



National
MPS
Society

Support for Families. Research for a Cure.

Maroteaux-Lamy Syndrome



A Guide to Understanding

MPS VI



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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) Autumn, (bottom) Claudio, Patricia, Isabel

Pictured on right: (top to bottom) Kendra, Holden, Savannah



What is MPS VI?

Mucopolysaccharidosis VI (MPS VI; pronounced “mew·ko·pol·ee·sak·ah·ri·doh·sis six”) is a very rare genetic disorder characterized by a large head, distinctive “coarse” features, and a large tongue. It is also known as Maroteaux-Lamy (pronounced “marr·ah·toe·la·mee”) syndrome, named after two French physicians, Dr. Pierre Maroteaux and his mentor, Dr. Maurice Emil Joseph Lamy, who first described the condition in 1963. Other names for MPS VI include polydystrophic dwarfism and arylsulfatase B deficiency.

MPS VI belongs to a group of inherited metabolic diseases called mucopolysaccharidoses (MPSs), which are 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 VI yourself, it is important to remember that there is a wide spectrum of disease severity in how MPS VI shows up and progresses:



ALEXANDRIA

- It can be a severe, rapidly progressing form that manifests before 3 years of age; OR
- It can be a slow progressing (attenuated) form that usually manifests after the age of 5 and often in the second or third decade of life.

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 VI, 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).

What causes MPS VI?

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 some cases, cognitive development.

MPS VI is caused by accumulation of a particular GAG called dermatan sulfate (DS), which is primarily found in the skin. It is also prevalent in blood vessels, heart

valves, tendons, lungs, intestinal mucosa, cornea, and sclera of the eye (the white outer layer of the eyeball). Although DS is not toxic, its storage due to accumulation in large amounts within cells can cause many physical and physiological problems. In the most severe cases, babies may show signs of the disease at birth. Symptoms start to appear due to progressive accumulation of DS and the resulting damage.

DS is broken down by an enzyme called arylsulfatase B. Enzymes are special types of proteins that help build and break down complex molecules inside a cell. Arylsulfatase B participates in the breakdown of two complex GAGs, DS and chondroitin sulfate. Deficiency in arylsulfatase B results in accumulation of both GAGs. Although accumulation of DS is considered the primary cause of MPS VI, accumulation of chondroitin sulfate also plays a significant part.

MPS VI is caused primarily by accumulation of the GAG dermatan sulfate (DS). Consuming sugar or foods normally eaten will not affect GAG accumulation.



15TH INTERNATIONAL SYMPOSIUM ON MPS AND RELATED DISEASES, SAN DIEGO, CA

How is MPS VI diagnosed?

As stated previously, MPS VI is one type of MPS, which is a subgroup of LSDs. As such, although each MPS type has its own specific combination of symptoms, there are many symptoms common to all types of MPS. In addition, since MPS VI has a range of disease severity, the symptoms of the disease also vary in severity. These issues make it complicated to diagnose the disease.

Doctors may consider testing for MPS VI 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 the results may be difficult to interpret.



LILAH

In individuals with severe MPS VI, symptoms begin appearing by 2 to 3 years of age and mobility is impaired by age 10. In individuals with attenuated MPS VI, symptoms begin to appear later in childhood or the early teens. In these individuals, diagnosis may occur at age 5 years or even older.

Usually, the first diagnostic test for MPS VI is to determine whether GAG levels in the urine are higher than normal for individuals of a comparable age. Most, but not all, individuals with MPS VI 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 VI. 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 VI, the enzyme activity levels are much lower or absent.

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

Doctors may consider testing for MPS VI when signs and symptoms of the disease are present and cannot be explained by other causes.

Early diagnosis of MPS VI is important so that potential treatment options can be explored and supportive care can be started sooner.

Prenatal diagnosis

If you have a child with MPS VI, 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. You may also want to consult with your doctor if one or more of your brothers or sisters had a child with MPS VI, as this may

mean that you are also a carrier. The decision to have prenatal testing is complex and personal. Talking with your genetic counselor or doctor can help you explore these options and other strategies, such as egg or sperm donation, for having additional children while limiting the probability that they will have or be carriers for MPS VI.

Neonatal (newborn) screening

Newborn screening is the testing of newborn babies to see whether they have specific disorders. The goal is to help with early diagnosis and treatment. In the US, each state makes its own decisions about which health conditions should be included in their newborn screening programs. The factors that are considered when deciding on newborn testing include:

- Is the disorder clearly defined?
- What is the incidence rate of the disorder?
- Does early diagnosis help?
- Are tests available to diagnose the disorder accurately and cost-effectively?
- Can the tests be done quickly or is there a long waiting time for results?
- Is there a current therapy? Is bone marrow transplant an option?

Currently, there is a growing movement towards promoting newborn screening for MPS disorders such as MPS VI. It is now more widely recognized that

for many families, just knowing about the diagnosis is helpful, along with the opportunity for genetic counseling and education about additional medical help and management options. Considering the potential benefits of early diagnosis, the current aim is to develop a test that would allow children with LSDs to take advantage of these options.

Research into newborn screening for LSDs is still in early stages. Important questions remain about the screening process and testing methods. There will likely continue to be debate over the appropriateness of screening. There also may be concern about the effect on the parent–child relationship when a newborn is identified with a condition before symptoms appear. The test may also not be able to tell how severe the child’s symptoms may become. This will leave many questions for families and healthcare professionals who want to choose the best treatment. As a community, those whose lives have been touched by MPS VI will likely continue to become more involved in the promotion of newborn screening.

There is a growing movement towards promoting newborn screening for MPS.

Specific treatment of MPS VI

Overview

The goals of managing MPS VI are to improve quality of life, to slow down the progression of the disease, and to prevent permanent tissue and organ damage. Currently, there is no cure for MPS VI; however, early intervention may help prevent irreversible damage. Treatment options for MPS VI include those aimed at disease management and supportive or palliative care (care focused on increasing comfort for a person with a disease that cannot be cured), as well as those aimed at treating the underlying enzyme deficiency.



HARVY

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 intravenous (IV) infusion, ERT provides an external source of the deficient enzyme. The enzyme travels through the bloodstream and enters cells in various organs, where it helps break down GAG buildup.

The first ERT for MPS VI was approved by the US Food and Drug Administration in 2005. It has subsequently been approved in the European Union, Australia, Brazil, and several countries in Asia. Naglazyme® (galsulfase) is a manufactured version of the body's natural arylsulfatase B enzyme. It is given via IV infusions. Once in the bloodstream, it is taken up into lysosomes (small organelles inside the cell), where it breaks down the GAGs that accumulate in individuals with MPS VI.

Naglazyme improves endurance (walking ability and stair climbing) and pulmonary function and decreases the GAG levels in the urine. Clinical and long-term follow-up studies show that long-term galsulfase ERT

results in improved life expectancy, continued growth, and stabilization of cardiac and quality of life measures. Early initiation of the therapy in individuals with MPS VI will probably lead to better outcomes as more damage can be prevented. Unfortunately, Naglazyme does not penetrate well into some tissues like cartilage and bone. It also does not cross the blood-brain barrier, so it cannot help with certain eye conditions.

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

Anecdotal side effects noted by some families include: flushing/redness on face and/or body, increased heart rate, and nausea/vomiting/abdominal discomfort. Often these begin around infusions 6 and 8 and may require treatment with premedications (such as antihistamines, steroids, antiemetics).

For parents or individuals to fully understand the risks, benefits, and limitations of ERT, it is important to talk with physicians familiar with MPS VI 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, an option for individuals with other types of MPS diseases, is to restore activity of the deficient enzyme. 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. HSCT has been successful in a few individuals with MPS VI. Successful HSCT can restore the activity

of the deficient enzyme, which may improve such symptoms as enlarged liver and spleen, joint stiffness, sleep apnea, heart disease, hydrocephalus, and hearing loss. HSCT does not correct bone or eye problems, frequently requiring future therapies and surgeries.

The disadvantages of HSCT include the risk of mortality, the problem of finding a suitable donor, graft-versus-host disease, and the necessity of a very specialized medical facility.



ISABELLA AND MACKENZIE

For parents or patients to fully understand the risks, benefits, and limitations of HSCT, it is important to talk with physicians familiar with MPS VI HSCT 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.

Are there different forms of MPS VI?

Unlike some other MPS diseases in which there are multiple forms based on where the defect lies, there is only one form of MPS VI. However, it can manifest

as a severe, rapidly progressing disease or as a milder, slowly progressing disease, or some severity in between.

MPS VI can manifest as a continuous spectrum ranging from a severe, rapidly progressing disease to a milder, slowly progressing disease.

How common is MPS VI?

MPS VI is one of the rarer MPS diseases. Reliable incidence figures are available only from areas where epidemiological studies have been conducted. Although not proven, there may be an association with ethnicity. The prevalence of MPS VI ranges from 1 in 12,739 live births in Saudi Arabia to 1 in 43,261 live births among the Turkish immigrant population living in Germany to 1 in 5 million live births in South Korea. Some available information by region or country is given in the table below.

Country	Prevalence*	Country	Prevalence*
Australia	1 in 248,372	Poland	1 in 7.5 million
Brazil	1 in 322,580	Saudi Arabia	1 in 12,739
British Columbia, Canada	~1 in 1 million	Scandinavia	1 in 1.5–2 million
Germany	1 in 432,610	South Korea	1 in 5.3 million
Germany (Turks)	1 in 43,261	Taiwan	~1 in 800,000
Japan	1 in 3.3 million	United States	1 in 2 million

*Incidence rate per live births.

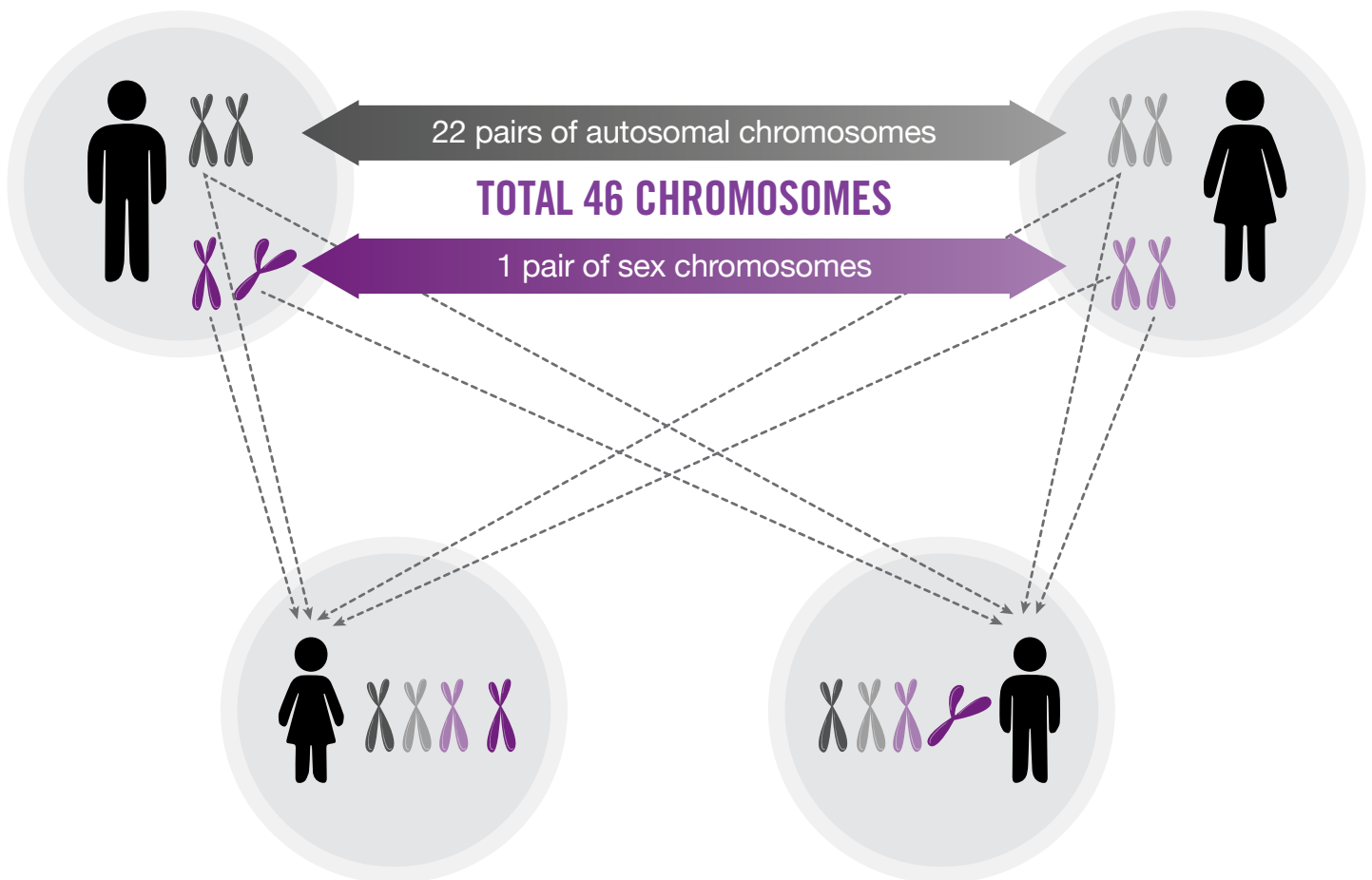
The prevalence of MPS VI varies considerably across the world and sometimes within people of specific ethnic origins within a country. It is important to discuss your ethnicity with your doctor so that the best care can be provided.

How is MPS VI inherited?

To understand inheritance of MPS VI, 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 hundreds of 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 (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 2 copies of each gene, 1 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” **(Figure 2)**. That is because the inappropriately functioning gene from the parent who 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 parent 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 **(Figure 3)**.

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 one of the 22 autosomal chromosomes or on the sex chromosomes, the disease is described as autosomal, X-linked, or Y-linked.

Figure 2. Autosomal dominant inheritance with one parent affected.

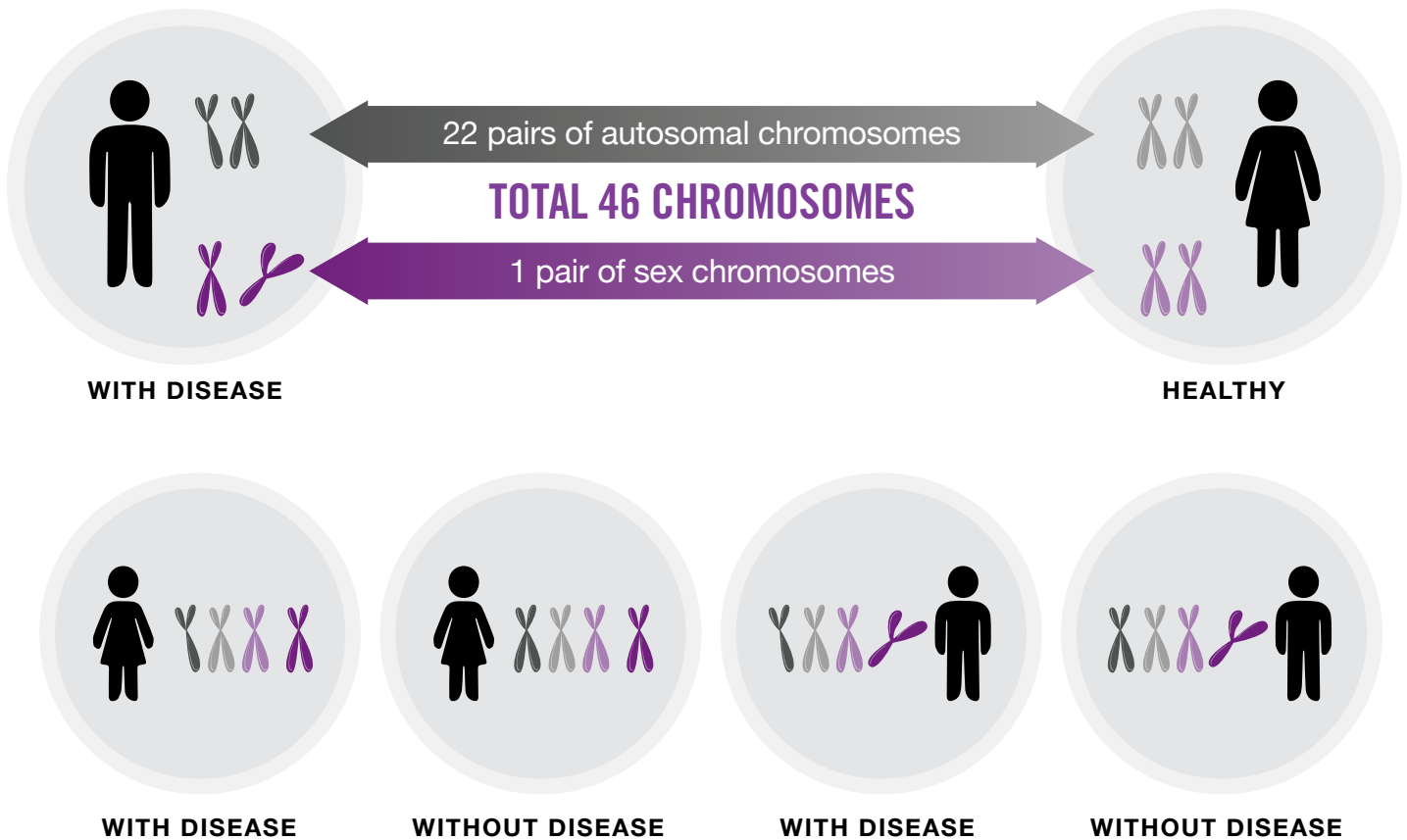
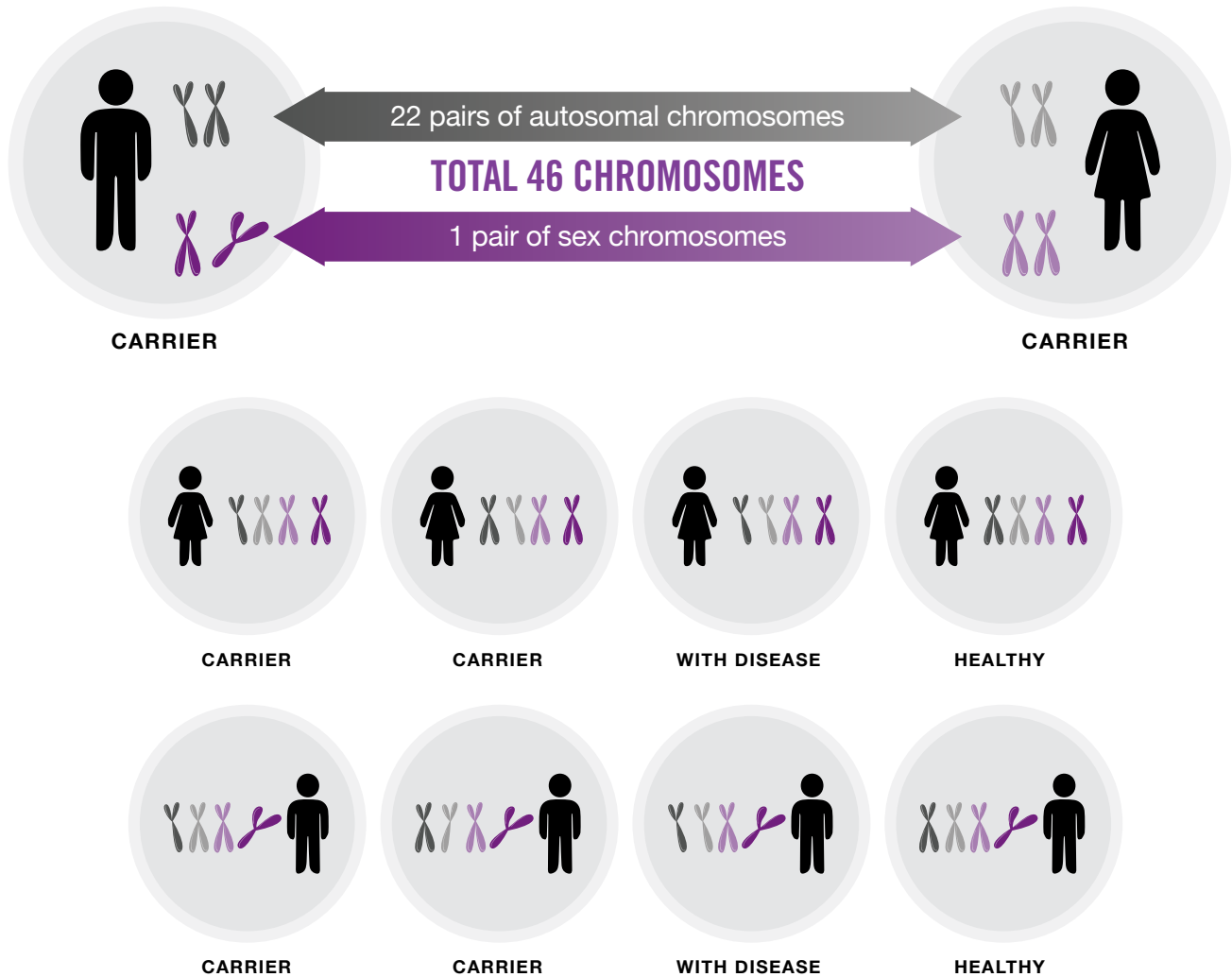


Figure 3. Autosomal recessive inheritance with both parents as carriers.



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 parents and thus having the disease;
- 25% chance of inheriting the normal gene from both parents; thus being healthy and also not being a carrier.



MITCHELL, AUTUMN, DR. HARMATZ, AND ISABEL

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 both genes inherited from the father and the mother are defective and producing very little or inactive enzyme does the individual exhibit symptoms.

MPS VI is an autosomal recessive genetic disease; that means that the gene for arylsulfatase B (*ARSB*) that causes this disease is on 1 of the 22 autosomal chromosomes, specifically on chromosome 5. MPS VI shows up only when both copies of the gene, one each inherited from the father and mother, are not functioning properly (**Figure 3**).

MPS VI is a genetic recessive disease caused by a deficiency in a specific enzyme, arylsulfatase B coded by the *ARSB* gene.

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

Why does disease severity vary so much?

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 structure 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 gene codes for an enzyme, this could mean too much or too little enzyme activity. In the case of MPS VI, all individuals lack the same enzyme, arylsulfatase B, which means that the gene coding for it (*ARSB*) is defective, resulting in highly reduced or completely absent enzyme activity. Currently, there is no reliable way of telling from biochemical tests how severe the disease will be.

The *ARSB* gene has been well studied and many mutations that cause enzyme deficiency have been identified. Some mutations result in absolutely no enzyme being produced. If both copies of the defective gene inherited by an individual are of this kind, evidence suggests that this individual’s symptoms will likely be at the severe end of the spectrum. Other common mutations cause very small amounts of defective enzyme to be produced, which may be sufficient to result in a milder (attenuated) form of the disease. Still, other mutations are not common at all and may

occur only in a single known family. In these cases, it is virtually impossible to predict severity of disease using DNA analysis. However, other than absence of enzyme activity being associated with manifestation of severe disease, there is as yet no clear correlation between gene mutations, enzyme activity, and disease severity. Thus, DNA tests or mutational analysis are not always sufficient to predict disease severity.

Disease severity can vary substantially even among individuals with the same level of enzyme activity. Similarly, disease severity can vary substantially among affected individuals within the same family. These data suggest that there are other, as yet not fully understood, factors beyond enzyme activity and DNA mutations involved in determining MPS VI disease severity. As such, there is no perfectly reliable way to determine the severity or the exact course of disease for individuals with MPS VI.

It is important to remember that whatever name is given to your condition or your child’s condition, MPS VI 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 VI 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 VI 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 VI live?

The lifespan of an individual with MPS VI depends on many factors including, but not limited to, severity of the disease, specific symptoms, what treatment is given, when the treatment was started, and how long the treatment continued. Individuals with less severe symptoms and more slowly progressing disease may have an almost normal lifespan; some individuals

are known to live into their 50s and 60s. However, individuals with more severe symptoms, fast-progressing disease, and lack of access to treatment options usually do not live beyond their teens or early 20s. There is always hope for better outcomes for individuals with MPS VI with ever-improving newer treatments, surgical procedures, and technology.

The lifespan of individuals with MPS VI can vary widely depending on severity of disease and treatment received.

Signs and symptoms of MPS VI

With tips for care and management

Except in the most severe cases, there are no symptoms at birth. Signs and symptoms generally appear in early childhood. Often the first sign is frequent ear infections that may require ventilation tubes. Two to 3 years later, symptoms can include a large head (macrocephaly), a buildup of fluid in the brain (hydrocephalus), distinctive facial features often described as “coarse,” and a large tongue (macroglossia). MPS VI affects multiple organ systems and is associated with a wide range of symptoms. The many signs and symptoms of MPS VI by organ class are summarized in the table below with detailed descriptions following.



BRANDON

Physical appearance	Gastrointestinal system (abdomen and intestines)
<ul style="list-style-type: none">• Coarse facial features (such as a flat-bridged nose or square jaw)• Large head (macrocephaly)• Severely short stature• Uneven, swaying gait	<ul style="list-style-type: none">• Enlarged liver and spleen (hepatosplenomegaly)• Umbilical and inguinal hernias

<h2>Mouth and teeth</h2>	<h2>Respiratory system (lungs and breathing)</h2>
<ul style="list-style-type: none"> • Thick lips • Enlarged tongue (macroglossia) • Abnormal teeth (widely spaced with small, sharp-pointed cusps and very thin enamel) 	<ul style="list-style-type: none"> • Narrowed trachea and bronchial airways • Thickened vocal cords • Lung problems and reduced lung function • Sleep apnea
<h2>Heart and blood vessels</h2>	<h2>Musculoskeletal system (bones and joints)</h2>
<ul style="list-style-type: none"> • Heart valve problems • High blood pressure (hypertension) • Arteriosclerosis • Ischemia • Infection of inner lining of heart (endocarditis) • Congestive heart failure • Angina • Sudden cardiovascular collapse 	<ul style="list-style-type: none"> • Disproportionately short trunk • Skeletal abnormalities (dysostosis multiplex) • Weak bones (osteopenia) • Joint stiffness • Loose ligaments, especially between atlas (C1) and axis (C2) bones of the spine • Tendon entrapment • Thickened, short finger (metacarpal) bones • Irregular, hypoplastic wrist (carpal) bones • Irregularly contoured foot (tarsal) bones • Carpal tunnel syndrome • Dysplastic femoral head • Abnormal hip formation (hip dysplasia) • Abnormal vertebral development (kyphosis, scoliosis) • Paddle-shaped widened ribs • Short, thick irregular clavicles
<h2>Ears, nose, and throat</h2>	
<ul style="list-style-type: none"> • Hearing loss • Frequent ear infections (otitis media) • Deformity of ossicles • Inner ear abnormalities • Progressive mouth (oral), throat (pharyngeal), and nose (upper airway) obstruction • Increased mucus secretion and blocked drainage, leading to nasal and sinus infections 	
<h2>Brain and nerves</h2>	<h2>Eyes</h2>
<ul style="list-style-type: none"> • Narrowing of spinal canal in the neck (spinal stenosis) • Cervical spine myelopathy • Fluid in the brain (hydrocephalus) • Pressure on the neck area of the spinal cord from abnormal tissue growth nearby (cervical spinal cord compression) 	<ul style="list-style-type: none"> • Vision problems, such as corneal clouding • Glaucoma • Chronic swelling of optic nerve (papilledema) • Retinal degeneration • Cross-eye (strabismus)

Growth

Children with MPS VI usually grow normally at first, but growth varies with severity of the disease. In severe disease, growth often slows down around 1 year of age and stops completely by 3 to 4 years of age, with

individuals reaching a final height between 3 and 4 feet. Less severely affected individuals continue growing into their teens and can reach 5 feet.

Physical appearance

Facial features of individuals with MPS VI are usually altered to some extent. They are often described as “coarse” with chubby cheeks, broad noses with a flat bridge, and wide nostrils. As they grow, the trunk is disproportionately short compared with limbs. They generally have a large head (macrocephaly) and short necks. The shoulders are narrow and rounded and the stomach tends to protrude. The hair on the body is coarser and more abundant than usual, and the eyebrows are bushy. The skin may become thickened and less elastic than usual.



MEEKEL AND CARISSAH

Mouth and teeth

Individuals with severe MPS VI usually have an enlarged tongue (macroglossia) and thick lips. Gum ridges are broad. The teeth can be widely spaced and poorly formed 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, children with MPS VI should be given daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and help avoid bad breath. 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 very young child, but they should be able to indicate the problem as they get older.

If an individual with MPS VI has a heart problem, it is advised that they speak with their cardiologist to determine whether it is appropriate for antibiotics to be given in association with 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 the individual is under an anesthetic, this should be done in the hospital under the care of both an experienced anesthetist and dentist, never in the dentist's office. Dentists should be informed of the diagnosis of MPS VI 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 VI should be given fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and avoid bad breath. For individuals with MPS VI, dental surgery must be done only in a hospital setting with appropriate anesthesia. Additional precautions may be required for those with heart conditions.

Nose, throat, chest, and ear problems

The problems described in this section are more common in individuals with more rapidly progressing disease. Individuals with attenuated MPS VI are likely to have fewer and less severe symptoms.

Runny nose

Typically, the bridge of the nose in individuals with MPS VI is flattened and the passage behind the nose may be smaller than in individuals without MPS. This is due to poor growth of the bones in the mid-face and thickening of the mucosal lining. The combination of abnormal bones with storage of GAG in the soft tissues in the nose and throat can cause the airway to become easily blocked. Common features of individuals with severe MPS VI are the chronic discharge of thick mucus from the nose (rhinorrhea) and chronic ear and sinus infections.

Throat

In individuals with MPS VI, the tonsils and adenoids often become enlarged and can partly block the airway. The neck is usually short, which contributes to problems in breathing. The windpipe (trachea) becomes narrowed by storage material and may be floppier or softer than in healthy individuals. This is due to abnormal cartilage rings in the trachea. Nodules or excess undulations of tissue can further block the airway.

Chest

Normally, the breastbone (sternum) is joined to the spine by the ribs. In individuals with MPS VI, the shape of the chest is abnormal and the junction between the ribs and the breastbone (sternum) is not as flexible as it should be. The chest is therefore rigid and cannot move freely to allow the lungs to take in a large volume of air. The muscle at the base of the chest (diaphragm) is pushed upward by the enlarged liver and spleen, further reducing the space for the lungs. When the lungs are not fully cleared, there is an increased risk of infection (pneumonia). A breathing test, called a pulmonary function test, can be used by a lung specialist to assess the amount of breathing restriction caused by abnormal bone growth.

Breathing difficulties

Noisy breathing, nighttime restlessness, and snoring even in the absence of infections is common among individuals with MPS VI. It is not uncommon for these individuals to stop breathing for short periods of 10–15 seconds while sleeping (sleep apnea). This sleep pattern of noisy breathing with occasional or periodic stops can be very frightening for parents who may think their child is dying. Frequent stoppage of breathing may result in low blood oxygen levels, which could cause

heart problems. Many individuals may breathe like this for years. If a parent or caregiver notices significant choking or episodes of interrupted breathing, the child or adult with MPS VI should be evaluated for sleep apnea by a sleep specialist using a polysomnogram.

Breathing difficulties may also be due to excessive mucus secretions in the air passages and settling in the lungs. This can be managed through chest postural drainage; a physiotherapist can teach this technique to parents or caregivers at school.

In certain cases, airways can be obstructed to the point that a tracheotomy (an incision in the windpipe to relieve obstruction) is required, and it is performed successfully for sleep apnea (see below) and occasionally prior to a planned surgery.

Managing sleep apnea

A sleep specialist will generally want the patient admitted to a special evaluation center for a sleep study. This involves attaching several electrical leads to the chest, arms, hands, and head to measure blood oxygen levels, brain and heart function during sleep, and other aspects of body function during sleep. These tests will help the doctor determine the individual's quality of sleep, and oxygen blockage during sleep and its effect on the body, especially the heart and the brain.

It is important that individuals with MPS VI who have sleep apnea be evaluated by a sleep specialist. Proper management of sleep apnea is important for overall health and to prevent heart problems associated with low blood oxygen levels.

Respiratory infections

Most individuals with colds do not require antibiotics. However, poor drainage of the sinuses and middle ear due to excess mucus production make individuals with MPS VI more prone to secondary bacterial infections,

Sleep apnea can be treated in various ways. For some individuals, mechanically opening up the airway with nighttime continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) can address the problem. These machines pump air at a prespecified pressure into the individual through a face mask worn each night during sleep. This keeps the airways from collapsing and maintains the individual's blood oxygen at a healthy level, thereby reducing the risk or preventing heart failure caused by low blood oxygen levels. Most individuals easily get used to the mask and machine, and they can greatly improve the overall quality of sleep.

For others, surgery, such as removing the tonsils and adenoids (adenoids may regrow), may resolve the sleep apnea. In severe cases, such as sleep apnea with heart failure, making an incision in the windpipe to relieve obstruction (tracheotomy) may be necessary. However, most families will try to avoid a tracheotomy because it is perceived to be very invasive and seemingly destructive of the patient's normal function. Conversely, many doctors feel that individuals with MPS should receive a tracheotomy earlier than most currently do, as it improves overall health when nighttime breathing is not obstructed.

which often promptly recur after the antibiotic course is over. Thus, treating and managing respiratory infections can be particularly difficult for individuals with MPS VI.

Although most individuals with colds do not require antibiotics, individuals with MPS VI may end up with secondary bacterial infections of the sinuses or middle ear requiring regular courses of antibiotic treatment.

Treatment of respiratory infections

These infections should be treated with antibiotics. However, individuals with MPS VI may respond differently to drugs than do individuals without this disease. It is, therefore, essential to consult your doctor rather than using over-the-counter medications.

Chronic antibiotic therapy can be used to help some individuals with recurring ear infections. Many people with MPS VI become allergic to antibiotics or the bacteria may acquire resistance to the antibiotics being used to treat the infections. Your doctor can prescribe other antibiotics to help manage this problem. Overusing antibiotics is not advised. Nevertheless, most people with MPS VI will require some type of treatment to manage recurrent infections. You will need a doctor with whom you can develop a good working relationship and who is experienced in treating MPS diseases to manage the frequent infections.

Ventilation tubes can be used to improve drainage from the ear and speed resolution of infections. It is important to consult with an ear, nose, and throat (ENT) specialist experienced in treating MPS diseases to determine which tube is best.



MAKAYLA

Many individuals with MPS VI will need multiple courses of antibiotics to treat recurrent infections. They may become allergic to antibiotics or may acquire resistant infections. You will need a doctor with whom you can develop a good working relationship and who is experienced in treating MPS diseases to manage the frequent infections.

Heart

Heart disease is common in individuals with MPS VI, progressively worsens with age, and is a major cause of death. However, heart disease may not develop or cause any real problems until later in life. Some individuals may have slowly progressive heart disease for years

without any apparent clinical effects. Endocarditis (infection of inner heart membrane) is also something to be considered especially in individuals fitted with a central venous access port for receiving ERT. Storage of GAGs may occasionally cause cardiomyopathy

(weak heart muscle) and endocardiofibroelastosis (stiff heart) in individuals with the severe form of MPS VI. This can place the heart under strain due to having to pump blood through abnormal lungs (cor pulmonale or right heart failure). Systemic hypertension (high blood pressure) is common and may occur due to narrowing of arteries or intermittent low blood oxygen levels (hypoxia).

Your doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAGs. Heart valves are designed to close tightly as blood passes from one chamber of the heart to another to stop blood from flowing back in the wrong direction. If a valve is

weakened, it may not shut firmly enough and a small amount of blood may shoot backward, leading to turbulence and a murmur. Most people with MPS VI have some degree of heart valve leakage or blockage. Some individuals with MPS VI may develop heart failure and have problems with the aortic or mitral valve. As heart problems occur in MPS VI, individuals should have a test known as an echocardiogram annually (or as often as your 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.

Heart disease is common in people with MPS VI but may not develop or cause any real problems until later in life.

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

Treatment of heart disease

Medications are available to help manage the heart problems that occur in MPS VI. Many individuals with MPS VI have some degree of heart valve leakage or blockage and may need surgery to repair and/or replace the damaged valves.

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



SAVANNAH AND PAIGE

For optimal treatment of heart disease caused by MPS VI, it is important to work with a cardiologist with specific knowledge of MPS diseases.

Liver and spleen

In most individuals with MPS VI, both the liver and spleen become substantially enlarged (hepatosplenomegaly) by storage of GAG.

The enlarged liver does not usually cause liver problems or lead to liver failure, but it can interfere with eating and breathing.

Abdomen and hernias

In most individuals with MPS VI, the abdomen bulges out due to posture, weakness of the muscles, and the enlarged liver and spleen. Frequently, part of the abdominal contents will push out behind a weak spot in the wall of the abdomen. This is called a hernia.

The hernia can come from behind the navel (umbilical hernia) or in the groin (inguinal hernia).

Inguinal hernias can be repaired by an operation but will sometimes recur. Umbilical hernias are not usually treated unless they are small and cause entrapment of the intestine or are very large and are causing problems. It is very common to have a reoccurrence of an umbilical hernia after a repair has been made.

In most individuals with MPS VI, the abdomen bulges out due to posture, weakness of the muscles, and the enlarged liver and spleen.

Bowel problems

Many individuals with MPS VI periodically experience loose stools and diarrhea. The reasons for these bowel movement problems are not fully understood. Occasionally the problem is caused by severe constipation and leakage of loose stools from behind the solid mass of feces. More often, however, parents of children with this problem describe it as “coming straight through.” The problem may resolve itself as the child gets older. However, diarrhea can be made worse by certain antibiotics prescribed to treat other problems experienced by individuals with MPS VI. Diet may also cause episodic diarrhea in some individuals with MPS VI. Constipation may become a problem as the child gets older and less active and as the muscles weaken.

An examination by your pediatrician, supplemented by an X-ray if necessary, may establish the cause of diarrhea.

The autonomic nervous system is the system that controls those bodily functions usually beyond voluntary control, such as breathing and bowel movement. Studies have found GAG storage in the nerve cells of the intestine, which may cause abnormal motility in the bowel, resulting in diarrhea. If the diarrhea is caused by diet, elimination of some foods can be helpful. If antibiotics are the cause, eating plain live-culture yogurt often is helpful during episodes of diarrhea. This provides a source of lactobacillus to help prevent the growth of harmful organisms within the bowel wall, which can cause diarrhea or make it worse. A diet low in roughage also may be helpful. On the other hand, if the individual is experiencing constipation, an increase in roughage is recommended. If this does not help or is not possible, the doctor may prescribe laxatives or a disposable enema.

Most individuals with MPS VI experience bowel problems. Consult your doctor to determine the cause and receive the optimum treatment.

Bones and joints

Individuals with MPS VI tend to have significant problems with bone formation and growth. This leads to multiple skeletal problems (called dysostosis multiplex) as well as neurological problems if nerves get compressed by bone.

Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Individuals with the severe form of MPS VI often have poorly formed vertebrae that may not stably support 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. This backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not need treatment.

Spinal cord compression, a serious condition caused by accumulation of GAGs in the membrane surrounding the spinal cord, is common among individuals with MPS VI and can lead to spinal cord

disease (myelopathy) and/or softening of the spinal cord (myelomalacia). Spinal cord compression can be caused by narrowing of the spinal canal (spinal cord stenosis) occurring as a result of other malformations of the spine and the base of the skull. Compression usually occurs in the neck (cervical region) and has been reported in individuals as young as 1 year old. It can be debilitating and even life-threatening.



KENDRA

Spinal cord compression is a serious condition common to individuals with MPS VI. It can be debilitating or even life-threatening. Consult your doctor to determine the cause and receive the optimum treatment.

The neck is short and sometimes restricted in movement. The bones that stabilize the connection between the head and neck can be malformed (odontoid dysplasia) in people with the severe form of MPS VI. In particular, individuals with MPS VI have loose ligaments, especially between atlas (C1) and axis (C2) bones of the spine (atlantoaxial instability), making the

neck unstable. Fusion surgery is required to connect all the bones to each other, so they do not slip further. If severe pain or pain associated with weakness or tremors in the lower legs occur, the individual should have studies of the neck (MRI and flexion-extension X-rays) to evaluate for slippage of the neck vertebrae.

Scoliosis

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

Joints

Joint stiffness is common in all forms of MPS, 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 heat and ordinary painkillers. The limited movement in the shoulders and arms may make dressing difficult. Anti-inflammatory drugs, such as ibuprofen, can help with joint pain, but their use should be monitored closely to make sure that irritation and ulcers in the stomach do not occur.

Joint stiffness is common in all forms of MPS, and the maximum range of movement of all joints may become limited.

Hands

The shape of the hands is very noticeable; the hands are short and broad with stubby fingers. The fingers stiffen and gradually become curved due to limited joint movement. The tips of the fingers can become permanently bent over.

Legs and feet

Many individuals with MPS VI stand and walk with their knees and hips flexed. This, combined with a tight Achilles tendon, may cause them to walk on their toes. They sometimes have knock-knees. Severe knock-knees can be treated by surgery on the tibia bones, but this is not common in MPS VI. The feet are broad and may be stiff with the toes curled under, similar to the hands.

Skin

Individuals with MPS VI tend to have thickened and tough skin, making it difficult to draw blood or place IV catheters. Excess hair on the face and back occurs in some individuals with MPS VI. Sweating and cold hands and feet also are common problems and are

possibly related to the heart, circulation, or other mechanisms that control temperature regulation. Periodic blue or cold hands or feet should be evaluated by a cardiologist to determine whether heart or aortic disease might be responsible for the problem.

Individuals with MPS VI may have thickened or tough skin, making it difficult to draw blood.

Body temperature may not be well regulated and should be evaluated by a cardiologist to determine the cause of the problem.

Neurological problems: brain, senses, and nerves

Brain

The brain and the spinal cord are protected from jolting by the cerebrospinal fluid that circulates around them. In some individuals with MPS VI, the circulation of the fluid can slowly (over months to years) become blocked so that it cannot be taken back into the bloodstream. The blockage (communicating hydrocephalus) causes increased pressure inside the head, which can press on the brain and cause headaches and delay development. If hydrocephalus is suspected, an imaging study of the brain (CT or MRI scan) should be performed. A lumbar puncture with pressure measurement is another way to assess whether hydrocephalus exists. If the doctor confirms that you or your child has communicating hydrocephalus, it can be treated by the insertion of a thin tube that drains fluid from the brain into the abdomen (ventriculoperitoneal or VP shunt). The shunt has a pressure-sensitive valve that allows spinal fluid to be drained to the abdomen when the pressure around the brain becomes too high.

The lack of papilledema (swelling around the optic disk) does not rule out hydrocephalus in an individual with MPS. Communicating hydrocephalus is more likely to occur in an individual with severe MPS VI.

Eyes

The circular window at the front of the eye (cornea) can become cloudy due to storage of GAGs. When corneal clouding becomes severe in individuals with MPS VI, it can impair sight especially in dim light. Some individuals cannot tolerate bright light, as the clouding causes uneven refraction of light. Wearing caps with visors or sunglasses can help. Corneal transplant usually improves vision. Other vision problems may be due to increased eye pressure (glaucoma) and retinal changes.

It is often difficult to determine the cause of decrease in eyesight. An ophthalmologist can conduct tests to help determine whether the problem lies in how light gets into the eye (the cornea) or how the eye responds to light (the retina or optic nerve disease), or a combination, and figure out how best to treat it.

Eyesight should be checked regularly. An ophthalmologist can help determine the cause of failing eyesight and how best to treat it.

Ears

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

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. This is called middle ear effusion and can lead to infections.

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

Sensorineural (nerve) deafness

In most cases, nerve deafness is caused by damage to the tiny hair cells in the inner ear. If it occurs together with conductive deafness, it is referred to as mixed deafness. Nerve or conductive deafness can be managed by the fitting of a hearing aid or aids in most individuals. In general, it is felt that hearing aids are underutilized in MPS diseases.

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.

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

Carpal tunnel syndrome and other nerve entrapments or compression

Individuals with MPS VI sometimes experience pain and loss of feeling in the fingertips caused by carpal tunnel syndrome. The wrist, or carpus, consists of 8 small bones known as the carpals, which are joined by fibrous bands of protein called ligaments. Nerves have to pass through the wrists in the space between the carpal bones and the ligaments. Thickening of the ligaments causes pressure on the nerves, and this can cause irreversible nerve damage. The nerve damage will cause the muscle at the base of the thumb to waste away and will make it difficult to oppose the thumb in position for a normal grasp. Although you may not feel pain or your child may not complain of pain, carpal tunnel syndrome may be severe. If you or your child experiences pain or numbness in the hands, particularly

at night, it would be advisable to have an electrical test called a nerve conduction study performed. This test will show whether carpal tunnel syndrome is the cause. If you or your child has any weakness at all in the hand or has decreased muscle mass at the base of the thumb, ask for the test from your neurologist. Be persistent, as many physicians may not believe carpal tunnel syndrome is present without the classic symptoms. Most individuals affected by MPS VI do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage. Healthy hand habits may help to combat occupational stresses. Taking time to rest and relax the hands, and simple stretching exercises may help to relieve the strain on wrists and hands.

It is important that individuals with MPS VI be evaluated for carpal tunnel syndrome and treated early to prevent loss of hand function.

Intelligence

There is no storage of GAGs in the brains of individuals with MPS VI; therefore, intelligence is not usually affected.

Living with MPS VI

Education

The majority of children and adolescents with MPS VI will attend mainstream school and should be able to maintain academic achievement. Obtaining a college education is not unusual. For individuals with MPS VI to reach their full academic potential, it is important to ensure that the school is aware of the resources required. It is important for parents or caretakers to

work with the school system and develop the best Individualized Education Program, Section 504 Plan, or medical plan for your child. For more information on education, see the booklet titled, *A Guide for Parents: Education Strategies and Resources*, published by the National MPS Society.

Puberty

Adolescents with MPS VI will go through normal developments of puberty, although the onset of menstruation in girls may be delayed. Individuals with MPS VI are fertile. Women whose stature is significantly restricted may be advised not to become pregnant

because of risks to their health. All children born to a parent with MPS VI are automatically carriers, but none will have the disease unless the other parent also is a carrier or has MPS VI too.

Reproduction

Individuals with MPS VI are fertile. Fertility studies in humans with any MPS type are rare. Spermatogenesis may be reduced among males with MPS VI. Individuals with MPS VI who have received an allogeneic (from a donor with a different genetic background) HSCT (see more on page 7) often experience an adverse impact on fertility due to the chemotherapy and radiotherapy associated with HSCT. Irradiation can also have adverse effects on the uterus including poor implantation and poor fetal growth. Premature termination or birth may occur. Women whose stature is significantly restricted may be advised not to become pregnant because of risks to their health. It is important to remember that all children born to a parent with MPS VI are automatically carriers, but none will have the disease unless the other parent also is a carrier or has MPS VI too. It is advisable for individuals with MPS VI to take the following points into account when considering having a child:

- Preconception genetic counseling
- Preconception medical evaluation
- Preconception discussion of risks during pregnancy and delivery, e.g., high probability of a caesarian delivery
- Health risks during pregnancy, e.g., difficulty with respiration due to the uterus pushing up, fluid overload, cardiopulmonary complications
- Health risks during delivery, e.g., premature delivery due to skeletal limitations, anatomical differences making diagnosis of delivery process difficult, problems with administering and managing anesthesia
- Newborns with skeletal problems will need immediate specialized medical care

All children born to a parent with MPS VI are automatically carriers, but none will have the disease unless the other parent also is a carrier or has MPS VI.

Independence

People with MPS VI should be encouraged to be as independent as possible to lead full and enjoyable lives. The teenage years may be difficult for those who have restrictions imposed by their disease. Teens with MPS VI may be helped by meeting or contacting other

teenagers and adults who also have MPS VI. 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 with MPS VI should not prevent people from accessing meaningful employment. The Americans with Disabilities Act helps both employees and employers. Individuals

with MPS VI may find it helpful to contact their local Vocational Rehabilitation office. These are in every state, usually with multiple offices in each state, and help provide information about and access to employment.



MPS VI FAMILY MEETING, DALLAS, TX

Home adaptations

Appropriately adapted living accommodations will greatly enhance the ability of an individual with MPS VI to develop independent living skills. Where stature is severely restricted, kitchen and bathroom facilities set at a lower height will be required. If mobility is restricted to such an extent that a wheelchair is used, plans for any home adaptations will need to allow adequate space to

accommodate this. Additional information about home adaptations can be found in the booklet titled *Daily Living with MPS and Related Diseases*, published by the National MPS Society.

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

Healthcare information

Assistance may be available from specialized agencies for individuals with disabilities and from genetics clinics. Explore Social Services, Social Security, Medicaid Waivers, and the Katie Beckett Law. Investigate these options and others that may be available for you on federal, state, and local levels. In most states, it is beneficial to start with the Department of Social Services or Department of Health and Human Services for additional information. If you already have Medicaid, calling the phone number on the card will help to get

you connected with a social worker or case manager who will serve as a “point person” to help you get set up with things for which you qualify. If you do not have Medicaid or an established social worker, you can ask to speak with one through your healthcare provider. Many physicians have access to social workers, as do most hospitals. Your social worker should be able to locate additional information and/or resources for your family.

Assistance may be available from specialized agencies for individuals with disabilities and from genetics clinics.

Psychosocial issues

Currently, there has been no research that explores the psychosocial development of individuals affected with MPS VI. As such, it is not possible to make definitive statements about this subject. As a parent of a child or young person with MPS VI, it is important to consider how their disability may cause them to experience additional challenges in life. Some children and young adults with MPS VI may adapt socially and emotionally by becoming socially inhibited or by internalizing problems or developing

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

Taking a break

Caring for a severely affected individual is hard work. Parents and caregivers need a break to rest and enjoy activities, and this may not be possible when their child or ward with MPS VI is with them. Brothers and sisters need their share of attention and need to be taken on outings that may not be feasible with a sibling with

MPS. Many parents use some form of respite care or have someone come to help at busy times.

Mildly affected individuals may need help to become more independent from their families and may benefit from a vacation, perhaps with others who have disabilities.

Taking care of yourself and others in the family is important and should not be sidelined.

General management of MPS VI

Diet

There is no scientific evidence that any symptoms of MPS VI can be managed with a particular diet. Digestive system problems, such as diarrhea, tend to come and go naturally or with moderate intervention. Some individuals and parents, however, 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 your problems

or your child's problems are eased, you could try reintroducing foods one at a time to test whether any particular item seems to increase symptoms. It is important to remember that GAGs are synthesized by cells as part of their natural process. This disease is not caused by overproduction of GAGs, but rather by the failure to break down GAGs. As such, there is no diet that can prevent GAG accumulation.

Please note:

Consuming sugar or foods normally eaten will not affect the buildup of GAGs in the body.

There is no scientific evidence that a particular diet has any helpful effect on individuals with MPS VI.

Swallowing

Swallowing may become difficult as an individual with MPS VI gets older and the disease progresses. If this occurs, the individual may choke or aspirate food or liquids into the lungs, which can result in recurrent pneumonia. During these episodes, there may be weight

loss and feeding can take much longer and become more problematic. It is often difficult for a family to consider alternate means of feeding, such as a gastrostomy tube (G-tube). Consult your medical geneticist and surgeon to help you with making your decisions.

Swallowing may become more difficult as the disease progresses. Consider alternate modes of feeding.

Physical therapy

Joint stiffness, a common feature of MPS VI, limits motion and can cause significant loss of joint function. Range-of-motion exercises (passive stretching and bending of the limbs) may offer some benefits in preserving joint function and should be started as early as possible for maximum benefit. Exercises that cause pain should be avoided. Once significant limitation has occurred, it may not be possible to regain the earlier range of motion although further limitation may be minimized. Individuals with MPS VI should be as active as possible to maintain their joint function and improve their general health. Your 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. It is important for children and adults to keep a balance between avoiding risks and leading as normal a life as possible. Activities such as somersaults, head stands, or diving should be avoided completely because of risk to the neck.



PAIGE AND ERIN

Mobility

Many individuals with MPS VI remain ambulatory into their teens and adult life. Others may need to use a wheelchair from an early age for longer periods of

activity. In such cases, an electric wheelchair is vital to encourage independence. Consult your physical therapist or occupational therapist for advice.

Individuals with MPS VI should be as active as possible to maintain their joint function and improve their general health. Your doctor or physical therapist may be able to suggest ways of achieving this.

Drugs and medications

Drugs for controlling mucus production may not help and may even be counterproductive. Antihistamines, which dry out the mucus, may make it thicker and harder to dislodge. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for individuals with MPS VI. Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea (see above) by depressing muscle tone and respiration.

Anesthetics

Giving an anesthetic to an individual with MPS VI 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 have to go to an unfamiliar hospital in an emergency, 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 a flexible bronchoscope.

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 VI.

For any elective surgery for a child with MPS VI, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical center, not at a local hospital. See additional information on anesthesia in the booklet titled *Is Your Child Having an Anesthetic?*, published by the National MPS Society.

For any elective surgery for a child with MPS VI, it is important to choose a pediatric anesthesiologist who has experience with difficult airways.

Research for the future

The mission of the National MPS Society is to find cures for MPS and mucopolidosis (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 families understand more about what is happening to those with MPS VI and what they can do to manage it. This booklet was updated by the National MPS Society in 2020.



PATRICIA

Updates

Medical professionals and researchers are constantly learning new things about MPS VI 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 VI 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.

Update: Date: Link to more information:	
Update: Date: Link to more information:	
Update: Date: Link to more information:	
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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, with each other.

Benefits of membership in the National MPS Society:

- *E-Courage*, our quarterly newsletter containing stories and information about individuals with MPS and ML
- Educational materials such as fact sheets, syndrome booklets, 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 of members 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, secretions, and 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 GAG, 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 2 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.mpssociety.org

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