

Pathways

*The Newsletter for
Glycoprotein & Related
Storage Diseases*



A publication of ISMRD

Crossing Oceans for a Cure

ISMRD's largest and most
successful fundraising
event yet!



Table of Contents

Between the Lines: "A Little Fighter" by Paul Murphy	Page 2
"An Exciting Journey Begins" by Terri Klein	Page 3
Crossing Oceans for a Cure: An International Family Workshop & Fundraiser	Page 4-9
"The View From Tromso" by Dag Malm Mutational Analysis for Mucopolipidosis I-Cell Medical Alert	Page 10-12
In Memoriam	Page 13
Current Events @ ISMRD	Page 14-15
How to Contact ISMRD Donation Acknowledgements Information - Volunteer - Donation Form	Page 16-17

The International Advocates for Glycoprotein Storage Diseases

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FEIN #: 52-2164838



Our Mission:

ISMRD is the leading advocate for families worldwide affected by a Glycoprotein & Related Storage Disease. Through partnerships built with medicine, science and industry, we seek to detect and cure these diseases, and to enable a network of support and information.

A Little Fighter

By Paul Murphy
President ISMRD

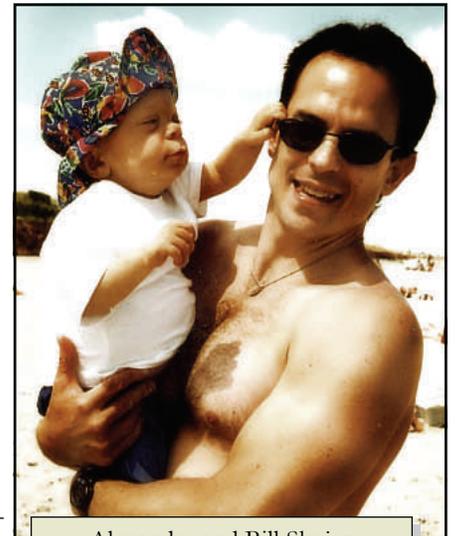


This year has been one of exciting change and achievement for ISMRD, yet also one of sadness. We are still a small organization with big goals and this newsletter, the first in over a year, reflects that reality. Our objective has always been to publish Pathways at least twice yearly, so as to keep families and friends informed, but our resources have not proven adequate to the task. Because we realize that ISMRD cannot make the progress that all of us want without more time commitments from our Board, we have decided to appoint an Executive Director beginning January of 2006. This is a major move for us, yet one we have wanted to make for several years. We did not have to go far to find a willing, excited person to fill that role; indeed, we found her on our Board of Directors!

So it is with great pleasure that I announce that Terri Klein has accepted our offer to be our visible presence and operations director. Terri is mother to Jenny Klein, a teenager affected by Mucopolipidosis III or Pseudo-Hurler Polydystrophy. Terri joined our Board about a year ago after demonstrating a rare zeal to help ISMRD take advantage of the goodwill arising from our first international conference in 2004. She has proven to be a tireless advocate and enthusiastic supporter for ISMRD's mission for all nine diseases we represent. With her leadership as Executive Director in the coming year, I feel we can finally break through the barriers that have prevented us from meeting our potential thus far. So, please join me in congratulating Terri on her new position and feel free to contact her or I about your ideas, comments or to volunteer to help.

The excitement of filling an important position within our organization, however, is tempered by the sadness to which I alluded above. For the first time in our seven year existence I must report that we have lost several children this year, all of whom passed away well before their time. We have prepared a small, dignified acknowledgement of their passing on page 13, which I will let speak for itself. For me, personally, one death was particularly affecting. Several years ago I was contacted by Bill Skojec, whose son, Alex, was born with Sialidosis. I was immediately impressed by Bill's fighting instinct and tenacity against such a very rare and serious disease (Sialidosis is among the rarest of all the Lysosomal Diseases worldwide). He became active in publicizing the disease, organizing benefits to raise money for research and seeking out resources for his quest to eventually find a cure. ISMRD became one of these resources and we developed a small website for Alex, "Alexander's Hope," which continues to be carried as part of ISMRD's overall online presence. You can find it by clicking the "Our Stories" link on ISMRD's home page.

Bill attended our first International Conference in Rockville, Maryland in 2004, which afforded me the opportunity to finally meet him personally. Unfortunately, he was unable to bring Alex with him and yet I held out hope that I would meet him sometime in the future. Thus, it was with shock that I learned from Bill this fall that Alex passed away. The email notice from him was brief, but to the point: *I am sending this e-mail to let you know that Alex lost his battle with Sialidosis Type II yesterday afternoon at 3:35. He was close to his 7th birthday, but was too tired and hurting to go on. I will be dedicating my life in some way to finding cures for these disorders as I already have been over the past 5 years. Alex was with his family at the time and died peacefully in his room. He was quite a little fighter having lived as long as he did.*



Alexander and Bill Skojec



For Bill, and for the parents of the other children who have passed away this past year, there is great sadness and a loss we can only imagine. For him and them, all of us at ISMRD send our condolences and our renewed dedication to finding therapies and eventual cures for Aspartylglucosaminuria, Alpha-Mannosidosis, Beta-Mannosidosis, Fucosidosis, Galactosialidosis, Mucopolipidosis II, Mucopolipidosis III, Schindler Disease and Sialidosis. Like Alex and Bill, ISMRD will continue to be a fighter. Please join us in this mission, won't you?

An Exciting Journey Begins

By Terri Klein
Executive Director ISMRD



Dear families, friends and supporters,

In November of 2004 I was elected to the Board of Directors for ISMRD and was excited to plan, organize and participate in the April workshop-fundraising event which you will read about beginning on page 4 of this issue. Since that exhilarating weekend in Michigan the Board felt it critical that we create an Executive Director position to continue making progress on our mission to find cures for our diseases. I feel privileged and honored that the Board has asked me to assume these duties and I have enthusiastically accepted the position beginning January 2006.

In 2006 ISMRD will continue to expand our advocacy for families through our global outreach to affected patients. We will strive to find new, innovative solutions that foster collaborative efforts among researchers and physicians who share our vision. This objective was the dream that inspired our founders, continues to motivate our current Board and will enable us to realize the breakthroughs we all seek. I am so very proud to be a part of this mission that seeks the early detection of and cures for Glycoprotein Storage Diseases, so that one day our children will be able to lead healthy lives. There is much work to be done and I look forward to contact with all of you. Please feel free to contact me any time by email; I will be accessible to guide you. Also, please feel free to drop by our website, if you are able, and join our growing online community the Penguin Cafe. We are particularly anxious to hear from those of you whose lives are affected by the “rare of the rare:” sialidosis, galactosialidosis, fucosidosis and schindler but, of course, want all of you to feel that ISMRD is your “home.”

This is an exciting journey on which we embark and I am so very pleased that it promises to provide more opportunities for all our Penguin families. May everyone have a joyous holiday and a Happy New Year!

Terri Klein
terri@terriklein.com

Upcoming Events!!

ISMRD's Board of Directors will be participating in the following conferences in 2006 and hope to enable our families, who live in the region, to meet with each other. As we did in Paris in 2001 our goal is to hold a “mini-conference” and review the latest developments in research and ISMRD's current mission. We will be updating everyone in the coming weeks and months on developments and hope to see you at one (or both)!!

1. 9th International Symposium on MPS & Related Disorders:
June 29-July 2, 2006; Venice, Italy
Information: <http://www.congress2006mps.it/>
2. National MPS Society, United States, Annual Member Meeting:
July 27-July 29, 2006; Covington, Kentucky
Information: <http://www.mpsociety.org>

For additional information please contact Paul Murphy or Terri Klein



Crossing Oceans for a Cure

By Terri Klein,
Executive Director, ISMRD

On April 21-22, 2005 thirty-two families gathered in Ann Arbor, to participate in "Crossing Oceans for a Cure," a Walk-Run benefit for ISMRD. The idea to hold this fundraising event in conjunction with a trip to the US by Jenny Noble, an ISMRD Board Member from New Zealand, grew into something more than any of us could have expected. Indeed, it took on a life of its own and became the largest gathering of ISMRD families in our six year history!

Attendees came from around the world, including Australia, Belgium, Canada, Germany, Italy, Mexico and United States. Among the families in attendance were 29 affected by Mucopolidosis and 3 affected by Alpha Mannosidosis. In fact, never had there been such a gathering of Mucopolidosis patients and families anywhere in the world prior to this.

Because there was such a high turnout of families, much more than originally anticipated, we decided to hold a one day Family Workshop the day before the Walk-Run. The scramble to put together a day-long agenda became easier and more feasible after securing the participation of four physicians with knowledge of these diseases: Professor David Sillence of Australia, Dr. Jules LeRoy of Belgium, Dr. Stephen Tiede of Germany and Dr. Mark Patterson (a member of ISMRD's Professional Advi-



sory Board) from the USA.

After months of working with many of these families online on ISMRD's Penguin Café, we saw the "fruit of our labor" by watching them gather one by one in the daycare room and then on into the conference. We had babies crying, parents crying, volunteers crying and of course the dreaded skies were crying, as well, with the clouds down pouring our first rainstorm this spring.

The workshop was all encompassing and began with an overview of Lysosomal Diseases by Dr. Patterson, followed by an introduction to Mucopolidosis II and III by Dr. LeRoy. Other sessions included disease management techniques and a discussion of the benefits of Pamidronate by Professor Sillence. Dr. Tiede spoke on the genetic mutations in Mucopolidosis and Dr. Patterson covered diagnostic techniques for Glycoprotein Storage Diseases.

In addition to these knowledgeable and qualified speakers we were also honored by the participation of Denise Crompton, the parent of an adult ML III patient, who discussed the art of communicating effectively with professionals and how to be an advocate for your child. Our own John Forman, a member of ISMRD's Board, led the audience through an overview of ISMRD, its past and future. At the end of the day, families benefited from meeting one another and having one-to-one contact with some of the world's most knowledgeable physicians. The professionals who attended were able to see actual patients with these rare diseases and to provide families with

(Continued on page 6)

Glycoprotein & Related Storage Disorders	Map & Directions to the Walk/Run	Crossing Oceans for a Cure...
<p>Glycoprotein & Related Storage Disorders are very rare inherited disorders caused by a defect in the breakdown of complex molecules in the cells, resulting in the "storage" of these molecules in small cellular organelles called lysosomes. This defect causes a multitude of physical and neurological symptoms for which there are currently no effective treatments or cures. Affected children suffer progressively deteriorating physical and mental skills, resulting in disability and often a premature death. These diseases include Alpha Mannosidosis, Asparaglycosaminuria, Beta Mannosidosis, Fucosidosis, Galactosialidosis, I-Cell Disease, Pseudo-Hurler Polydystrophy, Schindler Disease and Sialidosis.</p>		<p>ISMRD Walk/Run 2005 April 23 - Saturday</p> <p>Raising Funds to Research Rare Diseases</p>
<p>What do these 9 diseases all have in common?</p> <ul style="list-style-type: none"> • They are all Lysosomal Diseases • Course facial features • Skeletal Complications • Enlarged Liver and Spleen • Heart Involvement • Developmental Delay • Carpal Tunnel Syndrome • Short Stature • Clouding of the Cornea • Respiratory Infections • Ataxia 	<p>From I-275/M14 Go West on M-14 to US-23 North. North on US-23 to Exit 49 North Territorial Rd. Go West on North Territorial Rd. approximately 7 Miles. Turn South into Hudson Mills Metropark. West of Huron River Dr.</p> <p>From I-96/Brighton Go South on US-23 to Exit 49 North Territorial Rd. Go West on North Territorial approximately 7 Miles. Turn South into Hudson Mills. West of Huron River Dr.</p> <p>From I-94/Baker Rd. Exit 168 Go North on Baker Rd. Turn Left in Town at Dexter Ann Arbor Rd. Go Under Bridge & turn Right on Dexter Pinkney Rd. Go 3 Miles. Turn Right on North Territorial Rd. Go 1/2 Mile & turn South into Hudson Mills Metropark.</p> <p>From I-94/Zeab Rd. Exit 168 Go North on Zeab Rd. Turn Left on Huron River Dr. Turn Left on North Territorial Rd. Go 1/2 Mile turn South into Hudson Mills Metropark.</p>	<p>ISMRD International Advocate for Glycoprotein Storage Diseases www.ismrd.org</p>

Special Memories and a Defining Moment

By Jenny Noble,
Board Member, ISMRD

So many special memories were created from our benefit weekend, with what can only be described as a joining of families with one goal in mind - to raise funds to help find a cure for their children. Our conference was a huge success with 31 families attending. Of that group 28 were ML2 and ML3 families, 3 were families with Mannotosidosis and several families with MPS joining us and giving their support.

We were very honored to have Prof Sillence, Australia, Dr LeRoy Belgium, Dr Patterson, America, Dr Tiede Germany to make presentations to the conference. Dr Tiede gave the conference hope with his work on Gene Mutations in ML. He also stated that his cell cultures will no longer be just cells; he will forever have imprinted in his mind the many ML children he was able to meet and interact with. Prof Sillence went above and beyond the call of duty by being available to meet with families prior to the benefit weekend commencing on Friday.

I think the highlights of the whole weekend for Drs and Parents alike was to see the children talking playing and just plain having fun. They were all totally spoilt with gift bags which meant for some of us we went home with extra suitcases full of goodies. Language was no barrier for the children. Seeing Zack Haggett from America and Sergio Cardenas from Venezuela playing together are memories we will never forget. Hearing Brenda teach Ashton Keddy to say "Hey Baby" was so very cute.

The entire weekend created many special memories for all the families present. It was an even more incredibly defining moment for our attending physicians to see so many ML children and young adults all together for the first time! Given the huge success of this benefit weekend, it is now ISMRD's goal to hold a conference such as this again and to reach out to all families with a Glycoprotein Storage Disorder.

Imagine what could happen with desire, a goal and the joining of families from around the world. Imagine how much money we could raise for research for our super orphan diseases! Stay tuned....



Jenny Noble (left) with
daughter Sarah (middle) & Jenny Klein (right)
...and some special friends!



Sponsor Roll of Honor!

The following corporations, organizations and individuals provided significant financial support for ISMRD's Workshop & Walk-Run Fundraiser:

- | | |
|---------------------------|------------------------|
| * Real Estate One | * Adair Printing |
| * FM Global Engineering | * CareBags4Kids.org |
| * Webers Inn | * Aeschliman Equipment |
| * National MPS Society US | * All Sewn Up |
| * Australian MPS Society | * Colorbooks, Inc. |
| * Genzyme Australia | * Durolast, Inc. |
| * The MPS Society Germany | * Sallie Mae Mortgage |

Without such support as this, as well as those from numerous individual contributors, this event would not have achieved the success that it did!

Crossing Oceans for a Cure

By Terri Klein,
Executive Director, ISMRD

(Continued
from page 4)

the most current knowledge about them.

On Saturday the Walk-Run benefit brought in over \$46,000 in funds and donations, by far the most successful fundraiser in ISMRD's six year history. Despite the terrible weather (rain in the morning gave way to a snowstorm later in the day) \$11,800 was raised on Saturday alone from the community of walkers and runners who gathered despite these adverse conditions. It was quite a site... we had to light up the fireplaces inside Hudson Mills Metropark & Concessions for those who did not or could not brave the walk!

From Thursday thru Sunday the Benefit Weekend was overwhelming with emotions from families who wanted to gather for the purpose of knowledge, advocacy & family. Friendships for a lifetime were created – it is hard to express the amount of compassion and love for one another transcended all language barriers. Our penguin family should be so proud of themselves!

From rain to snow to ice storms... this was an historical weekend and it certainly showed each one of us how deep the need is for the most current knowledge, research & family advocacy for our children.

Thank you to all of our families and everyone who gave an abundance of unconditional time to help our endeavors. Our special thanks go to all the corporate sponsors who provided so much for so little, and also to families who raised sponsored funds for the event. If you haven't patted yourself on the back yet... please do!

Now that we've accomplished so much, we now must ask ourselves: "where do we go next??"



When doctors tell you that your child has a disease such as Mucopolidosis, the world falls down around you. My wife, Emanuela, and I have lived through moments that only those who've experienced such heartache can truly

understand. You find that you must force yourself from thinking about what the future holds, so that you might focus on dealing with the issues of the present. I found only one effective way to manage the situation in which I found myself, and that was to take this disease by the chest, face it head on and to fight it. When it was clear to me that the doctors who we'd consulted were fumbling in the dark, I began to seek out answers on my own. I did this despite many doctor's warnings that I should spend less time researching the disease and focusing more on my job!



Luis Catozzi

A Journey from Fear

By Luciano Catozzi

Yet, of course, I ignored such advice! Alone, I contacted the doctor who made the diagnosis. Alone, I found information about Pamidronate. Alone, I forced our doctors to consider Pamidronate as a therapy. Alone, I found a specialist for Carpal Tunnel Syndrome.

Fear of the unknown is what makes our lives most difficult. To overcome this fear, it is important to become acquainted with others who understand the source of your anguish. Thus, our journey to Ann Arbor to meet other families affected by Mucopolidosis was perfectly aligned with this overall strategy. And so it was that Emanuela and I saw our fears vanish with this journey. Meeting

(Continued on page 7)

A Priceless Experience

By Maria Elena Cardenas

When I was invited to go to Michigan to attend the benefit, I was not sure that I should attend, nor did I think that I would have the courage to see other affected children, especially those with more serious symptoms, since



that would be like seeing the future that waits for my Sergio .

Nevertheless, reading what the other mothers posted in the Penguin Cafe forum made me enthusiastic to be one of many coming face to face with all the others. And so it was at that point, then, that I decided that Sergio and I should go to Michigan to meet with other Mucopolidosis families.

When we arrived and I saw the other children with their families and they also saw us, my eyes filled with tears and the words did not manage to leave my mouth. I saw, too, that the same thing happened to them. I recognized that there are no words adequate to describe that moment and the weekend we shared together. Even now that memory is so fresh that it seems as if it occurred only yesterday.

To attend the conferences and listen to the Doctors explain to us so many important things and to have the Dr. LeRoy sharing his valuable knowledge with our children present indeed was an experience words are inadequate to describe. For me personally,

it was important as it was the place and date I felt no longer alone, but part of a great family. It is this extended family who truly understands how it feels and who can cry and laugh together through good or bad experiences. To be part of this in Michigan was truly a priceless experience!

Maria Elena Cardenas and family recently emigrated to the US from Venezuela this past year so that her son, Sergio, would benefit by better medical resources. She became aware of ISMRD via the Penguin Cafe and has become a regular in the King Colony for Mucopolidosis families. Sergio is affected by ML II. She is pictured with Sergio in the photo above.

(Continued from page 6)

other families traveling this same journey was tremendously beneficial to us and them.

Having witnessed the many changes wrought on Luis by Mucopolidosis it was confirmed to me in Ann Arbor that he is, indeed, affected in a dramatic fashion. Though this confirmation was startling in the present tense, it should prepare him better for the future when he is older and understands better. All this was of benefit to his sister, Maryuri, as she now has a better understanding of her brother's challenges.

So, I see now that there are three things in my life of which I can be proud: 1) to have married Emanuela 2) to have adopted two extraordinary children and 3) my journey to Ann Arbor!

Luciano Catozzi, his wife Emanuela and children Luis and Maryuri journeyed to Michigan for ISMRD's workshop and benefit from their home in Senegallia, Italy. Luis is affected by Mucopolidosis III.



Luis, Luciano, Maryuri and Emanuela

Crossing Oceans for a Cure

An Exchange of Ideas

By Dr. Stephen Tiede

For me this meeting was a great chance to meet ML II and III children. I was working on ML II and III during my doctoral thesis and I had fewer possibilities to make contact with affected children and their families. I was just working on anonymous cultured fibroblasts of patients I never met! So the scientific work in the laboratory was very abstract in regard to these diseases.

I was very interested, however, for whom I do all this work. For me it was very important to see, to fully comprehend the sense of what my work really is. And I realized the importance of my work when I was able to make personal contact with the children and families in Ann Arbor. A meeting like the one held in Ann Arbor is very important both for the affected people and also for the scientists to get information about the diseases.

In my case, I was able to glean a lot of information about Pamidronate therapy during this meeting. I was also able to take this information with me back to Germany, where no one is aware that this treatment exists. Since returning home I have followed up this important news by writing a letter to the German MPS Society, resulting in a lot of response from ML III families. So there is necessity here in Germany which nobody recognized before and physicians are now contemplating initiating the treatment.

In conclusion, I feel that the most important thing to be done is to meet people (patients, families and scientists from different fields), to stay in good contact and to exchange ideas and knowledge!

Stephen Tiede
Children's Hospital, Biochemistry
Hamburg, Germany
stiede@uke.uni-hamburg.de

Stephen Tiede is currently working on his doctoral thesis on the Molecular Analysis of GlcNAc-phosphotransferase. His presentation in Ann Arbor concerned gene mutations in ML II & ML III.



Dr. Marc Patterson
USA



Prof. David Sillence
Australia



Dr. Stephen Tiede
Germany



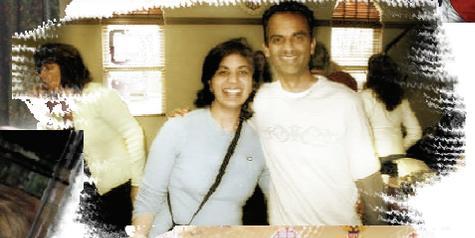
Dr. Jules LeRoy
Belgium

The Friday workshop material was specifically tailored to the families attending. Because the majority of them had children with Mucopolipidosis we focused the presentations to their needs, though also making the material encompassing enough for the Mannosidosis families. In the future our goal is to have another conference whose scope will cover all the Glycoprotein Storage Diseases. We will keep all our global families informed as we develop plans for this major conference in 2007.

ISMIRD Family Workshop Presentations:

1. Understanding Lysosomal Diseases: *Dr. Marc Patterson*
2. Introducing ML II & ML III: *Dr. Jules LeRoy*
3. Patterns of Inheritance/Metabolic Screening/Diagnosis/Sibling Testing/Prevention: *Dr. Marc Patterson*
4. Managing ENT/Dental/Cardiac & Other Problems in Mucopolipidosis and Mannosidosis: *Prof. David Sillence*
5. Pamidronate Treatment in Mucopolipidosis: *Prof. David Sillence*
6. Gene Mutations in Mucopolipidosis: *Dr. Stephen Tiede*
7. Communicating With Professionals: *Denise Crompton, ML III Parent*
8. ISMIRD: The Organization and Future Issues: *John Forman, ISMIRD Board Member and Mannosidosis Parent*

Ann Arbor Photo Collage



Photos from the weekend in Ann Arbor!!



The View from Tromsø: Mannosidosis Research Update

By Dag Malm, M.D., PhD.
Asst. Prof of Internal Medicine
University Hospital of Northern Norway



Greetings and best wishes to all from the land of eternal night (in winter, that is): Tromsø, Norway!

Progress proceeds on developments that will result in clinical trials for determining the efficacy of Enzyme Replacement Therapy for Alpha-Mannosidosis. The European Union, who is underwriting much of the cost, plans to begin a Natural History study to precede the actual randomized, double-blinded and placebo-controlled clinical trial over 6-12 months duration. In this trial half of the patients will receive the Enzyme Therapy, while the other half will receive a “placebo” or “fake medicine.” This is a standard format followed at the outset of all clinical trials and best determines whether the therapy actually succeeds. However, we are encouraged that in animal experiments with “knock-out mice” such Enzyme Therapy has had an unmistakable positive effect on substrate deposits—not only in the body, but in the brain!!

Although this study was originally designed by me it has been taken over by the company that will produce the enzyme. I had to agree to surrender such control since I had no economic means of doing it myself. The first question arising about the Natural History study is whether there are enough patients to fill the quota needed. To answer this, I am requesting information from Mannosidosis-affected families in North America, Australia and New Zealand who have not undergone a Bone Marrow Transplant. The qualifications are that there is a confirmed diagnosis of Alpha-Mannosidosis and that patients are able and willing to undergo normal examinations to include neurological, ENT, psychological testing and, perhaps, an MRI.

I would further need a letter containing the complete clinical information about the child/adult patient, which can be done by the family or with an MD’s assistance. If you have filled out such information for me before, then I would only require updated clinical information. The letter should contain postal and email addresses and phone/fax numbers should I need to contact you.

Patients outside Europe may be entitled to participate in the actual clinical trial if enough patients are not found for the study. So, therefore, I must reiterate that there is no guarantee that non-Europeans can participate in this first round of trials; however, the information you provide will be extremely helpful in our overall understanding of the disease. So, the “bottom line” is that we have made great progress and are hopeful that this important study will succeed!

Other news: I have recently authored the results of a study on psychiatric systems in patients with Alpha-Mannosidosis in the *Journal of Intellectual Disability Research*. We concluded that there appears to be an increased risk of psychiatric symptoms in Alpha-Mannosidosis, yet were unable to ascertain if this was caused by the disease or related to an outside factor. This will have to be the focus of follow-up studies. At any case, families and caregivers should be aware that patients appear to be susceptible to these symp-

toms and should be given adequate diagnostic work-up, treatment and support should they arise.

Finally, it is a pleasure to report that my daughter Emilie, who underwent a Bone Marrow Transplant in 1997 at the age of ten, is preparing to get her driver’s license! Recent evaluations indicate that substrate deposits in her brain from Mannosidosis have nearly completely normalized; thus, my outlook for Enzyme Replacement Therapy is that it could work!



Emilie Malm: Student, skier, tennis player,
auto driver & Mannosidosis patient



Gene Mutation Analysis For Mucopolipidosis II & III !

**GREENWOOD
GENETIC
CENTER**



**Greenwood Genetic Center
101 Gregor Mendel Circle
Greenwood, SC 29646**

The Greenwood Genetic Center in South Carolina, USA has begun to offer diagnostic Gene Mutation testing for Mucopolipidosis type II and type III at no charge for a limited time. This testing was initiated as a result of the recent publications that positively identified the ML II gene, also known as GNTPA. Their current goals are to provide DNA testing for this gene as well as the ML III gene, GNTPG. During the course of the identification period families will be contacted by the clinic to collect further clinical information that will help in understanding of specific genetic alterations.

The cost to families will be retained in blood & urine samples and the shipping of the kit back to Greenwood Clinic. The actual cost to have the identification completed is being absorbed by the clinic – **THEY ARE NOT CHARGING FOR THIS.** The results will be made available to your physician of choice when completed and each family must sign a waiver for this process to occur. The Greenwood Clinic is opening this opportunity up to families on an international level. This is a very large step into the research of Mucopolipidosis, one that has had many waiting years to see implanted. If you would like details on this opportunity and to be part of results in this study please contact: The Greenwood Genetic Center in South Carolina, USA has begun to offer diagnostic Gene Mutation testing for Mucopolipidosis type II and type III at no charge for a limited time. This testing was initiated as a result of the recent publications that positively identified the ML II gene, also known as GNTPA. Their current goals are to provide DNA testing for this gene as well as the ML III gene, GNTPG. During the course of the identification period families will be contacted by the clinic to collect further clinical information that will help in understanding of specific genetic alterations. The cost to families will be retained in blood & urine samples and the shipping of the kit back to Greenwood Clinic. The actual cost to have the identification completed is being absorbed by the clinic – **THEY ARE NOT CHARGING FOR THIS.** The results will be made available to your physician of choice when completed and each family must sign a waiver for this process to occur. The Greenwood Clinic is opening this opportunity up to families on an international level. This is a very large step into the research of Mucopolipidosis, one that has had many waiting years to see implanted. If you would like details on this opportunity and to be part of results in this study please contact:

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scathey@ggc.org



The James Cuthbert Self Genetic Laboratories at the Greenwood Genetic Center offers a full range of biochemical testing, including Lysosomal Enzymes, Oligosaccharides and Mucopolysaccharides. These diagnostic laboratories, located on the campus of the Greenwood Genetic Center, provide modern and well-equipped facilities where technology is put to work for the evaluation, treatment, and prevention of human genetic disorders. For more information about these services have your physician or genetics specialist call 800.473.8100 or 864.941.8111. Visit their website at <http://www.ggc.org/diagnostic.htm>

Medical Alert for Parents of Children with I-Cell Disease

I-Cell disease is a slowly progressive inborn error of metabolism for which, unfortunately, no curative treatment is available. Children with I-Cell disease have extreme growth failure, neurodevelopmental delay and disease of connective tissues in many organs, including the lungs and respiratory tract. Manifestations including swollen gums, stiff joints, thick-feeling skin, bone and tendon abnormalities are well known signs of the disorder.

Because of the poor growth potential, atrophied muscles, and poor compliance of the narrow thoracic cage, the baseline respiratory status of these children is compromised. Additionally, they have small mouths that do not open fully or easily. As the children grow older the airway becomes gradually more restricted as the initially swollen airway passages become stiff and easily traumatized. This combination of factors makes intubation (placing a tube within the airway in order to use mechanical assistance to breathe for the patient) very risky, so elective surgical procedures should be avoided as much as possible.

If a procedure is considered essential, it should be undertaken at a major medical facility where pediatric anesthesia and pediatric critical care services are available. Under all circumstances, medical staff should be prepared to perform fiber optic intubation, where a tiny camera is used to visualize the airway during the intubation procedure. Because children with I-Cell disease have much smaller airways than other children of the same age, a much smaller endotracheal tube will be required. However, a smaller tube may be less effective for ventilation (breathing for the patient) and may potentially lead to additional problems such as pneumothorax or collapsed lung.

All medical personnel involved with the elective procedure (surgeons, anesthesiologists, and critical care specialists) should be conversant with the clinical features and natural course of I-Cell disease. Parents and physicians must realize that intubation can easily cause more problems than an elective procedure may alleviate.

For many of the same reasons already described, extubation (removing the breathing tube) may also be unusually difficult and the patient's general condition in the first days following it, quite unpredictable. If prolonged intubation is required, a tracheotomy (making an artificial hole in the trachea through an incision in the neck) will be required. The probability of subsequent adequate healing in order to close the tracheostomy and having the patient breathe without mechanical assistance is slim indeed.

All humans have an airway protective reflex so as to continue to breathe when sleeping or even when artificially sedated. Deep anesthesia diminishes this reflex. Children with I-Cell disease do not necessarily respond differently to anesthesia. However, because of their precarious airway status from the start, the patients may lose that protective reflex very quickly, even from "light sedation". That is why a medical team must always be prepared for intubation, preferably fiber optically, if indeed a surgical procedure is considered of crucial importance.



Sara Cathey, M.D.
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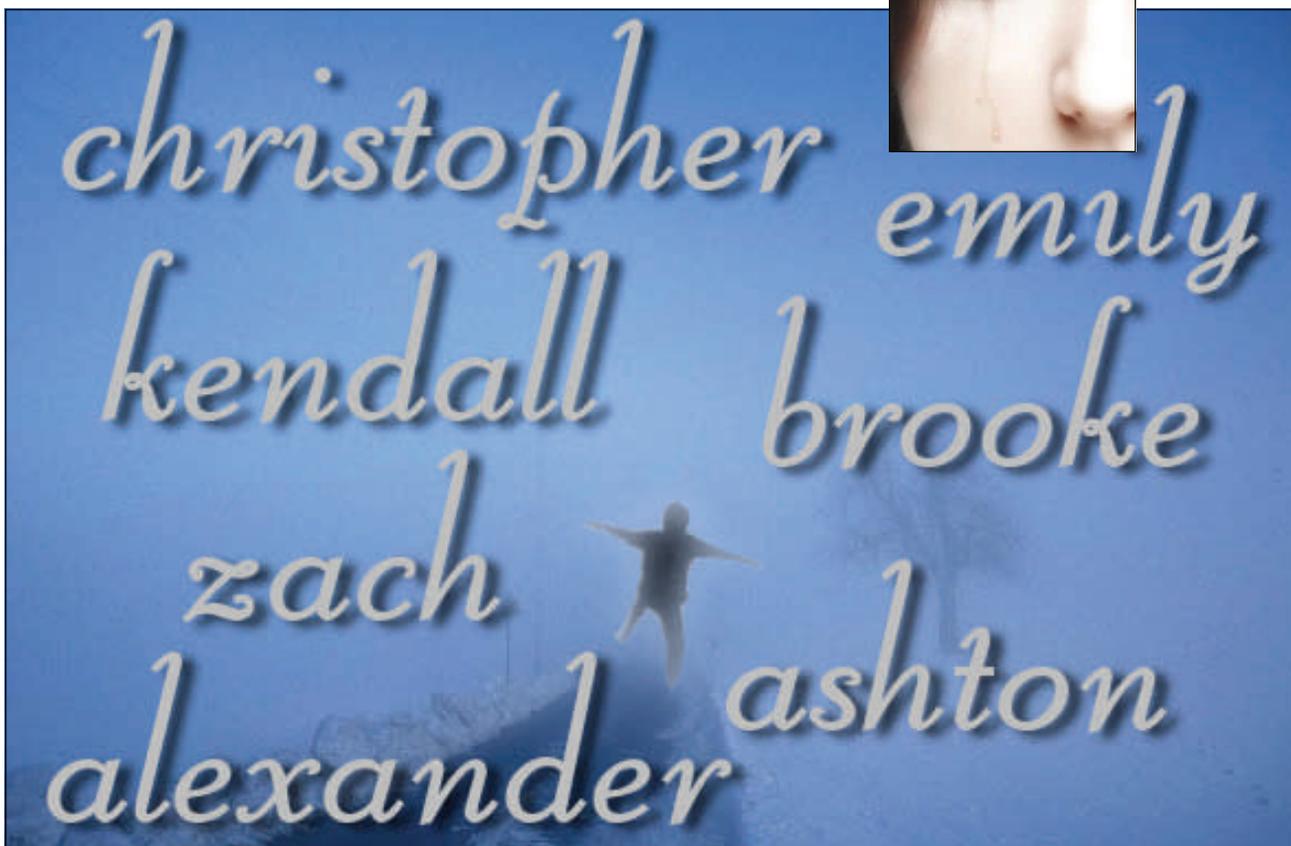
Where We Live

ISMARD is truly an international organization and though we are incorporated in the United States we do not recognize any national, ethnic, religious or philosophical barriers to our outreach. We continue to seek out families affected by all nine of our supported diseases wherever they may reside, and view no diagnosis as having any less importance than another simply because there are fewer individuals identified.

Our families currently reside in the following countries: *Australia, Canada, China, Czech Republic, England, Finland, France, Germany, Holland, Israel, Italy, Japan, Latvia, Netherlands, New Zealand, Norway, Poland, Russia, South Africa and the United States.*

ISMARD is not a dues-based organization: we rely on donations and grants to fund all our activities!

In Memoriam



Christopher Reese: Mucopolipidosis II/III, age 18; Emily Potter: Mucopolipidosis II, age 6; Kendall Moran: Mucopolipidosis II, age 5; Zach McGinnis: Alpha-Mannosidosis, age 1 1/2; Brooke Weddell: Mucopolipidosis II, age 3; Alexander Skojec: Sialidosis, age 6; Ashton Keddy: Mucopolipidosis II, age 6



Current Events



Board Governance News

ISMRD's Board of Directors gathered in Maryland for its annual meeting to elect new members and to formulate strategies for the coming year. Representing the international scope of our leadership, the Board members came from New Zealand, Canada and the United States which gave everyone the opportunity to meet face-to-face.

We were pleased to welcome our newest Board member, Harvey Trimman, a resident of Cockeysville, Maryland, who assumed the post of Treasurer. Harvey has years of experience in commercial accounting, is a CPA (Certified Public Accountant) and has a wealth of knowledge in budgeting, forecasting and cash management. His first task has been to assume responsibility for safeguarding ISMRD's financial assets and converting our traditional method of accounting to that used by US nonprofit organizations. Harvey is the father of two adult children and plays piano in his leisure time. He is eager to learn more about Glycoprotein Storage Diseases and to help all our families achieve the ultimate goal of a cure for these disorders.

Our annual meeting was also a time to say thanks and bid farewell to Debora Murphy, one of the four original founding members of ISMRD, who has stepped down to concentrate on her Massage Therapy practice and devote more time to daughter, Taryn. Debbie was instrumental in organizing ISMRD's first conference, the *First International Scientific & Family Conference on Glycoprotein Storage Diseases*, held in Rockville, Maryland in April 2004. Without Debora's considerable dedication and oversight the conference would not have been the resounding success that it turned out to be!



Executive Director Position Created

ISMRD's Board of Directors have created the new position of Executive Director, to be filled by Terri Klein of Whitmore Lake, Michigan effective January 1, 2006. Terri, who is the mother of Jenny Klein, a teenager with Mucopolipidosis III, will be ISMRD's "public face" and will be responsible for carrying out the mission and objectives of the Board of Directors. Terri will be a paid, non-voting member of the Board and work directly with ISMRD's President, Paul Murphy. Terri's accomplishments this past year included our most successful fundraising event to date in April that raised more than \$40,000. Both Terri and the entire Board of Directors are extremely excited by her appointment and anticipate even greater accomplishments in the coming year. We hope that all of you will share our excitement and wish her well!

World's Greatest Tag Sale: Coming 2006!



Everyone join other penguin families from around the World for our annual World's Greatest Tag Sale: a fundraiser (be it in a garage, an attic, a basement or a yard) that has the ability to include anyone who has a mission and determination as we do to raise funds for ISMRD! This event has been successful in the past and we are hoping to really give it a **BANG** and get the word out to everyone of our ISMRD families. All proceeds go to our continued mission to increase knowledge about Glycoprotein Storage Diseases and one day realize treatments and cures.

Look for dates sometime this coming Spring 2006 (Winter for those of you on the "bottom" of the world) to be posted soon! Box up items while you clean before Christmas and after the new year – every item has a price! We are so very excited about this endeavor and hope we can

all come up with some creative ideas to make your individual sale a success!! Think **BIG** and how to get family and friends involved too!



ISMRD Unveils Its New, Improved Website!

Among our accomplishments this past year we realized our goal of a new, improved (and continuously evolving) website. Designed by Cold Toast Media's Eric Szczerbinsky, our new online face provides a more pleasing and informative presentation of information for families and professionals alike.



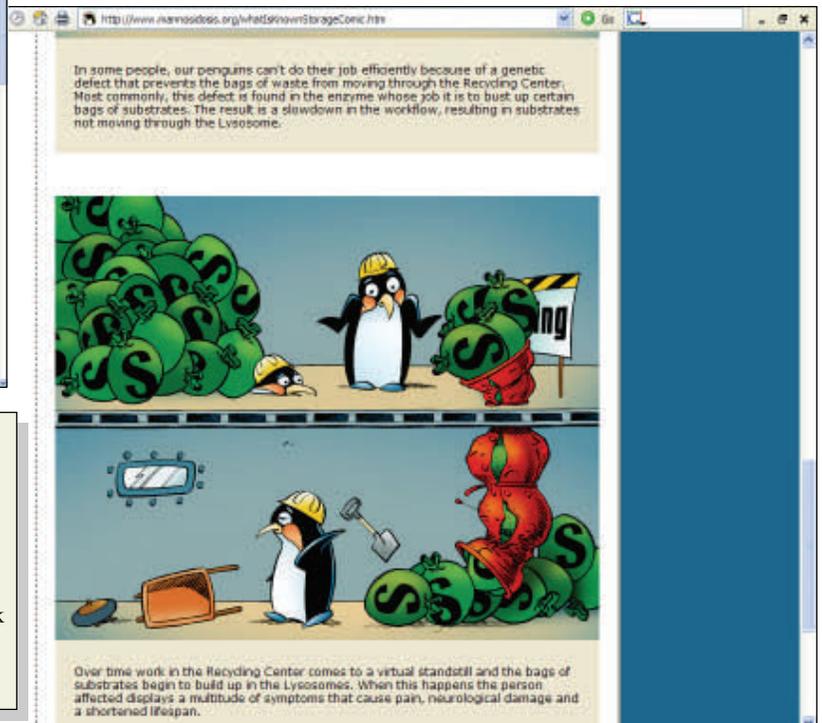
ISMRD's website opens to a clean, easy to navigate home page, featuring our specially commissioned penguin family logo created by artist Denis Rodier. This look is consistent throughout the interior pages, thanks to the layout created by our designer, Eric Szczerbinsky.

Features currently available are fact sheets on each disease, an overview of ISMRD's founding and accomplishments and, of course, the Penguin Café Discussion Forum.

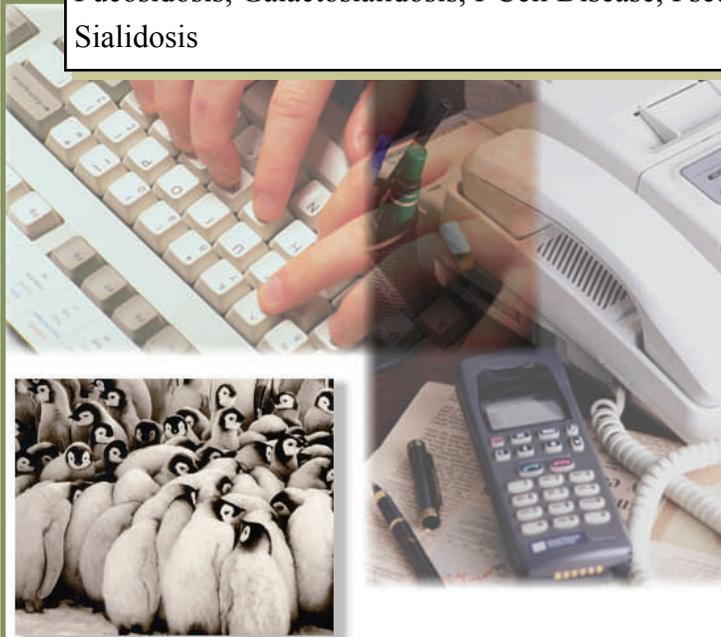
We continue to work on improvements to the website in order that it become the authoritative gateway to information about Glycoprotein Storage Diseases. If you have not yet visited the site, please do so and tell us what you think and what you would like to see in the future!



In the section called "The Diseases" is a layman's explanation of what we know about Glycoprotein Storage Diseases. Included in this information is a four panel comic strip created by Denis Rodier. The cartoon features ISMRD's penguins showing the process whereby material is "stored" in the cell's lysosomes. In the case of our penguins, the cell is like a recycling center whose efficient work schedule is interrupted when a crucial tool (a wheelbarrow) becomes unusable.



The International Advocates for Alpha Mannosidosis, Aspartylglucosaminuria, Beta Mannosidosis, Fucosidosis, Galactosialidosis, I-Cell Disease, Pseudo-Hurler Polydystrophy, Schindler Disease & Sialidosis



Contacting ISMRD

ISMRD Board of Directors

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Treasurer: Harvey Trimman | **Secretary:** Mark Stark

Asia/Pacific Coordinator: John Forman

Directors:

United States - Gretchen Oswald, M.S., C.G.C.

New Zealand - Jenny Noble

Canada - Bill Simpson

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Website: www.ismrd.org | FEIN: 52-2164838

A US 501 c3 Nonprofit Charity Incorporated in Maryland

Thank You for Your Support!

We are grateful to the following who made a donation to ISMRD during 2005:

Denise Crompton, Bill & Tina Skojec, Mark & Angie McGinnis, Barbara & Walter Marshall, John & Kimberly Nye, Judy Snyder, Meg Niehaus, Pamela Gibel, Alison Aldrich, Amy Whalen, Employees of FM Global Foundation, Friends & Relatives of Brooke Weddell (so many we do not have enough room to list individually!), St. Mary's Byzantine Catholic Church, Richard & Donna Yorkovich, Applied Materials Charitable Giving Program, Deanna Robbins, Mary Anne Carroll, Mike & June Sheard & friends (on behalf of Saffy Wooley), Joseph & Ann Marie Abt

A special thank you goes out to everyone who contributed money in memory of one of our children who passed away this year (see page 13) and to every individual, company and race participant who contributed to the success of our "Crossing Oceans for a Cure" in Ann Arbor, Michigan this past April.

To all who are acknowledged here, or who we have unintentionally omitted, we appreciate your faith and support that has resulted in almost \$50,000 in financial support this year. By a wide margin, this is the most successful year that we have enjoyed and we pledge to each and every donor that every dollar/pound & franc will be put to good use.

If you or someone you know would like to help our cause you may do so in a number of ways:

1. Make a donation using the tear-off slip on the facing page and send to us at the address above.
2. Make a secure online credit card donation using JustGive.org (accepted from any country):

- * Go to the JustGive website at www.justgive.org
- * Type "ISMRD" in the "Search for a Charity" box in the upper-left corner and press "GO"
- * In the page that follows click on ISMRD's organizational name
- * In the ensuing page click the purple "Donate Now" and follow the instructions
- * ISMRD will receive a check in the amount you specify within 3-4 weeks!

3. Donate by being a volunteer. To do so, fill out and return the "Join With Us" tear-off slip on the facing page.

Did You Know?

You can download this and previous editions of Pathways from our website!

Click on "Library" at our homepage to view or print a copy in Adobe Acrobat.



Feedback Form | Donation

ISMIRD would like to hear from you!

Send us your feedback, your request for further information or make a donation. Just fill out the appropriate boxes below, cut out this page and then return it to the address on the reverse side.

Donations: contributions to ISMRD are tax-deductible in many countries. Consult your nation's local or central tax-collection agency. A copy of our current financial statement is available upon request by contacting ISMRD at our address at 1030 Saxon Hill Drive, Cockeysville, MD 21030 USA. Documents and information submitted to the State of Maryland under the Maryland Charitable Solicitations Act are available from the Office of the Secretary of State for the cost of copying and postage. Please contact us for further information.

Join With Us!

We would like to hear from you and offer you a part in our vision to link families, support research, develop therapies and find cures. Send us names of friends, family and professionals who would be interested in receiving our newsletter or know more about our mission. Join an Action Team and contribute to ISMRD's success, no matter how small that contribution may seem, Your ideas are invaluable!

Please send Pathways to:

Name: _____
 Address: _____
 City: _____ State/Province: _____
 Country: _____ Postal Code: _____

Join an Action Team:

Action team members work together to fulfill parts of ISMRD's mission. For more information, check an area that interests you and we'll contact you.

- Family Support
- Fundraising
- Medical Outreach/Research
- Policy/Advocacy
- Public Awareness

My Name:

Email Address:

Phone:

Please Help Our Cause!

ISMIRD is a 501 (c)(3) charitable organization based in the United States serving a global constituency. We provide our services, which include our newsletter, website, outreach activities and support of research, without requiring monthly dues or any other financial restrictions. We gratefully accept donations that will enable us to continue toward our goal of a future free of the tragic consequences of Glyco-protein Storage Diseases.

Please give us your name & how to contact you:

YES! I would like to contribute the following (check one):

_____ \$100.00

_____ \$75.00

_____ \$50.00

_____ \$25.00

_____ Other: \$ _____

Please make your check payable to
ISMIRD
 Thank you!

Name: _____

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