

The Voice of the Patient

Summary report resulting from an externally conducted Patient-Focused survey

Hunter syndrome (MPS II)

Cognitive and Behavioral results from the Toileting Ability Survey

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The Voice of the Patient Report for Hunter syndrome (MPS II)

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Introduction

Hunter syndrome or Mucopolysaccharidosis type II (MPS II) is a rare, X-linked, lysosomal storage disease caused by a deficiency in the enzyme iduronate-2-sulfatase. In affected patients, glycosaminoglycans (GAGs) “accumulate in the lysosomes of many tissues and organs and contribute to the multisystem, progressive pathologies seen in Hunter syndrome. The nervous, cardiovascular, respiratory, and musculoskeletal systems can be involved in individuals with Hunter syndrome.” [1]

The incidence of Hunter syndrome is 1 in 170,000 male births. Severe neurologic involvement is present in 75% of all patients, who have cognitive impairment and developmental regression. [2,3]

Symptoms of MPS II can generally be categorized as somatic, neurocognitive, and neurobehavioral. Somatic symptoms often include coarse facial features, hepatosplenomegaly, skeletal abnormalities, hernias, obstructive sleep apnea, atrial and mitral valve regurgitation, carpal tunnel syndrome, hearing loss, stiff joints, restricted airway, elevated intracranial pressure, macroglossia, unexplained diarrhea, and frequent respiratory infections. Neurocognitive symptoms frequently include developmental delay, speech delay or lack of speech development, and progressive loss of cognitive abilities. Neurobehavioral symptoms often include short attention span and high distractibility, impulsivity, heightened activity, sensory seeking behavior, emotional dysregulation, abnormal social interaction, poor sleep, and a reduced sense of danger. [4]

In the severe or neuronopathic form, the onset of disease becomes apparent within 2–4 years of age, and without treatment for the associated neurodegeneration, death generally occurs in the second decade of life. [2,3] Such patients generally exhibit symptoms across the somatic, neurocognitive, and neurobehavioral spectrums, although with substantial heterogeneity among patients. In contrast, patients with the non-neuronopathic form, also known as attenuated or mild form, generally only exhibit the somatic symptoms of MPS II, which can be severe and debilitating, but without cognitive or behavioral symptoms other than, in some cases, impaired intelligence and reduced attention. [6]

The burden of caring for a child with MPS II is significant. A recent study of neuronopathic patients and their caregivers detailed the extensive demands of caregivers, spending on average over ten hours per day caring for the medical and daily living needs of their child with MPS II. [7] The neuronopathic and neurobehavioral symptoms specifically can contribute to a caregiver’s social withdrawal, psychological stress, exhaustion, hypervigilance, as well as financial and vocational strain. [4]

Because of the progressive neurological decline, the impact on families and caregivers, and early mortality in the neuronopathic form, there is an urgent need for treatments. As noted specifically in multiple panels at the U.S. Food and Drug Administration, in neurodegenerative disorders such as MPS II, the objective of an experimental therapy could include slowing down the progressive neurological decline, stabilizing cognitive abilities at the current level, or even reversing the neurological impact. [9,10]

Treating neuronopathic MPS II

Traditionally, treatment for MPS II focused on palliative care then moved forward with therapies to address the somatic symptoms. The approval of idursulfase (Elaprase®), and enzyme replacement therapy (ERT) in 2006 in the United States (and thereafter in many other countries) has brought reported stabilization and improvement in somatic symptoms such as reducing liver and spleen volumes, improving forced vital capacity, and an improvement in the 6-minute walk. [10] Patients receive ERT weekly with a duration of 4-6 hours. Unfortunately, ERT does not cross the blood-brain barrier, so neurocognitive functioning continues to decline.

Haematopoietic Stem Cell Transplantation (HSCT) has been used with varying degrees of success in the somatic symptoms and in some cases, with reported stability and improvement in the cognitive and behavioral profiles as well, but more research is needed given the high risk of morbidity and mortality in contrast with the standard of care and other promising research. [11] Specifically, there is no research on why neurodegeneration continues in many cases of HSCT and Bone Marrow Transplant (BMT) in MPS II.

Experimental therapies currently under exploration for treatment of the neuronopathic symptoms of MPS II include intrathecal enzyme replacement therapy, gene therapy, gene editing, fusion proteins to permit enzymes to cross the blood-brain-barrier from an intravenous infusion (for example, using the insulin receptor or the transferrin receptor), substrate reduction therapy, and chaperone molecules. [12]

However, there is currently no FDA-approved treatment that addresses the neurocognitive symptoms and decline in MPS II.

Hunter Syndrome/MPS II FDA-requested Listening session

In February 2020, the FDA conducted a listening session with parents and caregivers. There are some significant outcomes from that session that directly tie to the need for a solution to address the neurocognitive symptoms in Hunter syndrome. [13]

In the listening session, a “majority of caregivers indicated they would be willing to accept severe or life-threatening risks” to gain improvement in their child’s disease. The report goes on to say that “four of the seven people who said this specifically acknowledged that the prognosis of the disease is death if left untreated.”

When asked *“Of all the symptoms that your child experiences because of MPS II, can you tell us which symptom has the greatest impact on your child’s life and in what way,* a majority of the caregivers said cognitive delay is the most burdensome symptom experienced. This includes communication and adaptive skills. Some of the impacts described as a result of this symptom include a short attention span, impulsive behavior, irritability or aggression, and the constant need for attention.”

The caregivers were asked in the listening session: “When thinking about the most burdensome symptoms your child experiences, can you describe what improvement

would look like to you? Nearly all caregivers indicated that improvements in communication would signify improvement. This includes saying “hello,” writing, communicating at an age- appropriate level, and interacting and playing with siblings and/or peers. Caregivers shared that they want patients to not only communicate with them, but also with others. They want them to be able to communicate when they are in pain or when they need to use the bathroom. Showing emotion appropriately, improved focus, and less outbursts could also be indicative of improvement.

Caregivers also described improvement as patients becoming self-sufficient and independent. This was defined as the ability to care for their basic needs, including being potty-trained and performing daily routines such as brushing their teeth, using the bathroom, putting on shoes and taking showers independently. Caregivers expressed that improvement would also include patients participating in mainstream education.”

Recognizing the progressive nature of the disease, caregivers were asked if there are “specific activities your child cannot do as fully as you would like because of MPS II?” “A majority of caregivers indicated that patients cannot focus or maintain eye contact. Caregivers shared that patients are hyperactive, impulsive, and unable to self-entertain. Some caregivers shared that it is difficult for patients sit through a movie, sit down so they can be read to, and play with other kids. Most patients are unable to participate in activities because of their limited ability to focus and communicate.”

“Most parents indicated that patients’ symptoms either plateaued or worsened over time. Caregivers added that patients also plateaued in their learning ability and decreased in ability to control their body. Caregivers shared that patients developed hearing loss over time. Patients experienced worsening of attention span, hyperactivity, and memory loss. The impact of decreased body control includes being accident-prone and not being able to use the toilet, resulting in the use of diapers.” [13]

Understanding the Impact of Neurocognitive Decline

To further understand the impact of neurodegeneration on boys with Hunter syndrome and their caregivers, Project Alive conducted a survey, which was administered to caregivers of individuals with MPS II over a period of two weeks in August 2019. Data collection for this study was conducted through the Backpack Health application.

While Backpack Health users were asked to enter full or partial dates when completing the survey, this information was not provided directly to the authors for this study. Instead, only years, or dates shifted using the offset date method were provided. Because of this study design, ages and time periods were calculated with 2019 being the current date (data being collected in Q3 2019) and by subtracting and averaging years.

For this report, we looked at the cognitive and behavioral data (a subset of the Toileting Abilities Survey – [14]) from 104 caregivers of boys with the severe type of MPS II. Based on survey results from 104 boys with severe Hunter syndrome, the mean age of diagnosis was 2.63, the median age was 3, and the mode was 3. The age of diagnosis

ranged from less than one year to eight years of age. The age at the time of the survey for the boys ranged from 1 to 22, with a mean of 9.24, a median age of 9, and a mode of 9.

Of the boys with severe Hunter syndrome included in the survey, 99 were currently receiving enzyme replacement therapy (95%), and 5 were not.

For the cognitive and behavioral section of the survey, we asked caregivers to answer 14 questions with yes, no, or unsure.

Figure 1: Answers to Cognitive and Behavioral Questions for boys with severe Hunter syndrome (n=104)

Cognitive or Behavioral issue	Yes	No	Unsure
Aggressive or violent behavior	46	57	1
Cognitive delay	95	8	1
Cognitive regression/Loss of skills	65	37	2
Delayed speech	80	11	3
Hyperactivity	59	42	3
Loss of speech	59	40	5
Repetitive behaviors	68	34	2
Obsessive tendencies	60	40	4
Running away from caregivers	44	55	2
Self-injury	22	80	2
Short attention span	80	20	4
Reduced visual/spatial skills	46	43	15
Reduced gross motor planning	69	31	4
Reduced sense of danger	62	35	7

To further understand the responses to the survey questions, Project Alive interviewed caregivers of children with Hunter syndrome. The results of those interviews follow.

44% of caregivers of boys with Hunter syndrome said their boys are aggressive or exhibit violent behavior.

Many caregivers talked about their sons biting, hitting, kicking, lashing out and breaking things when they are tired, frustrated, or angry.

“Our son regularly seeks sensory input, colliding with family members, caregivers, and friends. While it is not often violent, it catches those around him off guard, and it's concerning for those who don't know him well. It also makes caregivers and teachers uneasy, which creates another challenge or barrier for our son to participate in a school or group peer environment. Our son also periodically lashes out with hitting, biting, kicking, or (recently) pinching when frustrated by a transition, a favored toy or object being taken away, or when asked to do a non-preferred activity. All of these things make it tough to manage our boy with Hunter syndrome.”

“My son does show aggressive behavior. However, I see more as an impulsive behavior due to lack of communication because he is not trying to intentionally hurt someone. When he realizes he has hurt someone he typically apologizes and feels bad that he did. Except when he is extremely tired and just becomes delirious and destructive and just laughs hysterically at everything. He hurts his brother at least once a day.”

91% of caregivers of boys with Hunter syndrome said their boys experienced cognitive delay.

Many caregivers talked about the speech delay they see with their children. In addition, they shared their children have missed several milestones with crawling, walking, and toilet training.

“Our son did not speak until late, when he did it’s his own language. He is delayed in that he did not understand many concepts or how to apply them. He did not imaginatively play with toys. He often became frustrated with one task and two would be out of the question. He does not recognize letters or numbers.”

“Our son has also been painfully slow in toilet training, with frequent accidents, lack of awareness, and lack of forward progress in toileting over months and months. He's still in diapers, even though most of his peers are well past them. We worry based on what we hear from other families and MPS neurocognitive experts that our son's behavioral issues now (impulsivity, eloping, poor safety awareness, "aggression", etc.) are the early manifestations of cognitive impacts of his disease.”

“There were all sorts of little things - he didn't wave or clap at the time he was supposed to. But language was the main one for me. Expressive language was obviously delayed, but it was the inability to understand/act on what I was saying that was more worrying.”

63% of caregivers of boys with Hunter syndrome said their boys had cognitive regression or loss of skills.

Many caregivers talked about the loss of speech as a particularly frustrating part of the cognitive regression both for the families and their children. Parents have to “guess” what their child needs because the child can no longer express himself. The loss of everyday skills has also had a tremendous impact because it has stripped the independence of the child and magnified the burden for the caregiver. Parents talk about the continuous exhaustion they suffer from years of taking care of a child who is nonverbal and essentially a toddler – having to bathe, dress, feed, and constantly watch the child for fear he will hurt himself.

My son lost “the ability to count, recognize family members, back and forth communication and ability to understand dangerous situations among other misc. things such as brushing his teeth, riding a bike, learning his ABC's and no longer able to do sign language with his grandparents who are deaf. It has impacted our family a great deal and most of them do not see my direct family anymore. We also have been turned

away from external caregivers over 15 times, only finding one person in the last 3-4 years that will help care for him. I lost my job and my husband's employer had to change benefit plans to adjust."

"Our son had reached the milestone of over 50 single words and a few phrases. All those have gone now. He is very passive now, finding it harder to move around, feed himself and so on, so needs much more support through the day. It is heartbreaking watching old videos of how he used to be able to engage with us and initiate play."

"He lost his ability to babble mama and dada, lost his ability to eat certain foods, lost his ability to throw a ball and walk without balance issues, much more. It has been an emotional impact for our family watching him decline but particularly not hearing the words mama or dada."

71% of caregivers of boys with Hunter syndrome said their boys had delayed speech.

Caregivers talked about the various ways they and their children have tried to overcome the delayed or loss of speech through sign language and picture exchange communication systems (PECS). But again, caregivers and the children are frustrated with the inability to communicate, and parents constantly worry about what the child cannot express.

"Lack of communication has caused frustration and aggression. It also makes it hard to assess any illness or medical issues. It also has been a barrier to making friends."

"His speech is definitely delayed, and it has affected our family in many ways. His speech delay made communication challenging and also affects his little brother who surpassed him cognitively and tries to communicate with him but sometimes doesn't understand or have the patience to take the time it takes to understand what he is trying to communicate."

"Communication has been a huge challenge with him having no words and no true form of communicating with us. It is always a guessing game of what he is wanting or how to make him comfortable."

57% of caregivers of boys with Hunter syndrome said their boys experienced loss of speech.

As might be expected, loss of speech is one of top concerns of caregivers of boys with Hunter syndrome. Going from having a child who is constantly talking and engaging with others to having a child stare into space and not talk at all is devastating. Many parents spoke of the frustration they see in their children who seem to know what they want to say, but they cannot find words to express themselves any longer.

“It has affected us so deeply because I see him trying so hard to speak and communicate and yet he can’t. It is so tough to see how frustrated he gets for us to understand him.”

“This is probably our hardest part of the disease thus far! Losing speech is devastating to both my children who can still understand and don’t know why they cannot talk.”

“My son is unable to express his desires or needs. We both get frustrated, and it causes distress for me as he goes to school. I worry he won’t be able to tell me if he is being mistreated.”

“It’s been very, very hard on him and us! I still try to hold on hope and not look back at videos of how much he talked.”

57% of caregivers of boys with Hunter syndrome said their boys experienced hyperactivity.

Caregivers expressed their fear for their sons’ safety because of the constant activity and inability to self-regulate. They also talked about the exhaustion of having to supervise 24/7.

“He cannot sit down for any length of time. He is all over the place and is moving constantly. Does not focus on things and constantly gets bored with one thing and moves on to another. Everyone gets exhausted being around him, making sure he is safe and not hurting himself or others.”

“Our son rarely slows down or stops, other than for meals (briefly) or watching a screen. He climbs onto -- and jumps off of -- chairs, tables, counters, and people regularly. Coaching and disciplinary measures like "time out" simply don't work. They may change his behavior for a few minutes but then he's back to his hyperactive self. His overexuberance is exhausting for caregivers and also damaging to his body and his physical environment. He regularly scrapes, cuts, and bruises himself, as well as breaking things in our home. We try to spend as much time as possible outside in environments where he can run and jump without injuring his environment or himself.”

“He is extremely hyper, and it has not gotten worse as he has gotten older. It is very dangerous because he doesn’t realize his strength and when he becomes hyper is when he is likely to hurt someone. He has a baby sister who needs a bodyguard 24/7 because he will try to grab her and pull her by an arm or leg when he becomes hyper. He also likes to throw things. I was holding baby a few days ago, and he grabbed a huge bottle of ketchup and threw it at me, and I have a huge bruise in the back of my shoulder. ...but fortunately, I was not facing him, so it hit me in the back because if I had been facing him, he would have hit his little sister, which is extremely scary.”

“It has limited where and when we go places. We split up family outings if his sister has something to go to -- one parent goes with her while the other stays home with him.”

65% of caregivers of boys with Hunter syndrome said their boys have repetitive behaviors.

Caregivers talked a lot about repetitive speech of their boys – asking the same questions, repeating the same words over and over, watching the same video over and over again, often replaying a certain part continuously. Some talked about self-harm behaviors.

“He likes things a certain way, and if they aren’t he reverts back to being physical and loud. Everyone has to live according to his routines.”

“Our son repeats himself very often and for mom, dad and brother we are used it, but when he does it to other people, they often get annoyed which is hard to watch. We understand he usually repeats himself because he is excited about something, but people who are not used to him react in ways that are hurtful to watch or ignore him.”

“His repetitive behavior is him hitting his chin so hard it bruises or him banging his hand so hard on a hard surface his hand swells so badly, and that is not easy for any parent to watch their son do.”

58% of caregivers of boys with Hunter syndrome said their boys have obsessive tendencies.

Caregivers shared their sons’ obsession with food – eating constantly without a sense of feeling full. Others talked about their sons’ obsession for certain objects or clothing items.

“Our son has obsessive issues. Once his mind is locked on to something until that item is found or action happens, he is extremely focused, no matter how clearly impossible. His siblings have the most issues with this because sometimes we have to let his obsession run its course before moving forward.

“My son has one shirt that he will wear. When it is being laundered, he will open and close the washer and dryer continuously until it is done – fussing loudly and crying. He refuses to wear any other shirt during this time.”

“Our son is obsessed with food, and when he is tired, he will go into the kitchen every 5 minutes and get something. He is also obsessed with cracking eggs.”

“My children cannot sit and watch a movie or show in its entirety and enjoy it like they used to without constantly rewinding forwarding or tapping the iPad screen”

42% of caregivers of boys with Hunter syndrome said their boys run away from their caregivers.

Many caregivers expressed safety concerns for their children because they have no sense of danger or impulse control and will run out into traffic or run away. Consequently, parents said they do not trust anyone outside of themselves to watch their children. They also shared the myriad of ways they try to keep their boys safe in their own homes through elaborate locks, alerts, fences, and keypads.

“We have a handicap placard so we can park closer to entrances, and my husband is having to take him to most of his appointments as I can't stop him from running away or making him go where he has to go.”

“We have installed a mechanism to prevent opening all exterior doors of our house to prevent our son from going outside on his own. He is so impulsive that he cannot keep himself from going outside, running from us in parking lots, etc. We have to hold him by the wrist or the arm when we are in parking lots or other potentially dangerous areas to keep him from bolting and injuring himself. Just this past weekend, we were leaving a friend's house and he bolted across the street by himself. Thankfully, there were no cars, but it underscored (yet again) his impulsiveness and lack of safety awareness. If an adult caregiver is not paying attention to him for 30 seconds (and not physically close enough to provide restraint), there could be devastating consequences.”

“When out and about I had to watch him constantly, never being able to concentrate properly on a conversation with other parents in the park. He would make a beeline for the gate onto the main road if anyone left it open. Once, when being looked after by a respite caregiver, he learned how to open her front door and escaped onto the main road. He thought it was funny when she was chasing after him and luckily another passerby managed to stop the traffic, so he wasn't hit.”

“Outings are much more difficult. We attend less events because it is so much work to ensure he does not elope and injure himself. As a result, not only does he lose out on experiences, so do his siblings. When we do go out, we have to use a safety harness or keep him in his stroller. We can only visit parks that are fenced in.”

21% of caregivers of boys with Hunter syndrome said their boys self-injure.

Caregivers expressed dismay as they talked about self-injuries including head banging, biting, smacking, and unintentional accidents that occur from dangerous behaviors such as climbing and jumping.

My son “knocks his head and causes open wounds then he picks the wounds open repeatedly. He also bites himself.”

“He bangs his own head into toys or walls, and he will act in a dangerous manner even if he knows it will hurt -- he doesn't care.”

“Our son does not deliberately self-injure, but he regularly hurts himself through his physicality. He climbs, jumps, falls, and runs into things, and he always has scrapes and

bruises to show for it. Friends and adults who are not regularly around our son are always nervous when with us, since our son will climb anything in sight, stand on tabletops, etc. and no amount of coaching gets him to stop.”

“Our son gets injured mostly when he is super tired and extra hyper because I feel that he is more careless and loses control of his body. He has fallen more times than I could count. Last week he got hurt at school as he threw himself to grab his friend and his friend moved so he ended up hitting his head on the corner of a cabinet and ended up bleeding from his head, and I had to take him to the hospital. We try to stay close to him at all times to avoid and catch him when he falls, but we are not able to catch him every time. The scariest thing when they get hurt is that they have such a high tolerance for pain that sometimes we don’t realize how bad it is and have to get him checked out to be in the safe side.”

77% of caregivers of boys with Hunter syndrome said their boys have short attention spans.

Caregivers talked about their boys’ inability to concentrate on tasks because of their short attention spans. This limits their ability to do well in school and to take the cognitive tests required by most clinical trials.

“My son’s attention span is about 5 minutes, 10 on a real good day. He has problems in a school setting, or a setting where he expected to behave a certain way.”

“Our son “can’t stay playing with one toy or doing one activity for more than a couple minutes. He makes HUGE messes and doesn’t pick them up. He is like a tornado that blows by you, and you have to pick up the pieces.”

Short attention span and impulsiveness are definite issues for our son. While our older daughter can sit with an activity for half an hour, our son with Hunter syndrome typically tires of an activity within a few minutes, and then is off to the next thing. This makes instruction and therapies difficult with him and hurts his ability to learn.”

44% of caregivers of boys with Hunter syndrome said their boys have reduced visual/spatial skills.

Many caregivers said reduced spatial skills have affected their boys’ ability to navigate the world – with a tendency to trip, stumble, miscalculate distance, and fall.

Our son “doesn’t notice things before he steps on it or trips over it.”

“He stumbles, falls, trips on/over things. It’s a safety concern.”

“He has always been wary of going from one surface to another or using steps as he finds it difficult to judge. This is now getting worse as his balance goes.”

He has difficulty “walking up and down stairs and getting out of the car. We have to pick him up for him to get out.”

68% of caregivers of boys with Hunter syndrome said their boys have reduced gross motor planning.

Caregivers expressed a tremendous deficit in their boys’ gross motor planning, such as running, jumping, standing, or walking, particularly in their ability to interact with their peers.

“He has a difficult time running or even catching a ball, so he can’t play like other boys can which is difficult to watch your child want to do something so badly and he can’t.”

“My child cannot do things on his own that he once was able to do! It’s extremely heartbreaking, especially when there are treatments that could help.”

“He needs help with dressing, bathing, and stairs. Not only does this take away from his independence, but we constantly worry that he could hurt himself.”

60% of caregivers of boys with Hunter syndrome said their boys have a reduced sense of danger.

One of the chief concerns caregivers expressed was the boys’ reduced recognition of danger. They feel they must constantly watch their children to keep them from harm and have various safety measures put in place. Parents expressed a continuous state of anxiety for what might happen to their children.

“He has no sense of danger whatsoever. He has been running out of the house and has no "Stranger Danger" and no sense of when a car is coming towards him. He has reached inside the oven, put the dog’s feet near the toaster and microwaved a tablet along with my husband’s phone and credit cards”

“Reduced sense of danger is a mild way to say it. Our son has no sense of danger. Running across the street or through a parking lot, climbing up 5-foot walls and jumping from them (repeatedly) onto concrete, and throwing heavy items (at glass windows) are just a few examples. He needs constant supervision to keep him from injuring himself or others, which is exhausting for our family and for other caregivers. We have not lost caregivers due to his behaviors yet, but we anticipate that may be a future reality. We also avoid or limit certain activities our family does for fun, the locations we choose for outings, or the people we socialize with because of our son's behavioral challenges and concerns for his/our safety. While his sister deeply loves her brother, it hurts our heart to see her flinch when he runs up to her. She's right to protect herself, but she shouldn't need to protect herself from her own brother. But his lack of sense of danger and his impulsiveness necessitates it.”

“We are always on high alert. “Relax” is not part of our vocabulary EVER! We have chains on the doors leading to outside, and the entire house is childproof! For this reason, we do not venture out much anymore.”

“We are living in a state of high alert all the time. The stress and anxiety that comes from it can be exhausting. He loves water and candles but does not realize the danger that can come from them. We worry that one day he may be seriously injured or worse.”

Why We Need a Cognitive Treatment

As the last part of the study, we asked caregivers why is it important for your child/children to have a treatment that addresses the cognitive part of Hunter syndrome? The answers were heartbreaking.

“Our boys have so many obstacles to face in this life, so many struggles and an outcome that at the moment has no solution. When I think of my son...I have been blessed with a beautiful gift, and it is my job to make sure that each day he is with me no matter how long that may be that each of those days be the best they can possibly be. His quality of life is the best it can be. My son can talk, he can laugh, he can tell you stories, he can play, he can love his animals. He can love his family. He can enjoy life. With cognitive treatment, he can continue to be him! Every day he blesses us with his presence. And he is a wonderful loving boy. To take away someone’s ability to communicate to express is, well there are just no words to define that scenario. It would be devastating for all.”

“Our son desperately needs a treatment for the cognitive impacts of Hunter syndrome. Impulse control, hyperactivity, poor communication and situational awareness, aggressive behaviors... We see the neurobehavioral manifestations of his disease everywhere. They prevent him from learning, and they cause real safety concerns for our home, our family, and our son. We hope, pray, and work for a cure, but anything that could help stabilize the neurodegenerative impacts would be a meaningful improvement for him and other boys with Hunter syndrome. The status quo is so hard for our boys and our families. We need better.”

“Life is hard with a child who is developmentally delayed. We work so hard to help our son do basic tasks to make his life easier. All we want is an approved treatment that helps the cognitive part of Hunter syndrome to make life easier on the child. To be able to communicate basic needs and enjoy playing. Even though it is hard, we keep trying. Keep doing therapies and everything we can to preserve what we have right now. A treatment for cognitive effects of Hunter syndrome will be one more thing to preserve our children’s minds and give them a chance to make life more enjoyable.”

“Because the cognitive part is what is slowly killing my children! It is a matter of life and death for us, and I can see their light slowly but surely dimming.”

“Because ultimately the cognitive aspect is what is taking my son from us. I want to see him function as normal as possible. I want him to be able to communicate with us. I want him to live.”

“No parent should have to watch their child lose skills. The devastation that comes from it cannot be put into words. While other children are rapidly learning and growing, ours are fighting like hell to keep the limited skills that they have. The medical appointments, procedures and the trauma that comes along with them are enough to endure.”

Conclusion

There is a dire need for a treatment to address the neuronopathic devastation of MPS II. The current ERT does not cross the blood-brain barrier, so it addresses only the somatic symptoms of Hunter syndrome. Looking at the current trajectory of the disease as seen in the natural history studies of the disease, boys usually begin to show cognitive decline between 18 months and 4 years of age. [1] Without an intervention, patients begin to lose their speech, lose their mobility, and move toward a non-responsive state. This is heartbreaking for parents and caregivers as they watch their children begin to slip away from them.

Caregivers are most devastated by the cognitive and behavioral impacts of Hunter syndrome. [13] We need a treatment to address this now. The introduction of ERT in 2006 brought hope to the Hunter syndrome community, but fifteen years is too long to wait for breakthroughs to address the cognitive decline in this devastating disease. Any improvement to the current trajectory of the disease – whether slowing decline, stabilization, or improvement – is welcomed by caregivers. These families are desperately clinging to the possibility of more time with their loved one before this disease robs them of their precious children. In the Hunter Syndrome/MPS II FDA-requested Listening session “Some caregivers stressed that time is of the essence while requesting the FDA work to discover new treatments and cures and approve new trials. [13] One more day is too long. Children need a treatment to address the cognitive manifestations of Hunter syndrome today.

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