A Guide to Understanding Mucopolysaccharidosis (MPS) II

Canadian MPS Society
for Mucopolysaccharide & Related Diseases

Founded in 1984, The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (The Canadian MPS Society) is committed to providing support to individuals and families affected with MPS and related diseases, educating medical professionals and the general public about MPS, and raising funds for research so that one day there will be cures for all types of MPS and related diseases.

Table of Contents

Introduction

Mucopolysaccharidosis II (MPS II, pronounced **mew**·ko·**pol**·ee·**sak**·ah·ri·**doh**·sis two), also called Hunter syndrome, is a mucopolysaccharide storage disease named after Charles Hunter, a professor of medicine in Manitoba who first described two brothers with the disease in 1917. MPS II comprises a wide spectrum of severity, and individuals may be categorized anywhere from severe (or "rapidly progressing") to attenuated (less severe or "slowly progressing"), with many individuals having an intermediate form somewhere in between. The term attenuated instead of mild is used to describe less severe patients because the effects of the disease on a less severe patient are too significant to be considered mild.

The word "mucopolysaccharide" can be broken down into its parts: Muco refers to the thick jelly like consistency of the molecules; poly means many; and saccharide is a general term for a sugar molecule (think of saccharin).

All individuals with MPS II have a deficiency of the enzyme iduronate 2 sulfatase (also called IDS or I2S, pronounced eye·**dur**·o·nate **two sul**·fa·tase), which results in the accumulation of glycosaminoglycans (GAG, pronounced **gly**·cose·a·**mee**·no·**gly**·cans), previously called muco-polysaccharides, inside special parts of the cell called lysosomes. This is why MPS II is part of a larger family of diseases called the lysosomal storage diseases (LSDs). The accumulation of GAG is responsible for numerous problems that affect individuals with MPS II.

As yet, there is no cure for individuals affected by MPS II, but there are ways to manage the challenges they will have, and ensure an improved quality of life. Hematopoietic stem cell transplant (HSCT) has been used to treat MPS II, but HSCT, including bone marrow transplant and cord blood transplant, is not generally recommended as results have been disappointing. Enzyme replacement therapy (ERT), approved by the US Food and Drug Agency (FDA) in 2006 and by Health Canada in 2007, is another available treatment. Scientists who study MPS continue to look for better and more effective ways to treat these diseases. As a result, patients will likely have more options available to them in the future.

Individuals with MPS II have a deficiency of the enzyme iduronate-2-sulfatase, which results in the accumulation of glycosaminoglycans (GAG). This accumulation is responsible for numerous problems that affect patients with MPS II.

What causes MPS II?

As mentioned previously, all MPS disorders are caused by the storage of complex molecules called glycosaminoglycans (GAG). GAG are long chains of sugar molecules used in the building of bones, cartilage, skin, tendons and many other tissues in the body. These sugar chains are submicroscopic and cannot be seen with the eye, but can be studied using special scientific instruments and analytical methods.

GAG form part of the structure of the body and also give the body some of the special features that make it work. For example, the slippery, gooey fluid that lubricates your joints contains GAG. The rubbery resilient cartilage in your joints is another example. All tissues have some of this substance as a normal part of their structure; however, individuals with MPS have too much GAG accumulation.

To understand how GAG accumulation causes MPS II, it is important to understand that in the course of the normal life process, there is a continuous process of building new GAG and breaking down the old - a recycling process. This ongoing recycling process is required to keep the body healthy. The breaking down of GAG occurs in a part of the cell called the lysosome. Lysosomes are basically bags full of digestive enzymes which break down worn-out cellular components. This is why MPS II is considered one of the approximately 40 different kinds of lysosomal storage diseases (LSDs). All LSDs are caused by a deficiency of an individual enzyme – a biochemical tool. The breakdown and recycling process requires a series of special enzymes. To break down GAG, a series of enzymes works in sequence one after another.

The GAG chain is broken down by removing one sugar molecule at a time starting at one end of the GAG chain. Each enzyme in the process has its special purpose in the body and does one very specific action - just like a screwdriver works on screws and a hammer works on nails.

Andrew

Individuals with MPS II have a defect in the gene that instructs the body to make a specific enzyme called iduronate sulfatase (IDS), which is essential in the breakdown of certain GAG called dermatan sulfate (DS) and heparan sulfate (HS). 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 are not toxic, but the amount and the effect of storage in the body lead to many physical problems. There is also evidence that GAG are bioactive. This means that their accumulation can cause activation of other chemical reactions in the body (i.e. they may trigger inflammation in joints).

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

Are there different forms of MPS II?

Individuals with a severe form of MPS II have progressive developmental delay and more severe and progressive physical problems. Individuals with attenuated MPS II can have normal intelligence, milder and less progressive physical problems, and can live into adult life. Many individuals with MPS II have normal or near normal intelligence with severe physical symptoms, confirming that MPS II is a highly variable disease.

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

All individuals with MPS II lack the same enzyme, and currently there is no reliable way of telling from biochemical tests how severe the disease will be. Detailed studies have shown that in individuals with attenuated MPS II, a very small amount of active enzyme is working as designed resulting in the attenuated form of MPS II.

How common is MPS II?

It has been estimated that about 0.6-1.3 in 100,000 male births are affected by MPS II. Although MPS II is individually rare, the incidence of all MPS diseases combined is 1 in 25,000 births and the larger family of lysosomal storage diseases collectively occur in about 1 in every 5,000 to 7,000 births. Even though these diseases are rare, each patient needs such extensive medical care that the effect on the medical system is much larger than their numbers suggest.

How is MPS II inherited?

MPS II is a genetic disease; however, it has a different form of inheritance from all the other MPS diseases—it is X-linked recessive. Girls may be carriers of the disease but except in very rare cases, only boys will be affected.

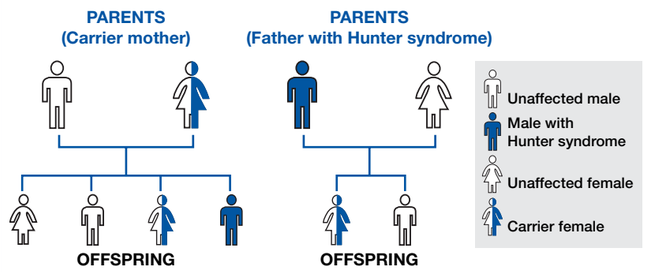
To understand this better, it is important to understand some basic concepts about genetics. DNA, or deoxyribonucleic acid, is the hereditary material in humans; nearly every cell in a person's body has the same DNA. Most DNA is located in the cell nucleus, but a small amount of DNA can also be found in the mitochondria. A gene mutation is a permanent change in the DNA sequence that makes up a gene. A gene is the basic physical and functional unit of heredity and genes act as instructions to make molecules called proteins. All humans are formed with two complete sets of genes - one set from each parent. So every individual has half his genes from his mother and half from his father. Enzymes are made from the instructions found in the genes.

A chromosome is an organized structure of DNA and protein found in cells. Most cells in the human body have 46 chromosomes: 23 from the mother and 23 from the father. X and Y chromosomes determine whether a baby will be a female or male. Females have two X chromosomes (one from the mother and the other from the father). Males have an X chromosome (from the mother) and a Y chromosome (from the father). The reason MPS II is called an X-linked disorder is that the gene needed to make 12S is found on the X chromosome.

Females who have one "MPS II" X chromosome (non-functioning) and one unaffected X chromosome (functioning) generally have enough enzyme to stay healthy because the unaffected X chromosome contains the gene needed to make enzyme. Although the body may only produce about 50 percent of the normal level of enzyme, this is often enough to keep the person healthy. This is why MPS II is very rare in females, although some cases have been reported. Females with one "MPS II" X chromosome are called "carriers," since they may pass this non-functioning chromosome on to their children. Males have an X chromosome and a Y chromosome; however, the Y chromosome does not have the full set of genes found on the X chromosome. In MPS II, since the change in the gene is on the X chromosome, there is no alternate copy of the gene on the Y chromosome, so the disease is seen almost always in males. Males who have one "MPS II" X chromosome lack the gene to make enough enzyme to prevent symptoms of the disease.

If a woman is a carrier for MPS II, there is a 50 percent risk that any of her sons will have the disease. In addition, there is a 50 percent risk that a daughter will be a carrier for the disease. However, it is important to understand that a woman may have a child with MPS II and not be a carrier of the abnormal gene, as it is possible for an X chromosome to be permanently changed spontaneously.

HOW HUNTER SYNDROME IS PASSED ON



Hunter syndrome (MPS II) shows X-linked inheritance. On average, a carrier mother will pass on the abnormal 12S gene to 50% of her sons and 50% of her daughters. A father with Hunter syndrome will pass on the abnormal 12S gene to all of his daughters and none of his sons.

MPS II is a genetic recessive disease. All families of affected individuals should seek further information from their medical/genetics doctor or from a genetic counsellor if they have questions about the risk for recurrence of the disease in their family or other questions related to inheritance of MPS diseases.

If only one individual in a family has MPS II, DNA testing can confirm the mother's carrier status. If she has the same genetic mutation in the I2S gene as her son with MPS II, then she is a carrier. Analysis of enzyme levels is not a reliable method to determine carrier status.

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

The sisters and maternal aunts of an individual with MPS II may be carriers of the disease and would also have a 50 percent chance of passing the non-functioning gene to a son. If the genetic mutation of the boy with MPS II is known, DNA testing can then determine the carrier status of other female relatives on the mother's side of the family. It is important for all female relatives on the mother's side to seek advice from their genetic doctor before planning to have children.

Kobe

How is MPS II diagnosed?

Doctors may consider testing for MPS II when signs and symptoms of the disease are present and are not explained by other causes. In many cases, a doctor with expertise in LSDs may put together the laboratory results with the features in the patient to provide the final diagnosis.

To diagnose MPS II, a doctor will typically first do a urine test to look for GAG levels that are higher than normal. The results are compared to GAG levels that are known to be normal for various ages. Most, but not all, individuals with an MPS disorder have GAG levels in their urine that are higher than those of individuals without an MPS disorder.

A urine test is only one of the first steps in diagnosing MPS II; a clear diagnosis requires a test to measure levels of enzyme activity in the blood or skin cells. In healthy individuals, the tests show white blood cells, serum and skin cells that contain normal levels of enzyme activity. In individuals with MPS II, the enzyme activity levels are much lower or absent. If the urine GAG test is normal but there is a strong suspicion of MPS II, enzyme testing should be considered.

MPS II is a highly variable disease

MPS II has a highly variable phenotype. Key variable features include the age at which symptoms and signs develop as well as the rate of progression of these symptoms. This means that some children may have many of the symptoms described below and may be severely affected while others may not experience all of the symptoms. There is currently no reliable way of telling how severe the disease will be. The age at which a child begins to develop symptoms is a clue to the severity of the disease, but only after detailed assessment and testing of a child can a physician make an educated guess as to where the child falls on the disease spectrum.

Detailed studies have shown that in individuals with attenuated, or slowly progressing, MPS II, a very small amount of active enzyme is working. This small amount of enzyme will digest some of the accumulating GAG, resulting in the disease being less severe than in an individual who has almost no enzyme activity.

DNA tests do not always provide the information that leads to the determination of the severity of MPS II. Many different kinds of mutations (changes) in the gene that produces the I2S have been identified (point mutations, small deletions or insertions), all of which result in I2S deficiency. The MPS II gene is located on the X chromosome and has been studied extensively to see if there is any relationship between specific genetic mutations and the symptoms of the disease. Approximately 20 percent of individuals with MPS II have a mutation of the gene that results in absolutely no enzyme being produced, suggesting that the individual's condition is likely to be at the severe end of the spectrum.

Other mutations of the gene cause very small amounts of defective enzyme to be produced, and still other mutations are not common at all and may only occur in a single known family. In these cases, it can be difficult or impossible to predict severity of disease.

There is therefore no perfectly reliable way to determine the exact course of disease for individuals with MPS II. Even with the same small amount of enzyme activity, and even within the same family, there can be variations in severity that cannot be explained by the enzyme level or DNA mutation. It is important to remember that whatever name is given to your child's condition, MPS II is a spectrum with a variety of symptoms, and is extremely varied in its effects. This booklet addresses a wide range of possible symptoms that individuals with MPS II may encounter; however, parents should be aware that their child(ren) may not experience them all or to the degree described.

Early diagnosis of MPS II is critical. The earlier MPS II is diagnosed, the sooner potential treatment options can be explored and supportive care may be started to help you or your loved one, and potentially prevent some of the permanent damage the disease may cause.

All relatives of affected individuals should seek further information from their medical/genetics doctor or from a genetic counsellor if they have questions about the risk for recurrence of the disease in their family, or other questions related to inheritance of MPS diseases.

Ryan

Prenatal diagnosis

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

Clinical concerns related to MPS II

The section below highlights the clinical features of MPS II disease and is largely based on historical data from patients. It does not take into account the impact of the recent emergence of treatments for MPS II, as well as other symptom-based management approaches.

Growth

Growth in height is usually significantly less than normal but varies according to the severity of the disease. Babies with severe MPS II may be quite large at birth and may grow faster than normal during the first year of life. Their growth may slow down by the end of the first year, usually stopping altogether around three years of age. The individual may not grow taller than 122 cm (4 feet). In contrast, individuals with attenuated MPS II usually grow to a relatively normal height, reaching 152 cm (5 feet) or more. The height of individuals who fall between these two extremes is variable but many are below the fifth percentile in height.

Intelligence

Children with severe (rapidly progressing) MPS II experience progressive storage of GAG in the brain that is primarily responsible for the slowing of development by two to four years of age, followed by a progressive regression in skills until death. There is great variation in the severity of the condition, however; some boys may say only a few words while others learn to walk well and to read a little. They can enjoy nursery rhymes and simple puzzles. Parents emphasize that it is important to help infants and children with MPS II learn as much as they can before the disease progresses. Even when children start to lose the skills they have 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.

It is important to remember that MPS II is a spectrum disease. Some patients have milder physical problems and impaired intelligence or learning disabilities, while others have more severe physical problems and normal intelligence.

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

Individuals with attenuated (slowly progressing) MPS II have normal or near normal intelligence. They may have the same physical features as those seen in individuals with severe MPS II, but they worsen at a greatly reduced rate. Some adults with attenuated MPS II have achieved high academic standards and have gone on to college and successful careers. Hearing impairment, joint stiffness, and airway and heart problems are commonly found in individuals with attenuated MPS II. These medical problems can hinder learning and communication. It is important to remember that MPS II is a spectrum and there is no correlation between the severity of the disease and the mental and physical condition of different individuals. Some patients have milder physical problems and impaired intelligence or learning disabilities, while others have more severe physical problems and normal intelligence.

Physical appearance

Individuals with severe MPS II tend to look remarkably similar due to their short necks and the coarsening of their facial features. They have short noses with flattened bridges, flat faces with chubby, rosy cheeks, and large heads. Their heads tend to be longer than normal from front to back with a bulging forehead (dolicocephalic). Their tongues are enlarged and their lips may be thickened. Their hair tends to be thick; their eyebrows are bushy and there may be more hair than usual on their bodies. They have protruding bellies and stand and walk with a bent-over stance due to joint contractures at the hips, shoulders, elbows and knees.

To understand the reason for the abnormal skull shape, it is important to understand more about how the bones of the skull form to create the shape of the skull. Babies' skulls are soft and the individual cranial bones are separated by thin fibrous tissue called sutures. In the front above the forehead and in the back near the hair whorl, are the anterior (front) and posterior (back) fontanelles or soft spots, which close during the first few years of life. In severe MPS II, the suture along the top of the head fuses earlier than normal so that the skull expands more in the front and the back creating the long head shape and prominent forehead. There is often a ridge across the forehead where the skull has closed prematurely.

The appearance of individuals with attenuated MPS II is extremely variable. Adults are often stocky in build and their trunks are shorter than their limbs. The neck may be short and stiff, although the facial appearance may be normal.

Nose, throat, chest and ear problems

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

Runny nose

Typically, the bridge of the nose is flattened and the passage behind the nose may be smaller than usual due to poor growth of the bones in the mid-face and thickening of the mucosal lining. This combination of abnormal bones, with storage in the soft tissues in the nose and throat, can cause the airway to become easily blocked. One of the common features of individuals with severe MPS II is the chronic discharge of thick mucous from the nose (rhinorrhea), and chronic ear and sinus infections.

Throat

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

Clinical concerns related to MPS II

Chest

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

Breathing difficulties

Many individuals with MPS II have frequent coughs, colds and throat infections. Individuals with MPS II who have narrowing of the large airways and increased secretions are at risk for asthma-like episodes. Many individuals are helped (decreased cough and easier breathing) by treatment with asthma medications during viral illness. A lung specialist can help determine if asthma-like episodes are occurring in individuals with MPS II during illnesses.

Many affected individuals breathe very noisily even when there is no infection. At night they may be restless and snore. Sometimes the individual may stop breathing for short periods while asleep (sleep apnea). Pauses of up to 10 to 15 seconds may be considered normal. This noisy breathing, which stops and starts, can be very frightening for parents to hear and may mean that the child's oxygen level may be low when sleeping, which can damage the heart over time. If a parent notices significant choking or episodes of interrupted breathing, the child should be evaluated by a sleep specialist using a polysomnogram (sleep study).

It is important to know that many individuals may breathe like this for years. Sleep apnea can be treated in some individuals by removing the tonsils and adenoids (adenoids may re-grow), opening up the airway with nighttime continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP) or tracheotomy, as discussed in the following paragraphs.

Management of breathing problems

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

CPAP or BiPAP can open up the airway at night using air pressure. A mask is placed on the face each night and air is pumped into the airway to keep it from collapsing. This may seem to be an extreme measure, but many individuals are able to tolerate it; it can greatly improve the quality of sleep, and help prevent or reduce the risk of heart failure caused by night time low oxygen levels. In severe cases of sleep apnea with heart failure, a tracheotomy (a hole in the airway made in the front of the neck) may be needed. Most families will try to avoid a tracheotomy because it is invasive and disruptive; however, many doctors feel that individuals with MPS II would benefit from receiving a tracheotomy earlier to improve their nighttime breathing and overall health.

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

Drugs often affect individuals with MPS II differently, so it is essential to consult your doctor rather than using over-the-counter medications.

Treatment of respiratory infections

Medication often affects individuals with MPS II differently, so it is essential to consult your doctor rather than using over-the-counter products. Medications for controlling mucous production may not help. Medications 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 individuals with MPS. Cough suppressants or medications that are too sedating may cause more problems with sleep apnea by depressing muscle tone and respiration.

Although most normal individuals with colds do not require antibiotics, individuals with MPS II almost always end up with secondary bacterial infections of the sinuses or middle ear. These infections should be treated with antibiotics. Poor drainage of the sinuses and middle ear make overcoming infections difficult. Therefore, it is common to have infections improve on antibiotics and then promptly recur after the antibiotic course is over. Chronic antibiotic therapy may be used to help some individuals with recurring ear infections. Ventilation tubes can be used to improve drainage from the ear and speed resolution of infections. It is important to consult with an ear, nose and throat (ENT) specialist experienced with MPS diseases to determine which tube is best.

Many individuals with MPS II become allergic to antibiotics or may acquire resistant infections. Your doctor can prescribe other antibiotics to help manage this problem. While overusing antibiotics is not advised, most individuals with MPS will require some type of treatment for most infections. You will need a doctor with whom you can develop a good working relationship to manage the frequent infections.

Mouth

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

Since individuals with MPS generally have heart problems, it may be advised by the individual's cardiologist 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, it should be done in a hospital that has experience working with patients affected with MPS disorders, and under the care of both an experienced anesthetist and a dentist, never in the dentist's office.

Clinical concerns related to MPS II

Heart	Heart disease is common in all individuals with MPS II, severe to attenuated; however, heart disease may not develop or cause any real problems until later in the individual's life. Medications are available to help manage the heart problems that occur in MPS II. Cardiomyopathy (weak heart muscle) and endocardiofibroelastosis (stiff heart) are conditions that can occur in young individuals with severe MPS II. Coronary artery disease caused by GAG storage in the heart blood vessels is like that seen in older adults and can lead to death. Some individuals with attenuated MPS II may develop problems with the aortic or mitral valves; they may have slowly progressive valvular heart disease for years without any apparent clinical effects. As the condition worsens, medications can be used to lessen the effect on the heart. However, an operation may be required to replace the damaged valves. Your doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAG. Heart valves are designed to close tightly as blood passes from one chamber of the heart to another in order to stop blood from flowing back in the wrong direction. If a valve is weakened, it may not shut firmly enough and a small amount of blood may shoot backward, leading to turbulence and a murmur. Most individuals with MPS II have some degree of heart valve leakage or blockage. Since heart problems occur so frequently in MPS II, all individuals with MPS II should have an echocardiogram (ECHO) annually (or as often as your doctor thinks necessary) to show whether any problems are beginning. The test is painless and similar to the ultrasound screening of babies in the womb. It can identify problems with the heart muscle, heart function and heart valves, but like many tests it cannot detect all possible problems, especially coronary artery disease. In individuals who are severely affected, the muscle of the heart may be damaged by the storage of GAG (cardiomyopathy) and the heart also may be put under strain by having to pump blood through abnormal lungs (cor pulmonale or right heart failure). A number of affected individuals have high blood pressure. Occasionally the coronary arteries of individuals with moderate to severe MPS II may become narrowed and cause episodes of chest pain (angina). If your child is distressed and crying and is at the same time pale and sweating while keeping still, you should consult your doctor who may refer your child for an electrocardiogram (ECG or EKG). Because of the unusual problems that can occur in these diseases, you should select a cardiologist with some knowledge of MPS II. At a minimum, you should inform the doctor about the heart problems experienced by individuals with MPS II.
Liver and spleen	In most individuals with MPS II, both the liver and spleen become enlarged by storage of GAG (hepatosplenomegaly). The enlarged liver does not usually cause liver problems or lead to liver failure, but it can interfere with eating and breathing and the proper fitting of clothes.
Abdomen and hernias	In most individuals with MPS II, the abdomen bulges out due to posture, weakness of the muscles, and the enlarged liver and spleen. Frequently part of the abdominal contents will push out behind a weak spot in the wall of the abdomen. This is called a hernia. A hernia can come from behind the navel (umbilical hernia) or in the groin (inguinal hernia). Inguinal hernias should be repaired by an operation, but hernias will sometimes recur. Umbilical hernias are not usually treated unless they are small and cause entrapment of the intestine or are very large and are causing problems.
Bowel problems	Many individuals with MPS II suffer periodically from loose stools and diarrhea. The cause of this is not fully understood. Occasionally, the problem is caused by severe constipation and leakage of loose stools from behind the solid mass of feces. More often, however, parents describe it as "coming straight through." It is thought there may be a defect in the autonomic nervous system, the system that controls those bodily functions usually beyond voluntary control. Studies have found storage in the nerve cells of the intestine and it seems likely that abnormal motility in the bowel is the cause of diarrhea. An examination by your pediatrician, who may use an additional test like an x-ray, may establish the cause of diarrhea. The problem may disappear as the child gets older, but it can be made worse by antibiotics prescribed for other problems. The episodic diarrhea in some individuals with MPS II appears to be affected by diet; elimination of some foods can be helpful. If antibiotics are the cause, treatment may involve eating plain live-culture yogurt to change the bacterial make-up in the intestines. This provides a source of lactobacillus to help prevent the growth of harmful organisms within the bowel, which can cause diarrhea or make it worse. A diet low in roughage also may be helpful. Constipation may become a problem as the child gets older and less active and as the muscles weaken. If an increase in roughage in the diet does not help or is not possible, the doctor may prescribe laxatives or a disposable enema.
Bones and joints	Individuals with MPS II tend to have significant problems with bone formation and growth. This leads to bone problems (called dysostosis multiplex) as well as neurological problems if nerves are compressed by bone.

Clinical concerns related to MPS II

Spine

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Individuals with severe MPS II often have poorly formed vertebrae that may not stably support each other. One or two of the vertebrae in the middle of the back are sometimes slightly smaller than the rest and set back in line. This backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not require treatment. In older children and adults with MPS II, spinal cord compression is common. The compression is due to accumulation of GAG in the membrane surrounding the spinal cord. Doctors will want to monitor this carefully and arrange surgical treatment if necessary.

Parents of children with MPS II should be cautious when handling the area of the spine around the neck. Children with MPS II should avoid high risk activities such as contact sports and gymnastics, including trampolines.

Joints

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

Hands

The shape of the hands in children with MPS II is very noticeable. The hands are short and broad with stubby fingers. The fingers stiffen and gradually become curved due to limited joint movement. The tips of the fingers can become permanently bent over. Finger joints may become locked, called trigger finger. Trigger fingers may be resolved with heat and massage or by surgery, if necessary.

Legs and feet

Many individuals with MPS II stand and walk with their knees and hips flexed. This, combined with a tight Achilles tendon, may cause them to walk on their toes. They sometimes have knock-knees but this is very unlikely to need treatment. Severe knock-knees can be treated by surgery on the tibia bones. The feet are broad and may be stiff with the toes curled under, rather like the hands. Lack of flexibility in the hips and legs often prevents individuals from sitting cross-legged (the seating position of choice for most kindergarten teachers) or putting on their own socks and shoes.

Skin

Individuals with MPS II tend to have thickened and tough skin, making it difficult to draw blood or place intravenous catheters. Excess hair on the face and back occurs in some individuals with MPS II. Sweating and cold hands and feet also are common problems, and are possibly related to the heart, circulation or other mechanisms that control temperature regulation. Periodic blue or cold hands or feet should be evaluated by a cardiologist to see if the heart or the aorta might be responsible for the problem.

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

Neurological problems: brain, senses and nerves

Brain

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

The brain and spinal cord are protected from jolting by the cerebrospinal fluid that circulates around them. In some individuals with severe MPS II, circulation of the fluid can slowly (over months to years) become blocked. The blockage causes increased pressure inside the head (communicating hydrocephalus), which can press on the brain and cause headaches, incontinence, delayed development, expansion of the skull and ultimately blindness. If hydrocephalus is suspected, an imaging study of the brain (CT or MRI scan) should be performed. A lumbar puncture with pressure measurement (ideally pressure monitoring) is another way to assess if hydrocephalus exists. If a doctor confirms an individual has communicating hydrocephalus, it can be treated by the insertion of a thin tube (shunt), which drains fluid from the brain into the abdomen (ventriculoperitoneal or VP shunt). The shunt has a pressure-sensitive valve, which allows spinal fluid to be drained to the abdomen when the pressure around the brain becomes too high. The lack of papilledema (swelling around the optic disk) or normal-sized ventricles does not rule out hydrocephalus in a child with MPS II. Communicating hydrocephalus is more likely to occur in a child with severe MPS II.

Eyes

Clouding of the cornea, which is a feature of some of the other MPS diseases, is not found in individuals with MPS II. Occasionally there may be problems with vision caused by changes to the retina or glaucoma (increased pressure) which should be checked during an eye examination. Storage in the retina can result in loss of peripheral vision and night blindness. Night blindness can result in a child not wanting to walk in the dark or waking up at night and being afraid. Sometimes the simple addition of a night light in a hall or bedroom is 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 MPS II. It may be conductive, or nerve deafness, or both (mixed deafness) and may be made worse by frequent ear infections. It is important that individuals with MPS II have their hearing monitored regularly so problems can be treated early to maximize their ability to learn and communicate.

Clinical concerns related to MPS II

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. Once the ventilation tube is in place, fluid should drain out and hearing should improve.
Sensorineural (nerve) deafness	In most cases, the cause of nerve deafness is damage to the tiny hair cells in the inner ear. It may accompany conductive deafness, in which case it is referred to as mixed deafness. Nerve or conductive deafness can be managed by the fitting of a hearing aid or aids in most individuals. Hearing aids are generally underutilized in MPS diseases.
Carpal tunnel syndrome and other nerve entrapments or compression	Individuals with MPS II sometimes experience pain and loss of feeling in the fingertips caused by carpal tunnel syndrome. The wrist, or carpus, consists of eight small bones known as the carpals, which are joined by fibrous bands 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, which can cause irreversible nerve damage. The nerve damage will cause the muscle at the base of the thumb to waste away and will make it difficult for a child to oppose his thumb in a position for a normal grasp. Although your child may not complain of pain, the carpal tunnel syndrome may be severe. If your child seems to have pain or numbness in the hands, particularly at night, an electrical test called a nerve conduction or electromyograph study should be performed, which will show whether carpal tunnel syndrome is the cause, or if there is a problem with nerve conduction in the neck or spine. If your child has any weakness at all in the hand or has decreased muscle mass at the base of the thumb, ask for the test from your neurologist. Be persistent, as many physicians may not believe carpal tunnel syndrome is present without the classic symptoms. Most individuals affected by MPS do not have the classic symptoms of carpal tunnel syndrome, even with severe nerve entrapment and damage. Uncorrected carpal tunnel syndrome may result in the loss of sensation in the hands and fingers. Carpal tunnel syndrome can be corrected through surgery; however, it may return in the future requiring additional surgeries. A similar type of nerve compression can happen elsewhere in the body, such as the feet, and cause localized weakness or pain.

General treatment and management

Diet

There is no scientific evidence that a particular diet has any helpful effect on individuals with MPS II, and symptoms such as diarrhea tend to come and go naturally. Some parents, however, find that a change in their child's diet can ease problems such as excessive mucous, diarrhea or hyperactivity. Reducing intake of milk, dairy products and sugar, as well as avoiding foods with too many additives and colouring, have helped some individuals. Consult your doctor or a dietician if you plan major dietary changes to make sure the proposed diet does not leave out essential items. If your child's problems are eased, you could try reintroducing foods one at a time to test whether any particular item seems to increase the child's symptoms.

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

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

Swallowing may become difficult as an individual with MPS II gets older and the disease progresses. If this occurs, the individual may choke or aspirate food or liquids into the lungs, which can result in recurrent pneumonia. During this time the individual may lose weight and require more and more time to be fed. It is often difficult for a family to consider alternate means of feeding, such as a gastrostomy tube (G-tube); consultation with your medical geneticist and pediatric surgeon can help with your decision making.

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

Physiotherapy/sports

Joint stiffness is a common feature of MPS II. Limitation of movement 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 although exercises that cause pain should be avoided. Once there is significant limitation of movement, it may not be possible to increase range-of-motion, but it may be possible to minimize further limitation. Individuals with MPS II should be as active as possible to maintain joint function and improve their general health; however, contact sports should be avoided. Your child's doctor, a physiotherapist, or a recreation therapist may be able to suggest ways of achieving optimal fitness through a combination of daily activities, adapted sports and passive range-of-motion exercises.

Trey

Mobility

Many individuals with MPS II remain ambulatory into their teens and adult life. Others may need to use a wheelchair or motorized scooter from an early age, at least for getting around outdoors or for periods of longer activity. Consult your physical therapist or occupational therapist for advice.

Pain

Many individuals with MPS II complain of pain. Pain may be caused by problems with bone formation and growth as mentioned above, but may also be due to inflammation (similar to arthritis). Pain management is important as it can help to improve general quality of life. Children and adults can benefit from seeing a pain specialist, such as a rheumatologist

Anesthetics

Various management options and surgical procedures to manage the symptoms of MPS II require that the person being treated be given an anesthetic. General anesthesia uses a medication or gas that "puts the person to sleep" before surgery. To make sure the person under anesthesia receives enough oxygen during surgery, a laryngeal mask airway (LMA) is used, if possible. In some cases, a LMA may not be possible and a tube is placed into the throat and connected to a machine that helps the person breathe.

Giving an anesthetic to an individual with MPS II requires skill and should always be undertaken by an experienced anesthetist familiar with MPS II. If the cervical spine is unstable, the individual with MPS II is at risk if the neck is flexed while unconscious, and special precautions must be taken. Inform your child's school or any other caregivers of this in case you cannot be contacted in the event of an emergency. Consider an emergency letter or a medical bracelet to indicate potential difficulties with intubation (placement of the breathing tube). If you have to go to a different hospital in an emergency, tell the anesthetist there may be problems with the neck and possibly with intubation. 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 with MPS II, it is difficult to remove the breathing tube after surgery is completed. Advise physicians of the critical nature of this difficulty, and that many problems have occurred during anesthesia of individuals with MPS II.

For any elective surgery in a child or adult with MPS II, it is important to choose a pediatric or general anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical centre instead of a local hospital.

Topical anesthetics, such as "EMLA" cream, used to freeze skin in order to more comfortably insert an IV line, may not be effective in individuals with MPS II. Use of nitrous oxide (laughing gas) for initial anesthesia in the operating room should be discussed with the operating surgeon and anesthesiologist.

See additional information on anesthesia in our booklet "Is Your Child Having an Anesthetic?" or in the Anesthesia Considerations section of the binder "MPS II: A resource for individuals and families affected by MPS II".

Sebastien and Kobe

Andrew with his brother Brad and parents Nick and Sonia

Life expectancy

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

Taking a break

Caring for a child with MPS II is hard work. Parents need a break to rest and enjoy activities, which may not be possible when their affected child is with them. Brothers and sisters also need their share of attention and need to be taken on outings that may not be feasible with a severely affected child. Many parents use some form of respite care or have someone come in regularly to help at busy times. Individuals with attenuated MPS II may need help to become more independent from their families and may benefit from a vacation, perhaps with others who have disabilities. The Canadian MPS Society has respite funding available through its Family Assistance Program – please visit our website or contact the office for more information.

Financial support and supportive care

Individuals with MPS II and their families may need help from case managers and support workers to access a variety of healthcare and supportive care services, including physical supportive care, emotional support, and financial assistance.

Families may benefit from financial assistance from health insurance or government programs to help cover the costs of medical treatment and devices. Health Canada's Service Canada website provides links to a number of programs for financial support of people with disabilities (www.servicecanada.gc.ca/eng/audiences/disabilities/index.shtml). Visit the Canadian MPS Society's website for a list of more links to programs which provide financial assistance (or refer to the lists included in the Society's MPS II resource binder "MPS II: A resource for individuals and families living with MPS II"). You may also wish to investigate private agencies and foundations.
The Canadian MPS Society's Family Assistance Program provides financial aid when it is not available through insurance or other sources - please contact the Canadian MPS Society office or visit www.mpssociety.ca for more details.

Living with a child with severe MPS II

While young, boys with MPS II may be overactive, strong, cheerful and hard to supervise. They have limited powers of concentration and their mental age will be lower than their physical capabilities. They could, for example, lock the bathroom door but be unable to understand how to get out again, even when told. They enjoy rough and tumble play; making a lot of noise and throwing toys rather than playing with them. They may be unaware of danger, and stubborn and unresponsive to discipline since they may not understand what is required. Some children may have outbursts of aggressive behavior. Boys with MPS II have an increased tolerance of pain; bumps and bruises or ear infections that would be painful for other boys often go unnoticed. 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.

It is very hard when a child cannot express him or herself to know whether crying is from pain or frustration. Children may have ear infections, toothache, aches and pains in their joints or feel discomfort from a full stomach. Do not hesitate to ask your doctor to check whether there is a physical reason for your child's distress.

Sebastien

Education

It is important to work with your school system and develop the best Individualized Education Program (IEP) possible for your child. Inclusive education is legally required in Canada; therefore, schools must have a means of identifying those students who are not completely able to adjust to a standard classroom situation as a result of a disability. Canadian human rights laws specify "a right to reasonable accommodation for a disability" which ensures that schools and other educational authorities have a legal obligation to take appropriate steps to eliminate discrimination resulting from a rule, practice, or barrier that has, or can have, an adverse impact on individuals with disabilities. This is referred to as the "duty to accommodate." For more information on education, see the Education Strategies section of our binder "MPS II: A resource for individuals and families affected by MPS II", which is available to families affected by MPS II through the Society's office, and posted on the Society's website.

Feeding

Most children with severe MPS II enjoy food, but the range of what they will eat may be limited. They often drink a great deal of fluids. Many do not progress to using a knife and fork or an ordinary cup and eventually need to be fed as if a baby. Eventually, they may find it difficult to chew properly, and food, especially meat, should be cut up into very small pieces.

Nathaniel and his sister Chelsea

Choking

When children cannot chew and have difficulty swallowing, there is a risk of choking. Even when food is cut up into very small pieces, children may still start to choke. If this happens, act quickly: turn him upside down, or lay him head down over your knee and pound sharply between the shoulders three or four times. Pounding on the back while the child is upright can make things worse by causing the child to breathe in rather than cough out the food. If necessary, put your finger down his throat to try to dislodge the food item. Consider registering for first aid and safety courses.

Chewing

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

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

The quieter stage

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

Slowly, weight will be lost as muscles waste away. Very occasionally, near the end of the child's life, there may be seizures which can be controlled with medication. Chest infections may be more frequent. Many children die peacefully after an infection or from the heart's gradual failure. You may find it helpful to prepare yourself in advance for the time of your child's death. The Society has a book available called "Choices – When Your Child is Dying," written by our founder Sheila Lee. Please contact the office to receive a copy if you think it might be helpful.

Living with a child or adult with attenuated MPS II

Education

Many children with attenuated MPS II attend mainstream school and succeed academically. Achieving post-secondary education is highly possible; however, it is important to ensure that the school is aware of the resources required. It is important to work with your school system and develop the best Individualized Education Program (IEP) possible for your child. Inclusive education is legally required in Canada; therefore, schools must have a means of identifying those students who are not completely able to adjust to a standard classroom situation as a result of a disability. Canadian human rights laws specify "a right to reasonable accommodation for a disability" which ensures that schools and other educational authorities have a legal obligation to take appropriate steps to eliminate discrimination resulting from a rule, practice, or barrier that has, or can have, an adverse impact on individuals with disabilities. This is referred to as the "duty to accommodate."
For more information on education, see the Education Strategies section of the binder "MPS II: A resource for individuals and families affected by MPS II", which is available to families affected by MPS II through the Society's office, and posted on the Society's website.

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

Puberty and reproduction

Adolescents with MPS II will go through normal developments of puberty and are fertile. All daughters born to a father with MPS II are automatically carriers but sons born to a father with MPS II will be only affected if the mother happens to be a carrier. In other words, the fact that the father has MPS II will have no effect on whether or not his son will have MPS II.

Transition to independence

As those with attenuated MPS II reach their teen years, it is helpful for them to start a gradual transition to advocate for their own medical care. More information on medical transition is available in our binder "MPS II: A resource for individuals and families affected by MPS II". Individuals with MPS II should be encouraged to be as independent as possible so that they can lead full and enjoyable lives. The teenage years may be difficult if those affected have restrictions imposed by their disease, but meeting or contacting other teenagers and adults who also have MPS II may help. If needed, a power wheelchair may be a helpful mode of transportation and provide further independence and an adapted vehicle can help teens and young adults with significant mobility issues achieve independence through driving. Learning to use the bus will also help affected teens and adults get around in their communities. It is a good idea for teens and adults to wear "Medic-Alert" bracelets and carry medical wallet-cards to ensure medical personnel are aware of any crucial health concerns in the case of an emergency.

Employment

Many individuals with attenuated MPS II do well at a variety of different jobs: one was a teacher of the deaf, one was a marine architect and another was an army sergeant. Some advice: Begin your search for the right job by assessing your physical capabilities. It's important to be practical about what you can and cannot do. Instead of using your limitations as a restriction, use them as a guide to finding the right career. A career counsellor can help you explore a type of work that you might enjoy and that is well suited to your individual strengths and interests. Section 15 of the Canadian Charter of Rights and Freedom guarantees equality rights plus freedom from discrimination for people who have a physical or mental disability. The Employment Equity Act (EEA) of 1995 ensures that persons with disabilities are granted full and equal access to employment and opportunity. An employer must accommodate the disabilities of employees, prospective employees, and clients or customers. More information is available in our binder "MPS II: A resource for individuals and families living with MPS II".

Compassionate leave legislation is overseen in Canada at the provincial level. A summary of the elements of the compassionate care leave provisions in employment standards in legislation published by Human Resources and Skills Development Canada can be found online at www.hrsdc.gc.ca/eng/labour/labour_law/esl/compass.shtml.

Home adaptations

Appropriately adapted living accommodations will greatly enhance the ability of an individual with MPS II to develop independent living skills. Where stature is severely restricted, kitchen and bathroom facilities at a low level will be required. If mobility is restricted to such an extent that a wheelchair is used, plans for any home adaptations will need to allow adequate space to accommodate this. Additional information about home adaptations can be found in the booklet published by the Canadian MPS Society, "Daily Living with MPS and Related Diseases", and funding is available through the Society's Family Assistance Program.

Psychosocial issues

To date, there has been no research carried out exploring the psychosocial development of individuals affected with MPS II, so it is not possible to make definitive statements about this subject. As a parent of a child or young adult with MPS II, it is important to consider how his disability may cause him to experience additional challenges in life.

Some children and young adults with MPS II may adapt socially and emotionally by becoming socially inhibited, or by internalizing problems or developing an aggressive, outgoing personality. Adolescence may be more of a challenge as they have to experience all of the physiological and psychosocial changes as well as any disease-related changes or limitations. Developing the necessary skills to lead independent adult lives can be challenging although important to achieving social maturity. Referral for counselling is recommended if problems such as depression are seen in teenagers and young adults with MPS II.

Parents and family members may need emotional support to help them cope. Families may need access to respite care, individual counselling, and support groups. The Canadian MPS Society has respite funding available through its Family Assistance Program. Please visit the Society's website or call its head office for more information.

Yusuf

Specific treatment of MPS II

Overview

The goals of managing MPS II are to improve quality of life, to slow down the progression of the disease, and to prevent permanent tissue and organ damage. Currently there is no cure for MPS II. However, early intervention may help prevent irreversible damage. Treatment options for MPS II include those aimed at disease management and supportive or palliative care (care that makes a person with a disease that cannot be cured more comfortable), as well as those aimed at treating the underlying enzyme deficiency.

Hematopoietic Stem Cell Transplant (HSCT)

For some years, HSCT (bone marrow and cord blood transplant) has been used to treat children with MPS. Some children with MPS I have benefited from HSCT, but this procedure currently is not recommended for most individuals with MPS II in Canada. HSCT in MPS II has not been proven to have any effect in preventing the damage to the brain that occurs with severe MPS II. The Canadian MPS Society may be able to put you in touch with parents whose children with MPS II have had this treatment so you may be better informed.

Enzyme replacement therapy (ERT)

ERT for MPS II was approved by the FDA in 2006, and by Health Canada in 2007. Elaprase® (Idursulfase) is a manufactured version of the body's natural iduronate sulfatase enzyme. Elaprase improves lung function, endurance, reduces the size of the liver and decreases the levels of GAG in the urine. It does not cross the blood-brain barrier at normal doses and thus is not anticipated to have an impact on any neurocognitive decline occurring in individuals with MPS II. Treatments of Elaprase are given weekly through intravenous infusions. For parents to fully understand the risks, benefits and limitations of ERT, it is important to talk with physicians familiar with MPS II ERT and families undergoing this treatment. The Canadian MPS Society can put you in touch with physicians and families so you can become better informed before reaching a decision.

Living with MPS II

Disease severity varies significantly for individuals with MPS II, and it is not possible to predict the expected life span for a given individual. Those on the more slowly progressing end of the disease spectrum may have a reasonably normal lifespan. However, the availability of new and ever-improving treatments, as well as other surgical procedures, provides hope for better future outcomes for all individuals affected by MPS II.

Research for the future

The Canadian MPS Society is committed to finding cures for MPS and related diseases, and therefore funds research grants. The Society recognizes the need for targeted research for treatment of bone and joint problems and for treating the brain, and Society research funding has focused on those areas. Information about Society funded research and promising new areas of research can be obtained by contacting the Society's office.

There are several different types of mucopolysaccharide (MPS) diseases. This booklet is intended as an introduction to mucopolysaccharidosis, type II (MPS II). A more thorough resource binder entitled "MPS II: A resource for individuals and families living with MPS II" is available for affected individuals and families through the Canadian MPS Society's office. "The Hunter Disease eClinic" is an excellent MPS II resource developed by the Lyosomal Research Group at Toronto's Hospital for Sick Children and is available online at www.lysosomalstorageresearch.ca.

This booklet was updated in 2013 by the Canadian MPS Society with help from the National MPS Society (USA), experts in the field, and parents of those with MPS II. This booklet is not intended to replace medical advice or care. The contents of and opinions expressed in "A Guide to Understanding MPS (Mucopolysaccharidosis) II" do not necessarily reflect the views of the Canadian MPS Society or its membership. This booklet may be reproduced and copies can be obtained through the Canadian MPS Society's office or its website.

Common bonds unite the lives of those affected by MPS and related diseases – all have a need for support and hope for a cure.

The Canadian MPS Society is committed to making a difference in the lives of families affected by MPS and related diseases through support, research, education and advocacy. Families gain a better understanding of these rare genetically determined diseases through the Society's assistance in linking them with health care professionals, researchers and, perhaps most importantly, each other.

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

- Our quarterly newsletter, the Connection, a valuable resource that helps members stay current on MPS-related news and events and stay in touch with each other, and our monthly e-newsletter, the e-Connection
- Our Family Referral Directory (Membership Directory): connecting families affected with the same syndrome or living in the same region
- Our Family Assistance Program: providing financial aid to affected families
- Advocacy support: to ensure our members receive the treatment and care they need
- Family conferences and regional meetings: providing families an opportunity to learn more about new research, treatments and care strategies, and to meet with other families, share experiences and form life-long friendships
- Bereavement support: for families dealing with the devastating loss of a child or family member to MPS or a related disorder

For more information or to join the Canadian MPS Society:
visit www.mpssociety.ca
contact us at **604-924-5130** or **1-800-667-1846**
or email us at **info@mpssociety.ca**