



National  
**MPS**  
Society

Support for Families. Research for a Cure.



# A Guide to Understanding MPS II

Hunter 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.

# Table of Contents

Introduction .....	2
What causes MPS II? .....	3
Are there different forms of MPS II? .....	4
How common is MPS II? .....	5
How is MPS II inherited? .....	6
How is MPS II diagnosed? .....	7
Prenatal diagnosis .....	8
Clinical problems in MPS II.....	8
Nose, throat, chest and ear problems.....	10
Mouth.....	13
Heart.....	14
Liver and spleen .....	15
Abdomen and hernias .....	15
Bowel problems.....	15
Bones and joints .....	16
Skin.....	18
Neurological problems: brain, senses and nerves .....	18
General treatment and management .....	21
Living with a severely affected child .....	24
Living with a child with attenuated MPS II .....	26
Specific treatment of MPS II .....	27
Research for the future .....	28

## 2 Introduction

MPS II, also called Hunter syndrome, is a mucopolysaccharide (MPS) storage disease, named after Charles Hunter, a professor of medicine in Manitoba, Canada, who first described two brothers with the disease in 1917. MPS II comprises a wide spectrum of severity, and individuals may be categorized anywhere from severe to attenuated (less severe), with many individuals having an intermediate form

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).

MPS II 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 II.

As yet, there is no cure for individuals affected by these diseases, but there are ways to manage the challenges they will have, and ensure an improved quality of life. Hematopoietic stem cell transplant

Individuals with MPS II have a deficiency of the enzyme iduronate sulfatase, which results in the accumulation of glycosaminoglycans (GAG). This accumulation of GAG is responsible for numerous problems that affect individuals with MPS II.

somewhere between severe and attenuated. 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.

All individuals with MPS II have a deficiency of the enzyme iduronate sulfatase, which results in the accumulation of glycosaminoglycans (GAG), previously called mucopolysaccharides, inside special parts of the cell called lysosomes. This is why

has been used to treat MPS II, but since results have been disappointing, bone marrow transplant is not recommended for MPS II. Enzyme replacement therapy (ERT), approved by the U.S. Food and Drug Administration (FDA) in 2006, is another available treatment. Scientists who study MPS continue to look for better and more effective ways to treat these diseases. As a result, individuals will likely have more options available to them in the future.

## What causes MPS II?

3

Glycosaminoglycans (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 causes MPS II, it is important to understand that in the course of the normal life process, there is a continuous cycle 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 II 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 the human body healthy. The breakdown and recycling process requires a series of special biochemical tools called enzymes. To break down GAG, a series of enzymes or tools work in sequence one after another to split the GAG into pieces. 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.



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Individuals with MPS II are missing one specific enzyme called iduronate sulfatase, which is essential in one step in the breakdown of certain GAG called dermatan sulfate and heparan sulfate. The incompletely broken down dermatan sulfate and heparan sulfate remain stored inside cells in the body and begin 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 leads to many physical problems.

- 4 Babies may show little sign of the disease, but as more and more GAG accumulates, symptoms start to appear. Sugar or other foods stored normally eaten will not affect whether there is more or less buildup of GAG.

## Are there different forms of MPS II?

MPS II has historically been divided into two broad groups (severe and mild) according to the severity of the symptoms. It is now more appropriate to view MPS II as a continuous spectrum of disease with the most severely affected individuals on one end, the less severely affected (attenuated) individuals on the other end, and a whole range of different severities in between.

All individuals with MPS II 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 II, a very tiny amount of active enzyme is working as designed resulting in the attenuated form of MPS II.

Individuals with a severe form of MPS II have progressive developmental delay and more severe and progressive physical problems. Individuals with attenuated MPS II have normal intelligence, milder and less progressive physical problems, and can live into adult life. Many individuals with MPS II have normal or near normal intelligence with severe physical symptoms, which confirms there is a wide range of severity within the disease.

DNA tests do not always correctly identify the severity of MPS II. Many different kinds of mutations (defects in the make-up of genes) in the gene that produces iduronate sulfatase have been identified (point mutations, small deletions or insertions), all of which result in iduronate sulfatase deficiency. This enzyme deficiency results in MPS II. The MPS II gene is located on the X chromosome and has been studied extensively to see if there is any relationship between specific genetic mutations and the symptoms of the disease. Approximately 20 percent of individuals with MPS II have a mutation of the gene that results in absolutely no iduronate sulfatase enzyme being produced, suggesting that the individual's condition is likely to be at the severe end of the spectrum. Other 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. Because MPS II is an X-linked disease, mutation analysis can be used to determine which women in an MPS II family may be carriers.

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



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## How common is MPS II?

It has been estimated that about 1 in 100,000 male births are affected by MPS II. Even though these diseases are rare, each individual needs such extensive medical care that the effect on the medical system is much larger than their numbers suggest. Although MPS II 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.

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.

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## 6 How is MPS II inherited?

MPS II is a genetic disease. However, MPS II has a different form of inheritance from all the other MPS diseases—it is X-linked recessive (also called sex-linked), like hemophilia. Girls may be carriers of the disease, but except in very rare cases only boys will be affected.

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 of his or her genes from his or her mother and half from his or her father. Together, the individual has 100 percent of the genes required to live. The X and the Y chromosomes determine whether the baby will be a boy or a girl. All girls have two X chromosomes, one from her mother and one from her father. All boys receive their Y chromosome from their father, and an X chromosome from their mother.

If a woman is a carrier for MPS II, there is a 50 percent risk that any boy born to her will have the disease. In addition, there is a 50



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percent risk that any girl born to her will be a carrier for the disease. However, it is important to understand that a woman may have an MPS II child and not be a carrier of the abnormal gene. If only one individual in a family has MPS II, the birth mother may or may not be a carrier. DNA testing can confirm the mother's carrier status. If she has the same genetic mutation in the iduronate sulfase gene as her son with MPS II, then she is a carrier.

Analysis of enzyme levels is not a reliable method to determine carrier status.

If the mother has two or more sons with MPS II or if there are additional affected individuals within the family, such as maternal uncles or maternal male cousins, then the mother of a child with MPS II is assumed to be a carrier.

The sisters and maternal aunts of an individual with MPS II may be carriers of the disease and also would have a 50 percent chance

of passing the abnormal gene to a son. All families of individuals with MPS II should seek further information from their medical genetic doctor or from a genetic counselor before planning to have more children. If the genetic mutation of the boy with MPS II is known, DNA testing can then determine the carrier status of other female relatives on the mother's side of the family. It is important for all female relatives on the mother's side to seek advice from their genetic doctor.

7

## How is MPS II diagnosed?

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

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



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A urine test is only one of the first steps in diagnosing MPS II; 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 II, the enzyme activity levels are much lower or absent.

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

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## Prenatal diagnosis

If you have a child with MPS II, it is possible to have tests during a subsequent pregnancy to find out whether the baby you are carrying is affected. It is important to consult your doctor early in the pregnancy if you wish to perform these tests. The decision to have prenatal testing is complex and personal. Talking with your genetic counselor or doctor can help you explore these options and other strategies for having additional children while limiting the probability that they will have or be carriers for MPS II.



OWEN

## Clinical problems in MPS II

### Growth

Growth in height is usually significantly less than normal, but varies according to the severity of the disease. Babies with severe MPS II may be quite large at birth and may grow faster than normal during the first two years of life. Their growth may slow down by the end of the second year. Their final height is likely to be between 4 feet and 4 feet 7 inches in individuals with severe MPS II. In contrast, individuals with attenuated MPS II usually grow to a relatively normal height.

### Intelligence

Children with severe MPS II experience progressive storage of GAG in the brain that is primarily responsible for the slowing of development by 2 to 4 years of age, followed by a progressive regression in skills until death. There is great variation in the severity of the condition, however; some boys may say only a few words while others learn to walk well and read a little. They can enjoy nursery rhymes and simple puzzles. Parents emphasize that it is important to help infants and children with MPS II learn as much as they can before the disease progresses. Even when the child starts to lose the skills he has learned, there may still be some surprising abilities left. Children will continue to understand and find enjoyment in life, even if they lose the ability to speak.

Individuals with severe MPS II commonly have other medical problems that can hamper their learning and performance, including chronic ear infections, poor peripheral vision, poor hearing, joint stiffness, communicating hydrocephalus and sleep apnea. Adequate treatment of these medical problems can improve their function; therefore, comprehensive medical assessments should be performed in individuals with significant developmental decline.

Individuals with attenuated MPS II have normal or near normal intelligence. They may have the same physical features as those seen in individuals with severe MPS II, but at a greatly reduced rate of progression. Some adults with attenuated MPS II have achieved high academic standards and have gone to college. Hearing impairment, joint stiffness, and airway and heart problems are commonly found in individuals with attenuated MPS II.

These medical problems can hinder learning and communication. It is important to remember that MPS II is a spectrum and the apparent severity of the disease on the mental and physical conditions of the individual may not correlate. In other words, some individuals have milder physical problems and impaired intelligence or learning disabilities, while others have more severe physical problems and normal intelligence.

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### Physical Appearance

Individuals with MPS II tend to look alike. When several of them are together, they can look like carbon copies of each other due to the coarsening of their facial features, short noses, flat faces and large heads. Their faces are chubby with rosy cheeks and their heads are large with prominent foreheads. The neck is short and the nose is broad with a flattened bridge. The tongue is enlarged and the lips may be thickened. The hair tends to be thick; the eyebrows bushy and there may be more hair than usual on the body. They have protruding bellies and stand and walk with a bent-over stance due to joint contractures at the hips, shoulders, elbows and knees.

## Nose, throat, chest and ear problems

The problems described in this section generally occur in more severely affected individuals. Individuals with attenuated MPS II are likely to have fewer and less severe symptoms, except for airway involvement.

### 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 II 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 partly block the airway. That, combined with a short neck, contributes to problems in breathing. The windpipe (trachea) becomes narrowed by storage material and may be 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

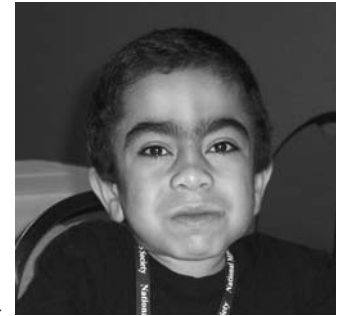
The shape of the chest is frequently abnormal and the junction between the ribs and the breastbone (sternum) is not as flexible as it should be. The chest is therefore rigid and cannot move freely to allow the lungs to take in a large volume of air. The muscle at the base of the chest (diaphragm) is 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 individuals with MPS II have frequent coughs, colds and throat infections. Individuals with MPS II who have narrowing of the large airways and increased secretions are at risk for asthma-

like episodes. Many individuals are helped (decreased cough and easier breathing) by treatment with asthma medications during viral illness. A lung specialist can help determine if asthma-like episodes are occurring in individuals with MPS II during illnesses.

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 to 15 seconds may be considered 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 which can damage the heart over time. 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 re-grow), opening up the airway with nighttime continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP) or tracheotomy, as discussed in the following paragraphs.



ZAYD

### 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, 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 his body.

CPAP or BiPAP can open up the airway at night using air pressure. This treatment involves 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 individuals 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 in 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 disruptive. However,



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many doctors feel that individuals with MPS II would benefit from receiving a tracheotomy earlier than they generally do for improving their nighttime breathing and overall health.

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

### Treatment of respiratory infections

Drugs often affect individuals with MPS II 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 II almost always 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 may 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

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

Many individuals with MPS II 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 individuals with MPS 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 MPS II generally have thick lips and an enlarged tongue. Gum ridges are broad. The teeth are widely spaced and poorly formed with fragile enamel. It is important that the teeth are well cared for, as tooth decay can be a major cause of pain. Teeth should be cleaned regularly, and if the water in your area has not been treated with fluoride give your child 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 affected individual.

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

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## Heart

Heart disease is common in all individuals with MPS II, severe to attenuated. However, heart disease may not develop or cause any real problems until later in the individual's life. Medications are available to help manage the heart problems that occur in MPS II. Cardiomyopathy (weak heart muscle) and endocardiofibroelastosis (stiff heart) are conditions that can occur in young individuals with severe MPS II. Coronary artery disease caused by GAG storage in the heart blood vessels is like that seen in older adults and can lead to death. Some individuals with attenuated MPS II may develop problems with the aortic or mitral valves; they may have slowly progressive valvular heart disease for years without any apparent clinical effects. As the condition worsens, medications can be used to lessen the effect on the heart. However, an operation may be required 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



BRYCE

weakened, it may not shut firmly enough and a small amount of blood may shoot backward, leading to turbulence and a murmur. Most individuals with MPS II have some degree of heart valve leakage or blockage.

Since heart problems occur so frequently in MPS II, all individuals with MPS II should have 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—especially coronary artery disease.

In individuals who are severely affected, the muscle of the heart may be damaged by the storage of GAG (cardiomyopathy) and 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.

Occasionally the coronary arteries of individuals with moderate to severe MPS II may become narrowed and cause episodes of chest pain (angina). If your child is distressed and crying and is at the same time pale and sweating while keeping still, you should consult your doctor who may refer your child for an electrocardiogram (EKG).

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



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## Liver and spleen

In most individuals with MPS II, 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 and the proper fitting of clothes.

## Abdomen and hernias

In most individuals with MPS II, 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. A 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.

## Bowel problems

Many individuals with MPS II 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

16 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 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



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antibiotics prescribed for other problems. The episodic diarrhea in some individuals with MPS II 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, 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 II tend to have significant problems with bone formation and growth. This leads to bone problems (called dysostosis multiplex) as well as neurological problems if nerves are compressed by bone.

### Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Individuals with severe MPS II can have poorly formed vertebrae that may not stably interact with each other. One or two of the vertebrae in the middle of the back are sometimes slightly smaller than the rest and set back in line. This

backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not require treatment. Older children and adults with MPS II occasionally develop compression of the spinal cord due to thickening of the ligaments around the bones of the neck. The doctor will want to monitor this carefully and arrange surgical treatment if necessary.

### Joints

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

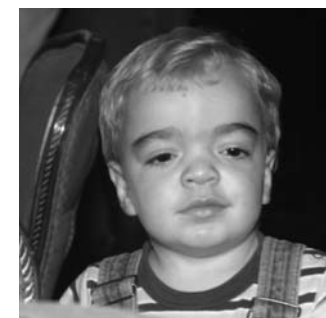
### Hands

The shape of the hands in children with MPS II 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. Finger joints may become locked—called trigger finger.

Trigger fingers may be resolved with heat and massage or by surgery, if necessary.



LOGAN

### Legs and feet

Many individuals with MPS II 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. The feet are broad and may be stiff with the toes curled under, rather like the hands. The lack of flexibility in the hips and legs often prevents individuals from tailor sitting (the seating position of choice for most kindergarten teachers) or putting on their own socks and shoes.

Individuals with MPS II 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 II. 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 see if the heart or the aorta might be responsible for the problem.

Some boys with MPS II have a characteristic white, nodular, pebble-like texture to their skin. This may occur on the back and shoulders and, in some boys, may extend to their arms and lower trunk. This is not a medical concern and is thought to be caused by storage of GAG in the skin.

## Neurological problems: brain, senses and nerves

### Brain

The decline in developmental function in individuals with severe MPS II may be related to storage in the neurons of the brain. Other aspects of MPS II that can affect brain function include inadequate oxygen levels, sleep deprivation due to sleep apnea, increased fluid pressure in and around the brain (hydrocephalus), and effects on the eyes and ears that affect the ability of the individual to see and hear normally.



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The brain and spinal cord are protected from jolting by the cerebrospinal fluid that circulates around them. In individuals with severe MPS II, circulation of the fluid becomes blocked over time 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, incontinence, delayed development, expansion of the skull and ultimately blindness. If hydrocephalus is suspected, an MRI should be performed. However, a lumbar puncture with

pressure measurement (ideally pressure monitoring) is the best 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) or normal-sized ventricles does not rule out hydrocephalus in a child with MPS II. Communicating hydrocephalus is more likely to occur in a child with severe MPS II.

### Eyes

Clouding of the cornea, which is a feature of some of the other MPS diseases, is not found in individuals with MPS II. Occasionally there may be problems with vision caused by changes to the retina or glaucoma (increased pressure) which should be checked during an eye examination. Storage in the retina can result in loss of peripheral vision and night blindness. Night blindness can result in a child not wanting to walk in the dark or waking up at night and being afraid. Sometimes the simple addition of a night light in a hall or bedroom is beneficial. 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).

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### Ears

Some degree of deafness is common in MPS II. 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 II have their hearing monitored regularly so 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 the 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 the 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 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. Hearing aids are generally underutilized in MPS diseases.

### **Carpal tunnel syndrome and other nerve entrapments or compression**

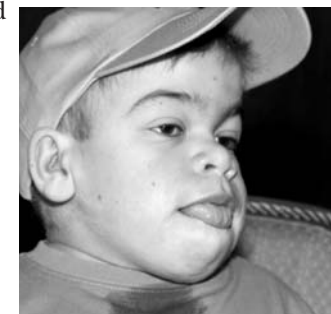
Individuals with MPS II sometimes experience pain and loss of feeling in the fingertips caused by carpal tunnel syndrome. The wrist, or carpus, consists of eight small bones known as the carpals, which are joined by fibrous bands of protein called ligaments. Nerves have to pass through the wrists in the space between the carpal bones and the ligaments. Thickening of the ligaments causes pressure on the nerves; 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 for a child



ASHTIN

to oppose his 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, an electrical test called a nerve conduction or electromyograph study should be 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. Uncorrected carpal tunnel syndrome may result in the loss of sensation in the hands and fingers. Carpal tunnel syndrome can be corrected through surgery. However, it may return in the future requiring additional surgeries.



SCOTTY

A similar type of nerve compression can happen elsewhere in the body, such as the feet, and cause localized weakness or pain.

## General treatment and management

### **Diet**

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

Swallowing may become difficult as an MPS II individual 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 the individual may lose weight and require more and more time to be fed. It is often difficult for a family to consider alternate means of feeding, such as a gastrostomy tube (G-tube); consultation with your medical geneticist and pediatric surgeon can help with your decision making.

Choking also can occur with liquids, including secretions made by the body such as saliva. As swallowing becomes more difficult, the individual may begin drooling and may need to be suctioned.

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

### Physical therapy/sports

Joint stiffness is a common feature of MPS II. 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 II should be as active as possible to maintain joint function and improve their general health. However, competitive or contact sports should be avoided. 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.

### Anesthetics

Giving an anesthetic to an individual with MPS II requires skill and should always be undertaken by an experienced anesthetist. Inform your child's school or any other caregivers of this in case you cannot be contacted in the event of an emergency. If you have to go to a different hospital in an emergency, you should tell the anesthetist that there might be problems with intubation (placement of the breathing tube). The airway can be very small and may require

Individuals with MPS II should be as active as possible to maintain joint function and improve their general health. However, competitive or contact sports should be avoided. Your child's doctor or physical therapist may be able to suggest ways of achieving this.

a very small endotracheal tube. Placing the tube may be difficult and require the use of advanced intubation techniques, such as a flexible bronchoscope, laryngeal mask airway or fiber optics. In addition, the neck may be somewhat lax and repositioning the neck during anesthesia or intubation could cause injury to the spinal cord. For some individuals, it is difficult to remove the breathing tube after surgery is completed due to excessive swelling. 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 in a child with MPS, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical center instead of a local hospital. See additional information on anesthesia in the booklet titled *Is Your Child Having an Anesthetic?* published by the National MPS Society.

### Puberty and marriage

Teenagers with MPS II will go through the normal stages of puberty and are able to have children. All daughters of an affected MPS II male will be carriers, but his sons will be affected only if the mother happened to be a carrier. In other words, the fact that the father has MPS II will have no effect on whether or not his son will have MPS II.

Teenagers with MPS II will go through the normal stages of puberty and are able to have children.

### Life expectancy

Life expectancy in MPS II is varied. Individuals with attenuated MPS II can have a reasonably normal life span, surviving into the fifth and sixth decades of life, and sometimes longer. Sadly, those who are severely affected are likely to die before reaching their mid-teens. Though parents often worry about their child's death, it is usually a peaceful event. Parents may find it helpful to prepare themselves in advance for the time of their child's death.

### Taking a break

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

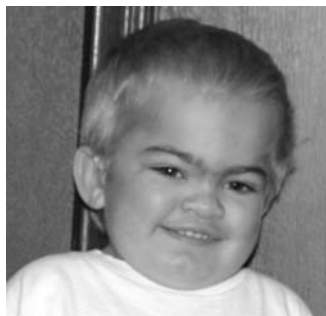
24 become more independent from their families and may benefit from a vacation, perhaps with others who have disabilities.

### 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 your Department of Health. If you have a social worker assigned to you, he or she should be able to help locate additional information and/or resources for your family.

## Living with a severely affected child

While young, boys with MPS II may be overactive, strong, cheerful and hard to supervise. They have limited powers of concentration and their mental age will be lower than their physical capabilities.



DANNY

They could, for example, lock the bathroom door but be unable to understand how to get out again, even when told. They enjoy rough and tumble play; making a lot of noise and throwing toys rather than playing with them. They may be unaware of danger, and stubborn and unresponsive to discipline since they may not understand what is required. Some children may have outbursts of aggressive behavior. Boys with MPS II have an

increased tolerance of pain. Bumps and bruises or ear infections that would be painful for other boys often go unnoticed in boys with MPS II. Toilet training may be achieved briefly by some, but most will remain in diapers. Getting enough sleep may be difficult for parents; they should not hesitate to ask their doctor for help.

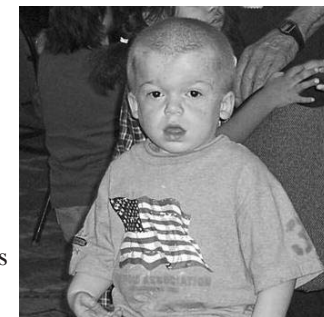
### Palliative care

Palliative care is any form of medical care or treatment that concentrates on reducing the severity of disease symptoms. The goal is to prevent and relieve suffering and to improve quality

of life for people facing serious, complex illness. This support encompasses aspects such as respite care, symptom management and bereavement support and may extend over a period of time. An assessment of medical need and a care plan can lead to support provided to the child and family so both can experience a better quality of life.

### Feeding

Severely affected MPS II boys generally enjoy their food, but may be very limited in the range of what they will eat. They often drink a great deal of fluids. Many do not progress to using a knife and fork or an ordinary cup and eventually need to be fed as if a baby. If the child becomes unable to chew and swallow, food will have to be mashed or puréed.



LEE

### Choking

When a child cannot chew and has difficulty swallowing, there is a risk of choking. Food, especially meat, should be cut up into very small pieces. However, the child may still start to choke. If this happens, act quickly; turn him upside down, or lay him head down over your knee and pound sharply between the shoulders three or four times. Pounding on the back while the child is upright can make things worse by causing the child to breathe in rather than cough out the food. If necessary, put your finger down his throat to try to dislodge the food item.

### Chewing

As they become more out of touch with their environment, many boys with severe MPS II will entertain themselves by rocking, or by chewing on their fingers, clothes or whatever they can lay their hands on. Because there is little one can do to stop this behavior, it is best to provide the individual with a wide range of safe items on which to chew, such as rubber toys, teething rings or soft cloths.

If the problem is severe and the child starts to injure his fingers, it is possible to splint the elbows for periods of the day so the hands cannot reach the mouth.

## The quieter stage

The change from the overactive noisy period is likely to be gradual. Parents will realize their son no longer runs everywhere and is happier sitting than standing. Many boys with severe MPS II will be easily pleased, perhaps by looking through the same little book of photographs or by having stories read to them. They may doze off quite often.

Slowly, weight will be lost as muscles waste away. Very occasionally, near the end of the child's life, there may be seizures which can be controlled with medication. Chest infections may be more frequent.

Many children die peacefully after an infection or from the heart's gradual failure. You may find it helpful to prepare yourself in advance for the time of your child's death.



MATTHEW

## Living with a child with attenuated MPS II

Boys with attenuated MPS II may be completely normal in behavior and are often affectionate, sunny natured children. They can be short-tempered at times from frustration when their physical limitations make life difficult.

### Education

Some children with MPS II may benefit from having a mainstreamed education and enjoy the social interaction with peers. It is important to work with your school system and develop the best Individualized Education Program (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.

### Independence

They should be encouraged to be as independent as possible since many adults with MPS II can lead full and enjoyable lives. The teenage years may be difficult; if ordinary adolescents worry about a pimple on the chin, think of how much more teenagers with MPS II must worry about their appearance and about the restrictions

imposed by their condition. They may be helped by meeting or writing to other teenagers or adults with MPS II. Ask the National MPS Society to put you in touch with other individuals. If emotional problems persist, help can be obtained through mental health services, which can include therapy and/or medications.

Many adults with attenuated MPS II have found satisfying work; one was a teacher of the deaf, one a marine architect and another an army sergeant. Some have married and have had children. There is every reason to encourage your son with MPS II to lead as full and independent a life as possible.

## Specific treatment of MPS II

### Overview

The goals of managing MPS II 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 II. However, early intervention may help prevent irreversible damage. Treatment options for MPS II 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) and Bone Marrow Transplant

For some years HSCT has been used to treat children with MPS. Some children with MPS I have benefited from HSCT, but this procedure currently is not recommended for individuals with MPS II. HSCT in MPS II has not been shown to have any effect in preventing the damage to the brain that occurs with severe MPS II. The National MPS Society may be able to put you in touch with parents whose children with MPS II have had this treatment so you may be better informed.

### Enzyme replacement therapy (ERT)

ERT for MPS II was approved by the FDA in 2006. Elaprased<sup>®</sup> is a manufactured version of the body's natural iduronate sulfatase enzyme. Elaprased improves lung

For parents to fully understand the risks, benefits and limitations of ERT, it is important to talk with physicians familiar with MPS II ERT and families undergoing this treatment.

28 function, endurance, reduces the size of the liver and decreases the levels of GAG in the urine. It does not cross the blood-brain barrier at normal doses and thus is not anticipated to have an impact on any neurocognitive decline occurring in individuals with MPS II. Treatments of Elaprase 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 II ERT and families undergoing this treatment. The National MPS Society can put you in touch with physicians and families so you can become better informed before reaching a decision.

## 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 II 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) II do not necessarily reflect the views of the National MPS Society or its membership. This booklet may be reproduced or copies can be made available upon request and written authorization from the National MPS Society.*



## 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.



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For more information or to join the National MPS Society:

Visit [www.mpsociety.org](http://www.mpsociety.org)  
Contact us at **877.MPS.1001**

Or e-mail us at [info@mpsociety.org](mailto:info@mpsociety.org)