people with disabilities. See details at www.servicecanada.gc.ca/eng/audiences/disabilities/index.shtml.

VIMIZIM™ (elosulfase alfa) Product Monograph, BioMarin Pharmaceutical (Canada) Inc. 2014

The following are some of the programs available in Canada that provide financial assistance for people with disabilities and/or their families:

- Canada Revenue Agency - Persons with disabilities (information on tax relief benefits): www.cra-arc.gc.ca/disability
- Human Resource and Skills Development Canada - Disability Issues: www.hrsdc.gc.ca/eng/disability_issues/index.shtml
- Child Disability Benefit (Canada Revenue Agency): www.cra-arc.gc.ca/cdb
- Registered Disability Savings Plan (Canada Revenue Agency): www.cra-arc.gc.ca/E/pub/tg/rc4460/rc4460-e.html
- Grant for Students with Permanent Disabilities (Service Canada): www.servicecanada.gc.ca/eng/goc/grant_disabilities.shtml
- Residential Rehabilitation Assistance Program for Persons with Disabilities (Canada Housing and Mortgage Corporation): www.cmhc-schl.gc.ca/en/co/prfinas/prfinas_003.cfm
- Children's Medical Equipment Recycling Loan Service: www.redcrossequipment.com/
- Canadian Bar Association Financial help for people with disabilities: www.cba.org/bc/public_media/employment/289.aspx
- Planned Lifetime Advocacy Network: www.plan.ca/
- President's Choice® Children's Charity: www.presidentschoice.ca/LCLOnline/aboutUsCharity.jsp
- Fuel Tax Refund for Persons with Disabilities (British Columbia): www.sbr.gov.bc.ca/documents_library/bulletins/mft_004.pdf

The Canadian MPS Society – support for your employee

The Canadian MPS Society provides programs and services to families affected by all forms of MPS and related diseases, including:

- Information and education for affected families and health care providers
- Support for families affected by MPS and related diseases, such as:
  - Providing emotional support and help accessing appropriate services

- Advocating for access to appropriate care and treatment
- Facilitating personal connections to other affected families
- Family Assistance Program to help offset costs associated with caring for someone living with MPS. Grants may be used for respite care, home renovations, durable medical goods, or other costs associated with disease management

For more information about the Canadian MPS Society, including financial program guidelines and application forms, call 1-800-667-1846 or visit www.mpssociety.ca.

Notes

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Emergency medical services notification

Please fax this to your local emergency medical services agency. If you need assistance finding who to send this to, contact your local emergency, police, or fire department for the appropriate fax number(s).

Patient's name: ____________________

Patient's age: ____________________

Patient's weight: ____________________

Patient's address: ____________________

____

Patient's phone #: ____________________

____________________ has mucopolysaccharidosis IV (MPS IV). MPS IV is a rare, autosomal recessive disorder that has progressive, pathologic manifestations in many organ systems including the respiratory, cardiovascular, gastrointestinal, and musculoskeletal systems. People with MPS IV may have reduced endurance and impaired vision and hearing.

People with MPS IV are at an increased risk during emergency medical situations due to narrow airways, increased potential for spinal injuries due to cervical spine instability, and other special circumstances.

This is a notification that the following special situations exist with this patient:

☐ HIGH RISK FOR SPINAL INJURY. STABILIZE NECK IMMEDIATELY
☐ Restricted airway
☐ Tracheostomy
☐ Supplemental oxygen: Amount ____________
☐ Wheelchair assistance
☐ Limited ability to move head/neck
☐ Difficulties with intubation
☐ Other medical assistance required and/or medications being taken:

____

____

____

____

FOR MORE INFORMATION ABOUT HOW MPS CAN IMPACT A PATIENT IN AN EMERGENCY SITUATION, VISIT WWW.MPSER.COM

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Glossary

acetyl CoA: alpha-glucosaminide acetyltransferase (acetyl CoA: α-glucosaminide acetyltransferase): Lysosomal enzyme deficient in MPS III-C.

adenoids: The collection of lymphatic tissue at the rear of the nose. Enlargement of the adenoids may cause obstruction of breathing through the nose.

adenoidectomy: A surgical procedure to remove adenoid growth.

airway patency: The openness of the airways (parts of the respiratory tract through which air passes).

alpha-L-iduronidase (α-L-iduronidase): Lysosomal enzyme deficient in MPS I.

alpha-N-acetylglucosaminidase (α-N-acetylglucosaminidase): Lysosomal enzyme deficient in MPS III-B.

amino acid: A class of chemical compounds that can be built up to form larger polymers called proteins. In most biological systems there are 20 common amino acids that can be linked in various combinations to generate larger molecules containing 100–10,000 amino acids. These larger molecules, or proteins, carry out most of the active functions within a cell or an organism.

amniocentesis: Procedure involving withdrawal of amniotic fluid, the fluid that surrounds the growing fetus in the uterus, generally performed between the 15th and 20th weeks of pregnancy by inserting a needle through the abdominal wall into the uterus. Cells that are contained in the fluid can be isolated and used for prenatal diagnosis of gender and for particular genetic conditions.

angioneurotic edema: Swelling under the skin of the face, throat, hands, or feet.

anterior: Front.

apneic episodes: Periods of time where breathing stops.

arrhythmia: An abnormal heartbeat.

arthralgia: Joint pain.

arylsulfatase B (ASB): Lysosomal enzyme deficient in MPS IV.

atrophy: A wasting of tissues, organs, or the entire body, as from death and reabsorption of cells, diminished cellular proliferation, decreased cellular volume, pressure, ischemia (blockage of blood flow), malnutrition, lessened function, or hormonal changes.

attenuated: Diminished, not as severe.

audiometry: Hearing tests.

autosomal recessive disease: A disease which follows an autosomal recessive pattern of inheritance requiring the presence of two copies of a particular gene mutation in order to express clinical signs and symptoms of a condition. A pattern of inheritance seen in all MPS disorders with the exception of MPS II.

autosomal recessive inheritance: A pattern of inheritance in which a non-dominant (recessive) gene on a non-sex-determining chromosome (autosome) results in a person either being a carrier of a trait or being affected. Males and females are affected with equal frequency. There is usually no family history of the trait. Instead, it is revealed when two unaffected parents who are both carriers of a particular recessive gene have a child who receives two copies of the recessive gene. A pattern of inheritance seen in all MPS disorders with the exception of MPS II.

beta-galactosidase (β-galactosidase, or GLB1): Lysosomal enzyme deficient in MPS IVB.

beta-glucuronidase (β-glucuronidase): Lysosomal enzyme deficient in MPS IVI.

blood-brain barrier: The walls of the blood vessels of the brain (and the retina) are much more difficult for large molecules to pass through than are blood vessels elsewhere in the body. This has important implications for the ability of the body to mount an immune response and to provide protection to these tissues, although the reason for the difference is not well understood. The implications for human genetic disease are that it is far more difficult to provide therapeutic treatment to neural (brain) tissues than to other tissues in the body. Since many lysosomal storage diseases have a specific involvement in the neural tissues, it is critical to provide access to these tissues during treatment.

bone marrow transplant: See stem cell transplant.

bone marrow: Tissue found in the centre of most bones. It is the site in which most blood cells are made, including red blood cells, which are involved in transport of oxygen in the blood, and white blood cells, which are involved in immune response.

BiPAP: Bilevel positive airway pressure, often used for people with sleep apnea to open the airway during sleep. It uses two pressure settings, one for while the person is breathing in and the other for while the person is breathing out.

cardiac arrhythmia: See arrhythmia.

cardiomyopathy: A general term referring to disease of, or damage to, the heart muscle.

carpal tunnel: The space between the carpal bones of the wrist and the connective tissue over the flexor tendons. The carpus (wrist) consists of eight small bones known as carpals, which are joined by a band of fibrous proteins called ligaments. Nerves have to pass through the wrists in the space between the carpal bones and the ligaments.

carpal tunnel syndrome: Thickening of the ligaments in the carpal tunnel causing pressure on the nerves. This can cause irreversible nerve damage if not surgically corrected. In individuals with MPS IV, carpal tunnel syndrome often occurs because of accumulation of glycosaminoglycan (GAG) deposits.

carrier: An individual who has a recessive, disease-causing version of a gene at a particular site on one chromosome of a pair and a normal version of a gene at the same location on the other chromosome. By definition, carriers of a recessive condition do not have clinical signs and symptoms of the condition.

cerebrospinal fluid (CSF): The fluid that surrounds the brain and spinal cord and that is produced in the ventricles of the brain.

cervical spinal cord compression: Pressure on the neck area of the spinal cord from abnormal tissue growth nearby.

chorionic villus sampling (CVS): Prenatal diagnostic procedure involving sampling the chorionic villi (part of the amniotic sac, which surrounds the growing fetus), generally performed between the 10th and 12th weeks of pregnancy. The test can reveal many, but not all, genetic abnormalities. The decision to have prenatal testing, and the appropriate method of prenatal diagnosis, should be discussed with your healthcare provider. Currently amniocentesis is more widely available than CVS for prenatal testing for MPS IV.

chromosome: The linear, double-stranded structural unit of genetic material consisting of DNA and supporting proteins called chromatin. Human cells are expected to contain 46 chromosomes identified as 23 pairs; 22 pairs are autosomes and one pair are the sex chromosomes.

cognitive function: The ability to think, reason, remember, pay attention, use judgment, and have insight (understanding one's self and situation).

contracture: Muscle shortening resulting in loss of motion of the joint.

cord blood transplant: See stem cell transplant.

cornea: The transparent circular part of the front of the eye.

corneal clouding: Disruption of the clear layers of the cornea in individuals with MPS IV due to storage of glycosaminoglycans (GAG), causing a milky appearance of the eye, decreased vision, and sensitivity to light. Cloudy corneas can be replaced with a corneal transplant.

corneal transplant: Surgical procedure to remove a cloudy cornea (see corneal clouding) and replace it with a healthy, donated cornea.

CPAP: Continuous positive airway pressure, often used for people with sleep apnea to open the airway during sleep using a constant pressure setting.

cranium: The part of the skeleton that encloses the brain.

deposits: See glycosaminoglycans (GAG).

DNA: The molecule that encodes the genes responsible for the structure and function of an organism and allows for transmission of genetic information to the next generation.

dyspnea: Shortness of breath.

dysostosis: The abnormal formation of bone caused by the lack of proper ossification (conversion of cartilage or tissues into bone).

dysostosis multiplex: The abnormal formation of many bones caused by the lack of proper ossification.

echocardiogram: Ultrasound of the heart to evaluate heart valve and heart muscle function.

electroencephalogram (EEG): A record of the electric potentials in the brain recorded by attaching electrodes on the scalp. Often this procedure is used to look for seizure activity.

electrocardiogram (ECG or EKG): A study of the currents in the heart that control its contraction.

electromyography (EMG): Continuous recording of the electrical activity of a muscle by means of electrodes inserted into the muscle fibres. Used, although not required, to diagnose carpal tunnel syndrome (which can be diagnosed by nerve conduction studies).

enamel: The hard outer covering of the crown of a tooth.

enzyme: A protein that facilitates a biological reaction without itself being used up in the reaction (i.e., it acts as a catalyst). An enzyme acts by binding with the substance involved in the reaction (the substrate) and converting it into another substance (the product of the reaction).

enzyme replacement therapy: A therapeutic approach for a genetic disorder whereby the missing protein is manufactured outside the body and given intravenously (injected into a vein) to the patient on a regular basis.

fontanelle: A soft spot on a baby's head.

galactosamine-6-sulfatase: Also known as N-acetylgalactosamine-6-sulfatase (GALNS), the lysosomal enzyme deficient in MPS IVA.

gastrostomy (G-tube): A surgical procedure in which an opening is made into the stomach from the outside. It is usually performed to allow nutrition and/or medications to be given directly into the stomach when swallowing is difficult because of disease or obstruction of the esophagus (the tube from the mouth to the stomach).

gene: Basic unit of heredity that codes for a specific protein leading to a particular characteristic or function – for example, details of physical appearance or organ function.

gene therapy: A therapeutic approach to a genetic disorder whereby a corrected copy of the gene or a new gene is inserted to replace the incorrect version.

genetic code: Information carried by the DNA molecules that decides the physical traits of an offspring. The code fixes the pattern of amino acids that build body tissue proteins within a cell.

genetic skeletal survey: See skeletal survey.

genu valgum: Knock-knees (knees curving inward in relation to the thigh).

gibbus: Abnormal angular curve of the vertebrae of the spine (synonym: kyphosis).

glaucoma: A condition in which loss of vision occurs because of an abnormally high pressure in the eye.

glycosaminoglycan (GAG): A long repeating chain of complex carbohydrate (sugar) molecules that is a common constituent of secretions and the connective tissue between cells. Formerly called mucopolysaccharide.

heparan N-sulfatase: Lysosomal enzyme deficient in MPS III-A.

hepatomegaly: Enlargement of the liver.

hepatosplenomegaly: Enlargement of the liver and the spleen. (Hepatomegaly: enlargement of the liver; splenomegaly: enlargement of the spleen.)

hernia: Protrusion of a part or structure (e.g., a loop of the small intestine) through the tissues normally holding it in.

heterozygote: An individual possessing a variant gene and a normal gene at identical sites of homologous chromosomes (adjective: heterozygous).

heterogeneity: Variations in clinical features (characteristics) within a specific disease.

hip dysplasia: Abnormal hip formation.

homologous chromosomes: A pair of chromosomes, one from each parent, having the same gene loci (locations) in the same order.

homozygote: An individual possessing a pair of identical genes, either both normal or both variant, at identical sites on homologous chromosomes.

Hurler syndrome: Historical term for the severe end of the clinical spectrum of MPS I.

Hurler-Scheie syndrome: Historical term for less-severe MPS I, the part of the clinical spectrum that is intermediate between Hurler and Scheie syndromes.

Hunter syndrome: See MPS II.

hyaluronidase: Lysosomal enzyme deficient in MPS IX.

hydrocephalus: An abnormal increase in the amount of cerebrospinal fluid within the ventricles of the brain. Communicating hydrocephalus or increased pressure may be caused by obstruction to the outflow of cerebrospinal fluid from the ventricles or a failure to reabsorb it into the cerebral sinuses. It can be treated using a ventriculoperitoneal shunt.

hypoxia: A deficiency of oxygen in the tissue or blood.

inguinal hernia: Hernia occurring in the lower abdomen and groin.

I-cell disease: See ML II.

iduronate sulfatase: Lysosomal enzyme deficient in MPS II.

individual education program (IEP): A program designed for each child within the public school system who receives special educational services. Its goals are to improve teaching, learning, and appropriate goal setting for each individual. Often, a team that includes members from the school system and the family is involved in designing the IEP.

intubation: The placement of a breathing tube during anesthesia.

joint contracture: Fibrosis of a muscle tissue producing shrinkage and shortening of the muscle without generating any strength. It is usually a consequence of pain in or disuse of a muscle or limb.

kyphosis: Abnormal angular curve of the vertebrae of the spine (synonym: gibbus).

lumbar puncture: A procedure in which cerebrospinal fluid is withdrawn by means of a needle inserted into the membrane space in the region of the lower back. This procedure may be performed to measure intracranial pressure (pressure inside the head) to aid in diagnosing hydrocephalus.

lysosomal enzyme: A protein found within the cytoplasm of most cells, especially leukocytes (white blood cells), kidney cells, and liver cells. It is a key component in the function of digestive processes within the cell.

lysosomal storage disorder (LSD): An inborn error of metabolism resulting in a particular lysosomal enzyme deficiency. At this time there are more than 40 identifiable lysosomal storage disorders.

lysosome: A specialized compartment (organelle) in the cytoplasm of cells that contains enzymes responsible for breaking down substances in the cell.

melatonin: A compound involved in circadian rhythms (biological variations during a 24-hour period). It is sometimes used as a sleep aid for those with MPS disorders.

Maroteaux-Lamy syndrome: See MPS IV.

menarche: A woman's first menstrual period.

mitral valve prolapse: A condition where flaps between two parts of the heart, the left atrium and the left ventricle, don't close evenly, allowing a small amount of blood to leak back into the left atrium.

ML II: Also called **I-cell disease**. Caused by a deficiency of the lysosomal enzyme N-acetylglucosaminyl-1-phosphotransferase. An autosomal recessive disease characterized by severe psychomotor developmental delay and by many of the clinical features seen in severe MPS I.

ML III: Also called **pseudo-Hurler polydystrophy**. Caused by a deficiency of the lysosomal enzyme N-acetylglucosaminyl-1-phosphotransferase. An autosomal recessive disease with a less severe disease course than ML II, becoming apparent later in life, with survival into adulthood.

Morquio syndrome: See MPS IV.

MPS I: Historically called **Hurler, Hurler-Scheie, and Scheie syndromes**. Caused by a deficiency of the lysosomal enzyme alpha-L-iduronidase. An autosomal recessive, heterogeneous disease characterized by a wide range of clinical involvement, including corneal clouding, bone changes, stiff joints, large liver and spleen, and heart disease.

MPS II: Also called **Hunter syndrome**. Caused by a deficiency of the lysosomal enzyme iduronate sulfatase. An X-linked recessive, heterogeneous disease characterized by a wide range of clinical involvement, including large liver and spleen, stiff joints, bone changes, and heart disease.

MPS III: Also called **Sanfilippo syndrome**. An autosomal recessive disease classified into four types based on the enzyme deficiency. The features in each type are similar and characterized by severe central nervous system degeneration but only mild somatic (body-related) problems.

MPS III-A: Caused by a deficiency of the lysosomal enzyme heparan N-sulfatase.

MPS III-B: Caused by a deficiency of the lysosomal enzyme alpha-N-acetylglucosaminidase.

MPS III-C: Caused by a deficiency of the lysosomal enzyme acetyl CoA: alpha-glucosaminide acetyltransferase.

MPS III-D: Caused by a deficiency of the lysosomal enzyme N-acetyl glucosamine 6-sulfatase.

MPS IV: Also called **Morquio syndrome**. An autosomal recessive disease classified into two types based on the enzyme deficiency, each with a wide range of clinical manifestations. Both types are characterized by short-trunk dwarfism, fine corneal deposits, and preservation of cognitive function.

MPS IVA: Caused by a deficiency of the lysosomal enzyme N-acetylgalactosamine-6-sulfatase (GALNS), also known as galactosamine-6-sulfatase.

MPS IVB: Caused by a deficiency of the lysosomal enzyme beta-galactosidase (GLB1).

MPS IV: Also called **Maroteaux-Lamy syndrome**. Caused by a deficiency of the lysosomal enzyme arylsulfatase B. An autosomal recessive heterogeneous disease characterized by a wide range of clinical involvement, including corneal clouding, bone abnormalities, stiff joints, large liver, heart disease, and normal cognitive function.

MPS IVI: Also called **Sly syndrome**. Caused by a deficiency of the lysosomal enzyme beta-glucuronidase. An autosomal recessive disease characterized by large liver and spleen, bone abnormalities, and a wide spectrum of severity.

MPS IX: An autosomal recessive disease caused by a deficiency of the lysosomal enzyme hyaluronidase, characterized by short stature, soft-tissue masses, normal joint movement, and normal cognitive function.

mucolipidosis: Term coined to denote diseases that combined clinical features common to both the mucopolysaccharidoses and the sphingolipidoses (diseases characterized by abnormal lipid or fat metabolism, affecting nerve tissue). See ML II and ML III.

mucopolysaccharide: A complex carbohydrate molecule that is a common constituent of secretions and the connective tissue between cells. Although the molecules were originally called “mucopolysaccharides” because of their ability to form thick, mucous-like solutions, the terminology was revised to “proteoglycans” and subsequently to “glycosaminoglycans” or GAGs in recent decades.

mutation: A change in the genetic material (DNA) of a cell that alters expected genetic processes.

N-acetylgalactosamine-6-sulfatase (GALNS): Also known as galactosamine-6-sulfatase, the enzyme that is deficient in MPS IVA.

N-acetylglucosamine 6-sulfatase: Lysosomal enzyme deficient in MPS III-D.

N-acetylglucosaminyl-1-phosphotransferase: Lysosomal enzyme deficient in ML II/III.

odontoid dysplasia: Malformation in the bones that stabilize the connection between head and neck.

otitis media: Inflammation of the middle ear occurring commonly in children as a result of an infection and often causing pain and temporary hearing loss.

papilledema: Swelling around the optic disc (the “blind spot” where the optical nerve joins the eye).

Port-a-Cath: Brand name for a long-term indwelling catheter into a central vein with access through the skin.

posterior: Back.

precocious puberty: The early onset of sexual maturation.

preimplantation genetic diagnosis (PGD): Also known as preimplantation testing. A procedure used to decrease the chance of a particular genetic condition for which a fetus is specifically at risk by testing one cell from embryos from in vitro fertilization for the DNA mutation known in the family. Only embryos found not to carry the DNA mutation are transferred to the mother's uterus.

pseudo-Hurler polydystrophy: See ML III.

psychomotor performance: The ability to coordinate mental activity with physical activity. For example, catching a ball, driving, and dancing are all examples of activities requiring good psychomotor performance.

pulmonary: Of the lung, or relating to the lung.

pulmonary hypertension: High blood pressure in the blood vessels supplying the lungs.

recessive disease: See autosomal recessive disease and X-linked recessive disease.

recombinant DNA: DNA that contains genes from different sources that have been combined by the techniques of genetic engineering.

retina: A part of the eye that turns light into nerve signals for the brain, allowing your brain to process the images that you see.

retinal: Of the retina, or relating to the retina.

retrosternal pain: Pain behind the chest area.

rhinorrhea: Thick, chronic discharge of mucus from the nose.

scaphocephalic: Having a long, narrow head shape.

Sanfilippo syndrome: See MPS III.

Scheie syndrome: Historical term for the less severe (attenuated) end of the clinical spectrum of MPS I.

scoliosis: Lateral (sideways) deviation of the spine.

seizures: Disruption of electrical signals in the brain. Seizures may cause brief changes in a person's body movements, awareness, emotions, or senses such as taste, smell, vision, or hearing.

sinusitis: A sinus infection. Sinus infections are common in people with MPS disorders.

skeletal survey: An X-ray to examine the skeleton (the bones of the body) for problems or abnormalities.

sleep apnea: A temporary cessation of breathing during sleep, generally caused by obstruction of the airway.

Sly syndrome: See MPS IVI.

spinal fusion: Surgery to connect the spinal bones to each other to prevent slippage.

spleen: A large organ situated on the left side of the body below and behind the stomach.

splenomegaly: Enlargement of the spleen.

stem cell: A cell whose "daughter" cells have the potential to develop into a variety of specialized cell types.

stem cell transplant: A therapeutic treatment where stem cells from bone marrow, peripheral blood, or umbilical cord blood are infused into the bloodstream after the original bone marrow cells have been ablated (destroyed) by chemotherapy and/or radiation therapy. The cells migrate to the interior of certain bones and begin producing immature cells called "committed progenitors." These committed progenitors produce colonies of cells that eventually mature into red blood cells, white blood cells, or platelets. The purpose is to allow the donor cells to repopulate the bone marrow and various other tissues of the recipient. If the cells can also provide the missing gene and function to the recipient, then clinical symptoms can sometimes improve. It is important to note that the process of destroying the recipient's bone marrow cells is extremely invasive and leaves the individual with a compromised immune system and susceptible to life-threatening infections. Also, it is critical to have donor cells come from an individual with compatible tissue types in order to avoid rejection of the donor cells after the transplant.

sternum: A long, flat bone, jointed with the cartilages of the first seven ribs and with the clavicle (collar bone), forming the middle part of the anterior (front) wall of the thorax (chest area). It is the vertical bone that can be felt in the middle of the chest between the ribs.

swallowing study (modified barium swallow study): Videotaped X-ray of a individual's oral (mouth) and pharyngeal (throat) mechanism during eating or drinking. This procedure is often ordered to evaluate for obstruction or aspiration (inhalation of foods). The results from this procedure may allow a therapist to better identify ways to safely feed the individual and ways to help the family make appropriate modifications.

trachea: The air tube from the mouth to the lungs. Around the level of the middle of the chest, it divides into the right and left main bronchi.

tracheostomy: A surgical procedure in which a hole is made into the trachea through the neck to relieve obstruction to breathing. A curved breathing tube is usually inserted through the hole.

trigger finger: A condition caused by a thickening of the tendon that bends the fingers, often experienced as swelling in the palm of the hand as the finger is moved.

umbilical hernia: A hernia in which bowel or connecting tissue protrudes through the abdominal wall under the skin at the umbilicus (navel).

urinary: Of the urine, or found in the urine.

urticaria: Hives.

ventriculoperitoneal shunt: A thin tube that drains fluid from the brain into the abdominal cavity. Used in the treatment and management of hydrocephalus.

X-linked recessive disease: A disease that follows a pattern of inheritance in which a mutation in a gene on the X chromosome causes males to have clinical features of a particular condition, as they only have one X chromosome. A pattern of inheritance seen in MPS II.

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