UMDF connect

UNITED MITOCHONDRIAL DISEASE FOUNDATION®

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UMDF and NIH Convene First Ever Workshop

Workshop organizers: Charles Mohan, Jr.; Vernon Anderson, Ph.D.; David Eckstein, Ph.D.; Carlos Moraes, Ph.D.; and Stephen Groft, Pharm.D.

In an unprecedented move to benefit the mitochondrial disease community, more than 80 clinicians, scientists, and researchers from leading medical institutions and universities gathered in Rockville, MD, for a first of a kind meeting with representatives from numerous institutes at the National Institutes of Health (NIH). The meeting, entitled, "Translational Research in Primary Mitochondrial Diseases: Obstacles and Opportunities," was developed and chaired by UMDF Scientific and Medical Advisory Board Chairman Carlos Moraes, Ph.D., of the University of Miami, and Vernon Anderson, Ph.D., of the National Institute of General Medical Sciences (NIGMS) at the NIH.

The day and a half long session, held on March 8-9, 2012, was designed to develop specific goals. The goals included sharing information about primary mitochondrial disease among researchers; developing ways to facilitate future collaboration and sharing of information; determining the obstacles, needs, and priorities of primary mitochondrial disease research; and developing ways to translate basic science discoveries into better diagnostic and therapeutic measures for patients. The outcome of the meeting is important for patients because findings will help form a plan to move mitochondrial medical research forward both inside and outside the NIH.

The meeting between the UMDF and the NIH was the result of a request from Sen. Barbara Boxer (D-CA). Sen. Boxer introduced legislation in the Senate and

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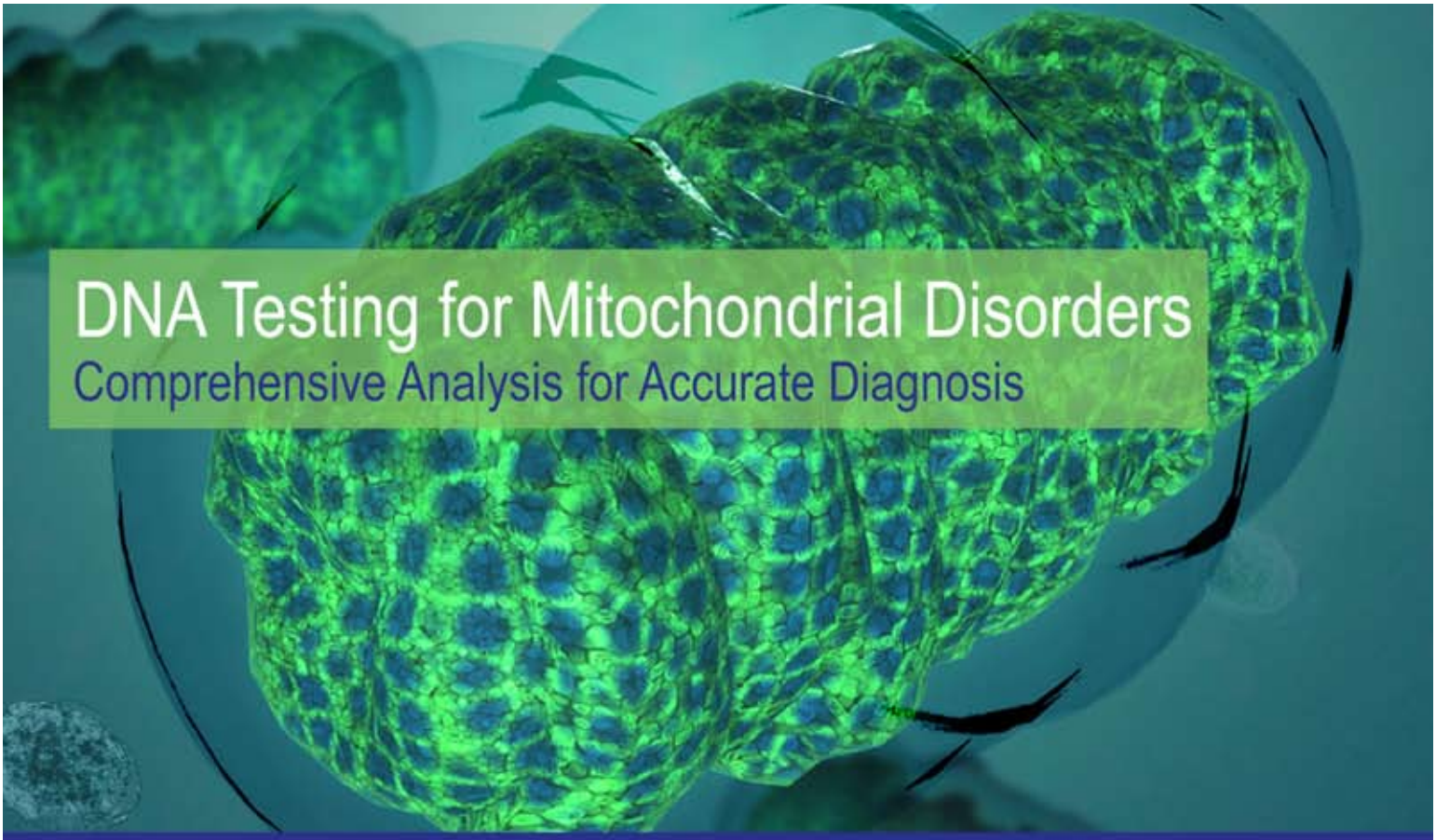
UMDF Hires Director of Development

Cindy Shafer

Chief Executive Officer and Executive Director Charles A. Mohan, Jr. is pleased to announce that Cindy Shafer has been hired as Director of Development. Shafer has a Bachelor of Arts degree in Communications, Literature, and Secondary Education and a Master of Science degree in Professional Leadership and Nonprofit Management. She has been working for non-profit organizations for 17 years and has held leadership positions in development departments for seven years.

Shafer will be working closely with Mohan; Leslie Heilman, J.D., Associate Director of Development; and Don Gielas, Grant Writer. She is anxious to meet the many donors that make the efforts of the UMDF possible.

Featured Articles:



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From the Chairman

I would like to share with you some of the exciting developments in the field of mitochondrial medicine that are taking place right now.

I was part of the team that recently represented the UMDF in Washington, DC, at two very important meetings that have far reaching implications for the mitochondrial disease community. The first set of meetings occurred during Rare Disease Day, which was February 29. The Office of Rare Disease Research (ORDR), part of the National Institutes of Health (NIH), conducted a daylong session that updated the rare disease community on the progress that has been made in rare disease research. One of the important discussions at this meeting was about NextGen Sequencing. The capability to sequence all of the nuclear and mitochondrial genes in an individual patient and if needed in their family has now arrived. This technology is advancing so quickly that we now obtain much more information about a patient than we ever could before. The first step of this sequencing is to compare this data with all known mutations. If we are very lucky, the source of the disease will be immediately known. However, if a mutation is not found, then the process becomes very tricky. The sequencing provides us with millions of points of data and most of that data will have to be reviewed by someone knowledgeable to try and find a needle in a haystack. The final result will be the discovery of the cause of many new primary mitochondrial disorders but we must have patience. The progress will be painfully slow until we determine those mutations and we devise a method to automate these discoveries.

While sequencing is important, we all need treatments and cures. A second set of meetings was held the next day at the Food and Drug Administration (FDA). UMDF and other patient advocacy groups were able to meet with FDA officials to share their opinions, with the hope that potential treatments that are in the pipeline can be fast tracked. The FDA was very responsive to our comments and provided a very informative session on their process, successes and barriers. You can read more about these meetings in this newsletter.

On March 8-9, 2012, the UMDF and the NIH convened a historic first-ever joint meeting between representatives from the various NIH institutes and UMDF mitochondrial researchers, scientists, physicians and representatives from several pharmaceutical companies. This meeting was critical to advance research into primary mitochondrial disease both inside and outside the NIH. It identified the barriers and obstacles that are faced in research, sharing resources, treatment and collaboration. A plan that could increase research for treatments and potential cures was discussed. This proposed plan of action will be unveiled at the UMDF's symposium, Mitochondrial Medicine: 2012, which will be held June 13-16, 2012, in Bethesda, MD.

While on the subject of the symposium, it is my hope that you can join us this year. We will have an outstanding scientific program as well as some very exciting topics for patients and families. I would also encourage you to participate in the second "Day on the Hill" where we explain to our Members of Congress about primary mitochondrial disease. Without your energy behind the UMDF, none of these exciting developments would be happening now! See you in Bethesda in June.

Energy to all,

W. Dan Wright, UMDF Chairman

UNITED MITOCHONDRIAL DISEASE FOUNDATION®

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UMDF and NIH Convene First Ever Workshop

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asked, among other things, for better collaboration between researchers around the country and at the NIH. Sen. Boxer has been a champion for mitochondrial medicine issues, not only for affected individuals in her own state, but around the country.

George Santangelo, Ph.D., Director of the Office of Portfolio Analysis in the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), detailed for the group the current funded research into mitochondrial disease and dysfunction with an aim to move forward. According to Dr. Santangelo, in the current year, the NIH has allocated $609 million in research projects across a variety of institutes. Dr. Santangelo told researchers $18 million was allocated to primary mitochondrial disease research, as defined by the UMDF. He reported 65 percent is being allocated for basic research, 27 percent has been allocated for non-primary mitochondrial disease research, and 5 percent has been allocated for secondary usage. It was also pointed out that the NIH has funded the North American Mitochondrial Disease Consortium (NAMDC). It has long been the UMDF's position that the NIH should fund research into primary mitochondrial disease at a higher level because research in that area could lead to better diagnostic tools and treatments in secondary mitochondrial disease research, such as diabetes, Parkinson's and Alzheimer's.

Vamsi Mootha, M.D., UMDF Scientific and Medical Advisory Board Member and Richard Leach, UMDF Board of Trustee talk at the meeting.

Attendees were presented with an update on the current states of research, therapeutic, and drug development with an eye towards moving patients closer towards treatments and potential cures. During his presentation, Douglas C. Wallace, Ph.D., Director of the Center for Mitochondrial and Epigenomic Medicine (CHOP) at Children's Hospital of Philadelphia Research Institute, urged the NIH to rethink the way they think about mitochondrial medicine. He urged them to break down the silos among the various institutes and consider research outside of organ specific diseases. "Mitochondrial disease is no longer a rare disease, but a major clinical problem in this country," Wallace told the group. He urged them to investigate the mitochondria as a path towards other breakthroughs.

Often times, the patient community wonders why therapeutic treatments and potential cures seem far in the future. The workshop provided researchers an opportunity to share their concerns on the issue. The workshop also gave representatives from NAMDC the chance to outline the successes it's making in the area of developing a clinical patient registry. UMDF serves as the patient advocacy representative to the NAMDC Consortia. Patients are able to receive a clinical diagnosis through their participation in NAMDC and they are offered an opportunity to learn about, and if they choose, participate in clinical trials that are offered through NAMDC.

Low participation in clinical trials by the patient community, while highly valued, can be a barrier to advancing potential treatments. Often times, patient recruitment is difficult. After outlining a host of recommendations on the issue, Peter W. Stacpoole, Ph.D., M.D., professor of medicine, biochemistry, and molecular biology at the University of Florida, told the attendees that "it is critical to the success of all clinical trials that the NIH remain committed to continuing this type of dialogue." That's not to say that potential drugs are not in the pipeline. Matt Klein of Edison Pharmaceuticals reported on two drugs in development that target primary mitochondrial diseases. Several other pharmaceutical companies, such as Colby, Cardero, and Biomarin, reported that they are focused on treatments that target the secondary causes of mitochondrial disease. The barrier to move these potential treatments remains within the regulatory approval process.

One of the exciting developments in the field of mitochondrial medicine is the advances made in the field of genome sequencing. Sequencing enables scientists to identify specific mutations. While this emerging technology will be the focus of the new National Center for Advancing Translational Sciences (NCATS) institute at the NIH, the good news for patients is the cost of this procedure is drastically falling. A few years ago, high powered sequencing cost tens of thousands of dollars to complete. With the advance of science and technology, the genome sequencing costs have dropped to under a thousand dollars.

Prior to the conclusion of the workshop, participants summed up the barriers and obstacles they believe exist in mitochondrial medicine. All agreed that additional meetings should be held with the NIH to learn about the many opportunities that exist amongst the institutes and for the NIH to understand the types of research that are being conducted outside the NIH. All of this information will be transformed into a white paper report, which will discuss the barriers and obstacles revealed in this meeting and will recomend ways to move progress forward. The report will generate an action list with a proposed roadmap to advance research into primary mitochondrial medicine. This report will be presented at the UMDF's symposium, June 13-16, 2012, in Bethesda, MD.

This meeting will also have a global impact. UMDF CEO/Executive Director Charles A. Mohan, Jr., has been invited to attend the meeting of the group, "International Mito Patients (IMP)" in April. Mohan has been asked to present to attendees of the Paris meeting information about the UMDF and the status of mitochondrial disease and research in the United States. "Mitochondrial disease knows no borders," Mohan said. The UMDF is a member of the IMP. "We are greatly impacting the lives of mitochondrial disease patients by having discussions on the barriers and obstacles that prevent researchers from delivering potential treatments to the affected community. Both the NIH and the IMP recognize that it is the UMDF that has the ability to bring everyone to the table to move us closer to a cure," Mohan said. "None of this would have been possible without the support and participation of the mitochondrial disease patient community. We are the voice that speaks the loudest on mitochondrial medical issues for everyone."

UMDF Represents Mitochondrial Disease Patients at Rare Disease Day

Representatives from more than 400 patient advocacy groups, scientists, researchers, and clinicians took part in the 5th Annual Rare Disease Day activities in a two day event that began February 29, 2012, at the National Institutes of Health (NIH) campus in Bethesda, MD. The all day sessions, which were organized in cooperation with the Office of Rare Disease Research (ORDR) at NIH, the National Organization for Rare Disorders (NORD), and Genetic Alliance were designed to showcase new technologies, new research paradigms, and to educate attendees about new rare diseases being investigated at the NIH and the ORDR.

Rare Disease Day was established to raise awareness with the public about rare diseases, the challenges encountered by those affected, the importance of research to develop diagnostics and treatments, and the impact of these diseases on patients' lives. There are about 7,000 rare diseases identified in the United States. About 80 percent of rare diseases are genetic in origin and it is estimated that about half of all rare diseases affect children.

The session opened with welcoming remarks by NIH Director Francis Collins, M.D., Ph.D. Dr. Collins took the opportunity to highlight the current successes made by the NIH in the study of rare diseases and to outline the plans for the National Center for Advancing Translational Science (NCATS), in moving towards potential treatments for rare diseases and fast tracked processes for drugs within the NIH. "There is an enormous gap between what we know and what we don't know about rare diseases," Collins told attendees. He stated the creation of NCATS will enable the location of a central point of collaboration that he envisions will help drop the barriers at the 27 institutes at NIH, bringing about faster therapeutics for rare diseases. The presentations that followed throughout the day highlighted the advancements being made at the NIH in biomedical research, genome sequencing, and other ways that will help the clinicians at the NIH work harder for the rare disease community in discovering faster and better potential therapies.

While the day at the NIH focused on the clinical side, the second half of the Rare Disease Day event shifted to the Silver Spring, Md., campus of the Food and Drug Administration (FDA) for a workshop on March 1, 2012. In her welcoming remarks, FDA Commissioner Dr. Margaret Hamburg emphasized the importance of the rare disease community and the patient organizations who represent the interests of those affected. Dr. Hamburg pointed out that one in 10 people in the United States is affected by a rare disease or disorder. Collectively, the patient community affected by one of the more than 7,000 rare diseases is very large, which is why she said the FDA shares in its concern of the NIH that drug development, therapies, and medical devices must be a priority. "Since the Orphan Drug Act was put into law in 1983, the FDA has approved more than 400 drugs or products for the treatment of rare diseases," said Dr. Hamburg. "In the decade before the law was enacted, the FDA only approved 10. It is the voice of the rare disease community that brings us to where we are today."

UMDF CEO/Executive Director Charles A. Mohan, Jr., Chairman of the Board of Trustees W. Dan Wright, and Director of Communications Clifford Gorski participated in the two events by providing information to attendees about UMDF's educational and support programs for patients with mitochondrial disease and sharing UMDF's advocacy efforts. They represented the mitochondrial disease patient community on behalf of all mitochondrial disease patients. UMDF is a member of NORD and the Coalition of Patient Advocates (CPAG), both of whom represent the rare disease community.

NIH Director Francis Collins, M.D., Ph.D., welcomes participants to 2012 Rare Disease Day

Strategic Plan Update

UMDF Launches New Strategic Plan Initiative in the Southeast – Continuing Support, Education, Advocacy, Fundraising, and Development through Regions

As part of its strategic planning process, the UMDF has initiated the first step in its new approach to serving our membership and volunteer needs – to better **connect** UMDF national with the mitochondrial community through regions. Over the next few years, you will see us expand our "regional look" in the newsletter, website, and other communication pieces as we continue to unify our members by region.

This new approach, designed by the strategic planning committee and approved by the UMDF Board of Trustees, enables all departments to work directly with members to determine their needs while providing them with an array of volunteer opportunities.

The process to regionalize the UMDF's membership kicked off at the 2011 symposium in Chicago. Based on that meeting, the strategic planning committee chose Southeastern United States as the pilot project. This region is made up of Alabama, Florida, Georgia, North Carolina, South Carolina, and Tennessee. Members in those states have been contacted and asked to participate in a survey to determine the types of activities they would like to see started in their own local communities and how they would like to get involved. The response to the survey has been very positive.

"Currently, and over the past 14 years, many of our volunteers have found themselves wearing too many hats," said Kara Strittmatter, Director of Member Services. "It is not uncommon to have one of our volunteers running support group meetings, hosting an educational activity, taking support calls, AND running a fundraiser – like the Energy for Life Walkathons. They might be affected or have affected kids. Many hold full-time jobs, and quite honestly, it has become too burdensome for them, but they are so dedicated to the mission they don't want to let anything drop. Under this new approach, we want to lighten the load and encourage them to focus on what they truly enjoy doing. If they have the experience for the task at hand, they will also avoid the frustration that comes with unknown territory."

Margaret Moore

Margaret Moore, newly-hired Regional Coordinator - Southeast, lives in Charlotte, NC. and brings nearly two decades of experience as an allied health professional to the position and to the UMDF.

Moore has been a longtime volunteer with the UMDF. She has been a member of the Carolina Foothills Chapter since 2008 and has served as a member of their board. Moore has also been involved with two successful Energy for Life Walkathons for the chapter.

Moore has a Bachelor of Arts degree from State University of New York at Fredonia and earned a Master of Science degree at the University of North Carolina at Chapel Hill. Moore began her new duties with the UMDF in January 2012.

Support and educational activities are quite popular across the US, and the Southeast is no exception. For example, the North Carolina Chapter recently decided to continue their focus on patient education. "We were pleased to help them secure three mitochondrial disease experts for one of their upcoming educational meetings," Strittmatter said. "While we still see value in webinars and phone conferences - especially for those who cannot travel, we also strongly feel our patients need that personal face-to-face interaction with these experts and that is what the UMDF does best." The chapter is also planning a regional mini-symposium in the fall to educate clinicians!

In response to the growing mitochondrial community and to also enhance this regional approach, the UMDF hired Margaret Moore in January as the Southeast Regional Coordinator. Moore is the main point of contact with the members in the Southeast Region – working with them and the National Office to bring programs and opportunities to life. Moore also collaborates with the UMDF Special Events Department in coordinating Energy for Life Walkathons in the Southeast Region.

"We are not doing away with Chapters, Support Groups, or Ambassadors," Strittmatter added. "We are saying that if, for example, you want to have an occasional support meeting in your local town in Tennessee, and nothing else, great – you're still a major part of the Tennessee Chapter. Each State will become and/or continue as a Chapter – with multiple Support Groups, Ambassadors, and activities growing within each Chapter. Bottom line, the regional approach gives our members more choices to better connect – especially those who live in an area that borders multiple states. With guidance from the National Office, this is truly a member- driven program by the UMDF."

The National Office will continue to evaluate the Southeast Region as a pilot project. In future steps, the UMDF will organize the rest of the country into regions and follow what we learn from the Southeast Region. The UMDF anticipates naming its next region(s) by the end of the summer to fully implement the new approach.

UMDF Support Group Provides Awareness to Community

Members of the Western New York Mito Group of the UMDF volunteered their time to help educate the general public about mitochondrial disease at a Health Expo in Erie County Fairgrounds in Hamburg, NY, on Sunday, February 26, 2012.

Theresa Eastman of *Western New York Health Magazine* contacted Linda Roesch of Cheektowaga, NY, to see if she would be willing to have a booth at the fair. Roesch was contacted because she regularly posts the Western New York Mito Group's support meetings in the magazine. She also tries to post them in other local publications, such as the *Buffalo News*.

Roesch was surprised that she was contacted but thrilled at the opportunity. She contacted Melinda O'Toole at the UMDF National Office for her input on the idea. Both women agreed that it was something Roesch should pursue.

Jane Dean and Linda Nieman, also members of the Western NY Mito Group, volunteered to help Roesch man the booth, and O'Toole helped Roesch secure the exhibit space and provided her with a UMDF tablecloth and educational materials to handout.

Roesch said it is estimated that more than 2,000 people attended the event. She felt that her time was well spent at the event and enjoyed being a part of the awareness activity. The women met people who had never heard of mitochondrial disease, as well as a few who were newly diagnosed with it and now may attend the group's support meetings.

In addition to educating others about mitochondrial disease, the women told people about their Energy for Life Walkathon scheduled for September 15, 2012 at Island Park in Williamsville, NY. They also obtained signatures on two petitions. One petition requests prescription coverage of the doctor-prescribed "Mito Cocktail," which is not currently covered by some insurance companies, and the other petition supports the reinstatement of the Rheumatology Fellowship Program at the University of Buffalo, which will bring vital awareness of mitochondrial diseases to the medical community.

UMDF Member Services Department Provides Support Thru Phone Calls and E-mails

The UMDF Member Services Department receives numerous phone calls and e-mails every day from people looking for help, direction, and information. But what you may not realize is that not all of them are patients, or parents of patients. With increasing frequency, inquiries are coming from physicians, nurses, therapists, and other allied health professionals – all looking for mitochondrial disease information relevant to their fields.

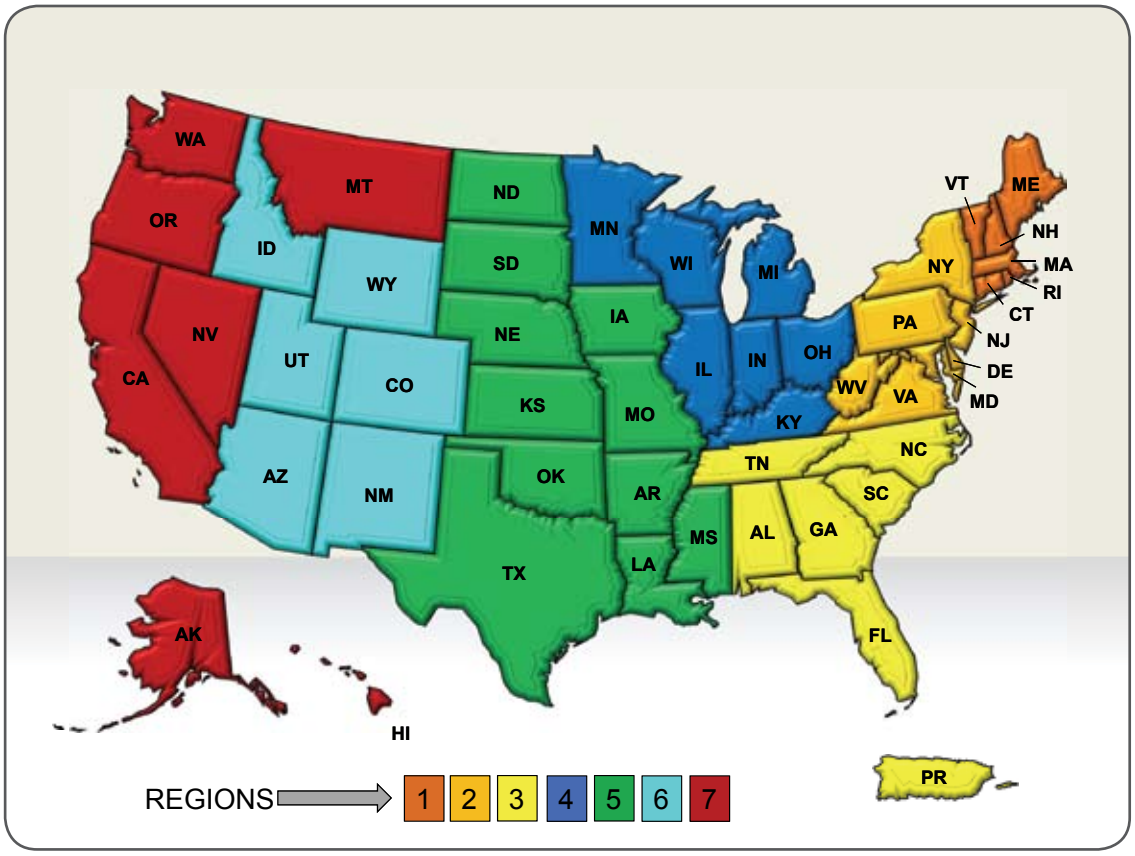
For example, just recently Jean Bassett received an e-mail from Donna Hornacek, a nurse anesthetist who encountered her first patient with MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes). Discovering that this disease was complex and required special anesthesia considerations, she contacted the UMDF not only for more information for herself but with a desire to do a hospital in-service presentation for 70 colleagues! Bassett was able to supply her with the necessary literature from the UMDF website, and also connect her with a nearby mito specialist who was willing to provide whatever assistance she needed. As a result, Hornacek now has the opportunity to give a presentation to a large group of health professionals that will far exceed her initial expectations.

Hornacek stated, "Jean was not only helpful, she responded to my requests in a very timely and efficient manner. She went above and beyond my expectations, and I appreciate all of her assistance."

Jane Dean, Roksolana Pikas, Linda Roesch, and Linda Nieman (All of these women have mitochondrial disease and are members of the Western New York Mito Group.)

UMDF connect
Resources for help & support.

In addition to the support staff at the UMDF National Office, help is available to you across the United States and around the World. To reach a state contact for support and/or if your state is not listed and you would still like to connect, simply e-mail to: connect@umdf.org. When sending the e-mail, please include the leader's name or city/state in the subject line for us to better serve your needs. Interested in getting involved? Visit: www.umdf.org/volunteeropps or call: 1-888-317-8633!



☆*Stars Denote Chapter and/or Chapter Leadership in that State*

New England Region (1)

MAINE
Amber Taylor, Bangor

VERMONT
MaryBeth LeFevre

CONNECTICUT, MASSACHUSETTS, NEW HAMPSHIRE, RHODE ISLAND
Contact the National Office to Connect

Northeast Region (2)

DELAWARE
Judy Weeks, Dover

☆DC – See Virginia

MARYLAND
☆Dawn Murphy, DC/Baltimore/Northern Virginia Chapter

NEW JERSEY
☆Laurel Smith, Delaware Valley Chapter

Northeast Region (2)

NEW YORK
☆Kim Zuzzolo, NY Metro Chapter
Linda Roesch, Buffalo, Western NY Mito Group
Jennifer Schwartzoff, Buffalo, Western NY Mito Group
Erica Beyea, Buffalo, Western NY Parents Mito Group
Sandy Sallaj, Buffalo, Western NY Parents Mito Group
Jacqueline Perrotta, Albany
Lori Piccirilli, Binghamton
Kimberly Dedrick, Utica

PENNSYLVANIA
Kimberly Dojonovic, Pittsburgh East Mito Group
Daria Grabowski, Erie
Jessica Myers, Erie Mito Group
Kim Olenderski, Central Pennsylvania
Heather Pallas, Pittsburgh (children)
Karen Wilson, Pittsburgh (adults)

VIRGINIA
Heather Meyer, Lynchburg
Judi Bartle, Central Virginia Mito Group
Sharon Hoffert, Central Virginia Mito Group
Molly McCaffrey Adams, Richmond

Northeast Region (2)

☆Sharon Goldin, DC/Baltimore/Northern Virginia Chapter
☆Anne Tuccillo, DC/Baltimore/Northern Virginia Chapter

WEST VIRGINIA
Contact the National Office to Connect

Southeast Region (3)

Regional Coordinator, Margaret Moore

☆ALABAMA
Margie Slemp, Huntsville, North AL Mito Group

☆FLORIDA
Amber Ferrell, Gainesville, Central FL Mito Group
Garry Krueger, North Central Florida
Joan Morris, Titusville, FL
Denise Richardson, Fort Lauderdale
Holly Schneider, Coconut Creek
Jennifer Slauter, Orlando, Central FL Mito Group
Sophie Szilagy, North East Florida

☆GEORGIA
Shelly Lorenzen, Sugar Hill
Hannah Bossie, Athens
Gail LaFramboise, West Central Georgia
Marybeth Morris, Atlanta area

☆NORTH CAROLINA
Heather Baudet, Raleigh Durham
Christy Koury, Charlotte
Adriana Smith, Raleigh Durham
Terry Holeman, Fayetteville
Jenny Hobbs, Winston-Salem

☆SOUTH CAROLINA
Karis Mott, Chapin

☆TENNESSEE
Courtney Fellers, Nashville area
Emily Culley, Memphis area
Karrie LaCroix, Memphis area

Great Lakes and Midwest Region (4)

ILLINOIS
☆Cherie Lawson, Chicago Area Chapter
Luke or Leslie Kirby, Philo
Patti Bauer, Springfield
Victoria Helms, St. Louis Area Mito Group
Hope Grover, St. Louis Area Mito Group

INDIANA
☆Jackie Parrish, Indiana Chapter

MICHIGAN
Julie Scott, Eastern Michigan Mito Group
Missy Leone, Eastern Michigan Mito Group

Great Lakes and Midwest Region (4)

Suzanne Arends, Western Michigan Mito Group
Carrie Gervasone, Fraser
Holly Worden, Lakeview

MINNESOTA
☆Stacey Pieper, Minneapolis/St. Paul Chapter
☆Anne Simonson, Minneapolis/St. Paul Chapter

OHIO
☆Darcy Zehe, Ohio Chapter
Ruth Gerke, Central Ohio
Jody Thompson, Central Ohio
Amanda & Jason Salensky, Cincinnati Mito Group
Chris & Alisa Rawski, Toledo

WISCONSIN
Jaqueline Bohne, Harshaw
Karen Loftus, Milwaukee
Terilyn Musser, LaCrosse/Eau Claire
Mindy Welhouse, Kimberly

KENTUCKY
Contact the National Office to Connect

Central Region (5)

ARKANSAS
Lacie Moore, Rogers

IOWA
Ronda Eick, Northern Iowa
Darla Klein, Des Moines, Iowa Mito Group
Kim Novy, Des Moines, Iowa Mito Group

KANSAS (see Missouri)

LOUISIANA
Mandy Poche, Baton Rouge
Anna Stewart, Bossier City
Chantel Wooley, Corington

MISSISSIPPI
Julie Manley, Greater Jackson Mito Group

MISSOURI (see also Illinois)
Theresa Edwards, Kansas City
Keli Stone, St. Louis Area Mito Group

TEXAS
☆Deb Schindler-Boultinghouse, Houston Chapter
Shawna McElween, Dallas/Fort Worth
Joshua Brewer, Dallas/Fort Worth
Manuel Castro, Austin
Shamayn Kennedy, Wichita Falls

NORTH DAKOTA, SOUTH DAKOTA, NEBRASKA, OKLAHOMA
Contact the National Office to Connect

Western Region (6)

ARIZONA
Gina Blair, Peoria

IDAHO
Jennifer Pfefferle, Boise, Idaho Mito Group

NEW MEXICO
Stephanie Cassady, Albuquerque

UTAH
Laura McCluskey, Orem

COLORADO, WYOMING
Contact the National Office to Connect

Pacific and Northwest Region (7)

CALIFORNIA
☆Norma Gibson, California Chapter
Cheryl Burge, Inland Empire
Cory Greenlee, La Verne

HAWAII
Kimo Phan, Honolulu

OREGON
Kimberli Freilinger, Monmouth

WASHINGTON
Joy Krumdiack, NW Washington

ALASKA, MONTANA, NEVADA
Contact the National Office to Connect

INTERNATIONAL
Rob Ryan, Australia
John Carreiro, British Columbia
Nilam Argawal, India
Saijad Haider, Pakistan
Anne Hansen, Norway
Vidar Hunstad Vik, Norway
Rowland Dicker, United Kingdom
Keely Schellenberg, Winnipeg

YOUTH AMBASSADORS
Joe Wise, California
Emily Swinn, Georgia
Briana Garrldo, Hawaii
Haley Wroth, Massachusetts/Connecticut
Alexandra Simonian, New York
Tyler Liebegott, Pennsylvania
Colleen Powell, Pennsylvania
Devin Shuman, Washington

UMDF MISSION
To promote research and education for the diagnosis, treatment, and cure of mitochondrial disorders and to provide support to affected individuals and families.

Adult Corner

Meet the Adult Advisory Council Team (AACT) - Representing, Serving, and Supporting Affected Adults

My name is Sharon Shaw, and I live in Arizona. I was diagnosed with Kearns Sayre Syndrome 11 years ago. I have been involved with UMDF since my diagnosis serving on the Board of Trustees as Vice-Chairman and as Chairman of the Adult Advisory Council Team.

My name is Gail Wehling, and I live in Illinois. I was diagnosed over 30 years ago with CPEO (Chronic Progressive External Ophthalmoplegia) a form of Kearns Sayre Syndrome. I have been involved with UMDF for over 10 years serving on the Chicago Chapter Board and as Co-Chairman of the Adult Advisory Council Team.

My name is Bob Brieff, and I live in New York. I was diagnosed with Mitochondrial Myopathy over 10 years ago. I have served on the Adult Advisory Council Team since it was established in 2007.

My name is Linda Cooper, and I live in So. California. My 17 year old son, Chad, is affected. I have been a UMDF volunteer for 13 years. I currently serve on the UMDF Board of Trustees, the California Chapter Board, and the Adult Advisory Council Team.

My name is Rev. David Hamm, and I live in Maryland. I was diagnosed with MELAS (Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, Stroke) in 2005. I have been a member of the Adult Advisory Council Team since April 2007.

Our names are Erica and Etan Harmelech, and we live in Connecticut. Erica was diagnosed in 2004 with Complex One Mitochondrial Myopathy. As a young adult with mito and a spouse of someone with mito, we have taken an interest in helping young adults and their families deal with the unique challenges that come along with being affected with mito during those transitional years.

They formed and oversee the Adult Advisory Council Team Young Adult Group Committee.

My name is Pam Johnson, and I live in Kansas. My diagnosis is clinical at this point, although I continue to seek a laboratory confirmation. I have been involved with UMDF through the Kansas City Support Group for 11 years.

My name is Debra Makowski, and I live in Arizona. I was diagnosed with Mitochondrial Myopathy in 2008 after numerous lifelong misdiagnoses. I have served on the Adult Advisory Council Team as the Adult Liaison Coordinator since 2009.

Established in 2007, the purpose of AACT is to represent and serve the unique needs of the affected adult community and to ensure that those needs are adequately represented to UMDF resulting in enhanced services to the affected adult population.

AACT is a liaison to the UMDF Board of Trustees and will assess and evaluate, provide advice and guidance, and make recommendations to UMDF on adult related issues.

Contact AACT at AACT@umdf.org or call 1-888-317-UMDF (toll free) to be connected with one of the council members of AACT.

Whit Davis and Gregory Yellen are also members of the Adult Advisory Council Team. Photos of them were not available at the time this publication was printed.

Whit Davis lives in Pennsylvania. He was diagnosed with Kearns Sayre Syndrome in 1981. He joined the Adult Advisory Council Team in 2011.

Gregory Yellen lives in Maryland. He was diagnosed with Kearns Sayre Syndrome in 1989 and has been learning about mitochondrial disease ever since then. He became involved with the Adult Advisory Council Team in 2007.

UNITED MITOCHONDRIAL DISEASE FOUNDATION®

HOPE. ENERGY. LIFE.

Ask The Mito Doc℠

Living with mitochondrial disease presents many twists and turns and a maze of questions. UMDF is pleased to offer answers to some of those questions as taken from Ask the Mito Doc℠ at: www.umdf.org. Please note that information contained in Ask the Mito Doc℠ is for informational and educational purposes only. Such information is not intended to replace and should not be interpreted or relied upon as professional advice, whether medical or otherwise.

Responders for this issue include: Fran D. Kendall, M.D., of Virtual Medical Practice in Atlanta, GA and Northside Alpharetta Medical Campus in Alpharetta, GA and Mary Kay Koenig, M.D., of The University of Texas Health Science Center at Houston, Houston, TX.

The Question is...

Our son, age 12, was diagnosed with mitochondria Complex I,II, IV at 12 months. He has low tone, amblyopia, and presents deficits in speech, language, fine motor, bowel control, and cognitive and tests within mental retardation ranges at school. He is currently taking methylphenidate ER 20 mg for attention deficit. There has been slight improvement with the medications but still requires CONSTANT re-direction or one-on-one attention with all activities. We are considering increasing his dosage, but cautious due to side effects. What treatments other than the traditional ADD medications are necessary and/or appropriate in the background of mitochondrial disease? How much does the mitochondrial disease cause symptoms that mimic ADD? Based on his 5 ft, 91 lbs, would you recommend an increase in dosage? Or even changing his prescription?

Fran D. Kendall, M.D.

Response from Fran D. Kendall, M.D.:

The decision to medicate a child with ADD/ADHD spectrum issues is a difficult one and is not typically something I do or recommend unless all other avenues of treatment such as educational modification with, for example, one-on-one teaching assistance has been tried. If all other avenues fail and the ability to learn is severely impacted in a child who has the capacity to do so but cannot, due to ADD/ADHD, then I am supportive of ADD/ADHD medication. Methylphenidate ER 20 mg per day is often a starting dose for this medication. However, modification of current dosage or the decision to switch to another medication must be determined by a treating physician who will weigh the risks and benefits of doing so.

The Question is...

I am 49 years old. I was diagnosed with mitochondrial myopathy five years ago, although I have had symptoms for 21 years. My balance has gotten worse to the point I must use a cane. I had some tests that showed the vertigo was coming from my Central Nervous System. I also have some hearing loss, kidney failure (lost one kidney to cancer some years ago), sleep apnea, seizures and increased BP and pulse rate. Many of these symptoms started very recently. Can these symptoms be attributed to worsening mitochondrial disease? What do you suggest I do?

Response from Mary Kay Koenig, M.D.:

Mary Kay Koenig, M.D.

All of the symptoms you are describing are symptoms commonly seen in people with mitochondrial disease and unfortunately, most adult patients do tend to have worsening of their symptoms over time. My recommendation to you would be to do everything possible to optimize your health status. A good "check-up" at the PCP can go a long way towards improving how you feel. In your case specifically, make sure to control your seizures, have a sleep study and/or use CPAP to improve sleep quality, and see a cardiologist to assess your elevated blood pressure and heart rate. Additionally, I would suggest seeing a physical therapist to help you develop a safe, low-intensity exercise plan. Studies have shown that routine exercise can improve quality of life in people with mitochondrial disease. Lastly, ensure that you are taking adequate doses of CoEnzyme Q10. Although not proven effective, most people with mitochondrial disease describe benefits in energy levels with it.

DID YOU KNOW?

You can quickly and easily find "Ask the Mito Doc" Q/As on topics of your choice by doing the following: Place your mouse arrow on the gray Resources for Life box near the top of the UMDF home page at www.umdf.org. A drop-down box will appear with various resources in it. Click on the "Ask the Mito Doc" link, which will take you to the Mito Doc main page. Scroll down the page and click on the orange Search "Ask the Mito Doc" link; this will pull up a search box. Type in a keyword or phrase you are interested in and click "Go." It will pull up every Q/A that mentions your word or phrase. If you are not satisfied with the results, try variations or synonyms of your word/phrase.

UMDF education
Bringing the experts to your community.

Family Meetings for Families and Grand Rounds for Health Care Providers

UMDF has made Grand Rounds a top priority to reach out to physicians through introducing and/or broadening the knowledge base on mitochondrial diseases. The primary purpose of our Grand Rounds program is to provide continuing education to health care providers on topics specific to mitochondrial disorders, which also furthers the UMDF mission to promote research and education for the diagnosis, treatment, and cure of mitochondrial disorders and to provide support to affected individuals and families.

With the generous support from various funders, the foundation hosts approximately 12-15 Grand Rounds per fiscal year throughout the United States. These meetings have received nothing but positive feedback from the medical community.

In addition to Grand Rounds, UMDF also schedules a special family meeting with our members during this time to not only help educate patients/families about mitochondrial disease but to allow them to speak one-on-one with a mitochondrial specialist. These family meetings are also suitable for outreach to nurses, therapists, educators, and various allied health professionals.

Please see the schedule below for family meetings and Grand Rounds. Perhaps you can get a health care provider to attend or you may want to go to a family meeting.

Contact Janet Owens, UMDF Executive Administrative Assistant for more information. She can be reached at the National Office, toll-free, at: 1-800-317-8633, ext. 107 or at: janet@umdf.org.

Upcoming Family Meetings and Grand Rounds

Date	Type	Time	Location
4-4	Family Mtg.	6:30 pm	Oregon Health & Science University - Portland, OR
4-5	Grand Rounds	8:00 am	Oregon Health & Science University - Portland, OR
5-23	Family Mtg.	6:30 pm	Columbus Regional Healthcare System - Columbus, GA
5-24	Grand Rounds	8:00 am	Columbus Regional Healthcare System - Columbus, GA
10/2	Family Mtg.	6:30 pm	St. Mary's Medical Center - Evansville, IN
10/3	Grand Rounds	8:00 am	St. Mary's Medical Center - Evansville, IN
10/15	Family Mtg.	6:30 pm	Cooks Children's Hospital - Fort Worth, TX
10/16	Grand Rounds	8:00 am	Cooks Children's Hospital - Fort Worth, TX

Visit the UMDF calendar on the UMDF website: www.umdf.org for complete meeting details.

You may have noticed that the newsletter has a new name. The newsletter name was changed from Mitochondrial News to UMDF Connect to better connect you with UMDF resources for help and support.

If you have news in your family, that you would like to share with us, send an e-mail to: news@umdf.org or call the UMDF toll-free phone number at: 1-888-317-8633 and ask for Alison Cooley.

North Carolina Chapter Special Patient/Family Educational Meeting

Friday, March 30, 2012,
6:30 pm to 9:00 pm
Charlotte Convention Center
Room 208AB, Charlotte, NC.

Through efforts of the UMDF National Office, the North Carolina Chapter of the UMDF, and the generosity of the organizers for the upcoming SIMD/ACMG Annual Meeting, the North Carolina Chapter is pleased to offer an evening with three outstanding mitochondrial specialists. UMDF CEO/ED Chuck Mohan will also provide an update.

To register for this meeting, please visit www.umdf.org/familymeetingreg -- the UMDF is pleased to offer this FREE educational opportunity!

If you have questions or you would like to register by telephone, contact: UMDF Member Services 888-317-UMDF (8633).

Munchausen-by-Proxy - Also known as Medical Child Abuse

The following information was extracted from a symposium talk by Sumit Parikh, M.D. and other experts. Additional comments were provided by Drs. Russell Saneto and Mark Tarnopolsky.

Munchausen-by-Proxy, also known as Medical Child Abuse (MCA), is a mental disorder in which a parent (usually the mother) abuses her child by creating or falsifying medical symptoms, or by seeking unnecessary medical care for the child, in order to gain attention and sympathy. The parent may exaggerate, misrepresent, or fabricate symptoms or test results, which can lead to the child undergoing numerous hospitalizations, invasive tests, needless therapies, and even surgeries. Some physicians who have a particular interest in unusual disorders may be eager to test and diagnose a child with complex, persistent, and confusing symptoms, often feeding the problem.

Physicians, especially pediatricians, are taught to listen to and trust parents, as a means of more quickly diagnosing a sick child. But the reality is that some parents do misrepresent information to their child's physicians. Sorting out whether there actually is an underlying disease, despite possible suspicions about the parent, can be a daunting task. There are no easy answers or solutions.

No provider enters a medical relationship suspecting MCA. There are certain "red flags" that physicians note when dealing with a difficult case that often raise suspicions. These include, but are not limited to, the following:

- No explanation for a persistent illness
- Symptoms/results don't fit the case; don't make sense
- Symptoms don't occur when witness is present; only the parent sees them
- Symptoms don't respond to appropriate and adequate treatments
- Numerous doctor visits or hospitalizations
- No medical documentation of alleged illnesses/symptoms
- Change in symptoms to another organ system when testing of one system is completed/negative
- Conflicting information from various medical sources
- Embellishing or over-exaggerating symptoms & test results
- Refusal to leave the child's bedside
- Symptoms improve in the hospital and return at home
- Requests from the parent to not send results or consultation notes to the primary care pediatrician
- Multiple tests ordered by experts are normal
- Insistent requests to repeat minimally abnormal tests even if subsequent tests are normal
- Frequent attempts to contact "World Experts" to garner support for a diagnosis
- "Doctor shopping" especially in regards to a primary care pediatrician
- Being evaluated at multiple centers
- Experts stumped
- Parent enthusiastic about invasive testing

The last several bullet points in particular can cause trouble for the parents of children with mitochondrial disease. In an effort to get a diagnosis for their child, parents of patients with possible mitochondrial disease may undergo a "diagnostic odyssey." They relentlessly pursue a diagnosis via the Internet, checklists, and multiple doctors. They may see non-existent symptoms, request too many tests, visit too many doctors, embellish or exaggerate, and use medical labels/terms. While these parents may not actually be guilty of MCA, their actions and responses can make a physician suspicious, and bring the parents' integrity into question.

Additionally, there is a concern about the overuse of a mitochondrial disease label by parents and physicians. Mitochondrial symptoms can overlap with other symptoms, and can be secondary to other medical/metabolic disorders. Mitochondrial disease can be an easy diagnosis for an MCA parent to reference.

Parents may assume that the first reaction of a physician is to report the parents to Child Protective Services. However, this is often not the case. Many facilities use a Child Advocacy Team approach. The team often includes physicians from several specialties, nurses, social workers and lawyers. The cases are evaluated in detail. These teams try very hard to be objective and not have an agenda going into the situation. If a concern of symptom over-reporting is raised, they may:

- Sit down and talk with the parents (may involve talking to each parent separately).
- Teach parents to accurately describe symptoms, and not over-report/embellish information.

(Continued on page 14)

Sumit Parikh, M.D.

Russell Saneto, D.O., Ph.D.

Mark Tarnopolsky, M.D., Ph.D., FRCP(C)

Munchausen-by-Proxy

(Continued from page 13)

When a physician suspects MCA, they will often first contact the primary care pediatrician to see if they have similar concerns and if they are aware of all of the testing/referrals that have been made with the child. If a concern exists regionally, a team meeting as described above is often pursued to decide whether it is necessary to notify child protection services.

Reporting suspected MCA is not always the simplest or best solution, but in some instances or hospital systems it may be the only option to get the parents' attention and response to the doctor's/team's concerns. It is a difficult moral and ethical dilemma. While only a small percentage of reported cases actually turn out to be MCA, the accused "vocal minority" makes it seem that the problem is more common than it is. Any stress placed on the family is with the intent of the safety and protection of the child. Bearing in mind that there is a difference between suspicion and confirmation of MCA, it may be necessary to separate the child from the parent and monitor the child's health after separation. The future of the child's safety must be assured, and the whole family may be involved in the treatment.

In order to avoid a mistaken diagnosis of MCA, recommendations include the following:

- Give full & accurate disclosure of information
- Avoid exaggerations
- Keep an organized copy of all medical records and share them openly with providers
- Have a letter from the principal provider stating the diagnostic dilemma of the patient.

In conclusion, the goal of medicine is to diagnose, treat, and enable the patient to return to their best state of health. Again, no provider begins a clinic/hospital visit with MCA in mind. However, when "red flags" appear, providers are legally, morally and ethically obligated to involve child advocacy teams and/or report their concerns to the local agencies responsible for the protection of children (and adults). Uncommon diseases can present the provider uncertainty about the signs and symptoms within a clinical situation. Repeated unexplained situations compound the dilemma a provider faces. Both care providers and patients and their families need to be open and proactive in all phases of medical care. The topic of MCA is sensitive and filled with emotion on both sides. Developing a dialogue between families and providers may help reduce a false MCA diagnosis.

Disclaimer:
The above information is not considered to be official hospital policy. Each hospital has its own policy for dealing with suspected child abuse cases, and such policies may vary widely.

Untangling the Knot of Mitochondrial Disease

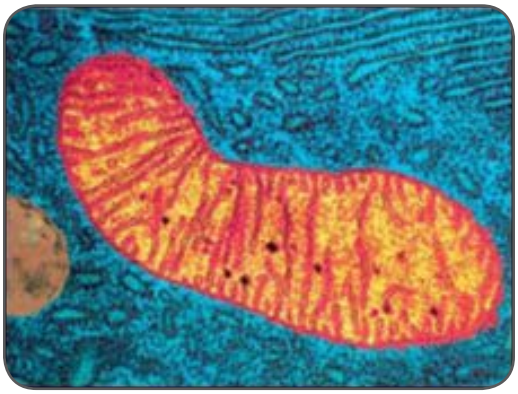
From CAP TODAY, September 2011. Reprinted with permission of the College of American Pathologists, Northfield, IL.

by Karen Titus
CAP TODAY Contributing Editor and Co-Managing Editor

Experts in mitochondrial disease are a persevering lot. Like Tristan and Isolde filling their lungs for Act 2, they're in it for the long haul.

"It's a field I've been in for 35 years," says Michael J. Bennett, Ph.D., Professor of Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania, and Director, Metabolic Disease Laboratory, Children's Hospital of Philadelphia. "And we're all still learning, basically."

"It's a difficult field," agrees Brian Robinson, Ph.D., Director of the Mitochondrial Research Laboratory, Hospital for Sick Children (SickKids), Toronto. "Even though I've been in it for 30 years, it's hard for me to figure out where it's headed."



Mitochondria

"I've been at this now for 40 years," says Douglas C. Wallace, Ph.D., the Michael and Charles Barnett Chair of Pediatric Mitochondrial Medicine and Metabolic Disease, and Director, Center for Mitochondrial and Epigenomic Medicine, CHOP. "When I started, nobody thought that studying mitochondrial DNA would be of any interest clinically." Only in recent years has medicine done an about-face on the matter, says Dr. Wallace, who likes to talk about the need to upend 150 years of Mendelian genetics in order to arrive at a proper diagnosis of mitochondrial disease.

If those are the experts talking, what are the prospects for physicians whose outlooks are less mitochondrial-centric?

The pace may be about to pick up, actually. While there's nothing easy about understanding and diagnosing mitochondrial disease—especially in children—breakthroughs appear imminent and could put laboratories in the thick of mitochondrial diagnostics. "These diseases are extraordinarily common, not rare," says Dr. Wallace, who is also Professor, Department of Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania. (A common estimate is one in 4,000 or 5,000 lifetime risk, though others, including those interviewed for this article, suggest the risk may be one in 2,000, or even less, for children.) "So the need for this testing is going to be great in almost every path lab."

Mitochondrial disorders are the Willy Lomans of disease—difficult to fathom, easy to overlook, dropping hints that don't quite add up to a full portrait. But now, attention must be paid.

Dr. Robinson hadn't planned on making mitochondrial disease his professional raison d'être. He fell into it almost by chance three decades ago when he was hired by the Hospital of Sick Children to look at why babies were developing hypoglycemia in the neonatal period.

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Untangling the Knot of Mitochondrial Disease

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Dr. Robinson, who trained as a biochemist, got busy with specific projects involving animal models. But early in his tenure, babies bumped the animals aside. "The clinicians kept coming to me, saying, 'We've got these babies with lactic acidosis, and we don't know what to do with them,'" recalls Dr. Robinson. He found himself trying to help his colleagues sort through a maze of individual metabolic defects and soon set up testing in his own laboratory.

In many ways, he's not much further than where he started. Such is the nature of diagnosing mitochondrial disease. "One of my colleagues here says, 'Mitochondrial disease can present at any age, any time, in any organ, with any set of symptoms,'" Dr. Robinson says. "And it's true."

There's been progress, of course. Dr. Robinson and other leaders in the field initially identified biochemical defects related to mitochondrial disease, then began identifying the underlying genetic defects. Next-generation sequencing has sped up that process. (See "Next-gen sequencing in clinical debuts," CAP TODAY, April 2011.) But while genetics has stormed all of medicine, mitochondrial disease has its own cruel twist: Diagnoses lie tangled within mutations both in mitochondrial DNA and in the nuclear genes. If genetics is a revolution, mitochondrial disease is an uprising within. Pathologists, it would appear, need to topple the king and set fire to the palace.

Michael J. Bennett, Ph.D.

Brian Robinson, Ph.D.

Douglas C. Wallace, Ph.D.

Rong Mao, M.D.

Richard H. Haas, M.D.

They've got their work cut out for them. "Mitochondrial disorder may be the most difficult disease to diagnose," says Rong Mao, M.D., Medical Director, Molecular Genetics and Genomics, ARUP Laboratories, and Assistant Professor of Pathology, University of Utah School of Medicine, Salt Lake City.

Why is it so difficult? Pull up a chair.

For starters, mitochondrial disease is given short shrift in medical training—understandably so. It's hard to teach what even the experts are only now starting to learn. Most physicians probably know that mitochondrial disease can be caused by mutations in the mitochondrial DNA, says Dr. Mao. "But the mutations in the nuclear genes are something new," she says, with the mitochondrial genome encompassing not only the mitochondrial DNA but more than a thousand nuclear DNA genes dispersed throughout the chromosomes.

On the biochemical end, the tests most physicians know about come up short. Says Dr. Bennett: "We have no good biomarkers whatsoever."

The lineup of traditional tests includes lactate and pyruvate analysis in blood and cerebrospinal fluid; plasma and CSF amino acids; urine organic acids; and plasma acylcarnitines. "All those provide clues without giving a diagnosis," says Dr. Bennett. (See Haas RH, et al. The in-depth evaluation of suspected mitochondrial disease. Mol Genet Metab. 2008;94:16–37; and Haas RH, et al. Mitochondrial disease: A practical approach for primary care physicians. Pediatrics. 2007;120:1326–1333.)

Lactate acid elevation should arouse suspicions, but it's not specific for mitochondrial disease. And some patients with mitochondrial disease may have normal lactate and pyruvate levels. A plasma amino assay might show an elevated alanine level, but again, this is a clue, not a diagnostic marker, Dr. Bennett says, since anyone with lactic acidemia will have an elevated alanine. "For the clinician, it should say, 'At least we're on the right track.' But these are soft clues without being particularly diagnostic," Dr. Bennett says.

Are clinicians good at spotting these clues? "Physicians are getting better," Dr. Bennett says. "There are some outstanding physicians out there. But it's a very, very difficult area."

Muscle biopsies have their own difficulties, especially in pediatric patients. There are the occasional slam-dunk cases—for example, ragged red fibers are a hallmark of mitochondrial myopathy. But generally, aimless dribbling seems to be the order of the day, particularly in the pediatric age group, where clues are much more subtle. "Probably the most common thing to find on muscle histology in pediatrics is nothing," says Richard H. Haas, M.D., Professor, Neurosciences and Pediatrics, and Director, UCSD Mitochondrial Disease Laboratory, UCSD Medical Center, La Jolla, CA.

"Then that blends into a few patients who do have ragged red fibers," Dr. Haas continues. "And in between you have patients with some evidence of mitochondrial proliferation. That middle group can be missed by people who aren't clued into this."

It doesn't help that effective treatments are scarce. Staple treatments include high doses of B vitamins and coenzyme Q10. EPI-743 (Edison Pharmaceuticals) looks promising in very early trials, says Dr. Haas, and MELAS patients are generally put on arginine or citrulline. Other approaches use antioxidants. Says Dr. Haas: "In the next few years we're going to be in a much better position in terms of having effective treatments for mitochondrial disease. We're not really there yet."

Even the phrase "mitochondrial disease" is suspect—it's a lumpy, almost useless definition, like saying someone has "cancer." "They're heterogeneous diseases clinically and biochemically," says Dr. Haas. Plotting out mitochondrial disease, with all its possible destinations, would produce an image resembling the iconic London Underground map, with its simplistic, geographically misleading routes. "We think in terms of primary genetic disease, and also secondary mito-

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Untangling the Knot of Mitochondrial Disease

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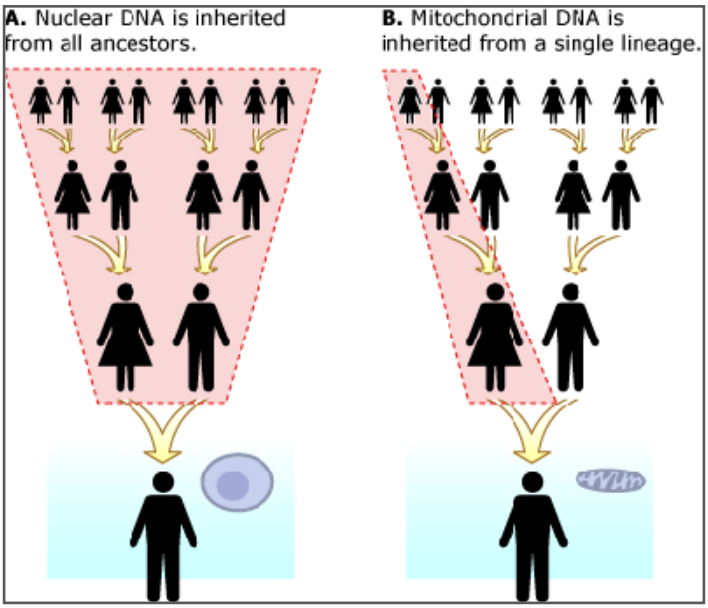
chondrial disease, which is another major category where there's evidence of mitochondrial dysfunction. And neurodegenerative, later-onset disease—Alzheimer's and Parkinson's disease—may have a combination of genetic predisposition and secondary mitochondrial failure. Type 2 diabetes has a major mitochondrial component to it," Dr. Haas says. In fact, "Almost any disease you care to mention, because mitochondria is so critical in metabolism, has some mitochondrial component."

Nonetheless, Dr. Haas says, physicians are getting better at considering mitochondrial disease. "They all know about it now. Ten years ago that wasn't the case."

Dr. Bennett suggests that physicians fail to detect cases because of the difficulties in attaching clinical clues to certain phenotypes. That will change as the underlying genetic defects come into sharper focus. "But it's been a slow molecular slog," he says, given the poor correlation between phenotype and genotype. "It's been a matter of working through the genes we know are associated with mitochondrial function. It's almost like a fishing expedition."

Dr. Wallace offers up Kearns-Sayre syndrome by way of explanation. The disease is severe, with onset typically before age 20, and is due to a deletion in the mitochondrial DNA. Because the mitochondrial DNA is inherited independent of the nuclear genes, however, and can be gained or lost during mitosis as well as meiosis, different types of tissue have different mitochondrial DNA genotypes, Dr. Wallace explains. "The muscle, the brain, the kidney—all the postmitotic organs have very high levels of this mutant, and that causes the disease."



Nuclear DNA vs. Mitochondrial DNA

The mutant, he continues, is selected against in the bone marrow stem cells. There is no deletion in blood.

This point has not always been understood, Dr. Wallace says. "Even today, pathologists ask me to rule out Kearns-Sayre and send me a blood sample. That simply can't work."

Dr. Wallace sees a bigger problem beyond this specific example. For him, the walls of Jericho need to tumble—and he's not shy about blowing the trumpet. "There's a real disconnect between this totally new genetics and biology, which is never taught to physicians, and the diagnostic tools that we need to address it," he says. "We're constantly asked to do things that might make sense from the traditional way of doing molecular pathology; for nuclear genes, it's actually not applicable to this novel set of genes."

That gap is only the first of several layers of complication that bedevil the diagnoses of mitochondrial disease, Dr. Wallace says. Understanding mitochondrial disease, as it turns out, quickly becomes a trip with as many twists as San Francisco's Lombard Street.

The second difficulty, he says, is that each cell contains thousands of copies of this mitochondrial DNA, whereas nuclear DNA contains only two copies. Thus, people with a mitochondrial DNA mutation can have a mixture of mutant and normal mitochondrial DNAs, a state known as heteroplasmy.

Genetic testing for nuclear DNA gene mutations is relatively simple since there are only three states: plus-plus, plus-minus, and "dead" (minus-minus). The possibilities explode for mitochondrial genotypes. Mutant levels could be low (0.1, one, three, five percent) or high (90, 95, 100 percent) or anywhere in between. "And different percentages of the same mutant give you totally different clinical presentations," Dr. Wallace says. For example, a mutation in the ATPase 6 gene of mitochondrial DNA at nucleotide position 8993, with a 75 percent mutation level in the body, will present as mild, so-called salt and pepper retinitis pigmentosa, Dr. Wallace says. Higher levels of mutation lead to macular degeneration and movement disorders. But at 95 percent, the result is Leigh syndrome.

In other words, he explains, the exact same mutation can result in very different clinical phenotypes depending simply on the percentage heteroplasmy: subclinical or with late adult onset, clinical with young adult onset, or severe with early pediatric death.

For another heteroplasmic mitochondrial DNA mutation, the MELAS tRNA mutation, high levels of mutant can cause stroke-like symptoms, cardiomyopathy, and/or myopathy. However, at low levels of heteroplasmy, this same mutant causes type 2 diabetes.

The heteroplasmy problem is particularly difficult for the mitochondrial medicine laboratory, Dr. Wallace says, "since someone can send me a blood sample to test for the MERRF mutation [which can cause myoclonic epilepsy], which is caused by a heteroplasmic mitochondrial DNA tRNA mutation. The mutation may be at 10 percent in the blood, but at 80 percent in the brain. So now you have this total disconnect between the numbers I give the physician, from the clinical lab, and the functional and genetic effect on the target organ."

The third major diagnostic dilemma is that the same clinical phenotype can be caused by mutations in totally different genes in the mitochondrial genome. For example, the severe childhood disease Leigh syndrome is now known to be caused by both mitochondrial DNA or nuclear DNA mutations in genes of the mitochondrial genome.

This is a striking difference from what most physicians were taught about nuclear mutations, with its linear approach: one gene, one polypeptide, one phenotype, Dr. Wallace says. With mitochondrial mutations, the same mutation can produce multiple phenotypes, simply from this statistical percentage of different mitochondrial DNAs. "That has been extraordinarily difficult for Western medicine, which is based on the differential diagnosis, the idea that there are given clinical presentations for given disease entities." In the case of mitochondrial disease, that approach is starting to look like a rusty one.

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Untangling the Knot of Mitochondrial Disease

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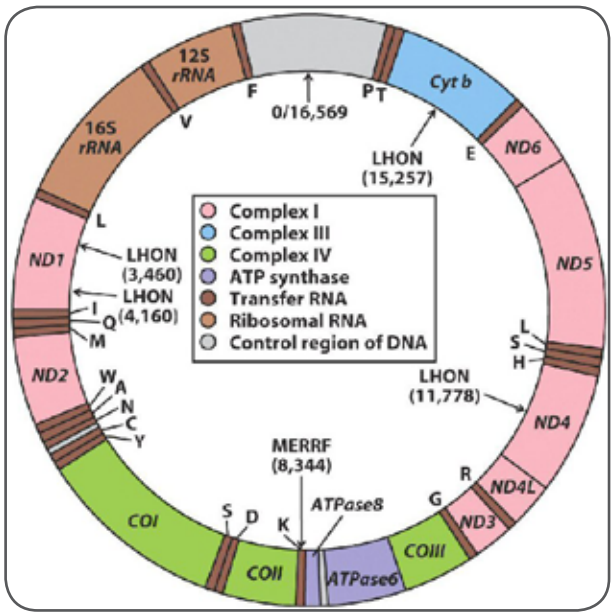
In short, every turn is different from the one physicians are used to taking. The road Dr. Wallace says needs to be taken is stochastic, not deterministic. "This has baffled the diagnostic systems of this country."

Not in other countries? Physicians in other countries are wrestling with it, Dr. Wallace concedes, but the paradigm in Western medicine is particularly difficult to transcend, he says. "Our clinical specialties, with the exception of the pediatrician, the internist, and the geneticist, are primarily based on anatomy. You're either a neurologist or a cardiologist or an ophthalmologist, etc." In China, by contrast, traditional medicine is based on "chi," the concept that the body's energy state causes symptoms. "The diseases we're talking about are diseases of energy flow, much more aligned with the concept of chi," Dr. Wallace says. "Since energy flow is essential for every organ in the body, but different organs of the body rely on energy flow to different extents, depending on the activity level, then you get systemic effects, genetic effects, that have organ-specific phenotypes.

"This is problematic for the way many people are trained in medicine in the U.S.," he continues. "If there's a symptom in a particular organ, then you tend to think of it as an organ-specific disease. We think of Alzheimer's disease as a brain disease. But in fact we and others have published papers showing that Alzheimer's disease is a systemic mitochondrial defect with tissue-specific symptomatology."

For all the complexities, Dr. Wallace does not see an insurmountable problem when he looks at the future of mitochondrial diagnostics. The concepts aren't hard to understand, he says. "But they are different."



Mitochondrial DNA

Biochemistry, typically the entree for most mitochondrial disease workups, is its own obstacle course. Looking to biochemistry to provide answers about mitochondrial dysfunction is "even more problematic" than the aforementioned DNA work, says Dr. Wallace.

Current biochemisty tests might raise suspicions, but don't expect that flag to snap smartly in the breeze, signaling mitochondrial disease. The testing tends to be reduced to a simplistic formula, says Dr. Wallace: that you can tell mitochondrial diseases by elevated lactate, or by pyruvate dehydrogenase deficiencies by the lactate-pyruvate ratio.

This is "mildly true," says Dr. Wallace. "But those are very, very insensitive approaches." Leber's hereditary optic neuropathy, though a mitochondrial DNA disease, rarely if ever has elevated lactate or altered lactate-pyruvate, he says; moreover, a muscle biopsy will show no altered mitochondrial morphology.

So at one end of the range are clinically relevant mutations that are so mild they pass under the variance of traditional assays, he says; at the other are devastating diseases, such as a severe Kearns-Sayre syndrome, which will show high levels of lactate in the blood, cerebrospinal fluid, and urine. "But those are the rare forms," Dr. Wallace says.

Dr. Bennett says he and his colleagues have developed an assay for measuring tissue levels of acyl-CoA. But better markers are not easy pickings.

"Some years ago," says Dr. Bennett, "we thought we had some clues toward defects of complex I of the respiratory chain," which essentially converts NADH into NAD for recycling. The NAD becomes limiting in complex I deficiency, "so what happened is it affected other metabolic pathways that actually require NAD. And so we've got some secondary clues based on metabolites that pointed to other diseases but in fact were primarily mitochondrial." To Dr. Bennett, this suggests there may be individual biomarkers for some of the mitochondrial diseases, and that the respiratory chain complexes—which relate to different parts of metabolism—might point the way. "But we're certainly not there yet."

Clinicians may not be aware of the many subtleties that can affect test results, Dr. Haas says. Some examples:

- Pyruvate is an unstable compound, a concern because it's often done as a send-out test, he says.
- If plasma amino acids are collected in a postprandial state, the elevated results can lead to false-positives.
- Patients who take carnitine will have a general elevation in acylcarnitine derivatives.
- Some drugs, including Valproate, will impair fatty acid oxidation, leading to a fatty acid oxidation defect in the acylcarnitine profile.
- Patients who are fasting tend to have elevated dicarboxylic acids and beta-hydroxybutyrate in the organic acids, which will also be reflected in the acylcarnitine profile.

"I don't think there's anywhere near the awareness of any of this that there should be," says Dr. Haas.

Most biochemical testing is done in academically based biochemical genetics labs, Dr. Haas says, as well as in commercial laboratories such as ARUP and Quest. But even with send-outs, labs can help their colleagues interpret confusing results. Inconclusive results aren't unusual during a diagnostic workup, Dr. Mao notes, which clinicians find unsettling. "They want to know how to interpret 'equivocal,'" she says.

"They wind up not knowing what to do," agrees Dr. Haas. "Often that generates a referral to us, often for things that are pretty trivial. We see patients where there's a question of whether they have severe disease—and in fact they were simply fasting when the sample was collected. Or eating Jell-O," Dr. Haas says with a laugh, noting that gelatin can cause adipic acid elevation in organic acids.

Dr. Bennett says clinicians might not fully appreciate the complexities of mitochondrial workups, or that interpretations are heavily dependent on skills of the interpreter. Many of the tests are in-house assays, with all the variability that implies. "Something I learned a long time ago is, if a physician suspects something strongly enough, and the tests don't give them the right answer, they should at least repeat it and maybe go somewhere else and see if they can get a different interpretation, particularly in this field, where interpretation is open to different skill sets," Dr. Bennett says.

(Continued on page 18

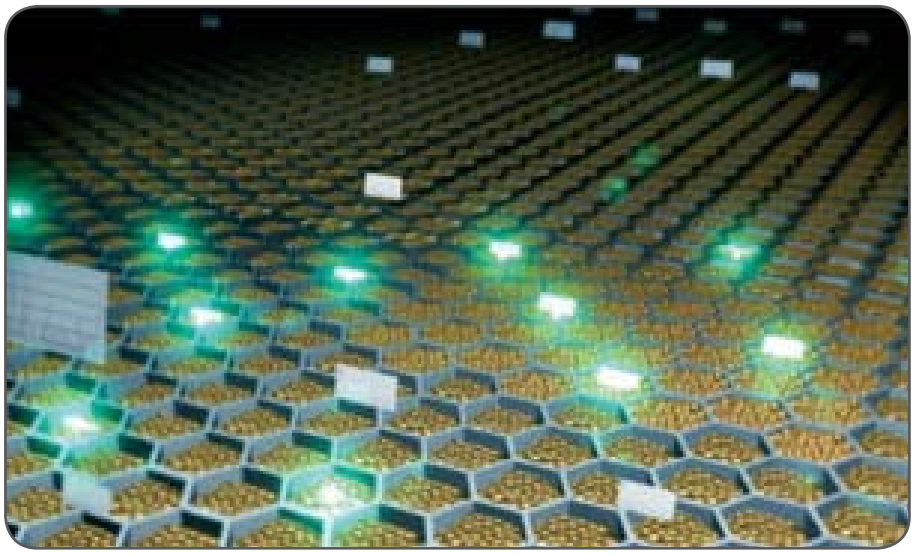
Untangling the Knot of Mito Disease

(Continued from page 17)

All this assumes that clinicians are even thinking to look for a mitochondrial disorder. Dr. Bennett suggests labs might be able to help raise the concern, but, mitochondrial disease being what it is, it resists facile advice, such as "start testing sooner." That, he says, could cause clinicians to pile on unnecessary tests. He wants labs to raise the flag of suspicion—but not too high, nor too quickly.

Typically, he says, patients with a mitochondrial disease first work their way through other subspecialties. Only at the end of the line, when no clear answer is forthcoming, will someone suggest a mitochondrial culprit. "If it's a GI presentation they would have been through the GI docs. Or, it's a neurological patient who goes through all the right testing for, say, a seizure disorder, but they don't get an answer. Then I think the thought begins to occur that it could be metabolic."

That's the sort of thinking Dr. Bennett would like to change. "People ought to be aware that it's a possibility from a clinical perspective, not something you suddenly realize you haven't done at the end."



Next Generation Sequencing

Perhaps the answer will lie in the happy, and apparently inevitable, confluence of next-generation sequencing and (to use Dr. Mao's phrase) next-generation pathologists.

Next-generation sequencing is the topic of lively discussions in pathology departments and universities, she says, since everyone has recognized the need to train residents and fellows in interpreting next-gen sequencing results. Ditto, she says, for the Association for Molecular Pathology, which is discussing educational guidelines for teaching the new technology.

Any lab that's currently embracing next-generation sequencing is on the right path, Dr. Wallace says. "That obviously is going to be a tremendous benefit for looking at these thousand-gene nuclear problem sets," he says.

But the answers still won't come easily—next-generation sequencing won't be turnkey. For mitochondrial DNA, "It would be tempting to say, 'Oh, we'll just throw it onto next-generation sequencing," Dr. Wallace says. But physicians need to be mindful that the tissue of interest has its own unique genotype. "So just throwing blood samples onto your automated sequencer to give you a result could well be misleading."

Researchers are beginning to look at other, accessible tissues as surrogates, he says. Urinary cell sediment sometimes contains mitochondrial DNA mutations that are not found in blood. Ditto for buccal swab tissue, as well as hair follicles. "But in the end, if it's a neuromuscular disease, you probably are going to many times be driven to actually get at least a small sample of muscle, say through a needle biopsy, if you're actually going to do a molecular diagnosis."

And there's nothing easy about tissue biopsies for mitochondrial diagnoses, especially in pediatric patients. Those with mitochondrial disease can be hypersensitive to the adverse effects of anesthesia, Dr. Wallace says; moreover, the large volume of tissue required can be disfiguring in small patients.

At CHOP, Dr. Wallace and his colleagues are building microchamber analysis tools, which will permit them to take a tiny segment of muscle from a needle biopsy, then perform traditional biochemical assays on one-hundredth the sample previously required.

Dr. Haas and colleagues are exploring new methods to extract useful information from muscle biopsies, using a high-resolution respirometer to look at oxygen consumption with different substrates of live mitochondria, using either intact tissue or with isolated mitochondria.

They're also looking at electron transport assays, again using either a frozen tissue sample or isolated mitochondria. These assays fall prey to lab-to-lab variability, Dr. Haas says. "They're not developed in a way CAP would like it, I'm sure, but it's kind of the state of the art at the moment."

Despite the abundant hurdles, a build-it-and-they-will-come hopefulness seems to prevail when it comes to next-generation sequencing. It's almost a foregone conclusion that the technology will eventually allow physicians to obtain a molecular diagnosis and confirmation of disease in the majority of patients. Some companies already offer next-generation sequencing of candidate mitochondrial genes. Dr. Haas says once this technology is brought to bear on mitochondrial disease, "The whole world's going to change."

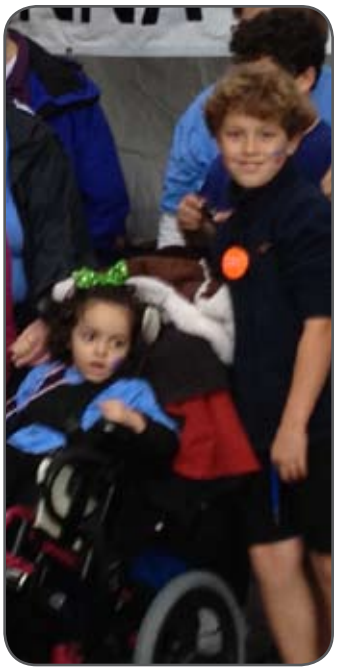
But on whose dime? "It's incredibly expensive," Dr. Haas warns.

Dr. Robinson sees a silver lining in that dark cloud, predicting a push to start, rather than end, with a genetic diagnosis. "The administrative people who look at costs will say, 'This is going to be cheaper than doing a muscle biopsy and getting the pathology and so on,'" he says. "That actually might be quite an efficacious way of doing things.

"But," he says, "it's going to take awhile to sort it all out." For mitochondrial disease—a disease that offers minimal diagnostic clues, few treatments, and an equally perplexing (and expensive) future—that's just par for the course.

UMDF
events
The energy providing education, support, and research.

Fundraisers Benefiting the UMDF



Sarah James snuggles with Stacy Navarrete as Nathan Lawson pushes the wheelchair at the Energy for Life Walkathon in Houston, TX. Meanwhile, Drew Vanchiere poses with his cousin, Anna Beth Vanchiere at the walk.

Jennifer Moore, Will Martin (also featured on the banner), Hank Goggan, Elliot Day, Carson Hayes, and Jerry Vinklarek at the walk in Houston, TX.

- **December 8, 2012.** The University of Florida's Agronomy Department held a raffle at their Annual Christmas Party for the UMDF this year. The faculty and families donated to the UMDF in honor of Nathan Ferrell, whose father William, is a professor at the University. The donations totaled more than $600. Thank you UF Agronomy Department for you generous donation!

- **December 17, 2012.** James Kedrow and Charlotte Gutwein celebrated their marriage on Saturday, December 17th. In lieu of gifts, the newly married couple asked that donations be made to the UMDF in honor of James' daughter, Rachel. They received about $1,600. The UMDF sends our congratulations and gratitude for your generous donation!

Brendan Maglish with his dog, Goldie

- **December 20, 2012.** The Family of Ted Tiller held a fundraiser at Friendly's Family Restaurant and raised more than $50. Thank you Ted and family for your amazing dedication to the UMDF!

- **January 2012.** Students at St. Bernadette's Roman Catholic School in Monroeville, PA, collected more than $2,000 for the second year in a row for the UMDF. They have raised $15,820 since 2002 when they first began collecting coins for a cure. Big hugs to all of the students for their continued support!

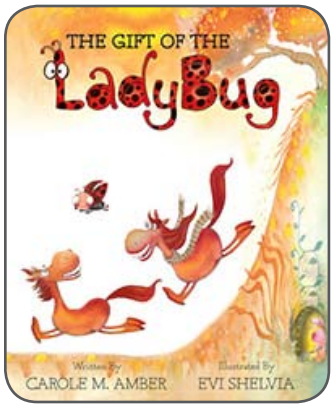
- **February 5, 2012.** The Houston Chapter hosted their Second Annual Energy for Life Walkathon in Sam Houston Park in Houston, TX. Approximately 450 walkers braved the rainy afternoon and raised more than $123,800. Thank you to the entire walk committee for coordinating this event.

- **February 8, 2012.** The Kouts Middle School of Kouts, IN, held an awareness week in honor of Brendan Maglish. The school held special days throughout the week and even held a bake sale! They raised over $250 for the UMDF! Thank you to the Kouts Middle School students and staff for an outstanding week!

- **December 4, 2012.** A Silpada Jewelry fundraiser was held in Exton, PA, at Weso's Restaurant in honor of Nathan Mowrer. Thank you for raising awareness about mitochondrial disease and for your donation of more than $600!

Gifts from the Heart

- Carole and Troy Amber of Columbus, OH, donated $2,607 to the UMDF, which includes a $250 donation from Thrivent Financial, from the sale of Carole's book, "The Gift of the Ladybug," to UMDF members and supporters on TJ's birthday, January 28, 2012. TJ, who suffered from Leigh syndrome, died at the age of fourteen months and his mom, Carole wrote a book about her journey with her son. "The Gift of the Ladybug" is still for sale and will continue to benefit the UMDF. For the story behind the story, visit: GiftoftheLadybug.com. Thank you Carole and Troy for sharing your story and for your donation to the UMDF!



Carole Amber's book, "The Gift of the Ladybug" and Carole and Troy's "ladybug" - TJ Amber.

- The family of John Garrett Evans of White Castle, LA, held a garage sale in honor of John Garrett Evans, Lydia Poche', Joe Reyes and all those fighting this incurable disease. Thank you to the Evans' family for holding the sale and for your donation of more than $1,100!

- Kristine & Trevor Miller of North Vernon, IN, participated in some local 5k races and an Ironman to spread awareness. They also collected donations in honor of their children, Zoe & Eliana, who have a mitochondrial disease. Thank you Kristine & Trevor for helping to spread awareness about mitochondrial diseases and for your donation of over $1,000!

- Grace Rennick of Rhode Island celebrated her birthday in October. She asked for donations to be made to the UMDF in lieu of presents, and she received about $150! Thank you Grace for your generosity! You are just too sweet! Happy Birthday!

- Anna Stewart of Benton, LA, held several awareness activities in the past few months, from a Chick-fil-A Day, to a Jeans Day at five local schools, and a raffle for some great prizes! Thank you Anna for an amazing job at raising awareness and collecting donations that totaled nearly $3,600!

- Alyssa Rogers of South Carolina held a lemonade stand in honor of her brother, Carson and raised about $30.00. Thank you so much Alyssa for your continued support of the UMDF! You are a very sweet sister!

- Pat Blankenship of Bronx, NY, sent in donations that she collected over the last month for the Coins for a Cure campaign. Her dontaions totaled about $255. She places boxes in her cafeteria at work, in honor of her niece, Michelle Mohan. Thank you Pat for your continued support of the UMDF!

- Ted Tiller of Syosset, NY sent in a donation of approximately $200 from selling his book, "The Bullies Learn Their Lesson." One dollar from each book sold will go to the UMDF! He has just received his third printing of 100 books! Way to go Ted!

- The Sales Employees of Relyco Business Printer Solutions of Dover, NH, chose the UMDF as their charity for their "Change for Change" program that is entirely employee-driven and managed. Thank you so much for your generous donation of nearly $250!

- Kimberli Freilinger of Monmouth, OR, had an 80s theme prom party for her 39th Birthday. She received $115 from family and friends and donated it to the UMDF. She also organized a fundraising event at Burgerville where 10 percent of all proceeds were donated to the UMDF. Thank you Kimberli for your donation and Happy Belated Birthday!

Mrs. Polk County International Kimberli Freilinger (a UMDF Oregon Ambassador), Mrs. Oregon International Kimberlee Buckingham, and Mrs. Multnomah County International Christine Wooley celebrated Rare Disease Day by fundraising for the UMDF. Freilinger said, "It was a great night and many people learned about mitochondrial disease! I love the UMDF!"

- The Publick House of Sturbridge, MA, held another wonderful fundraiser for the UMDF! A benefit dinner was held and raised $600 for the UMDF! Thank you, Cheryl Harrington and The Publick House, for your continued support!

- The RBC Capital Markets employees held a Jeans Day for the UMDF in the month of December. The total collected was just over $4,000! Thank you so much employees at RBC Capital Markets of New York City; your support is greatly appreciated!

- The Alpha Tau Omega Delta Kappa Chapter of Norman, OK, raised money in honor of Bailey Ferguson of Katy, TX. Thank you, ATO Fraternity for your philanthropy efforts to the UMDF and for your donation of more than $900!

- Melissa Fischer held an Art Party and Girls Night Out for Mito and raised $200 for the UMDF. Thank you Melissa for hosting this creative event!

Upcoming Events to Benefit the UMDF

- **March 31, 2012.** The Annual Bet on Baylee Casino Day & Auction Night will be held at the Roseville Community Center in Roseville, OH, in honor of Baylee Thompson. Join the Thompson family for great auction items, Texas Hold'em Tourney, wonderful food, and music. For more information, contact Jody Thompson by telephone at: 740-704-2994 or e-mail at: buff2506@hotmail.com.
- **April 1, 2012.** Think Spring! Bruster's of Ingomar on Perry Highway in Pittsburgh, PA will host an Easter Egg Hunt with 10 percent of all food sales being donated to the UMDF. For more information, contact the National office at: 1-888-317-8633.
- **April 14, 2012.** The Middle Tennessee Chapter will be holding their Second Annual Energy for Life Walkathon at the Nashville Zoo at Grassmere in Nashville, TN. Please join them again this year and help them raise funds and spread awareness of mitochondrial disease. For more information, go to: www.energyforlifewalk.org/nashville.
- **April 14, 2012.** The California Chapter will be holding their first annual Energy for Life Walkathon at Golden Gate Park in San Francisco, CA. Please join them to make their first Energy for Life Walkathon a success! For details, go to: www.energyforlifewalk.org/sanfrancisco.
- **April 14, 2012.** The St. Louis Metro Area Mito Group will be holding an Energy for Life Walkathon at Tower Grove Park in St. Louis, MO. Join them at their new location and help raise funds to find a cure. For more details, visit: www.energyforlifewalk.org/stlouis.
- **April 21, 2012.** The Atlanta Chapter will be holding their first annual Energy for Life Walkathon at Centennial Park in Atlanta, GA. Please join members of the chapter to make their first Energy for Life Walkathon a success! For details, go to: www.energyforlifewalk.org/atlanta.
- **April 28, 2012.** The Indiana Chapter will be holding their Second Annual Energy for Life Walkathon at IUPUI Campus outside of Taylor Hall. Please join them again this year and help them spread awareness and raise funds to find a cure. For more information, please visit: www.energyforlifewalk.org/indianapolis.
- **May 5, 2012.** The Binghamton Group will be holding their first annual Energy for Life Walkathon at Otsiningo Park in Binghamton, NY. Please join them for this inaugural event! For more information, go to: www.energyforlifewalk.org/binghamton.
- **May 5, 2012.** The Evansville Walk Committee is excited to announce their first annual Energy for Life Walkathon at Burdette Park in Evansville, IN. Please join them for this inaugural event! For details, visit: www.energyforlifewalk.org/evansville.
- **May 11, 2012.** The Western PA Mito Group invites you to join in on the fun at a home game for the Pittsburgh Pirates vs. the Houston Astros. For ticket information, please visit: www.umdf.org/pirates.
- **May 19, 2012.** The Michigan Mito Group will be holding their first annual Energy for Life Walkathon at Southeast Area Park in Ann Arbor, MI. Please join them for this inaugural event! For information, go to: www.energyforlifewalk.org/annarbor.
- **June 2, 2012.** The Western PA Mito Group will be holding their first annual Energy for Life Walkathon at Heinz Field in Pittsburgh, PA. Please join them for this inaugural event! For more information, go to: www.energyforlifewalk.org/pittsburgh.
- **June 9, 2012.** The Dobke Family of Waukesha, WI will host the sixth annual Greater Mito Open Golf Classic at Broadlands Golf Club in North Prairie, WI. For more information please e-mail: ddobke@wi.rr.com.
- **June 15, 2012.** Please join us for the inaugural Carson's Classic golf tournament hosted by the Dawg's for Mito collegiate chapter of the UMDF. All proceeds will benefit the UMDF in honor of Carson Coburn. For information on registering or sponsoring the event, go to: www.carsonsclassic.org.
- **June 23, 2012.** The Annual Lavallette 8K will be held in Lavallette, NJ, in honor of Lauryn and Owen Boyle. Please contact Kirk Tilton at: lavallette8k@gmail.com for details.
- **June 24, 2012.** Linda Wilkinson will be holding her first annual Bike Run for the Brittany Wilkinson Research Fund. For more information, contact Linda at: dotoheven@aol.com.
- **October 7, 2012.** Are you running in the Chicago Marathon? If so, please be sure to select the United Mitochondrial Disease Foundation as your official charity for the marathon! Also, visit: www.umdf.org/chicagomarathon to get more information, join our Team "Hope Energy Life," or make a donation!

If you are having or have held a fundraising event, or are in need of assistance, we want to talk to you!

Contact the Special Events Department via e-mail at: events@umdf.org or call them, toll free, at: 1-888-317-UMDF.

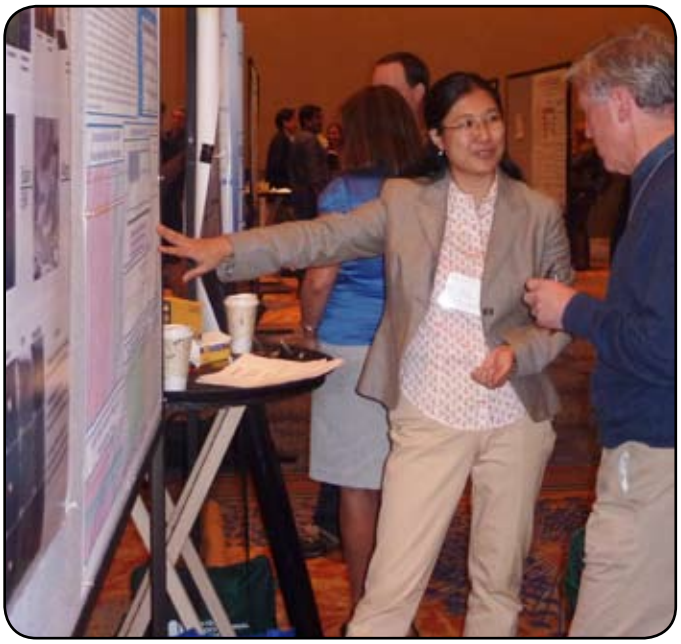
UMDF symposium

Providing education and networking.

The UMDF staff and the 2012 Family and Scientific Planning Committees are preparing for Mitochondrial Medicine 2012: Capitol Hill. The Scientific Program takes place Wednesday, June 13 thru Saturday, June 16, 2012, and the Family Program will be held Friday, June 15 and Saturday, June 16, 2012. All meetings will be held at the Bethesda North Marriott Hotel & Conference Center in Bethesda, MD. "Day on the Hill" is scheduled on Thursday, June 14, 2012.

Patients and families will have the opportunity to meet leading mitochondrial experts and many others who are in similar situations seeking information about mitochondrial disease and fellowship among peers with the same struggles. All those in the medical community are encouraged to attend and learn the latest information about mitochondrial disease and network with others in their field, as well as, meet patients and families affected by mitochondrial disease.

Please see the top ten reasons to attend either platform. To register, go to: www.umdf.org/symposium or call the National Office (toll-free): 1-888-317-UMDF. Scholarships are available; visit the website above for more information. The scholarship application deadline is April 30, 2012.



Hong Cui, Ph.D., with the Baylor College of Medicine in Houston, TX, talks to a symposium attendee.

Top 10 Reasons for Patients and Families to Attend:

1. Learn about current diagnostic testing and therapies from world-renown leaders in mitochondrial medicine.
2. Hear talks on living with mitochondrial disease; numerous topics, ranging from pediatric to adult issues.
3. Learn about medical, educational and vocational transitioning.
4. Attend an Ask the Mito Doc Panel session – Adult or Pediatric Q/As.
5. Meet with your congressman on Capitol Hill and advocate for mitochondrial medicine research funding.
6. Network with other mitochondrial disease patients and their families.
7. Learn about new products from exhibitors.
8. Speak one-on-one with a mitochondrial disease specialist at "The Doctor Is In."
9. Mingle with leading Mitochondrial Disease Researchers.
10. Involve your teen/young adult in impactful youth sessions.

Rachel Pipp and Chuck Mohan at the 2011 Symposium.

Top 10 Reasons for Scientists, Physicians, and those in the Medical Field to Attend:

1. Hear cutting edge lectures from world-renown leaders – including sessions on Genomics of Mitochondrial Biology and Mitochondrial Proteomics, Next Generation Sequencing, Translational Mitochondrial Medicine and much more.
2. Network with representatives from the National Institutes of Health.
3. Share common interests in mitochondrial research with physicians, researchers and scientists from around the world.
4. Attend a special panel discussion incorporating next-generation profiles into routine clinical use.
5. Participate in poster and abstract sessions – peer-reviewed poster presentations scheduled throughout the meeting with time given for questions and answers.
6. Attend a Special Clinical Director's Workshop – a new opportunity for clinicians. With an open discussion format, participants will work through the day-to-day challenges faced by clinicians in their practice (patient care and systems related).
7. Gain valuable information on the latest trends in mitochondrial medicine with ample time for professional discussion both in and out of the meeting room.
8. Interact with mitochondrial disease patients and their families.
9. Learn about new technologies and leading edge products from exhibitors.
10. Earn continuing education credits -- 23.25 CME Credits will be available to attendees.

UMDF advocacy

Your voice on important issues.

In June 2009, more than 150 members of the United Mitochondrial Disease Foundation were bussed to Capitol Hill. Prior to their arrival, appointments had been made for them with their representatives in the U.S. House and Senate. Armed with information, meeting times, maps, and good walking shoes, UMDF members were able to speak about mitochondrial disease and have their voices heard. It was our first ever "Day on the Hill" and it resulted in 253 meetings over an eight hour period. We're ready to do it again! Are you?

The UMDF's "Day on the Hill" will be held on Thursday, June 14, 2012, as part of our 14th Annual Symposium. Since the symposium takes place in Bethesda, MD, this year, the UMDF is giving everyone attending a chance to advocate for mitochondrial disease funding. Past participants found this experience important because they were able to tell their own personal stories to their elected officials in an effort to get them to learn more about mitochondrial disease and to work to involve the federal government in funding additional research towards a cure.

Amy Goldstein, M.D.; Leslie Heilman, J.D.; Representative Mike Doyle (D - PA), Heather and Hannah Pallas, and Chuck Mohan at "Day on the Hill" in 2009.

Those who participated in our 2009 "Day on the Hill" will remember some of the challenges we had at that time. Participants reported about meetings they had with their elected officials in hallways. They talked about the glazed look their elected official had when they mentioned the word 'mitochondria'. But, all of that work by UMDF members on that day in 2009 has paved the way for some incredibly positive developments.

We were able to have H.R. 3502 introduced in the House and S.2858 introduced in the Senate. Those bills asked the National Institutes of Health (NIH) to increase funding for research, create an office of Mitochondrial Medicine within the NIH, to create a biorepository and clinical patient registry, and for scientists and researchers at the NIH to better collaborate in order to bring about more effective treatments and potential cures.

Unfortunately, while each bill had significant bipartisan cosponsorship, neither made it out of their respective committees. Both bills expired in December 2010. The good news is that many of the things requested in those bills are coming into existence all because our members took the time to participate in" Day on the Hill" or scheduled a visit in their own communities with their elected officials.

While the bills may have expired, the champions of our legislation have remained solidly committed to our efforts. Senator Barbara Boxer (D-CA), through the efforts of the Wilkinson family, remains a champion of our efforts, as is Rep. Jim McDermott (WA-D-7). When the bills expired, Sen. Boxer and Rep. McDermott convened a meeting with several key NIH directors, the UMDF, and the UMDF's Scientific and Medical Advisory Board. The meeting identified the millions of dollars the NIH spends in the area of mitochondrial medicine and ways that the NIH and the UMDF can work together.

Sen. Boxer called for a follow up meeting between UMDF and the NIH. It was her hope that a workshop could be created to bring together the NIH institutes and mitochondrial medicine experts from around the country. The intent of the workshop was to formulate a plan to move research forward. You can read more about the results of that workshop in this newsletter.

Our previous bills sought the patient registry and a biorepository. As you known, the North American Mitochondrial Disease Consortium (NAMDC) has been funded by the NIH to continue its work in collecting patient information. This is critical because patients who participate in NAMDC are in a database that could match them to an important clinical trial. They are also eligible to receive a NAMDC certified diagnosis, which is so very important to our affected community. UMDF is the patient advocacy organization that is affiliated with NAMDC. We are also happy to tell you that a biorespoitry operates at the Mayo Clinic.

In 2009, many people on Capitol Hill had never heard of mitochondrial disease or the UMDF. But after your visits, and the continuation of meetings by the UMDF staff, we are recognized and we are getting results.

If you are ready to help us continue our forward motion, please sign up for our "Day on the Hill 2012." You can register online at: http://www.surveymonkey.com/dayonthehill2012. If you do not have computer access, feel free to call us, toll free, at: 1-888- 317-8633. In order for us to schedule a meeting for you, you must contact us by April 30, 2012.

Please note, while participating in Day on the Hill is free, if you are planning to attend the UMDF Symposium June 14-16, 2012, you must register separately at this website address: www.umdf.org/symposium. We look forward to seeing you in Bethesda, MD, and on Capitol Hill in June!

United Mitochondrial Disease Foundation LEAP Award

Living, Encouraging, Achieving & Persisting

Purpose: To recognize an individual living positively with mitochondrial disease, highlighting the person's accomplishments and volunteer service.

Eligibility: Age 14 years or older.

Criteria: Individual with confirmed or suspected mitochondrial disease who overcomes daily challenges to achieve goals in career, family and volunteer service. The individual demonstrates a positive attitude, hope for a brighter future, and an enthusiasm that inspires others.

Instructions: Any UMDF member can nominate an individual for this award. Fill out the form below and attach the requested information. The UMDF will announce the LEAP Award winner at the annual symposium and will present the winner with a plaque. The LEAP Award winner will be featured on the UMDF website and recognized in the UMDF newsletter.

In 100 words or less, please explain how this individual overcomes daily challenges to achieve goals in career, family and volunteer service. Please provide examples of how the individual demonstrates a positive attitude, hope for a brighter future, and an enthusiasm that inspires others. You may also attach copies of articles about the nominee and lists of projects, activities, or clubs the nominee is involved with.

Nominations may be submitted online at: www.surveymonkey.com/s/LEAP2012 or type your essay and attach it to the nomination form.

Mail the nomination by April 15, 2012 to:

United Mitochondrial Disease Foundation
Attn: LEAP Award
8085 Saltsburg Road, Suite 201
Pittsburgh, PA 15239

Or fax to 412-793-6477 or e-mail the nomination by April 15, 2012 to info@umdf.org.

Person Nominating

Name: _____

Address: _____

Phone: _____

E-mail: _____

Nominee for the Award

Name: _____

Address: _____

Phone: _____

Diagnosis (if known): _____

Age (must be at least 14 years old): _____

Winners will be announced at the symposium on Friday, June 15, 2012, at the awards ceremony.

United Mitochondrial Disease Foundation Heartstrings Award

Recognizing a youth commitment that tugs on the heartstrings

Purpose: To recognize a child or teen who has donated or raised funds for the UMDF, enabling the UMDF to continue its mission.

Eligibility: The individual recognized must be under 18 years of age at the time of the donation or fundraising activity.

Criteria: The winner is chosen based on related criteria of age, time invested, talents demonstrated, effectiveness and generosity. For nominees who implement fundraising projects, the judges will consider the uniqueness and creativity of the project, communication, time invested and the amount raised in comparison to the age of the individual. For nominees who donate funds, the judges will consider the generous spirit shown, communication, and amount donated in relation to the age of the individual.

Instructions: Any UMDF member can nominate an individual for this award. Fill out the form below and attach the requested information. The UMDF will announce the winner at the annual symposium and will present the winner with a plaque. The Heartstrings Award winner will be featured on the UMDF website and recognized in the UMDF newsletter.

In 100 words or less, please explain how this individual has "tugged at your heartstrings" through fundraising for or donating to the UMDF. Identify important features of the nominee's activity, such as the time invested, creativity, communication skills, determination, effectiveness and generosity. You may also attach supporting information on the fundraising project (published articles, pictures, comments from others involved with or participating in the project) or the communications of the nominee (letter explaining intended use of the gifted funds, thank you letters, letters sent with the donation, and so forth).

Nominations may be submitted online at: www.surveymonkey.com/s/Heartstrings2012 or type your essay and attach it to the nomination form.

Mail the nomination by April 15, 2012 to:
United Mitochondrial Disease Foundation
Attn: Heartstrings Award
8085 Saltsburg Road, Suite 201
Pittsburgh, PA 15239

Or fax to 412-793-6477 or e-mail the nomination by April 15, 2012 to info@umdf.org.

Person Nominating

Name: _____

Address: _____

Phone: _____

E-mail: _____

Nominee for the Award

Name: _____

Address: _____

Phone: _____

Diagnosis (if known): _____

Age (must be less than 18 years old at time of donation or event): _____

Winners will be announced at the symposium on Friday, June 15, 2012, at the awards ceremony.

UMDF
members
Uplifting stories about members.

Finding Our Way Through HOPE

by Lori Piccirilli

It's hard to believe it has been over a decade since our lives changed…for the better, at least partially, especially after learning about mitochondrial disorders. When our youngest was born on August 10, 2000, we had no idea what was in store for us, but we were fairly sure it was NOT as it turned out to be. After Ryan was born "blue" he continued to suffer from apnea events of over 20 episodes per day for the next two years. We, along with more than a dozen doctors, had no more information to help him than on his "birth" day. It felt like HOPE was more than a four letter word, it was an illusion, too abstract to grasp and embrace. After struggles far beyond anyone's control, and over a year's wait on a long list to see an expert on mitochondrial disorders, hope still seemed out of our grasp. Sure, it was comforting to hear we were not crazy, these were common symptoms, "we see a lot of this" as opposed to "we have never seen this," but that visit introduced the word…mitochondrial disease. It was hard to say, to understand, to describe. Fast forward a few years and many hospitalizations later, we realize hope may never be in sight. Our older son, Jonathan, of whom we had concerns but no convictions, showed more outward signs that something was just not right. It looked like Essential Tremor, it looked like Parkinson's, but at 7 years old, it was neither. It was another dash at finding hope. Again, that long confusing word, mitochondrial disease, entered our lives and dashed away any signs of hope sticking around.

Building HOPE - the Verde View Equestrian Center!

So, with the knowledge dispensed upon us, our protocols in hand, we embarked on a journey. We wondered if we would ever learn how to explain our children's unique conditions and fragility to others. Wondered if we would ever find hope, for the normalcy we experienced in raising our eldest, Marissa, who is 10 years older than our middle child. Wondered too many times to recount, if our youngest would live till his next birthday, or our older son, ever to stop the tremor in his hands. Hope was no longer part of our vocabulary. Striving to survive the journey, mentally, and physically was all we could concentrate on. Still, in the back of our minds, we felt we could never give up. We hoped for an eventual graduation from this life of chaos and crisis. Where does one begin with little hope and even less understanding of mitochondrial disease?

For our family, the end of this journey starts at the beginning - to reevaluate as any family reflects through the years. In this reflection: our kids are now a decade older, when we feared they would not make it a year older at times. That we lived through so many challenging medical, financial, and emotional times and are still here, together, as a family. Realizing we did survive and grow into our new roles, still paying it forward as the opportunities arise and our lives allowed. However, we still felt like we never really had hope in our grasp. We often struggled with a void in our lives, always feeling like we fought to keep our heads above water or recovering from the last crisis. There was an emptiness that came from struggling to graduate from therapies and programs that became benign. Despite the adaption to a normal routine, there was no sense of normalcy. We lacked a sense of what hopes we had in shaping our future and that of our medically fragile sons. Their future lacked the same hopes we had for our daughter, for obvious reasons.

Months before Marissa graduated from college, we had our worst struggle yet, the emergency plan and medical flight we prepared for that big crisis came on my birthday in 2009. Regardless of how much preparation went into that plan, it failed to relieve the anxiety such drastic measures instill. We prayed for hope to find its way into our lives and never leave. Later that year, after taking months to recover from the mental and physical stress an event leaves its mark on, we began to see hope materialize in ourselves and our home. Perhaps it was the crass reality that life is so precious, or the fact we survived, even after all the crises over the years or perhaps we realized that hope was really living amongst us. We found hope in our three children, guiding our way, despite their own challenges.

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Jonathan, Marissa, Lori, and Ryan at the Verde Equestrian Center.

Our daughter graduated with sights to attend a master's program in a college of a bordering state. She spent the summer helping with the care of her brothers, taking time to digest the materials associated with mitochondrial disorders, visited out of state doctors with them and attended their traditional and alternative therapies. It is here she learned their likes, dislikes, and where they excelled. Being a lifelong equestrian, a sport she shared with her mother, she took the initiative and brought home a horse to provide direct and appropriate riding and horsemanship skills for her brothers. She worked with their long time physical therapist to gain a better understanding of what and how being up on a horse was beneficial. Marissa and her brothers began to develop a rapport they lacked while she was away in college, the boys began to prosper in areas they previously showed stagnant. There was such excitement to interact with the horses, such growth in self esteem we had never experienced through countless hours in private practices and multiple sessions of brainstorming ideas. For our youngest we saw the core strength increase, like he had done with his Physical Therapy, when we snuck a pony into our sunroom to do Hippotherapy because he was too fragile to go outside! We had a summer of fun, watching the kids engage in a collective, yet independently enriching experience. So when fall was approaching, our daughter declined to head off for a Masters in Journalism, but instead insisted we head to a riding center to become certified to teach others the art of progressive riding and horsemanship. Those others were individuals like our boys, those with disabilities.

After six months of intensity on everyone's part, we passed our rigorous exams and riding test and became Professional Association of Therapeutic Horsemanship (PATH) International Certified Instructors. Of course, what came next was HOPE. We realized we had been searching for it this entire decade and yet it was with us all the time. Our family's HOPE was nestled inside our boys. This taught us that we can graduate from the program by adopting the program to fit their needs. Thus a Therapeutic Riding Center was born. Our hope transformed into an idea that creating a center around those with disabilities brought hope from abstract to concrete. It was more than just creating something for our children, it was creating something for all those with disabilities AND using HOPE to perhaps create a career, a way of life, a facility where our family could help others on a similar journey find their way too. There is a center of hope in the field next to our home. It is the home to Verde View Equestrian Center, staffed by Path International Instructors and designed with entire families in mind. Families who find themselves without hope, needing a place to network, renew, and watch their love ones grow their independence and individual progressive riding skills. It is our way to pay it forward and develop healing with horses, to nurture hope into everyone's lives. In March, we launch one of the most progressive teen centered volunteer programs in our area, working to build an inclusive environment. Come April 1st, we will partner with another local agency to offer riding programs through scholarships and programs for at-risk teenagers. Hope is finally sitting in plain sight…check it out on Facebook @ Verde View Equestrian Center!

Lori Piccirilli & Raymond Healy, parents to Marissa, Jonathan, and Ryan reside in Harpursville, NY. She is a UMDF Ambassador and is Co-Chair for the Energy for Life Walkathon scheduled for Saturday, May 5, 2012 at Otsiningo Park in Binghamton, NY.

Piccirilli has had horses all of her life. Her mother and grandmother rode, and her daughter, Marissa, her fellow instructor at the Verde View, has had professional riding lessons since she was 4 years old. Piccirilli said, "It's genetic."

A Norwegian Fjord horse called Thor at the center.

If you live in the Harpursville, NY, area, you may be interested in using the Therapeutic Riding Center as a resource for yourself or your loved ones. To learn more about this wonderful resource, please visit the Verde View Equestrian Center's Facebook page, e-mail verdeviewec@gmail, or call 607-656-9512. To get involved with UMDF Energy for Life Walk in Binghamton or one in the your area, visit: www.energyforlifewalk.org or call the National Office (toll-free) at: 1-888-317-8633.

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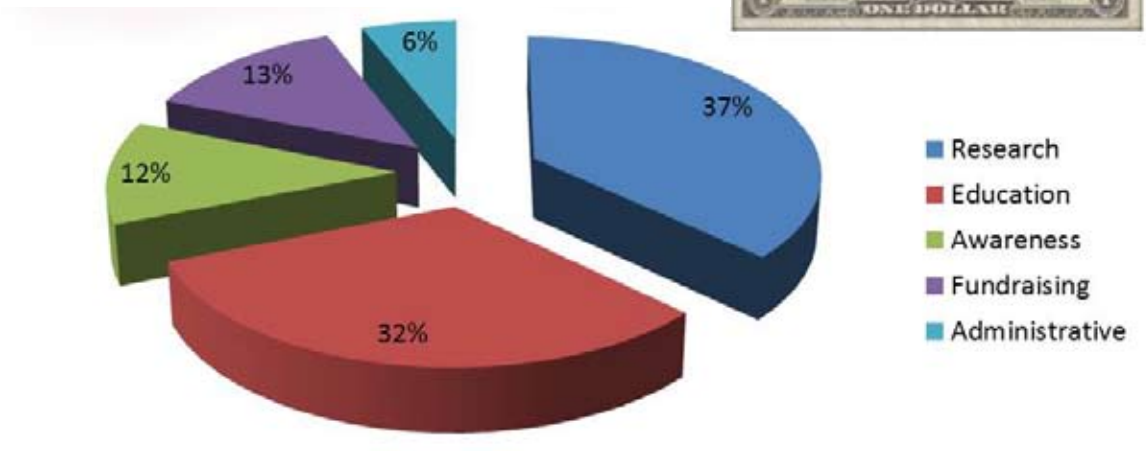

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