

## 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.*

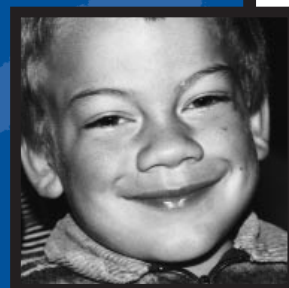
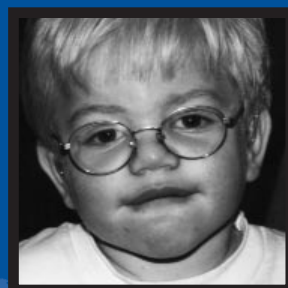
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## A Guide to Understanding Hunter Syndrome

### Mucopolysaccharidosis (MPS) II



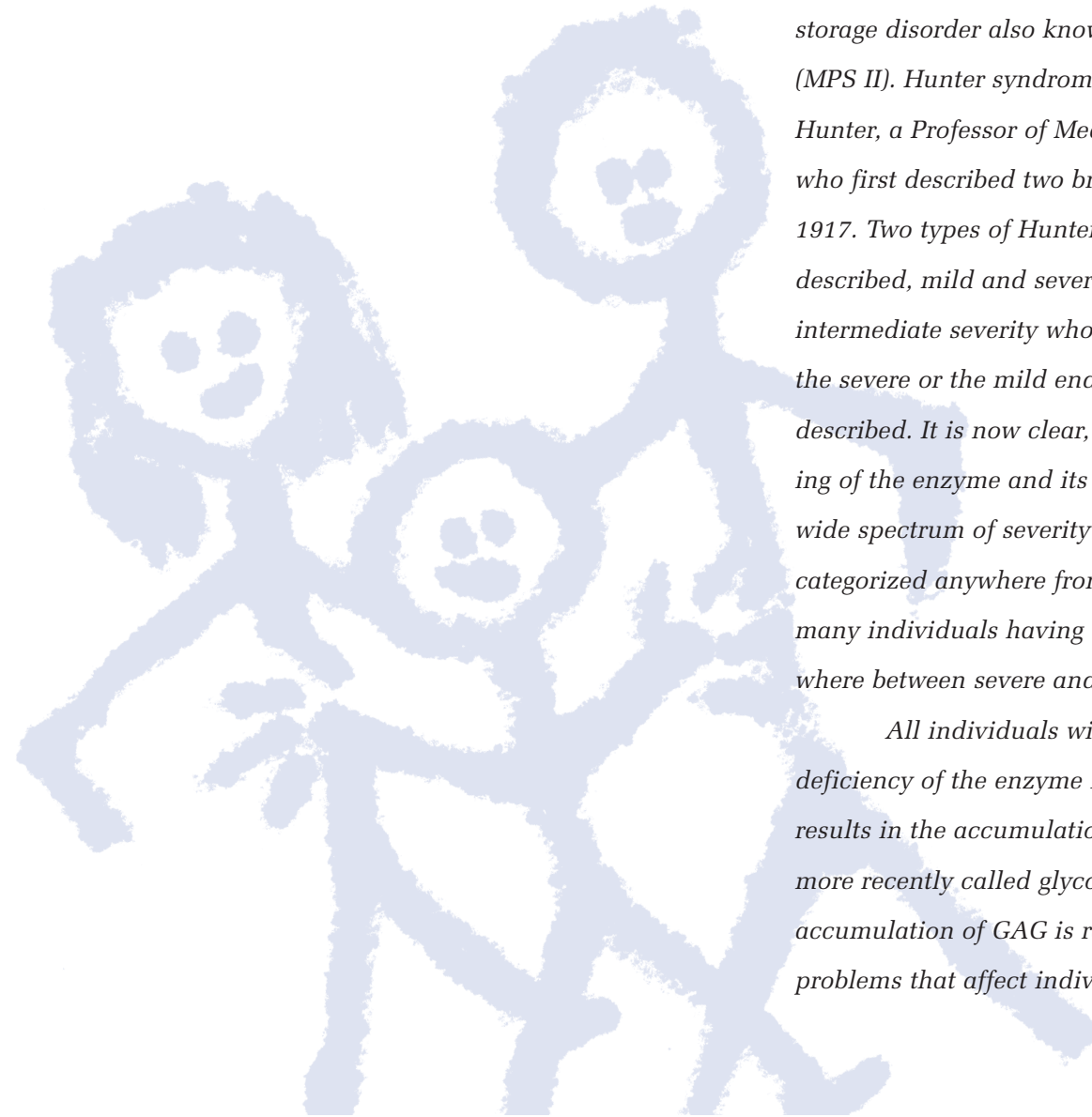
The National MPS Society, Inc.

## Introduction

*Hunter syndrome is a mucopolysaccharide storage disorder also known as Mucopolysaccharidosis II (MPS II). Hunter syndrome takes its name from Charles Hunter, a Professor of Medicine in Manitoba, Canada who first described two brothers with the disorder in 1917. Two types of Hunter syndrome have been described, mild and severe, but individuals with intermediate severity who do not fit clearly in either the severe or the mild end of the spectrum have been described. It is now clear, based on current understanding of the enzyme and its gene, that MPS II comprises a wide spectrum of severity and that individuals may be categorized anywhere from severe to mild Hunter with many individuals having an intermediate form somewhere between severe and mild.*

*All individuals with Hunter syndrome have a deficiency of the enzyme iduronate sulfatase, which results in the accumulation of mucopolysaccharides, more recently called glycosaminoglycans (GAG). The accumulation of GAG is responsible for numerous problems that affect individuals with MPS II.*

*front cover  
top: Chip, age 4  
middle: Gilberto, age 9  
bottom: Paul, age 7*



*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. Bone marrow transplantation (BMT) has been used to treat MPS II, but since results have been disappointing, BMT is not recommended for MPS II. Another MPS II treatment, an enzyme replacement therapy (ERT), is currently being studied and may help some problems that affect MPS II individuals. ERT is not yet available to MPS II individuals. Scientists who study MPS continue to look for better and more effective ways to treat these disorders, and it is likely that individuals will have more options available to them in the future.*

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

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 II 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.



Adrian, age 5

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).

## 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 II, 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 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. 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. Babies may show little sign of the disorder, but as more and more GAG accumulate, symptoms start to appear. Sugar or other foods normally eaten will not affect whether there is more or less buildup of GAG.

*The incompletely broken down dermatan sulfate and heparan sulfate remain stored inside cells in the body and begin to build up, causing progressive damage.*

### Are there different forms of the disorder?

MPS II is currently divided into two broad groups (severe and mild) according to the severity of the symptoms. Severely affected individuals are said to have severe Hunter syndrome. Severe Hunter individuals have progressive developmental delay and more severe and progressive physical problems. Mild Hunter individuals have normal intelligence, milder and less progressive physical problems, and can live into adult life. Many individuals with Hunter syndrome have normal or near normal intelligence, but severe physical symptoms can represent an intermediate form of MPS II.

All people with MPS II lack the same enzyme, and currently there is no 100% reliable way of telling from biochemical tests how

severe the disorder will be. Detailed studies have shown that in people with milder MPS II, there is a very tiny amount of the enzyme still remaining which is responsible for the milder disease. Specialized sensitive assays can detect small amounts of activity that, when present, would suggest a milder course.

Studies of the iduronate sulfatase gene can, in some cases, help describe the potential severity of an individual's disease. The MPS II gene is located on the X chromosome and has been studied extensively. There are many different iduronate sulfatase mutations (point mutations, small deletions or insertions) which are known to cause MPS II, but the severity of Hunter syndrome cannot usually be predicted from DNA analysis. Many MPS II families have a mutation, which has never been reported in another MPS II family. However, studies of the gene show that 20% of individuals with Hunter syndrome have a gene that should produce no iduronate sulfatase enzyme at all. The gene is either completely missing or changes have occurred that result in no iduronate sulfatase enzyme. If an individual with MPS II has these mutations (gene deletions or rearrangements), they would be expected to have a severe form of Hunter syndrome. Because MPS II is an X-linked disorder, mutation analysis can be used to determine which women in an MPS II family may be carriers. These mutational studies, however, are not widely available and can be very expensive.

It is important to remember that whatever label is given to your child's condition, the disorder is extremely varied in its effects. A whole range of possible symptoms is outlined in this booklet, but your child may not experience all of them.



Adam, age 12

## How common are these disorders?

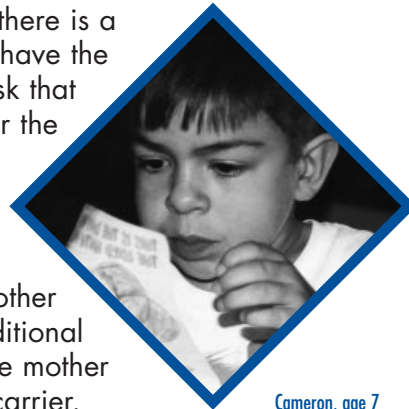
It has been estimated that about 1 in 100,000 male births are affected by MPS II. Even though these disorders are rare, each patient needs such extensive medical care that the effect on the medical system is much larger than their numbers suggest.

## How are the disorders inherited?

Hunter syndrome has a different form of inheritance from all the other MPS disorders, as it is X-linked recessive (also called sex-linked), like hemophilia. Girls may be carriers of the disorder but except in very rare cases, only boys will be affected.

If a woman is a carrier for MPS II, there is a 50% risk that any boy born to her will have the disorder. In addition, there is a 50% risk that any girl born to her will be a carrier for the disorder. It is important to note that not all women with only one MPS II child will be carriers of the abnormal gene. If only one individual in a family has MPS II, the carrier status of the birth mother cannot be determined. However, if additional affected individuals are known, then the mother of an MPS II child is assumed to be a carrier.

The sisters and maternal aunts of a person with Hunter syndrome may be carriers of the disorder and would also have a 50% chance of



Cameron, age 7

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.

passing the abnormal gene to a son. All families of individuals with Hunter syndrome should seek further information from their medical genetic doctor or from a genetic counselor before planning to have more children. There are DNA tests available to determine carrier status, so it is important for all female relatives on the mother's side to seek advice from their genetic doctor. Analysis of enzyme levels is not a reliable method to determine MPS II carrier status for many individuals.

## Prenatal diagnosis

If you already 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 tests to be arranged. Both amniocentesis and chorionic villus sampling can be used to diagnose MPS II in utero.

## Clinical problems in MPS II

### Growth

Growth in height is usually significantly less than normal, but varies according to the severity of the disorder. Babies with severe Hunter syndrome 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 2nd year; final height is likely to be between 4 feet and 4 feet 7 inches in individuals with severe Hunter syndrome. In contrast, individuals with mild Hunter syndrome usually grow to a relatively normal height.

### Intelligence

People with severe Hunter syndrome 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 a great variation in the severity of the condition; some boys may say only a few words while others learn to walk well and to read a little. They can enjoy nursery rhymes and simple puzzles. Parents emphasize that it is important to help infants and children with Hunter syndrome learn as much as they can before the disorder 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 Hunter syndrome 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 the function of Hunter children; therefore, comprehensive medical assessments should be performed in individuals with significant developmental decline.

Individuals with mild Hunter syndrome have normal intelligence. They may have the same physical features as those seen in severe Hunter syndrome, but at a greatly reduced rate of progression. Hunter adults have achieved high academic standards and many have gone to college. Hearing impairment, joint stiffness, and airway and heart problems are commonly found in individuals with mild Hunter syndrome. These medical problems can hinder learning and communication. It is important to remember that MPS II is a spectrum of clinical severity. Some patients have milder physical problems and learning disabilities, while others have more severe physical problems and normal intelligence.

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## Physical Appearance

Individuals with Hunter syndrome tend to look very 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 are common to children with severe Hunter syndrome. Individuals with mild Hunter syndrome can be relatively unaffected, except for airway involvement.

### *Runny nose*

Typically, the bridge of the nose is flattened and the passage behind the nose is smaller than usual due to poor growth of the bones in the midface and thickening of the mucosal lining. The combination of abnormal bones and storage in the soft tissues in the nose and throat can cause the nose to become easily blocked. One of the common features of children with Hunter syndrome is the chronic discharges of clear mucous from the nose (rhinorrhea), and chronic ear and sinus infections.

### *Throat*

The tonsils and adenoids often become enlarged and can partly block the airway. The neck is usually short, which contributes to problems in breathing. The windpipe (trachea) becomes narrowed by storage material and is often more floppy, or softer than usual, due to abnormal cartilage rings in the trachea. Nodules or excess undulations of tissue can further block the airway.

### *Chest*

The shape of the chest is abnormal and the junction between the ribs and the breastbone (sternum) is not as flexible as it should be. The chest is therefore rigid and cannot move freely to allow the lungs to take in a large volume of air. The muscle at the base of the chest (diaphragm) is pushed upwards 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*

Frequent coughs, colds and throat infections are common problems for many Hunter individuals. Individuals with Hunter syndrome 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 that their child is dying. If this is happening, the child's oxygen level may be low when sleeping, and can cause problems with the heart. If a parent notices significant choking or episodes of interrupted breathing, 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 can be treated in some individuals by removing the tonsils and adenoids, opening up the airway with nighttime CPAP (continuous positive airway pressure), BiPAP (bilevel positive airway pressure), or tracheostomy, as discussed below.

#### *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 and also breathing effort, brain waves during sleep and other monitors of the body's function. From this study, the doctors can assess how much blockage to breathing is present, how much trouble your child is having moving air into the lungs during sleep, and how much effect this has on his body.

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

Nighttime CPAP or BiPAP are methods to open up the airway at night using air pressure, which can help the child's airway stay open.



Chip, age 4

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 people are able to accept 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 tracheostomy (a hole into the airway made in the front of the neck) may be needed. Most families will try to avoid a tracheostomy because it is invasive and seemingly destructive of the child's normal function. In fact, many feel that MPS individuals should receive a tracheostomy much earlier than they do, and many feel much better after improving their nighttime breathing.

#### *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 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 Ears, Nose and Throat (ENT) specialist experienced with MPS II to determine which tube is best.

Many people with MPS 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

People 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 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.

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If an MPS II 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 the abnormal heart valve, potentially damaging it further. If teeth need to be removed while under an anesthetic, this should be done in the hospital under the care of both an experienced anesthesiologist and a dentist, never in the dentist's office.

## Heart

Heart disease can occur in people with Hunter syndrome but 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. 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 II have some degree of heart valve leakage or blockage. Some individuals with Hunter syndrome may develop problems with the aortic or mitral valve; 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.

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

In people who are severely affected, the muscle of the heart may be damaged by the storage of mucopolysaccharides (cardiomyopathy) and the heart may also be put under strain by having to pump blood through abnormal lungs (cor pulmonale or right heart failure).

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 the heart problems experienced by MPS II individuals.

### Liver and spleen

In most MPS II individuals, both liver and spleen become enlarged by storage of mucopolysaccharides (hepatosplenomegaly). The enlarged liver does not usually cause liver problems or lead to liver failure, but it can interfere with eating and breathing.

### Abdomen and hernias

In people 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. The hernia can come



Christian, age 4

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

### Bowel problems

Many Hunter 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 II 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 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 Hunter syndrome 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 is usually mild in MPS II and generally does not need treatment.

### Joints

Joint stiffness is common in all forms of MPS and the maximum range of movement of all joints may become limited. Later in the individual's life joint stiffness may cause pain, which may be relieved by 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

The shape of the hands is very noticeable and has been used as the symbol of the National MPS Society. The hands are short and broad with stubby fingers. The fingers stiffen and gradually become curved due to limited joint movement. The tips of the fingers can become permanently bent over.

### Legs and feet

Many people 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. Sometimes they 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 II. The feet are broad and may be stiff with the toes curled under, rather like the hands.

## Skin

People 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 people with Hunter syndrome. Sweating and cold hands and feet are also 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 Hunter syndrome have a characteristic 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 people with severe Hunter syndrome may be related to storage in the neurons of the brain. On the other hand, individuals with mild Hunter syndrome are not likely to be affected this way. 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.

The brain and the spinal cord are protected from jolting by the cerebrospinal fluid that circulates around them. In people with severe MPS II, the 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 and delayed development. If hydrocephalus is suspected, an imaging study of the brain (CT or MRI scan) should be performed. A lumbar puncture with pressure measurement is another way to assess if hydrocephalus exists. If the doctor confirms that your child has communicating hydrocephalus, it can be treated by the insertion of a thin tube (shunt), which drains fluid from the brain into the abdomen (ventriculoperitoneal or VP shunt). The shunt has a pressure sensitive valve, which allows spinal fluid to be drained to the abdomen when the pressure around the brain becomes too high. The lack of papilledema (swelling around the optic disk)

does not rule out hydrocephalus in an MPS child. 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 disorders, is not found in individuals with Hunter syndrome. 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 very 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).

### Ears

Some degree of deafness is common in all types of MPS 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 II 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 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. In general, it is felt that hearing aids are underutilized in MPS disorders.

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

People 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, and this can cause irreversible nerve damage. The nerve damage will cause the muscle at the base of the thumb to waste away and will make it hard for a child to oppose his thumb in a position for a normal grasp. Although your child may not complain of pain, the carpal tunnel syndrome may be severe. If your child seems to have pain or numbness in the hands, particularly at night, it would be sensible to have an electrical test called a nerve conduction study performed. This test will show whether carpal tunnel syndrome is the cause. If your child has any weakness at all in the hand or has decreased muscle mass at the base of the thumb, then ask for the test from your neurologist. Be persistent, as many physicians may not believe that carpal tunnel syndrome is present without the classic symptoms. Most individuals affected by MPS do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage.

## General treatment and management

### Diet

There is no scientific evidence that a particular diet has any helpful effect on people 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 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.

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

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 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 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.

### Physical therapy

Joint stiffness is a common feature of MPS. 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. 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 MPS II 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 very 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 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. 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.

### **Puberty and marriage**

Teenagers with Hunter syndrome will go through the normal stages of puberty. There are reports of adults with mild Hunter syndrome who have had 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.

### **Life expectancy**

Life expectancy in MPS II is varied. Individuals with mild Hunter syndrome can have a reasonably normal life span. Individuals with mild Hunter syndrome survive into the fifth and sixth decades of life, with the longest known survival of an individual to 87 years of age. Sadly, those who are severely affected are likely to die before reaching their mid-teens and some may die much earlier. 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, and this may not be possible when their MPS II child is with them. Brothers and sisters also need their share of attention and to be taken on outings that may not be feasible for the MPS child. Many parents use some form of respite care or have someone come in regularly to help at busy times.

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

### **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, 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, Hunter patients may be over-active, strong, usually cheerful, but hard work to look after. They have limited powers of concentration and their mental age will be lower than their physical capabilities. 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, as they cannot understand what is required. Some children may have outbursts of aggressive behavior. 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.

### *Feeding*

Hunter boys will usually enjoy their food but some 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 it may be necessary to feed your child as you would a baby. The child may become unable to chew and swallow in which case food will have to be mashed or puréed.

### *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, but even with this precaution, the child may 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.

### *The quieter stage*

The change from the overactive noisy period is likely to be gradual. Parents will realize that their son no longer runs everywhere and is happier sitting than standing. Many Hunter boys 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 by 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.

### **Living with a mildly affected child**

Mildly affected children may be completely normal in behavior and they are often affectionate, sunny natured children. They can be short-tempered at times from frustration when their physical limitations make life difficult.

They should be encouraged to be as independent as possible since many Hunter adults 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 Hunter teenagers must worry about their appearance and about the restrictions imposed by their condition. They may be helped by meeting or writing to other Hunter teenagers or adults. Ask the National MPS Society to put you in touch with other individuals.

Many mildly affected Hunter adults 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 Hunter child to lead as full and independent a life as possible.

## Education

Some MPS II 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 II

### 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.

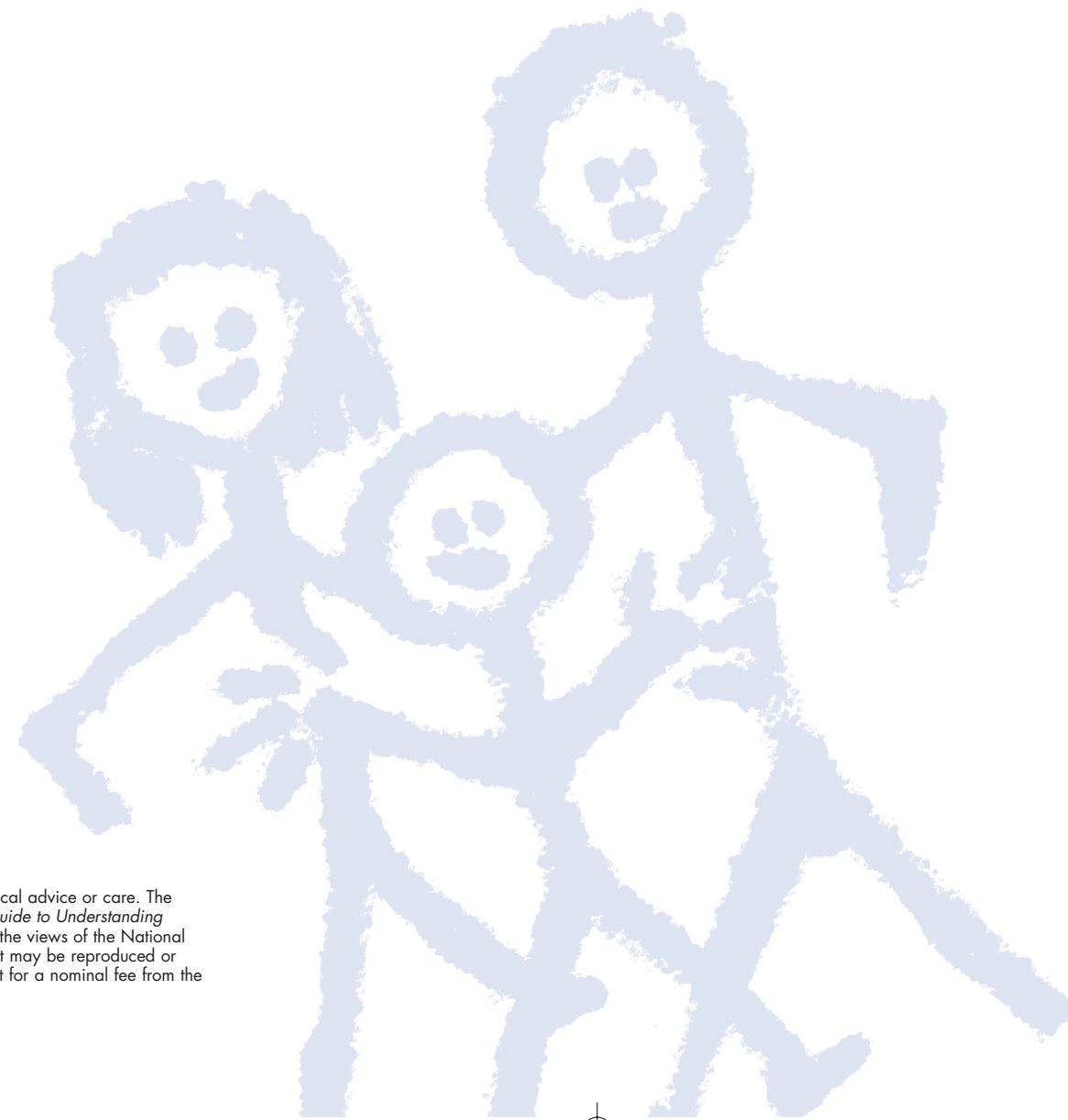
## Bone marrow transplant (BMT)

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

## Enzyme replacement therapy (ERT)

An experimental trial of enzyme replacement therapy is being planned for individuals with MPS II. The recombinant enzyme will initially be given in the clinical trial by repeated intravenous infusion. Although there is reason to hope that enzyme replacement therapy will help some of the physical problems, the blood-brain barrier may prevent enzyme therapy from directly helping the brain.

For 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 Hunter 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.