



National
MPS
Society

Support for Families. Research for a Cure.



A Guide to Understanding MPS VI

Maroteaux-Lamy Syndrome

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

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2 Introduction

MPS VI is one of the rarer mucopolysaccharide (MPS) diseases. It takes its name from two French doctors, Dr. Maroteaux and Dr. Lamy, who first described the condition in 1963. Historically MPS VI has

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).

been divided into severe and mild forms. It is now clear that this disease is more complex and more variable than was previously assumed. It is now perhaps more appropriate to view MPS VI as a continuous spectrum of disease, with the most rapidly progressing individuals on one end and the more slowly progressing individuals on the other end, and a wide range of different severities in between. The term attenuated instead of mild is used to describe less severe individuals because

the effects of the disease on a less severe individual are too significant to be considered mild. MPS VI varies enormously in the severity of the problems it causes. It is important to remember this variation if you are the parent of a newly diagnosed child. This booklet describes all the possible problems, however this does not mean your child will experience them all, or that he or she will be severely affected by them. In fact, some individuals have very few physical problems and are able to lead relatively normal lives.

There currently is no 100 percent reliable test that indicates how severe an individual’s MPS VI will eventually become.

All individuals with MPS VI have deficiency of the enzyme arylsulfatase B (ASB), which results in the accumulation of glycosaminoglycans (GAG), previously called mucopolysaccharides, inside special parts of the cell called lysosomes. This is why MPS VI is part of a larger family of diseases called the lysosomal storage diseases (LSDs). The accumulation of GAG is responsible for numerous problems that affect individuals with MPS VI.

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 help them enjoy life. Hematopoietic stem cell transplant (HSCT) has been used to treat MPS VI successfully in some individuals. Enzyme replacement therapy (ERT), approved by the U.S. Food and Drug Administration (FDA) in 2005, is another treatment. Scientists

who study MPS continue to look for better and more effective ways to treat these diseases, and it is likely that individuals with MPS VI will have more options available to them in the future.

What causes MPS VI?

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

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

To understand how GAG accumulates and cause MPS VI, it is important to understand that in the course of the normal life process, there is a continuous process of building new GAG and breaking down old ones—a recycling process. The breaking down of GAG occurs in a part of the cell called the lysosome. That is why MPS VI is considered one of the approximately 40 different kinds of LSDs. All of the LSDs are caused by the inherited deficiency of individual enzymes and are very rare. This ongoing recycling process is required to keep your body healthy.



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The breakdown and recycling process requires a series of special biochemical tools called enzymes. To break down GAG, a series of enzymes works in sequence one after another. The GAG chain is broken down by removing one sugar molecule at a time starting at one end of the GAG chain. Each enzyme in the process has its special purpose in the body and does one very specific action—just like a screwdriver works on screws and a hammer works on nails.

Individuals with MPS VI are missing one specific enzyme called arylsulfatase B (ASB), which is essential in the breakdown of certain

4 GAG called dermatan sulfate. The incompletely broken down dermatan sulfate remains stored inside cells in the body and begins to build up, causing progressive damage. The GAG itself is not toxic, but the amount of it and the effect of storing it in the body lead to many physical problems. Babies may show little sign of the disease, but as more and more GAG accumulates, symptoms start to appear. Sugar or other foods normally eaten will not affect whether there is more or less buildup of GAG.

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Is it possible to predict the severity of MPS VI?

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

DNA tests do not always correctly determine the severity of MPS VI. Many different kinds of mutations (defects in the make-up of

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genes) in the gene that produces ASB have been identified, all of which result in ASB deficiency. This enzyme deficiency results in MPS VI disease. The gene has been studied extensively to see if there is any relationship between specific genetic mutations and the symptoms of the disease. There are some common mutations of the gene that result in absolutely no

ASB enzyme being produced. If both copies of the defective gene inherited by an individual are of this kind, evidence suggests that the individual's condition is likely to be at the severe end of the spectrum. Other common mutations of the gene cause very small amounts of defective enzyme to be produced, and still other mutations are not common at all and may only occur in a single known family. In these cases, it is virtually impossible to predict severity of disease using DNA analysis.

Therefore, there is no perfectly reliable way to determine the exact course of disease for individuals with MPS VI. Even with the same small amount of enzyme activity, and even within the same family, there can be variations in severity of disease that cannot be explained by the enzyme level or DNA mutation. It is important to remember that whatever name is given to your child's condition, MPS 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, parents are forewarned that your child may not experience them all or to the degree described herein.

How common is MPS VI?

It has been estimated that about 1 in 215,000 births are affected by MPS VI. Although MPS VI is individually rare, the incidence of all MPS diseases is 1 in 25,000 births and the larger family of LSDs collectively occur in about 1 in every 5,000 to 7,000 births.

How is MPS VI inherited?

MPS VI is a genetic disease. When most individuals think of genetic disease, they think of a health problem that gets passed down from father or mother to child and so on. While many genetic diseases are passed down through generations in an obvious way, some genetic diseases are "hidden," or recessive, and only show up when both genes in an individual are affected. MPS VI is this type of genetic disease. Most families who have a child with MPS VI do not have a family history of genetic problems. MPS VI seems to show up suddenly even though the genetic mutation can be traced up the family tree to earlier generations through DNA testing.

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

Each enzyme in the body is produced by two genes—one from the mother and one from the father. If one gene happens to be defective (as is the case for a carrier), then the body may produce only 50

6 percent of the normal level of enzyme associated with that gene. However, 50 percent of the normal enzyme level is enough enzyme to keep the individual who is a carrier from having any symptoms of MPS VI. If, however, the genes from both the mother and the father are not functioning correctly, the individual will have little or no enzyme in the body and will experience symptoms of MPS VI.

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

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

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

How is MPS VI diagnosed?

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.

To diagnose MPS VI, the doctor will typically first do a urine test to look for levels of GAG that are higher than normal. The results are compared to levels of GAG that are known to be normal for various ages.

The earlier MPS VI is diagnosed, the sooner potential treatment options can be explored and supportive care may be started.

7 Most, but not all, individuals with MPS have GAG levels in their urine that are higher than those of individuals without MPS.

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

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. 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.

Clinical problems in MPS VI

Growth

Growth in height can be significantly less than normal for individuals with rapidly progressing MPS VI, but varies according to the severity of the disease. Individuals with the most severe form of MPS VI may not grow taller than 3 to 4 feet. Individuals with the more slowly progressing end of the disease spectrum of MPS VI usually grow to a relatively normal height, reaching 5 feet or more.

Intelligence

Intelligence is not affected by MPS VI; many children are of above average ability.

Physical appearance

Individuals with MPS VI, particularly those with severe disease, look remarkably similar due to large heads, short necks, chubby cheeks, broad noses with a flat bridge and wide nostrils. 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.

Nose, throat, chest and ear problems

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

Runny nose

Typically, the bridge of the nose is flattened and the passage behind the nose may be smaller than usual due to poor growth of the bones in the mid-face and thickening of the mucosal lining. This combination of abnormal bones, with storage in the soft tissues in the nose and throat, can cause the airway to become easily blocked. One of the common features of individuals with severe MPS VI is the chronic discharge of thick mucus from the nose (rhinorrhea), and chronic ear and sinus infections.

Throat

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 more floppy, or softer than usual, due to abnormal cartilage rings in the trachea. Nodules or excess undulations of tissue can further block the airway.

Chest

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).

Breathing difficulties

Many affected individuals breathe very noisily, even when there is no infection. At night they may be restless and snore. Sometimes the individual may stop breathing for short periods while asleep (sleep apnea). Pauses of up to 10–15 seconds may be considered

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normal. This noisy breathing, which stops and starts, can be very frightening for parents to hear. They may fear their child is dying. If this is happening, the child's oxygen level may be low when sleeping, and can cause problems with the heart.

If a parent notices significant choking or episodes of interrupted breathing, the child should be evaluated by a sleep specialist using a polysomnogram. It is important to know that many individuals may breathe like this for years. Sleep apnea can be treated in some individuals by removing the tonsils and adenoids (adenoids may regrow), opening up the airway with nighttime continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or tracheotomy, as discussed in the following paragraphs.

Management of breathing problems

The doctor may want the child to be admitted to the hospital overnight for a sleep study. Monitors are placed on the skin and connected to a computer to measure the levels of oxygen in the blood, breathing effort, brain waves during sleep and other monitors of the body's function. From this study, the doctors can assess how much blockage to breathing is present, how much trouble your child is having moving air into the lungs during sleep, and how much effect this has on the body.



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In some cases, removal of tonsils and adenoids will help to lessen the obstruction and make breathing easier, but adenoid tissue may grow back.

CPAP or BiPAP can open the airway at night using air pressure, which can help the child's airway stay open. This treatment involves

10 placing a mask on the face each night and having air pumped into the airway to keep it from collapsing. This may seem to be an extreme measure, but many people are able to tolerate it because it can greatly improve the quality of sleep, as well as help prevent or reduce the risk of heart failure caused by low oxygen levels at night.

In severe cases of sleep apnea with heart failure, a tracheotomy (a hole into the airway made in the front of the neck) may be needed. Most families will try to avoid a tracheotomy because it is so invasive and seemingly destructive of the child's normal function. In fact, many doctors feel that individuals with MPS should receive a tracheotomy earlier than they do, and many do much better after improving their nighttime breathing.

Chest postural drainage can be helpful in clearing secretions from the lungs. A physiotherapist will be able to teach the parents and someone at the child's school how to do this.

Treatment of respiratory infections

Drugs may affect people with MPS VI differently, so it is essential to consult your doctor rather than using over-the-counter medications. Drugs for controlling mucus production may not help. Drugs, such as antihistamines, 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 individuals with MPS. Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea by depressing muscle tone and respiration.

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

Although most normal individuals with colds do not require antibiotics, individuals with MPS VI may end up with secondary bacterial infections of the sinuses or middle ear. These infections should be treated with antibiotics. Poor drainage of the sinuses and middle ear make overcoming infections difficult. Therefore, it is common to have infections improve on antibiotics and then promptly recur after the antibiotic course is over. Chronic antibiotic therapy can be used to help some individuals with recurring ear infections. Ventilation tubes can be used to improve drainage from the ear and speed resolution of infections. It is important to consult with an ear,

nose and throat (ENT) specialist experienced with MPS diseases to determine which tube is best.

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

Mouth

Individuals with severe MPS VI generally have thick lips and an enlarged tongue. Gum ridges are broad. The teeth may be widely spaced and poorly formed with fragile enamel. It is important that the teeth are well cared for, as tooth decay can be a cause of pain. Teeth should be cleaned regularly, and if the water in your area has not been treated with fluoride the child should be given daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and help avoid bad breath. Even with the best dental care, an abscess around a tooth can develop due to abnormal formation of the tooth. Irritability, crying and restlessness can sometimes be the only sign of an infected tooth in a severely involved individual.

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

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

Heart

Heart disease is common across the spectrum of MPS VI disease, but may not develop or cause any real problems until later in the

individual's life. Heart disease is a major cause of death in individuals with MPS VI. Medications are available to help manage the heart problems that occur in MPS VI. Cardiomyopathy (weak heart muscle) and endocardiofibroelastosis (stiff heart) are conditions that can occur occasionally in individuals with the severe form of MPS VI because of the storage of GAG. 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. They may have slowly progressive heart disease for years without any apparent clinical effects. If the condition worsens, an operation may be needed to replace the damaged valves.

Your doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAG. Heart valves are designed to close tightly as blood passes from one chamber of the heart to another in order 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



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shoot backward, leading to turbulence and a murmur. Most people with MPS VI have some degree of murmur or leakage.

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

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

In individuals who are severely affected, the muscle of the heart may be damaged by GAG storage (cardiomyopathy). The heart also may be put under strain by having to pump blood through abnormal lungs (cor pulmonale or right heart failure). A number of affected individuals have high blood pressure.

Because of the unusual special problems that can occur in these diseases, you should select a cardiologist with some knowledge of

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MPS VI. At a minimum, you should inform the doctor about heart problems experienced by individuals with MPS VI.

Liver and spleen

In most individuals with MPS VI, both the liver and spleen become 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 should be repaired by an operation, but hernias will sometimes recur. Umbilical hernias are not usually treated unless they are small and cause entrapment of the intestine, or are very large and are causing problems. It is very common to have a reoccurrence of an umbilical hernia after a repair has been made.

Bowel problems

Many individuals with MPS VI suffer periodically from loose stools and diarrhea. The cause of this is not fully understood. Occasionally the problem is caused by severe constipation and leakage of loose stools from behind the solid mass of feces. More often, however, parents describe it as “coming straight through.” It is thought there may be a defect in the autonomic nervous system, the system that controls those bodily functions usually beyond voluntary control. Studies have found storage in the nerve cells of the intestine and it seems likely that abnormal motility in the bowel is the cause of the diarrhea.

An examination by your pediatrician, supplemented by an X-ray if necessary, may establish the cause of diarrhea. The problem may disappear as the child gets older, but it can be made worse by antibiotics prescribed for other problems. The episodic diarrhea

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

14 in some MPS individuals appears to be affected 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.

Constipation may become a problem as the child gets older and less active and as the muscles weaken. If an increase in roughage in the diet does not help or is not possible, the doctor may prescribe laxatives or a disposable enema.

Bones and joints

Individuals with MPS VI tend to have significant problems with bone formation and growth. This leads to bone problems (called dysostosis multiplex) as well as neurological problems if nerves 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. In the attenuated form of MPS VI spinal cord compression is common. The compression is due to accumulation of GAG in the membrane surrounding the spinal cord.

Neck

The neck is short and sometimes restricted in movement. The bones that stabilize the connection between head and neck can be malformed (odontoid dysplasia) in people with the severe form of MPS VI, 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 child 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 any case, the soft bone makes the 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.

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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 but this is very unlikely to need treatment. 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, rather like the hands.

Skin

Individuals with MPS VI tend to have thickened and tough skin, making it difficult to draw blood or place intravenous 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

16 other mechanisms that control temperature regulation. Periodic blue or cold hands or feet should be evaluated by a cardiologist to determine if the heart or the aorta might be responsible for 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

Communicating hydrocephalus is more likely to occur in a child with severe MPS VI.

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 delayed 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 if hydrocephalus exists. If the doctor confirms your child has communicating hydrocephalus, it can be treated by the insertion of a thin tube (shunt), which drains fluid from the brain into the abdomen (ventriculoperitoneal or VP shunt). The shunt has a pressure-sensitive valve, which 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 a child with MPS. Communicating hydrocephalus is more likely to occur in a child with severe MPS VI.

Eyes

The eye problems described are common to all forms of the MPS VI disease. The circular window at the front of the eye (cornea) becomes cloudy due to storage of GAG, which disrupts the clear layers of the cornea. If corneal clouding is severe it may reduce sight, especially in dim light. Some individuals with MPS VI cannot tolerate bright lights as the clouding causes uneven refraction of the light. Wearing caps with visors or sunglasses can help. Many individuals with MPS VI have had a corneal transplant, usually resulting in improved vision.

17 There may be problems with vision caused by changes to the retina or glaucoma (increased pressure) which should be checked during an eye examination. It is often difficult to determine which combination of problems is responsible for the decrease in eyesight. An ophthalmologist can perform special studies to help determine whether the problem is due to an effect on how light gets in the eye (the cornea) or on how the eye responds to light (the retina or optic nerve disease).

Ears

Some degree of deafness is common in all types of 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 treated early to maximize their ability to learn and communicate.

Conductive deafness

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

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

Sensorineural (nerve) deafness

In most cases, the cause of nerve deafness is damage to the tiny hair cells in the inner ear. It may accompany conductive deafness, in



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18 which case it is referred to as mixed deafness. Nerve or conductive deafness can be managed by the fitting of a hearing aid or aids in most individuals. In general, it is felt that hearing aids are under-utilized in MPS diseases.

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

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wrist, or carpus, consists of eight 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 hard for a child to oppose his or her thumb in a position for a normal grasp. Although your child may not complain of pain, the carpal tunnel syndrome may be severe. If your child seems to have 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 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 do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage.

General treatment and management

Diet

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

mucus, diarrhea or hyperactivity. Reducing intake of milk, dairy products and sugar, as well as avoiding foods with too many additives and coloring, have helped some individuals. It would be advisable to consult your doctor or a dietician if you plan major dietary changes to make sure the proposed diet does not leave out essential items. If your child's problems are eased, you could try reintroducing foods one at a time to test whether any particular item seems to increase the child's symptoms.

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

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 this time there also may be a decrease in weight, and feeding can take more and more time. It is often difficult for a family to consider alternate means of feeding, such as a gastrostomy tube (G-tube), and consultation with your medical geneticist and pediatric surgeon can help with your decision making.

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

Physical therapy

Joint stiffness is a common feature of MPS VI. Limitation of motion and joint stiffness can cause significant loss of function. 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 VI should be as active as possible to maintain their joint function and improve their general health. Your child's 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.

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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

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

you cannot be contacted in the event of an emergency. If you have to go to a different hospital in an emergency, tell the anesthetist there 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 MPS individuals. For any elective surgery for a child with MPS, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require 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.

Education

The majority of children with MPS VI will attend mainstream school and achieve academically. For the child to reach full academic potential, it is important to ensure the school and school personnel are aware of the resources required. This may include a one-on-one classroom assistant, appropriate classroom furniture and access to an individual computer. It is important to work with your school system and develop the best Individualized Education Program (IEP) for your child. For more information on education, see the booklet titled *A Guide for Parents: Education Strategies and Resources* published by the National MPS Society.

Puberty and marriage

Teenagers will go through the normal stages of puberty, though possibly later than their peers. MPS VI does not affect fertility, but a woman who is severely affected may be advised not to get pregnant because of the risk to her health. Children born to a parent who has MPS VI are automatically carriers, but none will have the disease unless the other parent also is a carrier.

Independence

Individuals with MPS VI should be encouraged to be as independent as possible to lead full and enjoyable lives. The teenage years may be difficult if they have restrictions imposed by their disease. This may be helped by meeting or contacting other teenagers and adults who also have MPS VI.

Employment

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

Home adaptations

Appropriately adapted living accommodation 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 at a low level 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 National MPS Society booklet *Daily Living with MPS and Related Diseases*.



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Psychosocial issues

Currently there has been no research that explores the psychosocial development of individuals affected with MPS VI, so 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 because children with MPS VI have to experience all the physiological and psychosocial changes as well as any disease-related changes or limitations. Developing the necessary skills to lead independent adult lives can be challenging although important to achieving social maturity. Referral for counseling is recommended if problems such as depression are seen in teenagers and young adults with MPS VI.

Taking a break

Caring for a severely affected child is hard work. Parents need a break to rest and enjoy activities, and this may not be possible when



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their MPS VI child is with them. Brothers and sisters need their share of attention, and need to be taken on outings that may not be feasible with an MPS child. 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.

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 locate additional information and/or resources for your family.

Developing the necessary skills to lead independent adult lives can be challenging although important to achieving social maturity.

Living with MPS VI

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

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 that makes a person with a disease that cannot be cured more comfortable), as well as those aimed at treating the underlying enzyme deficiency.

Hematopoietic Stem Cell Transplant (HSCT)

The goal of HSCT for MPS VI is to 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. Bone marrow and cord blood transplants are types of HSCT. For parents to fully understand the risks, benefits and limitations of HSCT, it is important to talk with transplant physicians and families who have had 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.

Enzyme replacement therapy (ERT)

ERT for MPS VI was approved by the FDA in 2005. Naglazyme® is a manufactured version of the body's natural ASB enzyme. Naglazyme improves endurance (walking ability and stair climbing) and

24 decreases the levels of GAG in the urine. Treatments of Naglazyme are given weekly through intravenous infusions. For parents 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.

Research for the future

The mission of the National MPS Society is to find cures for MPS and related diseases. As part of that mission, the Society funds research grants. The Society recognizes the need for targeted

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 2008.

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

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

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

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

Benefits of membership in the National MPS Society:

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



For more information or to join the National MPS Society:

Visit www.mpssociety.org

Contact us at 877.MPS.1001

Or e-mail us at info@mpssociety.org