Canadian MPS Society
for Mucopolysaccharide & Related Diseases

June, 2008

Dear Friends:

We are pleased to provide to you this resource entitled "MPS I: A resource for individuals and families living with MPS I." This comprehensive binder is designed to provide you with a source of information on the manifestations, concerns, and treatment of MPS I disease along with space for you to record and store your own experience.

Begin by reading the table of contents. You may find sections that are not relevant to you at this time but may be in the future. The chapters are separated by color so they can be easily updated when there is new information available. Please fill out and return the enclosed form so we can add you to our database to receive these updates.

The binder includes special extras, such as a business card holder, making it easy to track all the physicians you see. There are handouts about MPS I that you may copy for your physicians, teachers, and support workers. The MPS I Journal is designed to be your special place to write down information you receive during medical appointments, information about treatments, and observations for you or your child.

We encourage you to ask for copies of medical reports and evaluations and include these items in the binder. By having all information in one location, you can easily answer the questions asked by the various specialists you see.

We welcome your comments and suggestions about this resource and hope you find it to be a beneficial and functional tool.

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Canadian MPS Society
for Mucopolysaccharide & Related Diseases

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Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Mucopolysaccharidosis I (MPS I) disease

What is MPS I disease?

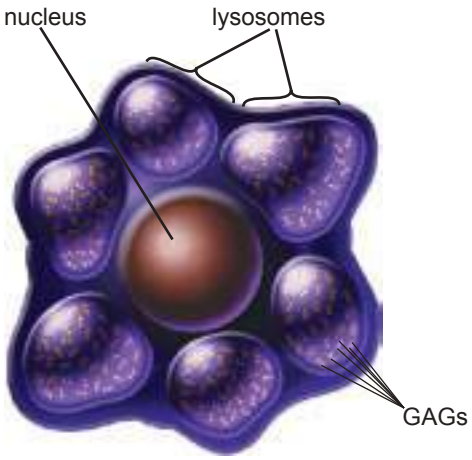
Mucopolysaccharidosis I (MPS I; pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis **one**) is a rare genetic disorder that affects many body systems and that may lead to damage of different body organs (e.g., the heart, lungs, joints, or eyes). It is caused by a defect in the gene that makes an enzyme called alpha-L-iduronidase (pronounced **al**-fa **el eye**-dur-**on**-i-dase). Because of this defect, cells either produce the enzyme in low amounts or cannot produce it at all. The enzyme is 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 cell, tissue, and organ damage.

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 mucopolysaccharides. 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 I have too much GAG in their body.

To understand how GAGs accumulate and cause MPS I, it is important to understand that in the course of normal life, there is a continuous process of building new 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 chemicals that are made by the body called enzymes.

Courtesy of Genzyme Corporation

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



Cell with GAG buildup

To break down GAGs, a series of enzymes work in sequence one after another. Each enzyme in the process has its special purpose in the body and does one very specific action, just like a screwdriver works on screws and a hammer works on nails. As mentioned earlier, people with MPS I are missing one specific enzyme called alpha-L-iduronidase, which is needed for the breakdown of certain GAGs called dermatan sulfate and heparan sulfate. If these GAGs are not completely broken down, they remain stored inside cells in the body and begin to build up. This interferes with how the cell normally works and causes damage that gets worse with time. Some individuals with MPS I may initially show few signs of the disorder, but as more and more GAGs build up, 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.

How is MPS I 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 these special parts of the cells called lysosomes. It is for this reason that MPS I is part of a larger family of diseases called the "lysosomal storage disorders" (or "LSDs" for short).

There are approximately 40 different conditions that can be caused by lysosomal storage disorders. These disorders share some common features: they are genetic; they are caused by a lack of 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, the exact enzyme is different in each case, so individual LSDs can cause completely different types of symptoms and affect different organ systems. Individual LSDs can also differ in the age that they begin to cause symptoms and in 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 family includes seven sub-types: MPS I, MPS II, MPS III, MPS IV, MPS VI, MPS VII, and MPS IX. All MPS are caused by the buildup of various GAGs in the lysosomes, but the exact GAGs that build up are different in each case. 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) – for example, corneal clouding, short stature, joint stiffness, speech and hearing problems, hernias, runny nose, and heart problems.


Courtesy of Genzyme Corporation

How do people inherit MPS I?

MPS I 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 I is one such disease.

Most families with a child with MPS I do not have a family history of any genetic problem – MPS I 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.

For each enzyme made in the body, there are two copies of the same gene 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. Because the body is

quite resilient, even the 50% level of enzyme can be more than enough to keep the person healthy.

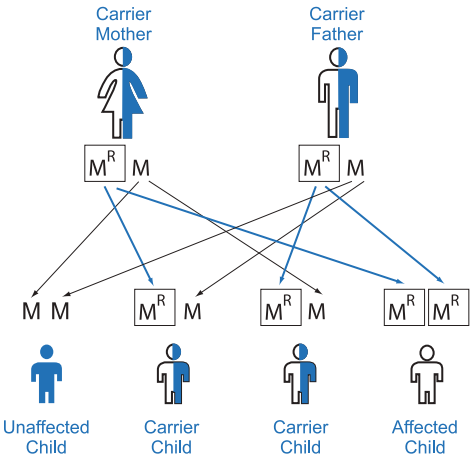
However, if the copies from both the mother and the father are not functioning correctly, the individual will have little or no enzyme in the body and will experience symptoms of MPS I disease.

The way genetic inheritance works, it is impossible to predict in advance of a pregnancy whether parents carrying the defective gene for MPS I will have an affected child. However, it is possible to calculate the probability that this will occur. As the figure describes, any child born of carrier parents has a 3 out of 4 (or 75%) chance

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

MPS I is a recessive disorder. This means it occurs only if both copies of the gene (one from each parent) inherited by the individual to produce alpha-L-iduronidase enzyme are defective. This happens 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 it properly.

The figure below shows how the MPS I gene may be passed from one generation to the next.



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 I

of having at least one normal gene and therefore no disease, while they have a 1 out of 4 (or 25%) chance of inheriting a copy of the defective gene from each parent and thus being affected with the disorder. There is also a 2 out of 3 (or 67%) chance that an unaffected offspring will still be a carrier of the defective gene that causes MPS I.

Because MPS I is an inherited disorder, family screening is extremely important. A genetic counselor can be a valuable resource to help you understand how MPS I is inherited in families and to help determine if others in the family may want to consider genetic testing for MPS I as well. Testing for MPS I is done by measuring the enzyme level in a blood or skin sample, and your doctor can arrange for this test. With early diagnosis, the disease may be better managed.

Prenatal testing allows pregnant women to find out if the baby they are carrying is affected by MPS I. 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 counselor or doctor can help you explore these options and other strategies for having additional children while limiting the probability that they will have MPS I.

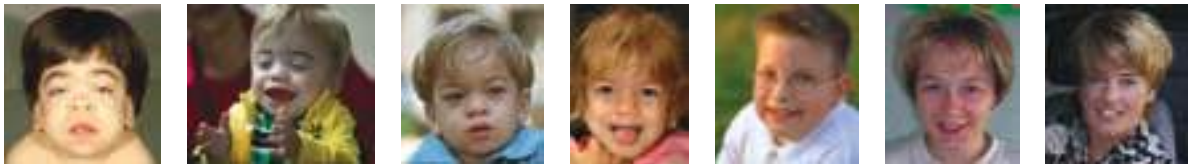
MPS I disease spectrum

MPS I has historically been divided into three groups (also known as phenotypes) according to the type, severity, and progression of the symptoms.

- The historical term for the most severe version of the disease is "Hurler syndrome," named after the doctor who first described this condition. The medical literature describes Hurler syndrome as a condition with very rapid disease progression, developmental delay, very severe physical problems, and early death.
- The historical term used for a less severe version of the disease is "Scheie syndrome," also named after the doctor who first described this condition. The medical literature describes Scheie syndrome as a condition with slow disease progression, normal cognitive function, mild symptoms, and normal lifespan. It was originally considered to be a completely different disease from Hurler, and was even referred to as "MPS V" for a while.
- The historical term used to describe individuals who do not neatly fit into the Hurler or Scheie categories is "Hurler-Scheie syndrome." The medical literature describes Hurler-Scheie syndrome as a condition with rapid disease progression, little or no developmental delay, and symptom severity and life expectancy in between what is associated with Hurler and Scheie.

Our understanding of the molecular basis and the signs and symptoms of MPS I has become more clear over time. It is becoming increasingly clear that this disease is more complex and more varied than was previously assumed, and that this Hurler–Hurler-Scheie–Scheie classification system is an oversimplification that does not adequately reflect the tremendous variation in symptoms, presentation, and progression.

It is now perhaps more appropriate to view MPS I as a continuous spectrum of disease, with the most severely affected individuals (historically known as Hurler) on one end and the less severely affected individuals (historically known as Scheie) on the other end, with a whole range of different severities in between.



1: courtesy of Dr. Emil Kakkis; 2–5: courtesy of Genzyme Corporation; 6: courtesy of Dr. N. Guffon; 7: courtesy of patient and family

It is important to understand that MPS I is a continuous spectrum of disease, and the historical "Hurler," "Hurler-Scheie," and "Scheie" terms are oversimplifications.

Some physicians choose to use the term "attenuated" to refer to all individuals who are not at the most severe end of the spectrum.

Is it possible to predict the severity of MPS I?

There is currently no 100% reliable way of telling from tests how severe MPS I will eventually become. All people with MPS I either completely lack the alpha-L-iduronidase enzyme needed to break down GAGs or only produce small amounts. Individuals who have as little as 0.1% to 0.3% of normal enzyme activity can still have an attenuated form of MPS I.

DNA tests do not always correctly identify someone with MPS I. Scores of different kinds of mutations (defects in the make-up of genes) in the gene that produces alpha-L-iduronidase have been identified, all of which result in alpha-L-iduronidase enzyme deficiency. This enzyme deficiency results in MPS I disease.

The gene has been studied extensively to see if there is any relationship between specific genetic mutations and the symptoms of the disease. There are some common mutations of the gene that result in absolutely no alpha-L-iduronidase enzyme being produced; if both copies of the defective gene inherited by an individual are of this kind, then there is some evidence to suggest that the individual's condition is likely to be at the severe end of the disease spectrum. But there are also other kinds of common mutations of the gene that cause very small amounts or defective enzyme to be produced. And then there are still other mutations that are not common at all, and only occur in a single known family. In all such cases, it is more difficult to predict severity of disease using DNA analysis.

Therefore, there is still today no perfectly reliable way to determine the exact effects that the disease will have on many individuals with MPS I. Even with the same small amount of enzyme activity, and even within the same family, there can be variations in severity of disease that cannot be explained by the enzyme level or DNA mutation. It is important to remember that whatever name is given to you or your child's condition, MPS I is a spectrum with a variety of symptoms, and the disorder is extremely varied in its effects. A whole range of possible symptoms is outlined later in this learning guide, but you or your child may not experience them all or to the degree pictured in those sections.

As MPS I is a condition that gets worse with time, all individuals will experience progression of symptoms no matter where they are on the spectrum of disease severity. However, it is important to understand that people do not progress from one "type" of MPS I to the other. For example, individuals with symptoms closer to the "attenuated" (historically known as "Scheie") end of the spectrum will never have their condition become as severe as it is for those closer to the most severe (historically known as "Hurler") end of the spectrum, or vice versa, as they get older.


Courtesy of Genzyme Corporation

Is it possible to predict lifespan?

Life expectancy varies significantly for people with MPS I and there is no 100% reliable way of predicting it for a given individual. Lifespan depends on many factors, such as position on the spectrum of disease severity, if and when an affected person receives treatment for MPS I or its symptoms, and the specific kinds of symptoms a person experiences. Those on the attenuated end of the disease spectrum (historically known as Scheie syndrome) can have a reasonably normal lifespan. Individuals who are more severely affected than attenuated patients (i.e., those with what was historically called Hurler-Scheie syndrome) die during their teenage years on average, although that average hides the fact that some may live to be adults. Unfortunately, the most severely affected children (those with what has historically been known as Hurler syndrome) rarely live more than 10 years, with some dying much younger. The availability of new treatments as well as other surgical procedures provides hope for better future outcomes for individuals affected by MPS I.

How common is MPS I?

It has been estimated through a study of babies born in British Columbia that about 1 in 100,000 babies born would have MPS I (severe and probably moderately severe MPS I, historically known as Hurler and Hurler-Scheie syndromes, respectively). The estimate for attenuated MPS I (historically known as Scheie syndrome) is 1 in 500,000 births. Studies in Australia and

the Netherlands have confirmed that MPS I occurs about 1 in every 100,000 births.

It is worth noting that while MPS I is individually rare, the larger family of lysosomal storage diseases collectively occur in about 1 in every 5000 to 7000 births.

alpha-L-iduronidase enzyme, the DNA mutations (genetic changes) responsible for the deficiency can differ among families. There are a handful of "common" mutations that cause MPS I. The term "common" does not mean that these mutations are the most frequent ones found in people with MPS I – it just means that these mutations

A clear diagnosis requires enzyme tests conducted by experts. Early diagnosis is critical.

How is a diagnosis made?

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

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

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

DNA testing can detect the specific changes in the genes that are responsible for making the missing enzyme. DNA testing is substantially more costly than enzyme testing, due to limited availability and the need for specialized lab techniques. For example, while we know that every individual with MPS I has a deficiency of have been seen over and over again in affected individuals who are not related to one another. In other words, unrelated people have these mutations "in common." Some laboratories offer specific testing for these types of mutations. Most of these "common" mutations are considered to be "severe," meaning that any combination of two genes with mutations is predicted to cause severe disease (historically known as "Hurler"). However, for many individuals with MPS I, at least one of their two genetic changes (also called mutations) is not one of the so-called "common" mutations. Instead, it is specific to their family and has not been found before (also called "novel" or "private" mutations). In these cases, it is difficult to predict the severity of the disease. Once the genetic mutations in the individual with MPS I have been identified, accurate testing is available for other interested relatives.

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


Courtesy of patient and family

An update on newborn screening

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

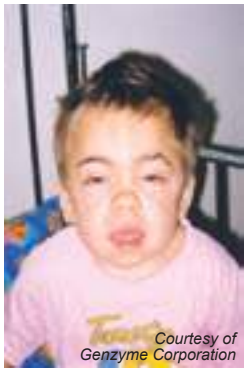
Currently, there is a growing movement promoting newborn screening for MPS disorders such as MPS I. It is now more widely recognized that to many families, information about the diagnosis alone is helpful with the opportunity for genetic counseling, education about additional treatment options, and improved quality of care with early medical help and therapy services.

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. As a community, those whose lives have been touched by MPS I will likely continue to become more involved in the promotion of newborn screening.

Signs and symptoms of MPS I and their management

Overview

MPS I has a wide range of symptoms, and people may experience different degrees of disease severity. Table 1 provides an overview of the signs and symptoms that may occur in individuals at different points on the disease spectrum. The content in later sections will provide more details about some of these signs and symptoms. Where possible, symptoms that are similar or linked or relate to a common organ system have been included together. Within the section devoted to each symptom or group of symptoms, there is also some information about disease management and relevant surgical procedures.



Severely affected child

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

Table 1: Clinical features of MPS I
A spectrum of disease from severe to attenuated MPS I

Symptom presentation	Severe MPS I	Attenuated MPS I
Stiffened joints	+++	++
Skeletal (bone) abnormalities	+++	++
Carpal tunnel syndrome	+++	++
Heart (valve) disease	+++	++
Recurrent upper airway infections	+++	+
Lung disease/ sleep apnea	+++	+
Corneal clouding	+++	+
Spinal cord compression	+++	+
Enlarged liver and spleen	+++	+
Hernia (inguinal or umbilical)	+++	+
Hearing loss	+++	+
Delayed mental development	+++	–
Coarse facial features	+++	–
Communicating hydrocephalus (fluid in the brain)	+++	–
Abnormally shaped teeth	+++	–

Physical appearance

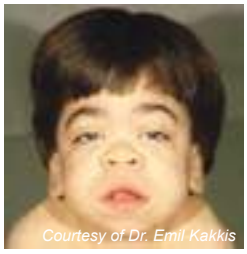
Stature

Growth in height is usually significantly less than normal for individuals with MPS I, but varies according to the severity of the disorder:

- Severely affected children (historically known as “Hurler”) may be quite large at birth, and grow faster than average at

first, but their growth usually slows down between 6 and 18 months of age and often stops altogether around 3 years of age. The individual may not grow taller than 4 feet.
- Individuals at the attenuated (historically known as "Scheie") end of the disease spectrum usually grow to a relatively normal height, reaching 5 feet or more.
- The height of individuals who fall between these two extremes (historically called "Hurler-Scheie") is variable, but many are below the 5th percentile in height (i.e., shorter than 95% of individuals their age).

Facial features



Severely affected child

Severely affected individuals look remarkably similar due to the facial features, which include short noses, flat faces, and large heads. Their heads tend to be "scaphocephalic": longer than normal from front to back, with a bulging forehead. This is because of how the bones of the skull form to create the shape of the skull. Babies' skulls are soft, and the individual bones are separated by thin tissue. In the front above the forehead and in the back near the hair whorl are the anterior (front) and posterior (back) fontanelles, or soft spots, which close during the first few years. In severely affected individuals, the bones along the top of the head fuse together earlier than normal, so the skull has to expand more in the front and the back, creating the long head shape and prominent forehead. There is often a ridge across the forehead where the skull has closed prematurely.

Woman with attenuated MPS I

Individuals with MPS I typically have a broad nose with a flat bridge and wide upturned nostrils. Their eye sockets tend to be shallow and their eyes tend to protrude slightly. They will have a large tongue, which may stick out. Their body hair is typically coarser and more abundant than usual. People with MPS I may have protruding bellies. They may also stand and walk with a bent-over stance due to joint stiffness (contractures) at the hips, shoulders, elbows, and knees. Attenuated individuals will vary considerably in appearance. Adults may be stocky in build and their trunks tend to be shorter than average. Their neck may be short and stiff. Alternatively, they may appear to be unaffected. The faces of many people with Scheie syndrome may not appear unusual.

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

Mouth

Particularly at the severe end of the disease spectrum, people with MPS I generally have thick lips and an enlarged tongue. Gum ridges are broad. The teeth are widely spaced and poorly formed, and their enamel (outer layer) is fragile. It is important that the teeth be well cared for, as tooth decay can be a cause of pain. Teeth should be cleaned regularly, and if the water in your area has not been treated with fluoride, a person with MPS I should have daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and help avoid bad breath. Even with the best dental care, an abscess (infec-

tion) around a tooth can develop because the tooth has not formed properly. Irritability, crying, and restlessness can sometimes be the only sign of an infected tooth in a severely affected child.

If an individual with MPS I has a heart problem, antibiotics should be given 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.

If teeth need to be removed while under an anesthetic, this should be done in the hospital under the care of both an experienced anesthetist and a dentist, never in the dentist's office. For more information on the risks of anesthesia, please see "Anesthesia considerations."

Skin

People with MPS I tend to have thickened and tough skin, making it difficult to draw blood or place intravenous catheters. Severely affected individuals may have extra hair on their face and back. If the hands or feet are blue or cold from time to time, a cardiologist (heart specialist) should check to see if the heart or the aorta (large blood vessel taking blood from the heart to other parts of the body) might be responsible for the problem. Heart or aorta problems can lead to poor blood circulation, which can cause cold hands and/or feet and the skin to appear to be blue.

Children with MPS I may also have "Mongolian spots." These are bluish-colored spots that appear on the skin, often in the lower back area. Mongolian spots occur because of clusters of unusually high levels of pigment-producing cells in the skin. It is not currently understood exactly why the pigment cells may cluster together in people with MPS I. One theory is that the clustering may be due to an interaction between the gene involved in MPS I and the genes associated with pigment cells. This sign should not be confused with temporary blueness of the hands or feet due to cold, which could be caused as a result of poor blood circulation due to heart problems that are also due to the underlying disease.

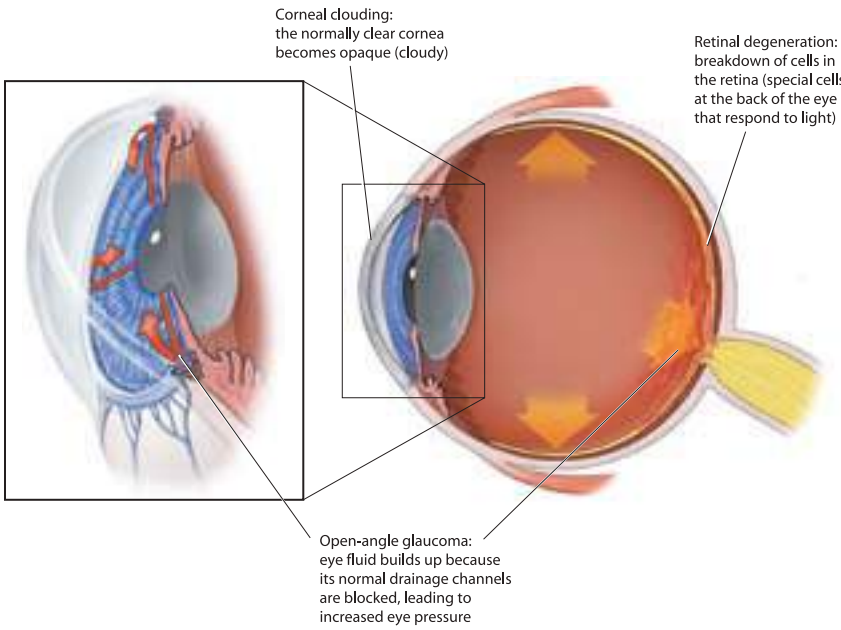
Eyes

Symptoms related to the eye are a very common feature in MPS I, and are found in people across the disease spectrum. 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 I cannot tolerate bright lights, as the clouding causes uneven refraction (bending) of the light. Wearing caps with visors or sunglasses can temporarily help. Many people with MPS I 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.

Corneal clouding

- *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. 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.



Eye problems in MPS I

It is often difficult to determine which combination of problems is responsible for the decrease in eyesight. An ophthalmologist (eye specialist) can perform special tests to help determine whether the problem with vision in an individual with MPS I is due to how light gets in the eye (i.e., related to the cornea) or on how the eye responds to light (i.e., related to the retina or optic nerve).

Ears

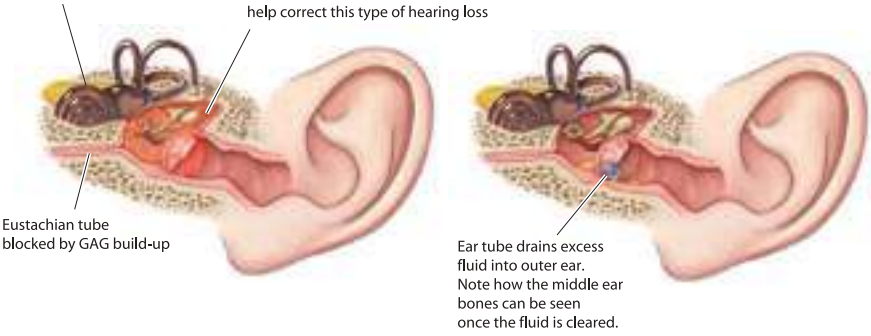
Deafness

Some degree of deafness is common across the disease spectrum of individuals with MPS I. This may be made worse by frequent ear infections. It is important that individuals with MPS I have their hearing checked regularly so that problems can be treated early to maximize their ability to learn and communicate.

With normal hearing, sound waves cause the eardrum (a thin membrane between the outer and middle ear) to vibrate. Three small bones in the middle ear amplify these vibrations. The middle ear needs to be at the same pressure as the outside air in order to work properly. The Eustachian tube, which reaches from the middle ear to the back of the throat, is used to regulate the pressure in the middle ear. The vibrations of the middle ear bones are picked up by the inner ear. Tiny hair cells in the inner ear sense these vibrations and send a message through the auditory nerve to the brain, which then interprets them as sound.

MPS I may cause problems at various points in the normal hearing process, potentially leading to hearing loss. Deafness in people with MPS I may be conductive deafness, sensorineural deafness, or mixed deafness (see definitions below).

- *Conductive deafness:* Conductive deafness occurs when something prevents the eardrum or middle ear bones from vibrating properly. This is often caused by excess fluid in the middle ear (middle ear effusion) because of a blocked Eustachian tube. The fluid interferes with the normal vibration of the eardrum. This condition can be managed by inserting ear tubes (also called tympanostomy tubes or T tubes) to drain the excess fluid.
- *Sensorineural (nerve) deafness:* In most cases, the cause of nerve deafness is damage to the tiny hair cells in the inner ear. Unlike conductive deafness, sensorineural deafness cannot be managed by inserting ear tubes. The hair cells are small, delicate, and difficult to repair. For this reason, sensorineural deafness is often not reversible. Using a hearing aid may help improve the person's ability to hear and understand speech.
- *Mixed deafness:* People who have both conductive and sensorineural deafness are said to suffer from mixed deafness. Treatment



Ear problems in MPS I

of mixed deafness involves treating both the conductive deafness (as described above under "conductive deafness") and the sensorineural deafness (as describe above under "sensorineural deafness").

Otitis media

For parents of children with MPS I

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 I. In children without MPS I, 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 with MPS I, 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 such as bulging eardrum often with pain, ear tugging, fever, irritability, decreased appetite, vomiting, and diarrhea. Complications, although rare, can include broken eardrum (tympanic membrane perforation), inflammation in the area surrounding the middle and inner ear (acute mastoiditis), a mass of cells and cholesterol in the middle ear (cholesteatoma), serious, potentially life-threatening inflammation of the membranes covering the brain (meningitis), and inflammation of the area between the skull bone and the membranes covering the brain (epidural abscess). 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. OME can lead to conductive deafness (see definition above), difficulty with learning speech and language (hearing problems interfere with speech and language development), thickening or scarring of the eardrum, and a mass of cells and cholesterol in the middle ear (cholesteatoma).

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

For some individuals with MPS I, a number of middle ear infections may occur before MPS I is diagnosed. The child may not have any symptoms, but hearing can be affected. Any child who has fluid in the middle ears for at least three months should have a hearing test. A careful examination of the ear may be difficult for a child with MPS I, but is essential for proper diagnosis. Ear, nose, and throat (ENT) specialists, also called otolaryngologists, can help diagnose

MPS I by identifying children with recurrent infections and abnormalities seen under examination. Once a diagnosis of MPS I 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 I 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.

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. Tympanostomy tube insertion 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. 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 I to determine which tube is best. (Please note that this should *always* be done at a properly equipped hospital and only after consultation with the anesthesiologist, because of anesthesia concerns for children with MPS I, which are also described in a separate section in this resource). After the procedure, a culture should be made from the drained fluid to identify the offending organism.

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

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 otitis media. 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. They 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 (steroid drugs which reduce inflammation) may also be helpful.

Removal of the adenoids (tissues at the back of the nasal cavity) and tonsils might also be recommended for children with MPS I 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

Children can receive a vaccine for *Streptococcus pneumoniae*, which is one of the more common bacteria that cause ear problems. This might help reduce the number of future bacterial infections. Vaccines may cause a mild fever or pain, redness, or swelling at the site of injection. More serious side effects include allergic reactions (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 seem to be a persistent problem in children with MPS I, 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.

lage rings in the trachea. Bumps or folds of excess tissue can further block the airway.

Respiratory system

Overview

Airway obstruction (blockage) is commonly seen in individuals with MPS I, who tend to have short necks and unusually narrow airways. In addition, the tonsils and adenoids (tissues at the back of the nasal cavity) can become enlarged and block the airway, which can also contribute to breathing difficulties. Finally, particularly for individuals at the more severe end of the disease spectrum, the shape of the chest is often abnormal, and the junction between the ribs and the breastbone (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. Individuals with MPS I can also have a small thorax (the part of the body that lies between the neck and the abdomen, is surrounded by the ribs and breastbone, and contains the heart and lungs). This can lead to a smaller amount of air in the lungs. The muscle at the base of the chest (diaphragm) is pushed upwards by the enlarged liver and spleen (hepato-

A speech therapist may help those with MPS I with their speech.

MPS I can cause frequent ear infections, hearing loss, an enlarged tongue, decreased mental capacity, and blocked airways. Any of these symptoms may lead to speech and language problems. A speech therapist may help those with MPS I with their speech. Hearing aids and sign language may also be useful for people with hearing loss.

Nose and throat

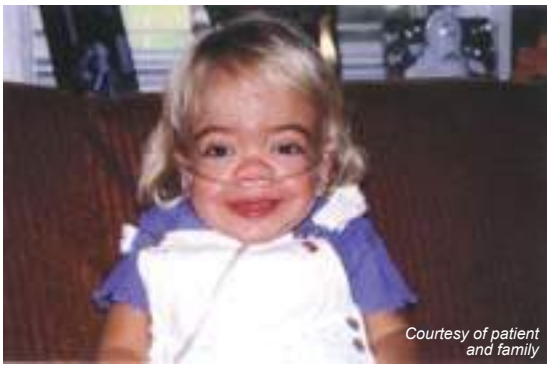
The problems described in this section are common to more severely affected individuals. Individuals with attenuated MPS I are likely to have fewer and less severe symptoms.

Runny nose

Typically, the bridge of the nose is flattened and the passage behind the nose may be smaller than usual because the bones in the mid-face have not grown well and the nose lining is thicker. GAG buildup in the soft tissues of the nose and throat, combined with abnormal bones, can cause the airway to become easily blocked. Severely affected individuals often have a chronic (long-term) discharge of thick mucus from the nose, and chronic ear and sinus infections.

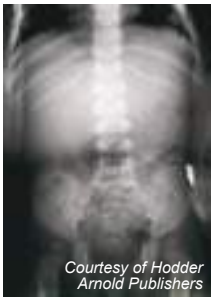
Throat

The adenoids (tissues at the back of the nasal cavity) and tonsils often become enlarged and can partly block the airway. The neck is usually short, which contributes to problems in breathing. The windpipe (trachea) becomes narrowed by stored GAGs and may be floppy, or softer than usual, due to abnormal carti-



Oxygen supply with nasal cannula

splenomegaly), further reducing the space for the lungs. A combination of these things can prevent the individual from breathing in adequate amounts of oxygen and can lead to difficulty breathing while awake or asleep. When the lungs cannot fully clear out, there is an increased risk of infection (pneumonia).



Chest X-ray of child with MPS I

Many affected individuals breathe very noisily even when there is no infection. At night they 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 I using a sleep study (see below for more information). It is important to know that many people may breathe like this for years. Sleep apnea can be treated in some patients by removing the tonsils and adenoids (which may regrow), opening up the airway with nighttime CPAP (continuous positive airway pressure), BiPAP (bilevel positive airway pressure), or tracheostomy.

Managing breathing problems

The doctor may want you or your child to be admitted to the hospital overnight for a sleep study. 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.

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 with heart failure, a tracheostomy (a hole into the airway made in the front of the neck) may be needed.

Infections

Treatment of respiratory infections

Drugs may affect people with MPS I differently, so it is essential to consult your doctor before using over-the-counter medications. Drugs for controlling mucus production may not help. Drugs such as antihistamines (allergy medications) may dry out the mucus, making it thicker and harder to dislodge. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for people with MPS I. Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea by decreasing muscle tone and breathing rates.

Colds are caused by viral infections and do not require antibiotic treatment. But many individuals with MPS I develop bacterial infections on top of their cold. These bacterial infections usually occur in the sinuses or middle ear. People with MPS I are more prone to ear infections because of GAG storage in the mouth and throat, which causes the Eustachian tube (which equalizes pressure in the ear, drains secretions from the ear, and protects the ear from mucus in the nose and throat) to malfunction. The risk of sinus infections is increased by GAG storage in the nose and throat, which leads to abnormal shapes and blockage of the sinus passages. Bacterial infections of the sinuses or middle ear should be treated with antibiotics as prescribed by the 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 sinuses and middle ear don't drain properly, 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.

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

Chest postural drainage is a technique that can be helpful in clearing secretions (collections of mucus) from the lungs. It involves placing the affected person in different positions to help mucus drain from the lungs. It may be used in combination with chest percussion, which involves tapping the chest or back with a cupped hand. This helps to loosen up the mucus. The physiotherapist (physical therapist) will be able to teach you and your family (and, for children affected by MPS I, someone at school) how to do this. Possible side effects of chest postural drainage include injury to the ribs, lungs, or diaphragm; bleeding in the lungs; vomiting and aspiration (inhaling mucus, saliva, or vomit into the breathing tubes); difficulty getting enough oxygen during treatment; and fainting (certain positions for chest postural drainage can cause the blood to rush from the head, leading to fainting).

Sleep apnea

Obstructive sleep apnea is a common airway problem for individuals with MPS I. It is defined as temporary breathing interruptions during sleep that occur when the airway in the neck becomes blocked as muscles in the airway relax. The risk of the airway becoming blocked is increased by some of the physical effects of MPS I, including a short neck, a narrow airway, and enlarged tonsils and adenoids. This airflow can be improved by using a CPAP (continuous positive airway pressure) or BiPAP (bi-level positive airway pressure) machine. If CPAP or BiPAP does not work or is not appropriate, an airway can be opened using the tracheostomy procedure.

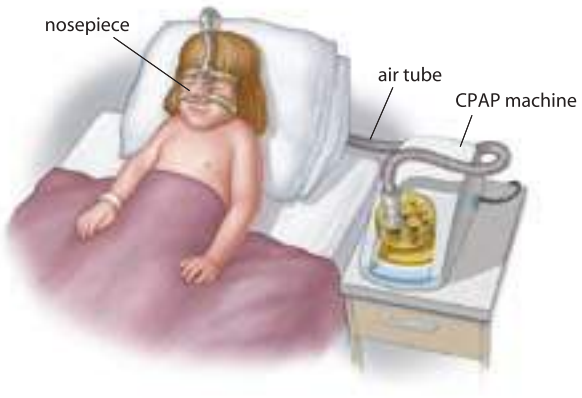
CPAP and BiPAP

Sleep apnea can be improved in some individuals by opening the airway with nighttime CPAP or BiPAP treatments. In cases where CPAP or BiPAP are not effective or appropriate, a tracheostomy (a surgical procedure to insert a breathing tube in the throat) may be used. For more information on tracheostomies, see "Tracheostomy," later in this section.

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

Both CPAP and BiPAP are noninvasive. 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 they sleep in order to receive the positive airway pressure to keep the airway open. CPAP and BiPAP treatments 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 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



CPAP device

making the work of breathing more difficult. The mask does not breathe for the person. The airflow creates enough pressure when inhaled 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. 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 traveling.

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.

Determining whether it's needed

To determine whether someone has sleep apnea and may benefit from CPAP or BiPAP, a doctor can arrange for a sleep study. During a sleep study, the person is continually monitored for apnea episodes or decreases (desaturations) in his or her oxygen level. An abnormal sleep study may suggest that CPAP or BiPAP would be helpful to maintain an open airway during the night. Before considering any therapy or treatment, consult your pulmonologist (lung doctor).

Individual with tracheostomy tube

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, or the 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 windpipe 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 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 I are at a higher risk of problems with 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 I. See "Anesthesia considerations" for more information about anesthesia and MPS I. 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.

A tracheostomy (also called an artificial airway or "trach") is a surgically created opening through the neck into the trachea, or the windpipe. A tube is usually placed through the opening into the trachea to open an airway and to remove secretions from the lungs.

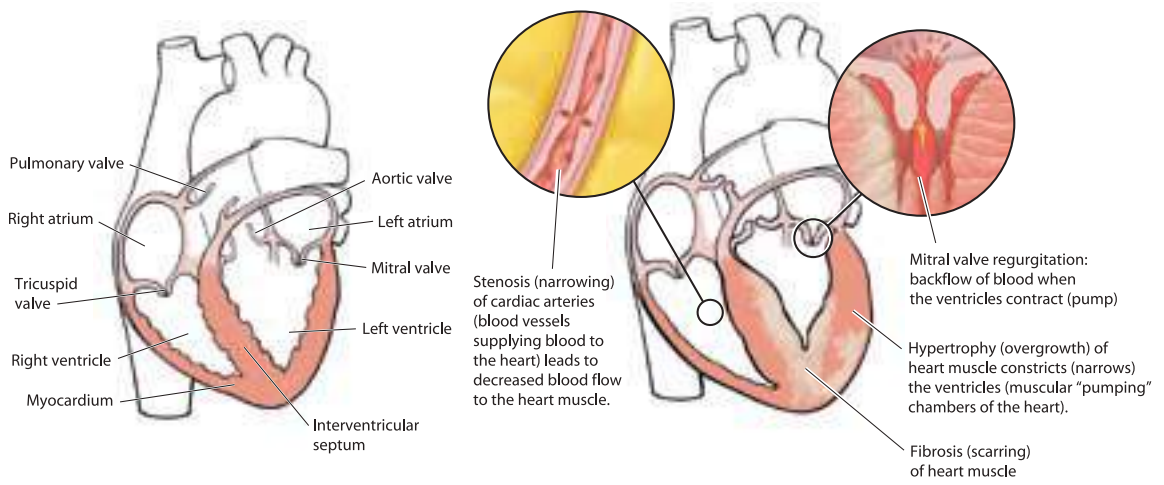
Adjusting to a tracheostomy

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-colored skin). If this occurs, the tube should be suctioned. People with tracheostomies also 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 for them.

From time to time, the tracheostomy tube will need to be changed. Changing an old tube for a new, fresh tube can be challenging but often 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 difficult 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.



Normal heart (left) and heart problems in MPS I (right)

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 I whose upper airway is blocked.

Heart

Heart disease is a major cause of death in individuals with MPS I. Heart disease is common in severely affected children, but it also affects those at the attenuated end of the disease spectrum.

Effects on the heart muscle

Cardiomyopathy (abnormal heart muscle) and endocardial fibroelastosis or fibrosis (scarred and stiff heart) are conditions that can occur in severely affected children. These types of heart damage are caused by the storage of GAGs. There are many different types of cardiomyopathy, and the type of cardiomyopathy often seen in individuals with MPS I 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 heart rhythm

Cardiomyopathy in individuals with MPS I can increase the risk of irregular heartbeat patterns (arrhythmias), which can lead to sudden death.

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. Occasionally, the coronary arteries of severely affected people may become narrowed and cause episodes of chest pain (angina). The narrowed blood vessels can also lead to poor circulation in the arms and legs. Signs of poor circulation in these areas include cold hands and feet. If you have MPS I and notice these symptoms, consult your doctor. If your child has MPS I 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 (EKG). A number of individuals with MPS I also have high blood pressure, which is related to the changes in blood vessels caused by GAG storage.

Effects on the heart valves

Most people with MPS I, including attenuated individuals, may develop problems with their heart valves (thickening or stiffening of the valves). Heart valves may thicken or stiffen because of GAG storage. There are four valves in the heart:

Heart valve damaged by MPS I

- 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.

Eventually the damaged heart valves may need to be replaced surgically.

The importance of regular heart checkups

Since heart problems occur so frequently in MPS I, all individuals with MPS I should 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.

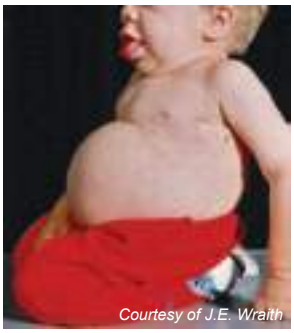
Because of the unusual special problems that can occur in these disorders, you should choose a cardiologist with some knowledge of MPS I. If this is not possible, you should inform the doctor about the heart problems experienced by individuals with MPS I. Medications are available to help manage the heart problems that occur as a result of MPS I.

Gastrointestinal system

Liver and spleen

In more severely affected individuals, accumulation of GAGs causes enlargement of both the liver and spleen (hepatosplenomegaly). The liver may also be enlarged in attenuated individuals. The enlargement of the liver and spleen does

not usually lead to problems with these organs, but it can interfere with eating and breathing.



Child with enlarged liver and spleen

Child with hernia

Abdomen and hernias

In most individuals with MPS I, the abdomen bulges out due to their posture, weakness of the muscles, and the enlarged liver and spleen. Frequently, part of the abdominal contents will 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 (intestine gets caught in the abdominal opening, which cuts off its blood supply) or are very large and are causing problems. People with attenuated MPS I are less likely to have hernias because they are less likely to have an enlarged liver and spleen.

Bowel problems

Many affected individuals suffer periodically from loose stools and diarrhea. The cause of this is not fully understood. Occasionally, the problem is caused by severe constipation and leakage of loose stools from behind the solid mass of feces. More often, however, it "comes straight through." It is thought that there may be a problem with the autonomic nervous system, the system that controls those bodily functions usually beyond voluntary control. Studies have found GAG buildup in the nerve cells of the intestine, and it seems likely that the diarrhea is caused by abnormal movement of the bowel.

An examination by a physician, supplemented by an X-ray if necessary, may establish the cause of diarrhea. For children, the problem may disappear as the child gets older, but it can be made worse by antibiotics prescribed for other problems. If the diarrhea in some individuals with MPS I appears to be affected by the diet, it can be helpful to eliminate some foods. If antibiotics have caused the diarrhea, eating plain live-culture yogurt is often helpful during episodes of diarrhea. This provides a source of lactobacillus (a "friendly" bacteria in the bowel) to help prevent the growth of harmful organisms within the bowel wall, which can cause diarrhea or make it worse. A diet low in roughage (fiber) may also be helpful. Before starting live-culture yogurt or a diet low in roughage, consult your physician.

Constipation may become a problem as children with MPS I get older and less active and as the muscles weaken. If an increase in roughage in the diet does not help or is not possible, the doctor may prescribe laxatives or a disposable enema. Depending on the type of laxative used, side effects may include bloating, gas, abdominal cramps, or diarrhea. Side effects of enemas include rectal irritation or damage.

Dietary considerations

There is no scientific evidence that a particular diet has any helpful effect on people with MPS I, and symptoms such as diarrhea tend to come and go naturally. Some parents, however, find that a change in their child's diet can ease problems such as excessive mucus, diarrhea, or hyperactivity.

Reducing intake of milk, dairy products, and sugar, as well as avoiding foods with too many additives and coloring, have helped some individuals. It would be advisable to consult your doctor or a dietician if you plan major dietary changes to make sure that the proposed diet does not leave out any essential items.

If your child's problems are eased, you could try reintroducing foods one at a time to test whether any particular item seems to increase the child's symptoms. It is important to note that there is no diet that can prevent the storage of mucopolysaccharides because they are actually created by the body. So reducing sugar intake or other dietary components cannot reduce GAG storage.

G-tubes and J-tubes

Tube feeding is usually done through either a gastrostomy tube (G-tube) or a jejunostomy tube (J-tube). A G-tube goes into the stomach through a surgical opening in the abdominal wall. A special kind of G-tube tube may be inserted by means of an endoscopic procedure (which uses a camera on a flexible tube to see inside the body) and is called a percutaneous endoscopic gastrostomy (PEG) tube. A J-tube is usually surgically placed through the abdominal wall into the part of the small intestine called the jejunum. Each tube is a flexible (usually silicone) catheter that remains in place at all times and is clamped between feedings to prevent leakage of stomach contents.

G-tube feeding can be done at regular mealtimes. It can be given at once, called bolus feeding, or it can be given slowly over a pe-

A process called "tube feeding" can be used to help individuals with MPS I get the nutrition they need and protect them from choking.

Feeding tubes

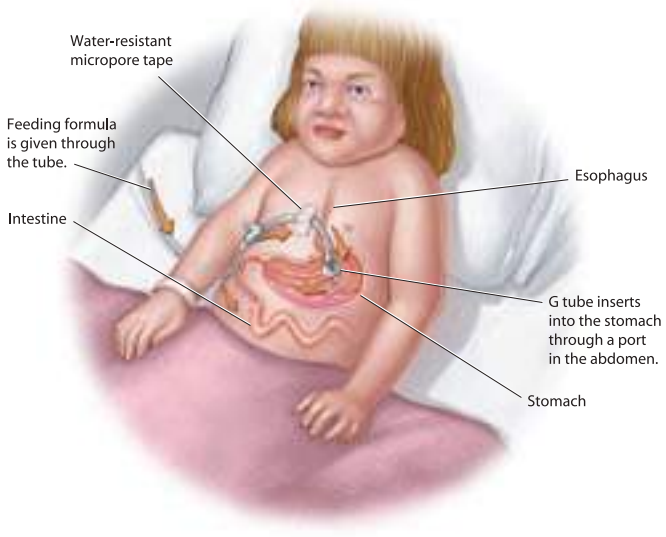
Why use tube feeding?

Individuals with severe MPS I may have problems chewing and swallowing. If so, they are at risk of poor nutrition, choking, and aspiration. "Aspiration" means inhaling food or other substances into the lungs. Aspiration can lead to pneumonia, which may be life threatening.

A process called "tube feeding" can be used to help individuals with MPS I get the nutrition they need and protect them from choking or aspirating. It also makes it easier for a caregiver to feed the individual with MPS I. A flexible feeding tube is inserted that bypasses the mouth and throat and goes directly into the stomach or intestine. NG tubes (which are inserted through the nose) are usually a temporary measure lasting days to weeks. Longer-term feeding issues require surgical placement of a G-tube or J-tube (see below). Tube feeding is also called "enteral nutrition."

Making the decision

The decision to change to enteral nutrition is a difficult one. You may wish to consult your pediatrician, geneticist, gastroenterologist, and nutritionist. To help with the decision, it's important to keep track of the affected person's intake of food, weight gain or loss, choking and gagging, episodes of pneumonia, and time required for feeding. This will help you and your health professionals decide whether enteral nutrition is needed.



Gastrostomy tube (G-tube)

riod of several hours using the gravity (drip) method or the pump-controlled method.

After the decision is made to insert a feeding tube, the doctor will perform X-rays of the gastrointestinal tract (stomach and intestines) to help decide which type of tube to use. The doctor will also check for gastroesophageal reflux disease (GERD) because tube placement may worsen existing GERD and a J-tube may be a better choice. A J-tube may also be an option if there is very poor motility (spontaneous movement) of the stomach. Because of special concerns regarding anesthesia in MPS I patients, you or your doctor should consult with an anesthesiologist before surgery is done to insert the tube. See "Anesthesia considerations" for more information about anesthesia and MPS I.

Caring for the tube

The surgical opening for the G-tube or J-tube is called a stoma. The stoma can be slow to heal after surgery. Proper care of the stoma site is very important to avoid infection or irritation from stomach and intestinal juices. The area should be kept covered with a dressing and changed as often as needed to keep dry. The skin around the stoma should stay snug around the tube. Swimming in lakes or ponds is not recommended because the bacteria living in these areas may infect the stoma site.

A G-tube is anchored inside the stomach by a small balloon at the tip of the tube. The balloon can deteriorate and deflate and the tube can fall out. If this happens, the doctor will provide you with a replacement tube and instructions on how to insert it. Only a doctor can reinsert the J-tube. Contact the doctor immediately if the J-tube falls out. Also, these tubes can become clogged. Prepare for this by discussing with your doctor appropriate methods to unclog them.

The Mic-key low-profile gastrostomy feeding tube/kit is a skin-level device to replace the gastrostomy tube. Because this device is level with the skin, it is less likely to be pulled out and can easily be covered by clothes. During feedings, a tube called an extension set is attached to the Mic-key opening in the skin. The feed is pumped in through this tube, which can be removed between feedings.

When and how to feed

The best tube feeding schedule will allow the person to maintain an adequate weight, tolerate the tube feedings comfortably, and be fed at convenient times. Caregivers should have contact with a nutritionist to regularly discuss the individual's feeding needs. For most individuals, regular solutions such as Pediasure, Resource, or Kindercal are sufficient to fill their needs. The addition of soluble fiber to their formula may help with the chronic diarrhea that is common in individuals with MPS I. The formulas are generally tolerated with little difficulty.

Good positioning during feedings is critical. If the individual is not positioned well, he or she may have trouble receiving food through the tube or breathing properly. The person should not be sitting slumped over, as this can put too much pressure on the stomach. If the individual has trouble maintaining an upright position, special equipment and supports are available to help.

If you or your loved one begin to have trouble eating, it is important to begin keeping track of food intake and weight. This will help to determine if another method of feeding needs to be considered. The decision to switch to enteral nutrition is not an easy one to make, but many individuals will thrive after the placement of their G-tube or J-tube. Difficulties that may be encountered are best dealt with by the medical team in charge of your medical care. Continued contact with them is essential for successful enteral feeding (i.e., enteral feeding that meets the child's nutritional needs).

Problems that may be associated with tube feeding

Feeding tubes may become blocked or clogged. Fortunately, they can often be unclogged at home. If the tube cannot be unclogged, it may be changed. Check with your doctor to find out how to unclog and change the tube so that you will be prepared in case this occurs.

The person receiving tube feeding may accidentally inhale food or liquid into the lungs. This is called "aspiration," and it can lead to pneumonia. Coughing around feeding time is a sign of possible aspiration. Coughing, difficulty breathing, and fever are signs that you or your child may have pneumonia. If any of these things occur, contact a physician.

The stoma may become infected. Signs of infection include fever, pain, swelling, warmth, or increased redness near the stoma. If you notice signs of infection, contact the doctor.

A person who is tube feeding may also experience bloating, diarrhea, or vomiting. These problems may be due to changes in feeding formula, giving too much feeding formula at once, problems digesting the feeding formula, or contamination of the feeding formula with germs.

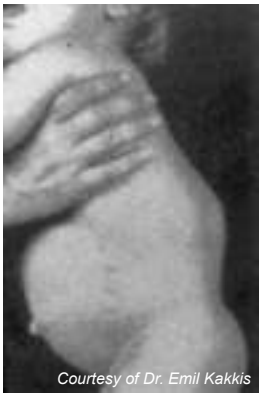
Musculoskeletal system (bones and joints)

People with MPS I 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 centers throughout the body (growth centers are near the ends of the bones).

Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. More severely affected individuals often have poorly formed vertebrae that may not stably interact with each other. One or two of the vertebrae in the middle of the back are sometimes slightly smaller than the rest and set back in line from them. This backward slippage of the vertebrae can cause an angular curve, called kyphosis or gibbus, to develop.

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 occurs in about 90% of children with severe MPS I. 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). Before enzyme replacement therapy and stem cell transplants were available, spine surgery for gibbus was not performed on children with MPS I because it would reduce the child's quality of life and because it was not expected that the child would have a long life of dealing with the problem. Now, with treatments available, a large number of gibbus will eventually require surgery to stop it from getting worse.



Child with gibbus

Some children with MPS I 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; however, this is less common. 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. Conditions determining a need for surgery vary, depending on the needs of the child and the desires of the family. Current experience suggests that, if possible, delaying spinal surgery to later ages allows the best growth of the spine and further development of already thin and brittle bone.

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. The procedure is called an instrumentation and fusion. The "fusion" is actually the placement of bone from the pelvis or ribs over the spine on the backside or between vertebrae on the front side. The "instrumentation," or metal hardware, is typically stainless steel or titanium, and provides temporary support to the spine until the fusion heals. Once placed, it is not usually removed unless there is a complication related to its presence, such as an infection. Most children 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 heals to form a strut between the vertebrae, which prevents 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.

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" for more information), infection, bleeding, blood clots, damage to the spinal cord, or death.

Neck

The bones that stabilize the connection between head and neck can be malformed (odontoid dysplasia) in more severely affected individuals, making the neck unstable. This puts people with MPS I at risk of spinal cord compression (a condition where fluid or tissues such as bones are pressing on the spinal cord). Fusion surgery is used to connect the bones to each other so they do not slip further. Some severely affected individuals appear to have occasional pain in the back of the neck. Parents of children with MPS I should be cautious about how the area of the spine around the neck is handled. It is recommended that children with MPS I 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.

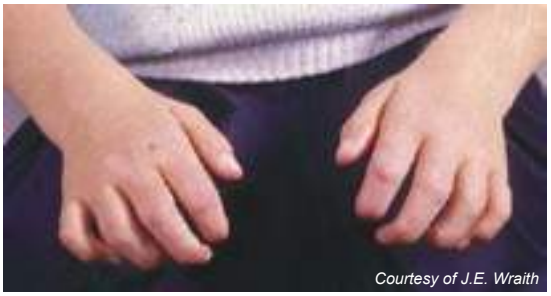
Joint stiffness

Joints

Joint stiffness is common in individuals with MPS I, and the maximum range of movement of all joints may become limited. Later in the individual's life, joint stiffness may cause pain, which may be relieved by warmth and pain medications. The limited movement in the shoulders and arms may make dressing difficult. Anti-inflammatory drugs, such as ibuprofen, can help with joint pain, but their use should be monitored closely to make sure that irritation and ulcers in the stomach do not occur.

Hands

The shape of the hands of people with MPS I is very noticeable and has been used as the symbol of MPS societies. The hands are short and broad with stubby fingers. Over time, the fingers stiffen and gradually become curved, due to limited joint movement caused by GAG buildup. The tips of the fingers can become permanently bent over, giving rise to the characteristic "claw hand."



"Claw hands"

Hips

Like the spine, the hip joint suffers from altered bone formation. The hip is a ball-and-socket joint 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). This combination of bone defects results in hip instability and sometimes dislocation.

Hip dysplasia is found to some degree in nearly all children with severe MPS I, and can also be found in children with attenuated MPS I. Most children with hip dysplasia eventually require corrective hip surgery. Surgery on the hips is done more easily at a younger age, around age 5–7, 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.

Hip surgery for dysplasia is a combination of precise bone cuts (osteotomies), which allow the surgeon to reposition the bones and optimize the working of the hip. 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, there is progressive pain and stiffness, and eventually dislocation of the hips, resulting in a greatly decreased ability to walk. Thus far, the results of hip surgery in some patients with MPS I have been promising.

Hip surgery carries a number of risks, including the risks associated with anesthesia (see "What is different for individuals with MPS I?" in "Anesthesia considerations" for more information), infection, bleeding, or blood clots.

Legs and feet

The feet of people with MPS I are broad and may be stiff with the toes curled under, similar to the fingers of the hands. Many people with MPS I stand and walk with their knees and hips flexed. This, combined with a tight Achilles tendon, may cause them to walk on their toes. Some children with MPS I have knock-knees (a condition in which the knees are bent in so much they touch each other when walking) severe enough to require surgery. During this surgery, staples are placed in the bone on the inner side of the knee through a relatively small incision. These staples prevent bone growth on the inner side of the knee, allowing the outer side to catch up. As a result, the knees straighten over time, and usually, the staples are removed with a second surgery. Occasionally, the staples can dislodge. When this happens, they are typically removed and, if necessary, new ones replace them. For children too small for staples to be used, osteotomies (bone cuts) in the large bones around the knee may be required. Although osteotomies are more invasive and painful, experience has shown that the children heal well.

Physical and occupational therapy

The joint stiffness and bone malformations caused by MPS I can make it hard to walk, dress, tie shoes, and do other activities. Physical therapy may help relieve symptoms and improve the person's ability to function. Occupational therapy teaches affected individuals how to adapt to their unique daily environment.

Physical therapy session

Range-of-motion exercises (passive stretching and bending of the arms and legs) may offer some benefits in preserving joint function. Exercises that cause pain should be avoided. Once joints become significantly stiff, it may not be possible to increase the range of motion (flexibility) in the joints. However, it may still be possible to limit further losses of flexibility. It makes sense for individuals to be as active as possible to maintain joint function and improve their general health. The doctor or physical therapist may be able to suggest ways of achieving this through a combination of daily activities and passive range-of-motion exercises.

Individuals with MPS I may need special learning programs and caregivers to help them with their daily activities.

Brain and central nervous system (CNS)

Overview

GAG storage in the neurons (nerve cells) in the brain can lead to a problem with brain function, including a decline in developmental ability in severely affected individuals. Other aspects of MPS I can affect brain function, including low oxygen levels, lack of sleep (sleep deprivation) due to sleep apnea, increased fluid pressure in and around the brain (hydrocephalus), and effects on the eyes and ears that affect the ability of the individual to see and hear normally. People who are closer to the attenuated end of the spectrum are less likely to experience these issues.

Cognitive function

Severely affected individuals experience a slowing of mental development by 1–3 years of age, followed by a progressive regression in skills (i.e., the child's mental development and skills gradually become less advanced over time) for the rest of their lives. There is great variation in the severity of the condition, however; some may say only a few words, while others learn to walk well and to read a little. They can enjoy nursery rhymes and simple puzzles.

Parents emphasize that it is important to help severely affected babies learn as much as they can before the disorder progresses. Even when the child starts to lose the skills he or she has learned, there may still be some surprising abilities left. Children will continue to understand and to find enjoyment in life even if they lose the ability to speak.

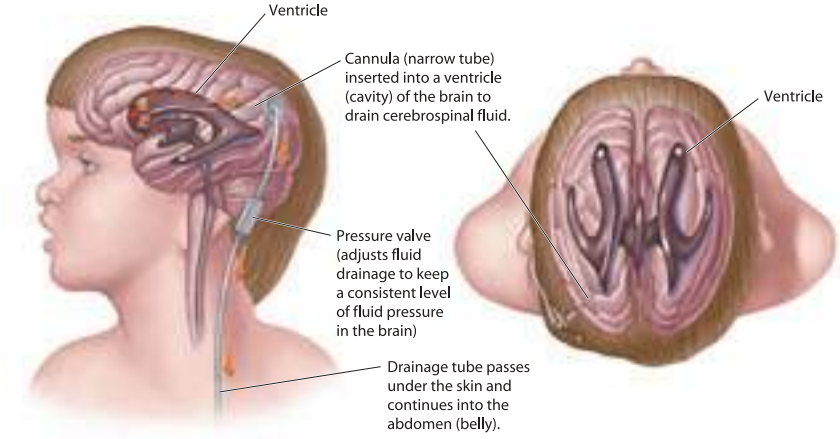
Severely affected individuals commonly have other medical problems that can reduce their learning and performance, including chronic ear infections, poor vision, poor hearing, communicating hydrocephalus (sometimes called "water on the brain"), and sleep apnea (temporarily stopping breathing while sleeping). Treating these medical problems can improve the function of severely affected individuals, so thorough medical checkups should be performed for individuals whose development is significantly affected.

Individuals who are moderately severely affected (historically called Hurler-Scheie individuals) can have normal cognitive (mental) function, but some may have moderate learning difficulties. They can also suffer from the effects of medical problems that hinder their learning and communication.

The least severely affected individuals (historically called Scheie individuals) usually have normal cognitive function, although there have been some reports of mental health issues in this group. One of Dr. Scheie's patients tested at near-genius level. It is important to remember that MPS I is a spectrum of disease conditions. Some patients have milder physical problems and learning disabilities, while others have more severe physical problems and normal cognitive (mental) function.

The effects of MPS I on the brain and nervous system may cause problems with learning and self-care for some individuals. Individuals with MPS I may need special learning programs and

caregivers to help them with their daily activities. More information on this is included in the section of this resource that describes "Educational Strategies" for individuals with MPS I.



Shunt for hydrocephalus

Hydrocephalus

MPS I can cause hydrocephalus, a condition where fluid accumulates in the brain, causing a pressure buildup that can lead to brain damage. This is more common in individuals with severe neurological (brain and nerve) symptoms.

Early detection and treatment of hydrocephalus is believed to improve quality of life. However, neurosurgeons are often unfamiliar with the unique aspects of diagnosing communicating hydrocephalus in MPS I, creating a frustrating situation for parents.

Hydrocephalus was once called "water on the brain."

Hydrocephalus was once known as "water on the brain." The "water" is actually cerebrospinal fluid (CSF), a clear fluid surrounding the brain and spinal cord. The CSF protects the brain and spinal cord from injury by providing a liquid cushion, and is continually being produced, circulated, and absorbed. Communicating hydrocephalus (also known as "non-obstructive hydrocephalus") is caused when the CSF is not absorbed properly. This causes the CSF to build up, leading to an abnormal enlargement of the spaces in the brain called ventricles. This causes potentially harmful pressure on the tissues of the brain.

Effects of hydrocephalus

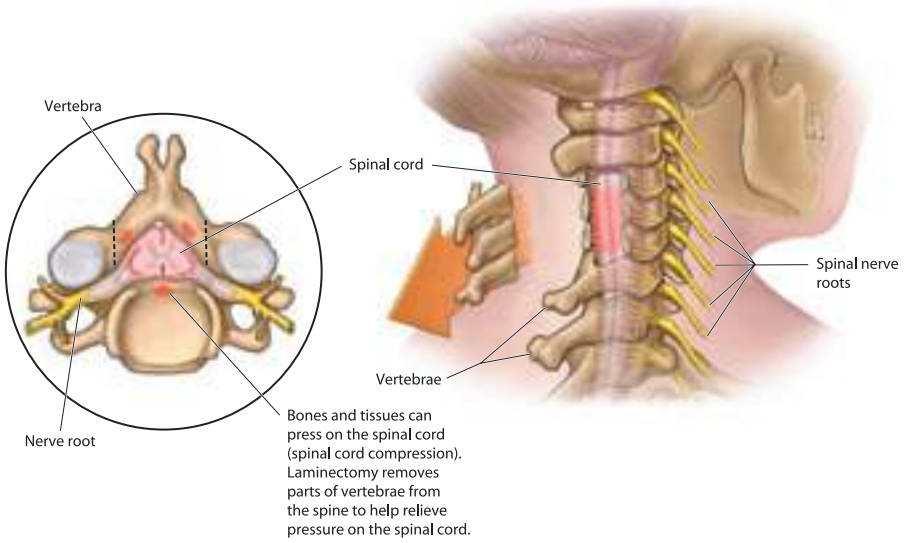
In infants, the most obvious sign of hydrocephalus is often a rapid increase in head circumference or an unusually large head size. In older children and adults, typical symptoms may include a headache followed by vomiting, nausea, blurred or double vision, downward deviation of the eyes (called "sunsetting"), problems with balance, poor coordination, abnormal walking patterns, urinary incontinence (difficulty holding urine), slowing or loss of development, lethargy, drowsiness, irritability, memory loss, or other changes in personality or thinking. If hydrocephalus develops slowly, these typical signs and symptoms may not be seen.

Diagnosing hydrocephalus

Hydrocephalus is diagnosed through clinical neurological evaluation (where the doctor checks the individual's brain and nerve function); by using imaging techniques such as ultrasound, computer tomography (CT), and magnetic resonance imaging (MRI); and through techniques to measure pressure, such as lumbar puncture (spinal tap).

It is recommended that individuals with MPS I have a "baseline" head scan (CT or MRI) at the time of diagnosis with regular follow-up scans (as frequently as the doctor recommends). Measuring intracranial pressure (pressure inside the brain) allows the doctor to diagnose

hydrocephalus. Intracranial pressure is measured in millimeters of mercury (mm Hg), and once the pressure is over 180–200 mm Hg, it is considered to be high. Once the fluid buildup is too severe, the doctor may recommend a shunt (see below).



Laminectomy for spinal cord compression

Use of shunts

Hydrocephalus is most often treated with the surgical placement of a shunt. A shunt is a flexible plastic tube (cannula) that diverts the flow of CSF from the brain to another area of the body where it can be absorbed as part of the circulatory process. If a shunt is placed, specialists recommend a high-pressure shunt to prevent rapid decompression (reduction of fluid in the ventricles). Shunts must be inserted surgically. Before surgery, doctors should check for signs of blockage in the form of spinal cord compression, which is described below.

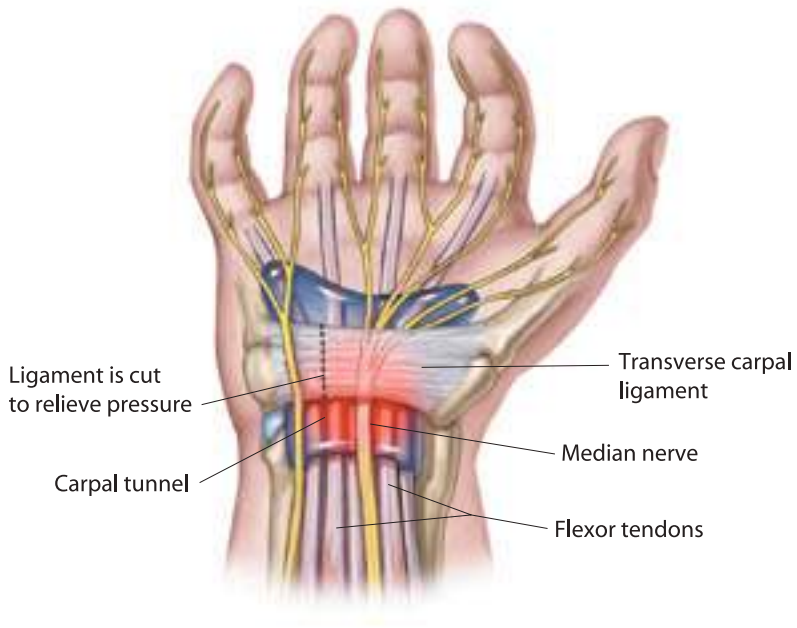
Spinal cord compression

In all people, the length of the spinal cord is surrounded by a system of tissue and ligaments and bones that are intended to protect it from damage when there is movement. However, as a result of GAG accumulation, over time these tissues and ligaments may gradually become thicker and start pressing against the spinal cord. This may result in a condition called spinal cord compression, particularly in the cervical (neck) region of the spinal column. This condition can be quite common in older individuals with MPS I. As a result of this compression, individuals may experience a range of symptoms including neck pain, weakness or numbness in the limbs, poor balance, and dizziness. The compression may also obstruct the proper flow of the CSF around the brain and spinal column, which can contribute to hydrocephalus (described earlier). Doctors usually can detect spinal cord compression with X-ray or MRI evaluation.

The main method used to relieve this condition is a surgical procedure called a laminectomy. In this procedure, the joints that surround the spinal cord may be trimmed and/or some of the cervical vertebrae (bones surrounding the spinal cord) are removed or adjusted to make more room for the spinal column and ease the compression.

Carpal tunnel syndrome

People with MPS I sometimes experience pain and loss of feeling in the fingertips as a result of carpal tunnel syndrome. The wrist, or carpus, consists of eight small bones known as the carpals, which are joined by bands called ligaments. A nerve called the median nerve passes through the space between the carpal bones and the ligaments in the wrists. Thickening of the ligament called the “transverse carpal ligament” causes pressure on the median nerve, and this can cause permanent nerve damage. The nerve damage will cause the muscle at the base of the



Carpal tunnel syndrome and carpal tunnel release surgery

thumb to waste away and will make it hard for the person with MPS I to use his or her thumb for grasping objects. In some cases, surgery may be used to cut the transverse carpal ligament and relieve the pressure on the median nerve. This surgery is also called "carpal tunnel release."

As with any surgical procedure for a person with MPS I, it is important to meet with the anesthesiologist prior to the surgery.

Although a person with MPS I may not experience pain, carpal tunnel syndrome may be severe. If an affected person has pain in his or her hands, particularly at night, he or she may wish to have an electrical test called a nerve conduction or electromyograph study performed. This test will show whether carpal tunnel syndrome is the cause. If there is any weakness at all in the hand or there are problems grasping objects, a test by the neurologist may be needed. Be persistent, as many doctors may not believe that carpal tunnel syndrome is present without the usual symptoms. Most individuals affected by MPS I do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage.

Treatment options

Overview

The goals of managing MPS I are to improve quality of life, to slow down the progression of the disease, and to prevent permanent tissue and organ damage. Currently there is no cure for MPS I. Early intervention may help prevent irreversible damage. Treatment options for MPS I 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), as well as those aimed at treating the underlying enzyme deficiency. Treatments that target the underlying enzyme deficiency include hematopoietic stem cell transplant (HSCT) and PrAldurazyme® (laronidase) enzyme replacement therapy (ERT). Supportive care measures are discussed in an earlier section of this resource.

This section only briefly describes some treatment options. However, the decision of which interventions and treatments are best for you or your child is an important and complex one that cannot be summarized here and that is best discussed with medical professionals who are experts in MPS I.

Importance of multi-disciplinary care

As described earlier in this resource, individuals with MPS I usually have a wide range of signs and symptoms. As a result, they often need to be managed by a large number and variety of medical specialists, including cardiologists, neurologists, pulmonologists, otolaryngologists, ophthalmologists, orthopedic surgeons, physical therapists, and speech therapists. All such health professionals involved in the care of somebody with MPS I 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 I 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 individual to other specialists as needed and help make sure they are receiving the best possible care. This physician might also become the focal point for coordinating the entry of disease- and treatment-related information to be added to the MPS I Registry (described in more detail in another section of this resource).

For many individuals with MPS I, 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

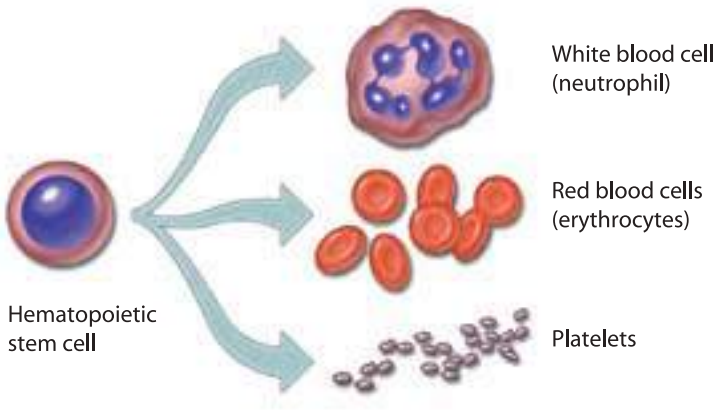
Disease management and nonspecific therapies do not address the underlying enzyme deficiency, but they can significantly improve lifespan or quality of life for many patients and their caregivers. Supportive care measures – such as the use of heart valve replacement surgery or shunts – have already been described earlier in this resource, and are included along with the description of the symptoms that they are intended to address. For individuals who plan to have medical interventions, it's important that the health professionals involved in the surgery, especially the anesthesiologist, have a good understanding of the potential risks and complications for individuals with MPS I.

Hematopoietic stem cell transplant (HSCT)

Overview of HSCT

The goal of hematopoietic stem cell transplant (HSCT) for MPS I is to restore the activity of the missing enzyme, alpha-L-iduronidase. Restoring enzyme activity may improve symptoms such as enlarged liver and spleen, joint stiffness, sleep apnea, heart disease, hydrocephalus, and hearing loss. However, HSCT also carries a number of health risks, which are described in this section. As a result, HSCT is usually recommended for selected individuals at the most severe end of the MPS I disease spectrum. It is important for parents to fully understand the risks, benefits, and limitations of HSCT.

** Please see the full product information for PrAldurazyme® inserted in the front pocket of your binder.*



Possible development of a hematopoietic stem cell

How HSCT works

Hematopoietic stem cells are blood cells at their earliest stage of development. At this stage, they can develop into three different types of blood cells: red blood cells, which carry oxygen in the blood; white blood cells, which help the immune system function; and platelets, which help the blood clot.

In a hematopoietic stem cell transplant (HSCT), the person with MPS I (recipient) is first conditioned with chemotherapy drugs (strong drugs that kill certain cells) to eliminate the MPS I bone marrow. Then stem cells from a person with normal enzyme activity (donor) are given intravenously (through a vein) to the person with MPS I (recipient). The cells are usually given through a central venous catheter, a tube that is inserted into a large vein called the superior vena cava. The healthy stem cells travel to the vacant bone marrow, where they grow inside the recipient and produce blood cells capable of making the missing enzyme. The goal is to help replace the enzyme that is missing.

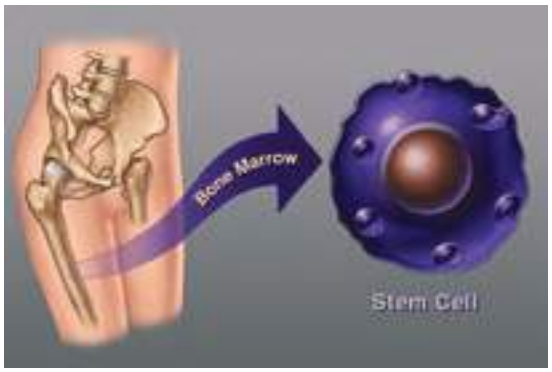
There are three types of HSCT: bone marrow transplant, cord blood transplant, and peripheral blood transplant. These three types of HSCT refer to the different potential sources of stem cells. Bone marrow transplants are procedures that make use of stem cells from the marrow within the bones of healthy donors, while cord blood transplants make use of stem cells from the blood of the umbilical cords of healthy newborns. HSCTs that make use of bone marrow have been used most frequently for individuals with MPS I. However, all three types of stem cell sources have been successfully used in people with MPS I. A successful transplant means that the recipient's body does not reject the transplanted stem cells. The choice of which HSCT type your doctor recommends may depend on the stage of disease, the rate of disease progression, the dose of cells to be given, and the safety of additional medications that may be required for the transplant.

Bone marrow transplant

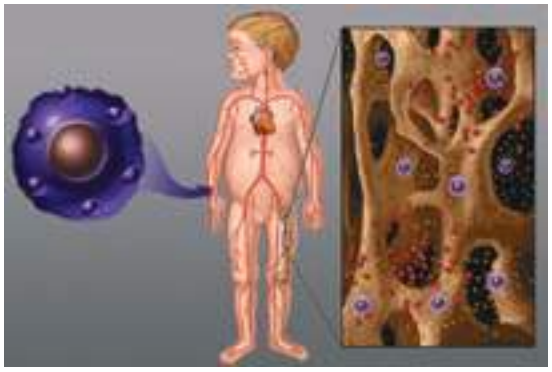
There are two types of bone marrow transplant: allogeneic (another person's bone marrow is used) and autologous (the person's own bone marrow is used). Allogeneic is used for people with MPS I, because they need to get bone marrow from a person (donor) not affected with MPS I since their own cells do not produce the enzyme.

The donor's bone marrow should be closely matched to the recipient's marrow. If there is not a good match, the recipient's immune system will strongly attack or reject the new bone marrow cells. The better the match, the better the chance that the recipient's body will accept the new bone marrow. Sometimes, a close relative

The goal of hematopoietic stem cell transplant (HSCT) for MPS I is to restore the activity of the missing enzyme, alpha-L-iduronidase.



Stem cells from donor bone marrow



Donor cells are transplanted into the recipient

will be a match. Other times, someone unrelated may be matched with the recipient through a bone marrow registry (an organization that stores information about potential donors).

Success (i.e., the recipient's body does not reject the donor's cells) is more likely for people who have a donor with bone marrow that is genetically identical to theirs (usually a brother or sister). In one study, people with a genetically identical donor had an approximately 85% rate of successful engraftment (i.e., the majority of the new blood cells in the recipient are made by the donor cells). In the same study, those whose donors were not genetically identical had a success rate of approximately 65%. Younger children (less than 2 years old) and children with higher levels of cognitive (mental) function (developmental quotient above 70) had improved long-term effects on brain function as a result of their transplants. The developmental quotient measures how close a child's developmental (mental) age is to their chronological (actual) age. A score below 70 indicates that the child has a severe developmental delay. As a result of this information, transplants are usually recommended for younger children with severe disease who are in the early stages of their disease.

Cord blood transplantation

A cord blood transplant uses blood from the umbilical cords of newborn babies. Cord blood is an excellent source of stem cells. Having a close match between donor and recipient is less important than with bone marrow sources. This is because the stem cells in cord blood are still immature enough that the body's immune system does not recognize them as easily as stem cells from another person.

Peripheral blood transplantation

A peripheral blood transplant uses blood from a healthy donor as the source of hematopoietic stem cells. As with a bone marrow transplant, the donor must be matched to the recipient to increase the chance that the recipient's body will accept the donor cells. This is because the body may recognize the donor's cells as a foreign invader and attack the newly transplanted cells.

Benefits and limitations of HSCT

If the recipient's body does not reject the donor stem cells, this is called a successful engraftment. Successful engraftment may have a number of benefits for people with MPS I:

- smaller liver and spleen
- reduced joint stiffness
- reduced coarseness of facial features
- improvement of sleep apnea

The better the match, the better the chance that the recipient's body will accept the new bone marrow.

- reduced risk of hydrocephalus (fluid buildup in the brain)
- hearing improvements
- improved long-term survival
- increased enzyme activity and less GAG buildup
- stabilization of mental ability
- improvements in heart problems (such as heart failure, narrowing of blood vessels in the heart, and abnormal heart rhythms)

While HSCT may help people with MPS I, there are some limitations:

- HSCT does not cure MPS I.
- HSCT does not correct bone and eye problems, although there may be small benefits.
- Effects on intellectual development vary between children.
- It may be difficult to find a matching donor, and this process may take a long time.
- Not everyone has a successful engraftment.
- Although every step is taken to make HSCT as safe as possible, there is a risk of death with the procedure.

Although HSCT may be an effective treatment (i.e., it can lead to improvements in the symptoms of MPS I) when performed early in life, it also has drawbacks. HSCT is a major procedure with serious health risks such as infection and graft-versus-host disease. It also relies on finding a suitable donor. HSCT is a promising treatment area for MPS I, but the risks limit its use to carefully selected individuals with the severe form of MPS I, who may experience early and rapid cognitive decline (decrease in mental abilities). Younger children (less than 2 years old) and children with higher initial levels of cognitive function do better. As a result of this information, stem cell transplants are now being recommended at a younger age. Families facing the severe form of MPS I should talk in detail with the transplant physician and with other families who have had the procedure in order to educate themselves as much as possible.

Possible complications of HSCT

HSCT may have a number of complications. Two of the more serious complications are infections and graft-versus-host disease (GVHD). Both complications may be life threatening.

With all stem cell options described, the immune system may still attack or reject the donor's stem cells. For this reason, the recipient has chemotherapy and/or radiation before the transplant to make their immune system less likely to attack or reject the donor's stem cells. With chemotherapy, medications are given (often into a vein) to reduce activity of the immune system and reduce the risk that it will attack the donor cells. Immune system activity can also be reduced by using doses of high-energy radiation delivered by a radiation machine. Both treatments are given in a hospital or clinic. Side effects of chemotherapy include fatigue, nausea and vomiting, loss of appetite, hair loss, mouth sores, and a risk of infertility. Side effects of radiation include fatigue, nausea and vomiting, diarrhea, mouth sores, hair loss, burning of skin, and dry mouth. Chemotherapy and radiation also increase the risk of infection. To prevent infection, the individual will be kept in an isolation unit after the transplant and carefully watched for signs of infection. Children receiving bone marrow transplants may be in the hospital for 30 days or more, of which approximately two weeks may be spent in isolation.

Graft-versus-host disease (GVHD) happens when the donor cells attack the recipient's cells despite treatments to reduce activity of the immune system. Severe GVHD occurs in nearly one third of children having bone marrow transplants for MPS I. GVHD causes symptoms such as skin rashes and stomach and liver problems. Severe GVHD can be life threatening, but many children experience at least some mild form of skin GVHD, which can be treated with creams. Most forms of GVHD resolve quickly with treatment. However, "chronic" forms may last for many years.

Studies report different risks of death after transplant. One study found that 18% of children with a genetically identical donor and 44% of children with a donor who was not genetically identical died from causes related to the transplant. This same study reported that 64% of children were

still alive 5 years after the transplant. Another study found that 49% of children survived for 2 years after the transplant. However, this was an older study and not as likely to be representative of today's outcomes. More recent studies have reported survival rates as high as 85%. Keep in mind, however, that these studies are based on small numbers of patients, and survival is affected by an individual's overall health, so it is difficult to predict with any certainty what the chances of survival will be after a transplant.

Enzyme replacement therapy (ERT)

Overview of ERT

Enzyme replacement therapy (ERT) is another treatment option that is designed to address the underlying enzyme deficiency in MPS I that leads to GAG buildup in the cells of various organs. ERT is designed to work by replacing the missing enzyme, alpha-L-iduronidase, in individuals with MPS I.

PrAldurazyme® (generic name: laronidase) is a manufactured version of the body's natural alpha-L-iduronidase enzyme. PrAldurazyme® was approved by the FDA in the US in 2003, and since then more than 600 patients have received it in more than 30 countries.

Enzyme replacement therapy (ERT) is designed to address the underlying enzyme deficiency in MPS I by replacing the missing alpha-L-iduronidase enzyme.

PrAldurazyme® Safety Information

PrAldurazyme® is indicated for: long-term enzyme replacement therapy in patients with Mucopolysaccharidosis I (MPS I; alpha-L-iduronidase deficiency) to treat the non-central nervous system manifestations of the disease. Pediatric patients from 6 months up to 18 years of age have been treated with PrAldurazyme® in clinical studies. Treatment with PrAldurazyme® is contraindicated in patients who are severely hypersensitive to this drug or to any ingredient in the formulation or component of the container. Caution should be exercised if PrAldurazyme® is to be used during pregnancy or administered to nursing women. The most serious adverse reaction reported with PrAldurazyme® (laronidase) was an anaphylactic reaction consisting of urticaria and airway obstruction, which occurred in one patient approximately three hours after the initiation of the infusion. This patient's pre-existing MPS I-related upper airway obstruction may have contributed to the severity of this reaction. The most common adverse reactions associated with PrAldurazyme® treatment in the clinical studies were upper respiratory tract infection, rash, injection site reaction, pyrexia and chills. The most common infusion-related reactions included flushing, fever, headache and rash (patients > 6 years of age). The most common adverse reactions requiring intervention were infusion-related reactions. Most infusion-related reactions requiring intervention were ameliorated with slowing of the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines.

Courtesy of Genzyme Corporation

For more information see consumer information section of PrAldurazyme® product monograph in the back of this binder.

The importance of regular treatment

Treatments with PrAldurazyme® should be given once weekly through intravenous (IV) infusions. The doctor will determine the dose or amount of medication to give on the basis of body weight. The infusions typically last about three to four hours.

** Please see the full product information for PrAldurazyme® inserted in the front pocket of your binder.*

Child receiving ERT

As MPS I is a lifelong illness, regular infusions are essential for reducing the buildup of GAG. Therefore, even if individuals with MPS I begin to feel better, it's important to continue to receive regular infusions of [Pr]Aldurazyme® as recommended by the doctor. If an infusion session is missed, talk to your doctor about rescheduling the next dose. Support is available to help individuals continue to receive regular infusions even when traveling for work or vacation.

Some patients prefer to have a permanent catheter (port) surgically implanted under the skin to reduce the trauma of having to find a vein each week. One end of the port is stitched into a major vein. The other end has a large rubber septum, which is easier to use for injecting medication into than the traditional method of finding a new IV site each week.

For additional information, call Genzyme Medical Information at 1-800-745-4447 (option 2) , see the full product information, or visit www.genzyme.ca.

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, below you will find additional sources of information to help you.

Canadian Society for MPS & Related Diseases

The Canadian MPS Society provides support for individuals and families living with MPS I. The Society can connect you with other families of people who have undergone HSCT and families of people who are currently receiving [Pr]Aldurazyme® ERT. The staff in the office can talk with you about the disease and treatment information you are looking for. Please call 1-800-667-1846 or visit www.mpssociety.ca. The Society also performs a variety of other functions that are not related to treatment, and that are described in another section of this resource (please see "Sources of support and information").

Genzyme Corporation

Genzyme Corporation is committed to providing [Pr]Aldurazyme® to help treat MPS I, and to supporting people with MPS I and their families as they face the daily challenge of living with the disease. In particular, Genzyme Treatment Support is a voluntary and confidential service where individuals living with MPS I can obtain information about:

- other organizations that provide support for people living with MPS I
- treatment centers that can help match your specific needs with specific services
- how to contact the doctors, nurses, genetic counselors, social workers, and other healthcare professionals in your area who can help you
- where to find more information about MPS I and [Pr]Aldurazyme®

To find out more about this and other services, please call Genzyme at 1-800-745-4447 (option 2), or visit one of the following websites:

- www.MPSIDisease.com
- www.genzyme.ca
- www.MPSIRegistry.com

Genzyme also performs a variety of other functions that are described in another section of this resource (please see "Sources of support and information").

** Please see the full product information for [Pr]Aldurazyme® inserted in the front pocket of your binder.*

Other websites

Other websites cans also provide you with more information about your current and future treatment and management options, including:

- www.cbmtg.org
  A website maintained by the Canadian Bone Marrow Transplant Group, with a wide variety of information for families about the kind of considerations that should go into the decision of obtaining transplantation.
- www.bmt.umn.edu
  A website maintained by the BMT program at the University of Minnesota that has a Frequently Asked Questions (FAQ) section for patients to learn more details about transplantation.
- www.clinicaltrials.gov
  Website maintained by the US government that includes an inventory of all active clinical studies, including those that relate to the study of various treatment options for individuals with MPS I.

Research for future treatment options

Overview

Although MPS I can be treated, there is currently no cure. Research is underway to find more treatments for MPS I and, hopefully, someday a cure.

The mission of the Canadian MPS Society is to find cures for MPS I and related diseases, and as part of that mission, the Society funds research grants. The Society recognizes the need for targeted research for treatment of bone and joint problems and for treating the brain, and recent research funding from the Society has focused on these specific areas. Information about this can be obtained through the Society office by calling 1-800-667-1846, or on the Society website at www.mpssociety.ca.

In addition to the work of the Canadian MPS Society, this section describes some promising new areas of research.

Gene therapy

Gene therapy involves replacing the defective gene with a healthy gene capable of producing the enzyme (alpha-L-iduronidase). The main issue with gene therapy is delivery (how to get the healthy gene to all cells of the body). A number of delivery methods are being researched. Gene therapy using cell transplantation is currently being investigated with mice. With this procedure, a sample of the person's own cells is removed and then treated outside the body. The treatment alters the genes in the cells so that they produce the enzyme. Then, the cells are put back into the person's body, where they begin to produce cells with a healthy copy of the gene for the enzyme. Another potential delivery method for gene therapy is *in utero* gene therapy. With this therapy, a healthy version of the gene would be injected into the fetus while it is still in the mother's womb, with the goal of producing a baby with healthy enzyme activity. *In utero* gene therapy is being investigated with mice, but has not yet been tested with people.

Intrathecal therapy

Researchers are now investigating ways of getting enzyme therapy to reach the tissues in the brain. Research in dogs suggests that intrathecal enzyme injections (injection of enzyme into the spinal fluid) can help increase enzyme levels in the brain, spinal cord, and membranes surrounding the spinal cord (meninges). In dogs, this led to improved motor function and less lysosomal storage around the meninges. A study has been initiated in the US by the MPS I Intrathecal Research Collaborative (MIRC) to assess the safety of this procedure in humans. Enzyme therapy has not been evaluated for effects on the central nervous system in humans.

Substrate deprivation therapy

MPS I is caused by insufficient levels of alpha-L-iduronidase, the enzyme needed to break down GAGs, leading to GAG buildup in the body. Substrate deprivation is a potential treatment method that works by slowing down the production of GAGs in order to reduce the rate at which they build up in lysosomes. So far, this treatment has not been tested for people with MPS I.

** Please see the full product information for [Pr]Aldurazyme® inserted in the front pocket of your binder.*


Courtesy of Genzyme Corporation

The MPS I Registry is an ongoing observational database that tracks natural history and outcomes for people with MPS I.

MPS I Registry

What is the MPS I Registry?

The MPS I Registry is an ongoing observational database that tracks natural history and outcomes for people with MPS I. It is designed to help doctors and other health professionals better understand, treat, and manage MPS I. Since MPS I is a rare condition, the information collected on known individuals with MPS I can help healthcare professionals learn from the collective experience of others. The goal is for all individuals with MPS I to be part of the registry. Patients are encouraged to participate, irrespective of where they are on the disease spectrum or whether they have received any therapy.

The MPS I Registry was started worldwide in April, 2003, and is expected to continue for a number of years. It is a program sponsored by Genzyme/BioMarin LLC and administered by Genzyme Corporation. As of July 2007, over 270 physicians are submitting data for over 636 individuals with MPS I from around the world.

The primary objectives of the MPS I Registry are:

- to evaluate the long-term effectiveness and safety of ^{Pr}Aldurazyme® (laronidase)
- to characterize and describe the MPS I population as a whole, including the variability, progression, and natural history of MPS I
- to help the MPS I medical community with development of recommendations for monitoring patients and reports on patient outcomes to help optimize patient care

** Please see the full product information for ^{Pr}Aldurazyme® inserted in the front pocket of your binder.*

It is up to you whether you would like to contribute information via your doctor to the MPS I Registry. Participating means that information about your health and treatment will be added to the database in a way that does not identify you by name. The MPS I Registry is maintained as confidential in accordance with applicable national privacy regulations and other state and local laws related to medical information.

Participating in the MPS I Registry does not mean that you will have experimental treatments. You will get the same care and treatment from your doctor regardless of whether you participate in the MPS I Registry. There are no expenses to you or your doctor for participating.

Why should I participate?

Participating in the MPS I Registry is voluntary. By participating, you are helping people with MPS I by adding to the information available to healthcare professionals. The information you provide will be grouped together with information from other people with MPS I. Once the information is put together, medical professionals can use it to learn more about MPS I, develop recommendations for care, and hopefully improve treatment for people with MPS I.

How do I join?

The MPS I Registry is open to anyone with a confirmed diagnosis of MPS I. If you are not sure whether this applies to you or your child, check with your doctor.

To participate in the MPS I Registry or learn more about it, talk to your doctor. Your doctor will ask you to complete a Patient Authorization Form. The form will tell you more about the MPS I Registry, the possible benefits to you, what is involved in participating, what personal information will be collected, and how this personal information will be used.


Courtesy of patient and family

You will need to give your permission to participate. Once your permission is obtained, your doctor will begin to regularly send information on your health and treatment to the MPS I Registry. However, your name will be confidential. A number will identify you, and only your doctor will know which number is yours. If you have any questions or concerns about confidentiality, talk to your doctor.

By participating, you are helping people with MPS I by adding to the information available to healthcare professionals.

The MPS I Registry provides the medical community with information about MPS I, treatment guidelines, and reports that are designed to help them better care for their patients with MPS I. Participating doctors can also use the database to answer specific questions they may have about MPS I or conduct research studies.

Participating in the Registry does not prevent you or your child from participating in clinical trials (studies) at the same time.

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Anesthesia considerations

Overview

Various treatments as well as surgical procedures to manage the symptoms of MPS I have been described in this resource. For many of these treatments, a person with MPS I may require an anesthetic. An anesthetic is 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 the surgery, a tube is placed into the throat and connected to a machine that helps the person breathe.

Individuals with MPS I, especially those at the more severe 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 are often narrow as a result of 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. Individuals with MPS I may also take longer to recover after anesthesia.

Courtesy of Genzyme Corporation

Individuals with MPS I in particular may need to receive anesthetics in a regional medical center or university hospital from a trained anesthesiologist.

For these reasons, it is important for individuals with MPS I to be properly assessed by an anesthesiologist prior to undergoing any medical interventions. It is also important for such interventions to be performed at a hospital with knowledge of and experience with MPS I in order to reduce the risk of potentially serious complications. A patient might consider, in consultation with his or her physician, having multiple procedures performed 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 in individuals with MPS I in more detail.

What is anesthesia?

The definition of "anesthesia" is 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 and during surgery.

There are two main types of anesthesia, which are briefly compared below:

- *Local 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.

- *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. 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 before the person fully wakes after it ends.

Normal procedure for general anesthesia

1. Gas or a medication given by injection is used to make the person 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. An endotracheal tube (a flexible tube that is placed into the trachea to help with breathing) is put into the trachea through the larynx and the laryngoscope is removed.
6. The endotracheal tube is connected to a machine that breathes for the individual during the procedure.
7. At the end of the surgical procedure, the anesthetic stops being given. The individual 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 I?

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. In individuals with MPS I, the effect of the storage of GAGs in many soft tissues, as well as its effect on bone formation, can create such difficulties. For example:

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

- The storage of the GAGs narrows the nasal passages; enlarges the tonsils, adenoids, and tongue; and causes loose extra tissues 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 premedications and/or by general anesthesia leads to further obstruction of the airway.
- A stiff cervical spine (the neck region of the spine) and the possibility of an unstable spine may prevent an anesthesiologist from placing the head and neck of the individual in the best position to view the larynx. The limited jaw movement and short neck often seen in individuals with MPS I make it even harder for even a very skilled anesthesiologist to see the larynx.

Individuals with MPS I may have other symptoms that can also contribute

to the increased risks associated with general anesthesia. For example:

- The storage of GAGs causes thick skin and joint stiffness, which can make it hard to give intravenous (IV) injections, especially in an emergency situation.
- The storage of GAGs in the heart and blood vessels of the heart, which can add to the overall burden to the cardiovascular system. The heart muscle may become sensitive to anesthetics and/or sensitive to oxygen needs.

Potential risks and complications

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

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 might 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).

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 individuals with MPS I will experience these problems. It should be noted that the risk of heart-related problems is much less than that of airway problems in individuals with MPS I under general anesthesia.

Courtesy of patient and family

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 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 I, it is possible to determine before undergoing anesthesia whether they will have a significantly increased risk associated with such a procedure. To avoid potential anesthetic complications in individuals with MPS I, the doctor(s) will need to consider preoperative examination and evaluation; anesthetic training and experience; and planning for the unusual or unexpected.

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

An evaluation by a pulmonologist (lung doctor) and cardiologist (heart doctor) can be helpful in determining pre-operative risks. The pulmonologist 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.

Picking and meeting the anesthesiologist

For individuals with MPS I, it is safer to have medical interventions at a hospital experienced with treating people with MPS I. This usually entails going to a regional medical center or university hospital, even if it means traveling far.

As there are no minor anesthetics for most individuals with MPS I, planned procedures should always involve careful assessment of the individual by an 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 both 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 person undergoing medical intervention. There are several aspects to this:

- Because people with MPS I 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 I, 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 will visit the individual before the procedure and prescribe the medication needed to prepare for the anesthetic.
- There are steps that can be taken 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.

Make sure that the anesthesiologist is aware of the individual's condition and possible problems. Inform the medical team of any developmental disabilities or hearing or vision problems, and bring hearing aids or glasses to assist the medical team in communicating with the individual. It may be useful to provide the anesthesiologist with information and experience from prior operations. For example, some people are nervous about of injections or hate the smell of the gas.

What does the overall process look like?

Preparation

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

Consent

The surgeon or members of the medical team will explain what is planned for the operation or procedure. The individual (or their parent if the individual is a child and unable to understand the procedure) will be asked to sign an official form of consent. One should continue to ask questions until completely comfortable with what is being agreed to.

"Nothing by mouth (NPO)"

The individual undergoing surgical intervention will be asked to not eat or drink anything for usually four to eight hours prior to receiving the anesthetic (the abbreviation "NPO" comes from the Latin for "nothing by mouth"). It is important to have the stomach empty, as people 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 I.

Pre-medication

Pre-medication is the medicine that is given to people before the general anesthetic. This can vary with the age of the individual and the type of procedure. Something 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 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. People can 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 would be better for him or her to lie on the bed or be held in a horizontal position, as blood pressure may drop while standing upright.

Anesthetic cream

If the anesthetic is to be given by IV injection, an anesthetic cream may be applied to the site of application an hour before the operation. This will numb the area so that the individual will 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.

In the operating room

A nurse always accompanies the individual into the operating room. If the individual is a child, a favorite teddy bear, doll, or blanket could go too, but it would be a good idea to bring it back for safekeeping. These procedures may vary from hospital to hospital.

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 individual 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 the individual is likely to be in the operating room. Many parents or family members like to go for a walk or have a meal. If the individual is going to intensive care 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 your loved one is doing. In many hospitals, you will be able to join your loved one once he or she has been taken to the recovery room.


Courtesy of Genzyme Corporation

Back in the recovery room

After having an anesthetic, the individual may seem drowsy and unaware, but hearing a loved one's 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 choosing a hospital with a intensive care unit is essential. 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

This section lists some of the risks and complications that are associated with general anesthesia in individuals with MPS I, as well steps to potentially minimize them. This material is intended to help caregivers and doctors better prepare individuals for anesthesia. With that comes the hope that these people can safely receive medical interventions intended to improve long-term health outcomes.

Living with MPS I

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 I, but some are also specifically included for individuals with MPS I.


Courtesy of Genzyme Corporation

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

Getting organized

MPS I Journal

Nobody cares more about your treatment or your child's treatment than you do. 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 I Journal included with this Learning Guide to help you keep all of this information in one convenient place.

Emotional support

For parents of children with MPS I

As a parent of a child with MPS I, 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, counseling, 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:

- **Talk to other families affected by MPS I.** 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 I. 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 I 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 eases their fears.
- **Draw strength from your family, friends, or religious community.** Although they may not have experience with MPS I, 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.
- **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 a severely affected child is hard work. Parents need a break to rest and enjoy activities, and this may not be possible when their child with MPS I is with them. Brothers and sisters also need their share of attention, and to be taken on outings that may not be feasible for the child with MPS I. Many parents use some form of respite care or have someone come in regularly to help at busy times. More mildly affected individuals may need help to become more independent from their families and may benefit from a vacation, perhaps with others who have disabilities.

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.

Talking with your family

Your immediate family

For parents of a child with MPS I

Receiving a diagnosis of MPS I 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 I, 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 I.

Talk about MPS I with both your affected child and their unaffected siblings.

Parents of children with MPS I 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 I 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.

Though parents cannot control having to accept the diagnosis of MPS I, they do control how the diagnosis affects their family.

Help your children deal with their feelings about the disease. Parents of children with MPS I 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 I. Providing support by listening and discussing these feelings is essential. Younger children may believe that MPS I 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 I. 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 I and their impact may change over time. As such, keeping the lines of communication open should be an ongoing task.

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 I by withholding


Courtesy of Genzyme Corporation

it is important for parents to help foster a greater sense of control. This can be accomplished by offering children choices whenever possible. When appropriate, children with MPS I 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 care-giving 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 I and siblings like any other child. While recognizing that children with MPS I 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. The parents should make sure siblings and playmates understand what types of activities are considered appropriate for child with MPS I.

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.

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 his or her 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.

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 I and their siblings may feel they have little control over their lives. Therefore,

Don't be afraid to discipline your child who has MPS I. 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 I 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 behavior. 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 I and their brothers and sisters in the household helps to foster healthy sibling relationships. Recommended discipline techniques in-


Courtesy of Genzyme Corporation

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 I 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 I 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 I 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 I.

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

clude praising appropriate behavior, using time-outs for young children, and restricting privileges of older children for inappropriate behavior.

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 I 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 I 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 I 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

Your extended family

For parents of a child with MPS I

Speaking with your extended family

Talking about MPS I may help both you and your family. Because MPS I is genetic, your other family members may be carriers and may have children affected by MPS I. Making them aware that MPS I 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 I, the more likely they will be able to help. For more information on genetic testing, see "How do people inherit MPS I?" in "Mucopolysaccharidosis I (MPS I) disease."

Getting ready to talk to your extended family

Telling your family about MPS I 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.

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

- What is MPS I? Explain the different severities and which one applies to you or your child.
- When did the symptoms start, and 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 I? 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 I?
- How can your family help?
- What does this mean to your relatives, and should they be tested for MPS I?

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. The answers to these questions depend on your individual situation. You can turn to your doctor, this learning guide, or the National 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 I. You may wish to plan ahead by making a list of a few resources (see 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 I. To help, you may want to explain how MPS I is inherited (see "How do people inherit MPS I?" in "Mucopolysaccharidosis I (MPS I) disease.").

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

MPS I can cause many physical and mental challenges, including difficulties with mobility, speech, and mental capabilities. Parents of a child with MPS I may feel helpless and uncertain about their child's future. Older individuals

with MPS I 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

It's important to choose a doctor that you and your child feel comfortable with. Consider the qualities that are important to you. 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 I is a rare condition, so many doctors may not have extensive experience with the condition. Finding a doctor who is knowledgeable about MPS I or willing to work through the issues with you is very important.

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

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.

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.

For your first visit to a new doctor, you might also want to include:

- all symptoms, when they began, how often they occur, and how they have changed over time
- any medications you or your child take
- your or your child's medical history, including a list of your other doctors and previous medical procedures
- any problems you or your child may have with daily activities

MPS I 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 I 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 about the condition. 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 in between your visits to the doctor, you can find more information by reading books on MPS I, 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.

Keep an open line of communication

Open and honest communication will help create a 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 options are available?
- Of these, which may be appropriate for me (or my child)?
- How and when is the treatment usually given (for example, is the treatment a one-time procedure, or are repeated treatments required on a regular basis)?
- What are the side effects?
- How will it interact with other medications and treatments?
- How much will it cost?
- Is it covered by my insurance policy?
- How long until it starts to work?
- For symptoms that cannot be treated, how else might I be able to manage them?

The doctor is your partner in managing MPS I. Good communication will help you get the most out of your visits to the doctor.

Working with employers

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

For parents whose child has MPS I

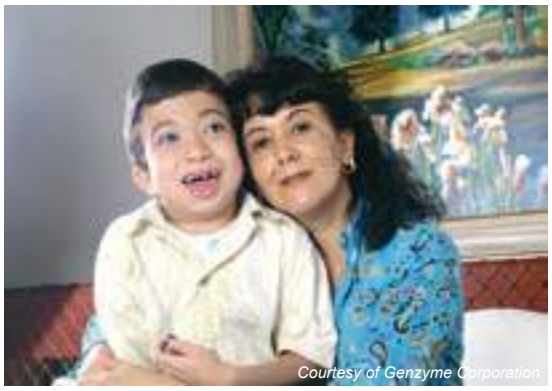
If your child has MPS I, you may find yourself struggling to meet the demands of the workplace while still giving your child the care and attention they need. You may need time off to take your child for medical appointments or treatment. You may also need to send them to a special daycare or school. Fortunately, there are programs to help working parents cope.

Family Medical Leave offers eligible employees of a covered employer up to 8 weeks within a period of 26 weeks of unpaid leave per year under the following circumstances:

- to care for an immediate family member (a child, parent, or spouse) who has a serious health condition
- to take medical leave if the employee is unable to work due to a medical condition

When you return from family leave, your employer must give you back your job, or an equivalent job with the same pay and benefits. Your employer cannot fire you or take away your benefits just because you took family leave. For more information on the FMLA, visit www.e-laws.gov.on.ca.

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.


Courtesy of Genzyme Corporation

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.

someone without a disability. "Reasonable" means that the accommodations can be offered without causing too much expense or disruption for the employer. Some examples of reasonable accommodations are modified equipment (such as chairs or computers), part-time work, or flexible work hours. The Canadian Human Rights Commission, www.chrc-ccdp.ca, has suggestions on accommodations that may be helpful, tips on asking your employer for accommodations, and more details on the EEA.

In Canada, each province has specific legislation that allows certain family members to take leave from employment to provide care or support to family members and people who consider the employee to be like a family member. For example, in Ontario, under the Employment Standards Act (2000) employees are entitled to 8 weeks in any 26 week period of Family Medical Leave.

A career counselor may help you choose a type of work that you will enjoy and that is well suited to your individual strengths and interests.

For individuals with MPS I

Some individuals with less severe forms of MPS I may do well at a variety of different jobs. A career counselor can help you explore a type of work that you might enjoy and that is well suited to your individual strengths and interests.

The Canadian Human Rights Act (CHRA) and the Employment Equity Act (EEA) help to protect the rights of people with disabilities. The EEA makes it illegal for employers to discriminate against qualified workers who have a disability. In order to be protected by the EEA, you must have a disability and also be qualified to do the activities essential for the job.

Under the EEA, you have the right to ask for "reasonable accommodations." These are changes to your job or working environment that help you do your job as well and easily as

For more information, http://www.labour.gov.on.ca/english/es/fml_index.html

Talking to educators

Educators can play a critical role in the development of your child, and need to understand the special issues that could affect his or her educational needs and learning capabilities. Please see "Education Strategies" and "An overview of MPS I for teachers" for information on this very important issue.

Sources of support and information

Resources from the Canadian MPS Society

The Canadian MPS Society's goal is to ultimately find cures for MPS I and related disorders. The Canadian MPS Society will achieve this goal by supporting research, providing support to individuals and their families affected by MPS I or related diseases, promoting public and professional awareness, and significantly increasing participation by regions. In addition to the disease and treatment information and family newsletters, the Society supports ongo-

ing research, hosts yearly family conferences, actively advocates for people with MPS I and other lysosomal storage disorders to government, and works to increase awareness.

The Canadian MPS Society is dedicated to supporting individuals and families affected with MPS and related diseases through such vital services as:

- The website: www.mpssociety.ca
- 1-800#: 1-800-667-1846
- Quarterly newsletter, the Connection: a valuable resource that helps members stay on top of MPS-related news and events and stay in touch with each other.
- A Family Referral Directory: connecting families affected with the same syndrome or living in the same region.
- A Family Assistance Program: financial aid to affected families.
- Advocacy support: to ensure our members receive the treatment and care they need.
- Biennial family conferences: providing families an opportunity to learn more about new research, treatments and care strategies, and to meet with other families, share experiences and form life-long friendships.
- Bereavement support, for families dealing with the devastating loss of a child to MPS or a related disorder.

The Society supports public awareness campaigns – like our Canadian MPS Jeans Days - develops, publishes, and distributes a variety of educational materials, issues press releases, and maintains this website, www.mpssociety.ca with important updates on the Canadian MPS Society's news and events as well as links to our international sister organizations. Our biennial conferences give medical professionals an opportunity to meet and share information with attendees and each other.

The Society's initiatives are funded primarily through private donations and fundraising. Events like our Canadian MPS Jeans Days and The MPS CUP enable us to fund annual Summer Studentship Research Grants as well as larger research grants at major university centres. Research into MPS and other lysosomal storage disorders has led to exciting new treatments.

You can support the Canadian Society for Mucopolysaccharide & Related Diseases by becoming a member, attending or organizing an event, sharing your story, volunteering, or simply by informing yourself and spreading the word to others about MPS and related diseases. The Canadian MPS Society has made great strides in providing support and services to its members and the community. Help us grow.

Living with a chronic, progressive illness can cause emotional and physical stress - the demands can be overwhelming. To find out how The Canadian MPS Society can help you deal with MPS or a related disorder in your family please call 1-800-667-1846.

Resources from Genzyme Corporation

Overview of resources at Genzyme

Many patients and their families have placed calls to Genzyme for a variety of reasons – to receive information about MPS I disease, to inquire about treatment options, to check the status of clinical trials, or to ask questions about insurance coverage. Genzyme encourages and welcomes this contact, and has teams of professionals standing by to help answer all of these questions and more. Below is a brief description of some of the resources available at Genzyme to help patients with MPS I and their families find the answers they may be seeking.

Please note that these Genzyme resources are available to all patients with MPS I disease and their families, regardless of how the disease is being managed. These resources are in addition to those already available to you through your treating physicians and through the Canadian MPS Society.

Genzyme Medical Information

When you call Genzyme Medical Information, you are reaching a team of pharmacists and other healthcare professionals who can answer a wide range of questions related to MPS I disease and PrAldurazyme® (laronidase) and who can also provide educational resources and brochures.

In addition, Medical Information professionals can supply healthcare professionals treating MPS I patients with medical literature, information from recent medical meetings, and other physician-oriented resources as requested.

They can be reached by calling 800-745-4447 and selecting option 2. They are available Monday through Friday from 8 am to 6 pm EST.

MPS I is a lifelong condition. Staying well informed can help you play a role in your or your child's health.

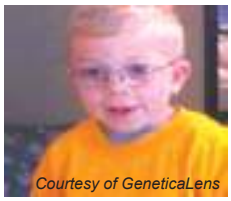
Learning from other individuals living with MPS I


Courtesy of GeneticaLens

Haley's story

Haley is nine months old. Her parents learned a month ago that Haley has a severe form of MPS I (historically known as Hurler syndrome). Watch Haley's story to learn how Haley was diagnosed, how her parents are coping, and their plans for Haley's future treatment.

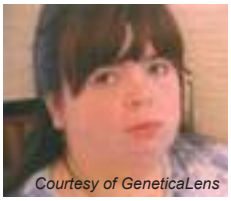
To watch a video of Haley's story, visit www.mps1disease.com


Courtesy of GeneticaLens

Bryce's story

Bryce has just turned six. Two years ago, he was diagnosed with an attenuated (less severe) form of MPS I. Watch Bryce's story to see how Bryce and his parents are coping with the diagnosis, the experience Bryce has had with treatment, and how the whole family works together to support each other.

To watch a video of Bryce's story, visit www.mps1disease.com


Courtesy of GeneticaLens

Alicia's story

Alicia is a 16-year-old with MPS I. She has known about her diagnosis of MPS I for nearly 10 years now. She has an attenuated form of MPS I. Watch Alicia's story for interviews with Alicia and her mother on how she was diagnosed, what life with MPS I is like for Alicia and her family, and how she dealt successfully with being bullied in school by educating her peers.

To watch a video of Alicia's story, visit www.mps1disease.com


Courtesy of Genzyme Corporation

Denise's story

Denise is a 40-year-old woman with MPS I. She was first diagnosed at the age of 10, but it wasn't until her early 30s that she began to experience many of the symptoms that she is living with today. Watch Denise's story to see how her positive attitude, solid support system, and active involvement in her treatment help her enjoy life to the fullest.

To watch a video of Denise's story, visit www.mps1disease.com

** Please see the full product information for PrAldurazyme® inserted in the front pocket of your binder.*

Other information sources

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

The following sites are created and maintained by Genzyme Corporation to help educate the community of individuals and caregivers involved with MPS I:

- www.MPS1disease.com
- www.genzyme.ca
- www.MPS1Registry.com
- www.lysosomallearning.com

Other resources that can help you:

- www.mpsforum.com (owned and operated by a family affected by MPS I)
- www.raredisorders.ca (Canadian Organization for Rare Disorders)
- www.marrow.org (National Marrow Donor Program)
- www.cbmtg.org (Canadian Blood and Marrow Transplant Group)

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Education strategies

For parents of children with MPS I

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 I ensure that their child has the best possible education.

This section is designed to provide a source of information for parents and educators. It is not meant to be an exhaustive resource, but 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 I. There has been very little research on the behavioral and educational aspects of MPS I. 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 useful techniques and have addressed difficulties commonly experienced by children with MPS I.

Courtesy of Genzyme Corporation

How schools work

Understanding how schools are organized can help parents work together with educators. Parents of children with MPS I 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 labor 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 and needed 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.

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

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 I, 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 relation-

ship 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.

teristics between mild and more severe forms of the disorders. 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.

Early intervention

Infants and very young children with MPS I may obtain substantial benefit from an early intervention and stimulation program where maximum intellectual gain can be encouraged. This is especially important for children with disorders in which early plateaus in learning occur. The child should be enrolled in a preschool early intervention program as soon as the diagnosis is made. All localities have early infant stimulation programs, but each state will likely operate the program from a variety of agencies, such as the school system, mental health and developmental delay services, or public health department. The school system can recommend to parents the appropriate agency to contact.

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

Relevant laws

Canadian Human Rights Laws state that schools and other educational authorities have a legal obligation to provide "reasonable accommodation" for a student's disability, as required by the personal circumstances of each student who has a learning disability or another disability. Such education accommodation is often developed partly through an individualized educational plan (IEP) that attempts to be consistent with the student's needs. For a list of "Rights to Appropriate Education" visit The Learning Disabilities Association of Canada website, www.ldac-taac.ca.

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 "An overview of MPS I for teachers") to help school personnel become more familiar with MPS I. This section covers some of the "big picture" issues schools should consider when developing an individual educational program (IEP) for a child with MPS I. It is difficult to write specific guidance that covers every child with MPS I, as there is such variation in charac-

Overall planning and monitoring considerations

Because of the rather rapid regression in skills and behavior experienced in severely affected individuals with MPS I, schools should frequently monitor changes in behavior so the IEP can quickly be adapted as needed to support a child who is losing skills. The IEP should be developed to encourage social and academic participation, new learning, and the preservation of established skills. It's frequently necessary to alter the learning environment and methods of instruction to adapt to difficulties with cognitive skills, mobility, or behavior problems. Teachers may need additional support to understand the child's capability and to cope with the limitations of the child's skills and disease progression. This will assist them in tailoring their teaching and expectations to the child.

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 and adaptive physical educators. 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.

Courtesy of Genzyme Corporation

Infants and very young children with MPS I may obtain substantial benefit from an early intervention and stimulation program where maximum intellectual gain can be encouraged.

Behavior problems

Some of the physical effects of MPS I, including limited language skills, poor hearing, and developmental delay, may lead to difficulty hearing or understanding a teacher's questions or instructions, difficulty interacting with peers, trouble participating in group activities, or failure to complete assigned work. For severely affected children, most behavior problems are likely caused by neurological issues, lack of understanding, difficulty with communication, or sensory limitations. It is important for school personnel to understand MPS I so that they recognize these issues as complications of the medical condition. Altering the learning environment and methods of instruction may help reduce some behavior problems. Teachers and administrators may need training and consultation in interventions for over-activity, restlessness, and fearfulness. Behavior support and management principles should be well known by teachers and school psychologists. There should be an emphasis on modifying the classroom environment and using of reinforcements to promote appropriate behavior. Children with MPS I should be disciplined consistently and appropriately according to their age and abilities. Parents should arrange to coordinate discipline strategies with teachers in advance to maintain consistency between home and school.

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 these disorders, but many skills they use in teaching non-disabled students will enable them to work well with children with MPS I. Teachers should have access to personnel with more expertise, such as school psychologists or behavior specialists, when needed. Teachers also may 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 limitations. Children with mild MPS I are likely to have normal or only mildly delayed intellectual development. It's important for teachers to be aware that the outward skeletal manifestations of the disorder do not mean that the child has a significant delay in intellectual development. 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. Planning for the transition from school to post-secondary education or work should focus on helping children with MPS I pursue vocations in a manner similar to that of their peers.


Courtesy of Genzyme Corporation

Socialization

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.

Placement issues

Overview

One of the most vexing issues in devising an educational plan for children is deciding where special education services will actually be delivered. The student's placement must be in the "least restrictive environment," the setting in which the student has the most contact possible with children without disabilities. Schools should first consider educating children in the regular classroom with supplemental aids and services to meet their needs. It should first be determined what supplementary aids and services would enable the child to be educated in the regular classroom. When deciding on the least restrictive environment, the team should consider the following factors:

- the educational benefit to the child
- the non-academic benefit to the child (for example, social benefits)
- the potential harmful effects of a setting (such as lack of stimulation)

The effects a disabled child will have on other students also must be evaluated. A child with disabilities may disrupt the education of other students in the classroom. The IEP team must consider a different placement for the child if it is determined that the child's needs cannot be met in the regular classroom, even with supplemental aids and services. Schools are required to have a variety of placements available, ranging from services in the general education classroom, to part-time services in a resource room, to services in self-contained classrooms or special schools. Special education law requires not that a student have the best placement, but only that the student have a placement in which he or she can obtain educational benefit. The best way to ensure the most appropriate placement is for parents to develop a list of the child's strengths, needs, and goals.

Inclusion

Inclusion is the practice of giving appropriate in-class support in the general education classroom to students with a full range of abilities and disabilities. The term "inclusion" can be used in different ways. Some use inclusion to mean inclusion in regular education programs for four of six periods with instruction adapted only in two of the child's special education classes. Others have abolished all separate classes for special education and provide supportive services to all children in regular classes.

As far as academic progress goes, inclusion seems to work for some students. Socially, there is no data to support whether inclusion is effective or not, and few studies have been conducted with children who have multiple disabilities. In theory, all required services could be provided in a regular education classroom.

In practice, it seems that despite having well-trained teachers and well-equipped classrooms, not every child will benefit from inclusion.

When deciding on goals and placements for children with disabilities, schools are required to consider the academic and social needs of students and where these needs can reasonably be met. At times, this may result in the school wanting to include the child in an inclusion program even though the parent may wonder if this is the best placement. If this is the case, have the school document these needs and how inclusion specifically meets the child's needs. Then you and the school can work together to find the best solution for your child.

Socialization

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

- Decide on overall socialization needs and goals for the child. Remember that for some children, increasing the number of friends and playmates is the goal, while for others it may be reducing interaction to a tolerable level.
- Form a social network in an inclusive setting. Meet with small groups of non-disabled students and have them develop a list of ideas on how to involve the disabled 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 disabled and non-disabled 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.

There are several parts of the IDEA that can be helpful to a parent who wants to advocate a full inclusion program.

Courtesy of Genzyme Corporation

Monitor your child's outcomes in terms of academics: Are they making academic progress? Are they meeting their academic goals? For non-academic areas: Are they making social/emotional progress? Do they have friends? Do they enjoy school? Do they feel safe? Do they feel they have enough boundaries?

If the answer to these questions is yes, inclusion may be a good option. If not, and the parents don't like a placement option recommended by other team members, have the team document how they will deal with these concerns. Usually any differences of opinion can be resolved to both the parents' and the school's satisfaction. But it's important to remember that parents have a right to mediation and appeal.

Behavior problems and placement

Some parents whose children have disruptive or challenging behavior have been told their child must be placed in a special class because the behavior is too disruptive to other students. Special education regulations do allow the consideration of whether a child's behavior is so disruptive that the education of other students is significantly affected. In such a case, the school can place the child in a special education class; however, the education of the other children must be "significantly impaired" and "all reasonable steps" must first be taken to minimize the burden on

the teacher and other students. Reasonable steps include a variety of services to assist the child and the teacher, including an individual aide for the child. If behavior is a problem, have the school system document what has been done to assess and intervene in the difficult behavior.

Courtesy of Genzyme Corporation

The individualized education plan (IEP)

IEP goal setting

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

- develop relationships with adults and children in school
- achieve as much self-help skill 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:** Appropriate academic learning goals such as reading, math, social studies, etc. These will vary according to the child's level of academic skill and potential. These goals also can include completing relevant tasks, becoming aware of the environment, etc.
- **emotional development:** Developing satisfaction with school, life, and self, improving self-control, and enhancing personal efficacy.
- **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 behavior.
- **communication skills:** Skills that develop understanding and communication with others. Improving and maintaining language skills, learning compensatory communication skills, and being exposed to and practicing appropriate language skills are examples.
- **sensory skills:** Improving 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:** 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 on the child that can be built into

the IEP program. Strengths and likes can be used as learning tools. For example, if the child likes animals, animal shapes can be used to teach addition and can be used to reinforce appropriate behavior. Animal stories can be read when the child is attentive. The focus on strengths and likes enhances motivation and allows everyone to enjoy the experience.

Parents should ask the IEP team to focus on the child's strengths and likes. The team can refer to these strengths and likes 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 favorite 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 favorite foods?

There are many more examples of 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 "wrap-around" approach to developing plans. The idea is to think in terms of what supports the teacher needs in order to help this student be successful (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 (success means 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 favorite 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 a few strengths of the teacher and school that have been identified before the IEP meeting.

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.


Courtesy of Genzyme Corporation

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

Managing disagreement with the IEP

If the parent 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 centers, 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.

Learning Disabilities Association Canada (LDAC) can advise you on how to suc-

cessfully partner with your local school district's special education officials.

www.ldac-taac.ca
1-877-238-5322

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 appropriate modifications made to simplify the environment?
- Are school-related tasks modified where appropriate but still similar to tasks other children do?

Behavior intervention plans

Overview

All children who receive special education services and have behaviors that get in the way of their learning or the learning of other children must have a behavior intervention plan as part of their individualized education plan (IEP). This should include an analysis of the problem behaviors, along with an assessment of the factors that might cause these behaviors.

The program also should specify strategies to help reduce the problem behavior. These strategies should include positive behavioral interventions, such as reinforcement (reward) for appropriate behavior, and teaching the skills necessary to perform the appropriate behavior. There also should be attention directed to arranging the classroom environment to reduce stress on the child and to provide support for appropriate behavior. An example of a situation where a classroom support is needed would be for a child who cannot communicate his needs clearly and has angry outbursts as a result. One possible solution would be to provide a communication board with

words or pictures that the child can point to as a way of communicating with the teacher or other children. If the communication need is met, there is less need for the child to become angry.

If their child's behavior problems interfere with learning, parents should make sure the IEP includes psychological services. This would allow the school psychologist to consult with the teacher in implementing behavioral interventions.

It is also important for the behavior intervention plan to be consistent with the discipline the child receives at home.

Suspension from school

Suspension from school for behavior problems should be a rare occasion for a child with MPS I. Children receiving special education services may not have their educational placement changed without an IEP team meeting and the change recommended in their IEP. Schools can suspend a child for up to 10 days before it is considered a change of educational placement. However, if a child is repeatedly suspended for less than 10 days, it may be considered a cumulative change of placement. In that case, an IEP meeting must be held to discuss the child's IEP, including developing a behavioral intervention plan or reviewing and modifying an existing plan to improve the child's behavior.

If a child is to be suspended or moved to an alternate educational setting for 10 or more days, then it is a change of placement. The IEP team must then conduct a manifest determination to establish whether the problem behavior is directly related to the child's disability. If so, the child may not be suspended for more than 10 days. The IEP team must review the child's placement and services and develop more effective ways to help the child. If the behavior is considered to be unrelated to the disability, the child can be suspended for more than 10 days, since this would be the same penalty that non-disabled students would receive if they engaged in

Courtesy of Genzyme Corporation

the same behavior. The IEP team must then meet within 10 days to plan for a functional behavior analysis, which is an individualized analysis of the problem behavior. This should include the revision or development of a behavior intervention plan, as well as looking at the suitability of the classroom and the supports provided to the child.

Dealing with difficult behavior

When dealing with difficult behavior, look closely at the environment and use consistent strategies to manage the behavior. Try to identify what the function of the behavior is. Possible functions include:

- to communicate anger, boredom, pain, or hunger
- to avoid a task the child finds unpleasant
- to get something the child wants
- to discharge pent-up energy

Look closely at the environment. Environmental change can often make a difference.

Simplify the environment. Frequent negative behavior results from an environment that is too complex, is difficult to understand, or has too high expectations. In these cases, try to simplify the environmental demands on the child.

Make the environment more attractive or stimulating. Other times, difficult behavior is the result of an environment that is boring or unattractive. Improving appropriate room decorations, activities, and levels of stimulation can improve the learning environment.


Courtesy of Genzyme Corporation

Use positive interventions first. Identify positive behavior and reinforce it as much as possible. Try to arrange it so the child is able to be successful at things and has more positive interactions with people than negative interactions. Attention, praise, and smiles are all examples of reinforcements.

Use mild penalties. Don't over-punish negative behavior. Usually mild penalties will result in behavior changes. Removing the child from the situation, taking away a privilege, and turning your back are all examples of mild penalties.

Don't take it personally. Much of the behavior of children with MPS I is not directed personally at caregivers. Taking it personally makes you angry and liable to punish more harshly.

Be consistent. Consistency is often reassuring for children, especially those who have limitations in understanding or communication. Changing the limits of what you are willing to tolerate can make difficult behavior less likely to resolve itself. Consistently reinforce positive behavior and penalize negative behavior.

Find people to help. School psychologists and special education teachers with experience in working with autistic children or children with emotional problems often are the best people to consult about behavior management.

Consider what others have done to assist with these specific behaviors:

Fears
- Consult/train teachers to intervene empathically.
- Use behavior management and medication.

Over-activity/restlessness
- Provide a quiet place with little stimulation and few choices until the child is calmer.
- Designate an activity table to include favorite books or toys for a one- to five-minute break.
- Have the child take a walk around school, then go back and continue the activity.

Aggressive/destructive
- Physically protect and block the child. Put your hand on top of the child's hand to tell him or her to "stop" or "let go."
- Be a role model for how to deal with anger.
- Label appropriate touching (i.e. no hitting) and use positive reinforcement of appropriate behavior.
- Teach other children to remind the child to use nice touching.
- Have other children leave a space around the child so he/she doesn't feel crowded.
- Teach others to approach the child from the front so as not to startle him/her.
- Arrange the environment to reduce the child's frustration.

Sensory stimulation
- Assess undesirable behaviors that may be adopted because the child is trying to manipulate the environment to increase or decrease stimulation to a desired level. The function of sensory stimulation/automatic reinforcement is to increase or reduce stimulation.
- Check for possible health problems (such as an ear infection) that may be uncomfortable.
- Provide an enriched environment, such as stimuli that match the behavior. For example, provide textured items to replace behavior that seems to provide tactile stimulation.
- Reduce sensory stimulation when over-stimulation may be causing the negative behavior. Move to a quieter area, and pad the area if necessary to prevent tactile stimulation.
- Change noise, crowding, and room temperature to provide a more optimal environment based on the child's preferences.

The discipline strategies used at school should be consistent with those used at home by the child's parents.

Adaptive physical education

Children with MPS I, like all children, must have a physical education program. The individualized education plan (IEP) should include the services of an adaptive physical educator. Adaptive physical educators learn how to adapt existing physical education activities and develop innovative activities to meet the physical, motor, personal, social, and learning needs of children with disabilities.

parents on how to provide physical education activities that meet a specific child's needs.

Every school district should have at least one adaptive physical educator. If not, one can be hired as a consultant. 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.

When dealing with difficult behavior, look closely at the environment and use consistent strategies to manage the behavior.

The adaptive physical education teacher 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

Adaptive physical educators may work directly with children with disabilities and/or may provide consultation to teachers and

Assistive technology

It should be the responsibility of the IEP team 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 and cognitive 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.


Courtesy of Genzyme Corporation

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

Communication

- Picture communication boards allow a child who doesn't speak understandably to point to pictures to communicate desires and needs.
- Augmentative communication devices use computerized devices to provide a "voice" for communication.

Educational activities

- Large-button calculators can assist with math.
- Color-coded organizers will help identify what goes where.
- Speech recognition software and other computer software 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
- commercially purchased devices take into account any cognitive limitations the child may have
- 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

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.

Daily activities

- 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.
- Picture directions can be put on or near the place where a child must perform an activity.
- 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.
- 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

Resources for more help

Web sites

- Learning Disabilities Association of Canada (LDAC) www.ldac-taac.ca
- Canadian Human Rights Commission www.chrc-ccdp.ca
- Special Needs Ontario Window (SNOW) http://snow.utoronto.ca

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Information hand-out

Additional copies of this information sheet are available at www.mpssociety.ca

An overview of MPS I for doctors

Definition, causes and incidence

Mucopolysaccharidosis I (MPS I) is a rare autosomal recessive disease that has progressive, pathologic manifestations in most organ systems. The disease is caused by a defect in the gene coding for the lysosomal enzyme alpha-L-iduronidase. As a result of this genetic defect, cells either are unable to produce the enzyme or produce it in low amounts. This results in an inability of the lysosome to catabolize certain glycosaminoglycans – a process essential for normal growth and homeostasis of tissues. These glycoasminoglycans, commonly referred to as GAGs, progressively accumulate in the lysosome, ultimately causing cell, tissue, and irreversible organ damage. The incidence of MPS I is estimated to range from one in 100,000 births for severe MPS I to one in 1.3 million for attenuated MPS I.

Clinical presentation and prognosis

MPS I has a wide spectrum of severity, ranging from the severe form (historically known as Hurler syndrome), through a more intermediate form (historically known as Hurler-Scheie syndrome), to an attenuated form (historically known as Scheie syndrome).

Individuals with the most severe form of MPS I typically suffer from a number of symptoms that worsen over time, including developmental delays. Their lifespan is approximately eight to ten years. Those at the other end of the spectrum may have symptoms that can be severe, but they generally have normal cognitive function and height. They also survive well into adulthood and may have a normal lifespan.

The signs and symptoms of MPS I involve most organ systems. Table 1 illustrates how the signs and symptoms vary across the spectrum of MPS I, from attenuated to more severely affected patients.

Table 1: Clinical features of MPS I
A spectrum of disease from severe to attenuated MPS I

Symptom presentation	Severe MPS I	Attenuated MPS I
Stiffened joints	+++	++
Skeletal (bone) abnormalities	+++	++
Carpal tunnel syndrome	+++	++
Heart (valve) disease	+++	++
Recurrent upper airway infections	+++	+
Lung disease/ sleep apnea	+++	+
Corneal clouding	+++	+
Spinal cord compression	+++	+
Enlarged liver and spleen	+++	+
Hernia (inguinal or umbilical)	+++	+
Hearing loss	+++	+
Delayed mental development	+++	–
Coarse facial features	+++	–
Communicating hydrocephalus	+++	–
Abnormally shaped teeth	+++	–

Diagnosis

More common childhood conditions are usually ruled out before considering a diagnosis of MPS I. The first step in diagnosis is an analysis of urinary GAG levels. If high levels suggesting MPS I are found, then alpha-L-iduronidase activity levels are measured in a blood or skin sample. Enzyme activity tests are essential for a definitive diagnosis. If alpha-L-iduronidase activity levels are abnormally low, the diagnosis

of MPS I is confirmed. DNA testing may be considered to determine the specific genetic mutations, which 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 counselor.

Treatment

Two types of treatment are available: treatment that affects the underlying enzyme deficiency and supportive care.

Treatments that target the underlying enzyme deficiency include enzyme replacement therapy (ERT) and hematopoietic stem cell transplant (HSCT). Both of these treatments aim to restore enzyme activity.

With ERT, a recombinant version of alpha-L-iduronidase called PrAldurazyme® (laronidase) is given as a weekly intravenous infusion. PrAldurazyme® is indicated for: long-term enzyme replacement therapy in patients with Mucopolysaccharidosis I (MPS I; -L-iduronidase deficiency) to treat the non-central nervous system manifestations of the disease. Pediatric patients from 6 months up to 18 years of age have been treated with PrAldurazyme® in clinical studies. Treatment with PrAldurazyme® is contraindicated in patients who are severely hypersensitive to this drug or to any ingredient in the formulation or component of the container. Caution should be exercised if PrAldurazyme® is to be used during pregnancy or administered to nursing women. The most serious adverse reaction reported with PrAldurazyme® (laronidase) was an anaphylactic reaction consisting of urticaria and airway obstruction, which occurred in one patient approximately three hours after the initiation of the infusion. This patient's pre-existing MPS I-related upper airway obstruction may have contributed to the severity of this reaction. The most common adverse reactions associated with PrAldurazyme® treatment in the clinical studies were upper respiratory tract infection, rash, injection site reaction, pyrexia and chills.

The most common infusion-related reactions included flushing, fever, headache and rash (patients > 6 years of age). The most common adverse reactions requiring intervention were infusion-related reactions. Most infusion-related reactions requiring intervention were ameliorated with slowing of the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines.

Side effects should be reported promptly to Genzyme at 800-745-4447. PrAldurazyme® is available by prescription only. For more information on PrAldurazyme® therapy, please see full prescribing information (www.genzyme.ca).

With HSCT, stem cells from a healthy donor are transplanted into the MPS I patient, where they produce leukocytes that make alpha-L-iduronidase. HSCT can improve long-term survival, joint stiffness, facial coarseness, sleep apnea, hepatosplenomegaly, heart disease, hydrocephalus, and hearing loss. It has a variable effect on neurological outcomes depending on the age and intellectual function of the child at the time of treatment. HSCT does not improve skeletal and vision problems. Because of the risks of transplantation (such as infection and graft-versus-host disease), HSCT is limited to people with severe MPS I. Younger children (less than 2 years old) and children with higher cognitive function have the best results. As a result of this information, early diagnosis and referral for possible stem cell transplant are critical. Choice of stem cell source (bone marrow vs. cord blood) is largely dependent on the judgment of the institution (e.g. hospital) or physician.

Neither ERT nor HSCT is a cure for MPS I.

Supportive care includes physical therapy, occupational therapy, shunts for hydrocephalus, feeding tubes, 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.

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Information hand-out

Additional copies of this information sheet are available at www.mpssociety.ca

An overview of MPS I for teachers

What is MPS I?

Mucopolysaccharidosis I (MPS I; pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis **one**) 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 an enzyme called alpha-L-iduronidase (pronounced **al**-fa **el eye**-dur-**on**-i-dase). This enzyme is needed to break up substances called glycosaminoglycans (GAGs; pronounced **gly**-cose-a-**mee**-no-**gly**-cans), which are long chains of sugar molecules. Without the enzyme, GAGs build up in cells throughout the body, leading to damage in many body systems and organs.

MPS I signs and symptoms range from mild to very severe, and include:

- developmental delays
- problems with speech and language
- "thickened" facial features and a large tongue
- hearing loss and vision problems
- breathing problems
- abnormal bone structure
- joint stiffness and movement problems
- heart damage

Table 1 shows how the signs and symptoms of MPS I vary between severely affected children and attenuated individuals.

Table 1: Clinical features of MPS I
A spectrum of disease from severe to attenuated MPS I

Symptom presentation	Severe MPS I	Attenuated MPS I
Stiffened joints	+++	++
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Corneal clouding	+++	+
Spinal cord compression	+++	+
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Hernia (inguinal or umbilical)*	+++	+
Hearing loss	+++	+
Delayed mental development	+++	–
Coarse facial features	+++	–
Communicating hydrocephalus (fluid in the brain)	+++	–
Abnormally shaped teeth	+++	–

** 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 I affect a child's school performance?

Some children with MPS I have developmental delays that make it more difficult for them to learn. In severe cases, abilities decline as the child gets older and skills and learning can be lost. Learning difficulties can be compounded by hearing loss and vision problems.

Changes in physical appearance (such as the bone problems and thickened facial features) make children with MPS I 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 I to do the physical tasks and activities that their classmates find easy, such as handwriting, artwork, putting on a coat, or attending gym class. If the physical problems are severe, they may require a personal care worker or nurse.

Some children with MPS I have developmental delays that make it more difficult for them to learn.

Children with the less severe forms of MPS I may have a different physical appearance from children without MPS I, but this does not mean that they also have a developmental delay. In the less severe cases, cognitive function is not impaired.

How teachers can help children with MPS I

Teachers are part of the educational team for the child with MPS I. Here are a few ways that teachers may be able to help children with MPS I:

- In children with severe MPS I, learning may plateau and start to decline with age. Teachers may find it helpful to adjust expectations and evaluations to focus on maintaining existing learning.
- Teachers may want to encourage children with MPS I 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 behavior and performance so the 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.
- For severely affected children, most behavior problems are likely caused by neurological issues, 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 behavior. Teachers may wish to request a consultation with a professional experienced in dealing with these behavior issues.
- Children with MPS I 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.
- Children with mild MPS I are likely to have normal or only mildly delayed intellectual development, even though they may appear to be severely affected physically.
- Appropriate expectations of academic achievement will foster realistic self-appraisal and enhanced academic achievement.
- Teachers need support too! The child with MPS I 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.

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An overview of MPS I for case managers and support workers

What is MPS I?

Mucopolysaccharidosis I (MPS I; pronounced **mew**-ko-**pol**-ee-**sak**-ah-ri-**doh**-sis **one**) is a rare autosomal recessive genetic disorder caused by a deficiency of an enzyme called alpha-L-iduronidase (pronounced **al**-fa **el eye**-dur-**on**-i-dase). It can damage many systems and organs of the body. MPS I is inherited when a child gets two faulty copies of a gene, one from each parent.

MPS I signs and symptoms range from mild to very severe, and include:

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- "thickened" facial features and a large tongue
- hearing loss and vision problems
- breathing problems
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Abnormally shaped teeth	+++	–

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Services that may help MPS I families

Individuals with MPS I and their families may need help from case managers and support workers to access a variety of services, including physical supportive care and emotional 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; 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 counseling, and support groups.

Relevant legislation

There are a number of federal legislations that may affect access to health care, education, and services for families affected by MPS I.

The Canadian MPS Society is dedicated to supporting individuals and families affected with MPS and related diseases through such vital services as:

- The website: www.mpssociety.ca
- 1-800#: 1-800-667-1846
- Quarterly newsletter, the Connection: a valuable resource that helps members stay on top of MPS-related news and events and stay in touch with each other.
- A Family Referral Directory: connecting families affected with the same syndrome or living in the same region.
- A Family Assistance Program: financial aid to affected families.
- Advocacy support: to ensure our members receive the treatment and care they need.
- Biennial family conferences: providing families an opportunity to learn more about new research, treatments and care strategies, and to meet with other families, share experiences and form life-long friendships.
- Bereavement support, for families dealing with the devastating loss of a child to MPS or a related disorder.

People with MPS I and their families may need help from case managers and support workers to access a variety of services, including physical supportive care and emotional support.

Canadian Society for MPS and Related Diseases

The Society supports public awareness campaigns – like our Canadian MPS Jeans Days – develops, publishes, and distributes a variety of educational materials, issues press releases, and maintains this website, www.mpssociety.ca with important updates on the Canadian MPS Society's news and events as well as links to our international sister organizations. Our biennial conferences give medical professionals an opportunity to meet and share information with attendees and each other.

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.

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 (including MPS I).

anterior: Front.

arylsulfatase B: Lysosomal enzyme deficient in MPS VI.

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. It is often associated with brain disease in children with MPS I.

attenuated: Diminished, not as severe.

autosomal recessive disease: A pattern of inheritance requiring the presence of two copies of a particular gene mutation in order to have 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 nondominant (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.

beta-galactosidase (β-galactosidase): Lysosomal enzyme deficient in MPS IV-B.

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

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 center 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 at nighttime. It uses two pressure settings, one for while the person is breathing in and the other for while the person is breathing out.

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 children with MPS I, carpel tunnel syndrome 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.

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 I.

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 I 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 and replace with a healthy, donated cornea.

CPAP: Continuous positive airway pressure, often used for people with sleep apnea to open the airway at nighttime 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.

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

echocardiogram: Ultrasound of the heart to evaluate for 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 (EKG or ECG): 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 fibers. 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 replacement therapy: A therapeutic approach for a genetic disorder whereby the missing protein is manufactured separately and given intravenously (injected into a vein) to the patient on a regular basis.

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).

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

galactose 6-sulfatase: Lysosomal enzyme deficient in MPS IV-A.

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.

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): Long repeating chain of complex sugar molecules. See 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.

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.

iduronate sulfatase: Lysosomal enzyme deficient in MPS II.

individualized 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 including members from the school system and the family are involved in designing the IEP, and federal legislation is in place to guide the development of appropriate IEPs.

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, 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 VI.

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.

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 IV-A: Caused by a deficiency of the lysosomal enzyme galactose 6-sulfatase.

MPS IV-B: Caused by a deficiency of the lysosomal enzyme beta-galactosidase.

MPS VI: Also called **Maroteaux-Lamy syndrome**. Caused by a deficiency of the lysosomal enzyme arylsulfatase B. An autosomal recessive disease with bone abnormalities, corneal clouding, and normal cognitive function.

MPS VII: 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.

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" in recent decades.

mutation: A change in the genetic material (DNA) of a cell that alters expected genetic processes.

N-acetylglucosamine 6-sulfatase: Lysosomal enzyme deficient in MPS III-D.

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.

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.

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 mild (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.

sleep apnea: A temporary cessation of breathing during sleep, generally caused by obstruction of the airway.

Sly syndrome: See MPS VII.

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 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 re-populate 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.

stem cell: A cell whose "daughter" cells have the potential to develop into a variety of specialized cell types.

sternum: A long, flat bone, jointed with the cartilages of the first seven ribs and with the clavicle, forming the middle part of the anterior (front) wall of the thorax (chest area).

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: 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).

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 mode 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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Author acknowledgments

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Updates and new information

Medical professionals and researchers are constantly learning new things about MPS I disease and treatments. Some of the support resources, websites, and laws mentioned in this guide may change over time. As a result, the content in this guide may become outdated over time. However, the good news is that this guide has been designed so that the existing content can be easily updated and new content can be easily added over time. You can make sure that you keep this resource guide up to date simply by completing this form and sending it back to the National MPS Society using the pre-addressed envelope included in this binder. By doing so, you will be added to a distribution list of individuals and families who will receive any future updates.

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