



National
MPS
Society

Support for Families. Research for a Cure.

Hunter Syndrome



A Guide to Understanding

MPS II



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

Pictured on cover: (top) Scotty, (bottom) Sebastian

Pictured on right: (top to bottom) Khalil, Noah, Kalel



What is MPS II?

Mucopolysaccharidosis II (MPS II; pronounced “mew·ko·pol·ee·sak·ah·ri·doh·sis two”) is a rare genetic disorder that affects many organs in the body. It is also known as Hunter syndrome, named after Dr. Charles A. Hunter, who first described it in 1917.

MPS II belongs to a group of inherited metabolic diseases called mucopolysaccharidoses (MPS), a subgroup of lysosomal storage disorders (LSDs). MPS is a disorder in which at least one long-chain sugar carbohydrate called glycosaminoglycan (GAG; pronounced “gly·cose·a·mee·no·gly·can”; and formerly called mucopolysaccharide) accumulates in the lysosome, an organelle within cells. There are seven distinct clinical types of MPS, some of which have several subtypes.

If you are a parent of a newly diagnosed child, or someone who has been diagnosed with MPS II yourself, it is important to remember that there is a wide spectrum of severity in how MPS II shows up and progresses:

- It can be an attenuated (mild) form that usually manifests in childhood and progresses slowly; OR
- It can be a severe form that manifests in infancy and progresses rapidly.

Even children from the same family may be affected differently. A range of possible problems is described in this booklet; however, this does not mean that you or your child will experience all of the symptoms described. Some complications arise early in childhood, while others present much later or may never occur. As yet, there is no cure for individuals affected by MPS II, but there are ways to manage the challenges they will have, and to ensure the best quality of life.

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



TREVOR

What causes MPS II?

In healthy individuals, GAGs are used in the building of bones, cartilage, skin, tendons, and many other tissues in the body. For instance, the slippery synovial fluid that lubricates your joints contains GAGs as does the rubbery cartilage in your joints. All tissues have some of this substance as a normal part of their structure. As more GAGs are produced, older GAGs get broken down; this is the normal cycle of events that maintains a healthy balance in the body. However, when this cycle does not function properly and GAGs are not broken down, they accumulate within the cells. This malfunction results in progressive, sometimes permanent, cellular damage that affects the individual's physical abilities, proper functioning of organs and systems, appearance, and, in most cases, cognitive development.

MPS II is caused by accumulation of two particular GAGs called dermatan sulfate (DS) and heparan sulfate (HS). DS is found in the skin and in the cornea and sclera of the eye, which helps to maintain corneal transparency and the shape of the eye, respectively. DS is also found in high quantities in blood vessel walls, heart valves, tendons, lungs, intestinal mucosa, and the umbilical cord. HS is ubiquitous and is found on the cell surface and in the extracellular matrix. HS is also one of the most complex GAGs in the body. When these GAGs are not degraded, they remain stored inside the cells in the body. The GAGs are not intrinsically toxic, but when they accumulate in large amounts, the effect



AIDEN

of storing them in the body can lead to many physical problems. Babies may show little sign of the disease, but as more and more GAGs accumulate, symptoms start to appear as a result of progressive damage.

Both DS and HS are broken down by an enzyme called iduronate-2-sulfatase (pronounced “eye-dur-onate two sul-fa-tace”), also called I2S. Enzymes are special types of proteins that help build and break down complex molecules inside a cell. Deficiency in iduronate-2-sulfatase results in accumulation of both types of GAGs.

MPS II is caused primarily by accumulation of the GAGs dermatan sulfate (DS) and heparan sulfate (HS). Consuming sugar or foods normally eaten will not affect the buildup of GAGs in the body.

How is MPS II diagnosed?

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

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

A urine test is only one of the first steps in diagnosing MPS II. To confirm the diagnosis, the doctor needs to measure the levels of enzyme activity in the blood and/or skin cells. In healthy individuals, normal levels of enzyme activity are seen in the serum, white blood cells, and skin cells. In individuals with MPS II, the enzyme activity levels are much lower or absent.

An early diagnosis can potentially prevent some of the permanent damage caused by the disease.

Supportive care from physicians and your family network will help you and your loved one moving forward.

A clear diagnosis of MPS II requires tests conducted by experts showing enzyme activity much lower than normal or absent.

Genetic testing

DS and HS are both degraded by the same enzyme, iduronate-2-sulfatase (I2S). The gene that encodes this enzyme is called *IDS*. When this gene contains mutations (genetic changes), little or no enzyme is made.

DNA tests can identify the specific changes in the *IDS* gene that are responsible for making the missing enzyme. For example, while we know that every individual with MPS II has a deficiency of iduronate-2-sulfatase enzyme, there are over 650 different DNA mutations in the gene that can cause the deficiency. There are two major types of gene mutations. Some mutations (missense mutations) encode for an enzyme that is just slightly modified, while other mutations (nonsense mutations) are so severe that no enzyme is produced at all. While the implications of each of the

many possible mutations are not understood at this time, individuals who have mutations where no enzyme is produced are more likely to have the severe form of MPS II.

Until recently, the common diagnostic genetic test was a chromosomal microarray that could detect approximately 15%-20% of cases with a genetic basis. However, new technologies are being developed that may allow DNA tests to become a first-line diagnostic tool for MPS diseases. Next-generation sequencing techniques can now quickly and more cost effectively analyze the whole exome or genome of individuals. Whole exome sequencing (WES) sequences all of the DNA that encode proteins and is about 1.5%-2% of the entire genome.



SAWYER AND DAXTON

New DNA technologies have been developed recently that include multi-gene panels to allow the sequencing of just the MPS disease-causing genes. Some of these panels are currently being offered free of charge. Please contact the National MPS Society for more details.

It is important to note that different methods of DNA analysis will detect different types of genetic variants. No test will perfectly cover all possible mutations. Many commercial DNA testing sites are now advertising relatively inexpensive DNA tests. Some are of little predictive value to individuals with MPS. Even when the complete genome is sequenced, the quality of testing can vary significantly.

If an individual chooses a personal DNA analysis, he or she should be sure to pick a clinical-grade laboratory that is accredited by the Clinical Laboratory Improvement Amendments and College of American Pathologists. Additionally, the results should be analyzed by someone familiar with genetics as the implications for disease are very specific, and not all mutations are harmful. Once the genetic mutations in the individual with MPS II have been identified, accurate testing is available for other interested relatives.

Individuals with MPS II should receive DNA testing prior to discussing treatment options.

DNA tests can be diagnostic in many situations when performed by a clinical-grade laboratory, and the results are analyzed by appropriate genetic counselors. Gene panels may offer an initial analysis that is more affordable. Consult your doctor or genetic counselor for more information.

Individuals with MPS II should have DNA testing after the initial diagnosis through analysis of urine or blood. In many cases, severity can be determined by mutational analysis.

Specific treatment of MPS II

Overview

The goals of managing MPS II are to improve quality of life, slow down the progression of the disease, and prevent permanent tissue and organ damage. Currently, there is no cure for MPS II; however, early intervention may help prevent some irreversible damage. Until

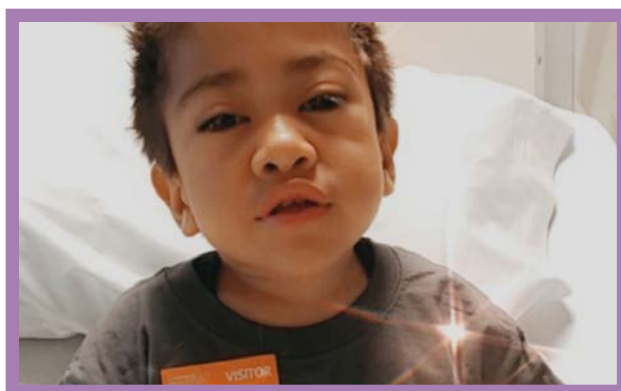
recently, the main treatments for MPS II have been symptom management, but newer treatments are entering clinical trials that may significantly improve disease outcomes in the future.

Enzyme replacement therapy (ERT)

Individuals with MPS have a deficiency in certain enzymes that break down GAGs, leading to their buildup in the cells of various organs. Given by an intravenous (IV) infusion, ERT provides an external source of the deficient enzymes. The enzyme travels through the bloodstream and enters cells in various organs where it helps break down GAG buildup.

The first ERT for MPS II was approved by the Food and Drug Administration (FDA) in 2006. It has subsequently been approved in many parts of the world. Elaprase® (idursulfase) is a manufactured version of the body's natural iduronate-2-sulfatase enzyme. (A second version of the enzyme, which appears to behave very similarly, was developed and approved in Korea in 2012.) Elaprase is administered via IV infusions. Once in the blood stream, it is taken up into lysosomes (small organelles inside the cell) where it breaks down the GAGs that accumulate in individuals with MPS II.

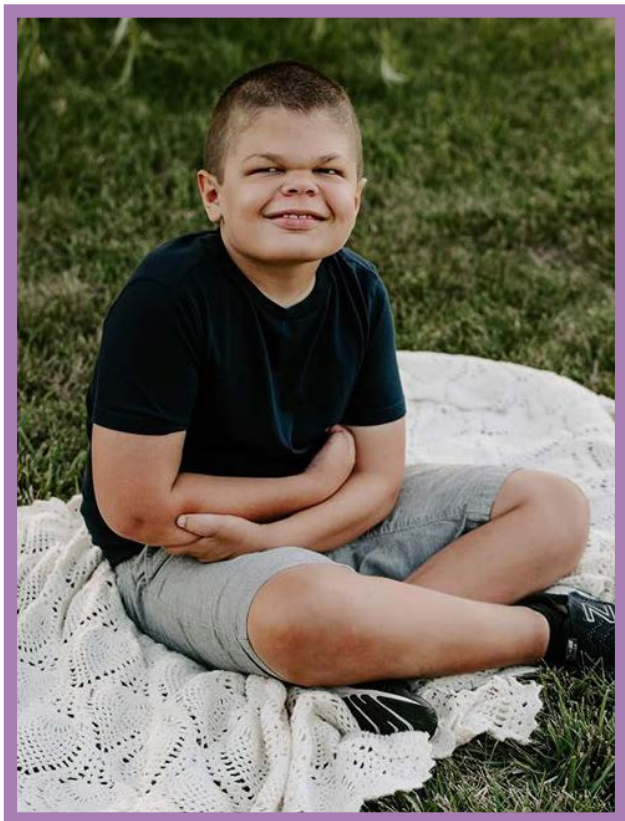
Elaprase improves lung function, walking capacity, endurance, reduces the size of the liver, and decreases the GAG levels in the urine in patients 5 years and older. Patients treated with Elaprase from 16 months to 5 years of age have reduced spleen size; however, other disease-related improvements have not yet been demonstrated. Safety has not been established for children under 16 months old.



EZRA

Elaprase, when administered normally via IV, does not reach certain parts of the body (i.e., bones and heart) well. More importantly, it does not cross the blood-brain barrier and has not shown significant effects on the neurocognitive decline that occurs in individuals with MPS II. Due to this issue some countries recommend ERT only for individuals with the attenuated form of MPS II, while in other countries all cases are eligible to receive ERT. In the United States, ERT is recommended regardless of the level of severity.

Treatment is generally well tolerated but must be delivered weekly for continued effectiveness. At times, serious hypersensitivity (allergic) reactions have been observed up to 24 hours after infusion. Initial treatments should be in a suitable medical setting where such reactions can be monitored and treated with the appropriate medications.



CARTER

Several new approaches are in development to get ERT into the brain successfully. Some methods include intrathecal (IT) delivery (into the spinal canal) that are currently in clinical trials in the United States, and intracerebroventricular administration (directly into the brain) currently in trials in Japan. The IT trials have had to overcome some problems with delivery methods, but the enzyme itself seems to be well tolerated, and clinical trials continue.

There are also approaches that modify the I2S enzyme so it will be able to cross the blood-brain barrier. I2S has been successfully fused to several different molecules that help transfer the enzyme directly into the brain. Early clinical trials of some of these modified enzymes are under way and have shown promise delivering the enzyme to the brain with normal IV administration.

Elaprase is a registered trademark of Shire, recently acquired by Takeda Pharmaceutical Co., Tokyo, Japan.

For parents or individuals to fully understand the risks, benefits, and limitations of ERT, it is important to talk with physicians familiar with MPS II ERT and families undergoing this treatment. The National MPS Society can put you in touch with physicians and families so you can become better informed before reaching a decision.

Hematopoietic Stem Cell Transplant (HSCT)

Like ERT, the goal of HSCT is to restore activity of the deficient enzyme. HSCT has become the treatment of choice for many individuals with MPS I; however, it has rarely been used on individuals with MPS II.

Stem cells (cells that are capable of differentiating into a wide variety of specific cell types) are harvested from the bone marrow, peripheral blood, or umbilical cord blood of a healthy donor. They are typed in advance to avoid rejection by the recipient. The stem cells are infused into the bloodstream of the recipient where they migrate into

the bone marrow and multiply into new, healthy, enzyme-producing blood cells. These healthy cells migrate back to many parts of the body where they produce properly functioning enzyme. Some of these new cells will migrate into the brain to produce enzyme, thereby preventing further neurological and cognitive damage.

When successful, this treatment only needs to be performed one time. It will provide a continuous source of healthy enzyme as the body is now creating the enzyme on its own in many parts of the body.

Donor stem cells must be carefully chosen to match the recipient as closely as possible to minimize rejection. Before a transplant, the individual needs a conditioning protocol. Typical protocols include chemotherapy and other medications to prepare the body to accept the transplanted stem cells and to avoid graft-versus-host disease (GVHD). This process eliminates the individual's immune system that will be "rebuilt" over time as the new donor cells reproduce and repopulate the individual. After a transplant procedure the individual will need to repeat all vaccinations received prior to the procedure.

The disadvantages of HSCT include the risk of mortality, the problem of finding a suitable donor, GVHD, and the necessity of a very specialized medical facility. The procedure and guidelines have been improved over time so that experienced centers now report up to 90% survival rates.

Transplants require very specialized medical centers and extended hospitalizations. They will also require frequent follow-ups and regular evaluations. Transplants should be performed at Centers of Excellence familiar with the unique needs of individuals with MPS.

As HSCT cannot reverse preexisting cognitive effects, it is generally recommended that HSCT be performed as early as possible. Although still controversial and not

frequently used in the United States, HSCT for MPS II is beginning to be offered as an option in some countries, including Japan, China, and Brazil.

As gene editing techniques have improved, new methods of HSCT are being attempted with the individual's own cells. A healthy copy of the *IDS* gene is edited into an individual's own stem or blood cells which are then reintroduced into the body. As the cells belong to the same individual, the possibility for rejection and immune complications are significantly less, and healthy enzyme can be produced.



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For individuals to fully understand the risks, benefits, and limitations of HSCT, it is important to talk with transplant physicians and families who are familiar with the procedure. The National MPS Society can put you in touch with physicians and families so you can become better informed before reaching a decision.

For more information, see the Mucopolysaccharide (MPS) Disorders and Hematopoietic Stem Cell Transplantation (HSCT) Fact Sheet mpssociety.org/hsct-facts.

Gene therapy



LIAM

Gene therapy is another promising treatment option that is currently in clinical trials. There are two approaches to gene therapy. Ex vivo therapies attempt to modify an individual's own cells (usually stem or blood) to correct the gene deficiency and then reintroduce these cells back into the individual.

In vivo gene therapy involves inserting a healthy gene for I2S into a type of vector (DNA transfer vehicle) that can introduce the corrected *IDS* gene into a person's body. The vector is usually a type of modified virus. Retroviral vectors actually insert the healthy gene into an individual's genome, but this method can lead to unintended disruption of other genes and is no longer the first choice of treatment.

Adeno-associated viral vectors do not integrate into the host genome. They can replicate within cells and are less likely to cause other genetic mutations or damage. This method of gene delivery is currently in early clinical trials. It was reported to be well tolerated following a one-time administration, and there were signs of neurocognitive stability in one patient and continued normal cognitive development in a second younger patient. Clinical trials are ongoing.

Genome editing techniques are also under investigation. For example, the *IDS* gene has been inserted into a gene-specific site in the livers of individuals with MPS II. A Phase I/II clinical trial is currently underway. These techniques may also be used to modify an individual's own stem or blood cells by correcting the mutated *IDS* gene. The healthy enzyme-producing cells can then be reintroduced into the body through HSCT.

While there are many promising new techniques and emerging clinical trials, they are mostly in early safety stages and will require further study to determine their long-term safety and efficacy. Be sure to consult with your doctor and genetics specialist to determine the best options to consider.

Many promising new treatments are currently entering clinical trials. Consult your doctor and genetics specialist to determine which options are the best to consider.

Are there different forms of MPS II?

MPS II has sometimes been classified based on clinical symptoms as mild (little cognitive involvement) or severe (rapidly progressing with intellectual decline), but there is only one form of MPS II caused by a deficiency in the enzyme I2S that is responsible for the breakdown

of both DS and HS. MPS II has a wide range of clinical severity. It is more appropriate to view MPS II as a continuous spectrum of disease from the most-severely affected individuals to the less-severely affected (attenuated) individuals.

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

How common is MPS II?

MPS II is a rare mucopolysaccharide disease. However, it is difficult to estimate exactly how rare since reliable incidence figures are not available. It is estimated that MPS II occurs in between 1 in 100,000 to 1 in 170,000 live *male* births. MPS II is extremely rare among females, although a few cases have been reported.

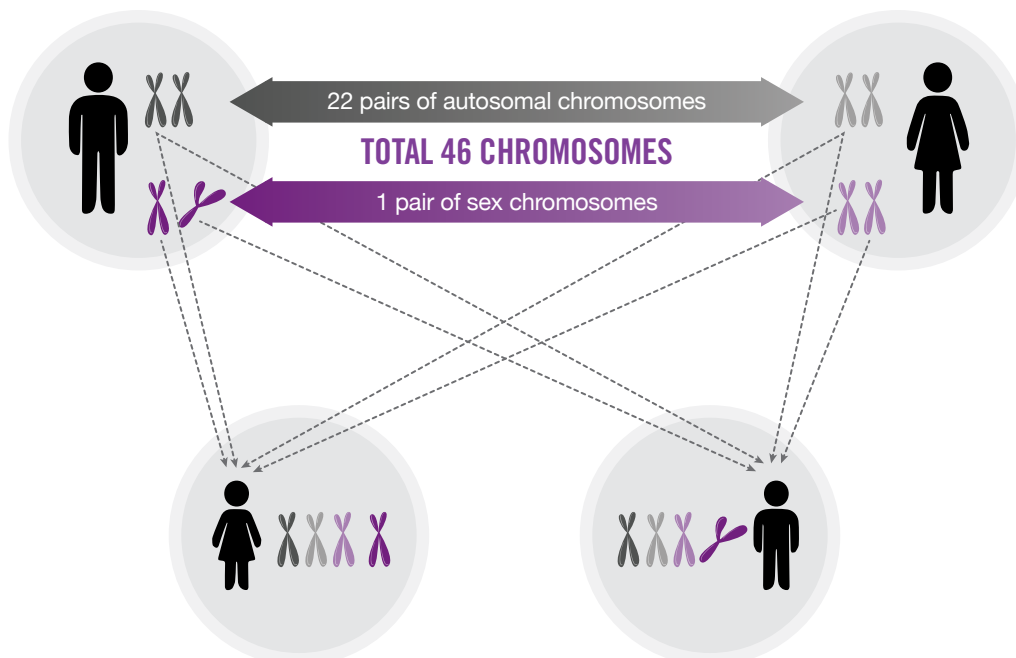
Although MPS II itself is rare, the cumulative incidence of all MPS diseases is 1 in 25,000 births, and part of the larger family of lysosomal storage disorders (LSDs), which collectively occur in about 1 in every 5,000 to 7,700 births.

How is MPS II inherited?

To understand inheritance of MPS II, it is important to grasp some basic concepts about genetics and inheritance (**Figure 1**). All humans have 2 complete sets of chromosomes—1 set of 23 from each parent for a total of 46 chromosomes. Each chromosome is a string of many genes. Twenty-two of the 23 chromosomes are matched and are termed “autosomal” and contain genes that are needed for all individuals regardless of gender. The remaining pair are the sex chromosomes that determine gender of the individual (XX for female and XY for male; the Y chromosome comes from the father). Each of the

matched autosomal chromosomes contain the same genes; i.e., chromosome 1 from the father has the same set of genes as does chromosome 1 from the mother; chromosome 2 from the father has the same set of genes as does chromosome 2 from the mother, and so on. Thus, every individual has two copies of each gene, one copy from each parent, located on the autosomal chromosomes. Consequently, every individual, other than those with certain chromosomal abnormalities, has 22 matched sets of autosomal chromosomes and 1 mismatched set of sex chromosomes totaling 46 chromosomes.

Figure 1. Normal inheritance.



Most people consider a genetic disease to be one that gets passed down from father or mother to child, in other words, at least one parent clearly has the disorder and so does the child. When only one parent is affected and so is the child, the disease is considered “dominant” because the inappropriately functioning gene from the parent that has the disease dominates over the healthy gene of the other parent.

However, there are some genetic disorders that appear to show up suddenly without any strong indication that either parent has the disease. These genetic diseases are termed “recessive” or “hidden” because they show up only when genes inherited from both parents are not functioning correctly. People with these recessive genes appear normal because they have one normally functioning gene from one of their parents that “hides” or overcomes the improperly functioning gene inherited from the other parent. Such individuals are termed “carriers” because although they themselves do not exhibit the disease, they carry the defective gene that can be passed on to their children.

Genetic testing can trace the defective gene back up the family tree for several generations, even if none of the ancestors showed signs of the disease. Depending on whether the affected gene is on 1 of the 22 autosomal chromosomes or on the sex chromosomes, the disease is described as autosomal, X-linked, or Y-linked.

Females have 2 X chromosomes, 1 each inherited from the father and the mother. Corresponding genes on both X chromosomes need to be mutated for the female to exhibit a recessive disorder. Males have 1 X chromosome inherited from the mother and 1 Y chromosome inherited from the father. Mutations in genes on either chromosome will result in the disease becoming manifest even in the case of rare disorders since there is no corresponding healthy counterpart to overcome the defective gene.

Any child born of carrier parents (those couples in which both have a recessive gene on an autosomal chromosome) has a:

- 50% chance of inheriting 1 normal gene and 1 diseased gene and be a carrier without evident disease, just like the parents;
- 25% chance of inheriting the defective gene from both the mother and the father and thus having the disease;
- 25% chance of inheriting the normal gene from both parents and thus being healthy and also not being a carrier.

Therefore, any child has a 75% chance of inheriting at least one normal gene and will not manifest disease.

Furthermore, there is a 67% chance that unaffected brothers and sisters of individuals with the disease will be carriers of the defective gene. This is why individuals who are related to each other should not conceive children. The probability of related parents having similar recessive gene mutations increases dramatically.

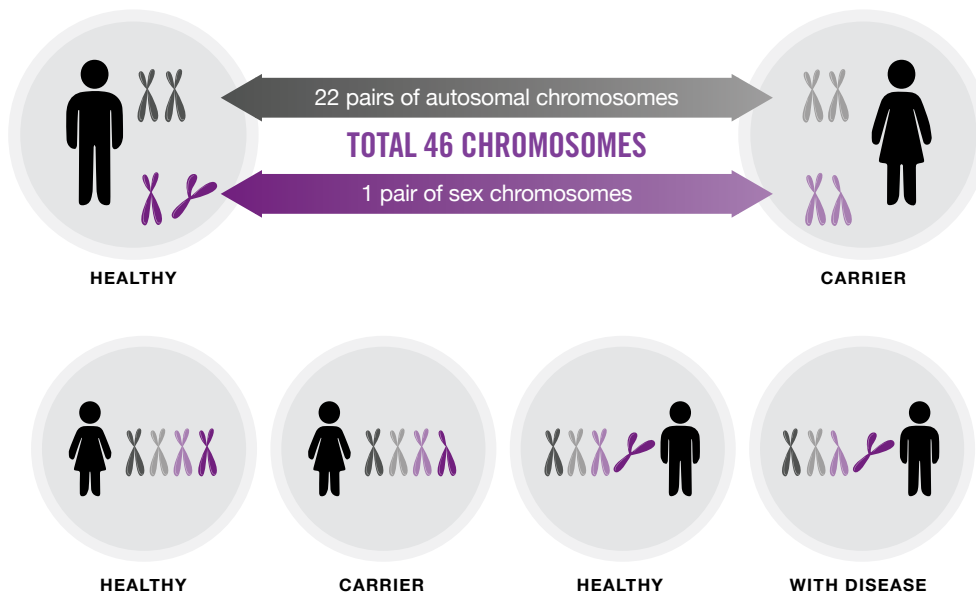
Some genes code for enzymes. Since there are two copies of each gene, one inherited from the father and the other from the mother, each enzyme is produced from two genes. A defective gene produces a defective enzyme, i.e., an enzyme that does not have full function or may even be completely inactive. If one of the two genes is defective (as is the case for carriers), the functional enzyme produced by the good gene helps the body compensate for the defective enzyme produced by the defective gene. This prevents the carrier from having symptoms of the disease. Only when genes inherited from both the father and the mother are defective and producing very little or inactive enzyme does the individual exhibit symptoms.

MPS II is an X-linked recessive genetic disease; that means that the gene that causes this disease is on the X chromosome (**Figure 2**). As such, every

male with a mutation in the gene coding for the I2S enzyme develops MPS II. Since they have only 1 X chromosome; they do not have a second X chromosome to compensate and the Y chromosome does not contain this gene. Females generally do not develop MPS II because they have 2 X chromosomes and the healthy gene inherited from 1 parent produces sufficient enzyme to overcome the deficiency in the mutated gene inherited from the other parent. Females develop MPS II *only* when the enzyme produced by both X chromosomes is defective.

If a male with MPS II has children, his male children will not be affected because they inherited his healthy Y chromosome; however, all female children will be carriers as they will all inherit his defective X chromosome. It is important to note, however, that spontaneous mutations are not uncommon in X-linked disorders, and they can also cause MPS II. Therefore, it is necessary to get confirmatory genetic testing to determine if a mother is actually carrying this disease.

Figure 2. X-linked recessive inheritance, mother with mutation.



MPS II is a genetic recessive disease caused by deficiency in a specific enzyme, iduronate-2-sulfatase encoded by the *IDS* gene.

MPS II is an X-linked disease and almost exclusively affects males, although a few cases among females have been reported.

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

Why does disease severity vary so much?



MARCUS

Any change in a gene is called a mutation. Many mutations do not have any effect on the gene function; in other words, the fundamental gene product does not change. These are called “silent” mutations. However, other mutations trigger changes in the gene structure that cause them to behave abnormally; i.e., a defective gene could result in either an overproduction or a deficiency in the gene product. When the defective gene codes for an enzyme, this could mean too much or too little enzyme activity. In the case of MPS II, the gene coding for *IDS* is defective, resulting in highly reduced or completely absent enzyme activity.

The gene coding for *IDS* has been studied extensively, and mutations that cause enzyme deficiency have

been identified. Approximately 1 in 5 individuals with MPS II (20%) have mutations that result in absolutely no enzyme being produced, suggesting that these individuals will have the more severe disease. Other mutations result in little or defective enzyme being produced. Still others are not common at all and may occur in only one family. However, to date, there has been no definite correlation between the mutation and enzyme activity, and consequently, no correlation with disease severity.

There is also little correlation between enzyme activity and disease severity. What has been demonstrated thus far is that complete absence of enzyme activity correlates with neuropathic disease and with intellectual disability and that even a small amount of active enzyme is sufficient to avoid neuropathic disease. Based on the available evidence to date, there is no definitive process known for prediction of disease severity. These data suggest that there are other, as yet not fully understood, factors involved in determining disease severity. Thus, DNA tests or mutational analysis are not always sufficient to predict disease severity.

It is important to remember that MPS II is a spectrum with a variety of symptoms, and the disease is extremely varied in its effects. This booklet addresses a wide range of possible symptoms that individuals with MPS II may encounter. However, readers are forewarned that you or your child may not experience all symptoms, or the degree described herein.

Although all individuals with MPS II lack the same enzyme, it is a complex disease with widely varying severity that is not always predictable based on DNA testing or assessment of the level of enzyme present in the body.

How long do individuals with MPS II live?

The lifespan of an individual with MPS II depends on many factors including, but not limited to, severity of the disease, specific symptoms, what treatment is given, when the treatment was started, how long the treatment continued, etc. With our current knowledge of the disease, it is not possible to predict how long individuals with MPS II will live. Individuals with slowly progressing disease may have a lifespan similar to

those without the disease, with the oldest known individual surviving to 87 years of age. On the other hand, individuals with rapidly-progressing disease experience a much shorter lifespan, usually into their mid-teens with some dying much earlier. There is always hope for better outcomes for individuals with MPS II with ever-improving newer treatments, surgical procedures, and technology.

The lifespan of patients with MPS II can vary widely depending on severity of disease, treatment received, and how fast the disease progresses.

Signs and symptoms of MPS II

With tips for care and management

Individuals with MPS II usually do not exhibit any symptoms at birth. Symptoms frequently begin to appear between 1 to 4 years of age or later depending upon the severity of the disease. Early symptoms are often abdominal hernias, frequent ear infections, and distinctive facial features often described as “coarse.”

MPS II affects multiple organ systems and is associated with a wide range of symptoms that are summarized in the table below with detailed descriptions following. Please note that not all individuals with MPS II will exhibit all symptoms or to the same degree. The symptoms and their severity can vary widely between individuals.



GIOVANNI

Table 1: List of symptoms exhibited by individuals with MPS II by organ systems.

General symptoms	Physical appearance
<ul style="list-style-type: none"> Reduced endurance 	<ul style="list-style-type: none"> Abnormal facial features (such as flat face, flat and depressed nasal bridge, slightly bulging eyes, enlarged tongue, thick lips) Large head (macrocephaly) Short stature Bent over stance
Eyes	
<ul style="list-style-type: none"> Vision problems Reduced field of vision Optic nerve damage Glaucoma (rare) 	
Gastrointestinal system (abdomen and intestines)	Respiratory system (lungs and breathing)
<ul style="list-style-type: none"> Enlarged liver and spleen (hepatosplenomegaly) Umbilical and inguinal hernias 	<ul style="list-style-type: none"> Lung problems Reduced lung function Frequent, recurrent lung infections Sleep apnea
Brain and nerves	Mouth and teeth
<ul style="list-style-type: none"> Potential developmental delays (some may have normal intelligence) Potential slowing of mental development Carpal tunnel syndrome Fluid in the brain (hydrocephalus) Compression of the cervical spinal cord 	<ul style="list-style-type: none"> Thick lips Enlarged tongue (macroglossia) Abnormal teeth (widely spaced and very thin enamel)
Ear, nose, and throat	
<ul style="list-style-type: none"> Frequent ear infections (otitis media) Hearing loss Frequent and recurrent sinus infections (sinusitis) 	
Heart and blood vessels	Musculoskeletal system (bones and joints)
<ul style="list-style-type: none"> Heart valve disease, especially aortic valve Abnormal heart muscle (cardiomyopathy) Irregular heartbeat (arrhythmia) Angina High blood pressure (hypertension) Poor circulation 	<ul style="list-style-type: none"> Joint stiffness Skeletal abnormalities (dysostosis multiplex) Abnormal hip formation (hip dysplasia) Bone deformities in the spine (scoliosis, gibbus, kyphosis), or knees (knock-knees or genu valgum)

MPS II affects many areas of the body and because its signs and symptoms are so variable, it can affect each individual very differently.

Growth

Individuals with MPS II are often taller than others of the same age until about 4 to 5 years of age after which

their growth slows down and they end up being shorter than those without the disease.

Physical appearance

Individuals with MPS II usually share common facial features, often described as “coarse”, which is not intended to be insensitive but rather help with quick and accurate diagnosis. These features include a short neck, a large head, a bulging forehead, and a broad nose with a flat bridge and wide upturned nostrils. Their faces are chubby with rosy cheeks and bushy eyebrows. The hair is often thick and more abundant

on the body than is usual (hirsute). They tend to have protruding bellies and often walk with a bent-over stance due to painful joint contractures at the shoulders, elbows, hips, and knees. Individuals with slowly progressing disease may vary considerably in appearance and may not display the typical features described above or exhibit only subtle differences.

The physical appearance of individuals with MPS II can vary considerably from distinctive features among those with fast progressing disease to very few differences from average among those with slowly progressing disease.

Mouth and teeth

Individuals with MPS II often have thick lips and enlarged tongue (macroglossia). Their gums are often overgrown. Their teeth are irregularly shaped (sometimes referred to as “peg shaped”), widely spaced, and poorly developed with a fragile outer layer (enamel). It is important that the teeth are well cared for, as tooth decay can be a cause of pain. Teeth should be cleaned regularly. If the water in your area has not been treated with fluoride, individuals with MPS II should speak with their dental and medical providers to determine a plan for fluoride administration. 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. However, even with the best dental care, an infection (abscess) around a tooth can develop due to its abnormal formation. Irritability, crying, and restlessness can sometimes be the only signs of an infected tooth in a severely affected young child.

If an individual with MPS II has a heart problem, it is advised that antibiotics be given before and sometimes after any dental treatment. This is because certain bacteria in the mouth may get into the bloodstream and cause an infection in the abnormal heart valve, potentially damaging it further. 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, but never in the dentist’s office. Dentists should be informed of the diagnosis of MPS II and provided contact information for other medical providers working with the individual.

Teeth should be cleaned regularly, and if the water in your area has not been treated with fluoride, individuals with MPS II should discuss supplemental fluoride with their dentist. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and avoid bad breath.

Dental surgery, including simple extractions, must be done only in a hospital setting with an experienced anesthetist and dentist or oral surgeon. Additional precautions must be taken for those with heart conditions. It is advised that antibiotics be given before and sometimes after any dental treatment.

Skin

Individuals with MPS II tend to have thickened and tough skin, making it difficult to draw blood or place IV catheters. Severely affected individuals may have coarser and extra hair on their face and back (hirsutism).

The skin of some individuals with MPS II may have an ivory color and pebble-like texture. This may be particularly noticeable on their back and shoulders, and sometimes, on arms and lower trunk. This is believed to be caused by storage of GAGs in the skin and medically is not considered to be of concern.

Excessive sweating and blue or cold hands or feet are common among individuals with MPS II. These may be a symptom of poor blood circulation. Please consult a cardiologist (heart specialist) to check whether there is a problem with the heart or the aorta (the large blood vessel that transports blood from the heart to rest of the body). Poor blood circulation can cause cold hands and/or feet and the skin to appear blue.



DOMINIC

Individuals with MPS II tend to have thickened and tough skin and extra hair. Cold and blue hands and feet are common and may indicate problems with circulation.

Eyes

Symptoms related to eyes include glaucoma and retinal degeneration among individuals with MPS II. Unlike other MPS diseases, individuals with MPS II do not have corneal clouding. It is often difficult to determine

Glaucoma

Storage of GAGs in the eyes can increase pressure in the eye (glaucoma), resulting in problems with vision. These should be checked by an eye doctor

Retinal degeneration

Storage of GAGs in the retina can cause changes in the retina, leading to night blindness and the loss of peripheral vision (ability to see things out of the corner of the eye). Night blindness may hamper a person's ability to go through dark areas or waking up at night

which combination of problems is responsible for the decrease in eyesight experienced by individuals with MPS II. An eye specialist (ophthalmologist) can perform special tests to help determine the cause.

(ophthalmologist) and corrective action taken to prevent further loss of vision. However, glaucoma is not common among individuals with MPS II.

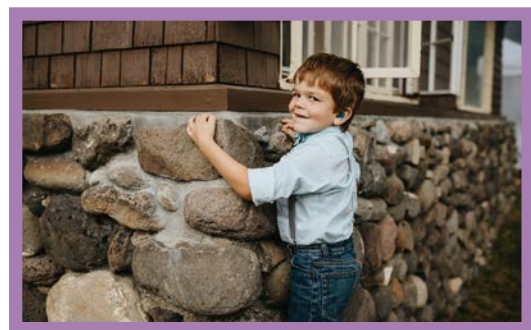
and being afraid. Adequate, but not too bright, night lighting in the bedroom or hall can help alleviate the last issue. It is important to consult an eye doctor (ophthalmologist) to take corrective action.

Problems with eyesight are common among individuals with MPS II. It is important to consult an eye doctor (ophthalmologist) to determine the cause for vision loss and take corrective action.

Ears

Some degree of deafness is common in MPS II. Deafness in individuals with MPS II may be conductive deafness, sensorineural deafness, or both (mixed deafness) and could be made worse by frequent ear infections. It is important that individuals with MPS II have their hearing monitored 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



ROWAN

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.

Conductive deafness

Conductive deafness occurs when something prevents the eardrum or middle ear bones from vibrating properly. Correct functioning of the middle ear depends on the pressure behind the eardrum being the same as that in the outer ear canal and the atmosphere. This pressure is equalized by the Eustachian tube, which runs to the middle ear from the back of the throat. If the tube is blocked, the pressure behind the eardrum will drop and the drum will be drawn in. If this negative pressure persists, fluid from the lining of the middle ear will build up and in time become thick like glue (middle ear effusion). This can prevent the eardrum or middle ear bones from vibrating properly, resulting in conductive deafness because of a blocked Eustachian tube. This is an important factor contributing to hearing loss in individuals with MPS II.



BRODY AND BENTLEY

If it is possible for the child to have a light general anesthetic, a small incision through the eardrum can be made (myringotomy) to remove the fluid by suction. A small ventilation tube may then be inserted to keep the hole open and allow air to enter from the outer ear canal until the Eustachian tube starts to work properly again. The tubes placed in the eardrum may quickly fall out. If this happens, the surgeon may decide to use tympanostomy tubes (see Use of T tubes, page), which usually stay in place much longer. It is expected that, once a ventilation tube is in place, fluid should drain out and hearing should improve.

Sensorineural (nerve) deafness

In most cases, nerve deafness is caused by 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. Nerve or sensorineural deafness can be managed by the fitting of a hearing aid or aids in most individuals. In general, it is felt that hearing aids are underutilized in MPS diseases.

Mixed deafness

When individuals experience both conductive and nerve deafness, it is referred to as mixed deafness. Managing mixed deafness involves treating both types of deafness as described above.

What is otitis media? (OM)

OM is the medical term for an infection of the middle ear. It is common for healthy children to have OM usually caused by blockage of the Eustachian tubes due to large adenoids or problems with drainage of fluid from the middle ear. In children with MPS II, this is complicated by the buildup of GAGs in the middle ear, nose, mouth, and throat and the infections become more stubborn, resulting in exacerbating the problems. There are two types of OM, acute and OM with effusion (OME).

Acute OM: 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), or a serious, potentially life-threatening inflammation of the membranes covering the brain (meningitis). Language development can also be affected by repeated ear infections.



JUSTIN

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, 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).

For some individuals with MPS II, a number of middle ear infections may occur before MPS II is diagnosed. The individual may not have any symptoms, but hearing can be affected. Any individual who has fluid in the middle ears for at least 3 months should have a hearing test. A careful examination of the ear may be difficult for a child with MPS II but is essential for proper diagnosis. Ear, nose, and throat (ENT) specialists, also called otolaryngologists, can help diagnose MPS II by identifying children with recurrent infections and abnormalities seen under examination. Once a diagnosis of MPS II 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 II tend to have many ear infections that can be very difficult to treat. If your child has ear infections that are hard to get rid of, it may be necessary for the doctor to do a “culture” of the fluid in the middle ear. The doctor will take a sample of this fluid and test it to see which bacteria, viruses, or fungi are living in the fluid. Identifying the bacteria, virus, or fungus that may be causing the infection allows the doctor to prescribe the appropriate medication. For example, if the infection is fungal, frequent antibiotic use will only worsen the situation.

Antibiotics are the usual treatment for OM. There is a wide array of antibiotics available for treatment. Some require refrigeration or frequent dosing. Antibiotic injections can be considered for a child who has difficulty taking medications by mouth. Some common side effects of antibiotics include diarrhea, nausea, and vomiting. 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, ear drops may be used to treat the infection. Steroid drugs that reduce inflammation (corticosteroids) may also be helpful. Always continue taking the full course of antibiotics as prescribed, even if the infection appears to clear quickly.

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- to 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 ENT specialist experienced with MPS II 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 II (described on page 49 in this resource). After the procedure, a culture should be made from the drained fluid to identify the offending organism.

Surgery: Removal of the adenoids (tissues at the back of the nasal cavity) and tonsils might also be recommended for children with MPS II 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. It is important to note that the adenoid tissue may “grow back” and individuals with MPS II can require more than one surgery to remove it.

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 their 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 secondhand cigarette smoke is recognized as a risk factor for OM, and every effort should be made to keep children away from smoke exposure.



DYMON JAREZ (“DJ”)

Ear infections seem to be a persistent and recurrent problem in children with MPS II, 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. MPS II can cause frequent ear infections, hearing loss, an enlarged tongue, decreased mental capacity, and blocked airway. Any of these symptoms may lead to speech and language problems. A speech therapist may help those with MPS II with their speech. Hearing aids and sign language may also be useful for people with hearing loss.

It is important that individuals with MPS II have their hearing monitored regularly.

It is important to consult with an ENT specialist experienced with MPS II to determine how best to treat ear infections and deafness.

Treatment for OM may include medication, ear tubes, or surgery. Surgery should only be performed in a hospital under appropriate anesthesia and under the care of specialists with expertise in treating MPS II or at least MPS in general.

Prevention of ear infections in individuals with MPS II may be an option. Please consult your doctor about vaccinations.

Nose and throat

Nose and throat problems are more common among individuals with more quickly progressing MPS II. Individuals with attenuated, slow-progressing disease

are likely to have fewer and less severe symptoms, except for airway involvement.

Runny nose

Typically, the bridge of the nose among severely affected individuals is flattened and the passage behind the nose may be smaller than among individuals not affected by MPS II. This is due to the bones in the mid-face not having grown well and the mucosal lining in the nose being thicker. GAG buildup in the soft

tissues of the nose and throat, combined with abnormal bones, can cause the airway to become easily blocked. Individuals with severe MPS II often have a long-term (chronic) discharge of thick mucus from the nose (rhinorrhea), 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. In addition, the neck is usually short, and both together contribute to problems in breathing. The windpipe (trachea) becomes narrowed by stored GAGs

and may be floppy or softer than among individuals without MPS II, due to abnormal cartilage rings in the trachea. Nodules, bumps, or folds of excess tissue can further block the airway.

Nose and throat problems are worse in individuals with more severe MPS II. Please consult an ENT specialist (otolaryngologist) to determine best course of action for nose and throat issues that arise.

A speech therapist may be able to help individuals with MPS II with their communication.

Respiratory system

Individuals with MPS II tend to have short necks and unusually narrow airway passages making airway blockage (obstruction) a common experience. In addition, the tonsils and adenoids (tissues at the back of the nasal cavity) can become enlarged and block the airway, thereby making breathing difficulties worse.

Chest

Individuals with MPS II often have a stiff chest; thus, it cannot move freely to allow lungs to take in larger air volumes. The diaphragm (muscle at the base of the

chest) is pushed upwards by the enlarged liver and spleen (hepatosplenomegaly). All of these structural abnormalities reduce the space available for the lungs allowing them to take in only small amounts of air and prevent intake of a large volume of air, as would be normal for someone with a healthy respiratory system. This reduced air intake prevents individuals with MPS II from breathing in adequate amounts of oxygen and can lead to difficulty breathing while awake or asleep. Individuals with MPS II are at an increased risk of infection (pneumonia).

Individuals with MPS II tend to have structural abnormalities of the chest resulting in breathing problems, including infections. Please consult your doctor for appropriate treatment.

Sleep apnea

Obstructive sleep apnea, defined as temporary breathing interruptions (usually 10–30 seconds) while asleep, is a common airway problem for individuals with MPS II. It occurs when the airway in the neck becomes blocked as muscles in the airway relax. The risk of the airway becoming blocked is increased among individuals with MPS II due to some of the structural issues stated earlier and enlarged tonsils and adenoids.

Many individuals with MPS II breathe very noisily, even when there is no infection. When sleeping, they are often restless and snore. This noisy breathing, which stops and starts, can sound very alarming to parents or bed partners who may fear that the person is dying. If the breathing is noisy during sleep, the individual's oxygen level may be low, which can cause heart problems. Although many individuals with MPS II may breathe like this for years, a sleep specialist should be consulted for an evaluation through a sleep study, especially if a parent or bed partner notices significant choking or episodes of interrupted breathing.

Individuals with MPS II may be admitted to the hospital overnight for a sleep study in which 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, sleep experts can assess the severity of breathing blockage, the difficulty in inhaling (moving air into the lungs) during sleep, and the effect on the body as a whole.

Sleep apnea can be treated in some patients by removing the tonsils and adenoids (which may regrow) or opening up the airway during sleep with a continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) machines, or a tracheostomy (a hole into the airway made in the front of the neck), which is only need in very severe cases of sleep apnea with heart failure.

Sleep apnea is common among individuals with MPS II. Sleep apnea can be treated by removing the tonsils and adenoids or airway pressure machines (CPAP/BiPAP), or a tracheostomy (in the most severe cases).

Infections

Colds are caused by viral infections and do not require antibiotic treatment. However, many individuals with MPS II develop secondary bacterial infections in addition to colds. These bacterial infections usually occur in the sinuses or middle ear (discussed earlier). In individuals with MPS II, storage of GAGs in the throat and nasal passages causes the sinuses to have abnormal shapes and become blocked, thereby increasing the risk for sinus infections. Furthermore, poor drainage of the sinuses and middle ear make treating infections difficult. Bacterial infections of the sinuses should be treated with antibiotics under the care of a physician knowledgeable about MPS.

There are many different antibiotics available and each one has its own spectrum of 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 do not 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 individuals with MPS II may become allergic to antibiotics or may develop resistant infections. Your doctor can prescribe other antibiotics to help manage this problem. While overusing antibiotics is never advised, most people with MPS II will require multiple treatments for most infections. Individuals with MPS II and caregivers will need a doctor with whom they can develop a good working relationship to manage the frequent infections.

Drugs may affect people with MPS II differently, so it is essential to consult your doctor before using over-the-counter (OTC) 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 II. Cough suppressants or drugs that have sedatives may cause more problems with sleep apnea by decreasing muscle tone and breathing rates.

Bacterial infections of the respiratory system are common among individuals with MPS II. Bacterial infections can be treated with antibiotics, but often recur when treatment is stopped. Multiple rounds of treatments may be needed.

Please consult a physician knowledgeable in treating MPS to treat infections. Please be aware that OTC medications can cause more harm than good or work differently in the body of an individual with MPS II.

Secretions

Individuals with MPS II often have collections of mucus (secretions) in the lungs. Chest postural drainage is a technique that can help with clearing such secretions. It involves placing the affected person in different positions to help mucus drain from the lungs. It may be used in combination with tapping the chest or back with a cupped hand (chest percussion), to help loosen the mucus. A physical therapist will be able to teach the technique to you, your family, and someone at school for children with MPS II. 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 causing the individual to lose consciousness).

There are also some mechanical devices that can help with clearing secretions. Inflatable vests (“shaky vests”) deliver high-frequency oscillations to the chest. The vibrations help to loosen and potentially thin the mucus in the lungs. The individual puts on the vest, connects it to the vest machine and breaths normally as the chest is massaged. After 5 minutes they stop the machine and attempt to cough. This procedure is repeated for about 30 minutes or as directed by the doctor. There are also cough assist machines that are basically a mask and mouthpiece connected to a machine. The cough assist device slowly blows air into the lungs through the mouthpiece and then quickly pulls the air out along with any mucus, simulating a cough. A nebulizer can also be used alone or in conjunction with these devices to deliver saline or prescribed medications into the lungs to help thin secretions.

Chest postural drainage, a technique to drain mucus from the lungs, may be required for some individuals with MPS II and must be done with training from a physical therapist or pulmonologist. Please be aware of the side effects of this technique and take the appropriate care. Cough assist vests and machines may help certain individuals.



PAYTON

Heart

Although heart disease is common in all individuals with MPS II across the spectrum from severe to attenuated, it may not develop or cause medical problems until later

in life. Heart disease can be categorized into effects on (a) heart valves, (b) the heart muscle, (c) heart rhythm, and (d) heart blood vessels.

Effects on the heart valves

Many individuals with MPS II across the disease spectrum experience problems, including thickening or stiffening and leakage, with their heart valves due to GAG storage. There are four valves in the heart, the tricuspid, the mitral, the pulmonary, and the aortic.

The tricuspid valve is on the right side of the heart between the right atrium (also known as “auricle,” a collecting chamber for blood flowing back from the body) and right ventricle (a muscular pumping chamber that pumps blood to the lungs). The valve prevents blood from flowing backward 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 left atrium (a collecting chamber for blood flowing back from the lungs) and the left ventricle (a muscular pumping chamber that pumps blood to the rest of the body). The valve prevents blood from flowing backward 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 transports blood from the heart to the lungs). The valve prevents blood from flowing backward into the heart between its contractions.

The aortic valve sits between the left ventricle and the aorta (the vessel that transports blood from the heart to the rest of the body). The valve prevents blood from flowing backward into the heart between its contractions.

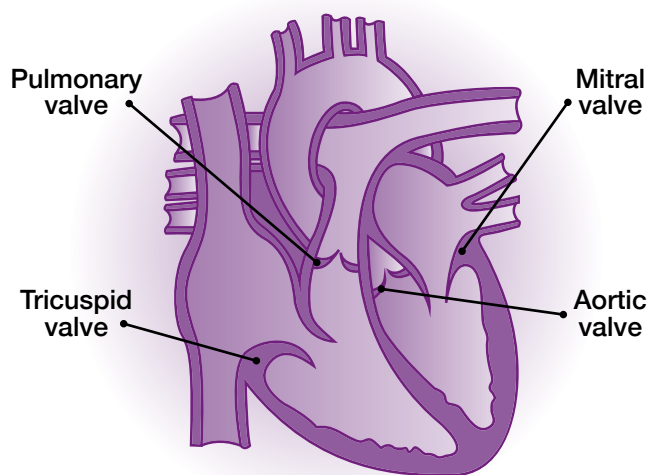
The doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAGs. The heart valves are designed to close tightly to prevent blood from flowing back in the wrong direction. Individuals with MPS II with defective valves due to damage by GAG accumulation may experience regurgitation (blood shooting backward) and/or stenosis (stiffening of the valve).

Regurgitation: This occurs when the weakened valve cannot shut firmly enough and a small amount of blood may shoot backward, causing turbulence and a murmur, e.g., when the mitral valve does not shut firmly causing blood from the left ventricle to flow back into the left atrium (mitral valve regurgitation), or when the aortic valve does not shut firmly causing blood from the aorta to flow back into the left ventricle (aortic valve regurgitation).

Stenosis: Stenosis refers to a stiffened heart valve. The valve may not be able to open completely thereby narrowing the opening through which the blood is pumped. When the problem becomes severe, the damaged heart valves may need to be replaced surgically.

Heart valve replacement is common for individuals with MPS II. There are two types of valves used for valve replacements – tissue or mechanical. Mechanical valves are made of strong durable materials that can last for a patient's lifetime; however, in order to prevent blood clots from forming, patients are usually treated

with blood thinning medication for the rest of their lives. Tissue valves are created from animal tissue and can last from 10 to 20 years in normal individuals without MPS. They do not usually require the need for blood thinners; however, GAGs can still build up on the replacement tissue possibly limiting their effectiveness. Most published cases used mechanical valves. Please consult with a heart specialist (cardiologist) knowledgeable in MPS diseases for appropriate treatment and care.



Individuals with MPS II often have abnormal heart valves, which make them susceptible to reverse blood flow (regurgitation) and/or stenosis (stiffened heart valves) that may require surgical intervention. Please consult with a heart specialist (cardiologist) knowledgeable in MPS diseases for appropriate treatment and care.

Effects on the heart muscle

Individuals with MPS II may have an abnormal heart muscle (cardiomyopathy) due to the storage of GAGs. Of the many types of cardiomyopathy, damage to the heart valves in individuals with MPS II often causes an abnormal thickening of the heart muscle (hypertrophic cardiomyopathy). As noted above, individuals with MPS II often suffer from insufficient oxygen. This

adds to the strain placed on the heart as it pumps blood through the affected lungs. When the condition worsens, the heart may become enlarged (cardiomegaly), especially the left and right ventricles (hypertrophy). This can lead to the heart pumping more weakly (dilated cardiomyopathy), resulting in heart failure due to inability of the heart to pump sufficient

blood to meet the needs of the body. In rare cases, adults with MPS II may develop a weakening of the wall of the left ventricle (ventricular aneurysm), the main

pumping chamber of the heart. These can be detected by MRI and should be treated promptly or else they may rupture and cause sudden death.

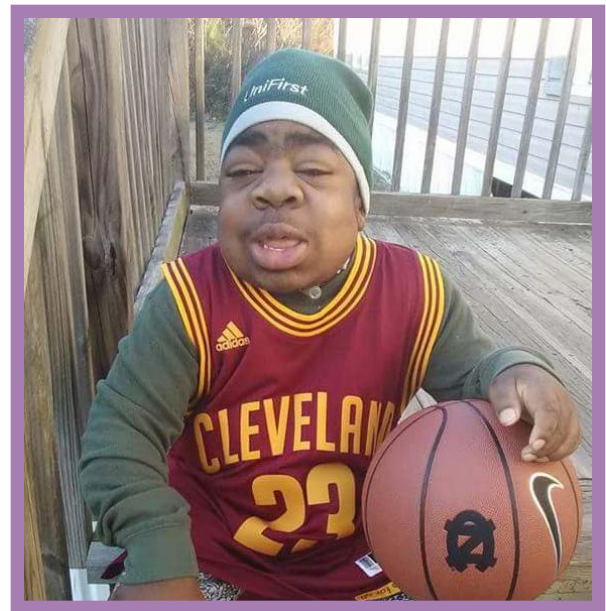
Individuals with MPS II often have abnormal heart valves, which make them susceptible to reverse blood flow (regurgitation) and/or stenosis (stiffened heart valves) that may require surgical intervention. Please consult with a heart specialist (cardiologist) knowledgeable in MPS diseases for appropriate treatment and care.

Effects on heart rhythm

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

Effects on the blood vessels of the heart

GAG storage in the heart blood vessels (coronary arteries) of individuals with MPS II can damage these vessels similar to that seen among older people and can lead to death. Sometimes, the coronary arteries of severely affected people may become narrowed and cause episodes of chest pain (angina). Many individuals with MPS II also have high blood pressure (hypertension), which is related to narrowing of blood vessels caused by GAG storage. 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 or the person you are caring for has MPS II and notice these symptoms,



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please consult your doctor and/or cardiologist. If your young child has MPS II and you notice that he (or rarely, she) is distressed, crying, pale, sweating, and keeping still, please consult your doctor as soon as possible.

Individuals with MPS II often have abnormal blood vessels, especially those in the heart, which make these individuals susceptible to chest pain (angina), poor circulation, and high blood pressure. Please consult with a heart specialist (cardiologist) knowledgeable in MPS diseases for appropriate treatment and care.

Since heart problems occur so frequently among individuals with MPS II, all those affected should have a test known as an echocardiogram annually (or as often as the doctor thinks necessary) to catch signs of problems as early as possible. 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 II. If this is not possible, you should inform the doctor about the heart problems experienced by individuals with MPS II. Medications are available to help manage the heart problems that occur as a result of MPS II.

Heart problems are common among individuals with MPS II. It is recommended that individuals with MPS II get regular tests of heart function. Please consult with a heart specialist (cardiologist) knowledgeable in MPS diseases for appropriate treatment and care.

Heart disease is a leading cause of death in individuals with MPS II.



JASON

Gastrointestinal system

Liver and spleen

In most individuals with MPS II, both the liver and spleen are enlarged (hepatosplenomegaly) due to accumulation of GAGs. The enlargement of these

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

Although enlargement of the liver and spleen itself may not be problematic, it can interfere with eating and breathing and cause hernias.

Abdomen and hernias

In most individuals with MPS II, the abdomen bulges out due to 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 surgically, but they may 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.

Inguinal (groin) hernias should be repaired surgically but may recur. Umbilical hernias are usually not treated unless they cause other, more serious, problems.

Bowel problems

It is unclear why many individuals with MPS II suffer periodically from loose stools and diarrhea. Sometimes, 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.” GAG buildup has been found in nerve cells of the intestine that may cause a problem with the autonomic nervous system, the system that controls those bodily functions usually beyond voluntary control, resulting in abnormal bowel movements and diarrhea.

An examination by a physician, supplemented by an X-ray if necessary, may establish the cause of diarrhea. Among children with MPS II, the problem may disappear as they get older. However, it can be made worse by antibiotics prescribed for other problems. If the diarrhea appears to be affected by the diet, it may help to eliminate those foods causing it.

If the diarrhea appears to be caused by antibiotics, eating plain live-culture yogurt may help, especially during episodes. This provides a source of lactobacillus (“friendly” bacteria in the bowel) to help prevent the growth of harmful organisms within the bowel wall, which can cause the diarrhea or make it worse. A diet low in roughage (fiber) may also be helpful. Please consult your doctor before starting live-culture yogurt or a diet low in roughage. Constipation may become a problem as children with MPS II get older, less active, and the muscles weaken. If an increase in roughage in the diet does not help or is not possible, the doctor may prescribe laxatives or a disposable enema.

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.

Most individuals with MPS II experience bowel problems. Please consult your doctor knowledgeable in MPS diseases to determine the cause and receive the optimum treatment.

Dietary considerations

There is no scientific evidence that any particular diet is helpful for people with MPS II. Symptoms such as diarrhea tend to come and go naturally. However, some parents 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. Please 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 the individual's problems are eased, foods can be reintroduced one at a time to test whether any particular item seems to increase symptoms. It is important to note that there is no diet that can prevent the storage of GAGs as these are naturally synthesized by the body as part of its normal functioning. So, reducing sugar intake or other dietary components cannot reduce GAG storage.

Although there is no evidence of specific diets being generally helpful for individuals with MPS II, eliminating certain foods may improve symptoms for some individuals. Diets cannot prevent storage of GAGs. Please consult your doctor and/or dietician knowledgeable in MPS diseases.

Musculoskeletal system (bones and joints)

People with MPS II tend to have significant problems with bone formation, bone abnormalities, joint stiffness, and growth. This leads to multiple abnormally shaped bones (called dysostosis multiplex) as well as neurological problems if nerves are squeezed by bone.

Dysostosis multiplex occurs when bones do not form correctly at cartilage growth centers near the ends of the bones throughout the body.

Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Those with severe MPS II 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 the rest. This backward slippage of the vertebrae can cause an

angular curve, called kyphosis (forward bend) or gibbus (bump in the lower back), to develop. Gibbus (also called thoracolumbar kyphosis) develops from poor bone growth in the upper front part of the vertebrae. This causes a wedging of the vertebrae (bones are smaller in the front than in the back).

Individuals with MPS II often develop a forward bending of the spine (kyphosis) or a bump in the lower back (gibbus).

Neck

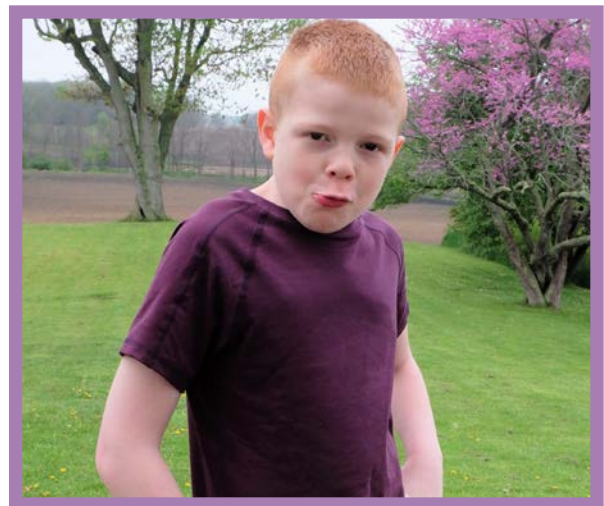
The spinal canal is narrowed in individuals with MPS II. Normally, a bone called odontoid process stabilizes the neck and is held in place by a strong tissue band called the transverse atlantal ligament. Among individuals with MPS II, this ligament can become overgrown. In individuals with rapidly progressing disease, the bones that stabilize the connection between head and neck are often malformed (odontoid dysplasia). All of these individually and together make the neck unstable. This puts individuals with MPS II at risk for spinal cord compression (a condition where fluid or tissues, such

as bones, are pressing on the spinal cord). Parents of children with MPS II should be cautious about how the area of the spine around the neck is handled. It is recommended that children with MPS II 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.

The bones that stabilize the head and neck may be malformed (odontoid dysplasia) and can be treated by fusion surgery to prevent further damage. Children with MPS II should avoid “high-risk” activities such as contact sports and gymnastics.

Joints

Joint stiffness is common in individuals with MPS II, 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. Many individuals with MPS II end up walking on their toes due to joint stiffness and tight heel cords. 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.



HUDSON

Joint stiffness and pain is common among individuals with MPS II making simple tasks, such as getting dressed, very difficult. Many individuals walk on their toes. Pain can be treated with anti-inflammatory drugs, but their uses should be carefully monitored.

Hands

The hands of individuals with MPS II 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 “bent/stiff” or “claw hand.” The finger joints may become locked producing a characteristic “trigger finger” look. Trigger fingers can be treated with heat and massage or through surgery, if needed.



RICKY

Individuals with MPS II have short hands with stubby fingers. The tips of fingers may become permanently bent and joints locked causing the “claw hand” and “trigger finger” appearance. Trigger fingers can be treated with heat and massage, or through surgery.

Hips

Like the spine, the hip joint suffers from altered bone formation. The hips are ball-and-socket joints situated at either side of the pelvis. The “ball” is the head of the thigh bone (femur) and the “socket” is the cupped part of the pelvis (the acetabulum) that surrounds the ball. In abnormal formation of the hip (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. Physical therapy, especially when started at a young age, can help preserve hip joint function and hip problems in individuals with MPS II.

Hip dysplasia is difficult to treat surgically in individuals with MPS II. Some experts believe that 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), allowing 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. Hip surgery carries a number of risks, including the risks associated with anesthesia, infection, bleeding, or blood clots.

Hip dysplasia is common among individuals with MPS II and can be corrected with surgery, which is best done at an early age.

Legs and feet

The feet of individuals with MPS II are broad and may be stiff with the toes curled under, similar to the fingers of the hands. In younger children, parents should check the skin around the toes and feet as it is a common area for blisters and skin infections. Wearing appropriately fitted (usually widely sized) shoes and engaging in routine cleaning and skin care around the toes can help to prevent and treat irritations. Many individuals with MPS II stand and walk with their knees and hips flexed. This, combined with a tight Achilles tendon in the heel and joint stiffness, may cause them

to walk on their toes. Some individuals with MPS II have genu valgum or knock-knees (a condition in which the knees are bent in so much they touch each other when walking), but rarely require treatment. When it is severe, knock-knees can be treated with surgery on the tibia, the bone in front of the leg below the knee. The lack of flexibility in the hips, legs, and ankles often prevents individuals with MPS II from putting on socks and shoes and sitting in a tailor position (the seating position of choice for most kindergarten teachers).

Many individuals with MPS II stand and walk on their toes with their knees and hips flexed and have difficulty sitting upright in the tailor position. Individuals with severe knock-knees can be treated with corrective surgery on the tibia.

Physical and occupational therapy

The joint stiffness and bone malformations caused by MPS II can make it hard to walk, dress, wash hair, tie shoes, and do other activities. The utility of physical therapy has not been extensively studied in individuals with MPS II. Physical therapy may help relieve symptoms and improve the person's ability to function. 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. Appropriate physical therapy may limit further losses of flexibility. Occupational therapy teaches affected individuals how to adapt to their unique daily environment. 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.

The many problems with bones and joints make it difficult for individuals with MPS II to perform daily activities and work. Physical therapy should be considered to help alleviate physical symptoms, improve joint motion, and the individual's ability to function. Occupational therapy can help individuals how to adapt to school, home, and the work environment.

Brain and central nervous system (CNS)



KHYE

GAG storage in the nerve cells (neurons) in the brain can adversely affect brain function, the extent of which depends on the severity of disease. Some, but not all, individuals with severe disease may experience a progressive and possibly severe decline in developmental function. It is less likely that individuals with mild, slow-progressing disease experience these symptoms and they often maintain normal or near normal intelligence.

When present, the problems with various organ systems discussed above can also contribute to poor brain function, including low oxygen levels, and lack of sleep due to sleep apnea. Additionally, effects on the eyes and ears can affect the ability of the individual to see and hear normally.

Cognitive function

It is important to remember that MPS II is a spectrum of disease conditions and that problems with mental function (cognition) vary with disease severity. Some individuals may exhibit milder learning disabilities while others may have more severe cognitive (mental) function.

At birth, most individuals with MPS II seem to have normal cognitive function reaching all developmental milestones at the normal timeline for about 1 year. However, shortly after this phase, there is a wide range of developmental outcomes.

More severely affected individuals with MPS II begin to show signs of developmental delay at 18-24 months of age followed by slower than normal development until reaching a plateau by 3-5 years of age, and gradual decline thereafter. Eventually, these individuals have severe mental handicaps and become dependent on caregivers for daily living activities.

Individuals with attenuated MPS II may have a normal or near normal intelligence and cognitive abilities. However, their brain scans may still display abnormalities.

Individuals with MPS II can exhibit a wide spectrum of cognitive dysfunction from mild, almost normal mental health among those with attenuated disease to significant loss of learning and mental skills among those with severe disease. Individuals with MPS II may need special learning programs and caregivers to help them with their daily activities.

Hydrocephalus

MPS II can cause hydrocephalus, a condition where fluid accumulates in the brain, causing a pressure buildup that can lead to brain damage. 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.

This condition is more common among individuals with severe neurological symptoms associated with the brain and nervous system. 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 II, creating a frustrating situation for parents and caregivers.

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 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, computed 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 II 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). Medications to reduce pressure may be attempted prior to surgical placement of a shunt. With these medications, electrolyte levels should be monitored.

An alternate method of measuring intracranial pressure is by CSF fluid opening pressure, also called opening pressure at lumbar puncture. A high measure can be an indication of intracranial pressure. A normal measurement is often considered less than 25-28 cm H₂O (sometimes also written as 250–280 mm H₂O); however, there are some doctors who report up to 29 cm H₂O as normal in certain children.



JACK

Sometimes lumbar puncture may be necessary for the diagnosis of hydrocephalus, as CT and MRI often do not demonstrate it conclusively for individuals with MPS. Additionally, if elevated pressure on the optic nerve is noticed during eye examinations, assessment should be made for signs of increased intracranial pressure.



GAVIN

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 of the brain). 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

Usually, the length of the spinal cord is surrounded by a system of tissue, ligaments, and bones that are intended to protect it from damage when there is movement. In individuals with MPS II, GAG accumulation over time causes these tissues and ligaments to gradually become thicker and start pressing against the spinal cord. This results in a condition called spinal cord compression, particularly in the neck (cervical) region of the spinal column. 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 that can contribute to hydrocephalus (described earlier). Doctors usually can detect spinal cord compression with an 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.

Complications of laminectomy include slowing of heart rate and difficulty breathing. Surgery should only be undertaken with an anesthesiologist and a surgical team knowledgeable in the complexities associated with MPS II.

Individuals with MPS II, especially those with severe disease, can have hydrocephalus (water on the brain). Hydrocephalus is diagnosed through a clinical neurological evaluation and when severe, is treated with a shunt. Individuals should be tested for spinal cord compression via X-ray or MRI, prior to surgical implantation of a shunt.

Seizures

Seizures (convulsions) are common in individuals with severe MPS II, with over 50% of sufferers older than 10 years of age. Seizures can be treated with

anticonvulsant medications. Seizures are not common among patients with attenuated MPS II.

Over 50% of individuals with severe MPS II suffer from seizures after 10 years of age. Seizures can be treated with anticonvulsant medication. Seizures are not common in patients with attenuated MPS II.

Carpal tunnel syndrome

Individuals with MPS II 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 thumb to waste away and will make it hard for the individual with MPS II to use his/her thumb for grasping objects. Some individuals with MPS II may have few or no symptoms of carpal tunnel syndrome.

If an individual with MPS II has pain in his/her hands, particularly at night, he/she may wish to have an electrical test called a nerve conduction or electromyography 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.

Carpal tunnel syndrome is often not diagnosed early enough in young children with MPS II. Some families



RICKY

may notice children running their hands under water of extreme temperatures (especially hot water) or biting their hands. If parents notice that the skin on their child’s hands doesn’t prune or wrinkle in warm water, this can also be a sign of carpal tunnel syndrome.

Most individuals affected by MPS II do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage. In some cases, surgery, called “carpal tunnel release”, may be used to cut the transverse carpal ligament and relieve the pressure on the median nerve. As with any surgical procedure for an individual with MPS II, it is important to meet with the anesthesiologist prior to the surgery. As excess GAGs are a continual problem for individuals with MPS II, it is possible that GAGs might build up again after surgery.

Individuals with MPS II may also experience tarsal tunnel syndrome, which is essentially the equivalent disorder in the ankles. In severe cases, surgery called “tarsal tunnel release” may be considered.

Individuals with MPS II, especially those with severe disease, can have carpal tunnel syndrome even without the classic symptoms. Be persistent with the doctor to ensure that it is diagnosed properly. If the syndrome is present, surgery to relieve the pressure on the median nerve may be needed.

At what age are people usually diagnosed with MPS II?

This varies between individuals depending on the severity of the disease. In general, individuals with severe MPS II tend to be diagnosed early between 2 and 4 years of age with symptoms beginning to appear at about 18 months. Individuals with attenuated MPS II tend to be diagnosed later.

Early diagnosis of MPS II is critical. The earlier that MPS II 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.

Early diagnosis of MPS II is critical and allows earlier intervention.

Neonatal (newborn) screening

Newborn screening is the testing of newborn babies to see whether they have specific genetic disorders. 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, only a few states in the USA have universal screening for MPS II. Several other countries also screen for MPS II.

Currently, there is a growing movement promoting newborn screening for MPS disorders such as MPS II. It is now widely recognized that for many families, information about the diagnosis alone is helpful with

the opportunity for genetic counseling, education about various and new 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 II will likely continue to become more involved in the promotion of newborn screening.

Prenatal diagnosis

If you have a child with MPS II, it is possible to have tests during a subsequent pregnancy to find out whether the baby you are carrying is affected. It is important to consult your doctor early in the pregnancy if you wish to perform these tests. The decision to have prenatal testing is complex and personal. Talking with

your genetic counselor or doctor can help you explore these options and other strategies, such as egg or sperm donation, for having additional children while limiting the probability they will have or be carriers for MPS II.

Newborn screening and prenatal diagnosis for MPS II may help with early diagnosis in the future. There is still much research to be done and these tests are not offered in all states. Please check with your doctor for the options in your community.

Living with MPS II

Living with MPS II or with an individual with MPS II can vary significantly depending on the severity of the disease. Individuals with severe MPS II usually are not be able to live independently, whereas individuals with

slowly-progressing, attenuated MPS II may be able to lead an almost normal life. The information below applies primarily to young boys with MPS II.



QUINN

Severe MPS II

Children with severe MPS II will vary considerably depending on which treatments they have received or are receiving. Boys with severe MPS II are often overactive, strong, happy, and are difficult to manage. Their mental age/cognitive abilities lag behind their physical capabilities. For example, they may lock themselves in a room but not understand how to unlock the door even when given specific directions. They may throw toys around rather than understanding how to play with them. They have a high tolerance

to pain which may result in bumps, bruises, and infections, which would be painful for children without MPS II, going unnoticed and untreated. They may have outbursts of aggressive behavior and be unresponsive to discipline as they may not understand what is required of them. Some boys will learn toilet training for a short time, but most will need diapers for their lifetime. When getting enough sleep becomes an issue for parents and caregivers, they should consult a doctor or social worker for guidance and help.

Education

Boys with severe MPS II may benefit from having a mainstreamed education and enjoy the social interaction with peers. It is important to work with your school system and develop the best Individualized Education Program for your child. You may need to educate the teachers and schools and give them a copy of *An Overview of MPS II for Teachers and A Teacher's Guide to MPS II*, published by the National MPS Society. It is important that the child's educational goals are appropriate for their level of intellectual and

emotional development. Hearing loss, vision difficulties, and mobility restrictions can lead to behavior problems, including difficulties in understanding questions and directions from the teacher. The learning environment needs to be supportive of these children, including modification of the classroom to accommodate their mobility needs. For more information on education, see the booklet titled *A Guide for Parents: Education Strategies and Resources*, published by the National MPS Society.

Children with severe MPS II may benefit from attending mainstream school but will need a multitude of resources from the school system, especially teachers.

Home adaptations

Individuals, especially children, with severe MPS II will become progressively less mobile and more dependent on their parents and/or caregivers to meet their everyday needs. The booklet *Daily Living with MPS and Related Diseases*, published by the National MPS Society, has many helpful suggestions for making adaptations in the home.

Taking a break

Caring for an individual or child with MPS is hard work. Parents and caregivers need a break to rest and enjoy activities, which may not be possible when their affected child or ward is with them. Siblings and others also need their share of attention and need to be taken on outings that may not be feasible with an affected individual or child. Many parents and caregivers use some form of respite care or have someone come in regularly to help at busy times.

Palliative care

Palliative care is any form of medical care or treatment that concentrates on providing relief from symptoms due to the disease. The goals are to prevent suffering and to improve quality of life as best possible for individuals facing serious, complex illnesses. This support encompasses aspects such as respite care, symptom management, and bereavement support. Palliative care may be short-term or extended, depending on the status of the patient.

Palliative care can be provided at any time it is needed by an individual with MPS II. Curative and preventative treatments continue as normal. This is in contrast to hospice care, which is also palliative, but is intended specifically to be end-of-life care. When an individual is receiving hospice care, treatments intended to cure the disease are stopped, and only comfort measures are provided.

For adults, hospice care is usually offered when the individual is expected to have fewer than 6 months to live. For children, hospice care may be offered as early as

the diagnosis is made. This varies significantly between regions, states, and insurance providers. Often the differentiation between palliative and hospice care is one made by insurance companies as hospice may provide different billing for medical care and supplies.

With both palliative and hospice care, an assessment of medical need and a care plan can lead to support provided to the individual and family so that all can experience a better quality of life.

Attenuated MPS II

Boys with attenuated MPS II may appear to be completely normal in behavior with a sunny and affectionate disposition. However, they can also

become short-tempered, especially when frustrated with their physical, mental, and emotional limitations.

Education

Some, but not all, children with attenuated MPS II will benefit from attending mainstream school/university. It is important to work with your school system and develop the best Individualized Education Program for your child. You may need to educate the teachers and schools and give them a copy of *An Overview of MPS II for Teachers and A Teacher's Guide to MPS II*, published by the National MPS Society. It is important that the child's educational goals are appropriate for their level of intellectual and emotional development. In order for the individual to reach full academic potential, it is important to ensure the academic institution and

associated personnel are aware of required resources. This may include a one-on-one classroom assistant, appropriate classroom furniture and access to an individual computer. For more information on education, see the booklet titled *A Guide for Parents: Education Strategies and Resources*, published by the National MPS Society.

It may be helpful to have a Section 504 plan in place in a school setting which allows for some modifications and supports as needed for those where an Individualized Education Program is not necessary.

Some, but not all, children with attenuated MPS II will attend mainstream school and achieve academically.

Independence

Individuals with attenuated MPS II should be encouraged to be as independent as possible to lead full and enjoyable lives. Contact with other teenagers and adults with attenuated MPS II can provide mutual support and helpful information for living an independent life, especially with strategies to cope with emotional issues. If problems persist, a doctor should be consulted for help with mental health services, which can include therapy and/or medications.

The Adult Resource Committee (ARC) exists to provide support for adults diagnosed with MPS and mucopolidosis. Contact the ARC at arc@mpssociety.org for more information. Individuals with short stature may find additional support and helpful information through Little People of America, www.lpaonline.org.

Employment

The physical disabilities of those suffering from attenuated MPS II should not prevent people from accessing meaningful employment. The Americans with Disabilities Act (ADA) affords protection against discrimination to Americans with disabilities. Vocational Rehabilitation is a state program to help people with disabilities make career plans, learn job skills and live independently. Many adults with MPS II have found satisfying and meaningful work.

Home adaptations

Appropriately adapted living accommodations will greatly enhance the ability of an individual with attenuated MPS II to develop independent living skills. Where mobility is restricted, a wheelchair may be helpful. Grants may be available through community or state agencies to cover the cost of home adaptations.

Puberty and marriage

Teenagers with attenuated MPS II will go through the normal stages of puberty and are able to have children. Some have married and had children of their own.

Healthcare information

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

General Management of MPS II



EASTON

The primary goals of treatment and management of MPS II are to improve quality of life, slow disease progression, and prevent permanent tissue and organ damage. At present, there is no cure for MPS II. Early diagnosis and intervention may prevent irreversible damage in some individuals. Treatment options for MPS II comprise those aimed at disease management (including treating underlying enzyme deficiency), and supportive or palliative care (care that focuses on comfort for an individual with an incurable disease).

This section only briefly describes some management and treatment options. However, the decisions of which interventions and treatments are best for the individual is an important and complex one that cannot be summarized here. These are best discussed with medical professionals with expertise in treating MPS II.

Importance of multidisciplinary care

As described earlier in this resource, individuals with MPS II usually have a wide range of signs and symptoms. As a result, they often need to be managed by many different medical specialists, including cardiologists, neurologists, pulmonologists, otolaryngologists, ophthalmologists, orthopedic surgeons, physical therapists, speech therapists, occupational therapists, and others. All healthcare professionals involved in the care of an individual with MPS II should have a basic understanding of the disease and how the condition may affect treatment decisions.

Dealing with so many specialists can be overwhelming for individuals with MPS II and their caregivers. It can be very helpful to have a single physician with experience in MPS II, usually either their primary care physician (who might be a pediatrician) or a geneticist, 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.

The coordinating physician might also become the focal point for facilitating the entry of disease and treatment-related information to the Hunter Outcome Survey (HOS), a global data registry sponsored by Shire Human Genetics Therapies, a subsidiary of Takeda Pharmaceuticals, for individuals with MPS II.

The goals of HOS are to collect data on patients with MPS II to better understand the natural history of the condition and monitor safety and efficacy of treatments, especially enzyme replacement therapy. This physician might also become the main contact for coordinating the entry of disease and treatment-related information to the MPS II registry.

A multidisciplinary approach to treatment and management coordinated by a single healthcare professional experienced in MPS II is recommended.

Diet

There is no scientific evidence that any symptoms of MPS II can be managed with a particular diet. Digestive system problems, such as diarrhea, tend to come and go naturally. However, some individuals and caregivers find that a change in diet can ease problems, such as excessive mucus, diarrhea or hyperactivity. Reducing intake of milk, dairy products, and sugar, as well as avoiding foods with too many additives and coloring, have helped some individuals. It would be advisable to consult your doctor or a dietician if you plan major dietary changes to make sure the proposed diet does

not leave out essential nutrients. If the individual's problems are eased, you could try reintroducing foods one at a time to test whether any particular item seems to increase the symptoms.

It is important to remember that GAGs are synthesized by cells as part of their natural process. This is not a disease caused by overproduction of GAGs, but rather the failure to break down GAGs. As such, there is no diet that can prevent GAG accumulation.

There is no scientific evidence that diet has an effect on this disease. However, it may help with some individuals. Please consult your doctor or dietician when making dietary decisions.

Feeding tubes

As the disease progresses, individuals with MPS II may have problems chewing and swallowing. If so, they are at risk for poor nutrition, choking, and aspiration (inhaling food or other substances into the lungs) that can lead to respiratory infections and pneumonia. During these episodes, the individual may need increasingly more time to be fed and may lose weight. Choking can also occur with liquids, including those made by the body, e.g., saliva. With swallowing becoming more difficult with disease progression, the individual often drools, which will need to be suctioned.

One option to ensure such individuals receive the nutrition they need and prevent choking or aspiration is to use feeding tubes (also called “enteral nutrition”). These may also make it easier for a caregiver to feed the individual with MPS II. However, the decision to use

feeding tubes is often a difficult one for family members and caregivers.

A flexible feeding tube is inserted that bypasses the mouth and throat and goes directly into the stomach or intestine. Nasogastric tubes are inserted through the nose and are usually a temporary measure lasting days to weeks. Longer-term feeding issues require surgical placement of a gastric (G)-tube, which is inserted into the stomach, or jejunal (J)-tube, which is inserted into the small intestine.

Because of special concerns regarding anesthesia in MPS II patients, you or your doctor should consult with an anesthesiologist before surgery is done to insert the tube.

Feeding tubes may be an option if the individual with MPS II can no longer chew or swallow. These need to be inserted with care and training. Long-term feeding tubes require surgery. Please consult your doctor and anesthesiologist to ensure that feeding tubes are inserted and used correctly.

Physical therapy

Joint stiffness is a common feature of MPS II. Limitation of motion and joint stiffness can cause significant loss of abilities. Range-of-motion exercises (passive stretching and bending of the limbs) may offer some benefits in preserving joint function and should be started early. Exercises that cause pain should be avoided. Once significant limitation has occurred, increased range-of-motion may not be achieved, although further limitation

may be minimized. Individuals with MPS II should be as active as possible to maintain joint function and improve their general health. However, competitive or contact sports should be avoided. 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 II should be as active as possible to maintain joint function and improve general health. However, competitive or contact sports should be avoided. Please consult the doctor or physical therapist for ways of achieving this.

Occupational therapy

While physical therapy targets gross motor or “large” movements of the body (such as walking), occupational therapy focuses on fine motor movements and targets activities of daily living. It is important to consider occupational therapy following surgery or if there are difficulties with dressing, toileting, transitioning, and other motions that involve the use of the hands. Occupational therapy may be helpful for young children with MPS II to help them and their families to learn strategies for making adaptations early on, so that these become more natural.



JIMMY

Occupational therapy can teach individuals with MPS II how to adapt to their learning and work environments.

Pain management

Pain management is an important topic for individuals with MPS II since many complications of the disease cause pain. Joint stiffness and pain, chronic headaches from increased intracranial pressure, hand or wrist pain from carpal tunnel syndrome, hip or back pain from abnormally shaped bones, mouth sores from dental cysts, and abdominal pain are just a few examples.

Many of the options to treat and/or manage the various symptoms have been discussed earlier in this resource, e.g., surgery to correct musculoskeletal issues, shunts to relieve hydrocephalus, physical therapy, etc. In addition to addressing the symptoms, these procedures also help decrease and better manage the pain caused by the symptoms. In addition, pharmaceutical options include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen and

naproxen), or narcotic pain relievers (such as codeine or morphine), which are usually prescribed for short-term quick relief. When pain is accompanied by muscle spasms, the doctor may recommend the addition of a muscle relaxant (such as methocarbamol, baclofen, or tizanidine). Special consideration should be taken with all pain medications to ensure they do not cause respiratory depression, causing difficulty in breathing.

The doctor can help you find an appropriate pain medication. Some individuals may need more than one pain medication to get their pain under control. If you are not getting the pain relief you need, speak to your doctor. If you have trouble swallowing, some pain medications are available in liquid or patch form. Ask your doctor for more information on which pain control options are best for you or your child.

Managing pain is one of the primary issues for individuals with MPS II. Many of the treatments for specific symptoms also help with pain relief. Please consult your doctor for any additional medications needed to help alleviate the pain.

CPAP and BiPAP

Sleep apnea can be improved in some individuals with MPS II by opening the airway using CPAP or BiPAP machines during sleep. These machines distribute oxygen to a patient if needed, using a mask covering the face or nose. Both CPAP and BiPAP are noninvasive (no surgery, breaking the skin, or inserting a device into a body cavity). Both require the individual to wear a mask covering the nose, and sometimes the mouth, when sleeping. These may be used at times for some individuals when they are awake for additional respiratory support. Both types

of support can improve breathing using pressurized air. While both CPAP and BiPAP are very effective in managing sleep apnea, they do not treat the underlying problem of GAG accumulation. Occasionally, CPAP can increase the work involved in natural breathing. In these cases, it may be advisable to switch to a BiPAP machine. Individuals will need to get acclimated to using these devices. In cases where CPAP or BiPAP are not effective or are not appropriate, a tracheostomy (a surgical procedure to insert a breathing tube in the throat) may be used.

CPAP and BiPAP are noninvasive options usually sufficient to address sleep apnea, although they do not address the underlying GAG accumulation.

Tracheostomy

A tracheostomy (tray-kee-ossta-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 (please see below). 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.

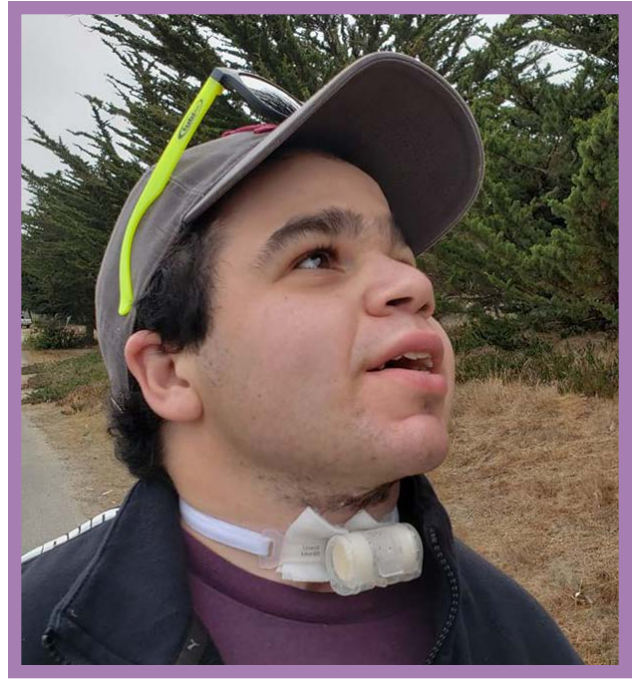
It is important to discuss trach care in detail with the doctors. The surgical incision needs to be cleaned frequently as it heals, perhaps as many as 4 to 5 times per day. Once the skin heals, it should be kept clean and dry. Most people use soap and water to clean the skin. Some people use a small 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.

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. There is also a risk of the new tube being inserted incorrectly. As the wound heals, the chance that either situation will occur will decrease.

One of the biggest challenges that people face following the insertion of the trach is adjusting to new breathing patterns and changes to the vocal cords. Communication is perhaps the biggest adjustment because it may be difficult for the individual 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. Special care needs to be taken during bathing to shield the tracheostomy tube opening from the water. A person with a trach also may benefit from using a cotton cover or scarf to protect from inhaling dust and other particles.

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



SPENCER

A tracheostomy is generally a routine procedure, but 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 individuals with MPS II are at a higher risk for 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 II.

Tracheostomy is an option to help with breathing when other methods have failed. It must be done in a hospital under anesthesia and the care of a surgeon who is knowledgeable in treating MPS.

Tracheostomies require life-long and specialized care of the tubes. This gets easier over time.

Anesthetics

Giving an anesthetic to an individual with MPS II requires skill and should always be undertaken by an experienced anesthetist. Inform your child's school or any other caregivers of this in case you cannot be contacted in the event of an emergency. If you must go to a different hospital in an emergency, be sure to tell the anesthetist there might be problems with intubation (placement of the breathing tube). The airway can be very small and may require a very small endotracheal tube. Placing the tube may be difficult and require the use of advanced intubation techniques, such as a flexible bronchoscope, laryngeal mask airway or fiber optics.

In addition, the neck may be somewhat lax, and repositioning the neck during anesthesia or intubation could cause injury to the spinal cord. For some individuals, it is difficult to remove the breathing tube after surgery is completed. It is important to advise physicians of the critical nature of these problems, and that many problems have occurred during anesthesia of individuals with MPS.

For any elective surgery in a child with MPS, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical center instead of a local hospital. See additional information on anesthesia in the booklet titled *Is Your Child Having an Anesthetic?*, published by the National MPS Society.

Giving an anesthetic to an individual with MPS II requires skill and should always be undertaken by an experienced anesthesiologist who has experience with difficult airways.



MICHAEL AND HUNTER

Research for the future

The mission of the National MPS Society is to find cures for MPS and mucopolipidosis (ML). As part of that mission, the Society funds research grants. The Society recognizes the need for targeted research for treatment of bone and joint problems and for treating the brain,

and Society research funding has focused on those areas. Information about Society-funded research and promising new areas of research can be obtained by contacting the Society's office.

This booklet is intended as an introduction into the nature of the disease as well as to help individuals and families understand more about what is happening to those living with MPS II and what they can do to manage it. This booklet was updated by the National MPS Society in 2020.



Updates

Medical professionals and researchers are constantly learning new things about MPS II disease and treatments. Some of the information provided in this booklet may change over time. To keep up to date on the latest information on MPS II and its management, visit www.mpssociety.org.

We have reserved the space below to call out new developments or updates we think deserve your attention.

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Benefits of the National MPS Society

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

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

The Adult Resource Committee (ARC) exists to provide support for adults diagnosed with MPS and ML. Contact the ARC at arc@mpssociety.org with any questions or for more information.

Benefits of membership in the National MPS Society:

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

Glossary

Term	Definition
Aspiration	To draw in or out by suction. For individuals with MPS, it most commonly means the accidental inhaling of a fluid or solid like saliva or food into the windpipe or lungs where it can lead to coughing, difficulty breathing, choking, or aspiration pneumonia.
Attenuated	Weakened, reduced, or diminished in size. Attenuated MPS means a mild form of the disease.
Bronchoscopy	A medical procedure that lets a doctor look into the lungs and airways. The doctor inserts a thin tube with a light and camera through the nose or mouth down the throat and into the lungs.
Carpal Tunnel Syndrome	Thickening of the ligaments in the carpal tunnel (space in the wrist where the nerves pass between the carpal bones and the connective tissue) that causes pressure on the nerves. This can cause irreversible nerve damage if not surgically corrected. In children with MPS, carpal tunnel syndrome occurs because of the accumulation of GAG deposits.
Carrier	An individual who has a recessive, disease-causing version of a gene on 1 chromosome of a pair and a normal version of that same gene 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 which cushions them from shock, brings nutrients to the brain, and carries waste away. It is produced in the ventricles (cavities) of the brain and is reabsorbed into bloodstream.
Chromosomes	Linear, double-stranded structural units of genetic material consisting of DNA and supporting proteins called chromatin. Human cells contain 46 chromosomes identified as 23 pairs; 22 pairs are autosomes (the same from each parent) and 1 pair are the sex chromosomes.
Echocardiogram	Ultrasound of the heart to evaluate heart valve and heart muscle function.

Enzyme	A protein that facilitates a biological reaction without itself being used up in the reaction (i.e. it acts as a catalyst). An enzyme acts by binding with the substance involved in the reaction (the substrate) and converting it into another substance (the product of the reaction).
Enzyme Replacement Therapy (ERT)	A medical treatment for a genetic disease whereby the missing protein (enzyme) is manufactured separately and given intravenously to the patient on a regular basis.
Gastrostomy Tube (G-Tube)	A tube surgically inserted through the abdomen into the stomach. It is used to deliver nutrition and/or medications directly into the stomach when swallowing is difficult because of disease or obstruction of the esophagus.
Gene	The basic unit of heredity. Genes are made up of sequences of DNA that code for specific proteins or other functional units. Hundreds of genes are arranged together in strings to form a chromosome.
Gene Therapy	A medical treatment for a genetic disease whereby normal genes are inserted into a patient's cells to replace or correct the effects of mutated or disease-causing genes.
Glycosaminoglycans (GAGs)	Complex linear sugar molecules that are widely found throughout the body in connective tissue, the area between cells, and secretions on the surfaces of many cell types. GAGs were previously called mucopolysaccharides.
Hernia	The bulging of an organ or tissue through some part of the body that should be containing it. Common examples are bulges in the umbilical (belly button) or inguinal (inner groin) regions of the body.
Hematopoietic Stem Cell Transplantation (HSCT)	A medical procedure that replaces enzyme-deficient cells with healthy enzyme-producing cells. Hematopoietic (blood) stem cells are capable of differentiating into a variety of specific cell types. The patient's bone marrow cells must first be eliminated by chemotherapy and/or radiation therapy. Then the healthy donor stem cells are infused into the bloodstream where they migrate into the bone marrow and multiply into new, healthy, enzyme-producing blood cells. These healthy cells migrate back to many parts of the body and brain where they produce properly functioning enzyme and "reboot" the immune system.

Hydrocephalus	A buildup of cerebrospinal fluid (CSF) in the cavities (ventricles) of the brain. This can put pressure on the brain and is sometimes characterized by an enlarged head in infants. Older children and adults can experience symptoms like headache, impaired vision, and cognitive difficulties. Communicating hydrocephalus can occur when the normal outflow of the fluid is blocked. It can be treated surgically by inserting a shunt into a ventricle to drain the excess fluid.
Individualized Education Program (IEP)	A specifically designed program for each child in the public school system who receives special educational services. The aim is to improve teaching, learning, and appropriate goal setting for each individual. A team including members from the school system and the family are generally involved in designing the IEP. Federal legislation is in place to guide the development of appropriate IEPs.
Kyphosis	An exaggerated, forward curve of the spine that causes a hunching of the back. (Similarly, a gibbus deformity is a type of kyphosis that involves a shorter section of the spine with a more angular curve.)
Lumbar Puncture	A lumbar puncture (also known as a spinal tap) is a procedure in which a needle is inserted into the space surrounding the spinal column in the lower back to withdraw cerebrospinal fluid (CSF) or to deliver medicine. This procedure may be performed to diagnose or treat a condition, but it is also used as a measure of intracranial pressure to aid in diagnosing hydrocephalus.
Lysosomal Storage Disorder (LSD)	An inborn error of metabolism, resulting in a particular lysosomal dysfunction. In the case of MPS disease, it is an inherited enzyme deficiency that blocks the natural breakdown of GAGs, causing a buildup of waste products in the lysosomes (specialized compartments within cells that contain the enzymes responsible for breaking down substances into smaller molecules so that they can be used again in various bodily processes).
Lysosome	Specialized compartments within cells that contain the enzymes responsible for breaking down substances into smaller molecules so that they can be either eliminated or used again in various bodily processes.
Mitral Valve Prolapse	When the flaps between the left atrium and the left ventricle of the heart don't close evenly or smoothly, the mitral valve that connects the two chambers forms a bulge (prolapse) into the left upper chamber (left atrium) as the heart contracts. This can lead to blood leaking backward into the left atrium, causing mitral valve regurgitation.

Mucopolipidosis (ML)	An inherited metabolic disease that affects the body's ability to break down various materials within cells. Patients with ML do not produce enough of one of the many enzymes required for a properly functioning lysosome. The name ML is used to classify all of the diseases with the clinical features common to both the mucopolysaccharidoses and the sphingolipidoses (diseases characterized by abnormal lipid or fat metabolism, affecting nerve tissue).
Mucopolysaccharidosis (MPS)	An inherited condition in which the body is unable to properly break down glycosaminoglycans (GAGs; formerly known as mucopolysaccharides). All of the various MPS diseases are characterized by defective lysosomal enzymes.
Mutation	Any change to the DNA sequence of a gene. Mutations are permanent alterations in the genetic code that can be passed down to future generations.
Otitis Media	Inflammation of the middle ear occurring commonly in children as a result of an infection, causing pain and temporary hearing loss.
Port-a-cath	A small medical device that allows easy access to a patient's veins. The port is installed beneath the skin and is connected to a catheter (a thin, flexible tube) that connects the port to a vein. A needle can be inserted through the skin into the port in order to draw blood or to give treatments, including drugs and blood transfusions. It can stay in place for many weeks or months.
Scoliosis	A sideways curve of the spine.
Shunt	A passage that will allow fluids to move from one part of the body to another. It is often used to treat hydrocephalus, where a tube is surgically placed into the brain to help drain cerebrospinal fluid (CSF) and redirect it to another part of the body where it can be reabsorbed.
Sleep Apnea	A sleep disorder where breathing stops repeatedly during sleep. It is frequently caused by an obstruction of the airway.
Tracheostomy	A surgical procedure in which a hole is made into the trachea (windpipe) through the front of the neck and a tube is inserted to help a person breathe.
Vocational Rehabilitation	A series of services that are designed to help individuals with disabilities get or keep a job, or to return to work or other useful occupation. These services are often provided by federal- or state-run programs.

You can find a complete list of terms in our online glossary at mpssociety.org/fact-sheet-glossary.



For more information or to join the National MPS Society:

Visit www.mpsociety.org

Contact us at 877.MPS.1001

Or email us at info@mpsociety.org

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

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