



National
MPS
Society

Support for Families. Research for a Cure.



A Guide to Understanding MPS III

Sanfilippo 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 III, also called Sanfilippo syndrome, is a mucopolysaccharide (MPS) storage disease named after Dr. Sylvester Sanfilippo, who described the condition in 1963. MPS III is characterized by developmental delay and cognitive regression, with usually mild physical problems.

All individuals with MPS III have deficiency of one of four enzymes, which results in the accumulation of glycosaminoglycans (GAG),

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).

previously called mucopolysaccharides, inside special parts of the cell called lysosomes. This is why MPS III 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 III.

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. Scientists who study MPS III continue to look for better and more effective ways to treat these diseases. As a result, hope for the future is promising.

What causes MPS III?

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 cause MPS III, 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 III 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. 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 III are missing one of four specific enzymes that are essential in the breakdown of one of the GAG called heparan sulfate. The incompletely broken down heparan 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.



BEN

Babies usually show no signs of the disease, but as more and more GAG accumulates, symptoms start to appear, usually from 2 to 6 years of age. Sugar or other foods normally eaten will not affect whether there is more or less buildup of GAG.

Are there different forms of MPS III?

There are four different enzyme deficiencies that have been found to cause MPS III; the disease is described as type A, B, C or D. The names of the deficient MPS III enzymes are heparan *N*-sulfatase (type A), alpha-*N*-acetylglucosaminidase (type B), acetyl-CoA-glucosaminide acetyltransferase (type C) and *N*-acetylglucosamine-6-

4 sulfatase (type D). There is little clinical difference among the four types of MPS III, since all four types accumulate the same GAG, heparan sulfate. All four enzymes are only involved with the breakdown of heparan sulfate. Heparan sulfate is primarily found in the central nervous system and its accumulation in the brain is responsible for the numerous problems that affect individuals with all types of MPS III.

How common is MPS III?

The estimated incidence of MPS III (all four types combined) based upon published studies is 1 in 70,000 births. Type A is the most common in northwestern Europe, type B in southeastern Europe, and types C and D are rare everywhere. Although the types of MPS III are 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 III inherited?

MPS III 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 the generations in an obvious way, some genetic diseases are “hidden,” or recessive, and only show up when both genes in an individual are affected. MPS III is that type of genetic disease. Most families who have a child with MPS III do not have a

Most families who have a child with MPS III do not have a family history of any genetic problems.

family history of any genetic problems. MPS III 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 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.

Each enzyme made 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 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 III. 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 III.



BRITTANY

That is why MPS III 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 III. There is a two in three (67 percent) chance that unaffected brothers and sisters of individuals with MPS III will be carriers of the defective gene that causes MPS III. 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 the family or other questions related to inheritance of MPS diseases.

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6 How is MPS III diagnosed?

Doctors may consider testing for MPS III 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 III, the doctor will typically first do a urine test to look for levels of GAG that are higher than normal. The results are



RHIANNA

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.

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

Early diagnosis of MPS III is critical. The earlier MPS III is diagnosed, the sooner a comprehensive medical care plan and supportive care may be started to ensure the best quality of life. As treatments are developed for MPS III, early diagnosis will be critical in potentially preventing some of the permanent damage that may be caused by the disease.

Prenatal diagnosis

If you have a child with MPS III, it is possible to have tests during a subsequent pregnancy to find out whether the baby you are carrying is affected. It is essential to know the type of MPS III (type A, B, C or D), because each one requires a specific test. 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 III.

7

How does the disease progress?

MPS III affects children differently, and its progress will be faster in some than in others. Babies usually show no signs of the disease, but symptoms start to appear from 2 to 6 years of age. Change will usually be very gradual and, therefore, easier to adjust to. The child's preschool years may be very frustrating for the parents.

They may begin to worry as their child starts to lag behind their friends' children in development, and they may feel they are being blamed for the child's overactive and difficult behavior.

Of all the MPS diseases, Sanfilippo produces the mildest physical abnormalities. Since the early symptoms also are common in unaffected children, diagnosis is often made late.

Diagnosis may be delayed, as some children do not have abnormal features, and their symptoms are very nonspecific with little evidence to suggest an MPS disease. A doctor has to be perceptive enough to recognize that something is seriously wrong and ask for urine and blood tests

to determine a diagnosis. Some families have had one or more affected children before a diagnosis is established.

As the disease progresses, children develop extreme activity, restlessness and often very difficult behavior. Some children sleep very little at night. Many will get into everything. Sadly, language and understanding will gradually be lost. Some children never become toilet trained, and those who do will eventually lose this ability.

Over time children with MPS III begin to slow down. They become more unsteady on their feet, tending to fall frequently as they walk or run. Eventually they lose the ability to walk. Some parents report episodes of muscle spasms, dystonia

(sustained muscle contractions) or continuous jerking movements. These may or may not be linked to seizures and can be difficult to



RACHEL

8 treat. Parents will need help with the physically tiring task of caring for an immobile child or teenager with severe developmental delay.

Clinical problems in MPS III

Of all the MPS diseases, MPS III produces the mildest physical abnormalities. It is important, however, that simple and treatable conditions such as ear infections and toothaches not be overlooked because of behavior problems that make examination difficult.

Children with MPS III often have an increased tolerance of pain. Bumps and bruises or ear infections that would be painful for



MEAGAN

other children often go unnoticed in children with MPS III. Parents may need to search for a doctor with the patience and interest in treating a child with a long-term illness. Do not hesitate to consult a doctor if you think your child might be in pain.

Some children with MPS III may have a blood-clotting problem during and after surgery. It is advised that pre-operative

tests be done to see if this might be a problem for your child. Discuss this with your surgeon.

Physical appearance

Children with MPS III grow to a fairly normal height, and changes in appearance may be less than in other MPS diseases. The hair tends to be thick and there may be more hair than usual on the body. The eyebrows are often dark and bushy and may meet in the middle.

Nose, throat, chest and ear problems

The problems described in this section are common to children with MPS diseases, but occur less often in individuals with MPS III. The severity of the problems depends greatly on the individual child.

Runny nose

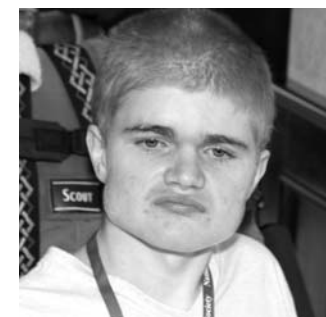
The bridge of the nose can be flattened and the passage behind the nose may be smaller than usual due to poor growth of the bones in the mid-face and thickening of the mucosal lining. This combination of abnormal bones, with storage in the soft tissues in the nose and throat, can cause the airway to become easily blocked. Some children with MPS III have chronic drainage of clear mucus from the nose (rhinorrhea). This chronic nasal discharge is due to the abnormal drainage of normal secretions and chronic ear and sinus infections.

Throat

The tonsils and adenoids often become enlarged and partly block the airway. The windpipe (trachea) can become narrowed by storage material and may be floppy, or softer than usual, due to abnormal cartilage rings in the trachea.

Breathing difficulties

Frequent coughs and colds are common problems in individuals with MPS III. At night they may be restless and awoken frequently. 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. 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 (sleep study). It is important to know that many individuals may breathe like this for years.



JOEY

Sleep apnea, which rarely occurs in MPS III, can be treated in some individuals by removing the tonsils and adenoids (adenoids may re-grow), or by opening up the airway with nighttime continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP).

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.

Treatment of respiratory infections

Drugs can affect individuals with MPS III 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



RUSSELL

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

Many individuals with MPS III 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.

Many individuals with MPS III become allergic to antibiotics or may acquire resistant infections.

Individuals with MPS III may have enlarged tongues. Gum ridges can be broad. The teeth can 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 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.

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If an individual with MPS III 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 an 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.

Heart

Heart disease is common in most MPS diseases, but serious heart problems rarely occur in individuals with MPS III. If heart problems develop, they may not cause any real problems until later in the individual's life. Medications are available to help manage the heart problems that occur in MPS III. 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



KARINA

12 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 shoot backward, leading to turbulence and a murmur. Most individuals with MPS III have



MACKENZIE

some degree of heart valve leakage or blockage, but the problem is usually mild and surgery is rarely needed. They may have slowly progressive valvular heart disease for years without any apparent clinical effects. If 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.

Although major heart problems are rare in MPS III, individuals should still have a test known as an echocardiogram annually (or as often as your doctor thinks necessary) to determine whether any problems are beginning. The test is painless, and similar to the ultrasound screening of babies in the womb. It can identify problems with the heart muscle, heart function and heart valves, but like many tests it cannot detect all possible problems.

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

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Liver and spleen

The liver and spleen may become slightly enlarged, due to GAG accumulation, but this usually does not cause problems.

Abdomen and hernias

In most individuals with MPS III the abdomen bulges out due to posture, weakness of the muscles, and due to the enlarged liver and spleen. Frequently, part of the abdominal contents will push out

13 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 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 III 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.



MICHAEL

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 some individuals with MPS 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 III tend to have minimal problems with bone formation and growth. Features of osteoporosis can, however, develop as early as the teen years. As the bones become fragile and brittle there is increased risk of fractures, and the decrease of overall stability increases the risk of falling. Prolonged use of seizure drugs combined with decreased mobility can lead to brittle bones. Recent research has shown that high-dose vitamin D therapy can improve bone mineral density.



ERIN

Joints

Joint stiffness occurs in all types of MPS, and the maximum range of movement of all joints may become limited. Individuals with MPS III tend to have minimal problems with joints. Later in the individual's life, joint stiffness may cause pain, but this 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

Children with MPS III have fingers that occasionally become bent due to contractures, and they may not be able to fully extend their arms.

Hips

In some individuals with MPS III, the hips may become dislocated, but this is often not a problem and treatment may not be necessary.

Legs and feet

Many individuals with MPS III 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 III. The feet are broad and may be stiff with the toes curled under, rather like the hands.

Cold hands and feet

Cold hands and feet may occur in MPS III as the disease progresses, resulting from disruption of the normal neurologic regulation of blood vessels (autonomic dysfunction). It may not bother the child, but if it does the obvious remedies of heavy socks and warm gloves may be useful. Late in the disease, the temperature control mechanism in the child may become damaged and the child may sweat at night, as well as having cold hands and feet by day. Some children have episodes when their body temperature drops (hypothermia). If this happens, keep your child warm and ask your doctor for advice on the best ways of managing the problem.

Skin

Individuals with MPS III 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 III.

Neurological problems: brain, senses and nerves

Seizures

At a later stage of the disease, children with MPS III can have frequent, minor seizures, during which they momentarily lose the ability to focus and concentrate (petit mal). When this is occurring, the child may seem more out of touch or harder to feed.



HAILEE

Some may have generalized seizures (grand mal), which can be controlled by medications. During the seizure you should place your child on his or her side to prevent the inhalation of vomit. The child should be left in that position until the seizure is over. Check that the airway is clear, and do not put anything in the child's mouth.

Seizures can usually be prevented or reduced in frequency with conventional anti-seizure medications. It is not unusual to try several

16 medications before finding what works best for your child. Some doctors may recommend the individual wear a helmet to prevent head injury.

Movement Disorders

A constellation of physical problems has been reported by parents of teenagers with MPS III beginning with eye fluttering, fast breathing and extreme restlessness. This can lead to sweating, arm and leg jerking and kicking and, in some individuals, dystonia-like spasms with rigid arms and legs. Some individuals may appear to be in pain, while others may not. Parents have tried therapies such as physical therapy, massage and water therapy, with varied success. Talk with your physician about the use of prescription and over-the-counter medications.

Eyes

There may be problems with vision caused by changes to the retina. GAG storage in the retina can result in loss of peripheral vision and night blindness. Night blindness can result in an individual not wanting to walk in a dark area at night or waking up at night and being afraid. Sometimes the addition of a night-light in a hall or bedroom is beneficial. If you have concerns about your child's vision, an ophthalmologist can perform special studies to help determine whether the problem is due to how the retina responds to light.

Ears

Deafness is common in all types of MPS III. 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 III 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 in 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



KEVIN

17 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 a ventilation tube is in place, fluid should drain out and hearing should improve.

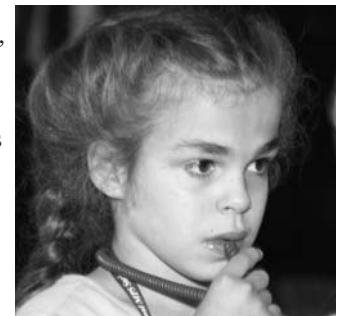
Sensorineural (nerve) deafness

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 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 general, it is felt that hearing aids are underutilized in MPS diseases.

General treatment and management

Diet

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



TAYLOR

18 Early feeding of children with MPS III usually causes few problems, but some do not progress to eating food that needs chewing. Others learn to chew but find it increasingly difficult to eat “lumpy” foods, particularly if they are mixed with food of a smooth texture. Many become quite picky and reject a number of foods for no clear reason.

As children lose the rhythm of swallowing, they may start to splutter and cough while eating. It is better to serve food of a mashed consistency. Meat will be tolerated more easily if it is made through slow cooking rather than just chopped into small pieces. You can help by moving your hand gently backward under the chin and slowly down the throat to help move the tongue and encourage swallowing. Choking is frightening and you can provide reassurance by rubbing your child’s back and holding his or her hands.

You can help by moving by moving your hand gently backward under the chin and slowly down the throat to help move the tongue and encourage swallowing.

Swallowing becomes more difficult as a child with MPS III gets older and the disease progresses. When 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. Families often consider alternate means of feeding, such as through a gastrostomy tube (G-tube). 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 GAG, because they are actually made by the body. So reducing sugar intake or other dietary components cannot reduce GAG storage.

Choking

When a child cannot chew and has difficulty swallowing, there is a risk of choking. Food, especially meat, should be cut into very small pieces or made soft by slow cooking. Even with this precaution, the child may choke. If this happens, act quickly and turn him or her upside down, or lay him or her head-down over your knee and pound sharply between the shoulders three or four times. If necessary, put your finger down

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19 his or her throat to try to dislodge the food item. Pounding on the back while the child is sitting upright can make things worse because the child might breathe in the food rather than coughing it out.

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.

If a child develops a fever within a few days of a choking episode, consult your doctor. It is possible that some food particles entered the lungs (aspiration); treatment is required for pneumonia that may have developed.

Chewing

As they become more out of touch with their environment, many children with MPS III 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.



MAGGIE

If the problem is severe and the child starts to injure his or her fingers, the elbows may be splinted for periods of the day so the hands cannot reach the mouth.

Physical therapy

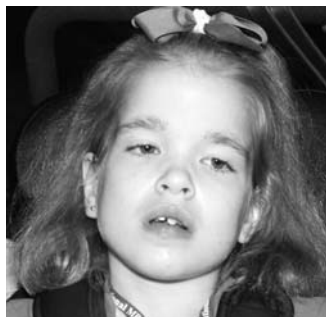
When the child is young and mobile, physical therapy may not be needed. Chest physiotherapy may be needed later to help clear an infection.

As the child gets older, the joints of the feet and ankles may become tight and spastic. Hydrotherapy may be a great help in keeping the joints mobile. Some range-of-motion physical therapy may be useful but need not be intensive. Exercises that cause pain should be avoided.

When the child is immobile, it is important to ensure that he or she is sitting with proper support to avoid uneven pressure on particular joints. If a deformity at the ankle joint develops, making walking difficult, special braces may help.

Giving an anesthetic to an individual with MPS III 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, tell the anesthetist there might be problems with intubation (placement of the breathing tube). The airway can be small and may require a very small endotracheal tube. Placing the tube may be difficult and require the use of advanced intubation techniques, such as a flexible bronchoscope, laryngeal mask airway or fiber optics. In addition, the neck



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may be somewhat lax and repositioning it during anesthesia or intubation could cause injury to the spinal cord. For some individuals, it is difficult to remove the breathing tube after surgery due to excessive swelling. 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 an MPS child, it is important to choose a pediatric anesthesiologist who has experience with difficult airways. This may require the surgery to be performed at a regional medical center instead of a local hospital. Generally, individuals with MPS III have fewer problems with anesthesia than other individuals with MPS. See additional information on anesthesia in the booklet titled *Is Your Child Having Anesthesia?* published by the National MPS Society.

Puberty

Children with MPS III will go through the normal changes associated with puberty.

Life expectancy

Life expectancy in MPS III is extremely varied. Individuals with MPS III typically live into their teenage years. Some children will not live this long, while others will live into their twenties. Mildly affected individuals have lived into their thirties, and in a few rare cases, into their forties. Although 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.

Behavioral problems

The behavior problems seen in children with MPS III are generally not altered by medications or behavioral therapy. It is helpful to adapt family life as much as possible, and to seek regular breaks for parents and other family members.

Some parents may try to modify their child's behavior with the support of a local psychologist, and a few have reported some limited success. However, the child's behavior will continue to change as the disease progresses, and the usefulness of a particular behavior modification technique may be short-lived.

Adapting the house

Parents find it very helpful to designate a room or part of a room for their child with MPS III. The room should be within a caregiver's

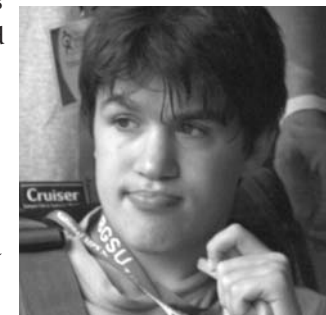
Some parents find it very helpful to designate a room or part of a room in the house especially for their child with MPS III.

hearing distance and be made safe for the child to play without constant supervision, so the parent can interact with other children or deal with household tasks. Furniture that is fragile or has sharp edges should be removed and replaced by large cushions on the floor. Windows may need to be fitted with strengthened

glass or Plexiglas, and the floor should be easy to clean. Replacing the door to the room with a Dutch door allows the child to see the parent, increasing the child's sense of security while keeping him or her safe. Favorite durable toys and playthings should be accessible to the child. A television or stereo speakers can be placed high on a shelf or suspended from the ceiling and operated by parents using remote control.

Sleeping difficulties

Many children with MPS III are very restless at night, not sleeping for more than a couple of hours at a time. The reason for this is not known. It is sometimes possible to improve this situation with medications, but it may take a period of trial and error to establish which drug will work best. Drugs often lose their effect after a while. Some parents choose to ration their use to a few nights a week or accept that after a few weeks the medication will have to be discontinued



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for a while. It is vital for parents to get sleep if they are to cope during the day; do not hesitate to ask your doctor for help.

Some parents find they can achieve a longer period of unbroken sleep by putting the child to bed later and following a regular routine. The thought of the child getting up in the middle of the night and having an accident while the rest of the household is asleep worries many parents. Some find it helpful to put a lock on the outside of the child's bedroom door, to replace the bedroom door with a Dutch door and lock the bottom section, to fit a stair gate in the doorway, or to place special pads under the carpet by the door which cause a bell to ring if the child leaves his or her room.

Removing furniture and using only a mattress on the floor helps to prevent falls or injury in the night. Some parents find that special beds that help contain the child may be effective.

Hyperactivity

Most children with MPS III go through a hyperactive stage where they get into everything, are difficult to control and are unaware of danger. Medications used to treat hyperactivity generally do not modify this behavior in children with MPS III; instead it is better to adapt the house in the way previously described. A yard where the child can run around safely is a great asset.



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It is most helpful if the child can join a play group or attend a school or after-school program where a variety of activities occupy the child. Ideally there should

be space for the child to run around and keep fit for as long as possible. Many children are calmed by the movement of a car and will travel well.

Enjoying your child

A child with MPS III will have a life that is different from the majority of children, but they have delightful personalities and are extremely lovable.

Children affected by MPS III will give you love that is totally unconditional. They will make you laugh when you think you may never laugh again. Their love is infectious to everyone around them. They communicate with you even when they lose their verbal

skills. Their eyes will beguile you, their smiles will entice you and their spirit will raise yours when you think nothing else can.

Taking a break

Caring for a severely affected child is hard work. Parents will need regular breaks so they can continue caring for the child with MPS III without becoming exhausted. Brothers and sisters also need to have their share of attention, and to be taken on outings that are not feasible with an affected child.

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.



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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 or the Katie Beckett Law. Investigate these options and others in your state or with your Department of Health. If you have a social worker assigned to you, he or she should be able to help locate additional information and/or resources for your family.

Education

Some children with MPS III 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.

Some children with MPS III may benefit from having a mainstreamed education and enjoy the social interaction with peers.

Specific treatment of MPS III

Overview

The goals of managing MPS III are to improve quality of life and to slow down the progression of the disease. Currently there is no cure for MPS III. Treatment options for MPS III 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).

Hematopoietic Stem Cell Transplant (HSCT)

The goal of HSCT is to restore the activity of the deficient enzyme. Initial transplants in children with MPS III using stem cells from



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bone marrow did not improve the neurological deterioration. In recent years transplants have been performed using stem cells from umbilical cord blood.

Long-term data is not available to show the benefits of this procedure in children with MPS III. 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)

Because ERT does not cross the blood-brain barrier at normal doses and the physical problems in children with MPS III are less severe than other forms of MPS, it is unlikely this intravenous (IV) treatment will be developed for MPS III. Research is being conducted to assess the benefit of IV injection of ERT into cerebral spinal fluid as a method of treating the brain.

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 research for treatment of bone and joint problems and for treating the brain, and Society research funding has focused on those areas. Information about Society funded research and promising new areas of research can be obtained by contacting the Society's office.

This booklet is intended as an introduction into the nature of the disease, as well as to help families understand more about what is happening to those with MPS III and what they can do to manage it. This booklet was updated by the National MPS Society in 2008.

This booklet is not intended to replace medical advice or care. The contents of and opinions expressed in A Guide to Understanding Mucopolysaccharidosis (MPS) III 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 for a nominal fee 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