

# 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.*

For more information or to join the National MPS Society, please visit:

[www.mpssociety.org](http://www.mpssociety.org)

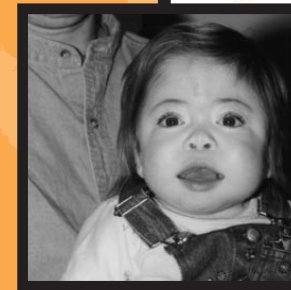
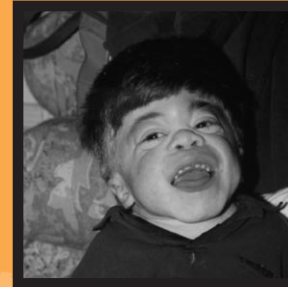
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## A Guide to Understanding I-Cell Disease and Pseudo-Hurler Polydystrophy

Mucopolipidoses (ML) II and III



The National MPS Society, Inc.

## Introduction

*I-cell disease and Pseudo-Hurler polydystrophy are closely related diseases, first described in the 1960s. The more severe of the two, I-cell disease, was named by Jules Leroy, a Belgian pediatrician, for the inclusions he saw in his patients' cells under a microscope. Pseudo-Hurler polydystrophy was described by the French physicians, Maroteaux and Lamy, who found the disease reminiscent of Hurler syndrome, though milder in its manifestations. Both diseases were assigned to the class of mucopolipidosis, I-cell disease as mucopolipidosis II and Pseudo-Hurler polydystrophy as mucopolipidosis III (or simply, ML II and ML III). Even though the reasons for this assignment were soon shown to be incorrect, the names remained for the sake of simplicity.*

*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 mucopolipidosis disorders continue to look for better and more effective ways to treat them, and it is likely that patients will have more options available to them in the future.*

*front cover*

*top: Chris, age 8, ML II*

*middle: Emily, age 2, ML II*

*bottom: Dakota, age 11, ML III*

## What causes these disorders?

Both ML II and ML III are disorders of the lysosomes. Lysosomes are the recycling plants of our cells – places where large and complex molecules are broken down to constituent parts, to be reused or disposed. Within the lysosomes, there are several dozen enzymes that carry out this breakdown of complex molecules.

In ML II and ML III, many of the enzymes are either missing completely from the lysosomes or are present in inadequate amounts. Instead, they are found outside of the cell in excessive amounts in the blood. That happens because, when they are first made (in other parts of the cell), these enzymes must be equipped with a signal that guides them to lysosomes. In ML II and ML III, signals are not attached to enzymes and, failing to reach lysosomes, are secreted out of the cell instead. The major problem is that the deficiency of these enzymes within lysosomes causes an accumulation of molecules that should have been broken down. The accumulation, in turn, causes progressive damage to cells and organs. The inclusions that Jules Leroy, MD had observed as black dots under the microscope, and for which ML II was named, are lysosomes engorged with stored material.

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 ML II and ML 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 enzyme deficiency within lysosomes causes an accumulation of molecules that should have been broken down. The accumulation, in turn, causes progressive damage to cells and organs.***

The biochemical cause of ML II and ML III is therefore different from that of other lysosomal storage diseases, such as the mucopolysaccharide disorders. In the latter, there is only one lysosomal enzyme that is missing because of a mutation in its gene – for example, alpha-L-iduronidase is lacking in MPS I. But in ML II and ML III, alpha-L-iduronidase is one of the many enzymes lacking in lysosomes, because it is not targeted correctly. This explains why I-cell disease has some of the same clinical problems as Hurler syndrome (MPS I), and additional problems. The enzyme responsible for attaching the targeting signal has the unwieldy name of "phospho-N-acetylglucosamine-transferase," referred to as "targeting enzyme."

## Are there different forms of the disorder?

Although ML II and ML III have the same biochemical cause, they are different in how they affect children. It is now apparent that a wide spectrum of severity exists within and between ML II and ML III. ML II is the severe form of the targeting enzyme deficiency, while ML III is a milder form of the same deficiency. The lack of lysosomal enzymes is not quite as profound in ML III, probably because a very small amount of the targeting enzyme can be made. Because the gene encoding the targeting enzyme has been cloned only recently, the mutations that cause ML II and ML III have not yet been described.

I-cell disease starts to affect babies in the womb and there are usually obvious signs from an early age. Many children are born with dislocated hips, an early sign of the skeletal problems of the disease. In contrast, some children with ML III are mildly affected and their condition may not be recognized for a year or more. The two disorders are not distinguished from each other by biochemical tests, so the doctor will have to use clinical examinations of the child or observe the child's actions for a period of time to arrive at a diagnosis. There are also forms of the disease that are intermediate in severity between ML II and ML III. It is important to remember, however, that regardless of the label given to your child's condition, the disorder is extremely varied in its effects. A wide range of possible symptoms is outlined in this booklet but your child may not experience them all.

***Regardless of the label given to your child's condition, ML disorders are extremely varied in their effects. A wide range of possible symptoms is outlined in this booklet, but your child may not experience them all.***

## How common are these disorders?

These disorders are very rare and sometimes misdiagnosed, so it is difficult to give accurate figures on frequency. Recent reports from Australia and the Netherlands indicate 2 or 3 patients of ML II and ML III combined, per one million births. There may be parts of the world where the disease occurs more often. Even though these disorders are rare, each patient needs such extensive medical care that the effect on the medical system is larger than their numbers suggest.

## 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 through generations in an obvious way, some genetic diseases are "hidden," or recessive and only show up when both genes in an individual are affected. ML II and ML III are such diseases. Most families with a ML II or ML III child do not have a family history of any genetic problem – ML II or ML 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.



Tristan, age 3, ML II

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 are recessive. This means it is hidden until an individual inherits two genes for the same enzyme that are not working.

Because the parents of the child with ML II or ML III have another gene that does work, there is a 3 out of 4 chance 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 ML II or ML 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.

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 mucopolysaccharidoses disorders.



Savannah, age 12, ML III

## Prenatal diagnosis

If you already have a child with ML II or ML III, 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.

## Clinical problems in ML II and III

### Growth

Growth in height is usually significantly less than normal but varies according to the severity of the disorder. Children with ML II will be severely restricted in growth. Usually they have stopped growing by the age of three and are unlikely to be taller than about 3 feet. Those who have ML III may grow taller, to between 4 feet, 6 inches and 5 feet.

### Intelligence

There is a wide variation in both disorders regarding intelligence. Many children with ML III have normal intelligence, but some may have learning disabilities.

Individuals with ML II experience progressive storage of mucopolysaccharides and glycosaminoglycans in the brain leading to the slowing of development by ages 6 months to two years, followed by a progressive regression in skills until death. There is a great variation in the severity of the condition. Those affected by



ML II are likely to be restricted in what they learn, but there are reports of children who have learned to talk, sing and do simple math. Parents emphasize that it is important to help ML II babies 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 to find enjoyment in life even if they lose the ability to speak.

Individuals with ML II and ML III commonly have other medical problems that will hamper their learning and performance, including chronic ear infections, poor vision, poor hearing, hip pain, and sleep apnea. Adequate treatment of these complications can improve the function of ML II and ML III individuals, so they should be assessed in patients with significant developmental decline.

## Physical appearance

Birth weight and length are often below normal, and the clinical features of the disease may be present at birth or in the first few months of life. In people with ML II, the neck is short, cheeks are often rosy, and the nose may be broad with a flattened bridge and upturned nostrils. The mouth may be wide, and children with I-cell can have very prominent gums. Eyebrows may be bushy and meet in the middle, and the eye sockets are usually shallow making the eyes appear prominent. The head shape of children with ML II may change with the early closing of the soft part of the baby's skull.

The facial appearance of most people with ML III is usually not affected by the disorder, though a few individuals may have some of the features found in people with ML II.



Kylie and Kendall, age 9 months, ML II

## Nose, throat, chest and ear problems

The problems described in this section are common to ML II children, and to a lesser degree to ML III individuals. Children with ML II are prone to frequent chest and ear infections, and tend to have runny noses.

### Runny nose

Typically, the bridge of the nose is flattened and the passage behind the nose may be smaller than usual due to poor growth of the bones in the midface 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. Individuals with ML II can have chronic discharge of thick 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 may be floppy, or softer than usual, due to abnormal cartilage rings in the trachea.

### Chest

The shape of the chest is frequently abnormal and the junction between the ribs and the breastbone (sternum) is not as flexible as it should be. The chest is therefore rigid and cannot move freely to allow the lungs to take in a large volume of air. The muscle at the base of the chest (diaphragm) is pushed upwards if the liver and spleen are enlarged, further reducing the space for the lungs. When the lungs are not

fully cleared, there is an increased risk of infection (pneumonia).

### *Breathing difficulties*

Many affected individuals breathe very noisily even when there is no infection. At night they may be restless and snore. Sometimes the individual may stop breathing for short periods while asleep (sleep apnea). Pauses of up to 10-15 seconds may be considered 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 which can cause problems with the heart. If a parent notices significant choking or episodes of interrupted breathing, the child should be evaluated by a sleep specialist using a polysomnogram. It is important to know that many individuals may breathe like this for years. Sleep apnea can be treated in some patients by removing the tonsils and adenoids, opening up the airway with nighttime CPAP treatment (continuous positive airway pressure), BiPAP (bilevel positive airway pressure), or tracheostomy, as discussed in the following paragraphs.

### *Management of breathing problems*

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

Nighttime CPAP or BiPAP can open the airway at night using air pressure, which can help the child's airway stay open. 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 so invasive and seemingly destructive of the child's normal function.

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

### *Treatment of respiratory infections*

Drugs may affect people with mucopolysaccharidoses 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 ML II and ML III. Cough suppressants or drugs that are too sedating may cause more problems with sleep apnea by depressing muscle tone and respiration.

Although most individuals with colds do not require antibiotics, individuals with mucopolysaccharidoses 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 makes overcoming infections difficult. Therefore, it is common to have infections improve on antibiotics and then promptly recur after the antibiotic course is over. Chronic antibiotic therapy can be used to help some individuals with recurring ear infections. Ventilation tubes can be used to improve drainage from the ear and speed resolution of infections. It is important to consult with an Ears, Nose and Throat (ENT) specialist experienced with ML disorders to determine which type of tube is best.

Many people with mucopolysaccharidoses 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 mucopolysaccharidoses 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

Children with ML II generally have overgrown and swollen gums, which are characteristic of the disease. Their teeth may be late and troublesome in breaking through the gum. Teeth may appear just above or below the edge of the gum and are often widely spaced and poorly formed with fragile enamel. Sometimes the tongue may be enlarged, and the roof of the mouth may have a high arch. The mouths of children with ML III, on the other hand, are generally normal.

***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.***

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

## Heart

Children with ML II or ML III may develop heart disease, but to a very different degree. Those who have ML III may not experience problems until much later in life. In general, the heart will be much more severely affected in children with ML II.

During examinations, your doctor may hear an unusual sound in your child's heart, called a heart murmur, if heart valves have been damaged. A simple and painless test called an echocardiogram (similar to ultrasound screening of babies in the womb) is used to identify the



problem. Heart valves are designed to close tightly to prevent blood from flowing in the wrong direction as blood passes from one chamber of the heart to another. If a valve becomes weakened or hardened, it may not shut firmly enough and a small amount of blood may leak through the valve. It is possible to have heart valve problems for years without any ill effects. If problems do occur, it may be possible to treat them with surgery.

Children with I-cell disease can also develop the more serious problems of thickening and weakness of the heart muscle (cardiomyopathy), often as a result of the damaged heart valves. In some cases, medication may be prescribed to try to help the problem. Because of the unusual special problems that can occur in these disorders, you should select a cardiologist with some knowledge of MPS/ML. At a minimum, you should inform the doctor about the problems experienced by people with ML disorders.

## Abdomen and hernias

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A child with I-cell disease is likely to have a protruding abdomen due to posture, weakness of the muscles, and enlarged liver and spleen.

Frequently, part of the abdominal contents will push out behind a weak spot in the wall of the abdomen. This is called a hernia. The hernia can come from behind the navel (umbilical hernia) or in the groin (inguinal hernia). Inguinal hernias should be repaired by an operation, but hernias 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. People with ML III are less likely to have hernias.

## Bowel problems

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Many ML II and ML III 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/ML individuals appears to be affected by the 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 wall, 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

There is a wide variation in the severity of problems that affect bones and joints, even between affected brothers and sisters. Those with ML II are more severely affected, and skeletal problems may even be evident at birth.

### Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Individuals with ML II often have poorly formed vertebrae that may not stably interact with each other. One or two of the vertebrae in the middle of the back are sometimes slightly smaller than the rest and set back in line. This backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not need treatment unless severe.

*It makes common sense for individuals to be as active as possible to maintain their joint function and improve their general health. Your child's doctor or physical therapist may be able to suggest ways of achieving this.*

### Neck

The bones that stabilize the connection between head and neck may be malformed (odontoid dysplasia) in people with ML II. If the neck becomes unstable, which is unusual in ML II, surgery (spinal fusion) is required to connect all the bones to each other so they do not slip further.

### Scoliosis

Abnormal curvature of the spine, or scoliosis, can also occur and if severe, may require intervention. In general, fusion with bone is the best alternative, and hardware-like rods may not be well tolerated. In any case, the soft bone makes the surgery and recovery difficult. Some patients need multiple procedures.

### Joints

Joint stiffness is common in both ML II and ML III and the maximum range of movement of all joints may become limited. Later in the individual's life this may cause pain, which may be relieved by warmth and ordinary painkillers. 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.

Many people with ML II and ML 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.

The hips are sometimes dislocated, and the knees may become "knocked" (genu valgum). The breastbone (sternum) may be curved outward (pigeon chest). The bones of the feet are sometimes deformed. Restriction of movement in the shoulders makes it difficult for the child to raise his or her arms above the head and may cause problems with dressing. Those who have ML III may have very stiff hips, as the supporting socket is not formed properly, and they may have pain in the joints if they are very active. Surgery on the hips may be used as a last resort if pain becomes a real problem. Hip surgery may not be successful until after puberty. Total hip replacement has been effective in individuals with ML III, if done after puberty.

### Hands

The shape of the hands is very noticeable and is 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.

## Skin

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People with ML II and ML 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 occasionally occurs. Sweating and cold hands and feet are also occasional 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 determine if the heart or the aorta might be responsible for the problem.

## Neurological problems: brain, senses and nerves

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### Eyes

Children with both conditions may be affected by mild corneal clouding. The circular window at the front of the eye (cornea) becomes cloudy which disrupts the clear layers of the cornea. If corneal clouding is severe, it may reduce sight, especially in dim light. Some people with ML II and ML III cannot tolerate bright lights as the clouding causes uneven refraction of the light. Wearing caps with visors or sunglasses can help. For individuals with severe corneal clouding causing severely limited vision, a corneal transplant may be recommended.

There may be problems with vision caused by changes to the retina. 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.

### Ears

Some degree of deafness is common in both ML II and ML 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 ML II and ML 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 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 eventually 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 due to 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 patients. In general, it is felt that hearing aids are underutilized in ML and MPS disorders.

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

People with ML III 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, carpal tunnel syndrome may be severe. If your child seems to have pain in the hands, particularly at night, it would be sensible to have an electrical test called a nerve conduction or electromyograph 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 ML II and ML III may 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 ML II and ML 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 the 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.

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

## Physical therapy

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Joint stiffness is a common feature of ML II and ML III. 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. It makes common sense for individuals to 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.

*It makes common sense for individuals to be as active as possible to maintain their joint function and improve their general health. Your child's doctor or physical therapist may be able to suggest ways of achieving this.*

## Anesthetics

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Giving an anesthetic to a ML II or ML 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 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 the surgery is completed.

Please advise physicians of the critical nature of these problems, and that many problems have occurred during anesthesia of ML and MPS individuals. For any elective surgery, 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

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Teenagers with ML III will go through the normal stages of puberty, although the stages may be delayed. A woman with ML III could bear children, but her doctor may advise against it due to the physical challenges it would present.

Remember that affected individuals are automatically carriers of the recessive genes that cause ML disorders. All children born to an ML parent are also carriers, but none will have the disease unless the other parent is also a carrier.

## Life expectancy

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Sadly, children with ML II may die before the age of three or four. Some who are less severely affected have lived to the age of ten or twelve. Parents often worry about their child's death, how it will happen, and whether their child will suffer. Many children with I-cell disease have a peaceful death during a chest infection or from the heart's gradual failure. Parents may find it helpful to prepare themselves in advance for the time of their child's death.

Those with ML III may live well into adult life. It is hard to be precise about life expectancy, as the condition has been recognized for less than thirty-five years. Therefore, there may be older adults who have never been diagnosed with ML III.

## Taking a break

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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 ML 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 ML 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 who have disabilities.

## Health care information

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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 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.

## Living with ML II

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Children with ML II can bring great joy to their families and those who know them. They are usually very content and, as they remain small, they tend to continue as the baby of the family who is loved and spoiled by everyone.

Babies may weigh less than normal and are rather unsteady. Most learn to sit without support and some manage to stand on their own. Some learn to walk with a little help. The children smile, laugh and show pleasure and some learn to say a few words. They often have a good understanding and have the ability to communicate without speech. They enjoy playing with simple toys. Some have progressed further and have learned to read simple books and do easy math. Some learn to sing songs, although the voice is often rather hoarse.

Most do not become toilet trained or manage to feed themselves. It may be difficult for them to chew and swallow solid food. Food may have to be provided in liquid form.

## Living with ML III

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Children with ML III can lead very active and full lives, many at ordinary schools, joining in clubs and other activities. They should be helped to be as independent as possible and to achieve as much as they are able.

Many children with disabilities are helped by knowing others with the same or similar conditions. As they become teen-agers and adults, they want the privileges that come with growing up (privacy, independent living, bank accounts, etc.). The National MPS Society sponsors activities for teenagers and adults with MPS/ML.



## Education

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Some ML 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.

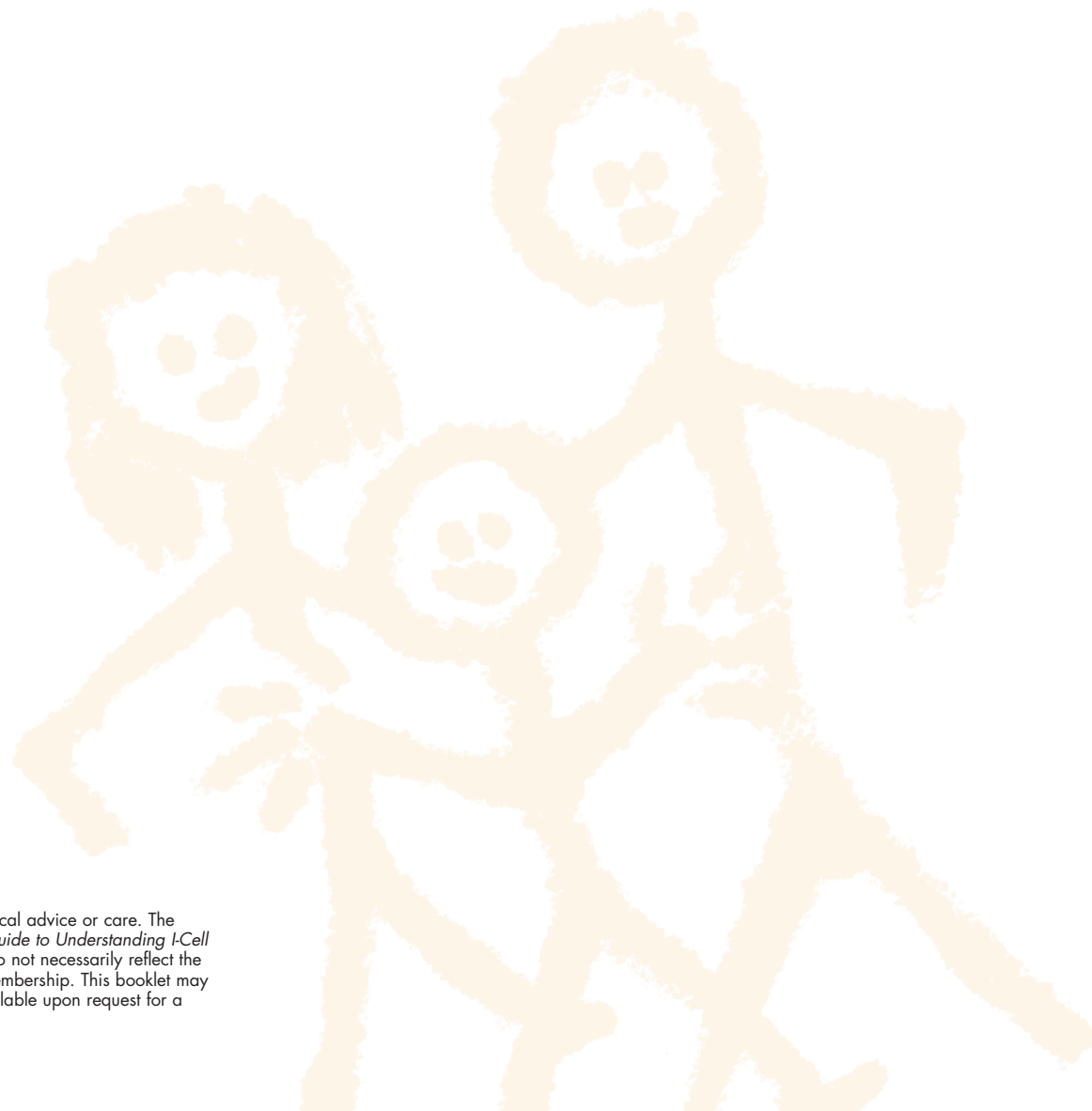
## Specific treatment of ML II and III

### The theory behind the treatment of ML disorders

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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.

At present there is no cure for the disorders, although the symptoms may be managed to create a better life for children. The biochemical cause of ML II and ML III, a lack of the targeting enzyme, suggests that treatments being developed for mucopolysaccharide disorders, such as bone marrow transplantation (BMT) and enzyme replacement, would likely not work well (if at all) in ML II and ML III. However, researchers continue their work in this area – keep in touch with the National MPS Society to learn of any new developments.



The National MPS Society, Inc.

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