

The National MPS Society

Families Joining Together

Common bonds unite the lives of those affected by mucopolysaccharidoses (MPS) and mucopolipidoses (ML) disorders – the need for support and the hope for a treatment.

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

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

Join the National MPS Society and enjoy a variety of benefits, including:

- *Courage, our quarterly newsletter that shares stories and information about people with MPS or ML.*
- *News about various National MPS Society-sponsored conferences and gatherings, where families and leading MPS and ML scientists, physicians and researchers are brought together.*
- *Information on local events like regional picnics and fundraisers. Opportunities for families to meet each other and help raise community awareness of these rare genetic diseases.*
- *A listing in our annual directory of members, which assists families in locating each other.*

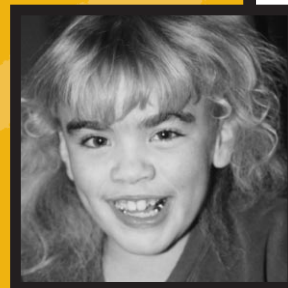
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A Guide to Understanding Sanfilippo Syndrome

Mucopolysaccharidosis (MPS) III



The National MPS Society, Inc.

Introduction

Sanfilippo syndrome is a mucopolysaccharide storage disorder, also known as Mucopolysaccharidosis III (MPS III). It takes its name from Dr. Sylvester Sanfilippo, who described the condition in 1963. MPS III is characterized by developmental delay, with usually mild physical problems.

As yet, there is no cure for individuals affected by these disorders, but there are ways to manage the challenges they will have, and to help them enjoy life. Scientists who study MPS III continue to look for better and more effective ways to treat these disorders, and it is likely that patients will have more options available to them in the future.



front cover
top: Kirby, age 8, MPS III B
middle: Katie, age 9, MPS III B
bottom: Sarah, age 8, MPS III A

What causes these disorders?

Mucopolysaccharides are long chains of sugar molecules used in the building of bones, cartilage, skin, tendons and many other tissues in the body. They 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 joint fluid that lubricates your joints contains mucopolysaccharides. The rubbery resilient cartilage in your joints is another example. All tissues have some of this substance as a normal part of their structure.

The more modern word for mucopolysaccharides is glycosaminoglycans or GAG, which stands for the sugar-amino-sugar polymer or long repeating sugar chains found in these materials. These sugar chains are submicroscopic and cannot be seen with the eye, but can be studied using special scientific instruments and analytical methods.

To understand how GAG accumulate and cause MPS III, it is important to understand that in the course of normal life, there is a continuous process of building new mucopolysaccharides and breaking down old ones – a recycling process. This ongoing process is required to keep your body healthy. The breakdown and recycling process requires a series of special biochemical tools called

The incompletely broken down heparan sulfate remains stored inside cells in the body and begins to build up, causing progressive damage.

This booklet is intended as an introduction into the nature of the disorder, 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. In April 2000, this booklet was updated by the National MPS Society with help from experts in the field and MPS/ML parents to provide families with the latest information.

The word "mucopolysaccharide" can be broken down into its parts to help understand it: *muco-poly-saccharide* *muco* refers to the thick jellylike consistency of the molecules; *poly* means many; *saccharide* is a general term for a sugar molecule (think of saccharin).

enzymes. To break down GAG, a series of enzymes or tools work 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. Babies usually show no signs of the disorder, but as more and more GAG accumulate, 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 the disorder?

There are four different enzyme deficiencies that have been found to cause Sanfilippo syndrome; the disorder is described as type A, B, C, or D. The names of the deficient Sanfilippo enzymes are heparan N-sulfatase (type A), alpha-N-acetylglucosaminidase (type B), acetyl-CoA-glucosaminide acetyltransferase (type C) and N-acetylglucosamine-6-sulfatase (type D). There is little clinical difference among the four types of Sanfilippo syndrome, 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.

The accumulation of heparan sulfate in the brain is responsible for the numerous problems that affect individuals with all types of MPS III.

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 disorders.

How are the disorders inherited?

When most people 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 one such disease. Most families with an MPS III child do not have a family history of any genetic problem — MPS III seems to show up suddenly.

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

For each enzyme made in the body, there are two genes for it, one from the mother and one from the father. For most enzymes, if only one of the genes actually works, the nearly 50% level of enzyme is more than enough to keep the person healthy. Basically, half as much enzyme can do twice the usual amount of work. However, if both genes for the enzyme from mother and father are not functioning correctly, the individual will have little or no enzyme and then will suffer from the disease. Disease occurs only when both genes from mother and father are not working right, or recessive. This means it is hidden until an individual inherits two genes for the same enzyme that are not working.

How common is MPS III?

A frequently quoted figure from a study in the Netherlands is a rate of 1 in 24,000 births; more recent studies in the Netherlands and in Australia have shown that this figure was too high and that the incidence of Sanfilippo syndrome (all four types combined) is closer to 1 in 70,000 births. Type A is the most common one in Northwestern Europe, type B in South-eastern Europe, and types C and D are rare everywhere. Even though these disorders are rare, each patient needs such extensive medical care that the effect on the medical system is much larger than their numbers suggest.

Because the parents of the child with MPS III each have another gene that does work, there is a 3 out of 4 chance with each pregnancy that a repeat pregnancy will result in a child with at least one normal gene and no disease. There is also a 1 in 4 chance with every pregnancy that the child will inherit the defective gene from each parent and will be affected with the disorder. There is a 2 in 3 chance that unaffected brothers and sisters of MPS III individuals will be carriers. Carriers have one good gene and one defective gene. In general, the disorder is so rare that the likelihood of one carrier marrying another carrier is very low.



Karina, age 7
MPS III A

Prenatal diagnosis

If you already 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 Sanfilippo syndrome (type A, B, C, or D), because each one requires a different test, and it is generally not feasible to run all four tests for a prenatal diagnosis. It is important to consult your doctor early in the pregnancy if you wish tests to be arranged.

How does the disorder progress?

Sanfilippo syndrome affects children differently, and its progress will be faster in some than in others. Babies usually show no signs of the disorder, 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 disorder tends to have three main stages.

The first stage, during the child's pre-school years, may be a very frustrating one 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.

Diagnosis is often made very late, as some children do not look abnormal, and their symptoms are very nonspecific with little evidence to suggest a storage disorder. The doctor has to be perceptive enough to recognize that something is seriously wrong and ask for urine and blood tests to help reach a diagnosis. It is not unusual for families to have had one or more affected children before diagnosis is established.

The second phase of the disorder is characterized by 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, and parents may find it hard not being able to have a conversation with their child.

Of all the MPS disorders, Sanfilippo produces the mildest physical abnormalities. And since the early symptoms are also common in healthy children, diagnosis is often made late.

Some children never become toilet trained, and those who do will eventually lose this ability.

In the third phase of the disorder, children with Sanfilippo syndrome 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. Life may be more peaceful in some ways, but 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 disorders, Sanfilippo produces the mildest physical abnormalities. It is important, however, that simple and treatable conditions such as ear infections and toothaches not be overlooked because behavior problems make examination difficult. Parents may need to search until they find 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 Sanfilippo syndrome 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.



Jonathan, age 12
MPS III B

Physical Appearance

Children with Sanfilippo syndrome grow to a fairly normal height, and changes in appearance may be less than in other MPS disorders. 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 disorders, but occur less often in individuals with Sanfilippo syndrome. 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 midface and thickening of the mucosal lining. The 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 can have chronic drainage of clear mucous 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 can 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 Sanfilippo individuals. At night they may be restless and awaken 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, a sleep specialist using a polysomnogram (sleep study) should evaluate the child. It is important to know that many individuals may breathe like this for years. Sleep apnea, which rarely occurs in MPS III, can be treated in some individuals by removing the tonsils and adenoids, or by opening up the airway with nighttime CPAP (continuous positive airway pressure) or BiPAP (bilevel positive airway pressure).

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



Nathan, age 11
MPS III A

present, how much trouble your child is having moving air into the lungs during sleep, and how much effect this has on his body.

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

Treatment of respiratory infections

Drugs may affect people with MPS differently, so it is essential to consult your doctor rather than using over-the-counter medications. Drugs for controlling mucous production may not help. Drugs, such as antihistamines, may dry out the mucous, making it thicker and harder to dislodge. Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for people with MPS. 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 Ears, Nose and Throat (ENT) specialist experienced with MPS disorders to determine which tube is best.

Many people 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 people with MPS will require some 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 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, the child should have daily fluoride tablets or drops. Cleaning inside the mouth with a small sponge on a stick soaked in mouthwash will help keep the mouth fresh and help avoid bad breath. Even with the best dental care, an abscess around a tooth can develop due to abnormal formation of the tooth. Irritability, crying and restlessness can sometimes be the only sign of an infected tooth in a severely involved individual.

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

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Heart

Heart disease is common in most MPS disorders, but serious heart problems rarely occur in people with Sanfilippo syndrome. The heart problems 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 III. Your doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored mucopolysaccharides. The heart valves are designed to close tightly as blood passes from one chamber of the heart to another in order to stop blood from flowing back in the wrong direction. If a valve is weakened, it may not shut firmly enough and a small amount of blood may shoot backwards, leading to turbulence and a murmur. Most people with MPS III have 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, an operation may be needed 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 disorders, 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 MPS individuals.

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 MPS III individuals, 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 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.



Allison, age 4
MPS III A

Bowel problems

Many Sanfilippo individuals 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 that there may be a defect in the autonomic nervous system, the system that controls those bodily functions usually beyond voluntary control. Studies have found storage in the nerve cells of the intestine and it seems likely that abnormal motility in the bowel is the cause of the diarrhea.

An examination by your pediatrician, supplemented by an X-ray if necessary, may establish which is the cause. 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 MPS individuals appears to be affected by diet; elimination of some foods can be helpful.

If antibiotics have caused the diarrhea, eating plain live-culture yogurt is often 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 may also 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

People with MPS III tend to have minimal problems with bone formation and growth.

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

Hands

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

Hips

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

Legs and feet

Many people 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 in the later phases, 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



Sean, age 20
MPS III A

heavy socks and warm gloves may be useful. Late in the disorder, 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, you should keep your child warm and ask your doctor for advice on the best ways of managing the problem.

Skin

People 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 people with Sanfilippo syndrome

Neurological problems: brains, senses and nerves

Seizures

At a later stage of the disorder, children with Sanfilippo syndrome 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.

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.

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 disorders. It may be conductive or nerve deafness or both (mixed deafness) and may be made worse by frequent ear infections. It is important that MPS III individuals have their hearing monitored regularly so that problems can be treated early to maximize their ability to learn and communicate.

Conductive deafness

Correct functioning of the middle ear depends on the pressure behind the eardrum being the same as that in the outer ear canal and 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 and the drum will be drawn in. If this negative pressure persists, fluid from lining of the middle ear will build up and in time become thick like glue. This is called middle ear effusion.

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

General treatment and management

Diet

There is no scientific evidence that a particular diet has any helpful effect on people 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 mucous, 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 that the proposed diet does not leave out any 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.

Early feeding of MPS III children 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 soft through slow cooking rather than just chopped into small pieces. You can help by moving your hand gently backwards



Jennifer, age 22
MPS III A

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

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.

Swallowing becomes more difficult as a Sanfilippo child 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 may also be a decrease in weight and feeding can take more and more time. It is often difficult for a family to consider alternate means of feeding, such as 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 that there is no diet that can prevent the storage of mucopolysaccharides, because they are actually made by the body. So reducing sugar intake or other dietary components cannot reduce GAG storage.

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 upside down, or lay him head down over your knee and pound sharply between the shoulders three or four times. If necessary, put your finger down his 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.

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 Sanfilippo syndrome 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 things on which to chew – rubber toys, teething rings, and large Lego blocks are examples.

If the problem is severe and the child starts to injure his or her fingers, it is possible to splint the elbows for periods of the day so that 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.

Anesthetics

Giving an anesthetic to an MPS III individual requires skill and should always be undertaken by an experienced anesthetist. You should inform your child's school or any other caregivers of this in case you cannot be contacted. 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 small and may require a very small endotracheal tube. Placing the tube may be difficult and require the use of a flexible bronchoscope to place it gently. In addition, the neck 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. Please 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 that the surgery be performed at a regional medical center, not at a local hospital. Generally, MPS III individuals have fewer problems with anesthesia than other MPS individuals.

Puberty

Children with Sanfilippo syndrome 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. 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.

Some parents find it very helpful if they can set aside a room or part of a room in the house especially for their child with Sanfilippo syndrome.

Ways of making life more tolerable

Those who know children with Sanfilippo syndrome will agree that there is not much that can be done to change the behavior of the child. The way to survive is to adapt family life as much as possible, and to seek regular breaks for the 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 disorder progresses, and the usefulness of a particular behavior modification technique may be short-lived.

Adapting the house

Parents find it very helpful to set aside a room or part of a room for their child with Sanfilippo syndrome. The room should be within a caregiver's hearing distance and be made safe for the child to play without constant supervision, so the parent can cook or make a phone call in relative peace. 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. 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 the parents using remote control.

Sleeping difficulties

Many children with Sanfilippo syndrome 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 for a while. It is vital for parents to get sleep if they are to cope in the day, so do not hesitate to ask your doctor for help.

Some parents find that 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 helps to put a lock on the outside of the child's bedroom door, 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/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 helpful.

Hyperactivity

Most children with Sanfilippo syndrome go through a hyperactive stage when they get into everything, are difficult to control, and are unaware of danger. It is difficult to modify this behavior with medication; instead it is better to adapt the house in the way described above. A yard where the child can run around safely is a great asset.

It is most helpful if the child can join a playgroup, attend school or an 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 Sanfilippo syndrome 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 that 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 Sanfilippo syndrome 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 the MPS III child.

Health care 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 Wavers, 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 MPS III children 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.

Specific treatment of MPS III

The theory behind the treatment of MPS disorders

It was shown by Dr. Elizabeth Neufeld that small amounts of lysosomal enzymes, although they are intracellular in nature, could be secreted from normal cells. The secreted enzymes could then be taken up by adjacent cells and directed to the lysosome where they functioned normally. It was then shown that the biochemical defect in a cell that is deficient in a lysosomal enzyme could be corrected by taking up the small amount of enzyme secreted from an adjacent normal cell. This phenomenon, referred to as "cross section," forms the basis of all of the therapeutic strategies being developed.

Bone marrow transplant (BMT)

For some years, bone marrow transplants have been used selectively to treat children with MPS. Some children with Hurler syndrome (MPS I H) have benefited from bone marrow transplantation, but this procedure is currently not recommended for MPS III individuals. BMT in MPS III has not been shown to have any effect in preventing the damage to the brain. To get up-to-date information on treatment options, contact the National MPS Society.

This booklet is not intended to replace medical advice or care. The contents of, and opinions expressed in *A Guide to Understanding Sanfilippo Syndrome* 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.



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