



National
MPS
Society

Support for Families. Research for a Cure.



Management

of Mucopolysaccharidosis (MPS)
and Related Diseases

The National MPS Society exists to find cures for MPS and related diseases. We provide hope and support for affected individuals and their families through research, advocacy and awareness of these devastating diseases.

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Introduction

Management of MPS and related diseases consists of supportive care, treatment of complications and treatment of the MPS disease, if available. Information about treatment options for specific MPS diseases can be found in MPS Society booklets dedicated to each disease type. The progressive nature of organ involvement dictates the need for constant evaluation of clinical status. The goal of systematic evaluation is to improve the quality of life for the individual and family suffering from MPS and related diseases. This booklet is organized based on a systems approach to clinical problems. No one physician or medical care provider is able to deal with all the medical problems that can occur in an individual with MPS. Each system or subspecialty area will be presented as a section with a review of the clinical features, diagnostic procedures that are available and management/treatment options. A glossary of common terms begins on page 18.

Medical Overview

Central nervous system (Neurology)

The brain and the spinal cord are protected from injury by the cerebrospinal fluid that circulates around them. In individuals with MPS, the circulation of the fluid over time may become blocked so

Individuals with MPS often have an increased tolerance of pain. It is not unusual for an ear infection or abscessed tooth to be diagnosed in the absence of any outward signs of discomfort.

that it cannot be taken back into the bloodstream. The blockage (communicating hydrocephalus) causes increased pressure inside the head, which can press on the brain and cause headaches and possible delayed development. Physical signs of hydrocephalus may include decreased consciousness, ataxia (unbalanced movements), headaches, vomiting and blindness. Because the hydrocephalus that occurs in MPS develops very slowly over months to

years, the typical signs are not commonly seen or are assumed to be due to the progressive brain involvement that occurs in MPS. The lack of papilledema (swelling around the optic disk) does not rule out hydrocephalus in individuals with MPS.

If hydrocephalus is suspected, a magnetic resonance imaging (MRI) scan should be performed. A lumbar puncture with pressure

measurement is another way to assess if hydrocephalus exists. If your doctor confirms that communicating hydrocephalus is present, 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 into the abdomen when the pressure around the brain becomes too high.

Shunting of communicating hydrocephalus is believed to improve quality of life. It is suspected, but not proven, that hydrocephalus may contribute to neurologic deterioration. Therefore, early detection and treatment of hydrocephalus should be considered.

An MRI scan should be performed routinely at diagnosis. Periodic MRI scans to monitor for communicating hydrocephalus should be performed on all children with MPS. The frequency of imaging studies depends on the degree of neurologic involvement of each child and the results of the previous scan. For management purposes, it is important to keep in mind that children with greater neurologic involvement have a higher risk for developing hydrocephalus. Progressive enlargement of the ventricles and/or elevated cerebral spinal fluid (CSF) pressure are two criteria for considering shunting in individuals with MPS who are at risk for hydrocephalus.

Hydrocephalus with elevated CSF pressure commonly occurs in MPS I, MPS II, MPS VI and MPS VII and may be associated with some degree of cortical atrophy (loss of brain cells). Children with MPS III routinely develop enlarged ventricles, but elevated CSF pressure has never been documented. In MPS III, the enlarged ventricles are believed to be due to cortical atrophy and not elevated CSF pressure. However, Robertson et al, *European Journal of Pediatrics*, 157: 635, 1998, have reported that shunting in individuals with MPS III may decrease hyperactivity and aggressive behavior.

Seizures are a complication most common among individuals with the severe forms of MPS. Seizures are common in individuals with MPS III and may occur in up to one half of these individuals, typically in the late stages of the diseases.



CARLY (MPS IV)

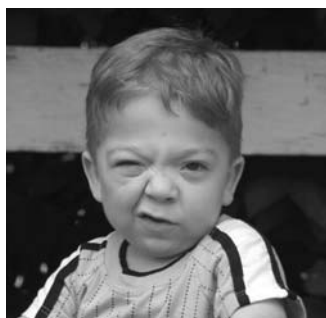
Seizures are a complication most common among individuals with the severe forms of MPS.

4 In MPS diseases, seizures are most likely secondary to the progressive brain damage that occurs due to the stored material. There are many effective medications to treat seizures, and the specific medication prescribed depends on the type of seizure experienced. Evaluation by a neurologist is recommended to determine the best medication to use. An electroencephalogram may be needed to confirm the diagnosis of a seizure disease and aid your neurologist in selecting the best medication to control the seizures. In general, seizures that occur in individuals with MPS are not difficult to control, but can be very alarming to parents.

Vision

There may be problems with vision caused by changes to the retina due to glaucoma or due to corneal clouding. It is often difficult to determine which combination of problems is responsible for the decrease in eyesight. An ophthalmologist (eye doctor) can perform special studies to help determine whether the problem is due to an effect on how light enters the eye (the cornea) or on how the eye responds to light (the retina or optic nerve disease). An initial evaluation at the time of diagnosis and routine evaluations by a pediatric ophthalmologist are recommended for all individuals with MPS.

Corneal clouding, glaucoma and retinal degeneration are common eye problems in MPS. The cornea (circular window at the front of



CALEB (MPS I)

the eye) can become cloudy due to storage of glycosaminoglycans (GAG), previously called mucopolysaccharides, which disrupt the clear layers of the cornea. Individuals with corneal clouding may not tolerate bright lights (photophobia) due to uneven refraction of the light. Wearing caps with visors or sunglasses can help. If corneal clouding is severe, it usually will reduce sight, especially in dim light. Glaucoma (increased pressure in the globe of the

eye) also may occur in MPS, especially MPS I, and is typically treated with medications. Glaucoma is another cause of photophobia in MPS.

Storage in the retina (the tissue in the back of the eye involved in vision) can result in degeneration of the retina. Retinal degeneration often leads to night blindness (difficulty seeing in lower light) and

5 loss of peripheral vision. 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. The addition of a night light in a hall or bedroom may be beneficial.

For individuals with significantly reduced vision due to corneal clouding, cornea transplantation has been performed. Cornea transplantation is usually beneficial, but poor vision may persist because of underlying involvement of the retina or optic nerve. It is usually very difficult for the ophthalmologist to visualize the retina prior to surgery. If retinal degeneration and/or optic nerve atrophy is present, even with a clear cornea, decreased vision may persist. Recurrence of corneal clouding in the transplanted cornea has been reported in some individuals. The recurrence is believed to be due to GAG slowly diffusing into the cornea from the surrounding tissues.

Hearing

Hearing loss (deafness) is common in all types of MPS diseases. Hearing loss may be conductive or sensorineural (nerve) deafness or both (mixed deafness) and may be made worse by frequent ear infections. Conductive hearing loss is an abnormality in the conduction of sound, involving the middle ear bones, while sensorineural hearing loss is a defect in the transmission of sound along the nerve.

Conductive deafness

Correct functioning of the middle ear depends on the pressure behind the eardrum being the same as the pressure in the outer ear canal and in the atmosphere. This pressure is equalized by the Eustachian tube, which runs to the middle ear from the back of the throat. If the tube is blocked due to GAG deposits and/or inflammation, 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 may build up. The buildup of fluid can result in frequent otitis media (ear infections) as seen in MPS. The continued presence of fluid (middle ear infections) after antibiotic treatment is common and in time can become thick like glue.

To remove the fluid, a small incision is made in the eardrum (myringotomy) and the fluid is sucked out. A small ventilation tube (standard or T-tube) is then inserted to keep the hole open and

6 allow air to enter from the outer ear canal and fluid to drain out. In MPS, the storage in the Eustachian tube may require long-term tube placement.

Standard ventilation 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, resulting in fewer ear infections and improved hearing. Most children with MPS require a light, general anesthetic for myringotomy and tube placement.

Sensorineural (nerve) deafness

In most cases, the cause of permanent nerve deafness is damage to the tiny hair cells in the inner ear. It may be accompanied by conductive deafness, in which case the hearing loss 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 is traditionally tested with an audiogram. However, children with MPS often have trouble cooperating with the hearing test, so an auditory brain stem response (ABR) can be done to assess hearing. For many individuals with MPS, sedation or general anesthesia may be required to perform an ABR.

In general, it is felt that hearing aids are underutilized in MPS diseases. It is important that individuals with MPS have their hearing monitored regularly so problems can be treated early to maximize the child's ability to learn and communicate. Frequency of hearing evaluations should be determined by an ear nose and throat specialist, such as an audiologist and/or otolaryngologist.

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Airway obstruction

A very common and severe problem for many individuals with MPS is airway obstruction. Obstruction of the airway can be caused by narrowed or blocked nasal passages, a large tongue, enlarged adenoids and tonsils, abnormal trachea (windpipe) and decreased rib movement with breathing.

Tonsils and adenoids often become enlarged and can partly block the airway. It is not uncommon for adenoids to re-enlarge after having been once removed. The neck is usually short, which contributes to problems in breathing. The trachea becomes narrowed by storage material and is often more floppy or softer than usual

7 due to abnormal cartilage rings in the trachea. Nodules or excess folding of airway tissue above the vocal cords can further block the airway. The normal relaxation of the airway muscles and decreased tone during sleep also is a significant contributing factor to airway narrowing. The combination of storage in the airway and normal narrowing during sleep explains why airway obstruction in MPS is initially a problem during sleep. As storage progresses, airway obstruction can occur at any time and is usually worse with upper respiratory illness.

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 expanded, there is an increased risk of infections (pneumonia).

Obstructive sleep apnea (temporary stopping of breathing during sleep) is the most common airway problem in MPS. Obstructive sleep apnea is characterized by loud snoring, apnea, frequent awakenings or arousals, and fatigue during the day. Apnea may occur for short periods while asleep. Pauses in breathing of up to 10–15 seconds are considered normal. This noisy breathing which stops and starts can be very frightening for family or friends to hear. Parents may fear that their child is dying. Fatigue during the day can be caused by never achieving a deep sleep due to frequent awakening caused by decreased oxygen levels in the blood.



ROBIN (ML)

Airway obstruction and valvular heart disease is a serious problem which can lead to heart failure with right-sided hypertrophy (increase in size) of the heart because the heart strains to provide enough oxygen in the blood by attempting to work harder.

If an individual with MPS has significant snoring or episodes of interrupted breathing (apnea), he or she should be evaluated by a pulmonologist (lung specialist) using a polysomnogram (sleep study). Many individuals with MPS may be very noisy breathers for years and not develop significant airway obstruction. A sleep study is a non-invasive way to assess the airway status.

8 A sleep study is performed by spending a night in a special room at the hospital. Monitors are placed on the skin and connected to a computer to measure the levels of oxygen in the blood, heart rate, breathing rate and effort, airflow through the nose and brain waves during sleep. From this study doctors can assess how much blockage to breathing is present, how much trouble the person is having moving air into the lungs during sleep, and how much effect this

Routine pulmonary function testing and sleep studies are recommended in individuals with attenuated MPS to assess airway problems.

has on his or her body. Flexible bronchoscopy can be used to directly visualize the airway to better determine the problem areas causing narrowing and/or obstruction. Routine pulmonary function testing and sleep studies are recommended in individuals with attenuated MPS to assess airway problems. Individuals with MPS who have airway disease are at increased

risk for problems associated with anesthesia. See the booklet *Is Your Child Having an Anesthetic?* published by the National MPS Society.

Sleep apnea can be improved in some individuals by removing the tonsils and adenoids, opening the airway with nighttime continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) treatment or tracheotomy. Removal of tonsils and adenoids will help in some cases to lessen the obstruction and make breathing easier, but adenoid tissue may grow back. Nighttime CPAP or BiPAP are methods to open the airway using air pressure, which can help the 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 tolerate it. CPAP or BiPAP can greatly improve the quality of sleep, as well as help prevent or reduce heart failure caused by low oxygen levels at night.

In severe cases of sleep apnea, in particular with heart failure, a tracheotomy (a permanent opening made in the trachea in the front of the neck) may be needed. Most families will try to avoid a tracheotomy because it is invasive and seemingly disruptive of normal daily activities. In fact, many feel that individuals with MPS should receive a tracheotomy earlier than they do. Individuals with a tracheotomy have improved nighttime breathing and decreased episodes of sleep apnea.

Heart

9

The progressive storage of GAG in individuals with MPS can result in abnormal heart valves, narrowing of the coronary arteries and

The progressive storage of GAG in individuals with MPS can result in abnormal heart valves, narrowing of the coronary arteries and weakening of the heart muscle. Individuals with MPS should be seen on a regular basis by a cardiologist.

weakening of the heart muscle (cardiomyopathy). The aortic and mitral valves are affected in many individuals with MPS. Heart valves are designed to open and close in combination to allow blood to be pumped in one direction and to prevent blood from flowing back in the opposite direction. The damaged valves in individuals with MPS may not open fully (resulting in stenosis) or are unable to close tightly (resulting in regurgitation). Both conditions cause the heart to pump harder and increase the risk of heart failure. Individuals

with MPS may have slowly progressive valvular heart disease for years without any apparent clinical effects. Coronary artery disease due to narrowing of the blood vessels in the heart can lead to heart attacks and death. Cardiomyopathy (weak heart muscle) and endocardiofibroelastosis (stiff heart) are conditions that can occur in children with severe MPS I and other severe types of MPS.

Your doctor may hear heart murmurs (sounds caused by turbulence in blood flow in the heart) if the valves become damaged by stored GAG. If a valve is damaged, it may not open fully and/or shut firmly, leading to abnormal flow, turbulence and a murmur. Most individuals with MPS have some degree of murmur or leakage due to abnormal heart valves.

As heart problems occur so frequently in MPS, all such individuals should be seen on a regular basis by a cardiologist. All individuals with MPS should have an electrocardiogram (EKG) and an echocardiogram as often as your cardiologist thinks necessary to show whether any heart problems are beginning. The EKG is painless and similar to the ultrasound screening of

Medications are available to help manage the congestive heart failure and hypertension that can occur in MPS. If the heart failure is due to valvular disease, an operation may be possible to replace the damaged valves. Heart valve replacement has been performed on many individuals with attenuated (milder) forms of MPS, such as MPS I, MPS II and MPS VI.

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, such as coronary artery disease.

In people who are severely affected, the muscle of the heart may be damaged by storage of GAG resulting in cardiomyopathy. The heart also may be put under strain by having to pump blood through abnormal lungs causing cor pulmonale or right heart failure. A number of affected individuals have high blood pressure, which is probably due to blockage of blood vessels. Obstructive airway disease and associated upper respiratory infections can lead to pulmonary hypertension and eventually cause cardiac failure. Management of airway disease can help prevent further stress on the heart.

Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of the median nerve in the wrist due to accumulation of GAG in the nerve canal. The wrist, or carpus, consists of eight small bones known as the carpals, which are joined by a band of fibrous proteins 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; this can cause irreversible nerve damage.

Physical signs of carpal tunnel syndrome are numbness, tingling, pain, clumsiness and weakness of the hand. The nerve damage may cause the muscle at the base of the thumb to waste away and will make it more difficult for a child to oppose his or her thumb in a position for a normal grasp. Loss of function of the thumb is a significant sign of carpal tunnel syndrome. Although many individuals with MPS may not complain of pain, carpal tunnel syndrome may be severe.

Children with MPS should be monitored for carpal tunnel syndrome with nerve conduction studies on a regular basis. Detection and treatment of the problem is most effective prior to severe nerve damage. 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. Similar types of nerve compression can happen elsewhere in the body, such as the feet, and cause localized weakness or pain.

Carpal tunnel syndrome can be treated with splinting, anti-inflammatory medications and surgery to decompress the nerve. A study by Haddad et. al. (1997) found that the majority of children with MPS who have carpal tunnel syndrome did not complain of symptoms. None of the cases in the study worsened after surgical decompression of the nerve. Better neurophysiological recovery was seen in children with mild cases of carpal tunnel syndrome. Therefore, detection and treatment in the early stages of nerve compression, before severe nerve damage occurs, allows for the best outcome.

Bowel problems

Many children with MPS 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 a 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, which controls those bodily functions usually beyond voluntary control. Studies have found storage in the nerve cells in the intestine and it seems likely that abnormal motility in the bowel is the cause of diarrhea.



JONATHAN (MPS II)

An examination by your pediatrician, supplemented by an X-ray if necessary, may establish the cause of diarrhea. The problem may disappear as the child gets older, but it can be made worse by antibiotics prescribed for other problems. Episodic diarrhea in some individuals with MPS appears to be affected by diet; elimination of some foods can be helpful.

If antibiotics are the cause, eating plain, live-culture yogurt is often helpful during episodes of diarrhea. This provides a source of lactobacillus to help prevent the growth of harmful organisms within the bowel, which can cause diarrhea or make it worse. A diet low in roughage also may be helpful.

Constipation may become a problem as the child gets older and less active and as the abdominal 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, which is easy to use.

Liver and kidney

Although the liver can be very enlarged and occasionally affect the ability to breathe, problems associated with significant abnormal function of the liver have not been reported in individuals with MPS. Individuals with MPS usually have elevated GAG in their urine, but significant kidney problems have not been reported.

Hernia

In many individuals with MPS, the abdomen bulges out due to poor posture, weakness of the muscles and the enlarged liver and spleen.



ERIN (MPS III)

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 commonly occur before the individual has been diagnosed with MPS. Inguinal hernias should be repaired because of the high risk of entrapment and subsequent damage to the bowel in the area of

herniation. Umbilical hernias usually occur later than inguinal hernias and are not usually repaired unless they are causing problems. It is very common for an umbilical hernia to recur even with the best surgeon. The abnormal connective tissue secondary to GAG storage is believed to be the cause of the very high recurrence rates after attempted repair.

Dental issues

The teeth can be widely spaced and poorly formed with fragile enamel. Delayed eruption of the permanent teeth is common. It is important that the teeth are well cared for because tooth decay is more likely to occur and may be the cause of unexplained 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 avoid bad breath. Even with the best of dental care, an abscess around a tooth can develop due to abnormal formation and/or a microfracture of the

tooth. Irritability, crying and restlessness can sometimes be the only sign of an infected tooth in a severely affected individual.

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

Skeletal system (Orthopedics)

Most individuals with MPS tend to have problems with bone formation (dysostosis multiplex) and growth. This leads to bone and joint problems as well as neurological problems if nerves get compressed by bone or deposits of glycosaminoglycans.

Neck

The bones that stabilize the connection between head and neck can be malformed (odontoid dysplasia) in individuals with MPS, making the neck unstable. If severe pain or pain associated with weakness or tremors in the arms or legs occurs, studies of the neck (MRI and flexion-extension X-rays) should be performed to evaluate for slippage (subluxation) of the neck vertebrae. Cervical fusion surgery is usually required to connect the bones to each other so they do not slip anymore.

Problems in the cervical spine are perhaps the most serious facing individuals with MPS IV. The neck problems need to be discussed at the time of diagnosis because serious problems can occur before 5 to 6 years of age. With odontoid dysplasia the neck can become unstable, which places the spinal cord at risk for life-threatening injury. The spinal cord is a large bundle of nerves that carries messages between the brain and the rest of the body. If the cord is compressed or squeezed (cervical myelopathy), there may be gradual worsening of nerve damage with paralysis or death occurring if left untreated. Children with MPS IV should be referred to an orthopedic surgeon at an early age and a close watch should be kept on the condition of the cervical spine. MRI studies or X-rays should be performed with the head bent forward and with the neck straight (flexion and extension view) and repeated as the years pass to monitor the situation. A baseline study of the neck is recommended at the time of diagnosis.

The bones of the spine (vertebrae) normally line up from the neck to the buttocks. Individuals with MPS often have poorly formed vertebrae that may not stably rest on top of each other. One or two

Severe curvature of the spine, kyphosis or scoliosis, may require surgical intervention.

of the vertebrae in the middle of the back are sometimes abnormally shaped or slightly smaller than the rest. Backward slippage of the vertebrae can cause an angular curve (kyphosis or gibbus) to develop, but it usually does not need treatment. Bracing is sometimes used for

management of kyphosis (front-to-back curvature of the spine) and scoliosis (side-to-side curvature of the spine).

Severe curvature of the spine, kyphosis or scoliosis, may require surgical intervention. In general, fusion with bone is the best alternative because hardware-like rods are not tolerated well. In any case, the soft bones make the surgery and recovery difficult. Many individuals end up needing multiple procedures. An orthopedic surgeon who has previous experience with individuals with MPS may need to be consulted to obtain the best outcome.

Hip

Some individuals with MPS have been recognized to have significant abnormalities of the hip joint (hip dysplasia) resulting in increased pain and decreased ability to walk normally. Abnormal formation of the hip joint may result in an increased risk of injury to the hip. Treatment with non-steroidal anti-inflammatory medications has been beneficial for some individuals.

Miscellaneous issues

Physical therapy

Joint stiffness is common in all forms of MPS, and the maximum range of motion of all joints may become limited, which 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 in the clinical course. 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 is common sense for individuals to be as active as possible to maintain joint function and improve their general health. A physical therapist may be able to suggest ways of achieving this through a combination of daily activities and passive range-of-motion exercises.

Later in the individual's life, joint stiffness may cause pain, but this may be relieved by heat and ordinary pain medication. Limited movement in the shoulders and arms may make dressing difficult. Stiff hips and knees with tight heel cords can make walking more 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.

Individuals should be as active as possible to maintain joint function and improve general health. A physical therapist may be able to suggest ways of achieving this through a combination of daily activities and passive range-of-motion exercises.

Anesthetics

Giving a general anesthetic to an individual with MPS requires skill and should always be undertaken by an experienced anesthesiologist. Inform your child's school or any other caregivers of this in case you cannot be contacted in the event of an emergency. If you must go to a different hospital in an emergency, be sure to tell the anesthesiologist 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 advanced intubation techniques, such as the use of a flexible bronchoscope, laryngeal mask airway or fiber optics. 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 also is difficult to remove the breathing tube after surgery is completed, due to excessive swelling. It is important to advise physicians of the critical nature of these problems and that many problems have occurred during anesthesia of individuals with MPS. For any elective surgery in a child with MPS, it is important to



ELLIOT (MPS I)

16 select a pediatric anesthesiologist who has experience with difficult airways. This may require that the surgery be performed at a regional medical center instead of a local hospital. Parents often find it helpful to schedule more than one procedure when their child receives anesthesia, e.g. dental work and PE tubes. Additional information on anesthesia can be found in the booklet *Is Your Child Having an Anesthetic?* published by the National MPS Society.

Diet

There is no scientific evidence that a particular diet has any helpful effect on people with MPS, and symptoms such as diarrhea tend to come and go naturally. Some parents, however, find that a change in their child's diet can ease problems such as excessive mucus,

Consult your doctor or a dietician if you plan major dietary changes to make sure the proposed diet does not leave out essential items.

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 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 food appears to increase the child's symptoms.

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

Some individuals with MPS have severe neurological problems in the late stages of their disease, resulting in increasing problems with feeding. As chewing and swallowing become more difficult, the individual with MPS begins to lose weight and the time required by the caregiver for feeding can become very prolonged. Aspirating because of swallowing problems can lead to pneumonia. Placement of a gastrostomy tube (G-tube) may be needed to allow adequate nutrition to prevent weight loss and to improve the quality of life for the individual with MPS and caregivers. Any individual being considered for G-tube placement should be evaluated for gastroesophageal reflux (GERD) because G-tube placement may worsen existing GERD.

Hyperactivity

17 Hyperactivity is a common and sometimes very severe problem in individuals with MPS, especially MPS III. Many children with MPS II and MPS III go through a hyperactive stage when they are into everything, difficult to control and unaware of danger. In general, the hyperactivity reaches a peak at the time of maximum development and then decreases slowly as the child with MPS starts to regress. It is better to adapt the house to the child because the behavior problems are generally not altered by medications. A yard where the child can run about safely is a great asset. Consistency in behavior modification programs by all caregivers can be helpful for some hyperactive children with MPS. See additional information about home modifications in the booklet *Daily Living with MPS and Related Diseases* published by the National MPS Society.

It can be helpful if the child can join a play group, attend school or an after-school program where a variety of activities occupy the child. Ideally there should be space for the child to run about and expend energy. This also allows the child to keep fit for as long as possible. Many children are calmed by the movement of a car and travel well. Some children with MPS have difficulty with loud and busy environments. Some parents find it very helpful if they can set aside a room or part of a room in the house especially for their child with MPS.

Acetyl CoA: α -glucosaminide acetyltransferase: Lysosomal enzyme deficient in MPS III C.

Adenoids: The collection of lymphatic tissue at the rear of the nose. Enlargement of the adenoids may cause obstruction of breathing through the nose.

Adenoidectomy: Surgical procedure to remove adenoid growth.

α -L-Iduronidase: Lysosomal enzyme deficient in MPS I.

α -N-Acetylglucosaminidase: Lysosomal enzyme deficient in MPS III B.

Amino acid: A class of chemical compounds that can be built up to form larger polymers called proteins. In most biological systems there are 20 common amino acids that can be linked in various combinations to generate larger molecules containing 100–10,000 amino acids. These larger molecules, or proteins, carry out most of the active functions within a cell or an organism.

Amniocentesis: Procedure involving withdrawal of amniotic fluid, the fluid that surrounds the growing fetus in the uterus, generally performed between the 15th–20th weeks of pregnancy by inserting a needle through the abdominal wall into the uterus. Cells that are contained in the fluid can be isolated and used for prenatal diagnosis of gender and for particular genetic conditions (including MPS).

Anterior: Front.

Arylsulfatase B: Lysosomal enzyme deficient in MPS VI.

Atrophy: Wasting of tissues, organs or the entire body, as from death and reabsorption of cells, diminished cellular proliferation, decreased cellular volume, pressure, ischemia, malnutrition, lessened function or hormonal changes. Often associated with brain disease in children with MPS.

Autosomal recessive inheritance: A pattern of inheritance in which a nondominant (recessive) gene on a non-sex determining chromosome (autosome) results in a person either being a carrier of a trait or being affected. Males and females are affected with equal frequency. There is usually no family history of the trait. Instead, it is revealed when two unaffected parents who are both carriers of a particular recessive gene have a child who receives two copies of the recessive gene.

β -Galactosidase: Lysosomal enzyme deficient in MPS IV B.

β -Glucuronidase: Lysosomal enzyme deficient in MPS VII.

Blood-brain barrier: The blood vessels of the brain (and the retina) are much more impermeable to large molecules than blood vessels elsewhere in the body. This has important implications for the ability of the organism to mount an immune response and to provide protection to these tissues, although the basis for the difference in blood vessel permeability is not well understood. The implications for human genetic disease are that it is far more difficult to provide therapeutic treatment to neural (brain) tissues than in other tissues in the body. Since many lysosomal storage diseases have a specific involvement in the neural tissues it is critical to provide access to these tissues during treatment.

Bone marrow transplant: See **stem cell transplant**.

Bone marrow: Tissue found in the center of most bones. It is the site in which most blood cells are made, including red blood cells involved in transport of oxygen in the blood and white blood cells.

BiPAP: Bi-level positive airway pressure, often used for people with sleep apnea to open the airway at night using two pressure settings.

Carpal tunnel: The space between the carpal bones of the wrist and the connective tissue over the flexor tendons. The wrist or carpus consists of eight small bones known as carpals, which are joined by a band of fibrous proteins called ligaments. Nerves have to pass through the wrists in the space between the carpal bones and the ligaments.

Carpal tunnel syndrome: Thickening of the ligaments in the carpal tunnel that causes pressure on the nerves. This can cause irreversible nerve damage if not surgically corrected. In children with MPS carpal tunnel syndrome occurs because of accumulation of GAG deposits.

Carrier: An individual who has a recessive, disease-causing version of a gene at a particular site on one chromosome of a pair, and a normal version of a gene at that location on the other chromosome. By definition, carriers of a recessive condition do not have clinical signs and symptoms of the condition.

Cerebrospinal fluid (CSF): The fluid that surrounds the brain and spinal cord which is produced in the ventricles of the brain.

Chorionic villus sampling (CVS): Prenatal diagnostic procedure involving sampling the chorionic villi, generally performed between the 10th and 12th weeks of pregnancy. The test can reveal many, but not all, genetic abnormalities. The decision to have prenatal testing and the appropriate method of prenatal diagnosis should be discussed with your healthcare provider. Currently amniocentesis is more widely available than CVS for prenatal testing for MPS diseases.

Chromosome: The linear, double-stranded structural unit of genetic material consisting of DNA and supporting proteins called chromatin. Human cells are expected to contain 46 chromosomes identified as 23 pairs; 22 pairs are autosomes and one pair is the sex chromosomes.

Contracture: Muscle shortening resulting in loss of motion of the joint.

Cord blood transplant: See **stem cell transplant**.

Cornea: The transparent circular part of the front of the eye.

Corneal clouding: Disruption of the clear layers of the cornea in individuals with MPS due to storage of GAG, causing a milky appearance of the eye, decreased vision and sensitivity to light. Cloudy corneas can be replaced via a corneal transplant.

Corneal transplant: Surgical procedure to remove cloudy cornea and replace with a healthy, donated cornea.

CPAP: Continuous positive airway pressure, often used for people with sleep apnea to open the airway at night using a constant pressure setting.

Cranium: The part of the skeleton that encloses the brain.

Deposits: See **glycosaminoglycans (GAGs)**.

DNA: The molecule that encodes the genes responsible for the structure and function of an organism and allows for transmission of genetic information to the next generation.

Dysostosis: The abnormal formation of bone caused by the lack of proper ossification.

Echocardiogram: Ultrasound of the heart to evaluate for heart valve and heart muscle function.

Electroencephalogram (EEG): A record of the electric potentials in the brain recorded by attaching electrodes on the scalp. Often this procedure is used to look for seizure activity.

Electrocardiogram (EKG or ECG): A study of the currents in the heart that control its contraction.

Electromyography (EMG): Continuous recording of the electrical activity of a muscle by means of electrodes inserted into the muscle fibers. Used, although not required, to diagnose carpal tunnel syndrome (can be diagnosed by nerve conduction studies).

Enamel: The hard outer covering of the crown of a tooth.

Enzyme replacement therapy: A therapeutic approach for a genetic disease whereby the missing protein is manufactured separately and given intravenously to the patient on a regular basis.

Enzyme: A protein that facilitates a biological reaction without itself being used up in the reaction (i.e. it acts as a catalyst). An enzyme acts by binding with the substance involved in the reaction (the substrate) and converting it into another substance (the product of the reaction).

Fontanelle: The soft spot on a baby's head.

Galactose 6-sulfatase: Lysosomal enzyme deficient in MPS IV A.

Gastrostomy (G-tube): A surgical procedure in which an opening is made into the stomach from the outside. It is usually performed to allow nutrition and/or medications to be administered directly into the stomach when swallowing is difficult because of disease or obstruction of the esophagus.

Gene: Basic unit of heredity that codes for a specific protein leading to a particular characteristic or function.

Gene therapy: A therapeutic approach to a genetic disease whereby treatment is achieved by inserting a corrected copy of the gene or a new gene to replace the incorrect version.

Genetic code: Information carried by the DNA molecules that decides the physical traits of an offspring. The code fixes the pattern of amino acids that build body tissue proteins within a cell.

Genu valgum: Knock-knee (knees curving inward in relation to the thigh).

Gibbus: Kyphosis (curvature of the upper spine).

Glaucoma: A condition in which loss of vision occurs because of abnormally high pressure in the eye.

Glycosaminoglycans (GAGs): Long repeating chains of complex sugar molecules. See **mucopolysaccharide**.

Hematopoietic stem cell transplantation (HSCT): Blood stem cell transplant (hematopoietic refers to the blood). Possible sources of blood stem cells include bone marrow, peripheral blood and umbilical cord blood. See **stem cell transplant**.

Heparan N-sulfatase: Lysosomal enzyme deficient in MPS III A.

Hepatosplenomegaly: Enlargement of the liver and spleen. (Hepatomegaly: enlargement of the liver; Splenomegaly: enlargement of the spleen).

Hernia: Protrusion of a part or structure through the tissues normally containing it.

Heterozygote: An individual possessing a variant gene and a normal gene at identical sites of homologous chromosomes. (adjective: heterozygous).

Heterogeneity: Variations in clinical features (characteristics) within a specific disease.

Homologous chromosomes: A pair of chromosomes, one from each parent, having the same gene loci in the same order.

Homozygote: An individual possessing a pair of identical genes, either both normal, or both variant, at identical sites on homologous chromosomes (adjective: homozygous).

Hurler syndrome: Severe end of a clinical spectrum of MPS I. See **MPS I**.

Hurler-Scheie syndrome: Clinical spectrum that is intermediate between Hurler and Scheie syndromes. See **MPS I**.

Hunter syndrome: See **MPS II**.

Hyaluronidase: Lysosomal enzyme deficient in MPS IX.

Hydrocephalus: An abnormal increase in the amount of cerebrospinal fluid within the ventricles of the brain. Communicating hydrocephalus or increased pressure may be caused by obstruction to the outflow of cerebrospinal fluid from the ventricles or a failure of its reabsorption into the cerebral sinuses. It can be treated using a ventriculoperitoneal shunt.

Hypoxia: A deficiency of oxygen in the tissue or blood.

Inguinal hernia: Hernia occurring in the lower abdomen and groin.

I-Cell disease: See **ML II**.

Iduronate sulfatase: Lysosomal enzyme deficient in MPS II.

Individualized Education Plan (IEP): An IEP is a program designed for each child within the public school system who receives special educational services with goals to improve teaching, learning and appropriate goal setting for each individual. Often a team including members from the school system and the family are involved in designing the IEP, and federal legislation is in place to guide the development of appropriate IEPs.

Intubation: The placement of a breathing tube during anesthesia.

Joint contracture: Fibrosis of muscle tissue producing shrinkage and shortening of the muscle without generating any strength. It is usually a consequence of pain in or disuse of a muscle or limb.

Kyphosis: Abnormal angular curve of the vertebrae of the spine (also called gibbus).

Lumber puncture: A procedure in which cerebrospinal fluid is withdrawn by means of a needle inserted into the membrane space in the region of the lower back. This procedure may be performed to measure intracranial pressure to aid in diagnosing hydrocephalus.

Lysosomal enzyme: A protein found within the cytoplasm of most cells, especially leukocytes, kidney and liver cells, which are key components in the function of digestive processes within the cell.

Lysosomal storage disease (LSD): An inborn error of metabolism resulting in a particular lysosomal enzyme deficiency. At this time there are more than 40 identifiable lysosomal storage diseases.

Lysosome: A specialized compartment (organelle) in the cytoplasm of cells that contains enzymes responsible for breaking down substances in the cell.

Maroteaux-Lamy syndrome: See **MPS VI**.

Melatonin: A compound involved in circadian rhythms sometimes used as a sleep aid for those with MPS and related diseases.

Mitral valve prolapse: Flaps between two parts of the heart, the left atrium and the left ventricle, don't close evenly allowing a small amount of blood to leak back into the left atrium.

ML II: Also called **I-Cell disease**, caused by a deficiency of the lysosomal enzyme N-acetylglucosaminyl-1-phosphotransferase. Autosomal recessive disease characterized by severe psychomotor retardation and by many of the clinical features seen in severe MPS I.

ML III: Also called **Pseudo-Hurler Polydystrophy**, caused by a deficiency of the lysosomal enzyme N-acetylglucosaminyl-1-phosphotransferase. Autosomal recessive disease with less severe disease course than ML II, presenting later in life, with survival into adulthood.

Morquio syndrome: See MPS IV.

MPS I: Also called **Hurler**, **Hurler-Scheie** and **Scheie**, caused by a deficiency of the lysosomal enzyme α -L-Iduronidase. Autosomal recessive, heterogeneous disease characterized by a wide range of clinical involvement, including corneal clouding, bone changes, stiff joints, large liver and spleen, and heart disease.

MPS II: Also called **Hunter syndrome**, caused by a deficiency of the lysosomal enzyme Iduronate sulfatase. X-linked recessive, heterogeneous disease characterized by a wide range of clinical involvement, including large liver and spleen, stiff joints, bone changes and heart disease.

MPS III: Also called **Sanfilippo syndrome**, an autosomal recessive disease classified into four types based on the enzyme deficiency. Features in each type are similar and characterized by severe central nervous system degeneration but only mild somatic (relating to the body) problems.

MPS III A: Caused by a deficiency of the lysosomal enzyme heparan N-sulfatase.

MPS III B: Caused by a deficiency of the lysosomal enzyme α -N-acetylglucosaminidase.

MPS III C: Caused by a deficiency of the lysosomal enzyme acetyl CoA: α -glucosaminide acetyltransferase.

MPS III D: Caused by a deficiency of the lysosomal enzyme N-acetylglucosamine 6-sulfatase.

MPS IV: Also called **Morquio syndrome**, autosomal recessive disease classified into two types based on the enzyme deficiency, each with a wide range of clinical manifestations. Both types are characterized by short trunk dwarfism, fine corneal deposits and preservation of intelligence.

MPS IV A: Caused by a deficiency of the lysosomal enzyme galactose 6-sulfatase.

MPS IV B: Caused by a deficiency of the lysosomal enzyme β -galactosidase.

MPS VI: Also called **Maroteaux-Lamy syndrome**, caused by a deficiency of the lysosomal enzyme arylsulfatase B. Autosomal recessive disease with bone abnormalities, corneal clouding and normal intelligence.

MPS VII: Also called **Sly syndrome**, caused by a deficiency of the lysosomal enzyme β -Glucuronidase. This is an autosomal recessive disease characterized by large liver and spleen, bone abnormalities and a wide spectrum of severity.

MPS IX: An autosomal recessive disease, caused by a deficiency of the lysosomal enzyme Hyaluronidase, characterized by short stature, soft-tissue masses and normal joint movement and intelligence.

Mucopolipidosis: Term coined to denote diseases that combined clinical features common to both the mucopolysaccharidoses and the sphingolipidoses (diseases characterized by abnormal lipid or fat metabolism, affecting nerve tissue). See **ML II** and **ML III**.

Mucopolysaccharide: A complex carbohydrate molecule that is a common constituent of secretions and the connective tissue between cells. Although the molecules were originally called "mucopolysaccharides" because of their ability to form viscous, mucin-like solutions, the terminology was revised to "proteoglycans" and subsequently to "glycosaminoglycans" in the last decades.

Mutation: A change in the genetic material (DNA) of a cell that alters expected genetic processes.

N-acetylglucosamine 6-sulfatase: Lysosomal enzyme deficient in MPS III D.

N-acetylglucosaminyl-1-phosphotransferase: Lysosomal enzyme deficient in ML II and ML III.

Odontoid dysplasia: Malformation in the bones that stabilize the connection between head and neck.

Otitis media: Inflammation of the middle ear occurring commonly in children as a result of an infection and often causing pain and temporary hearing loss.

Papilledema: Swelling around the optic disc.

Port-a-cath: Brand name for a long-term indwelling catheter into a central vein with access through the skin.

Posterior: Back.

Precocious puberty: The early onset of sexual maturation.

Preimplantation Genetic Diagnosis (PGD): Also known as preimplantation testing. A procedure used to decrease the chance of a particular genetic condition for which a fetus is specifically at risk by testing one cell from embryos from in vitro fertilization for the DNA mutation known in the family. Only embryos found not to carry the DNA mutation are transferred to the mother's uterus.

Pseudo-Hurler Polydystrophy: See **ML III**.

Recessive disease:

Autosomal recessive: A pattern of inheritance requiring the presence of two copies of a particular gene mutation in order to have express clinical signs and symptoms of a condition. Pattern of inheritance seen in all MPS diseases with the exception of MPS II.

X-linked recessive: A mode of inheritance in which a mutation in a gene on the X chromosome causes males to have clinical features of a particular condition as they only have one X chromosome. Pattern of inheritance seen in MPS II.

Recombinant DNA: DNA that contains genes from different sources that have been combined by the techniques of genetic engineering.

Rhinorrhea: Thick, chronic discharge of mucus from the nose.

Scaphocephalic: Having a long, narrow head shape.

Sanfilippo syndrome: See **MPS III**.

Scheie syndrome: Mild end of a clinical spectrum of MPS I. See **MPS I**.

Scoliosis: Lateral (sideways) deviation of the spine.

Seizure: Disruption of electrical signals in the brain. Seizures may cause brief changes in a person's body movements, awareness, emotions or sense such as taste, smell, vision or hearing.

Sleep apnea: A temporary cessation of breathing during sleep generally caused by obstruction of the airway.

Sly syndrome: See **MPS VII**.

Spinal fusion: Surgery to connect the spinal bones to each other to prevent slippage.

Spleen: A large organ situated on the left side of the body below and behind the stomach.

Stem cell transplant: A therapeutic treatment for patients where stem cells from bone marrow, peripheral blood, or from umbilical cord blood are infused into the bloodstream after the original bone marrow cells have been ablated (destroyed) by either chemotherapy and/or radiation therapy. The cells migrate to the interior of certain bones and begin producing immature cells called "committed progenitors." These committed progenitors produce colonies of cells that eventually mature into red blood cells, white blood cells or platelets. The purpose is to allow the donor cells to repopulate the bone marrow and various other tissues of the recipient. If the cells also can provide the missing gene and function to the recipient then it can sometimes improve clinical symptoms. It is important to note that the process of destroying the recipient's bone marrow cells is extremely invasive and leaves the individual immunocompromised and susceptible to life-threatening infections. Also it is critical to have donor cells come from an individual with compatible tissue types in order to avoid rejection of the donor cells after the transplant bloodstream and the immune cells that provide protection from infection.

Stem cells: A cell whose daughter cells may differentiate into other cell types.

Sternum: A long flat bone, articulating with the cartilages of the first seven ribs and with the clavicle, forming the middle part of the anterior wall of the thorax.

Swallowing study (modified barium swallow study): Videotaped X-ray of a individual's oral (mouth) and pharyngeal (throat) mechanism during eating or drinking. This procedure is often ordered to evaluate for obstruction or aspiration. The results from this procedure may allow for a therapist to better identify ways to safely feed the individual and ways to help the family make appropriate modifications.

Trachea: The air tube extending from the larynx to the thorax (level of the fifth or sixth thoracic vertebra) where it divides into the right and left main bronchi.

Tracheostomy: A surgical procedure in which a hole is made into the trachea through the neck to relieve obstruction to breathing. A curved metal, plastic or rubber tube is usually inserted through the hole.

Trigger finger: Caused by a thickening of the tendon that bends the fingers, often experienced as swelling in the palm of the hand as the finger is moved.

Ventriculoperitoneal shunt: A thin tube that drains fluid from the brain into the abdominal cavity used in the treatment and management of hydrocephalus.

Umbilical hernia: A hernia in which bowel or omentum protrudes through the abdominal wall under the skin at the umbilicus (navel).

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

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

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

Benefits of membership in the National MPS Society:

- *Courage*, our quarterly newsletter containing stories and information about individuals with MPS and related diseases;
- Educational materials such as fact sheets and an MPS glossary;
- Conference and education scholarships;
- The Family Assistance Program, which provides financial support for durable medical goods;
- News about various Society sponsored conferences and gatherings, where families and leading MPS scientists, physicians and researchers join together for a common cause;
- Information on local events, such as regional social events and fundraisers. These events create opportunities for families to meet each other and help raise community awareness of these rare genetic diseases; and
- A listing in our annual directory of members that assists families to connect with one another.



For more information or to join the National MPS Society:

Visit www.mpssociety.org

Contact us at **877.MPS.1001**

Or email us at info@mpssociety.org